Theilheimer's

Synthetic Methods

of Organic Chemistry

78 2011

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Preface

This volume of *Theilheimer* contains abstracts of new synthetic methods and supplementary data mainly from papers published in the literature up to November 2010.

For browsing purposes, abstracts are displayed according to the Systematic Classification (symbol notation: summary p. VIII) so that reactions of the same type and associated data appear together. For example, all deprotections appear in the early symbols (under HO⇓↑, HN⇓↑, HS⇓↑); reduction of oxo compds., imines and carbon-carbon multiple bonds under the HC⇓ sections; C-defunctionalization under the HC sections; oxy-functionalization under the OC sections; aminations, nitrations, peptide coupling etc. under the NC sections; halogenation under the HalC sections; sulfurations under the SC sections; selenation, stannylation, phosphorylation, etc. under the RemC sections; syntheses involving C-C bond formation in the latter half of the book under the CC sections; and data on resolutions (Res) at the end. A list of reaction symbols and references thereto is given in the Systematic Survey (p. XVIII).

The displayed data are supported by the customary in-depth Subject Index (p. 432) and access to supplementary data can be made in the usual manner via the Supplementary Reference section, e.g. the reader interested in updates on the Biginelli synthesis (Synth. Meth. *55*, 337) will note from p. 489 that additional references can be found on p. 284 of this volume.

As usual, the volume contains a 'Reviews' section (p. 415), covering reviews published up to and including April 2011, and a 'Trends' section (p. XI) incorporating key developments in synthetic chemistry up to and including June 2011.

I would like to express my gratitude to Alan Finch for his continuing help and enthusiasm during the preparation of these volumes, as well as to Julian Hayward and Chris Hardy. We are also very grateful for the assistance and support of Jill Entwistle, Eliot Cartwright-Finch, Daniel Scarborough, Chloë Cyrus-Kent and Andrew Hotchkiss.

July 2011 *G. Tozer-Hotchkiss*, Editor

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Advice to the User

General Remarks

New methods for the synthesis of organic compounds and improvements of known methods are being recorded continuously in this series.

Reactions are classified on a simple though purely formal basis by symbols, which can be arranged systematically. Thus searches can be performed without knowledge of the current trivial or author names (e.g. 'Oxidation' and 'Friedel-Crafts reaction').

Users accustomed to the common notations will find these in the subject index (see page 432). By consulting this index, use of the classification system may be avoided. It is thought that the volumes should be kept close at hand. The books should provide a quick survey, and obviate the immediate need for an elaborate library search. Syntheses are therefore recorded in the index by starting materials and end products, along with the systematic arrangement for the methods. This makes possible a sub-classification within the reaction symbols by reagents, a further methodical criterion. Complex compounds are indexed with cross reference under the related simpler compounds. General terms, such as synthesis, replacement, heterocyclics, may also be brought to the attention of the reader.

A brief review, *Trends and Developments in Synthetic Organic Chemistry* (see page XI), stresses highlights of general interest and calls attention to key methods too recent to be included in the body of the text.

The abstracts are limited to the information needed for an appraisal of the applicability of a desired synthesis. In order to carry out a particular synthesis it is therefore advisable to have recourse to the original papers or, at least, to an abstract journal. In order to avoid repetition, selections are made on the basis of most detailed description and best yields whenever the same method is used in similar cases. Continuations of papers already included will not be abstracted, unless they contain essentially new information. They may, however, be quoted at the place corresponding to the abstracted papers. These supplementary references (see page 489) make it possible to keep abstracts of previous volumes up-to-date.

Syntheses that are divided into their various steps and recorded in different places can be followed with the help of the notations such as *startg. m. f.* (starting material for the preparation of ...).

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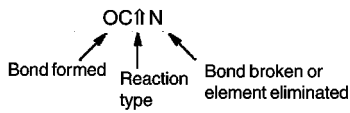
Method of Classification

Reaction Symbols. As summarized in the Systematic Survey (page XVIII), reactions are classified firstly according to the bond formed in the synthesis, secondly according to the reaction type, and thirdly according to the bond broken or the element eliminated. This classification is summarized in the reaction symbol, e.g

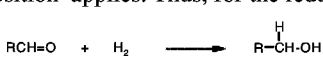


The first part of the symbol refers to the chemical bond formed during the reaction, expressed as a combination of the symbols for the two elements bonded together, e.g. HN, NC, CC. The order of the elements is as follows:

H, O, N, Hal (Halogen), S, Rem (Remaining elements), and C.

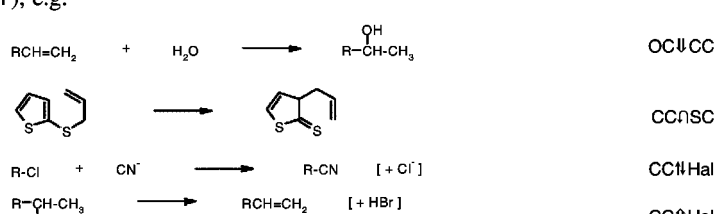
Thus, for the formation of a hydrogen-nitrogen bond, the notation is HN, not NH.

If two or more bonds are formed in a reaction, the 'principle of the latest position' applies. Thus, for the reduction



in which both hydrogen-oxygen and hydrogen-carbon bonds are formed, the symbol is HC⇓OC and not HO⇓OC.

The second part of the symbol refers to the reaction type. Four types are distinguished: addition (⇓), rearrangement (∩), exchange (⇅), and elimination (⇑), e.g.



Monomolecular reactions are either rearrangements (∩), where the molecular weight of the starting material and product are the same, or

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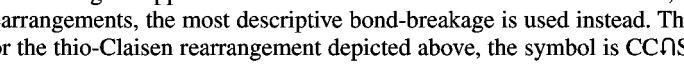
eliminations (⇑), where an organic or inorganic fragment is lost; bimolecular and multicomponent reactions are either additions (⇓), such as intermolecular Diels-Alder reactions, Michael addition and 1,4-addition of organometallics, or exchanges (⇓⇑), such as substitutions and condensations, where an organic or inorganic fragment is lost.

The last part of the symbol refers to the essential bond broken or, in the case of exchange reactions and eliminations, to a characteristic fragment which is lost. While the addition symbol is normally followed by the two elements denoting the bond broken, in the case of valency expansion, where no bonds are broken, the last part of the symbol indicates the atom at which the addition occurs, e.g.

For addition, exchanges, and eliminations, the 'principle of the latest position' again applies if more than one bond is broken. However, for rearrangements, the most descriptive bond-breakage is used instead. Thus, for the thio-Claisen rearrangement depicted above, the symbol is CC∩SC, and not CC∩CC.

Deoxygenations, quaternizations, stable radical formations, and certain rare reaction types are included as the last few methods in the yearbook. The reaction symbols for these incorporate the special symbols El (electron pair), Het (heteropolar bond), Rad (radical), Res (resolutions), and Oth (other reaction types), e.g.



The following rules simplify the use of the reaction symbols:

1. The chemical bond is rigidly classified according to the structural formula without taking the reaction mechanism into consideration.

2. Double or triple bonds are treated as being equivalent to two or three single bonds, respectively.

3. Only stable organic compounds are usually considered: intermediates such as Grignard compounds and sodiomalonic esters, and inorganic reactants, such as nitric acid, are therefore not expressed in the reaction symbols.

Reagents. A further subdivision, not included in the reaction symbols, is based on the reagents used. The sequence of the reagents usually follows that of the periodic system. Reagents made up of several components are

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arranged according to the element significant for the reaction (e.g. $KMnO_4$ under Mn, NaClO under Cl). When a constituent of the reagent forms part of the product, the remainder of the reagent, which acts as a 'carrier' of this constituent, is the criterion for the classification; for example, phosphorus is the carrier in a chlorination with PCl_5 and sodium in a nitrosation with $NaNO_2$.

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Trends and Developments in Synthetic Organic Chemistry 2011

Organocatalyzed asymmetric synthesis via enamine catalysis has developed rapidly in recent years, notably in the context of asymmetric α-functionalization of aldehydes with electrophiles. This has now been elaborated with an 'oxidative' version, whereby the intermediate enamine is oxidized *in situ* to the corresponding α,β-unsaturated iminium ion, which then undergoes 1,4-addition with various nucleophiles to give chiral β-functionalized aldehydes[1]. In another key development of asymmetric synthesis, a catalytic asymmetric S_N2'-displacement with organolithium compounds has been established for a new asymmetric synthesis of ethylene derivatives from allyl bromides under copper(I) catalysis in the presence of a chiral ferrocenyldi(phosphine)[2]. Chiral ammonium salts may be applied in the enantioselective reduction and alkylation reaction of α,β-ethylene-aldehydes with alcohols via iminium catalysis, enamine catalysis, and acid catalysis[3]. Chiral organocatalysts incorporated in size-selective metal-organic frameworks have been applied in asymmetric aldol reactions[4]. Chiral organo-Brønsted acid-catalyzed asymmetric allylic alkylation has been developed as an alternative to traditional transition metal-catalyzed routes[5].

C-H Activation of hydrocarbons may be described as the 'Holy Grail'. Highly selective and efficient terminal hydroxylation of *n*-alkanes is possible under mild conditions using an artificial self-sufficient cytochrome P450[6], while the berberine bridge enzyme has been employed for the first preparative oxidative biocatalytic asymmetric intramolecular C-C coupling[7]. Amazingly, methane has succumbed to an efficient functionalization by carbene insertion, courtesy of a new electron-poor silver(I) catalyst with a polyhalogenated scorpionate ligand. Here, coupling with ethyl diazoacetate yields ethyl propionate, but the trick is to use supercritical CO_2 as solvent to suppress side reactions and ease solubility problems[8]. α- or β-Ketopyranosides may be prepared by activation of anomeric C-H groups with carbenoids[9]. Note also an eco-friendly, metal-free, regioselective functionalization of hydrocarbons with an N-triflylamino-λ^3-bromane, providing N-triflylamines (preferentially by reaction at tertiary sites), and perhaps one day offering an alternative to high-valent iodine reagents[10]. An alternative amination of hydrocarbon groups uses copper amides[11], while a highly efficient iron-catalyzed conversion of ethylene derivatives affords α,β-ethylenenitriles[12]. Remarakably, *n*-alkanes are reported to undergo catalytic dehydro-aromatization mediated by pincer-ligated iridium complexes[13].

On the theme of one-pot sequential conversions, there is an interesting heterogeneous adaptation based on the principle of harnessing the power of multiple catalyst interfaces. This is exemplified by a 'stacked' multi-layered catalyst composed of platinum nanocubes on silica with CeO_2 nanocubes on platinum, which efficiently converts ethylene and methanol to propanal in tandem fashion: methanol is converted to H_2 and CO at the Pt/CeO_2 interface then ethylene undergoes hydroformylation at the Pt/SiO_2 interface[14]. A multistep microreactor has also been developed as a safer, more controllable and scalable alternative to batch processes. This is illustrated by a direct ['one-flow'] conversion of phenols to biaryls via Suzuki coupling: here, the phenol is converted to the aryl triflate in a 100 µl reaction tube and in a second tube the formed aryl triflate reacts with the arylboron compound over a palladium catalyst – the process being coupled with a microfluidic liquid-liquid extraction unit to purify the intermediate[15]. The multistep, 'one-flow' synthesis of nucleosides under mild Brønsted acid catalysis is also worth a mention[16]. Continuous flow microreactors are finding increasing applications, e.g. in the cycloisomerization of *o*-acetylenephenols with a highly active heterogeneous Pd-nanoparticle catalyst[17]; a safe tetrazole synthesis without a metal promotor[18]; and continuous flow palladium-catalyzed N-arylation in a packed-bed microreactor[19]. A two-chamber process has also been devised for safe, laboratory-scale carbonylations based on *in situ*-generation of carbon monoxide from a solid source: 9-chlorocarbonyl-9-methylfluorene. This is converted to CO under palladium catalysis in the first chamber and passes to a second for the desired carbonylation in the presence of another catalyst, as illustrated by the palladium-catalyzed carbonylation of aryl halides[20].

On the theme of challenging cycloadditions, nature has given up its first demonstrable, specific Diels-Alderase – well, almost! The microbe, *Saccharopolyspora spinosa* is a source of the insecticide spinosyn A and presumed to deliver the molecule through the intramolecular [4+2]-cycloaddition of a metabolite. The gene pool has now thrown up a protein (SpnF) which truly catalyzes the conversion *in vitro*, which is surely evidence of a '[4+2]-cycloadditionase'. But, alas, the jury has yet to confirm the existence of a true Diels-Alderase which effects the conversion concertedly[21]. In another interesting development, a dimerizing cycloaddition – impossible in bulk solution – has been 'forced' on the nanoscale. Here, the trick is to tether two potentially reactive molecules at adjacent sites on a thiolate-treated gold surface, in such a way that they are geometrically oriented to interact: one recent outcome is the first [4+4]-cyclodimerization of anthracenes[22]. The nature of the catalyst may also be important in directing otherwise impossible

reactions, as illustrated in a novel [2+2+2]-cycloaddition with ketenes through the agency of a nickel phosphine complex, which suppresses the undesirable, and all-too-familiar, decarbonylation[23].

Continuing with the theme of transition metal catalyses, a new nickel-catalyzed hydrogenolytic cleavage of diaryl ethers has evolved, of potential application to the depolymerization of lignins to provide energy-rich fuels and commercially viable materials[24]. Several new ruthenium N-heterocyclic carbene complexes have been fashioned for specific aspects of olefin metathesis, the most notable being another offering of Grubbs, based on 1-adamantyl-3-mesitylimidazolidin-2-ylidene as ligand, specifically designed for efficient synthesis of challenging (Z)-olefins[25] and considered an improvement/alternative to recently reported molybdenum complexes for the same purpose[26]. An efficient cross-metathesis and ring-closing metathesis of ethyleneammonium salts (including primary amine salts) is also reported[27], reaction with ethyleneamines generally being unsuccessful. One-pot cross-metathesis-reduction may be performed using Grubbs catalyst followed by addition of triethylsilane under microwave irradiation, especially for polymer-based substrates[28]. An iridium-catalyzed asymmetric S_N2' displacement of 2-ethylenecarbonates procures chiral sec. allyl alcohols[29], while a homogeneous ruthenium-catalyzed conversion of sec. alcohols with ammonia affords the corresponding prim. amines[30], and application of bimetal nanoclusters allows selective aerobic oxidation of alcohols to aldehydes/carboxylic acids or esters[31].

Turning our attention to supported catalysts, magnetically recoverable SiO_2-coated Fe_3O_4 nanoparticles serve as a support for a chiral rhodium catalyst, applicable to asymmetric transfer-hydrogenation in aqueous medium[32]. Polypeptidal titanium phosphonate scaffolds find application for dihydroxylation of styrenes[33]. $CeCaPO_4$ supports are suited to ruthenium-catalyzed aerobic oxidation of alcohols[34] while size-selective non-porous silicodecatungstates are applicable to oxidation of a variety of compounds[35]. Mesoporous graphitic carbon nitride [mpg-C_3N_4][36] serves to support palladium nanoparticles for selective hydrogenation of phenols and derivatives, but is also important as a photocatalyst in its own right, finding application in metal-free aerobic oxidation of amines[37]. Finally here, note also the critical study of silica supports for palladium-catalyzed oxidation of alcohols, where dispersion of the catalyst is maximized on those possessing a 3D network of interconnected channels[38].

The design of a new silylium salt (paired with a carborane anion) is notable as initiator for the challenging Friedel-Crafts reaction with aryl fluorides. Here, capture of fluoride by the cation is the driving force for C-F cleavage,

and the presence of a stoichiometric silane facilitates regeneration of the silyl cation via trapping of the liberated proton[39]. Self-regeneration of silylium ion catalysts has been achieved in carbonyl reduction using a ferrocenyl-substituted silane[40]. A new source of fluorine is also at hand based on a zwitterionic, non-hygroscopic, solid fluoride sensor which has been manipulated to return fluoride ion via a labile fluoroborate for mild nucleophilic displacements, such as the conversion of aromatic nitro compounds to fluorides at room temperature[41]. Calcium salts have found novel applications, e.g. for formation of chiral 3-hydroxyoxindole derivatives using chiral VAPOL calcium phosphate[42]. Regarding frustrated ion pairs, a bisfluorenyl-substituted allene may now be used instead of tris(pentafluorophenyl)borane for their generation and utilized in cleavage of disulfides[43], while chiral examples have found application in asymmetric hydrogenation of imines[44]. An aldehyde decarbonylase catalyzes conversion of fatty aldehydes to alk(a,e)nes[45]. An organocatalyzed reduction of enamides with diimide in water also comes to mind[46].

Oligosaccharide synthesis may now be performed with S-benzimidazolyl glycosides that may be activated under a variety of conditions[47], or via an ionic-liquid-supported 'catch-and-release' strategy [ICROS][48]. Also note Danishefsky's new peptide ligation[49], and a new medium for peptide coupling[50]. To close, a new one-pot, Fischer-inspired indole synthesis from ar. halides via halogen-magnesium exchange, quenching with di-*tert*-butyl azodicarboxylate, and reaction with ketones[51], and a metal-free intramolecular Ullmann synthesis of chromones[52], also deserve a mention.

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Systematic Survey

Reaction symbol	Page
HO⇓OC	1
HO⇓Rem	1
HO⇓C	2
HO⇑O	3
HN⇓O	4
HN⇓S	5
HC⇓OC	6
HC⇓NC	11
HC⇓CC	13
HC⇓O	21
HC⇓N	22
HC⇓Hal	23
HC⇓Rem	24
HC⇓C	25
HC⇑O	26
HC⇑C	27
ON⇑OC	28
OS⇓S	28
ORem⇓HRem	31
ORem⇓H	31
ORem⇓N	32
ORem⇓Hal	32
ORem⇓Rem	32
OC⇓HC	33
OC⇓OC	33
OC⇓NC	35
OC⇓CC	36
OC∩ON	47
OC∩OS	48
OC∩CC	48
OC⇓H	51
OC⇓O	57
OC⇓N	62
OC⇓Hal	65
OC⇓S	67
OC⇓Rem	69
OC⇓C	71
OC⇑H	79
OC⇑O	84
OC⇑N	84
OC⇑Hal	85
OC⇑S	85
OC⇑Rem	86
OC⇑C	86
NN⇓H	87
NN⇑O	87
NN⇑N	88
NS⇓H	88
NS⇓Hal	88
NS⇓S	89
NRem⇓NC	89
NRem⇓O	90
NC⇓OC	90
NC⇓NN	91
NC⇓NC	93
NC⇓CC	94
NC∩HO	99
NC∩HC	99
NC∩ON	100
NC∩OC	100
NC∩NN	101
NC∩CC	102
NC⇓H	104
NC⇓O	107
NC⇓N	121
NC⇓Hal	123
NC⇓S	133
NC⇓Rem	135
NC⇓C	137
NC⇑H	138
NC⇑O	141
NC⇑N	142
NC⇑Hal	144
NC⇑S	146
NC⇑Rem	146
NC⇑C	146
HalC⇓OC	147
HalC⇓NC	147
HalC⇓CC	148
HalC⇓H	150
HalC⇓O	157
HalC⇓Hal	159
HalC⇓Rem	159
HalC⇓C	160
SS⇓H	161
SS⇑H	162
SC⇓NC	163
SC⇓CC	163
SC⇓O	165
SC⇓Hal	170
SC⇓S	171
SC⇓Rem	172
SC⇓C	172
SC⇑N	173

Reaction symbol	Page
SC⇑Hal	173
RemRem⇓⇑H	174
RemC⇓⇑Hal	174
RemC⇓⇑Rem	174
RemC⇓OC	174
RemC⇓NC	175
RemC⇓CC	175
RemC∩HO	180
RemC⇓⇑H	181
RemC⇓⇑O	182
RemC⇓⇑N	184
RemC⇓⇑Hal	184
RemC⇓⇑S	186
RemC⇓⇑Rem	186
RemC⇓⇑C	191
RemC⇑H	193
CC⇓HC	193
CC⇓OC	194
CC⇓NC	205
CC⇓CC	211
CC∩HC	256
CC∩OC	259
CC∩NC	262
CC∩CC	262
CC⇓⇑H	265
CC⇓⇑O	275
CC⇓⇑N	311
CC⇓⇑Hal	319
CC⇓⇑S	345
CC⇓⇑Rem	351
CC⇓⇑C	384
CC⇑H	398
CC⇑O	399
CC⇑N	402
CC⇑Hal	403
CC⇑S	405
CC⇑Rem	405
CC⇑C	406
ElS⇑O	411
Het⇓N	411
Het⇓Rem	411
Res	411

Abbreviations and Symbols

abs.	absolute
alc.	alcoholic
aq.	aqueous
ar.	aromatic
atm.	atmosphere(s)
compd(s).	compound(s)
deriv(s).	derivative(s)
e.e.	enantiomeric excess
eq(s).	equivalent(s)
E.	Example
F.e.s.	Further example(s) see
M	molar
prepn.	preparation
prim.	primary
s*78*	supplementary reference in Volume *78*
sec.	secondary
startg. m.f.	starting material for (the preparation of …)
subst.	substituted
sym.	symmetrical
tert.	tertiary
v.i.	via intermediates
w.a.r.	without additional reagents
Y *	Yield

ϟ	Electrolysis
///	Irradiation
[\\\\]	Microwave irradiation
○	Ring closure
◌⁾	Ring contraction
◌⁾	Ring expansion
⊂	Ring opening
Ⓗ	Ring hydrogenation
←	'see title or reagent on the left half of the page'

* Yields in parentheses refer to the immediately preceding step of a multi-step reaction

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Formation of H-O Bond

Uptake ⇓

Addition to Oxygen and Carbon HO ⇓ OC

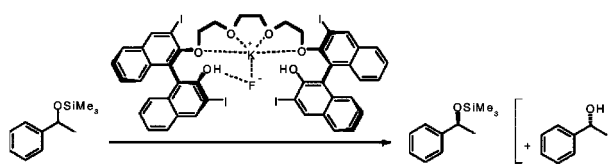
Tetra-n-butylammonium fluoride *Bu_4NF*
1,2,3-Triols from 2,3-epoxyalcohols ▽O → C(OH)C(OH)
with inversion of configuration s. *78*, 46

Exchange ⇓↑

Remaining Elements ↑ HO ⇓↑ Rem

Potassium fluoride/chiral 3,3′-diiodo-1,1′-bi-2-naphthol-based polyethers *[F⁻]**
Kinetic resolution by asym. O-desilylation OSi⩽ → OH
with a chiral polyether-complexed ['naked'] fluoride ion

1.



(rac)

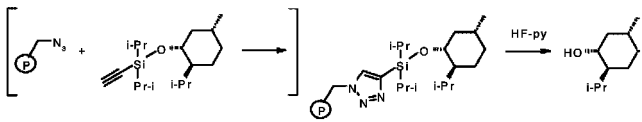
Spray-dried KF (0.35 mmol) added in one portion to a soln. of the chiral 3,3′-diiodo-1,1′-bi-2-naphthol-based polyether (20 mol%) and startg. racemic trimethylsilyl ether (0.5 mmol) in dioxane (2.5 ml), stirred at 20° for 5 d, the mixture concentrated under reduced pressure, and worked up with chromatographic purification → remaining (S)-trimethylsilyl ether. Conversion 60% (e.e. 95%; selectivity factor s = 16). The procedure is applicable to a wide range of silylated aryl(alkyl)-, aryl(propargyl)- and aryl(styryl)-carbinols, permitting the recovery of the lesser reactive (S)-trimethylsilyl ethers with high enantioselectivity (eleven examples; e.e. 91-97.3%; s factor up to 30). The high activity of the reagent is due to complexation of the potassium ion by *both* the ethereal oxygens and the Lewis basic iodine atoms of the polyether, which leave the associated fluoride ion free to desilylate the substrate while being retained within the chiral environment. The corresponding [less bulky] 3,3′-dichlorinated analog was less active, and dehalogenated reagents were inactive. The free phenolic residues are also critical for high activity as the corresponding methyl ethers were inactive. F.e.s. H. Yan, H.B. Jang, J.-W. Lee, H.K. Kim, S.W. Lee, J.W. Yang, C.E. Song, Angew. Chem., Int. Ed. *2010*, *49* (47), 8915-7 [DOI: 10.1002/anie.201004777].

Acetic acid *AcOH*
Protection of hydroxyl groups
as polymer-based diisopropyl(1,2,3-triazol-4-yl)silyl ethers – Removal of the protective group under mild conditions s. *78*, 2

Sulfamic acid *H_2NSO_3H*
O-Detrimethylsilylation in water s. *29*, 415s*78*

Hydrogen fluoride-pyridine *HF-C_5H_5N*
Protection of hydroxyl groups OSi⩽ → OH
as polymer-based diisopropyl(1,2,3-triazol-4-yl)silyl ethers
Removal of the protective group under mild conditions

2.

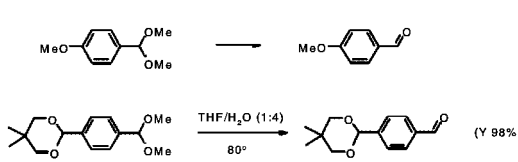


The startg. triazole-linked resin (200 mg) allowed to swell in dry THF (2 ml) for 20 min, 70% HF-pyridine (2 eq.) added, the mixture stirred *at room temp.* for 2 h, the reaction quenched by addition of 2 eq. methoxy(trimethyl)silane (to remove excess of cleavage reagent), the resin filtered and washed with THF, the combined organic layer evaporated, and the residue passed through a short bed of silica gel → menthol. Y 72%. The starting polymer-based silyl ethers were simply prepared by coupling the appropriate alcohol or phenol with ethynyl(diisopropyl)silyl chloride using DMAP/Et_3N in methylene chloride, and then linked with polystyryl azide by classical 'click' chemistry under mild conditions. The protective group is robust (for example, under the conditions of Wittig synthesis and in the presence of Grignard reagents) but readily removed with HF-pyridine or (in lower yield) with 6:6:1 acetic acid/THF/water. F.e. incl. protection of secondary, benzyl and allyl alcohols s. P. Sharma, J.E. Moses, Org. Lett. *2010*, *12* (12), 2860-3 [DOI: 10.1021/ol100968t].

Carbon ↑ HO ↓↑ C

Without additional reagents *w.a.r.*
Uncatalyzed cleavage of acyclic acetals in water under mild conditions $C(OR)_2$ → CO

3.



Neat deionized water (15 ml; pH 6.4) added to the startg. acetal (12.5 mmol) in a round-bottomed flask, heated to 80° for 2 h (with no special precautions being taken to exclude oxygen), and the water simply removed by evaporation → product. Y 97% (>98% purity). This simple, water-promoted and catalyst-free cleavage is generally applicable to dimethyl or diethyl acetals of *acyclic* aromatic or aliphatic acetals or ketals, although hydrophobic substrates with long alkyl chains required more forcing conditions: heating at 80° in a mixed aq. solvent (ether/THF/water) in a stainless-steel reactor under 8 atm. N_2. Significantly, **selective cleavage** of acyclic acetals or ketals can be conducted **with retention of cyclic acetals or ketals**. Certain substrates (e.g. acetals of cinnamaldehyde) underwent cleavage efficiently *at room temp.*! F.e. (ca. twenty; high yield) s. D.B.G. Williams, A. Cullen, A. Fourie, H. Henning, M. Lawton, W. Mommsen, P. Nangu, J. Parker, A. Renison, Green Chem. *2010*, *12* (11), 1919-21 [DOI: 10.1039/c0gc00280a]; cleavage of cyclic or acyclic aromatic acetals in water catalyzed by [inexpensive] $Fe(OTs)_3 \cdot 6H_2O$ (1-5 mol%) s. M.E. Olson, J.P. Carolan, M.V. Chiodo, P.R. Lazzara, R.S. Mohan, Tetrahedron Lett. *2010*, *51* (30), 3969-71 [DOI: 10.1016/j.tetlet.2010.05.112].

Irradiation ///
Cleavage of O-protective groups ←
cleavage of photo-labile protective groups s. *30*, 5s*76*; photo-cleavage of α-carboxy-6-nitroveratryl esters s. A.G. Russell, M.-E. Ragoussi, R. Ramalho, C.W. Wharton, D. Carteau, D.M. Bassani,

J.S. Snaith, J. Org. Chem. *2010, 75* (13), 4648-51 [DOI: 10.1021/jo100783v]; cleavage of tetrahydropyran-2-yl (cf. *48*, 120s*73*) and tetrahydrofuran-2-yl ethers with $Al(OTf)_3$, also formation of the former with $Al(OTf)_3$/dihydropyran s. D.B.G. Williams, S.B. Simelane, M. Lawton, H.H. Kinfe, Tetrahedron *2010, 66* (25), 4573-6 [DOI: 10.1016/j.tet.2010.04.053]; orthogonal cleavage of sulfonic acid *tert*-butyl (with BBr_3) and 2,2,2-trifluoroethyl (with NaOH) esters s. S.C. Miller, J. Org. Chem. *2010, 75* (13), 4632-5 [DOI: 10.1021/jo1007338]; cleavage of methoxy- and ethoxymethyl ethers (cf. *38*, 3s*76*) in [Hmim][HSO_4] as Brønsted acidic catalyst and ionic liquid under thermal or microwave heating s. I. Mohammadpoor-Baltork, M. Moghadam, S. Tangestaninejad, V. Mirkhani, A.R. Khosropour, A. Mirjafari, Monatsh. Chem. *2010, 141* (10), 1083-8 [DOI: 10.1007/s00706-010-0373-6]; safe and practical procedure for **global deprotection of oligoribonucleotides** s. D. Zewge, F. Gosselin, R. Sidler, L. DiMichele, R.J. Cvetovich, J. Org. Chem. *2010, 75* (15), 5305-7 [DOI: 10.1021/jo100648e].

Microwaves s. under 1-n-Butyl-3-methylimidazolium bromide and 1-Methylimidazolium hydrogen sulfate [\\\\]

Sodium hydroxide or Boron bromide *NaOH or BBr_3*
Orthogonal cleavage of arenesulfonic acid esters s. *30*, 5s*78* $SO_2OR \rightarrow SO_2OH$

Sodium hydroxide/hydrogen chloride *NaOH/HCl*
Cleavage of 5-acylene-1,3-dioxolan-4-ones s. *78*, 442 ⊂

Aluminum triflate *$Al(OTf)_3$*
Cleavage of tetrahydropyran-2-yl and tetrahydrofuran-2-yl ethers OTHP or OTHF → OH
s. *30*, 5s*78*; *48*, 120s*78*

1-n-Butyl-3-methylimidazolium bromide/microwaves *[Bmim]Br/[\\\\]*
1-Decyl mercaptan *RSH*
O-Demethylation of methyl phenolethers OMe → OH
with $AlHal_3$/EtSH cf. *35*, 7s*77*; in 1-butyl-3-methylimidazolium bromide as ionic liquid under microwaves s. J. Park, J. Chae, Synlett *2010* (11), 1651-6 [DOI: 10.1055/s-0030-1258087]; with 1-decyl mercaptan for an odor-free procedure with a simple aq. work-up s. B. Kale, A. Shinde, S. Sonar, B. Shingate, S. Kumar, S. Ghosh, S. Venugopal, M. Shingare, Tetrahedron Lett. *2010, 51* (23), 3075-8 [DOI: 10.1016/j.tetlet.2010.04.012]; demethylation of 6-(2,4-dimethoxybenzoyl)-chromen-2-one and other aryl methyl ethers with pyridine hydrobromide in sulfolane s. A. Srivastava, J. Yang, B. Zhao, Y. Jiang, W. Blackmon, B. Kraemer, Synth. Commun. *2010, 40* (12), 1765-71 [DOI: 10.1080/00397910903161769].

Saccharin-2-sulfonic acid/wet silica ←
Cleavage of acylals s. *78*, 45 $C(OAc)_2 \rightarrow CO$

1-Methylimidazolium hydrogen sulfate/microwaves *[Hmim]HSO_4/[\\\\]*
Cleavage of (m)ethoxymethyl ethers in Brønsted acidic ionic liquids $OCH_2O(Me,Et) \rightarrow OH$
s. *30*, 5s*78*; *38*, 3s*76*

Pyridine hydrobromide *$C_5H_5N{\cdot}HBr$*
O-Demethylation of methyl phenolethers s. *35*, 7s*78* OMe → OH

Hydrogen chloride *HCl*
N-Hydroxyureas from N-*tert*-butoxyureas s. *78*, 157 $\geq NC(O)NHOBu\text{-}t \rightarrow \geq NC(O)NHOH$

Iron(III) tosylate *$Fe(OTs)_3$*
Cleavage of acetals in water s. *78*, 3 $C(OR)_2 \rightarrow CO$

Elimination ⇑

Oxygen ↑ HO ⇑ O

Copper(I) chloride/ammonium chloride or diisopropylamine hydrochloride/N,N′,N′,N″,N″-pentamethyldiethylenetriamine/acetic acid ←
1,4-Chlorohydrins from hydroperoxides ←
via copper-catalyzed 1,5-hydrogen atom transfer s. *78*, 225

Formation of H-N Bond

Exchange ↓↑

Oxygen ↑ HN ↓↑ O

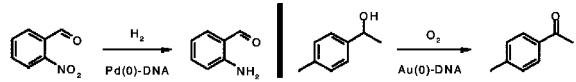
Copper(II) phthalocyanine ←
Chitosan-bioconjugated silver nanoparticles/sodium tetrahydridoborate ←
Silver nanoparticles-on-silica gel/sodium tetrahydridoborate *Ag-SiO$_2$/NaBH$_4$*
Silver/silver(I) or Gold/silver(I) *Ag/Ag(I) or Au/Ag(I)*
Cobalt(II) phthalocyanine ←
Nickel nanoparticles-on-silica/alumina *Ni-on-SiO$_2$/Al$_2$O$_3$*
Ar. amines from nitro compds. $NO_2 \rightarrow NH_2$

with gold nanoclusters-on-iron(III) hydroxide cf. *75,* 7; with $NaBH_4$ and Ag nanoparticles-on-silica gel (in aq. medium), chemoselectivity, s. A.R. Kiasat, R. Mirzajani, F. Ataeian, M. Fallah-Mehrjardi, Chin. Chem. Lett. *2010, 21* (9), 1015-9 [DOI: 10.1016/j.cclet.2010.05.024]; with $NaBH_4$ and chitosan-bioconjugated Ag nanoparticles s. D. Wei, Y. Ye, X. Jia, C. Yuan, W. Qian, Carbohydr. Res. *2010, 345* (1), 74-81 [DOI: 10.1016/j.carres.2009.10.008]; by silver(I)-promoted Ag- or Au-catalyzed hydrogenation for the chemoselective reduction of halogenonitrobenzenes s. R. Crook, J. Deering, S.J. Fussell, A.M. Happe, S. Mulvihill, Tetrahedron Lett. *2010, 51* (39), 5181-4 [DOI: 10.1016/j.tetlet.2010.07.143]; chemo- and regio-selective reduction with recyclable copper(II) or cobalt(II) phthalocyanine s. U. Sharma, P. Kumar, N. Kumar, V. Kumar, B. Singh, Adv. Synth. Catal. *2010, 352* (11-12), 1834-40 [DOI: 10.1002/adsc.201000191]; reduction of nitrophenol with Ni nanoparticles-on-silica/alumina s. I. Hamdy, A. El Maksod, E.Z. Hegazy, S.H. Kenawy, T.S. Saleh, ibid. *352* (7), 1169-78 [DOI: 10.1002/adsc.200900873].

Palladium nanoparticles-in-aluminum oxohydroxide *Pd-Al(O)OH*
Ar. amines from nitro compds. s. *3,* 46s*78*

Palladium(0) nanoparticles-DNA/tris buffer ←
Chemoselective oxidation and reduction catalyzed by DNA-supported metal nanoparticles

4.

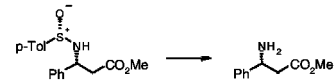


Palladium(0)-catalyzed hydrogenation of ar. nitro compds. A mixture of 2-nitrobenzaldehyde (1 mmol) and Pd(0)-DNA (1.8 mol%) in aq. tris buffer (4 ml) and ethanol (2 ml) stirred under H_2 (balloon) at 25° until reaction complete (TLC; 6 h), excess ethanol (2-3 volumes) added, the mixture centrifuged, and purified by chromatography on silica → 2-aminobenzaldehyde. Y 83%. Air-stable and recyclable palladium(0)-nanoparticles, stabilized and supported by DNA [Pd(0)-DNA], were prepared from K_2PdCl_4 and inexpensive fish sperm DNA as a homogeneous, highly dispersed aq. suspension. The catalyst was effective for the hydrogenation of electron-diverse nitrobenzenes (ten examples; Y 80-99%) in the presence of ester, carboxylic acid, aldehyde, sulfonate and ether functionality. Work-up involved simple precipitation of the catalyst, which was recycled up to 5 times without significant reduction in yield. Other metal (Au, Ag, Pt) nanoparticle-DNA catalysts were similarly prepared, with Au-DNA proving an effective catalyst for the mild oxidation (using O_2) of electron-diverse sec. benzylic alcohols to **ketones** (seven examples; Y 82 to >99%), with 1-pyrid-2-ylethanol (at 50°) and cyclohexanol affording moderate yields (both 60%) of the corresponding ketones. F.e. and catalyst preparation s. Y. Wang, G. Ouyang, J. Zhang, Z. Wang, Chem. Commun. *2010, 46* (42), 7912-4 [DOI: 10.1039/c0cc02632h].

Sulfur ↑ HN ↓↑ S

Irradiation ///
Photochemical N-desulfinylation under neutral conditions NS(O)R → NH

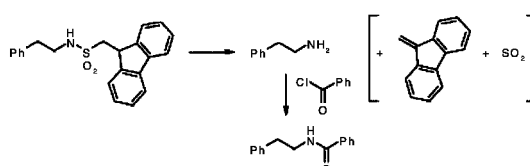
5.



with retention of configuration. Argon bubbled through a soln. of the startg. sulfinamide (0.15 mmol) in 1:1 ether/methanol (10 ml), contained in a quartz tube, for 5 min, the tube capped, placed in a Rayonet UV chamber, the mixture irradiated at 2537 Å for 16 h, the soln. concentrated, ethyl acetate (10 ml) added, washed with satd. Na_2CO_3, worked up, the crude residue dissolved in ether (15 ml), washed with 15% HCl, the aq. phase and washings neutralized to pH 7.5 with solid Na_2CO_3, and worked up with chromatographic purification → (R)-product. Y 82% (enantiopure). Neither acid nor base was required, and yields were high from a number of chiral N-*p*-toluenesulfinylamines, incl. N-*p*-toluenesulfinylaziridines, with no loss of α-chirality (six examples; Y 71-85%). The corresponding N-*tert*-butylsulfinylamine, however, decomposed under these conditions, as did an α-dibenzylamino-β-(*p*-toluenesulfinylamino)carboxylic acid ester. F.e.s. F.A. Davis, R.E. Szewczyk, J.F.A. Davis, T. Ramachandar, Y. Zhang, J. Chai, H. Qiu, J. Deng, V. Velvadapu, Tetrahedron Lett. *2010*, *51* (31), 4042-4 [DOI: 10.1016/j.tetlet.2010.05.114].

Sodium tert-butoxide *NaOBu-t*
Piperidine $(CH_2)_5NH$
Protection of amino groups NSO$_2$R → NH
as (9*H*-fluoren-9-yl)methanesulfonamides [NFms derivs.]
Removal of the protective group

6.



Piperidine (2.5 mmol) added to a Young's-type Schlenk flask containing 1-(9*H*-fluoren-9-yl)-*N*-phenethylmethanesulfonamide (0.5 mmol), mesitylene (0.5 mmol as internal standard) and DMF (2.5 ml), the resulting clear soln. stirred at 25° for 1 min, and the liberated amine isolated as the N-benzoyl deriv. after purification by chromatography on silica gel → N-benzoylphenethylamine. Y 96%. The new protective group is readily incorporated by reaction of the amine (primary or secondary, incl. N-*tert*-alkyl derivs.) with storable (9*H*-fluoren-9-yl)methanesulfonyl chloride in methylene chloride containing ethyldiisopropylamine. It has similar characteristics to the classical Fmoc but, unlike the latter, can be used for preparing **chiral N-protected α-aminophosphonic acid amide esters** (s.a. *78*, 131) by direct condensation of the N-protected α-aminophosphonic acid monoesters with sec. amines (which is complicated by oxazaphospholine formation when the more nucleophilic Fmoc group is present). The NFms group also has a weaker metal-coordinating sulfonamide group as compared with carbamates, thereby increasing the applicability of Fms-protected compounds in metal-catalyzed reactions. Deprotection takes place readily under the same conditions used for cleavage of the NFmoc group, with elimination of 9-methylene-9*H*-fluorene and SO_2. F.e.s. Y. Ishibashi, K. Miyata, M. Kitamura, Eur. J. Org. Chem. *2010* (14), 2670-3 [DOI: 10.1002/ejoc.201000682]; **N-desulfonylation of indoles and azaindoles** (cf. *23*, 31) using NaOBu-*t* (in dioxane in a sealed tube at 80°) s. C. Chaulet, C. Croix, J. Basset, M.-D. Pujol, M.-C. Viaud-Massuard, Synlett *2010* (10), 1481-4 [DOI: 10.1055/s-0029-1219918].

Lithium tetrahydridoaluminate $LiAlH_4$
1,2-Diamines from 2,1,3-thiadiazolidine 2,2-dioxides s. *78*, 201 C

Carbon ↑ HN ↓↑ C

Potassium carbonate/n-butanol $K_2CO_3/BuOH$
Amines from ureas $\geq NC(O)N\leq \rightarrow \geq NH$
β-Branched sec. benzylamines s. *78*, 301

Ethanol *EtOH*
Cleavage of N-[2,2-bis(carbethoxy)vinyl] protective groups $NHCH{=}C(COOEt)_2 \rightarrow NH_2$
from protected prim. amines s. *5*, 32s*78*

Flavin/oxygen/irradiation ←
Trifluoroacetic acid CF_3COOH
Trifluoromethanesulfonic acid CF_3SO_3H
Cleavage of N-protective groups ←
N-debenzylation with alkali metals in silica gel cf. *5*, 32s*76*; N-debenzylation of N-benzylamides with triflic acid s. F. Rombouts, D. Franken, C. Martínez-Lamenca, M. Braeken, C. Zavattaro, J. Chen, A.A. Trabanco, Tetrahedron Lett. *2010, 51* (37), 4815-8 [DOI: 10.1016/j.tetlet.2010.07.022]; of sec. benzylamines with flavin/oxygen under visible-light photocatalysis s. R. Lechner, B. König, Synthesis *2010* (10), 1712-8 [DOI: 10.1055/s-0029-1218709]; **cleavage of N- and S-(2,2,4,6,6-pentamethyl-2,3-dihydrobenzofuran-5-ylmethyl groups** as an alternative to the trityl group for the side-chain protection of cysteine and asparagine/glutamine (deprotection with trifluoroacetic acid) s. O. Garcia, J.M. Bofill, E. Nicolas, F. Albericio, Eur. J. Org. Chem. *2010* (19), 3631-40 [DOI: 10.1002/ejoc.201000201]; **cleavage of N-[2,2-bis(ethoxycarbonyl)vinyl] groups** from protected prim. amines in ethanol, application to the conversion of amino acids to esters, s. A. Ilangovan, R.G. Kumar, Chem. Eur. J. *2010, 16* (13), 2938-43 [DOI: 10.1002/chem.200902054]; deprotection of amidine-type protecting groups for nucleobases under acidic conditions during oligonucleotide synthesis s. A. Ohkubo, Y. Kuwayama, Y. Nishida, H. Tsunoda, K. Seio, M. Sekine, Org. Lett. *2010, 12* (11), 2496-9 [DOI: 10.1021/ol100676j].

Formation of H-C Bond

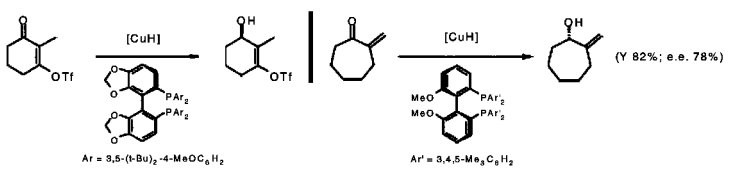
Uptake ⇓

Addition to Oxygen and Carbon HC ⇓ OC

Potassium fluoride s. under Co(OAc)$_2$ *KF*

Copper(II) acetate/diethoxy(methyl)silane/chiral 2,2′-bis(diarylphosphino)biphenyls ←
2-Ethylene-*sec*-alcohols from α,β-ethyleneketones CO → CHOH
Copper(I) hydride-mediated regioselective asym. reduction

7.



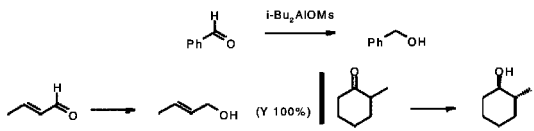
under mild conditions. Diethoxy(methyl)silane (3 eq.) added to a mixture of $Cu(OAc)_2 \cdot H_2O$ (3 mol%) and (R)-DTBM-SegPhos (3 mol%) in ether (0.4 ml) under argon at room temp. in a vial

capped with a rubber septum, the mixture stirred for 10 min, the brown soln. stirred at -25° for 5 min, startg. enone (0.25 mmol) added in one portion, the mixture stirred until reaction complete (TLC; 5 h), quenched with satd. methanolic NH_4F, warmed to room temp., filtered through silica, concentrated *in vacuo*, and purified by chromatography on silica → (R)-3-hydroxy-2-methylcyclohex-1-en-1-yl triflate. Y 90% (e.e. 86%). Copper(I) hydride, generated *in situ* via silane-reduction of Cu(II), efficiently reduced di- and tri-subst. vinyl alkyl ketones exclusively at the carbonyl function, generally with high enantioselectivity even in the presence of a vinyl triflate (sixteen examples; Y 82-99%; e.e. 62-99%). F.e., optimization and substrate prepn. s. R. Moser, Z.V. Boškovic, C.S. Crowe, B.H. Lipshutz, J. Am. Chem. Soc. *2010*, *132* (23), 7852-3 [DOI: 10.1021/ja102689e].

Tris(pentafluorophenyl)borane/triphenylphosphine/phenylsilane $(C_6F_5)_3B/Ph_3P/PhSiH_3$
Alcohols from oxo compds. via metal-free hydrosilylation s. *78*, 14 CO → CHOH

Diisobutylaluminum methanesulfonate $i\text{-}Bu_2AlOSO_2Me$
Selective reduction of oxo compds. under mild conditions

8.

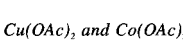


As well as being an excellent reductant for the regiospecific ring opening of epoxides (*76*, 13), diisobutylaluminum methanesulfonate is highly efficient for the selective reduction of aldehydes and ketones, leaving carboxylic acids, esters, amides, acid chlorides and sulfur compounds (excepting DMSO) unaffected. **E:** A stock soln. of diisobutylaluminum methanesulfonate (5.5 mmol) in ether (3.7 ml) added at 25° with stirring (at time intervals of 0.5, 1 and 3 h) to a soln. of benzaldehyde (5 mmol) in ether (4.5 ml) containing tridecane as internal standard, the mixture hydrolyzed with 3 *N* HCl for 2 h, the aq. layer satd. with K_2CO_3, and the organic layer dried over anhydrous $MgSO_4$ before chromatographic analysis → benzyl alcohol. Y 88% (99.9% after 24 h). Significantly, ketones were reduced relatively slowly under these conditions but efficient reduction was achieved with 2 eq. of the reagent. Furthermore, both α,β-ethylenealdehydes (with 1.1 eq. reductant) and α,β-ethyleneketones (with 2 eq. reductant) were reduced *solely* to the corresponding allyl alcohols in 98-100% yield *with 100% purity,* while substituted cyclic ketones gave the thermodynamically more stable (*trans*) cyclic alcohols (seven examples; Y 95-100%). F.e.s. J.S. Cha, M. Noh, Bull. Korean Chem. Soc. *2010*, *31* (4), 840-4 [DOI: 10.5012/bkcs.2010.31.04.840]; regioselective ring cleavage of phenyl- and/or alkyl-subst. epoxides with *diisobutylaluminum triflate* and comparison of its reactivity with diisobutylaluminum methanesulfonate s. J.S. Cha, S.J. Park, ibid. *31* (8), 2135-6 [DOI: 10.5012/bkcs.2010.31.8.2135].

Isopropanol s. under $FeCl_2$ *i-PrOH*
Chiral o,o′-bis(Δ²-oxazolin-2-yl)diphenylamines s. under $Co(OAc)_2$ ←
Phenylsilane s. under $(C_6F_5)_3B$ $PhSiH_3$
Diethoxy(methyl)silane s. under $Cu(OAc)_2$ and $Co(OAc)_2$ $(EtO)_2MeSiH$
Triphenylphosphine s. under $(C_6F_5)_3B$ Ph_3P
Chiral 2,2′-bis(diarylphosphino)biphenyls s. under $Cu(OAc)_2$ ←
(S)-Bis(3,3-dimethyl-2-isonitrilobutyl) phenylphosphonate s. under $FeCl_2$ ←

Diphosphorus tetraiodide/tetraethylammonium bromide P_2I_4/Et_4NBr
Regiospecific reductive ring opening of epoxides ▽ → C(OH)CH

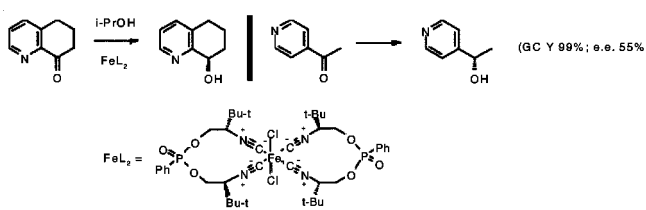
9.



2(R)-Phenyloxirane (0.01 mol) added to a stirred soln. of P_2I_4 (10 mmol) and a catalytic amount of tetraethylammonium bromide in *moist* methylene chloride, stirred at room temp. until startg.

m. completely consumed (6 h; TLC), filtered, the filtrate washed successively with satd. aq. $NaHCO_3$ and water, the organic layer separated, dried, concentrated *in vacuo*, and worked up with purification by chromatography on silica gel → 1(R)-phenylethanol. Y 87%. The procedure is mild, reliable, convenient and suitable for the *completely* regioselective reductive ring opening of a wide range of aliphatic, cycloaliphatic and styrene oxides possessing electron-donating or -withdrawing groups (MeO, NO_2, COOEt, Cl, Br, OH) on the benzene ring, reaction with chiral substrates taking place **with retention of configuration** (fifteen examples; Y 80-90%). Reaction failed with other quaternary ammonium salts as additive as well as in dry solvents. F.e.s. V.N. Telvekar, R.A. Rane, Synth. Commun. *2010*, *40* (14), 2108-12 [DOI: 10.1080/00397910903219492].

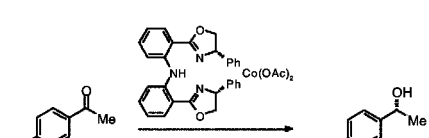
Tetra-n-butylammonium fluoride s. under Co(OAc)$_2$ *Bu_4NF*
Tetraethylammonium bromide s. under P_2I_4 *Et_4NBr*
Iron(II) chloride/(S)-bis(3,3-dimethyl-2-isonitrilobutyl) phenylphosphonate/potassium tert-butoxide/isopropanol ←
Sec. alcohols from ketones CO → CHOH
by iron(II) bis(isonitrile) complex-catalyzed asym. transfer-hydrogenation



10.

A mixture of iron complex [generated from $FeCl_2 \cdot 4H_2O$ (5 mol%) and bis(isonitrile) ligand (10 mol%)], *t*-BuOK (0.5 eq.) and isopropanol (1.7 ml) stirred at room temp. under N_2 for 5 min, 5,6,7,8-tetrahydroquinol-8-one (0.34 mmol) added, and the mixture stirred for 24 h → (R)-8-hydroxy-5,6,7,8-tetrahydroquinoline. Y 80% by GC (e.e. 91%). This novel use of isonitriles as chiral transfer agents in the hydrogenation of ketones was applicable to cyclic and acyclic (het)aryl alkyl ketones (twenty-one examples; conversions 50 to >99%; 3-acetylthiophene gave 36%). Enantiomeric excesses of 72-91% were achieved with cyclic ketones *ortho* to a pyridine ring, although most examples gave more modest selectivity (e.e. 30-64%). Aryl ketones gave (S)-alcohols in all cases, whereas in the hetaryl ketone series, only 2-acetylthiophene and 4-acetylpyridine afforded the (S)-alcohol, the remaining acetyl-pyridines, -thiophenes, -furans and bicyclic pyridine-based ketones giving (R)-alcohols. Infra-red measurements indicate that hydrogenation may involve hydride transfer from a reduced isonitrile species. F.e.s. A. Naik, T. Maji, O. Reiser, Chem. Commun. *2010*, *46* (25), 4475-7 [DOI: 10.1039/c0cc00508h].

Cobalt(II) acetate/chiral o,o′-bis(Δ²-oxazolin-2-yl)diphenylamines/diethoxy(methyl)silane/ tetra-n-butylammonium fluoride/potassium fluoride ←
Cobalt(II)-catalyzed asym. reduction of ketones via hydrosilylation



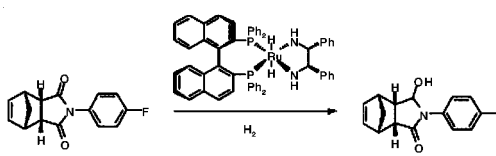
11.

p-(*n*-Butyl)acetophenone (1 mmol), (R,R)-[*o,o′*-bis(4-phenyl-Δ²-oxazolin-2-yl)diphenyl]amine (Bopa-*ph*) (0.06 mmol) and $Co(OAc)_2$ (0.05 mmol) placed in a flask under argon, THF (3 ml)

added, the mixture stirred for 1 h at 65°, treated with *diethoxy(methyl)silane* (2 mmol), stirring continued for 24 h at 65°, tetra-*n*-butylammonium fluoride in THF (1 ml; 1 *M*), KF (112 mg), methanol (1 ml) and water (1 ml) added at 0°, and worked up with purification by chromatography on silica gel → product. Y 99% (e.e. 96%). The procedure is convenient, environmentally friendly, relatively inexpensive, safe and generally applicable to the asym. reduction of a wide range of aryl ketones (incl. naphthyl ketones) possessing electron-donating or -withdrawing groups at the *o-*, *m-* or *p*-site (twenty examples; Y 95-99%; e.e. generally 91-98%); enantioselectivity was low, however, with linear aliphatic ketones (e.e. 15%), and generally lower with $Fe(OAc)_2$ in place of $Co(OAc)_2$ or with other chiral Bopa derivs. **Asym. reduction of β-subst. α,β-ethyleneketones via hydrosilylation** was also effected with related chiral cobalt(II) Bopa complexes (five examples; Y 85-93%; e.e. 65-72%). F.e. and comparison of organosilicon hydrides s. T. Inagaki, L.T. Phong, A. Furuta, J. Ito, H. Nishiyama, Chem. Eur. J. *2010*, *16* (10), 3090-6 [DOI: 10.1002/chem.200903118].

trans-Dihydrido[(R,R)-1,2-diphenylethylenediamine][(R)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl]ruthenium(II)/potassium tert-butoxide ←
Lactamols from *meso*-dicarboxylic acid imides ←
Asym. homogeneous hydrogenation with desymmetrization

12.



A soln. of the startg. imide (2.5 mmol) in THF placed in a stainless steel autoclave, the latter flushed with H_2 for ca. 3 min at 0°, a soln. of *trans*-[Ru((R)-BINAP)((R,R)-dpen)$(H)_2$] (0.2 mol%) and KOBu-*t* (1.8 mol%) in THF (substrate molarity 0.625 *M*) added by cannula under H_2 pressure, the autoclave pressurized with H_2 to 50 atm., stirred at 0° under this pressure for 17 h, the autoclave vented slowly at 0°, and the precipitate collected → product. Y 99% (d.r. >99:1; e.e. 97%). This is the first instance of a diastereo- and enantio-group-selective *mono*hydrogenation of a *meso*-imide, reaction being applicable to mono-, bi- and tri-cyclic substrates with generation of up to 5 chiral centers and with retention of isolated olefin functionality (eight examples; Y 44-99%; d.r. 93:7 to >99:1; e.e. 83-97%). The *cis-trans* selectivity at the C-OH groups was not preserved during hydrogenation, but the *trans*-isomer is favored on thermodynamic grounds, control experiments showing that *cis-trans* isomerization is catalyzed by base. Monohydrogenation takes place at lower temperatures when the imide structure disfavors ring-opening tautomerization (cf. *78*, 16). F.e. and comparison of chiral complexes s. S. Takebayashi, J.M. John, S.H. Bergens, J. Am. Chem. Soc. *2010*, *132* (37), 12832-4 [DOI: 10.1021/ja105783u].

Chiral ruthenium(II) complexes *[Ru(II)]**
Asym. homogeneous hydrogenation of ketones CO → CHOH
s. *67*, 22s*74*; *43*, 51s*75*; asym. hydrogenation of aryl and alkyl ketones with $RuCl_2[(PPh_3)]$[(S,R)-indan-ambox]] s. W. Li, G. Hou, C. Wang, Y. Jiang, X. Zhang, Chem. Commun. *2010*, *46* (22), 3979-81 [DOI: 10.1039/b927028k]; of aryl ketones with a [(R,R)-DPEN]ruthenium(II) complex and a chiral-bridged di(phosphine) as ligand s. Y.M. Ciu, L.L. Wang, F.Y. Kwong, W. Sun, Chin. Chem. Lett. *2010*, *21* (12), 1403-6 [DOI: 10.1016/j.cclet.2010.05.027]; of bicyclic ketones with $RuCl_2$[(S)-binap][(R)-iphan] s. N. Arai, M. Akashi, S. Sugizaki, H. Ooka, T. Inoue, T. Ohkuma, Org. Lett. *2010*, *12* (18), 3380-3 [DOI: 10.1021/ol101200z]; of α-chloro-β-keto-esters and phosphonate analogs with a [DifluorPhos]ruthenium(II) complex **with dynamic kinetic resolution** s. S. Prévost, S. Gauthier, M.C. Caño de Andrade, C. Mordant, A.R. Touati, P. Lesot, P. Savignac, T. Ayad, P. Phansavath, V. Ratovelomanana-Vidal, J.-P. Genêt, Tetrahedron: Asym. *2010*, *21* (11-12), 1436-46 [DOI: 10.1016/j.tetasy.2010.05.017].

Chiral ruthenium(II) complexes/H-donor *[Ru(II)]*/H-donor*
Asym. transfer-hydrogenation of ketones CO → CHOH

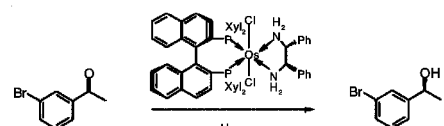
s. *46,* 42s*72*; in aq. medium with a chiral fluorinated dendritic ruthenium(II) TsDPEN complex having polyfluoroalkoxy substituents s. W. Wang, Q. Wang, Chem. Commun. *2010, 46* (25), 4616-8 [DOI: 10.1039/c002168g]; in the presence of a chiral N-pyroglutamyl-2-aminoalcohol as ligand s. P. Geoghegan, P. O'Leary, Tetrahedron: Asym. *2010, 21* (7), 867-70 [DOI: 10.1016/j.tetasy.2010.04.055]; with a chiral oxalamide-based bis(phosphinite) as ligand s. M. Aydemir, N. Meric, A. Baysal, B. Gümgüm, M. Togrul, Y. Turgut, ibid. *2010, 21* (6), 703-10 [DOI: 10.1016/j.tetasy.2010.04.002]; asym. transfer-hydrogenation of α-aminoketones with $[Ru(cymene)Cl_2]_2$ and (1S,2S)-TsDPEN as ligand s. Z. Xu, S. Zhu, Y. Liu, L. He, Z. Geng, Y. Zhang, Synthesis *2010* (5), 811-7 [DOI: 10.1055/s-0029-1218619]; with a chiral ruthenium(II) TsDPEN complex confined in a silica-nanocage for the enhancement of catalytic activity by microenvironmental engineering s. S. Bai, H. Yang, P. Wang, J. Gao, B. Li, Q. Yang, C. Li, Chem. Commun. *2010, 46* (43), 8145-7 [DOI: 10.1039/c0cc01401j].

Chiral rhodium complexes/H-donor *[Rh]*/H-donor*
Asym. transfer-hydrogenation of ketones

s. *46,* 42s*72*; with chiral α-(carbo-*tert*-butoxyamino)carboxylic acid N-(1,2,3-triazol-4-ylmethyl)-thioamides as ligand s. F. Tinnis, H. Adolfsson, Org. Biomol. Chem. *2010, 8* (20), 4536-9 [DOI: 10.1039/c0ob00400f]; with chiral 3-aminomethyl-1,2,3,4-tetrahydroisoquinolines as ligand s. B.K. Peters, S.K. Chakka, T. Naicker, G.E.M. Maguire, H.G. Kruger, P.G. Andersson, T. Govender, Tetrahedron: Asym. *2010, 21* (6), 679-87 [DOI: 10.1016/j.tetasy.2010.04.055]; with a helical-chiral *Tropos* sandwich-shaped rhodium complex having a tris(diphenylphosphinophenyl)benzene ligand s. K. Wakabayashi, K. Mikami, Heterocycles *2010, 80* (2), 933-9 [DOI: 10.3987/com-09-s(s)134].

Chiral (1,2-diamine)dichloro[di(phosphine)]osmium(II) complexes/sodium ethoxide ←
Osmium(II)-catalyzed asym. homogeneous hydrogenation of ketones

13.



A novel class of chiral (1,2-diamine)dichloro[di(phosphine)]osmium(II) complexes has proven highly active for the asym. homogeneous hydrogenation of ketones, in certain instances affording higher enantioselectivities and TOF values than traditional chiral ruthenium analogs (cf. *50*, 17). **E:** A 0.5 *M* soln. of the startg. ketone in ethanol containing 0.01 mol% chiral Os(II) complex [readily prepared from $[Os_2Cl_4(P(m\text{-tolyl})_3)_2]$, (R)-xylbinap and (R,R)-dpen in toluene at reflux] and NaOEt (1 mol%) hydrogenated under 5 atm. H_2 at 60° for 1 h, quenched with ether, filtered over a short silica pad, and worked up → (S)-product. Conversion >99% (e.e. 99%). The procedure is applicable to the asym. hydrogenation of a wide range of aryl ketones, incl. trifluoromethyl phenyl ketone and β-naphthyl methyl ketone (ten examples in all; e.e. 86-99%), at catalyst loadings *as low as 0.001 mol%* with TOF values up to 4.1×10^4. Enantioselectivity was slightly lower with *tert*-butyl methyl ketone (e.e. 71%), although for *tert*-butyl ketones in general the result was a significant improvement over asym. hydrogenation with established chiral *trans*-$[RuCl_2(BINAP)(1,2\text{-diamine})]$ complexes. A further advantage is that such chiral osmium complexes are more stable than related ruthenium complexes and can be used at higher temperatures and in more polar media (the downside being that they are more expensive). The catalytic cycle is thought to involve intermediate formation of a chiral osmium dihydride complex. F.e. and a preliminary study of the **hydrogenation of oxo compds.** with racemic osmium(II) complexes (six examples; conversion 95 to >99% *at 0.01 to 0.0005 mol%* catalyst levels) s. W. Baratta, C. Barbato, S. Magnolia, K. Siega, P. Rigo, Chem. Eur. J. *2010, 16* (10), 3201-6 [DOI: 10.1002/chem.200902809]; with chiral pincer ruthenium or osmium complexes, [MCl(CNN)(PP)] [M = Ru, Os; HCNN = (*S*)-2-(1-aminoethyl)-6-arylpyridine; PP = Josiphos di(phosphine)], s. W. Baratta, F. Benedetti, A.

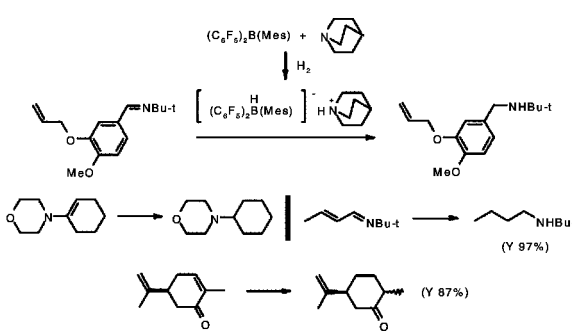
Del Zotto, L. Fanfoni, F. Felluga, S. Magnolia, E. Putignano, P. Rigo, Organometallics *2010*, *29* (16), 3563-70 [DOI: 10.1021/om1004918].

Addition to Nitrogen and Carbon HC ⇓ NC

1,4-Dihydropyridines or benzothiazolines/1,1′-binaphthyl-2,2′-diyl hydrogen phosphates ←
Asym. transfer-hydrogenation of carbon-nitrogen double bonds C=N → CHNH
s. *69*, 20s*72*; of N-unsubst. *o*-hydroxyketimines with (S)-3,3′-bis(triphenylsilyl)-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate as Brønsted acid s. T.B. Nguyen, H. Bousseroul, Q. Wang, F. Gueritte, Org. Lett. *2010*, *12* (20), 4705-7 [DOI: 10.1021/ol102043x]; with chiral 3,3′-diaryl-analogs for the asym. transfer-hydrogenation of 2(1*H*)-quinoxalones and quinoxalines s. M. Rueping, F. Tato, F.R. Schoepke, Chem. Eur. J. *2010*, *16* (9), 2688-91 [DOI: 10.1002/chem.200902907]; of 3*H*-indoles with chiral 3,3′-bis(9-anthracen-9-yl)-derivs. s. M. Rueping, C. Brinkmann, A.P. Antonchick, I. Atodiresei, Org. Lett. *2010*, *12* (20), 4604-7 [DOI: 10.1021/ol1019234]; of α-imino-esters with benzothiazolines as H-donor s. C. Zhu, T. Akiyama, Adv. Synth. Catal. *2010*, *352* (11-12), 1846-50 [DOI: 10.1002/adsc.201000328].

Bis(pentafluorophenyl)mesitylborane/quinuclidine or triethylenediamine $(C_6F_5)_2BMes/R_3N$
Tris(pentafluorophenyl)borane/triphenylphosphine/phenylsilane $(C_6F_5)_3B/Ph_3P/PhSiH_3$
Selective metal-free hydrogenation with 'frustrated' Lewis pairs ←

14.



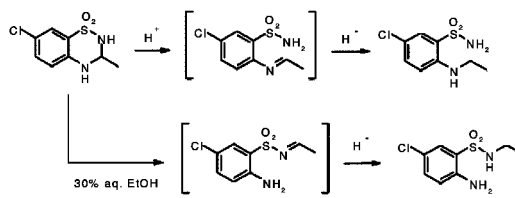
The concept of metal-free hydrogenation with 'frustrated' Lewis pairs (*72*, 24; *75*, 31) has been extended by catalyst design, thereby achieving, for the first time, unprecedented orthogonal reactivity and chemoselectivity. **E: Sec. amines from azomethines**. The startg. allyloxyaldimine (1 mmol), bis(pentafluorophenyl)mesitylborane (10 mol%), quinuclidine [or DABCO] (10 mol%) and dry benzene-d_6 (0.75 ml) placed in a Schlenk bomb (inside a glove box), the bomb attached to a double manifold H_2/vacuum line and degassed (3 freeze-pump-thaw cycles), the mixture cooled in liquid N_2, H_2 introduced (1 atm.), the flask sealed, warmed up to room temp., stirred at 20° (now under ca. 4 atm. H_2) for 42 h, and worked up → product. Y 72% (with quinuclidine) or 100% (with DABCO). Compared with the previously used tris(pentafluorophenyl)borane, the mesityl analog is more bulky which results in lower intrinsic Lewis acidity, but still sufficiently high to form a Lewis pair with the amine with the required heterolytic activity towards hydrogen. The result is a system which is suitable for the efficient hydrogenation of azomethines, notably without affecting isolated allyloxy groups, as well as the hydrogenation of the C=C double bond of enamines; furthermore, with quinuclidine (but not DABCO) as Lewis base, α,β-ethylene-aldimines are completely reduced to sec. amines, while DABCO (but not quinuclidine) is effective for the reduction of enones to saturated ketones. A variety of aliphatic and cyclic amines were compared, but no others compared in any way with the above two, indicative of the importance of

both structural and electronic features of the Lewis pair. F.e.s. G. Erős, H. Mehdi, I. Pápai, T.A. Rokob, P. Király, G. Tárkányi, T. Soós, Angew. Chem., Int. Ed. *2010*, *49* (37), 6559-63 [DOI: 10.1002/anie.201001518]; metal-free catalytic reduction of oxo compds. and azomethines via hydrosilylation using $(C_6F_5)_3B/Ph_3P$ and $PhSiH_3$ s. H. Matsuoka, K. Kondo, Chin. Chem. Lett. *2010*, *21* (11), 1314-7 [DOI: 10.1016/j.cclet.2010.05.029].

Sodium trihydridocyanoborate/acetic acid *$NaBH_3CN/AcOH$*

o-Aminosulfonic acid amides from 3,4-dihydro-2*H*-1,2,4-benzothiadiazine 1,1-dioxides C
pH-Dependent regioselective reductive ring opening

15.

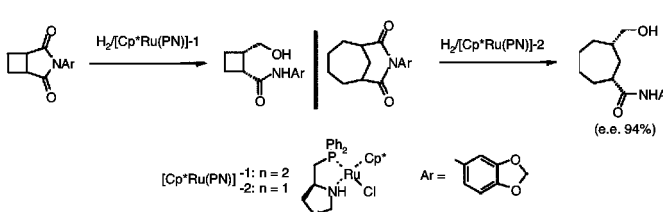


$NaBH_3CN$ (6 mmol) added to a soln. of 7-chloro-3-methyl-3,4-dihydro-2*H*-1,2,4-benzothiadiazine 1,1-dioxide (1 mmol) in glacial acetic acid (20 ml), stirred at room temp. for 3 h, the mixture neutralized with NaOH (10 *M*), extracted with ethyl acetate, and worked up with chromatographic purification → 5-chloro-2-ethylaminobenzenesulfonamide. Y 93%. Under acidic conditions protonation of N^2 promotes ring opening to give the *o*-(ethylideneamino)sulfonamide, which is then reduced to give the *o*-ethylaminosulfonamide. However, under neutral conditions in 30% aq. ethanol at 70°, cleavage of the ring takes place at the 3,4-position to give the isomeric *o*-amino-N-ethylidenebenzenesulfonamide which is then reduced to the *o*-amino-N-ethylsulfonamide (Y 86% after 6 h). F.e. incl. reductive ring opening of N^4-alkyl derivs. s. U.M. Battisti, G. Cannazza, M.M. Carrozzo, D. Braghiroli, C. Parenti, F. Rosato, L. Troisi, Tetrahedron Lett. *2010*, *55* (33), 4433-6 [DOI: 10.1016/j.tetlet.2010.06.08].

Benzothiazolines s. under 1,4-Dihydropyridines ←
Phenylsilane s. under $(C_6F_5)_3B$ *$PhSiH_3$*
Triphenylphosphine s. under $(C_6F_5)_3B$ *Ph_3P*
1,1′-Binaphthyl-2,2′-diyl hydrogen phosphates s. under 1,4-Dihydropyridines ←

Chiral β-aminophosphine-ruthenium(II) complexes/potassium tert-butoxide *[Ru(II)]*/KOBu-t*
Hydroxycarboxylic acid amides from *meso*-dicarboxylic acid imides
Asym. homogeneous hydrogenation with desymmetrization

16.



Degassed isopropanol (9 ml) added to a mixture of startg. succinimide (1.51 mmol), chiral Cp*Ru(PN) catalyst (10 mol%) and KOBu-*t* (10 mol%) under argon in a stainless-steel autoclave, the mixture stirred vigorously under H_2 (3 MPa) at 80° for 24 h, excess H_2 vented with care, the

mixture concentrated *in vacuo*, and purified by chromatography on silica → (+)-*cis*-N-[3,4-(methylenedioxy)phenyl]-2-hydroxymethylcyclobutanecarboxamide. Conversion >99% (e.e. 91%). By use of the appropriate catalyst a series of mono- and bi-cyclic glutarimide and succinimide derivs. were hydrogenated (>99% conversion) to synthetically useful chiral hydroxyamides (incl. 1,2- and 1,3-disubst. C4-C7 cycloalkane derivs.) not readily accessible by other routes (eleven examples; e.e. 81-98%). Cleavage of cyclopropano-fused succinimides, however, was less selective (e.e. 62%, 71%). Absolute configuration was determined by X-ray analysis in one case. F.e. and substrate prepn. s. M. Ito, C. Kobayashi, A. Himizu, T. Ikariya, J. Am. Chem. Soc. *2010*, *132* (33), 11414-5 [DOI: 10.1021/ja105048c].

Addition to Carbon-Carbon Bonds — HC ⇓ CC

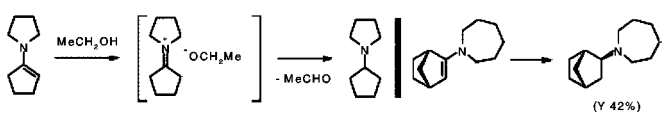
Microwaves s. under Prim. alcohols [\\\\\]
Potassium fluoride s. under Co(OAc)$_2$ *KF*
1,4-Dihydropyridines s. under Pd-C ←

Bis(pentafluorophenyl)mesitylborane/quinuclidine or triethylenediamine *$(C_6F_5)_2BMes/R_3N$*
Selective metal-free hydrogenation with 'frustrated' Lewis pairs ←
of enamines, α,β-ethylenealdimines and α,β-ethyleneketones s. *78*, 14

Aluminum oxyhydroxide s. under Pd nanoparticles *Al(O)OH*

Prim. alcohols/microwaves *RCH_2OH/[\\\\]*
Amines from enamines using prim. alcohols as reducing agents C=C(N≤) → CHCHN≤

17.

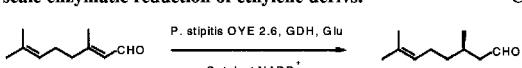


A soln. of N-(1-cyclopent-1-enyl)pyrrolidine in anhydrous ethanol subjected to microwave heating at 160° for 1 h → N-cyclopentylpyrrolidine. Y 100%. Prim. alcohols (methanol, benzyl alcohol and anhydrous ethanol) effected rapid reduction of cyclic enamines under microwave irradiation. No reaction occurred in the absence of alcohol, while heating under reflux in ethanol produced 62% conversion after 42 h in one case. The reaction gave best results (four examples; Y 79-100%) with pyrrolidine-derived enamines, while hexamethyleneimine (two examples; Y 42-68%), piperidine (two examples; Y 13-26%) and morpholine analogs (one example; Y 13%) were less effective. Exocyclic enamines gave low yields (4-9%) as did the use of sec. alcohols as reducing agents, while tert. alcohols were unreactive. A norbornenyl deriv. was diastereoselective, affording the *endo* isomer in 42% yield. The proposed mechanism was based on deuterium labelling experiments. F.e.s. A.G. Cook, Tetrahedron Lett. *2010*, *51* (29), 3762-4 [DOI: 10.1016/j.tetlet.2010.05.053].

Dimethylformamide/potassium hydroxide s. under Pd(OAc)$_2$ *DMF/KOH*
Chiral o,o′-bis(Δ²-oxazolin-2-yl)diphenylamines s. under Co(OAc)$_2$ ←

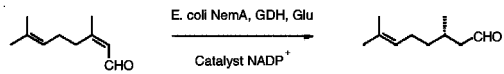
Alkene reductase ←
Preparative-scale enzymatic reduction of ethylene derivs. C=C → CHCH

18.



Asym. reduction of α,β-ethylenealdehydes. A preparative *gram-scale* procedure has evolved for the enzymatic reduction of alkenes, designed specifically for routine laboratory use and without requiring specialized apparatus. **E:** A sample of KP$_i$ (100 m*M*; 85 ml; pH 7.5) containing glucose (44.4 mmol) degassed for 1 h, transferred to a round-bottomed flask under argon, glucose dehydrogenase 102 (for NADPH regeneration; 100 U; 1 mg), NADPH (12 mmol) and ammonium sulfate-purified *Pichia stipitis* old yellow enzyme 2.6 (100 U, 13 ml) added, stirred for 15 min at

room temp., geranial (5.2 mmol) in ethanol (0.83 ml) added, the pH maintained at 7.5 using a pH stat (with 1 *M* KOH as titrant), additional 5.2 mmol portions of geranial added after 1.5 and 3 h, the mixture acidified to pH 4 after 5.75 h (95% conversion) with 1 *M* HCl, stirred overnight with methylene chloride (100 ml), the aqueous portion extracted, filtered over Celite, washed with brine, dried, passed over a small bed of silica gel, concentrated under vacuum, and purified on a silica column → (R)-citronellal. Y 67% (e.e. 98%). Various yeast-derived old yellow enzymes (as fusion proteins with glutathione S-transferase) produced mainly (R)-citronellal, while those from bacterial or plant origin showed the opposite stereo-preference, (S)-citronellal being obtained (Y 69%; e.e. >99%) from neral with the old yellow enzyme from *Escherichia coli* NemA.

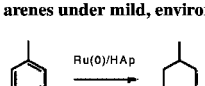


Although enzyme activity decreased in time, this was more than offset by the high volumetric productivity and final product titre. Significant, also, is the fact that there was no reduction of the carbonyl group. F.e.s. D.J. Bougioukou, A.Z. Walton, J.D. Stewart, Chem. Commun. *2010*, *46* (45), 8558-60 [DOI: 10.1039/c0cc03119d]; investigation of the stereochemistry of double bond reduction of (E)-α-(hydroxymethyl)nitrostyrene and of (Z)-α-ethoxycinnamaldehyde using Baker's yeast (cf. *17*, 82) in the presence of deuterated water s. E. Brenna, G. Fronza, C. Fuganti, F.G. Gatti, Eur. J. Org. Chem. *2010* (26), 5077-84 [DOI: 10.1002/ejoc.201000442].

Diethoxy(methyl)silane s. under Co(OAc)$_2$ *(EtO)$_2$MeSiH*
(R)-2,2′-Bis(diphenylphosphino)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl s. under Pd(OCOCF$_3$)$_2$ *H$_8$-BINAP*
Chiral 1-phosphinooctahydroisophosphindoles s. under [Rh(nbd)$_2$]BF$_4$ ←
Multiply-chiral sec-phosphine oxide-phosphines s. under [Rh(cod)Cl]$_2$ *JoSPOphos*
N^1-(4-Butylphenyl)-N^2-[2-[((11bS)-dinaphtho[2,1-d:1′,2′-f][1,3,2]dioxaphosphepin-4-yloxy)methyl]benzyl]phthalamide s. under [Rh(cod)$_2$]BF$_4$ ←
L-Camphorsulfonic acid s. under Pd(OCOCF$_3$)$_2$ *RSO$_3$H*
Tetra-n-butylammonium fluoride s. under Co(OAc)$_2$ *Bu$_4$NF*
Tetra-n-butylammonium bromide s. under Pd nanoparticles *Bu$_4$NBr*
Magnetite s. under Pd nanoparticles *Fe$_3$O$_4$*
1,1′-Bis[4,5-dihydro-3H-binaphtho[2,1-c;1′,2′-e]phosphepino]ferrocene s. under [Ir(cod)Cl]$_2$ *(S,S)-f-Binaphane*
Chiral iron(II) phosphoromonoamidite complexes s. Chiral polymeric rhodium(I)/iron(II) phosphoromonoamidite complexes ←
Cobalt(II) acetate/chiral o,o′-bis(Δ^2-oxazolin-2-yl)diphenylamines/diethoxy(methyl)silane/tetra-n-butylammonium fluoride/potassium fluoride ←
Ketones from [β-subst.] α,β-ethyleneketones C=C → CHCH
Cobalt(II)-catalyzed asym. reduction via hydrosilylation s. *78*, 11

Ruthenium(0) nanoclusters-on-hydroxyapatite *Ru(0)/HAp*
Heterogeneous hydrogenation of arenes under mild, environmentally friendly conditions Ⓗ

19.



Ruthenium(0) nanoclusters-on-hydroxyapatite serve as a highly active, reusable catalyst for the total hydrogenation of benzene and methylbenzenes at room temperature under an initial H_2 pressure of 42 psi. **E:** Ruthenium(0) nanoclusters-on-hydroxyapatite (150 mg; ruthenium content: 0.42 wt% corresponding to 6.23 μmol Ru) weighed into a borosilicate culture tube (in a N_2-filled, O_2- and moisture-free dry box), toluene (0.5 ml) in cyclohexane (1.5 ml) added via gas-tight syringe, the tube placed inside a Fischer-Porter pressure bottle, the latter sealed, removed from

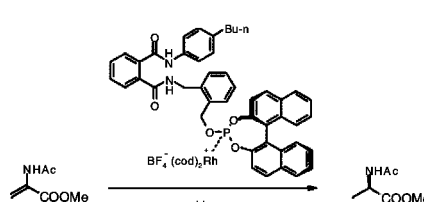
the dry box, placed inside a water bath at 25°, connected via Swagelock TFE-sealed quick-connects to an O_2- and moisture-free hydrogenation line, the bottle filled with purified H_2 *at 42 psig*, and hydrogenated at 25° until ^{1}H-NMR analysis confirmed completion of reaction → methylcyclohexane. Conversion 100%. Significantly, *record catalytic lifetimes* (with TTO up to 192,600 over 400 h) were reported for the total hydrogenation of benzene **without solvent** under the same conditions (with an average TOF of 480 h^{-1} before deactivation). The catalyst is easy to prepare, readily removed by suction filtration to give a dark-grey powder, and can be stored in a bottle under ambient conditions for repeated use. F.e.s. M. Zahmakiran, Y. Tonbul, S. Özkar, Chem. Commun. *2010*, *46* (26), 4788-90 [DOI: 10.1039/c0cc00494d].

Oxygen- and sulfur-bridged dirhodium di(phosphine) complexes *[Rh]*
Hydrogenation of carbon-carbon double bonds s. *3*, 46s*78* C=C → CHCH

Chiral rhodium di(phosphine), bis(aminophosphine), phosphine-phosphoromonoamidite or aminophosphine-phosphinite complexes *[Rh]*
Asym. homogeneous hydrogenation
of enacylamines s. *71*, 26s*76*; of β-(acylamino)acrylates with chiral BINOL-based N-(*o*-diphenylphosphino)-α-methylbenzylphosphoramidites as ligand s. X.-M. Zhou, J.-D. Huang, L.-B. Juo, C.-L. Zhang, X.-P. Hu, Z. Zheng, Org. Biomol. Chem. *2010, 8* (20), 2320-2 [DOI: 10.1039/c000268b]; of dehydroamino esters with chiral bis(aminophosphines) as ligand s. X. Sun, W. Li, L. Zhou, X. Zhang, Adv. Synth. Catal. *2010, 352* (7), 1150-4 [DOI: 10.1002/adsc.201000038]; of β-aminoacrylonitriles with TangPhos as ligand s. M. Ma, G. Hou, T. Sun, X. Zhang, W. Li, J. Wang, X. Zhang, Chem. Eur. J. *2010, 16* (18), 5301-4 [DOI: 10.1002/chem.201000325]; of N-protected α-(perfluoroalkyl)enamines with (R,R)-ChiraPhos as ligand s. K. Mikami, T. Murase, L. Zhai, Y. Itoh, S. Ito, Tetrahedron: Asym. *2010, 21* (9-10), 1158-61 [DOI: 10.1016/j.tetasy.2010.04.055]; of α-aminomethylacrylates with Et-Duphos as ligand s. Y. Guo, G. Shao, L. Li, W. Wu, R. Li, J. Li, J. Song, L. Qiu, M. Prashad, F.Y. Kwong, Adv. Synth. Catal. *2010, 352* (9), 1539-53 [DOI: 10.1002/adsc.201000122]; rapid identification of scalable catalysts for asym. hydrogenation of sterically demanding arylenacylamines s. L. Lefort, J.A.F. Boogers, T. Kuilman, R.J. Vijn, J. Janssen, H. Straatman, J.G. de Vries, A.H.M. de Vries, Org. Process Res. Dev. *2010, 14* (3), 568-73 [DOI: 10.1021/op100011y]; asym. hydrogenation **of prochiral olefins** (cf. *27*, 57s*76*,*77*) with chiral (diene)rhodium(I) di(phosphine) complexes s. A. Preetz, H.-J. Drexler, S. Schulz, D. Heller, Tetrahedron: Asym. *2010, 21* (9-10), 1226-31 [DOI: 10.1016/j.tetasy.2010.03.017]; with substituted $[Rh((R,R)\text{-SMS-Phos})(MeOH)_2]BF_4$ complexes s. B. Zupancic, B. Mohar, M. Stephan, Org. Lett. *2010, 12* (13), 3022-5 [DOI: 10.1021/ol101029s]; with σ-bonded calix[4]arene-subst. P-chiral aminophosphine-phosphinites as ligand s. N. Khiri, E. Bertrand, M.-J. Ondel-Eymin, Y. Rousselin, J. Bayardon, P.D. Harvey, S. Jugé, Organometallics *2010, 29* (16), 3622-31 [DOI: 10.1021/om100520u].

Bis(cyclooctadiene)rhodium(I) fluoroborate/N^1-(4-butylphenyl)-N^2-[2-[((11bS)-di-naphtho[2,1-d:1′,2′-f][1,3,2]dioxaphosphepin-4-yloxy)methyl]benzyl]phthalamide *[Rh(I)]**
Asym. homogeneous hydrogenation under supramolecular catalysis with chiral phthalamide-linked 1,1′-binaphthyl-2,2′-diyl phosphites as ligand

20.

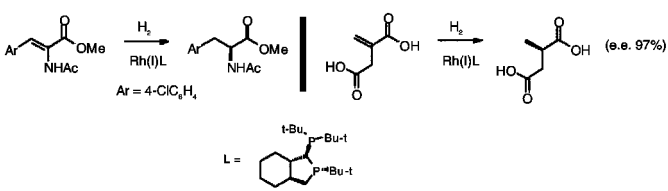


of enacylamines. An oven-dried test tube containing N^1-(4-butylphenyl)-N^2-[2-[((11bS)-dinaphtho[2,1-*d*:1′,2′-*f*][1,3,2]dioxaphosphepin-4-yloxy)methyl]benzyl]phthalamide (0.022 eq.) placed in a Schlenk flask and subjected to three vacuum/N_2 cycles, a soln. of $[Rh(cod)_2]BF_4$

(0.01 eq.) in methylene chloride (2.12 ml) added, the mixture stirred for 10 min under N_2, a 0.1909 *M* soln. of the startg. enacylamine (1 eq.) in the same solvent (1 ml) added, followed by more methylene chloride (2.1 ml), the mixture subjected to three vacuum/H_2 cycles, left stirring overnight at room temp. under 1 bar H_2, and worked up → methyl (R)-2-acetamidopropanoate. Conversion 100% (e.e. >99%). On complexation with rhodium(I) in solution, *chiral monodentate* phthalamide-linked 1,1′-binaphthyl-2,2′-diyl phosphites (PhthalaPhos ligands) self-assemble to form highly active cationic rhodium(I) bis(phosphite) species wherein the two phthalamide residues are linked by hydrogen bonds. The formed supramolecular bidentate ligand correspondingly has a reduced degree of freedom relative to simple chiral aryl 1,1′-binaphthyl-2,2′-diyl phosphites with enhanced enantioselectivity for the asym. hydrogenation of diverse enacylamines, incl. the challenging 1-acetylamino-3,4-dihydronaphthalene (five examples; e.e. up to 96%) and the sluggish (E)-methyl 2-(acetamidomethyl)-3-phenylacrylate (e.e. 91-98% at 50 atm. H_2). The ligands are also easy to prepare and modular in nature so that tuning for the particular substrate can be effected combinatorially. F.e.s. L. Pignataro, S. Carboni, M. Civera, R. Colombo, U. Piarulli, C. Gennari, Angew. Chem., Int. Ed. *2010*, *49* (37), 6633-7 [DOI: 10.1002/anie.201002958].

Bis(norbornadiene)rhodium(I) fluoroborate/chiral 1-phosphinooctahydroisophosphindoles ←
Asym. rhodium(I)-catalyzed hydrogenation C=C → CHCH
of α,β-ethylenecarboxylic acid derivs.
with a rigid, chiral 1-phosphinooctahydroisophosphindole as ligand

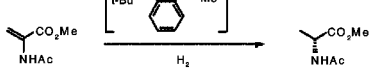
21.



A soln. of rhodium catalyst [freshly prepared from $[Rh(nbd)_2]BF_4$ (0.1 mol%) and (1S,2R,3aS,7aS)-2-*tert*-butyl-1-(di-*tert*-butylphosphino)octahydro-1*H*-isophosphindole (0.11 mol%) in THF/methanol (1:1; 2 ml) at room temp. for 20 min] in deoxygenated methanol (0.1 ml) added to a soln. of methyl α-acetamido-4-chlorocinnamate (0.1 mmol) in the same solvent (1 ml), the mixture hydrogenated (50 psi) in an autoclave at room temp. for 12 h, pressure released cautiously, and the mixture filtered through silica → methyl 2-acetamido-3-(4-chlorophenyl)propionate. Y 100% (e.e. >99%). The rhodium catalyst, incorporating a novel rigid three-hindered quadrant bisphosphine ligand, was successful for the hydrogenation of both α- and β-acetamidoacrylic acid and itaconic acid derivs. at low catalyst loadings (twenty-five examples; 100% conversions; e.e. 94 to >99%) with turnover numbers of up to 10,000 achieved. F.e. and ligand prepn. s. K. Huang, X. Zhang, T.J. Emge, G. Hou, B. Cao, X. Zhang, Chem. Commun. *2010*, *46* (45), 8555-7 [DOI: 10.1039/c0cc02620d].

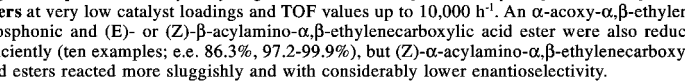
(R,R)-1,2-Bis[tert-butyl(methyl)phosphino]benzene(1,5-cyclooctadiene)rhodium(I) hexafluoroantimonate ←
Asym. homogeneous hydrogenation of functionalized ethylene derivs.
with (R,R)-1,2-bis[*tert*-butyl(methyl)phosphino]benzene as ligand

22.



at very low catalyst loading. A hydrogen bottle containing (R,R)-1,2-bis[*tert*-butyl(methyl)-phosphino]benzene(1,5-cyclooctadiene)rhodium(I) hexafluoroantimonate (0.01 mol%) and the

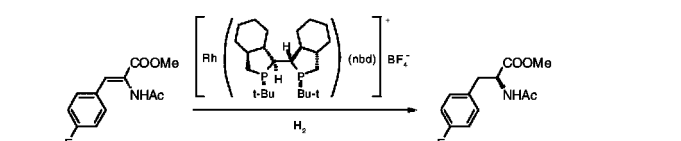
startg. functionalized olefin (2 mmol) evacuated and filled with H_2 several times, degassed methanol (3 ml) added, the H_2 pressure adjusted to 5 atm., stirred vigorously until H_2 uptake ceased (1 h), the mixture evaporated under reduced pressure, the residue passed through a short column of silica gel to remove the rhodium catalyst, and the solvent removed under reduced pressure → (R)-N-acetylalanine methyl ester. Conversion 100% (e.e. 99.9%). The novel chiral ligand is an easy-to-prepare, crystalline, air-stable solid which offers enantioselectivities of 99.1 to 99.9% (eight examples) for the asym. hydrogenation **of (E)-α-acylamino-α,β-ethylenecarboxylic acid esters** at very low catalyst loadings and TOF values up to 10,000 h^{-1}. An α-acoxy-α,β-ethylene-phosphonic and (E)- or (Z)-β-acylamino-α,β-ethylenecarboxylic acid ester were also reduced efficiently (ten examples; e.e. 86.3%, 97.2-99.9%), but (Z)-α-acylamino-α,β-ethylenecarboxylic acid esters reacted more sluggishly and with considerably lower enantioselectivity.



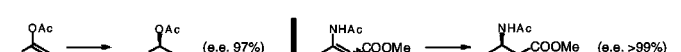
F.e. and preparation of the ligand (and its (S,S)-antipode) s. K. Tamura, M. Sugiya, K. Yoshida, A. Yanagisawa, T. Imamoto, Org. Lett. *2010*, *12* (19), 4400-3 [DOI: 10.1021/ol101936w].

Chiral [2,2′-di-tert-butylhexadecahydro-1H,1′H-1,1′-bi(isophosphindole)]-(norbornadiene)rhodium(I) fluoroborate *[Rh(I)]**

Asym. homogeneous hydrogenation of functionalized ethylene derivs. with a rigid, electron-donating P-chiral hexadecahydro-1*H*,1′*H*-1,1′-bi(isophosphindole) as ligand C=C → CHCH



23.



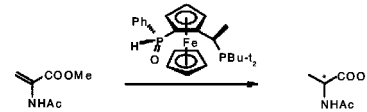
The startg. functionalized olefin (1 mmol) added to a soln. of [Rh(ZhangPhos)(nbd)]BF_4 [1 mol%; ZhangPhos = (1*S*,1′*S*,2*R*,2′*R*,3a*S*,3′a*S*,7a*S*,7′a*S*)-2,2′-di-*tert*-butylhexadecahydro-1*H*,1′*H*-1,1′-bi-(isophosphindole)] in methanol (10 ml) under N_2 (in a glovebox), the mixture transferred to an autoclave and charged with 20 psi H_2, the mixture hydrogenated *at room temp.* for 12 h, the pressure released carefully, the soln. passed through a short silica-gel plug to remove the catalyst, and worked up → (S)-product. Conversion 100% (e.e. >99%). With the two cyclohexane rings, ZhangPhos is conformationally more rigid and electron-donating than the established TangPhos and enantioselectivities correspondingly higher with TON values of 50,000 and TOF of 12,500/h at catalyst loadings *as low as 0.002%*. A further advantage is that, unlike TangPhos and related less rigid ligands, ZhangPhos is also effective at higher temp. and can be readily prepared from commercially available material. The scope of the method is extensive, highly efficient asym. hydrogenation of α-acylamino-α,β-ethylenecarboxylic acids and esters (fourteen examples; e.e. all >99%), α-arylenacylamines (eleven examples; e.e. all >99%), α-arylenol acetates (five examples; e.e. 97 to >99%), β-acylamino-α,β-ethylenecarboxylic acid esters (five examples; e.e. 92 to >99%) and itaconic acid esters (two examples; e.e. >99%) being achieved. Reaction also supports electronically diverse substituents on the aromatic ring. F.e.s. X. Zhang, K. Huang, G. Hou, B. Cao, X. Zhang, Angew. Chem., Int. Ed. *2010*, *49* (36), 6421-4 [DOI: 10.1002/anie.201002990].

Chloro(1,5-cyclooctadiene)rhodium(I) dimer/multiply-chiral sec-phosphine oxide-phosphines [Rh]*

Asym. homogeneous hydrogenation C=C → CHCH

with multiply-chiral *sec*-phosphine oxide-phosphines as ligand

24.



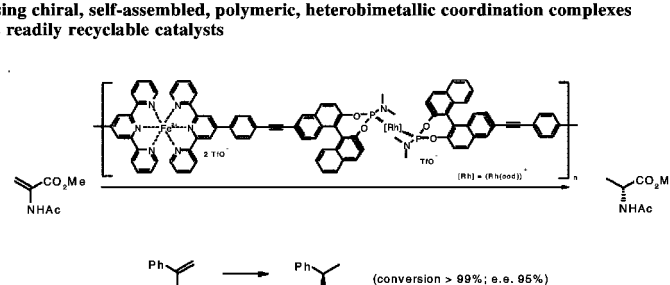
Modular, readily accessible *sec*-phosphine oxide-phosphines [termed *JoSPOphos*], having a planar chiral ferrocenyl backbone with both central (sp^3) and P-chirality, are highly effective ligands for rhodium-catalyzed asym. hydrogenation of functionalized alkenes, offering both high activity (at 0.1 to 1 mol%) and enantioselectivity (e.e. 98-99%) by appropriate choice of substituents at the P-centers. **E:** $[Rh(cod)Cl]_2$ (1 mol%) and chiral 1-(phenylphosphinoyl)-2-[1-(*tert*-butylphosphino)ethyl]ferrocene (1.1 mol%) mixed in 1,2-dichloroethane at room temp., the startg. alkene added to the *in situ*-generated rhodium(I) complex, and hydrogenated under 1 atm. H_2 until reaction complete (within 2 h) → product. Conversion 100% (e.e. 99%). High enantioselectivity (e.e. 90 to >99%) was recorded for the hydrogenation of a broad range of functionalized olefins, namely (Z)-α-acylamino-α,β-ethylenecarboxylic acid esters, (E)- or (Z)-β-acylamino-α,β-ethylenecarboxylic acid esters (both undergoing the *same* face-selectivity!) and dimethyl itaconate. With two substrates (an α-acylamino-enoate and the itaconate) the procedure was also carried out with a range of ligands at catalyst loading of 0.1 to 0.5 mol% (under 1 atm. H_2 in a 50 ml reactor), reaction normally being complete within 5 min, implying turnover frequencies of 2000-20,000 h^{-1}. The high catalytic activity is associated with the fact that coordination to the metal is stronger with two P-ligands, leading to better-defined complexes. The face-selectivity, however, appears to be dependent solely on the chirality of the *sec*-phosphine oxide residue. Related chiral menthyl(*o*-phosphinophenyl)phosphine oxides (termed *TerSPOphos*) lacking the planar chirality, also proved effective ligands (e.e. 68-99%), and preliminary experiments proved positive with analogous ligands based on biaryl-type planar-chirality and other terpene functionality. Only moderate enantioselectivity, however, was recorded for Ru-catalyzed asym. hydrogenation of ketocarboxylic acid esters. F.e.s. H. Landert, F. Spindler, A. Wyss, H.-U. Blaser, B. Pugin, Y. Ribourduoille, B. Gschwend, B. Ramalingam, A. Pfaltz, Angew. Chem., Int. Ed. *2010, 49* (38), 6873-6 [DOI: 10.1002/anie.201002225].

Chiral polymeric rhodium(I)/iron(II) phosphoromonoamidite complexes ←

Asym. heterogeneous hydrogenation

using chiral, self-assembled, polymeric, heterobimetallic coordination complexes as readily recyclable catalysts

25.



Chiral heteroditopic ligands bearing two orthogonal metal-ligating residues self-assemble in the presence of two different metals (in this case Fe(II) and Rh(I)) to form polymeric coordination

complexes which serve as highly efficient, readily recyclable catalysts for *heterogeneous* asym. hydrogenation of olefins, and are considered a significant improvement on established, but much less accessible, covalently bonded equivalents. **E:** The startg. enacylamine (1 mmol) and anhydrous toluene (1 ml) added under N_2 [in a glove box] to a test-tube containing the chiral bimetallic polymeric complex (1 mol%) [formed as a purple powder by self-assembly of $[Rh(cod)_2]OTf$ with the chiral iron(II)-coordinated heteroditopic phosphoromonoamidite ligand (1 eq. relative to Rh(I)) in methylene chloride at room temp. over 30 min], the test-tube placed inside a stainless steel autoclave, the latter sealed, purged with H_2 five times, the final H_2 pressure adjusted to 40 atm., stirred at room temp. for 2 h, H_2 released, the catalyst removed by filtration through a short pad of silica gel, the solvent removed from the filtrate under reduced pressure, and the residue worked up → product. Conversion >99% (e.e. 95%). High yields (>99% conversion), excellent enantioselectivities (90-96% e.e.) and very high turnover frequencies (up to 4560 h^{-1}) were recorded for the asym. hydrogenation of α-dehydroamino acids, enamides and itaconic acid derivs., comparing favorably with the homogeneous rhodium-catalyzed conversions [and in the above examples offering a significantly higher e.e. than with MonoPhos as ligand (e.e. 56%)]. Furthermore, the catalyst was readily recovered by filtration and retained its activity after 10 cycles without significant loss of enantioselectivity. The nature of the associated anions (triflate being optimal for both Rh(I) and Fe(II)), however, is critically important. F.e.s. L. Yu, Z. Wang, J. Wu, S. Tu, K. Ding, Angew. Chem., Int. Ed. *2010, 49* (21), 3627-30 [DOI: 10.1002/anie.200906405].

Palladium-carbon/1,4-dihydropyridines ←
Poly(N-vinyl-2-pyrrolidone)-stabilized palladium nanoparticles ←
Palladium nanoparticles/tetra-n-butylammonium bromide *Pd/Bu_4NBr*
Palladium(II) acetate/dimethylformamide/potassium hydroxide *Pd$(OAc)_2$/DMF/KOH*
Ethylene from acetylene derivs. C≡C → CH=CH

with $Pd_2(dba)_3$/*o*-Tol_3P cf. *45,* 24s*77*; **(Z)-ethylene derivs.** from aliphatic alkynes with recyclable poly(N-vinyl-2-pyrrolidone)-stabilized palladium nanoparticles by hydrogenation in ethanol, also Heck arylation in N-methyl-2-pyrrolidone, s. C. Evangelisti, N. Panziera, A. D'Alessio, L. Bertinetti, M. Botavina, G. Vitulli, J. Catal. *2010, 272* (2), 246-52 [DOI: 10.1016/j.jcat.2010.04.006]; with Pd nanoparticles in tetra-*n*-butylammonium bromide as ionic liquid s. J.K. Lee, D.W. Kim, M. Cheong, H. Lee, B.W. Cho, H.S. Kim, D. Mukherjee, Bull. Korean Chem. Soc. *2010, 31* (8), 2195-200 [DOI: 10.5012/bkcs.2010.31.8.2195]; (Z)-styrenes with Pd-C and diethyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate as H-donor (cf. *75,* 35) s. Y. Zhao, Q. Liu, J. Li, Z. Liu, B. Zhou, Synlett *2010* (12), 1870-2 [DOI: 10.1055/s-0030-1258122]; (Z)-ethylene derivs. with $Pd(OAc)_2$ and *DMF/KOH as source of hydrogen* s. J. Li, R. Hua, T. Liu, J. Org. Chem. *2010, 75* (9), 2966-70 [DOI: 10.1021/jo100247a].

Palladium nanoparticles-in-aluminum oxyhydroxide *Pd-Al(O)OH*
Palladium nanoparticles-in-mesoporous MCM-48 *Pd-MCM-48*
Palladium nanoparticles-on-magnetite *Pd-Fe_3O_4*
Hydrogenation of carbon-carbon double bonds C=C → CHCH

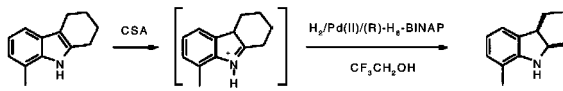
with sepiolite-immobilized Pd nanoparticles cf. *3,* 46s*75*; with magnetically retrievable Pd nanoparticles-on-magnetite s. Y. Kim, M.-J. Kim, Bull. Korean Chem. Soc. *2010, 31* (5), 1368-70 [DOI: 10.5012/bkcs.2010.31.1368-70]; with Pd nanoparticles encapsulated in mesoporous MCM, regio- and chemo-selectivity, s. S. Banerjee, V. Balasanthiran, R.T. Koodali, G.A. Sereda, Org. Biomol. Chem. *2010, 8* (19), 4316-21 [DOI: 10.1039/c0ob00183j]; with Pd nanoparticles-in-aluminum oxyhydroxide for the solvent-free hydrogenation of solid alkenes and ar. nitro compds. s. F. Chang, H. Kim, B. Lee, S. Park, J. Park, Tetrahedron Lett. *2010, 51* (32), 4250-2 [DOI: 10.1016/j.tetlet.2010.06.024]; with oxygen- and sulfur-bridged dirhodium di(phosphine) complexes s. C. Zhu, N. Yukimura, M. Yamane, Organometallics *2010, 29* (19), 2098-103 [DOI: 10.1021/om100067r].

Palladium(II) trifluoroacetate/(R)-2,2′-bis(diphenylphosphino)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl/L-camphorsulfonic acid ←

2-Subst. indolines from indoles C=C → CHCH

Palladium(II)-catalyzed asym. hydrogenation with activation by Brønsted acids

26.



A mixture of (R)-H_8-BINAP (2.4 mol%) and $Pd(OCOCF_3)_2$ (2 mol%) in a dried Schlenk tube stirred under N_2 in degassed anhydrous acetone at room temp. for 1 h, solvent removed *in vacuo*, a soln. of L-CSA (1 eq.) and 1-methyl-5,6,7,8-tetrahydro-9*H*-carbazole (0.25 mmol) in methylene chloride/*2,2,2-trifluoroethanol* (1:1; 1 ml) stirred at room temp. for 5 min, a soln. of the catalyst in the same solvents (2 ml) added, the mixture stirred under H_2 (700 psi) in a stainless steel autoclave for 24 h, pressure released cautiously, the mixture concentrated *in vacuo*, dissolved in satd. aq. $NaHCO_3$, stirred for 10 min, extracted with methylene chloride, and purified by chromatography on silica → (+)-(2R,3R)-1-methyl-5,6,7,8,8a,9-hexahydro-4b*H*-carbazole. Y 83% (e.e. 96%). Initial Brønsted acid activation of the indole (to an iminium ion) is crucial to the success of this novel enantioselective hydrogenation of unprotected indole derivs. A variety of 2-alkyl and 2-benzyl derivs. were reduced with high enantioselectivity (seventeen examples; Y 78-99%; e.e. 84-99%), apparently unaffected by 3- or 7-alkyl substituents but with e.e. marginally decreased (by 3-7%) for 5-methyl- or 5-fluoro-substituted indoles. Deuterium labelling experiments demonstrated that 2-H and 3-H are provided by H_2 and trifluoroethanol respectively. F.e., optimization and substrate prepn. s. D.-S. Wang, Q.-A. Chen, W. Li, C.-B. Yu, Y.-G. Zhou, X. Zhang, J. Am. Chem. Soc. *2010, 132* (26), 8909-11 [DOI: 10.1021/ja103668q]; chiral 2- or 3-subst. N-protected [Boc, Ts, Ac] indolines **under iridium catalysis** (cf. *75*, 37) using chiral N,P ligands s. A. Baeza, A. Pfaltz, Chem. Eur. J. *2010, 16* (7), 2036-9 [DOI: 10.1002/chem.200903105]; chiral N-Boc-indoline-2-carboxylic acid esters **under rhodium catalysis** (cf. *68*, 36) using Walphos-type chiral ligands (and sometimes a base) s. A.M. Maj, I. Suisse, C. Méliet, F. Agbossou-Niedercorn, Tetrahedron: Asym. *2010, 21* (16), 2010-4 [DOI: 10.1016/j.tetasy.2010.06.030].

Chiral iridium phosphine, aminophosphine, aminophosphine oxide or phosphite complexes *[Ir]**

Asym. homogeneous hydrogenation

s. *62*, 39s*75*; with chiral cationic iridium(I) *o*-diphenylphosphino-*o*′-Δ^2-oxazolin-2-ylbiphenyl complexes for asym. hydrogenation of exocyclic enones s. F. Tian, D. Yao, Y. Liu, F. Xie, W. Zhang, Adv. Synth. Catal. *2010, 352* (11-12), 1841-5 [DOI: 10.1002/adsc.201000185]; of olefins with chiral bicyclic N-phosphino-α-(thiazol-2-yl)amines as ligand s. J.-Q. Li, A. Paptchikhine, T. Govender, P.G. Andersson, Tetrahedron: Asym. *2010, 21* (11-12), 1328-33 [DOI: 10.1016/j.tetasy.2010.03.023]; of unfunctionalized (E)- or (Z)-trisubst. and 1,1-disubst. terminal alkenes with chiral thiazolyl- or oxazolyl-subst. biaryl phosphites as ligand s. J. Mazuela, A. Paptchikhine, O. Pàmies, P.G. Andersson, M. Diéguez, Chem. Eur. J. *2010, 16* (15), 4567-76 [DOI: 10.1002/chem.200903350]; with chiral spirocyclic P,N-ligands s. Z. Han, Z. Wang, X. Zhang, K. Ding, Tetrahedron: Asym. *2010, 21* (11-12), 1529-33 [DOI: 10.1016/j.tetasy.2010.05.022].

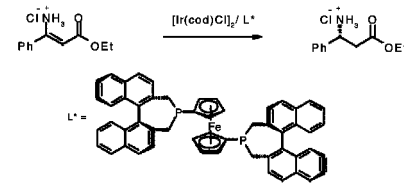
Chiral iridium(I) di(phosphine) complexes *[Ir(I)]**

Asym. homogeneous hydrogenation of N-heteroarenes Ⓗ

asym. hydrogenation of quinolines s. *66*, 42s*72*; **of quinolines and pyridines** with a chiral iridium(I) DifluorPhos complex s. W. Tang, Y. Sun, L. Xu, T. Wang, Q. Fan, K.-H. Lam, A.S.C. Chan, Org. Biomol. Chem. *2010, 8* (15), 3464-71 [DOI: 10.1039/c002668a]; **of quinoxalines** s. D. Cartigny, T. Nagano, T. Ayad, J.-P. Genêt, T. Ohshima, K. Mashima, V. Ratovelomanana-Vidal, Adv. Synth. Catal. *2010, 352* (11-12), 1886-91 [DOI: 10.1002/adsc.201000513]; of quinolines and quinoxalines with a chiral iridium(I) (R)-SegPhos complex by activation of the substrate with piperidine·triflic acid as Brønsted acid s. D.-S. Wang, Y.-G. Zhou, Tetrahedron Lett. *2010, 51* (22), 3014-7 [DOI: 10.1016/j.tetlet.2010.04.004].

Chloro(cyclooctadiene)iridium(I) dimer/(S,S)-1,1′-bis[4,5-dihydro-3H-binaphtho-[2,1-c;1′,2′-e]-phosphepino]ferrocene/hydrochlorides ←
Iridium(I)-catalyzed asym. homogeneous hydrogenation C=C → CHCH
of β-*prim*-amino-α,β-ethylenecarboxylic acid esters

27.



A soln. of $[Ir(cod)Cl]_2$ (0.003 mmol) and (S,S)-f-Binaphane (0.006 mmol) in methylene chloride (5 ml) stirred in a vial (inside a glove box) for 20 min at room temp., one-tenth of the soln. placed in a second vial, a soln. of the startg. ester hydrochloride (0.6 mmol) in methanol (2 ml) added, the vial placed in a steel autoclave, the inert atmosphere replaced by H_2, stirred under 50 atm. H_2 at room temp. for 12 h, the mixture concentrated under vacuum, dissolved in satd. aq. $NaHCO_3$, stirred for 10 min, extracted with methylene chloride, dried, and worked up → (S)-3-ethoxy-3-oxo-1-phenylpropan-1-aminium chloride. Conversion >99% (e.e. 97% as determined after conversion to the corresponding acetamide). **Chiral β-*prim*-amino-β-arylcarboxylic acid esters** were thus obtained with ca. quantitative conversion and high enantioselectivity (thirteen examples; e.e. 84%, 90-97%), with an unprecedented high reactivity (TON >5000) and with a substrate/catalyst ratio *as high as 10,000*. The ester group of the substrate is variable, and the β-aryl substituent may possess an electron-withdrawing or -donating group and includes naphthyl or 2-thienyl. Enantioselectivity was considerably lower with more established chiral ligands (e.g. BINAP, TangPhos, Me-DuPhos, SegPhos, MonoPhos and *t*-Bu-JosiPhos). The high reactivity suggests that hydrogenation proceeds via a 'non-chelate' mechanism, i.e. without an iridium-nitrogen interaction. F.e. and comparison of solvents s. G. Hou, W. Li, M. Ma, X. Zhang, X. Zhang, J. Am. Chem. Soc. *2010*, *132* (37), 12844-6 [DOI: 10.1021/ja105674y].

Exchange ⇓⇑

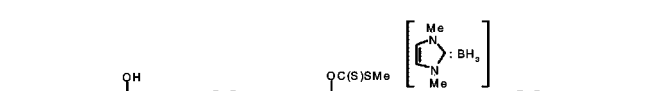
Oxygen ↑ HC ⇓⇑ O

1,4-Dihydropyridines s. under Et_3SiH ←

Zinc/trimethylsilyl chloride/alcohols *Zn/Me_3SiCl/ROH*
Methylene groups from ketones CO → CH_2
Clemmensen reduction – Also one pot ozonolysis-Clemmensen reduction s. *78*, 34

1,3-Dimethylimidazol-2-ylidene-borane/azodiisobutyronitrile ←
Radical deoxygenation OC(S)- → H
using low molecular-weight N-heterocyclic carbene-boranes

28.



via xanthates. AIBN (0.1 mmol) added in one portion to a soln. of 1,3-dimethylimidazol-2-ylidene-borane (0.1 mmol) and the startg. xanthate (0.1 mmol) in deoxygenated benzene (1 ml), the colorless soln. refluxed for 2 h, cooled to room temp., the solvent removed under vacuum, and

the residue purified by flash column chromatography → octyloxymethylbenzene. Y 79% (81% with Et_3B/air as radical initiator). This NHC-borane and related 2,4-dimethyl-1,2,4-triazolidin-3-ylidene-borane are superior to bulkier 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene-borane and bicyclic analogs for the radical deoxygenation of alcohols via xanthates, thionocarbonates or imidazole-based thionocarbamates. They are also easier to handle, relatively inexpensive, readily soluble, even in water, and function efficiently and rapidly in stoichiometric amount, although (as is true of most radical reducing agents) yields were lower (30-50%) with prim. xanthates. F.e. via sec. xanthates, **thionocarbonates or thionourethans** (ca. twelve; Y 50-88%) s. S.-H. Ueng, L. Fensterbank, E. Lacôte, M. Malacria, D.P. Curran, Org. Lett. *2010, 12* (13), 3002-5 [DOI: 10.1021/ol101015m].

Sodium tetrahydridoborate/potassium carbonate/polyethylene glycol s. under $SOCl_2$ ←

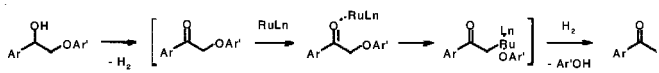
Triethylsilane/trifluoromethanesulfonic anhydride/2-fluoropyridine/1,4-dihydropyridines ←
Sec. amines from N-subst. carboxylic acid amides C(O)NHR → CH_2NHR
Chemoselective reduction under mild, metal-free conditions s. *78*, 35

Trimethylsilyl chloride/alcohols s. under Zn *Me_3SiCl/ROH*
4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene s. under $RuH_2(CO)(PPh_3)_3$ *XantPhos*
Trifluoromethanesulfonic anhydride s. under Et_3SiH *Tf_2O*

Thionyl chloride/sodium tetrahydridoborate/potassium carbonate/polyethylene glycol-400 ←
Prim. alcohols from carboxylic acids COOH → COCl → CH_2OH
via carboxylic acid chlorides in a 2-phase medium s. *78*, 30

Carbonyl(dihydrido)tris(triphenylphosphine)ruthenium(II)/4,5-bis(diphenylphosphino)-9,9-dimethylxanthene ←
Acetophenones from 2-arylglycol 1-monoaryl ethers $CH(OH)CH_2OAr$ → $C(O)CH_3$
Ruthenium(II)-catalyzed redoxidative C-O bond cleavage

29.



Ar = 3,4-$(MeO)_2C_6H_3$ Ar' = 2-$MeOC_6H_4$

under neutral conditions. A soln. of 2-(2-methoxyphenoxy)-1-(3,4-dimethoxyphenyl)ethanol (1 mmol), $RuH_2(CO)(PPh_3)_3$ (10 mol%) and XantPhos (10 mol%) in anhydrous xylenes (2.5 ml) sealed in a Biotage Microwave reaction vial with an aluminum crimp-top, heated at 135° for 4 h, and purified by chromatography on silica → 3,4-dimethoxyacetophenone. Y 89%. The method was developed to provide small molecules, via depolymerization of lignins, as potential biofuel components. The C-O bond cleavage was successful for a series of phenyl and methoxyphenyl derivs., with increasing methoxy substitution on the O-aryl substituent leading to reduced yields (five examples; Y 62-98%). The method was applied to the cleavage of poly(4′-hydroxy-1-phenylethanol), affording 4′-hydroxyacetophenone in 99% yield. Experimental evidence suggests that α-aryloxyketones are key intermediates in this transformation. F.e., optimization and substrate prepn. s. J.M. Nichols, L.M. Bishop, R.G. Bergman, J.A. Ellman, J. Am. Chem. Soc. *2010, 132* (36), 12554-5 [DOI: 10.1021/ja106101f].

Nitrogen ↑ HC ↓↑ N

o-Iodoxybenzoic acid/ammonia *$ArIO_2/NH_3$*
Aldehydes from carboxylic acid hydrazides s. *78*, 91 $C(O)NHNH_2$ → CHO

Triethylsilane/triflimide *Et_3SiH/Tf_2NH*
Alkylarenes from benzyl-N-tosylamines $NHTs$ → H
with retention of ethylene or acetylene moieties s. *78*, 487

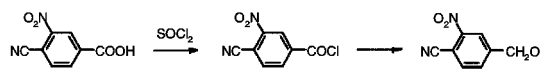
Triethylsilane/trifluoromethanesulfonic anhydride/2-fluoropyridine/citric acid ←
Aldehydes from N-subst. carboxylic acid amides C(O)NHR → CHO
Chemoselective reduction under mild, metal-free conditions s. *78*, 35

Halogen ↑ HC ↓↑ Hal

tert-Butylmagnesium chloride s. under Fe(acac)$_3$ *t-BuMgCl*

Sodium tetrahydridoborate/potassium carbonate/polyethylene glycol-400 *$NaBH_4/K_2CO_3$/PEG*
Prim. alcohols from carboxylic acid chlorides in a 2-phase medium COCl → CH_2OH

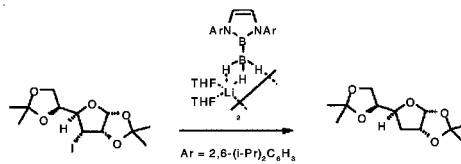
30.



The startg. crude acid chloride [prepared by boiling a soln. of 4-cyano-3-nitrobenzoic acid (2.6 mmol) in methylene chloride (10 ml) with thionyl chloride (3.91 mmol) for 3 h, followed by concentration] redissolved in fresh, dry methylene chloride (2.5 ml), added dropwise with stirring to a precooled (0-15°) mixture of methylene chloride (2.5 ml) and water (2.5 ml) containing K_2CO_3 (5.2 mmol), PEG-400 (20 mol%) and a portion of $NaBH_4$ (0.2 eq.), a further 2 eq. of the reductant added over 5 min, stirring continued at the same temp. for another 10 min, and worked up with purification on a short column of silica gel → 4-hydroxymethyl-2-nitrobenzonitrile. Y 97%. The procedure is simple, mild, rapid, efficient and high-yielding for the reduction of a wide range of aroyl and hetaroyl chlorides, leaving a variety of common functional groups unaffected (aromatic Cl, Br, NO_2, OMe, COOMe, CN, OAc, AcNH, as well as CCl_3, CF_3 and SMe groups). Furthermore, the method can be *scaled up to the 200 g level* with exactly the same result. Phthalimide and phthalic anhydride, under these conditions, gave phthalimidine and phthalic acid, respectively. F.e. (ca. twenty; Y 51-98%), also comparison of phase transfer catalysts, bases and solvents, s. R. Rajan, S. Badgujar, K. Kaur, Y. Malpani, P.R. Kanjilal, Synth. Commun. *2010, 40* (19), 2897-907 [DOI: 10.1080/00397910903340645].

Lithium [1,3-bis(2,6-diisopropylphenyl)-2,3-dihydro-1H-1,3,2-diazaborol-2-yl]trihydrido-borate/azodiisobutyronitrile ←
Dehalogenation using a novel borylhydridoborate anion Hal → H

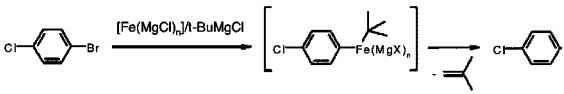
31.



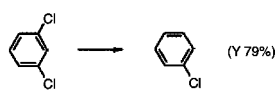
Replacement of iodine by hydrogen. A soln. of 1,2,5,6-di-O-isopropylidene-3-iodo-3-deoxy-α-D-glucofuranose (0.05 mmol) and the boryltrihydridoborate (1 eq.) in benzene-d6 (0.5 ml) added to AIBN (1 eq.) in a flame-dried quartz NMR tube, the tube sealed, heated at 80° for 2 h, solvent removed *in vacuo*, and the residue purified by flash chromatography on silica → 1,2,5,6-di-O-isopropylidene-3-deoxy-α-D-glucofuranose. Y 73% (78% conversion). This novel boryl anion shares characteristics of traditional borohydrides and N-heterocyclic carbenes (with which it is isoelectronic) and was able to effect reductions specific to both types of compound. Ionic reduction of an alkyl iodide in THF (>95% conversion; Y 75%), palladium(II)-catalyzed reduction of an aryl iodide (>95% conversion; Y 65%) and the illustrated radical reduction gave similar or improved results compared to examples of existing borohydride and borane reductants. F.e., reagent prepn. and characterization (incl. X-ray analysis) s. K. Nozak, Y. Aramaki, M. Yamashita, S.-H. Ueng, M. Malacria, E. Lacôte, D.P. Curran, J. Am. Chem. Soc. *2010, 132* (33), 11449-51 [DOI: 10.1021/ja105277u].

Polyethylene glycol-400 s. under $NaBH_4$ *PEG*

Tri-n-butyltin hydride *Bu_3SnH*
1,3-Dihydroisobenzofurans from 1-α-iodo-1,3-dihydroisobenzofurans s. *78*, 460 I → H
Iron(III) acetoacetonate/tert-butylmagnesium chloride *$Fe(acac)_3$/t-BuMgCl*
Iron-catalyzed replacement of ar. halogen by hydrogen under mild conditions Hal → H



32.



Selective conversion. Dry THF (4 ml) added to a septum-sealed Schlenk tube charged with $Fe(acac)_3$ (1 mol%) under argon, the soln. stirred *at 0°*, *tert*-butylmagnesium chloride (1.5 eq.; 1.7 *M* in THF) as hydride source added via syringe, after 2 min *p*-bromochlorobenzene (1 mmol) added, the mixture quenched after 90 min with satd. aq. NH_4Cl, and worked up with purification by flash chromatography on silica gel → chlorobenzene. Y 89%. Ar. bromides and iodides were reduced in high yield at 0°, but ar. chlorides required a more elevated temp. (20° or above) over a longer period (3 h). The procedure is environmentally friendly, mild and generally applicable to a wide range of ar. chlorides, bromides and iodides, tolerating electron-donating and -withdrawing groups and *o*-substitution, while leaving F, OR, SR, CN, COOR and vinyl groups unaffected. Interestingly, aromatic dichlorides were *monodechlorinated*; reaction is also applicable to heteroaromatic halides, as well as aromatic bromides possessing acidic functions (OH, NH_2), which required excess of the Grignard reagent (twenty examples in all; Y 54-99%). $FeCl_3$ and $FeCl_2$ were slightly less active, while $CuCl_2$, $CoCl_2$, $Pd(acac)_2$ and $Ni(acac)_2$ were ineffective. Reduction is presumed to involve iron-centered β-hydride elimination from an intermediate aryl(*tert*-butyl)-iron complex with elimination of isobutene. F.e. and preliminary study of reduction of alkyl bromides (three examples; Y 79-93%) s. W.M. Czaplik, S. Grupe, M. Mayer, A. Jacobi von Wangelin, Chem. Commun. *2010, 46* (34), 6350-2 [DOI: 10.1039/c0cc01980a].

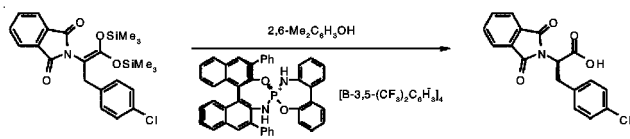
Nickel-aluminum or Rhodium nanoparticles or Palladium-carbon/ triethylamine *Ni-Al or Rh or Pd-C/Et_3N*
Replacement of ar. halogen by hydrogen
with Pd-C/$NaHCO_3$ cf. *11*, 633s*74*; pilot-plant study of the hydrogenation of PCBs at ambient pressure and temp. with Pd-C/Et_3N s. Y. Monguchi, S. Ishihara, A. Ido, M. Niikawa, K. Kamiya, Y. Sawama, H. Nagase, H. Sajiki, Org. Process Res. Dev. *2010, 14* (5), 1140-6 [DOI: 10.1021/op100107r]; dehalogenation of halogenoanilines with powdered Raney Ni-Al alloy (cf. *21*, 100s*75*) s. T. Weidlich, A. Krejcová, L. Prokeš, Monatsh. Chem. *2010, 141* (9), 1015-20 [DOI: 10.1007/s00706-010-0362-9]; hydrogenation of ar. mono-, di- and tri-chlorides with Rh nanoparticles (cf. *29*, 77s*37*) s. M.L. Buil, M.A. Esteruelas, S. Niembro, M. Oliván, L. Orzechowski, C. Pelayo, A. Vallribera, Organometallics *2010, 29* (19), 4375-83 [DOI: 10.1021/om1003072].

Remaining Elements ↑ HC ↓↑ Rem

Silver fluoride/methanol *AgF/MeOH*
Removal of the traceless 2-pyridylsilyl directing group s. *78*, 78 Si⩽ → H

Chiral diaminodioxyphosphonium barfates/2,6-di-tert-butylpyridine/2,6-dimethylphenol ←
Carboxylic acids from ketene disilyl acetals C=C(OSi≤)$_2$ → CHCOOH
via asym. proto-desilylation

33.



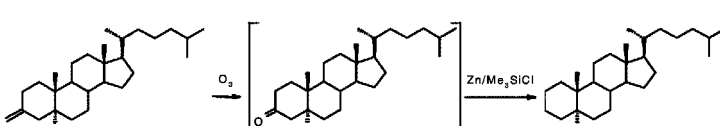
Chiral α-aminocarboxylic acids. A soln. of the startg. ketene disilyl acetal (0.1 mmol) in toluene (0.4 ml) added slowly to a soln. of 2,6-dimethylphenol (1.1 eq.), chiral phosphonium catalyst (1 mol%) and 2,6-di-*tert*-butyl-pyridine (2 mol%) in the same solvent (0.6 ml) at -20°, the mixture stirred for 6 h, and purified by chromatography on silica → (R)-N-phthalimido-α-(4-chlorobenzyl)glycine. Y 100% (e.e. 90%). Novel diaminodioxyphosphonium salts were developed as chiral proton-transfer agents and, in catalytic amounts, using 2,6-dimethylphenol as the stoichiometric proton source, were successful for preparation of diverse α-alkyl- and α-benzyl-glycines. The reaction rate was strongly affected by steric hindrance (reaction times of 2-20 h) but yields were quantitative and enantioselectivity high in all cases (seven examples; e.e. 90-95%), with products characterized as their methyl esters (MeI/Ag_2O). Use of stoichiometric amounts of the illustrated proton-transfer agent in one case gave similar enantioselectivity, indicating direct proton transfer from the diaminodioxyphosphonium cation. F.e., optimization and reagent prepn./characterization s. D. Uraguchi, N. Kinoshita, T. Ooi, J. Am. Chem. Soc. *2010, 132* (35), 12240-2 [DOI: 10.1021/ja105945z].

Hydrogen fluoride *HF*
Cleavage of a 'volatilizable' silica support s. *78*, 245 ←

Carbon ↑ HC ↓↑ C

Ozone/zinc/trimethylsilyl chloride/alcohols *O_3/Zn/Me_3SiCl/ROH*
Methylene groups from 1,1-disubst. ethylene derivs. via ketones >C=C → >CH_2
One-pot conversion via ozonolysis-Clemmensen reduction under mild conditions

34.



A one-pot conversion of 1,1-disubst. ethylene derivs. to methylene groups has been achieved efficiently via ozonolysis and a modified Clemmensen reduction without using hazardous or expensive reagents. **E:** Ozone passed through a soln. of the startg. olefin (0.2 mmol) *in 3:1 isopropanol/methylene chloride* (20 ml) at -78°, allowed to react until the olefin was consumed (TLC monitoring), excess of ozone removed by a stream of argon for 10 min, the mixture treated at the same temp. with Zn powder (20 mmol), followed dropwise by trimethylsilyl chloride (10 mmol), gradually warmed to 0°, stirred for 30 min, filtered, the filtrate concentrated, and the residue worked up with purification by chromatography on silica gel → product. Y 87%. Key to the conversion is the use of a mixed alcohol/methylene chloride solvent for the Clemmensen reduction, the efficiency of which was demonstrated preliminarily by reducing a wide range of aliphatic and cyclic ketones with methanol, ethanol or isopropanol as the alcoholic component

(five examples; Y 77-98%). The one pot conversion is applicable to both terminal and trisubst. ethylene derivs. (four examples; Y 72-86%). F.e.s. S. Xu, T. Toyama, J. Nakamura, H. Arimoto, Tetrahedron Lett. *2010*, *51* (34), 4534-7 [DOI: 10.1016/j.tetlet.2010.06.102].

Hydrogen chloride *HCl*
Indan-1,3-diones from indan-1,3-dione-2,2-dicarboxylic acid esters $C(COOR)_2 \rightarrow CH_2$
s. *78*, 395

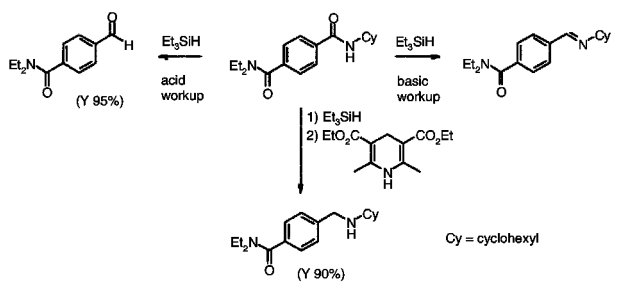
Elimination ↾

Oxygen ↑ HC ↾ O

(Acetonitrile)[dicyclohexyl(2,4,6-triisopropylbiphenyl-2′-yl)-phosphine]gold(I) hexafluoroantimonate *[(MeCN)(XPhos)Au]SbF$_6$*
Allenes from benzyloxy-2-acetylenes C(OBn)C≡C → C=C=CH
via gold(I)-catalyzed 1,5-hydride shift and loss of benzaldehyde s. *78*, 532

Triethylsilane/trifluoromethanesulfonic anhydride/2-fluoropyridine *Et$_3$SiH/Tf$_2$O/2-FC$_5$H$_4$N*
Chemoselective metal-free reduction C(O)NHR → C=NR
of N-subst. carboxylic acid amides under mild conditions

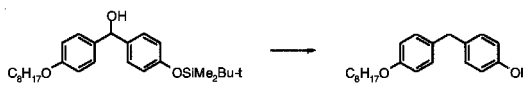
35.



Aldimines. 2-Fluoropyridine (1.1 eq.) added to a soln. of startg. amide (2 mmol) in anhydrous methylene chloride (8 ml), the soln. cooled to -78°, stirred for 10 min, triflic anhydride (1.05 eq.) added dropwise via syringe, the mixture stirred for 10 min, warmed to 0°, triethylsilane (1.1 eq.) added, the mixture stirred at 0° for 10 min then at room temp. for 5 h, *quenched with satd. aq. $NaHCO_3$*, extracted with methylene chloride, solvents removed *in vacuo*, and 2-fluoropyridine and silane residues removed in a vacuum oven (1-5 mmHg) at 50° for 4 h → N,N-diethyl-4-(E)-(cyclohexyl-iminomethyl)benzamide. Y 99%. Pure imines were stored at -20° under argon. Reduction of electron-neutral or -poor (het)ar. and aliphatic sec. amides with mild, inexpensive and commercially available triethylsilane afforded imines after basic work-up (eighteen examples; Y 66-99%) or **aldehydes** following acid (aq. citric acid/THF) treatment (eighteen examples; Y 64-96%). Wide functional group tolerance was observed (*tert. amide, aldehyde, azide, alkene*, ester, nitrile, nitro, alkyne, phosphate, ether and silyl ether), and reduction of a chiral sec. amide to an aldehyde occurred with only slight loss of optical activity (e.e. 98% → 93%; Y 70%). The method was extended to the prepn. of **sec. amines** by *in situ* reduction of imine products with Hantzsch ester (fourteen examples; Y 71-90%). F.e., optimization and substrate prepn. s. G. Pelletier, W.S. Bechara, A.B. Charette, J. Am. Chem. Soc. *2010*, *132* (37), 12817-9 [DOI: 10.1021/ja105194s].

Hydrogen chloride/ethanol *HCl/EtOH*
Mild and efficient deoxygenation of diarylcarbinols OH → H
under metal-free, hydrolytic conditions

36.



A soln. of concd. HCl (1 ml) in ethanol (10 ml) added to a soln. of [4-(*tert*-butyldimethylsilyloxy)phenyl][4-(octyloxy)phenyl]methanol (2.26 mmol) in the same solvent (50 ml) at 0°, the mixture heated under reflux for 48 h, cooled to room temp., poured into satd. aq. $NaHCO_3$ (25 ml), extracted with hexanes and ether, the combined extracts washed with water, dried ($MgSO_4$), filtered, solvent removed *in vacuo*, and the residue purified by recrystallization → 4-[4-(octyloxy)benzyl]-phenol. Y 79%. Diphenylmethanol and various 4,4′-disubst. (hydroxyl, long-chain alkoxy and silyloxy) derivs. were similarly deoxygenated (seven examples; Y 68-90%), with silyl ethers cleanly hydrolyzed under the conditions. The method avoids the need for toxic or expensive reagents, such as stannanes, silanes or dialkyl phosphites, and is selective for the reduction of diarylmethanols; 1-arylethanols are unaffected. F.e.s. K.A. Hope-Ross, J.F. Kadia, Can. J. Chem. *2010*, *88* (10), 1003-8 [DOI: 10.1139/V10-090].

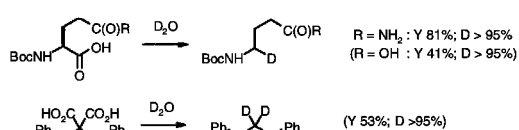
Carbonyl(dihydrido)tris(triphenylphosphine)ruthenium(II)/4,5-bis(diphenylphosphino)-9,9-dimethylxanthene ←
Acetophenones from 2-arylglycol 1-monoaryl ethers $CH(OH)CH_2OAr$ → $C(O)CH_3$
Ruthenium(II)-catalyzed redoxidative C-O bond cleavage s. *78*, 29

Via intermediates *v.i.*
Radical deoxygenation via xanthates, thionocarbonates or thionourethans OH → OC(S)- → H
using low molecular-weight N-heterocyclic carbene-boranes s. *78*, 28

Carbon ↑ HC ⇑ C

Phenanthrene/1,4-dicyanobenzene/tert-dodecanethiol/irradiation ←
Photo-assisted decarboxylative deuteriation of aliphatic carboxylic acids COOH → D

37.



A soln. of N-Boc-*L*-glutamine (0.6 mmol), phenanthrene (1 eq.), 1,4-dicyanobenzene (1 eq.) and *tert*-dodecanethiol (2 eq.) in acetonitrile/D_2O (98:2; 60 ml) under argon irradiated (400 *W* high-pressure mercury lamp) for 8 h, solvent removed *in vacuo*, and the residue purified by chromatography on silica → N-Boc-4-deuterio-4-aminobutanamide. Y 81% (D content >95%). Efficient deuterium exchange (>95%) was observed for aliphatic (incl. amino-subst.) carboxylic acids (eight examples; Y 73-92%; 50% for N-Boc-proline), and occurred exclusively at the more reactive α-carboxylic acid for N-Boc-*L*-glutamic acid, albeit in modest yield (41%). A 2-carboxyfuranose, however, achieved only 82% incorporation of deuterium (Y 67%). A radical mechanism has been proposed. F.e. and optimization s. T. Itou, Y. Yoshimi, K. Nishikawa, T. Morita, Y. Okada, N. Ichinose, M. Hatanaka, Chem. Commun. *2010*, *46* (33), 6177-9 [DOI: 10.1039/c0cc01464h].

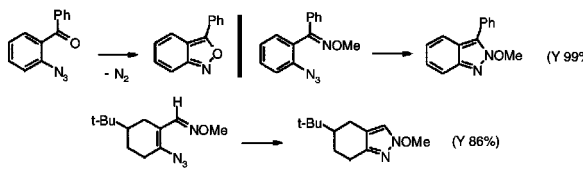
Formation of O-N Bond

Elimination ⇑

Nitrogen ↑ ON ⇑ N

Iron(II) bromide $FeBr_2$

Iron(II)-catalyzed denitrogenative ring closures of 2-functionalized unsatd. azides ○



38.

2,1-Benzisoxazoles from *o*-azidoketones. Methylene chloride (0.25 ml) added to a conical flask (fitted with a Teflon septum) containing a mixture of *o*-azidobenzophenone (0.1 mmol), 100 w/w% crushed 4 Å molecular sieves and $FeBr_2$ (5 mol%), heated for 16 h, filtered through silica, the filtrate concentrated *in vacuo*, and the residue worked up with purification by MPLC → 3-phenyl-2,1-benzisoxazole. Y 98%. The procedure is mild, eco-friendly, and applicable to a range of *o*-azidobenzophenones and -acylophenones (eleven examples; Y 57-98%); there was no reaction, however, with *o*-azidoaldehydes or with *o*-azidoketones possessing electron-withdrawing groups on the aromatic ring. Similarly, **2-alkoxyindazoles** (both 3-subst. and 3-unsubst. derivs.) were obtained, more broadly, **from (E)-*o*-azidoalkoximes**, irrespective of the electronic nature of ring substituents (eleven examples; Y 44-99%), while **1-alkoxypyrazoles** were prepared **from (E)-β-azido-α,β-ethylenealkoximes** (four examples; Y 79-99%). The fact that (Z)-*o*-azidoalkoximes were unreactive suggests that N-O and N-N bond formation takes place through a planar iron(II)-azide complex. F.e. and comparison of transition metal catalysts s. B.J. Stokes, C.V. Vogel, L.K. Urnezis, M. Pan, T.G. Driver, Org. Lett. *2010, 12* (12), 2884-7 [DOI: 10.1021/ol101040p].

Formation of O-S Bond

Addition ⇓

Addition to Sulfur OS ⇓ S

Boric acid/hydrogen peroxide H_3BO_3/H_2O_2

Flavin-functionalized β-cyclodextrin/hydrogen peroxide ←

S-Oxidation of thioethers $>S \rightarrow >SO$ or $>SO_2$

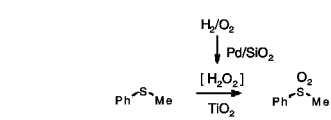
sulfoxides s. *5*, 101s*76*; sulfoxides or sulfones with boric acid/H_2O_2 without solvent s. A. Rostami, J. Akradi, Tetrahedron Lett. *2010, 51* (27), 3501-3 [DOI: 10.1016/j.tetlet.2010.04.103]; with aq. NaOCl and an imide as catalyst s. N. Fukuda, T. Ikemoto, J. Org. Chem. *2010, 75* (13), 4629-31 [DOI: 10.1021/jo100719w]; with solid-supported aq. NaOCl under microwaves, also oxidation of selenides and tellurides (cf. *41*, 102), s. J.M. Khurana, B. Nand, Can. J. Chem. *2010, 88* (9), 906-9 [DOI: 10.1139/V10-060]; multi-phase procedure with Keggin-type heteropolyacids/H_2O_2 at room temp., also oxidation of alcohols (cf. *47*, 192s*73*), s. P. Tundo, G.P. Romanelli, P.G. Vazquez, F. Aricò, Catal. Commun. *2010, 11* (15), 1181-4 [DOI: 10.1016/j.catcom.2010.06.015];

sulfoxides with the polyoxometalate, $H_5PV_2Mo_{12}O_{40}$, as catalyst s. A.M. Khenkin, G. Leitus, R. Neumann, J. Am. Chem. Soc. *2010, 132* (33), 11446-8 [DOI: 10.1021/ja105183w]; sulfoxides with NaOCl in PEG with H_2SO_4 as catalyst s. A. Amoozadeh, F. Nemati, Phosphorus, Sulfur Silicon Relat. Elem. *2010, 185* (7), 1381-5 [DOI: 10.1080/10426500903055204]; with benzyltriphenylphosphonium tribromide in aq. methanol, selectivity, s. F. Shirini, G.H. Imanzadeh, A.R. Mousazadeh, A.R. Aliakbar, ibid. *2010, 185* (8), 1640-4 [DOI: 10.1090/10426500903176539]; with 1,2-bis(pyridinio)ethane bis(tribromide) s. A. Ghorbana-Choghamarani, M.A. Zolfigol, T. Azadbakht, ibid. *185* (3), 573-7 [DOI: 10.1080/10426500902849565]; with poly(N-vinyl-2-pyrrolidone)-based hydroperoxide, also carboxylic acids from aldehydes (cf. *22*, 116), s. M.M. Lakouraj, B. Aghajani, M. Mokhtary, ibid. *185* (12), 2393-401 [DOI: 10.1080/10426501003671437]; with β-cyclodextrin-flavin conjugates/H_2O_2 in aq. media s. V. Mojr, V. Herzig, M. Budesinsky, R. Cibulka, T. Kraus, Chem. Commun. *2010, 46* (40), 7599-601 [DOI: 10.1039/c0cc02562c].

Titanium dioxide nanoparticles/palladium nanoparticles-on-silica/hydrogen/oxygen ←
Sulfones from thioethers $\geq S \rightarrow \geq SO_2$

Dual nanoparticle-catalyzed oxidation with *in situ*-generated hydrogen peroxide in supercritical carbon dioxide/water as 2-phase medium

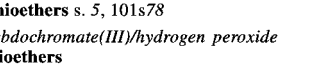
39.



A stainless-steel high-pressure reactor charged with thioanisole (0.5 mmol), distilled water (1 ml), Pd/SiO_2 (100 mg; 0.078 mmol Pd; average particle size: ca. 12 nm) and TiO_2 nanoparticles (2.5 mmol; average particle size 21 nm), the reactor pressurized with CO_2 (0.5 MPa), O_2 (0.5 MPa) and H_2 (0.5 MPa), the overall pressure adjusted with CO_2 to 13 MPa, the mixture stirred for 24 h, the reactor cooled using an ice bath and depressurized slowly, and the supercritical phase worked up → methyl phenyl sulfone. Y 96% (conversion 99%). The procedure is efficient, selective (no sulfoxide isolated), safe (outside the explosive regime for H_2/O_2 mixtures), eco-friendly (no organic solvents!) and benefits from reversible acidification of the aq. phase with CO_2. It also illustrates the concept of *compartmentalizing* catalytic processes in consecutive reactions by using two different nanoparticulate catalysts in a 2-phase medium: in this instance, the supported palladium catalyzes *in situ*-generation of H_2O_2 in the aq. phase with supercritical carbon dioxide as the second phase in which oxidation of the thioether takes place in the presence of TiO_2 nanoparticles at the interface. Each catalyst was essential for reaction and the slightly acidic medium (due largely to the presence of trifluoroacetic acid used in the preparation of the palladium nanoparticles) was an added bonus for the conversion. Water was also essential, the selectivity being significantly lower in its absence. Pd/C and Pd nanoparticles generated *in situ* from $Pd_2(dba)_3$ were less active. F. details and optimization s. S.K. Karmee, L. Greiner, A. Kraynov, T.E. Müller, B. Niemeijera, W. Leitner, Chem. Commun. *2010, 46* (36), 6705-7 [DOI: 10.1039/c0cc01443e].

Hydrogen peroxide s. under H_3BO_3, Flavin-functionalized β-cyclodextrin and $Na_3[CrMo_6O_{24}H_6]$ H_2O_2
Poly(N-vinyl-2-pyrrolidone)-based hydroperoxide ←
Heteropolyacids/hydrogen peroxide ←
S-Oxidation of thioethers s. *5*, 101s*78* $\geq S \rightarrow \geq SO$ or $\geq SO_2$
Sodium hexamolybdochromate(III)/hydrogen peroxide $Na_3[CrMo_6O_{24}H_6]/H_2O_2$
Sulfones from thioethers $\geq S \rightarrow \geq SO_2$

40.



The Anderson-type polyoxometalate, sodium hexamolybdochromate(III), is highly effective for the *direct and clean* conversion of a range of thioethers to the corresponding sulfones, contrasting with the established oxidation with ammonium molybdate and MoO_3 which yields sulfoxides.

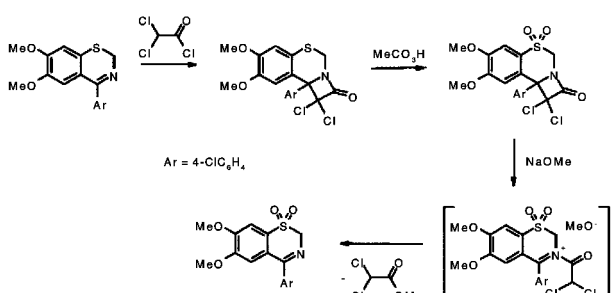
E: Thioanisole (1 mmol) and 30% H_2O_2 (2 mmol) dissolved in 60% acetonitrile (v/v; 10 ml), Na-hexamolybdochromate(III) (2 mol%) added, stirred at 60° for 10 min (TLC monitoring), and worked up with purification by chromatography on silica gel → methyl phenyl sulfone. Y 94%. The procedure is mild, rapid, eco-friendly, efficient and generally applicable [with a simple work-up] to the selective formation of dialkyl, alkyl aryl and diaryl sulfones (twelve examples; Y 74-95%). Dialkyl sulfides reacted more rapidly than aromatic sulfides, and oxidation of the latter was more facile with substrates possessing electron-donating groups on the aromatic ring. Reaction is believed to involve initial oxidation of chromium(III) to oxochromium(V) species which are the effective oxidants in the catalytic cycle. F.e., solvent effect, and simple preparation of the catalyst s. A.R. Supale, G.S. Gokavi, Phosphorus, Sulfur Silicon Relat. Elem. *2010*, *185* (4), 725-31 [DOI: 10.1080/10426500902922958].

Sodium hypochlorite/polyethylene glycol/sulfuric acid or Sodium hypochlorite/imides ←
1,2-Bis(pyridinio)ethane bis(tribromide) or Benzyltriphenylphosphonium tribromide ←
S-Oxidation of thioethers s. *5*, 101s*78* $\geq S \rightarrow \geq SO$ or $\geq SO_2$

Palladium nanoparticles-on-silica s. under TiO_2 *Pd-SiO_2*

Via intermediates *v.i.*
4-Aryl-2*H*-1,3-benzothiazine 1,1-dioxides $\geq S \rightarrow \geq SO_2$
from 4-aryl-2*H*-1,3-benzothiazines via S,S-dioxidation
of 9b-aryl-1,1-dichloro-1,9b-dihydroazeto[2,1-*c*][1,3]benzothiazin-2-ones

41.



Dichloroacetyl chloride (1.5 eq.) added to a soln. of 4-(4-chlorophenyl)-6,7-dimethoxy-2*H*-1,3-benzothiazine (2 mmol) in anhydrous toluene (10 ml), the soln. heated under reflux for 1 h during addition of triethylamine (1.5 eq.), cooled, filtered and triturated with ethanol, the initially-formed β-lactam (Y 95%) dissolved in acetic acid (10 ml/g), peroxyacetic acid (15 ml/g) added, the soln. allowed to stand at room temp. for 24 h, poured onto ice, filtered, the S,S-dioxide (Y 94%) dissolved in dry methanol (60 ml/mmol), Na-methoxide (2 eq.) added, the mixture refluxed for 15 min, solvent removed *in vacuo*, the residue dissolved in methylene chloride, washed with water, and concentrated → 4-(4-chlorophenyl)-6,7-dimethoxy-2*H*-1,3-benzothiazine 1,1-dioxide (Y 93%). The dioxides were not available by direct S-oxidation of the bicyclic due to facile ring contraction to 1,2-benzisothiazole derivs. (s. *43*, 241), but conversion to the fused β-lactam via Staudinger reaction allowed clean and efficient conversion to the dioxide under mild conditions, with retro-Staudinger reaction releasing the final product. Yields for this novel method (three examples) were in the range 92-98% for each step. F.e.s. L. Fodor, P. Csomós, A. Csámpai, P. Sohár, Tetrahedron Lett. *2010*, *51* (24), 3205-7 [DOI: 10.1016/j.tetlet.2010.04.051].

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Formation of O-Rem Bond

Addition ⇓

Addition to Remaining Elements ORem ⇓ Rem

Solid-supported sodium hypochlorite/microwaves ←
Se- and Te-Oxidation s. *41*, 102s*78* ←

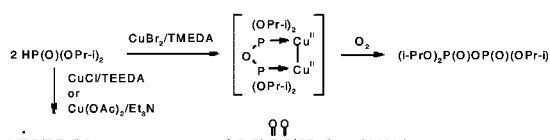
Iodine I_2
Nucleoside, nucleotide and oligonucleotide synthesis ←
oligonucleotide synthesis s. *17*, 169; synthesis of oligodeoxynucleotides using fully protected deoxynucleoside 3′-phosphoramidite building blocks, suppression of cyanoethylation side-reactions, s. H. Tsunoda, T. Kudo, A. Ohkubo, K. Seio, M. Sekine, Molecules *2010*, *15* (11), 7509-31 [DOI: 10.3390/molecules15117509]; synthesis of oligodeoxynucleotides acylated by the chemically stable 2-(trimethylsilyl)benzoyl (TMSBz) group at the 5′ or 3′ terminus s. K. Yamada, H. Taguchi, A. Ohkubo, K. Seio, M. Sekine, Tetrahedron Lett. *2010*, *51* (39), 5173-6 [DOI: 10.1016/j.tetlet.2010.07.121]; solid-phase synthesis of nucleoside 5′-*O*-β,γ-methylene-triphosphate derivs. s. Y. Ahmadibeni, C. Dash, S.F.J. Le Grice, K. Parang, ibid. *51* (22), 3010-3 [DOI: 10.1016/j.tetlet.2010.04.005]; chemical primer extension at submillimolar concentration of deoxynucleotides s. M. Röthlingshöfer, C. Richert, J. Org. Chem. *2010*, *75* (12), 3945-52 [DOI: 10.1021/jo1002467]; safe and practical procedure for global deprotection of oligoribonucleotides s. *30*, 5s*78*; deprotection of amidine-type protecting groups for nucleobases under acidic conditions during oligonucleotide synthesis s. *5*, 32s*78*.

Exchange ↓↑

Hydrogen ↑ ORem ↓↑ H

Copper(II) bromide/N,N,N′,N′-tetramethylethylenediamine *$CuBr_2$/TMEDA*
Chemoselective aerobic dehydrogenative coupling of dialkyl phosphites (H-phosphonates) ←

42.



A novel copper-catalyzed aerobic dehydrogenative coupling of dialkyl phosphites affords sym. diphosphoric acid esters or elusive tetraalkoxydiphosphine P,P-dioxides (hypophosphates) by only a minor alteration in the reaction conditions. **E: Sym. diphosphoric acid esters**. *TMEDA* (0.1 mmol) added to a suspension of *$CuBr_2$* (0.01 mmol) in acetone (1 ml), the mixture stirred at room temp. for 5 min, the startg. dialkyl phosphite (1 mmol) added, stirring continued under dry air for 6 h, chilled satd. aq. NH_4Cl added, extracted with chloroform, dried, and concentrated under vacuum → tetraisopropyl diphosphate. Y 99%. The same product was formed with $CuBr_2$ (2 mol%) and TMEDA (15 mol%) in tetrahydrofuran (seven examples in all; Y 90-99%). However, with *CuCl* (10 mol%) and the more bulky N,N,N′,N′-tetraethylethylenediamine (*TEEDA*) in acetone [or with $Cu(OAc)_2$ (2 mol%) and triethylamine (0.2 ml) in the absence of solvent] the corresponding **sym. tetraalkoxydiphosphine P,P-dioxides** were formed instead (seven examples; Y 80-93%). It

is thought that P-P bond formation takes place via an electron-transfer (ET) process of the dialkyl phosphite to copper(II), followed by coupling of the resulting phosphoryl radicals; the diphosphate, however, is formed via a tetranuclear dicopper phosphorous anhydride complex. F.e. and solvent effect s. Y. Zhou, S. Yin, Y. Gao, Y. Zhao, M. Goto, L.-B. Han, Angew. Chem., Int. Ed. *2010*, *49* (38), 6852-5 [DOI: 10.1002/anie.201003484].

Nitrogen ↑ — ORem ↓↑ N

N,N′-Diiodo-N,N′-1,2-ethanediylbis(p-toluenesulfonamide)/microwaves ←
12-Tungstophosphoric acid-doped mesoporous silica $H_3PW_{12}O_{40}$*-SBA 15*
Poly(4-vinylpyridinium tribromide)/microwaves ←

Catalytic O-trimethylsilylation with hexamethyldisilazane OH → OSi≤

s. *60*, 55s*76*; heterogeneous procedure for the O-trimethylsilylation of alcohols or phenols with poly(4-vinylpyridinium tribromide) s. A. Ghorbani-Choghamarani, M.A. Zolfigol, M. Hajjami, K. Darvishi, L. Gholamnia, Collect. Czech. Chem. Commun. *2010*, *75* (5), 607-15 [DOI: 10.1135/cccc2009560]; O-trimethylsilylation and N-carbo-*tert*-butoxylation [using $(Boc)_2O$] with 12-tungstophosphoric acid-doped mesoporous silica (SBA15) s. B. Karmakar, J. Banerji, Tetrahedron Lett. *2010*, *51* (29), 3855-8 [DOI: 10.1016/j.tetlet.2010.05.080]; O-trimethylsilylation of alcohols and phenols with *N,N′*-diiodo-*N,N′*-1,2-ethanediylbis(*p*-toluenesulfonamide) under solvent-free and microwave conditions s. R. Ghorbani-Vaghei, S.M. Malaekehpoor, Phosphorus, Sulfur Silicon Relat. Elem. *2010*, *185* (3), 582-7 [DOI: 10.1080/10426500902849581]; of alcohols or phenols with sulfamic acid in acetonitrile or in the absence of solvent, also reverse reaction with the same catalyst in water (cf. *29*, 415), s. A. Rostami, F. Ahmad-Jangi, M.R. Zarebin, J. Akradi, Synth. Commun. *2010*, *40* (10), 1500-7 [DOI: 10.1080/00397910903097344].

Halogen ↑ — ORem ↓↑ Hal

Via intermediates *v.i.*

Protection of hydroxyl groups OH → OSi≤

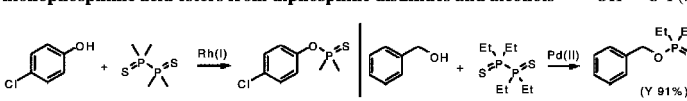
as polymer-based diisopropyl(1,2,3-triazol-4-yl)silyl ethers via 'click' reaction s. *78*, 2

Remaining Elements ↑ — ORem ↓↑ Rem

Hydridotetrakis(triphenylphosphine)rhodium(I)/1,2-bis(dimethylphosphino)ethane ←
Palladium(II) acetate/o-bis(diphenylphosphino)benzene ←

Thionophosphinic acid esters from diphosphine disulfides and alcohols OH → O-P(S)R_2

43.



Rhodium(I)-catalyzed reaction with phenols. Dry THF (2 ml) and dmpe (2 mol%) added to a mixture of $RhH(PPh_3)_4$ (1 mol%), tetramethyldiphosphine disulfide (1 eq.) and 4-chlorophenol (1 mmol) under argon, the soln. refluxed for 3 h, solvent removed *in vacuo*, and the residue purified by flash chromatography on silica → O-(4-chlorophenyl) dimethylphosphinothioate. Y 98%. Base-free phosphinothioation of electron-diverse phenols with tetraalkyldiphosphine disulfides and tetraphenyldiphosphine dioxide was successful under rhodium catalysis (twelve examples; Y 94-100%), whereas prim. and sec. aliphatic alcohols required higher temp. (80°) and the use of $Pd(OAc)_2$ and *o*-bis(diphenylphosphino)benzene as catalyst (eleven examples; Y 71-99%) but reactions were slow with hindered 2- (Y 23%) and 1-adamantanol (Y 7%). Reaction of 1,2-propanediol with 1 eq. of reagent occurred selectively at the prim. hydroxyl group (Y 79%; plus 6% of the bis-phosphinothioate), while protected serine and tyrosine derivs. reacted with minimum racemization. F.e.s. M. Arisawa, M. Yamaguchi, Tetrahedron Lett. *2010*, *51* (37), 4840-2 [DOI: 10.1016/j.tetlet.2010.07.040].

Formation of O-C Bond

Uptake ⇓

Addition to Hydrogen and Carbon OC ⇓ HC

3,3-Dimethylbut-1-ene/chlorobis(cyclopentadienyl)-hydridozirconium(IV)/tert-butyl hydroperoxide $CH_2{=}CHBu\text{-}t/Cp_2Zr(H)Cl/t\text{-}BuOOH$
s. under $IrH_3(PPr\text{-}i_3)_2$

Poly(N-vinyl-2-pyrrolidone)-based hydroperoxide ←
Carboxylic acids from aldehydes s. *22*, 116s*78* CHO → COOH

Potassium permanganate $KMnO_4$
Rapid oxidations with potassium permanganate under continuous flow ←
Carboxylic acids from aldehydes s. *78*, 92

Pentahydridobis(triisopropylphosphine)iridium/3,3-dimethylbut-1-ene/chlorobis(cyclopentadienyl)hydridozirconium(IV)/tert-butyl hydroperoxide ←
Regioselective functionalization of alkanes via terminal ethylene derivs. H → OH
Alcohols s. *78*, 224

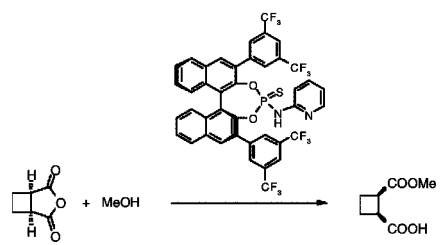
Via intermediates *v.i.*
Ar. hydroxylation via silylation s. *78*, 102 ArH → ArSi⩽ → ArOH

Addition to Oxygen and Carbon OC ⇓ OC

Zinc salphens or Polymer-based α-aminocarboxylic acids or Lewis basic ionic liquids ←
1,3-Dioxolan-2-ones from epoxides by fixation of carbon dioxide ○
s. *23*, 139s*76*; with an inexpensive, robust and eco-friendly zinc salphen s. A. Decortes, M. Martínez Belmonte, J. Benet-Buchholz, A.W. Kleij, Chem. Commun. *2010, 46* (25), 4580-2 [DOI: 10.1039/c000493f]; fixation of CO_2 with epoxides or aziridines (cf. *32*, 278s*70*) using polymer-based α-aminocarboxylic acids s. C. Qi, J. Ye, W. Zeng, H. Jiang, Adv. Synth. Catal. *2010, 352* (11-12), 1925-33 [DOI: 10.1002/adsc.201000261]; with Lewis basic ionic liquids, e.g. bicyclic amidine and guanidine hydrohalides, as catalyst s. Z.-Z. Yang, L.-N. He, C.-X. Miao, S. Chanfreau, ibid. *352* (13), 2233-40 [DOI: 10.1002/adsc.201000239].

Chiral 2-amino(thio)ureas ←
Chiral 3,3′-diaryl-1,1′-binaphthyl-2,2′-diyl N-(2-pyridyl)thionophosphoromonoamidates ←
Succinic acid monoesters from *meso*-succinic acid anhydrides ⊂
Desymmetrization using a bifunctional organo-Brønsted acid/base

44.



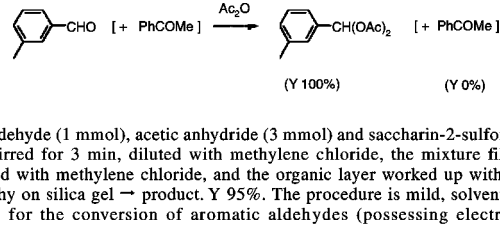
Fully synthetic chiral 3,3′-diaryl-1,1′-binaphthyl-2,2′-diyl N-(2-pyridyl)thionophosphoromonoamidates, possessing both Lewis acidic and Lewis basic sites, offer more scope for diversification

than cinchona-based equivalents (cf. *41*, 118s*67*) for the alcoholytic desymmetrization of *meso*-anhydrides, and generally induce equivalent or higher enantioselectivity. **E:** Methanol (5 mmol) added dropwise to a stirred soln. of the startg. anhydride (0.5 mmol) and chiral 3,3′-diaryl-1,1′-binaphthyl-2,2′-diyl N-(2-pyridyl)thionophosphoromonoamidate (10 mol%) in toluene (0.4 *M*) at -35° under argon, the solvent evaporated under vacuum after 1.5 h, the residue taken up in methylene chloride, the soln. washed with satd. Na_2CO_3, the combined aq. layers acidified with excess 2 *N* HCl, and worked up → cyclobutane-1,2-dicarboxylic acid monomethyl ester. Y 97% (e.r. 99:1). The catalytic activity of a wide range of chiral BINOL-derived bifunctional N-pyridyl- and N-pyrimidyl-phosphoromonoamidates and -thionophosphoromonoamidates was compared, the latter showing superior enantioselectivity with the electronic characteristics of the amine component (4-dimethylamino-2-pyridyl > 4-trifluoromethyl-2-pyridyl) having a significant effect. Enantioselectivity was high for mono-, bi- and tri-cyclic anhydrides (Y 81-97%; e.r. 91:9 to 99:1) with a range of alcohols (methanol, ethanol, propanol, isopropanol, propargyl alcohol), and in one instance (with *meso*-cyclobutane-1,2-dicarboxylic acid anhydride) the enantioselectivity was even higher than that recorded with cinchona-based catalysts. Furthermore, the face-selectivity was *reversed* with the same enantioselectivity by using the (R)-catalyst, and there was no significant variation on changing the concentration (from 0.1 to 1 *M*). F.e. and application to the synthesis of (+)-grandisol s. V.N. Wakchaure, B. List, Angew. Chem., Int. Ed. *2010*, *49* (24), 4136-9 [DOI: 10.1002/anie.201000637]; of *meso*-glutaric anhydrides with cinchona-based sulfonamide catalysts s. S.E. Park, E.H. Nam, H.B. Jang, J.S. Oh, S. Some, Y.S. Lee, C.E. Song, Adv. Synth. Catal. *2010*, *352* (13), 2211-7 [DOI: 10.1002/adsc.201000289]; of mono-, bi- or tri-cyclic anhydrides with chiral 2-amino(thio)ureas derived from D- or L-valine s. R. Manzano, J.M. Andrés, M.-D. Muruzábal, R. Pedrosa, J. Org. Chem. *2010*, *75* (15), 5417-20 [DOI: 10.1021/jo100792r].

Saccharin-2-sulfonic acid *SaSA*

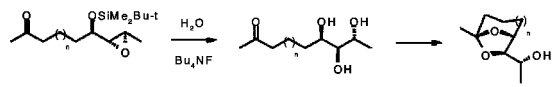
Acylals from aldehydes under mild conditions in the absence of solvent $CHO \rightarrow CH(OAc)_2$

45.

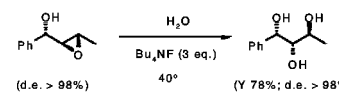


o-Nitrobenzaldehyde (1 mmol), acetic anhydride (3 mmol) and saccharin-2-sulfonic acid [SaSA] (0.2 mmol) stirred for 3 min, diluted with methylene chloride, the mixture filtered, the solid residue washed with methylene chloride, and the organic layer worked up with purification by chromatography on silica gel → product. Y 95%. The procedure is mild, solvent-free, rapid and high-yielding for the conversion of aromatic aldehydes (possessing electron-donating or -withdrawing groups) as well as aliphatic aldehydes (seventeen examples in all; Y 85-95%). This contrasts with many established procedures which require strong acids and/or harsh conditions and in certain cases expensive and highly toxic reagents. There was no reaction with ketones, exemplified by the **selective conversion** of 3-methylbenzaldehyde in the presence of acetophenone. **Cleavage of acylals** was also effected in good to high yield with the same reagent in the presence of wet silica at 90°. F.e.s. F. Shirini, M. Mamaghani, T. Mostashari-Rad, M. Abedini, Bull. Korean Chem. Soc. *2010*, *31* (8), 2399-401 [DOI: 10.5012/bkcs.2010.31.8.2399]; saccharin-2-sulfonic acid as efficient and recyclable catalyst for **acetylation** of alcohols, phenols and amines with Ac_2O s. F. Shirini, M.A. Zolfigol, M. Abedini, Monatsh. Chem. *2009*, *140* (12), 1495-8 [DOI: 10.1007/s00706-009-0214-7]; acylal formation in the absence of solvent with the catalyst prepared by H_2SO_4-catalyzed copolymerization of *p*-toluenesulfonic acid and paraformaldehyde s. D.-H. Fan, H. Wang, X.-X. Mao, Y.-M. Shen, Molecules *2010*, *15* (9), 6493-501 [DOI: 10.3390/molecules15096493].

Tetra-n-butylammonium fluoride *Bu_4NF*
1,2,3-Triols from 3-siloxyepoxides or 2,3-epoxyalcohols ▽/O → C(OH)C(OH)
Fluoride-mediated regioselective hydrolytic ring opening with inversion of configuration



46.

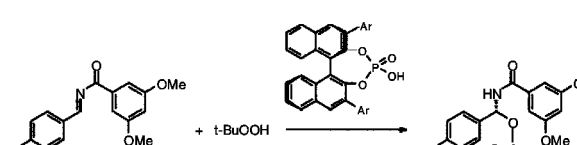


under mild conditions. $Bu_4NF{\cdot}3H_2O$ (3 eq.) added to a soln. of startg. siloxyepoxide (0.35 mmol) in acetonitrile (2 ml) in a screw cap vial, the mixture stirred at room temp. for 12 h, concentrated *in vacuo*, water (20 µl) and *acetonitrile* (80 µl) added, the mixture stirred at 35-40° until reaction complete (TLC; 24 h), concentrated *in vacuo*, diluted with minimal methylene chloride, filtered through silica, and purified by flash chromatography on silica → (8R,9R,10R)-8,9,10-trihydroxy-undecan-2-one. Y 82%. This experimentally simple method affords a general synthesis of *lyxo*- and *arabino*-configured consecutive triols from readily available epoxyalcohols or O-silyl derivs. via *unexpected α-hydrolysis* with high stereoretention (five examples; Y 76-85%). The keto moiety was not essential (for anchimeric assistance) and was replaced with alkyl, alkene and phenyl functionality. Analogous nonan- and decan-2-one-derived substrates underwent further reaction to afford bicyclic acetals (three examples; Y 73-87%) allowing rapid and unambiguous assignment of stereochemistry (by NMR). Other tetrabutylammonium salts gave reduced yields and/or selectivity as did the use of alternative solvents or increased amounts of water. F.e. and optimization s. P. Mukerjee, M. Abid, F.C. Schroeder, Org. Lett. *2010*, *12* (18), 3986-9 [DOI: 10.1021/ol1015306].

Addition to Nitrogen and Carbon OC ⇓ NC

(R)-3,3′-Di-9-anthracenyl-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate ←
1,1-(Acylamino)peroxides from N-acylimines C=NAc → C(OOR)NHAc
under asym. organo-Brønsted acid catalysis

47.



Startg. imine (0.1 mmol) and (R)-3,3′-di-9-anthracenyl-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate (5 mol%) placed in a flame-dried reaction tube, dry isopropyl acetate (0.6 ml) added, stirred for 5 min, the startg. hydroperoxide (0.2 mmol) added, stirring continued for an additional 24 h at room temp., and the mixture directly subjected to column chromatography on silica gel → product. Y 88% (e.e. 95%). This is the first example of an asym. addition of a hydroperoxide to an imine, reaction being high-yielding (75-97%; eighteen examples) and highly enantioselective (e.e. 84-98%). The procedure is applicable to a wide range of aromatic N-acylimines, incl. substrates with F, Cl or Br at the *p*-position and electron-donating groups at the *o*- or *p*-position. The N-benzoyl group may be substituted by methyl, methoxy (preferably at the *m*-position) or dimethoxy (at the

3- and 5-positions). The bifunctional nature of the catalyst is responsible for the concurrent activation of both the nucleophile and electrophile through hydrogen bonding (involving the P=O and P-OH groups, respectively), which holds the substrates in close vicinity to the chiral binaphthyl system for face-selectivity. F.e.s. W. Zheng, L. Wojtas, J.C. Antilla, Angew. Chem., Int. Ed. *2010*, *49* (37), 6589-91 [DOI: 10.1002/anie.201002972].

Addition to Carbon-Carbon Bonds OC ⇓ CC

Ammonium hydroxide s. under Ni(cod)$_2$ *NH_4OH*

Triethylamine *Et_3N*

γ-Acoxy-β-ketonitriles from α,β-acetylene-γ-hydroxynitriles and carboxylic acids ←
s. *78*, 381

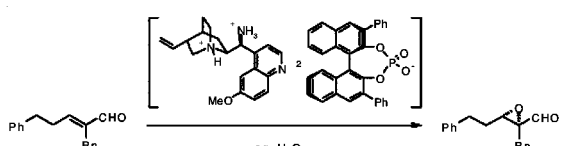
2(S)-[p-Methoxyphenyl(2-naphthyl)(hydroxy)methyl]pyrrolidine s. under t-BuOOH ←

(S)-2-[Fluoro(diphenyl)methyl]pyrrolidine/hydrogen peroxide ←

9-Amino-9-deoxy-epi-quinine/(R)-3,3′-diphenyl-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate/hydrogen peroxide ←

Asym. epoxidation of α-subst. α,β-ethylenealdehydes under synergistic cooperative catalysis with a chiral prim. amine and a chiral organo-Brønsted acid C=C → ▽o

48.



(R)-3,3′-Diphenyl-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate (0.2 eq.) and 9-amino-9-deoxy-*epi*-quinine (0.1 eq.) in dry THF (2 ml) stirred for 5 min under an ambient atmosphere at room temp., the startg. α-subst. enal (25 mmol; 1 eq.) added, stirred for an additional 5 min at room temp., aq. H_2O_2 (50% w/w; 5 eq.) added, the reaction vessel sealed, stirred for 24 h at 50° under air, excess peroxide quenched by stirring with 10% aq. $Na_2S_2O_3$ (1 ml) for 10 min, and worked up with purification by flash column chromatography → product. Y 77% (d.r. 9:1; e.r. 99:1). High epoxide yields were generally secured from *α,β-disubst.* (E)-acroleins (seven examples; Y 43%, 64-94%) with high stereoselectivity (d.r. 76:24 to 95:5; e.r. 85:15 to 99:1), whereas the yield and enantioselectivity were poor with an aliphatic α-unsubst. enal and there was no reaction with a tetrasubst. enal (2-methylcyclohex-1-enecarboxaldehyde). With challenging *α-subst. acroleins*, however, (R)-3,3′-bis(2,4,6-triisopropylphenyl)-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate was the Brønsted acid of choice (four examples; Y 53-78%; e.r. 96:4 to 99:1). The two catalysts provide excellent enantiocontrol *synergistically*, the prim. amine activating the enal by formation of an iminium ion, which undergoes enantioselective 1,4-addition with the peroxide prior to ring closure; importantly, the chiral Brønsted acid fulfils a dual role: as a chiral counterion enhancing enantiodiscrimination in the 1,4-addition, and as an acid catalyst for the ring closure. The reaction rate and selectivity were compromised with α,β-disubst. (Z)-acroleins. F.e. and comparison of catalysts s. O. Lifchits, C.M. Reisinger, B. List, J. Am. Chem. Soc. *2010*, *132* (30), 10227-9 [DOI: 10.1021/ja1037935]; asym. epoxidation of α,β-ethylenealdehydes using (S)-2-[fluoro(diphenyl)-methyl]pyrrolidine as organocatalyst (and H_2O_2) s. C. Sparr, E.-M. Tanzer, J. Bachmann, R. Gilmour, Synthesis *2010* (8), 1394-7 [DOI: 10.1055/s-0029-1218636].

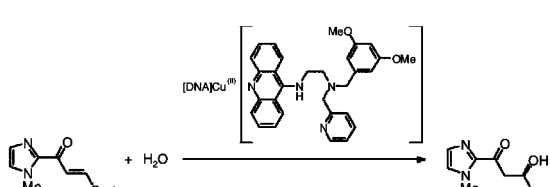
5-Bromo-3-carbomethoxypyridine N-oxide s. under [o-Biphenyl(dicyclohexyl)-phosphine]gold(I) triflimide ←

8-Alkylquinoline N-oxides s. under [1,3-Bis(2,6-diisopropylphenyl)imidazol-2-ylidene]-gold(I) triflimide ←

Supported transition metal catalysts/tert-butyl hydroperoxide or hydrogen peroxide ←
Heterogeneous epoxidation with supported transition metal catalysts C=C → ▽o
s. *28*, 113s*72*; with recyclable copper(II)-coordinated nanotubes and H_2O_2 or *t*-BuOOH as oxidant for epoxidation of alkenes and oxidation of hydrocarbons, alcohols and phenols s. T. Chattopadhyay, M. Kogiso, M. Asakawa, T. Shimizu, M. Aoyagi, Catal. Commun. *2010*, *12* (1), 9-13 [DOI: 10.1016/j.catcom.2010.07.013]; with an *n*-octyl-stabilized colloidal soln. of gold nanoparticles for the aerobic epoxidation of *trans*-stilbene s. M. Boualleg, K. Guillois, B. Istria, L. Burel, L. Veyre, J.-M. Basset, C. Thieuleux, V. Caps, Chem. Commun. *2010*, *46* (29), 5361-3 [DOI: 10.1039/c0cc00664e]; with polydimethylsiloxane membrane-immobilized tripodal titanium silsesquioxane complexes/aq. H_2O_2 s. E.H. Aish, M. Crocker, F.T. Ladipo, J. Catal. *2010*, *273* (1), 66-72 [DOI: 10.1016/j.jcat.2010.05.003]; with robust, reusable $Mo(CO)_6$ supported on amine-modified carbon nanotubes/*t*-BuOOH s. M. Moghadam, S. Tangestaninejad, V. Mirkhani, I. Mohammadpoor-Baltork, N.S. Mirbagheri, Appl. Organomet. Chem. *2010*, *24* (10), 708-13 [DOI: 10.1002/aoc.1671]; with mesoporous silica-supported arene(tricarbonyl)molybdenum complexes/*t*-BuOOH s. A.C. Coelho, S.S. Balula, S.M. Bruno, J.C. Alonso, N. Bion, P. Ferreira, M. Pillinger, A.A. Valente, J. Rocha, I.S. Gonçalves, Adv. Synth. Catal. *2010*, *352* (10), 1759-69 [DOI: 10.1002/adsc.201000042]; with robust and reusable dimeric Mn-salen complexes entrapped within the nanocages of a 3-dimensional periodic mesoporous organosilica support s. J. Hu, Q. Wu, K. Li, W. Li, F. Ma, S. Zhang, F. Su, Y. Guo, Y. Wang, Catal. Commun. *2010*, *12* (3), 238-42 [DOI: 10.1016/j.catcom.2010.09.001].

Copper(II) nitrate/N-acridin-9-yl-N′-(3,5-dimethoxybenzyl)-N′-2-pyridylmethyl-1,2-ethylenediamine/DNA *Cu(II)L/DNA*
β-Hydroxy- from α,β-ethylene-ketones by catalytic asym. Michael addition of water C=C → C(OH)CH

49.

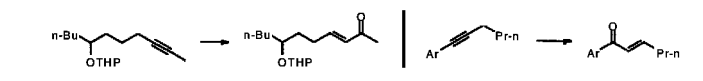


The first example is reported of a non-enzymatic, homogeneous asym. Michael addition of water, the sole source of chirality being DNA. **E:** An aq. soln. (15 ml) of copper(II)-N-acridin-9-yl-N′-(3,5-dimethoxybenzyl)-N′-2-pyridylmethyl-1,2-ethylenediamine complex (0.3 m*M*) and salmon testes DNA (st-DNA; 1.3 mg/ml) in 2-(N-morpholino)ethanesulfonic acid (MES) buffer (20 m*M*; pH 5.5) [prepared by mixing a st-DNA stock soln. (10 ml; 2 mg/ml st-DNA in MES buffer (30 m*M*), pH 5.5, prepared 24 h in advance) with a filtered soln. (5 ml) of $Cu(NO_3)_2$ (0.3 m*M*) and the diamine ligand (0.39 m*M*) in water], treated with the startg. α,β-ethylenecarbonyl compd. (1 m*M*) in acetonitrile (30 ml), mixed by continuous inversion at 5° for 24 h, extracted with ether, and worked up with purification by chromatography on silica gel → (R)-product. Conversion 55% (e.e. 72%). The procedure benefits from the synergistic action of copper(II), the achiral ligand and DNA, reaction taking place under kinetic control via *re*-face addition of water within the asymmetric environment created by complexation of copper to both carbonyl oxygen and the DNA helix. By studying the asym. Michael addition of D_2O, it was demonstrated that ***syn*-hydration** takes place exclusively, the highest enantioselectivity being recorded at 82% with two particular samples of st-DNA. Enantioselectivity, however, is markedly dependent on the size of the alkyl group at the β-position (being highest with *tert*-butyl), but there was no reaction with β-phenyl derivs. F.e. and comparison of achiral ligands, also scale-up to the 17 mg level, s. A.J. Boersma, D. Coquière, D. Geerdink, F. Rosati, B.L. Feringa, G. Roelfes, Nature Chem. *2010*, *2* (11), 991-5 [DOI: 10.1038/nchem.819].

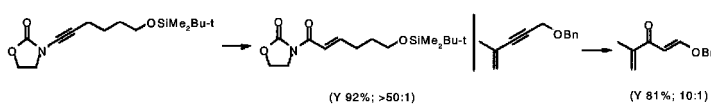
Copper(II) chloride s. under $PdCl_2$ *$CuCl_2$*

[1,3-Bis(2,6-diisopropylphenyl)imidazol-2-ylidene]gold(I) triflimide/8-alkylquinoline N-oxides ←

(E)-α,β-Ethylenecarbonyl compds. from [internal] acetylene derivs. $CH_2C{\equiv}C \rightarrow C{=}C\text{-}CO$
Regio- and stereo-selective gold(I)-catalyzed oxidation under mild conditions



50.



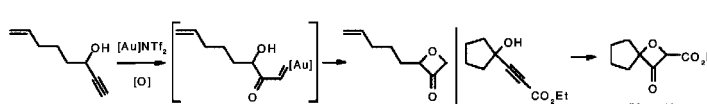
The regioselective gold(I)-catalyzed oxidation of propargyl moieties to α,β-unsatd. carbonyl compds. with 8-alkylquinoline N-oxides has been shown to proceed with high *trans*-selectivity, complementing the high *cis*-selectivity obtained from the rhodium-catalyzed decomposition of α-diazoketones (cf. *37*, 946s*51*). **E: (E)-α,β-Ethyleneketones**. $IPrAuNTf_2$ (5 mol%) added to an oven-dried reaction tube charged with 2-(1-butylhept-5-ynyloxy)tetrahydropyran (0.2 mmol), 8-isopropylquinoline N-oxide (1.2 eq.) and THF (2 ml) at -20°, the mixture stirred at that temp. until reaction complete (48 h), concentrated *in vacuo*, and purified by flash chromatography on silica gel → (E)-7-(tetrahydro-2*H*-pyran-2-yloxy)undec-3-en-2-one. Y 82% (regioselectivity 12:1). Excellent (E)-selectivities were obtained from a wide variety of internal alkynes, the mild, *acid-free* conditions tolerating sensitive functionality including THP ether, MOM ether, azide, silyl ether and N-Boc. Regioselectivity was generally very high (10:1 to >50:1), but dictated by steric effects for aliphatic alkynes (in which the O-atom is delivered to the least-hindered site) and electronic effects for ar., vinyl and heteroatom-subst. alkynes (in which the O-atom is delivered adjacent to the substituent). Enynes afforded divinyl ketones optimally using 8-*ethyl*quinoline N-oxide as oxidant, while for aryl subst. alkynes, optimal selectivity required the more Lewis acidic $[(2,4\text{-}t\text{-}Bu_2PhO)_3P]AuNTf_2$ with 2-bromopyridine N-oxide as oxidant. Surprisingly, cyclopentylalkynes afforded mainly ring-enlarged products, presumably promoted by release of ring-strain. F.e. (ca. twenty; Y 71-92%) s. B. Lu, C. Li, L. Zhang, J. Am. Chem. Soc. *2010*, *132* (40), 14070-2 [DOI: 10.1021/ja1072614].

(Tert. phosphine)gold(I) triflimides *$(R_3P)AuNTf_2$*
Furans from 1,3-diynes
2,5-Diaryl-, 2,5-dialkyl- and 2,5-bis(tosylamino)-furans s. *78*, 141

[o-Biphenyl(dicyclohexyl)phosphine]gold(I) triflimide/5-bromo-3-carbomethoxypyridine N-oxide/triflimide ←

2-Subst. oxetan-3-ones from 2-acetylenealcohols
Gold(I)-catalyzed oxidative ring closure

51.

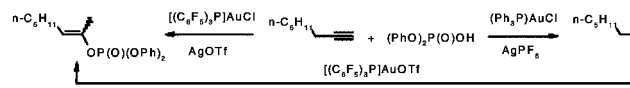


under mild conditions. 5-Bromo-3-carbomethoxypyridine N-oxide (2 eq.), a soln. of triflimide (1.2 eq.) in dichloroethane (1.8 ml), and $[(o\text{-biphenyl})Cy_2P]AuNTf_2$ (5 mol%) added sequentially to a soln. of oct-1-en-7-yn-6-ol (0.3 mmol) in the same solvent (4.2 ml) at room temp., the mixture stirred until reaction complete (TLC; 3 h), quenched with satd. aq. $NaHCO_3$, extracted with

methylene chloride, concentrated, and purified by flash chromatography on silica → 2-(pent-4-enyl)oxetan-3-one. Y 65%. The reaction is presumed to involve the formation of gold-carbene intermediates (formal equivalents of hazardous and relatively inaccessible α-diazoketones), affording 2-subst. (incl. 2-phenyl) oxetan-3-ones from readily available sec. propargylic alcohols (eight examples; Y 57-81%; parent oxetan-3-one was obtained from the prim. propargylic alcohol in 71% yield). The reaction was compatible with acetal, alkene, phenyl, azide and halo functionality, and partial decomposition of Boc-amines was minimized by reaction at lower temp. (-20°). The cyclization was extended to tert. propargylic alcohols, requiring an electron-withdrawing group (CO_2Et) on the alkyne terminus to reduce the formation of propargylic cations, affording 2-subst. 4-ethoxycarbonyl derivs. (eight examples; Y 72-92%). F.e., optimization and substrate prepn. s. L. Ye, W. He, L. Zhang, J. Am. Chem. Soc. *2010*, *132* (25), 8550-1 [DOI: 10.1021/ja1033952].

(Triphenylphosphine)gold(I) chloride/silver hexafluorophosphate $(Ar_3P)AuCl/Ag^+$
or [Tris(pentafluorophenyl)phosphine]gold(I) chloride/silver triflate
Enol phosphates from acetylene derivs. $C{\equiv}C \rightarrow CH{=}C\text{-}OPO(OR)_2$
Regioselective gold(I)-catalyzed conversion under kinetic *vs.* thermodynamic control

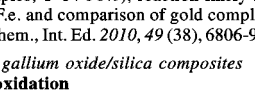
52.



The nature of the gold catalyst determines whether kinetic or thermodynamic control operates in the regioselective addition of diphenyl phosphate to acetylene derivs. **E: Kinetic isomers.** 1-Octyne (0.6 mmol) added to a suspension of *[(Ph$_3$P)Au]Cl* (5 mol%), *AgPF$_6$* (5 mol%) and diphenyl phosphate (0.5 mmol) in toluene (2 ml) at room temp., the mixture stirred (in a V Vial) *for 9 h*, the solvent removed under reduced pressure, and the crude product purified by chromatography on silica gel → oct-1-en-2-yl diphenyl phosphate. Y 88%. With *[(C$_6$F$_5$)$_3$PAu]Cl/AgOTf over 24 h* (under otherwise identical conditions) the thermodynamic isomer was formed (Y 86%; thermodynamic/kinetic isomer 35:1; E/Z 1:2.6). High yields and regioselectivities were recorded for a wide range of terminal acetylene derivs. substituted by alkyl, benzylthio or electron-diverse aryl groups, as well as for internal acetylene derivs., e.g. dialkylacetylenes or alkyl(aryl)acetylenes (both at 100°) and ethyl phenylpropiolate (twenty examples in all; Y 69-98%). The kinetic isomers were simply isomerized to the less accessible thermodynamic isomers on treatment with [(C$_6$F$_5$)$_3$PAu]OTf (eight examples; Y 84-90%), reaction likely involving intermediate formation of an oxocarbenium species. F.e. and comparison of gold complexes s. P.H. Lee, S. Kim, A. Park, B.C. Chary, S. Kim, Angew. Chem., Int. Ed. *2010*, *49* (38), 6806-9 [DOI: 10.1002/anie.201001799].

Mesoporous nanoparticulate gallium oxide/silica composites $mpGa_2O_3$-*x*
Heterogeneous catalytic epoxidation $C{=}C \rightarrow$
with mesoporous nanoparticulate gallium oxide/silica composites

53.



A new class of mesoporous materials ($mpGa_2O_3$-x), comprising gallia nanoparticles homogeneously embedded and stabilized in a silica matrix, combine the intrinsic assets of nanoparticulate material (high surface area...) and their organization in a mesoporous structure, rendering them highly active in catalytic epoxidation. **E:** A soln. containing *cis*-cyclooctene (1 mmol), di-*n*-butyl ether (0.5 mmol) and ethyl acetate (1308 μl) added to $mpGa_2O_3$-100 (20 mg), H_2O_2 (2 mmol; 50 wt% aq. soln.) added, stirred for 4 h at 80° in a capped glass vial (pierced with a sharp needle to prevent the development of an overpressure), the mixture centrifuged, and the cyclooctene conversion and yield determined by gas chromatographic analysis of the supernatant → cyclooctene oxide. Conversion 25.8%; selectivity 95.6%. Although conversions were low, the selectivity was virtually 100% for the catalytic samples tested, while yields and selectivities were clearly lower

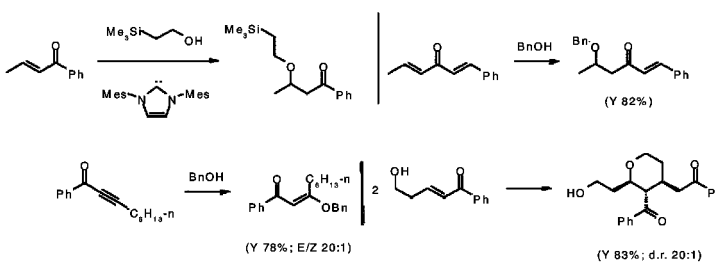
with less stable and less organized pre-Ga_2O_3 from which the composite materials were simply prepared with tetraethyl orthosilicate. This is the first report of a mesoporous material containing gallium oxide nanoparticles and the first time such ordered mesoporous material has been synthesized by high-throughput experimentation. The catalyst was reused with only a slight decrease in the yield, and the initial activity was restored for subsequent cycles by re-calcining at 300° for 3 h. F.e. and details of catalyst preparation s. C. Aprile, E. Gobechiya, J.A. Martens, P.P. Pescarmona, Chem. Commun. *2010*, *46* (41), 7712-4 [DOI: 10.1039/c0cc02729d].

Pinacolatoboron s. under Ni(cod)$_2$ *$(RO)_2BH$*

Graphene oxide *GO*
Heterogeneous metal-free carbocatalysis with readily recyclable graphene oxide ←
under mild, slightly acidic conditions – Ketones from acetylene derivs. s. *78*, 117

15-Crown-5 polyether s. under $Pt_2Cl_4(CH_2{=}CH_2)_2$ *crown*
Carbohydrate-based crown ethers s. under t-BuOOH ←

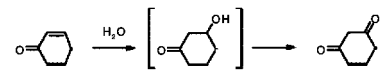
1,3-Dimesitylimidazolium chloride/n-butyllithium/lithium chloride *IMes·HCl/BuLi/LiCl*
N-Heterocyclic carbene-catalyzed Michael addition of alcohols to α,β-ethylene-ketones or -carboxylic acid esters C=C → C(OR)CH



β-Alkoxyketones. THF (0.4 ml) added to a mixture of 1,3-dimesitylimidazolium chloride (5 mol%) and LiCl (1 eq.) in a sealed vial under N_2, the mixture cooled to -78°, *n*-BuLi (5 mol%; 2.49 *M* in hexanes) added via syringe, warmed to room temp., solvent removed *in vacuo*, the vial back-filled with N_2, a mixture of (E)-1-phenylbut-2-en-1-one (0.4 mmol), 2-(trimethylsilyl)ethanol (5 eq.) and toluene (0.4 ml) added via cannula, the resulting mixture stirred at room temp. until reaction complete (ca. 20 h), diluted with ethyl acetate, filtered through a small silica pad, the filtrate concentrated, and the residue purified by flash chromatography on silica gel → 1-phenyl-3-[2-(trimethylsilyl)ethoxy]butan-1-one. Y 80%. This mild procedure was suitable for the addition of a variety of prim. and sec. alcohols to unsatd. alkyl and aryl enones (fifteen examples; Y generally 70-89%, 50% for methyl vinyl ketone) and esters (single example; Y 60%), with no evidence of polymerization observed. Substrates with β-alkyl substituents were ideal, but those with β-aryl substituents were inert, leading to regioselective addition to a differentially-substituted bis-enone (illustrated). Cyclic enones (cyclohexenone and cyclopentenone) were less reactive (ca. 50% conversion) than their acyclic counterparts. Under the same conditions, an **(E)-β-alkoxy-α,β-ethyleneketone** was selectively obtained **from an α,β-acetyleneketone** (Y 78%; E/Z 20:1) and an α,β-ethylene-δ-hydroxyketone underwent tandem 1,4-addition-intramolecular Michael reaction to afford a **3-acyl-2-β-hydroxy-4-β-ketotetrahydropyran** deriv. with excellent diastereoselectivity (d.r. 20:1; Y 83%). Mechanistic observations support the free carbene acting as a Brønsted base, with enhanced yields obtained in the presence of a lithium counterion. F.e., incl. initial studies towards asym. induction, s. E.M. Phillips, M. Riedrich, K.A. Scheidt, J. Am. Chem. Soc. *2010*, *132* (38), 13179-81 [DOI: 10.1021/ja1061196].

Michael hydratase/alcohol dehydrogenase/methylene blue ←
β-Keto- from α,β-ethylene-oxo compds. CH=CH → CH_2CO
via enzymatic Michael addition of water

55.



Cell extracts of anaerobically grown *Alicycliphilus denitrificans* DSMZ 14773 serve *as a bifunctional enzyme source* combining the rare Michael hydratase activity with alcohol dehydrogenase activity, as manifest in the **one-pot conversion** of α,β-ethyleneoxo compds. to β-ketooxo compds. **E:** The cell extract (0.1 ml) of *Alicycliphilus denitrificans* DSMZ 14773 added to a quartz cuvette containing 2-cyclohexenone (1 m*M*) and methylene blue (60 m*M*) [or dichlorophenol indophenol] as H-acceptor in Tris-HCl (100 m*M*; 0.9 ml; pH 7.8) at room temp., and the course of the reaction followed spectroscopically → 1,3-cyclohexanedione. Y undisclosed. Relative rate data were obtained for six substrates, the intermediate (although detectable) eluding isolation due to its volatility and high solubility. Although not, as yet, a synthetically defined process, sufficient evidence points to the identification of a quite unusual combination of enzyme activities which might be less uncommon in nature than previously thought. F.e. and comparison of the dehydrogenase activity on preformed (3R)-cyclohexan-3-olone and its racemate s. J. Jin, P.C. Oskam, S.K. Karmee, A.J.J. Straathof, U. Hanefeld, Chem. Commun. *2010, 46* (45), 8588-90 [DOI: 10.1039/c0cc03229h].

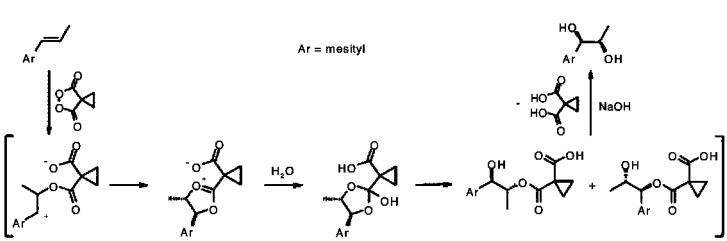
Monooxygenase ←
Anomalous enzymatic Baeyer-Villiger oxidation s. *36,* 129s*78* ←

Nitrosobenzene s. under Ni(cod)$_2$ *PhNO*
tert-Butyl hydroperoxide s.a. under [Pd(II)] *t-BuOOH*

tert-Butyl hydroperoxide/2(S)-[p-methoxyphenyl(2-naphthyl)(hydroxy)methyl]pyrrolidine or carbohydrate-based crown ethers ←
Organocatalyzed asym. epoxidation of α,β-ethyleneketones C=C → ▽
s. *70,* 63s*74*; asym. epoxidation of α-arylidene-β-diketones with 2(S)-[*p*-methoxyphenyl(2-naphthyl)(hydroxy)methyl]pyrrolidine as catalyst s. A. Russo, A. Lattanzi, Org. Biomol. Chem. *2010, 8* (11), 2633-8 [DOI: 10.1039/c002587a]; with carbohydrate-based crown ethers s. A. Makó, Z. Rapi, G. Keglevich, Á. Szöllősy, L. Drahos, L. Hegedűs, P. Bakó, Tetrahedron: Asym. *2010, 21* (8), 919-25 [DOI: 10.1016/j.tetasy.2010.05.009]; with a *Cinchona*-based phase-transfer catalyst/NaOCl in toluene s. M.-S. Yoo, D.-G. Kim, M.W. Ha, S. Jew, H. Park, B.-S. Jeong, Tetrahedron Lett. *2010, 51* (42), 5601-3 [DOI: 10.1016/j.tetlet.2010.08.056].

α,α-Cyclopropanomalonoyl peroxide/water ←
***syn*-Glycols from ethylene derivs.** C=C → C(OH)C(OH)
Stereoselective dihydroxylation under mild, metal-free conditions

56.

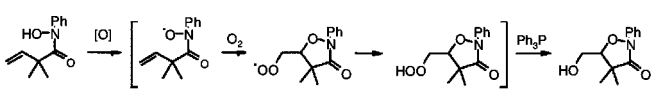


Startg. alkene (1.26 mmol) added dropwise to a soln. of α,α-cyclopropanomalonoyl peroxide (1.2 eq.) in chloroform (2 ml), water (1 eq.) added, the mixture heated at 40° until reaction

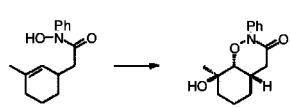
complete (TLC; ca. 24 h), evaporated to dryness, 1 *M* NaOH (10 ml) added, the resulting mixture heated at 60° until reaction complete (TLC; ca. 4 h), the aq. layer extracted with chloroform, washed with brine (10 ml), dried ($MgSO_4$), and solvent removed *in vacuo* → 1-(2,4,6-trimethylphenyl)propane-1,2-diol. Y 93% (*syn/anti* >50:1). The reagent is bench-stable, conveniently prepared on a multi-gram scale in one step from commercially available cyclopropanomalonic acid (using methanesulfonic acid/urea hydroperoxide) and is particularly suitable for the dihydroxylation of styrenes (incl. indene), *trans*-β-subst. styrenes and *trans*-stilbene derivs. (twenty-two examples; Y 56-93%), with internal olefins affording *syn*-glycols (selectivity 10:1 to >50:1; ten examples). A single aliphatic example (ethylidenecyclohexane) afforded a reduced yield of only 40%, while the *syn/anti* selectivity for *cis*-stilbene fell to 3:1 (Y 84%), consistent with the proposed mechanism, which was also supported by isolation of intermediates and $H_2{}^{18}O$-labelling studies. The corresponding cyclobutano- and cyclopentano-malonoyl peroxides were significantly less reactive, as a result of decreased ring strain. F.e.s. J.C. Griffith, K.M. Jones, S. Picon, M.J. Rawling, B.M. Kariuki, M. Campbell, N.C.O. Tomkinson, J. Am. Chem. Soc. *2010*, *132* (41), 14409-11 [DOI: 10.1021/ja1066674].

Acetic acid/triphenylphosphine *AcOH/Ph_3P*

Metal-free aerobic intramolecular radical 1,2-dioxylation of ethylenehydroxamic acids ○

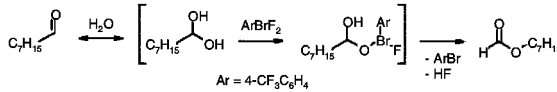


57.

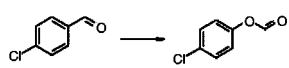


5-α-Hydroxy-3-isoxazolidones. A soln. of the startg. hydroxamic acid dissolved in glacial acetic acid (to 0.1 *M*), the reaction vial fitted with a PTFE-lined screw cap, O_2 bubbled through the mixture for 10 min, stirred under 1 atm. O_2 at 60° until TLC indicated completion of reaction (generally 3-40 h), cooled to room temp., triphenylphosphine (1 eq.) added to decompose any hydroperoxides in soln., and worked up with chromatographic purification → product. Y 88%. Both 5-*exo*- and 6-*exo*-cyclization were effected cleanly to give the corresponding hydroxylated cyclic hydroxamic acid esters in high yield (62-98%; ten examples) from substrates possessing terminal, 1,2-disubst. or trisubst. alkene groups (d.r. 55:45 to >95:5), while cycloalkene analogs gave bicyclic derivs. via *trans*-difunctionalization (complementing *cis*-difunctionalization under transition metal catalysis). The N-O bond was readily cleaved to give the corresponding ***vic*-dihydroxycarboxylic acid amides**, and a **one-pot dihydroxylation** was effected via *in situ*-reduction of the cyclic hydroxamates with added zinc (one example; Y 83%). Reaction was also successful in air, this representing the first such example of a metal-free dioxygenation. Overall the procedure is mild, simple and environmentally friendly, being (as a consequence of the attenuated reactivity of the generated amidoxyl radical) more reliable than the corresponding ring closures of ethylenealcohols via promiscuous alkoxyl radicals. Reaction is also possible in dimethyl sulfoxide at 90°, *in situ*-generated dimethyl sulfide serving to reduce the intermediate hydroperoxide (instead of triphenylphosphine) in the last phase of the reaction. F.e.s. V.A. Schmidt, E.J. Alexanian, Angew. Chem., Int. Ed. *2010*, *49* (26), 4491-4 [DOI: 10.1002/anie.201000843].

4-(Trifluoromethyl)bromobenzene difluoride $4\text{-}CF_3C_6H_4BrF_2$
Formic acid esters from aldehydes $RCHO \rightarrow ROCHO$
Baeyer-Villiger-type oxidation via novel Criegee intermediates



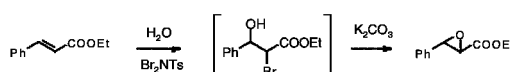
58.



Water (2 eq.) added to a stirred soln. of octanal (0.1 mmol) in methylene chloride (0.5 ml) at 0° under argon, a soln. of 4-(trifluoromethyl)bromobenzene difluoride (1.5 eq.) in the same solvent (1.7 ml) added dropwise, the mixture stirred for 1 h, quenched with satd. aq. NaCl, extracted with methylene chloride, and purified by preparative TLC → heptyl formate. Y 91% (as a 95:5 mixture with octanoic acid). Classical Baeyer-Villiger treatment of linear alkyl and aromatic aldehydes results in simple oxidation to carboxylic acids, while this novel procedure, based on the use of a hypervalent λ^3-bromane, forms reactive Criegee intermediates which enable 1,2-migration of alkyl or aryl groups, affording formate esters. Selectivity for formate ester vs. carboxylic acid formation was high for linear alkyl (79-95%; ten examples; Y 55-91%) and essentially exclusive for branched alkyl and ar. aldehydes (thirteen examples; Y 45-98%). Acetaldehyde gave only 4% of the formate ester (methyl groups have low migratory aptitude) and electron-poor 4-(trifluoromethyl)benzaldehyde was less selective (64:36; Y 53%). The corresponding λ^3-iodane was unreactive under similar conditions. F.e.s. M. Ochiai, A. Yoshimura, K. Miyamoto, S. Hayashi, W. Nakanishi, J. Am. Chem. Soc. *2010*, *132* (27), 9236-9 [DOI: 10.1021/ja104330g].

N,N-Dibromo-p-toluenesulfonamide/potassium carbonate $TsNBr_2/K_2CO_3$
Uncatalyzed epoxidation of styrenes $C{=}C \rightarrow \triangledown$

59.



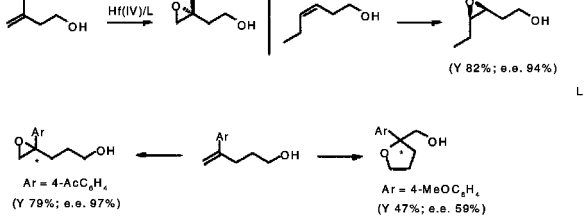
***trans*-Cinnamate oxides.** N,N-Dibromo-*p*-toluenesulfonamide (1.2 mmol) added at room temp. to a soln. of ethyl cinnamate (1.1 mmol) in a mixture of acetonitrile (4 ml) and water (1 ml), stirred for 10 min, K_2CO_3 (1.5 mmol) added, stirring continued for a further 45 min at room temp. (to convert the formed 1,2-bromohydrin to the epoxide *in situ*), quenched by adding $Na_2S_2O_3$ (ca. 200 mg), stirred for a further 20 min, and worked up with purification by flash chromatography on silica gel → *trans*-ethyl cinnamate oxide. Y 85%. The procedure is high-yielding for the *trans*-selective epoxidation of cinnamic acid esters (seven examples; Y 70-85%) and the epoxidation of styrenes (three examples; Y 50-80%). F.e.s. I. Saikia, B. Kashyap, P. Phukan, Synth. Commun. *2010*, *40* (17), 2647-52 [DOI: 10.1080/00397910903318617].

Silica s. under Gallium oxide SiO_2

Hafnium(IV) tetra-tert-butoxide/chiral bis(hydroxamic acids)/cumene hydroperoxide/ N,N′-dimethyl N,N′-propyleneurea ←

Asym. epoxidation of 3- and 4-ethylenealcohols catalyzed by hafnium(IV) or zirconium(IV) C=C →

60.



A mixture of $Hf(OBu\text{-}t)_4$ (2 mol%), chiral bis(hydroxamic acid) (2 mol%), DMPU (4 mol%) and powdered 4 Å molecular sieves (100 mg) in toluene (0.5 ml) stirred at room temp. for 1 h, cooled to 0°, 3-methyl-3-buten-1-ol (0.5 mmol) and 85% cumene hydroperoxide (1.5 eq.) added sequentially, the mixture stirred at 0° for 4 h, then at room temp. for 36 h, quenched with methanol, stirred for 10 min, and purified by flash chromatography on silica gel → (R)-2-(2-methyloxiran-2-yl)ethanol. Y 81% (e.e. 97%). Both Hf(IV) and Zr(IV) catalyzed the asym. epoxidation, with the latter giving significantly better results in some cases. Reactivity and enantioselectivity of homoallylic alcohols were variable (ten examples; Y 31-82%; e.e. 63-97%), and determined by substituents on the alkene moiety, with high enantioselectivity observed for 1,1- (high for methyl and ar. substituents; e.e. 91-98%, moderate for *t*-butyl and H; e.e. 63-71%) and (Z)-1,2-disubst. derivs. (e.e. 94-96%). The authors note that substrates carrying a (Z)-substituent favor 3S-products (cf. 3R) but it is not clear if this is general, since some products have unassigned stereochemistry. The more challenging 4-ethylenealcohols, 4-aryl-4-pentenols, were also good substrates (five examples; Y 53-75%; e.e. 97-99%) with reactivity reduced for a sterically-hindered 2,5-dimethoxyphenyl deriv. (Y 25%; e.e. 97%), while a 4-methoxyphenyl deriv. gave a **2-(hydroxymethyl)tetrahydrofuran** (Y 47%; e.e. 59%), as did the 1,2-disubst. deriv., 4-heptenol (Y 43%; e.e. 95%). F.e. and optimization s. Z. Li, H. Yamamoto, J. Am. Chem. Soc. *2010, 132* (23), 7878-80 [DOI: 10.1021/ja100951u].

Triphenylphosphine s. under Acetic acid Ph_3P

(R)-3,3′-Diphenyl-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate s. under 9-Amino-9-deoxy-epi-quinine ←

DNA s. under $Cu(NO_3)_2$ *DNA*

Oxygen s. under [Pd(II)] O_2

Hydrogen peroxide s.a. under 9-Amino-9-deoxy-epi-quinine H_2O_2

Hydrogen peroxide/axially-chiral polycyclic guanidines ←

Asym. epoxidation s. *78*, 285

Hydrogen peroxide/silica-supported sulfonic acid ←

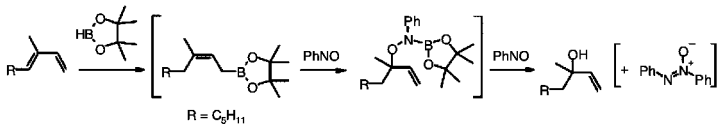
Baeyer-Villiger oxidation ←

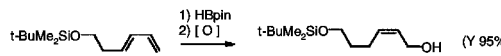
s. *36*, 129s*75*; eco-friendly procedure with a silica-supported sulfonic acid and aq. H_2O_2 in hexafluoroisopropanol s. C.G. Piscopo, S. Loebbecke, R. Maggi, G. Sartori, Adv. Synth. Catal. *2010, 352* (10), 1625-9 [DOI: 10.1002/adsc.201000076]; with molecular oxygen and benzaldehyde in ionic liquids s. A. Chrobok, Tetrahedron *2010, 66* (16), 2940-3 [DOI: 10.1016/j.tet.2010.02.082]; regiospecific oxidation of N-protected β-aminoketones with Baeyer-Villiger monooxygenase to give the expected N-protected 2-aminoalcohols and unexpected β-aminocarboxylic acids s. J. Rehdorf, M.D. Mihovilovic, U.T. Bornscheuer, Angew. Chem., Int. Ed. *2010, 49* (26), 4506-8 [DOI: 10.1002/anie.201000511].

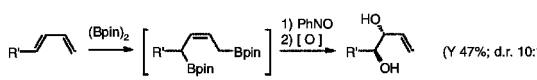
Triflimide s. under [o-Biphenyl(dicyclohexyl)phosphine]gold(I) triflimide ←

Sodium hypochlorite/cinchona-based quaternary ammonium salts ←
Organocatalyzed asym. epoxidation of α,β-ethyleneketones s. *70*, 63s*78* C=C →

Bis(1,5-cyclooctadiene)nickel(0)/tricyclohexylphosphine/pinacolatoboron/nitrosobenzene/ ammonium hydroxide ←
2-Ethylenealcohols from 1,3-dienes via β,γ-ethyleneboronic acid esters CHC(OH)C=C
Regioselective conversion







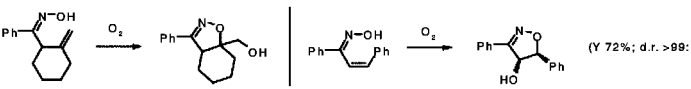
61.

2-Ethylene-*sec*-alcohols. $Ni(cod)_2$ (2.5 mol%), tricyclohexylphosphine (2.5 mol%), toluene (1.45 ml), pinacolborane (1.5 eq.), and *trans*-3-methyl-1,3-nonadiene (0.36 mmol) added sequentially to a vial, the vial sealed with a polypropylene cap, the mixture stirred at room temp. for 3 h, cooled to 0°, nitrosobenzene (3 eq.) and THF (2 ml) added, the soln. stirred at room temp. for 1 h, cooled to 0°, aq. NH_4OH added, the mixture stirred for 14 h while warming to room temp., diluted with brine, extracted with methylene chloride, concentrated *in vacuo*, and purified by chromatography on silica gel → 3-methylnon-1-en-3-ol. Y 58%. Under conventional oxidative work-up (H_2O_2/NaOH) the intermediate boronates are converted to prim. allylic alcohols (nine examples; Y 56-95%), whereas treatment with nitrosobenzene effects allylic rearrangement via formation of an N-O adduct which is cleaved under surprisingly mild, basic conditions to afford the isomeric sec. allylic alcohols (nine examples; Y 33-66%). The rearrangement is tolerant of silyl ether, benzyl ether and 3-methyl functionality but a low yield (33%) was obtained for a substrate with a 2-methyl substituent. A single example of a *1,4-diboryl-2-alkene* intermediate subjected to nitrosobenzene treatment before final oxidative work-up at low temp. (-78°) was converted to the 3,4-dihydroxy-1-alkene with good *anti*-selectivity (Y 47%; d.r. 10:1). F.e., substrate prepn. and optimization s. R.E. Kyne, M.C. Ryan, L.T. Kliman, J.P. Morken, Org. Lett. *2010, 12* (17), 3796-9 [DOI: 10.1021/ol101472k].

Palladium(II) salts or complexes/tert-butyl hydroperoxide or oxygen [Pd(II)]/t-BuOOH or O_2
Methyl ketones from terminal ethylene derivs. by Wacker oxidation $CH=CH_2 \rightarrow C(O)CH_3$
s. *19*, 200; with dichloropalladium(II) bis(isonitrile) complexes under O_2 without cocatalyst (cf. *57*, 69s*76*) s. A. Naik, L. Meina, M. Zabel, O. Reiser, Chem. Eur. J. *2010, 16* (5), 1624-8 [DOI: 10.1002/chem.200901560]; oxidation of natural allylbenzenes with $PdCl_2/O_2$ in aq. DMF s. L.A. Parreira, L. Menini, J.C. da Cruz Santos, E.V. Gusevskaya, Adv. Synth. Catal. *2010, 352* (9), 1533-8 [DOI: 10.1002/adsc.201000050]; N-protected α-aminoketones from allylamines with a palladium(II) quinoxaline complex and *tert*-butyl hydroperoxide s. B.W. Michel, J.R. McCombs, A. Winkler, M.S. Sigman, Angew. Chem., Int. Ed. *2010, 49* (40), 7312-5 [10.1002/anie.201004156].

Palladium(II) acetate/1,10-phenanthroline/acetic acid/air $Pd(OAc)_2/phen/AcOH/O_2$
4-Hydroxy- or 5-α-hydroxy-Δ^2-isoxazolines from α,β- or β,γ-ethyleneoximes
Palladium(II)-catalyzed intramolecular 1,2-dioxylation with molecular oxygen as oxidant

62.

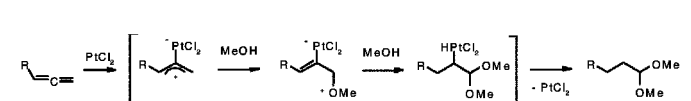


A mixture of startg. oxime (0.3 mmol), $Pd(OAc)_2$ (10 mol%), 1,10-phenanthroline (12 mol%), acetic acid (10 eq.), water (15 eq.) and 1,2-dichloroethane (1 ml) stirred at 40° in air until reaction complete (TLC; 12-48 h), cooled to room temp., quenched with satd. aq. $NaHCO_3$, extracted with ethyl acetate, concentrated *in vacuo*, the residue stirred with methanol (3 ml) and K_2CO_3 (2 eq.) at room temp. for 1 h, and purified by chromatography on silica → (3-phenyl-3a,4,5,6,7,7a-hexahydrobenzo[*d*]isoxazol-7a-yl)methanol. Y 74% (d.r. >99:1 by crude ^1H NMR; stereochemistry not assigned). This intramolecular dioxygenation utilizes O_2 as the optimal oxidant, affording 5-hydroxymethyl- or 4-hydroxy-isoxazolines with β,γ- or α,β-unsaturated oximes, respectively. The reaction appears general for α-alkyl and (het)aryl substituents and was tolerant of a single aliphatic β-substituent (twelve examples; Y 66-75%), but dialkyl or phenyl substitution at the β-position resulted in significant yield reduction (three examples; Y 36-46%). Reaction initially affords mixtures of products and their acetate esters that are conveniently hydrolyzed during work-up. Attempts to form larger rings by this method were unsuccessful. F.e., substrate prepn. and optimization s. M.-K. Zhu, J.-F. Zhao, T.-P. Loh, J. Am. Chem. Soc. *2010*, *132* (18), 6284-5 [DOI: 10.1021/ja100716x].

Palladium(II) chloride/copper(II) chloride $PdCl_2/CuCl_2$
α-Diketones from acetylene derivs. $C{\equiv}C \rightarrow C(O)C(O)$
en route to quinoxalines s. *78*, 156

Platinum(II) chloride $PtCl_2$
Acetals from terminal allenes $C{=}C{=}CH_2 \rightarrow CHCH_2CH(OR)_2$
by regiospecific platinum(II)-catalyzed double addition of alcohols

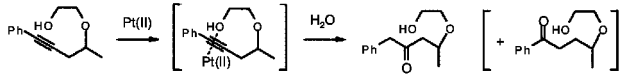
63.



A soln. of the startg. allene (0.2 mmol) in dry THF (2 ml) added to $PtCl_2$ (5 mol%) under argon, followed by methanol (2-4 eq.), the mixture heated at 70° for 20 h, cooled to room temp., filtered through Celite, the solvent evaporated, and the residue worked up with purification by flash chromatography on silica gel → product. Y 80%. This is the first example of a double addition of two molecules of an alcohol to the terminal carbon of an allene, reaction being clearly distinct from gold-catalyzed addition of alcohols which yields the corresponding allyl ethers. Monosubst. allenes gave moderate to good product yields with a variety of alcohols (prim., sec., tert., benzylic and propanediol), complicated in some instances by formation of aldehydes and ketones. Unsatd. alcohols, e.g. propargyl alcohol, however, underwent polymerization (ca. ten examples in all; Y 20-85%), while 1,1-disubst. and 1,3-disubst. allenes either decomposed or gave complex mixtures of products. Alkyl, aryl, ester and imide groups were tolerated. Deuteriation experiments suggest that reaction involves an unprecedented [formal] 1,3-dipolar addition of the alcohol to an intermediate zwitterionic platinum carbene complex as the key step. F.e.s. M. Paz Muñoz, M.C. de la Torre, M.A. Sierra, Adv. Synth. Catal. *2010*, *352* (13), 2189-94 [DOI: 10.1002/adsc.201000342].

Dichloro(ethylene)platinum(II) dimer/15-crown-5 polyether $Pt_2Cl_4(CH_2{=}CH_2)_2$*/crown*
β-(2-Hydroxyalkoxy)ketones from (2-hydroxyalkoxy)-3-acetylenes via regiospecific platinum(II)-catalyzed intramolecular hydroalkoxylation C≡C → CH_2CO

64.



17 : 1

A soln. of Zeise's dimer (2.5 mol%) and 15-crown-5 (5 mol%) in dry DME (1.5 ml) stirred under argon at room temp. for 30 min, the reaction vessel placed in a glove bag, the startg. acetylene deriv. (0.15 mmol) added, stirred at room temp. for 2.5 h, water (25 μl) added, stirred for a further 10 min, quenched with triethylamine, the solvent evaporated, and the residue worked up with purification by flash chromatography on silica gel → product. Y 68% (17:1 β-alkoxyketone/γ-alkoxyketone). The procedure is applicable to substrates possessing an alkyl or aryl group at the alkyne terminus (the proportion of β-alkoxyketone increasing with the size of the alkyl group and with the electron-withdrawing nature of the benzene ring substituent). The substituent at the propargylic position also affected regioselectivity, larger groups also favoring the β-alkoxyketone, while the hydroxyl group may be prim., sec. or tert. Reaction involves initial activation of the acetylene bond by Pt(II), followed by preferential 7-*exo-dig*-cyclization [through *trans*-addition of the appended hydroxyl group] prior to hydrolysis to give the β-alkoxyketone. The crown ether effectively coordinates to platinum, thereby inhibiting *cis*-attack of the hydroxyl group which would favor formation of the γ-alkoxyketone. The products were readily converted to the corresponding β-hydroxyketones so that overall the procedure is seen as an **alternative to the aldol condensation**. F.e. (thirteen; Y 59-98%; β-alkoxyketone/γ-alkoxyketone 2.6:1 to 17:1) s. D. Yang, J. Huang, B. Liu, Eur. J. Org. Chem. *2010* (22), 4185-8 [DOI: 10.1002/ejoc.201000484].

Rearrangement ∩

Oxygen/Nitrogen Type OC ∩ ON

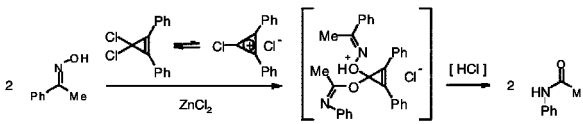
Without additional reagents *w.a.r.*
4-α-Acetoxy-5-alkoxypyrimidines from 5-alkoxypyrimidine N-oxides s. *78*, 175 ∩

Zinc chloride s.a. under 3,3-Dichloro-1,2-diphenylcyclopropene, $[Me_2SBr]Br$ *and* H_2NSO_3H $ZnCl_2$

Zinc nitrate or chloride or Indium(III) nitrate $Zn(NO_3)_2$ *or* $ZnCl_2$ *or* $In(NO_3)_3$
Beckmann rearrangement ∩
s. *64*, 83s*73*; with catalytic amounts of $Zn(NO_3)_2$, $ZnCl_2$ or $In(NO_3)_3$ s. C.L. Allen, C. Burel, J.M.J. Williams, Tetrahedron Lett. *2010, 51* (20), 2724-6 [DOI: 10.1016/j.tetlet.2010.03.048]; with bromodimethylsulfonium bromide/$ZnCl_2$ s. L.D.S. Yadav, R. Patel, V.P. Srivastava, Synthesis *2010* (11), 1771-6 [DOI: 10.1055/s-0029-1218730]; with sulfamic acid/$ZnCl_2$ s. J.-T. Li, X.-T. Meng, Y. Yin, Synth. Commun. *2010, 40* (10), 1445-52 [DOI: 10.1080/00397910903097286]; with ordered mesoporous silica chlorides having 2D P_6 *mm* hexagonal structures s. B. Karimi, H. Behzadnia, Synlett *2010* (13), 2019-23 [DOI: 10.1055/s-0030-1258484]; with N-tosylimidazole/Cs_2CO_3/silica s. M.N.S. Rad, A. Khalafi-Nezhad, S. Behrouz, Z. Amini, M. Behrouz, Phosphorus, Sulfur Silicon Relat. Elem. *2010, 185* (8), 1658-71 [DOI: 10.1080/10426500903176554]; with *p*-TsCl/tetramethylguanidinium tosylate for rearrangement of cyclohexanone oxime s. M. Vilas, E. Tojo, Tetrahedron Lett. *2010, 51* (31), 4125-8 [DOI: 10.1016/j.tetlet.2010.05.145].

3,3-Dichloro-1,2-diphenylcyclopropene/zinc chloride ←
Cyclopropenium-catalyzed Beckmann rearrangement of ketoximes R(R′)C=NOH → RC(O)NHR′

65.



3,3-Dichloro-1,2-diphenylcyclopropene (3 mol%) and $ZnCl_2$ (3 mol%) added at room temp. to a soln. of the startg. ketoxime (1 mmol) in dry acetonitrile (3 ml), the mixture heated at reflux under N_2 for 2 h, quenched with satd. aq. $NaHCO_3$, and worked up with purification by chromatography on silica gel → acetanilide. Y 98%. This is the first example of organocatalysis with a cyclopropenium ion, opening up a new aspect of **catalysis with an aromatic cation**. With $ZnCl_2$ as co-catalyst, the procedure is rapid, highly selective and applicable to a wide range of alkyl aryl, diaryl and dialkyl ketoximes as well as 10- and 12-membered carbocyclic ketoximes (fifteen examples; Y 86-99%). Yields were low, however, with cyclooctanone and cyclohexanone oximes. Reaction is presumed to take place via electrophilic activation of the oxime hydroxyl group, and a plausible mechanism is proposed. Other Lewis acids ($InCl_3$, $FeCl_3$, $SnCl_4$, $MgCl_2$ and $CuCl_2$) in place of $ZnCl_2$ were ineffective. F.c. and solvent effect s. V.P. Srivastava, R. Patel, Garima, L.D.S. Yadav, Chem. Commun. *2010*, *46* (31), 5808-10 [DOI: 10.1039/c0cc00815j].

Bromo(dimethyl)sulfonium bromide/zinc chloride *$[Me_2SBr]Br/ZnCl_2$*
Mesoporous silica chlorides *SBA-Cl*
N-Tosylimidazole ←
p-Toluenesulfonyl chloride/tetramethylguanidinium tosylate *$TsCl/(Me_2N)_2C{=}NH{\cdot}HOTs$*
Sulfamic acid/zinc chloride *$H_2NSO_3H/ZnCl_2$*
Beckmann rearrangement s. *64*, 83s*78* ∩

Oxygen/Sulfur Type OC ∩ OS

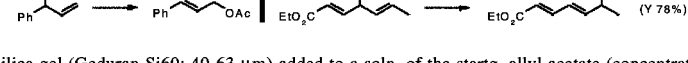
1,8-Diazabicyclo[5.4.0]undec-7-ene/triphenylphosphine *DBU/Ph_3P*
(E)-α,β-Ethylene-γ-hydroxyketones ∩
from α,β-ethylene-α-sulfinylketones via rearrangement with chirality transfer s. *78*, 125

Carbon/Carbon Type OC ∩ CC

Microwaves s. under Silica gel [\\\\]
Copper(II) triflate *$Cu(OTf)_2$*
(Triphenylphosphine)gold(I) chloride or chiral dichloro[di(phosphine)]digold complexes/silver triflate *[Au(I)]/AgOTf*
Lanthanide(III) bis(trimethylsilyl)amides or triflates ←
Cycloisomerization of unsatd. alcohols ○
with Au(III) cf. *36*, 148s*76*; (Z)-1-alkylidenephthalans from *o*-acetylenebenzyl alcohols with $Cu(OTf)_2$ s. C. Praveen, C. Iyyappan, P.T. Perumal, Tetrahedron Lett. *2010*, *51* (36), 4767-71 [DOI: 10.1016/j.tetlet.2010.07.030]; planar-chiral tricarbonylchromium-complexed isochromenes by **asym. cycloisomerization** with chiral dichloro[di(phosphine)]digold complexes/AgOTf s. M. Murai, J. Uenishi, M. Uemura, Org. Lett. *2010*, *12* (21), 4788-91 [DOI: 10.1021/ol1019376]; 2-subst. 2,5-dihydrofurans from 2-allenealcohols with $[(Ph_3P)]Cl/AgOTf$ s. D. Eom, D. Kang, P.H. Lee, J. Org. Chem. *2010*, *75* (21), 7447-50 [DOI: 10.1021/jo101474s]; oxabicyclic β-lactams under gold(I)- or Ag(I)-catalysis s. B. Alcaide, P. Almendros, T. Martínez del Campo, R. Carrascosa, Eur. J. Org. Chem. *2010* (25), 4912-9 [DOI: 10.1002/ejoc.201000710]; double cycloisomerization of bis(acetylenealcohols) with lanthanide(III) bis(trimethylsilyl)amides (cf. *65*, 86s*75*) s. S.Y. Seo, T.J. Marks, Chem. Eur. J. *2010*, *16* (17), 5148-62 [DOI: 10.1002/chem.200903027]; cyclo-

isomerization of unactivated ethylenealcohols with recyclable lanthanide(III) triflates in ionic liquids s. A. Dzudza, T.J. Marks, ibid. 3403-22 [DOI: 10.1002/chem.200902269].

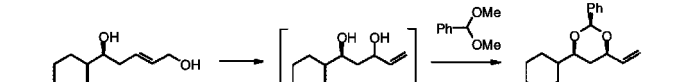
Silica gel/microwaves SiO_2/[\\\\\]
Silica gel-mediated isomerization of acoxy-2-ethylenes C=C-C(OAc) → C(OAc)C=C

66. 

Silica gel (Geduran Si60; 40-63 μm) added to a soln. of the startg. allyl acetate (concentration: 100 mg/ml; silica gel/substrate weight ratio 4/1) in 1,2-dichloroethane contained in a microwave vial, the latter sealed, the mixture subjected to microwave heating at 120° for 30 min, filtered, and the volatiles removed from the filtrate under reduced pressure → acetic acid (*E*)-3-phenylallyl ester. Y 63% (conversion 100%). The yield was 69% at the same temp. *after 20 h without* microwave irradiation. This mild, *metal-free* procedure is inexpensive, environmentally friendly and applicable to a range of aryl-subst. allyl acetates affording the more stable regioisomer in good yield and tolerating a variety of functional groups on the aromatic ring: rearrangement is especially facile with electron-donating substituents but substrates with electron-withdrawing groups (e.g. NO_2) were more sluggish, requiring H_2SO_4-doped silica gel to secure high yields (nine examples in all; Y 54-98%). Pyridyl analogs, however, were unreactive. 3-Acoxy-1,4-enynes also underwent isomerization to give **(E)-2,4-enynol acetates** (six examples; Y 23-71%), while aryl-subst. 2-ene-1,4-diol acetates gave the corresponding (E)-3-ene-1,2-diol acetates, and a 2,4-dienol acetate underwent double rearrangement. Trimethylsilyl and carbalkoxy groups on the alkyne terminus were tolerated as were *tert*-butyldimethylsilyl ethers. An S_N1 mechanism is suggested, the acetate carbonyl group being activated by silica gel through hydrogen bonding. F.e.s. A. Serra-Muns, A. Guérinot, S. Reymond, J. Cossy, Chem. Commun. *2010*, *46* (23), 4178-80 [DOI: 10.1039/c0cc00035c].

1,3,5-Triaza-7-phosphaadamantane s. under [Rh(cod)(MeCN)$_2$]BF$_4$ *PTA*

Rhenium heptoxide Re_2O_7
***syn*-4-Ene-1,3-diol O,O-alkylidene derivs. from 2-ene-1,5-diols**
via regio- and stereo-selective rhenium-catalyzed allylic rearrangement-O,O-alkylidenation

67. 

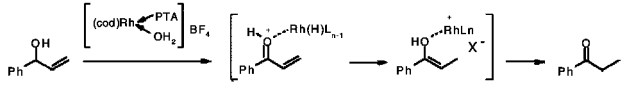
in one pot under mild conditions. Methylene chloride (5 ml) added under argon to a dry flask containing rhenium(VII) oxide (0.025 mmol), the startg. diol (1 mmol) in the same solvent (5 ml) added, followed by benzaldehyde dimethyl acetal (2 mmol), stirred for 20 h at room temp., satd. aq. $NaHCO_3$ added, the biphasic mixture stirred vigorously for 10 min, and the aq. layer worked up with purification by chromatography on silica → *cis,cis*-4-cyclohexyl-2-phenyl-6-vinyl-1,3-dioxane. Y 94%. The catalyst fulfils a dual role: as promoter of the initial allyl rearrangement and as an acid catalyst for the subsequent acetalation, the thermodynamically more stable *syn*-product being formed by a slow equilibration in the last phase of the reaction. This is a significant improvement on prior art which ordinarily delivers a mixture of diastereoisomers with low regioselectivity and fails with primary alcohol derivs. Reaction is also applicable to 2-ene-1,5-diols protected on O[5] (e.g. by silyl, *p*-methoxybenzyl or *p*-methoxybenzoyl), the protecting group first being removed *in situ* under the slightly acidic conditions. F.e. and comparison of Re catalysts, also with retention of carbobenzoxyamino groups and with O,O-alkylidene rearrangement, s. A.T. Herrmann, T. Saito, C.E. Stivala, J. Tom, A. Zakarian, J. Am. Chem. Soc. *2010*, *132* (17), 5962-3 [DOI: 10.1021/ja101673v].

Bis(acetonitrile)(cyclooctadiene)rhodium(I) fluoroborate/1,3,5-triaza-7-phospha-adamantane ←

Oxo compds. from 2-ethylenealcohols CH(OH)C=C → C(O)CHCH

Rhodium-catalyzed redox isomerization in water under very mild conditions

68.

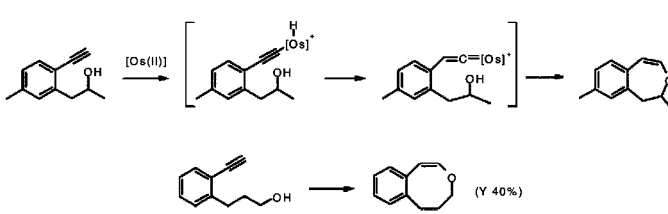


A soln. of $[Rh(cod)(MeCN)_2]BF_4$ (2 mol%) and *water-soluble* 1,3,5-triaza-7-phosphaadamantane (PTA; 4 mol%) in degassed ionized water added to the startg. allyl alcohol (0.4 mmol), the mixture stirred vigorously (1500 rpm) under N_2 in a closed tube *at 23° for 5 min*, and worked up via ethereal extraction → propiophenone. Y >99%. The procedure is very fast, mild, atom-economical, eco-friendly and applicable, generally in very high yield, to a range of aryl- and alkyl-subst. prim. and sec. allyl alcohols with catalyst loadings as low as 0.5 mol%. Yields were highest with aryl-subst. allyl alcohols with only one substituent on the double bond, but higher temperatures (50-80°) were required with substrates having a high degree of substitution. Deuterium isotope studies indicated that reaction involves an intramolecular 1,3-hydrogen shift after initial formation of a water-soluble hydroxorhodium(I) phosphine complex as the active catalyst; this reacts with the allyl alcohol to give a protonated, hydridorhodium-complexed α,β-ethyleneoxo compd., which leads to a rhodium enolate prior to hydrogen shift and elimination of the catalyst. F.e. and gram-scale procedure, also comparison of catalysts and ligands, and study of pH effects s. N. Ahlsten, H. Lundberg, B. Martín-Matute, Green Chem. *2010*, *12* (9), 1628-33 [DOI: 10.1039/c004964f].

Cyclopentadienyltris(pyridine)osmium(II) hexafluorophosphate/pyridine $[CpOs(py)_3]PF_6/py$

Regioselective osmium(II)-catalyzed *endo*-cycloisomerization of (*o*-ethynylaryl)alcohols ○

69.

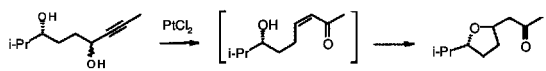


1,2-Dihydro-3-benzoxepins from 2-(*o*-ethynylaryl)alcohols. A mixture of the startg. alcohol (0.29 mmol) and $[CpOs(py)_3]PF_6$ (0.029 mmol) in pyridine (2 ml) stirred in a sealed tube under argon for 1 h at 90°, cooled to room temp., and worked up with purification by flash chromatography on silica gel → product. Y 68%. This is the first such *endo*-cyclization in synthetically useful yield, the conversion being inefficient with ruthenium, rhodium or tungsten catalysts. The procedure is applicable to a range of prim., sec. and tert. 2-(*o*-ethynylaryl)alcohols, reaction being faster with substrates possessing electron-donating groups on the aromatic ring. There was no reaction, however, with internal alkyne derivs., confirming the proposition that cycloisomerization takes place **via osmium vinylidene complexes**. A more challenging *o*-propargylbenzyl alcohol and an even more challenging 3-(*o*-ethynylaryl)alcohol also underwent *endo*-cycloisomerization (Y 40% in each case), although harsher conditions (130°) were required for the latter. Here, ruthenium complexes failed completely. F.e. (eight; Y 56-69%) and with $[Cp^NOs(MeCN)_2]PF_6$ (Cp^N = $CpCH_2CH_2NHMe$), also outline of mechanistic considerations, s. A. Varela-Fernández, C. García-Yebra, J.A. Varela, M.A. Esteruelas, C. Saá, Angew. Chem., Int. Ed. *2010*, *49* (25), 4278-81 [DOI: 10.1002/anie.201000455].

Platinum(II) chloride $PtCl_2$

2-β-Ketotetrahydrofurans from 5-yne-1,4-diols
via Meyer-Schuster rearrangement-intramolecular Michael addition

70.



A soln. of the startg. 5-yne-1,4-diol in toluene treated with $PtCl_2$ (40 mol%) at room temp. for 18 h, and the mixture worked up → product. Y 84% (as a 1:1 mixture of diastereoisomers). It was established that reaction proceeds via Meyer-Schuster rearrangement-intramolecular oxa-Michael addition, rather than by a redox-isomerization. Undec-6-yne-2,5,10-triol reacted similarly to give the isomeric 2-ε-hydroxy-β-ketotetrahydrofuran. F.e. (three; Y 50-74%) and with $[(Ph_3P)Au]Cl/AgBF_4$ s. C. Schwehm, M. Wohland, M.E. Maier, Synlett *2010* (12), 1789-92 [DOI: 10.1055/s-0030-1258109].

Via intermediates *v.i.*

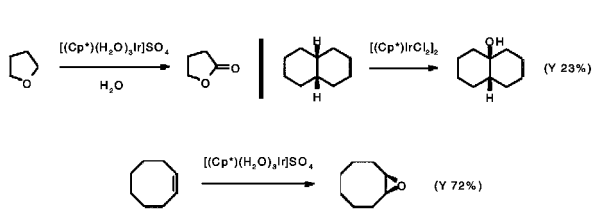
1,3-Dihydroisobenzofurans from *o*-vinylbenzyl alcohols
via 1-iodomethyl-1,3-dihydroisobenzofurans s. *78*, 460

Exchange ↓↑

Hydrogen ↑ OC ↓↑ H

Irradiation s. under CBr_4 and Rose Bengal ///
Sodium acetate s. under $PhI(OAc)_2$ *NaOAc*
Silver(I) acetate s. under $Pd(OAc)_2$ *AgOAc*
Copper(I) iodide s. under $Pd(OAc)_2$ *CuI*
Ammonium cerium(IV) nitrate/tris(aqua)(pentamethylcyclopentadienyl)iridium(III) sulfate ←
Iridium(III)-catalyzed oxidations with cerium(IV) ←

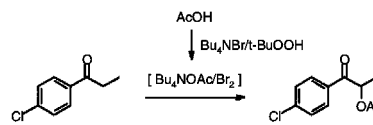
71.



Carbonyl from methylene groups. CAN (8 eq.), THF (0.05 ml) and $[(Cp^*)(H_2O)_3Ir]SO_4$ (1 mol%) added sequentially to 50% aq. *tert*-butanol (4 ml), the mixture stirred under N_2 for 20 min, diluted with water, extracted with methylene chloride, and purified chromatographically → γ-butyrolactone. Y 72%. Ir-Cp* complexes successfully catalyzed the oxygenation of alkanes and alkenes using CAN as the primary oxidant and water as source of oxygen. Cyclooctene and ethylbenzene afforded cyclooctene oxide (Y 72%) and acetophenone (Y 55%), respectively, while *cis*-decalin and *cis*-1,4-dimethylcyclohexane were partially mono-hydroxylated (Y 23% and 27%, respectively), with retention of stereochemistry and significant recovery of substrate. Pyrrolidine, however, gave only recovered substrate (Y 82%). Other terminal oxidants were significantly less effective as were reactions run under air. F.e.s. M. Zhou, N.D. Schley, R.H. Crabtree, J. Am. Chem. Soc. *2010*, *132* (36), 12550-1 [DOI: 10.1021/ja1058247].

tert-Butyl hydroperoxide/tetra-n-butylammonium bromide *t-BuOOH/Bu$_4$NBr*
α-Acoxylation of ketones under redox catalysis with bromide ion H → OAc

72.



tert-Butyl hydroperoxide (70% aq.; 0.25 eq.) added to a soln. of tetra-*n*-butylammonium bromide (*30 mol%*) and *p*-chloropropiophenone (1.5 mmol) in acetic acid (0.25 ml) at 110°, stirred for 3 h, a second portion of oxidant (0.25 eq.) added, followed by further amounts every 3 h (total: 1.25 eq.), stirred for 12 h after the final addition of *tert*-butyl hydroperoxide, cooled to 0°, diluted with water, the mixture poured into satd. aq. $NaHCO_3$, the dried methylene chloride extract concentrated *in vacuo*, the residue placed on the top of a short-path silica gel column and eluted using hexane/ethyl acetate (3/2) (to remove tetra-*n*-butylammonium salts), evaporated, and the residue chromatographed on silica gel → product. Y 70%. This is a unique example of *atom-transfer redox catalysis* wherein the ultimate nucleophilic reactant (tetra-*n*-butylammonium acetate) and the catalytic oxidant (Br_2) are formed in the *same* step of the catalytic cycle. The procedure is applicable to the α-acetoxylation of a range of acylophenones, incl. acetophenones substituted by an electron-withdrawing or -donating group (eight examples; Y 41-74%), but the yield with acetophenone itself and *tert*-butyl ethyl ketone was low (15-40%). Conversions were poor with H_2O_2 as reoxidant, and other halide sources were inefficient. F.e.s. T. Nagano, Z. Jia, X. Li, M. Yan, G. Lu, A.S.C. Chan, T. Hayashi, Chem. Lett. *2010, 39* (9), 929-31 [DOI: 10.1246/cl.2010.929].

tert-Butyl peroxyacetate/acetic acid/acetic anhydride/dimethylformamide s. under Pd(OAc)$_2$ ←
Iodosocarboxylates s.a. under Pd(OAc)$_2$ *RI(OCOR)$_2$*

Phenyl iodosoacetate [s.a. under Pd(OAc)$_2$] *PhI(OAc)$_2$*
δ-Phosphoryloxy-γ-lactones from γ,δ-ethylenecarboxylic acids ○
and phosphoric acid diesters s. *78*, 75

8-Functionalized spiro[5.5]undeca-1,4,7-trien-3-ones from terminal 5-(*p*-hydroxyaryl)acetylenes
Oxidative Prins-type ring closure

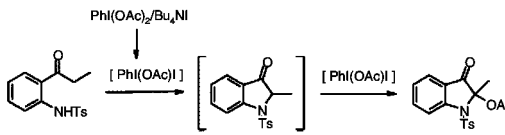
73.

A soln. of phenyl iodosoacetate (1.1 eq.) in hexafluoroisopropanol (0.25 ml) added over 5 s to a vigorously stirred soln. of the startg. phenol (0.1 mmol) in the same solvent (0.75 ml) at 0°, the mixture stirred for 2 min, quenched with acetone, filtered directly over silica gel, the filtrate concentrated under reduced pressure, and worked up with purification by chromatography on silica gel → product. Y 61%. Substitution at each position of the aromatic ring was tolerated, incl. *o,o'*-dibromophenol derivs., while substrates disubstituted at the benzylic site readily produced spirocyclics with two contiguous quaternary centers as exist in such natural products as laurencenone B. Mechanistically, a phenoxonium ion is generated on initial oxidation of the aromatic ring, which then couples intramolecularly, Prins-fashion, with the alkyne residue to give a strained sp-hybridized carbonium species, which is quenched with even weakly reactive nucleophiles, e.g. hexafluoroisopropanol, methylene chloride (as source of Cl^-), trifluoroacetic acid and benzene. Reaction with the latter effectively secures a tandem oxidative Prins-type cyclization-Friedel-Crafts reaction. F.e. (ca. twelve; Y 50-86%), also ring closure of a terminal 3-methylene-5-(*p*-hydroxyaryl)acetylene (two examples; Y 64-65%) and reaction with an internal alkyne deriv., s. J.-C. Andrez, M.-A. Giroux, J. Lucien, S. Canesi, Org. Lett. *2010, 12* (19), 4368-71 [DOI: 10.1021/ol101851z].

Phenyl iodosoacetate/sodium hydrogen carbonate *$PhI(OAc)_2/NaHCO_3$*
1-Oxaspiro[5.5]undeca-7,10-diene-3,9-diones from 1-(*p*-hydroxyaryl)cyclobutanols ○
s. *78*, 119

Phenyl iodosoacetate/tetra-n-butylammonium iodide/sodium acetate *$PhI(OAc)_2/Bu_4NI/NaOAc$*
2-Acoxy-1-tosyl-3-indolones from *o*-tosylaminoketones ○
Metal-free oxidative ring closure-acoxylation

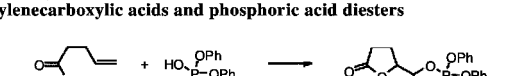
74.



A mixture of the startg. *o*-tosylaminoketone (0.2 mmol), $PhI(OAc)_2$ (3 eq.) and NaOAc (1 eq.) in dioxane (1 ml) treated with tetra-*n*-butylammonium iodide (2.5 eq.), stirred at 25° for 1 h, quenched with satd. $Na_2S_2O_3$, and worked up with purification by chromatography on silica gel → 2-methyl-3-oxo-1-tosylindolin-2-yl acetate. Y 89%. High yields (50%, 75-92%; eight examples) were obtained with *o*-tosylaminoketones bearing electron-withdrawing or -donating groups on the aromatic ring (with acetyl, propionyl or 3-phenylpropionyl as the acyl residue), but there was no reaction with substrates possessing other N-protective groups. Addition of iodide ion was essential for generation of a more reactive iodine(III) reagent [PhI(OAc)I] from phenyl iodosoacetate. This initially undergoes ligand exchange with the ketone (in enolate form) prior to ring closure, followed by iodine(III)-mediated 2-acoxylation of the resulting 3-indolone terminated by a second reductive elimination. Other iodine(III) reagents were ineffective and α-methoxylation was a problem with added KOH in methanol. The products underwent Friedel-Crafts reaction with electron-diverse arenes in the presence of TfOH to give the corresponding **2-aryl-1-tosyl-3-indolones** (eleven examples; Y 52-86%). F.e.s. Y. Sun, R. Fan, Chem. Commun. *2010*, *46* (36), 6834-6 [DOI: 10.1039/c0cc01911a].

Iodobenzene/m-chloroperoxybenzoic acid *$PhI/ArCOO_2H$*
δ-Phosphoryloxy-γ-lactones
from γ,δ-ethylenecarboxylic acids and phosphoric acid diesters

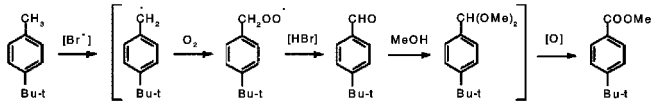
75.



Catalytic procedure under mild conditions. 4-Pentenoic acid (0.3 mmol), diphenyl phosphate (1 eq.), *m*CPBA (75%; 1 eq.), and iodobenzene (0.1 eq.) added to 2,2,2-trifluoroethanol (2 ml), the mixture stirred at room temp. for 8 h, quenched with water (5 ml), satd. aq. $Na_2S_2O_3$ (2 ml) and satd. aq. Na_2CO_3 (2 ml), extracted with methylene chloride, the organic layer washed with brine, dried ($MgSO_4$), filtered, concentrated under reduced pressure, and the residue purified on a silica gel plate → 5-[bis(phenyloxy)phosphoryloxy]-4-pentanolactone. Y 65%. Yields were slightly higher with dibenzyl phosphate (70-77%; three examples) than with diphenyl phosphate (63-66%; four examples), while bis(4-nitrophenyl) phosphate afforded a product that decomposed during purification (Y 58%). Reaction of 3-butenoic acid or 2-cyclopentene-1-acetic acid did not afford phosphoryloxylactones; furthermore, as in the previously-described method from iodoso(hydroxy)phosphates (*43*, 169), reaction of hexenoic acid provided an unstable δ-lactone. The proposed mechanism for the catalytic cycle involves the electrophilic addition of a hypervalent iodine species, generated from iodobenzene by oxidation with *m*CPBA, to the double bond, then intramolecular addition of carboxyl, followed by nucleophilic substitution by phosphate. Use of other stoichiometric oxidants such as Oxone, $NaBO_3$ or $Na_2S_2O_8$ proved unsuccessful. F.e.s. Z.-S. Zhou, X.-H. He, Tetrahedron Lett. *2010*, *51* (18), 2480-2 [DOI: 10.1016/j.tetlet.2010.02.153]; with $PhI(OAc)_2$ in acetonitrile cf. idem., Chin. Chem. Lett. *2010*, *21* (9), 1041-4 [DOI: 10.1016/j.cclet.2010.04.011].

Carbon tetrabromide/irradiation *CBr_4/hν*
Arylcarboxylic acid methyl esters $CH_3 \rightarrow COOCH_3$
from methylarenes by aerobic photooxidation

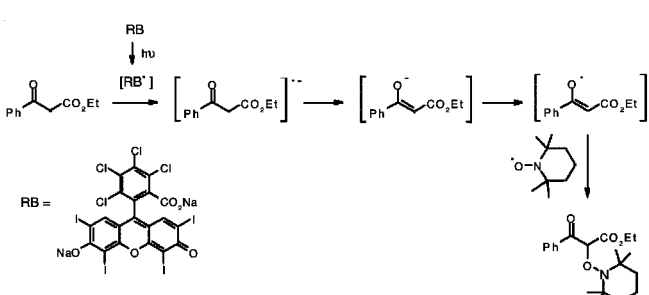
76.



A soln. of 4-*tert*-butyltoluene (0.3 mmol) and carbon tetrabromide (10 mol%) in dry methanol (1 ml) purged with O_2 (balloon pressure) in a Pyrex test-tube, the mixture stirred under irradiation with four 22 W fluorescent lamps for 24 h, concentrated *in vacuo*, and purified by PTLC (toluene) → methyl 4-*tert*-butylbenzoate. Y 92%. This is the first example of the direct conversion of a methylarene to a methyl benzoate. The procedure is simple, inexpensive and applicable to a range of methylarenes, electron-rich derivs. giving good yields (70-92%; five examples), but electron-deficient substrates (notably those possessing a CN or NO_2 group) affording lower yields under irradiation with a 500 W xenon lamp (22-80%; eight examples). 2-Picoline, however, was a poor substrate (Y 2%). Reaction is initiated by abstraction of a hydrogen atom from the methyl group by a generated bromine radical prior to trapping of the formed benzyl radical with O_2; the corresponding ar. aldehyde is then formed by dehydration and converted to the dimethyl acetal prior to a second abstraction of hydrogen and oxidation to the product. F.e. and comparison of bromine sources s. S. Hirashima, T. Nobuta, N. Tada, T. Miura, A. Itoh, Org. Lett. *2010, 12* (16), 3645-7 [DOI: 10.1021/ol1014575].

Rose Bengal/irradiation ←
Photocatalyzed α-aminooxylation of β-ketocarbonyl compds. $H \rightarrow ON\lesssim$
under visible light irradiation

77.



An inexpensive, eco-friendly *organic dye* has been used for the first time as a one-electron photoredox catalyst under irradiation with a *household fluorescent bulb*. **E:** TEMPO (0.05 mmol), Rose Bengal (0.00025 mmol), a stirring bar and distilled acetonitrile (0.5 ml) introduced in this sequence into a clear vial, the mixture stirred at room temp. for a while, ethyl benzoylacetate (0.05 mmol) added in one portion, the vial placed under an 11 W household fluorescent bulb, the soln. concentrated after 24 h, and loaded onto a short silica gel column followed by flash chromatography → product. Y 97%. This simple *metal-free* procedure affords complete conversions with high product yields for the α-aminooxylation of a range of β-keto-esters and β-diketones, and is notably applicable to α-fluoro-β-keto-esters, leading, for the first time, to quaternary α-fluoro-α-oxycarboxylic acid derivs. (twelve examples in all; Y 64-97%). Substrates may possess

electron-withdrawing or -donating groups on the aromatic ring, but those with the latter required a longer reaction time. Reaction was also possible **in water**, and one example is cited for the α-aminooxylation of an α-nitroketone (Y 72%). There was no reaction, however, with aliphatic β-keto-esters. Other organic dyes and the familiar photocatalyst, $Ru(bpy)_3Cl_2$, were also tested, but conversions were very low. A mechanistic proposal is advanced. F.e.s. H. Liu, W. Feng, C.W. Kee, Y. Zhao, D. Leow, Y. Pan, C.-H. Tan, Green Chem. *2010*, *12* (6), 953-6 [DOI: 10.1039/b924609f].

Oxygen s. under $Pd(OAc)_2$ O_2

Chromium(IV) oxide CrO_2

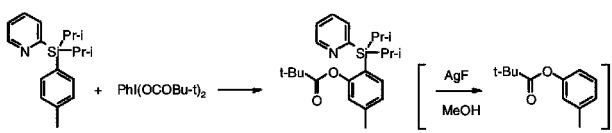
Oxidation of organic substrates using metal oxides under flow conditions ←
with inductive heating by admixed magnetite nanoparticles – Carbonyl from methylene groups s. *78*, 120

Tetra-n-butylammonium bromide s. under t-BuOOH Bu_4NBr

Tetra-n-butylammonium iodide s. under $PhI(OAc)_2$ Bu_4NI

Palladium(II) acetate/silver acetate/iodosocarboxylates $Pd(OAc)_2/AgOAc/RI(OCOR)_2$
Palladium(II)-catalyzed ar. acoxylation H → OCOR
2-Pyridylsilyl as a traceless directing group

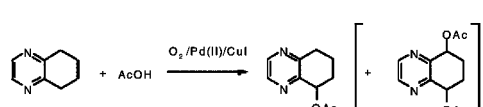
78.



Startg. silane (0.5 mmol), $Pd(OAc)_2$ (10 mol%), phenyl iodosopivalate (2 eq.), AgOAc (1 eq.) and dry 1,2-dichloroethane (10 ml) added sequentially to an oven-dried vial under N_2, the vial sealed with a pressure screw cap, the mixture heated at 80° until reaction complete (GC/MS; 5 h), quenched with triethylamine, filtered through silica, concentrated *in vacuo*, and purified by chromatography on silica → (2-pivaloxy-4-methylphenyl)diisopropyl(2-pyridyl)silane. Y 93%. This novel silane directing group ['PyDipSi'] is readily prepared from the corresponding haloarene, can be removed under mild conditions, and promotes general and efficient C-H activation for electron-diverse arenes via catalyst coordination and subsequent mono-acetoxylation or -pivaloxylation (twenty-five examples; Y 60-93%). The reaction was compatible with ether, halo, amide, ester and acetal functionality but less-bulky silane directing groups were unstable under the reaction conditions. Removal of the PyDipSi group (AgF/MeOH/room temp.; Y 92%) and conversion to B(pin), D, I, OH and phenyl derivs. (Y 89-100%) is also described. F.e., optimization and substrate prepn. s. N. Chernyak, A.S. Dudnik, C. Huang, V. Gevorgyan, J. Am. Chem. Soc. *2010*, *132* (24), 8270-2 [DOI: 10.1021/ja1033167].

Palladium(II) acetate/copper(I) iodide/oxygen $Pd(OAc)_2/CuI/O_2$
N-Directed *o*-α-acoxylation of pyridines and pyrazines H → OAc
Palladium(II)-catalyzed oxidation using molecular oxygen

79.



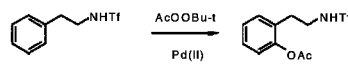
A mixture of $Pd(OAc)_2$ (5 mol%), *CuI* (1 eq.), acetic acid (3 ml) and 5,6,7,8-tetrahydroquinoxaline (1 mmol) stirred under O_2 (8 atm.) in an autoclave at 70° for 24 h, cooled to 0°, pressure released,

the residual oil dissolved in ethyl acetate, washed with water and satd. aq. $NaHCO_3$, concentrated, and purified by chromatography on silica → 5-acetoxy-5,6,7,8-tetrahydroquinoxaline. Y 88% (as a 97:3 mixture with the 5,8-diacetoxy deriv.). Selective α-oxygenation of a series of cyclic and acyclic 2-alkyl-pyridine and -pyrazine derivs. using O_2 as the sole oxidant, afforded acetoxy derivs. as major products at 40-120° (twelve examples; Y 55-92%), with lower temp. required for active substrates to minimize over-oxidation to ketone by-products. 2-Ethyl-3-methylpyrazine underwent selective oxidation at the ethyl group to afford an 85:15 mixture of 2-(1-acetoxyethyl)-3-methyl- and -formyl-pyrazines (Y 82%). Other copper co-catalysts (and KI) gave reduced yields, as did reactions performed under 1 atm. of O_2. The mechanism of the reaction was not clear, but is unlikely to involve vinyl-pyridine/-pyrazine intermediates. F.e. and optimization s. H. Jiang, H. Chen, A. Wang, X. Liu, Chem. Commun. *2010*, *46* (38), 7259-61 [DOI: 10.1039/c0cc00841a].

Palladium(II) acetate/tert-butyl peroxyacetate/acetic acid/acetic anhydride/ dimethylformamide ←

Palladium-catalyzed *o*-acoxylation of N-triflyl-2-arylamines under mild conditions H → OAc

80.

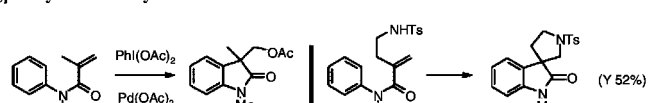


A soln. of the startg. triflamide (0.5 mmol), $Pd(OAc)_2$ (0.1 eq.), *tert*-butyl peroxyacetate (2 eq.), dimethylformamide (6 eq.), acetic acid (1 eq.) and acetic anhydride (2 eq.) in 1,2-dichloroethane (0.32 ml) stirred in a sealed tube under air at 70° for 48 h, the mixture cooled to room temp., concentrated under vacuum, and purified by chromatography on silica gel → product. Y 55%. The procedure is applicable to a wide range of N-triflyl-2-arylamines bearing electron-donating or -withdrawing groups on the aromatic ring, and optionally being substituted at the benzylic site or α to the amino function by ketal, OTBS, triflate or ester groups (incl. phenylalanine, tyrosine and ephedrine derivs.). The highest reactivity was achieved with acetonitrile as additive (notably preferred for the less reactive *o*-substituted and electron-poor substrates), while DMF is preferred for *o*-acetoxylation of electron-rich or *o*-unsubstituted substrates (ca. twenty-five examples in all; Y 38-98%). Regarding electron-deficient substrates, *o*-trifluoromethyl derivs. gave high yields but substrates with NO_2 or Ac groups on the aromatic ring gave markedly lower yields. Significantly, aromatic halogen was unaffected. An N-triflyl-3-arylamine also underwent *o*-acoxylation but in low yield, reaction likely proceeding via a rare 7-membered palladacyclic (one example; Y 33%). F.e.s. C.J. Vickers, T.-S. Mei, J.-Q. Yu, Org. Lett. *2010*, *12* (11), 2511-3 [DOI: 10.1021/ol1007108].

Palladium(II) acetate/phenyl iodosoacetate *$Pd(OAc)_2$/PhI$(OAc)_2$*

Stereoselective palladium-catalyzed intramolecular carboacoxylation of α,β-ethylenecarboxylic acid anilides

81.



3-α-Acoxyoxindoles. Phenyl iodosoacetate (2 eq.) and $Pd(OAc)_2$ (10 mol%) added to a soln. of the startg. anilide in acetic acid (0.1 *M*), the mixture heated under argon to 100°, stirred for 20 h, cooled to room temp., volatiles evaporated under reduced pressure, and the residue worked up with purification by flash chromatography on silica gel → (1,3-dimethyl-2-oxoindolin-3-yl)methyl acetate. Y 54%. This is a rare example of an intramolecular carbo-heterofunctionalization involving an initial C-H activation, and is an alternative to routes based on aryl halides. The procedure is applicable to substrates possessing electron-donating or weakly electron-withdrawing groups (e.g. Cl) at the *p*-position, but there was no reaction with *p*-cyanoanilides (twelve examples; Y 43-83%). *m*-Subst. anilides gave mixtures of regioisomers. Good yields were obtained with a number of palladium catalysts and other oxidants (AgOAc, IBX, $K_2S_2O_8$, H_2O_2 or Oxone) but phenyl iodosoacetate was the most efficient in neat acetic acid (non-polar or weakly polar solvents being unsuitable). A tertiary anilide (incl. N-benzyl derivs.) was mandatory. With $PdCl_2$ in place

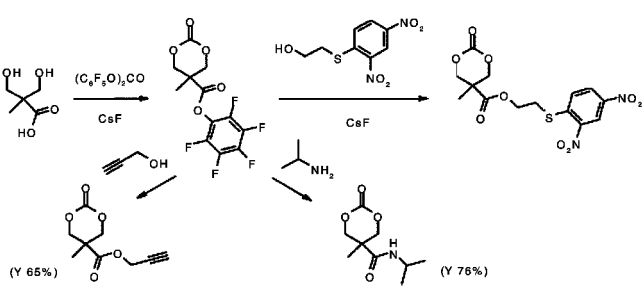
of $Pd(OAc)_2$ at 80° in acetonitrile substrates with a homoallylic tosylamino group underwent double ring closure to give **1′-tosylspiro[indoline-3,3′-pyrrolidin]-2-ones** (seven examples; Y 37-58%) **via stereoselective intramolecular carboacoxylation-N-alkylation**. F.e. and diastereoselectivity, also preliminary mechanistic considerations, s. S. Jaegli, J. Dufour, H. Wei, T. Piou, X.-H. Duan, J.-P. Vors, L. Neuvill, J. Zhu, Org. Lett. *2010*, *12* (20), 4498-501 [DOI: 10.1021/ol101778c].

Tris(aqua)(pentamethylcyclopentadienyl)iridium(III) sulfate s. under $[(Cp^*)(H_2O)_3Ir]SO_4$
Ammonium cerium(IV) nitrate

Oxygen ↑ OC ↓↑ O

Irradiation s. under CuOTf ///
Microwaves s. under Tosylhydrazine [\\\\]
Potassium carbonate s.a. under Tosylhydrazine K_2CO_3
Potassium carbonate/tetra-n-butylammonium iodide K_2CO_3/Bu_4NI
O-Benzylation with soluble oligomeric benzyl phosphates s. *78*, 159 $OH \rightarrow OCH_2Ar$
Cesium fluoride *CsF*
Synthesis and reactions of 1,3-dioxan-2-one-5-carboxylic acid pentafluorophenyl esters ○

82.



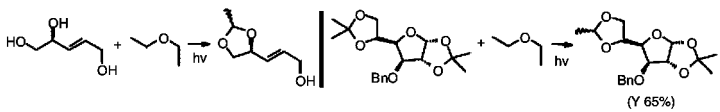
Stable, crystalline pentafluorophenyl 5-methyl-2-oxo-1,3-dioxane-5-carboxylate (or its 5-ethyl analog), prepared on a kilogram scale in one step from readily available starting materials, has been shown to be a versatile, common intermediate for the preparation of a wide variety of functionalized cyclic carbonate monomers (via transesterification with prim. alcohols or amidation with prim. amines), which in turn can be used to synthesize an array of novel functionalized polymers. The method provides a convenient, safe alternative to the use of hazardous phosgene or inefficient phosgene surrogates, such as chloroformates, nitro-subst. diphenyl carbonates or N,N′-carbonyldiimidazole. **E:** A heterogeneous mixture of 2,2-bis(hydroxymethyl)propionic acid (22 mmol), bis(pentafluorophenyl) carbonate (2.5 eq.), CsF (0.2 eq.) and anhydrous THF (70 ml) stirred at room temp. for 21 h (becoming homogeneous after 1 h), solvent removed *in vacuo*, the residue dissolved in methylene chloride, precipitated pentafluorophenol collected by filtration after 10 min, the filtrate washed with aq. $NaHCO_3$ and water, dried over $MgSO_4$, solvent evaporated *in vacuo*, and the product purified by recrystallization → pentafluorophenyl 5-methyl-2-oxo-1,3-dioxane-5-carboxylate (Y 75%), 7.43 mmol of which stirred for 24 h with CsF (0.27 eq.) and 2-(2,4-dinitrophenylthio)ethanol (1.1 eq.) in anhydrous THF (35 ml), filtered to remove precipitated pentafluorophenol, solvent evaporated *in vacuo*, the residue dissolved in methylene chloride, allowed to stand for ca. 30 min, filtered to remove additional precipitated pentafluorophenol, the filtrate washed with satd. $NaHCO_3$, brine and water, dried over $MgSO_4$, concentrated *in vacuo*, and the crude product purified chromatographically → 2-(2,4-dinitrophenylthio)ethyl 5-methyl-2-oxo-1,3-dioxane-5-carboxylate (Y 90%). F.e. (twelve alcohols: Y 50-90%; three amines: Y 64-

76%), also polymerization [using 1-[3,5-bis(trifluoromethyl)phenyl]-3-cyclohexyl-2-thiourea and DBU] to generate polymers (six examples, Y 60-86%) with predictable molecular weights and narrow polydispersities, s. D.P. Sanders, K. Fukushima, D.J. Coady, A. Nelson, M. Fujiwara, M. Yasumoto, J.L. Hedrick, J. Am. Chem. Soc. *2010*, *132* (42), 14724-6 [DOI: 10.1021/ja105332k].

Copper(I) triflate/irradiation *CuOTf/hν*

2-Methyl-1,3-dioxolanes by copper(I)-catalyzed photochemical [trans]acetalation with diethyl ether ○

83.



(Y 65%)

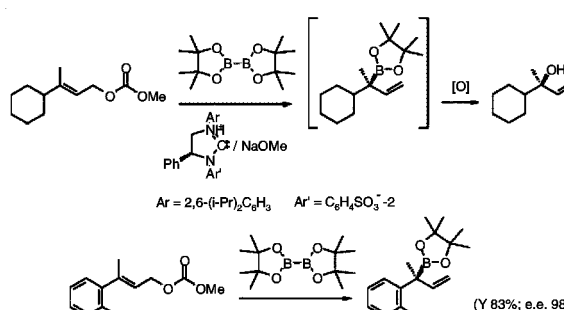
under neutral conditions. A soln. of (S)-pent-2-ene-1,4,5-triol (1.74 mmol) in dry ether (120 ml) in a Pyrex cell degassed with argon for 30 min, $[CuOTf]_2{\cdot}C_6H_6$ (15 mol%) added, the mixture irradiated with a Hanovia medium pressure lamp (450 *W*) until reaction complete (TLC; 4 h), quenched with aq. ammonia at 0°, the organic layer concentrated *in vacuo*, and the residue purified by chromatography on silica → (4S)-2-methyl-4-(3-hydroxyprop-1-enyl)-1,3-dioxolane. Y 70%. This novel acetalation provides experimentally simple access to protected glycols under *neutral conditions without use of carbonyl compds.* from unprotected glycols or their acetonides (thirteen examples; Y 55-70%). No acetalation occurred in the absence of copper. F.e.s. S. Mondal, R.N. Yadav, S. Ghosh, Tetrahedron Lett. *2010*, *51* (33), 4452-4 [DOI: 10.1016/j.tetlet.2010.06.082].

Copper(II) triflate/(S)-3-(2,6-diisopropylphenyl)-5-phenyl-1-(2-sulfonatophenyl)-imidazolinium/sodium methoxide/bis(pinacolato)diboron/hydrogen peroxide/sodium hydroxide ←

2-Ethylenealcohols from 2-ethylenecarbonic acid esters via β,γ-ethyleneboronic acid esters C=C-C(OCOOR) → C(OH)C=C

Asym. copper(II)-catalyzed conversion with allyl shift using a chiral imidazolidin-2-ylidene as ligand

84.



(Y 83%; e.e. 98%)

under mild conditions. A mixture of imidazolinium salt (6 mol%), $Cu(OTf)_2$ (5 mol%), NaOMe (0.8 eq.) and DME (1 ml) stirred under N_2 at -30° in a PTFE sealed vial for 30 min, bis(pinacolato)-diboron (2 eq.) added to the blue soln., the resulting brown soln. stirred for 30 min, neat (E)-(3-cyclohexylbut-2-en-1-yl) methyl carbonate (0.2 mmol) added by syringe, the mixture stirred for 24 h, quenched by passage through Celite/silica, cooled to 0°, H_2O_2 (11 eq.) and 2 *M* NaOH (5 eq.) added, the soln. stirred for 1 h, diluted with water, extracted with ether, concentrated *in*

vacuo, and purified by chromatography on silica → (S)-3-cyclohexylbut-1-en-3-ol. Y 95% (e.c. 96%). Catalyst optimization produced a method that was general, clean, regio- and enantioselective for boronation of di- and tri-subst. (incl. aryl) allylic carbonates, with *alkene stereochemistry determining absolute configuration of the products* (nineteen examples; Y 71-97%; e.e. 72-98%). α-Aryl-α-methyl derivs. were cleanly converted to the allylic substitution products but replacing methyl with ethyl resulted in loss of selectivity, affording a 4:1 mixture of S_N2' and S_N2 derived products. Intermediate boronates were oxidized *in situ* to the allylic alcohols, but boronates containing a C-B quaternary center were sufficiently stable to be isolated and purified (silica chromatography). F.e., substrate prepn. and optimization s. A. Guzman-Martinez, A.H. Hoveyda, J. Am. Chem. Soc. *2010, 132* (31), 10634-7 [DOI: 10.1021/ja104254d].

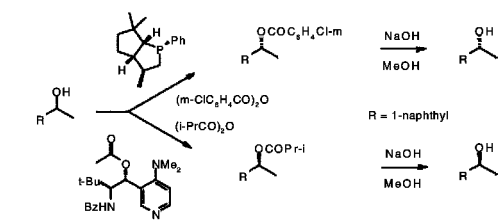
4-Dimethylaminopyridinium perfluorooctanoate *DMAP·$C_7F_{15}COOH$*
N,N′-Diiodo-N,N′-1,2-ethanediylbis(p-toluenesulfonamide) *TsN(I)CH_2CH_2N(I)Ts*
O-Acylation OH → OAc

with DMAP cf. *29*, 184; with readily recoverable and recyclable 4-dimethylaminopyridinium perfluorooctanoate under base- and solvent-free conditions s. D. Vuluga, J. Legros, B. Crousse, D. Bonnet-Delpon, Chem. Eur. J. *2010, 16* (6), 1776-9 [DOI: 10.1002/chem.200902982]; O-acylation of alcohols and phenols with the recyclable, Brønsted acidic ionic liquid, N-methyl-N-(3-sulfopropyl)morpholinium hydrogen sulfate, as catalyst under solvent-free conditions s. C. Yue, Q. Liu, T. Yi, Y. Chen, Monatsh. Chem. *2010, 141* (9), 975-8 [DOI: 10.1007/s00706-010-0353-x]; under heterogeneous conditions with benzyltriphenylphosphonium tribromide for the acetylation and methoxymethylation of alcohols s. F. Shirini, G.H. Imanzadeh, S.A.R. Mousazadeh, I. Mohammadpoor-Baltork, M. Abedin, Chin. Chem. Lett. *2010, 21* (10), 1187-90 [DOI: 10.1016/j.cclet.2010-04.031]; O-acylation of prim., sec. and tert. alcohols and phenols, also N-acylation and S-acylation, with N,N′-diiodo-N,N′-1,2-ethanediylbis(*p*-toluenesulfonamide) as catalyst under solvent-free conditions s. R. Ghorbani-Vaghei, Z. Toghraei-Semiromi, Phosphorus, Sulfur Silicon Relat. Elem. *2010, 185* (8), 1701-7 [DOI: 10.1080/10426500903241721]; acetylation of alcohols, phenols and amines with melamine-trisulfonic acid s. F. Shirini, M.A. Zolfigol, A.-R. Aliakbar, J. Albabii, Synth. Commun. *2010, 40* (7), 1022-8 [DOI: 10.1080/00397910903029941]; mild, solvent-free procedure for the acetylation of alcohols and phenols, also formylation with formic acid, with *p*-toluenesulfonyl chloride as catalyst s. A. Khazaei, A. Rostami, F. Mantashlo, Chin. Chem. Lett. *2010, 21* (12), 1430-4 [DOI: 10.1016/j.cclet.2010.05.025].

Polyethylene glycol-based bis(imidazolium methanesulfonates) s. under I_2 ←
Silica s. under Sulfonic acid and $H_3W_{12}O_{40}$ *SiO_2*
Titanium dioxide-zirconium dioxide s. under H_3PO_4 *TiO_2-ZrO_2*

Chiral 4,8,8-trimethyl-2-phenyl-2-phosphabicyclo[3.3.0]octane/(R,R)-3-(1-acetoxy-2-benzoylamino-3,3-dimethylbutyl)-4-(dimethylamino)pyridine/triethylamine ←
Catalytic parallel kinetic resolution of sec. alcohols via O-acylation

85.



A soln. of the startg. sec. alcohol (0.1 mmol), *m*-chlorobenzoic anhydride (0.1 mmol), degassed isobutyric anhydride (0.1 mmol) and triethylamine (0.15 mmol) in toluene (0.8 ml) cooled to -40° in a Cryocool, a soln. of chiral 4,8,8-trimethyl-2-phenyl-2-phosphabicyclo[3.3.0]octane·3HBF$_4$ (0.0022 mmol) in methylene chloride (0.088 *M*) and (R,R)-3-(1-acetoxy-2-benzoylamino-3,3-

dimethylbutyl)-4-(dimethylamino)pyridine (0.001 mmol) in the same solvent (0.04 ml) added, the mixture stirred for 3 h, quenched with isopropylamine (0.1 ml), concentrated, worked up with purification by flash chromatography, and the isolated (R)-*m*-chlorobenzoate and (S)-isobutyrate hydrolyzed with 5% NaOH in methanol by warming for 5 min and standing at room temp. for 24 h → (R)-alcohol (Y 44%; e.e. 87%) and (S)-alcohol (Y 33%; e.e. 76%). The mutually compatible [orthogonal] 2-phosphabicyclo[3.3.0]octane and chiral 4-dimethylaminopyridine selectively activate *m*-chlorobenzoic anhydride and isobutyric anhydride, respectively, and the *in situ*-formed acylating agents react preferentially with the (R)- and (S)-enantiomer, respectively, of the startg. alcohol to achieve a unique parallel kinetic resolution via two enantiodivergent pathways. The *m*-chlorobenzoate is obtained with near-ideal enantioselectivity, but the isobutyrate is contaminated by ca. 8% of the (R)-enantiomer as a result of formation of the mixed anhydride (*m*-chlorobenzoic isobutyric anhydride) as by-product, which is preferentially activated by the 2-phosphabicyclo-[3.3.0]octane. F.e. and mechanistic considerations s. T.A. Duffey, J.A. MacKay, E. Vedejs, J. Org. Chem. *2010, 75* (14), 4674-85 [DOI: 10.1021/jo100695z].

Phosphoric acid/titanium dioxide-zirconium dioxide H_3PO_4/TiO_2-ZrO_2
Carboxylic acid esters from acids under acid catalysis COOH → COOR
s. *48,* 169; green procedure for esterification of arylcarboxylic acids with H_3PO_4/TiO_2-ZrO_2 s. R.J. Kalbasi, A.R. Massah, Z. Barkhordari, Bull. Korean Chem. Soc. *2010, 31* (8), 2361-7 [DOI: 10.5012/bkcs.2010.31.8.2361]; with $Bi(OTf)_3$ as precursor of triflic acid s. C. Lherbeti, Synth. Commun. *2010, 40* (7), 1082-7 [DOI: 10.1080/00397910903046846]; methyl esters with methoxy-silica gel in the presence of a protic acid, e.g. 12-phosphotungstic acid, s. J. Li, Y. Peng, J. Chin. Chem. Soc. *2010, 57* (3A), 305-8; with nanoporous sulfonic acid-silica having octyl spectator groups for increased acid strength and hydrophobicity s. J.-P. Dacquin, H.E. Cross, D.R. Brown, T. Düren, J.J. Williams, A.F. Lee, K. Wilson, Green Chem. *2010, 12* (8), 1383-91 [DOI: 10.1039/c0gc00045k].

Bismuth(III) triflate $Bi(OTf)_3$
Carboxylic acid esters from acids s. *48,* 169s*78*

Tosylhydrazine/potassium carbonate/microwaves $K_2CO_3/TsNHNH_2$/[\\\\]
Ethers from oxo compds. CO → C=NNHTs → CH(OR)
via metal-free reductive coupling with *in situ*-prepared tosylhydrazones s. *78,* 88

(S)-3-(2,6-Diisopropylphenyl)-5-phenyl-1-(2-sulfonatophenyl)imidazolinium s. under ←
Cu(OTf)$_2$

p-Toluenesulfonyl chloride *TsCl*
N-Methyl-N-(3-sulfopropyl)morpholinium hydrogen sulfate ←
O-Acylation s. *29,* 184s*78* OH → OAc

Poly(vinylsulfonic acid)-on-polystyrene ←
Syntheses using a polymer-grafted poly(vinylsulfonic acid) as solid acid catalyst ←
Heterogeneous esterification s. *78,* 411

p-Toluenesulfonic acid *TsOH*
Phosphonic acid esters from phosphonic acids $PO(OH)_2$ → $PO(OR)_2$
2-Aryltetrahydrofuran-2-ylphosphonic acid diethyl esters s. *78,* 267

Saccharin-2-sulfonic acid *SaSA*
O-Acetylation s. *78,* 45 OH → OAc

Nanoporous sulfonic acid-silica RSO_3H-SiO_2
Carboxylic acid esters from acids under acid catalysis s. *48,* 169s*78* COOH → COOR

Melamine-trisulfonic acid ←
O-Acylation s. *29,* 184s*78* OH → OAc

12-Phosphotungstic acid-silica $H_3W_{12}O_{40}$-SiO_2
Carboxylic acid esters from acids under acid catalysis s. *48,* 169s*78* COOH → COOR

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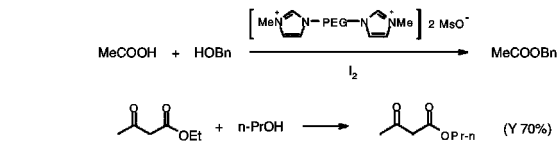
Iodine/polyethylene glycol-based bis(imidazolium methanesulfonates) ←
Carboxylic acid esters from acids COOH → COOR
Iodine-catalyzed esterification in ionic liquids with a simplified work-up

86.

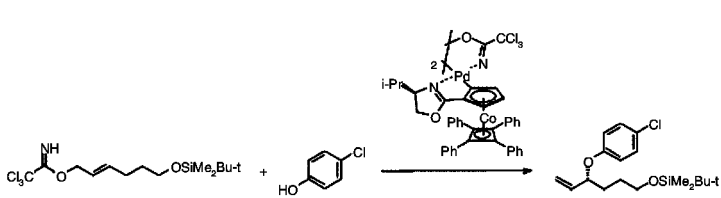


Iodine (0.06 mmol) added to a soln. of acetic acid (2 mmol), benzyl alcohol (1 ml), and toluene (1.5 ml) in IL 1000 (1 ml; prepared by condensing PEG 1000 with 1-methylimidazole in the presence of methanesulfonyl chloride), the mixture refluxed for 6 h (with TLC monitoring), the *homogeneous* soln. cooled to room temp. (whereupon the toluene and ionic liquid phases separated), the upper toluene layer (containing the product) separated by decantation, the solvent evaporated, and the residue worked up with chromatographic purification → benzyl acetate. Y 85%. The ionic liquid containing the catalyst and water was set aside and can be recycled up to 4 times without significant loss of activity (after removal of the water under reduced pressure). The procedure is simple, neutral, environmentally friendly (no metals or toxic reagents) and generally applicable to the esterification of aliphatic carboxylic acids with aliphatic or benzylic alcohols possessing electronically diverse substituents (Cl, NO_2, MeO, Me) on the benzene ring (thirteen examples; Y 80-94%). The yield with *tert*-butanol, however, was only moderate (61%), and there was no reaction with arylcarboxylic acids. F.e., **also catalytic transesterification of β-ketocarboxylic acid esters** (twelve examples; Y 51-80%) s. Y. Ren, C. Cai, Synth. Commun. *2010*, *40* (11), 1670-6 [DOI: 10.1080/00397910903161660].

Benzyltriphenylphosphonium tribromide *$[Ph_3PBn]Br_3$*
O-Acylation s. *29*, 184s*78* OH → OAc

Chiral cobaltocene-functionalized palladacyclic Δ^2-oxazoline complex ←
Aryloxy-2-ethylenes from (E)-2-ethylenetrichloroacetimidates and phenols C(OAr)C=C
Palladium(II)-catalyzed asym. conversion with allyl shift

87.



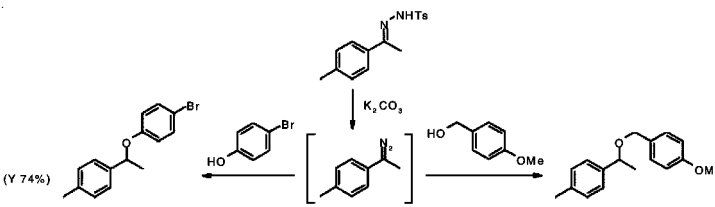
Chiral cobaltocene-functionalized palladacyclic oxazoline complex [((S$_p$,R)-COP-NHCOCCl$_3$)$_2$] (1 mol%) added to a soln. of (E)-6-(*tert*-butyldimethylsilyloxy)hex-2-enyl 2,2,2-trichloroacetimidate (0.26 mmol) and 4-chlorophenol (5 eq.) in chloroform (0.26 ml) in a glass vial, the vial sealed under argon, the mixture heated at 38° for 12 h, concentrated *in vacuo*, and purified by flash chromatography on silica → (R)-*tert*-butyl[4-(4-chlorophenoxy)hex-5-enyloxy]dimethylsilane. Y 86% (e.e. 95%). Previous work [s. S.F. Kirsch, L.E. Overman, N.S. White, Org. Lett. *2007*, *9* (5), 911-3 [DOI: 10.1021/ol070110b]] using the closely-related chiral COP-acetate analog as catalyst had demonstrated similar transformations with a series of (*Z*)-allyl trichloroacetimidates, whereas (E)-isomers had undergone preferential [3.3]-sigmatropic rearrangement (cf. *72*, 183). The present, modified catalyst inexplicably and dramatically altered the course of the reaction for (E)-isomers, however, affording allyl phenyl ethers with electron-diverse phenols, with high selectivity for the branched isomer (twenty-one examples; Y 45-88%; e.e. 78-98%; 3-nitrophenol

gave poor enantioselectivity due to solubility problems). The reaction was successful using methylene chloride or chloroform as solvent and was compatible with *ester*, carbamate, silyl ether, aldehyde, ketone, halo and ether functionality. F.e.s. A.C. Olson, L.E. Overman, H.F. Sneddon, J.W. Ziller, Adv. Synth. Catal. *2009*, *351* (18), 3186-92 [DOI: 10.1002/adsc.200900678].

Nitrogen ↑ OC ↓↑ N

Potassium carbonate/microwaves K_2CO_3/[\\\\]
Ethers from tosylhydrazones by metal-free reductive coupling C=NNHTs → CH(OR)

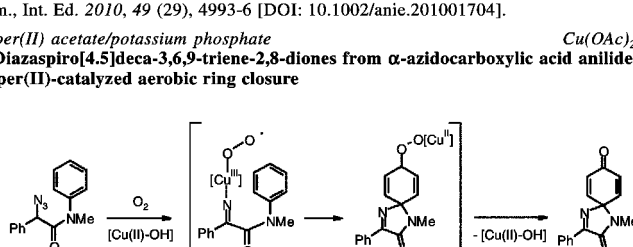
88.



A microwave vial containing K_2CO_3 (3.5 eq.), *p*-methoxybenzyl alcohol (0.3 mmol), the startg. tosylhydrazone (2 eq.) and fluorobenzene (1-1.5 ml) sealed with a septum, the vessel placed into the microwave cavity of a Biotage Initiator microwave apparatus, irradiated for 2 h at 155°, cooled to room temp. under a propelled air flow, and worked up with purification by chromatography on silica gel → 1-methoxy-4-[(1-*p*-tolylethoxy)methyl]benzene. Y 66%. The procedure is simple, environmentally friendly (no metals!), and is generally applicable to the coupling of a wide range of alcohols (primary, secondary, tertiary, benzylic and allylic) in good yield (57-74%; six examples). More significant pharmaceutically, it is also suitable for preparing **phenolethers** from phenols (up to the 25 mmol level), irrespective of the electronic nature or position of ring substituents, and notably tolerating a range of functionality, incl. halogen, ester, aldehyde, nitro and CF_3. The tosylhydrazones may be derived from electronically diverse aromatic or aliphatic aldehydes and ketones (incl. cyclic ketones) (fifteen examples; Y 40-82%), the corresponding thermal method required longer reaction times and high temperatures. A one-pot conversion **from oxo compds.** was also effected by preliminary heating of the substrate with tosylhydrazine under microwave irradiation for 30 min prior to coupling with the phenol (two examples; Y 63-75%). Reaction is presumed to involve initial cleavage of the tosylhydrazone to give the corresponding diazo compd. which then undergoes denitrogenation to the carbene before insertion into the H-O bond. F.e.s. J. Barluenga, M. Tomás-Gamasa, F. Aznar, C. Valdés, Angew. Chem., Int. Ed. *2010*, *49* (29), 4993-6 [DOI: 10.1002/anie.201001704].

Copper(II) acetate/potassium phosphate $Cu(OAc)_2/K_3PO_4$
1,4-Diazaspiro[4.5]deca-3,6,9-triene-2,8-diones from α-azidocarboxylic acid anilides ○
Copper(II)-catalyzed aerobic ring closure

89.

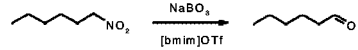


$Cu(OAc)_2$ (0.105 mmol) and K_3PO_4 (0.515 mmol) added to a soln. of 2-azido-N-methyl-N,2-diphenylacetamide (0.515 mmol) in dry DMF (5.1 ml), stirred at 80° for 3.5 h under O_2, filtered

through Celite, the filtrate cooled to room temp., quenched with 1 *M* aq. HCl, and worked up with flash chromatographic purification → 1-methyl-3-phenyl-1,4-diazaspiro[4.5]deca-3,6,9-triene-2,8-dione. Y 77%. The procedure is applicable to a range of α-arylated substrates possessing electron-withdrawing or -donating groups (notably chloroaryl derivs.), but there was no reaction with α-alkylated analogs. An electron-donating (e.g. MeO) group on the anilide ring was also supported, but mixtures of products were obtained with chloroanilides (sixteen examples in all; Y 42%, 60-83%). Reaction is presumed to involve initial denitrogenation to give an iminylcopper(II) species which undergoes intramolecular 1,4-addition across the anilide ring prior to oxygenation and elimination of a copper(II) hydroxide species to continue the cycle. One of the oxygen atoms of O_2 was incorporated, as determined by studies with $^{18}O_2$. F.e.s. S. Chiba, L. Zhang, J.-Y. Lee, J. Am. Chem. Soc. *2010*, *132* (21), 7266-7 [DOI: 10.1021/ja1027327].

Sodium perborate/1-n-butyl-3-methylimidazolium triflate *$NaBO_3$/[bmim]OTf*
Oxo compds. from aliphatic nitro compds. $CHNO_2 \rightarrow CO$
Nef reaction in ionic liquids under mild conditions with a simplified work-up

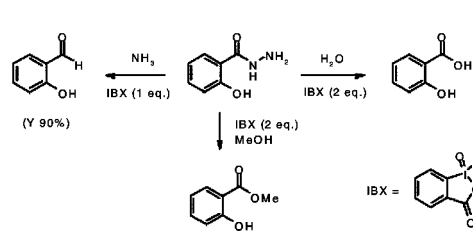
90.



A mixture of the startg. nitro compd. and $NaBO_3$ (1.5 eq.) in 1-*n*-butyl-3-methylimidazolium triflate (1 ml) heated at 70° for 6 h, cooled to room temp., the product extracted with ether, and worked up → hexanal. Conversion 80% (Y 75%). For recycling of the ionic liquid, it was added (without any treatment) to further amounts of substrate and oxidant, and a further oxidation carried out without significant decrease in efficiency. The procedure is mild, safe, and efficient, and permits a simple recovery of the ionic liquids for reuse; furthermore, unlike many established methods, it is applicable to both aliphatic (or cycloaliphatic) sec. nitro compds. *as well as* prim. nitro compds. with no overoxidation of the products. Basic aq. hydrogen peroxide was also an effective oxidant *at room temp.* affording almost identical yields (40-96%; conversion 60-98%; eight examples). F.e. and comparison of ionic liquids s. O. Bortolini, A. De Nino, A. Garofalo, L. Maiuolo, B. Russo, Synth. Commun. *2010*, *40* (16), 2483-7 [DOI: 10.1080/00397910903267921].

o-Iodoxybenzoic acid *$ArIO_2$*
Controlled oxidation of carboxylic acid hydrazides with hypervalent iodine $C(O)NHNH_2 \rightarrow COOH,R$

91.



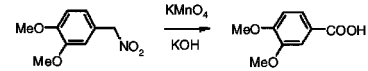
Carboxylic acids. 2-Hydroxybenzoic acid hydrazide added in one portion to a stirred soln. of *o*-iodoxybenzoic acid (2 eq.) in chloroform/water (1:1), the mixture stirred at room temp. until substrate consumed (15 min), diluted with chloroform and 10% aq. $NaHCO_3$, the aq. layer separated, acidified with dil. HCl, extracted with chloroform, the extracts washed with water, dried (Na_2SO_4), concentrated *in vacuo*, and purified by chromatography on silica → 2-hydroxybenzoic acid. Y 92%. Conversion to electron-diverse (het)ar. and aliphatic carboxylic acids was complete within 10-60 min under these mild conditions (eight examples; Y 75-92%), with electron-rich derivs. affording the fastest reaction rates and highest yields. Replacing water with methanol allowed selective formation of the corresponding **carboxylic acid methyl esters** (eight examples;

Y 70-85%), while use of ammonia (with only 1 eq. oxidant) gave rise to **aldehydes** (eight examples; Y 73-94%). F.e.s. B.S. Takale, V.N. Telvekar, Chem. Lett. *2010*, *39* (6), 546-7 [DOI: 10.1246/cl.2010.546].

Phenyl iodosoacetate or Sodium periodate *$PhI(OAc)_2$ or $NaIO_4$*
p-Quinones from p-diamines s. *78*, 200 ←

Potassium permanganate/potassium hydroxide *$KMnO_4$/KOH*
Rapid oxidations with potassium permanganate under continuous flow ←

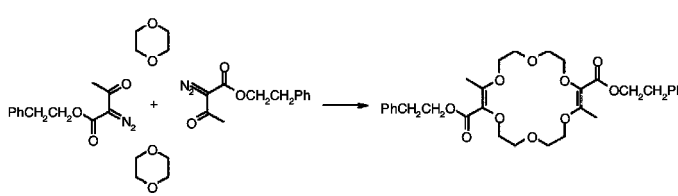
92.



Carboxylic acids from prim. nitro compds. A soln. of the startg. nitroalkane (1 eq.) and KOH (1.2 eq.) in methanol (0.167 *M*) pumped via a T-piece into a coiled [perfluoroalkoxy] tube reactor (0.5 mm internal diameter) together (via a second inlet) with a soln. of $KMnO_4$ (2 eq.) and Na_2HPO_4 (2 eq.) in water (0.33 *M*) with a residence time of 10 min at room temp., the outlet mixture (as a fine suspension) eluted into a stirred 2-phase mixture of aq. 1 *M* HCl (30 ml) (saturated with NaCl and $Na_2S_2O_3$) and ethyl acetate (15 ml), extracted several times with ethyl acetate, dried, and the solvent removed *in vacuo* → product. Y 97%. To avoid possible blockages with MnO_2 within the T-piece mixer, the latter was submerged in an ultrasound bath during reaction and briefly pulsed every few minutes. The methodology is simple, cheap, efficient and rapid for the classical permanganate oxidation of alcohols, aldehydes and nitroalkanes, delivering clean products with excellent purity with a simple non-chromatographic work-up; significantly, by using a larger 14 ml coil reactor, operating under continuous flow at steady state over several hours, the process can be scaled up to the 50 mmol level! F.e.s. J. Sedelmeier, S.V. Ley, I.R. Baxendale, M. Baumann, Org. Lett. *2010*, *12* (16), 3618-21 [DOI: 10.1021/ol101345z].

Rhodium(II) octanoate *$Rh_2(OCOC_7H_{15})_4$*
Regio- and stereo-selective rhodium(II)-catalyzed 2-component (4 molecule) synthesis of sym. polyether macrocyclics ○

93.



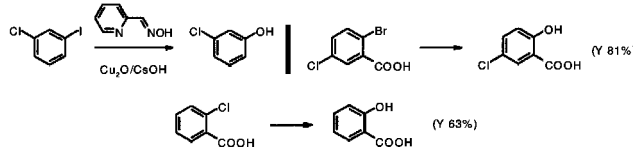
at high concentration. A 10 mmol soln. of $[Rh_2(OCOC_7H_{15})_4]$ in dioxane (0.64 ml) added in one portion to the startg. α-diazo-β-keto-ester (0.64 mmol) in a screw-cap vial, the latter flushed with argon and capped, the mixture stirred at 60° for 12 h, cooled to 20°, the solvent removed under reduced pressure, and the residue worked up with purification by flash chromatography on neutral Al_2O_3 → product. Y 62%. Reaction takes place in moderate to high yield within the concentration range of 2 to 0.5 *M* (up to the 7 mmol scale) for this non-templated condensation of α-diazo-β-ketoesters with 1,4-dioxane, tetrahydropyran or tetrahydrofuran, yields, surprisingly, decreasing with higher dilution! Several rhodium(II) carboxylates were effective but the lipophilic octanoate was preferred on the grounds of solubility. Steric hindrance was a complicating factor with diazo-esters bearing larger alkyl groups attached to the keto group, longer reaction times at room temp. being necessary to achieve acceptable yields. Significantly, there was no loss of the diazo-ester by intramolecular lactonization. The elevated yields at high concentration are in accord with the mechanistic proposition that reaction involves intermediate formation of stabilized oxonium ylids. F.e. (eleven; Y 14-75%) s. W. Zeghida, C. Besnard, J. Lacour, Angew. Chem., Int. Ed. *2010*, *49* (40), 7253-6 [DOI: 10.1002/anie.201003559].

Halogen ↑ OC ↓↑ Hal

Without additional reagents *w.ar.*
3-Alkoxyphthalides from 2-acyl-7-chlorotropones s. *78*, 178 ○

Copper(I) oxide/pyridine-2-aldoxime/cesium hydroxide/tetra-n-butylammonium bromide ←
Copper(I) iodide/lithium pipecolinate/sodium hydroxide/tetra-n-butylammonium fluoride ←
Copper(I) iodide/N,N′-dimethylethylenediamine/potassium phosphate/microwaves ←
Phenols from ar. halides in water under copper(I) catalysis Hal → OH

94.



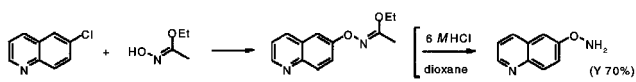
m-Chloroiodobenzene (1 mmol) and water (1 ml) added sequentially via syringe to a Schlenk tube containing Cu_2O (0.05 mmol), CsOH (3 mmol), pyridine-2-aldoxime (0.1 mmol) and tetra-*n*-butylammonium bromide (0.2 mmol) under N_2 at room temp., the tube sealed, placed in a preheated oil bath at 110° for 48 h under N_2, cooled to room temp., HCl (1 *N*; 2 ml) added (to pH 2-3), and worked up with purification by chromatography on silica gel → *m*-chlorophenol. Y 71%. The procedure is simple, mild, practical, inexpensive (relative to palladium-catalyzed methods), environmentally friendly and applicable to a wide range of aryl iodides and bromides in good yield (ca. twenty examples; Y 45-95%), substrates possessing electron-withdrawing groups being more reactive than those with electron-donating groups. Furthermore, various functional groups remained unaffected (F, NO_2, CHO, OH and COOH). Ar. chlorides were also generally unreactive, with the exception of *o*-chlorocarboxylic acids for which an interesting *ortho*-effect was at play; this was also evident with N-(*o*-bromoaryl)anilides, while N-(*o*-bromophenyl)acetamide underwent simultaneous N-deacetylation to give *o*-aminophenol. Pyridine-2-aldoxime was the most efficient ligand for the conversion, and tetra-*n*-butylammonium bromide and CsOH the optimum phase transfer catalyst and base, respectively. F.e.s. D. Yang, H. Fu, Chem. Eur. J. *2010*, *16* (8), 2366-70 [DOI: 10.1002/chem.200903468]; with CuI, lithium pipecolinate, NaOH and Bu_4NF in water [at 130°] s. L. Jing, J. Wei, L. Zhou, Z. Huang, Z. Li, X. Zhou, Chem. Commun. *2010*, *46* (26), 4767-9 [DOI: 10.1039/c0cc00434k]; with CuI/DMEDA/K_3PO_4 under microwave irradiation s. A. Mehmood, N.E. Leadbeater, Catal. Commun. *2010*, *12* (1), 64-6 [DOI: 10.1016/j.catcom.2010.07.011].

Silver acetate s. under Pd(OAc)₂ *AgOAc*
2-(Dicyclohexylphosphinomethyl)-1,3-bis(2,6-diisopropylphenyl)imidazolium iodide/cesium carbonate s. under Bis(cinnamylpalladium chloride) ←

Palladium(II) acetate/silver acetate *Pd(OAc)₂/AgOAc*
Palladium(II)-catalyzed acoxylation of arenes with iodosocarboxylates H → OCOR
2-Pyridylsilyl as a traceless directing group s. *78*, 178

Bis(π-allylpalladium chloride)/2-di-tert-butylphosphino-2′,4′,6′-triisopropyl-3,6-dimethoxybiphenyl/cesium carbonate ←
Palladium(II)-catalyzed O-arylation of hydroximinoesters with ar. halides C(OR)=NOH → C(OR)=NOAr

95.



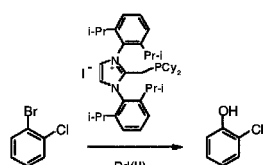
Ethyl acetohydroximate (1.25 eq.) added to an oven-dried vial containing a mixture of $[allylPdCl]_2$ (2.5 mol%), 2-di-*tert*-butylphosphino-2′,4′,6′-triisopropyl-3,6-dimethoxybiphenyl (5 mol%),

Cs_2CO_3 (1.5 eq.) and 6-chloroquinoline (1 mmol) in toluene (2 ml) under argon, the vial sealed, the mixture stirred vigorously at 65° for 2 h, cooled, diluted with ethyl acetate, filtered through silica, concentrated *in vacuo*, and purified by flash chromatography on silica → ethyl N-quinolin-6-yloxyacetimidate. Y 92%. Use of acetohydroximate as a hydroxylamine equivalent allowed synthesis of inaccessible O-arylhydroxylamine derivs. under relatively mild conditions. The method was successful for electron-diverse (het)ar. chlorides, bromides and iodides, with electron-poor or -neutral bromides being most effective (fifteen examples; Y 70-95%) and sterically-hindered *o*-subst. ar. halides giving optimal results with a less bulky ligand [*tert*-Butyl XPhos]. Products were hydrolyzed rapidly (aq. HCl/0°/1 h) to the corresponding **aroxylamines** (four examples; Y 70-91%), and in the presence of a ketone at 70° provided rapid one-pot access (1-2 h) to **2,3-di-subst. benzofurans** (six examples; Y 55-88%). F.e.s. T.J. Maimone, S.L. Buchwald, J. Am. Chem. Soc. *2010*, *132* (29), 9990-1 [DOI: 10.1021/ja1044874].

Bis(cinnamylpalladium chloride)/2-(dicyclohexylphosphinomethyl)-1,3-bis(2,6-di-isopropylphenyl)imidazolium iodide/cesium carbonate ←

Homogeneous palladium-catalyzed coupling with 2-phosphinomethyl-1,3-bis(2,6-diisopropylphenyl)imidazolium iodides as readily recyclable, hindered ligands ←

96.



A new family of hindered, *cationic* phosphine ligands has evolved for homogeneous palladium-catalyzed Buchwald-Hartwig amination, Sonogashira and Suzuki coupling, and C-O coupling, with the particular advantage of ready retrievability for recycling many times without significant loss of activity. Such ligands are notably invaluable for the challenging formation of **phenols from ar. bromides** for which there exists, up to now, no simple means for recycling of the catalyst. **E:** A Schlenk tube containing [(cinnamyl)PdCl]$_2$ (1 mol%), 2-(dicyclohexylphosphinomethyl)-1,3-bis(2,6-diisopropylphenyl)imidazolium iodide (4 mol%) and CsOH·H_2O (3 eq.) sealed with a septum and secured under argon, the startg. aryl bromide (1 eq.) and dried dioxane (1.2 ml) added, stirred and heated to 100° for 20 h, and worked up after acidification → product. Y 97%. Although the ligand is insoluble at room temp., it forms a soluble palladium phosphine complex which can be easily separated from the precipitated phenolate. It was thus retrieved and recycled eight times (without addition of any further ligand) with effectively no decrease in yield (up to the 20 mmol scale), and offering the highest turnover numbers ever recorded for this conversion. The ligand is stable in air and can be stored for several months under water without significant decomposition. Commercially available mono- and bi-dentate phosphine ligands are inadequate for the conversion, affording low yields or no product formation at all. The startg. aryl bromides may possess electron-donating or -withdrawing groups (incl. *o*- and *o,o'*-di-subst. derivs.), and aromatic chlorine remains unaffected (seven examples; Y 70-97%). Examples are also given of Suzuki coupling, Buchwald-Hartwig amination, and copper-free Sonogashira coupling using the same ligand or 4,5-dimethylimidazolium analogs. F.e. and comparison of dicyclohexylphosphinomethyl with [less effective] di-*tert*-butylphosphinomethyl and diphenylphosphinomethyl ligands, also coupling under microwave enhancement, s. A. Dumrath, X.-F. Wu, H. Neumann, A. Spannenberg, R. Jackstell, M. Beller, Angew. Chem., Int. Ed. *2010*, *49* (47), 8988-92 [DOI: 10.1002/anie.201001787].

Via intermediates *v.i.*

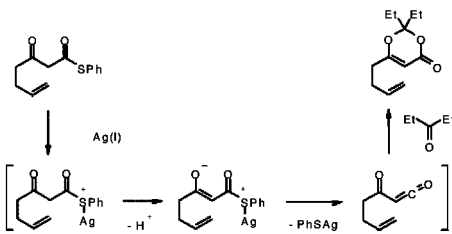
Phenols from ar. bromides via arylsilanes s. *78*, 102 ArBr → ArSi⩽ → ArOH

Sulfur ↑ OC ↓↑ S

Sodium alkoxide *NaOR*
Replacement of sulfonyl groups in 1,1-alkoximinosulfones s. *78*, 463 ←

Silver trifluoroacetate *$AgOCOCF_3$*
2,2,6-Trisubst. 1,3-dioxin-4-ones from β-ketothiolic acid esters and ketones ○
Silver(I)-catalyzed ring closure via α-ketoketenes

97.



under mild conditions. $AgOCOCF_3$ (1.1 eq.) added to a soln. of startg. keto-thiolester (0.577 mmol) and 3-pentanone (3 eq.) in $CDCl_3$ (2 ml), the mixture stirred for 1.5 h, filtered through silica, concentrated *in vacuo*, and purified by flash chromatography → 6-but-3-en-1-yl-2,2-diethyl-1,3-dioxin-4-one. Y 75%. This mild and experimentally simple method requires stoichiometric amounts of Ag(I) for activation of the substrate. To minimize competing reaction of the substrate ketone moiety, acylketene intermediates were trapped with excess (3-fold) ketones (four examples; Y 72-82%). The method failed, however, for relatively hindered ketones (*i*-Pr_2CO and Bn_2CO). Competitive experiments, using diacetone alcohol as the trapping agent, showed exclusive reaction of the tert. alcohol moiety to form the simple β-ketocarboxylic acid ester, with none of the cyclic product observed. F.e.s. A.E. May, T.R. Hoye, J. Org. Chem. *2010, 75* (17), 6054-6 [DOI: 10.1021/jo101372v].

Silver triflate (s.a. under N-Iodosuccinimide and p-Nitrobenzenesulfenyl chloride) *AgOTf*
Oligosaccharide synthesis ←
s. *75*, 108; by a combination of traceless solid-phase and solution-phase synthesis under sonication s. C.T. Tanifum, J. Zhang, C.-W.T. Chang, Tetrahedron Lett. *2010, 51* (33), 4323-7 [DOI: 10.1016/j.tetlet.2010.06.027]; oligosaccharide combinatorial library synthesis using a special hydroxyl protecting group, the uni-chemo hydroxy protection (UCHP) group (composed of oligomeric amino acid derivs.), s. S. Komba, S. Machida, J. Carbohydr. Chem. *2010, 28* (6), 369-93 [DOI: 10.1080/07328300903100661]; polymer-supported synthesis of oligosaccharides using a diisopropylsiloxane linker and trichloroacetimidate donors s. M.M. Kayser, J.L. de Paz, P.M. Nieto, Eur. J. Org. Chem. *2010* (11), 2138-47 [DOI: 10.1002/ejoc.200901445]; use of an acylsulfonamide safety-catch linker for the polymer-based synthesis of hyaluronic acid oligosaccharides s. J.L. de Paz, M.M. Kayser, G. Macchione, P.M. Nieto, Carbohydr. Res. *2010, 345* (5), 565-71 [DOI: 10.1016/j.carres.2009.12.021]; comparison of armed/disarmed building blocks of the D-gluco and D-glucosamino series for chemoselective oligosaccharide synthesis s. T. Kamkhachorn, A.R. Parameswar, A.V. Demchenko, Org. Lett. *2010, 12* (13), 3078-81 [DOI: 10.1021/ol101089u].

Gold(I) chloride-dimethyl sulfide *$AuCl(SMe_2)$*
Sulfoxonium ylids as metal carbene precursors C=S(O)< → CH(OR)
α-Alkoxycarbonyl compds. s. *78*, 192

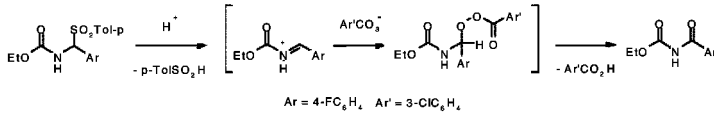
Fluoroboric acid-silica or imidazolium salts s. under N-Iodosuccinimide ←

m-Chloroperoxybenzoic acid/1,1,3,3-tetramethylguanidine $ArCOO_2H/(Me_2N)_2C{=}NH$

N-Functionalized carboxylic acid amides from α-aminosulfones $CH(SO_2Ar)N- \rightarrow C(O)N-$

Mild metal-free oxidation via N-functionalized iminium ions

98.



Ar = 4-FC_6H_4 Ar' = 3-ClC_6H_4

N-Aroylurethans. *m*-Chloroperoxybenzoic acid (4 eq.) added to a soln. of startg. amido-sulfone (1 mmol) in methylene chloride (10 ml) at room temp., *tetramethylguanidine* (1.1 eq.) added dropwise, the mixture stirred for 4 h, diluted with methylene chloride, washed with aq. $NaHSO_3$ and $NaHCO_3$, concentrated *in vacuo*, and purified chromatographically → ethyl N-(4-fluorobenzoyl)carbamate. Y 85%. This direct conversion to imides was successful with electron-diverse α-amidobenzyl sulfones derived from amides, carbamates or sulfonamides, with significantly higher yields obtained for electron-poor derivs. (attributed to the greater acidity of the benzylic proton) and a low yield (46%) for a sterically-hindered *o*-chloro-deriv. (thirteen examples; Y 40-85%). α-Amidoalkyl derivs. were unreactive under these conditions. F.e. and optimization s. F. Martinelli, A. Palmieri, M. Petrini, Eur. J. Org. Chem. *2010* (26), 5085-9 [DOI: 10.1002/ejoc.201000634].

N-Iodosuccinimide/silver triflate or fluoroboric acid-silica or imidazolium salts or trifluoromethanesulfonic acid ←

Glycosides from thioglycosides SR → OR

s. *39*, 189s*75*; selective β-arabinofuranosylation using 2,3-O-xylylenethioglycosides with NIS/AgOTf s. A. Imamura, T.L. Lowary, Org. Lett. *2010, 12* (16), 3686-9 [DOI: 10.1021/ol1015209q]; with a 2-[(*p*-fluorophenyl)sulfonyl]ethoxycarbonyl [Fsec]-protected thioglycoside s. S. Spjut, W. Qian, M. Elofsson, Molecules *2010, 15* (8), 5708-20 [DOI: 10.3390/molecules15085708]; glycosylation of *prim*-hydroxyl groups with thioglucosaminide derivs. using NIS/HBF_4-silica gel s. M. Kurosu, K. Li, Heterocycles *2010, 80* (1), 115-23 [DOI: 10.3987/COM-09-S(S)24]; with NIS and an imidazolium ionic liquid in methylene chloride s. M.C. Galan, K. Jouvin, D. Alvarez-Dorta, Carbohydr. Res. *2010, 345* (1), 45-9 [DOI: 10.1016/j.carres.2009.09.034]; glycosylation from the non-reducing end with a glycosyl sulfoxide as acceptor using NIS/TfOH s. T. Kajimoto, K. Arimitsu, M. Ozeki, M. Node, Chem. Pharm. Bull. *2010, 58* (5), 758-64; α-selective glycosylation with acetyl-protected 2-deoxy- and 2,6-dideoxy-thioglycosides using BSM/Tf_2O s. Y.-S. Lu, Q. Li, Y. Wang, X.-S. Ye, Synlett *2010* (10), 1519-24 [DOI: 10.1055/s-0029-1219943].

1,3-Dibromo-5,5-dimethylhydantoin ←

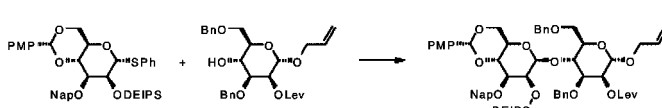
Aldehydes from cyclic mercaptals s. *28*, 182s*78* $C(SR)_2 \rightarrow CO$

p-Nitrobenzenesulfenyl chloride/silver triflate/2,6-di-tert-butyl-4-methylpyridine ←

Oligosaccharide synthesis SPh → OR

based on a versatile set of orthogonal O-protective groups

99.



PMP = p-$MeOC_6H_4$, Nap = 2-naphthylmethyl, DEIPS = $SiEt_2Pr$-*i*, Lev = $C(O)CH_2CH_2C(O)CH_3$

Orthogonally protected β-*D*-mannosyl-(1→4)-*D*-mannosides. Flame-activated 4 Å molecular sieves added to a mixture of phenyl 4,6-*p*-methoxybenzylidene-2-*O*-(diethylisopropylsilyl)-3-*O*-(2-naphthylmethyl)-1-thio-α-*D*-mannopyranoside (1 mmol), AgOTf (2 mmol) and DTBMP (3 mmol) in methylene chloride (10 ml), stirred for 15 min at room temp. in the dark, cooled to -78°, *p*-nitrobenzenesulfenyl chloride (1.1 mmol) in the same solvent (2 ml) added dropwise,

stirred for 10 min at -78°, allyl 3,6-di-*O*-benzyl-2-*O*-levulinoyl-α-*D*-mannopyranoside (1.25 mmol) in methylene chloride (2 ml) added dropwise, stirred for 1 h at -78°, slowly warmed to -35° over 3 h, quenched with satd. aq. $NaHCO_3$, and worked up with purification by chromatography on silica gel → allyl 4,6-di-*O*-*p*-methoxybenzylidene-2-*O*-(diethylisopropylsilyl)-3-*O*-(2-naphthylmethyl)-β-*D*-mannopyranosyl-(1→4)-3,6-di-*O*-benzyl-2-*O*-levulinoyl-α-*D*-mannopyranoside. Y 73% (β/α >20:1). The combination of diethylisopropylsilyl and 2-naphthylmethyl at C(2) and C(3), respectively, of the glycosyl donor with levulinoyl at C(2) of the accepting *allyl* glycoside are ideal for this disaccharide synthesis with excellent anomeric selectivity; more importantly, each of the four protecting groups can be removed selectively without affecting the other by established methods, thereby freeing up further hydroxyl groups for subsequent elaboration of **highly branched oligosaccharides** (e.g. part-structures of the lipopolysaccharide of *Francisella tularensis*). N-Benzenesulfinylpiperidine/Tf_2O was also a suitable coupling agent (Y 40% with the same stereoselectivity), but other combinations of orthogonol protective groups were less effective. F.e.s. T.J. Boltje, C. Li, G.-J. Boons, Org. Lett. *2010*, *12* (20), 4636-9 [DOI: 10.1021/ol101951u].

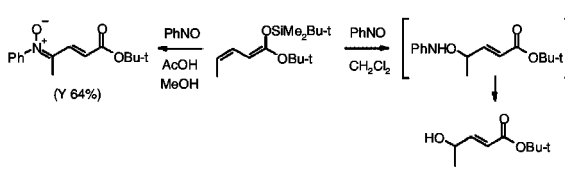
Trifluoromethanesulfonic acid s. under N-Iodosuccinimide *CF_3SO_3H*

Chloro(cyclooctadiene)iridium(I) dimer *$[Ir(cod)Cl]_2$*
Sulfoxonium ylids as metal carbene precursors C=S(O)< → CH(OR)
α-Alkoxycarbonyl compds. s. *78*, 192

Remaining Elements ↑ OC ↓↑ Rem

Nitrosobenzene/pyridine hydrofluoride *PhNO/Py·HF*
α,β-Ethylene-γ-hydroxycarboxylic acid esters C(OH)C=C-COOR
from O-silyl O-alkyl vinylketene acetals
via stereospecific vinylogous [Mukaiyama] aldol-type reaction with nitrosobenzene

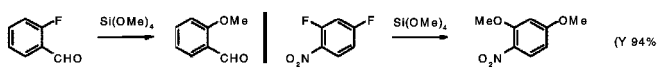
100.



under mild conditions. Py·HF (2 eq.) and ((1Z,3Z)-1-*tert*-butoxypenta-1,3-dien-1-yloxy)(*tert*-butyl)dimethylsilane (0.2 mmol) added sequentially to a soln. of nitrosobenzene (2.2 eq.) in methylene chloride (1 ml) at -78°, the mixture stirred for 48 h, warmed to 10° over 2 h, and purified by flash chromatography on silica → (E)-*tert*-butyl 4-hydroxypent-2-enoate. Y 67%. Novel use of nitrosobenzene in the Mukaiyama aldol reaction effected near exclusive γ-aminoxylation of acyclic substrates, affording (E)-allylic alcohols via *in situ* hydrolysis (eleven examples; Y 39-77%), with phenyl-terminated and cyclic substrates giving mixtures of α/γ-hydroxy derivs. (1:4 and 1.9:1; Y 70% and 72% respectively). Low yields in some cases were attributed to substrate instability or product volatility, and poor yields were also obtained with β-subst. substrates (Y 20% and 34%). Other solvents and fluoride sources were inferior and, unexpectedly, conducting the illustrated reaction in acetic acid/methanol afforded a **γ-nitrone** (Y 64%). Alternative formation of the aminoxy intermediate via a [4+2]-cycloaddition pathway was discounted on the basis of experimental evidence. F.e.s. G.-Q. Tian, J. Yang, K. Rosa-Perez, Org. Lett. *2010*, *12* (21), 5072-4 [DOI: 10.1021/ol11021433].

m-Chloroperoxybenzoic acid *$ArCO_2OH$*
Oxidative cleavage of cyclic boronic acid monoesters C
α-(*o*-Hydroxyaryl)-β-hydroxyketones s. *78*, 307

Tetra-n-butylammonium fluoride *Bu_4NF*
Phenolethers from electron-deficient ar. fluorides and alkoxysilanes F → OR
Fluoride-mediated coupling under mild, solvent-free conditions



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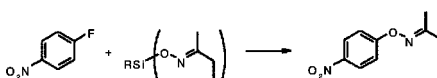
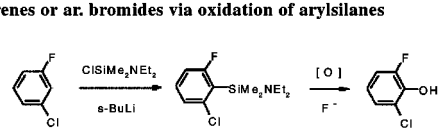
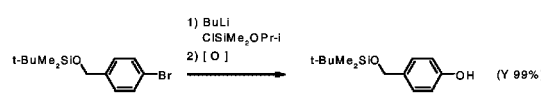


A mixture of 2-fluorobenzaldehyde (1 mmol), tetramethoxysilane (0.6 eq.) and $Bu_4NF{\cdot}3H_2O$ (1 eq.) heated at 80°, with stirring, in a Schlenk tube until reaction complete (TLC; 9 h), and the crude mixture purified directly by chromatography on silica gel → 2-methoxybenzaldehyde. Y 85%. A variety of *p*-subst. (formyl, acetyl, cyano, nitro) ar. fluorides similarly afforded the corresponding methyl (or ethyl) phenolethers in yields of 84-99% (eight examples). Steric hindrance was not a problem, as evidenced by the illustrated *o*-subst. ar. fluoride, but the yield for the less-activating *m*-subst. analog fell to 41%. No reaction occurred with electron-neutral or -rich ar. fluorides. High yields were also obtained using trimethoxy(phenyl)silane in place of the orthosilicates, and use of either methyl- or vinyl-tri(ethylmethyl ketoximo)silane gave rise to **O-aryloximes** in high yield. F.e. incl. gram-scale reactions s. W. Xiong, Q. Ding, J. Chen, J. Ding, H. Wu, J. Chem. Res. *2010*, *34* (7), 395-8 [DOI: 10.3184/030823410X12791804205820].

Tetra-n-butylammonium fluoride/potassium hydrogen carbonate/hydrogen peroxide ←
Phenols from arenes or ar. bromides via oxidation of arylsilanes ArSi⩽ → ArOH



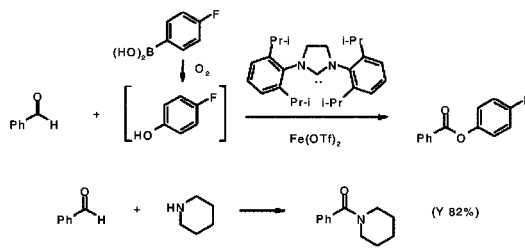
102.



One-pot conversion via *o*-directed silylation. A soln. of *sec*-butyllithium (1.2 eq.) in hexanes (0.92 ml) added to a soln. of 1-chloro-3-fluorobenzene (1.91 mmol) and TMEDA (1.2 eq.) in THF (5 ml) at -78°, the mixture stirred for 3 h, diethylaminodimethylsilyl chloride (1.4 eq.) added, the mixture stirred for 4 h, warmed to room temp., concentrated *in vacuo*, methanol/THF (1:1; 3 ml), $KHCO_3$ (2 eq.), a soln. of *n*-Bu_4NF (0.1 eq.) in THF (0.2 ml) and 35% aq. H_2O_2 (6 eq.) added to the residue, the soln. stirred at room temp. for 16 h, quenched with aq. NH_4Cl, extracted with ether, concentrated *in vacuo*, and purified by flash chromatography → 2-chloro-6-fluorophenol. Y 99%. This versatile and efficient phenolation strategy produced stable arylsilane intermediates via *o*-directed lithiation or halogen→lithium exchange protocols (eighteen examples; Y 63-99%), which were subjected to subsequent oxidation in the presence of fluoride (Y 35-99%). The one-pot procedure, however, gave comparable (and sometimes significantly better) results (seventeen examples; Y 43-99%) in the presence of carbamate, amide, fluoride, chloride, ether and silyl ether functionality. F.e. and optimization s. S. Bracegirdle, E.A. Anderson, Chem. Commun. *2010*, *46* (20), 3454-6 [DOI: 10.1039/b924135c].

Iron(II) triflate/1,3-bis(2,6-diisopropylphenyl)imidazolidin-2-ylidene *$Fe(OTf)_2$/NHC*
Carboxylic acid aryl esters from aldehydes and arylboronic acids by iron(II)-catalyzed aerobic oxidation CHO → COOAr

103.

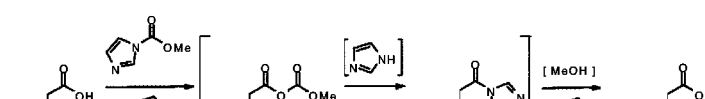


Arylcarboxylic acid aryl esters. A mixture of dry dioxane (1.5 ml), 1,3-bis(2,6-diisopropylphenyl)-Δ^2-imidazolinium chloride (20 mol%) and sublimed KOBu-*t* (0.247 mmol) allowed to react under N_2 at room temp. for 20 min, $Fe(OTf)_2$ (20 mol%) added, left for a further 5 min at room temp., the startg. arylboronic acid (0.247 mmol) and aldehyde (0.247 mmol) added sequentially, the N_2 atmosphere replaced by air, the mixture heated at 90°, volatiles removed after 24 h under reduced pressure, and the product isolated by preparative thin layer chromatography → 4-fluorophenyl benzoate. Y 91%. The procedure is mild, eco-friendly [based on aerobic oxygen], efficient with the two reactants in stoichiometric amount, and unaffected by the electronic nature of substituents on either aromatic ring (although poor yields were obtained with *o*-subst. arylboronic acids). Furthermore, reaction was also effected with cyclohexanecarboxaldehydes indicating that it is not limited to ar. aldehydes. The nature of the iron catalyst and the NHC ligand are critical, suggestive of *in situ*-generation of a catalytically active iron(II)-NHC complex, and reaction likely involving intermediate formation of a phenol from the arylboronic acid prior to oxidative esterification. There was no reaction under copper catalysis. F.e. (sixteen; Y 53-97%), also one-pot preparation of **arylcarboxylic acid amides** by interception of the aryl esters with sec. amines (three examples; Y 30-82%), s. J.N. Rosa, R.S. Reddy, N.R. Candeias, P.M.S.D. Cal, P.M.P. Gois, Org. Lett. *2010*, *12* (12), 2686-9 [DOI: 10.1021/ol100302e].

Carbon ↑ OC ↓↑ C

Without additional reagents *w.a.r.*
Carboxylic acid esters from carboxylic acids and N-carbalkoxyimidazoles COOH → COOR

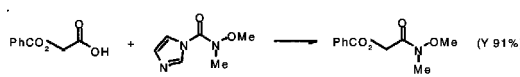
104.



R = Bn

Dry acetonitrile (1 ml) added to a vial containing N-benzyloxycarbonylglycine (0.5 mmol) and methyl imidazolecarbamate (2 eq.), the vial quickly sealed with a plastic cap [*Caution!* gas is evolved during the course of the reaction], the mixture stirred at 23° for 15 min, then at 80° for 24 h, cooled to room temp., the vial opened carefully [*Caution!* vial under pressure], volatiles removed *in vacuo*, the residue dissolved in ether, washed with 1 *M* aq. HCl, and concentrated *in vacuo* → methyl N-benzyloxycarbonylglycinate. Y 93%. This novel procedure utilizes inexpensive, stable and non-toxic reagents and appears general for esterification (methyl, benzyl, allyl) of

electron-diverse ar. (using DMF as solvent) and aliphatic carboxylic acids (thirty-eight examples; Y 70-97%) in the presence of amide, carbamate (Fmoc amines are cleaved), ar. ether, halo, ketone and *phenol* functionality. A sulfonamide was partially N-acylated under these conditions (Y 7%) and the method is unsuitable for esterification of chiral amino acid derivs. due to extensive racemization. The mechanism is thought to involve formation of an O-acyl carbonate which acylates imidazole (an N-acylimidazole was isolated from a reaction where generated methanol was allowed to escape). The method also proved useful for the prepn. of **hydroxamic acid esters** [Weinreb amides] **from carboxylic acids** and N-methoxy-N-methylimidazole-1-carboxamide (five examples; Y 88-92%).



F.e. and substrate prepn. s. S.T. Heller, R. Sarpong, Org. Lett. *2010*, *12* (20), 4572-5 [DOI: 10.1021/ol1018882].

Irradiation s. under I_2 ///

Sodium azide s. under BF_3 NaN_3

Potassium hydrogen phosphate or Lithium bromide/diethylamine K_2HPO_4 *or LiBr/*Et_2NH

Transesterification $COOR \rightarrow COOR'$

s. *47*, 182s*76*; methyl esters with K_2HPO_4 s. T. Shinada, M. Hamada, K. Miyoshi, M. Higashino, T. Umezawa, Y. Ohfune, Synlett *2010* (14), 2141-5 [DOI: 10.1055/s-0030-1258491]; with LiBr/Et_2NH, also carboxylic acid amides with amines (cf. *42*, 338), s. M.S. Abaee, E. Akbarzaadeh, R. Sharifi, M.M. Mojtahedi, Monatsh. Chem. *2010*, *141* (7), 757-61 [DOI: 10.1007/s00706-010-0315-1]; with $NaBH_4$ s. G. Sereda, S. Pothula, J. Dreessen, Synth. Commun. *2010*, *40* (9), 1312-22 [DOI: 10.1080/00397910903072438]; transesterification of β-keto esters with BF_3-etherate s. J. Yang, C. Ji, Y. Zhao, Y. Li, S. Jiang, Z. Zhang, Y. Ji, W. Liu, ibid. *2010*, *40* (7), 957-63 [DOI: 10.1080/00397910903029842].

Cesium fluoride *CsF*

Transesterification $COOC_6F_5 \rightarrow COOR$

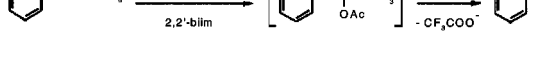
of 1,3-dioxan-2-one-5-carboxylic acid pentafluorophenyl esters s. *78*, 82

Copper(II) acetate/2,2′-biimidazole/phenyl iodosoacetate/potassium carbonate ←

α-Acetoxyketones from trifluoromethyl β-diketones $COCF_3 \rightarrow OAc$

Oxidative C-cleavage under mild conditions

105.



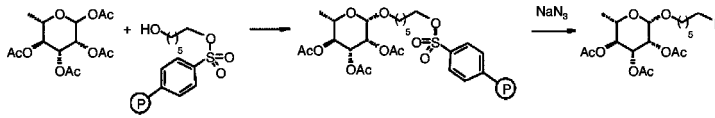
α-Acetoxyacetophenones. A mixture of 4,4,4-trifluoro-1-phenylbutane-1,3-dione (1 mmol), phenyl iodosoacetate (1 mmol), K_2CO_3 (2 mmol), $Cu(OAc)_2$ (0.15 mmol), 2,2′-biimidazole (0.15 mmol) and DMSO (1 ml) heated at 45° for 2.5 h (TLC monitoring), and worked up with purification by chromatography on silica gel → benzoylmethyl acetate. Y 93%. The procedure is efficient at a relatively low temperature for the formation of α-acetoxyacetophenones (as well as naphthalene and 2-thienyl analogs), substrates with electron-donating groups on the benzene ring affording higher yields (92-97%) than those with electron-withdrawing groups (56-66% for *p*-fluoro- and *m*-bromo-derivs.), while 4,4,4-trifluoro-1-(*m*-nitrophenyl)butane-1,3-dione was unreactive. Reaction is presumed to involve intermediate formation of the α-acetoxy-β-diketone which, possessing the strongly electron-withdrawing CF_3 group, readily cleaves to give the product with elimination of trifluoroacetate. With 1-phenylbutane-1,3-dione, itself, there was no such C-cleavage, the α-acetoxy deriv. being isolated (Y 86%). F.e. and optimization (by comparing copper salts, bases and solvents) s. C. Zhou, R. Zeng, J. Zou, Chin. J. Chem. *2010*, *28* (2), 294-8.

Calcium hydroxide s. under I_2 $Ca(OH)_2$

Sodium tetrahydridoborate $NaBH_4$
Boron fluoride (s.a. under Chiral lactate-based o-alkoxyaryl iodosoacetates) BF_3
Transesterification s. *47*, 182s*78* $COOR \rightarrow COOR'$

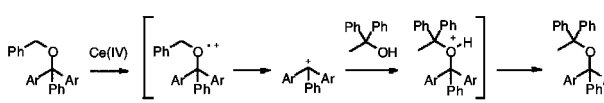
Boron fluoride/sodium azide BF_3/NaN_3
Sequential solid- and solution-phase synthesis of active glycosyl donors by means of a traceless linker ←

106.

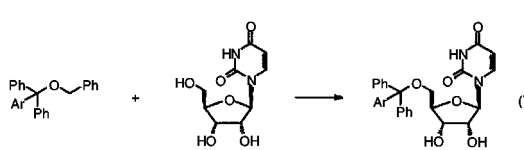


under mild conditions. Resin-bound hexanediol deriv. (prepared by treatment of polystyrene-bound tosyl chloride with 1,6-hexanediol) swollen in anhydrous methylene chloride for 1 h, tetraacetylrhamnopyranose (3-6 eq.) and BF_3-etherate added, the mixture sonicated for 20-25 min at room temp., the resin washed with methanol and methylene chloride, dried *in vacuo*, swollen in DMF, NaN_3 (2 eq.) added, the mixture sonicated for 30 min, filtered through Celite, concentrated, and purified by flash chromatography → α-1-(6-azidohexyl)-2,3,4-triacetyl-rhamnopyranose. Y 75%. The use of a solid-phase approach in conjunction with sonication provided an experimentally simple, clean and efficient preparation of monosaccharide glycosyl donor intermediates from readily available substrates in variable yields (nine examples; Y 14-80%). Product stereochemistry at the anomeric carbon was variable, generally exclusively α or β, but pentaacetyl-*D*-galactopyranose gave a 1:1 mixture. The method was applied to the synthesis of some di- and tri-mannoside and rhamnoside analogs (five examples; Y 44-54% based on startg. resin). F.e.s. C.T. Tanifum, J. Zhang, C.-W.T. Chang, Tetrahedron Lett. *2010*, *51* (33), 4323-7 [DOI: 10.1016/j.tetlet.2010.06.027].

Diethyl azodicarboxylate/cerium(IV) triflate $ROOC\text{-}N{=}N\text{-}COOR/Ce(OTf)_4$
Protection of alcohols as trityl ether derivs. via cerium(IV)-catalyzed transetherification $OH \rightarrow OCAr_3$



107.



under mild conditions. $Ce(OTf)_4$ (10 mol%) and activated 4 Å molecular sieves (2 g) added to a soln. of 1,1-diphenylethanol (5 mmol), DEAD (1.5 eq.) and benzyl 4,4′-dimethoxytrityl ether (1.5 eq.) in acetonitrile (50 ml), the mixture stirred at room temp. until reaction complete (TLC; 2 h), quenched with 5% aq. $NaHCO_3$, extracted with chloroform, concentrated *in vacuo*, and purified by chromatography on silica → 1,1-diphenylethyl 4,4′-dimethoxytrityl ether. Y 75%.

The method provides simple and efficient protection of prim. (12-15 min), sec. (45-90 min) and tert. (120 min) aliphatic alcohols as 4,4′-dimethoxytrityl (DMTr) ethers at room temp. (eight examples; Y 75-95%), incl. selective protection of propane-1,2-diol as its prim. ether. The method was also applied to the selective 5′-O-protection of nucleosides as DMTr (two examples; Y 87-90% after 2-3 h) and 4-methoxytrityl ethers (two examples; Y 70-75% after 7-7.5 h) but reaction with the less active benzyl trityl ether gave lower yields (three examples; Y 18-57% after 10-12 h), with attempts to increase yields by using additional tritylating agent leading to the formation of poly-tritylated by-products. A radical mechanism has been proposed. F.e. and optimization s. N. Zekri, R.F. Alamdari, Can. J. Chem. *2010, 88* (6), 563-8 [DOI: 10.1139/V10-042].

Polyethylene glycol-based bis(imidazolium methanesulfonates) s. under I_2 ←

Lipase or Ionic liquid-coated lipase ←

Kinetic resolution of alcohols by asym. transesterification OH → OAc

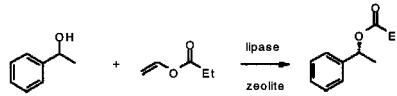
with vinyl acetate s. *44*, 214s*72*; resolution of α-quaternary α-(hydroxymethyl)cycloalkanones s. Z. Guerrab, S. Schweiger, B. Daou, M. Ahmar, B. Cazes, Tetrahedron: Asym. *2010, 21* (13-14), 1752-7 [DOI: 10.1080/00397910903072438]; of β-(2-furyl)-β-hydroxynitriles s. M.C. Turcu, P. Perkiö, L.T. Kanerva, ibid. *2010, 21* (6), 739-45 [DOI: 10.1016/j.tetasy.2010.04.025]; of benzothiazole-subst. 2-furylcarbinols s. L. Csaba Bencze, C. Paizs, M.I. Tosa, M. Trif, D. Irimie, ibid. *2010, 21* (16), 1999-2004 [DOI: 10.1016/j.tetasy.2010.06.010]; of ethyl α-hydroxyphosphinates with Et_3N as additive s. P. Majewska, B. Lejczak, P. Kafarski, Phosphorus, Sulfur Silicon Relat. Elem. *2010, 185* (9), 1915-20 [DOI: 10.1080/10426500903365595]; of sec. alcohols with an ionic liquid-coated lipase s. Y. Abe, K. Yoshiyama, Y. Yagi, S. Hayase, M. Kawatsura, T. Itoh, Green Chem. *2010, 12* (11), 1976-80 [DOI: 10.1039/c0gc00151a]; general method for activation of enzymes in organic solvents with hydrogel supports based on surfactant gelators s. D. Das, S. Roy, S. Debnath, P.K. Das, Chem. Eur. J. *2010, 16* (16), 4911-22 [DOI: 10.1002/chem.200903205].

Immobilized lipase s.a. under Tris(triphenylsilyl) vanadate or polymer-based vanadyl phosphonate ←

Immobilized lipase/butyltrimethylammonium triflimide-coated zeolite ←

Dynamic kinetic resolution of sec. benzyl alcohols under continuous flow conditions OH → OCOR

108.

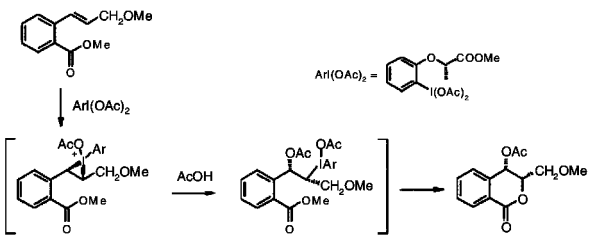


Equimolar solns. of 1-phenylethanol and vinyl propionate in hexanes passed through a single column containing a mixture of *Candida antarctica* lipase B immobilized on supported butylmethylimidazolium chloride and zeolite CP811E-150 coated with butyltrimethylammonium triflimide using $scCO_2$ as carrier at 50°/10 mPA and flow rate of 10.6 μmol/min → (R)-1-phenylethanol propionate. Y 92% (e.e. 99.9%). Development of supported lipases for batch kinetic resolution was successfully extended to dynamic resolution using a solid acid catalyst (zeolite) to racemize unreacted alcohol. Initial attempts using columns of lipase-zeolite-lipase in series were encouraging, but limited to a maximum theoretical yield of 75%. Key to the success of the final process was limiting the reactivity of the zeolite by coating with an ionic liquid and using a relatively slow flow rate to afford the single ester enantiomer in high yield, containing only traces of the (R)- (Y 2%) and (S)-alcohols (Y 6%). F.e., catalyst prepn. and optimization s. P. Lozano, E. García-Verdugo, N. Karbass, K. Montague, T. De Diego, M.I. Burguete, S.V. Luis, Green Chem. *2010, 12* (10), 1803-10 [DOI: 10.1039/c0gc00076k].

Phenyl iodosoacetate s. under Cu(OAc)$_2$ *PhI(OAc)$_2$*

Chiral lactate-based o-alkoxyaryl iodosoacetates/boron fluoride *Ar*I(OAc)$_2$/BF$_3$*
4-Acoxy-3,4-dihydroisocoumarins from *o*-ethylenecarboxylic acid esters via regioselective asym. intramolecular oxylactonization

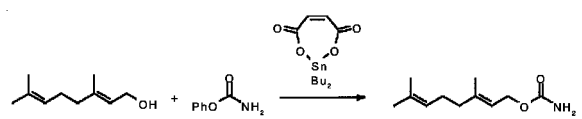
109.



BF_3-etherate (0.1 ml) added to a soln. of the startg. *o*-vinylbenzoate (0.22 mmol), the chiral lactate-based *o*-alkoxyaryl iodosoacetate (0.3 mmol) and acetic acid (0.25 ml) in methylene chloride (5 ml) at -80°, the mixture gradually warmed to -40° over 3 h, quenched by adding water, and worked up with purification by chromatography on silica gel → *cis*-4-acetoxy-3-(methoxymethyl)isochroman-1-one. Y 84% (e.e. 84%). Remarkably, the procedure is almost exclusively *endo*-selective, yielding chiral 3,4-*cis*-disubst. products via initial face-selective addition of the iodine(III) reagent to the double bond to give an iodonium compd., followed by nucleophilic displacement by acetoxy at the benzylic site and subsequent intramolecular nucleophilic displacement by the ester group, each taking place with inversion of configuration. F.e. (thirteen; Y 57-84%; e.e. 84-97%) and with chiral valine-based *o*-alkoxyaryl iodosoacetates, also application to natural product synthesis, s. M. Fujita, Y. Yoshida, K. Miyata, A. Wakisaka, T. Sugimura, Angew. Chem., Int. Ed. *2010*, *49* (39), 7068-71 [DOI: 10.1002/anie.201003503].

Dibutyltin maleate ←
N-Unsubst. urethans from alcohols by tin-catalyzed O-transcarbamylation OH → $OCONH_2$

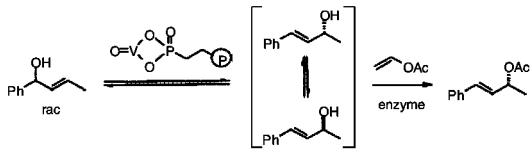
110.



A soln. of geraniol (32.4 mmol), phenyl carbamate (1.5 eq.) and dibutyltin maleate (3 mol%) in toluene heated at 90° for 150 min, cooled to 0°, diluted with 5% aq. NaOH (25 ml), stirred at 0° for 5 min, and worked up with purification by chromatography on silica gel → geranyl carbamate. Y 98%. The procedure is mild, simple, inexpensive and based on readily accessible, air-stable reagents. High yields were obtained with prim. or sec. aliphatic and allyl alcohols (twenty-three examples; Y 80-99%), but the yield was low with a tert. alcohol, even with 30 mol% of the catalyst over 24 h, while the challenging 3-methyl-2-cyclohexenol required both a high catalyst loading and lower reactant concentration (Y 72%). Significantly, the method tolerates a wide range of functionality, e.g. acetyl, benzoyl, tosyl, glycosyl, ketal, carbamate and silyl groups. F.e. and preparation of the phenyl carbamate s. Y. Ichikawa, Y. Morishita, S. Kusaba, N. Sakiyama, Y. Matsuda, K. Nakano, H. Kotsuki, Synlett *2010* (12), 1815-8 [DOI: 10.1055/s-0030-1258102].

Tris(triphenylsilyl) vanadate or polymer-based vanadyl phosphonate/immobilized lipase ←
(E)-Acoxy-2-ethylenes from 2-ethylenealcohols C=C-C(OH) → C(OAc)C=C
Dynamic kinetic resolution

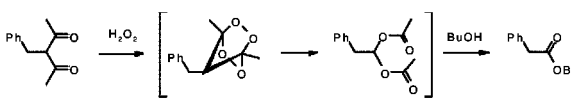
111.



via vanadium-catalyzed racemizing allyl rearrangement-enzymatic asym. O-acylation. Immobilized *Candida antarctica* lipase B (150 mg), the polymer-bound vanadyl phosphonate (0.034 mmol) and vinyl acetate (0.68 mmol) added in this order at room temp. under N_2 to a soln. of racemic (E)-1-phenyl-2-buten-1-ol (0.34 mmol) in acetonitrile (4.2 ml), the mixture stirred at 35° for 1 d, filtered through a Celite pad, the filtrate evaporated under reduced pressure, and the residue purified by chromatography on silica gel → (R,E)-4-phenyl-3-buten-2-yl acetate. Y 77% (e.e. 94%). Reaction is initiated by vanadium-catalyzed allyl shift with continuous racemization to produce a mixture of racemic allyl alcohols in thermodynamic equilibrium, which undergo lipase-catalyzed asym. O-acylation to secure a dynamic kinetic resolution. The same result is achieved from either of the regioisomeric allyl alcohols [secondary or tertiary], or from a mixture of the two, the compatibility of the transition metal catalyst and the enzyme being critical (fourteen examples; Y 65-99%; e.e. 94 to >99%). For substrates possessing an electron-rich aryl (or hetaryl) group, tris(triphenylsilyl) vanadate [$VO(OSiPh_3)_3$] was the catalyst of choice, while the polymer-based vanadyl phosphonate was preferred with aliphatic substrates. **Chiral 2,4-dienolesters** were obtained similarly (e.e. 64-99%) **by dynamic kinetic resolution of the corresponding 2,4-dienols** (or isomeric 1,4-dien-3-ols). F.e.s. S. Akai, R. Hanada, N. Fujiwara, Y. Kita, M. Egi, Org. Lett. *2010*, *12* (21), 4900-3 [DOI: 10.1021/ol102053a].

Hydrogen peroxide/sulfuric acid H_2O_2/H_2SO_4
Carboxylic acid esters from α-subst. β-diketones $RCH(COR')_2 \rightarrow RCOOR''$
One-pot conversion via oxidative cleavage of two acyl groups

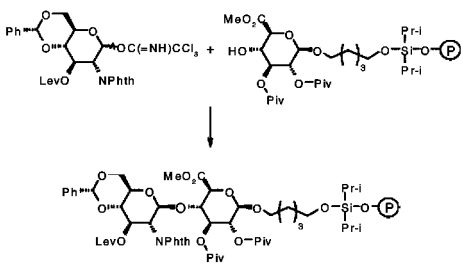
112.



37% Aq. H_2O_2 (13.15 mmol) and a soln. of H_2SO_4 (10.2 mmol) in *n*-butanol (4 ml) added to a soln. of the startg. diketone (2.63 mmol) in the same solvent (6 ml) at room temp., the mixture refluxed for 1 h, diluted with chloroform, water removed by azeotropic distillation (ca. 2 h), and the mixture worked up with purification by chromatography on silica gel → *n*-butyl phenylacetate. Y 86%. This simple, direct procedure is applicable to α-alkyl- and α-benzyl-β-diketones in good yield (eight examples; Y 67-88%). Reaction proceeds **with initial formation of 3,6-alkylidene-1,2,4,5-tetraoxanes**, which had previously been isolated under the same oxidative treatment; these in turn undergo acid-catalyzed rearrangement (related to Baeyer-Villiger oxidation and Hock processes) to give intermediate acylals which are then oxidized to the esters. F.e. and with aq. $HClO_4$ and HBF_4 s. A.O. Terent'ev, D.A. Borisov, I.A. Yaremenko, Y.N. Ogibin, G.I. Nikishin, Synthesis *2010* (7), 1145-9 [DOI: 10.1055/s-0029-1219225].

Trimethylsilyl triflate *Me_3SiOTf*
Soluble polymer-based synthesis of oligosaccharides OH → OR
using a diisopropylsiloxane linker

113.



The PEG-supported glucuronic acid deriv. (360 mg; ca. 36 mmol of sugar) and glycosyl donor (0.22 mmol), previously co-evaporated with toluene and dried under vacuum, dissolved in methylene chloride (3 ml), trimethylsilyl triflate (0.11 *M* soln. in methylene chloride; 102 ml) added at 0°, stirred for 30 min, quenched with triethylamine, excess diethyl ether added at 0°, the precipitated white solid collected by filtration, rinsed with more cold diethyl ether, and dried under high vacuum → product. Y >71%. Acid- and base-resistant siloxane linkers are more advantageous than related silyl ethers since even sterically hindered alcohols can be directly loaded onto the commercially available polymeric support without its prior manipulation and without using silyl chlorides. Products can be easily detached from the support by mild fluoridolysis to afford oligo-saccharides with free hydroxyl groups for further elaboration. Soluble PEG was selected as the support in view of the high reactivity of bound sugars and facile monitoring. Reaction takes place under homogeneous conditions, the supported product being simply retrieved via precipitation with ether. Interestingly, this is the first time a glycosyl trichloroacetimidate has been used as glycosyl donor in the presence of siloxane linkers. The procedure was applied to the synthesis of two biologically important oligosaccharides, but partial cleavage of the diisopropylsiloxane linker presented a problem in the synthesis of a glycosaminoglycan-type disaccharide. F.e.s. M.M. Kayser, J.L. de Paz, P.M. Nieto, Eur. J. Org. Chem. *2010* (11), 2138-47 [DOI: 10.1002/ejoc.200901445].

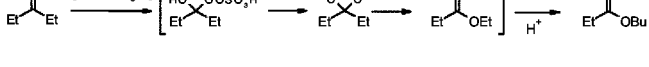
Trimethylsilyl triflate or N-Trimethylsilyltriflimide *Me_3SiOTf or Me_3SiNTf_2*
Glycosides from glycosyl trichloroacetimidates $OC(=NH)CCl_3$ → OR
s. *60*, 103s*75*; β-selectivity with per-methacrylated glycosyl trichloroacetimidates using N-trimethylsilyltriflimide s. C. Zandanel, L. Dehuyser, A. Wagner, R. Baati, Tetrahedron *2010, 66* (18), 3365-9 [DOI: 10.1016/j.tet.2010.02.068]; C-β-mannosylation of electron-rich phenols with Me_3SiOTf or $ZnCl_2$ cf. S. Weck, T. Opatz, Synthesis *2010* (14), 2393-8 [DOI: 10.1055/s-0029-1218772]; **from glycosyl N-trichloroacetylcarbamates**, also one-pot conversion from aldoses via initial treatment with trichloroacetyl isocyanate, s. T. Shirahata, J. Matsuo, S. Teruya, N. Hirata, T. Kurimoto, N. Akimoto, T. Sunazuka, E. Kaji, S. Ômura, Carbohydr. Res. *2010, 345* (6), 740-9 [DOI: 10.1016/j.carres.2010.01.011].

Butyltrimethylammonium triflimide-coated zeolite s. under Supported lipase ←

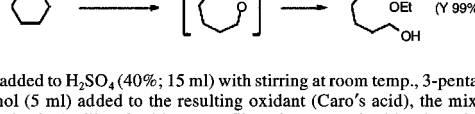
Sulfamic acid *H_2NSO_3H*
Transesterification of carbamic acid esters NCOOR → NCOOR′
Hindered carbamates s. *78*, 167

Sulfuric acid s. under H_2O_2 and $K_2S_2O_8$ *H_2SO_4*

Potassium persulfate/sulfuric acid $K_2S_2O_8/H_2SO_4$
Baeyer-Villiger oxidation-transesterification under mild conditions C(O)R + R'OH → COOR'



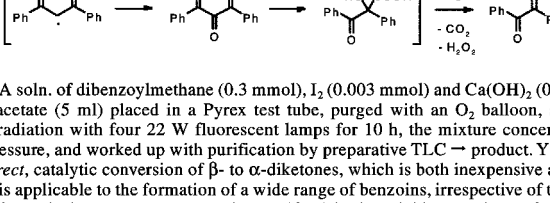
114.



$K_2S_2O_8$ (16 mmol) added to H_2SO_4 (40%; 15 ml) with stirring at room temp., 3-pentanone (8 mmol) and excess *n*-butanol (5 ml) added to the resulting oxidant (Caro's acid), the mixture stirred for 15 h (with GC monitoring), diluted with water, filtered, extracted with ether, the organic layer washed with 5% $NaHCO_3$, then with distilled water, dried ($MgSO_4$), filtered, and concentrated under vacuum → *n*-butyl propanoate. Y 97%. The acid serves a dual role: for the generation of Caro's acid and as catalyst for the transesterification. The procedure is efficient, mild, clean, based on readily available reagents, and has been applied in high yield to the reaction of sym. dialkyl ketones and cycloalkanones (affording hydroxy esters) with a range of prim. or sec. aliphatic alcohols and cyclohexanol (fourteen examples; Y 81-99%). The yield was much lower, however, with the hindered *tert*-butanol (one example; Y 54%). F.e.s. S. Zarrabi, N.O. Mahmoodi, O. Marvi, Monatsh. Chem. *2010*, *141* (8), 889-91 [DOI: 10.1007/s00706-010-0338-9].

Iodine/calcium hydroxide/irradiation $I_2/Ca(OH)_2/h\nu$
α-Diketones from β-diketones $COCH_2COR \rightarrow COCOR$
Photoaerobic C-cleavage via decarboxylative benzilic rearrangement

115.



Benzoins. A soln. of dibenzoylmethane (0.3 mmol), I_2 (0.003 mmol) and $Ca(OH)_2$ (0.15 mmol) in dry ethyl acetate (5 ml) placed in a Pyrex test tube, purged with an O_2 balloon, stirred under external irradiation with four 22 W fluorescent lamps for 10 h, the mixture concentrated under reduced pressure, and worked up with purification by preparative TLC → product. Y 75%. This is the first *direct*, catalytic conversion of β- to α-diketones, which is both inexpensive and safe. The procedure is applicable to the formation of a wide range of benzoins, irrespective of the electronic nature of ring substituents (seven examples; Y 56-75%), but yields were lower from alkyl aryl β-diketones (32-58%; two examples). A dialkyl β-diketone, however, gave the corresponding 1,2,3-triketone while there was no reaction with α-methylated dibenzoylmethane. Reaction is presumed to involve intermediate formation of a β-diketone α-radical which is converted to a 1,2,3-triketone prior to base-catalyzed benzilic rearrangement and photoaerobic decarboxylative cleavage. F.e.s. N. Tada, M. Shomura, H. Nakayama, T. Miura, A. Itoh, Synlett *2010* (13), 1979-83 [DOI: 10.1055/s-0030-1258134].

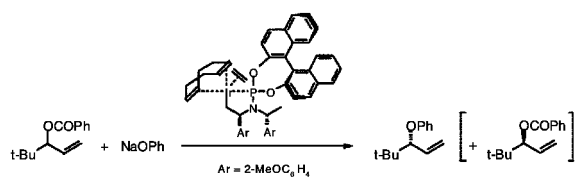
Iodine/polyethylene glycol-based bis(imidazolium methanesulfonates) ←
Catalytic transesterification of β-ketocarboxylic acid esters s. *78*, 86 COOR → COOR'

Sodium periodate s. under OsO_4 $NaIO_4$

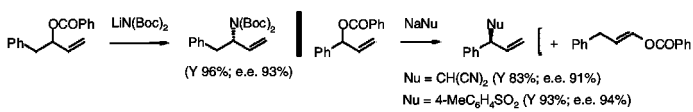
Rhenium heptoxide Re_2O_7
syn-4-Ene-1,3-diol O,O-alkylidene derivs. from 2-ene-1,5-diols
One-pot conversion via regio- and stereo-selective rhenium-catalyzed allylic rearrangement-O,O-alkylidenation s. *78*, 67

Osmium tetroxide/sodium periodate/pyridine $OsO_4/NaIO_4/py$
Ketones from enesilanes C=C(Si⩽) → CO
δ,δ′-Dihydroxyketones *en route* to 1,7-dioxaspiro[5.5]undecanes s. *78*, 528

Chiral iridium(I) 1,1′-binaphthyl-2,2′-diyl phosphoramidite σ-complex *[Ir]**
Allylation with acoxy-2-ethylenes ←
Kinetic asym. transformation with retention of the double bond



116.



3-Benzoyloxy-4,4-dimethyl-1-pentene (2.2 eq.) added to a degassed soln. of Ir catalyst (2 mol%), Na-phenoxide (0.25 mmol) and THF (2 ml) in a sealed vial, the mixture stirred for 12-16 h, filtered through silica, concentrated *in vacuo*, and purified by flash chromatography on silica → (R)-[(4,4-dimethylpent-1-en-3-yl)oxy]benzene. Y 88% (based on phenoxide; e.e. 96%). Branched aliphatic allylic benzoates were more reactive than their linear analogs in this versatile iridium-catalyzed reaction (incl. the illustrated rare *substitution at a neopentyl site*). High enantioselectivity was achieved with C-, O-, N- and S-based nucleophiles using only 2.2 eq. of the racemic substrate (eleven examples; Y 74-96%; e.e. 88-98%). For aromatic substrates [i.e. α-(het)ar. allylic benzoates] the more reactive enantiomer underwent competing linear isomerization, and slight modification of the protocol enabled selective transformation of the less reactive enantiomer (fourteen examples; Y 75-95%; e.e. 84-98%). F.e. and substrate prepn. s. L.M. Stanley, C. Bai, M. Ueda, J.F. Hartwig, J. Am. Chem. Soc. *2010*, *132* (26), 8918-20 [DOI: 10.1021/ja103779e].

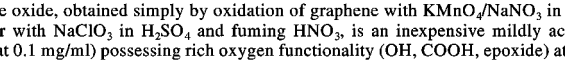
Elimination ⇑

Hydrogen ↑ OC ⇑ H

Poly(anilinesulfonic acid)-supported gold nanoparticles or gold nanoparticles-in-(S)-2-pyrrolidone-5-carboxylic acid-modified SBA-15/oxygen Au/O_2
Gold-catalyzed aerobic oxidation of alcohols s. *70*, 119s*78* CHOH → CO

Gold nanoparticles-DNA/oxygen $Au\text{-}DNA/O_2$
Aryl ketones from sec. benzyl alcohols s. *78*, 4 CHOH → CO

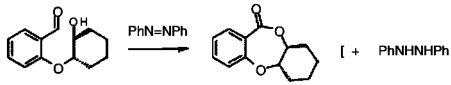
Graphene oxide *GO*
Heterogeneous metal-free carbocatalysis ←
with readily recyclable graphene oxide under mild, slightly acidic conditions

117. 

Graphene oxide, obtained simply by oxidation of graphene with $KMnO_4/NaNO_3$ in concentrated H_2SO_4 or with $NaClO_3$ in H_2SO_4 and fuming HNO_3, is an inexpensive mildly acidic material (pH 4.5 at 0.1 mg/ml) possessing rich oxygen functionality (OH, COOH, epoxide) attached to the 2D array of carbon atoms. Its value as a metal-free, readily recyclable heterogeneous oxidant and hydrating agent has now been demonstrated. **E: Oxo compds. from alcohols.** The startg. benzyl alcohol and graphene oxide (100 mg; 200 wt%) charged into a Teflon-lined vial (7.5 ml), the latter sealed under ambient atmosphere, heated at 100° for 24 h, diluted with deuteriochloroform (1 ml), filtered to remove the catalyst, and the filtrate worked up → product. Conversion >98%. A number of benzyl alcohols and cyclohexanol were efficiently oxidized, as was *cis*-stilbene to benzoin (Y 49%; conversion 56%), the spent catalyst being simply recovered by filtration and multiply recycled [after reoxidation] (with TON values of 10^{-2} mol/g irrespective of the catalyst loading or temperature). Aerobic oxygen does appear to be required as a terminal oxidant although the catalyst itself does undergo partial reduction during the process. Its acidic properties were also tapped for the mild **hydration of acetylene derivs.** to ketones (five examples; conversion 26 to >98%) under the same conditions, conversions being equal or higher than those previously recorded for non-metal-mediated alkyne hydration. F.e. and preparation of the catalyst s. D.R. Dreyer, H.-P. Jia, C.W. Bielawski, Angew. Chem., Int. Ed. *2010*, *49* (38), 6813-6 [DOI: 10.1002/anie.201002160].

Chiral spirobis(isoxazolines)/p-benzoquinone s. under Pd(OCOCF$_3$)$_2$ *SPRIX/BQ*
2,2,6,6-Tetramethylpiperidine nitroxyl/phenyl iodosoacetate/potassium bromide/sodium dodecyl sulfate ←
Saponite-supported 2,2,6,6-tetramethylpiperidine nitroxyl/oxidant ←
Ionic liquid-supported 2,2,6,6-tetramethylpiperidine nitroxyl/tetra-n-butylammonium peroxymonosulfate/1-butyl-3-methylimidazolium hexafluorophosphate ←
Soluble polymer-based 2,2,6,6-tetramethylpiperidine nitroxyl/potassium peroxymonosulfate ←
Oxo compds. from alcohols under catalysis with TEMPO CHOH → CO
with TEMPO as catalytic oxidant s. *39*, 225s*48*; in water with PhIO as reoxidant and KBr/SDS s. C. Zhu, Y. Wei, L. Ji, Synth. Commun. *2010*, *40* (14), 2057-66 [DOI: 10.1080/00397910903219427]; with recyclable saponite-supported TEMPO s. C. Röben, A. Studer, W.L. Hemme, H. Eckert, Synlett *2010* (7), 1110-4 [DOI: 10.1055/s-0029-1219587]; with recyclable ionic liquid-supported 2,2,6,6-tetramethylpiperidine nitroxyl and tetra-*n*-butylammonium peroxymonosulfate/1-butyl-3-methylimidazolium hexafluorophosphate s. C. Zhu, L. Ji, Y. Wei, Catal. Commun. *2010*, *11* (12), 1017-20 [DOI: 10.1016/j.catcom.2010.05.002]; s.a. A. Fall, M. Sene, M. Gaye, G. Gomez, Y. Fall, Tetrahedron Lett. *2010*, *51* (34), 4501-4 [DOI: 10.1016/j.tetlet.2010.06.086]; with soluble PEG-supported TEMPO and Oxone as reoxidant s. K. Matsumoto, T. Iwata, M. Suenaga, M. Okudomi, M. Nogawa, M. Nakano, A. Sugahara, Y. Bannai, K. Baba, Heterocycles *2010*, *81* (11), 2539-53 [DOI: 10.3987/COM-10-12027].

3-Mesityl-4-methylthiazolium perchlorate/triethylamine/azobenzene ←
Lactones from hydroxyaldehydes ○
by N-heterocyclic carbene-catalyzed intramolecular oxidative O-acylation

118. 

2,3-Dihydro-1,4-benzodioxepin-5-ones. A soln. of 2-(2-hydroxycyclohexyloxy)benzaldehyde (0.6 mmol) and THF (0.6 ml) stirred for 5 min, the thiazolium perchlorate (5 mol%) and azobenzene

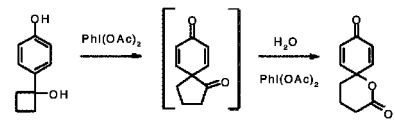
(1 eq.) added, triethylamine (8 mol%) added via syringe, the vial sealed under argon, the mixture stirred at 80° for 20 h, cooled, concentrated *in vacuo*, and purified by chromatography on silica → *trans*-5a,6,7,8,9,9a-hexahydrodibenzo[*b*,*e*][1,4]dioxepin-11-one. Y 78%. This mild and experimentally simple N-heterocyclic carbene-catalyzed oxidative lactonization gave only minor amounts (<5%) of the dimeric macrolide, even at high substrate concentration (1 *M*) and the by-product, hydrazobenzene, was efficiently separated and recycled (Y 90%) using inexpensive $FeCl_3$ as re-oxidant. The reaction was successful with both prim. and sec. alcohol substrates (ten examples; Y 74-95%) in the presence of ether, halo and *unprotected alcohol* functionality. In a final development, a substrate was generated *in situ* from the corresponding benzylic alcohol, using MnO_2 as oxidant, and cyclized in 58% overall yield. F.e., optimization and substrate prepn. s. C.A. Rose, K. Zeitler, Org. Lett. *2010*, *12* (20), 4552-5 [DOI: 10.1021/ol101854r].

Phenyl iodosoacetate s.a. under Pd(OAc)₂ *PhI(OAc)₂*

Phenyl iodosoacetate/sodium hydrogen carbonate *PhI(OAc)₂/NaHCO₃*

1-Oxaspiro[5.5]undeca-7,10-diene-3,9-diones from 1-(*p*-hydroxyaryl)cyclobutanols

119.



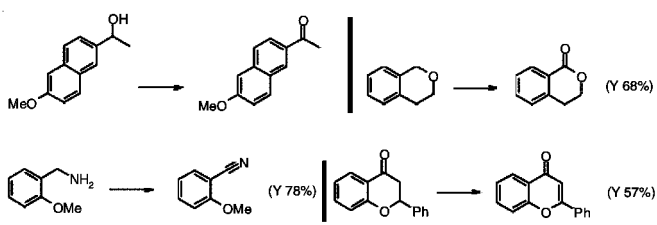
Phenyl iodosoacetate (0.366 mmol) added to a stirred soln. of 1-(*p*-hydroxyphenyl)cyclobutanol (0.183 mmol) and $NaHCO_3$ (0.732 mmol) *in 9:1 hexafluoroisopropanol/water* (2 ml) at 0° under N_2, stirred at the same temp. for 30 min, the mixture quenched by the addition of satd. aq. $NaHCO_3$, and worked up with purification by chromatography on silica gel → product. Y 75%. The procedure is applicable to a number of substrates, incl. *o*-subst., *o,o'*-disubst. and *m*-subst. phenol derivs. (five examples; Y 54-77%), while 2-alkylcyclobutanol derivs. gave regioisomeric mixtures of 4- and 6-alkylated products (two examples; Y 71-74%; regioisomer ratio 5:1 to 6.7:1 in favor of the 6-alkylated products). This one-pot *domino* reaction is presumed to involve sequential iodine(III)-mediated oxidation via a spiro[5.4]decadienedione with release of 4 molecules of acetic acid (neutralized with the bicarbonate). Other solvents and phenyl iodosotrifluoroacetate were less effective. F.e. and labelling experiments with $H_2{}^{18}O$ s. H. Fujioka, H. Komatsu, T. Nakamura, A. Miyoshi, K. Hata, J. Ganesh, K. Murai, Y. Kita, Chem. Commun. *2010*, *46* (23), 4133-5 [DOI: 10.1039/b925687c].

Oxygen s. under Au nanoparticles *O_2*

Chromium(IV) oxide *CrO_2*

Oxidations using metal oxides under flow conditions with inductive heating by admixed magnetite nanoparticles CHOH → CO

120.



Ketones from sec. alcohols. A soln. of 1-(6-methoxynaphth-2-yl)ethanol in acetonitrile (0.15 *M*) passed (flow rate 0.1 ml/min; residence time ca. 40 min) over CrO_2 and silica-coated Fe_3O_4

nanoparticles heated to 135° by magnetic induction in a polyether ether ketone (PEEK) reactor, the effluent concentrated *in vacuo*, and purified by flash chromatography on silica → 2-acetyl-6-methoxynaphthalene. Y 92%. In an oscillating magnetic field, ferromagnetic Fe_3O_4 particles are heated by induction in a controlled and efficient manner, and in the presence of metal oxides (CrO_2, NiO_2) provided an oxidation system for organic substrates. Careful optimization of concentration, temperature and flow rates allowed efficient conversion with residence times of 40-80 min (cf. up to 22 h for similar reactions performed in flasks). Initial reactions performed in glass reactors were successful but limited by pressure considerations, whereas the PEEK reactor could operate at higher pressures (100 psi) allowing use of higher temps. (60-135°) and shorter residence times. Alcohols, benzylic amines, isochroman, 2-phenylchroman-4-one and anthracene were oxidized to ketones (five examples; Y 78-95%), **ar. nitriles** (two examples; Y 78-82%), isochromanone (Y 68%), 2-phenylchromone (Y 57%) and anthraquinone (Y 80%), respectively. F.e. and optimization s. J. Wegner, S. Ceylan, C. Frieste, A. Kirschning, Eur. J. Org. Chem. *2010* (23), 4372-5 [DOI: 10.1002/ejoc.201000628].

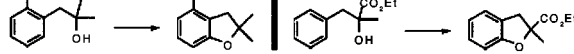
Keggin-type heteropolyacids/hydrogen peroxide ←
Oxidation of alcohols s. *47*, 192s*78* CHOH → CO

Potassium permanganate $KMnO_4$
Rapid oxidations with potassium permanganate under continuous flow ←
Oxo compds. from alcohols s. *78*, 92

Cobalt(II), ruthenium hydride/cobalt(II), rhodium(III) or palladium(II) complexes ←
Transition metal-catalyzed aerobic oxidation of alcohols CHOH → CO
with Co(II)-trifluoroacetoacetonate cf. *26*, 463s*71*; with cobalt(II) Schiff base complexes derived from amino acids s. S.M. Seyedi, R. Sandaroos, G.H. Zohuri, Chin. Chem. Lett. *2010*, *21* (11), 1303-6 [DOI: 10.1016/j.cclet.2010.06.009]; with rhodium(III) porphyrin complexes for the oxidation of aliphatic, functionalized aliphatic and benzylic alcohols in water s. L. Liu, M. Yu, B.B. Wayland, X. Fu, Chem. Commun. *2010*, *46* (34), 6353-5 [DOI: 10.1039/c0cc01406k]; *under bifunctional hybrid catalysis* with Shvo's ruthenium hydride complexes and a cobalt(II) Schiff base complex for oxidation of sec. alcohols under ambient conditions s. E.V. Johnston, E.A. Karlsson, L.-H. Tran, B. Åkermark, J.-E. Bäckvall, Eur. J. Org. Chem. *2010* (10), 1971-6 [DOI: 10.1002/ejoc.201000033]; with a palladium(II) complex *under continuous flow* for a safe and scalable oxidation s. X. Ye, M.D. Johnson, T. Diao, M.H. Yates, S.S. Stahl, Green Chem. *2010*, *12* (7), 1180-6 [DOI: 10.1039/c0gc00106f]; with $Pd(OAc)_2$ and anionic pyridine- or quinoline-based N,O-ligands, e.g. pyridine-2,6-dicarboxylic acid, as highly active catalysts for the oxidation of unactivated alcohols in the presence of tetrabutylammonium acetate s. D.S. Bailie, G.M.A. Clendenning, L. McNamee, M.J. Muldoon, Chem. Commun. *2010*, *46* (38), 7238-40 [DOI: 10.1039/c0cc01138j]; with poly(anilinesulfonic acid)-supported gold nanoparticles in water (cf. *70*, 119s*75*) s. D. Saio, T. Amaya, T. Hirao, Adv. Synth. Catal. *2010*, *352* (13), 2177-82 [DOI: 10.1002/adsc.201000451]; with small gold nanoparticles stabilized in the mesopores of (*S*)-2-pyrrolidone-5-carboxylic acid-modified SBA-15 s. L. Wang, X. Meng, B. Wang, W. Chi, F.-S. Xiao, Chem. Commun. *2010*, *46* (27), 5003-5 [DOI: 10.1039/c000226g].

Palladium(II) acetate/lithium carbonate/phenyl iodosoacetate $Pd(OAc)_2/Li_2CO_3/PhI(OAc)_2$
2,2-Disubst. 2,3-dihydrobenzofurans from 2-aryl-*tert*-alcohols ○
Oxidative ring closure via palladium(II)-catalyzed C-H activation

121.

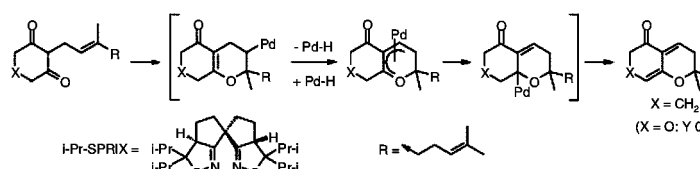


(Y 50%)

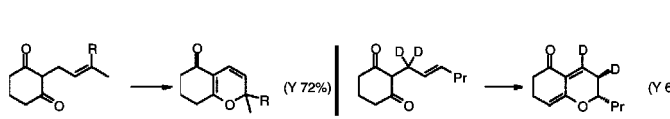
Hexafluorobenzene (2 ml) added to a mixture of startg. alcohol (0.2 mmol), $Pd(OAc)_2$ (5 mol%), Li_2CO_3 (1.5 eq.) and $PhI(OAc)_2$ (1.5 eq.) under air, the sealed mixture stirred at 100° for 36 h, cooled to room temp., diluted with ether, filtered through Celite, the filtrate concentrated *in vacuo*, and the residue purified by chromatography on silica gel → 4-bromo-2,2-dimethyl-2,3-dihydro-

benzofuran. Y 88%. Mechanistically, reaction likely proceeds via Pd(II)-catalyzed C-H cleavage, followed by oxidation of Pd(II) to Pd(IV) and subsequent C-O bond formation via a reductive elimination process, the procedure being entirely complementary to the equivalent Pd(0)- and Cu(I)-catalyzed intramolecular O-arylations (cf. *52*, 128s*60*) in which the Br atom is substituted. Twenty-two examples (tolerating a variety of electron-donating and -withdrawing groups on the aromatic ring, and alkyl and aryl substitution both α and β to the hydroxyl group) afforded yields generally in the range 70-90% (incl. two spirocyclic examples), falling to 50% for an α-carboxy analog, while a secondary alcohol afforded only 42% due to competing oxidation to the ketone. Other similar I(III) oxidants [PhI(OCOCF$_3$)$_2$ and PhI(OCOBu-*t*)$_2$] gave lower yields, as did the strongly oxidizing fluorinating agent, N-fluorobenzenesulfonimide, while a variety of commonly-used alternatives were ineffective. The reaction proceeds to some extent without added base (Li_2CO_3 and Na_2HPO_4 being most effective), albeit accompanied by significant decomposition of starting material. F.e.s. X. Wang, Y. Lu, H.-X. Dai, J.-Q. Yu, J. Am. Chem. Soc. *2010*, *132* (35), 12203-5 [DOI: 10.1021/ja105366u].

Palladium(II) trifluoroacetate/chiral spirobis(isoxazolines)/p-benzoquinone Pd(II)/SPRIX/BQ
Asym. intramolecular Wacker-type ring closure of α-allyl-β-diketones



122.

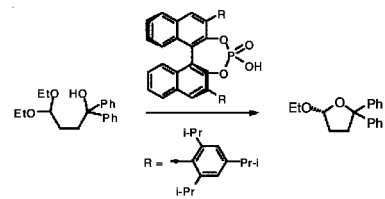


Chiral 2,3,6,7-tetrahydro-5-chromenones. *p*-Benzoquinone (2 eq.) and startg. diketone (1 mmol) added to a soln. of Pd(OCOCF$_3$)$_2$ (10 mol%) and (M,S,S)-*i*-Pr-SPRIX (12 mol%) in diglyme (0.5 ml) (previously stirred at room temp. for 2 h), the resulting mixture stirred for 12 h, filtered through a short pad of silica, the filtrate concentrated under reduced pressure, and the residue purified by flash chromatography on silica gel → 2-methyl-2-(4-methylpent-3-enyl)-6,7-dihydro-2*H*-chromen-5(3*H*)-one. Y 80% (e.e. 81%). Reaction was only applicable to *2-allylcyclohexane-1,3-dione* derivs. (seven examples; Y 38-80%; e.e. 51-84%), with no reaction observed for pyran-3,5-dione, cyclopentane-1,3-dione or acetylacetone analogs. Reaction proceeds via oxypalladation, followed by β-hydride elimination and, crucially, re-insertion of Pd-H to afford a π-allyl intermediate, which undergoes further β-hydride elimination to give the product. Substituents on the double bond of the allyl group had a dramatic effect on the outcome, however, with the (Z)-isomer of the illustrated reaction taking an alternative pathway to afford a racemic non-isomerized heterocycle as the major product, steric effects likely preventing re-insertion of Pd-H. The strong Lewis acidity of the Pd-SPRIX complex is also crucial, with alternative chiral ligands, such as (-)-sparteine, (R,R)-Bn-BOX, (S,S)-*i*-Pr-BOXAX and (R)-BINAP being ineffective. F.e.s. K. Takenaka, S.C. Mohanta, M.L. Patil, C.V.L. Rao, S. Takizawa, T. Suzuki, H. Sasai, Org. Lett. *2010*, *12* (15), 348-3 [DOI: 10.1021/ol1013069]; cf. *61*, 121 ; 2-homoallylchromenes by asym. 6-*endo-trig* ring closure of *o*-geranylphenols (e.e. up to 55%), incl. application to synthesis of (–)-cordiachromene, s. K. Takenaka, Y. Tanigaki, M.L. Patil, C.V.L. Rao, S. Takizawa, T. Suzuki, H. Sasai, Tetrahedron: Asym. *2010*, *21* (7), 767-70 [DOI: 10.1016/j.tetasy.2010.04.060].

Oxygen ↑ OC ⇑ O

(S)-3,3′-Bis(2,4,6-triisopropylphenyl)-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate ←
Lactolides from hydroxyacetals ○
by organo-Brønsted acid-catalyzed asym. intramolecular transacetalation

123.



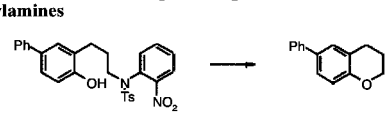
4 Å Molecular sieves (150 mg) and a soln. of (S)-TRIP (0.003 mmol, co-crystallized with acetonitrile, 1:1) in dry benzene (4 ml) added to a soln. of 4,4-diethoxy-1,1-diphenylbutan-1-ol (0.3 mmol) in dry benzene (8 ml), stirred at 20° for 24 h, triethylamine (42 µl) added to the mixture after 48 h, concentrated under reduced pressure, and purified by chromatography on silica gel → (R)-5-ethoxy-2,2-diphenyltetrahydrofuran. Y 95% (e.r. 94.5:5.5). The procedure is mild and applicable to the preparation of chiral 5- and 6-membered lactolides from the corresponding *prim*- or *tert*-hydroxyacetals, which (in the case of the latter) may possess an alkyl or aryl group α to the hydroxyl group, irrespective of the electronic character of the aromatic substituent (sixteen examples; Y 76-99%; e.r. 79:21 to 98:2). Reaction is presumed to involve initial acid-catalyzed formation of an oxocarbenium ion, followed by intramolecular nucleophilic attack of the hydroxyl group within the sphere of the hydrogen-bonded chiral phosphate group. F.e. and application to the parallel kinetic resolution of an unsym. γ,γ-disubst. γ-*tert*-hydroxyacetal s. I. Coric, S. Vellalath, B. List, J. Am. Chem. Soc. *2010*, *132* (25), 8536-7 [DOI: 10.1021/ja102753d]; correction to structure of intermediate oxocarbenium ion s. ibid. (34), 12155 [DOI: 10.1021/ja105707w].

p-Toluenesulfonic acid *TsOH*
1,7-Dioxaspiro[5.5]undecanes from δ,δ′-dihydroxyketones s. *78*, 528

Nitrogen ↑ OC ⇑ N

Potassium phosphate K_3PO_4
Ring closures via intramolecular nucleophilic displacement ○
of N-aryl-N-sulfonylamines

124.



N-(*o*-Nitrophenyl)- and N-(*p*-methoxyphenyl)-N-sulfonylamino groups are readily displaced intramolecularly by O-, N- and C-nucleophiles, providing an efficient entry into a wide range of O-heterocyclics (incl. cyclic ethers and lactones), N-heterocyclics and *gem*-subst. carbocyclics. **E: Chromans**. A mixture of 2-[3-[(*o*-nitrophenyl)(*p*-toluenesulfonyl)amino]propyl]-4-phenylphenol (0.101 mmol) and K_3PO_4 (2 eq.) in DMF (2 ml) stirred at 150° for 24 h, cooled to room temp., diluted with water, extracted with ethyl acetate, and worked up with purification by chromatography on silica gel → 6-phenylchroman. Y 83%. The substrates are readily prepared

from the corresponding prim. amines (by sulfonylation-arylation or the reverse), and chiral N-aryl-N-sulfonyl groups were predictably displaced **with inversion of configuration**. Yields depend to some extent on the nature of the N-sulfonyl group, the order of reactivity being Ms < Ts < Ns < Tf. F.e. (ca. twenty; Y 63-94%) s. Y. Kato, D.H. Yen, Y. Fukudome, T. Hata, H. Urabe, Org. Lett. *2010*, *12* (18), 4137-9 [DOI: 10.1021/ol101541p].

Halogen ↑ OC ↑ Hal

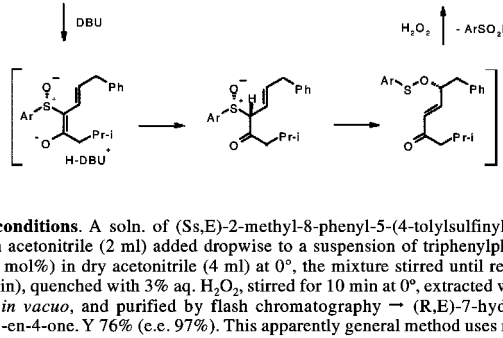
Tetra-n-butylammonium salts *$[Bu_4N]^+$*
Functionalized arenes $Ar(Ar')IX \rightarrow ArX\ [+Ar'I]$
by regioselective reductive elimination of diaryliodonium salts s. *78*, 209

Palladium(II) acetate/tri-tert-butylphosphine/potassium carbonate *$Pd(OAc)_2/t\text{-}Bu_3P/K_2CO_3$*
Palladium-catalyzed intramolecular O-vinylation
Benzofurans s. *78*, 210

Sulfur ↑ OC ↑ S

1,8-Diazabicyclo[5.4.0]undec-7-ene/triphenylphosphine/hydrogen peroxide *$DBU/Ph_3P/H_2O_2$*
(E)-α,β-Ethylene-γ-hydroxyketones
from α,β-ethylene-β′-ketosulfoxides with chirality transfer

125.

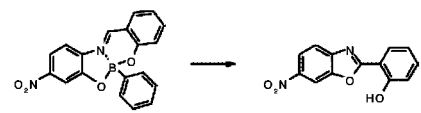


under mild conditions. A soln. of (Ss,E)-2-methyl-8-phenyl-5-(4-tolylsulfinyl)oct-5-en-4-one (0.5 mmol) in acetonitrile (2 ml) added dropwise to a suspension of triphenylphosphine (3 eq.) and DBU (10 mol%) in dry acetonitrile (4 ml) at 0°, the mixture stirred until reaction complete (TLC; 5-30 min), quenched with 3% aq. H_2O_2, stirred for 10 min at 0°, extracted with chloroform, concentrated *in vacuo*, and purified by flash chromatography → (R,E)-7-hydroxy-2-methyl-8-phenyloct-5-en-4-one. Y 76% (e.e. 97%). This apparently general method uses readily available substrates and gives rapid conversion with good to excellent chirality transfer for phenyl and alkyl ketone derivs. (eleven examples; Y 55-92%; e.e. 71 to >99). Phenyl ketones gave lowest yields, presumed due to instability at room temp., and a diphenylmethyl ketone, while giving an excellent yield (97%), gave reduced enantioselectivity (e.e. 58%). Absolute configuration was determined via conversion to Mosher esters. F.e., optimization and substrate prepn. s. M. Miura, M. Toriyama, T. Kawakubo, K. Yasukawa, T. Takido, S. Motohashi, Org. Lett. *2010*, *12* (17), 3882-5 [DOI: 10.1021/ol1015724].

Remaining Elements ↑ OC ⇑ Rem

Potassium cyanide *KCN*
2-(*o*-Hydroxyaryl)benzoxazoles ○
via cyanide-promoted arylboronate elimination

126.

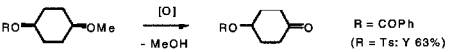


under mild conditions. A soln. of startg. boracycle (1 eq.) and KCN (3 eq.) in methanol (45 ml) stirred at room temp. for 4 h, solvent removed *in vacuo*, and the residue purified by crystallization → 2-(2-hydroxyphenyl)-6-nitrobenzoxazole. Y 94%. Attempted hydrocyanation of the readily available azadioxoboracycle at the imine moiety unexpectedly resulted in efficient ring-contraction to the title products under experimentally simple conditions. The reaction appears general for electron-diverse substituents (six examples; Y 61-94%) with products being fully characterized and structure confirmed by X-ray analysis in one case. F.e.s. H. López-Ruiz, H. Briseño-Ortega, S. Rojas-Lima, R. Santillán, N. Farfán, Tetrahedron Lett. *2010*, *51* (19), 2633-5 [DOI: 10.1016/j.tetlet.2010.03.027].

Carbon ↑ OC ⇑ C

m-Chloroperoxybenzoic acid/manganese(II) chloride/4,4′,4″-tri-tert-butyl-2,2′:6′,2″-terpyridyl ←
Ketones from methyl ethers CHOMe → CO
Mild, manganese-catalyzed direct C-H oxidation

127.



cis-1-Benzoyloxy-4-methoxycyclohexane (0.5 mmol) added at room temp. to a soln. of $MnCl_2$-$4H_2O$ (1 eq.), 4,4′,4″-tri-*tert*-butyl-2,2′:6′,2″-terpyridyl (1 eq.), and distilled water (50 ml) in acetonitrile (5 ml) (previously stirred at room temp. for 30 min), the resulting mixture cooled to 0°, treated with *m*-chloroperoxybenzoic acid (4 eq.), stirred at 0° for 2 h, filtered through a short column of alumina, concentrated, and purified by flash chromatography on silica gel → 4-benzoyloxy-1-cyclohexanone. Y 64%. Reaction occurs via direct oxidation of the tertiary C-H group, followed by elimination of methanol, rather than via oxidation of the methyl group. Similar oxidation of a variety of cyclic or acyclic methyl ethers afforded ketones generally in yields of 50-80% (seven examples), although yields were lower with steroidal (46%) and sterically-hindered substrates (*cis*-1-benzoyloxy-2-methoxycyclohexane gave 30%). A cyclododecyl *n*-octyl ether afforded a 59% yield, while corresponding isopropyl (29%) and *tert*-butyl ethers (trace) were less successful. Benzyl ethers (especially electron-poor ones) were moderately successful (three examples; Y 46-55%), the outcome of the Mn-catalyzed reaction contrasting sharply with oxidation using RuO_4, which generally affords benzoate esters. The oxidation was completely retarded with electron-poor analogs, such as O-methoxymethyl, O-benzoyl or O-tosyl derivs., which are, therefore, suitable as orthogonal protecting groups. Reaction was sluggish in the absence of the electron-rich (tri-*tert*-butyl subst.), tridentate 2,2′:6′,2″-terpyridyl ligand; and other oxidants (magnesium monoperoxyphthalate or tetra-*n*-butylammonium Oxone) were less successful. F.e.s. S. Kamijo, Y. Amaoka, M. Inoue, Chem. Asian J. *2010*, *5* (3), 486-9 [DOI: 10.1002/asia.200900420].

(S)-3,3′-Bis(2,4,6-triisopropylphenyl)-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate ←
Lactolides from hydroxyacetals ○
by organo-Brønsted acid-catalyzed asym. intramolecular transacetalation s. *78*, 123

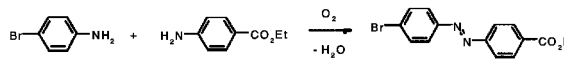
Formation of N-N Bond

Exchange ↓↑

Hydrogen ↑ NN ↓↑ H

Copper(I) bromide/pyridine/oxygen *$CuBr/C_5H_5N/O_2$*
Azo compds. from prim. ar. amines $RNH_2 + H_2NR' \rightarrow RN{=}NR'$
Copper(I)-catalyzed coupling using molecular oxygen as oxidant

128.



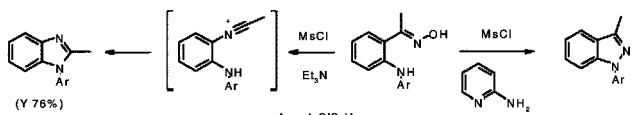
A mixture of ethyl 4-aminobenzoate (*5 eq.*), *CuBr* (10 mol%), *pyridine* (30 mol%) and 4-bromoaniline (0.2 mmol) in toluene (4 ml) stirred at 60° under O_2 for 24 h, cooled, concentrated *in vacuo*, and purified by flash chromatography on silica → (E)-1-(4-bromophenyl)-2-(4-ethoxycarbonylphenyl)diazene. Y 73%. This novel and atom-economical reaction generates water as the only by-product and was successful for homo-coupling of electron-diverse anilines (twelve examples; Y 61-97%) as well as for cross-coupling, using an excess of the less reactive electron-poor partner (thirteen examples; Y 42-73%), in the presence of halo, ester, ether and nitrile functionality. Other additives gave inferior results, as did the use of other copper salts, while other transition metal salts (Ag, Fe, Au, Co, Mn) were ineffective. No coupling took place under an inert atmosphere. F.e. and optimization s. C. Zhang, N. Jiao, Angew. Chem., Int. Ed. *2010*, *49* (35), 6174-7 [DOI: 10.1002/anie.201001651].

Elimination ↑↑

Oxygen ↑ NN ↑↑ O

Methanesulfonyl chloride/2-aminopyridine *$MeSO_2Cl/2\text{-}H_2NC_5H_4N$*
1-Aryl-indazoles or -benzimidazoles from *o*-(arylamino)oximes ○

129.



3-Subst. 1-arylindazoles. A soln. of startg. oxime (1 mmol) and *2-aminopyridine* (2 eq.) in methylene chloride (15 ml) stirred at room temp. for 15 min, cooled to 0°, a soln. of methanesulfonyl chloride (2 eq.) in the same solvent (5 ml) added over 1.5 min, the mixture warmed to room temp. over 5 h, concentrated *in vacuo*, and purified via flash chromatography → 1-(4-chlorophenyl)-3-methyl-1*H*-indazole. Y 72%. Initial attempts at preparing relatively inaccessible 1-arylindazoles from readily available *o*-(arylamino)oximes gave isomeric benzimidazoles as by-products, the ratio varying with choice of amine base (weaker bases generally favoring indazole formation). 2-Aminopyridine was optimal for the formation of indazoles from electron-diverse ar. aldoximes (reaction at -78 to -23°) or ketoximes (fifteen examples; Y 59-94%) but gave low yields of electron-poor 4-nitro- (20%) and 4-trifluoromethyl-phenyl (44%) derivs. Use of stronger tert. amine bases (e.g. Et_3N) afforded benzimidazoles as major products (thirteen examples; Y 39-86%) with 4- and 3-methoxyphenyl derivs. giving the lowest yields, while an electron-rich 4,5-dimethoxy-ketoxime gave only indazole under these conditions. Formation of benzimidazoles is presumed

to involve initial **Beckmann rearrangement** and intramolecular trapping of the generated nitrilium ion. F.e., optimization and substrate prepn. s. B.C. Wray, J.P. Stambuli, Org. Lett. *2010*, *12* (20), 4576-9 [DOI: 10.1021/ol101899q].

Nitrogen ↑ NN ⇑ N

Iron(II) bromide *$FeBr_2$*

Iron(II)-catalyzed denitrogenative ring closures of 2-functionalized unsatd. azides ○

2-Alkoxyindazoles from (E)-*o*-azidoalkoximes – N-Alkoxypyrazoles from (E)-α-azido-α,β-ethylene-alkoximes s. *78*, 38

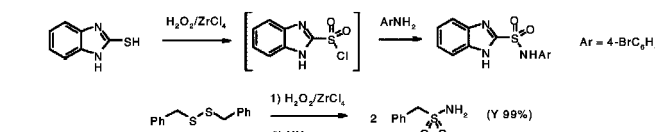
Formation of N-S Bond

Exchange ↓↑

Hydrogen ↑ NS ↓↑ H

Zirconium tetrachloride/hydrogen peroxide/pyridine *$ZrCl_4/H_2O_2/C_5H_5N$*

Sulfonic acid amides from mercaptans or disulfides and amines SH → SO_2N≺



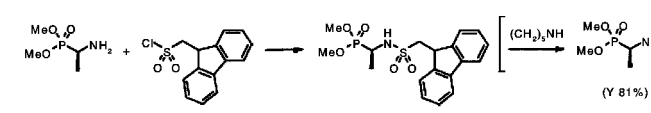
130.

A mixture of 2-mercaptobenzimidazole (1 mmol), 30% aq. H_2O_2 (3 eq.) and $ZrCl_4$ (1 eq.) in acetonitrile stirred at 25° until substrate consumed (TLC; 3 min), a soln. of 4-bromoaniline (1 eq.) in pyridine (0.5 ml) added, the mixture stirred until reaction complete (TLC), acidified with 2 *M* aq. HCl, extracted with ethyl acetate, washed with water and brine, concentrated *in vacuo*, and purified by recrystallization → N-(4-bromophenyl)benzimidazole-2-sulfonamide. Y 91%. This novel and experimentally simple reaction utilizes inexpensive reagents for conversion of commercially available electron-diverse ar. and benzyl thiols or disulfides to prim., sec. and tert. sulfonamides (twenty-two examples; Y 91-99%). The reaction occurs via sulfonyl chloride formation, which was extremely rapid (1-3 min) at room temperature, and advantageous in the described example as *benzimidazole-2-sulfonyl chloride is unstable at room temperature.* F.e. and optimization s. K. Bahrami, M.M. Khodaei, M. Soheilizad, Tetrahedron Lett. *2010*, *51* (37), 4843-6 [DOI: 10.1016/j.tetlet.2010.07.056].

Halogen ↑ NS ↓↑ Hal

Ethyldiisopropylamine *$i\text{-}Pr_2NEt$*

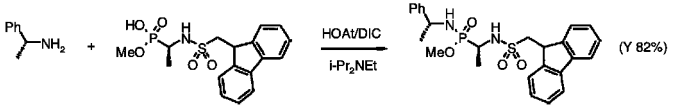
9-Fluorenylmethanesulfonyl [Fms] as N-protective group NH → NSO_2R



131.

complementing carbo-9-fluorenylmethoxy [Fmoc]. Ethyldiisopropylamine (2 eq.) and 9-fluorenylmethanesulfonyl chloride (1.5 eq.) added to a soln. of dimethyl (R)-1-aminoethylphosphonate

(1 mmol) in methylene chloride (5 ml) at 0°, the mixture stirred at 30° for 3 h, quenched with water, extracted with methylene chloride, concentrated, and purified by chromatography on silica → dimethyl (R)-1-aminoethylphosphonate-9-fluorenylmethanesulfonamide. Y 87%. The method is applicable to protection of *prim*-, *sec*- and *tert*-alkyl prim. or sec. amines, and aniline, (thirteen examples; Y 79-95%), with deprotection (piperidine/DMF) being rapid (<1 to 10 min) at 25° (thirteen examples; Y 78-96%). While this novel N-protecting group can be introduced and removed using classical Fmoc methodology (s.a. *78*, 6), it is free from the formation of cyclodehydrated by-products often associated with peptide coupling of Fmoc-protected amino acids, making it a good candidate for N-protection of α-aminophosphonic acid analogs of peptides; thus under standard conditions (DCI/HOAt), an Fms-protected α-aminophosphonic acid monoester coupled cleanly with (R)-2-phenylethylamine (Y 82%), while the Fmoc analog gave only 20% of the coupled product, the major compound being an oxazaphospholine.



Similar condensations with H-Phe-OBu-*t*, H-Pro-Gly-OBu-*t* or H-Phe-Phe-OBu-*t* gave yields of 89-91% after deprotection. F.e. and optimization s. Y. Ishibashi, K. Miyata, M. Kitamura, Eur. J. Org. Chem. *2010* (22), 4201-4 [DOI: 10.1002/ejoc.201000682].

Sulfur ↑ NS ↓↑ S

Zirconium tetrachloride/hydrogen peroxide/pyridine $ZrCl_4/H_2O_2/C_5H_5N$
Sulfonic acid amides from disulfides and amines s. *78*, 130 $RSSR \rightarrow 2\,RSO_2N<$

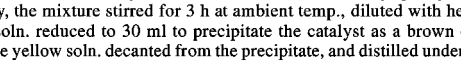
Formation of N-Rem Bond

Uptake ⇓

Addition to Nitrogen and Carbon NRem ⇓ NC

Bis(acetonitrile)(cyclopentadienyl)(triisopropylphosphine)ruthenium(II) hexafluorophosphate ←
N-Silylaldimines from nitriles $CN \rightarrow CH{=}NSiR_3$
Chemoselective ruthenium(II)-catalyzed hydrosilylation under mild conditions

132.



Bis(acetonitrile)(cyclopentadienyl)(triisopropylphosphine)ruthenium(II) hexafluorophosphate (1.5 mol%) loaded in air into a round-bottom flask, the latter purged with N_2, charged with methylene chloride (30 ml), isobutyronitrile (6.7 mmol) and dimethyl(phenyl)silane (7.1 mmol) added sequentially, the mixture stirred for 3 h at ambient temp., diluted with hexane (30 ml), the resulting cloudy soln. reduced to 30 ml to precipitate the catalyst as a brown oil (contaminated with siloxanes), the yellow soln. decanted from the precipitate, and distilled under reduced pressure → product. Y 86%. The procedure is very mild and high-yielding (thirteen examples) for a range of aliphatic and electron-diverse aromatic nitriles, notably leaving keto, formyl, nitro and carbethoxy groups on the benzene ring intact. A β,γ-ethylenenitrile was also hydrosilylated with retention of the alkene group, but acrylonitrile gave a low product yield while an acetylenenitrile underwent preferential hydrosilylation of the alkyne residue. Significantly, with 1 eq. of the

organosilicon hydride, monohydrosilylation was exclusive but conversion of aromatic nitriles (excepting *m*-nitrobenzonitrile) to **N-aryldisilazanes** was achieved with excess (2 eq.) hydride (enolizable nitriles giving mixtures of disilazane and disilylenamine). More conveniently, the catalyst can be formed *in situ* from commercially available $[CpRu(MeCN)_3]PF_6$ and triisopropylphosphine; it is insensitive to moisture and can be readily recycled. Reaction is thought to involve intermediate formation of a neutral ruthenium hydride complex. F.e. and solvent-free procedure, also hydrosilylation of 3-cyanopyridine (over 14 h), s. D.V. Gutsulyak, G.I. Nikonov, Angew. Chem., Int. Ed. *2010*, *49* (41), 7553-6 [DOI: 10.1002/anie.201003069].

Exchange ⇃↾

Oxygen ↑ NRem ⇃↾ O

1-Hydroxy-7-azabenzotriazole/N,N′-diisopropylcarbodiimide/ethyldiisopropylamine ←
Phosphonic acid amide esters from monoesters PO(OR)OH → PO(OR)N≤
α-[(9*H*-Fluoren-9-ylmethanesulfonyl)amino]phosphonic acid amide esters s. *78*, 131

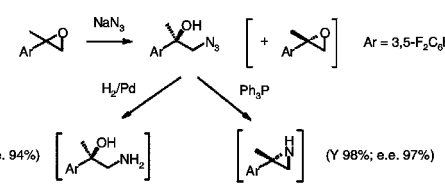
Formation of N-C Bond

Uptake ⇓

Addition to Oxygen and Carbon NC ⇓ OC

Sodium azide/halohydrin dehalogenase *NaN_3/dehalogenase*
Kinetic resolution of 1,1-disubst. epoxides via regioselective enzymatic azidolysis ▽o → C(N_3)C(OH)

133.

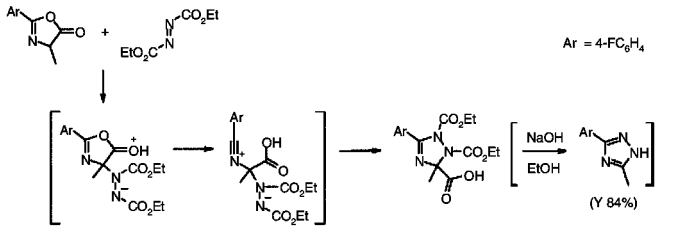


NaN_3 (0.55 eq.) and a soln. of startg. epoxide (3.73 mmol) in DMSO (5 ml) added sequentially to a soln. of the enzyme (HHDH P2E2; 250 mg) in 0.1 *M* K_2HPO_4 (70 ml) at room temp., the mixture stirred overnight, diluted with ethyl acetate and water, separated by centrifugation, solvent removed *in vacuo*, and the residue purified by chromatography on silica → (R)-1-azido-2-(3,5-difluorophenyl)propan-2-ol. Y 45% (regioselectivity >25:1; e.e. 99%). Of 96 screened Codex halohydrin dehalogenases, only 4 showed complete regioselectivity (>25:1) for the prim. azide product, with enzyme P2E2 giving high enantioselectivity for 2-methyl/ethyl-2-aryl/benzyl-derivs. (Y 38-45%; e.e. 98-99%). 2-Trifluoromethyl and 2-naphthyl derivs. gave moderate enantioselectivity (e.e. 34-71%) under these conditions (a 2-isopropyl deriv. was unreactive) and, although enantioselectivity was improved (e.e. 88-96%) using enzyme P1H2, yields were decreased (19-22%). Uncatalyzed azidolysis produced mixtures of prim. and tert. azides (ratio dependent on substituent effects). F.e., substrate prepn. and conversion to chiral **2-amino-*tert*-alcohols** (Y 98%; e.e. 97-98%) and **aziridines** (Y 60-94%; e.e. 94-97%) s. C. Molinaro, A.-A. Guilbault, B. Kosjek, Org. Lett. *2010*, *12* (17), 3772-5 [DOI: 10.1021/ol101406k].

Addition to Nitrogen-Nitrogen Bonds NC ⇓ NN

Without additional reagents *w.a.r.*
1,2-Dicarbalkoxy-Δ^3-1,2,4-triazoline-5-carboxylic acids ○C
from Δ^2-oxazol-5-ones and azodicarboxylic acid esters

134.



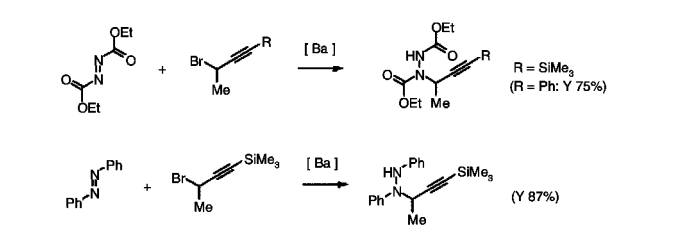
under mild conditions. A mixture of 2-(4-fluorophenyl)-4-methyl-Δ^2-oxazolin-5-one (0.5-0.8 mmol) and diethyl azodicarboxylate (1 eq.) in acetonitrile (10 ml) stirred at room temp. until reaction complete (TLC; 11 h), shaken with methylene chloride and aq. $NaHCO_3$, the aq. layer acidified with aq. HCl, extracted with methylene chloride, and concentrated *in vacuo* → 1,2-bis-(ethoxycarbonyl)-5-(4-fluorophenyl)-3-methyl-2,3-dihydro-1*H*-1,2,4-triazole-3-carboxylic acid. Y 98%. This simple and efficient conversion proceeds without need of a catalyst and appears general for electron-diverse 2-aryl-5-alkyloxazolin-5-ones (nine examples; Y 82-100%). Reactions were somewhat slower (22 h) in acetonitrile for sterically-hindered (e.g. isopropyl) 5-substituents or electron-poor (e.g. 4-nitrophenyl) 2-substituents, but use of methylene chloride effected efficient conversion within 9 h. The products were converted to the corresponding **2,5-disubst. triazoles** by refluxing in ethanolic NaOH (four examples; Y 74-84%). Structures were confirmed by X-ray methods in some cases. Oxazolinone substrates were readily available via dehydration (trifluoro-acetic anhydride) of the corresponding N-acylamino acids. F.e. and optimization s. R.S.Z. Saleem, J.T. Tepe, J. Org. Chem. *2010*, *75* (12), 4330-2 [DOI: 10.1021/jo100716m].

Microwaves s. under Proline [\\\\]
Lithium biphenylide s. under BaI_2 ←

Copper(II) triflate/chiral bicyclic bis(α-carbamyl-N-oxides) ←
Asym. α-amination with azodicarboxylic acid esters s. *75*, 132*s78* H → NNH

Barium diiodide/lithium biphenylide ←
2-Acetylenehydrazines from azo compds. and β,γ-acetylenehalides N=N → N(R)NH
Regioselective barium-promoted Barbier-type addition

135.



3-Hydrazo(silylacetylenes). Anhydrous BaI_2 (2.2 eq.) in an oven-dried, two-necked flask under argon covered with anhydrous THF (5 ml) then stirred for 20 min at room temp., treated with a

THF soln. of Li-biphenylide [prepared by stirring freshly cut Li (4.4 eq.) and biphenyl (4.4 eq.) in anhydrous THF (5 ml) in a Schlenk flask under argon for 1.5 h at room temp. (until Li completely consumed)], the mixture stirred for 30 min at room temp., a soln. of (3-bromobut-1-ynyl)trimethylsilane (1 mmol; 2 eq.) and diethyl azodicarboxylate (2.2 *M* toluene soln.; 0.5 mmol) in anhydrous THF (4 ml) added dropwise to the resulting dark brown suspension of reactive barium (1.1 mmol) in THF (10 ml) at -78°, the mixture stirred for 2 h at this temp., treated with satd. aq. NH_4Cl soln. (10 ml) at -78°, the aq. layer extracted with ether, the organic extracts washed with 1 *N* $Na_2S_2O_3$ soln. (20 ml), dried ($MgSO_4$), filtered, concentrated *in vacuo*, and the residue purified by chromatography on silica gel → product. Y 80%. The method is applicable to ar. azo compds. (four examples; Y 52-92%), those bearing electron-withdrawing groups being more reactive than those with electron-donating ones, as well as to azodicarboxylates (thirteen examples; Y 45-85%) in reaction with γ-trialkylsilylated, γ-alkylated or γ-arylated propargylic bromides or [less efficiently] chlorides. It is noteworthy that 3-bromo-1-phenylbut-1-yne, which afforded a mixture of α- and γ-adducts in its reaction with an imine, exhibited exclusive α-selectivity. F.e.s. A. Yanagisawa, T. Koide, K. Yoshida, Synlett *2010* (10), 1515-8 [DOI: 10.1055/s-0029-1219944].

L-Proline/microwaves *Pro-OH/[\\\\]*

Chiral 2-siloxymethyl-4,5-diphenyl-1-tosylimidazolidine or N-carbamyl-N′-thiocarbamyl-cyclohexane-1,2-diamines ←

Axially-chiral polycyclic guanidines ←

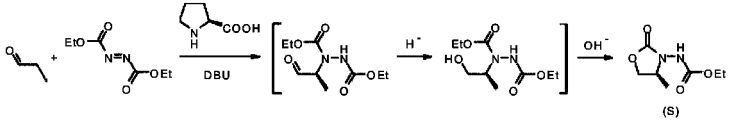
Asym. α-amination with azodicarboxylic acid esters H → NNH

s. *75*, 132s*76*; of aromatic α-(polyfluoroalkyl)aldehydes and deuteriated aldehydes with *L*-proline (cf. *63*, 142) under microwave irradiation, also conversion to chiral α,α-disubst. α-aminocarboxylic acid amides, s. C.E. Hartmann, T. Baumann, M. Bächle, S. Bräse, Tetrahedron: Asym. *2010*, *21* (11-12), 1341-9 [DOI: 10.1016/j.tetasy.2010.04.026]; of α-branched aldehydes with chiral [bifunctional] N-carbamyl-N′-thiocarbamylcyclohexane-1,2-diamines s. J.-Y. Fu, X.-Y. Xu, Y.-C. Li, Q.-C. Huang, L.-X. Wang, Org. Biomol. Chem. *2010*, *8* (20), 4524-6 [DOI: 10.1039/c0ob00406e]; with a chiral 2-siloxymethyl-4,5-diphenyl-1-tosylimidazolidine based on (R,R)-TsDPEN, also organocatalyzed asym. Diels-Alder reaction (CC⇓CC; cf. *59*, 301s*76*), s. S. Gosiewska, R. Soni, G.J. Clarkson, M. Wills, Tetrahedron Lett. *2010*, *51* (32), 4214-7 [DOI: 10.1016/j.tetlet.2010.06.017]; asym. α-amination of enacylamines with $Cu(OTf)_2$ and a chiral bicyclic bis(α-carbamyl-N-oxide) to give the corresponding chiral α-amino-N-acylimines s. L. Chang, Y. Kuang, B. Qin, X. Zhou, X. Liu, L. Lin, X. Feng, Org. Lett. *2010*, *12* (10), 2214-7 [DOI: 10.1021/ol100540p]; asym. α-amination of β-dicarbonyl compds. using axially-chiral polycyclic guanidines s. *78*, 285.

L-Proline/1,8-diazabicyclo[5.4.0]undec-7-ene *Pro-OH/DBU*

Organocatalyzed asym. α-amination of aldehydes with azodicarboxylic acid esters
Reversal of face-selectivity with added base

136.

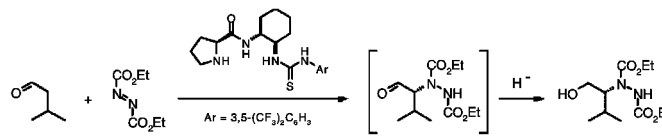


Interestingly, the face-selectivity of the established organocatalyzed asym. α-amination of aldehydes with azodicarboxylates in the presence of *L*-proline (cf. *63*, 142) is reversed on addition of a tertiary amine as co-catalyst. **E:** Diethyl azodicarboxylate [DEAD] (0.5 mmol) and the startg. aldehyde (1.5 mmol) added sequentially to a stirred soln. of *L*-proline (0.1 mmol) and DBU (0.09 mmol) in methylene chloride (2.5 ml) at 0°, stirred until complete consumption of DEAD (as indicated by the disappearance of the orange color), diluted with methanol (2.5 ml), treated portionwise with $NaBH_4$ (50 mg), stirred for a further 20 min (to reduce the aldehyde to the less sensitive alcohol), and the product isolated and characterized as the corresponding 2-oxazolidone by adding 0.5 *N* aq. NaOH (2.5 ml), stirring vigorously for 15 h, and purifying by flash chromatography on silica gel → (S)-product. Y 60% (e.e. 46%). Without added DBU the (R)-product

was formed in 67% yield (e.e. 85%). The result with L-proline alone is rationalized in terms of *anti*-addition to a *syn*-enamine rotamer, whereas with added DBU the electrophile approaches the rotamer from the opposite face to the carboxylate. Other tertiary amines and certain phosphazene bases gave similar results, correlating roughly with their pK_a value, but there was no reaction with bulky P_4-*t*-Bu. Similar face reversal was observed with chiral 5-(2-pyrrolidinyl)-1*H*-tetrazole in place of L-proline, and with tetraalkylammonium prolinates in place of the combination, but reaction failed with alkali metal prolinates on their own. F.e. (seven of reversal; Y 35-74%; e.e. (S) 25-46%) s. D.G. Blackmond, A. Moran, M. Hughes, A. Armstrong, J. Am. Chem. Soc. *2010*, *132* (22), 7598-9 [DOI: 10.1021/ja102718x].

Chiral 2-(L-prolylamino)thiourea ←
Organocatalyzed asym. α-amination of aldehydes H → NNH
with azodicarboxylic acid esters

137.



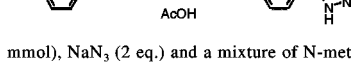
under mild conditions. A mixture of isopentanal (1.5 eq.), catalyst (20 mol%) and diethyl azodicarboxylate (0.2 mmol) in xylene (0.8 ml) stirred at 0° for *1 min*, and treated with $NaBH_4$ (1.5 eq.) in methanol → (R)-diethyl N-(1-hydroxymethyl-2-methylpropyl)hydrazinedicarboxylate. Y 97% (e.e. 99%). A series of novel pyrrolidine-thiourea catalysts derived from L-proline were effective for coupling (rapidly in some cases) of linear and branched aliphatic aldehydes (incl. acetaldehyde) with azodicarboxylate esters (Et, Bn, *i*-Pr). Products were conveniently isolated by reduction to prim. alcohols (eighteen examples; Y 68-97%; e.e. 85 to >99%; 3-phenylpropanal gave Y 65%; e.e. 77%). The authors suggest that the bifunctional catalyst acts via enamine formation with the aldehyde and hydrogen-bonding of the thiourea group to the azo moiety. F.e. and optimization s. J.-Y. Fu, Q.-C. Huang, Q.-W. Wang, L.-X. Wang, X.-Y. Xu, Tetrahedron Lett. *2010*, *51* (37), 4870-3 [DOI: 10.1016/j.tetlet.2010.07.042].

Addition to Nitrogen and Carbon NC ⇓ NC

Without additional reagents *w.a.r.*
2-Oxazolidones from aziridines and carbon dioxide ○
s. *32*, 278; catalyst-free procedure with tunable, compressed CO_2 (9 MPa) at 120° s. X.-Y. Dou, L.-N. He, Z.-Z. Yang, J.-L. Wang, Synlett *2010* (14), 2159-63 [DOI: 10.1055/s-0030-1258510]; with a recyclable DABCO-based quaternary ammonium ionic liquid, chemo- and regio-selectivity, s. Z.-Z. Yang, L.-N. He, S.-Y. Peng, A.-H. Liu, Green Chem. *2010*, *12* (10), 1850-4 [DOI: 10.1039/c0gc00286k]; with NH_4I as catalyst under mild conditions s. C. Phung, A.R. Pinhas, Tetrahedron Lett. *2010*, *51* (34), 4552-4 [DOI: 10.1016/j.tetlet.2010.06.110].

Sodium azide/acetic acid/microwaves *NaN_3/AcOH/[\\\\]*
Sodium azide/ammonium salts or γ-iron(III) oxide ←
5-Subst. tetrazoles from nitriles under batch or continuous flow conditions ○

138.



4-Chlorobenzonitrile (1 mmol), NaN_3 (2 eq.) and a mixture of N-methylpyrrolidine/acetic acid/water (7:2:1; 1 ml) in a microwave vial sealed with a Teflon septum, the mixture heated by microwaves (Biotage) at 220° (ca. 7 bar) for 5 min, cooled to 45°, residual pressure released by piercing the septum in a fume hood, the mixture added dropwise to aq. $NaNO_2$ (1 eq.) (*caution!* gas evolution), acidified (pH 1) with concd. HCl (*caution!* gas evolution), cooled in an ice-bath,

the precipitate collected by filtration, and washed with cold 1 *M* HCl → 5-(4-chlorophenyl)tetrazole. Y 98%. This unprecedented process, wherein electron-diverse (het)ar. and benzylic nitriles were heated at 220° in the presence of NaN_3, as a convenient and inexpensive source of azide, effected rapid (5-15 min) and clean conversion to 5-subst. tetrazoles (sixteen examples; Y 69-98%). Many products were isolated simply by precipitation from water with acid (water-soluble examples used an extractive process). A continuous flow system was also developed (for scalability and acid sensitive substrates), wherein HN_3 was generated in a mixing chamber. Yields by this method (fourteen examples) were essentially the same as those from the batch process. In a final development, the use of an SiC reactor plate allowed the simultaneous batch synthesis (10 min) of fourteen tetrazoles with yields practically identical to those from the microwave reactions. F.e.s. B. Gutmann, J.-P. Roduit, D. Roberge C.O. Kappe, Angew. Chem., Int. Ed. *2010*, *49* (38), 7101-5 [DOI: 10.1002/anie.201003733]; with NaN_3 and amine salts as catalyst s. Y. Zhou, C. Yao, R. Ni, G. Yang, Synth. Commun. *2010*, *40* (17), 2624-32 [DOI: 10.1080/00397910903318583]; with magnetically retrievable and recyclable $NaN_3/\gamma\text{-}Fe_2O_3$ s. G. Qi, Y. Dai, Chin. Chem. Lett. *2010*, *21* (9), 1029-32 [DOI: 10.1016/j.cclet.2010.05.003].

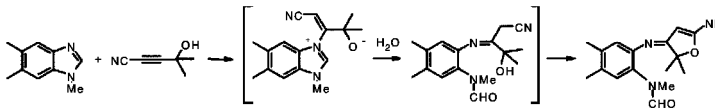
Polymer-based α-aminocarboxylic acids ←
Cyclic N-alkyltriethylenediammonium salts or Ammonium iodide ←
2-Oxazolidones from aziridines and carbon dioxide s. *32*, 278s*78* ○
(with polymer-based α-aminocarboxylic acids s. under *78*, 186)

Addition to Carbon-Carbon Bonds NC ⇓ CC

Without additional reagents *w.a.r.*
Aza-Michael addition C=C → C(N<)CH
of amines in water cf. *56*, 129s*69*; addition of anilines to enones, enoates or N-acryloylpyrroles **on water** under mild conditions s. C.B.W. Phippen, J.K. Beattie, C.S.P. McErlean, Chem. Commun. *2010*, *46* (43), 8234-6 [DOI: 10.1039/c0cc02502j]; addition of amines and polyamines to α,β-ethylenephosphorus(V) compds. (incl. P-oxides) in water or in imidazolium ionic liquids/water s. E.V. Matveeva, P.V. Petrovskii, Z.S. Klemenkova, N.A. Bondarenko, I.L. Odinets, Compt. Rend. Chim. *2010*, *13* (8-9), 964-70 [DOI: 10.1016/j.crci.2010.03.005]; simple procedure in water under microwave irradiation s. A. Kall, D. Bandyopadhyay, B.K. Banik, Synth. Commun. *2010*, *40* (12), 1730-5 [DOI: 10.1080/00397910903134634]; addition of 2-(aryloxymethyl)benzimidazoles to acrylonitrile with K_2CO_3 under microwaves s. T.-B. Wei, M.-T. Hua, H.-X. Shi, Y. Liu, Y.-M. Zhang, J. Chem. Res. *2010*, *34* (8), 452-4 [DOI: 10.3184/030823410X12798039668476]; in [bmim] methosulfate as ionic liquid **under supramolecular catalysis** s. S.R. Roy, A.K. Chakraborti, Org. Lett. *2010*, *12* (17), 3866-9 [DOI: 10.1021/ol101557t]; addition of amines to acrylates with lipase B from [promiscuous] *Candida antarctica* in toluene s. K.P. Dhake, P.J. Tambade, R.S. Singhal, B.M. Bhanage, Tetrahedron Lett. *2010*, *51* (33), 4455-8 [DOI: 10.1016/j.tetlet.2010.06.089]; addition of N-heterocyclics with K_3PO_4 as catalyst in acetonitrile s. X. Hou, H. Hemit, J. Yong, L. Nie, H.A. Aisa, Synth. Commun. *2010*, *40* (7), 973-9 [DOI: 10.1080/00397910903029867]; addition of N-unsubst. acylamines to enones with trimethylsilyl triflate as catalyst s. A.S.-Y. Lee, M.-C. Lin, C.-C. Lin, Y.-T. Chang, J. Chin. Chem. Soc. *2010*, *57* (4B), 795-9; addition of indoline to enones and subsequent aromatization to indole derivs. s. S. Bayindir, E. Erdogan, H. Kilic, N. Saracoglu, Synlett *2010* (10), 1455-8 [DOI: 10.1055/s-0029-1219923].

(E)-N-Formyl-N′-(5-amino-2,3-dihydrofuran-3-ylidene)-*o*-diamines from benzimidazoles and α,β-acetylene-γ-hydroxynitriles C○

139.



A mixture of 1,5,6-trimethyl-1*H*-benzimidazole (1 mmol), the startg. nitrile (1 mmol) and water (1 mmol) in dry acetonitrile (0.5 ml) stirred at 45-50° for 6 h, the mixture cooled to room temp., and the precipitate filtered off then recrystallized → [2-[((3E)-5-amino-2,2-dimethylfuran-3(2*H*)-

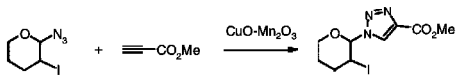
ylidene)amino]-4,5-dimethylphenyl]methylformamide. Y 99%. Reaction is thought to involve a cascade sequence of skeletal rearrangements and prototropic isomerizations after initial reaction of the two variables to give an intermediate zwitterion. The benzimidazole ring opening is extraordinarily facile (even at room temperature after several days), proceeding without transition metal catalyst, acid or base. F.e. (thirteen; Y 84-99%) s. B.A. Trofimov, L.V. Andriyankova, L.P. Nikitina, K.V. Belyaeva, A.G. Mal'kina, A.V. Afonin, Synthesis *2010* (9), 1536-42 [DOI: 10.1055/s-0029-1218704].

Microwaves (s.a. under K_2CO_3, $CuO\text{-}Mn_2O_3$ and Bu_4NOAc) [\\\\]
Potassium carbonate/microwaves K_2CO_3/[\\\\]
Potassium phosphate K_3PO_4
Aza-Michael addition s. *56*, 129s*78* C=C → CHC(N<)

Tetramethylammonium hydroxide Me_4NOH
1,2,3-Triazoles from acetylene derivs. and azides s. *64*, 141s*78* ○

Copper-manganese spinel oxide/microwaves $CuO\text{-}Mn_2O_3$/[\\\\]
1,2,3-Triazoles from terminal acetylene derivs. and azides
Ligand-free heterogeneous [3+2]-cycloaddition under bimetal catalysis with recyclable copper-manganese spinel oxide

140.



Copper(I), which is prone to redox processes, is stabilized within the tetrahedral sites of copper-manganese spinel oxide, thereby forming a robust, readily recyclable heterogeneous catalyst for classical 'click' chemistry under mild conditions, with or without solvent, and is free from by-product formation, as a valuable alternative to classical, but more limited, procedures based on stabilization of copper(I) by ligand interaction. **E:** A soln. of the startg. azide (1 mmol) and alkyne (1 mmol) in acetonitrile (0.5 ml) adsorbed on the bimetallic Cu-Mn spinel oxide (10 mg/g of reactant) in a beaker, the mixture subjected to microwave irradiation (100 W) (ramping the temp. to 120°), held at this temp. *for 3 min*, diluted with ethyl acetate/acetone (5:1), stirred for 15 min, centrifuged, the catalyst washed and dried for further use, and the organic phase worked up with purification of the product by recrystallization or by chromatography on silica gel → 4-carbomethoxy-1-(3-iodotetrahydropyran-2-yl)-1,2,3-triazole. Y 99%. The yield was 95% after 4 h by classical solution-phase cycloaddition. Very high yields of pure products (fifteen examples; Y 97-99%) were obtained with retention of a range of functionality (e.g. carbohydrate OAc and acetonide groups; hydroxyl and iodine), and the method is notably applicable to ethynyl(trimethyl)-silane which cannot be coupled under classical homogeneous catalysis. Furthermore the catalyst was recycled 10 times with effectively no loss of activity and only minimal (ca. 110 ppb) leaching of the catalyst into the product after the 10th run. The catalyst is easy to prepare and the active copper-manganese oxide phase can be simply monitored [the sample with a lin (count) of 800 being the most active]. The active copper(I) sites are presumed to be formed within the matrix by electron-transfer between Mn(III) and Cu(II), and stabilized at tetrahedral sites in such a way that no external ligand is required. F.e. and preparation of catalyst samples s. S.K. Yousuf, D. Mukherjee, B. Singh, S. Maity, S.C. Taneja, Green Chem. *2010*, *12* (9), 1568-72 [DOI: 10.1039/c005088a].

Copper nanoparticles or Copper(I) oxide nanoparticles *Cu(0) or Cu_2O*
Copper(I) zeolite ←
Copper(I) carboxylates or Copper(II) sulfate/carboxylic acids *CuOCOR or $CuSO_4$/RCOOH*
Copper(I) bromide/triethylamine *CuBr/Et_3N*
Copper(I) salt/polymer-based 1,5,7-triazabicyclo[4.4.0]dec-5-ene or N-alkylimidazole or PEG-based quaternary ammonium methosulfate ←

1,2,3-Triazoles from acetylene derivs. and azides

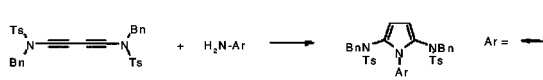
s. *64*, 141s*76*; with readily generated copper nanoparticles for ligand-free cycloaddition to terminal acetylene derivs. s. F. Alonso, Y. Moglie, G. Radivoy, M. Yus, Eur. J. Org. Chem. *2010* (10), 1875-84 [DOI: 10.1002/ejoc.200901446]; with stabilized poly(N-vinyl-2-pyrrolidone)-coated copper(I) oxide nanoparticles **in water** s. Z. Zhang, C. Dong, C. Yang, D. Hu, J. Long, L. Wang, H. Li, Y.

Chen, D. Kong, Adv. Synth. Catal. *2010*, *352* (10), 1600-4 [DOI: 10.1002/adsc.201000206]; with copper(0) *under ultrasonication* in aq. dioxane s. G. Cravotto, V.V. Fokin, D. Garella, A. Binello, L. Boffa, A. Barge, J. Comb. Chem. *2010*, *12* (1), 13-5 [DOI: 10.1021/cc900150d]; green procedure with recyclable copper(I)-doped zeolite, also other 1,3-dipolar cycloadditions and oxidative dimerization of terminal acetylene derivs. (cf. *16*, 780s*76*), s. S. Chassaing, A. Alix, T. Boningari, K.S.S. Sido, M. Keller, P. Kuhn, B. Louis, J. Sommer, P. Pale, Synthesis *2010* (9), 1557-67 [DOI: 10.1055/s-0029-1218733]; with *dinuclear* copper(I) acetate in cyclohexane or without solvent s. C. Shao, G. Cheng, D. Su, J. Xu, X. Wang, Y. Hu, Adv. Synth. Catal. *2010*, *352* (10), 1587-92 [DOI: 10.1002/adsc.200900768]; preparation of 1-sulfonyl-1,2,3-triazoles with copper(I) thiophene-2-carboxylate in toluene or water s. J. Raushel, V.V. Fokin, Org. Lett. *2010*, *12* (21), 4952-5 [DOI: 10.1021/ol102087r]; under carboxylic acid-promoted catalysis with $CuSO_4$/Na-ascorbate in water/*tert*-butanol s. C. Shao, X. Wang, J. Xu, J. Zhao, Q. Zhang, Y. Hu, J. Org. Chem. *2010*, *75* (20), 7002-5 [DOI: 10.1021/jo101495k]; with CuBr/Et_3N for **desilylative cycloaddition** to silylacetylenes (NCIIRem) s. F. Cuevas, A.I. Oliva, M.A. Pericàs, Synlett *2010* (12), 1873-7 [DOI: 10.1055/s-0030-1258120]; with a copper(I) salt and polymer-based 1,5,7-triazabicyclo[4.4.0]dec-5-ene as ligand for a mild eco-friendly procedure, also 3-component conversion with NaN_3/alkyl halide (cf. *68*, 184s*78*), s. A. Coelho, P. Diz, O. Caamaño, E. Sotelo, Adv. Synth. Catal. *2010*, *352* (7), 1179-92 [DOI: 10.1002/adsc.200900680]; with an N-alkylimidazole as ligand, notably for reaction with bulky acetylene derivs., s. K. Asano, S. Matsubara, Org. Lett. *2010*, *12* (21), 4988-91 [DOI: 10.1021/ol101990d]; with CuI and PEG-based quaternary ammonium methosulfate as ionic liquid for preparation of 1,4-disubst. 1,2,3-triazoles s. A. Vecchi, A. Chambery, C. Chiappe, A. Marra, A. Dondoni, Synthesis *2010* (12), 2043-8 [DOI: 10.1055/s-0029-1218760]; solvent-free method, also with a metallic salt other than copper, for reaction with ethynyl ketones s. H. Elamari, I. Jlalia, C. Louet, J. Herscovici, F. Meganem, C. Girard, Tetrahedron: Asym. *2010*, *21* (9-10), 1179-83 [DOI: 10.1016/j.tetasy.2010.06.013]; preparation of fluorescent triazole-subst. α-amino-esters s. C. Li, E. Henry, N.K. Mani, J. Tang, J.-C. Brochon, E. Deprez, J. Xie, Eur. J. Org. Chem. *2010* (12), 2395-405 [DOI: 10.1002/ejoc.201000042]; of moisture-sensitive sol-gel silylated triazoles s. N. Moitra, J.J.E. Moreau, X. Cattoën, M.W.C. Man, Chem. Commun. *2010*, *46* (44), 8416-8 [DOI: 10.1039/c0cc03417g]; with azidoboronates for sequential cycloaddition-Suzuki coupling s. J.R. White, G.J. Price, S. Schiffers, P.R. Raithby, P.K. Plucinski, C.G. Frost, Tetrahedron Lett. *2010*, *51* (30), 3913-7 [DOI: 10.1016/j.tetlet.2010.05.104]; application of azide/alkyne resins for the polymer-based synthesis of 1,4-disubst. triazoles s. U. Sirion, J.H. Lee, Y.J. Bae, H.J. Kim, B.S. Lee, D.Y. Chi, Bull. Korean Chem. Soc. *2010*, *31* (7), 1843-7 [DOI: 10.5012/bkcs.2010.31.7.1843]; transition *metal-free* cycloaddition with aq. Me_4NOH in DMSO, 1,5-diaryl-1,2,3-triazoles, s. S.W. Kwok, J.R. Fotsing, R.J. Fraser, V.O. Rodionov, V.V. Fokin, Org. Lett. *2010*, *12* (19), 4217-9 [DOI: 10.1021/ol101568d]; **protection of hydroxyl groups** as polymer-based diisopropyl(1,2,3-triazol-4-yl)silyl ethers via 'click' chemistry s. *78*, 2.

Copper(II) hexafluoroacetoacetonate/chiral bis(Δ^2-oxazolines) *$Cu[CH(COCF_3)_2]_2$/box*
Copper(II) chloride/tetra-n-butylammonium chloride *$CuCl_2/Bu_4NCl$*
N-Sulfonyloxazolidines from N-sulfonyloxaziridines and ethylene derivs. ○
regioselective ring expansion with $CuCl_2/Bu_4NCl$ s. *72*, 170s*77*; 1,4-diaryl-N-nosyloxazolidines s. S.M. DePorter, A.C. Jacobsen, K.M. Partridge, K.S. Williamson, T.P. Yoon, Tetrahedron Lett. *2010*, *51* (40), 5223-5 [DOI: 10.1016/j.tetlet.2010.08.015]; **asym. variant** with $Cu(F_6acac)_2$/(R)-Ph-box in acetone (e.e. up to 84%) s. D.J. Michaelis, K.S. Williamson, T.P. Yoon, Tetrahedron *2009*, *65* (26), 5118-24 [DOI: 10.1016/j.tet.2009.03.012].

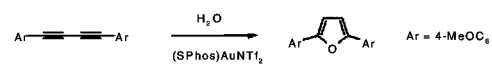
Copper(I) chloride *CuCl*
(Triphenylphosphine)gold(I) triflimide *$(Ph_3P)AuNTf_2$*
Pyrroles from 1,3-diynes and prim. amines via double gold(I)-catalyzed hydroamination ○

141.



2,5-Bis(tosylamino)pyrroles. Ethyl 4-aminobenzoate (1.05 eq.) added to a stirred mixture of startg. di(ynamide) (0.2 mmol), $[(Ph_3P)AuNTf_2]_2$·toluene (1 mol%) and methylene chloride (1 ml)

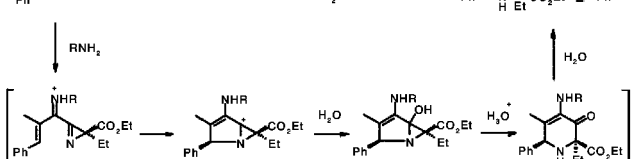
in a vial, the vial sealed, the mixture stirred at 30° for 30 min, concentrated *in vacuo*, and purified by flash chromatography → ethyl 4-[2,5-bis(N-benzyl-4-methylphenylsulfonamido)-1*H*-pyrrol-1-yl]benzoate. Y 94%. This novel and atom-economical cyclization was general for N-aryl and N-alkyl-sulfonamides reacting with electron-diverse anilines, incl. *o*-subst. derivs., (eight examples; Y 90-96%, incl. a *3,4-dideutero* deriv.), with electron-poor anilines requiring prolonged reaction time (1 h); cyclization, in one case, with phenylhydrazine afforded an *N-phenylaminopyrrole* in moderate yield (51%). Cyclization of terminal diaryl diynes was less effective, requiring more forcing conditions (80°/24 h) for incomplete conversions to 1,3,5-trisubst. pyrroles (two examples; Y 49-58%), while a di-*n*-hexyl diyne gave only 24% yield. The method was extended to the prepn. of **2,5-bis(tosylamino)furans** (four examples; Y 51-85%) and **2,5-diaryl- and 2,5-dialkylfurans** (seven examples; Y 59-84%) via hydration at 60°, optimally with (SPhos)AuNTf$_2$ as catalyst.



Cyclization of diphenylbutadiyne with phenylhydrazine gave a mixture of *N-phenyl-3(5)-benzyl-5(3)-phenylpyrazoles* (Y 28% and 20%). F.e. and optimization s. S. Kramer, J.L.H. Madsen, M. Rottländer, T. Skrydstrup, Org. Lett. *2010*, *12* (12), 2758-61 [DOI: 10.1021/ol1008685]; **1,2,5-trisubst. pyrroles** with CuCl (10 mol%) at 100° s. Q. Zheng, R. Hua, Tetrahedron Lett. *2010*, *51* (34), 4512-4 [DOI: 10.1016/j.tetlet.2010.06.092].

N-Cyclohexyl-(R,R)-cyclohexane-1,2-diamine monotrifluoroacetate ←
Organocatalyzed ring expansion with kinetic resolution ⓘ
of 2-cinnamoyl-Δ^1-azirines via aza-Nazarov ring closure

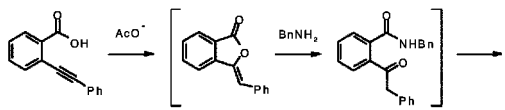
142.



Water (1.2 eq.) and a soln. of 1,2-diamine catalyst as its mono-trifluoroacetic acid salt (20 mol%) in methylene chloride added to a soln. of startg. azirine (0.1 mmol) in acetonitrile (0.13 ml) at 21°, the mixture stirred for 9 d, brine added, the mixture extracted with ethyl acetate, concentrated *in vacuo*, and purified by chromatography on silica → (2S,6S)-ethyl 2-ethyl-1,2,3,6-tetrahydro-4-hydroxy-5-methyl-3-oxo-6-phenylpyridine-2-carboxylate. Y 28% (and unreacted (R) enantiomer; Y 36%). This unexpected and rare cyclization/resolution occurred with other cinnamyl derivs. (two examples; Y 28.5%, 25%), while crotonyl analogs were unreactive. The ring expansion is rationalized by diastereospecific formation of an iminium ion via reaction with the catalyst, and subsequent cleavage of the azirine ring driving the process to completion. Absolute stereochemistry of the products was determined in one case by X-ray crystallography. F.e., optimization and substrate prepn. s. N. Shimada, B.O. Ashburn, A.K. Basak, W.F. Bow, D.A. Vicic, M.A. Tius, Chem. Commun. *2010*, *46* (21), 3774-5 [DOI: 10.1039/b927564a].

Tetra-n-butylammonium acetate/microwaves *Bu_4NOAc/[\\\\]*
3-Hydroxyphthalimidines from *o*-acetylenecarboxylic acids and prim. amines ○
Mild, regiospecific conversion under phase transfer catalysis in water

143.



Tetra-*n*-butylammonium acetate (5 mol%) added to a suspension of 2-(phenylethynyl)benzoic acid (0.1 mmol) in water (3 ml), the mixture heated to 100° under argon for 10 min under microwave irradiation performed in an Initiator™ EXP microwave system (Biotage, Inc.), benzylamine (0.2 mmol) added, microwave heating continued at 100° under argon for a further 10 min, cooled, concentrated in vacuum, and worked up with purification by flash chromatography → product. Y 94%. The procedure is mild, eco-friendly, metal-free, atom-economical and applicable to the coupling of *o*-acetylenebenzoic acids with electron-diverse benzylamines, heterocyclic analogs and aliphatic prim. amines, tolerating a wide range of functionality (ca. twenty examples; Y 70-95%). The position and nature of substituents on the benzylamine ring had little effect on the reaction, although yields were slightly reduced with *o*- and/or *m*-subst. benzylamines (steric effect). Significantly, 5-*exo*-cyclization was the rule, reaction taking place in tandem fashion with intermediate formation of an enollactone, ultimately generating two new C-N bonds and one C-O bond from 2 simple substrates. The protocol can also be scaled up to the gram level. F.e. and comparison of phase transfer catalysts s. Y. Zhou, Y. Zhai, J. Li, D. Ye, H. Jiang, H. Liu, Green Chem. *2010*, *12* (8), 1397-404 [DOI: 10.1039/c004745g].

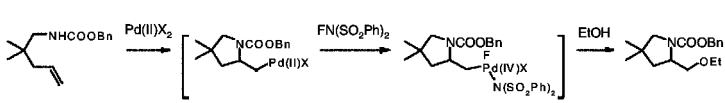
Chiral bis(Δ^2-oxazolines) s. under $Cu(F_6acac)_2$ *box*

Imidazolium ionic liquids or Lipase or Trimethylsilyl triflate ←
Aza-Michael addition s. *56*, 129s*78* C=C → C(N≤)CH

Tetra-n-butylammonium chloride s. under $CuCl_2$ *Bu_4NCl*

Palladium(II) trifluoroacetate/N-fluorobenzenesulfonimide *$Pd(OCOCF_3)_2$/$(PhSO_2)_2NF$*
Palladium-catalyzed intramolecular oxyamination of ethylene derivs. ○
Effect of catalyst and medium on regioselectivity
with N-fluorobenzenesulfonimide as oxidant under mild conditions

144.



N-Protected 2-(alkoxymethyl)pyrrolidines. $Pd(OCOCF_3)_2$ (10 mol%) and N-fluorobenzenesulfonimide (2 eq.) weighed into a round-bottomed flask containing 3 Å molecular sieves, the flask capped with a rubber septum and filled with N_2, the startg. N-protected ethyleneamine (0.25 mmol) *in ethanol* (5 ml) added, the mixture stirred overnight, diluted with ethyl acetate, the resulting soln. decanted into another flask, concentrated under reduced pressure, and purified chromatographically → benzyl 2-(ethoxymethyl)-4,4-dimethylpyrrolidine-1-carboxylate. Y 52%. Interestingly, with $PdCl_2(MeCN)_2$ as catalyst, or with $Pd(OCOCF_3)_2$ containing added halide ion, a 1:1 mixture of *exo*/*endo*-regioisomers was obtained, and *in DMF* (with either catalyst) the *endo*-isomer was formed almost exclusively, although yields were only moderate (38-80%; four examples). Higher alcohols (e.g. benzyl or *p*-methoxybenzyl alcohol) were also effective nucleophiles *in non-polar medium* (e.g. benzene), the latter always favoring the *exo*-regioisomer. The *exo*-isomers are presumed to be formed via initial intramolecular aminopalladation followed by

oxidative addition of N-fluorobenzenesulfonimide to give a palladium(IV) species prior to cleavage with the nucleophile. The mechanism of the *endo*-cyclization is less clear but an aziridinium ion may be involved. F.e. (ten of *exo*-regioisomers; Y 48-62%) incl. reaction with branched alcohols and with acetic acid as nucleophile s. D.V. Liskin, P.A. Sibbald, C.F. Rosewall, F.E. Michael, J. Org. Chem. *2010*, *75* (18), 6294-6 [DOI: 10.1021/jo101171g].

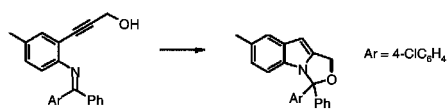
Rearrangement ∩

Hydrogen/Oxygen Type NC ∩ HO

Copper(I) bromide *CuBr*

Copper(I)-catalyzed double ring closure of *o*-(alkylideneamino)acetylenealcohols ○

145.



1*H*,3*H*-Oxazolo[3,4-*a*]indoles. DMF (2 ml) added to a mixture of startg. imine (0.5 mmol) and CuBr (10 mol%), the mixture stirred at 80° until reaction complete (TLC), quenched with water, extracted with ethyl acetate, concentrated *in vacuo*, dissolved in hexane/ethyl acetate, and filtered through silica → 3-(4-chlorophenyl)-1,3-dihydro-7-methyl-3-phenyloxazolo[3,4-*a*]indole. Y 78%. This efficient and relatively mild cascade cyclization does not occur in the absence of CuBr and gives reduced yields in the presence of other copper salts. The method was successful for the preparation of oxazolo-, **dihydrooxazino-** and **oxazepino-[3,4-*a*]indoles** by use of the appropriate acetylenealcohol (sixteen examples; Y 69-89%) in the presence of halo and ether functionality. F.e. and optimization s. W. Fu, M. Zhu, G. Zou, Appl. Organomet. Chem. *2010*, *24* (7), 499-502 [DOI: 10.1002/aoc.1648].

Hydrogen/Carbon Type NC ∩ HC

Iron(II) chloride *$FeCl_2$*

N-Unsubst. indoles from 3-aryl-Δ¹-azirines
via iron(II)-catalyzed intramolecular *o*-amination with (Z)-β-styrylnitrenes ○

146.

2,3-Disubst. indoles. $FeCl_2$ (5 mol%) added to the startg. azirine (1 mmol; vacuum dried) under N_2, *THF* (1 ml) added, the mixture stirred at 70° for 24 h, cooled to room temp., and worked up with purification by chromatography on silica gel → product. Y 79%. The procedure is less expensive and less toxic than routes based on Pd- or Rh-catalysis, and is of broader scope (ca. twenty examples; Y 46-93%), notably tolerating electron-diverse substituents (e.g. OMe, NO_2) on the aromatic ring, alkyl or aryl substitution of the azirine ring, and leaving a wide range of functionality unaffected (notably Br, F, CF_3, OTBS, alkenes and OPiv). $FeBr_2$ and FeI_2 were also effective in slightly lower yield, but other iron salts, CuCl, $CuCl_2$ and Lewis or Brønsted acids gave poor yields or complex mixtures of unidentified products. The solvent is critical, no rearrangement taking place in THF, DME, methylene chloride, 1,2-dichloroethane or toluene at room temp. F.e. and mechanistic rationale, also adaptation for the synthesis of **6-azaindoles**, s. S. Jana, M.D. Clements, B.K. Sharp, N. Zheng, Org. Lett. *2010*, *12* (17), 3736-9 [DOI: 10.1021/ol101130e].

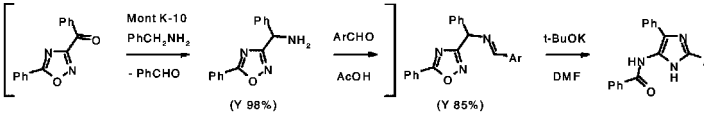
Oxygen/Nitrogen Type NC ∩ ON

Potassium tert-butoxide *KOBu-t*

4(5)-Acylamino-2-arylimidazoles from 3-α-(benzylideneamino)-1,2,4-oxadiazoles C,O

Boulton-Katritzky-type rearrangement with a 'CN=C' side-chain

147.



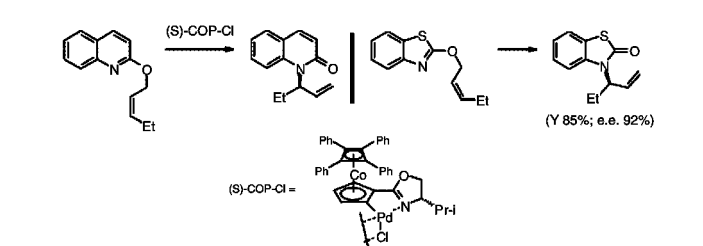
A soln. of N-(4-fluorobenzylidene)phenyl(5-phenyl-1,2,4-oxadiazol-3-yl)methanamine (1 mmol) in DMF (5 ml) treated with K-*tert*-butoxide (1.1 eq.), the mixture heated under reflux for 1 h, cooled, solvent evaporated, the dry residue treated with water, neutralized with 1 *N* HCl, extracted with ethyl acetate, and purified by flash chromatography on silica gel → 2-(4-fluorophenyl)-4(5)-phenyl-5(4)-N-(benzoylamino)imidazole. Y 76%. Nine similar examples afforded yields of 52-89%, with lowest yields being obtained for substrates having electron-donating groups (4-Me_2N and 4-MeO substituents) on the ring of the ar. imine. Decomposition of starting material was observed in the absence of base (simply by heating in a variety of organic solvents; protic solvents, such as methanol or ethanol, giving rise to simple hydrolysis of the startg. imine). F.e., also prepn. of startg. imines by novel montmorillonite-K10 catalyzed **non-reductive trans-amination** of a 3-benzoyl-1,2,4-oxadiazole with benzylamine, followed by condensation of the resulting prim. amine (Y 98%) with benzaldehyde derivs. (nine examples; Y 80-95%), s. A.P. Piccionello, S. Buscemi, N. Vivona, A. Pace, Org. Lett. *2010*, *12* (15), 3491-3 [DOI: 10.1021/ol1013087]; **5-acylamino-1,2,4-triazoles** from N-(1,2,4-oxadiazol-3-yl)hydrazones thermally in the absence of solvent cf. ibid., *2009*, *11* (17), 4018-20 [DOI: 10.1021/ol901687n]; temperature-dependence of base-catalyzed **ring rearrangements of 3-acylamino-1,2,4-oxadiazoles** s. A. Pace, I. Pibiri, A.P. Piccionello, S. Buscemi, N. Vivona, G. Barone, J. Org. Chem. *2007*, *72* (20), 7656-66 [DOI: 10.1021/jo701306t].

Oxygen/Carbon Type NC ∩ OC

Chiral cobaltocene-functionalized palladacyclic Δ^2-oxazoline complex/ silver trifluoroacetate ←

Palladium(II)-catalyzed asym. [3.3]-sigmatropic rearrangement of *o*-allyloxy-N-heterocyclics ∩

148.

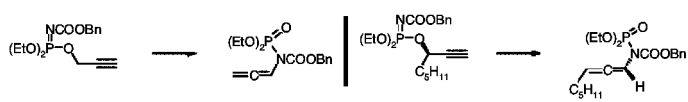


A soln. of 2-pent-2-enyloxyquinoline (1 mmol) in methylene chloride (1 ml) added to a stirred soln. of (S)-COP-Cl (5 mol%) and $Ag(OCOCF_3)$ (10 mol%) in the same solvent in a flame dried

vial under N_2, the vial sealed, heated at 35° for 20 h, the mixture concentrated, and purified chromatographically → N-pent-1-en-3-yl-1*H*-quinolin-2-one. Y 85% (e.c. 95%). Under optimized conditions using the commercially available chiral catalyst, 2-allyloxypyridines and quinoline, isoquinoline and benzothiazole analogs underwent clean and enantioselective 3-aza-1-oxa-Cope rearrangement to the corresponding **chiral N-allyllactams** (seventeen examples; Y 61-95%; e.e. 83-96%) in the presence of silyl and benzyl ethers. Absolute configuration (confirmed by X-ray analysis in one case) was determined by substrate stereochemistry, with (Z)-allyloxy derivs. generally affording higher yields and enantioselectivities. The reaction is sensitive to steric effects, however, and was only successful for linear-alkyl terminated-allyloxy substituents (cyclohexyl or phenyl-terminated analogs were poor substrates). The reaction also failed with 2-allyloxypyrimidines. F.e., also prepn. of substrates from *o*-halogeno-N-heterocyclics and readily available 2-ethylenealcohols, s. A. Rodrigues, E.E. Lee, R.A. Batey, Org. Lett. *2010, 12* (2), 260-3 [DOI: 10.1021/ol9025759].

Bis(acetonitrile)dichloropalladium(II) $PdCl_2(MeCN)_2$
N-Protected N-allenylphosphoromonoamidates ∩
from 2-acetylene-P-iminophosphoric acid esters
Palladium-catalyzed [3.3]-sigmatropic rearrangement

149.



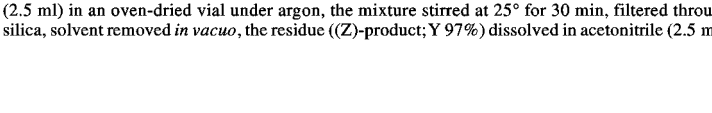
(Y 70%; e.e. 80%)

The startg. phosphorimidate (0.2 mmol) and 3 mol% $PdCl_2(MeCN)_2$ added to methylene chloride (20 ml), stirred at room temp. for 5-7 h (TLC), the solvent removed under vacuum, and the crude mixture *immediately* subjected to flash chromatography → benzyl diethoxyphosphoryl(propa-1,2-dienyl)carbamate. Y 76%. The procedure is applicable in good yield (58-76%; twelve examples) to the formation of mono-, di- and tri-subst. alleneamine derivs. from aliphatic [linear or branched alkyl-substituted] terminal or internal propargyl derivs., chiral substrates reacting with **central-to-planar transfer of chirality**. There was no reaction, however, with tertiary propargyl derivs. and substrates possessing an aryl group at the terminal site were more challenging [electron-rich primary arylacetylene derivs., for example, giving lowish yields (25-41%)]. The substrates were simply obtained by condensation of the corresponding propargyl alcohols with dialkyl chlorophosphites and carbobenzoxy azide ($CbzN_3$) and used directly. The thermal rearrangement failed. F.e.s. A.M. Danowitz, C.E. Taylor, T.M. Shrikian, A.K. Mapp, Org. Lett. *2010, 12* (11), 2574-7 [DOI: 10.1021/ol1007845].

Nitrogen/Nitrogen Type NC ∩ NN

Copper(II) acetate $Cu(OAc)_2$
β-Amino-α,β-ethylenenitriles from α,β-acetylenehydrazones ∩
Copper(II)-catalyzed 1,4-N→C-amine migration

150.



Startg. (Z)-hydrazone (0.25 mmol) added to a mixture of $Cu(OAc)_2$ (10 mol%) and acetonitrile (2.5 ml) in an oven-dried vial under argon, the mixture stirred at 25° for 30 min, filtered through silica, solvent removed *in vacuo*, the residue ((Z)-product; Y 97%) dissolved in acetonitrile (2.5 ml),

acetic acid (5 eq.) added under N_2, the mixture stirred at 25° for 2 h, filtered through silica, and purified by chromatography on silica → (E)-3-(cyclohex-2-en-1-yl)-3-morpholinoacrylonitrile. Y 83%. This migration appears general for cyclic and acyclic N,N-dialkylpropynal hydrazones terminated with electron-diverse aryl and alkyl groups (nine examples; Y 75-89%) with a less active N-methyl-N-*phenyl*hydrazone requiring heating at 130° (Y 45%) and a H-terminated deriv. giving only 82% conversion (65% isolated yield). The initially formed (Z)-products were prone to isomerization during chromatography, resulting in lower yields, but underwent efficient isomerization by treatment with acetic acid. Other catalysts (incl. gold and platinum complexes) were less effective, with CuI affording significant amounts (Y 20%) of a pyrazole by-product. F.e., substrate prepn. and optimization s. I. Nakamura, N. Shiraiwa, R. Kanazawa, M. Terada, Org. Lett. *2010*, *12* (18), 4198-200 [DOI: 10.1021/ol1017504].

Carbon/Carbon Type NC ∩ CC

Microwaves s. under $(Ph_3P)AuNTf_2$ [\\\\]

(R)-N,N′-Dilithio-2,2′-di(benzylamino)-1,1′-binaphthyl bis(etherates) ←

Catalytic asym. intramolecular hydroamination ○

with chiral gold(I) complexes cf. *72*, 185; chiral 2-vinyl-N-heterocyclics from amino-1,3-dienes with (R)-N,N′-dilithio-2,2′-di(benzylamino)-1,1′-binaphthyl bis(etherates) s. J. Deschamp, C. Olier, E. Schulz, R. Guillot, J. Hannedouche, J. Collin, Adv. Synth. Catal. *2010*, *352* (13), 2171-6 [DOI: 10.1002/adsc.201000302]; asym. intramolecular hydroamination of alkenes with (R)-1,1′-binaphthyl-based yttrium(III) triamide complexes s. I. Aillaud, J. Collin, J. Hannedouche, E. Schulz, A. Trifonov, Tetrahedron Lett. *2010*, *51* (35), 4742-5 [DOI: 10.1016/j.tetlet.2010.07.023]; of *1,2-disubst.* alkenes with tetrakis(trimethylsilylmethyl)yttrium(III) ate complexes/(R)-2,2′-bis-(benzylamino)-1,1′-binaphthyl s. Y. Chapurina, J. Hannedouche, J. Collin, R. Guillot, E. Schulz, A. Trifonov, Chem. Commun. *2010*, *46* (37), 6918-20 [DOI: 10.1039/c0cc01064b].

Copper(I) bromide *CuBr*

Copper(I)-catalyzed double ring closure of *o*-(alkylideneamino)acetylenealcohols s. *78*, 145

Acyclic gold(I) 1,1-diaminocarbene complexes *[Au(I)]*

Catalytic intramolecular hydroamination of carbon-carbon multiple bonds

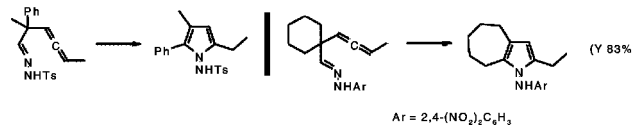
with poly(N-vinyl-2-pyrrolidone)-stabilized gold nanoclusters s. *70*, 147s76; 2-vinyl-N-heterocyclics from alleneamines with acyclic gold(I) 1,1-diaminocarbene complexes, also cycloisomerization of allenealcohols and phenyl homopropargyl sulfoxides, s. C. Bartolomé, D. García-Cuadrado, Z. Ramiro, P. Espinet, Organometallics *2010*, *29* (16), 3589-92 [DOI: 10.1021/om100507r]; intramolecular hydroamination of alkynes with electronically and sterically modifiable methylzinc β-diketiminato complexes and dimethyl(phenyl)amine·TfOH as co-catalyst s. M. Biyikal, K. Löhnwitz, N. Meyer, M. Dochnahl, P.W. Roesky, S. Blechert, Eur. J. Inorg. Chem. *2010* (7), 1070-80 [DOI: 10.1002/ejic.200900998]; of ethylene derivs. with methylzinc aminotroponiminato complexes s. M. Dochnahl, K. Löhnwitz, A. Lühl, J.-W. Pissarek, M. Biyikal, P.W. Roesky, S. Blechert, Organometallics *2010*, *29* (12), 2637-45 [DOI: 10.1021/om901012f]; with phenylenediamine-based (dimethylamine)aluminum triamide complexes s. J. Koller, R.G. Bergman, Chem. Commun. *2010*, *46* (25), 4577-9 [DOI: 10.1039/c002760j]; with pincer-type dimethyl[2,6-bis(aryloxymethyl)phenyl]aluminum complexes s. Organometallics *2010*, *29* (15), 3350-6 [DOI: 10.1021/om100278b]; with (1,2-diaminato)(trimethylsilylmethyl)-scandium(III) or bis(trimethylsilylmethyl)yttrium(III) α-aminatoketimine complexes s. H. Kaneko, H. Tsurugi, T.K. Panda, K. Mashima, ibid. 3463-6 [DOI: 10.1021/om1002667]; with dibenzyluranium(IV) bis(N-silylamide) complexes s. E.M. Broderick, N.P. Gutzwiller, P.L. Diaconescu, ibid. 3242-51 [DOI: 10.1021/om9006328]; with zirconium(IV) 2-imidazolone complexes s. Y.-C. Hu, C.-F. Liang, J.-H. Tsai, G.P.A. Yap, Y.-T. Chang, T.-G. Ong, ibid. 3357-61 [DOI: 10.1021/om100296m]; with iridium(I) *o*-(diisopropylphosphino)phenolate complexes s. K.D. Hesp, R. McDonald, M. Stradiotto, Can. J. Chem. *2010*, *88* (8), 700-8 [DOI: 10.1139/V09-181]; intramolecular hydroamination of alkynes with cationic rhodium(I) or iridium(I) 1-[2-(diphenylphosphino)ethyl]pyrazole complexes s. S.R. Beeren, S.L. Dabb, G. Edwards, M.K. Smith, A.C. Willis, B.A. Messerle, New J. Chem. *2010*, *34* (6), 1200-8 [DOI: 10.1039/b9nj00759h].

(Triphenylphosphine)gold(I) triflimide/microwaves *$(Ph_3P)AuNTf_2$*

1-Aminopyrroles from β-allenehydrazones

Gold(I)-catalyzed cycloisomerization with selective 1,2-alkyl or -aryl migration under microwave irradiation

151.



$[(Ph_3P)AuNTf_2]_2{\cdot}C_6H_5Me$ (5 mol%) added to a soln. of startg. allenehydrazone (0.2 mmol) in dry 1,2-dichloroethane (3.5 ml) under argon, the soln. heated by microwaves at 100° for 20 min, cooled to room temp., filtered through silica, concentrated *in vacuo*, and purified by flash chromatography over silica → N-(5-ethyl-3-methyl-2-phenyl-1*H*-pyrrol-1-yl)-4-methylbenzenesulfonamide. Y 99%. This novel and experimentally simple cycloisomerization occurs with exclusive migration of α-phenyl or -ethyl substituents in the presence of α-methyl to afford 2,3,5-trisubst. 1-aminopyrroles (twenty-one examples; Y 51-99%). The reaction apparently requires an electron-withdrawing group on the N-terminus (tosyl, 2,4-dinitrophenyl or *ethoxycarbonyl* are suitable). Spiro-linked allenehydrazones afforded bicyclic 1-aminopyrroles, but a less-reactive β-alleneimine gave only 15% yield of a N-phenylpyrrole. Structures were confirmed by X-ray analysis in one case. F.e., optimization and substrate prepn. s. E. Benedetti, G. Lemière, L.-L. Chapellet, A. Penoni, G. Palmisano, M. Malacria, J.-P. Goddard, L. Fensterbank, Org. Lett. *2010*, *12* (19), 4396-9 [DOI: 10.1021/ol101889h].

Methylzinc β-diketiminato or aminotroponiminato complexes *[Zn(II)]*

(Dimethylamine)aluminum triamide complexes or Pincer-type dimethyl[2,6-bis(aryloxymethyl)phenyl]aluminum complexes *[Al(III)]*

(1,2-Diaminato)(trimethylsilylmethyl)scandium(III) or Bis(trimethylsilylmethyl)yttrium(III) α-aminatoketimine complexes or Dibenzyluranium(IV) bis(N-silylamide) complexes ←

Catalytic intramolecular hydroamination of carbon-carbon multiple bonds

s. *70*, 147s*78*

(R)-1,1′-Binaphthyl-based yttrium(III) triamide complexes or tetrakis(trimethylsilylmethyl)yttrium(III) ate complexes/(R)-2,2′-bis(benzylamino)-1,1′-binaphthyl *[Y(III)]*

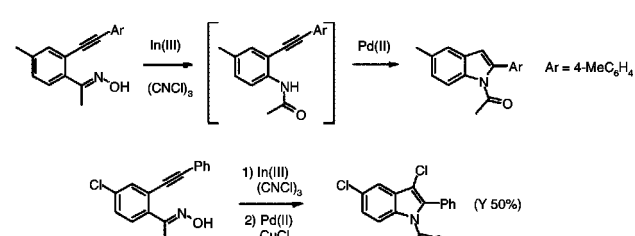
Catalytic asym. intramolecular hydroamination s. *72*, 185s*78*

Cyanuric chloride/indium(III) chloride/bis(acetonitrile)dichloropalladium(II) ←

1-Acylindoles from *o*-acetyleneketoximes

Beckmann rearrangement-intramolecular hydroamination under sequential catalysis

152.



in one pot. Cyanuric chloride (10 mol%) and $InCl_3$ (10 mol%) added to a soln. of startg. ketoxime (0.2 mmol) in acetonitrile (2 ml), the mixture stirred at reflux under N_2 until substrate consumed

(TLC), $PdCl_2(MeCN)_2$ (10 mol%) added, the mixture stirred at reflux overnight, and purified by flash chromatography on silica → 1-(5-methyl-2-*p*-tolyl-1*H*-indol-1-yl)ethanone. Y 70%. Aryl- and alkyl-terminated *o*-acetyleneoximes derived from alkyl aryl ketones underwent initial $InCl_3$- (or $ZnCl_2$ to a lesser extent) catalyzed Beckmann rearrangement to ***o*-acetyleneacylamines** (isolated in one case in 90% yield), with subsequent palladium-promoted cyclization affording 2-subst. 1-acylindoles (twelve examples; Y 52-80%). Trimethylsilyl terminated acetylenes, however, produced complex mixtures, while a diaryl ketone derived oxime afforded only the initial Beckmann product. Addition of a suitable chlorinating agent ($CuCl_2$) during the cyclization step provided a synthesis of **2-subst. 1-acyl-3-chloroindoles** (six examples; Y 50-66%). F.e. and optimization s. G. Qiu, Q. Ding, H. Ren, Y. Peng, J. Wu, Org. Lett. *2010*, *12* (18), 3975-7 [DOI: 10.1021/ol101487q].

Zirconium(IV) 2-imidazolone complexes *[Zr(IV)]*
Catalytic intramolecular hydroamination of carbon-carbon multiple bonds ○
s. *70,* 147s*78*

Chiral 1,1′-binaphthyl-2,2′-diyl hydrogen phosphates ←
Δ²-Pyrazolines from (E)-α,β-ethylenehydrazones
via organo-Brønsted acid-catalyzed asym. 6π-electrocyclization
of α,β-ethylenehydrazonium salts s. *77,* 159; s.a. S. Müller, B. List, Synthesis *2010* (13), 2171-8 [DOI: 10.1055/s-0029-1218792].

Cationic rhodium(I) or iridium(I) 1-[2-(diphenylphosphino)ethyl]pyrazole complexes or Iridium(I) o-(diisopropylphosphino)phenolate complexes *[Rh(I)] or [Ir(I)]*
Catalytic intramolecular hydroamination of carbon-carbon multiple bonds
s. *70,* 147s*78*

Exchange ↓↑

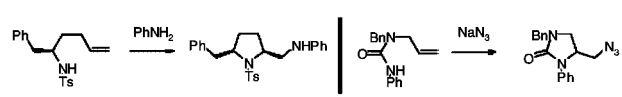
Hydrogen ↑ NC ↓↑ H

Sodium, potassium or ammonium nitrate/sulfuric acid *MNO_3/H_2SO_4*
Metal nitrates/potassium hydrogen sulfate *$MNO_3/KHSO_4$*
Nitration of phenols H → NO_2
s. *1,* 343s*41*; inexpensive, clean and eco-friendly mono-*o*-nitration of phenols with various metal nitrates and $KHSO_4$ as catalyst s. B. Baghernejad, H.A. Oskooie, M.M. Heravi, Y.Sh. Beheshtiha, Chin. J. Chem. *2010*, *28* (3), 393-6 [DOI: 10.1002/cjoc.201090085]; trinitration of phloroglucinol and its mono-, di- and tri-methyl ethers with an inorganic salt ($NaNO_3$, KNO_3 or NH_4NO_3) and H_2SO_4 s. N.A. Straessler, Synth. Commun. *2010*, *40* (17), 2513-9 [DOI: 10.1080/00397911.2010.481743]; mild mononitration of phenols with bismuth subnitrate/charcoal and trichloroisocyanuric acid s. A.R. Pourali, F. Fatemi, Chin. Chem. Lett. *2010*, *21* (11), 1283-6 [DOI: 10.1016/j.cclet.2010.05.016]; rapid nitration of salicylic acid and other aromatics with nitric acid and H_3PO_4/TiO_2-ZrO_2 s. R.J. Kalbasi, A.R. Massah, F. Zamani, H.J. Naghash, Chin. J. Chem. *2010*, *28* (3), 397-403 [DOI: 10.1002/cjoc.201090086].

Copper(II) acetate s. under I_2 *$Cu(OAc)_2$*

Copper(II) 2-ethylhexanoate/cesium carbonate *$Cu(OCOR)_2/Cs_2CO_3$*
2-α-Functionalized N-heterocyclics from 4-ethyleneamines and N-nucleophiles ○
Copper(II)-catalyzed stereoselective diamination

153.



(Y 85%)

Benzotrifluoride (0.75 ml) and aniline (3 eq.) added via syringe to a mixture of (R)-N-tosyl-2-benzylpent-4-enylamine (0.15 mmol), Cs_2CO_3 (1 eq.) and Cu(II)-2-ethylhexanoate (2 eq.) in a

glass tube, the tube capped, the mixture heated at 120° for 24 h, cooled to room temp., diluted with ethyl acetate, washed with aq. Na_2EDTA and aq. NaOH, concentrated *in vacuo*, and purified by flash chromatography on silica → (2S,5R)-N-tosyl-2-anilinomethyl-5-benzylpyrrolidine. Y 82% (d.r. >20:1). This novel and selective diamination appears general for the preparation of 2-aminomethyl derivs. of **5-imidazolidone, 5-pyrrolidone, pyrrolidine** and **indoline**, using sulfonamide, benzamide and electron-diverse anilines as well as azide (NaN_3) as N-nucleophiles (thirty examples; Y 42-97%). The reaction generally required excess (3 eq.) nucleophile to minimize side-reactions, and the use of stoichiometric amounts of copper(II), but for sulfonamide nucleophiles the reaction was catalytic in copper (four examples; Y 69-87%). A single example using 3 eq. $Cu(OTf)_2$ and a chiral bis(oxazoline) effected moderate chiral induction (Y 64%; e.e. 73%). F.e.s. F.C. Sequeira, B.W. Turnpenny, S.R. Chemler, Angew. Chem., Int. Ed. *2010*, *49* (36), 6365-8 [DOI: 10.1002/anie.201003499].

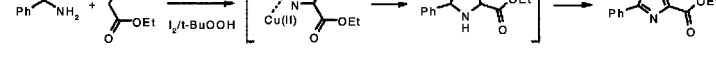
Copper(II) acetoacetonate/2,2′-bipyridyl/lithium or sodium tert-butoxide/N-chlorosuccinimide ←
Regiospecific copper(II)-catalyzed *tert*-amination of azoles H → N≤
with *in situ*-generated N,N-disubst. chloramines s. *78*, 183

Copper(II) chloride s. under $PdCl_2$ *$CuCl_2$*
1,3-Bis(2,6-diisopropylphenyl)imidazolidin-2-ylidene/arylboronic acids s. under $Fe(OTf)_2$ ←
Acetonitrile/1,3-diisopropylimidazolium bromide/sodium hydride s. under $RuH_2(PPh_3)_4$ ←
tert-Butyl hydroperoxide s. under I_2 *t-BuOOH*
N-Chlorosuccinimide s. under $Cu(acac)_2$ *NCS*

Phosphoric acid/titanium dioxide-zirconium dioxide *H_3PO_4/TiO_2-ZrO_2*
Bismuth subnitrate/charcoal/trichloroisocyanuric acid ←
Nitration of phenols s. *1*, 343s*78* H → NO_2

Air s. under $Fe(OTf)_2$ *O_2*

Iodine/copper(II) acetate/tert-butyl hydroperoxide *$I_2/Cu(OAc)_2$/t-BuOOH*
2-Aryloxazole-4-carbonyl from β-ketocarbonyl compds. and benzylamines ○
Copper(II)-catalyzed ring closure via sequential oxidation under mild conditions

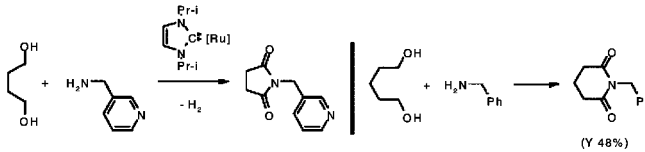
154. 

Iodine (1.2 mmol), the startg. β-keto-ester (1 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.1 mmol) and *tert*-butyl hydroperoxide (2 mmol) added sequentially to a soln. of benzylamine (1.5 mmol) in DMF (3 ml), the mixture stirred for 4 h at room temp., a second portion of benzylamine (0.5 mmol) added, reaction allowed to reach completion, and worked up with chromatographic purification → ethyl 5-methyl-2-phenyloxazole-4-carboxylate. Y 76%. The procedure is mild, economical, eco-friendly, based on readily accessible substrates, and high-yielding for the reaction of β-keto-esters and β-diketones having alkyl, aryl or vinyl substitution, irrespective of electronic or steric factors. The benzylamines may possess an electron-withdrawing or -donating group, but the former afforded higher yields; heterocyclic analogs, e.g. 2-aminomethylfuran, also participated, but aliphatic prim. amines were unreactive (ca. twenty examples in all; Y 49-91%) while reaction with a β-keto-amide was low-yielding. Reaction is thought to involve sequential oxidation with iodine and *tert*-butyl hydroperoxide to give an intermediate copper(II)-complexed α-(benzylideneamino)ketone, which undergoes intramolecular cyclization prior to oxidative aromatization. F.e. and comparison of oxidants, copper salts and solvents s. C. Wan, J. Zhang, S. Wang, J. Fan, Z. Wang, Org. Lett. *2010*, *12* (10), 2338-41 [DOI: 10.1021/ol100688c].

Iron(II) triflate/1,3-bis(2,6-diisopropylphenyl)imidazolidin-2-ylidene/arylboronic acids/air ←
Carboxylic acid amides from aldehydes and sec. amines CHO → CON≤
via iron(II)-catalyzed aerobic oxidation – Arylcarboxylic acid amides s. *78*, 103

Dihydridotetrakis(triphenylphosphine)ruthenium(II)/acetonitrile/1,3-diisopropyl-imidazolium bromide/sodium hydride ←
Dicarboxylic acid imides from diols and prim. amines ○
Ruthenium-catalyzed dehydrogenative ring closure

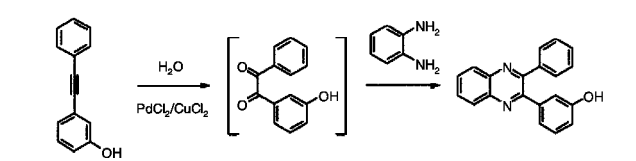
155.



in one pot. A mixture of $[RuH_2(PPh_3)_4]$ (5 mol%), 1,3-diisopropylimidazolium bromide (5 mol%), NaH (20 mol%) and acetonitrile (5 mol%) in toluene (0.5 ml) refluxed under argon in an oven-dried Schlenk tube for 20 min, 1,4-butanediol (0.5 mmol) and 3-aminomethylpyridine (1.1 eq.) added, the mixture refluxed under a flow of argon (to remove H_2) for 24 h, cooled to room temp., concentrated *in vacuo*, and purified by chromatography on silica → N-3-picolinylsuccinimide. Y 73%. This novel procedure provides atom-economical and experimentally simple access to **succinimides** from 1,4-butanediol derivs. and aliphatic amines (twenty examples; Y 36-88%), with low yields obtained from sterically hindered amines (α-aminoethylbenzene: 36%; cyclohexylamine: 57%) or from 2-aminomethylpyridine (44%), presumed due to catalyst inhibition. The reaction was extended to the prepn. of **glutarimides** (two examples; Y 48-51%) from 1,5-diols, but cyclization of a 1,6-diol was unsuccessful as was the prepn. of acyclic imides from amines or amides and 2 or 1 eq. of alcohol, respectively. F.e. and optimization s. J. Zhang, M. Senthilkumar, S.C. Ghosh, S.H. Hong, Angew. Chem., Int. Ed. *2010*, *49* (36), 6391-5 [DOI: 10.1002/anie.201002136].

Palladium(II) chloride/copper(II) chloride/water $PdCl_2/CuCl_2/H_2O$
Quinoxalines from *o*-diamines and acetylene derivs.
via palladium(II)/copper(II)-catalyzed oxidation to α-diketones

156.



in one pot. $PdCl_2$ (5 mol%) and $CuCl_2$ (5 mol%) added to a soln. of 1-(3-hydroxyphenyl)-2-phenylethyne (1 mmol) in PEG/water (4:1; 10 ml), the mixture stirred at room temp. until oxidation complete (TLC), 1,2-diaminobenzene (1 eq.) added, the mixture stirred for 16 h, diluted with ether, cooled in ice, the ether layer concentrated *in vacuo*, and the residue purified chromatographically → 2-(3-hydroxyphenyl)-3-phenylquinoxaline. Y 80%. Five 2,3-diarylquinoxalines were prepared by this method (Y 75-81%) but the efficient and recyclable (up to five cycles) catalyst system was applicable to the oxidation of diaryl and *aryl-alkyl* ethynes, with the α-diketone products (cf. *27*, 145*s49*) isolated and fully characterized (nine examples; Y 63-87%). F.e.s. S. Chandrasekhar, N.K. Reddy, V.P. Kumar, Tetrahedron Lett. *2010*, *51* (28), 3623-5 [DOI: 10.1016/j.tetlet.2010.05.006].

Oxygen ↑ NC ↓↑ O

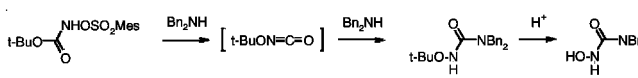
Without additional reagents *w.a.r.*
N-Formylation NH → NCHO

with formic acid s. *13,* 442*s36*; of aliphatic and heterocyclic sec. amines without catalyst or solvent s. M. Rahman, D. Kundu, A. Hajra, A. Majee, Tetrahedron Lett. *2010, 51* (21), 2896-9 [DOI: 10.1016/j.tetlet.2010.03.097]; using thiamine hydrochloride as catalyst under solvent-free conditions s. M. Lei, L. Ma, L. Hu, Tetrahedron Lett. *2010, 51* (32), 4186-8 [DOI: 10.1016/j.tetlet.2010.06.005]; of prim. amines with indium as catalyst under solvent-free conditions s. J.-G. Kim, D.O. Jang, Synlett *2010* (8), 1231-4 [DOI: 10.1055/s-0029-1219784]; notably for N-formylation of α-amino-esters without epimerization with iodine as catalyst without solvent s. J.-G. Kim, D.O. Jang, ibid. *2010* (14), 2093-6 [DOI: 10.1055/s-0030-1258518]; with DMF in the presence of methyl benzoate as promoter cf. D. Yang, H.B. Jeon, Bull. Korean Chem. Soc. *2010, 31* (5), 1424-6 [DOI: 10.5012/bkcs.2010.31.5.1424].

Irradiation s. under Ag-TiO_2 ///
Microwaves s. under KI, ZnO or $ZnCl_2$, $NaBH_3CN$ and NH_4OAc [\\\\]

Sodium hydride *NaH*
N-Hydroxyureas from amines via N-*tert*-butoxyureas ≥NH → ≥NC(O)NHOBu-*t*

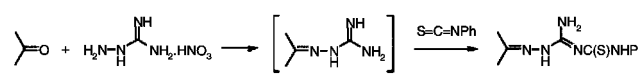
157.



A soln. of *tert*-butyl mesitylenesulfonyloxycarbamate (prepared almost quantitatively in crude form from *tert*-butyl N-hydroxycarbamate and mesitylenesulfonyl chloride) and dibenzylamine (1 eq.) in DMF (1 *M*) treated with NaH (1 eq.) for 1 h at 0°, ice-water added, and the precipitate collected → intermediate N-*tert*-butoxyurea (Y 85%), refluxed in concd. HCl for 10 min → N,N-dibenzyl-N′-hydroxyurea (Y 70%). Significantly, the procedure is applicable to both prim. and sec. amines (aliphatic or aromatic), affording the respective N′-subst. and N′,N′-disubst. N-hydroxyureas in good yield (ten examples; 1st step: Y 45-85%; 2nd step: Y 43-92%). The first step is presumed to involve Lossen rearrangement of the startg. carbamate to give N-*tert*-butoxyisocyanate prior to addition of the amine. F.e. and comparison of bases, acids and solvents s. J.G. Krause, B.D. Leskiw, M.L. Emery, M.E. McGahan, M.P. McCourt, R. Priefer, Tetrahedron Lett. *2010, 51* (27), 3568-70 [DOI: 10.1016/j.tetlet.2010.05.002].

Sodium hydroxide *NaOH*
N-(Alkylideneamino)amidinothioureas from thiocyanates, oxo compds. and aminoguanidine CO → C=NHNC(NH$_2$)=NC(S)NHR

158.

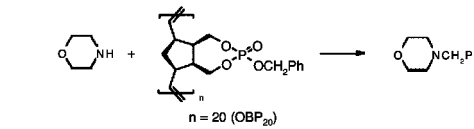


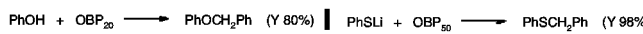
Acetone (0.01 mol) added to a well-stirred suspension of aminoguanidine nitrate (0.01 mol) and NaOH (0.01 mol) in DMF (5 ml), the mixture stirred for 1 h, treated with the startg. isothiocyanate (0.009 mol), stirring continued for another 50 min, and the mixture worked up with purification by crystallization → N-(isopropylideneamino)-N′-(phenylthiocarbamyl)guanidine. Y 70%. The determining feature of the method is the initial *in situ* blocking of the amino group of aminoguanidine by Schiff base formation so that reaction with isothiocyanate takes place solely at the guanidine nitrogen. The procedure is mild, convenient and rapid, and was applied in high yield to the coupling of aryl isothiocyanates with aromatic aldehydes and aromatic or [cyclo]aliphatic ketones. F.e. and application to **library generation** by solution-phase parallel synthesis s. K.G. Sreejalekshmi, Phosphorus, Sulfur Silicon Relat. Elem. *2010, 185* (9), 1830-7 [DOI: 10.1080/10426500903329237].

Sodium/alcohol *NaOR*
4-(*o*-Hydroxyaryl)pyrimidines from chromones C,O
s. *23*, 407; 5-aryl-4-(*o*-hydroxyaryl)-2-thioureidopyrimidines from isoflavones and amidinothiourea, incl. application for library synthesis in drug discovery, s. W.-Y. Han, Z.-T. Zhang, Y.-C. Zhang, D. Xue, G. Li, Helv. Chim. Acta *2010*, *93* (8), 1641-9 [DOI: 10.1002/hlca.200900438].

Potassium or cesium carbonate/tetra-n-butylammonium iodide *K_2CO_3 or Cs_2CO_3/Bu_4NI*
Benzylation with soluble oligomeric benzyl phosphates NH → NCH_2Ar

159.





ROMP-derived oligomeric benzyl phosphates are readily available, purifiable, bench-stable, pure-white, free-flowing solids which are soluble in organic solvents and effective for the benzylation of a variety of O-, N- and S-nucleophiles (phenols, thiophenols, cyclic and acyclic amines), yielding pure products courtesy of a simple, non-chromatographic work-up. **E: N-Benzylation of cyclic sec. amines**. The oligomeric (20-mer) benzyl phosphate (1.3-2 eq.) [simply prepared by standard ruthenium-catalyzed ring-opening metathetical polymerization (ROMP) of the norbornene-based monomeric benzyl phosphate], tetra-*n*-butylammonium iodide (0.1-0.2 eq.), K_2CO_3 or Cs_2CO_3 (3 eq.) and chloroform (0.3 *M*) added sequentially to a Teflon-capped 1-dram vial, stirred rapidly until the oligomer dissolved (<30 s), morpholine (1 eq.) added, the vial sealed under argon, heated to 80° with stirring (2-24 h), the mixture added with continued stirring to ether in order to complete precipitation of the oligomeric phosphate anion as by-product, filtered through silica, and the filtrate and washings concentrated *in vacuo* → N-benzylmorpholine. Y 99% (purity 98%). The oligomeric benzylating agent, as well as ring-substituted and heteroaromatic analogs, were prepared on the multigram scale as 20-, 50- and 100-mers, each displaying different solubility profiles. F.e. (ca. thirty; Y 70-99%) incl. N-benzylation of 3,4-dihydro-2*H*-5,1,4-benzothioxazepine S,S-dioxides s. T.R. Long, P.K. Maity, T.B. Samarakoon, P.R. Hanson, Org. Lett. *2010*, *12* (13), 2904-7 [DOI: 10.1021/ol1006604].

Sodium azide *NaN_3*
Tandem solid- and solution-phase synthesis of active glycosyl donors ←
by means of a traceless linker – Azidoalkyl glycosides s. *78*, 106

Sodium azide/copper(I)-zeolite *NaN_3/Cu(I)-zeolite*
1,2,3-Triazoles from terminal acetylene derivs. and tosylates in water O
s. *68*, 184s*78*

Sodium azide/propylphosphonic anhydride/triethylamine or benzotriazol-1-yloxy-tris(dimethylamino)phosphonium hexafluorophosphate/ethyldiisopropylamine ←
Carboxylic acid azides from acids s. *36*, 355s*78* COOH → $C(O)N_3$

Cesium fluoride *CsF*
1,3-Dioxan-2-one-5-carboxylic acid amides $COOC_6F_5$ → CON<
from 1,3-dioxan-2-one-5-carboxylic acid pentafluorophenyl esters s. *78*, 82

Lithium bromide/diethylamine *LiBr/Et_2NH*
Carboxylic acid amides from carboxylic acid esters and amines COOR → CON<
s. 42, 338s*78*

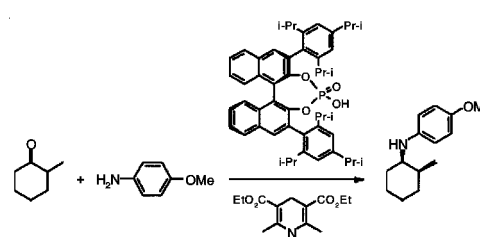
Lithium iodide s. under [Ir(cod)Cl]$_2$ *LiI*

Potassium iodide/air/microwaves *KI/air/[\\\\]*
Benzimidazoles from *o*-diamines and aldehydes ○
s. *69*, *171s76*; *46*, 321s*76*; rapid and inexpensive procedure with KI/air under microwaves s. Z. Mao, Z. Wang, J. Li, X. Song, Y. Luo, Synth. Commun. *2010, 40* (13), 1963-77 [DOI: 10.1080/00397910903219328]; with a highly acidic nanoporous aluminosilicate (AlKIT-5) s. M.A. Chari, D. Shobha, E.-R. Kenawy, S.S. Al-Deyab, B.V.S. Reddy, A. Vinu, Tetrahedron Lett. *2010, 51* (39), 5195-9 [DOI: 10.1016/j.tetlet.2010.07.132]; with the natural, eco-friendly acidic zeolite, scolecite, s. L.S. Gadekar, B.R. Arbad, M.K. Lande, Chin. Chem. Lett. *2010, 21* (9), 1053-6 [DOI: 10.1016/j.cclet.2010.03.038]; with $FeCl_3$-doped polyaniline nanoparticles s. M. Abdollahi-Alibeik, M. Moosavifard, Synth. Commun. *2010, 40* (18), 2686-95 [DOI: 10.1080/00397910903318658]; 8-subst. **xanthenes** from 5,6-diaminouracils with bromo(dimethyl)sulfonium bromide s. P. LaBeaume, M. Dong, M. Sitkovsky, E.V. Jones, R. Thomas, S. Sadler, A.E. Kallmerten, G.B. Jones, Org. Biomol. Chem. *2010, 8* (18), 4155-7 [DOI: 10.1039/c003382k].

1,4-Dihydropyridines/adenosine 5′-diphosphate ←
Reductive N-alkylation with oxo compds. s. *17*, 436s*78* CO → CHN≤

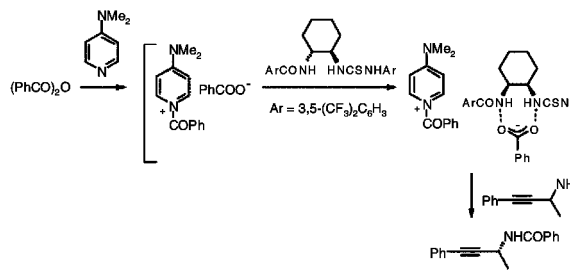
1,4-Dihydropyridines/(R)-3,3′-bis(2,4,6-triisopropylphenyl)-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate ←
Organo-Brønsted acid-catalyzed transfer-hydrogenative N-alkylation with α-subst. ketones with dynamic kinetic resolution

160.



The first example of a catalytic reductive N-alkylation with α-subst. ketones *with dynamic kinetic resolution* is reported, notably for preparing pharmaceutically important **chiral 2-subst. cyclohexylamines**. **E:** The startg. racemic ketone (0.5 mmol), *p*-anisidine (1.1 eq.), Hantzsch ester (1.4 eq.) and (*R*)-TRIP (1 mol%) introduced into a Schlenk tube under argon, 5 Å molecular sieves (500 mg) and anhydrous cyclohexane (5 ml) added, the mixture stirred at 50° for 72 h, and worked up with purification by flash chromatography on silica gel → (1R,2S)-4-methoxy-*N*-(2-methylcyclohexyl)aniline. Y 82% (d.r. 5:1; e.r. of the *cis*-isomer 93:7). α-Alkyl-, α-allyl- and α-chlorocyclohexanones afforded high product yields and enantioselectivities at a catalyst loading of 1 mol% (six examples; Y 76-96%; d.r. 5:1 to 10:1; e.r. 93:7 to 98:2), but less active α-benzyl- and α-aryl-cyclohexanones required 5 mol% catalyst. Stereoselectivity was lower, however, with cyclopentanone derivs. and, surprisingly, there was no reaction with cycloheptanone derivs. An α-subst. 2-cyclohexenone reacted similarly with simultaneous reduction of the C=C bond. F.e.s. V.N. Wakchaure, J. Zhou, S. Hoffmann, B. List, Angew. Chem., Int. Ed. *2010, 49* (27), 4612-4 [DOI: 10.1002/anie.201001715].

4-Dimethylaminopyridine/(R,R)-N-[3,5-bis(trifluoromethyl)benzoyl]-N′-[N-[3,5-bis-(trifluoromethyl)phenyl]thiocarbamyl]cyclohexane-1,2-diamine ←
Kinetic resolution of 2-acetylene-*prim*-amines by N-benzoylation under cooperative nucleophilic catalysis and anion-binding organocatalysis $NH_2 \rightarrow NHCOPh$



161.

DMAP (0.0125 mmol) in toluene (1 ml) added to a mixture of benzoic anhydride (0.15 mmol) and 4 Å molecular sieves (100 mg), diluted with freshly distilled toluene (21 ml), cooled to -78° over 15 min, a soln. of (R,R)-N-[3,5-bis(trifluoromethyl)benzoyl]-N′-[N-[3,5-bis(trifluoromethyl)-phenyl]thiocarbamyl]cyclohexane-1,2-diamine (0.0125 mmol) in toluene (2 ml) added, followed after 15 min by a soln. of the startg. amine (0.25 mmol) in the same solvent (1 ml), stirred at -78° for 3 h, reaction quenched by adding 3 *M* methylmagnesium chloride in THF (0.5 mmol in 0.167 ml solvent) at -78°, stirring continued for another 10 min, excess Grignard reagent quenched with 1 *M* aq. HCl, allowed to warm to room temp., and worked up with purification by flash chromatography → (R)-N-(4-phenylbut-3-yn-2-yl)benzamide. Y 43% (conversion 48%; s-factor 39). The unreacted amine was isolated by basifying the aq. layer with 15% NaOH (pH 10), followed by extraction and characterization by standard benzoylation (no further details). Highly efficient kinetic resolution of a series of aromatic or aliphatic primary *sec*-propargylamines (regardless of the electronic nature of substituents) was effected with an s-factor *up to 56* based on cooperative catalysis with a classical nucleophile (DMAP) and a novel, easily prepared chiral N-aroyl-N′-thiocarbamyl-1,2-diamine. Mechanistically, reaction involves initial formation of an N-benzoyl-4-(dimethylamino)pyridinium ion rendered chiral by hydrogen-bonding of the associated anion with the chiral organocatalyst in the form of a chiral ion pair which efficiently discriminates between the two enantiomeric propargylamines. **Kinetic resolution of α-subst. prim. benzylamines** was achieved similarly with s-factors of 13 to 38. F.e. and comparison of organocatalysts s. E.G. Klauber, C.K. De, T.K. Shah, D. Seidel, J. Am. Chem. Soc. *2010*, *132* (39), 13624-6 [DOI: 10.1021/ja105337h]; kinetic resolution of α-subst. prim. benzylamines s.a. C.K. De, E.G. Klauber, D. Seidel, ibid. *2009*, *131* (47), 17060-1 [DOI: 10.1021/ja9079435].

Silver nanoparticles *Ag*
β-Amino-α,β-ethylene- from β-keto-carbonyl compds. $COCH \rightarrow C(N\leq)=C$
s. *26*, 331s*69*; β-amino-α,β-ethylene-ketones and -esters with recyclable silver nanoparticles s. K.D. Bhatte, P.J. Tambade, K.P. Dhake, B.M. Bhanage, Catal. Commun. *2010, 11* (15), 1233-7 [DOI: 10.1016/j.catcom.2010.06.011]; with $Ni(OAc)_2$ under solvent-free conditions s. J.-Y. Liu, G.-E. Cao, W. Xu, J. Cao, W.-L. Wang, Appl. Organomet. Chem. *2010, 24* (10), 685-91 [DOI: 10.1002/aoc.1667]; β-amino-α,β-ethyleneketones with $Yb(OTf)_3$ s. R. Chen, P. Li, J. Li, W. Su, Synth. Commun. *2010, 40* (17), 2506-12 [DOI: 10.1080/00397911.2010.493722].

Silver-titanium dioxide/montmorillonite/air/irradiation ←
Benzimidazoles from *o*-diamines and prim. alcohols s. *68*, 174s*78* ○

Copper(I)-zeolite s. under NaN_3 *Cu(I)-zeolite*

Strontium chloride $SrCl_2$
4(3*H*)-Quinazolones ○
from *o*-aminocarboxylic acids, prim. amines and orthoformic acid esters
s. *66*, 178s*69*; with $SrCl_2$ as catalyst under solvent-free conditions s. M. Wang, Z.G. Song, T.T. Zhang, Chin. Chem. Lett. *2010*, *21* (10), 1167-70 [DOI: 10.1016/j.cclet.2010.05.021]; with $Ce(OMs)_3$ dihydrate without solvent s. M. Wang, Z.-G. Song, T.-T. Zhang, Monatsh. Chem. *2010*, *141* (9), 993-6 [DOI: 10.1007/s00706-010-0352-y]; with silica gel-supported phosphomolybdic acid without solvent s. G. Sabitha, N.M. Reddy, M.N. Prasad, G.S.K. Raja, J.S. Yadav, J. Heterocycl. Chem. *2010*, *47* (3), 589-93 [DOI: 10.1002/jhet.361].

Zinc oxide or chloride/hydroxylamine hydrochloride/microwaves ←
Nitriles from aldehydes CHO → CN
s. *55*, 146s*70*; rapid, eco-friendly procedure for preparing ar. nitriles with hydroxylamine hydrochloride and reusable ZnO under microwaves without solvent s. M.B.M. Reddy, M.A. Pasha, Chin. Chem. Lett. *2010*, *21* (9), 1025-8 [DOI: 10.1016/j.cclet.2010.05.004]; with $ZnCl_2$ in place of ZnO s. M.A. Pàsha, A. Nizam, Synth. Commun. *2010*, *40* (9), 1276-9 [DOI: 10.1080/00397910903069657]; with hydroxylamine hydrochloride-on-melamine formaldehyde and ammonium acetate as catalyst under microwaves s. R. Rezaei, M.K. Mohammadi, N. Rastin, Chin. J. Chem. *2010*, *28* (6), 993-6 [DOI: 10.1002/cjoc.201090184]; general procedure in aq. ammonia with tetra-*n*-butylammonium tribromide as oxidant s. Y.-Z. Zhu, C. Cai, Monatsh. Chem. *2010*, *141* (6), 637-9 [DOI: 10.1007/s00706-010-0305-5].

Indium *In*
N-Formylation with formic acid s. *13*, 442s*78* NH → NCHO

Sodium tetrahydridoborate-Amberlyst 15 or -cellulose sulfuric acid or Zinc bis(tetrahydridoborate)/N-methylpyrrolidine *[BH_4^-]*
Sodium trihydridocyanoborate/microwaves *$NaBH_3CN$/[\\\\]*
Borane-ammonia/titanium tetraisopropoxide *$BH_3{\cdot}NH_3/Ti(OPr\text{-}i)_4$*
Borane-α-picoline ←
Reductive N-alkylation with oxo compds. CO → CHN<
s. *17*, 436s*69*; prim., sec. and tert. amines with $BH_3{\cdot}NH_3/Ti(OPr\text{-}i)_4$ s. P.V. Ramachandran, P.D. Gagare, K. Sakavuyi, P. Clark, Tetrahedron Lett. *2010*, *51* (24), 3167-9 [DOI: 10.1016/j.tetlet.2010.04.014]; N-benzyl- and N,N-dibenzyl-protected α-amino acid esters or amino alcohols with α-picoline-borane in methanol/acetic acid s. Y. Kawase, T. Yamagishi, T. Kutsuma, T. Kataoka, K. Ueda, T. Iwakuma, T. Nakata, T. Yokomatsu, Synthesis *2010* (10), 1673-7 [DOI: 10.1055/s-0029-1218707]; reduction with $NaBH_4$-Amberlyst 15 in THF or without solvent s. H. Alinezhad, M. Tajbakhsh, N. Mahdavi, Synth. Commun. *2010*, *40* (7), 951-6 [DOI: 10.1080/00397910903026731]; with $NaBH_4$ in the presence of cellulose sulfuric acid in ethanol or without solvent s. H. Alinezhad, Z. Tollabian, Bull. Korean Chem. Soc. *2010*, *31* (7), 1927-30 [DOI: 10.5012/bkcs.2010.31.7.1927]; sec. or tert. methylamines with $Zn(BH_4)_2$/N-methylpyrrolidine s. H. Alinezhad, M. Tajbakhsh, F. Salehian, K. Fazli, Synth. Commun. *2010*, *40* (16), 2415-20 [DOI: 10.1080/00397910903249606]; prim. amines from ketones and NH_4OAc with $NaBH_3CN$ under microwaves s. L. Dong, S. Aleem, C.A. Fink, Tetrahedron Lett. *2010*, *51* (39), 5210-2 [DOI: 10.1016/j.tetlet.2010.07.156]; **biomimetic reductive N-alkylation** with adenosine 5′-diphosphate as catalyst and diethyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate as reductant s. A. Kumar, S. Sharma, R.A. Maurya, Adv. Synth. Catal. *2010*, *352* (13), 2227-32 [DOI: 10.1002/adsc.201000178]; reductive N-alkylation of sec. amines with aldehydes using phenylsilane and a high-valent oxorhenium(V) or oxorhenium(VII) complex, notably $ReIO_2(PPh_3)_2$ s. S.C.A. Sousa, A.C. Fernandes, ibid. *2010*, *352* (13), 2218-26 [DOI: 10.1002/adsc.201000246]; diastereoselective formation of N-subst. 2-fluoroamines with trichlorosilane/thiourea s. R.M. Malamakal, W.R. Hess, T.A. Davis, Org. Lett. *2010*, *12* (10), 2186-9 [DOI: 10.1021/ol100647b].

Nanoporous aluminosilicate or Scolecite ←
Benzimidazoles from *o*-diamines and aldehydes s. *69*, 171s*78*; *46*, 321s*78* ○

Montmorillonite s. under Ag-TiO_2 *clay*

Fluoroboric acid-silica HBF_4-SiO_2
Benzazoles from *o*-functionalized amines and orthocarboxylic acid esters ○
Heterogeneous acid catalysis under mild solvent-free conditions – Benzimidazoles – Benzoxazoles – Imidazo[4,5-*b*]pyridines s. *78*, 241

Cerium(III) methanesulfonate $Ce(OMs)_3$
4(3*H*)-Quinazolones from *o*-aminocarboxylic acids, prim. amines
and orthoformic acid esters s. *66*, 178s*78*

Ytterbium(III) triflate $Yb(OTf)_3$
β-Amino-α,β-ethylene- from β-keto-carbonyl compds. COCH → C(N≤)=C
s. *26*, 331s*78*

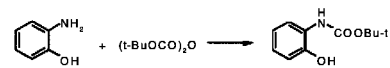
Ammonium acetate or Ammonium acetate/microwaves or copper(II) nitrate impregnated on zeolite or 1-methyl-3-(4-sulfobutyl)imidazolium hydrogen sulfate or silica-based sulfonic acid or iron(III) phosphate ←
3-Component synthesis of imidazoles from α-diketones and aldehydes ○
s. *23*, 423s*75*; 2,4,5-trisubst. imidazoles under continuous flow in a microreactor under pressure and with superheating s. L. Kong, X. Lv, Q. Lin, X. Liu, Y. Zhou, Y. Jia, Org. Process Res. Dev. *2010, 14* (4), 902-4 [DOI: 10.1021/op100058h]; rapid procedure without catalyst or solvent under microwaves s. J.-F. Zhou, G.-X. Gong, X.-J. Sun, Y.-L. Zhu, Synth. Commun. *2010, 40* (8), 1134-41 [DOI: 10.1080/00397910903043025]; **in water** under microwaves s. E. Chauveau, C. Marestin, F. Schiets, R. Mercier, Green Chem. *2010, 12* (6), 1018-22 [DOI: 10.1039/b925177d]; with 1-methyl-3-(4-sulfobutyl)imidazolium hydrogen sulfate as acidic catalyst without solvent s. M.M. Heravi, M. Zakeri, N. Karimi, M. Saeedi, H.A. Oskooie, N. Tavakoli-Hosieni, Synth. Commun. *2010, 40* (13), 1998-2006 [DOI: 10.1080/00397910903219377]; heterogeneous procedure with a readily removable silica-based sulfonic acid without solvent s. K. Niknam, M.R. Mohammadizadeh, S. Mirzaee, D. Saberi, Chin. J. Chem. *2010, 28* (4), 663-9 [DOI: 10.1002/cjoc.201090129]; with anhydrous iron(III) phosphate s. F.K. Behbahani, T. Yektanezhad, A.R. Khorrami, Heterocycles *2010, 81* (10), 2313-21 [DOI: 10.3987/com-10-12019]; with DABCO, also 1,2,4,5-tetrasubst. imidazoles by **4-component synthesis** (with prim. amines and ammonium acetate) s. S.N. Murthy, B. Madhav, Y.V.D. Nageswar, Tetrahedron Lett. *2010, 51* (40), 5252-7 [DOI: 10.1016/j.tetlet.2010.07.128]; 4-component synthesis with copper(II) nitrate impregnated on zeolite, **also from α-hydroxyketones**, s. K. Sivakumar, A. Kathirvel, A. Lalitha, ibid. *2010, 51* (22), 3018-21 [DOI: 10.1016/j.tetlet.2010.04.013]; with TsOH or MCM-41 s. R.H. Shoar, G. Rahimzadeh, F. Derikvand, M. Farzaneh, Synth. Commun. *2010, 40* (9), 1270-5 [DOI: 10.1080/00397910903068204]; with 1-methyl-3-(4-sulfobutyl)imidazolium hydrogen sulfate as acidic catalyst in the absence of solvent s. A. Davoodnia, M.M. Heravi, Z. Safavi-Rad, N. Tavakoli-Hoseini, ibid. *2010, 40* (17), 2588-97 [DOI: 10.1080/00397910903289271]; with covalently bound 3-mercaptopropylsilica s. C. Mukhopadhyay, P.K. Tapaswi, M.G.B. Drew, Tetrahedron Lett. *2010, 51* (30), 3944-50 [DOI: 10.1016/j.tetlet.2010.05.102]; with NaH_2PO_4 under solvent-free conditions s. Z. Karimi-Jaberi, M. Barekat, Chin. Chem. Lett. *2010, 21* (10), 1183-6 [DOI: 10.1016/j.cclet.2010.06.012].

Ammonium acetate/hydroxylamine hydrochloride-on-melamine formaldehyde/microwaves ←
Nitriles from aldehydes s. *55*, 146s*78* CHO → CN

Formic acid/triethylamine s. under Cyclometalated chloro(cyclopentadienyl)-iridium(III) aryl ketimine complexes *HCOOH/Et₃N*

N,N′-Bis(2,6-diisopropylphenyl)imidazolium chloride/sodium tert-butoxide s. under Ni(cod)₂ *IPr·HCl/t-BuONa*

1,1,3,3-Tetramethylguanidinium acetate $(Me_2N)_2C{=}NH{\cdot}HOAc$
Efficient and selective N-carbo-*tert*-butoxylation of amines NH → NCOOBu-*t*
catalyzed by an ionic liquid



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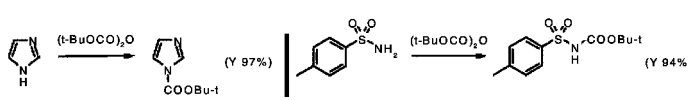


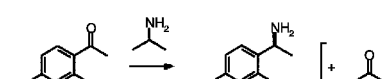
under mild solvent-free conditions. 2-Aminophenol (1 mmol) added to a mixture of di-*tert*-butyl dicarbonate (1 eq.) and 1,1,3,3-tetramethylguanidinium acetate (10 mol%), the mixture stirred at room temp. until reaction complete (TLC; 6 min), diluted with ether, filtered, and concentrated *in vacuo* → 2-(*tert*-butoxycarbonylamino)phenol. Y 98%. Use of the inexpensive and recyclable ionic liquid provided clean, selective and experimentally simple mono-N-protection of sterically hindered and electron-diverse ar. (incl. *4-nitroaniline*) and aliphatic prim. and sec. amines (fourteen examples; Y 93-98%) in the presence of prim. alcohol, phenol and additional amine functionality. Reactions were rapid (5-30 min) with no evidence of side-reactions, and products were obtained pure without the need for chromatographic purification. The method was also applicable to imidazole (Y 97%), tosylamine (Y 94%) and N,N-dimethylhydrazine (Y 94%). Other tetramethylguanidinium salts were less effective. F.e.s. J. Akbari, A. Heydari, L. Ma'mani, S.H. Hosseini, Compt. Rend. Chim. *2010, 13* (5), 544-7 [DOI: 10.1016/j.crci.2009.10.003].

Oxime-based uronium salts ←
Peptide synthesis s. *77,* 179s*78* COOH → CON≤

Lipase or protease/mercaptans ←
Immobilized lipase/palladium nanoparticles ←
Dynamic kinetic resolution of amines NH → NAc
by enzymatic N-acylation-catalytic racemization
of benzylamines with Novozyme and supported palladium catalysts s. *53,* 500s*73*; of prim. amines via racemization with palladium nanoparticles s. Y. Kim, J. Park, M.-J. Kim, Tetrahedron Lett. *2010, 51* (42), 5581-4 [DOI: 10.1016/j.tetlet.2010.08.050]; **via thiiyl-mediated racemization** with mercaptans in the presence of CAL-B or alkaline protease, (R)- or (S)-selectivity, s. L. El Blidi, N. Vanthuyne, D. Siri, S. Gastaldi, M.P. Bertrand, G. Gil, Org. Biomol. Chem. *2010, 8* (18), 4165-8 [DOI: 10.1039/c0ob00054j]; dynamic kinetic resolution of *cis*-N-(carbalkoxy)cyclopentane-1,2-diamines with CAL-B **via spontaneous racemization** s. F.J. Quijada, V. Gotor, F. Rebolledo, Org. Lett. *2010, 12* (16), 3602-5 [DOI: 10.1021/ol101378k].

ω-Transaminase/alcohol dehydrogenase/formate dehydrogenase/isopropylamine ←
α-Subst. prim. benzylamines from aryl ketones CO → $CHNH_2$
Reductive amination using a cooperative enzyme system

163.



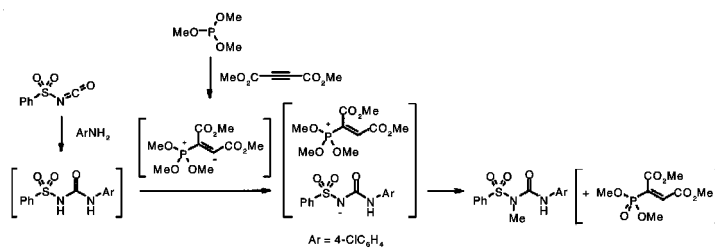
A mixture of 2,4-dihydroxyacetophenone (0.02 mmol), isopropylamine (28 eq.), *Arthrobacter citreus* S9 transaminase (1 mg; 0.97 U), yeast alcohol dehydrogenase (600 U), formate dehydrogenase (0.2 U), NADH (10 mol%) and Na-formate (1.25 eq.) in Na-phosphate buffer (1 ml; pH 7) stirred at 37° for 24 h → (S)-1-(2,4-dihydroxyphenyl)ethylamine. Y >99% (e.e. >99.9%). The use of the dehydrogenase system was essential to remove acetone formed in the reaction, thereby driving the conversion to completion (in the absence of dehydrogenase the illustrated reaction plateaued at 68% conversion). The dehydrogenase system is essentially

unreactive towards the substrate as it accepts only a narrow range of small ketones. Four acetophenones (4-H, 4-NO_2, 4-Me and 2,4-$(OH)_2$) were, however, excellent substrates for the system, affording the corresponding amines with >99% conversion and >99.9% e.e. F.e.s. K.E. Cassimjee, C. Branneby, V. Abedi, A. Wells, P. Berglund, Chem. Commun. *2010*, *46* (30), 5569-71 [DOI: 10.1039/c0cc00050g].

Dimethyl acetylenedicarboxylate *ROOC-C≡C-COOR*

N-Sulfonylureas from N-sulfonylisocyanates and prim. amines RNHC(O)N(R′)SO_2R″
via acetylenedicarboxylate-mediated *in situ*-N-alkylation with trialkyl phosphites

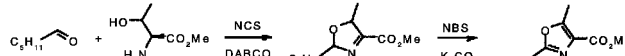
164.



in one pot. A soln. of 4-chloroaniline (1 mmol) and benzenesulfonyl isocyanate (1 eq.) stirred in dry methylene chloride (5 ml) at 25° for 5 min, trimethyl phosphite (1 eq.) and a soln. of dimethyl acetylenedicarboxylate (1 eq.) in the same solvent (3 ml) added, the mixture stirred for 2 h, concentrated *in vacuo*, and purified by chromatography on silica → N-benzenesulfonyl-N′-4-chlorophenyl-N-methylurea. Y 95%. This simple and efficient procedure generates N-sulfonylureas *in situ* which are subsequently alkylated at the sulfonamide nitrogen under mild and neutral conditions. The method was successful with electron-diverse ar. and benzyl amines and prim./sec. alkyl phosphites (seventeen examples; Y 85-98%). The authors propose the formation of an ene(trialkoxy)phosphonium salt as the active alkylating agent. F.e.s. M. Adib, E. Sheikhi, G.S. Moghaddam, H.R. Bijanzadeh, Tetrahedron Lett. *2010*, *51* (43), 5646-8 [DOI: 10.1016/j.tetlet.2010.06.054].

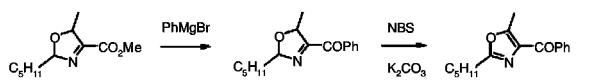
Amberlyst 15 s. under [BH_4^-] ←
tert-Butyl hydroperoxide s. under I_2 *t-BuOOH*
Mercaptans s. under Lipase or protease *RSH*
Thiourea s. under $HSiCl_3$ *$(H_2N)_2CS$*
(R,R)-N-[3,5-Bis(trifluoromethyl)benzoyl]-N′-[N-[3,5-bis(trifluoromethyl)-phenyl]thiocarbamyl]cyclohexane-1,2-diamine s. under 4-Dimethylaminopyridine ←
2-Chloro-4,6-dimethoxy-1,3,5-triazine ←
N-Acylation with carboxylic acids s. *23*, 415s*78* NH → NAc
Peptide synthesis s. *77*, 179s*78* COOH → CON≤
N-Chlorosuccinimide/triethylenediamine *NCS/DABCO*
Oxazole-4-carbonyl compds. from aldehydes ○
via Δ^3-oxazoline-4-carboxylic acid esters

165.



Oxazole-4-carboxylic acid esters. DABCO (3 eq.) added to a suspension of L-threonine methyl ester hydrochloride (1.1 eq.) in methylene chloride (5.9 ml) at room temp., the mixture stirred for 20 min, a soln. of hexanal (1.07 mmol) in the same solvent (5.35 ml) added, the mixture stirred

for 30 min, cooled to 0°, NCS (1.1 eq.) added, the mixture stirred until reaction complete (TLC; 78 min), quenched with satd. aq. $Na_2S_2O_5$ (*sic*), extracted with methylene chloride, concentrated *in vacuo*, and purified by chromatography on silica → intermediate 3-oxazoline-4-carboxylate (Y 83%), 0.256 mmol of which suspended in dichloroethane (2.6 ml) under N_2, NBS (1.2 eq.) and K_2CO_3 (1.2 eq.) added at room temp., the mixture refluxed until reaction complete (TLC; 30 min), cooled to 0°, quenched with satd. aq. $Na_2S_2O_3$ and $NaHCO_3$, extracted with methylene chloride, washed with aq. $NaHCO_3$, and purified by chromatography on silica → methyl 5-methyl-2-pentyl-oxazole-4-carboxylate (Y 97%). This novel approach involves cyclization of aliphatic aldehydes with serine or threonine esters to afford the corresponding 2-subst. or 2,5-disubst. 3-oxazoline-4-carboxylates (eleven examples; Y 82-96%), which were oxidized to oxazoles in a separate step (eleven examples; Y 70-97%). The method was compatible with silyl ethers, esters, benzyl ethers and carbamates. In a further development, the oxazolinecarboxylates were treated with Grignard reagents (MeMgBr, PhMgBr) to afford the corresponding 4-acyl-derivs. (four examples; Y 81-92%) which were subsequently oxidized to **4-acyloxazoles** (four examples; Y 74-99%).



F.e. and optimization s. K. Murai, Y. Takahara, T. Matsushita, H. Komatsu, H. Fujioka, Org. Lett. *2010*, *12* (15), 3456-9 [DOI: 10.1021/ol1012789]; oxazole-4-carboxylic acid esters with Et_3N/$MgSO_4$ in THF or K_2CO_3 in DMA for oxazolidine formation and $BrCCl_3$/DBU for oxazole via oxazoline formation s. T.H. Graham, ibid. (16), 3614-7 [DOI: 10.1021/ol101346w].

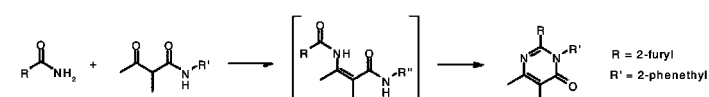
Bromo(dimethyl)sulfonium bromide — $Me_2(Br)S^+ Br^-$
Imidazole ring from *o*-diamines and aldehydes ○
8-Subst. xanthenes s. *46*, 321s*78*; *69*, 171s*78*

Phenylsilane/high-valent oxorhenium(V) or oxorhenium(VII) complexes — $PhSiH_3$/[Re]
Trichlorosilane/thiourea — $HSiCl_3/(H_2N)_2CS$
Reductive N-alkylation with oxo compds. s. *17*, 436s*78* — $CO \rightarrow CHN<$

Silica s. under HBF_4 and Phosphomolybdic acid — SiO_2
Mesoporous silica s. under Phosphotungstic acid — *SBA 15*
Titanium dioxide s. under Silver — TiO_2

Titanium tetraisopropoxide (s.a. under $BH_3{\cdot}NH_3$) — $Ti(OPr\text{-}i)_4$
4(3*H*)-Pyrimidinones ○
from β-ketocarboxylic acid amides and N-unsubst. carboxylic acid amides
Titanium(IV)-mediated double amide condensation

166.



$Ti(OPr\text{-}i)_4$ (4 eq.) added to a mixture of startg. β-ketoamide and prim. amide (1.2 eq.) in an oven-dried reaction vessel under argon, the vessel sealed, the mixture stirred at room temp. for 10 min, then stirred vigorously at 150° for 24 h, cooled to room temp., diluted with toluene, quenched with 2 *N* HCl, stirred vigorously for 2 h, extracted thoroughly with methylene chloride, washed with brine, dried (Na_2SO_4), concentrated *in vacuo*, and the residue purified by flash chromatography on silica gel → 2-(2-furanyl)-5,6-dimethyl-3-(2-phenylethyl)-4(3*H*)-pyrimidinone. Y 74%. This mild, versatile method for prepn. of both tri- and tetra-subst. pyrimidines (> twenty examples; Y generally 40-80%) is tolerant of a wide range of functionality, notably of O-, S- and N-heterocyclics, but yields are diminished with pivalamide (trace) and with bulky N-substituents on the β-ketoamide (N-isopropyl: 7%). F.e., also prepn. of β-ketoamide substrates, scale-up to 130 g,

and a proposed mechanism in which $Ti(OPr\text{-}i)_4$ acts both as Lewis acid, chelating to both substrates, and as dehydrating agent, s. J.M. Ramanjulu, M.P. DeMartino, Y. Lan, R. Marquis, Org. Lett. *2010*, *12* (10), 2270-3 [DOI: 10.1021/ol100624p].

2-Azido-1,3-dimethyl-Δ^2-imidazolinium chloride/triethylamine ←

Carboxylic acid azides from acids COOH → CON_3

s. *36*, 355; with 2-azido-1,3-dimethyl-Δ^2-imidazolinium chloride/triethylamine, notably applicable to α-amino acids without racemization s. M. Kitamura, N. Tashiro, Y. Takamoto, T. Okauchi, Chem. Lett. *2010*, *39* (7), 732-3 [DOI: 10.1246/cl.2010.732]; with NaN_3, propylphosphonic anhydride and Et_3N, also one-pot preparation of α-ureidopeptides from N-protected α-amino acids, s. Basavaprabhu, N. Narendra, R.S. Lamani, V.V. Sureshbabu, Tetrahedron Lett. *2010*, *51* (22), 3002-5 [DOI: 10.1016/j.tetlet.2010.04.002]; with BOP and *i*-Pr_2NEt, notably for preparing N-Fmoc/Boc/Z-protected α-aminocarboxylic acid azides, s. B. Vasantha, V.V. Sureshbabu, Indian J. Chem. *2010*, *49B* (6), 812-7.

Polymer-based triphenylphosphine/iodine/ethyldiisopropylamine ←

N-Subst. carboxylic acid amides from acids COOH → CON≤

s. *23*, 415s*75*; with triphenylphosphine (or polymer-based triphenylphosphine) and I_2 in the presence of ethyldiisopropylamine s. A. Kumar, H.K. Akula, M.K. Lakshman, Eur. J. Org. Chem. *2010* (14), 2709-15 [DOI: 10.1002/ejoc.200901420]; **N-acylation** of deoxy- and ribo-cytidine **with carboxylic acids** activated by 2-chloro-4,6-dimethoxy-1,3,5-triazine s. A.B. Rode, S.J. Son, I.S. Hong, Bull. Korean Chem. Soc. *2010*, *31* (7), 2061-4 [DOI: 10.5012/bkcs.2010.31.7.2061]; N-acetylation of prim. or sec. amines with various metal acetates or oxides without solvent s. G. Brahmachari, S. Laskar, S. Sarkar, J. Chem. Res. *2010*, *34* (5), 288-95 [DOI: 10.3184/030823410X12746305905926].

Di(1-adamantyl)[o-(dimethylamino)phenyl]phosphine s. under [(cinnamyl)PdCl]$_2$ *Mor-DalPhos*

Benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate s. under NaN_3 ←

[O-[(1-Cyano-2-ethoxy-2-oxoethylidene)amino]oxy]tris(pyrrolidin-1-yl)phosphonium salts ←

Peptide synthesis

with Oxyma as additive s. *77*, 179; coupling with Oxyma-derived [O-[(1-cyano-2-ethoxy-2-oxoethylidene)amino]oxy]tris(pyrrolidin-1-yl)phosphonium hexafluorophosphate [PyOxP] and tetrafluoroborate (PyOxB) for **solution-phase peptide synthesis** with reduced racemization s. R. Subirós-Funosas, A. El-Faham, F. Albericio, Org. Biomol. Chem. *2010*, *8* (16), 3665-73 [DOI: 10.1039/c003719b]; with uronium salts based on the sodium salt of isonitroso-Meldrum's acid cf. A. El-Faham, R. Subirós-Funosas, F. Albericio, Eur. J. Org. Chem. *2010* (19), 3641-9 [DOI: 10.1002/ejoc.201000314]; with Oxyma-based uronium salts or 2-chloro-4,6-dimethoxy-1,3,5-triazine s. T.I. Al-Warhi, H.M.A. Al-Hazimi, A. El-Faham, F. Albericio, Molecules *2010*, *15* (12), 9403-17 [DOI: 10.3390/molecules15129403]; use of cysteine orthoesters for **solid-phase peptide synthesis** s. Z. Huang, D.J. Derksen, J.C. Vederas, Org. Lett. *2010*, *12* (10), 2282-5 [DOI: 10.1021/ol100645t]; with a new safety-catch protecting group (N-carbo-2-methoxy-4-methylsulfinylbenzoxy) and polymer-based linker s. S. Thennarasu, C.-F. Liu, Tetrahedron Lett. *2010*, *51* (24), 3218-20 [DOI: 10.1016/j.tetlet.2010.04.047]; solid-phase synthesis of (ω-aminoalkyl)peptoids s. D. Fritz, S. Bräse, Synlett *2010* (10), 1544-8 [DOI: 10.1055/s-0029-1219925]; of phosphoramidate-linked glycopeptides s. D.M.M. Jaradat, H. Hamouda, C.P.R. Hackenberger, Eur. J. Org. Chem. *2010* (26), 5004-9 [DOI: 10.1002/ejoc.201000627]; of O-phosphonylpeptides s. M. MacDonald, M. Lanier, J. Cashman, Synlett *2010* (13), 1951-4 [DOI: 10.1055/s-0030-1258132].

Cyclic phosphoromonoamidites s. under [Ir(cod)Cl]$_2$ ←

Propylphosphonic anhydride s. under NaN_3 ←

Adenosine 5′-diphosphate s. under 1,4-Dihydropyridines ←

(R)-3,3′-Bis(2,4,6-triisopropylphenyl)-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate s. under 1,4-Dihydropyridines ←

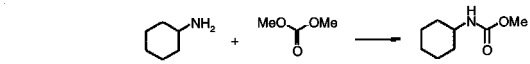
Air s. under KI and Ag-TiO_2 *air*

1-Methyl-3-(4-sulfobutyl)imidazolium hydrogen sulfate or silica-based sulfonic acid s. under NH_4OAc ←

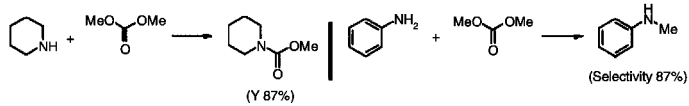
p-Toluenesulfonic acid s. under Pd[CH(COBu-t)$_2$]$_2$ *TsOH*

Saccharin-2-sulfonic acid ←
N-Acetylation s. *78*, 45 NH → NAc

Sulfamic acid [s.a. under [Ir(cod)Cl]$_2$] *H_2NSO_3H*
Urethans from carbonic acid esters and amines >NH + OC(OR)$_2$ → >NCOOR
Mild and efficient N-carbalkoxylation using sulfamic acid as recyclable catalyst



167.

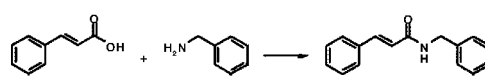


A mixture of cyclohexylamine (24 mmol) and dimethyl carbonate (5 eq.) treated with H_2NSO_3H (20 mol%) at 100° for 8 h, excess dimethyl carbonate and methanol removed by distillation, methylene chloride added to precipitate the catalyst, the mixture filtered, and the filtrate evaporated to dryness → methyl cyclohexylcarbamate. Y 95%. This environmentally-friendly synthesis (avoiding heavy metal catalysts, phosgene and chloroformates) was used for the prepn. of N-alkyl carbamates from a variety of prim. and sec. *aliphatic* amines (nine examples, incl. bis-acylation of 1,6-hexamethylenediamine; Y 87-95%). The catalyst is stable, non-volatile, non-hygroscopic and non-toxic, and could be easily recycled by precipitation and filtration, with no loss of activity observed after four cycles. With ar. amines as substrates, the predominant reaction was **mono-N-alkylation** rather than N-acylation, with unoptimized selectivity of 75-99% obtained from three prim. and sec. aniline derivs. F.e.s. B. Wang, J. He, R.C. Sun, Chin. Chem. Lett. *2010*, *21* (7), 794-7; halogen-free process, influence of leaving and entering groups, also trans-esterification of methyl carbamates to hindered carbamates, e.g. N-Boc-amines, s. P. Tundo, C.R. McElroy, F. Aricò, Synlett *2010* (10), 1567-71 [DOI: 10.1055/s-0029-1219927].

Cellulose sulfuric acid s. under [BH_4] ←

Sulfated tungstate ←
Carboxylic acid amides from carboxylic acids and amines COOH → C(O)NHR
using a novel, recyclable solid acid catalyst

168.



Sulfated tungstate (15 w/w%) and benzylamine (14.9 mmol) added in one portion to a soln. of cinnamic acid (1.1 eq.) in toluene (20 ml), the mixture heated under reflux for 12 h with azeotropic removal of water in a Dean-Stark trap, cooled to 50-60°, filtered, concentrated *in vacuo*, dissolved in ethyl acetate, washed with 10% aq. $NaHCO_3$ and 5% aq. HCl, and concentrated → N-benzylcinnamide. Y 95%. This novel, environmentally benign, heterogeneous catalyst (prepared from Na_2WO_4 and 2 eq. $ClSO_3H$) is cleaner and more efficient than other activators, can be removed by simple filtration, and recycled up to four times without loss of efficiency. The method was successful for ar. and aliphatic acids/amines (ten examples; Y 72-98%) but gave lower yields for N-phenyl- (45%) and morpholino-benzamides (33%). F.e. and catalyst prepn. s. P.S. Chaudhari, S.D. Salim, R.V. Sawant, K.G. Akamanchi, Green Chem. *2010*, *12* (10), 1707-10 [DOI: 10.1039/c0gc00053a].

Phosphomolybdic acid-silica ←
4(3*H*)-Quinazolones from *o*-aminocarboxylic acids, prim. amines ○
and orthoformic acid esters s. *66*, 178s*78*

12-Phosphotungstic acid-doped mesoporous silica $H_3W_{12}O_{40}$*-SBA 15*
N-Carbalkoxylation NH → NCOOR

N-carbo-*tert*-butoxylation with Boc_2O s. *60,* 135s*69*; with 12-phosphotungstic acid-doped mesoporous silica (SBA 15) without solvent s. B. Karmakar, J. Banerji, Tetrahedron Lett. *2010, 51* (29), 3855-8 [DOI: 10.1016/j.tetlet.2010.05.080]; N-carbo-*tert*-butoxylation of prim. amines via N-carbomethoxylation cf. P. Tundo, C.R. McElroy, F. Aricò, Synlett *2010* (10), 1567-71 [DOI: 10.1055/s-0029-1219927]; introduction of Fmoc and Alloc groups with the corresponding [crystalline] oxime carbonates, notably for protecting glycine, s. S.N. Khattab, R. Subirós-Funosas, A. El-Faham, F. Albericio, Eur. J. Org. Chem. *2010* (17), 3275-80 [DOI: 10.1002/ejoc.201000028].

Iodine I_2
N-Formylation with formic acid s. *13,* 442s*78* NH → NCHO

Iodine/tert-butyl hydroperoxide/sodium hydrogen carbonate I_2*/t-BuOOH/*$NaHCO_3$
Iodine/tert-butyl hydroperoxide/pyridine I_2*/t-BuOOH/*C_5H_5N
2-Arylquinazolines from *o*-aminoketones and prim. benzylamines via sp³ C-H functionalization under mild, metal-free conditions ○

169.

(2-Aminophenyl)(4-fluorophenyl)methanone (0.2 mmol), benzylamine (2.5 eq.), I_2 (10 mol%), pyridine (10 mol%) and *tert*-butyl hydroperoxide (70% soln. in water; 2 eq.) heated in a balloon-sealed tube at 90° for 12 h, the mixture worked up, and purified by chromatography on silica gel → 4-(4-fluorophenyl)-2-phenylquinazoline. Y 92%. 2,4-Diarylquinazolines were obtained from a variety of *o*-aminobenzophenone derivs. (seventeen examples; Y generally 70-90%), with best yields obtained for products in which the 4-aryl substituent was phenyl or electron-poor (but not sterically hindered, a mesityl example being unreactive); the nature or position of substituents on the benzylamine ring had relatively little effect on the outcome (1-aminomethylnaphthalene afforded a reduced yield of 63%, however), but electron-donating substituents on the aniline moiety had a detrimental effect. *α-Alkyl-subst. o*-aminoacetophenone derivs. were also suitable substrates (six examples; Y 83-90%), although *o*-aminoacetophenone itself afforded a complex mixture and a chalcone deriv. was low-yielding (31%). Higher yields were sometimes obtained in the absence of pyridine, but no reaction occurred in the absence of I_2, and other oxidants (*t*-BuOOBu-*t*, O_2, H_2O_2) were ineffective. F.e. incl. a tentative mechanism involving oxidation of an initially-formed imine s. J. Zhang, D. Zhu, C. Yu, C. Wan, Z. Wang, Org. Lett. *2010, 12* (12), 2841-43 [DOI: 10.1021/ol100954x]; **2,5-diaryloxazoles** from ar. aldehydes and α-amino-acetophenones under similar conditions (with $NaHCO_3$ as base) s. C. Wan, L. Gao, Q. Wang, J. Zhang, Z. Wang, ibid. (17), 3902-5 [DOI: 10.1021/ol101596s].

Hydroxylamine hydrochloride s. under ZnO or $ZnCl_2$ $NH_2OH{\cdot}HCl$
Hydroxylamine hydrochloride-on-melamine formaldehyde s. under NH_4OAc ←
Tetra-n-butylammonium iodide s. under K_2CO_3 Bu_4NI

Thiamine hydrochloride ←
N-Formylation with formic acid s. *13,* 442s*78* NH → NCHO

Tetra-n-butylammonium tribromide Bu_4NBr_3
Nitriles from aldehydes and ammonia s. *55,* 146s*78* CHO → CN

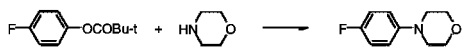
High-valent oxorhenium(V) or oxorhenium(VII) complexes s. under $PhSiH_3$ ←
Iron(III) phosphate s. under NH_4OAc ←

Iron(III) chloride/polyaniline nanoparticles ←
Benzimidazoles from *o*-diamines and aldehydes s. *46,* 321s*78*; *69,* 171s*78* ○

Bis(1,5-cyclooctadiene)nickel(0)/N,N′-bis(2,6-diisopropylphenyl)imidazolium chloride/ sodium tert-butoxide ←

Tert. ar. amines from sec. amines and aryl pivalates NH → NAr

Selective nickel(0)-catalyzed N-arylation

170. 

A mixture of $Ni(cod)_2$ (5 mol%), N,N′-bis(2,6-diisopropylphenyl)imidazolium chloride (10 mol%), *t*-BuONa (1.4 eq.), 4-fluorophenyl pivalate (0.5 mmol), morpholine (1.2 eq.) and toluene (2.5 ml) stirred at 70° under N_2 in a screwcap vial for 3 h, and purified by flash chromatography on silica → N-(4-fluorophenyl)morpholine. Y 73%. Careful optimization was required to minimize formation of by-products via O-acyl cleavage. Aryl pivalates *or N,N-diethylcarbamates* were good substrates under these conditions, while benzoates or acetates gave none of the aminated products. The reaction was successful for electron-diverse pivalates reacting with cyclic and acyclic sec. amines (twenty-one examples; Y 56-99%) in the presence of acetal, ether, *fluoro*, trifluoromethyl, *aldehyde* and alkene functionality. No amination occurred with the less nucleophilic cyclohexylamine or N-methylaniline, nor in the absence of the imidazolium ligand (tricyclohexylphosphine as ligand gave a reduced yield). F.e. and optimization s. T. Shimasaki, M. Tobisu, N. Chatani, Angew. Chem., Int. Ed. *2010*, *49* (16), 2929-32 [DOI: 10.1002/anie.200907287].

Nickel(II) acetate *Ni(OAc)₂*

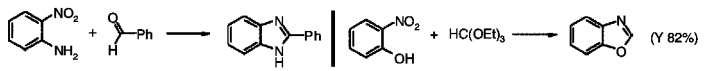
β-Amino-α,β-ethylene- from β-keto-carbonyl compds. COCH → C(N≤)=C

s. *26*, 331s*78*

Palladium nanoparticles s. under Immobilized lipase *Pd*

Palladium(II) 2,2,6,6-tetramethyl-3,5-heptanedionate/p-toluenesulfonic acid ←

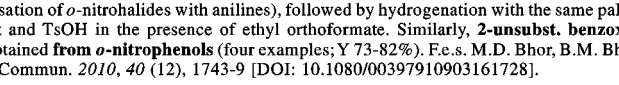
2-Arylbenzimidazoles from *o*-nitramines and ar. aldehydes ○

171. 

2-Nitroaniline (2 mmol), benzaldehyde (4 mmol), Pd(II)-2,2,6,6-tetramethyl-3,5-heptanedionate (5 mol%), *p*-TsOH (10 mol%) and ethyl acetate (10 ml) introduced into a high-pressure reactor (100 ml), heated to 80° for 1 h (to generate the intermediate imine), 500 psi of H_2 charged into the reactor at 80°, the mixture stirred for another 7 h, removed from the reactor, and worked up with chromatographic purification → product. Y 78%. This well-defined palladium catalyst is effective for the coupling of *o*-nitramines with a range of aromatic (and heteroaromatic) aldehydes possessing electron-donating (e.g. MeO, BnO, MeO, OH, Me_2N) or withdrawing (Cl) groups, reaction taking place by hydrogenative N-arylation followed by hydrogenation of the nitro group and ring closure (eleven examples; Y 65-82%). 2-Unsubst. N-arylbenzimidazoles were also obtained (in low overall yield) by initial N-arylation of *o*-nitramines with aryl halides (or by condensation of *o*-nitrohalides with anilines), followed by hydrogenation with the same palladium catalyst and TsOH in the presence of ethyl orthoformate. Similarly, **2-unsubst. benzoxazoles** were obtained **from *o*-nitrophenols** (four examples; Y 73-82%). F.e.s. M.D. Bhor, B.M. Bhanage, Synth. Commun. *2010*, *40* (12), 1743-9 [DOI: 10.1080/00397910903161728].

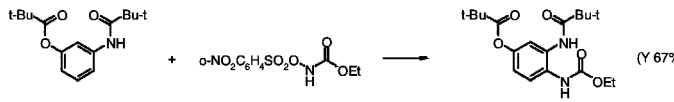
Bis(acetonitrile)palladium(II) ditosylate *[(MeCN)₂Pd(OTs)₂]*

Palladium(II)-catalyzed *o*-carbalkoxyamination of N-protected anilines H → NHCOOR

172. 

2,2,2-Trichloroethyl nosyloxycarbamate (1.2 eq.) added in one portion to a vial containing a mixture of 2,4-dimethylpivalanilide (0.2 mmol) and $[Pd(OTs)_2(MeCN)_2]$ (10 mol%) in 1,4-dioxane

(2 ml), the vial sealed with a Teflon cap, the mixture stirred at 80° for 6 h, cooled to room temp., diluted with ethyl acetate, quenched with satd. aq. $NaHCO_3$, extracted with ethyl acetate, concentrated *in vacuo*, and purified chromatographically → 2,2,2-trichloroethyl 3,5-dimethyl-2-(pivalamido)phenylcarbamate. Y 87%. This novel prepn. of diprotected *o*-diaminobenzene derivs. (incl. two *orthogonally diprotected* examples) is presumed to involve C-H activation via cyclopalladation (no reaction occurs in the absence of palladium). The method was successful for electron-diverse N-protected anilines using a variety of nosyloxycarbamate esters (twenty-one examples; Y 45-85%) in the presence of halo, ether and ester functionality. Interestingly, 3-pivaloyloxypivalanilide reacted exclusively at the 6-position, indicating the stronger directing effect of the amide moiety.



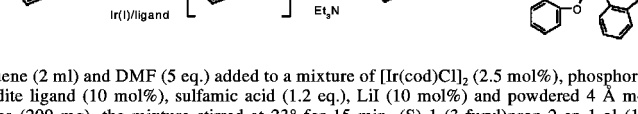
A 2-vinylaniline reacted sluggishly affording a 50% yield after prolonged reaction (40% recovered startg. m.). F.e., optimization and substrate prepn. s. K.-H. Ng, A.S.C. Chan, W.-Y. Yu, J. Am. Chem. Soc. *2010*, *132* (37), 12862-4 [DOI: 10.1021/ja106364r].

Bis(cinnamylpalladium chloride)/di(1-adamantyl)[o-(dimethylamino)phenyl]-phosphine/sodium tert-butoxide ←
Prim. ar. amines from aryl triflates s. *78*, 189 $OTf \rightarrow NH_2$

N-Unsubst. arylhydrazines from aryl triflates s. *78*, 190 $OTf \rightarrow NHNH_2$

Chloro(cyclooctadiene)iridium(I) dimer/cyclic phosphoromonoamidites/lithium iodide/sulfamic acid ←
2-Ethylene-*prim*-amines from 2-ethylenealcohols $OH \rightarrow NH_2$
Regioselective iridium(I)-catalyzed conversion with retention of chirality

173.



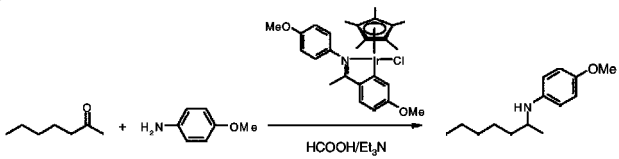
Toluene (2 ml) and DMF (5 eq.) added to a mixture of $[Ir(cod)Cl]_2$ (2.5 mol%), phosphoromonoamidite ligand (10 mol%), sulfamic acid (1.2 eq.), LiI (10 mol%) and powdered 4 Å molecular sieves (200 mg), the mixture stirred at 23° for 15 min, (S)-1-(3-furyl)prop-2-en-1-ol (1 mmol) added via syringe to the yellow soln., the mixture stirred until reaction complete (TLC; 18 h), triethylamine (5 eq.) added, the mixture cooled to 0°, a soln. of distilled benzoyl chloride (2 eq.) in methylene chloride (1 ml) added slowly via syringe, the mixture stirred at 0-23° during 3 h, solvents removed *in vacuo*, and the residue purified by flash chromatography on silica → (S)-N-[1-(fur-3-yl)allyl]benzamide. Y 70% (e.e. >98%). This novel, scaleable (6 mmol) and general stereospecific Ir-catalyzed substitution affords prim. amines exclusively from electron-neutral and -rich α-(het)ar. allylic alcohols (seven examples; Y 60-70%; e.e. 94 to >98%). 5-Phenylpent-1-en-3-ol was also a good substrate (Y 63%; e.e. 96%) but required heating at 50°, while other aliphatic derivs. were less enantioselective (Y 46-52%; e.e. 74-84%). Products were conveniently isolated via benzoylation *in situ*. F.e., substrate prepn. and isolation/characterization of an $Ir(ligand)_2I$ complex s. M. Roggen, E.M. Carreira, J. Am. Chem. Soc. *2010*, *132* (34), 11917-9 [DOI: 10.1021/ja105271z].

Chiral iridium(I) 1,1′-binaphthyl-2,2′-diyl phosphoramidite σ-complex/N-sodio compd. *[Ir]*/NaN≤*
N-Allylation with acoxy-2-ethylenes ←
Kinetic asym. transformation with retention of the double bond s. *78*, 116

Cyclometalated chloro(cyclopentadienyl)iridium(III) aryl ketimine complexes/ formic acid/triethylamine ←

Iridium(III)-catalyzed transfer-hydrogenative N-alkylation with oxo compds. CO → CH(NHR)

174.



Modular, air-stable and readily available cyclometalated iridium(III) aryl ketimine complexes are highly efficient and versatile catalysts for the transfer-hydrogenative N-alkylation of prim. or sec. amines, as well as ammonia, with a wide array of ketones and aldehydes, the procedure rivalling classical boron hydride routes in chemoselectivity, activity and substrate scope. **E:** A carousel reaction tube charged with *p*-anisidine (0.6 mmol) degassed and recharged with N_2 three times, 2-heptanone (0.5 mmol) added via syringe, followed by a soln. of the iridium(III) complex (0.5 μmol) in methanol (1 ml), a further quantity of methanol (2 ml) and $HCOOH/Et_3N$ azeotrope (0.5 ml) added sequentially, stirred at 80° for 1 h, cooled to room temp., quenched with water, basified with aq. KOH, and worked up with purification by flash chromatography → product. Y 98%. The procedure is safe, inexpensive, and highly efficient at catalyst loadings as low as 0.01 mol% for N-alkylation with aliphatic ketones, cyclic ketones and aldehydes, while less reactive aromatic ketones (which are demanding reaction partners in the boron hydride route) and α- and β-keto-esters required 0.5 mol% of the complex. Aromatic, benzylic and aliphatic prim. amines (incl. aminoalcohols and amino-acids) and cyclic sec. amines all underwent N-alkylation, but aliphatic sec. amines were less reactive (only 50% conversion with acetophenone). Significantly, there was no reduction of the keto or aldehyde group to the alcohol, and both isolated and conjugated double bonds, as well as CN and NO_2 groups, remained unaffected; furthermore, aromatic ketones may be substituted by electron-donating or -withdrawing groups on the aromatic ring. An ionic mechanism involving generation of an iridium hydride species is proposed. F.e. and diastereoselectivity s. C. Wang, A. Pettman, J. Basca, J. Xiao, Angew. Chem., Int. Ed. *2010, 49* (41), 7548-52 [DOI: 10.1002/anie.201002944].

Via intermediates *v.i.*

N-Carbo-*tert*-butoxylation of prim. amines NH → NCOOMe → NCOOBu-*t*

via N-carbomethoxylation s. *60,* 135s*78*

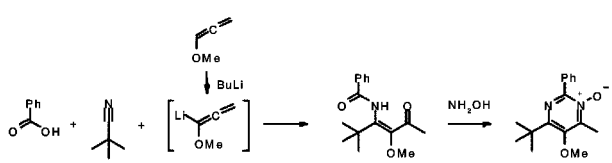
Nitrogen ↑ NC ↓↑ N

Microwaves s. under Methyl benzoate [\\\\]

Butyllithium/hydroxylamine *BuLi/NH$_2$OH*

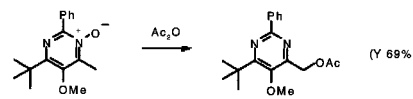
Pyrimidine N-oxides from allenyllithium compds., nitriles and carboxylic acids via β-acylamino-α,β-ethyleneketones under mild conditions ○

175.



5-Alkoxypyrimidine N-oxides. *n*-BuLi (2.5 *M* in hexanes; 1.1 eq.) added to a soln. of methoxyallene (28.5 mmol) in ether (60 ml) at -40°, the soln. stirred for 25 min, pivaloylnitrile (1.5 eq.)

added, the soln. stirred for 30 min, cooled to -78°, stirred for 4 h, benzoic acid (3 eq.) added, the mixture warmed to room temp. overnight, quenched with satd. aq. $NaHCO_3$, extracted with methylene chloride, concentrated *in vacuo*, and purified by chromatography on silica → intermediate enamide (Y 33%), 5.08 mmol of which dissolved in methanol (16 ml), hydroxylamine hydrochloride (3.12 eq.) added, the mixture stirred at room temp. for 24 h, diluted with water, extracted with methylene chloride, concentrated, and purified by chromatography on silica → 4-*tert*-butyl-5-methoxy-6-methyl-2-phenylpyrimidine-1-oxide (Y 97%). A series of multi-substituted 5-methoxy or 5-[2-(trimethylsilyl)ethoxy]-6-methyl derivs. containing additional alkyl, alkenyl and (het)ar. substituents were prepared by this method (nine examples; Y 59-97% from the intermediate enamides). The triethylsiloxyethyl protecting group was readily removed (using CF_3COOH) in quantitative yield. In a further development, the N-oxide products were treated with refluxing Ac_2O to afford the corresponding **4-α-acetoxy-5-alkoxypyrimidines** via O-acetylation and acetoxy migration to the adjacent 6-methyl group.

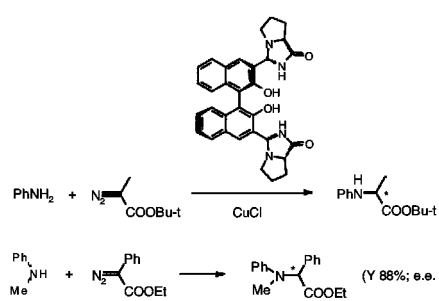


F.e.s. R. Zimmer, T. Lechel, G. Rancan, M.K. Bera, H.-U. Reissig, Synlett *2010* (12), 1793-6 [DOI: 10.1055/s-0030-1258088].

Copper(I) chloride/chiral 3,3′-bis(1,3-diazabicyclo[3.3.0]octan-4-on-2-yl)-1,1′-bi-2-naphthols *[Cu(I)]**

Catalytic asym. insertion of carbenes into nitrogen-hydrogen bonds under mild conditions NH → NCH≺

176.



Planar chiral [BINOL-based] 3,3′-bis(1,3-diazabicyclo[3.3.0]octan-4-on-2-yl)-1,1′-bi-2-naphthols possessing bicyclic L-prolinamide residues serve as excellent ligands for copper(I)-catalyzed asym. insertion of carbenes into the N-H bond of both anilines and challenging N-alkylanilines. **E: Chiral α-arylaminocarboxylic acid esters.** Methylene chloride (2 ml) added under an inert atmosphere to a dry test tube charged with the chiral ligand (10 mol%), CuCl (10 mol%), and 4 Å molecular sieves (50 mg), the tube sealed with a septum, the mixture stirred at 30° for 1 h, cooled to 0°, the startg. aniline (0.2 mmol) and α-diazo-ester (3 eq.) introduced successively via syringe, the mixture carefully shaken for a few sec, and again *for several sec every 2 h* over the next 6 h to ensure homodispersity, the soln. left *without stirring* for a further 12 h at 0°, and directly uploaded onto a column of silica gel eluting with petroleum ether/ethyl acetate (10:1) → product. Y 99% (e.e. 93%). High yields and enantioselectivities were recorded (nineteen examples; Y 90-99%; e.e. 87-98%) for the reaction of *tert*-butyl α-diazo-esters with prim. anilines, irrespective of the position or electronic character of ring substituents. Unprecedented enantioselectivities (67-70%

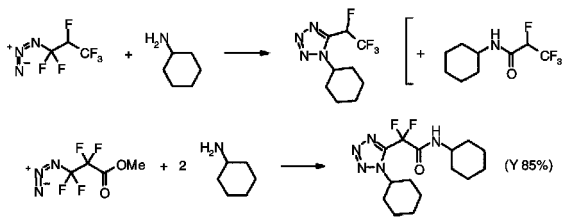
e.e.) were also registered with a sec. amine [N-ethylaniline] on reaction with alkyl diazo(phenyl)-acetate (two examples; Y 82-88%). The nature of the solvent is critical and, surprisingly, results were better if stirring was *not* continuous. The hydroxyl groups of the ligand are essential, but the face-selectivity was dictated by the planar chirality rather than by the bicyclic *L*-prolinamide residues. Other ligands (the corresponding N,N′-dioxides and BINOL-derived bis(oxazolines) or tertiary amines) gave poor results. F.e.s. Z. Hou, J. Wang, P. He, J. Wang, B. Qin, X. Liu, L. Lin, X. Feng, Angew. Chem., Int. Ed. *2010*, *49* (27), 4763-6 [DOI: 10.1002/anie.201001686].

Methyl benzoate/microwaves *PhCOOMe/[\\\\]*
N-Formylation with dimethylformamide s. *13*, 442s*78* NH → NCHO

Halogen ↑ NC ↓↑ Hal

Without additional reagents *w.a.r.*
Tetrazoles from 1-azido-1,1-difluorides and prim. amines ○

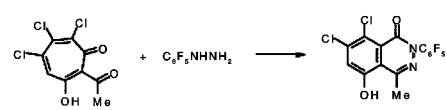
177.



A mixture of startg. azide (5 mmol) and cyclohexylamine (4 eq.) in dry ethanol (50 ml) stirred for 8 h, quenched with 5% aq. $NaHCO_3$ (100 ml), extracted with ethyl acetate, the extracts dried (Na_2SO_4), the solvent evaporated, the residue subjected to column chromatography on silica, crystallized from ethanol, then dried *in vacuo* → 1-cyclohexyl-5-(1,2,2,2-tetrafluoroethyl)tetrazole. Y 60%. The crude product was a 3:2 mixture of tetrazole and amide. A 45% yield of the tetrazole was obtained in THF after 12 h, with the same tetrazole/amide ratio in the crude mixture. The starting azidodifluorides are stable, safe compounds, readily prepared from fluoroolefins. The method is sensitive to steric hindrance but even adamantyl- and *tert*-alkyl-amines were reactive. With methyl 3-azido-2,2,3,3-tetrafluoropropionate the corresponding difluoro(tetrazol-5-yl)acet-amides were obtained. F.e. (seven; Y 40-85%) s. A.G. Polivanova, S.V. Shkavrov, A.V. Churakov, A.S. Lermontov, S.A. Lermontov, Tetrahedron Lett. *2010*, *51* (32), 4205-7 [DOI: 10.1016/j.tetlet.2010.06.016].

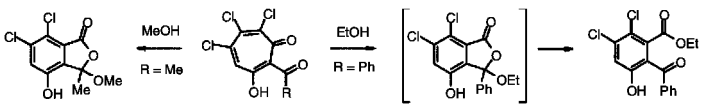
1(2*H*)-Phthalazones from 2-acyl-7-chlorotropones and hydrazines ○

178.



7,8-Dichloro-5-hydroxy-1(2*H*)-phthalazones. A mixture of 2-acetyl-3-hydroxy-5,6,7-trichlorotropone (0.1 mmol) and pentafluorophenylhydrazine (3 eq.) in *tert*-butanol (1 ml) under N_2 heated at 100° for 2 h → 7,8-dichloro-5-hydroxy-4-methyl-2-pentafluorophenyl-1(2*H*)-phthalazone. Y 86%. This novel synthesis selectively affords phthalazones via ring contraction of 2-acetyl- or -benzoyl-tropone derivs. using electron-poor 2,4-dinitrophenyl- and pentafluorophenyl-hydrazines (five examples; Y 68-94%). 2,5-Difluorophenylhydrazine, however, gave a mixture of the phthal-azone (Y 74%) and a pyrazolotropone (Y ca. 6%), while for phenylhydrazine, a ca. 1:1 mixture of the two products was obtained (Y 85%). The ring contraction of a 2-*acetyl*-7-chlorotropone was

also induced with alcohols to afford **3-alkoxyphthalides**, with methanol being most effective (Y 95%) and yields somewhat reduced for ethanol (85%), isopropanol (70%), ethylene glycol (mono-reaction; 68%) and 2-hydroxymethyltetrahydrofuran (54%). Interestingly, a 2-benzoyl deriv. afforded an *o*-benzoyl-*m*-hydroxycarboxylic acid ester (Y 79%) presumed via transesterification of the intermediate alkoxyphthalide.



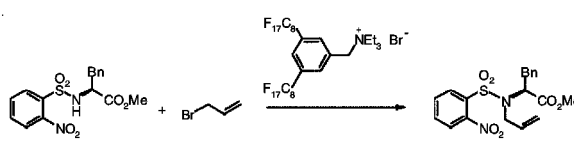
F.e.s. W. Li, H. Li, Z. Li, Tetrahedron Lett. *2010*, *51* (41), 5448-50 [DOI: 10.1016/j.tetlet.2010.08.017].

Microwaves s. under CuI [\\\\]

Sodium hydroxide/hydrogen chloride *NaOH/HCl*
2-Hydroxyfumaric acid monoamides
from (Z)-2,2-dimethyl-5-chlorocarbonylmethylene-1,3-dioxolan-4-one s. *78*, 442

Potassium carbonate/[3,5-bis(n-perfluorooctyl)benzyl]triethylammonium bromide
Solid-liquid phase transfer catalysis
with a readily recyclable fluorous quaternary ammonium bromide

179.



N-Alkylation. K_2CO_3 (1.5 eq.) added to a screw-cap vial containing a soln. of the startg. sulfonamide (0.5 mmol), 3,5-bis(*n*-perfluorooctyl)benzyltriethylammonium bromide (10 mol%) and allyl bromide (1.1 eq.) in anhydrous acetonitrile (3 ml), the heterogeneous mixture stirred at 80° for 12 h (TLC monitoring), cooled to room temp., filtered through Celite to remove inorganic salts, the filtrate evaporated under reduced pressure, the catalyst removed *by addition of cold toluene followed by filtration*, and the filtrate and washings evaporated under reduced pressure → product. Y 98%. Being both hydrophobic and lipophilic, with two fluorous ponytails, the catalyst was simply recovered in quantitative yield and reused several times without loss of activity. High yields (84-98%; nine examples) were obtained for the N-alkylation of a series of chiral N-(2- or 4-nitrobenzenesulfonyl)-α-aminocarboxylic acid esters. F.e.s. G. Pozzi, V. Mihali, F. Foschi, M. Penso, S. Quici, R.H. Fish, Adv. Synth. Catal. *2009*, *351* (18), 3072-6 [DOI: 10.1002/adsc.200900631].

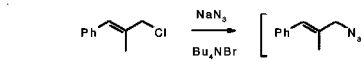
Sodium azide [s.a. under Cu or Cu(I)] *NaN_3*
4-Acyl-2*H*-1,2,3-triazoles from α,β-acetyleneketones s. *68*, 184s*78*

Sodium azide/copper or copper(I)-zeolite *NaN_3/Cu or Cu(I)-zeolite*
Sodium azide/copper(I) iodide/polyethylene glycol *NaN_3/CuI/PEG*
1,2,3-Triazoles from terminal acetylene derivs. and halides
s. *68*, 184s*75*; eco-friendly procedure **in water** with Cu(I)-zeolite, also from tosylates, s. V. Bénéteau, A. Olmos, T. Boningari, J. Sommer, P. Pale, Tetrahedron Lett. *2010*, *51* (28), 3673-7 [DOI: 10.1016/j.tetlet.2010.05.036]; with copper wire in an inductively heated flow microreactor, also decarboxylation of α,β-acetylenecarboxylic acids and lactonization of bromocarboxylic acids, s. S. Ceylan, T. Klande, C. Vogt, C. Friese, A. Kirschning, Synlett *2010* (13), 2009-13 [DOI: 10.1055/s-0030-1258487]; 1-aryl-1,2,3-triazoles **from diaryliodonium halides** with CuI in aq. PEG-400 s. D. Kumar, V.B. Reddy, Synthesis *2010* (10), 1687-91 [DOI: 10.1055/s-0029-1218765];

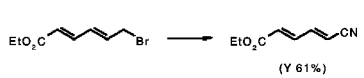
metal-free procedure in DMSO for preparing 4-acyl-2*H*-1,2,3-triazoles from ynones s. J. Li, Y. Zhang, D. Wang, W. Wang, T. Gao, L. Wang, J. Li, G. Huang, B. Chen, Synlett *2010* (11), 1617-22 [DOI: 10.1055/s-0030-1258086].

Sodium azide/18-crown-6 polyether or tetra-n-butylammonium bromide/2,3-dichloro-5,6-dicyanoquinone ←

α,β-Ethylenenitriles from β,γ-ethylene-*prim*-halides via 2-ethyleneazides $CH_2Hal \rightarrow CH_2N_3 \rightarrow CN$



180.



under mild conditions. A one-pot, two-step conversion of allyl halides to unsatd. nitriles is reported, extending previous work on the conversion of methylarenes to ar. nitriles [using NaN_3/$PhI(OAc)_2$/$CuSO_4$], in which it was observed that reaction proceeds via novel oxidative rearrangement of intermediate benzyl azides (s. *76*, 155). **E:** An oven-dried Schlenk tube charged with (E)-(3-chloro-2-methyl-1-propenyl)benzene (0.5 mmol), NaN_3 (1.2 eq.), *n*-Bu_4NBr (5 mol%) and 1,2-dichloroethane (2 ml), flushed three times with N_2 at -40°, the mixture stirred at room temp. for 24 h, DDQ (1.3 eq.) added, the mixture heated under reflux until reaction complete (TLC), cooled to room temp., solvent evaporated, and the residue purified by flash chromatography on silica gel → 2-methyl-3-phenyl-2-propenenitrile. Y 96% (E/Z 8:1). Nine cinnamyl chloride or bromide derivs. afforded corresponding unsatd. nitriles in yields of 73-96%. Linear examples were lower-yielding, however (only 35% for an allyl chloride). (E)-Products predominated in all cases, even with trisubst. olefins. Other oxidants, such as $PhI(OAc)_2$, CAN or benzoquinone were less effective than DDQ and a range of alternative common solvents were also lower-yielding; notably, 18-crown-6 could be used effectively as phase transfer catalyst in place of Bu_4NBr. F.e., also **(het)ar. nitriles from benzyl halides** (fifteen examples; Y 57-96%, highest for electron-rich ar. groups), notably tolerating ar. iodides and thioethers, s. W. Zhou, J. Xu, L. Zhang, N. Jiao, Org. Lett. *2010*, *12* (12), 2888-91 [DOI: 10.1021/ol101094u].

Potassium fluoride s. under Pd(OAc)₂ *KF*

2,2′-Bipyridyl s. under Cu(acac)₂ *bipy*

Copper s.a. under NaN_3 *Cu*

Copper/sodium azide/pipecolinic acid/ascorbic acid ←

Copper(I)/sodium azide *Cu(I)/NaN_3*

Prim. ar. amines from ar. halides s. *75*, 180s*78* $Hal \rightarrow NH_2$

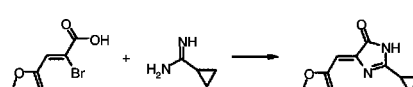
Copper(I)-zeolite s. under NaN_3 *Cu(I)-zeolite*

Copper(I) oxide/cesium carbonate *Cu_2O/Cs_2CO_3*

4-Alkylidene-Δ²-imidazol-5-ones from α-bromo-α,β-ethylenecarboxylic acids and amidines ○

Simple and efficient copper(I)-catalyzed ring closure

181.

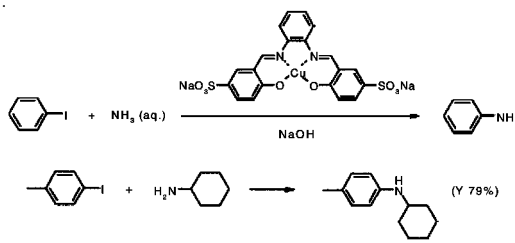


A mixture of 2-bromo-3-fur-2-ylacrylic acid (1.4 eq.), startg. amidine hydrochloride (0.5 mmol), Cs_2CO_3 (2 eq.) and Cu_2O (20 mol%) in *DMF* (2 ml) stirred at 80° under N_2 for 12 h, filtered, concentrated, and purified by chromatography on silica → (Z)-2-cyclopropyl-4-(fur-2-yl-

methylene)-4,5-dihydro-1*H*-imidazol-5-one. Y 94%. This simple and efficient method uses readily available substrates and affords 2-(het)aryl- or 2-alkyl-4-(het)arylidene derivs. without requirement for additives or ligands (twenty-two examples; Y 44-94%) with lowest yields observed for 2-*n*-alkyl derivs. F.e., optimization and substrate prepn. s. X. Gong, H. Yang, H. Liu, Y. Jiang, Y. Zhao, H. Fu, Org. Lett. *2010*, *12* (14), 3128-31 [DOI: 10.1021/ol1008813].

Water-soluble copper(II) salen complex/sodium hydroxide *Cu(II)-salen/NaOH*
Ar. amines from ar. halides in water Hal → N≤

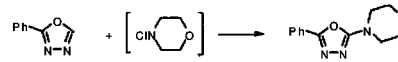
182.



Prim. ar. amines. The water-soluble copper(II) salen complex (0.025 mmol), iodobenzene (0.5 mmol), NaOH (1 mmol), aq. ammonia (1 ml), and water (2 ml) stirred in a sealed tube at 120° for 12 h, cooled to room temp., and worked up with purification by chromatography on silica gel → aniline. Y 83%. The procedure is simple, inexpensive, environmentally friendly and applicable to a wide range of ar. iodides and [with 10 mol% catalyst] ar. bromides. The yields were generally higher with substrates possessing electron-withdrawing groups, and *o*-substitution was not a problem; reaction was also applicable to heteroaromatic iodides or bromides, and tolerated a wide range of functional groups (e.g. NO_2, acetyl, ether, Cl, and F). Other copper salts gave only trace amounts of product, but several other bases were effective, e.g. K_2CO_3, K_3PO_4, Na_2CO_3 or Cs_2CO_3 (NaOAc and Et_3N giving low yields). F.e. (twenty-three in all; Y 64-95%), **also benzimidazoles from *o*-iodo-acylamines** and ammonia in one pot (one example; Y 90%), s. Z. Wu, Z. Jiang, D. Wu, H. Xiang, X. Zhou, Eur. J. Org. Chem. *2010* (10), 1854-7 [DOI: 10.1002/ejoc.201000060]; **sec. ar. amines from ar. iodides or bromides** and aliphatic (or benzylic) prim. amines (incl. 2-*prim*-aminoalcohols and α- or β-*prim*-aminocarboxylic acids) under the same conditions s. Z. Wu, L. Zhou, Z. Jiang, D. Wu, Z. Li, X. Zhou, ibid. (26), 4971-5 [DOI: 10.1002/ejoc.201000840]; N-arylation of nitrogen-containing heterocyclics and aliphatic amines in water using CuBr or CuCl, (1E,2E)-oxalaldehyde dioxime [OADO] as ligand, Bu_4NBr and NaOH, functional group tolerance, s. X. Li, D. Yang, Y. Jiang, H. Fu, Green Chem. *2010*, *12* (6), 1097-105 [DOI: 10.1039/c002172e]; of amines with ar. bromides or iodides using CuI, N′-phenyl-1*H*-pyrrole-2-carbohydrazide, Bu_4NBr and KOH under microwave irradiation s. J. Xie, X. Zhu, M. Huang, F. Meng, W. Chen, Y. Wan, Eur. J. Org. Chem. *2010* (17), 3219-23 [DOI: 10.1002/ejoc.201000361].

Copper(II) acetoacetonate/2,2′-bipyridyl/lithium or sodium tert-butoxide ←
Regiospecific copper(II)-catalyzed *tert*-amination of azoles H → N≤
with N,N-disubst. chloramines under mild conditions

183.



2-*tert*-Amino-1,3,4-oxadiazoles. Toluene (2 ml) and morpholine (0.75 mmol) added to N-chlorosuccinimide (0.83 mmol) under N_2 using standard Schlenk technique, the mixture stirred for 30 min *at room temp.* in the dark, the resulting suspension of N-chloromorpholine transferred via syringe to another reaction flask containing $Cu(acac)_2$ (0.05 mmol), 2,2′-bipyridyl (0.05 mmol),

LiOBu-*t* (1.8 mmol) and dibenzyl (as internal standard), a soln. of 2-phenyl-1,3,4-oxadiazole (0.5 mmol) in toluene (1 ml) added, the mixture stirred for 2 h at room temp., quenched with water, and worked up with purification by chromatography on silica gel → 4-(5-phenyl-1,3,4-oxadiazol-2-yl)morpholine. Y 73%. Although reaction is equally effective with preformed chloramines, their generation *in situ* is more convenient. This is a useful alternative to copper-catalyzed reaction of 2-halogeno-1,3,4-oxadiazoles with amines, which ordinarily requires harsh conditions. The substituent at the 5-position of the product may be alkyl or aryl, and either electron-donating or -withdrawing groups (notably Cl) are tolerated on the aromatic ring; furthermore, N-benzyl and N-Boc groups remained unaffected (twelve examples in all; Y 51-84%). **2-*tert*-Aminobenzoxazoles** were obtained similarly (six examples; Y 38-76%) with NaOBu-*t* in place of LiOBu-*t*.

The mechanism of the reaction possibly involves initial base-assisted cupration, followed by oxidative addition of the chloramines and reductive elimination of a copper(III) species. F.e.s. T. Kawano, K. Hirano, T. Satoh, M. Miura, J. Am. Chem. Soc. *2010*, *132* (20), 6900-1 [DOI: 10.1021/ja101939r].

Copper(I) iodide s.a. under NaN_3 *CuI*

Copper(I) chloride or bromide/(1E,2E)-oxalaldehyde dioxime/tetra-n-butylammonium bromide/sodium hydroxide ←

Copper(I) iodide/N′-phenyl-1H-pyrrole-2-carbohydrazide/tetra-n-butylammonium bromide/potassium hydroxide/microwaves ←

N-Arylation in water s. *78*, 182 NH → NAr

Copper(I) 2-(dimethylaminomethyl)phenylmercaptide/potassium carbonate *$CuSAr/K_2CO_3$*

Copper(I) iodide/potassium hydroxide/tetra-n-butylammonium bromide *$CuI/KOH/Bu_4NBr$*

Copper(I) iodide/potassium phosphate *CuI/K_3PO_4*

Copper(I) iodide/N,N′-dimethylethylenediamine/potassium carbonate *$CuI/DMEDA/K_2CO_3$*

Copper(I) iodide/1,4-bis(2-hydroxy-5-methoxybenzyl)piperazine/tetra-n-butylammonium bromide/potassium hydroxide ←

Copper(I) iodide/3-acetylcoumarin ←

Copper(I) iodide/8-acetyl-5,6,7,8-tetrahydroquinoline/cesium carbonate ←

Copper(II) fluoride *CuF_2*

Copper(I) siloxane cage compds. ←

Copper-catalyzed N-arylation

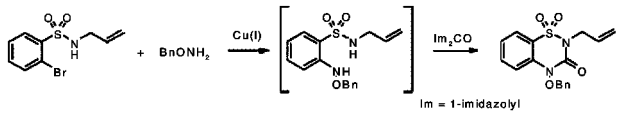
s. *62*, 171s*76*; of amines and N-heterocyclics with [het]aryl bromides using thermally stable Cu(I)-2-(dimethylaminomethyl)phenylmercaptide (and analogs) as pre-catalyst and K_2CO_3 as base s. E. Sperotto, G.P.M. van Klink, J.G. de Vries, G. van Koten, Tetrahedron *2010, 66* (19), 3478-84 [DOI: 10.1016/j.tet.2010.03.040]; N-[het]arylation of imidazoles **in water** with CuI and 1,4-bis(2-hydroxy-5-methoxybenzyl)piperazine as ligand, Bu_4NBr as phase transfer catalyst and KOH as base s. Y. Zhu, Y. Shi, Y. Wei, Monatsh. Chem. *2010, 141* (9), 1009-13 [DOI: 10.1007/s00706-010-0363-8]; mono-N-arylation of unprotected 2-imidazolidone with added DMEDA/K_2CO_3 s. P. Stabile, A. Lamonica, A. Ribecai, D. Castoldi, G. Guercio, O. Curcuruto, Tetrahedron Lett. *2010, 51* (24), 3232-5 [DOI: 10.1016/j.tetlet.2010.04.064]; N-arylation of aliphatic amines and imidazoles with ar. iodides (at room temp.) and ar. bromides (at 80°) using 3-acetylcoumarin as ligand s. C.-Z. Tao, W.-W. Liu, J.-Y. Sun, Z.-L. Cao, H. Li, Y.-F. Zhang, Synthesis *2010* (8), 1280-4 [DOI: 10.1055/s-0029-1218661]; of imidazoles with 8-acetyl-5,6,7,8-tetrahydroquinoline as ligand and Cs_2CO_3 as base s. H. Chen, D. Wang, X. Wang, W. Huang, Q. Cai, K. Ding, ibid. (9), 1505-11 [DOI: 10.1055/s-0029-1218691]; *ligand-free* N-arylation of amides and imidazoles with KOH/Bu_4NBr s. M.A. Ali, P. Saha, T. Punniyamurthy, ibid. (6), 908-10 [DOI: 10.1055/s-0029-1218643]; N-arylation of azoles with halogenothiophenes using CuF_2 s. P. Arsenyan, E. Paegle, A. Petrenko, S. Belyakov, Tetrahedron Lett. *2010, 51* (38), 5052-5 [DOI: 10.1016/j.tetlet.2010.07.094]; N-arylation of semicarbazones for the synthesis of aza-arylglycine-containing aza-peptides s. C. Proulx, W.D. Lubell, Org. Lett. *2010, 12* (13), 2916-9 [DOI: 10.1021/ol100932m]; N-thien-2-ylation of N-heterocyclics with copper(I) siloxane cage compds. s. G. Tan, Y. Yang, C.

Chu, H. Zhu, H.W. Roesky, J. Am. Chem. Soc. *2010, 132* (35), 12231-3 [DOI: 10.1021/ja1056104]; **prim. ar. amines** from ar. halides and aq. ammonia with CuI/K_3PO_4 in DMF at room temp. (cf. *75,* 180) s. C. Tao, W. Liu, A. Lv, M. Sun, Y. Tian, Q. Wang, J. Zhao, Synlett *2010* (9), 1355-8 [DOI: 10.1055/s-0029-1219922]; via N-arylation of fluorous N-Boc-protected alkoxylamines as a *fluorous ammonia equivalent* with a simple fluorous work-up s. S.D. Nielsen, G. Smith, M. Begtrup, J.L. Kristensen, Eur. J. Org. Chem. *2010* (19), 3704-10 [DOI: 10.1002/ejoc.201000367]; prim. ar. amines from ar. halides or azides *with* NaN_3 and Cu(I) cf. J.T. Markiewicz, O. Wiest, P. Helquist, J. Org. Chem. *2010, 75* (14), 4887-90 [DOI: 10.1021/jo101002p]; with Cu powder/NaN_3 and pipecolinic acid/ascorbic acid s. S. Messaoudi, J.-D. Brion, M. Alami, Adv. Synth. Catal. *2010, 352* (10), 1677-87 [DOI: 10.1002/adsc.201000149].

Copper(I) iodide/1,10-phenanthroline/cesium carbonate/N,N′-carbonyldiimidazole/ triethylamine/microwaves ←

4-Functionalized 1,2,4-benzothiadiazin-3-one 1,1-dioxides from *o*-bromosulfonic acid amides and functionalized amines Copper(I)-catalyzed N-arylation-cyclocarbonylation ○

184.

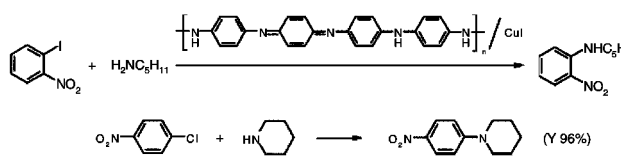


4-Benzyloxy-1,2,4-thiadiazin-3-one 1,1-dioxides in one pot. N-Allyl-2-bromobenzenesulfonamide (0.17 mmol), CuI (10 mol%), 1,10-phenanthroline (20 mol%), Cs_2CO_3 (4 eq.), *dry DMF* (0.3 ml) and O-benzylhydroxylamine (1.2 eq.) added sequentially to a microwave vial, the mixture heated by microwaves at 150° for 11 min, triethylamine (2 eq.) and N,N′-carbonyldiimidazole (4 eq.) added, the mixture heated at 150° for 11 min, cooled to room temp., concentrated *in vacuo*, diluted with methylene chloride, washed with aq. HCl and water, and purified by flash chromatography → 2-allyl-4-benzyloxybenzo-1,2,4-thiadiazin-3-one 1,1-dioxide. Y 73%. The choice of solvent was optimized for the one-pot process (three examples; Y 68-73%), but overall yields were generally higher for the two-step procedure. Thus, initial N-arylation of alkyl-, benzyl- and allyl-amines and ethyl carbamate gave optimal results in DMSO (eleven examples; Y 80-96%; propargylamine gave 69%), with DMF preferred for the cyclization step (eight examples; Y 92-98%). F.e.s. A. Rolfe, P.R. Hanson, Tetrahedron Lett. *2009, 50* (50), 6935-7 [DOI: 10.1016/j.tetlet.2009.09.090].

Polyaniline nanofiber-supported copper(I) iodide/potassium carbonate ←

Ar. amines from halides under mild, heterogeneous copper(I) catalysis Hal → N≤

185.



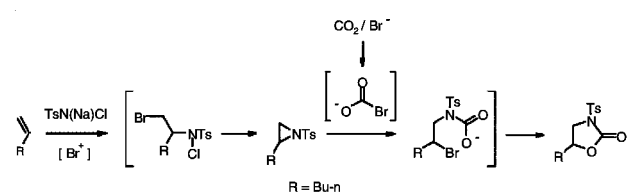
Polyaniline nanofibers, comprising linear polymeric chains of *p*-quinone imine and *p*-phenylenediamine residues, coordinate copper(I) iodide between the chains to form a readily recyclable heterogeneous catalyst [CuIPANInf] which is highly active for the N-arylation of a wide range of aromatic, aliphatic and heterocyclic amines with aryl halides under mild conditions, thereby obviating the familiar recourse to high temperatures, high catalyst loadings and the use of additives. **E:** *o*-Iodonitrobenzene (1 mmol), *n*-pentylamine (1.2 mmol), K_2CO_3 (1.2 mmol), CuIPANInf (Cu: 5 mol%) and DMF (2 ml) stirred *at room temp.* under N_2 for 2 h, the mixture centrifuged to remove the solid catalyst, the filtrate diluted with water, extracted with ethyl acetate, and worked

up with purification by flash chromatography on silica gel → product. Y 99%. The washed and air-dried catalyst was recycled five times with *only 1%* decrease in the yield. A wide range of aryl iodides coupled with both prim. amines and cyclic sec. amines in high yields, substrates possessing electron-withdrawing groups affording higher yields than those with electron-donating groups. Reaction was also applied to electron-diverse ar. chlorides at 80-100°, reactivity following the same electronic trend (but chlorobenzene itself was unreactive even after 24 h). The high reactivity of the catalyst is associated with high basicity of the polymeric matrix, which not only serves as support but also *as a macroligand* for copper(I). Interestingly, *o*-iodonitrobenzene is more reactive than *p*-iodonitrobenzene, the electron-withdrawing *o*-nitro group serving as an additional chelating group for the metal. F.e. incl. selective displacement of iodine in the presence of chlorine s. R. Arundhathi, D.C. Kumar, B. Sreedhar, Eur. J. Org. Chem. *2010* (19), 3621-30 [DOI: 10.1002/ejoc.201000149].

Polyethylene glycol s. under NaN_3	*PEG*
18-Crown-6 polyether s. under NaN_3	*crown*
3-Acetylcoumarin s. under CuI	←
8-Acetyl-5,6,7,8-tetrahydroquinoline s. under CuI	←
(1E,2E)-Oxalaldehyde dioxime s. under CuCl or CuBr	←
N′-Phenyl-1H-pyrrole-2-carbohydrazide s. under CuI	←
N,N′-Carbonyldiimidazole s. under CuI	*Im_2CO*
Ascorbic acid s. under Cu	←
L-Proline s. under $MnCl_2$	*L-Pro-OH*
Pipecolinic acid s. under Cu	←
2,3-Dichloro-5,6-dicyanoquinone s. under NaN_3	*DDQ*
Tert. phosphines or di(phosphines) s. under Pd-charcoal and $Pd(OAc)_2$	*≥P*
Di(1-adamantyl)[o-(dimethylamino)phenyl]phosphine s. under [(allyl)PdCl]$_2$ or [(cinnamyl)PdCl]$_2$	←
Air s. under $Pd(OAc)_2$	*air*
Tetra-n-butylammonium bromide s. under NaN_3, CuCl, CuBr, CuI and Bu_4NBr_3	*Bu_4NBr*
[3,5-Bis(n-perfluorooctyl)benzyl]triethylammonium bromide s. under K_2CO_3	*F-TEBA*
Tetra-n-butylammonium tribromide/tetra-n-butylammonium bromide/N-sodio salt	←
N-Tosyl-2-oxazolidones from ethylene derivs.	○

One-pot regioselective conversion via N-tosylaziridines

186.

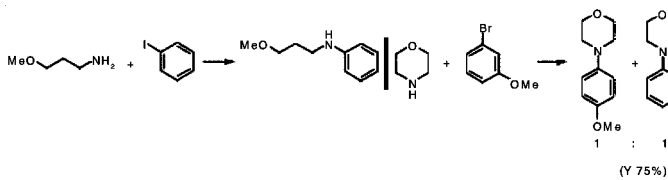


CO_2 introduced into a stainless steel autoclave charged with 1-hexene (3 mmol), freshly dried Chloramine-T (4 mmol), *n*-Bu_4NBr (0.3 mmol), *n*-Bu_4NBr_3 (0.3 mmol), *hydroquinone* (0.15 mmol), biphenyl (100 mg; as internal standard) and acetonitrile (10 ml), the mixture stirred at 100° for 15 min to allow equilibration, the CO_2 pressure adjusted to 8 MPa, stirred continuously for 24 h, the reactor cooled in ice-water, CO_2 vented slowly, and worked up with purification by chromatography on silica gel → 5-butyl-3-tosyl-2-oxazolidone. Y 63.7% (and 6% 2-butyl-1-tosylaziridine). This simple and effective one-pot procedure is perfectly regioselective and applicable to a range of aliphatic and aromatic olefins, reaction of the latter being favored by electron-donating groups on the benzene ring (Y 0% with *p*-chlorostyrene). With cyclohexene, however, the only isolated product was the corresponding aziridine (Y ca. 40%), while yields were low

with aliphatic olefins having long alkyl chains (Y 14.6% with 1-dodecene). Mechanistically, a dual catalytic cycle is proposed, based on initial tribromide ion-mediated aziridination, followed by bromide ion-mediated addition of CO_2. Reaction was optimized by comparing a range of tetraalkylammonium tribromides and halides, solvents, CO_2 pressures and temperatures. F.e. (eleven; Y 38.2-63.7% with isolation of 4-12.6% N-tosylaziridine as by-product) s. D.-L. Kong, L.-N. He, J.-Q. Wang, Catal. Commun. *2010, 11* (11), 992-5 [DOI: 10.1016/j.catcom.2010.04.003]; regioselective formation of 4-alkyl-2-oxazolidones from aziridines with NH_4I at a low CO_2 pressure, 5-aryl-2-oxazolidones under compressed CO_2 conditions, and use of a Lewis basic ionic liquid catalyst s. *32, 278s78*; with α-amino acids (0.6 mol%) in the absence of solvent s. H.-F. Jiang, J.-W. Ye, C.-R. Qi, L.-B. Huang, Tetrahedron Lett. *2010, 51* (6), 928-32 [DOI: 10.1016/j.tetlet.2009.12.031].

Manganese(II) chloride/L-proline/sodium tert-butoxide *$MnCl_2$/Pro-OH/NaOBu-t*
Manganese(II)-catalyzed N-arylation of prim. or sec. amines NH → NAr

187.



A mixture of 3-methoxypropylamine (1.47 mmol), iodobenzene (2 eq.), Na-*tert*-butoxide (2 eq.), $MnCl_2 \cdot 4H_2O$ (5 mol%) and L-proline (10 mol%) in DMSO (0.75 ml) stirred at 135° for 24 h → N-(3-methoxypropyl)aniline. Y 45%. This experimentally simple method uses an inexpensive and readily available catalyst system for N-arylation of cyclic and acyclic amines with iodo- and bromo-benzene derivs. The reaction was successful with electron-diverse *m*- and *p*-subst. ar. halides (seventeen examples; Y 43-80%) but *o*-subst. derivs. were unsuitable (Y 0-16%) as was benzylamine (Y 22%). Subst. ar. halides gave mixtures of isomeric *cine*-substitution products in some cases. Other bases or Mn(II) salts were less effective, while other solvents (e.g. DMF, toluene) were almost completely ineffective. F.e. and optimization s. F.-F. Yong, Y.-C. Teo, Tetrahedron Lett. *2010, 51* (30), 3910-2 [DOI: 10.1016/j.tetlet.2010.05.098].

Palladium-charcoal/2-dicyclohexylphosphinobiphenyl/sodium tert-butoxide ←
Palladium(II) acetate/tert. phosphines or di(phosphines)/base ←
Palladium-catalyzed N-arylation

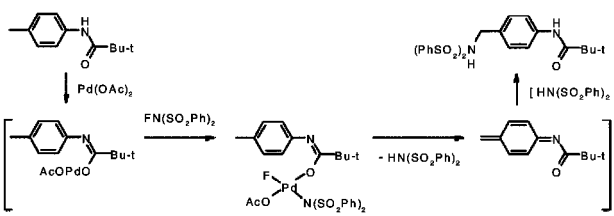
s. *51,* 171s*76*; *52,* 171s*76*; of sec. and functionalized aromatic amines with recyclable Pd-on-charcoal (Selcat Q6) in the presence of 2-dicyclohexylphosphinobiphenyl/NaOBu-*t* s. A. Komáromi, Z. Novák, Adv. Synth. Catal. *2010, 352* (9), 1523-32 [DOI: 10.1002/adsc.201000048]; preparation of sterically congested [*o,o'*-disubst.] triarylamines with $Pd(OAc)_2$/tri-*tert*-butylphosphine s. R. Kuwano, Y. Matsumoto, T. Shige, T. Tanaka, S. Soga, Y. Hanasaki, Synlett *2010* (12), 1819-24 [DOI: 10.1055/s-0030-1258125]; *tert*-amino-subst. from halogeno-subst. nitrobenzaldehydes (without aldehyde protection) s. J. Cao, J.X. Feng, Y.X. Wu, Y.Y. Tuo, Chin. Chem. Lett. *2010, 21* (8), 935-8 [DOI: 10.1016/j.cclet.2010.03.028]; 4-amino-2-fluoropyridines from 2-fluoro-4-iodopyridine with $Pd(OAc)_2$/BINAP/K_2CO_3 under microwaves s. M. Koley, M. Schnürch, M.D. Mihovilovic, Synlett *2010* (10), 1505-10 [DOI: 10.1055/s-0029-1219940]; 4-arylamino-2-hetarylamino- from 4-arylamino-2-chloro-pyrimidines with $Pd_2(dba)_3$/Xantphos/K_3PO_4 in a heated sealed tube s. B.I. Bliss, F. Ahmed, S. Iyer, W. Lin, J. Walker, H. Zhao, Tetrahedron Lett. *2010, 51* (25), 3259-62 [DOI: 10.1016/j.tetlet.2010.04.062]; 1-unsubst. amino- from halogeno-7-azaindoles s. J.L. Henderson, S.M. McDermott, S.L. Buchwald, Org. Lett. *2010, 12* (20), 4438-41 [DOI: 10.1021/ol101928m]; benzo-condensed 5-membered amino- from halogeno-N-heteroarenes s. J.L. Henderson, S.L. Buchwald, ibid. *12* (20), 4442-5 [DOI: 10.1021/ol101929v]; 4-amino- from 4-chloro-isoquinolines with $Pd_2(dba)_3$/BINAP/Na_2CO_3 under microwaves s. K. Prabakaran, P. Manivel, F.N. Khan, Tetrahedron Lett. *2010, 51* (33), 4340-3 [DOI: 10.1016/j.tetlet.2010.06.045]; 6-arylamino- from 6-halogeno-purine nucleosides with $Pd(OAc)_2$/Xantphos/

Cs_2CO_3 s. P.F. Thomson, P. Lagisetty, J. Balzarini, E. De Clercq, M.K. Lakshman, Adv. Synth. Catal. *2010, 352* (10), 1728-35 [DOI: 10.1002/adsc.200900728]; N-arylation **of N-unsubst. carboxylic acid amides** with aryl halides or triflates with $Pd_2(dba)_3$/BINAP/Cs_2CO_3 s. C. Barfoot, G. Brooks, P. Brown, S. Dabbs, D.T. Davies, I. Giordano, A. Hennessy, G. Jones, R. Markwell, T. Miles, N. Pearson, C.A. Smethurst, Tetrahedron Lett. *2010, 51* (20), 2685-9 [DOI: 10.1016/j.tetlet.2010.03.051]; preparation of N-Boc-protected prim. ar. amines by N-arylation of *tert*-butyl carbamate with $Pd(OAc)_2$/Xantphos/Cs_2CO_3 s. L. Qin, H. Cui, D. Zou, J. Li, Y. Wu, Z. Zhu, Y. Wu, ibid. *51* (33), 4445-8 [DOI: 10.1016/j.tetlet.2010.06.083].

Palladium(II) acetate/potassium fluoride/air *$Pd(OAc)_2$/KF/air*

Remote palladium-catalyzed benzylic disulfonylamination of carboxylic acid *p*-toluidides $H \rightarrow N(SO_2R)_2$

188.



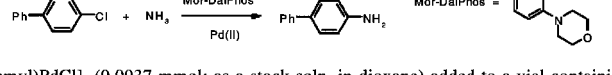
N-Fluorobenzenesulfonimide (1 mmol), KF (1.6 mmol) and $Pd(OAc)_2$ (0.04 mmol) added to a soln. of N-*p*-tolylpivalamide (0.4 mmol) in 1,2-dichloroethane (4 ml), stirred for 5.5 h at 90° under air, the mixture poured onto ice-water, and worked up with chromatographic purification → N-[4-[(N-(phenylsulfonyl)phenylsulfonamidomethyl]phenyl]pivalamide. Y 86%. This is the first example of a direct benzylic C-H amination *with a non-nitrene source*, which circumvents the classical *o*-functionalization characteristic of directed palladium-catalyzed C-H activation. The catalytic cycle is thought to involve initial formation of an acetoxypalladium(II) imidate which undergoes oxidative addition of the N-fluorodisulfonylamine to give a palladium(IV) complex prior to elimination of a key *N-acylimino-p-quinone methid*; the latter then simply undergoes 1,6-amination with the liberated disulfonylamine. The procedure is applicable to a range of N-acyl- and N-benzoyl-*p*-toluidines, reaction being facilitated by electron-donating groups on the aromatic ring (thirteen examples; Y 57-94%). The yield was lower, however, with N-(carbo-*tert*-butoxy)-*p*-toluidine (51%). F.e. and with $NaHCO_3$ (in place of KF), also solvent effects and comparison of palladium complexes s. T. Xiong, Y. Li, Y. Lv, Q. Zhang, Chem. Commun. *2010, 46* (36), 6831-3 [DOI: 10.1039/c0cc02175j].

Bis(π-allylpalladium chloride)/di(1-adamantyl)[o-(dimethylamino)phenyl]phosphine/sodium tert-butoxide ←

Bis(cinnamylpalladium chloride)/di(1-adamantyl)[o-(dimethylamino)phenyl]-phosphine/sodium tert-butoxide ←

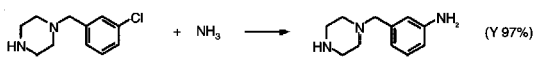
Palladium-catalyzed N-arylation with di(1-adamantyl)[*o*-(dimethylamino)phenyl]phosphine [Mor-DalPhos] as ligand Prim. ar. amines from ar. chlorides under mild conditions $Cl \rightarrow NH_2$

189.

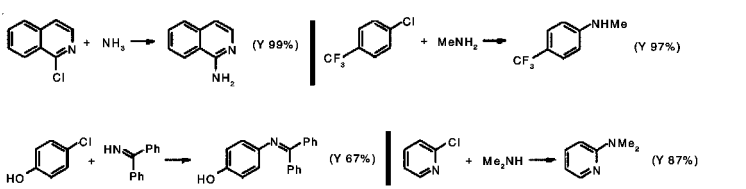


$[(Cinnamyl)PdCl]_2$ (0.0037 mmol; as a stock soln. in dioxane) added to a vial containing Mor-DalPhos (0.0149 mmol) and diluted with additional dioxane (to 3 ml), stirred for 5 min, 880 µl of the soln. (0.0021 mmol Pd) added to another vial containing 4-phenylchlorobenzene (0.6 mmol) and NaOBu-*t* (1.2 mmol), diluted with dioxane (to 7.5 ml), the vial sealed with a cap fitted with

a PTFE septum and removed from the glovebox, treated with ammonia (1.8 mmol as a 0.5 *M* soln. in dioxane), the soln. heated at 110° for 1 h (or 14 h at room temp.), cooled, and worked up with chromatographic purification → 4-phenylaniline. Y 90%. With Mor-DalPhos as ligand, prim. ar. amines are readily obtained from a wide range of ar. chlorides, notably **from deactivated ar. chlorides** *possessing electron-donating groups and lacking o-substitution* which ordinarily fail to react with established P-ligands; furthermore, in certain instances reaction can even be achieved **at room temp. with a relatively low catalyst loading**. A range of additional functionality (N-, O-, F- and S-heteroatoms) on the aromatic ring is supported, and excellent chemoselectivity was recorded for amination of ar. chlorides possessing additional aliphatic or aromatic *prim-*, *sec-* or *tert*-amino groups.



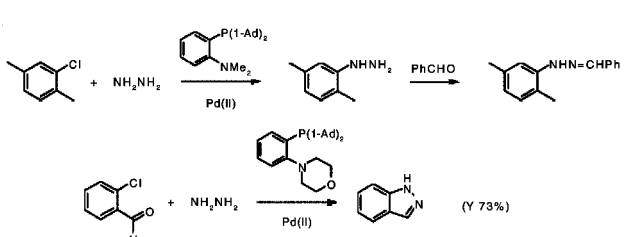
The products can also be obtained conveniently and inexpensively **from aryl tosylates** (unhindered or *o*-subst.) with good yields at room temp. Reaction is presumed to involve intermediate formation of a square-planar aryl(chloro)(Mor-DalPhos)palladium(II) complex. F.e. (ca. forty; Y good to excellent) and comparison of related P,N-ligands s. R.J. Lundgren, B.D. Peters, P.G. Alsabeh, M. Stradiotto, Angew. Chem., Int. Ed. *2010*, *49* (24), 4071-4 [DOI: 10.1002/anie.201000526];



palladium-catalyzed coupling of (het)ar. chlorides with ammonia, $LiNH_2$, prim. and sec. ar./alkyl-amines, N-unsubst. imines and hydrazones (*ninety-six* examples) using $[(\pi\text{-allyl})PdCl]_2$ s. R.J. Lundgren, A. Sappong-Kumankumah, M. Stradiotto, Chem. Eur. J. *2010*, *16* (6), 1983-91 [DOI: 10.1002/chem.200902316].

Bis(cinnamylpalladium chloride)/di(1-adamantyl)[o-(tert-amino)phenyl]-phosphine/sodium tert-butoxide ←

N-Unsubst. arylhydrazines from ar. chlorides under palladium catalysis Cl → $NHNH_2$



190.

A mixture of $[Pd(cinnamyl)Cl]_2$ (5 mol%) and Me-DalPhos (7.5 mol%) in toluene stirred for 5 min in a vial fitted with a PTFE septum (contained in a glove box under inert atmosphere), NaOBu-*t* (1.8-2 eq.) and the startg. ar. chloride (1 eq.) added, the vial removed from the glovebox, hydrazine hydrate (2 eq.) added, stirred at 90° for 1 h, cooled to room temp., filtered through a short plug of neutral alumina, the filtrate concentrated, diluted with methanol, acidified with

acetic acid or HCl in methanol, the soln. added portionwise to a vial containing benzaldehyde in methanol (1 eq.), the soln. concentrated after ca. 10 min, and the residue purified chromatographically → product. Y 88%. Purification of the formed hydrazines was simpler as their benzaldehyde hydrazones. This is the first example of a transition metal-catalyzed coupling of ar. halides with hydrazine. Significantly, there was no dehalogenation by hydrazine, no N-N cleavage, no degradation of the catalyst to inactive palladium(0) nor poly-N-arylation. The procedure is rapid, mild and generally applicable to a range of ar. chlorides and heterocyclic analogs on the 0.4 mmol to 2 g scale (ca. twenty examples; Y 49-95%). Substrates with alkyl, oxygen, sulfur or fluorine at the *m*-position, and MeO or CF_3 at the *p*-position, afforded high yields, as did *o*-methyl-derivs., but poor yields were generally recorded with substrates possessing electron-poor substituents, e.g. 4-trifluoromethyl(chloro)benzene (Y 50%). JosiPhos also gave good yields but other phosphine and di(phosphine) ligands tested were ineffective or gave low yields, as did other bases (KOH, Cs_2CO_3). The same products were obtained **from aryl tosylates** (seven examples; Y 51-97%) but, surprisingly, ar. bromides were poor substrates. F.e. and comparison of Pd-catalysts, **also indazoles from *o*-chloraldehydes** (three examples; Y 51-73%), s. R.J. Lundgren, M. Stradiotto, Angew. Chem., Int. Ed. *2010*, *49* (46), 8686-90 [DOI: 10.1002/anie.201003764].

Bis(cinnamylpalladium chloride)/2-(dicyclohexylphosphinomethyl)-1,3-bis(2,6-di-isopropylphenyl)imidazolium iodide/cesium carbonate ←

Homogeneous palladium-catalyzed coupling ←

with readily recyclable, hindered 2-phosphinomethyl-1,3-bis(2,6-diisopropylphenyl)imidazolium iodides as ligand s. *78*, 96

Sulfur ↑ NC ↓↑ S

Without additional reagents *w.a.r.*

Replacement of sulfonyl groups in 1,1-alkoximinosulfones ←

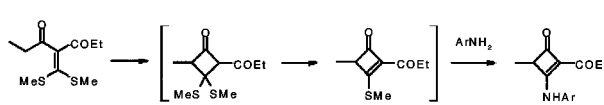
by amino groups s. *78*, 463

Microwaves s. under Et_3N [\\\\]

Potassium tert-butoxide *KOBu-t*

3-Aminocyclobutenones from α-ketoketene mercaptals and amines □

191.



Ar = p-MeC_6H_4

t-BuOK (2 mmol) added in one portion to a soln. of 4-[bis(methylthio)methylene]heptane-3,5-dione (1 mmol) and 4-methylaniline (1 mmol) in DMSO (2 ml), stirred for 0.5 h at room temp., the mixture poured into satd. aq. NaCl, neutralized with aq. HCl, and worked up with purification by chromatography on silica gel → product. Y 76%. The procedure is simple, mild, rapid, based on readily available substrates, and generally applicable to the condensation of α-ketoketene mercaptals with electron-diverse anilines, 2-pyridylamine, cyclic sec. amines and prim. or sec. aliphatic amines to give 3-aminocyclobutenones possessing an acyl, carbalkoxy or phenyl group at the 2-position and alkyl or phenyl at the 4-position. Mechanistically, one possibility is that reaction involves initial deprotonation of the mercaptal to give a vinyl enolate which undergoes 4-electron electrocyclization and elimination of alkyl thiol to give an intermediate 3-(alkylthio)-cyclobutenone; nucleophilic addition of the amine then takes place with elimination of a second alkyl thiol molecule to give the product. F.e. (nine; Y 66-76%), also ring expansion of the formed 3-arylamino-derivs. to **3-acyl-4(1*H*)-quinolones** (three examples; Y 70-72%), s. Y.-L. Zhao, S.-C. Yang, C.-H. Di, X.-D. Han, Q. Liu, Chem. Commun. *2010*, *46* (40), 7614-6 [DOI: 10.1039/c0cc02470h].

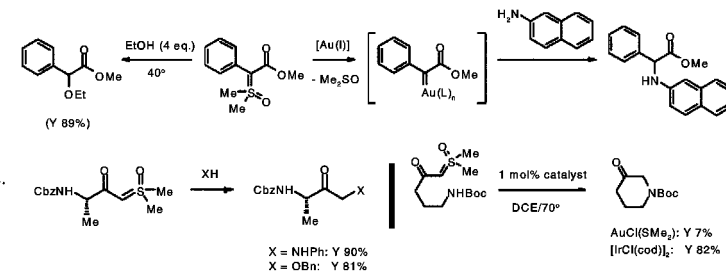
Sodium azide *NaN_3*

Replacement of sulfonyl groups in 1,1-alkoximinosulfones by azido s. *78*, 463 ←

Triethylamine/microwaves *Et_3N/[\\\\]*
(Z)-5-Arylidenerhodanines from prim. amines ○
via sequential one-pot Holmberg reaction-Knoevenagel condensation under microwave irradiation s. *78*, 382

Gold(I) chloride-dimethyl sulfide *$AuCl(SMe_2)$*
Sulfoxonium ylids as metal carbene precursors C=S(O)≤ → CHN≤

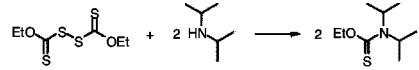
192.



Thermally stable sulfoxonium ylids act as safe alternatives to traditional diazo compds. in metal carbene chemistry. **E: α-Aminocarbonyl compds. under gold(I) catalysis.** Degassed methylene chloride (6.6 ml) added to a mixture of startg. sulfoxonium ylid (1.33 mmol) and $AuCl(SMe_2)$ (0.01 eq.) under N_2, 2-aminonaphthalene (1.5 eq.) added to the resulting suspension, the resulting soln. stirred at 23° for 4 h (TLC), concentrated, and the residue purified by chromatography on silica gel → product. Y 92%. High yields were obtained from a range of anilines, tolerating electron-donating or -withdrawing groups, and the ester-based ylid (ten examples; Y 84-94%) or chiral amino acid-derived ketone-based ylids (five examples; Y 80-91%). For formation of **α-alkoxycarbonyl compds.** from alcohols a higher temperature was required for optimal conversion (seven examples; Y 60-89%). However, in contrast to reactions under iridium catalysis, $AuCl(SMe_2)$ did not mediate the N–H insertion of carbamates efficiently; for example, intramolecular N–H insertion of an NHBoc-deriv. proceeded in only 7% yield with $AuCl(SMe_2)$ (1 mol%) whereas an 82% yield was obtained with $[Ir(cod)Cl]_2$. F.e.s. I.K. Mangion, M. Weisel, Tetrahedron Lett. *2010*, *51* (41), 5490-2 [DOI: 10.1016/j.tetlet.2010.08.038]; **under iridium(I) catalysis** with $[Ir(cod)Cl]_2$, also insertion of mercaptans, and intramolecular insertions, s. I.K. Mangion, I.K. Nwamba, M. Shevlin, M.A. Huffman, Org. Lett. *2009*, *11* (16), 3566-9 [DOI: 10.1021/ol901298p].

Peroxyacetic acid *$MeCOO_2H$*
Sodium hypochlorite *NaOCl*
Manganese(II) acetate/triethylamine/oxygen *$Mn(OAc)_2/Et_3N/O_2$*
Thionocarbamic acid esters from disulfur dicarbothionates and amines NH → NC(S)OR

193.



under manganese(II) catalysis. Diisopropylamine (2 eq.) added dropwise with vigorous stirring to a soln. of diethyl dixanthogenate (150 mmol) in water (100 ml), the temp. allowed to reach 30°, triethylamine (2 eq.) and $Mn(OAc)_2 \cdot 4H_2O$ (0.08 mol%) added, the mixture stirred at 50° under O_2 (0.2 MPa) for 1 h, extracted with ether, concentrated *in vacuo*, and purified by fractional vacuum distillation → N,N-diisopropyl-O-ethyl thiocarbamate. Y 90%. Three oxidizing systems were examined for the prepn. of thiocarbamates from diethyl dixanthogenate, a waste product from certain industrial processes. Peroxyacetic acid, NaOCl and $Mn(II)/O_2$ were all shown to give

better yields with prim. and sec. amines than existing methods based on reaction of sodium ethyl xanthogenacetate with amines, or of sodium ethyl xanthate with amines in the presence of sulfated nickel zeolite catalyst. The Mn(II)/O_2 system was superior on a laboratory scale (eight examples; Y 90-96%) but NaOCl was more convenient for industrial use due to lower cost of the reagent. F.e. and optimization s. M.M. Milosavljevic, M. Sovrlic, A.D. Marinkovic, D.D. Milenkovic, Monatsh. Chem. *2010, 141* (7), 749-55 [DOI: 10.1007/s00706-010-0328-y].

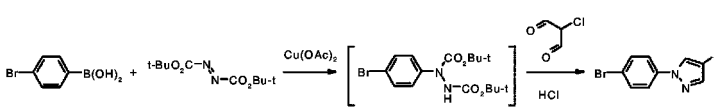
Chloro(cyclooctadiene)iridium(I) dimer *[Ir(cod)Cl]$_2$*
Sulfoxonium ylids as metal carbene precursors C=S(O)< → CH(N<)
α-Aminocarbonyl compds. s. *78*, 192

Remaining Elements ↑ NC ↓↑ Rem

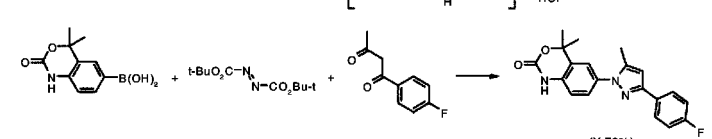
Microwaves s. under Bu_4NF [\\\\]

Copper(II) acetate/sodium acetate or pyridine/air *$Cu(OAc)_2$/NaOAc or py/air*
Copper(II) acetate/oxygen *$Cu(OAc)_2/O_2$*
Water-soluble copper(II) salen complex/air *[Cu(II)]/air*
Copper(II) sulfate/sodium hydroxide/air *$CuSO_4$/NaOH/air*
Copper(I)-fluorapatite/air ←
Copper-catalyzed [Chan-Lam-Evans] N-substitution with boronic acids NH → NR
s. *55*, 166s*76*; **N-alkylation** of prim. ar. amines with alkylboronic acids using $Cu(OAc)_2$/py s. M. Larrosa, C. Guerrero, R. Rodríguez, J. Cruces, Synlett *2010* (14), 2101-5 [DOI: 10.1055/s-0030-1258523]; N^{im}-arylation of Cbz-protected histidines using $Cu(OAc)_2$/NaOAc s. C. DalZotto, J. Michaux, E. Martinand-Lurin, J.-M. Campagne, Eur. J. Org. Chem. *2010* (20), 3811-4 [DOI: 10.1002/ejoc.201000591]; **N-[het]arylation and N-vinylation** of azoles with copper(I)-fluorapatite s. M.L. Kantam, G.T. Venkanna, K.B.S. Kumar, V.B. Subrahmanyam, Helv. Chim. Acta *2010, 93* (5), 974-9 [DOI: 10.1002/hlca.200900326]; N-[het]arylation of imidazoles *in water* using a water-soluble copper(II) salen complex (cf. *78*, 182) without base s. L. Wang, Z. Jiang, L. Yu, L. Li, Z. Li, X. Zhou, Chem. Lett. *2010, 39* (7), 764-5 [DOI: 10.1246/cl.2010.764]; **prim. ar. amines from arylboronic acids** with aq. ammonia using $CuSO_4 \cdot 5H_2O$/NaOH s. Z. Jiang, Z. Wu, L. Wang, D. Wu, X. Zhou, Can. J. Chem. *2010, 88* (9), 964-8 [DOI: 10.1139/V10-105]; **N-vinylation of carboxylic acid amides**, imides and carbamates *with potassium trifluoro(vinyl)-borates* using $Cu(OAc)_2/O_2$ (with added N-methylimidazole for substrates of low pK_a) s. Y. Bolshan, R.A. Batey, Tetrahedron *2010, 66* (27-28), 5283-94 [DOI: 10.1016/j.tet.2010.03.076]; N-arylation of N-heterocyclics in water *with potassium aryl(trifluoro)borates* without base (cf. *55*, 166s*66*) s. N. Joubert, E. Baslé, M. Vaultier, M. Pucheault, Tetrahedron Lett. *2010, 51* (22), 2994-7 [DOI: 10.1016/j.tetlet.2010.03.118].

Copper(II) acetate/hydrogen chloride *$Cu(OAc)_2$/HCl*
1-Arylpyrazoles from β-dioxo compds. and arylboronic acids ○



194.



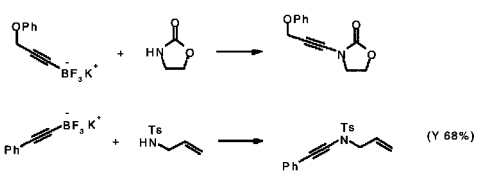
1-Aryl-4-halogenopyrazoles. A mixture of 4-bromophenylboronic acid (1.5 eq.), di-*tert*-butyl azodicarboxylate (0.5 mmol) and $Cu(OAc)_2 \cdot H_2O$ (0.05 eq.) in methanol (3 ml) heated for 1 h at 65° in a scintillation vial, cooled to room temp., 2-chloromalonaldehyde (1.5 eq.) added followed

by 4 *N* HCl in dioxane (2 ml), the mixture stirred for 10 min at room temp. then heated for 10 min at 80°, cooled to room temp., volatiles removed *in vacuo*, the crude oil treated with water (15 ml) followed by dropwise addition of satd. aq. $NaHCO_3$ until pH ca. 7, organics extracted with ethyl acetate, dried ($MgSO_4$), filtered, concentrated *in vacuo*, and the residue purified by flash chromatography through silica gel → 1-(4-bromophenyl)-4-chloro-1*H*-pyrazole. Y 53%. This operationally simple method, involving generation of arylhydrazines via Chan-Lam-type coupling with readily-available boronic acids, is an improvement on the one involving halogen-lithium exchange (*76*, 189), being compatible with sensitive groups. Eight further examples of 4-chloro-derivs. (Y 32-78%), three of 4-bromo-derivs. (Y 53-78%), five of 4-aryl-derivs. (Y 40-78%) and one 4-unsubst. deriv (Y 72%) are reported from aryl- or hetaryl-boronic acids and β-dialdehydes or β-diketones, while Celecoxib was obtained as a 2:1 regioisomeric mixture (Y 35%). F.e.s. R.E. Beveridge, D. Fernando, B.S. Gerstenberger, Tetrahedron Lett. *2010*, *51* (38), 5005-8 [DOI: 10.1016/j.tetlet.2010.07.077]; *multistep process* for synthesis of 1-heteroaryl-3-(trifluoromethyl)-1*H*-pyrazole-5-carboxylic acid N-benzylamides s. M. Allan, S. Manku, E. Therrien, N. Nguyen, S. Styhler, M.-F. Robert, A.-C. Goulet, A.J. Petschner, G. Rahil, A.R. MacLeod, R. Deziel, J.M. Besterman, H. Nguyen, A. Wahhab, Bioorg. Med. Chem. Lett. *2009*, *19* (4), 1218-23 [DOI: 10.1016/j.bmcl.2008.12.075].

Copper(II) chloride/1,2-dimethylimidazole — *$CuCl_2$/1,2-Me_2Im*

Copper(II)-catalyzed N-alk-1-ynylation with potassium alk-1-ynyl(trifluoro)borates — C≡C-BF_3K^+ → C≡C-N≤

195.

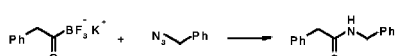


N-Alk-1-ynyl-2-oxazolidones. *1,2-Dimethylimidazole* (0.4 eq.), *$CuCl_2 \cdot 2H_2O$* (15 mol%), 4 Å molecular sieves (700 mg) and K-3-phenoxyprop-1-yn-1-yl(trifluoro)borate (1 mmol) added sequentially to a soln. of 2-oxazolidone (5 eq.) in dry methylene chloride (5 ml) at room temp., the blue-greenish heterogeneous mixture stirred vigorously under O_2 for 40-48 h, filtered through silica, concentrated *in vacuo*, and purified by flash chromatography on silica → 3-(3-phenoxyprop-1-yn-1-yl)oxazolidin-2-one. Y 100%. This efficient and general formation of ynamide derivs. was successful for alkynylation of 2-oxazolidones, 2-imidazolidones and tosylamines (incl. N-tosylaniline) with trimethylsilyl, ar. and alkyl-terminated acetylene(trifluoro)borates (thirty-three examples; Y 43-100%) in the presence of alkyl chloride and propargyl alcohol/ether functionality. 2-Pyrrolidone, however, gave only 20% yield with K-phenylacetylene(trifluoro)borate, and failed with the 1-hexyne deriv. Careful selection of the ligand and copper catalyst (Pd and Fe salts were ineffective) was essential to minimize the formation of homo-coupled products. F.e., optimization and substrate prepn. s. K. Jouvin, F. Couty, G. Evano, Org. Lett. *2010*, *12* (14), 3272-5 [DOI: 10.1021/ol101322k].

Fluoroboric acid — *HBF_4*

Potassium acyl(trifluoro)borates as acylating agents N-Subst. carboxylic acid amides from azides — N_3 → NHC(O)R

196.

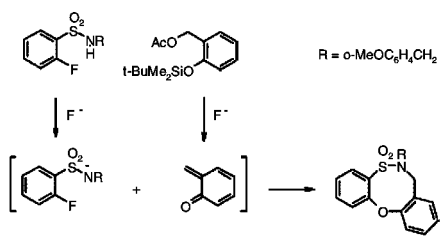


Anhydrous acetonitrile (1.5 ml) and benzyl azide (1 eq.) added to K-(2-phenylacetyl)trifluoroborate (0.3 mmol) under N_2, the mixture cooled to 0°, *$HBF_4 \cdot OEt_2$* (2 eq.) added dropwise via PTFE needle, the mixture stirred at room temp. for 4 h, quenched with water, extracted with ethyl

acetate, washed with brine, concentrated *in vacuo*, and purified by flash chromatography → N-benzyl-2-phenylacetamide. Y 75%. The trifluoroborate, a novel acyl anion equivalent, proved surprisingly stable but reacted with azides to afford sec. amides in moderate yields (six examples; Y 68-75%) in the presence of phthalimide, ester and nitrile functionality. The method lacks generality, however, giving mainly decomposition products in the presence of ar. or alkene functionality, and failing to form sulfonamides from sulfonyl azides. Other Lewis acids/fluorophiles were less effective activators. F.e. and K-acyl(trifluoro)borate prepn. s. G.A. Molander, J. Raushel, N.M. Ellis, J. Org. Chem. *2010*, *75* (12), 4304-6 [DOI: 10.1021/jo1004058].

Tetra-n-butylammonium fluoride/microwaves *Bu_4NF/\\\\]*
6,7-Dihydrodibenzo[*b*,*g*][1,4,5]oxathiazocine 5,5-dioxides ○
from *o*-fluorosulfonic acid amides and *in situ*-generated *o*-quinone methids
via a formal dipolar [4+4]-cycloaddition

197.



Two substrates, each possessing 1,4-disposed electrophilic and nucleophilic sites, have been united in a formal [4+4]-cycloaddition to afford a previously unreported tricyclic 8-membered sultam. **E:** The startg. sulfonamide (0.29 mmol), *o*-silyloxybenzyl acetate (0.584 mmol), THF (0.58 ml) and tetra-*n*-butylammonium fluoride (0.88 mmol) charged into a dry vial, the latter quickly sealed, stirred for 30 min under microwave irradiation at 100°, the mixture concentrated under reduced pressure, and purified chromatographically → 6-(2-methoxybenzyl)-6,7-dihydrodibenzo[*b*,*g*]-[1,4,5]oxathiazocine 5,5-dioxide. Y 71%. The pairing involves initial aza-Michael addition to the *o*-quinone methid, followed by intramolecular nucleophilic displacement of fluoride ion by the generated phenoxide ion. Conveniently, fluoride ion serves the dual role of desilylating agent for generating the *o*-quinone methid as well as base to deprotonate the sulfonamide nitrogen. The procedure is applicable to a range of sulfonamides substituted on nitrogen by alkyl, propargyl or benzyl, notably tolerating chlorine or bromine on the aromatic ring (twelve examples; Y 71-94%). Yields were lower with *o*-hydroxybenzyl alcohol or *o*-acetoxybenzyl acetate as quinone methid precursor. F.e.s. T.B. Samarakoon, M.Y. Hur, R.D. Kurtz, P.R. Hanson, Org. Lett. *2010*, *12* (10), 2182-5 [DOI: 10.1021/ol100495w].

Carbon ↑ NC ↓↑ C

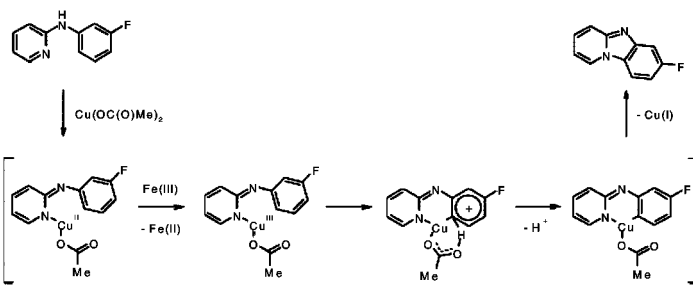
Without additional reagents *w.a.r.*
Ureas from β-ketocarboxylic acid amides and amines ≥NC(O)C-C(O)R → ≥NC(O)N≤
s. *28*, 417; from β-ketocarboxylic acid anilides by heating in xylene s. Y. Wei, J. Liu, S. Lin, H. Ding, F. Liang, B. Zhao, Org. Lett. *2010*, *12* (19), 4220-3 [DOI: 10.1021/ol101474f].

Hydroxamic acid esters from carboxylic acids COOH → CON(OR)R
and N-methoxy-N-methylimidazole-1-carboxamide s. *78*, 104

Elimination ⇑

Hydrogen ↑ NC ⇑ H

Copper(II) acetate/iron(III) nitrate/oxygen/pivalic acid $Cu(OAc)_2/Fe(NO_3)_3/O_2/t\text{-}BuCOOH$
Pyrido[1,2-*a*]benzimidazoles from 2-(arylamino)pyridines ○
Regioselective intramolecular amination
via copper(II) and iron(III) cocatalyzed C-H activation



198.

A mixture of N-(3-fluorophenyl)-2-aminopyridine (0.5 mmol), $Cu(OAc)_2$ (100 mol%), $Fe(NO_3)_3{\cdot}9H_2O$ (10 mol%), pivalic acid (2.5 mmol) and DMF (1 ml) stirred at 130° under O_2 (balloon pressure) until reaction complete (TLC; 66 h), cooled to room temp., water (10 ml), triethylamine (1 ml), and ethyl acetate (10 ml) added successively, extracted with ethyl acetate, the extracts dried (Na_2SO_4), concentrated, and the residue purified chromatographically → 7-fluoropyrido[1,2-*a*]benzimidazole. Y 72%. A variety of substituents (incl. bromo) were tolerated on the phenyl ring, with electron-poor substrates being most reactive and requiring only 20 mol% Cu(II) catalyst; unsymmetrically-subst. examples reacted exclusively at the least-hindered C-atom (sixteen examples; Y 68-85%). Electron-withdrawing groups on the pyridine ring were not well-tolerated, however, with reactions not proceeding to completion, and a low yield (24%) was obtained for a 2-methyl-subst. pyridine, presumably due to steric hindrance. **Benzo-fused pyrido[1,2-*a*]-benzimidazoles** were obtained from N-phenyl-2-aminoquinoline and N-phenyl-2-amino-isoquinoline (Y 77% and 96%), respectively. Mechanistic experiments demonstrated the role of Fe(III) in facilitating formation of an electrophilic Cu(III) species, the S_EAr reaction being reversible and much less efficient in its absence. F.e.s. H. Wang, Y. Wang, C. Peng, J. Zhang, Q. Zhu, J. Am. Chem. Soc. *2010*, *132* (38), 13217-9 [DOI: 10.1021/ja1067993].

Aluminum nitrate/silica-sulfuric acid $Al(NO_3)_3/SiO_2\text{-}OSO_3H$
Pyridines from 1,4-dihydropyridines s. *25*, 649s*78* ←

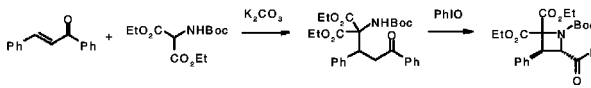
Imidazolium ionic liquids s. under $Fe(ClO_4)_3$ ←

Enzymes ←
Oxidative enzymatic desymmetrization of 3,4-disubst. pyrrolidines ←
s. *78*, 371, 420

Pivalic acid s. under $Cu(OAc)_2$ *t-BuCOOH*
Dimethyl sulfoxide s. under $Pd(OCOCF_3)_2$ *DMSO*

Iodosobenzene/tetra-n-butylammonium iodide *PhIO/Bu$_4$NI*
N-Protected 4-acylazetidine-2,2-dicarboxylic acid esters from α,β-ethyleneketones and N-protected α-aminomalonic acid esters via α-amino-δ-ketomalonic acid esters
Solvent-free Michael addition-stereoselective oxidative ring closure

199.



***anti*-4-Aroyl-3-aryl-1-carbo-*tert*-butoxyazetidine-2,2-dicarboxylic acid esters**. A mixture of diethyl 2-Boc-aminomalonate (0.2 mmol), chalcone (0.4 mmol), K_2CO_3 (1 eq.) and $PhEt_3NCl$ (1 eq.) ground at room temp. until addition complete (TLC; 10-30 min), quenched with satd. aq. NH_4Cl, extracted with ethyl acetate, concentrated *in vacuo*, the residue dissolved in toluene (1 ml), PhIO (2 eq.) and Bu_4NI (1.2 eq.) added, the mixture stirred at 25° until reaction complete (TLC; 12-24 h), quenched with satd. aq. $Na_2S_2O_3$, extracted with ethyl acetate, concentrated *in vacuo*, and purified by chromatography → 1-*tert*-butyl 2,2-diethyl 4-benzoyl-3-phenylazetidine-1,2,2-tricarboxylate. Y 75%. Stepwise formation of a Michael adduct and subsequent oxidative cyclization provided an efficient and highly diastereoselective route to functionalized azetidines for chalcones carrying electron-diverse (het)ar. termini (twenty-one examples; Y 46-75%; *anti/syn* >95:5). The reaction failed for aliphatic analogs of the chalcones and with strongly electron-withdrawing substituents (NO_2) on the aryl ketone moiety. The initial grinding reaction in the absence of solvent was more efficient than solution-based reactions. Attempted one-pot reactions were less efficient due to partial decomposition of the adduct and product in the presence of unconsumed base from the first step. F.e. and optimization s. Y. Ye, H. Wang, R. Fan, Org. Lett. *2010*, *12* (12), 2802-5 [DOI: 10.1021/ol100885f].

Phenyl iodosoacetate *PhI(OAc)$_2$*
Pyrimidines from 1,4-dihydropyrimidines ←
2-(Alkylthio)pyrimidine-5-carboxylic acid esters s. *21*, 528s*78*

1,4-Dicyano-1,3-dienes from *o*-diamines s. *78*, 200 C

Oxygen or air s. under Cu(OAc)$_2$, Fe(ClO$_4$)$_3$ and Pd(OCOCF$_3$)$_2$ *O$_2$*
Silica-sulfuric acid s. under Al(NO$_3$)$_3$ and Fe(NO$_3$)$_3$ *SiO$_2$-OSO$_3$H*

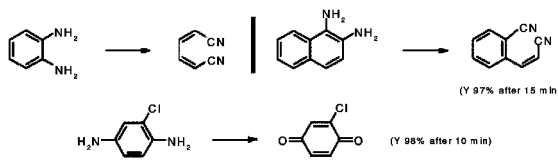
Hexadecyltrimethylammonium persulfate *[C$_{16}$H$_{33}$NMe$_3$]$_2$[S$_2$O$_8$]*
Sodium chlorite *NaClO$_2$*
Pyridines from 1,4-dihydropyridines ←
s. *25*, 649s*75*; with hexadecyltrimethylammonium persulfate, also enhancement of potassium persulfate reactivity with added hexadecyltrimethylammonium bromide as phase transfer catalyst, s. P. Kumar, A. Kumar, Bull. Korean Chem. Soc. *2010, 31* (8), 2299-303 [DOI: 10.5012/bkcs.2010.31.8.2299]; with $NaClO_2$ in aq. ethanol containing concd. HCl s. X. Liao, W. Lin, J. Lu, C. Wang, Tetrahedron Lett. *2010, 51* (29), 3859-61 [DOI: 10.1016/j.tetlet.2010.05.091]; with $Fe(ClO_4)_3$ in an imidazolium ionic liquid under air s. D. Liu, J. Gui, C. Wang, F. Lu, Y. Yang, Z. Sun, Synth. Commun. *2010, 40* (7), 1004-8 [DOI: 10.1080/00397910903029925]; under heterogeneous conditions with $Fe(NO_3)_3{\cdot}9H_2O$ or $Al(NO_3)_3{\cdot}9H_2O$ in the presence of silica-sulfuric acid s. A. Ghorbani-Choghamarani, J. Zeinivand, Synth. Commun. *2010, 40* (16), 2457-63 [DOI: 10.1080/00397910903262195]; **pyrimidines from 1,4-dihydropyrimidines** (cf. *21*, 528s*70*) with $PhI(OAc)_2$, 2-(alkylthio)pyrimidine-5-carboxylic acid esters, s. N.N. Karade, S.V. Gampawar, N.P. Tale, S.B. Kedar, J. Heterocycl. Chem. *2010, 47* (3), 740-4 [DOI: 10.1002/jhet.389].

Chromium(IV) oxide *CrO$_2$*
Oxidation of organic substrates using metal oxides under flow conditions ←
with inductive heating by admixed magnetite nanoparticles – Ar. nitriles from prim. benzylamines s. *78*, 120

Sodium chlorite *NaClO$_2$*
Pyridines from 1,4-dihydropyridines s. *25*, 649s*78* ←

Sodium periodate *$NaIO_4$*
1,4-Dicyano-1,3-dienes from *o*-diamines

200.



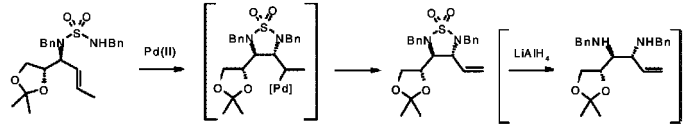
$NaIO_4$ (2 eq.) in water (10 ml) stirred at room temp. for 2 min, 1,2-diaminobenzene (4.62 mmol) added, after *10 min* (TLC) the aq. phase extracted with chloroform, the organic extracts washed with dil. HCl, followed by water, dried (Na_2SO_4), concentrated *in vacuo*, and the residue purified by chromatography on silica gel → *cis,cis*-muconanitrile. Y 98%. The method is mild, rapid and high-yielding (90-98%; nine examples) in the presence of electron-donating or -withdrawing groups, although it failed with a strongly electron-withdrawing group (nitro) and with 3,4-diamino-pyridine. For water-insoluble diamines 1:1 ethyl acetate/water may be used. No reaction was observed with oxidants such as $KMnO_4$, CAN, $NaICl_2$ or $K_2Cr_2O_7$, even at higher temperature with longer reaction times. F.e., **also *p*-quinones from *p*-diamines**, s. V.N. Telvekar, B.S. Takale, Tetrahedron Lett. *2010*, *51* (30), 3940-3 [DOI: 10.1016/j.tetlet.2010.05.103]; with $PhI(OAc)_2$ in acetone at room temp. s. V.N. Telvekar, H.M. Bachhav, Synlett *2010* (14), 2059-62 [DOI: 10.1055/s-0030-1258511].

Tetra-n-butylammonium iodide s. under PhIO *Bu_4NI*
Iron(III) nitrate s.a. under Cu(OAc)$_2$ *$Fe(NO_3)_3$*

Iron(III) nitrate/silica-sulfuric acid *$Fe(NO_3)_3/SiO_2$-OSO_3H*
Iron(III) perchlorate/imidazolium ionic liquids/air ←
Pyridines from 1,4-dihydropyridines s. *25*, 649s*78* ←

Palladium(II) trifluoroacetate/dimethyl sulfoxide/sodium benzoate/oxygen ←
4-Vinyl-2,1,3-thiadiazolidine 2,2-dioxides from 2-ethylenesulfamides ○
Palladium(II)-catalyzed oxidative ring closure

201.



under mild conditions. A soln. of DMSO (10 mol%) in THF (3 ml) added via syringe to a mixture of startg. sulfamide (0.3 mmol), $Pd(OCOCF_3)_2$ (5 mol%), Na-benzoate (20 mol%) and powdered 3 Å molecular sieves (80 mg) under O_2, the soln. stirred vigorously at room temp. for 10 h, and purified by flash chromatography → product. Y 99% (d.r. >20:1). This general, experimentally simple and efficient method uses readily available materials and can be performed on a gram scale, with analytically pure products obtained in most cases by filtration of the reaction mixture through alumina and concentrating *in vacuo* (twenty-one examples; Y 73-99%). The reaction tolerates α- and β-substitution on the allylic amine moiety, and can be performed in the presence of acetal, silyl ether, ether and carbamate functionality. Experimental evidence favors aminopalladation as the initial step (cf. allylic C-H activation). A 3-ethylene-1,2-diamine was generated in one case by reductive desulfonation of the product with $LiAlH_4$ (Y 89%). F.e. and optimization s. R.I. McDonald, S.S. Stahl, Angew. Chem., Int. Ed. *2010*, *49* (32), 5529-32 [DOI: 10.1002/anie.200906342].

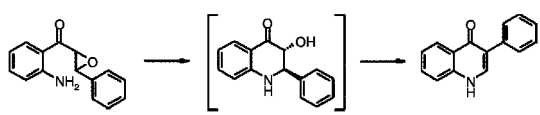
Oxygen ↑ NC ⇑ O

Triphenylphosphine/molybdenyl chloride-dimethylformamide $Ph_3P/MoO_2Cl_2(dmf)_2$
N-Unsubst. benzo-condensed *o*-vinyl-N-heterocyclics from (nitroaryl)ethylene derivs. ○
regiospecific reductive ring closure with $(EtO)_3P$ under microwave irradiation or thermally, 3-vinyl-3,4-dihydro-2*H*-1,4-benzoxazines, 2-vinyl-1,2,3,4-tetrahydro-quinoxalines or -quinolines cf. *72*, 264; with Ph_3P and $MoO_2Cl_2(dmf)_2$ as catalyst under microwave irradiation or in a sealed tube, especially for 3-vinyl-3,4-dihydro-2*H*-1,4-benzothiazines, s. C.C. Malakar, E. Merisor, J. Conrad, U. Beifuss, Synlett *2010* (12), 1766-70 [DOI: 10.1055/s-0030-1258119].

Methanesulfonyl chloride/triethylamine $MeSO_2Cl/Et_3N$
1-Arylbenzimidazoles from *o*-(arylamino)oximes s. *78*, 129

Trifluoromethanesulfonic acid *TfOH*
3-Aryl-4(1*H*)-quinolones [azaisoflavones] ○C
from *trans-o'*-aminochalcone epoxides via 1,2-aryl migration

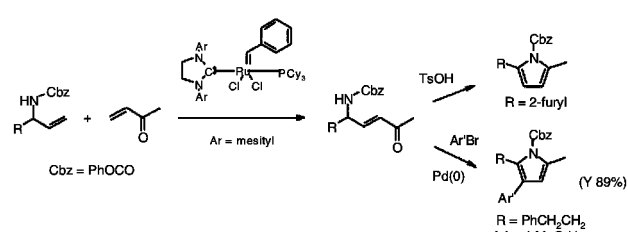
202.



A stirred soln. of 2′-aminochalcone epoxide (1 mmol) in anhydrous methylene chloride (1 ml) treated dropwise at 0° with trifluoromethanesulfonic acid (3 eq.), after 0.3 h (TLC) the mixture quenched with ice-cold water, the pH adjusted to 7.5 with $NaHCO_3$, extracted with methylene chloride, the organic extracts dried (Na_2SO_4), concentrated under reduced pressure, and purified chromatographically → 3-phenyl-4(1*H*)-quinolone. Y 90%. This provides a straightforward preparation of azaisoflavones from simple starting materials **under mild conditions**. Yields were higher, with shorter reaction times, for substrates bearing electron-releasing groups. The intermediate *trans*-2-phenyl-3-hydroxy-2,3-dihydro-4(1*H*)-quinolone may be isolated in 80% yield with *0.5 eq.* triflic acid at 0° *for 10 min*. The corresponding *cis*-isomer did not undergo rearrangement-dehydration, indicating that an anti-periplanar orientation is essential for migration of a phenonium ion. F.e. (ten; Y 73-94%) s. C. Praveen, K. Parthasarathy, P.T. Perumal, Synlett *2010* (11), 1635-40 [DOI: 10.1055/s-0030-1258091].

p-Toluenesulfonic acid *TsOH*
N-Protected pyrroles from α,β-ethyleneketones and 2-ethyleneamines ○
via *trans*-γ-amino-α,β-ethyleneketones

203.



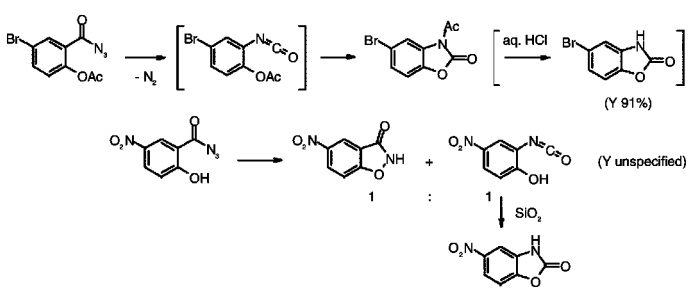
Methylene chloride (4.6 ml) and methyl vinyl ketone (5 eq.) added via syringe to a mixture of benzyl 1-fur-2-ylallylcarbamate (0.23 mmol) and Hoveyda-Grubbs 2nd generation catalyst (10 mol%) under argon in a vial sealed with a rubber septum, the septum replaced with a screw

cap, the mixture heated at 40° for 48 h, cooled to room temp., concentrated *in vacuo*, and purified by flash chromatography → intermediate subst. enone (Y 69%), 0.03 mmol of which dissolved in methylene chloride (0.6 ml), the soln. added to *p*-toluenesulfonic acid (20 mol%) under argon in a vial, the vial sealed with a screw cap, the mixture heated at 70° until reaction complete (TLC; 3 h), cooled to room temp., concentrated *in vacuo*, filtered through silica, and purified by flash chromatography → benzyl 2-(furan-2-yl)-5-methyl-1*H*-pyrrole-1-carboxylate. (Y 94%). This general and efficient preparation of γ-aminoenones was successful for a variety of enone and enal derivs., and is compatible with carbamate, sulfonamide and trifluoroacetyl N-protecting groups (thirteen examples; Y 55-73%). The versatile enone intermediates were cyclized with acid (TsOH) to afford 2,5-disubst. pyrroles (thirteen examples; Y 55-97%, incl. a **dihydroindolizinone**) or under Heck arylation conditions to afford 2,3,5-trisubst. pyrroles (eight examples; Y 54-89%; a 2,3-diaryl deriv. gave 32%). The method was less efficient as a one-pot process. Furan analogs cf. *77*, 130. F.e., substrate prepn. and use of the method in a synthesis of atorvastatin pyrrole sub-unit s. T.J. Donohoe, N.J. Race, J.F. Bower, C.K.A. Callens, Org. Lett. *2010*, *12* (18), 4094-7 [DOI: 10.1021/ol101681r].

Nitrogen ↑ NC ⇑ N

Without additional reagents *w.a.r.*

3-Acylbenzoxazol-2(3*H*)-ones from *o*-acoxycarboxylic acid azides via 1,4-O→N-acyl migration ○



204.

A soln. of crude 2-acetoxy-5-bromobenzoyl azide (50 mmol) in dry toluene (50 ml) warmed slowly [*caution:* azides are potentially explosive] in a water bath, gas evolution commenced at 50°, temp. gradually increased (to ca. 80°) during 6 h to maintain gas evolution until reaction complete, concentrated *in vacuo*, and the residue purified by recrystallization → 3-acetyl-5-bromobenz[*d*]oxazol-2(3*H*)-one. Y 85%. The reactivity of the O atom was limited by acetylation, providing smooth conversion to the heterocycle, presumed via Curtius reaction to an intermediate isocyanate, which suffered acetyl group migration on subsequent ring closure (five examples; Y 82-91%), reaction taking place in the presence of halo, nitro and acetoxy functionality. The N-acetyl group was subsequently cleaved by hydrolysis (5 *M* aq. HCl; Y 49-91%). It was reasoned that the presence of a strong electron-withdrawing group might decrease rearrangement of the intermediate isocyanate and, in fact, refluxing 5-nitro-*2-hydroxy*-benzoyl azide in toluene produced a 1:1 mixture (unspecified yield) of *5-nitrobenzo[d]isoxazol-3(2H)-one* and the isocyanate, with the latter cyclizing to the benz[*d*]oxazolone during chromatography. F.e. and substrate prepn. (stable for a few days under refrigeration) s. S. Ray, S. Ghosh, Synth. Commun. *2010*, *40* (16), 2377-88 [DOI: 10.1080/00397910903245158].

Potassium phosphate K_3PO_4

Ring closures

via intramolecular nucleophilic displacement of N-aryl-N-sulfonylamino groups s. *78*, 124

Copper(I) iodide/tert-butyl hydroperoxide *CuI/t-BuOOH*
Nitriles from prim. azides in water $CH_2N_3 \rightarrow CN$

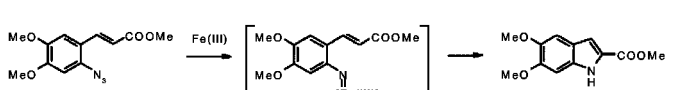
205.

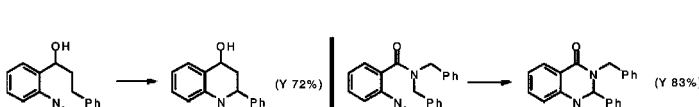
Aq. *tert*-butyl hydroperoxide (70% soln.; 2.5 mmol) added to a stirred suspension of 1-(azidomethyl)-4-methoxybenzene (1 mmol) and CuI (0.05 mmol) in water (2 ml), the mixture heated at reflux for 1 h, cooled to room temp., and worked up with purification by chromatography on silica gel → *p*-methoxybenzonitrile. Y 92%. The procedure is generally applicable to a wide range of prim. and sec. benzyl azides possessing electron-withdrawing or -donating groups, as well as to aliphatic azides, 2-azidomethylpyridine, cinnamyl azide and an α-azidocarboxylic acid ester (ca. twenty examples; Y 51-94%). Significantly, various oxidizable functions and allyl ethers remained unaffected. Other oxidants (molecular oxygen, N-methylmorpholine N-oxide, TEMPO/O_2, H_2O_2 and sodium perborate) were ineffective, and yields were lower with other copper salts. Reaction was also efficient in toluene. Nitrogen was generated during the reaction, but no radical species were detected. F.e. incl. conversion of a diazide to a dinitrile s. M. Lamani, K.R. Prabhu, Angew. Chem., Int. Ed. *2010*, *49* (37), 6622-5 [DOI: 10.1002/anie.201002635].

Magnesium monoperoxyphthalate ←
Nitriles from aldehyde hydrazones $CH{=}NN{\leq} \rightarrow CN$
Chiral γ-benzoylamino-α,β-ethylenenitriles s. *78*, 295

Molybdenum hexacarbonyl $Mo(CO)_6$
4-Pyridone ring closure via reductive isoxazole ring opening
1,6-Dihydropyrrolo[3,4-*b*]pyrid-4-ones s. *78*, 474

[5,10,15,20-Tetrakis(pentafluorophenyl)porphyrinato]iron(III) chloride *[Fe(F20TPP)Cl]*
Iron-catalyzed ring closures of *o*-subst. ar. azides
via intramolecular insertion of nitrenoids into carbon-hydrogen bonds



206. 

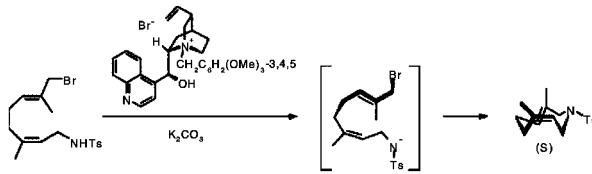
A wide range of **benzo-condensed N-heterocyclics** familiar to the alkaloid chemist can now be prepared simply *under mild, green conditions* from *o*-subst. aromatic azides via intramolecular insertion of iron nitrenoids into sp^2 or sp^3 carbon-hydrogen bonds. **E: Indole-3-carboxylic from *o*-azidocinnamic acid esters.** [Fe(F_{20}TPP)Cl] (0.004 mmol), 4 Å molecular sieves (60 mg) and 1,2-dichloroethane (1 ml) added to the startg. azide (0.2 mmol), the mixture heated to reflux under N_2 for 16 h, concentrated under reduced pressure, and the residue purified chromatographically → product. Y 86%. High yields were obtained from substrates with electron-withdrawing or -donating groups on the aromatic ring (86-91%; seven examples). **2-Aryl-indolines and -1,2,3,4-tetrahydroquinolines** were obtained under the same conditions via intramolecular nitrenoid insertion into the benzylic sp^3 C-H bond, although *o*-(1-hydroxy-2-phenylethyl)aryl azides and the corresponding O-methyl derivs. gave 2-phenylindoles via dehydration/dealcoholation (twelve examples in all; Y 72-82%); similarly, **N-subst. 1,2-dihydro-4(3*H*)-quinazolones** were obtained predominantly **from N,N-disubst. *o*-azidocarboxylic acid amides** (eight examples; Y 63-83%). The catalyst is commercially available, air-stable and a useful, non-toxic alternative to rhodium and other transition metal catalysts. F.e. and mechanistic considerations s. Y. Liu, J. Wei, C.-M. Che, Chem. Commun. *2010*, *46* (37), 6926-8 [DOI: 10.1039/c0cc01825b].

Halogen ↑ NC ⇑ Hal

Sugar-derived lithium alkoxides or Potassium carbonate/N-(3,4,5-trimethoxybenzyl)-cinchonidinium bromide ←

Planar-chiral 9-membered N-heterocyclics by intramolecular asym. N-alkylation ○

207.

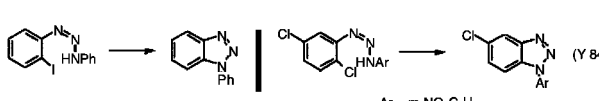


A planar-chiral N-heterocyclic has been produced for the first time by an unprecedented *prochiral face-selective ring closure* using a chiral promoter. **E:** A soln. of N-(3,4,5-trimethoxybenzyl)-cinchonidinium bromide (7.5 μmol) and K_2CO_3 (7.45 mmol) in water (1 ml) added to a soln. of N-[(2Z,6E)-8-bromo-3,7-dimethylocta-2,6-dienyl]-*p*-toluenesulfonamide (0.0745 mmol) in methylene chloride (7.5 ml) at 0°, the mixture stirred vigorously at the same temp. for 24 h, quenched by diluting with water, and worked up with purification by chromatography on silica gel → (S)-product. Y 97% (e.e. 37%). A number of cinchona-based quaternary ammonium salts were effective as the chiral phase transfer catalyst, affording e.e. of 28-37%, the (S)-product being formed via re-face selective cyclization (and the (R)-product via si-face cyclization with the antipodal reagent). More significantly, the enantioselectivity was enhanced to 80-89% e.e. *with sugar-derived lithium alkoxides* as base, a *D*-galactose-deriv. affording the same (S)-product (Y 89%; e.e. 80%) while the corresponding *D*-glucose-deriv. gave the (R)-product (Y 89%; e.e. 93%). A mono-methylated substrate reacted similarly (Y 79-90%; e.e. 62-66%). F.e.s. K. Tomooka, K. Uehara, R. Nishikawa, M. Suzuki, K. Igawa, J. Am. Chem. Soc. *2010*, *132* (27), 9232-3 [DOI: 10.1021/ja1024657].

Copper(I) iodide/potassium carbonate/polyethylene glycol-400 or cesium carbonate or 1,10-phenanthroline/sodium tert-butoxide ←

1,2,3-Triazole ring from *o*-halogenotriazenes
by copper(I)-catalyzed intramolecular N-arylation in aq. medium

208.



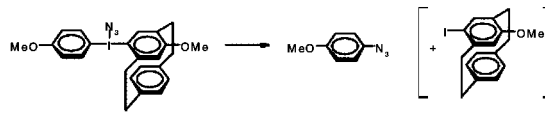
1-Arylbenzotriazoles. Startg. triazene (1 mmol), CuI (10 mol%), K_2CO_3 (2 eq.), PEG-400 (0.2 ml) and water (2 ml) heated in an Erlenmayer flask at 110° until reaction complete (TLC; 2.5 h), the mixture cooled, poured into a beaker containing crushed ice, stirred for 10 min, filtered, and the filtrate worked up with purification by chromatography on silica gel → 1-phenylbenzotriazole. Y 92%. The procedure is simple, eco-friendly and high-yielding for the conversion of *o*-iodo-, *o*-bromo- and [at 130°] *o*-chloro-triazenes, as well as pyridine analogs (twenty-seven examples; Y 75-92%). DMSO and DMF were also effective solvents, but yields were higher in the eco-friendly aq. medium. F.e. and regioselectivity, also comparison of bases, solvents, phase transfer catalysts and copper salts, s. C. Mukhopadhyay, P.K. Tapaswi, R.J. Butcher, Org. Biomol. Chem. *2010*, *8* (20), 4720-9 [DOI: 10.1039/c0ob00177e]; with CuI/Cs_2CO_3 s. R.R. Kale, V. Prasad, H.A. Hussain, V.K. Tiwari, Tetrahedron Lett. *2010*, *51* (43), 5740-3 [DOI: 10.1016/j.tetlet.2010.08.083]; with CuI/1,10-phenanthroline/NaOBu-*t* in DMSO s. Q.-L. Liu, D.-D. Wen, C.-C. Hang, Q.-L. Li, Y.-M. Zhu, Helv. Chim. Acta *2010*, *93* (7), 1350-4 [DOI: 10.1002/hlca.200900384].

Copper(I) iodide/phenanthridine or L-proline/sodium hydride or potassium carbonate ←
Copper-catalyzed intramolecular N-arylation ○

s. *63,* 191s*75*; of 4(3*H*)-quinazolones for a convergent approach to (-)-circumdatins H and J s. U.A. Kshirsagar, N.P. Argade, Org. Lett. *2010, 12* (16), 3716-9 [DOI: 10.1021/ol101597p]; of 1-aminoindolines for the synthesis of indolo[1,2-*b*]indazoles with CuI/phen/K_2CO_3 s. J. Chi, C. Hang, Y. Zhu, H. Katayam, Synth. Commun. *2010, 40* (8), 1123-33 [DOI: 10.1080/00397910903043017]; synthesis of reversed 3-prenyloxindoles, also 3-methyleneindan-1-carboxylic acid amides by intramolecular Heck arylation (cf. *43,* 965s*75*) s. V.A. Ignatenko, N. Deligonul, R. Viswanathan, Org. Lett. *2010, 12* (16), 3594-7 [DOI: 10.1021/ol1012372].

Tetra-n-butylammonium azide *$[Bu_4N]N_3$*
Functionalized arenes $Ar(Ar')IX \rightarrow ArX\ [+\ Ar'I]$
by regioselective reductive elimination of diaryliodonium salts

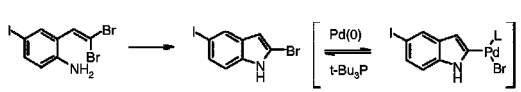
209.



Unsym. diaryliodonium salts possessing an electron rich aryl residue and a stereoelectronically 'locked' cyclophane residue undergo regioselective reductive elimination with incorporation of the counter anion *solely* onto the electron-rich aryl residue. **E:** A soln. of the startg. unsym. diaryliodonium hexafluorophosphate (0.025 mmol) in dry acetonitrile-d_3 (0.3 ml) combined with a soln. of tetra-*n*-butylammonium azide (7.1 mg; 1 eq.) in the same solvent (0.3 ml) [in a N_2-charged glove box], the mixture transferred into a J-Young NMR tube, sealed, taken out of the glove-box, wrapped with aluminum foil, placed into an oil bath at 45°, and worked up when ^1H NMR indicated completion of reaction → *p*-azidoanisole. Y 96%. High yields (51-96%; five examples) were recorded for incorporation of azide, acetate, phenoxide, thiocyanate and phenylthio onto the anisole ring but trifluoroethoxide was non-selective, consistent with a change of mechanism favoring benzyne intermediates. In all other instances it is presumed that an increase in the steric demand above the plane of the aromatic ring destabilizes the transition state to such an extent as to provide stereoelectronic control of the reductive elimination. F.e. and comparison of various electron-diverse unsym. diaryliodonium salts with or without the paracyclophane residue s. B. Wang, J.W. Graskemper, L. Qin, S.G. DiMagno, Angew. Chem., Int. Ed. *2010, 49* (24), 4079-83 [DOI: 10.1002/anie.201000695].

Palladium(II) acetate/tri-tert-butylphosphine/potassium carbonate *$Pd(OAc)_2$/t-Bu_3P/K_2CO_3*
2-Bromoindoles from *o*-amino-β,β-dibromostyrenes ○
Unusual ligand effect during palladium-catalyzed intramolecular N-vinylation

210.



under mild conditions. Toluene (1 ml) added to a mixture of startg. *gem*-dibromoalkene (0.2 mmol), $Pd(OAc)_2$ (5 mol%), tri-*tert*-butylphosphine·HBF_4 (10 mol%), and K_2CO_3 (2 eq.) under argon in a vial, the vial sealed, the mixture stirred at room temp. for 5 min then at 100° for 24 h, cooled, and purified directly by flash chromatography on silica → 2-bromo-5-iodoindole. Y 68%. The method was successful for electron-diverse (incl. sterically crowded) *gem*-*o*-dibromovinyl-anilines (twelve examples; Y 68-82%) in the presence of ester, ether, *halo* and trifluoromethyl functionality. Experimental evidence suggests that initial Pd(0)-catalyzed cyclization is accompanied by oxidative addition of Pd, which is *irreversible in the absence of the phosphine ligand*. The ligand is therefore essential for catalytic turnover. This effect appears to be general, with several previously problematic Pd-catalyzed cyclizations to **benzofurans** and **1-aminoindoles** resolved by the use of the tri-*tert*-butylphosphine ligand. F.e. and substrate prepn. s. S.G. Newman, M. Lautens, J. Am. Chem. Soc. *2010, 132* (33), 11416-7 [DOI: 10.1021/ja1052335].

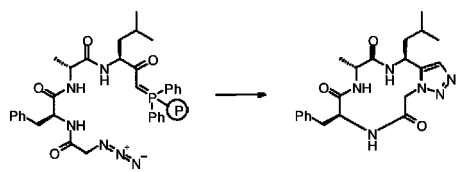
Sulfur ↑ NC ⇑ S

Chloro(cyclooctadiene)iridium(I) dimer *[Ir(cod)Cl]$_2$*
Intramolecular insertions with sulfoxonium ylids as metal carbene precursors ○
Cyclic α-aminocarbonyl compds. s. *78*, 192

Remaining Elements ↑ NC ⇑ Rem

Without additional reagents *w.a.r.*
Traceless polymer-based synthesis of 1,2,3-triazole-linked cyclic peptides from peptidyl azido(α-acylalkylidene)phosphoranes via 1,3-dipolar cycloaddition ○

211.



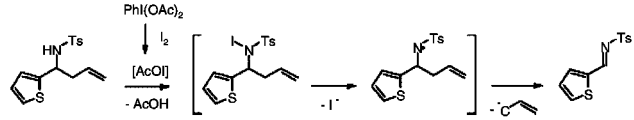
Monomeric products. The startg. azidophosphorane (0.315 mmol) swollen in anhydrous DMF (4 ml), heated at 80° for 14 h, cooled to room temp., filtered, and concentrated *in vacuo* → product. Y 67% (purity 89%). Use of supported azidopeptidylphosphoranes minimized formation of oligomeric products which characterize solution-phase approaches, affording intermolecular (dimeric) *cis*-locked triazolylcyclopeptides exclusively with dipeptide derivs. (two examples; Y 54% and 78%), while longer chain tetra-, penta- and octa-peptide analogs afforded monomers (via intramolecular reaction) as major or sole products with up to 24-membered rings (six examples; Y 32-72%). Tripeptide derivs. gave mixtures of mono- and di-meric products, formation of the latter indicating a significant degree of site separation within the polymer support, which in turn is influenced by the flexibility of the polymer. It was thereby demonstrated, for one tripeptide example, that use of a rigid macroporous polystyrene (with >20% divinylbenzene cross-linking) did indeed enhance monomer formation (75:25 from 12:88) compared with use of a more flexible microporous polystyrene (with 2% divinylbenzene cross-linking). F.e. and substrate prepn. s. Ahsanullah, J. Rademann, Angew. Chem., Int. Ed. *2010, 49* (31), 5378-82 [DOI: 10.1002/anie.200904980].

Carbon ↑ NC ⇑ C

Sodium methoxide *NaOMe*
2*H*-1,3-Benzothiazine 1,1-dioxides ⊂
from 1,1-dichloro-1,9b-dihydroazeto[2,1-*c*][1,3]benzothiazin-2-one S,S-dioxides s. *78*, 41

Phenyl iodosoacetate/iodine/sodium acetate *PhI(OAc)$_2$/I$_2$/NaOAc*
N-Sulfonylimines CH(N-SO$_2$R)C-C=C → C=NSO$_2$R
from 3-ethylene-N-sulfonylamines via β-fragmentation

212.



under mild conditions. 1,2-Dichloroethane (10 ml) and I$_2$ (0.5 eq.) added to a mixture of startg. homoallylic sulfonamide (2 mmol), phenyl iodosoacetate (1 eq.) and NaOAc (1 eq.) under argon,

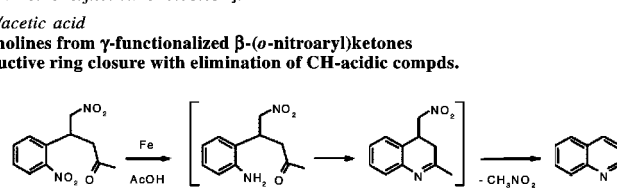
the mixture stirred at 0° until reaction complete (TLC; 30 min), quenched with aq. $Na_2S_2O_3$, extracted with ethyl acetate, concentrated, and purified by recrystallization → N-tosyl-N-(thien-2-ylmethylene)imine. Y 83%. N-Benzene- and N-*p*-toluene-sulfonyl derivs. of electron-diverse 1-(het)aryl-3-butenylamines afforded sulfonimines in moderate to good yields (eleven examples; Y 50-83%), with a sterically hindered 1-*o*-chlorophenyl deriv. affording only 30%. The reaction failed for alkanesulfonamide analogs (Me, CF_3, *i*-Bu, *t*-Bu), and, while 1-fur-2-yl and 1-thien-2-yl derivs. were good substrates, the corresponding pyridine deriv. was unreactive. Removal of acids formed during the reaction (with NaOAc) is thought to prevent inhibition of intermediate sulfamidyl radicals, but use of amine bases was not successful, attributed to instability under the oxidative conditions. F.e. and optimization s. W. Li, J. Gan, R. Fan, Tetrahedron Lett. *2010*, *51* (32), 4275-7 [DOI: 10.1016/j.tetlet.2010.06.031].

Iron/acetic acid *Fe/AcOH*

Quinolines from γ-functionalized β-(*o*-nitroaryl)ketones ○

Reductive ring closure with elimination of CH-acidic compds.

213.



Elimination of nitromethane. Powdered iron (6 eq.) added to a stirred soln. of 5-nitro-4-(2-nitrophenyl)pentan-2-one (1 mmol) in acetic acid (5 ml), the mixture refluxed for 2 h, cooled to room temp., the acetic acid removed under reduced pressure, diluted with ethyl acetate, stirred for 2 min, filtered to remove any iron impurities, the insoluble iron residue washed with ethyl acetate, the filtrate and washings combined and dried, the solvent removed under reduced pressure, and the residue worked up with purification by flash chromatography → product. Y 79%. The substrates are readily obtained by Michael addition of ketones to 1-nitro-2-(2-nitrovinyl)benzenes. The procedure is mild, inexpensive, clean and applicable to a wide range of nitroketones derived from acyclic, alicyclic or heterocyclic ketones (nineteen examples; Y 41-85%), irrespective of the electronic character of substituents on the aromatic ring. Furthermore, acid-sensitive groups, e.g. MeO, remained unaffected. Mechanistically, aromatization is the driving force for the reaction, with possible elimination of nitromethane or methylammonium acetate. F.e. **and** with **elimination of malononitrile or dimethyl malonate** (Y 73-75%) s. C. Ramesh, V. Kavala, C.-W. Kuo, C.-F. Yao, Tetrahedron Lett. *2010*, *51* (40), 5234-7 [DOI: 10.1016/j.tetlet.2010.07.063].

Formation of Hal-C Bond

Uptake ⇓

Addition to Oxygen and Carbon HalC ⇓ OC

Iminophosphoranylferrocenes/trimethylsilyl chloride ←

1,2-Halogenhydrins from epoxides → C(Hal)C(OH)

under nucleophilic organocatalysis with ferroceno[*d*][1,3]azaphosphinines and Me_3SiCl, regioselectivity, cf. *50*, 55*s65*; with novel iminophosphoranylferrocenes s. N. Sk, V.-D. Minhhoang, T.-J. Kim, Bull. Korean Chem. Soc. *2009*, *30* (12), 3075-8 [DOI: 10.5012/bkcs.2009.30.12.3075].

Addition to Nitrogen and Carbon HalC ⇓ NC

Tetra-n-butylammonium fluoride *Bu_4NF*

2-Fluorosulfonylamines from N-sulfonylaziridines C(F)C(NHSO$_2$R)

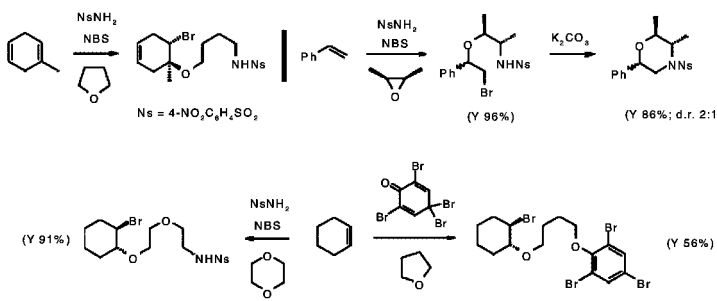
in 1,1,1,3,3-pentafluorobutane as environmentally friendly solvent s. *78*, 280

Addition to Carbon-Carbon Bonds — HalC ⇓ CC

Without additional reagents *w.a.r.*
N-Protected α,β-dibromolactams from α,β-ethylenelactams s. *78*, 540 C=C → C(Br)C(Br)

Diisobutylaluminum hydride s. under $NiCl_2(dppp)$ *i-Bu_2AlH*
Scandium(III) triflate/chiral cyclic bis(N-oxides) s. under N-Bromosuccinimide ←
2(S)-[Diphenyl(trimethylsiloxy)methyl]pyrrolidine s. under N-Fluorobenzenesulfonimide ←

N-Bromosuccinimide [s.a. under $NiCl_2(dppp)$] *NBS*
N-Protected 1,2-(aminoalkoxy)bromides from ethylene derivs. and cyclic ethers Regio- and diastereo-selective conversion C



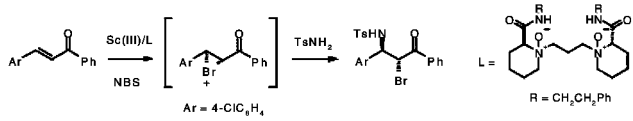
214.

2-(ω-Sulfonylaminoalkoxy)bromides. N-Bromosuccinimide (1.2 eq.), 4-nitrophenylsulfonylamine (0.5 mmol) and 1-methyl-1,4-cyclohexadiene (1.2 eq.) added to THF (4 ml) at 0°, the mixture shielded from light, stirred for 8 h at 25°, concentrated under reduced pressure, and the residue purified by flash chromatography on silica gel → N-[4-[*trans*-(6-bromo-1-methylcyclohex-3-en-1-yl)oxy]butyl]-4-nitrobenzenesulfonamide. Y 90%. Similar results were obtained for a variety of cyclic and acyclic mono-, di- and tri-subst. olefins (thirteen examples; Y 58-91%). Where applicable, reaction was exclusively *trans*-selective, chemoselective for the most electron-rich olefin and regioselective, affording Markovnikov-type addition products. The cyclic ether component could be successfully varied, with oxirane, oxetane and tetrahydropyran derivs. (incl. 1,4-dioxane) all giving high yields (five examples; Y 79-97%), but varying the amine component (alkyl or aryl amines, or *electron-rich* benzenesulfonamides) was unsuccessful, and various alternative brominating agents (Br_2, $PyHBr_3$, *n*-Bu_4NBr_3, 2,4,4,6-tetrabromo-2,5-cyclohexadienone or $Et_2SBr{\cdot}SbCl_5Br$) proved less effective than NBS, with 2,4,4,6-tetrabromo-2,5-cyclohexadienone giving rise to competing **alkoxyetherification**, affording a 2,4,6-tribromophenoxy deriv. (Y 21%; 56% in the absence of $NsNH_2$). Other oxygen nucleophiles (phenols and carboxylic acids) in the presence of NBS could replace the amine component with varying results (six examples; Y 33-48%, 85%; no reaction with 4-*tert*-butylphenol). F.e. incl. application to the prepn. of biologically active **morpholine** derivs. s. L. Zhou, C.K. Tan, J. Zhou, Y.-Y. Yeung, J. Am. Chem. Soc. *2010*, *132* (30), 10245-7 [DOI: 10.1021/ja104168q].

N-Bromosuccinimide/molecular sieves *NBS/MS*
1,2-Acoxybromides from ethylene derivs. s. *35*, 351s*78* C=C → C(OAc)C(Br)

N-Bromosuccinimide/scandium(III) triflate/chiral cyclic bis(N-oxides) *NBS/[Sc(III)]**
α-Bromo-β-(sulfonylamino)- from α,β-ethylene-ketones C=C → C(Br)C(NHSO$_2$R)
Regioselective Lewis acid-catalyzed asym. conversion

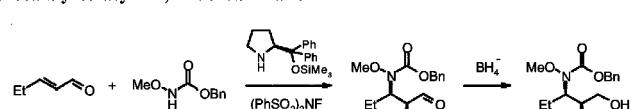
215.



under mild conditions. A soln. of Sc(OTf)$_3$ (0.05 mol%) and ligand (0.05 mol%) in THF (0.05 ml) concentrated *in vacuo*, 3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (0.2 mmol), 4 Å molecular sieves (40 mg) and methylene chloride (0.4 ml) added, the mixture stirred at 35° for 5 min, cooled to 0°, 4-toluenesulfonamide (1.1 eq.) and N-bromosuccinimide (1.2 eq.) added, the mixture stirred for 24 h, and purified by flash chromatography on silica → (3R-*trans*)-2-bromo-3-(4-chlorophenyl)-3-(4-tosylamino)-1-phenylpropan-1-one. Y 93% (d.r. >99:1; e.e. 96%). This novel and experimentally simple bromoamination of chalcones proceeds via bromonium ion intermediates under low catalyst loadings to afford the corresponding vicinal bromoamines with high regio-, diastereo- and enantio-control (thirty-nine examples; d.r. >99:1; e.e. 92-98%). Reaction tolerated electronic variation in both phenyl moieties of the chalcone for methane-, toluene- and benzenesulfonamides, with yields >89% (a penta-1,3-dien-5-one analog gave 80%), but were somewhat lower (Y 38-70%) for chloro- and methoxy-benzenesulfonamides. Absolute stereochemistry was determined by X-ray crystallography in one case. F.e. and optimization s. Y. Cai, X. Liu, Y. Hui, J. Jiang, W. Wang, W. Chen, L. Lin, X. Feng, Angew. Chem., Int. Ed. *2010*, *49* (35), 6160-4 [DOI: 10.1002/anie.201002355].

N-Fluorobenzenesulfonimide/2(S)-[diphenyl(trimethylsiloxy)methyl]pyrrolidine ←
N-Protected *syn*-β-alkoxylamino-α-fluoroaldehydes C=C → C(F)C-N(OR)
from α,β-ethylenealdehydes
Organocatalyzed asym. 1,2-fluoroamination

216.

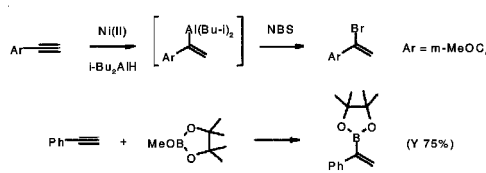


The startg. enal (0.125 mmol) added to a stirred soln. of 2(S)-[diphenyl(trimethylsiloxy)methyl]-pyrrolidine (20 mol%) and benzyl N-methoxycarbamate (1.2 eq.) in *tert*-butyl methyl ether (0.2 ml) at room temp., allowed to react until the enal was consumed (^{1}H NMR monitoring), diluted with more *tert*-butyl methyl ether (0.3 ml), cooled to 0°, N-fluorobenzenesulfonimide (1 eq.) added in one portion, stirred vigorously at 0°, monitoring continued until reaction complete (generally 24-48 h), cooled to -78°, diluted with ether (0.5 ml), filtered through a pad of Davisil® Silica Gel, dimethyl sulfide (0.1 ml) added, worked up, the resulting crude fluoroamine dissolved in methanol (1 ml), cooled to 0°, $NaBH_4$ (2 eq.) added in small portions, stirred for 15 min to reduce the aldehyde to the more manageable prim. alcohol, quenched by the addition of satd. aq. NH_4Cl, and worked up with purification by chromatography on silica gel → benzyl (2S,3R)-2-fluoro-1-hydroxypentan-3-yl(methoxy)carbamate. Y 73% (*syn/anti* 95:5; e.e. 99%). This is the first highly diastereoselective asymmetric addition of two different hetero-functions across the double bond of an achiral substrate. Significantly, the *same* chiral organocatalyst facilitates the incorporation of both nucleophile and electrophile within the catalytic cycle: the initial aza-Michael addition taking place via iminium activation of the aldehyde function and the resulting β-alkoxylamino-aldehyde then being activated as the enamine prior to attack of the electrophilic fluorine source. The procedure is applicable to a range of alkyl-subst. enals (alkyl = primary, branched or hindered), notably tolerating isolated olefinic double bonds, ether protective groups and remote cyano groups (nine examples; Y 24%, 41-73%; *syn/anti* 87:13 to 98:2; e.e. 80%, 98-99%). F.e. and conversion

to **chiral *syn*-β-amino-α-fluorocarboxylic acids** s. C. Appayee, S.E. Brenner-Moyer, Org. Lett. *2010, 12* (15), 3356-9 [DOI: 10.1021/ol101167z].

Dichloro[1,3-bis(diphenylphosphino)propane]nickel(II)/diisobutylaluminum hydride/ N-bromosuccinimide ←

Syntheses via α-selective nickel-catalyzed hydroalumination of terminal acetylene derivs. ←



217.

α-Subst. vinyl bromides. Commercial grade *$NiCl_2(dppp)$* (0.03 mmol) purged with N_2 for ca. 10 min in a dry test tube, THF (1 ml) added via syringe, followed by dropwise addition of *i*-Bu_2AlH (1.3 mmol) at 22° (gas evolution!), the resulting black soln. allowed to cool to 0°, 1-ethynyl-3-methoxybenzene (1 mmol) added slowly over 5 min (exothermic!), allowed to warm to 22°, stirring continued for 2 h, a soln. of NBS (2 mmol) in THF (3 ml) transferred via syringe to the *in situ*-formed enalane at 0°, the dark brown soln. allowed to warm up to 22°, stirred for 1 h, quenched by addition to a satd. soln. of Rochelle's salt and ether, and worked up with purification by chromatography on silica gel → 1-(1-bromovinyl)-3-methoxybenzene. Y 87% (α-selectivity >98%). Hydroalumination is highly α-selective (95% to >98% by ^1H NMR analysis) at low catalyst loading (as little as 0.1 mol%) and on the gram scale, whereas reaction with the more familiar $NiCl_2(PPh_3)_2$ is highly β-selective! The procedure is also simple, mild and inexpensive, and, unlike uncatalyzed hydroalumination, is very clean; it is applicable to a wide range of terminal arylacetylenes (incl. congested substrates and those with electron-donating or -withdrawing substituents) and alkylacetylenes (incl. linear and branched alkyl derivs.), the intermediate enalanes being trapped by NBS or NIS to give the corresponding α-subst. vinyl halides (four examples; Y 79-88%; α-selectivity >98%). **α-Subst. vinylboronic acid esters** were obtained similarly by quenching the intermediate enalanes with methoxy(pinacolato)borane (five examples; Y 68-94%; α-selectivity 95 to >98%). F.e. and comparison of Ni catalysts s. F. Gao, A.H. Hoveyda, J. Am. Chem. Soc. *2010, 132* (32), 10961-3 [DOI: 10.1021/ja104896b].

Exchange ⇅

Hydrogen ↑ HalC ⇅ H

Irradiation s. under HBr ///

Electrolysis s. under HBr ϟ

Lithium diisopropylamide s. under PhC(Cl)(F)CN and $(PhSO_2)_2NF$ *i-Pr_2NLi*

Potassium phosphate *K_3PO_4*

Metal-free halogenocarbocyclization of 1,5-enynes ○

1-Iodo-1,4-cyclohexadienes s. *78*, 364

Potassium iodide/sodium hydroxide *KI/NaOH*

Ar. iodination H → I

with KI/NaOH s. *9*, 613; mono- and poly-iodination **of phenols** possessing electron-withdrawing groups (e.g. NO_2, F) with I_2/KI/NaOH s. R. Francke, G. Schnakenburg, S.R. Waldvogel, Eur. J. Org. Chem. *2010* (12), 2357-62 [DOI: 10.1002/ejoc.201000161]; rapid and eco-friendly iodination of hydroxylated ar. aldehydes and ketones *on grinding* with I_2/iodic acid *without solvent* s. A. Vibhute, S. Mokle, K. Karamunge, V. Gurav, Y. Vibhute, Chin. Chem. Lett. *2010, 21* (8), 914-8 [DOI: 10.1016/j.cclet.2010.03.006].

Potassium bromide/hydrogen peroxide/silica-supported copper(II) perfluorophthalocyanine ← *Potassium iodide/ammonium persulfate* $KI/(NH_4)_2S_2O_8$

Oxidative ar. halogenation H → Hal

s. *43*, 420s67; eco-friendly *o*-iodination of activated aromatics, e.g. phenols and anilines, and hydroxycoumarins with $KI/(NH_4)_2S_2O_8$ in aq. methanol, selectivity, s. N.C. Ganguly, S.K. Barik, S. Dutta, Synthesis *2010* (9), 1467-72 [DOI: 10.1055/s-0029-1218698]; ar. bromination with NH_4Br/H_2O_2 in aq. medium containing SBA-15-supported sulfated zirconia under nearly neutral conditions, *p*-selectivity, s. A.-J. Chen, X.-R. Chen, C.-Y. Mou, J. Chin. Chem. Soc. *2010*, *57* (4B), 820-8; with NH_4Br/Oxone in methanol or water s. M.A. Kumar, C.N. Rohitha, S.J. Kulkarni, N. Narender, Synthesis *2010* (10), 1629-32 [DOI: 10.1055/s-0029-1218723]; with KBr/H_2O_2 and a silica gel-supported Cu(II)-perfluorophthalocyanine in acetic acid s. R.K. Sharma, C. Sharma, Tetrahedron Lett. *2010*, *51* (33), 4415-8 [DOI: 10.1016/j.tetlet.2010.06.067].

Silver acetate or sulfate $AgOAc\ or\ Ag_2SO_4$

Silver-catalyzed ar. halogenation

with Ag_2SO_4 s. *7*, 563; *7*, 564; multi-gram *o*-iodination and *o*-bromination of unprotected arylboronic acids in ethanol s. R.M. Al-Zoubi, D.G. Hall, Org. Lett. *2010*, 12 (11), 2480-3 [DOI: 10.1021/ol100537x]; iodination of N-heteroarenes, e.g. isoxazoles, with I_2/AgOAc s. M. Iglesias, O. Schuster, M. Albrecht, Tetrahedron Lett. *2010*, *51* (41), 5423-5 [DOI: 10.1016/j.tetlet.2010.07.178].

Copper(II) triflate/N-fluorobenzenesulfonimide $Cu(OTf)_2/(PhSO_2)_2NF$

5-Fluoro-2-cyclopentenones from cross-conjugated dienones ○

Stereospecific fluorinative Nazarov cyclization s. *78*, 223

Copper(I) chloride/ammonium chloride or diisopropylamine hydrochloride/ N,N′,N′,N″,N″-pentamethyldiethylenetriamine/acetic acid ←

Remote radical chlorination H → Cl

1,4-Chlorohydrins from hydroperoxides via copper-catalyzed 1,5-hydrogen atom transfer s. *78*, 224

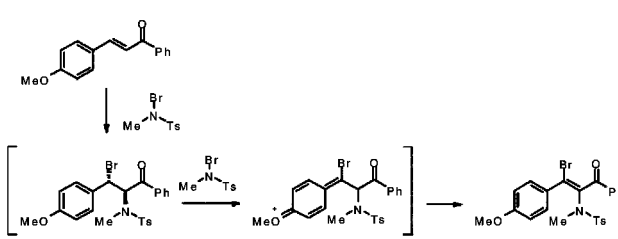
Copper(II) chloride (s.a. under Cyanuric chloride) $CuCl_2$

(E)-β-Bromo-α,β-ethylene-α-tosylamino- CH=CH → C(Br)=C(N-Ts)

from α,β-ethylene-carbonyl compds. and N-bromo-N-tosylamines

Copper-catalyzed aminobromination-elimination

218.



Startg. olefin (1 mmol), $CuCl_2$ (5 mol%), 4 Å molecular sieves (500 mg; pre-dried at 200° overnight *in vacuo*), and freshly distilled methylene chloride (3 ml) added to a dry vial under N_2, a soln. of N-bromo-N-methyltosylamine (1.8 eq.) in methylene chloride (3 ml) added dropwise, the mixture stirred at 35° for 36 h in the capped vial, quenched with satd. aq. Na_2SO_3, the organic phases separated, the aq. phase extracted with ethyl acetate, the combined organic layers washed with brine, dried (Na_2SO_4), concentrated, and purified chromatographically → (E)-product. Y 76% (after purification; E/Z by ^1H NMR of the crude mixture 5:1). The same product was obtained in 66% yield (E/Z 5:1) using TsNHMe/N-bromosuccinimide. This novel aminobromination-elimination reaction provides easy access to α,β-unsatd. β-bromo-α-(tosylamino)-ketones (eight examples; Y 58-81%) or -esters (two examples; Y 62%, 64%), which may serve as building blocks for unusual amino acids and biologically active natural products. $CuBr_2$ was also effective

(Y 73%) but copper(I) salts less so. The presence of an electron-donating group in the *para* position is essential, *o*- or *m*-methoxy-derivs. giving only the usual halogenamines. F.e. and optimization s. H. Sun, G. Zhang, S. Zhi, J. Han, G. Li, Y. Pan, Org. Biomol. Chem. *2010*, *8* (19), 4236-9 [DOI: 10.1039/c0ob00283f].

Indium(III) chloride s. under Cyanuric chloride $InCl_3$

3-Butylimidazolium fluoroborate s. under N′-Chloromethyl-N-fluoro-1,4-diazonia-bicyclo[2.2.2]octane bis(fluoroborate) [Hbim]BF_4

3,3-Dimethylbut-1-ene s. under $IrH_5(PPr\text{-}i_3)_2$ *t-BuCH=CH*$_2$

1-Butyl-3-methylimidazolium fluoroborate s. under PhI(OH)OTs [bmim]BF_4

(S)-2,6-Bis[diphenyl(trimethylsiloxy)methyl]-4,5-dihydro-3H-dinaphth[2,1-c;1′,2′-e]-azepine s. under 4,4-Dibromo-2,6-di-tert-butyl-2,5-cyclohexadienone ←

(1R,2R)-N-[3,5-Bis(trifluoromethyl)phenyl]-N′-[2-(dipentylamino)cyclohex-1-yl]urea s. under N-Iodo-4-fluorophthalimide ←

(R,R)-Jacobsen's salen s. under N-Fluorobenzenesulfonimide ←

Phenyl iodosoacetate/methylene chloride $PhI(OAc)_2/CH_2Cl_2$

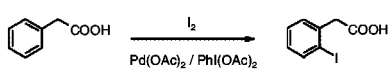
8-Chlorospiro[5.5]undeca-1,4,7-trien-3-ones ○

from terminal 5-(*p*-hydroxyaryl)acetylenes – Oxidative Prins-type cyclization s. *78*, 73

Phenyl iodosoacetate/palladium(II) salts/iodine $PhI(OAc)_2/Pd(II)/I_2$

Palladium-catalyzed *o*-iodination of arylacetic acids H → I

219.



o-Iodination of arylacetic acids, which cannot be achieved via classical *o*-lithiation, can now be carried out simply and efficiently under palladium-catalyzed *carboxyl-directed* *o*-activation. **E:** A soln. of phenylacetic acid (0.5 mmol), $Pd(OAc)_2$ (5 mol%), phenyl iodosoacetate (0.75 eq.) and I_2 (0.75 eq.) in anhydrous DMF (3 ml) charged into a tube under air, the latter sealed with a Teflon-lined cap, wrapped with aluminum foil to exclude light (eliminating the possibility of light-induced decarboxylation), the mixture stirred at 60° for 12 h, cooled to room temp., concentrated under vacuum, and the residue subjected to column chromatography → *o*-iodophenylacetic acid. Y 70%. The procedure is applicable to a wide range of substrates possessing electron-withdrawing or -donating groups on the aromatic ring (notably OAc, Cl, Br and amide groups) and the catalyst can be readily retrieved by precipitation and reused at least 5 times without a significant decrease in yield (from 92% to 80% after the fifth cycle). The method is also applicable on the gram scale and the products readily converted to pharmacologically important ***o*-arylaminoarylacetic acids** via Ullmann coupling. Other palladium(II) salts were also effective, irrespective of the nature of the anion, the key active catalyst being *in situ*-generated PdI_2. F.e.s. T.-S. Mei, D.-H. Wang, J.-Q. Yu, Org. Lett. *2010*, *12* (14), 3140-3 [DOI: 10.1021/ol1010483].

Phenyl iodoso(hydroxy)tosylate/1-butyl-3-methylimidazolium fluoroborate ←

α-Chloro-α-fluorophenylacetonitrile/lithium diisopropylamide *PhC(Cl)(F)CN/i-Pr*$_2$*NLi*

α-Halogenation H → Hal

α-chlorination with hexachloro-2,4-cyclohexadienone s. *38*, 473; mild α-chlorination of deprotonated nitriles and ketone/ester enolates with α-chloro-α-fluorophenylacetonitrile/*i*-Pr_2NLi s. B.R. Pitta, F.F. Fleming, Org. Lett. *2010*, *12* (12), 2810-3 [DOI: 10.1021/ol100897y]; comparison of the electrophilicities of α-chlorinating agents used in organocatalysis s. X.-H. Duan, H. Mayr, ibid. *12* (10), 2238-41 [DOI: 10.1021/ol100592j]; α-iodination of alkyl aryl ketones with I_2 or MeI in the presence of Koser's reagent in 1-butyl-3-methylimidazolium fluoroborate as ionic liquid s. J.C. Lee, J. Kim, H.J. Park, B. Kwag, S.B. Lee, Bull. Korean Chem. Soc. *2010*, *31* (5), 1385-6 [DOI: 10.5012/bkcs.2010.31.5.1385]; anodic α-monobromination of alkyl aryl ketones with HBr in acetonitrile s. R.S. Kumar, K. Kulangiappar, M.A. Kulandainathan, Synth. Commun. *2010*, *40* (12), 1736-42 [DOI: 10.1080/00397910903161710].

Methylene chloride s. under PhI(OAc)$_2$ CH_2Cl_2

4,4-Dibromo-2,6-di-tert-butyl-2,5-cyclohexadienone/(S)-2,6-bis[diphenyl(trimethylsiloxy)-methyl]-4,5-dihydro-3H-dinaphtho[2,1-c;1′,2′-e]azepine ←
Synthesis of chiral *anti*-1,2-bromhydrins from aldehydes CHCHO → C(Br)CH(OH)R
via organocatalyzed asym. α-bromination s. *78*, 282

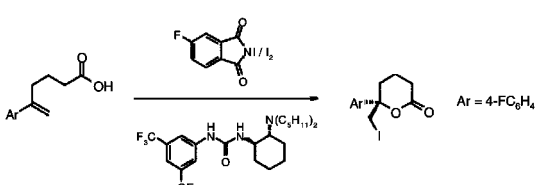
N-Bromosuccinimide/molecular sieves or Bis(collidine)iodonium hexafluorophosphate ←
Electrophilic halogenocyclization ○
halogenolactonization s. *35*, 351; bromolactonization with NBS and molecular sieves as catalyst, also 1,2-acoxybromides from ethylene derivs., s. F. Chen, X. Jiang, J.C. Er, Y.-Y. Yeung, Tetrahedron Lett. *2010, 51* (26), 3433-5 [DOI: 10.1016/j.tetlet.2010.04.113]; polysubst. 2-iodomethyl-3,6-dihydro-2*H*-pyrans from 2,5-dienols with I_2 and $FeCl_3{\cdot}6H_2O$ s. M. Xie, J. Zhang, X. Zhao, G. Lin, Chin. J. Chem. *2010, 28* (6), 961-6 [DOI: 10.1002/cjoc.201090178]; N-protected 2-iodomethylazetidines from 3-ethyleneamines with I_2, and conversion to N-protected 3-iodopyrrolidines, s. A. Feula, L. Male, J.S. Fossey, Org. Lett. *2010, 12* (21), 5044-7 [DOI: 10.1021/ol102215e]; 4-iodo-Δ^3-pyrazoline-1,2-dicarboxylic acid esters from 2-acetylenehydrazo-dicarboxylic acid esters with bis(collidine)iodonium hexafluorophosphate, also 4-iodopyrazole-1-carboxylic acid esters with NIS/BF_3 (HalC⇊C), s. T. Okitsu, K. Sato, A. Wada, Org. Lett. *2010, 12* (15), 3506-9 [DOI: 10.1021/ol101365x]; 4-α-alkoxy-3-iodofurans from 2-acyl-1,3-enynes s. C.-H. Cho, R.C. Larock, Tetrahedron Lett. *2010, 51* (26), 3417-21 [DOI: 10.1016/j.tetlet.2010.04.108]; 3-iodomethyl-3,4-dihydro-2*H*-benzoxazines from *o*-(allyloxy)tosylamines, also 1,2,3,4-tetrahydroquinoxaline analogs, s. K.C. Majumdar, K. Ray, S. Ponra, *2010, 51* (41), 5437-9 [DOI: 10.1016/j.tetlet.2010.08.016].

N-Bromo- or N-Iodo-succinimide *NBS or NIS*
3-Halogeno-1-vinylindenes from *o*-(alk-1-ynyl)styrenes
Also 1-α-alkoxy-3-iodoindenes s. *78*, 363

N-Iodosuccinimide *NIS*
Metal-free halogenocarbocyclization of 1,5-enynes
Iodoarene ring – 1-Iodo-4-formyloxycyclohexenes s. *78*, 364

N-Iodo-4-fluorophthalimide/iodine/(1R,2R)-N-[3,5-bis(trifluoromethyl)phenyl]-N′-[2-(dipentylamino)cyclohex-1-yl]urea ←
Organocatalyzed asym. iodolactonization

220.



Chiral δ-aryl-δ-iodomethyl-δ-lactones. N-Iodo-4-fluorophthalimide (1 eq.) and I_2 (0.15 mol%) added to a stirred soln. of 5-(4-fluorophenyl)-5-hexenoic acid (0.2 mmol) and chiral urea catalyst (15 mol%) in toluene at -80° under N_2, the mixture stirred for 5 d, quenched with aq. $Na_2S_2O_4$ and 1 *M* aq. NaOH, extracted with methylene chloride, concentrated *in vacuo*, and purified by flash chromatography on silica → product. Y 95% (e.e. 96%). The use of stoichiometric N-iodo-4-fluorophthalimide and optimized levels of catalytic I_2 was essential for effective iodolactonization of 5-aryl-5-hexenoic acids, with electron-poor substrates giving the highest enantioselectivity (seven examples; Y 71-96%; e.e. 87-94%). A 4-methoxyphenyl deriv. was less selective (Y 91%; e.e. 48%), as was a 5-isopropyl analog (Y 85%; e.e. 76%). Absolute stereochemistry was confirmed in one case by deiodination and X-ray analysis of the resultant methyl lactone. Cyclization of 4-phenyl-4-*pentenoic* acid to the corresponding **chiral γ-aryl-γ-iodomethyl-γ-lactone** (*with reverse configuration*), was only successful at low levels (0.1 mol%) of iodine catalysis (Y 82%; e.e. 90%), while the 2,2-dimethyl deriv. gave only the racemic product (Y 98%). F.e. and optimization

s. G.E. Veitch, E.N. Jacobsen, Angew. Chem., Int. Ed. *2010, 49*, (40), 7332-5 [DOI: 10.1002/anie.201003681].

Cyanuric chloride/indium(III) chloride/bis(acetonitrile)dichloropalladium(II)/copper(II) chloride ←

1-Acyl-3-chloroindoles from *o*-acetyleneketoximes s. *78*, 152 ○

N-Fluorobenzenesulfonimide s.a. under Cu(OTf)$_2$ and Fe(OTf)$_2$ *(PhSO$_2$)$_2$NF*

N′-Chloromethyl-N-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(fluoroborate)/3-butyl-imidazolium fluoroborate ←

N-Fluorobenzenesulfonimide/lithium diisopropylamide *(PhSO$_2$)$_2$NF/i-Pr$_2$NLi*

N-Fluorobenzenesulfonimide/cobalt(II) acetoacetonate/(R,R)-Jacobsen's salen ←

α-Fluorination H → F

with Selectfluor s. *39*, 458s*75*; α-fluorination of β-ketosulfones with Selectfluor under ultrasonication in [Hbim]BF$_4$ with methanol as co-solvent at room temp. s. M.R.P. Heravi, Chin. Chem. Lett. *2010, 21* (12), 1399-402 [DOI: 10.1016/j.cclet.2010.06.030]; of N-protected β- and γ-aminocarboxylic acid esters with N-fluorobenzenesulfonimide/LDA **with asym. induction** (cf. *39*, 458s*70*) s. V. Peddie, M. Pietsch, K.M. Bromfield, R.N. Pike, P.J. Duggan, A.D. Abell, Synthesis *2010* (11), 1845-59 [DOI: 10.1055/s-0029-1218743]; **asym. α-fluorination** of β-ketocarboxylic acid esters with Co(acac)$_2$/(R,R)-Jacobsen's salen/N-fluorobenzenesulfonimide (cf. *60*, 186s*75*), also α-chlorination, s. M. Kawatsura, S. Hayashi, Y. Komatsu, S. Hayase, T. Itoh, Chem. Lett. *2010, 39* (5), 466-7 [DOI: 10.1246/cl.2010.466].

Zirconia s. under NH$_4$Br *ZrO$_2$*

Chlorobis(cyclopentadienyl)hydridozirconium(IV) s. under IrH$_3$(PPr-i$_3$)$_2$ *Cp$_2$ZrHCl*

Triphenylphosphine *Ph$_3$P*

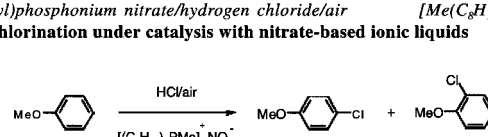
2-Dichloromethyl-1-sulfonyl-Δ^2-imidazolines from ethylene derivs. ○

from enones or enoates with FeCl$_2$/Ph$_3$P cf. *62*, 193s*64*; with Ph$_3$P alone, also conversion to differentially protected 1,2-diamines by hydrolysis in the presence of SnCl$_4$, s. H. Wu, X. Ji, H. Sun, G. An, J. Han, G. Li, Y. Pan, Tetrahedron *2010, 66* (25), 4555-9 [DOI: 10.1016/j.tet.2010.04.054].

Methyl(trioctyl)phosphonium nitrate/hydrogen chloride/air *[Me(C$_8$H$_{17}$)$_3$P]NO$_3$/HCl/air*

Aerobic ar. chlorination under catalysis with nitrate-based ionic liquids H → Cl

221.



in the absence of solvent. Aq. HCl (37%; 3.14 mmol) added to anisole (1.4 mmol) and methyl(trioctyl)phosphonium nitrate (1 eq.), the resulting mixture heated at 80° for 3 h with exposure to atmospheric oxygen, cooled, and worked up with chromatographic purification → chloroanisole. Y 97% (75% *p*- and 22% *o*-isomers). The phosphonium salt may be prepared in a waste-free process from trioctylphosphine, dimethyl carbonate and HNO$_3$ with liberation of only methanol and CO$_2$. The procedure is simple, eco-friendly, non-toxic and applicable in high yield to the monochlorination of a range of activated arenes. Only traces of product were obtained, however, with deactivated arenes (chloro- and nitro-benzene), while acetophenone and methoxyacetophenone underwent benzylic oxidation to give a mixture of products. The catalyst was simply recycled with no loss of activity by extracting the product, removing residual water under vacuum, adding fresh substrate and 1 eq. HCl, and heating again at 80° for a further 120 h. A stepwise conversion of anisole to 2,4-dichloroanisole was also achieved by adding a further 1 eq. aq. HCl to the intermediate monochlorinated anisole and heating for a further 5 days (Y 92%). The truly catalytic nature of the onium nitrate was revealed, and a mechanism (based on initial generation of HOCl as the effective chlorinating agent) proposed. F.e. and large-scale (13-fold) procedure, also comparison of onium nitrates, s. M. Noè, A. Perosa, M. Selva, L. Zambelli, Green Chem. *2010, 12* (9), 1654-60 [DOI: 10.1039/c0gc00004c].

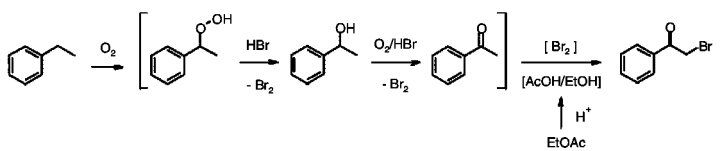
Air s. under $[Me(C_8H_{17})_3P]NO_3$ *air*
Hydrogen peroxide/SBA-15-supported sulfated zirconia s. under NH_4Br ←
Potassium peroxymonosulfate s. under NH_4Br *$KHSO_5$*
Ammonium persulfate s. under KI *$(NH_4)_2S_2O_8$*
Iodine s. under $PhI(OAc)_2$ and N-Iodo-4-fluorophthalimide *I_2*

Iodic acid *HIO_3*
Ar. iodination of phenols on solid-state grinding s. *9*, 613s*78* H → I

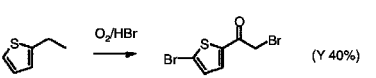
Ammonium bromide/hydrogen peroxide/SBA-15-supported sulfated zirconia ←
Ammonium bromide/potassium peroxymonosulfate *$NH_4/KHSO_5$*
Oxidative ar. bromination s. *43*, 420s*78* H → Br

Hydrogen chloride s. under $[Me(C_8H_{17})_3P]NO_3$ *HCl*

Hydrogen bromide/irradiation *HBr/hν*
α-Bromoacylophenones from alkylarenes $CH_2CH \rightarrow C(O)C(Br)$



222.



A soln. of ethylbenzene (0.3 mmol) in dry *ethyl acetate* (5 ml), water (50 or 100 µl) and 48% aq. HBr (0.38 mmol) in a Pyrex test-tube equipped with an O_2 balloon stirred under irradiation with four 22 W fluorescent lamps (at a distance of 65 mm) for 10 h (temp. of the final stage ca. 40°), concentrated under reduced pressure, and the residue subjected to preparative TLC → phenacyl bromide. Y 68%. Fourteen further examples afforded yields of 40-76%, highest yields being obtained with substrates bearing an electron-withdrawing group in the *para* position, while *p*-ethylanisole, bearing an electron-donating group, produced 4-methoxyphenol in 4% yield with 74% recovered starting material. 2-Ethylthiophene underwent ring bromination as well (using 3 eq. HBr). The mechanism probably involves generation of a bromine radical, followed by formation of a benzyl radical which traps molecular oxygen to give the hydroperoxide after abstraction of hydrogen from HBr or ethyl acetate, reduction to the alcohol with formation of bromine from HBr, further oxidation to the acylophenone by a similar pathway, and bromination with bromine accelerated by HBr or photoirradiation; furthermore, during the course of the reaction ethyl acetate is hydrolyzed to acetic acid and ethanol which play a key role in the bromination, but if present from the start inhibit the oxidation stage. F.e. and optimization s. N. Tada, K. Ban, S.-i. Hirashima, T. Miura, A. Itoh, Org. Biomol. Chem. *2010*, *8* (20), 4701-4 [DOI: 10.1039/c0ob00101e].

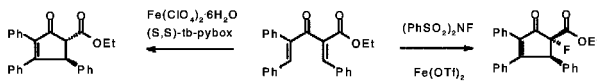
Ammonium chloride or diisopropylamine hydrochloride s. under CuCl ←

Hydrogen bromide/electrolysis *HBr/⚡*
Anodic α-bromination of acylophenones s. *38*, 473s*78* H → Br

Bis(pyridine)iodonium fluoroborate *$[Py_2I]BF_4$*
Metal-free halogenocarbocyclization of 1,5-enynes ○
1-Iodo-4-fluorocyclohexenes s. *78*, 364

Iron(II) triflate/N-fluorobenzenesulfonimide *$Fe(OTf)_2/(PhSO_2)_2NF$*
Iron(II) triflate or perchlorate or cobalt(II) perchlorate/chiral bis(Δ^2-oxazolines) ←
5-Fluoro-2-cyclopentenones from cross-conjugated dienones ○
Stereospecific fluorinative Nazarov cyclization

223.



(Y 69%; e.e. 83%)

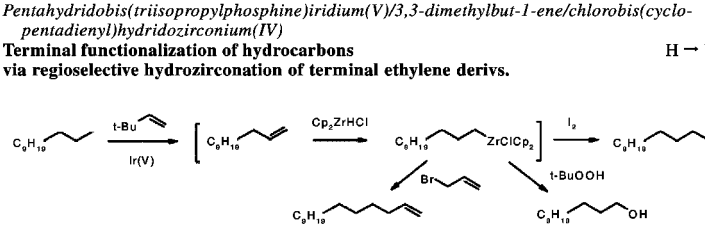
2-Subst. 3,4-diaryl-5-fluoro-2-cyclopentenone-5-carboxylic acid esters. $Fe(OTf)_2$ (10 mol%), ethyl 2-benzylidene-3-oxo-4,5-diphenylpent-4-enoate (0.1 mmol) and N-fluorobenzenesulfonimide (2 eq.) mixed in toluene (0.2 ml) at room temp. for 15 h, and worked up with purification by silica gel chromatography → product. Y 91% (single stereoisomer). Six further examples afforded yields of 51-80%, mostly as single stereoisomers. **Asym. Nazarov cyclization** may be effected (seven substrates; e.e. up to 83%) with $Fe(OTf)_2$, $Fe(ClO_4)_2{\cdot}6H_2O$ or $Co(ClO_4)_2{\cdot}6H_2O$ and a chiral pybox ligand (in the absence of fluorinating agent), especially in methylene chloride/hexane (2:1). F.e.s. M. Kawatsura, K. Kajita, S. Hayase, T. Itoh, Synlett *2010* (8), 1243-6 [DOI: 10.1055/s-0029-1219782]; fluorinative Nazarov cyclization with $Cu(OTf)_2$ as catalyst (Y up to 95%; *trans/cis* up to 49:1), **also asym. fluorinative cyclization** with added (R)-Ph-bis(oxazoline) (three examples; Y 60-80%; *trans/cis* 19:1 to 49:1; e.e. 43.5-95.5%), s. J. Nie, H.-W. Zhu, H.-F. Cui, M.-Q. Hua, J.-A. Ma, Org. Lett. *2007, 9* (16), 3053-6 [DOI: 10.1021/ol071114j]; **2-fluoro-1-indanone-2-carboxylic acid esters** from aroylacetic acid esters and aldehydes via stereospecific $AlCl_3$-mediated **Knoevenagel condensation-fluorinative Nazarov cyclization** with N-fluorobenzenesulfonimide (Y 12-72%; *cis/trans* 3:1 to 29:1) s. H.-F. Cui, K.-Y. Dong, G.-W. Zhang, L. Wang, J.-A. Ma, Chem. Commun. *2007* (22), 2284-6 [DOI: 10.1039/b702114c].

Iron(III) chloride *$FeCl_3$*
Polysubst. 2-iodomethyl-3,6-dihydro-2*H*-pyrans from 2,5-dienols s. *35,* 351s*78*

Cobalt(II) acetoacetonate s. under N-Fluorobenzenesulfonimide *$Co(acac)_2$*
Bis(acetonitrile)dichloropalladium(II) s. under Cyanuric chloride *$PdCl_2(MeCN)_2$*
Palladium(II) salts/iodine s. under PhI(OAc)$_2$ *Pd(II)/I_2*

Pentahydridobis(triisopropylphosphine)iridium(V)/3,3-dimethylbut-1-ene/chlorobis(cyclopentadienyl)hydridozirconium(IV) ←
Terminal functionalization of hydrocarbons H → Hal
via regioselective hydrozirconation of terminal ethylene derivs.

224.



(Y 57% (nmr)) (Y 58%)

in one pot. A mixture of $IrH_5(i\text{-}Pr_3P)_2$ (11 mol%), 3,3-dimethylbut-1-ene (2 eq.) and dodecane (40 eq.) stirred under argon at 150° for 6 h, cooled, concentrated *in vacuo*, the mixture of alkenes dissolved in THF (2.5 ml), Cp_2ZrHCl (1 eq.) added under argon, the mixture stirred at 40° for 12 h, cooled to 25°, I_2 (0.05 mmol) added, the mixture stirred for 1 h, concentrated, and filtered through silica → 1-iodododecane. Y 74%. Sequential iridium-catalyzed dehydrogenation, alkene isomerization, hydrozirconation and zirconium exchange was successful with a number of electrophiles (NBS, I_2, *t*-BuOOH, allyl bromide and CO), affording terminally functionalized dodecanes as single products (Y 44-74%). Attempted functionalization of branched alkanes, alkylarenes or dialkyl ethers gave low conversion to the initial alkene mixture, but butylbenzene was converted to 4-iodobutylbenzene in 30% yield using a large excess (20 eq.) of the

dehydrogenating agent (3,3-dimethylbut-1-ene). F.e.s. Y. Kuninobu, T. Ureshino, S. Yamamoto, K. Takai, Chem. Commun. *2010*, *46* (29), 5310-2 [DOI: 10.1039/c0cc00243g]; bromination or, especially, chlorination of aliphatic C-H bonds with peroxyacetic acid and halide salts (e.g. NaCl) in acetonitrile or water s. Y. He, C.R. Goldsmith, Synlett *2010* (9), 1377-80 [DOI: 10.1055/s-0029-1219832].

Oxygen ↑ HalC ↓↑ O

Microwaves s. under Bu_4NBr or Bu_4NI [\\\\]

Cesium fluoride/polymer-based pentaethylene glycol/tert-amyl alcohol ←

Heterogeneous nucleophilic fluorination under weakly basic conditions ←

Fluorides from mesylates or tosylates s. *78*, 228

Potassium chloride or bromide s. under $Pd_2(dba)_3$ *KCl or KBr*

Phenylcopper/cobalt(II) acetoacetonate/4-fluorostyrene/tetra-n-butylammonium iodide ←

Ar. iodides from aryl sulfonates $ArOSO_2Ar' \rightarrow [ArCu] \rightarrow ArI$

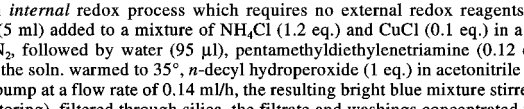
via arylcopper compds. s. *78*, 438

Copper(I) chloride/ammonium chloride or diisopropylamine hydrochloride/ N,N′,N″,N‴-pentamethyldiethylenetriamine/acetic acid ←

1,4-Chlorohydrins from hydroperoxides ←

via copper-catalyzed 1,5-hydrogen atom transfer

225.



Remote radical chlorination of alkyl hydroperoxides has been effected under copper catalysis, based on an *internal* redox process which requires no external redox reagents. **E:** Degassed acetonitrile (5 ml) added to a mixture of NH_4Cl (1.2 eq.) and CuCl (0.1 eq.) in a septum-sealed vial under N_2, followed by water (95 µl), pentamethyldiethylenetriamine (0.12 eq.) and acetic acid (4 eq.), the soln. warmed to 35°, *n*-decyl hydroperoxide (1 eq.) in acetonitrile (4.5 ml) added via syringe pump at a flow rate of 0.14 ml/h, the resulting bright blue mixture stirred for 1 d (with HPLC monitoring), filtered through silica, the filtrate and washings concentrated under vacuum, and worked up with purification by flash chromatography on silica → 4-chlorodecanol. Y 41%. The procedure is simple, inexpensive, eco-friendly and applicable to a wide range of primary, secondary and tertiary alkyl hydroperoxides (diisopropylamine hydrochloride being preferred as chlorine source for secondary substrates, while ascorbic acid was required as an added reducing agent for the more sluggish tertiary derivs.). Reaction is presumed to involve initial copper(I)-mediated reduction of the hydroperoxide to yield an oxyl radical (or copper(III) alkoxide), which abstracts a hydrogen atom regioselectively from the alkyl chain with generation of a copper(II) chloride for the ensuing radical chlorination. Controlled addition of water is important for reproducibility and acetic acid is necessary to facilitate regeneration of copper(I) chloride from copper(I) hydroxide to complete the cycle. There was no significant diastereoselectivity with a 3-methoxyhydroperoxide. F.e. (twelve; Y 33-74%) and with retention of ester groups s. R. Kundu, Z.T. Ball, Org. Lett. *2010*, *12* (11), 2460-3 [DOI: 10.1021/ol100472t].

Triisobutylaluminum s. under $Pd_2(dba)_3$ *$i\text{-}Bu_3Al$*

1-Butyl-3-methylimidazolium tetrachloroindate s. under Bu_4NBr or Bu_4NI *[bmim][$InCl_4$]*

4-Fluorostyrene s. under PhCu *$ArCH{=}CH_2$*

Polymer-based pentaethylene glycol/tert-amyl alcohol s. under CsF ←

2-Butanone s. under $Pd_2(dba)_3$ *EtC(O)Me*

2-Di-tert-butylphosphino-2′,4′,6′-triisopropyl-3,6-dimethoxybiphenyl s. under $Pd_2(dba)_3$ ←

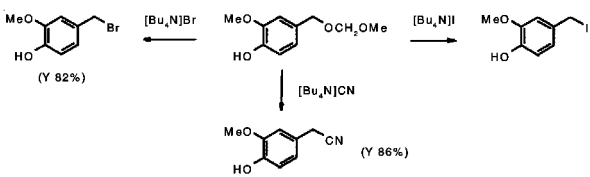
Ammonium chloride or diisopropylamine hydrochloride s. under CuCl ←

Tetra-n-butylammonium iodide s.a. under PhCu *Bu_4NI*

Tetra-n-butylammonium bromide or iodide/1-butyl-3-methylimidazolium tetrachloroindate/ microwaves ←

Bromides or iodides from (m)ethoxymethyl ethers with a Lewis acidic ionic liquid as catalyst under microwave irradiation $OCH_2OR \rightarrow Br$ or I

226.



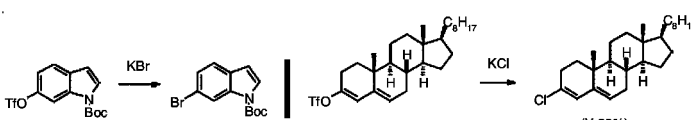
A mixture of startg. benzyl methoxymethyl ether (1 mmol), tetra-*n*-butylammonium iodide (2 eq.) and 1-butyl-3-methylimidazolium tetrachloroindate (0.28 eq.) subjected to microwave irradiation (170 W; 135-140°) for 4.5 min → product. Y 86% (83% from the ethoxymethyl ether). This method is experimentally simple, avoiding toxic organic solvents and an inert atmosphere, and is applicable to a wide range of structurally diverse benzylic, allylic and aliphatic methoxy- or ethoxy-methyl ethers bearing electron-withdrawing or -donating groups (chloro, bromo, nitro, methoxy, hydroxy or benzyloxy). Primary methoxymethyl ethers reacted selectively in the presence of secondary, tertiary or phenolic ones. The ionic liquid may be reused four times without significant loss of activity. It is water-stable and more active than $InCl_3$, [bmim][$AlCl_4$] or [bmim][$FeCl_4$]. F.e. (bromides: nineteen, Y 77-89%; iodides: eighteen, Y 78-92%), **also nitriles** with [Bu_4N]CN (nineteen, Y 80-92%), s. A. Mirjafari, I. Mohammadpoor-Baltork, M. Moghadam, S. Tangestaninejad, V. Mirkhani, A.R. Khosropour, Tetrahedron Lett. *2010, 51* (25), 3274-6 [DOI: 10.1016/j.tetlet.2010.04.056].

Cobalt(II) acetoacetonate s. under PhCu *$Co(acac)_2$*

Tris(dibenzylideneacetone)dipalladium/2-di-tert-butylphosphino-2′,4′,6′-triisopropyl-3,6-dimethoxybiphenyl/potassium chloride or bromide/2-butanone/triisobutylaluminum ←

Unsatd. bromides/chlorides from triflates under palladium(0) catalysis OTf → Hal

227.



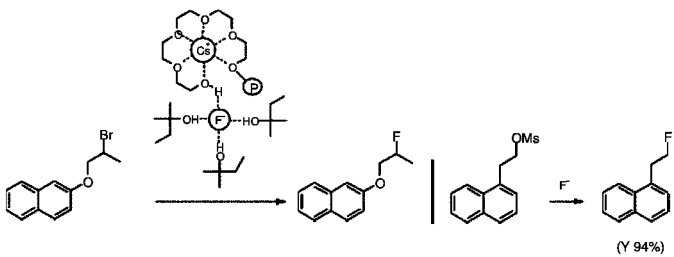
Ar. bromides. 2-Butanone (1.5 eq.) and toluene (6-8 ml) added to a mixture of $Pd_2(dba)_3$ (1.5 mol%), *t*-BuBrettPhos (3.75 mol%), KBr (1.5 eq.), PEG-3400 (120 mg) and N-*tert*-butoxycarbonylindol-6-yl triflate (1 mmol) in a screw-cap tube under argon, the mixture stirred for 1 min, *i*-Bu_3Al (1.5 eq.) in toluene (1.5 ml) added dropwise, the mixture stirred vigorously at 100° for 20-24 h, cooled to room temp., diluted with ether, filtered through silica, concentrated *in vacuo*, and purified by flash chromatography on silica → *tert*-butyl 6-bromo-1*H*-indole-1-carboxylate. Y 76%. This novel conversion requires the use of sterically-hindered phosphine ligands and a suitable additive to scavenge for generated KOTf (found, surprisingly, to inhibit the conversion). Dialkylaluminum alkoxides (generated *in situ* from ketones and trialkylaluminum) were effective scavengers and also suppressed the formation of C-C coupled by-products obtained with trialkylaluminum alone. The conversion was successful for the formation of bromides (seventeen examples; Y 63-92%) and chlorides with KCl (six examples; Y 65-94%) from a range of electron-diverse vinyl/aryl (incl. steroid) and hetaryl (indole, quinoline, benzothiazole) triflates.

F.e. and optimization s. X. Shen, A.M. Hyde, S.L. Buchwald, J. Am. Chem. Soc. *2010, 132* (40), 14076-8 [DOI: 10.1021/ja107481a].

Halogen ↑ HalC ↓↑ Hal

Cesium fluoride/polymer-based pentaethylene glycol/tert-amyl alcohol ←
Heterogeneous nucleophilic fluorination under weakly basic conditions ←

228.

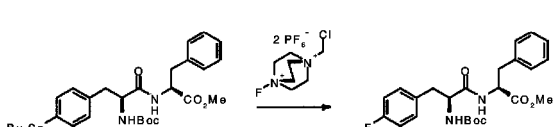


The nucleophilicity of alkali metal fluorides is significantly enhanced by coordination of the cation to Merrifield resin-supported pentaethylene glycol in the presence of a tertiary alcohol for attenuating basicity through hydrogen bonding, thereby delivering a more 'flexible' source of fluoride ion, notably suitable for reactions with base-sensitive substrates. **E: Replacement of halogen by fluorine**. CsF (3 eq.) added to a mixture of 2-(2-bromopropoxy)naphthalene (1 mmol) and polymer-supported pentaethylene glycol (PSpentaEG ; 1 eq.) in *tert*-amyl alcohol (4 ml), the mixture stirred for 2.5 h at 100°, filtered to remove PSpentaEG, and the filtrate subjected to flash column chromatography → 2-(2-fluoropropoxy)naphthalene. Y 80%. Bromine and iodine are replaced at both primary and more challenging *secondary* sites where side reactions, such as dehydrohalogenation, are normally problematic under basic conditions (four examples; Y 80-92%). The system also provides an interesting protic microenvironment for reaction, and the polymer-based reagent is readily recovered by filtration for repeated use without loss of activity. Comparisons were made with less efficient routes using non-immobilized polyethylene glycols or crown ethers. **Fluorides** were also obtained efficiently **from mesylates or tosylates** under the same conditions (six examples; Y 87-96%). F.e.s. H. Jadhav, S.H. Jang, H.-J. Jeong, S.T. Lim, M.-H. Sohn, D.Y. Chi, D.W. Kim, Org. Lett. *2010, 12* (17), 3740-3 [DOI: 10.1021/ol101485n].

Remaining Elements ↑ HalC ↓↑ Rem

N′-Chloromethyl-N-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate)/ silver(I) oxide/sodium hydrogen carbonate/sodium triflate ←
Ar. fluorides from arylstannanes $SnR_3 \rightarrow F$
Silver(I)-catalyzed substitution

229.



under mild conditions. Ag_2O (5 mol%), $NaHCO_3$ (2 eq.), NaOTf (1 eq.) and F-TEDA·$2PF_6$ (1.5 eq.) added to a soln. of methyl N-Boc-4-(tributylstannyl)-*L*-phenylalanyl-*L*-phenylalaninate (2 mmol) in acetone (40 ml) at 23°, the mixture stirred at 65° in a sealed vial for 5 h, cooled to 23°, diluted

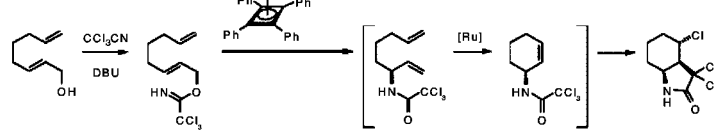
with methylene chloride, filtered through Celite, concentrated *in vacuo*, and purified by chromatography on silica → methyl N-Boc-4-fluoro-*L*-phenylalanyl-*L*-phenylalaninate. Y 92%. The novel use of inexpensive Ag_2O to promote late stage fluorination of arenes was applicable, on a gram scale, to peptide, steroid, carbohydrate and macrocyclic substrates (thirteen examples; Y 65-92%) in the presence of ester, carbamate, alcohol, ether and alkene functionality. Addition of methanol was required in some cases to minimize protodestannylation (<10% in all examples). Optimized conditions required the use of $NaHCO_3$ as base, to remove acids formed during the reaction and facilitate work-up by precipitation of Bu_3SnHCO_3, and the addition of stoichiometric NaOTf (presumed to assist in Ag(I) solubilization). The reaction failed in the presence of thioethers and tert. amines containing β-hydrogens (due to N-fluorination and HF elimination) and carboxylic acids were problematic due to formation of less active silver carboxylates. F.e. and substrate prepn. s. P. Tang, T. Furuya, T. Ritter, J. Am. Chem. Soc. *2010*, *132* (34), 12150-4 [DOI: 10.1021/ja105834t].

Carbon ↑ HalC ↓↑ C

N-Iodosuccinimide/boron fluoride *NIS/BF_3*
4-Iodopyrazole-1-carboxylic acid esters
from 2-acetylenehydrazodicarboxylic acid esters s. *35*, 351s*78*

Chiral cobaltocene-functionalized palladacyclic Δ²-oxazoline complex/ benzylidene(dichloro)bis(tricyclohexylphosphine)ruthenium(II) ←
4,5-Condensed 3,3,4-α-trichloro-2-pyrrolidones from 2,n-dienol trichloroacetimidates via asym. Overman rearrangement-ring-closing metathesis-intramolecular Kharasch reaction

230.



The startg. dienol trichloroacetimidate [prepared, crude, from (2E)-octa-2,7-dien-1-ol (0.8 mmol) by routine DBU-mediated coupling with trichloroacetonitrile in methylene chloride] in toluene (10 ml) transferred to a Schlenk tube containing the chiral cyclopalladated Δ²-oxazoline complex (3 mol%) for 36 h at 38°, further catalyst (3 mol%) added and stirred at the same temp. for 72 h, followed by a third portion (3 mol%) with stirring for another 24 h, Grubbs 1st generation catalyst added, the solvent degassed, stirred for 1 h at room temp., 4 Å molecular sieves added, the mixture sealed under argon, stirred at 155° for 3 h, filtered, and worked up with chromatographic purification → (1S,5S,6S)-5,7,7-trichloro-8-oxo-9-azabicyclo[4.3.0]nonane. Y 70% (from the startg. dienol; e.e. 89%). Three contiguous chiral centers are generated in one pot (three examples; Y 51-70%; e.c. 89-94%). F.e. and diastereoselective process [with $PdCl_2(MeCN)_2$] for preparing racemic [3.3.0]-, [4.3.0]- and [5.3.0]-fused analogs (five examples; Y 39-87%) [heteroatom-tethered dienol trichloroacetimidates affording higher yields via *thermal* Overman rearrangement] s. F.I. McGonagle, L. Brown, A. Cooke, A. Sutherland, Org. Biomol. Chem. *2010*, *8* (15), 3418-25 [DOI: 10.1039/c004695g].

Formation of S-S Bond

Exchange ↓↑

Hydrogen ↑ SS ↓↑ H

Silver-titanium dioxide/montmorillonite/air/irradiation ←
Sym. disulfides from mercaptans 2 RSH → $(RS)_2$
s. *47*, 468s*76*; sym. bis(*o*-aminoaryl) disulfides from *o*-aminomercaptans with Ag-TiO_2 on montmorillonite K10 under photocatalysis (UV or solar) in air, also benzimidazoles from *o*-diamines and prim. alcohols (cf. *68*, 174s*77*), s. K. Selvam, M. Annadhasan, R. Velmurugan, M. Swaminathan, Bull. Chem. Soc. Jpn. *2010, 83* (7), 831-7 [DOI: 10.1246/bcsj.20090319]; with a novel manganese(III) Schiff base complex based on the quadridentate ligand, bis(2-hydroxyphenyl)phthaldiimine under O_2 at room temp. s. M. Montazerozohori, L.Z. Fradombe, Phosphorus, Sulfur Silicon Relat. Elem. *2010, 185* (3), 509-15 [DOI: 10.1080/10426500902839830]; **unsym. disulfides from two different mercaptans** (cf. *43*, 445), one-pot conversion with 1-chlorobenzotriazole/benzotriazole via sulfenyl chlorides and 1-(organothio)benzotriazoles, general method, s. N. Stellenboom, R. Hunter, M.R. Caira, Tetrahedron *2010, 66* (17), 3228-41 [DOI: 10.1016/j.tet.2010.02.077]; application to the formation of unsym. glycosyl disulfides s. N. Stellenboom, R. Hunter, M.R. Caira, L. Szilágyi, Tetrahedron Lett. *2010, 51* (40), 5309-12 [DOI: 10.1016/j.tetlet.2010.07.176].

1-Butyl-3-methylimidazolium salts s. under Air *[bmim]⁺*

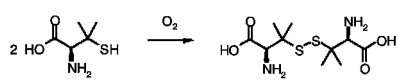
1-Chlorobenzotriazole/benzotriazole *BtCl/BtH*
Disulfides from two different mercaptan molecules s. *47*, 468s*78* RSH + HSR′ → RSSR′

Titanium dioxide s. under Ag *TiO_2*

Oxygen or Air s.a. under Ag-TiO_2, Nanophase manganese(VII) oxide-coated clay, Manganese(III) Schiff base complex and Iron metal-organic frameworks *O_2 or air*

Air/1-butyl-3-methylimidazolium salts/sodium carbonate *air/[bmim]⁺/Na_2CO_3*
Sym. disulfides from mercaptans 2 RSH → $(RS)_2$
Metal-free aerobic coupling

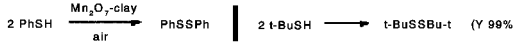
231.



under mild conditions. A mixture of penicillamine (1 mmol) and Na_2CO_3 (2 eq.) in [bmim]BF_4 (1.5 ml) stirred in an open Schlenk tube while air bubbled through the mixture for 30 min, extracted with methylene chloride, washed with water, and recrystallized from water → penicillamine disulfide. Y 88%. This efficient and experimentally simple method can be carried out on a multigram scale, utilizes inexpensive base, and is general and rapid for electron-diverse (het)ar. and aliphatic thiols, affording symmetrical disulfides within 30 min at room temp. (fourteen examples; Y 83-99%). A number of 1-butyl-3-methylimidazolium salts were effective in this reaction, with the marginally more effective fluoroborate salt being recycled up to six times without loss in reactivity. F.e. and optimization s. D. Singh, F.Z. Galetto, L.C. Soares, O.E.D. Rodrigues, A.L. Braga, Eur. J. Org. Chem. *2010* (14), 2661-5 [DOI: 10.1002/ejoc.201000126].

Nanophase manganese(VII) oxide-coated clay/air ←
Sym. disulfides from mercaptans under heterogeneous aerobic coupling 2 RSH → $(RS)_2$

232.

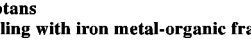


The startg. mercaptan in chloroform treated with excess nanophase manganese(VII) oxide-coated clay (1:2 molar ratio of mercaptan/Mn, based on a Mn content of 7%) at room temp. for 2 h in the presence of air, the solid catalyst filtered off, the filtrate concentrated under reduced pressure, and worked up with chromatographic purification → product. Y 99% (pure). The procedure is facile, convenient, mild and rapid; it also avoids handling activating agents, proceeds with minimal accumulation of waste, and is generally applicable in quantitative yield to a range of aromatic thiols [substituted by electron-withdrawing (NO_2) or -donating (MeO) groups], as well as benzyl thiols and aliphatic thiols [incl. trityl thiol for which the yield of dityrityl disulfide (60%) is the highest yet reported]. The catalyst is stable, inexpensive and readily recyclable (multiple times), suggesting that reaction involves catalysis on the surface of the clay. Toluene was also an effective solvent, as was water for water-soluble mercaptans. F.e. (eleven), incl. formation of a cyclic disulfide from a dithiol, and preparation of the catalyst s. S.R. Gondi, D.Y. Son, E.R. Biehl, R.K. Vempati, Phosphorus, Sulfur Silicon Relat. Elem. *2010*, *185* (1), 34-9 [DOI: 10.1080/10426500903147175].

Manganese(III) Schiff base complex/oxygen *[Mn(III)]/O_2*
Sym. disulfides from mercaptans s. *47*, 468s*78*

Iron metal-organic frameworks/oxygen *Fe(BTC)/O_2*
Sym. disulfides from mercaptans
Heterogeneous aerobic coupling with iron metal-organic frameworks

233.



The iron metal-organic framework, Fe(BTC) - a commercially available solid, formed as a dual mesoporous cage system with microporous windows, comprising trimers of iron octahedra with benzene-1,3,5-tricarboxylate (BTC) moieties - is an excellent, environmentally friendly redox catalyst for the heterogeneous oxidation of mercaptans to disulfides **under mild conditions** *without* over-oxidation to oxygenated by-products. **E:** Fe(BTC) (100 mg; 840 m^2g^{-1} BET specific surface area) added to a stirred soln. of thiophenol (2.27 mmol) *in acetonitrile* (4 ml), the temp. raised to 70°, the system purged with O_2 through a balloon, allowed to react for 1 h, filtered, and the filtrate (and washings) evaporated → diphenyl disulfide. Y 91%. The procedure is applicable in high yield to a range of aromatic mercaptans (incl. *o*- and *p*-subst. derivs.), heteroaromatic analogs, cyclohexyl and hexyl mercaptans (nine examples; Y 72-91%), but yields were moderate with benzyl mercaptan (61%) and thioacetic acid (55%), while thiobenzoic acid decomposed. 1,5-Pentanedithiol gave a mixture of cyclic products. The catalyst is simply retrieved by filtration and was reused without loss of activity. Other metal-organic frameworks based on copper and aluminum showed poor catalytic activity. Reaction is presumed to involve coupling of generated thiyl radicals with re-oxidation of iron to the native state with oxygen. F.e. and solvent effect s. A. Dhakshinamoorthy, M. Alvaro, H. Garcia, Chem. Commun. *2010*, *46* (35), 6476-8 [DOI: 10.1039/c0cc02210a].

Elimination ⇑

Hydrogen ↑ SS ⇑ H

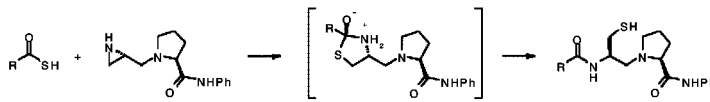
Nanophase manganese(VII) oxide-coated clay/air ←
Cyclic disulfides from dithiols under heterogeneous aerobic coupling s. *78*, 232 ○

Formation of S-C Bond

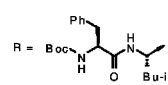
Uptake ⇓

Addition to Nitrogen and Carbon SC ⇓ NC

Without additional reagents *w.a.r.*
Peptidomimetic ligation C
with peptidyl thiolic acids and N-(aziridin-2-ylmethyl)-α-aminocarboxylic acid amides



234.



The concept of generating **2-acylaminomercaptans from thiolic acids and aziridines** has been adapted in a new peptide ligation to give **reduced cysteine-linked peptides**. **E:** A 0.1 *M* soln. of the startg. aziridine-terminated amino-acid anilide in ethanol stirred at room temp. under N_2, the startg. C-terminal peptidyl thiolic acid (1 eq.) added, stirred overnight until ESI MS showed reaction complete, ethanol removed under reduced pressure, and the newly ligated peptide purified using preparative HPLC → Boc-Phe-Leu-Cys-red-Pro-anilide. Y 86%. The procedure is highly efficient at the micromolar level and unaffected by competing addition of exogenous thiols, such as glutathione. It is also regioselective, devoid of epimerization and double acylation (as takes place with thiobenzoic acid), uncomplicated by aza-Payne rearrangement, and can be performed with unprotected acid-terminated peptides. Mechanistically, reaction is presumed to involve initial regiospecific aziridine ring opening with the thioacid, followed by trapping of the adjacent amino groups and S→N-acyl migration via the intermediate thiazolidine. F.e. (eleven; Y 51-100%) s. N. Assem, A. Natarajan, A.K. Yudin, J. Am. Chem. Soc. *2010, 132* (32), 10986-7 [DOI: 10.1021/ja104488d].

Addition to Carbon-Carbon Bonds SC ⇓ CC

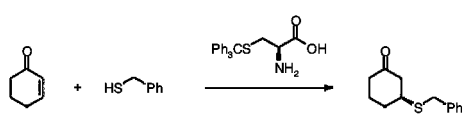
Without additional reagents *w.a.r.*
Thia-Michael addition C=C → CHC(SR)
uncatalyzed conversion s. *47*, 487*s75*; Michael addition of thioacetic acid without solvent s. S. Sobhani, S. Rezazadeh, Phosphorus, Sulfur Silicon Relat. Elem. *2010, 185* (10), 2076-84 [DOI: 10.1080/10426500903496713]; eco-friendly addition of mercaptans to chalcones in a phosphonium ionic liquid s. S.R. Sarda, W.N. Jadhav, A.S. Shete, K.B. Dhopte, S.M. Sadawarte, P.J. Gadge, R.P. Pawar, Synth. Commun. *2010, 40* (14), 2178-84 [DOI: 10.1080/00397910903221050]; biomimetic addition of thiophenols to enones using a disubst. benzoate-bridged dinuclear bis(urea)nickel(II) complex s. W.-Z. Lee, H.-S. Tseng, T.-L. Wang, H.-L. Tsai, T.-S. Kuo, Organometallics *2010*, *29* (13), 2874-81 [DOI: 10.1021/om100103u]; *reductive procedure* by addition of disulfides to enones and enoates with Rongalite dihydrate/K_2CO_3 in DMF cf. W. Guo, G. Lv, J. Chen, W. Gao, J. Ding, H. Wu, Tetrahedron *2010, 66* (13), 2297-300 [DOI: 10.1016/j.tet.2010.02.001].

Lanthanum(III) triflate/chiral bis(N-oxides) *[La(III)*]*
Squaramide-based 9-deoxyquinines ←
Chiral α-prim-aminocarboxylic acids ←
9-Thioureido-9-deoxyquinines ←
Asym. thia-Michael addition C=C → CHC(SR)

organocatalyzed asym. Michael addition s. *75,* 223; with a *bifunctional* squaramide-based 9-deoxyquinine s. L. Dai, S.-X. Wang, F.-E. Chen, Adv. Synth. Catal. *2010, 352* (13), 2137-41 [DOI: 10.1002/adsc.201000334]; study of self-aggregation of chiral bifunctional organocatalysts, incl. squaramide-based 9-deoxyquinines and 9-thioureido-9-deoxyquinines, effect of concentration on enantioselectivity, s. H.B. Jang, H.S. Rho, J.S. Oh, E.H. Nam, S.E. Park, H.Y. Bae, C.E. Song, Org. Biomol. Chem. *2010, 8* (17), 3918-22 [DOI: 10.1039/c0ob00047g]; asym. Michael addition of thioglycolate to chalcones with $La(OTf)_3$ and a chiral bis(N-oxide) for high enantioselectivity at low catalyst loading (1 mol%) and a remarkable *asym. amplification* (using 2 mol% of the catalyst *with 2% e.e.*) s. Y. Hui, J. Jiang, W. Wang, W. Chen, Y. Cai, L. Lin, X. Liu, X. Feng, Angew. Chem., Int. Ed. *2010, 49* (25), 4290-3 [DOI: 10.1002/anie.201000105].

S-Trityl-L-cysteine/dimethyl sulfoxide ←
Organocatalyzed asym. thia-Michael addition of benzyl mercaptans to cyclic α,β-ethyleneketones

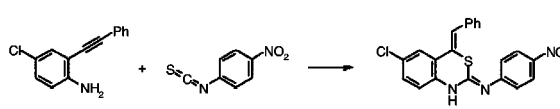
235.



Chiral β-(benzylthio)ketones. A soln. of cyclohex-2-enone (0.5 mmol), benzyl mercaptan (1.1 eq.), DMSO (50 mol%) and S-trityl-L-cysteine (10 mol%) in methylene chloride (1 ml) heated at 37° for 72 h → (S)-3-(benzylmercapto)cyclohexanone. Y 85% (e.e. 55%). Cycloheptenone afforded an 81% yield (e.e. 23%) (Y 82%; e.e. 30% after 7 days), while cyclopentenone gave only a 44% yield (e.e. 24%). Good yields were obtained from the reaction of cyclohexenone with 4-chloro- and 4-methoxy-benzyl mercaptan (Y 81% for both; e.e. 27% and 50%, respectively), with the α-subst. benzhydryl and trityl mercaptan affording yields of 86% and 69% (e.e. 39% and 8%), respectively. Although enantioselectivity is only modest, it is the highest yet reported for such an organocatalyzed thia-Michael addition. F.e., optimization, and a suggested mechanism, (involving initial reaction between enone and amino acid to afford a chiral α,β-unsatd. imine, which acts as Michael acceptor, followed by hydrolysis with adventitious water to regenerate the catalyst; DMSO acts as a weak Lewis base, helping to dissolve the amino acid and activate the mercaptan), s. M. Yoshida, Y. Ohno, S. Hara, Tetrahedron Lett. *2010, 51* (39), 5134-6 [DOI: 10.1016/j.tetlet.2010.07.089].

Silica gel *SiO_2*
4-Alkylidene-2-imino-2,4-dihydro-1*H*-3,1-benzothiazines from *o*-acetyleneamines and isothiocyanates under heterogeneous catalysis in the absence of solvent

236.



in one pot. A mixture of 4-chloro-2-phenylethynylaniline (0.2 mmol), 4-nitrophenyl isothiocyanate (1.5 eq.) and silica gel (pore size 50-70 μm; 200 mg) stirred at 80° until reaction complete (TLC; 24 h), washed with ethyl acetate, concentrated *in vacuo*, and purified by chromatography on silica → N′-(4-nitrophenyl)-4-benzylidene-6-chloro-1*H*-benzo[*d*][1,3]thiazin-2(4*H*)-imine. Y 92%. This experimentally simple, atom-efficient, solvent- and metal-free tandem cyclization-cycloaddition was effective for aryl-terminated *o*-acetyleneanilines reacting with electron-diverse ar.

and aliphatic isothiocyanates (fifteen examples; Y 63-98%; a butyl-terminated acetyleneaniline gave 27%), but 4-dimethylaminophenyl isothiocyanate did not apparently take part in the reaction as only indole derivs. were isolated (no details given). After washing and drying (80°) the silica gel was reused with only minimal loss in yield (from 98% to 89% on the 4th cycle). Structures were confirmed by X-ray analysis in one case. F.e.s. Q. Ding, B. Cao, Z. Zong, Y. Peng, J. Comb. Chem. *2010*, *12* (3), 370-3 [DOI: 10.1021/cc100012a].

Phosphonium ionic liquids ←
Thia-Michael addition in ionic liquids s. *47*, 487s*78* C=C → CHC(SR)

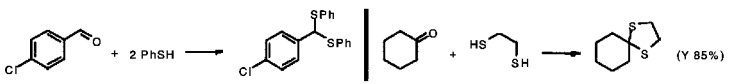
Sodium hydroxymethylsulfinate/potassium carbonate $HOCH_2S(O)ONa/K_2CO_3$
Reductive thia-Michael addition s. *47*, 487s*78*

Benzoate-bridged dinuclear bis(urea)nickel(II) complex *[Ni(II)]*
Thia-Michael addition of arylmercaptans s. *47*, 487s*78*

Exchange ⇓↑

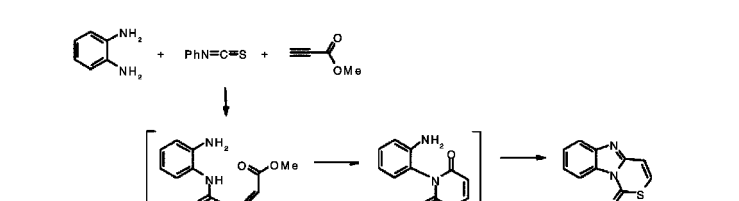
Oxygen ↑ SC ⇓↑ O

Without additional reagents *w.a.r.*
Mercaptals from oxo compds. CO → $C(SR)_2$
Uncatalyzed thioacetalation in glycerol

237. 

Benzenethiol (2 eq.) added to a mixture of 4-chlorobenzaldehyde (1 mmol) and glycerol (3 ml), the mixture stirred at 90° for 6 h, extracted with hexanes, concentrated *in vacuo*, and purified chromatographically → 4-bis(phenylthio)methyl-1-chlorobenzene. Y 96%. This efficient thioacetalation uses an inexpensive and recyclable solvent, and appears general in scope for electron-diverse (het)ar. and alkyl aldehydes and ketones, using benzenethiol or 1,2-ethanedithiol as sulfur component (seventeen examples; Y 65-96%; 4-dimethylaminobenzaldehyde gave 50%). In a competitive experiment between benzaldehyde and acetophenone, the ketone-derived thioacetal was the major product (Y 96%; 97:3). The solvent may be recycled 5 times without significant reduction in yield. F.e.s. G. Perin, L.G. Mello, C.S. Radatz, L. Savegnago, D. Alves, R.G. Jacob, E.J. Lenardão, Tetrahedron Lett. *2010*, *51* (33), 4354-6 [DOI: 10.1016/j.tetlet.2010.06.049].

3-Component synthesis of 1-imino-1*H*-[1,3]thiazino[3,4-*a*]benzimidazoles from *o*-diamines, isothiocyanates and methyl propiolate ○

238. 

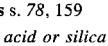
Phenyl isothiocyanate (1 mmol) added with stirring to a soln. of *o*-phenylenediamine (1 mmol) in methylene chloride (2 ml), after 15 min methyl propiolate (1 mmol) in toluene (5 ml) added, stirring continued under reflux for ca. 10 h, the solvent removed under reduced pressure, and the

residue worked up with crystallization from methylene chloride → product. Y 70%. The procedure is simple, mild, non-catalytic, based on readily accessible substrates, and efficient for the coupling of a range of aryl isothiocyanates with *o*-phenylenediamines (six examples; Y 60-70%). It is not, however, regioselective, as reaction of 4-methyl-1,2-benzenediamine with 2- and 4-methylphenyl isothiocyanate or 4-fluorophenyl isothiocyanate gave inseparable mixtures of isomers. The proposed mechanism of the conversion, involving formation of four carbon-heteroatom bonds in one operation, is outlined. F.e.s. A. Alizadeh, Z. Noaparast, H. Sabahnoo, N. Zohreh, Synlett *2010* (10), 1469-72 [DOI: 10.1055/s-0029-1219934].

Microwaves s. under Aluminum-containing helical mesoporous silica, Polyethylene glycol and Silica-sulfuric acid [\\\\]

Potassium carbonate K_2CO_3
Thiolic acid esters from carboxylic acid anhydrides $(RCO)_2O \rightarrow RC(O)SR'$
and mercaptans s. *3,* 569s*78*

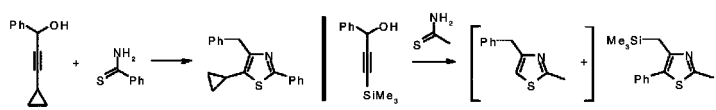
Potassium carbonate/tetra-n-butylammonium iodide K_2CO_3/Bu_4NI
S-Benzylation with soluble oligomeric benzyl phosphates s. *78,* 159 $SH \rightarrow SCH_2Ar$

Ammonium thiocyanate/1-hydroxyethane-1,1-diphosphonic acid or silica chloride ←
Thiiranes from epoxides  →
s. *52,* 214s*75*; with NH_4SCN and etidronic acid as catalyst s. L. Wu, Y. Wang, F. Yan, C. Yang, Bull. Korean Chem. Soc. *2010, 31* (5), 1419-20 [DOI: 10.5012/bkcs.2010.31.5.1419]; with silica chloride as catalyst in the absence of solvent with a simple work-up s. L. Wu, L. Yang, L. Fang, C. Yang, F. Yan, Phosphorus, Sulfur Silicon Relat. Elem. *2010, 185* (10), 2159-64 [DOI: 10.1080/10426500903544298]; O-carbamyl-2,3-sulfidoalcohols from 2,3-epoxyalcohols with N,N-dimethylthiocarbamyl choride/NaH, inversion of configuration, s. P. Kalicki, M. Karchier, K. Michalak, J. Wicha, J. Org. Chem. *2010, 75* (15), 5388-91 [DOI: 10.1021/jo101000u].

Copper/acetic acid/air *Cu/AcOH/air*
Benzothiazoles from bis(*o*-aminoaryl) disulfides and aldehydes s. *19,* 674s*78* ○

Copper(II) bis(dodecyl sulfate) $Cu(OSO_2OC_{12}H_{25})_2$
Mecaptals from oxo compds. $CO \rightarrow C(SR)_2$
with $AlCl_3$ cf. *8,* 667s*36*; in water with copper(II) bis(dodecyl sulfate) as a reusable Lewis acid/surfactant, also mercaptals from acetals, s. S.-S. Weng, S.-C. Chang, T.-H. Chang, J.-P. Chyn, S.-W. Lee, C.-A. Lin, F.-k. Chen, Synthesis *2010* (9), 1493-9 [DOI: 10.1055/s-0029-1218693]; dithioacetalation, monothioacetalation and acetalation with recyclable 1-carbomethoxymethyl-3-methylimidazolium fluoroborate as catalyst in THF (cf. *60,* 194s*76*) s. L. Myles, R. Gore, M. Špulák, N. Gathergood, S.J. Connon, Green Chem. *2010, 12* (7), 1157-62 [DOI: 10.1039/c003301d]; cyclic mercaptals (1,3-dithianes and 1,3-dithiolanes) from aldehydes with retention of ketones under mild conditions with 1,3-dibromo-5,5-dimethylhydantoin, also reverse reaction (OCHS) with the same reagent (cf. *28,* 182s*36*), s. H. Veisi, M. Amiri, A.H. Hamidian, J. Malakootikhah, L. Fatolahi, A. Faraji, A. Sedrpoushan, B. Maleki, S.G. Saremi, M. Noroozi, F. Bahadoori, S. Veisi, Phosphorus, Sulfur Silicon Relat. Elem. *2010, 185* (4), 689-96 [DOI: 10.1080/10426500902917669].

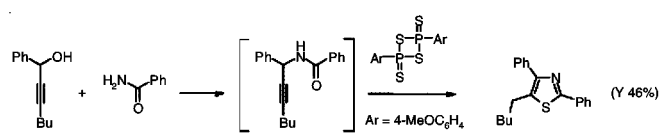
Silver(I) triflate *AgOTf*
Thiazoles from 2-acetylenealcohols and carboxylic acid thioamides or amides ○

239. 

(24:76; Y 83%)

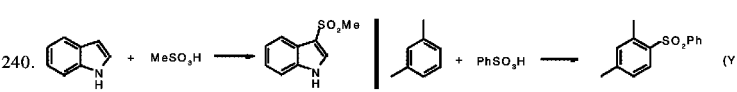
1-Cyclopropyl-3-phenylprop-1-yn-3-ol (0.5 mmol), benzenethioamide (1.2 eq.), chlorobenzene (2 ml) and AgOTf (10 mol%) added sequentially to a flask, the mixture stirred under reflux until reaction complete (TLC; 0.3 h), concentrated *in vacuo*, and purified by chromatography on silica → 4-benzyl-5-cyclopropyl-2-phenylthiazole. Y 89%. A series of sec. and tert. terminal/internal

propargylic alcohols were cyclized via Lewis acid catalysis under experimentally simple conditions with electron-diverse ar. and aliphatic thioamides, apparently via an allenyl cation intermediate (cf. propargylic cation), to afford unexpected di- and tri-subst. thiazoles exclusively, with broad functional group tolerance (alkene, halo, nitro, ether, ester, cyclopropyl). Highest yields were obtained for substrates carrying one or more electron-diverse aromatic groups at the propargylic position (twenty-three examples; Y 68-95%) with yields reduced somewhat (two examples; Y 42%, 58%) for dialkyl propargylic substrates. Sec. propargylic alcohols carrying terminal H- or -$SiMe_3$, afforded the isomeric thiazoles (via the propargylic cation) as major products in most cases (five examples; Y 72-87%; selectivity 71-97%) with $SiMe_3$ groups directly attached to the thiazole ring lost during work-up. In a final development, sec. propargylic alcohols were treated with electron-diverse *benzamides* to generate propargylic amides *in situ*, which were cyclized with Lawesson's reagent in moderate overall yields (41-53%; eight examples).



F.e. and optimization s. X. Gao, Y.-m. Pan, M. Lin, L. Chen, Z.-p. Zhan, Org. Biomol. Chem. *2010, 8* (14), 3259-66 [DOI: 10.1039/c002093]; from thioamides under Brønsted acid catalysis with *p*-TsOH·H_2O at 100° without exclusion of air and moisture s. X. Zhang, W.T. Teo, S. Chan, P.W.H. Chan, J. Org. Chem. *2010, 75* (18), 6290-3 [DOI: 10.1021/jo101292r].

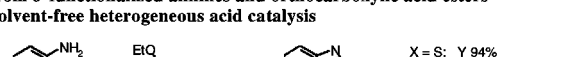
Polystyrene-supported aluminum triflate Ⓟ-*Al(OTf)*$_3$
Chemoselective sulfonation of (het)arenes with sulfonic acids using a supported Lewis acid catalyst H → SO_2R

240. 

under mild solvent-free conditions. Supported catalyst (10 mol%) added to a mixture of indole (1.33 eq.) and methanesulfonic acid (7.5 mmol), the mixture stirred at 40° until reaction complete (TLC/GC; 4.2 h), filtered, diluted with methylene chloride, washed with 10% aq. $NaHCO_3$ and water, concentrated *in vacuo*, and the residue recrystallized → 3-methanesulfonylindole. Y 88%. This apparently general reaction utilizes a stable, inexpensive and recyclable catalyst (up to five times without reduction in yield) for sulfonation of indole and benzene derivs. (incl. weakly deactivated examples) with benzene-, *p*-toluene- and methane-sulfonic acids (thirty-three examples; Y 76-93%). Unsymmetrically subst. arenes gave mixtures of isomers with the *para* or less crowded isomer generally predominating (ca. 90%). F.e. and catalyst prepn. s. K.P. Boroujeni, Bull. Korean Chem. Soc. *2010, 31* (7), 1887-90 [DOI: 10.5012/bkcs.2010.31.7.1887].

Aluminum-containing helical mesoporous silica/microwaves ←
1,3-Oxathiolanes from oxo compds. and 2-mercaptoethanol ○
under heterogeneous catalysis s. *78*, 243

Fluoroboric acid-silica *HBF*$_4$-*SiO*$_2$
Benzazoles from *o*-functionalized anilines and orthocarboxylic acid esters under mild solvent-free heterogeneous acid catalysis

241. 

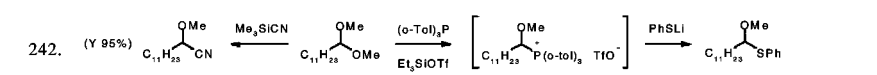
2-Subst. benzothiazoles. A mixture of ethyl orthoacetate (2 eq.), 2-mercaptoaniline (5 mmol) and HBF_4-SiO_2 (2 mol%) stirred at room temp. until reaction complete (TLC; 45 min), diluted

with ethyl acetate, filtered through a plug of cotton, concentrated *in vacuo*, and purified by chromatography on silica → 2-methylbenzothiazole. Y 94%. This simple and efficient procedure uses an inexpensive and recyclable catalyst (up to three cycles without significant reduction in yield) to afford 2-subst. (incl. H) benzothiazoles (five examples; Y 84-97%), **benzoxazoles** (seven examples; Y 92-94%), **benzimidazoles** (six examples; Y 90-94%) and **imidazo[4,5-*b*]pyridines** (three examples; Y 70-85%). The catalyst was removed from the reaction by simple filtration, and reactivated by heating at 80°. In comparison with catalysts previously used in this cyclization, the supported catalyst gave similar (and often superior) results at lower catalyst loadings. F.e., optimization and catalyst prepn. s. A.V. Patil, B.P. Bandgar, S.-H. Lee, Bull. Korean Chem. Soc. *2010, 31* (6), 1719-22 [DOI: 10.5012/bkcs.2010.31.6.1719].

Polyethylene glycol-200 or -400/p-toluenesulfonic acid/microwaves *PEG/TsOH/[\\\\]*
β-Cyclodextrin ←
Benzothiazoles from *o*-aminomercaptans and aldehydes ○

s. *19,* 674s*75*; clean, eco-friendly synthesis of 2-aryl-derivs. under microwave irradiation in PEG-200 or -400 with added TsOH, also from bis(*o*-aminoaryl) disulfides, s. T.G. Deligeorgiev, S. Kaloyanova, A. Vasilev, J.J. Vaquero, Phosphorus, Sulfur Silicon Relat. Elem. *2010, 185* (11), 2292-302 [DOI: 10.1080/10426501003598648]; **in water** with β-cyclodextrin as supramolecular catalyst s. B.S. Londhe, U.R. Pratap, J.R. Mali, R.A. Mane, Bull. Korean Chem. Soc. *2010, 31* (8), 2329-32 [DOI: 10.5012/bkcs.2010.31.8.2329]; with P_2O_5 at room temp. s. S.V. Nalage, S.V. Bhosale, D.S. Bhosale, W.N. Jadhav, Chin. Chem. Lett. *2010, 21* (7), 790-3 [DOI: 10.1016/j.cclet.2010.03.006]; with recyclable silica-sulfuric acid under microwave irradiation without solvent s. K.S. Niralwad, B.B. Shingate, M.S. Shingare, Bull. Korean Chem. Soc. *2010, 31* (4), 981-3 [DOI: 10.5012/bkcs.2010.31.04.981]; synthesis of pyrimidine nucleosides substituted by benzothiazole residues under catalytic oxidation with $RuCl_3$ in [bmim]PF_6 under air s. X. Fan, Y. Wang, Y. He, X. Zhang, J. Wang, Tetrahedron Lett. *2010, 51* (27), 3493-6 [DOI: 10.1016/j.tetlet.2010.04.050]; f. method **from bis(*o*-aminoaryl) disulfides** via a DBU-mediated thiol-disulfide dynamic interchange, and f. syntheses of benzo-condensed N,S-heterocyclics, s. N. Zhu, F. Zhang, G. Liu, J. Comb. Chem. *2010, 12* (4), 531-40 [DOI: 10.1021/cc100042v]; with Cu in acetic acid under air cf. J. Hyvl, J. Srogl, Eur. J. Org. Chem. *2010* (15), 2849-51 [DOI: 10.1002/ejoc.201000174]; **from bis[*o*-(alkylideneamino)aryl] disulfides** with low-valent titanium ($TiCl_4$/Sm) s. D.-Q. Shi, S.-F. Rong, G.-L. Dou, Synth. Commun. *2010, 40* (15), 2302-10 [DOI: 10.1080/00397910903227230].

1-Butyl-3-methylimidazolium hexafluorophosphate s. under $RuCl_3$ *[bmim]PF_6*
1-Carbomethoxymethyl-3-methylimidazolium fluoroborate ←
Mercaptals from oxo compds. or acetals s. *60,* 194s*78* CO or $C(OR)_2$ → $C(SR')_2$
1,3-Dibromo-5,5-dimethylhydantoin ←
Cyclic mercaptals from aldehydes s. *8,* 667s*78* CHO → $CH(SR)_2$
Silica s. under HBF_4 *SiO_2*
Silica chloride s. under NH_4SCN *SiO_2-Cl*
Tri-o-tolylphosphine/triethylsilyl triflate *o-Tol_3P/Et_3SiOTf*
α-Functionalized ethers from acetals via 1-alkoxyphosphonium salts $C(OR)_2$ → C(OR)Nu

242. 

Tri-*o*-tolylphosphine serves as an excellent nucleophile for the generation of reactive 1-alkoxyphosphonium salts from acetals and as a good leaving group for subsequent nucleophilic displacement, affording a variety of α-functionalized ethers in a **one-pot conversion. E: Monothioacetals.** Triethylsilyl triflate (2 eq.) added slowly to a stirred soln. of the startg. acetal (1 eq.) and tri-*o*-tolylphosphine (3 eq.) in dry methylene chloride (0.1 *M*) under N_2 at -5°, the mixture stirred for 0.5 h at the same temp., Li-phenylmercaptide (1.2 eq.) added, stirred at room temp. for 1 h, aq. $NaHCO_3$ added, and the mixture worked up with purification by chromatography on silica gel → (1-methoxydodecyl) phenyl sulfide. Y 97%. The structure and the electronic nature of the phosphine

is critical, tri-*o*-tolylphosphine giving consistently high yields with various nucleophiles (LiSPh, Me_3SiCN, PhMgBr and water), while tri-*m*-tolyl-, tri-*p*-tolyl-, trimesityl-, tri-*n*-butyl-, tri-*o*-methoxyphenyl- and tris[*o*-(trifluoromethyl)phenyl]-phosphine gave poor results for a variety of reasons. Reaction is applicable to both aliphatic and aromatic acetals (the latter requiring addition of ethyldiisopropylamine). F.e. (thirteen; Y 72-99%) s. H. Fujioka, A. Goto, K. Otake, O. Kubo, K. Yahata, Y. Sawama, T. Maegawa, Chem. Commun. *2010*, *46* (22), 3976-8 [DOI: 10.1039/c0cc00170h].

Phosphorus pentoxide P_2O_5

Benzothiazoles from *o*-aminomercaptans and aldehydes s. *19*, 674s*78* ○

1-Hydroxyethane-1,1-diphosphonic acid s. under NH_4SCN $MeC(OH)(PO_3H_2)_2$

Air s. under Cu/AcOH and $RuCl_3$ *air*

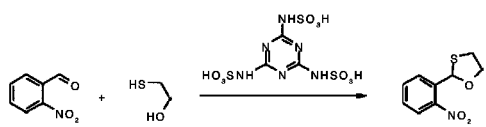
Triethylsilyl triflate s. under Tri-o-tolylphosphine Et_3SiOTf

p-Toluenesulfonic acid s. under Polyethylene glycol *TsOH*

Melamine trisulfonic acid *MTSA*

1,3-Oxathiolanes from aldehydes and 2-mercaptoethanol under heterogeneous catalysis using a novel recyclable sulfamic acid

243.

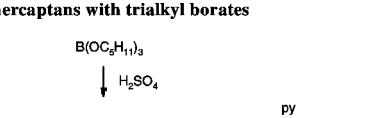


A mixture of 2-nitrobenzaldehyde (1 mmol), 2-mercaptoethanol (1.05 eq.) and melamine trisulfonic acid [MTSA] (3 mol%) in hexane stirred at reflux until reaction complete (TLC; 3 min), concentrated *in vacuo*, dissolved in methylene chloride, filtered, washed with water, concentrated *in vacuo*, and purified by chromatography on silica → 2-(2-nitrophenyl)-1,3-oxathiolane. Y 90%. This efficient thioacetalation utilizes a readily available heterogeneous catalyst and was rapid for electron-poor and neutral benzaldehydes (3-15 min) but somewhat slower (18-35 min) for electron-rich benzaldehydes and aliphatic aldehydes (twelve examples; Y 75-95%). No reaction occurred in the absence of catalyst, while ketones were unreactive under these conditions. The catalyst was used three times without significant reduction in yield and, in comparison with previously used catalysts, generally produced more rapid reaction (4-60 fold) with similar yields at lower catalyst loading. F.e. and catalyst prepn. (from melamine and $ClSO_3H$; Y 87%) s. F. Shirini, J. Albadi, Bull. Korean Chem. Soc. *2010, 31* (5), 1119-20 [DOI: 10.5012/bkcs.2010.31.5.1119]; **from oxo compds.** with Al-containing helical mesoporous silicas under microwave irradiation s. A.I. Carrillo, E. Serrano, R. Luque, J.G. Matínez, Chem. Commun. *2010*, *46* (28), 5163-5 [DOI: 10.1039/c0cc00030b].

Sulfuric acid/pyridine H_2SO_4/py

S-Alkylation of mercaptans with trialkyl borates SH → SR

244.



Concd. H_2SO_4 (0.15 mol) added dropwise with stirring to tri-*n*-pentyl borate (0.1 mol) at 0°, stirring continued for 30 min, a mixture of butanethiol (0.3 mol) and pyridine (0.3 mol) added portionwise within 10 min, heated at 100° for 24 h, cooled, neutralized with NaOH soln. (2 *M*), the oily phase washed twice with satd. NaCl soln., dried, and distilled under vacuum → butyl *n*-pentyl sulfide. Y 81.2%. The procedure is high-yielding for the S-alkylation of *aliphatic* mercaptans with tri-*prim*-alkyl and tri-*sec*-alkyl borates (seven examples; Y 58-93%), but reaction failed with thiophenol due to formation of 2-(butylthio)phenol by electrophilic ring substitution.

Furthermore, there was no O-alkylation of alcohols. Reaction involves initial *in situ*-generation of dialkyl sulfates, followed by S-alkylation of the mercaptan in the presence of pyridine. Hence, the approach is considered a useful **alternative to classical S-alkylation with preformed dialkyl sulfates** which are less manageable and more toxic than the corresponding [simply prepared] trialkyl borates. F.e.s. D. Gunes, O. Sirkecioglu, N. Bicak, Phosphorus, Sulfur Silicon Relat. Elem. *2010*, *185* (8), 1685-90 [DOI: 10.1080/10426500903213563].

Silica-sulfuric acid/microwaves SiO_2-OSO_3H/[\\\\]
Benzothiazoles from *o*-aminomercaptans and aldehydes s. *19*, 674s*78* ○

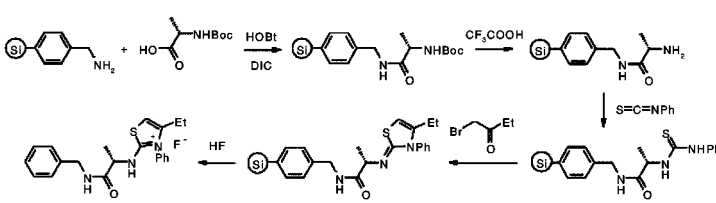
Tetra-n-butylammonium iodide s. under K_2CO_3 Bu_4NI

Ruthenium trichloride/1-butyl-3-methylimidazolium hexafluorophosphate/air ←
Benzothiazoles from *o*-aminomercaptans and aldehydes s. *19*, 674s*78*

Halogen ↑ SC ↓↑ Hal

Without additional reagents *w.a.r.*
Solid-phase synthesis of 2-aminothiazolium salts from thioureas and α-bromoketones ○
Improved work-up using a 'volatilizable' silica support

245.



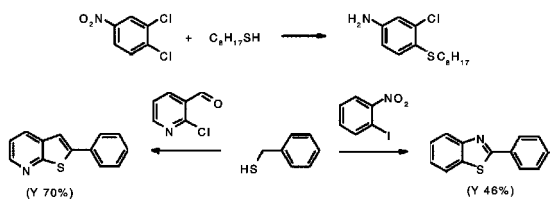
A soln. of the startg. N-Boc-amino acid (5 eq.; 0.1 *M* in DMF), N-hydroxybenzotriazole (5 eq.; 0.1 *M* in DMF) and diisopropylcarbodiimide [DIC] (5 eq.; 0.1 *M* in DMF) added to a polypropylene bottle containing functionalized aminomethylphenyl silica gel (200 mg), the mixture shaken at room temp. for 2 h, the resulting supported amine washed, treated with 55% trifluoroacetic acid in methylene chloride at room temp. for 30 min to remove the Boc group, the support washed again and neutralized with 5% ethyldiisopropylamine in methylene chloride, the resulting supported amine treated overnight with the startg. isothiocyanate (5 eq.; 0.1 *M* in methylene chloride), the supported thiourea washed and air dried, the startg. α-bromoketone (10 eq.; 0.1 *M* in DMF) added, heated at 65° for 24 h, the resulting supported 2-iminothiazoline washed, treated with 10% HF (4 ml) at room temp. for 1 h to cleave the support (*with liberation of volatile SiF_4 and water*), and the mixture lyophilized to remove the solvent → product. Y 84% (purity 92%). The procedure is more advantageous than those with traditional supports, the removal of which can be less efficient and more costly when dealing with large numbers of compounds. F.e. and from N-Fmoc-protected α-amino acids and side-chain-protected N-Boc-amino acids (fourteen examples in all; Y 73-99%; purity 70-92%) s. Y. Li, M. Giulianotti, R.A. Houghten, Tetrahedron Lett. *2010*, *51* (43), 5637-9 [DOI: 10.1016/j.tetlet.2010.08.026].

Sodium hydroxide/tetra-n-butylammonium chloride $NaOH/Bu_4NCl$
Thiolic acid esters from carboxylic acid chlorides COCl → COSR
and arylmercaptans s. *3*, 569s*75*; under phase transfer catalysis with $NaOH/Bu_4NCl$ s. C. Simion, I. Hashimoto, Y. Mito, A.M. Simion, N. Egashira, Phosphorus, Sulfur Silicon Relat. Elem. *2010*, *185* (12), 2480-8 [DOI: 10.1080/10426501003713072]; with diaryl disulfides in place of mercaptans by reduction with In in $[bmim]PF_6$ cf. G. Tabarelli, E.E. Alberto, A.M. Deobald, G. Marin, O.E.D. Rodrigues, L. Dornelles, A.L. Braga, Tetrahedron Lett. *2010*, *51* (43), 5728-31 [DOI: 10.1016/j.tetlet.2010.08.076]; **from carboxylic acid anhydrides** and mercaptans with

K_2CO_3, **also** selective **S-carbo-*tert*-butoxylation** with *tert*-butoxyformic anhydride, s. A. Temperini, D. Annesi, L. Testaferri, M. Tiecco, ibid. *51* (41), 5368-71 [DOI: 10.1016/j.tetlet.2010.07.126].

Potassium hydroxide *KOH*
Metal-free reductive sulfenylation of activated ar. halides Hal → SR

246.



Ar. aminothioethers from nitrohalides in one pot. A mixture of PEG-600 (3 ml), 3,4-dichloronitrobenzene (0.5 mmol), octanethiol (1.5 eq.), and KOH (3 eq.) stirred at 100° until reaction complete (TLC; 2 h), cooled to room temp., diluted with water, extracted with ethyl acetate, concentrated *in vacuo*, and purified by chromatography on silica → 3-chloro-4-octylthioaniline. Y 80%. This efficient reaction apparently effects simultaneous nitro-reduction and nucleophilic substitution of *o*- and *p*-nitro-halo-benzenes and -2-pyridines with electron-diverse ar. and aliphatic thiols (fifteen examples; Y 61-96%; 50% for 4-nitrobenzenethiol). In the illustrated example, the *p*-product was formed exclusively, whereas 2,4-dichloronitrobenzene gave the bis-thiolated aniline (Y 68%). With benzylic thiols, 2-nitroiodobenzene underwent thiolation/reductive cyclization to afford **2-arylbenzothiazoles** (two examples; Y 40% and 46%) and 2-chloro/fluoro-benzaldehydes or 2-chloropyridine-3-carboxaldehyde suffered thiolation/dehydrative cyclization to **2-arylbenzo[*b*]thiophenes** (eight examples; Y 72-87%, incl. 2-phenylbenzo[*b*]thiophene: Y 78% on a 5 mmol scale) or a **thieno[2,3-*b*]pyridine** (Y 70%), respectively. Notably, the PEG solvent could be recycled up to three times without reduction in yield. F.e. and optimization s. Z. Duan, S. Ranjit, X. Liu, Org. Lett. *2010*, *12* (10), 2430-3 [DOI: 10.1021/ol100816g].

Copper(I) iodide/potassium fluoride-alumina *CuI/KF-Al$_2$O$_3$*
Copper(I) iodide/cis-1,2-cyclohexanediol/potassium phosphate ←
Ar. thioethers from ar. halides and mercaptans
under copper catalysis s. *31*, 522s*76*; from ar. iodides and alkyl or aryl mercaptans with CuI and KF-Al_2O_3 as base in DMF s. Y.-S. Feng, Y.-Y. Li, L. Tang, W. Wu, H.-J. Xu, Tetrahedron Lett. *2010*, *51* (18), 2489-92 [DOI: 10.1016/j.tetlet.2010.02.155]; from ar. bromides or iodides with CuI/K_3PO_4 and *cis*-1,2-cyclohexanediol as ligand, **also thioenolethers** from α,β-ethylenehalides with stereoretention (cf. *68*, 230s*76*), s. M.S. Kabir, M. Lorenz, M.L. Van Linn, O.A. Namjoshi, S. Ara, J.M. Cook, J. Org. Chem. *2010*, *75* (11), 3626-43 [DOI: 10.1021/jo1004179]; ligand-free procedure from ar. iodides with readily recyclable iron/graphite in DMF with KOH as base s. V.K. Akkilagunta, V.P. Reddy, K.R. Rao, Synlett *2010* (8), 1260-4 [DOI: 10.1055/s-0029-1219801].

Tetra-n-butylammonium chloride s. under NaOH *Bu$_4$NCl*

Iron/graphite/potassium hydroxide *Fe/C/KOH*
Ar. thioethers from ar. iodides and mercaptans s. *31*, 522s*78*

Sulfur ↑ SC ↓↑ S

Lithium arylmercaptides *LiSAr*
Replacement of sulfonyl groups in 1,1-alkoximinosulfones ←
by arylthio groups s. *78*, 463

Phenylcopper/cobalt(II) acetoacetonate/4-fluorostyrene/tetra-n-butylammonium iodide ←
Ar. thioethers from aryl sulfonates $ArOSO_2Ar' \rightarrow [ArCu] \rightarrow ArSR''$
via arylcopper compds. s. *78*, 438

Indium/1-butyl-3-methylimidazolium hexafluorophosphate *In/[bmim]PF_6*
Thiolic acid esters from carboxylic acid chlorides and disulfides COCl → C(O)SR
s. *3*, 569s*78*

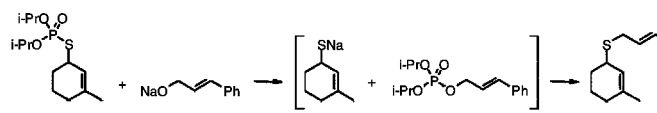
Cobalt(II) acetoacetonate/4-fluorostyrene/tetra-n-butylammonium iodide s. under PhCu ←

Chloro(cyclooctadiene)iridium(I) dimer *$[Ir(cod)Cl]_2$*
Sulfoxonium ylids as metal carbene precursors C=S(O)< → CH(SR)
α-(Organothio)carbonyl compds. s. *78*, 192

Remaining Elements ↑ SC ↓↑ Rem

Sodium hydride *NaH*
2-Ethylenethioethers OH → S-C-C=C
from S-(2-ethylene)monothiophosphoric acid esters and alcohols

247.

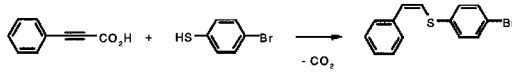


A soln. of startg. phosphorothioate (0.34 mmol) in *tert*-butyl methyl ether (1 ml) added to a soln. of Na-cinnamoxide [freshly prepd. from NaH (1.3 eq.) and cinnamyl alcohol (1.5 eq.)] in the same solvent (1.3 ml) at room temp. to 55°] at 55°, the reaction vessel sealed, the soln. stirred overnight, quenched with satd. aq. $NaHCO_3$, extracted with ether, washed with brine, concentrated *in vacuo*, and purified by chromatography on silica → cinnamyl 3-methylcyclohex-2-enyl thioether. Y 92%. This preparation of allylic thioethers is considerably more efficient and general than previously reported methods and avoids the use of malodorous sulfur compds. The method was successful for cyclic (5- to 7-membered) and acyclic allyl phosphorothioates reacting with alkyl, allylic and benzylic alkoxides (seventeen examples; Y 44-93%) in the presence of ester, nitrile and N-, O- and S-heterocyclic functionality. A single chiral benzylic alcohol was converted to its allylic thioether **with** complete **inversion of configuration** (Y 58%). F.e. and substrate prepn. s. F. Robertson, J. Wu, Org. Lett. *2010, 12* (11), 2668-71 [DOI: 10.1021/ol1009202].

Carbon ↑ SC ↓↑ C

Copper(I) iodide/cesium carbonate *CuI/Cs_2CO_3*
(Z)-Thioenolethers C≡C-COOH → CH=CH(SR)
from α,β-acetylenecarboxylic acids and mercaptans
Copper(I)-catalyzed decarboxylative cross-coupling

248.

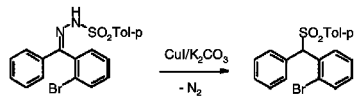


(Z)-β-Styryl thioethers. CuI (4 mol%) and Cs_2CO_3 (2.4 eq.) added to a soln. of phenylpropiolic acid (0.5 mmol) and 4-bromothiophenol (1.5 eq.) in N-methyl-2-pyrrolidone (3 ml), the mixture stirred at 90° for ca. 24 h, cooled to room temp., quenched with 1 *M* aq. HCl, extracted with ethyl acetate, washed with water and brine, concentrated *in vacuo*, and purified by chromatography on silica → (Z)-(4-bromophenyl) β-styryl sulfide. Y 88% (Z/E 100:0). This copper(I)-catalyzed coupling (copper(II) salts were less effective) occurred under relatively mild conditions without need of a palladium catalyst, and demonstrated *high Z-selectivity* and broad functional group tolerance (amine, ether, phenol, halo) for phenylpropiolic acid reacting with electron-diverse (het)ar. and aliphatic thiols (twenty examples; Y 75-95%; Z/E 79:21 to 100:0). The *o*-methyl subst. phenylpropiolic acid gave the Z-isomer exclusively (Y 95%), but *p*-chloro/bromo derivs. showed low selectivity (six examples; Y 89-95%; Z/E 70:30 to 30:70). F.e. and optimization s. S. Ranjit, Z. Duan, P. Zhang, X. Liu, Org. Lett. *2010, 12* (18), 4134-6 [DOI: 10.1021/ol101729k].

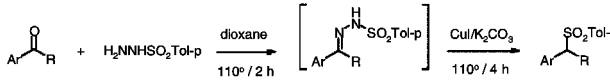
Elimination ⇑

Nitrogen ↑ SC ⇑ N

Copper(I) iodide/potassium carbonate *CuI/K₂CO₃*
Copper(I)-catalyzed formation of sulfones from sulfonylhydrazones with elimination of molecular nitrogen C=NNHSO₂R → CHSO₂R



249.



Ar = p-Me₂NC₆H₄, R = H (Y 50%)
Ar = p-MeOC₆H₄, R = Me (Y62%)

A mixture of startg. sulfonylhydrazone (0.3 mmol), *CuI* (20 mol%), K_2CO_3 (2 eq.) and dioxane (2 ml) in a Schlenk tube heated at 110° for 2 h, cooled to room temp., diluted with methylene chloride, filtered through silica, concentrated *in vacuo*, and purified chromatographically → 1-bromo-2-[phenyl(tosyl)methyl]benzene. Y 88%. The presence of a copper salt and base were essential for this experimentally simple and efficient conversion, but the addition of ligands produced a slight reduction in yield. The method was successful for electron-diverse ar. and aliphatic sulfonylhydrazones derived from ketones (fifteen examples; Y 46-90%), with diaryl ketone-derived substrates affording the highest yields (although a fluorenone-derived substrate gave the lowest yield). A single sulfonylhydrazone derived from an aldehyde (4-dimethylaminobenzaldehyde) required longer heating (4 h) and afforded a 54% yield. The method was extended to generate the hydrazones *in situ*, thereby providing one-pot formation of **sulfones from oxo compds.** *with only slight reduction in overall yield* (two examples; Y 50%, 62%). F.e. and optimization s. X.-W. Feng, J. Wang, J. Zhang, J. Yang, N. Wang, X.-Q. Yu, Org. Lett. *2010*, *12* (19), 4408-11 [DOI: 10.1021/ol101955x].

Halogen ↑ SC ⇑ Hal

Tetra-n-butylammonium salts *[Bu₄N]⁺*
Functionalized arenes Ar(Ar′)IX → ArX [+ Ar′I]
by regioselective reductive elimination of diaryliodonium salts – Ar. thiocyanates or diaryl sulfides s. *78*, 209

Sulfur ↑ SC ⇑ S

Titanium tetrachloride/samarium *$TiCl_4$/Sm*
Benzothiazoles from bis[*o*-(alkylideneamino)aryl] disulfides s. *19*, 674s*78* ○

Formation of Rem-Rem Bond

Exchange ↓↑

Hydrogen ↑ RemRem ↓↑ H

Copper(II) acetate/triethylamine $Cu(OAc)_2/Et_3N$
Copper(I) chloride/N,N,N′,N′-tetraethylethylenediamine *CuCl/TEEDA*
Sym. tetraalkoxydiphosphine P,P-dioxides from dialkyl phosphites $(RO)_2P(O)\text{-}P(O)(OR)_2$
Chemoselective aerobic dehydrogenative coupling s. *78*, 42

Halogen ↑ RemRem ↓↑ Hal

Titanium(III) [tert-butyl(3,5-dimethylphenyl)amide] $Ti[N(Bu\text{-}t)Ar]_3$
Silyl- or stannyl-phosphines from chloro-silanes or stannanes s. *78*, 266

Remaining Elements ↑ RemRem ↓↑ Rem

Titanium(III) [tert-butyl(3,5-dimethylphenyl)amide] $Ti[N(Bu\text{-}t)Ar]_3$
Silyl- or stannyl-phosphines from chloro-silanes or stannanes s. *78*, 266 ←

Formation of Rem-C Bond

Uptake ⇓

Addition to Oxygen and Carbon RemC ⇓ OC

Diethylaluminum chloride/chiral hydrogenated aluminum Schiff base complex *[Al(III)]**
Ytterbium(III) triflate/chiral bis(N-oxide)/pyridine *[Yb(III)]*/py*
α-Hydroxyphosphonic acid esters from oxo compds. $CO \rightarrow C(OH)PO(OR)_2$
Asym. hydrophosphonylation
from aldehydes with Et_2AlCl and a chiral 3-α,3′-α-di-*tert*-amino-1,1′-bi-2-naphthol as ligand cf. *49*, 510s*74*; with a chiral hydrogenated aluminum Schiff base complex as ligand for the asym. hydrophosphonylation of trifluoromethyl ketones s. X. Zhou, Q. Zhang, Y. Hui, W. Chen, J. Jiang, L. Lin, X. Liu, X. Feng, Org. Lett. *2010, 12* (19), 4296-9 [DOI: 10.1021/ol101737b]; from aldehydes with $Yb(OTf)_3$ and a chiral bis(N-oxide) as ligand s. W. Chen, Y. Hui, X. Zhou, J. Jiang, Y. Cai, X. Liu, L. Lin, X. Feng, Tetrahedron Lett. *2010, 51* (32), 4175-8 [DOI: 10.1016/j.tetlet.2010.05.137].

Lanthanum(III) bis(trimethylsilyl)amide·lithium chloride complex *[La(III)]*
β-Cyclodextrin *cyclodextrin*
α-Hydroxyphosphonic acid esters from oxo compds.
from aldehydes with NaOEt cf. *41*, 556s*76*; **in water** with β-cyclodextrin as supramolecular catalyst for hydrophosphonylation of isatins s. J. Shankar, K. Karnakar, B. Srinivas, Y.V.D. Nageswar, Tetrahedron Lett. *2010, 51* (30), 3938-9 [DOI: 10.1016/j.tetlet.2010.05.096]; from aldehydes and dialkyl phosphites with the lanthanum(III) bis(trimethylsilyl)amide·LiCl complex,

$[(Me_3Si)_2N]_3La(\mu\text{-}Cl)Li(THF)_3$, at low catalyst loading (0.1 mol%) s. Q. Wu, J. Zhou, Z. Yao, F. Xu, Q. Shen, J. Org. Chem. *2010, 75* (21), 7498-501 [DOI: 10.1021/jo101743e]; from aldehydes in water by dealkylative addition of triethyl phosphite (cf. *59*, 234s*77*) with iodine as catalyst s. H.-S. Wang, J.-E. Zeng, Phosphorus, Sulfur Silicon Relat. Elem. *2010, 185* (7), 1425-8 [DOI: 10.1080/10426500903061541].

Addition to Nitrogen and Carbon — RemC ⇓ NC

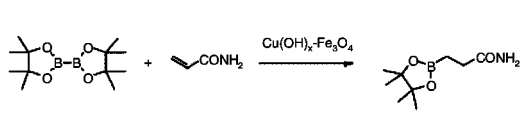
Without additional reagents — *w.a.r.*
Diethylzinc or Hydrogen chloride — *Et_2Zn or HCl*
α-Aminophosphorus(V) compds. from azomethines — C=N- → C(NH-)P(O)≤

α-aminophosphonates with TsCl cf. *41*, 556s*74*; catalyst- and solvent-free addition of phosphorous acid diesters to 3-iminooxindoles s. G.I. Shakibaei, S. Samadi, R. Ghahremanzadeh, A. Bazgir, J. Comb. Chem. *2010, 12* (2), 295-7 [DOI: 10.1021/cc900169p]; dealkylative addition of phosphorus(III) acid esters with HCl cf. W. Goldeman, M. Soroka, Synthesis *2010* (14), 2437-45 [DOI: 10.1055/s-0029-1218817]; α-(sulfinylamino)phosphine oxides from S-chiral N-sulfinylimines and sec. phosphine oxides in the presence of Et_2Zn *with asym. induction*, s. D. Zhao, L. Mao, D. Yang, R. Wang, J. Org. Chem. *2010, 75* (20), 6756-63 [DOI: 10.1021/jo1014917]; α-(phosphinylamino)phosphonic acid esters from N-phosphinylimines and TADDOL-based cyclic phosphorous acid diesters with asym. induction s. F. Palacios, T.K. Olszewski, J. Vicario, Org. Biomol. Chem. *2010, 8* (19), 4255-8 [DOI: 10.1039/c003004j].

Addition to Carbon-Carbon Bonds — RemC ⇓ CC

Copper-on-magnetite/potassium carbonate — *$Cu(OH)_x$-Fe_3O_4/K_2CO_3*
Boronic acid esters — C=C → CHC-B(OR)$_2$
from ethylene derivs. and tetraalkoxydiboranes
Regioselective copper-catalyzed conversion under mild conditions at low catalyst loading

250.



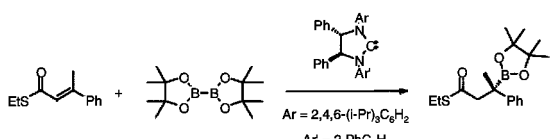
β-Borylcarboxylic acid amides. Impregnated copper-on-magnetite [$Cu(OH)_x/Fe_3O_4$] (*50 mg*), K_2CO_3 (0.45 mmol), the startg. olefin (0.5 mmol) and methanol (1 mmol) added under argon to a stirred soln. of bis(pinacolato)diboron (0.7 mmol) in toluene (0.5 ml), the mixture stirred *at 60°* for 16 h, the catalyst removed by a magnet, the resulting soln. quenched with satd. aq. NH_4Cl, and worked up with purification by chromatography on silica gel → 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propanamide. Y 86%. The procedure is simple and broadly applicable to the conjugate borylation of α,β-ethylene-carboxylic acid amides, esters, -nitriles and -ketones (eight examples; Y 91-99%) as well as the regioselective borylation of simple styrenes (incl. α-methylstyrene) and a terminal aliphatic olefin (five examples; Y 56%, 85-99%; regioselectivity >95%). The catalyst is readily prepared (by a basic precipitation-adsorption of aq. CuCl on the surface of commercially available magnetite powder (<5 μm) with incorporation of 1.37-1.62% Cu); it is easily retrieved with the aid of a magnet and may be recycled 8 times with little change in the product yield. Significant, also, is the fact that no phosphine ligand is required. Reaction is presumed to involve formation of an intermediate copper-boryl species. F.e. and comparison of bases s. R. Cano, D.J. Ramón, M. Yus, J. Org. Chem. *2010, 75* (10), 3458-60 [DOI: 10.1021/jo100325e].

Tetrakis(acetonitrile)copper(I) hexafluorophosphate/chiral 1,2-di-sec-amines/lithium tert-butoxide/isopropanol ←

Copper(I) chloride/(4S,5S)-1-biphenyl-2-yl-3-(2,4,6-triisopropylphenyl)-4,5-diphenyl-imidazolinium fluoroborate/sodium tert-butoxide ←

Regioselective asym. hydroboration of α,β-ethylenecarbonyl compds. with bis(pinacolato)diboron C=C → CHC-B(OR)$_2$

251.



under mild conditions. A mixture of imidazolinium salt (5 mol%), NaOBu-*t* (13 mol%) and CuCl (5 mol%) in THF (1 ml) stirred at 22° under dry N_2 for 2 h, filtered through Celite, bis-(pinacolato)diboron (1.1 eq.) added, the mixture cooled to -50°, (E)-ethyl 3-phenylbut-2-thioenoate (0.33 mmol) and methanol (1.2 eq.) added, the mixture stirred for 18 h, quenched with 30% methanolic HCl, warmed to 22°, neutralized with satd. aq. $NaHCO_3$, extracted with ether, concentrated *in vacuo*, and purified by chromatography on silica → (R)-ethyl 3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butanethioate. Y 87% (e.e. 98%). Alkyl and ar. trisubst. alkenes derived from acyclic esters, ketones and thioesters (but not amides) underwent 1,4-addition with the commercially available diboronate (eighteen examples; Y 71-98%; e.e. 81-98%) with electron-rich ar. or bulky alkyl subst. derivs. giving poorer results, and a β-isopropyl deriv failing completely. Esters reacted optimally at -78°, whereas thioesters were less reactive and required stirring at -50° for complete conversion, but gave more consistent enantioselectivity and were readily converted to ester and ketone analogs without loss of chirality. F.e.s. J.M. O'Brien, K.-s. Lee, A.H. Hoveyda, J. Am. Chem. Soc. *2010, 132* (31), 10630-3 [DOI: 10.1021/ja104777u]; with a highly active chiral chloro(2,3,5,6-tetrahydroimidazo[1,2-*c*]quinazolin-5-ylidene)copper(I) complex (10,000 turnovers at 0.01 mol%) and NaOBu-*t* as base s. J.K. Park, H.H. Lackey, M.D. Rexford, K. Kovnir, M. Shatruk, D.T. McQuade, Org. Lett. *2010, 12* (21), 5008-11 [DOI: 10.1021/ol1021756]; with $(MeCN)_4CuPF_6$/*t*-BuOLi/isopropanol in the presence of (S,S)-N,N′-diethyl-1,2-diphenylethylene-diamine as ligand for the highly enantioselective conjugate borylation of linear β,β-disubst. enones s. I.-H. Chen, M. Kanai, M. Shibasaki, ibid. *2010, 12* (18), 4098-101 [DOI: 10.1021/ol101691p].

Calcium oxide *CaO*

Phospha-Michael addition of dialkyl phosphites C=C → CHC(PO(OR)$_2$)

with Me_3Al cf. *45,* 340; 1,4-addition to α,β-ethylene-sulfones and -carboxylic acid esters with CaO in the absence of solvent, also 1,2-addition to α,β-ethyleneoxo compds., s. E. Martínez-Castro, Ó. López, I. Maya, J.G. Fernández-Bolaños, M. Petrini, Green Chem. *2010, 12* (7), 1171-4 [DOI: 10.1039/c0gc00026d]; catalyst- and solvent-free Michael addition of phosphorous acid diesters to 3-(dicyanomethylene)oxindoles s. G.I. Shakibaei, S. Samadi, R. Ghahremanzadeh, A. Bazgir, J. Comb. Chem. *2010, 12* (2), 295-7 [DOI: 10.1021/cc900169p]; solvent-free dealkylative 1,4-addition **of trialkyl phosphites** to a range of electron-deficient ethylene derivs. with recyclable perchloric acid-silica (cf. *22,* 675) s. S. Sobhani, S. Rezazadeh, Synlett *2010* (10), 1485-8 [DOI: 10.1055/s-0029-1220069].

Diethylzinc/2,6-bis[2(S)-[hydroxy(di-2-thienyl)methyl]pyrrolidin-1-ylmethyl]phenol/pyridine ←

Asym. phospha-Michael addition C=C → CHC(P(O)<)

diethylzinc-mediated asym. addition of dialkyl phosphites to enones s. *76,* 267; of dialkylphosphine oxides with 2,6-bis[2(S)-[hydroxy(di-2-thienyl)methyl]pyrrolidin-1-ylmethyl]phenol as ligand in the presence of pyridine s. D. Zhao, L. Mao, D. Yang, R. Wang, J. Org. Chem. *2010, 75* (20), 6756-63 [DOI: 10.1021/jo1014917]; asym. addition **of sec. phosphines** with bis(acetonitrile)-[1-[1(R)-(dimethylamino)ethyl)]-2-naphthyl]palladium(II) perchlorate as catalyst s. Y. Huang, S.A. Pullarkat, Y. Li, P.-H. Leung, Chem. Commun. *2010, 46* (37), 6950-2 [DOI: 10.1039/c0cc00925c].

Diisobutylaluminum hydride s. under $NiCl_2(dppp)$ *i-Bu_2AlH*

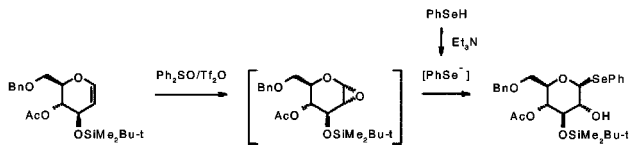
(4S,5S)-1-Biphenyl-2-yl-3-(2,4,6-triisopropylphenyl)-4,5-diphenylimidazolinium fluoroborate/sodium tert-butoxide s. under CuCl ←

2,6-Bis[2(S)-[hydroxy(di-2-thienyl)methyl]pyrrolidin-1-ylmethyl]phenol s. under Et_2Zn ←

Diphenyl sulfoxide/trifluoromethanesulfonic anhydride/2,4,6-tri-tert-butylpyridine/methanol/triethylamine ←

β-Selenoglycosides from glycals C=C → C(OH)C(SeR)

252.



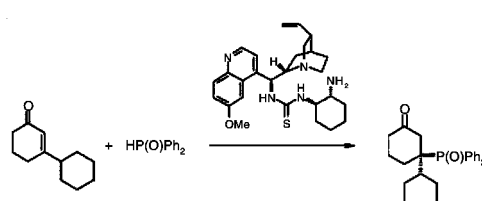
Trifluoromethanesulfonic anhydride (1.5 eq.) added to a soln. of diphenyl sulfoxide (3 eq.) and 2,4,6-tri-*tert*-butylpyridine (3.5 eq.) in anhydrous methylene chloride (80 ml) at -78°, the mixture stirred at this temp. for 10 min, a soln. of 4-O-acetyl-6-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-D-glucal (1.92 mmol) in anhydrous methylene chloride (6 ml) added, stirred again for 30 min and then at -40° for 1 h, methanol (1 eq.) and triethylamine (4 eq.) added sequentially at -40°, stirred for 30 min at the same temp. then at 0° for 2 h, benzeneselenol (3 eq.) added, stirred at 0° for 1 h and at 23° for 12 h, diluted with methylene chloride, and worked up with purification by flash chromatography on silica gel → phenyl 4-O-acetyl-6-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-1-seleno-β-D-glucopyranoside. Y 78%. Under these conditions, through interaction with triethylamine, benzeneselenol is in equilibrium with nucleophilic phenyl selenide anion which attacks the intermediate glycal epoxide in typical, direct S_N2 fashion to give the β-selenoglycoside. This contrasts totally with the more familiar Danishefsky procedure wherein benzeneselenol is presumed to remain undissociated and initially protonates the epoxide oxygen, thereby remaining associated as an ion-polar pair from which the selenide attacks C_1 *intramolecularly* from beneath to give the more familiar α-anomer. The process is general, as demonstrated by three further examples (Y 58-78%), incl. a disaccharide. F.e.s. V. Di Bussolo, A. Fiasella, F. Balzano, G.U. Barretta, P. Crotti, J. Org. Chem. *2010*, *75* (12), 4284-7 [DOI: 10.1021/jo100145s].

Quinine-derived chiral 2-prim-aminothiourea ←

β-Phosphinylketones from α,β-ethyleneketones C=C → CHC-P(O)R_2

Organocatalyzed asym. phospha-Michael addition

253.



under mild conditions. Diphenylphosphine oxide (1 mmol) and chiral quinine-based thiourea catalyst (10 mol%) added to a soln. of 3-cyclohexylcyclohex-2-enone (3 eq.) in methylene chloride (2 ml) at room temp., the mixture stirred until reaction complete (TLC; 6 d), and purified by chromatography on silica → (R)-3-cyclohexyl-3-diphenylphosphinylcyclohexanone. Y 85% (e.e. 90%). This efficient and highly enantioselective method appears general for cyclic (cyclo-

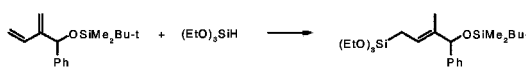
hexenone, cycloheptenone) and electron-diverse ar. enones, and tolerates bulky β-substituents, affording *synthetically challenging* ***chiral quaternary centers*** *attached to phosphorus* (twenty examples; Y 82-97%; e.e. 84-98%), with absolute stereochemistry determined by X-ray analysis in one case. Less sterically hindered acyclic enones (pent- and oct-3-en-2-one) gave lower enantioselectivity (Y 92%, 70%; e.e. 70%, 67%), while 4,4′-dibromodiphenylphosphine oxide was unreactive. From optimization of the chiral catalyst it was noted that, while the 1,2-diaminocyclohexane scaffold determined the sense of enantioselectivity ((S,S) analogs gave opposite selectivity), thiourea and alkaloid moieties were essential for the level of enantioselectivity, and substitution of the prim. amine resulted in a dramatic decrease in selectivity. F.e., optimization and catalyst prepn., s. S. Wen, P. Li, H. Wu, F. Yu, X. Liang, J. Ye, Chem. Commun. *2010*, *46* (26), 4806-8 [DOI: 10.1039/c0cc00094a].

Chiral poly(quinoxaline)-based tert. phosphines s. under [(π-allyl)PdCl]$_2$ ←
Trifluoromethanesulfonic anhydride s. under Ph_2SO *Tf_2O*
Magnetite s. under $Cu(OH)_x$ *Fe_3O_4*

Bis(o-dimethylaminomethylphenyl)(pyridine)iron(II)/(E)-N-[1,2-dihydropyrid-2-yl-methylene]-2,6-diisopropylaniline ←

Regio- and stereo-selective 1,4-hydrosilylation of 1,3-dienes C=C → CHC(Si⩽)

254.

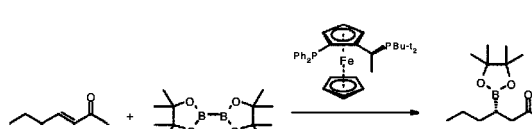


2-Ethylene(trialkoxy)silanes under mild conditions. Solns. of (E)-N-[1,2-dihydropyrid-2-yl-methylene]-2,6-diisopropylaniline (15 mol%) in toluene (0.2 ml), startg. 1,3-diene (0.299 mmol) in toluene (0.4 ml) and triethoxysilane (1.21 eq.) added to Fe(II) pre-catalyst (15 mol%) in a vial, the mixture stirred at 23° for 20 h, quenched with satd. aq. $NaHCO_3$, extracted with ether, filtered through Celite, concentrated *in vacuo*, and purified by bulb-to-bulb distillation → (E)-1-*tert*-butyldimethylsiloxy-2-methyl-1-phenylbut-2-en-4-yl(triethoxy)silane Y 80% (E/Z >99:1). Preparation of allylsilanes via hydrosilylation provided a milder and more general alternative to treatment of chlorosilanes with allylmetal species, and was successful for 1-, 2- and 2,3-di-subst. 1,3-dienes, with the linear adduct predominating in all cases (ten examples; Y 66-91%; selectivity 94 to >99%). The method was compatible with ether, ester, oxirane, amine and silyl ether functionality, with stereoselectivity >99:1 in all cases. The catalyst was presumed to be a low-valent Fe species, formed by reductive ligand exchange. F.e., also catalyst and substrate prepn. s. J.Y. Wu, B.N. Stanzl, T. Ritter, J. Am. Chem. Soc. *2010*, *132* (38), 13214-6 [DOI: 10.1021/ja106853y].

(R)-(S)-1-[1-(Di-tert-butylphosphino)ethyl]-2-(diphenylphosphino)ferrocene/cesium carbonate ←

Metal-free asym. hydroboration of α,β-ethylenecarbonyl compds. C=C → CHC-B(OR)$_2$

255.



A mixture of chiral ferrocenyldi(phosphine) ligand (4 mol%), Cs_2CO_3 (15 mol%) and bis-(pinacolato)diboron (1.1 eq.) in THF (2 ml) stirred at room temp. for 10 min under argon, *trans*-3-hepten-2-one (0.5 mmol) and methanol (5 eq.) added, and the mixture stirred at 70° for 6 h → (S)-4-pinacolatoborylheptan-2-one. Y 89% (GC; e.e. 95%). This challenging boration gave good isolated yields (91-99%; six examples) for sterically unhindered α,β-unsaturated esters and ketones (incl. 1-phenylbut-2-en-1-one) using *triphenylphosphine* as catalyst (*iso*- and *tert*-butyl ester derivs. gave Y 46-54%). Using the chiral phosphine catalyst, highest reactivity/enantioselectivity was observed for unsaturated methyl/ethyl ketones and ethyl esters (five examples; conversion 79-99%; e.e. 80-95%), with modest results achieved for sterically hindered ester, phenyl ketone

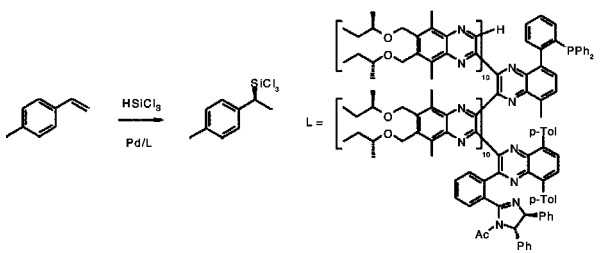
and 2-cyclohexenone derivs. (three examples; conversion 42-75%; e.e. 36-57%). F.e. and optimization s. A. Bonet, H. Gulyás, E. Fernández, Angew. Chem., Int. Ed. *2010*, *49* (30), 5130-4 [DOI: 10.1002/anie.201001198].

Dichloro[1,3-bis(diphenylphosphino)propane]nickel(II)/diisobutylaluminum hydride ←
Syntheses via α-selective nickel-catalyzed hydroalumination ←
of terminal acetylene derivs. – α-Subst. vinylboronic acid esters s. *78*, 217

Bis(acetonitrile)[1-[1(R)-(dimethylamino)ethyl]-2-naphthyl]palladium(II) perchlorate ←
β-Phosphino- from α,β-ethylene-ketones and sec. phosphines C=C → CHC(PR$_2$)
Asym. phospha-Michael addition s. *76*, 267s*78*

Bis(π-allylpalladium chloride)/helically-chiral poly(quinoxaline)-based tert. phosphines ←
Regioselective asym. hydrosilylation of styrenes C=C → CHC(Si⩽)
under palladium catalysis with helically-chiral tert. phosphines as ligands

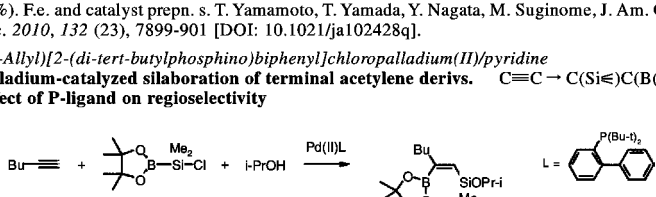
256.



A soln. of [(π-allyl)PdCl]$_2$ (0.05 mol%) in toluene (0.05 ml) added to a soln. of the helically-chiral phosphine ligand (0.2 mol% based on P) in toluene (1 ml), solvent removed *in vacuo*, 4-methylstyrene (0.99 mmol) added to the residue, the mixture cooled to 0°, $HSiCl_3$ (2 eq.) added, the mixture stirred for 12 h, and purified by bulb-to-bulb distillation → (S)-1-trichlorosilyl-1-(4-tolyl)ethane. Y 96% (e.e. 95%). The low-molecular weight catalyst (prepared by block copolymerization) is based on a nominal chain of 22 quinoxaline units containing chiral spacers with a single phosphine moiety incorporated in the 11th unit, and exists as a single-handed helix. The ligand efficiently catalyzed the regio- and enantio-selective hydrosilylation of electron-diverse styrenes (nine examples; Y 91-96%; e.e. 84-96%). A subsequent catalyst based on random copolymerization of 1000 units was more efficiently recycled (8 cycles before re-activation with additional Pd) and could exist as P-(right-handed) and M-(left-handed)-helical forms in different solvents. Tests with parent styrene showed the P-form afforded the (S)-trichlorosilyl adduct (Y 94%; e.e. 97%) while the (R)-enantiomer was obtained in the presence of the M-form (Y 93%; e.e. 93%). F.e. and catalyst prepn. s. T. Yamamoto, T. Yamada, Y. Nagata, M. Suginome, J. Am. Chem. Soc. *2010*, *132* (23), 7899-901 [DOI: 10.1021/ja102428q].

(η^3-Allyl)[2-(di-tert-butylphosphino)biphenyl]chloropalladium(II)/pyridine ←
Palladium-catalyzed silaboration of terminal acetylene derivs. C≡C → C(Si⩽)C(B(OR)$_2$)
Effect of P-ligand on regioselectivity

257.



While classical P-ligands (Ph_3P, *n*-Bu_3P and Cy_3P) direct silaboration of terminal alkynes with attack of boron at the terminal carbon (cf. *52*, 227s*58*), the *sterically demanding and electron-*

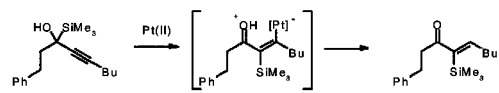
rich 2-(di-*tert*-butylphosphino)biphenyl *reverses* the regioselectivity almost completely to give the *abnormal* product. **E:** Hex-1-yne (1.2 eq.) and the B-(chlorosilyl)boronate (0.4 mmol) added to a soln. of (η^3-allyl)[2-(di-*tert*-butylphosphino)biphenyl]chloropalladium(II) (1 mol%) in toluene (0.2 ml), stirred at room temp. for 2 h, pyridine (1.8 eq.) and isopropanol (1.5 eq.) added, stirring continued at room temp. for 1 h, and worked up with purification by bulb-to-bulb distillation → (E)-1-[isopropoxy(dimethyl)silyl]-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-hex-1-ene. Y 99% (97:3 mixture of regioisomers). Reaction is applicable with high yields and regioselectivity (seven examples; Y 80-99%; abnormal regioselectivity 97-98%) to a range of *prim*-alkylacetylenes (notably possessing siloxy, acoxy, Cl, and CN functionality); yields and selectivity were slightly lower with the more bulky *sec*- and *tert*-alkylacetylenes, as well as with arylacetylenes, there being no reaction with 4-trifluoromethylphenylacetylene. The mechanism for the reversal of regioselectivity is thought to involve a unique ligand control of reductive elimination. F.e.s. T. Ohmura, K. Oshima, H. Taniguchi, M. Suginome, J. Am. Chem. Soc. *2010*, *132* (35), 12194-6 [DOI: 10.1021/ja105096r].

Platinum(II) chloride $PtCl_2$
(E)-α,β-Ethylene-α-silylketones from α,β-acetyleneketones COC(Si∈)=CHR
by regio- and stereo-selective platinum-catalyzed hydrosilylation s. *78*, 258

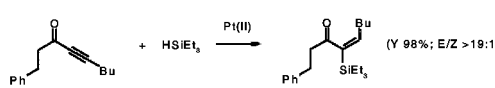
Rearrangement ∩

Hydrogen/Oxygen Type RemC ∩ HO

Platinum(II) chloride $PtCl_2$
Regio- and stereo-selective platinum-catalyzed formation of α,β-ethylene-α-silylketones COC(Si∈)=CHR



258.



(Z)-α,β-Ethylene-α-silylketones from 2-acetylene-1,1-hydroxysilanes. $PtCl_2$ (5 mol%) added to a soln. of the startg. α-hydroxypropargylsilane in toluene (0.1 *M*) under argon, the reaction flask placed in an oil bath at 80°, stirred for 1.5 h (TLC monitoring), diluted with ether, the mixture filtered through silica gel, and worked up with purification by flash chromatography on silica gel → product. Y 99% (Z/E 10:1). This interesting **1,2-silyl migration** was applicable to a range of readily accessible substrates (incl. hindered compds.) at low catalyst loading and with retention of esters, carbamates, silyl ethers, acetals and distal olefin functionality to give (Z)-isomers predominantly (thirteen examples; Y 76-99%; Z/E >19:1 in all but one case). Reaction is thought to involve initial activation of the alkyne residue by platinum(II), followed by *anti*-selective silyl migration to give a vinylplatinum species prior to protodemetalation. The corresponding **(E)-α,β-ethylene-α-silylketones** were obtained **from α,β-acetyleneketones**, however, by regiospecific hydrosilylation with triethylsilane or benzyldimethylsilane (1.1-1.2 eq.) in toluene using the catalyst (six examples; Y 87-99%; E/Z >19:1 in all but the illustrated case). F.e. and stereospecific Hiyama coupling of the products with iodobenzene s. D.A. Rooke, E.M. Ferreira, J. Am. Chem. Soc. *2010*, *132* (34), 11926-8 [DOI: 10.1021/ja1058197].

Exchange ↓↑

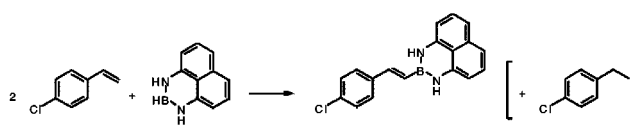
Hydrogen ↑ RemC ↓↑ H

P4-Phosphazene base/1-trimethylsilylpropyne/dimethyl sulfoxide-d_6 ←
Metal-free deuteration of 5-membered heteroarenes s. *78*, 287 H → D

Ruthenium/carbon *Ru/C*
Carbonyl(chloro)(hydrido)tris(triphenylphosphine)ruthenium(II) *RuH(Cl)(CO)(PPh_3)$_3$*
Deuteration
of glycosides with Ni cf. *23*, 642s*42*; regio-, chemo- and stereo-selective deuterium labelling of sugars with D_2O based on C-H bond activation with Ru/C under H_2 (1 atm.) s. Y. Fujiwara, H. Iwata, Y. Sawama, Y. Monguchi, H. Sajiki, Chem. Commun. *2010, 46* (27), 4977-9 [DOI: 10.1039/c0cc01197e]; deuteration of terminal and internal olefins (at both the double bond and in the alkyl chain) with activation by RuH(Cl)(CO)(PPh_3)$_3$ s. S.K.S. Tse, P. Xue, Z. Lin, G. Jia, Adv. Synth. Catal. *2010, 352* (9), 1512-22 [DOI: 10.1002/adsc.201000037].

Bis(1,5-cyclooctadiene)rhodium(I) fluoroborate/styrenes *[Rh(cod)$_2$]BF_4/ArCH=CH_2*
Rhodium(I)-catalyzed dehydrogenative β-diaminoborylation of styrenes C=C-B(N<)$_2$

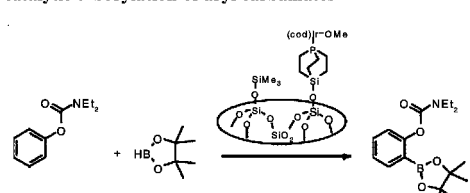
259.



Cyclic β-aryl-α,β-ethyleneboronic acid amides. Naphthalene-1,8-diaminatoborane [(dan)BH] (0.369 mmol) and 4-chlorostyrene (2.5 eq.) added to a soln. of [Rh(cod)$_2$]BF_4 (0.5 mol%) in dioxane at room temp. under N_2 in a glass tube, the tube sealed with a PTFE stopper, the soln. stirred at 60° for 4 h, concentrated *in vacuo*, and purified by chromatography on silica → (E)-2-(4-chlorostyryl)-2,3-dihydro-1*H*-naphtho[1,8-*de*][1,3,2]diaza-borinine. Y 83%. Efficient catalysis by the cationic rhodium(I) compd. and use of excess styrene (as receptor for eliminated hydrogen) provided a route to stable, electron-diverse (E)-β-boryl-styrene derivs. (nine examples; Y 59-94%) in the presence of halo, ether, ester and pinacolatoboron functionality. 4-Bromostyrene, however, failed to give the desired product. Neutral rhodium compds. were less effective catalysts, as were iridium and ruthenium complexes, and the addition of a triphenylphosphine ligand produced a significant reduction in yield. The products were subjected to cross-coupling reactions to afford highly conjugated compds. F.e. and optimization s. N. Iwadate, M. Suginome, Chem. Lett. *2010, 39* (6), 558-60 [DOI: 10.1246/cl.2010.558].

Covalently-linked silica-supported iridium(I) phosphine complex *[Ir(SiO$_2$-SMAP)]*
Heterogeneous catalytic *o*-borylation of aryl carbamates H → B(OR)$_2$

260.



The covalently-linked silica-supported 1-phospha-4-silabicyclo[2.2.2]octane ligand (silica-SMAP; 0.064 mmol P g^{-1}; 0.0025 mmol), anhydrous degassed hexane (1.1 ml) and [Ir(OMe)(cod)]$_2$ (0.00125 mmol) in hexane (0.4 ml) placed in a glass tube (inside a glove box), the mixture stirred for 1 min at 25°, phenyl N,N-diethylcarbamate (1 mmol) and pinacolatoborane (0.5 mmol) added,

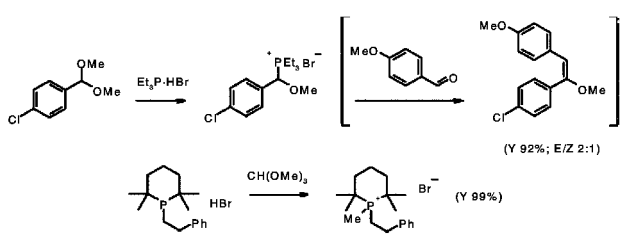
the tube sealed with a screw cap, removed from the glove box, stirred at 70° for 12 h, the mixture filtered through a glass pipette equipped with a cotton filter, the solvent removed under reduced pressure, and the crude residue purified by GPC → product. Y 64%. *o*-Boration takes place uniquely with a range of mono- or di-subst. aryl N,N-diethylcarbamates leaving MeO, CF_3, Ph, Cl, F, $MeOCOCH_2$, *t*-BuOCOO and ketal-protected acetyl groups at the *m*- or *p*-site unaffected. With a methoxycarbonyl group at the *p*-position, however, a 61:39 mixture of regioisomers was obtained with preference for *o*-borylation relative to the carbamate residue. Various other O-protected phenols (methyl and methoxymethyl phenolethers, phenol carbonates, phenyl methanesulfonates and phenyl phosphorodiamidates) were also tested but *o*-borylation was either very low-yielding or gave mixtures of regioisomers. F.e., also Suzuki coupling of the products (crude, if necessary) using $Pd(PPh_3)_4/Na_2CO_3$ and Ni(II)-catalyzed [Nakamura-type] coupling with ar. bromides, s. K. Yamazaki, S. Kawamorita, H. Ohmiya, M. Sawamura, Org. Lett. *2010, 12* (18), 3978-81 [DOI: 10.1021/ol101493m].

Oxygen ↑ RemC ↓↑ O

Without additional reagents *w.a.r.*

α-Alkoxyphosphonium salts from tert. phosphines and acetals $C(OR)_2 \rightarrow C(OR)P^+\leqslant$

261.



Triethylphosphine·HBr (1 eq.) added to 4-chlorobenzaldehyde dimethyl acetal (2 mmol) in a flame-dried flask under argon, the mixture stirred at 80° for 50 min, solvent removed, and the residue placed *in vacuo* for 50 min → (α-methoxy-4-chlorobenzyl)triethylphosphonium bromide. Y 98%. Reaction of triphenylphosphine with dimethyl acetals afforded methyl(triphenyl)-phosphonium salts, whereas *trialkylphosphines* afforded the title compounds (cf. *78*, 242). This novel and efficient process was apparently general for dimethyl acetals derived from α,β-unsaturated and electron-diverse ar. aldehydes (eight examples; Y 97-99%), with the water-sensitive products isolated, without need for chromatography, by simple removal of methanol *in vacuo*. The products are useful intermediates for Wittig reaction with ar. or unsaturated aldehydes to form **enolethers** or **1- or 2-alkoxy-1,3-dienes** (sixteen examples; Y 87-95%; undecanal gave 75%). Interestingly, replacing dimethyl acetals with methyl orthoformate generated the softer and less discriminating oxonium ion intermediate, which was able to P-methylate *both* triphenyl- and trialkyl-phosphines, thereby providing a general and environmentally benign route to quaternary **methylphosphonium salts** (seven examples; Y all 99%). F.e. and substrate prepn. s. P. Das, J. McNulty, Eur. J. Org. Chem. *2010* (19), 3587-91 [DOI: 10.1002/ejoc.201000601].

Microwaves [\\\\]

Aluminum dihydrogen phosphate $Al(H_2PO_4)_3$

Acetic anhydride/acetyl chloride $Ac_2O/AcCl$

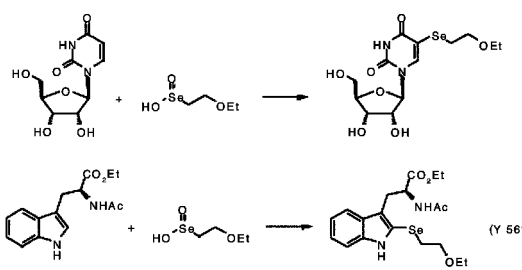
3-Component synthesis of α-aminophosphonic acid esters from aldehydes $CHO \rightarrow CH(NHR)PO(OR)_2$

by coupling with prim. amines and phosphorous acid diesters s. *33,* 593s*76*; *uncatalyzed* conversion under microwave irradiation s. A.J. Rao, P.V. Rao, V.K. Rao, C. Mohan, C.N. Raju, C.S. Reddy, Bull. Korean Chem. Soc. *2010, 31* (7), 1863-8 [DOI: 10.5012/bkcs.2010.31.7.1863]; with $Al(H_2PO_4)_3$ under solvent-free conditions s. M.T. Maghsoodlou, S.M. Habibi-Khorassani, R.

Heydari, N. Hazeri, S.S. Sajadikhah, M. Rostamizadeh, Chin. J. Chem. *2010, 28* (2), 285-8 [DOI: 10.1002/cjoc.201090067]; with an acyclic acidic ionic liquid in water for dealkylative coupling with trimethyl phosphite (cf. *59*, 234s*76*) s. D. Fang, C. Jiao, B. Ji, Phosphorus, Sulfur Silicon Relat. Elem. *2010, 185* (12), 2520-6 [DOI: 10.1080/10426501003724905]; with $Bi(OTf)_3$ as catalyst under solvent-free conditions s. A. Banik, S. Batta, D. Bandyopadhyay, B.K. Banik, Molecules *2010, 15* (11), 8205-13 [DOI: 10.3390/molecules15118205]; with $KHSO_4$ cf. P. Thirumurugan, A. Nandakumar, N.S. Priya, D. Muralidaran, P.T. Perumal, Tetrahedron Lett. *2010, 51* (43), 5708-12 [DOI: 10.1016/j.tetlet.2010.08.066]; synthesis of N-protected α-aminophosphorus(V) compds. in acetic anhydride/acetyl chloride s. P. Thirumurugan, A. Nandakumar, N.S. Priya, D. Muralidaran, P.T. Perumal, ibid. *2010, 51* (43), 5708-12 [DOI: 10.1016/j.tetlet.2010.08.066].

Trifluoroacetic acid or Heptafluorobutyric acid *CF_3COOH or C_3F_7COOH*
(Het)ar. selenylation with 2-ethoxyethaneseleninic acid H → SeR

262.

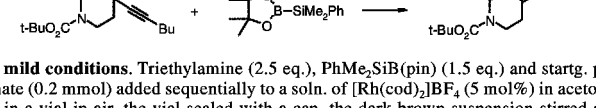


5-(Alkylseleno)uridines in water. Uridine (0.041 mmol) and heptafluorobutyric acid (1 drop) added to a soln. of 2-ethoxyethaneseleninic acid (3 eq.) in water (1 ml), the mixture refluxed for 24 h, concentrated, and purified by chromatography on silica → 5-(2-ethoxyethylseleno)uridine. Y 71%. The seleninic acid reacts with electron-rich (het)arenes (pyrimidines, indoles, phenols) to afford the corresponding selenoethers, with experimental observations suggesting initial formation of a selenoxide (ten examples; Y 30-71%). The reaction was generally conducted in trifluoroacetic acid/acetonitrile but water-soluble substrates were able to utilize aq. heptafluorobutyric acid. F.e., transformations of the selenoether moiety, and activity of a family of 5-uridinyl derivs. as human and malarial orotate phosphoribosyltransferase [OPRT] inhibitors s. M. Abdo, Y. Zhang, V.L. Schramm, S. Knapp, Org. Lett. *2010, 12* (13), 2982-5 [DOI: 10.1021/ol1010032].

Bismuth(III) triflate *$Bi(OTf)_3$*
Potassium hydrogen sulfate *$KHSO_4$*
3-Component synthesis of α-aminophosphonic acid esters $CHO \rightarrow CH(NHR)PO(OR)_2$
from aldehydes s. *33*, 593s*78*

Bis(1,5-cyclooctadiene)rhodium(I) fluoroborate/triethylamine *$[Rh(cod)_2]BF_4/Et_3N$*
Allenylsilanes $C(OCOOR)C{\equiv}C \rightarrow C{=}C{=}C(Si{\in})$
from 2-acetylenecarbonic acid esters and silylboronic acid esters
Regioselective rhodium(I)-catalyzed substitution

263.



under mild conditions. Triethylamine (2.5 eq.), $PhMe_2SiB(pin)$ (1.5 eq.) and startg. propargylic carbonate (0.2 mmol) added sequentially to a soln. of $[Rh(cod)_2]BF_4$ (5 mol%) in acetone or DMF (1 ml) in a vial in air, the vial sealed with a cap, the dark brown suspension stirred at 50° until

reaction complete (TLC; 12 h), filtered through silica, concentrated *in vacuo*, and purified by flash chromatography on silica → *tert*-butyl 4-[2-(dimethylphenylsilyl)-1-hexenylidene]piperidine-1-carboxylate. Y 96%. The method provides a general synthesis of allenylsilanes not readily available by other routes, affording the S_N2' substitution products exclusively (ten examples; Y 80-97%) for internal mono/di-α-alkyl-propargylic carbonates in the presence of ester, carbamate, silyl ether, alcohol and ether functionality. Reaction of an optically active propargylic carbonate proceeded with excellent chirality transfer to afford an axially chiral allenylsilane. A substrate lacking an α-substituent gave a low yield (17%), a terminal propargylic carbonate gave complex mixtures and other silylboron reagents were unreactive. The reaction can be carried out in a number of alternative solvents but yields are significantly reduced in the absence of triethylamine. F.e., optimization and substrate prepn. s. H. Ohmiya, H. Ito, M. Sawamura, Org. Lett. *2009*, *11* (24), 5618-20 [DOI: 10.1021/ol902339a].

Nitrogen ↑ — RemC ↓↑ N

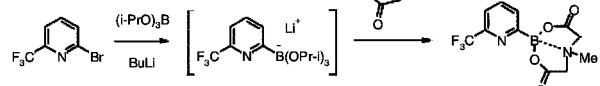
Palladium(II) acetate/potassium iodide/cesium carbonate — $Pd(OAc)_2/KI/Cs_2CO_3$
Arylphosphonic acid esters from diazonium fluoroborates — $N_2^+ \rightarrow PO(OR)_2$
Also ar. phosphine oxides or tert. arylphosphines s. *78*, 277

Halogen ↑ — RemC ↓↑ Hal

n-Butyllithium — *BuLi*
Arylsilanes from arenes or ar. bromides — ArSi≤
en route to phenols s. *78*, 102

n-Butyllithium/triisopropyl borate — *BuLi/(i-PrO)$_3$B*
Hetarylboronic acid N-methyliminodiacetates — Br → B≤
from hetar. bromides and N-methyliminodiacetic acid [MIDA]

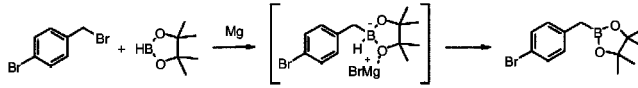
264.



A soln. of *n*-butyllithium (2.5 *M*; 0.99 eq.) in hexanes (3.4 ml) added dropwise over 15 min to a mixture of 2-bromo-6-trifluoromethylpyridine (8.6 mmol) and triisopropyl borate (1.16 eq.) in THF (17 ml) at -78°, the mixture stirred for 1 h, then at 23° for 3 h, the Li-pyridylborate soln. added dropwise to a soln. of N-methyliminodiacetic acid (1.7 eq.) in DMSO (17 ml) at 115° so as to maintain a temp. of 115-120° (ca 1 h; with rapid collection of THF distillate), the mixture cooled to 50°, DMSO removed *in vacuo*, the residue adsorbed onto Celite from an acetonitrile suspension, stored *in vacuo* for 12 h, and purified by chromatography on silica → (2-trifluoromethylpyridin-6-yl)-N-methyliminodiacetoxyboronate. Y 89%. This practical, scalable and cost effective prepn. of MIDA boronates ('slow release' sources of otherwise unstable boronic acids for cross-couplings: cf. *76*, 501) appears general for electron-diverse 2-bromopyridines, affording air- and heat-stable (130° in aq. DMSO) MIDA boronates (ten examples; Y 42-89%) with rapid MIDA complexation at 115° minimizing protodeborylation of the initial pyridine-borate. 2,5-And 2,6-dibromopyridine both gave monosubst. 2-MIDA boronates. The reaction also gave moderate yields with 5-bromothiazole (Y 30%) and 2-bromopyrazine (Y 43%). F.e. and optimization s. G.R. Dick, D.M. Knapp, E.P. Gillis, M.D. Burke, Org. Lett. *2010*, *12* (10), 2314-7 [DOI: 10.1021/ol100671v].

Magnesium/triethylamine *Mg/Et$_3$N*
Benzylboronic acid esters from benzyl halides Hal → B(OR)$_2$
Grignard-type coupling with pinacolborane using magnesium metal in catalytic amount

265.

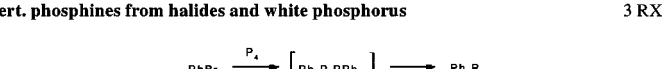


Mg turnings (10 mol%), distilled THF (10 ml), 4-bromobenzyl bromide (1 mmol), triethylamine (1 eq.) and pinacolborane (1 eq.) added successively to a round-bottom flask under N_2, the resulting mixture heated under reflux, with stirring, for 15 h, followed by hydrolytic work-up and purification by chromatography on silica gel → 2-[(4-bromophenyl)methyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane. Y 88% (100% conversion). A variety of ring-subst. (alkyl, methoxy, chloro, bromo) benzyl bromides reacted similarly (seven examples; Y 62-92%), albeit with hindered examples giving <100% conversion (*o*-methyl: 80%; *p-tert*-butyl: 90%). The hindered α-methylbenzyl bromide afforded a reduced yield (30%; 40% conversion) and *benzyl chlorides* were similarly sluggish and low-yielding (three examples; Y 41-42%; conversion 39-41%) even on prolonged heating (24 h) at elevated temp. (refluxing DME). Interestingly, the only by-products were methylarenes, with no benzyl dimers (Wurtz coupling products) observed. Mechanistic considerations, including DFT calculations, concluded that the reaction proceeds via an unusual magnesium dialkoxy(alkyl)borohydride intermediate, which preferentially reacts with a further molecule of benzyl halide deriv. to give a benzylmagnesium halide, rather than eliminating HMgBr. It is noteworthy that pinacolborane acts as both electrophile and reducing agent. F.e.s. C. Pintaric, S. Olivero, Y. Gimbert, P.Y. Chavant, E. Duñach, J. Am. Chem. Soc. *2010*, *132* (34), 11825-7 [DOI: 10.1021/ja1052973].

Triisopropyl borate s. under BuLi *(i-PrO)$_3$B*

Titanium(III) [tert-butyl(3,5-dimethylphenyl)amide] *Ti[N(Bu-t)Ar]$_3$*
Tert. phosphines from halides and white phosphorus 3 RX → R$_3$P

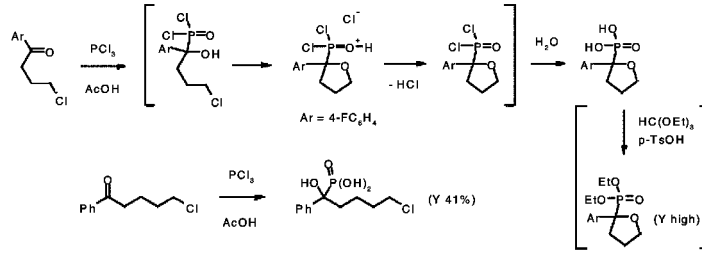
266.



The direct functionalization of white phosphorus (P_4), a known radical trap, obviates the need for the intermediacy of PCl_3 in the synthesis of a variety of phosphine derivs. Ti[N(Bu-*t*)Ar]$_3$ (Ar = 3,5-$Me_2C_6H_3$) rapidly abstracts a halogen atom from RX (X = I, Br or Cl; R = aryl, cyclohexyl, Ph_3Sn or Me_3Si), conveniently in the presence of P_4, to afford XTi[N(Bu-*t*)Ar]$_3$ and R·, giving rise to **triaryl-, trialkyl-, stannyl- and silyl-phosphines** in high yield. **E: Triarylphosphines**. Ti[N(Bu-*t*)Ar]$_3$ (*5 eq.*) added to a soln. of P_4 (0.04 *M*) in benzene (0.04 *M*) at room temp., bromobenzene (*5 eq.*) added by syringe, and the reaction worked up after 1 min → triphenylphosphine. Y 72% (after repeated crystallizations from ether at -35°). Using less than 5 eq. of the reagents gave rise to increasing amounts of Ph_4P_2, which became the major product (Y 80%) when quantities were reduced to only 2 eq. Asymmetric phosphines (Ph_2PMes, Ph_2PCy and Ph_2PSnPh_3) were obtained quantitatively by treatment of the latter with 2 eq. of the appropriate reagents. This apparent stepwise radical degradation of P_4 was exploited further to prepare novel disubst. ***cis,trans*-tetraphosphabicyclobutanes** (78% yield using the highly hindered 2,6-$Mes_2C_6H_3I$ as radical precursor). F.e., also catalyst recycling by treatment of XTi[N(Bu-*t*)Ar]$_3$ with Na/Hg, and experimentation towards a catalytic variant, s. B.M. Cossairt, C.C. Cummins, New J. Chem. *2010*, *34* (8), 1533-6 [DOI: 10.1039/c0nj00124d].

Phosphorus trichloride/acetic acid *PCl_3/AcOH*
2-Aryltetrahydrofuran-2-ylphosphonic acids from aryl γ-chloroketones ○

267.



PCl_3 (1.375 eq.) added dropwise to 4-chloro-1-(4-fluorophenyl)-1-butanone (10 mmol) with stirring at 0°, the mixture allowed to warm to room temp., stirred for 30 min, cooled to 0°, glacial acetic acid added dropwise, the mixture stirred at 0° for 20 h, quenched with ice (50 g), heated at 90° for 40 min to ensure complete hydrolysis, solvents evaporated *in vacuo*, the resulting oil re-evaporated with water (3 x 20 ml), the crystalline residue washed with cold water and benzene, and dried under vacuum → 2-(4-fluorophenyl)tetrahydrofuran-2-ylphosphonic acid. Y 83%. Four similar examples afforded yields of 57-94%, lowest for substrates containing electron-rich ar. groups; a 2-naphthyl analog gave only 20%. A mechanism is proposed, in which it is suggested that anchimeric assistance of the P=O group is crucial to the success of the reaction. Attempted extension of the method to the prepn. of tetrahydropyranyl analogs afforded only α-hydroxyphosphonic acid addition products (Y 41% reported for one example), with no cyclization observed. F.e., also conversion of the products to their diethyl esters (by treatment with ethyl orthoformate/TsOH), s. V.V. Komissarov, A.M. Kritzyn, J.J. Vepsäläinen, Beilstein J. Org. Chem. *2010*, *6*, No. 63 [DOI: 10.3762/bjoc.6.63].

Nickel(II) mixed phosphine complexes/triethylamine *[Ni(II)]*
Pinacolboryltris(triethylphosphine)rhodium(I) *$PinB(Et_3P)_3Rh(I)$*
Arylboronic acid esters from ar. halides s. *76*, 278s*78* Hal → $B(OR)_2$

Sulfur ↑ RemC ↓↑ S

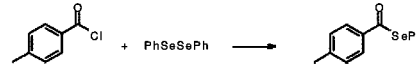
Sodium salt *Na^+*
Replacement of sulfonyl groups in 1,1-alkoximinosulfones ←
by phosphonyl groups s. *78*, 463

Remaining Elements ↑ RemC ↓↑ Rem

Microwaves s. under Pd(OAc)$_2$ [\\\\]

Copper(II) oxide nanoparticles/cesium carbonate/1-butyl-3-methylimidazolium hexafluorophosphate ←
Selenolic acid esters from carboxylic acid chlorides and diselenides COCl → C(O)SeR

268.

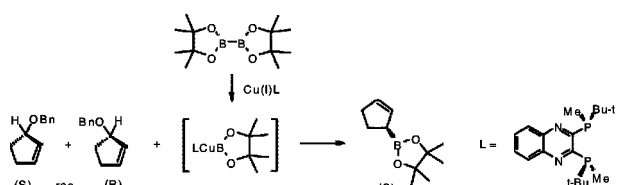


in an ionic liquid solvent. A Schlenk tube charged under N_2 with 4-methylbenzoyl chloride (1 mmol) and CuO nanopowder (5 mol%), followed by diphenyl diselenide (0.5 mmol) and Cs_2CO_3 (1 mmol) in [bmim]PF_6 (1 ml), the mixture stirred at 80° for 60 min (TLC monitoring), and

worked up with purification by chromatography on silica → product. Y 90%. The procedure is mild, eco-friendly, highly efficient, byproduct-free, based on an inexpensive catalyst and a harmless, non-volatile solvent, and is applicable to the coupling of both aroyl and acyl chlorides with diaryl diselenides (twelve examples; Y 57-91%). Yields were lower with diaryl diselenides and aroyl chlorides possessing electron-withdrawing groups than those possessing electron-donating groups. Both the catalyst and ionic liquid were simply retrieved and recycled three times with effectively the same outcome. F.e. and comparison of ionic liquids and bases s. D. Singh, S. Narayanaperumal, K. Gul, M. Godoi, O.E.D. Rodrigues, A.L. Braga, Green Chem. *2010*, *12* (6), 957-60 [DOI: 10.1039/c002648d]; with In in [bmim]PF_6, also thiolic acid esters from disulfides (*3*, 569s*78*), s. G. Tabarelli, E.E. Alberto, A.M. Deobald, G. Marin, O.E.D. Rodrigues, L. Dornelles, A.L. Braga, Tetrahedron Lett. *2010*, *51* (43), 5728-31 [DOI: 10.1016/j.tetlet.2010.08.076]; selenolic acid esters **from carboxylic acid** chlorides or **anhydrides** with $FeCl_2$ and Mg-dust in 1,4-dioxane at 100° s. K. Ren, M. Wang, P. Liu, L. Wang, Synthesis *2010* (7), 1078-82 [DOI: 10.1055/s-0029-1219229].

Copper(I) tert-butoxide/(R,R)-2,3-bis[tert-butyl(methyl)phosphino]quinoxaline ←
Direct enantioconvergent S_N2'-substitution of racemic cyclic 2-ethyleneethers ←

269.

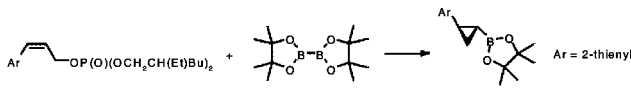


Dynamic kinetic resolutions and deracemizations are in vogue for the one-pot conversion of racemic substrates to single enantiomers in high chemical yield, these proceeding either by racemization of the chiral center (cf. *53*, 500s*78*) or intermediate formation of a prochiral molecule (cf. *78*, 546). An alternative methodology has now been demonstrated in the direct enantioconvergent S_N2'-substitution of a cyclic allyl ether. **E: Chiral cyclopent-2-enylboronic acid acid esters.** A soln. of Cu(I)-*tert*-butoxide (0.025 mmol), (R,R)-2,3-bis[*tert*-butyl(methyl)-phosphino]quinoxaline [QuinoxP] (0.025 mmol) and bis(pinacolato)diboron (0.75 mmol) in dry diethyl ether (0.5 ml) stirred in a vial (kept in a nitrogen-filled glove box), the vial sealed with a rubber septum, removed from the glove box, connected to an argon line through a needle, the startg. allylic ether (0.5 mmol) added dropwise at 30°, stirred for 12 h, and the mixture directly subjected to chromatography on silica gel → (S)-product. Y 92% (e.e. 92%). Here, *under exclusive reagent control*, each enantiomer of the racemic substrate *gives the same chiral product*: the (R)-enantiomer being attacked in *syn*-S_N2' fashion by the intermediate copper(I) boronate, while the (S)-enantiomer is attacked in *anti*-S_N2' fashion. Reaction was applied to both tertiary and secondary cyclopent-2-enyl ethers with the same chiral ligand (three examples; Y 91-98%; e.e. 92-97%), with (R,R)-Me-DuPhos affording slightly lower enantioselectivity and (R)-BINAP requiring a considerably longer reaction time with low enantioselectivity. The potential of the methodology is clearly high for the enantioconvergent conversion of racemic substrates which cannot readily, or at all, be racemized or symmetrized. The products were converted to the corresponding **chiral cyclopent-2-enylcarbinols** (possessing quaternary or tertiary carbon centers) by classical allylboration. F.e.s. H. Ito, S. Kunii, M. Sawamura, Nature Chem. *2010*, *2* (11), 972-6 [DOI: 10.1038/nchem.801].

Copper(II) triflate/(S)-3-(2,6-diisopropylphenyl)-5-phenyl-1-(2-sulfonatophenyl)-imidazolinium/sodium methoxide ←
Regioselective asym. copper(II)-N-heterocyclic carbene catalyzed boronation C(B≺)C=C of 2-ethylenecarbonic acid esters with allyl shift s. *78*, 84

Copper(I) chloride/1,3-bis(diphenylphosphino)propane/potassium tert-butoxide ←
Cyclobutaneboronic acid esters from sulfonyloxy-3-ethylenes □
via stereospecific copper(I)-catalyzed hydroboration – *cis*-2-Silylcyclobutaneboronic acid esters s. *78*, 388

Copper(I) chloride/1,2-bis((2R,5R)-2,5-diisopropylphospholano)benzene or (R,R)-2,3-bis-[tert-butyl(methyl)phosphino]quinoxaline/potassium tert-butoxide ←
***trans*-2-Arylcyclopropaneboronic acid esters** ▽
from 3-aryl-2(Z)-ethylenephosphoric acid esters
via copper(I)-catalyzed asym. hydroboration

270. 

under mild conditions. Bis(pinacolato)diboron (1.2 eq.), CuCl (5 mol%), (R,R)-*i*-Pr-DuPhos (6 mol%) and toluene (1.2 ml) added to a vial under N_2, the vial sealed, the mixture stirred at room temp. for 30 min, startg. allylic phosphate (0.4 mmol) added by syringe, followed by dropwise addition of K-*tert*-butoxide (1 eq.; 1.2 *M* in THF), the mixture stirred until reaction complete (72 h), passed through a short column of Florisil, concentrated, and purified by chromatography on silica gel → 4,4,5,5-tetramethyl-2-[(1R,2R)-2-(thiophen-2-yl)cyclopropyl]-1,3,2-dioxaborolane. Y 70% (*trans/cis* 48:1; e.e. 92%). The reaction was successful with a range of aryl-subst. allyl phosphates (twelve examples; Y 50-90%; *trans/cis* 16:1 to 48:1; e.e. 64%, 82-94%), with highest enantioselectivity obtained for substrates carrying electron-rich aryl groups. Chloro, ether, ester, acetal and N-Boc groups were tolerated but the presence of bromo or acetyl ring-substituents led to dramatically diminished yields (8% and 11%, respectively). Replacing the aryl group with cyclohexen-1-yl gave none of the desired cyclopropane. Optimal results were obtained using bulky bis(2-ethylhexyl)phosphates as leaving groups (although low yields were obtained for diisopropyl analogs). While *(E)-allylic phosphates* gave rise to the analogous *cis* products using (R,R)-*i*-Pr-DuPhos as ligand, surprisingly the diastereoselectivity was switched using (R,R)-QuinoxP, giving rise to predominantly *trans* products; a plausible mechanistic explanation is presented. F.e.s. C. Zhong, S. Kunii, Y. Kosaka, M. Sawamura, H. Ito, J. Am. Chem. Soc. *2010*, *132* (33), 11440-2 [DOI: 10.1021/ja103783p].

Magnesium s. under $FeCl_2$ *Mg*

Indium/1-butyl-3-methylimidazolium hexafluorophosphate *In/[bmim]PF_6*
Selenolic acid esters from carboxylic acid chlorides and diselenides COCl → C(O)SeR
in an ionic liquid solvent s. *78*, 268

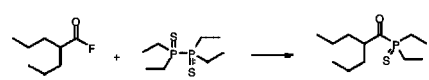
p-Benzoquinone s. under $Pd(OAc)_2$ *BQ*
1-Butyl-3-methylimidazolium hexafluorophosphate s. under CuO and In *[bmim]PF_6*
1,3-Bis(diphenylphosphino)propane s. under CuCl *dppp*
Bis[2-(diphenylphosphino)ethyl]phenylphosphine s. under $RhH(PPh_3)_4$ *$(Ph_2PCH_2CH_2)_2PPh$*
1,2-Bis((2R,5R)-2,5-diisopropylphospholano)benzene s. under CuCl *(R,R)-i-Pr-DuPhos*
(R,R)-2,3-Bis[tert-butyl(methyl)phosphino]quinoxaline s. under CuOBu-t and CuCl *QuinoxP*
Air s. under $Pd(OAc)_2$ *air*

Iron(II) chloride/magnesium *$FeCl_2$/Mg*
Selenolic acid esters from carboxylic acid chlorides or anhydrides
and diselenides s. *78*, 268

Bis(1,5-cyclooctadiene)rhodium(I) fluoroborate/triethylamine *$[Rh(cod)_2]BF_4/Et_3N$*
Allenylsilanes from 2-acetylenecarbonic acid esters C(OCOOR)C≡C → C=C=C(Si≤)
and silylboronic acid esters – Regioselective rhodium(I)-catalyzed substitution s. *78*, 263

Hydridotetrakis(triphenylphosphine)rhodium(I)/bis[2-(diphenylphosphino)ethyl]phenylphosphine ←
Acylphosphine sulfides C(O)F → C(O)P(S)≤
from carboxylic acid fluorides and diphosphine disulfides under rhodium(I) catalysis

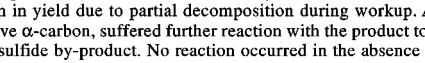
271.



A soln. of 2-propylpentanoyl fluoride (0.5 mmol), tetraethyldiphosphine disulfide (1 eq.), $RhH(PPh_3)_4$ (1 mol%) and bis[2-(diphenylphosphino)ethyl]phenylphosphine (2 mol%) in THF (1 ml) stirred and refluxed under argon for 3 h, concentrated *in vacuo*, and purified by flash chromatography on silica → diethyl(2-propylpentanoyl)phosphine sulfide. Y 93%. The use of electron-rich acyl fluorides and the tetraethyldiphosphine disulfide (rather than tetramethyl) were key to minimizing the formation of by-products from product decomposition. The method was successful with electron-rich aroyl fluorides and with acyl fluorides containing a sec. or tert. α-carbon (ten examples; Y 63-97%), with both benzoyl (Y 63%) and its 4-chloro deriv. (Y 18%) suffering reduction in yield due to partial decomposition during workup. A linear acyl fluoride, containing a reactive α-carbon, suffered further reaction with the product to afford an α-carboxyvinylphosphine disulfide by-product. No reaction occurred in the absence of a phosphine ligand or with acyl chlorides. F.e. and optimization s. M. Arisawa, T. Yamada, M. Yamaguchi, Tetrahedron Lett. *2010*, *51* (38), 4957-8 [DOI: 10.1016/j.tetlet.2010.07.038].

Palladium(II) acetate/2,9-dimethyl-1,10-phenanthroline/p-benzoquinone/microwaves or air ←
Arylphosphonic acid esters from phosphorous acid diesters ≥P(O)H → ≥P(O)Ar
and arylboronic acid or potassium aryl(trifluoro)borates
Chemoselective palladium(II)-catalyzed P-arylation

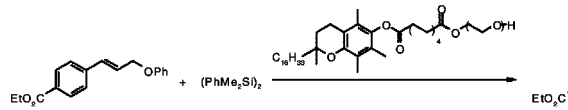
272.



A soln. of $Pd(OAc)_2$ (4 mol%) and 2,9-dimethyl-1,10-phenanthroline (6 mol%) in DMF (1 ml) stirred at room temp. for 30 min, added to a soln. of 4-bromobenzeneboronic acid (2 eq.), diethyl phosphite (0.5 mmol) and *p*-benzoquinone (1 eq.) in DMF (1 ml) in a microwave vial under air, the vial capped, the mixture stirred under microwave irradiation at 100° for 30 min, cooled, diluted with methylene chloride, washed with aq. NaOH, filtered through silica, and purified by chromatography on silica → diethyl 4-bromophenylphosphonate. Y 75%. This novel, efficient and apparently general P-arylation gave none of the alternative coupling products and utilized arylboronic acids and K-aryl(trifluoro)borates as arylating agents (thirteen examples; Y 51-90%) in the presence of halo, ketone and ester functionality. Comparable yields were obtained, in some cases, in the absence of microwaves at room temp. (24-48 h) using air as the reoxidant. A single vinylboronic acid example gave a low yield (37%). F.e., optimization and use of the procedure in the synthesis of a glutamine synthetase inhibitor s. M. Andaloussi, J. Lindh, J. Sävmarker, P.J.R. Sjöberg, M. Larhed, Chem. Eur. J. *2009*, *15* (47), 13069-74 [DOI: 10.1002/chem.200901473].

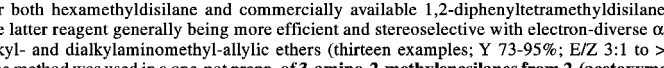
Dichloro[bis[2-(diphenylphosphino)phenyl] ether]palladium(II)/polyoxyethanyl α-tocopheryl sebacate/triethylamine ←
2-Ethylenesilanes from aryloxy-2-ethylenes OAr → Si≤
Palladium-assisted conversion under micellar catalysis

273.



in water only. Triethylamine (4 eq.) and an aq. soln. of PTS amphiphile (2%; 1.5 ml) added via syringe to a vial containing $PdCl_2$(DPEphos) (6 mol%), (E)-4-ethoxycarbonylcinnamyl phenyl

ether (0.25 mmol) and 1,2-diphenyltetramethyldisilane (1.5 eq.) in a glove-bag under argon at room temp., the vial closed with a Teflon coated cap, the mixture stirred vigorously for 20 h, poured into brine, extracted with ethyl acetate, filtered through silica, and purified chromatographically → dimethyl[(E)-4-(ethoxycarbonyl)cinnamyl]phenylsilane. Y 95% (E/Z >25:1; linear/branched 25:1). This regioselective and efficient silylation is achieved under *mild conditions* in a micellar environment in the absence of organic solvent (previous experiments with more reactive allylic acetates required heating in DMF). The reaction was selective (25:1) for the linear product for both hexamethyldisilane and commercially available 1,2-diphenyltetramethyldisilane, with the latter reagent generally being more efficient and stereoselective with electron-diverse α-aryl-, alkyl- and dialkylaminomethyl-allylic ethers (thirteen examples; Y 73-95%; E/Z 3:1 to >25:1). The method was used in a one-pot prepn. of **3-amino-2-methylenesilanes from 2-(acetoxymethyl)-aryloxy-2-ethyleneethers** (two examples; Y 68%, 70%).

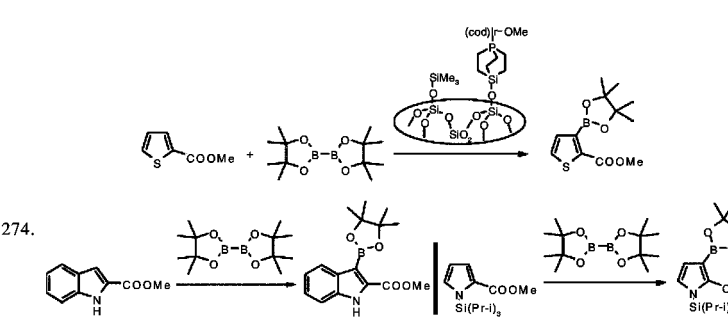


F.e. and optimization s. R. Moser, T. Nishikata, B.H. Lipshutz, Org. Lett. *2010, 12* (1), 28-31 [DOI: 10.1021/ol9023908].

Cyclopalladated ferrocenylimine-phosphine complex *[Pd(II)]*
Arylboronic acid esters from ar. halides Hal → $B(OR)_2$

and bis(pinacolato)diboron under copper(I) catalysis cf. *76,* 278; pinacolborylation of [het]ar. chlorides with phosphine-ligated cyclopalladated ferrocenylimine complexes as catalyst s. L. Wang, J. Li, X. Cui, Y. Wu, Z. Zhu, Y. Wu, Adv. Synth. Catal. *2010, 352* (11-12), 2002-10 [DOI: 10.1002/adsc.201000085]; neopentylglycolboration of *o*-subst. ar. halides possessing electron-withdrawing or -donating groups with a nickel(II) mixed phosphine complex as catalyst and Et_3N as base s. C. Moldoveanu, D.A. Wilson, C.J. Wilson, P. Leowanawat, A.-M. Resmerita, C. Liu, B.M. Rosen, V. Percec, J. Org. Chem. *2010, 75* (16), 5438-52 [DOI: 10.1021/jo101023t]; with highly active pinacolboryltris(triethylphosphine)rhodium(I) for converting pentafluoropyridine to 3,4,5,6-tetrafluoro-2-pinacolborylpyridine in hexamethyldisilane s. M. Teltewskoi, J.A. Panetier, S.A. Macgregor, T. Braun, Angew. Chem., Int. Ed. *2010, 49* (23), 3947-51 [DOI: 10.1002/anie.201001070].

Covalently-linked silica-supported iridium(I) phosphine complex *[Ir(SiO2-SMAP)]*
Heterogeneous catalytic *o*-borylation of heteroarylcarboxylic acid esters H → $B(OR)_2$



274.

Silica-SMAP (0.064 mmol P g^{-1}; 0.0025 mmol), bis(pinacolato)diboron (1 mmol), and anhydrous, degassed hexane (1.6 ml) placed in a glass tube (in a glove box), the mixture stirred for 1 min at

25°, a soln. of $[Ir(OMe)(cod)]_2$ (0.00125 mmol) in hexane (0.4 ml) and thiophene-2-carboxylic acid methyl ester (1 mmol) added, the tube sealed with a screw cap and removed from the glove box, the mixture stirred at 70° for 10 h, filtered through a glass pipette equipped with a cotton filter, the solvent removed under reduced pressure, and the residue worked up with purification by Kugelrohr distillation → product. Y 99%. *o*-Borylation is selective for a range of carbomethoxy-subst. thiophenes, benzo[*b*]thiophenes, furans, benzofurans, N-TIPS-protected pyrroles, and N-methyl- or N-unsubst. indoles, as well as N-carbalkoxy-indoles and -carbazoles (seventeen examples; Y 56-99%). This is complementary with borylation under homogeneous conditions with (4,4′-di-*tert*-butyl-2,2′-bipyridyl)iridium(I) complexes which, in earlier studies (cf. *64*, 219), was shown to be dictated more by steric and/or electronic rather than carbonyl-directing effects. There was no diborylation and no reaction in the absence of the P-ligand. F.e.s. S. Kawamorita, H. Ohmiya, M. Sawamura, J. Org. Chem. *2010*, *75* (11), 3855-8 [DOI: 10.1021/jo100352b].

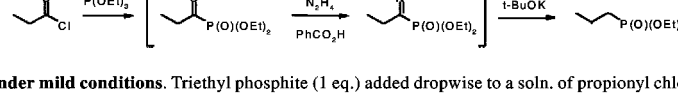
Chloro(1,5-cyclooctadiene)iridium(I) dimer/2,2′-bipyridyl-4,4′-dicarboxylic acid *[Ir(I)]*
Arylboronic acid esters from arenes H → $B(OR)_2$
and bis(pinacolato)diboron under iridium(I) catalysis cf. *64*, 219s*76*; under continuous flow with $[Ir(cod)Cl]_2$/2,2′-bipyridyl-4,4′-dicarboxylic acid (without loss of catalyst) s. T. Tagata, M. Nishida, A. Nishida, Adv. Synth. Catal. *2010*, *352* (10), 1662-6 [DOI: 10.1002/adsc.201000160].

Carbon ↑ RemC ↓↑ C

Potassium iodide s. under Pd(OAc)₂ *KI*

Hydrazine/benzoic acid/potassium tert-butoxide *N_2H_4/PhCOOH/t-BuOK*
Phosphonic acid esters from carboxylic acid chlorides COCl → $CH_2P(O)(OR)_2$
One pot procedure via acyl phosphonates

275.



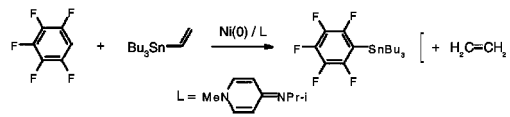
under mild conditions. Triethyl phosphite (1 eq.) added dropwise to a soln. of propionyl chloride (1 mmol) in methylene chloride (8 ml) at 0°, the mixture stirred at room temp. for 1 h, concentrated *in vacuo*, benzoic acid (2 eq.) and benzene (10 ml) added, the mixture stirred until homogeneous, hydrazine (1.05 eq.) in THF (1.05 ml) added dropwise, the mixture stirred vigorously for 1 h, flash-frozen and lyophilized (to remove water formed in the reaction), the solid dissolved in THF/*tert*-butanol (1:1; 10 ml), a soln. of *t*-BuOK (3 eq.) in the same solvent mixture (5 ml) added, the mixture stirred at room temp. for 6 h, diluted with ethyl acetate, quenched with 1 *M* aq. HCl, washed with satd. aq. $NaHCO_3$ and brine, concentrated *in vacuo*, and purified by flash chromatography on silica → diethyl *n*-propylphosphonate. Y 74%. Traditionally, alkyl phosphonates have been prepared from alkyl halides and trialkyl phosphites by the Arbuzov reaction, which is limited by use of high temps., and inefficient due to formation of one eq. alkyl halide by-product. The illustrated procedure generates acylphosphonates from commercially available acid chlorides [or ones formed *in situ* from the carboxylic acid and $(COCl)_2$] which, due to the electron-withdrawing phosphonate group, are readily reduced under Wolff-Kishner-type conditions at room temp. Prim. alkylcarboxylic acids were converted efficiently by this three/four step process (seven examples; Y 58-74%) in the presence of nitrile and ether functionality. Benzoyl chloride and branched alkyl derivs. gave lower yields (21-45%) due to decomposition of the intermediate acylphosphonates in some cases, and ester- or amide-containing products were labile under the reaction conditions. Removal of water formed during hydrazone formation was key to the success of the procedure. F.e. and optimization s. S.M.A. Kedrowski, D.A. Dougherty, Org. Lett. *2010*, *12* (18), 3990-3 [DOI: 10.1021/ol1015493].

Iodine *I_2*
α-Hydroxyphosphonic acid esters from aldehydes in water CO → $C(OH)PO(OR)_2$
s. *59*, 234s*78*

Perchloric acid-silica $HClO_4$-SiO_2
Phospha-Michael addition of trialkyl phosphites s. *22*, 675s*78* C=C → CHC-PO(OR)$_2$

Bis(1,5-cyclooctadiene)nickel(0)/4-isopropylimino-1-methyl-1,4-dihydropyridine or triisopropylphosphine *[Ni(0)]*
Nickel-catalyzed ar. stannylation of polyfluoroarenes with enestannanes H → Sn≤

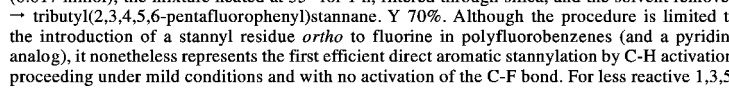
276.



A soln. of pentafluorobenzene (1.11 mmol) and tributyl(vinyl)tin (0.555 mmol) in benzene-d_6 (0.6 g) added to 4-isopropylimino-1-methyl-1,4-dihydropyridine (0.033 mmol) and Ni(cod)$_2$ (0.017 mmol), the mixture heated at 35° for 1 h, filtered through silica, and the solvent removed → tributyl(2,3,4,5,6-pentafluorophenyl)stannane. Y 70%. Although the procedure is limited to the introduction of a stannyl residue *ortho* to fluorine in polyfluorobenzenes (and a pyridine analog), it nonetheless represents the first efficient direct aromatic stannylation by C-H activation, proceeding under mild conditions and with no activation of the C-F bond. For less reactive 1,3,5- and 1,2,3-trifluorobenzene and 1,2-difluorobenzenes, however, the more thermally-stable triisopropylphosphine was the ligand of choice at elevated temperature (80°), affording di- and tristannylated products from the trifluorobenzenes (twenty-two examples in all; generally in 80-99% yield). Reaction is also applicable to trimethyl(vinyl)stannane and *cis*- or *trans*-tributyl-(1-propenyl)stannane, but replacement of these reagents with Bu_4Sn, Ph_4Sn, Bu_3SnPh or $Me_3SnSnMe_3$ was unsuccessful. Reaction is thought to involve oxidative addition of C-H and Sn-C bonds to the Ni center, terminating with elimination of alkene. F.e.s. M.E. Doster, J.A. Hatnean, T. Jeftic, S. Modi, S.A. Johnson, J. Am. Chem. Soc. *2010*, *132* (34), 11923-5 [DOI: 10.1021/ja105588v].

Palladium(II) acetate/potassium iodide/cesium carbonate $Pd(OAc)_2$/KI/Cs_2CO_3
Arylphosphonic acid esters from diazonium fluoroborates N_2^+ → PO(OR)$_2$

277.



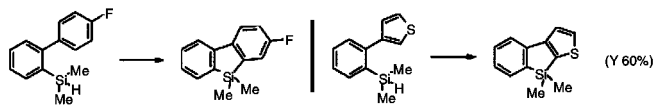
and trialkyl phosphites. $Pd(OAc)_2$ (5 mol%), triethyl phosphite (1.5 eq.) and Cs_2CO_3 (2 eq.) added with acetonitrile (2 ml) to a stirred mixture of 4-methoxybenzenediazonium fluoroborate (0.5 mmol) and KI (3 eq.) in anhydrous acetonitrile (1 ml) at room temp. under argon (the reactor being protected from light with Al film), the mixture stirred for 18 h at 80° under argon, cooled to room temp., diluted with ethyl acetate, washed with brine, dried (Na_2SO_4), concentrated under reduced pressure, and the residue purified by chromatography on silica gel → diethyl 4-methoxyphenylphosphonate. Y 84%. The same product was obtained from diethyl phosphite in 81% yield after 24 h. Fifteen further diazonium fluoroborates bearing electron-donating or -withdrawing groups (bromo, chloro, nitro, cyano, keto or ester as well as ether) reacted with triethyl phosphite under these optimized conditions (Y 54-95%), *ortho* substituents also being tolerated. Reaction is believed to take place via iododediazonation in the presence of KI, and may be carried out in one pot **from prim. ar. amines** (three examples; Y 50-66%), provided volatiles are removed under reduced pressure after diazonium salt formation. The method has been extended to the formation of **ar. phosphine oxides** from diphenylphosphine oxide (six examples; Y 50-90%; two *o*-subst. derivs. reacting poorly) or **tert. arylphosphines** from dicyclohexylphosphine (Y 70%). F.e.s. R. Berrino, S. Cacchi, G. Fabrizi, A. Goggiamani, P. Stabile, Org. Biomol. Chem. *2010*, *8* (20), 4518-20 [DOI: 10.1039/c0ob00243g].

Elimination ⇑

Hydrogen ↑ RemC ⇑ H

Chlorotris(triphenylphosphine)rhodium(I) $RhCl(PPh_3)_3$
Silacyclopentadiene [silole] ring by rhodium(I)-catalyzed dehydrogenative cyclization ○

278.



Silafluorenes from 2-(hydridosilyl)biaryls. A mixture of 2-(dimethylsilyl)-4′-fluorobiphenyl (0.125 mmol), $RhCl(PPh_3)_3$ (0.5 mol%) and 1,4-dioxane (0.125 ml) stirred at 135° for 15 min in a sealed tube, solvent removed *in vacuo*, and the product isolated by chromatography on silica → 9,9-dimethyl-2-fluoro-9-silafluorene. Y 95%. This efficient and rapid cyclization involves both Si-H and C-H activation, producing H_2 as the only by-product, and was successful for electron-diverse 2-dimethylsilylbiphenyls (ten examples; Y 66-96%). A 4′-chloro deriv. (Y 72%) suffered partial protodechlorination (Y 11%) and while an electron-rich 4′-methoxy deriv. was less reactive (Y 60%) under these conditions, prolonged reaction (1 h) in the presence of 3,3-dimethylbutene as hydrogen acceptor increased the yield to 91% (similarly for the 2′-methoxy isomer; Y 93%). Cyclization of the hetar. analog, 2-dimethylsilylphenyl-3-thiophene, gave the corresponding tricyclic in 60% yield and a 2,2″-bis(silyl)terphenyl gave the pentacyclic analog (Y 87%). F.e. and substrate prepn. s. T. Ureshino, T. Yoshida, Y. Kuninobu, K. Takai, J. Am. Chem. Soc. *2010*, *132* (41), 14324-6 [DOI: 10.1021/ja107698p].

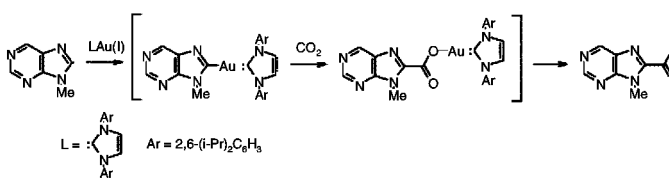
Formation of C-C Bond

Uptake ⇓

Addition to Hydrogen and Carbon CC ⇓ HC

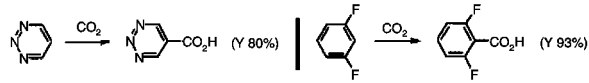
[N,N′-Bis(2,6-diisopropylphenyl)imidazol-2-ylidene]gold(I) hydroxide/potassium hydroxide ←
Gold(I)-catalyzed regioselective carboxylation of (het)arenes with carbon dioxide under mild conditions H → COOH

279.



8-Carboxypurines. A soln. of [(IPr)AuOH] (1.5 mol%) and KOH (1.05 eq.) in THF (1.2 ml) stirred (1450 rpm) under CO_2 (1.5 bar) at 20° for 15 min, a soln. of 9-methylpurine (1 mmol) in the same solvent (0.3 ml) introduced via CO_2-flushed syringe, the mixture stirred for 12 h, quenched with 1 *M* aq. HCl, extracted with ethyl acetate, washed with brine, concentrated *in vacuo*, and

purified by flash chromatography → 9-methylpurine-8-carboxylic acid. Y 91%. A series of hetarenes (azoles, purines, pyridazines, triazines) and activated arenes were carboxylated exclusively at the most acidic C-H (twenty-one examples; Y 69-94%; thiazole gave a 2.3:1 mixture of 2- and 5-carboxylic acids in 88% yield). In some cases the more basic N,N′-di-*tert*-butylimidazolylidene-derived complex was required for activation.

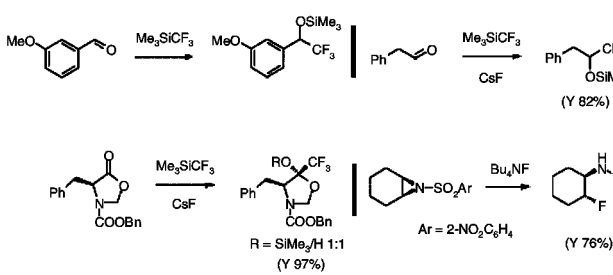


The method was **also** amenable to generation of **methyl esters**, in one pot, by quenching intermediate potassium carboxylates with MeI (six examples; Y >80%). The proposed mechanism was supported by isolation of the two gold intermediates in one case (oxazole) in 86-93% yields and their subsequent conversion to the product (Y both 88%). F.e. and optimization s. I.I.F. Boogaerts, S.P. Nolan, J. Am. Chem. Soc. *2010*, *132* (26), 8858-9 [DOI: 10.1021/ja103429q].

Addition to Oxygen and Carbon — CC ⇓ OC

Potassium hydroxide or Cesium fluoride — *KOH or CsF*

1,1,1,3,3-Pentafluorobutane as environmentally friendly solvent for fluorine chemistry ←

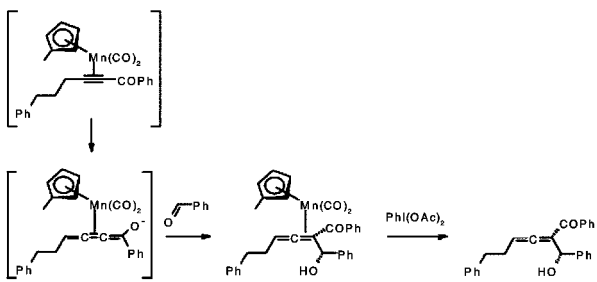


280.

Non-toxic and ozone-friendly 1,1,1,3,3-pentafluorobutane (commercially available as Solkane® 365mfc) is reported to be a viable alternative to the use of DMF or chlorinated solvents in the nucleophilic trifluoromethylation of oxo compds. and the fluorinative ring opening of N-sulfonylaziridines. **E: 2-Siloxy-1,1,1-trifluorides from aldehydes**. Ruppert's reagent [trifluoromethyl(trimethyl)silane] (2 eq.) added to a stirred soln. of 3-methoxybenzaldehyde (0.2 mmol) and KOH (1 eq.) in 1,1,1,3,3-pentafluorobutane (0.5 ml) at room temp. under N_2, the mixture stirred for 1 h, solvent removed *in vacuo* (89% recovery), and the residue purified by chromatography on silica gel → trimethyl[2,2,2-trifluoro-1-(3-methoxyphenyl)ethoxy]silane. Y 92%. A variety of ar. (incl. naphthyl), α,β-unsatd. and enolizable aldehydes or ketones were similarly trifluoromethylated under the conditions in yields of 72-97% (fifteen examples). Inorganic bases (KOH, CsOH and CsF) were preferred to the more commonly used *n*-Bu_4NF, LiOAc, *t*-Bu_3P and K_2CO_3, which were largely ineffective. The solvent was also successfully employed for the nucleophilic trifluoromethylation of a single oxazolid-5-one deriv. and in the prepn. of **2-fluorosulfonylamines from N-sulfonylaziridines** using *n*-Bu_4NF (two examples; Y 76-77%). F.e.s. A. Kusuda, H. Kawai, S. Nakamura, N. Shibata, Green Chem. *2009*, *11* (11), 1733-5 [DOI: 10.1039/b913984b].

Potassium tert-butoxide/dicarbonylmanganese η^2-(α,β-acetylenecarbonyl compds.) ←
Regio- and diastereo-selective synthesis of β-hydroxy-α-vinylidene- ←
from α,β-acetylene-carbonyl compds. and aldehydes
via aldol-type condensation with manganese η^2-(α,β-acetylenecarbonyl compds.)

281.



A soln. of *t*-BuOK in dry THF (1 *M*; 1.35 mmol) added dropwise to a soln. of the startg. dicarbonylmanganese η^2-alkyne complex (0.54 mmol) [readily prepared by UV-irradiation of a soln. of tricarbonyl(1-methylcyclopentadienyl)manganese in dry THF for 30 min, followed by complexation with the unassociated α,β-acetyleneketone in dry THF at room temp. for 24 h] in dry THF (10 ml) at 0°, the startg. aldehyde (1.35 mmol) added slowly after 5 min, stirred for ca. 1 h at 0°, quenched with satd. aq. NH_4Cl, extracted with ether, dried over Na_2SO_4, evaporated under reduced pressure, the crude product taken up in dry acetone (20 ml) under argon, treated with $PhI(OAc)_2$ (1.08 mmol) for 1.5 h (to remove the manganese residue), solvent evaporated, and the residue worked up with flash chromatographic purification → product (as a 12:1 mixture of *rel*-(S)-2-[(S)-hydroxy(phenyl)methyl]-1,6-diphenylhexa-2,3-dien-1-one and *rel*-(S)-2-[(R)-hydroxy(phenyl)methyl]-1,6-diphenylhexa-2,3-dien-1-one). Y 79%. The procedure is mild, convenient, inexpensive and applicable to the coupling of α,β-acetylene-ketones and -carboxylic acid esters with ar. aldehydes possessing electron-withdrawing or -donating groups (twenty-three examples; Y 52-92%). Significantly, deprotonation of the startg. manganese alkyne complex leads to a cumulenolate which reacts *preferentially at the α-position*: a reaction which hitherto has not been accomplished efficiently from the corresponding uncomplexed acetylene derivs. The predominant (S*,S*)-diastereoisomer is thought to derive from an E(O)-cumulenolate and is rationalized on the basis of a metal-chelated cyclic transition state. There was no coupling, however, with aliphatic aldehydes, the startg. manganese alkyne complex undergoing isomerization to the manganese allene complex. F.e.s. M. Bhowmick, S.D. Lepore, Org. Lett. *2010*, *12* (21), 5078-80 [DOI: 10.1021/ol1021096].

n-Butyllithium *BuLi*
o-Vinylbenzyl alcohols from o-bromostyrenes and oxo compds. ←
en route to 1,3-dihydroisobenzofurans s. *78*, 460

Chiral aminoalcohols s. under R_2Zn ←
Chiral N,N′-bis(prolyl)-1,2-diphenylethylenediamine s. under $Zn(OTf)_2$ ←

Chitosan aerogel or Chiral α-subst. picolylamines ←
Organocatalyzed asym. aldol condensation in water s. *68*, 259s*78* CHO → CH(OH)C-CO

Quinidine or desmethoxyquinidine s. under $Ti(OPr\text{-}i)_4$ ←

Chiral 3-aminopyrrolidines or Brucine N-oxide/(R)- or (S)-proline ←
Asym. Baylis-Hillman reaction CHO → CH(OH)C(=CH_2)CO
s. *58*, 233s*74*; with chiral 3-aminopyrrolidines, e.g. (R)-3-(dimethylamino)-1-methylpyrrolidine, s. M. Pouliquen, J. Blanchet, M. De Paolis, B.R. Devi, J. Rouden, M.-C. Lasne, J. Maddaluno,

Tetrahedron: Asym. *2010, 21* (11-12), 1511-21 [DOI: 10.1016/j.tetasy.2010.04.038]; *under dual catalysis* with a chiral α-guanidinocarboxylic acid ester and triphenylphosphine s. J. Shah, Z. Yacob, A. Bunge, J. Liebscher, Synlett *2010* (14), 2079-82 [DOI: 10.1055/s-0030-1258531]; with brucine N-oxide and (R)- or (S)-proline as co-catalyst, notably for the asym. Baylis-Hillman reaction with electron-deficient ar. aldehydes, s. K. Oh, J.-Y. Li, J. Ryu, Org. Biomol. Chem. *2010, 8* (13), 3015-24 [DOI: 10.1039/c003667f].

Chiral bis(N-oxide) s. under Sc(OTf)$_3$ and Scandium(III) dodecyl sulfate ←

Chiral copper(II) α-phenylethylamine, aminopyridine, Δ^2-oxazolin-2-yl-Schiff base or Δ^2-oxazolin-2-yl-1,2,3,4-tetrahydroisoquinoline complexes ←

Copper(II) triflate/ chiral spirocyclic bis(oxazolidines)/tri-n-butylamine ←

Copper(I) chloride/chiral N-sulfonyl-1,2-diphenylethylenediamines/pyridine ←

Catalytic asym. Henry reaction CO → C(OH)C(NO$_2$)

update s. *62,* 250s*76*; 3-component modular synthesis and application of a library of copper(II) Δ^2-oxazolin-2-yl-Schiff base complexes s. W. Yang, H. Liu, D.-M. Du, Org. Biomol. Chem. *2010, 8* (13), 2956-60 [DOI: 10.1039/b923835b]; with a novel family of copper(II) Δ^2-oxazolin-2-yl-1,2,3,4-tetrahydroisoquinoline complexes, also comparison with other metal complexes having the same ligands, s. R.B. Kawthekar, S.K. Chakka, V. Francis, P.G. Andersson, H.G. Kruger, G.E.M. Maguire, T. Govender, Tetrahedron: Asym. *2010, 21* (7), 846-52 [DOI: 10.1016/j.tetasy.2010.04.053]; asym. Henry reaction with trifluoromethyl ketones using chiral spirocyclic copper(II) bis(oxazolidine) complexes, selectivity, s. H. Xu, C. Wolf, Chem. Commun. *2010, 46* (42), 8026-8 [DOI: 10.1039/c0cc02378g]; with CuCl and a chiral 1,1′-binaphthyl-based N-sulfonyl-1,2-diphenylethylenediamine having multiple stereogenic centers in the presence of pyridine, diastereo- and enantio-selective conversion with chiral α-subst. aldehydes, s. T. Arai, Y. Taneda, Y. Endo, ibid. *46* (42), 7936-8 [DOI: 10.1039/c0cc03022h]; asym. Henry reaction with methyl 4-nitrobutyrate in the presence of chiral copper(II) aminopyridine complexes, also conversion to chiral δ-lactones, δ-hydroxy-γ-lactams and δ-hydroxy-γ-ketocarboxylic acid esters, s. G. Blay, V. Hernández-Olmos, J.R. Pedro, Org. Lett. *2010, 12* (13), 3058-61 [DOI: 10.1021/ol1010888]; with chiral copper(II) or zinc(II) bis(α-phenylethylamine) complexes s. M. Luo, B. Yan, Tetrahedron Lett. *2010, 51* (42), 5577-80 [DOI: 10.1016/j.tetlet.2010.08.055]; asym. Henry reaction with α,β-acetylenealdehydes, and elaboration of the adducts, s. D. Uraguchi, S. Nakamura, T. Ooi, Angew. Chem., Int. Ed. *2010, 49* (41), 7562-5 [DOI: 10.1002/anie.201004072]; generation of chiral quaternary hydrocarbon groups from trifluoromethyl ketones and trifluoromethylpyruvates with chiral lanthanide(III) 3,3′-bis[(diethylamino)methyl]-1,1′-bi-2-naphthoxide complexes in the presence of Proton Sponge s. F. Tur, J. Mansilla, V.J. Lillo, J.M. Saá, Synthesis *2010* (11), 1909-23 [DOI: 10.1055/s-0029-1218751].

Tetrakis(acetonitrile)copper(I) hexafluorophosphate/1,2-((R,R)-2,5-diphenylphospholano)ethane/lithium p-methoxyphenoxide ←

(Sparteine)copper(II) chloride/triethylamine ←

Catalytic asym. aldol condensation CHO → CH(OH)C-CO

with Sn(OTf)$_2$/chiral diamines cf. *37,* 630; asym. condensation of methyl vinyl ketone with ar. aldehydes with (sparteine)copper(II) chloride/Et$_3$N, and reversal of face-selectivity with (sparteine)-nickel(II) chloride, also asym. aldol-type condensation with enoxysilanes (and added KF), s. H. Maheswaran, P.J.A. Joseph, K.L. Prasanth, S. Priyadarshini, P. Satyanarayana, P.R. Likhar, M.L. Kantam, Tetrahedron: Asym. *2010, 21* (17), 2158-66 [DOI: 10.1016/j.tetasy.2010.07.008]; direct asym. condensation of ar. aldehydes with thioamides using [Cu(MeCN)$_4$]PF$_6$/(R,R)-Ph-BPE/Li-*p*-methoxyphenoxide as soft Lewis acid/hard Brønsted base s. M. Iwata, R. Yazaki, N. Kumagai, M. Shibasaki, ibid. *21* (13-14), 1688-94 [DOI: 10.1016/j.tetasy.2010.04.034]; asym. α-hydroxymethylation of ketones *in water or aq. ethanol* with Zn(OTf)$_2$/chiral N,N′-bis(prolyl)-1,2-diphenylethylenediamine s. M. Pasternak, J. Paradowska, M. Rogoziñska, J. Mlynarski, Tetrahedron Lett. *2010, 51* (31), 4088-90 [DOI: 10.1016/j.tetlet.2010.05.134]; *in water* with scandium(III) dodecyl sulfate/chiral bis(N-oxide) and a little pyridine cf. S. Kobayashi, M. Kokubo, K. Kawasumi, T. Nagano, Chem. Asian J. *2010, 5* (3), 490-2 [DOI: 10.1002/asia.200900442]; asym. aldol condensation of 3-subst. oxindoles with glyoxal derivs. and ethyl trifluoropyruvate using Sc(OTf)$_3$/chiral bis(N-oxides) s. K. Shen, X. Liu, K. Zheng, W. Li, X. Hu, L. Lin, X. Feng, Chem. Eur. J. *2010, 16* (12), 3736-42 [DOI: 10.1002/chem.200903471]; rapid asym. aldol condensation with a

ruthenium(III)-(S)-BINAP complex at room temp. under ultrasonication s. K. Tabatabaeian, E. Keshavarz, M. Mamaghani, N.O. Mahmoodi, ARKIVOC *2010* (ix) 155-162.

Silver hexafluoroantimonate s. under $InCl_3$ *$AgSbF_6$*

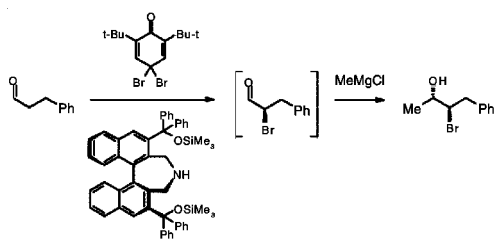
Magnesium/mercury(II) chloride *$Mg/HgCl_2$*

2,2,2-Trifluoroalcohols from aldehydes $CHO \rightarrow CH(OH)CF_3$

Synthesis with addition of one C-atom s. *78*, 465

Magnesium/4,4-dibromo-2,6-di-tert-butyl-2,5-cyclohexadienone/(S)-2,6-bis[diphenyl-(trimethylsiloxy)methyl]-4,5-dihydro-3H-dinaphth[2,1-c;1′,2′-e]azepine ←

Synthesis of *anti*-1,2-bromohydrins from aldehydes via organocatalyzed asym. α-bromination $CHCHO \rightarrow C(Br)CH(OH)R$



282.

One-pot conversion. A mixture of (S)-2,6-bis[diphenyl(trimethylsiloxy)methyl]-4,5-dihydro-3*H*-dinaphth[2,1-*c*;1′,2′-*e*]azepine (0.01 mmol) and 3-phenylpropanal (0.1 mmol) in methylene chloride (2 ml) stirred at -20°, 4,4-dibromo-2,6-di-*tert*-butyl-2,5-cyclohexadienone (0.1 mmol) added, stirred for 24 h at -20°, the mixture diluted with diethyl ether (2 ml) at -78°, stirred for a further 30 min, a THF soln. of methylmagnesium chloride added slowly at -78°, stirred for 2 h at this temp., treated with methanol (1 ml) and satd. NH_4Cl (1 ml), stirred for 30 min at room temp., and worked up with purification by preparative TLC → (2S,3R)-3-bromo-4-phenyl-2-butanol. Y 82% (*anti/syn* >20:1; e.e. 95%). Initial asym. α-bromination proceeds through face selective addition of bromonium ion to an intermediate chiral enamine to give predominantly the (R)-α-bromoaldehyde, which reacts with the Grignard compd. *in situ* to give the chiral *anti*-1,2-bromohydrin in high yield with high *anti/syn*-diastereoselectivity (>20:1) and high enantioselectivity (three examples; Y 73-83%; e.e. 96-99%). This followed a preliminary study of the initial organocatalyzed asym. α-bromination which (after reductive work-up with $NaBH_4$) gave (R)-1,2-bromohydrins in high yield and enantioselectivity (seven examples; Y 71-94%; e.e. 92-99%). F.e. and comparison of brominating agents, also with the less effective (S)-2,6-bis[diphenyl(hydroxy)-methyl]-4,5-dihydro-3*H*-dinaphth[2,1-*c*;1′,2′-*e*]azepine as organocatalyst, s. T. Kano, F. Shirozu, K. Maruoka, Chem. Commun. *2010*, *46* (40), 7590-2 [DOI: 10.1039/c0cc2739a].

Dialkylzinc/chiral 2-aminoalcohols or 3-aminoalcohols or Schiff bases or o-hydroxy-hydrazones or N-phosphoryl-1,2-diamines ←

Asym. synthesis of sec. alcohols from aldehydes $CHO \rightarrow CH(OH)R$

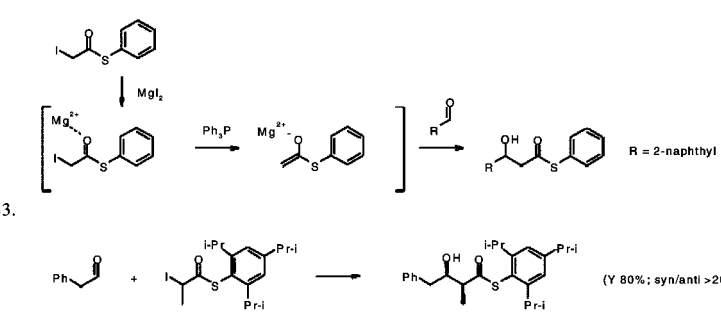
update s. *42*, 616s*76*; with chiral 2-*tert*-aminoalcohols as ligand (with e.e. up to 100%) s. C.-h. Zhang, S.-j. Yan, S.-q. Pan, R. Huang, J. Lin, Bull. Korean Chem. Soc. *2010, 31* (4), 869-73 [DOI: 10.5012/bkcs.2010.31.04.869]; with chiral 2-aminocyclohexylcarbinols s. X. Wang, K. Kodama, T. Hirose, G. Zhang, Chin. J. Chem. *2010, 28* (1), 61-8 [DOI: 10.1002/cjoc.201090036]; with chiral brominated [2.2]paracyclophane-based Schiff bases s. N.V. Vorontsova, G.S. Bystrova, D.Y. Antonov, A.V. Vologzhanina, I.A. Godovikov, M.M. Il'in, Tetrahedron: Asym. *2010, 21* (6), 731-8 [DOI: 10.1016/j.tetasy.2010.03.038]; with chiral *o*-hydroxyhydrazones s. S. Banerjee, G.M. Ferrence, S.R. Hitchcock, ibid. *21* (7), 837-45 [DOI: 10.1016/j.tetasy.2010.04.021]; asym. 1,2-addition of di-*sec*-alkylzincs (prepared by refined Charette method) to aldehydes and ketones (cf. *65*, 247s*75*) with chiral N-phosphoryl-1,2-diamines as ligand s. M. Hatano, T. Mizuno, K.

Ishihara, Chem. Commun. *2010, 46* (30), 5443-5 [DOI: 10.1039/c0cc01301c]; asym. addition of Charette-derived (commercially *unavailable*) di-*n*-alkylzincs (e.g. di-*n*-nonylzinc) to aldehydes and ketones s. M. Hatano, T. Mizuno, K. Ishihara, Synlett *2010* (13), 2024-8 [DOI: 10.1055/s-0030-1258129].

Zinc triflate/chiral N,N′-bis(prolyl)-1,2-diphenylethylenediamine ←
Catalytic asym. aldol condensation s. *37*, 630s*78* CHO → CH(OH)C-CO

Magnesium iodide/triphenylphosphine *MgI_2/Ph_3P*
β-Hydroxythiolic acid esters CHO → CH(OH)C-COSR
from enolizable aldehydes and α-iodothiolic acid esters
via non-basic reductive generation of thiolic acid ester enolates

283.



The first example of a direct aldol condensation of *enolizable* aldehydes with α-halogenothiolic acid esters is reported, obviating the need for prior enolization and being conducted under non-basic ['soft'] conditions so that there is no complicating deprotonation of the aldehyde. Furthermore, where appropriate, the coupling affords ***syn*-β-hydroxythiolic acid esters**, contrasting with the more familiar *anti*-coupling under conventional 'hard' (e.g. with *i*-Pr_2NLi) enolization. **E:** 2-Naphthaldehyde (0.15 mmol) added to a stirred soln. of S-phenyl α-iodothioacetate (1.2 eq.) in methylene chloride (3 ml), treated with MgI_2 (1.2 eq.), followed by Ph_3P (1.2 eq.), stirring continued for 16 h at room temp., followed by addition of 10% HCl (3 ml), the biphasic mixture stirred for 10 min then partitioned between ethyl acetate (40 ml) and water (3 ml), the organic layer isolated, washed with 1 *M* $Na_2S_2O_3$ soln. and brine, dried ($MgSO_4$), filtered, concentrated under reduced pressure, and the obtained yellow solid subjected to flash chromatography over silica gel → product. Y 63%. Similarly phenylacetaldehyde and S-2,4,6-triisopropylphenyl α-iodothiopropionate → product. Y 80% (*syn/anti* >20:1). The procedure is mild, can be performed in air and in untreated solvents, and is generally applicable to the condensation of a range of enolizable aldehydes with α-iodothiolic acid esters, the diastereoselectivity increasing with the bulk of the ester group (ten examples; Y 65-89%; *syn/anti* >20:1). Coupling is notably efficient with phenylacetaldehyde possessing more acidic α-protons than aliphatic aldehydes, and base-sensitive functional groups remain unaffected. Reaction is presumed to involve intermediate formation of a thermodynamically stabilized Z-(O)-enolate, which undergoes irreversible kinetic addition to the aldehyde to give the *syn*-product through a Zimmerman-Traxler transition state. Significant also is the fact that the intermediate magnesium aldolate is sufficiently stable to prevent retro-aldol cleavage, thereby resulting in the kinetic addition step. In all, therefore, α-halogenothiolic acid esters serve as valuable and convenient *shelf-stable latent enolates*. F.e., also with a chiral α-siloxyaldehyde **with asym. induction**, s. S.J. Sauer, M.R. Garnsey, D.M. Coltart, J. Am. Chem. Soc. *2010, 132* (40), 13997-9 [DOI: 10.1021/ja1057407].

Mercury(II) chloride s. under Mg $HgCl_2$

Indium *In*
Indium/polyethylene glycol or facial amphiphilic fructopyranosides *In/PEG*
Barbier-type synthesis of 3-ethylenealcohols CO → C(OH)C-C=C
in aq. medium s. *40,* 567s*75*; from cyclohexanones in water, effect of facial amphiphilic fructopyranosides on stereoselectivity, s. A. Bellomo, R. Daniellou, D. Plusquellec, Tetrahedron Lett. *2010, 51* (38), 4934-6 [DOI: 10.1016/j.tetlet.2010.07.028]; from aldehydes in PEG-400 or PEG-400/water s. Z. Du, F. Wang, W. Zhou, J.-X. Wang, J. Chem. Res. *2010, 34* (8), 475-7 [DOI: 10.3184/030823410X12813608471242]; synthesis of 3-deoxy-2-uloses s. C. Schmölzer, M. Fischer, W. Schmid, Eur. J. Org. Chem. *2010* (25), 4886-92 [DOI: 10.1002/ejoc.201000623]; 3′-hydroxyenolethers from oxo compds. and 2-(alkoxy)allyl bromides with added Bu_4NI in DMF, also 3′-(sulfonylamino)enolethers from N-sulfonylimines (cf. *48,* 626), and with asym. induction s. H. Dhanjee, T.G. Minehan, Tetrahedron Lett. *2010, 51* (42), 5609-12 [DOI: 10.1016/j.tetlet.2010.08.064].

Montmorillonite s. under (S)-Prolinamides *clay*

Indium(III) chloride/silver hexafluoroantimonate/chiral bis(Δ^2-oxazolines) ←
Asym. carbonyl-ene reaction CHO → CH(OH)C-C=C
s. *56,* 242s*72*; of aliphatic or aromatic 1,1-disubst. olefins with ethyl glyoxylate using $InCl_3$/pybox and $AgSbF_6$ (illustrating a significant counterion effect on enantioselectivity) s. J.-F. Zhao, T.-B.W. Tjan, T.-P. Loh, Tetrahedron Lett. *2010, 51* (43), 5649-52 [DOI: 10.1016/j.tetlet.2010.06.066]; with trifluoropyruvate using the same catalyst in an ionic liquid, e.g. [hmim]PF_6, for efficient recycling (up to 7 times) of the chiral complex s. J.F. Zhao, B.H. Tan, M.K. Zhu, T.B.W. Tjan, T.P. Loh, Adv. Synth. Catal. *2010, 352* (11-12), 2085-8 [DOI: 10.1002/adsc.201000170]; using chiral palladium(II) or platinum(II) bis(phosphine) complexes, e.g. (R)-Binaphane, (S)-Binapine, (S,S,R,R)-TangPhos or (R,R)-*i*-PrDuPhos for asym. ene reaction with phenylglyoxal and ethyl trifluoropyruvate s. H.-K. Luo, Y.-L. Woo, H. Schumann, C. Jacob, M. van Meurs, H.-Y. Yang, Y.-T. Tan, ibid. *352* (8), 1356-64 [DOI: 10.1002/adsc.200900888].

Scandium(III) triflate/chiral bis(N-oxides) ←
Catalytic asym. aldol condensation with 3-subst. oxindoles CHO → CH(OH)C-CO
s. *37,* 630s*78*

Scandium(III) dodecyl sulfate/chiral bis(N-oxide)/pyridine ←
Asym. α-hydroxymethylation of ketones in water s. *68,* 259s*78* H → CH_2OH

Chiral lanthanide(III) 3,3′-bis[(diethylamino)methyl]-1,1′-bi-2-naphthoxide complexes/1,8-bis(dimethylamino)naphthalene ←
Asym. Henry reaction with trifluoromethyl ketones s. *62,* 250s*78* CO → C(OH)C(NO_2)

Homochiral cerium-based metal-organic frameworks ←
Asym. synthesis of α-siloxynitriles from aldehydes s. *43,* 576s*78* CHO → CH(OSi≤)CN

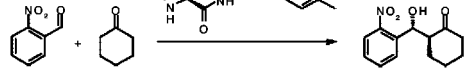
Polyethylene glycol s. under In *PEG*

(R)- or (S)-Proline (s.a. under Brucine N-oxide) *Pro-OH*
(S)-Prolinamides or 2(S)-[Bis[3,5-bis(trifluoromethyl)phenyl](hydroxy)methyl]pyrrolidine or Camphorsulfonamide-based (S)-prolinamide or Montmorillonite-supported (S)-N-(2-thienylsulfonyl)prolinamide or Polystyrene-based N-sulfonyl-(R)-binam-(S)-prolinamide ←
Organocatalyzed asym. aldol condensation CHO → CH(OH)C-CO
update s. *58,* 245s*75*; of α-keto-esters with cyclopentanone using L-proline s. J. Xiang, B. Li, Chin. J. Chem. *2010, 28* (4), 617-21 [DOI: 10.1002/cjoc.201090122]; *in cyclic carbonates* (ethylene or propylene carbonate) as solvent with added water for asym. coupling with cyclic or acyclic ketones s. W. Clegg, R.W. Harrington, M. North, F. Pizzato, P. Villuendas, Tetrahedron:

Asym. *2010, 21* (9-10), 1262-71 [DOI: 10.1016/j.tetasy.2010.03.051]; effect of chiral 1,3-dioxolan-2-ones as solvent on enantioselectivity (with (R)-proline and (R)-4-methyl-1,3-dioxolan-2-ones as a matched pair) s. M. North, P. Villuendas, Org. Lett. *2010, 12* (10), 2378-81 [DOI: 10.1021/ol1007313]; *solvent-free* condensation with glucosamine-based prolinamides for high *anti*-diastereoselectivity and enantioselectivity s. J. Agarwal, R.K. Peddinti, Tetrahedron: Asym. *2010, 21* (15), 1906-9 [DOI: 10.1016/j.tetasy.2010.06.009]; condensation of aldehydes with commercially available *polymeric* ethyl glyoxylate using 2(S)-[bis[3,5-bis(trifluoromethyl)phenyl]-(hydroxy)methyl]pyrrolidine as catalyst s. T. Urushima, Y. Yasui, H. Ishikawa, Y. Hayashi, Org. Lett. *2010, 12* (13), 2966-9 [DOI: 10.1021/ol1009812]; *heterogeneous* asym. aldol condensation with recyclable (S)-N-(2-thienylsulfonyl)prolinamide entrapped (via ion exchange) in montmorillonite, notable for coupling isatin with acetone or acetaldehyde s. N. Hara, S. Nakamura, N. Shibata, T. Toru, Adv. Synth. Catal. *2010, 352* (10), 1621-4 [DOI: 10.1002/adsc.201000214]; with recyclable polystyrene-based N-sulfonyl-(R)-binam-(S)-prolinamide (binam = 2,2′-diamino-1,1′-binaphthyl) in the presence of benzoic acid under solvent-free or aq. conditions, general procedure (incl. reaction between aldehydes), s. A. Bañón-Caballero, G. Guillena, C. Nájera, Green Chem. *2010, 12* (9), 1599-606 [DOI: 10.1039/c002967j]; aldol condensation of ketones with ar. aldehydes using a chiral camphorsulfonamide-based prolinamide s. R. Rani, R.K. Peddinti, Tetrahedron: Asym. *2010, 21* (7), 775-9 [DOI: 10.1016/j.tetasy.2010.04.018]; with a chiral bifunctional 2-*tert*-aminothiourea for the asym. 3-hydroxymethylation of N-protected oxindoles with paraformaldehyde s. X.-L. Liu, Y.-H. Liao, Z.-J. Wu, L.-F. Cun, X.-M. Zhang, W.-C. Yuan, J. Org. Chem. *2010, 75* (14), 4872-5 [DOI: 10.1021/jo100769n]; study of the role of thioureas as cocatalyst in (S)-proline-catalyzed coupling of acetone with aldehydes, substrate-dependent nonlinear effects, s. N. El-Hamdouni, X. Companyó, R. Rios, A. Moyano, Chem. Eur. J. *2010, 16* (4), 1142-8 [DOI: 10.1002/chem.200902678]; **organo-Brønsted acid-catalyzed asym. aldol condensation** with chiral H_8-BINOL-based 1,1′-binaphthyl-2,2′-diyl hydrogen phosphates as a complementary approach to enamine catalysis cf. G. Pousse, F. Le Cavelier, L. Humphreys, J. Rouden, J. Blanchet, Org. Lett. *2010, 12* (16), 3582-5 [DOI: 10.1021/ol101176j].

Chiral N-prolyl-N′-p-toluyl-1,2-diamines/acetic acid ←
Organocatalyzed asym. aldol condensation CHO → CH(OH)C-CO

284.

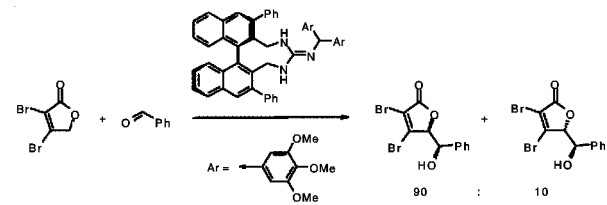


(S)-N-[2-(4-Methylbenzamido)ethyl]pyrrolidine-2-carboxamide (20 mol%) and acetic acid (20 mol%) stirred in toluene (2 ml) for 20 min at -20°, *o*-nitrobenzaldehyde (0.5 mmol) and cyclohexanone (1 eq.) added, stirring continued for 24 h, and worked up with purification by flash chromatography on silica gel → 2-[hydroxy(2-nitrophenyl)methyl]cyclohexanone. Y 98% (*anti*/*syn* 91:9; e.e. *anti*-diastereomer 94%). Yields were highest (93-98%) with benzaldehydes possessing electron-withdrawing groups (NO_2, CN, Cl), but lower with benzaldehyde itself and *p*-methylbenzaldehyde (50-63%). Enantio- and diastereo-selectivity, however, were uniformly high with all benzaldehydes (d.r. 86:14 to 95:5; e.e. 90-96%) in favor of the *anti*-product, and the enantioselectivity was the highest ever recorded for benzaldehyde and *p*-methylbenzaldehyde. Analogous chiral N-prolyl-N′-*p*-toluyl-1,2-diamines possessing chirality at both the proline residue and one of the C-N bonds of the diamine (incl. *ent*- and regio-isomers) were also prepared and tested, but, although chemical yields were improved in certain instances (notably for benzaldehyde and *p*-methylbenzaldehyde), the enantio- and diastereo-selectivity remained effectively the same, indicating that the stereochemistry of the 1,2-diamine component was not critical. F.e. and solvent effect s. R. Pedrosa, J.M. Andrés, R. Manzano, P. Rodríguez, Eur. J. Org. Chem. *2010* (27), 5310-9 [DOI: 10.1002/ejoc.201000616].

Chiral bis(Δ^2-oxazolines) s. under InCl$_3$ *box*
Chiral Schiff bases or o-hydroxyhydrazones s. under R$_2$Zn ←

Axially-chiral polycyclic guanidines ←
5-α-Hydroxy-2(5*H*)-furanones from 2(5*H*)-furanones and aldehydes H → CH(OH)R
Organocatalyzed asym. vinylogous aldol condensation
using an axially-chiral guanidine as basic catalyst

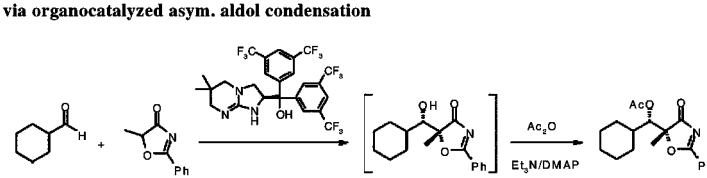
285.



The first enantioselective, direct, catalytic vinylogous aldol reaction of furanone derivs. is reported. **E: Chiral 3,4-dihalogeno-5-α-hydroxy-2(5*H*)-furanones**. A soln. of 3,4-dibromo-2(5*H*)-furanone (0.1 mmol) and benzaldehyde (1.2 eq.) in acetone (0.25 ml) and THF (0.25 ml) at -40° treated with the (R)-guanidine catalyst (5 mol%), stirred for 5 h, quenched with aq. NH_4Cl, extracted with ethyl acetate, the organic phase dried (Na_2SO_4), filtered, and, after removal of solvents, the residue purified chromatographically → product. Y 77% (*syn/anti* 90:10; e.e. *syn* 98%, e.e. *anti* 84%). The halo groups enhance the acidity of the furanones at the γ-position and prevent bond formation at the α-position, while providing a useful handle for further functionalization. The addition of acetone as co-solvent enhanced the diastereoselectivity while maintaining a high yield (Y 82%, d.r. 85:15 in THF alone; Y 52%, d.r. 92:8 in acetone alone). Seven further examples of dibromo-derivs. from ar. (incl. 2-furyl) aldehydes proceeded in good yields (58-95%) under these conditions, except for substrates bearing electron-donating methyl or methoxy groups which required THF alone as solvent, while stereoselectivities were high regardless of substituents (*syn/anti* 85:15 to 91:9; e.e. *syn* 96-99%). Diastereoselectivity was lower for a dichloro-analog (one example in THF at -40°; Y 90%; *syn/anti* 77:23; e.e. *syn* 99%, e.e. *anti* 87%). An α-monobrominated furanone gave a mixture of double bond isomers, but reaction of 3-(phenylthio)-2(5*H*)-furanone at -80° to give a chiral 3-(arylthio)-5-α-hydroxy-2(5*H*)-furanone was regiospecific (Y >99%; *syn/anti* 85:15; e.e. *syn* >99%, e.e. *anti* 91%). F.e. and optimization of catalyst s. H. Ube, N. Shimada, M. Terada, Angew. Chem., Int. Ed. *2010*, *49* (10), 1858-61 [DOI: 10.1002/anie.200906647]; asym. α-amination of β-dicarbonyl compds. with azodicarboxylates (cf. *68*, 143s*77*,*78*) using analogous catalysts s. M. Terada, M. Nakano, H. Ube, J. Am. Chem. Soc. *2006*, *128* (50), 16044-5 [DOI: 10.1021/ja066808m]; asym. epoxidation of enones with aq. H_2O_2 in toluene (e.e. 51-65%) s. M. Terada, M. Nakano, Heterocycles *2008*, *76* (2), 1049-55 [DOI: 10.3987/com-08-s(n)105].

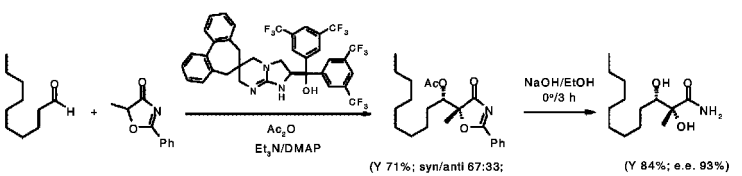
Chiral bicyclic hydroxyguanidines ←
5-α-Acoxy-Δ^2-4-oxazolones from Δ^2-4-oxazolones and aldehydes H → CH(OAc)R
via organocatalyzed asym. aldol condensation

286.



A novel, direct, catalytic, asym. aldol reaction for construction of *chiral quaternary α-carbon atoms* is reported, using 4-oxazolone enolates which have high nucleophilicity (cf. *67*, 374) without requiring the preparation of silyl enolates. **E:** A stirred soln. of startg. 5*H*-oxazol-4-one 2 (0.3 mmol) and cyclohexanecarboxaldehyde (2 eq.) in THF (1 ml) treated with (S)-8-[bis[3,5-bis(trifluoro-

methyl)phenyl](hydroxy)methyl]-3,3-dimethyl-1,5,7-triazabicyclo[4.3.0]non-5-ene (5 mol%) at 0-5°, after stirring at 0-5° for 5 h under N_2, acetic anhydride (1.5 eq.), triethylamine (1.5 eq.) and 4-dimethylaminopyridine (20 mol%) added successively with stirring at 0-5°, the mixture stirred at room temp. for 1 h, quenched with water, extracted with ethyl acetate, the combined organic phase dried ($MgSO_4$), concentrated, and the crude mixture purified by chromatography on silica → product. Y 84% (*syn/anti* >98:2 by ^1H NMR before chromatography; e.e. *syn* 96%, e.e. *anti* 26%). Eight further examples with branched aldehydes, including benzaldehyde, gave high diastereo- and enantio-selectivities (Y 43-92%; *syn/anti* 95:5 to >98:2; e.e. *syn* 95-97%). With seven examples of linear (non-α-branched) aldehydes, (S)-8-[bis[3,5-bis(trifluoromethyl)-phenyl](hydroxy)methyl]-[1,5,7-triazabicyclo[4.3.0]non-5-ene-3-spiro-6′-(6′,7′-dihydro-5′*H*-dibenzo[*a*,*c*]cycloheptene)] was used as catalyst, affording moderate diastereoselectivities but high enantioselectivities (Y 65-84%; *syn/anti* 67:33 to 80:20; e.e. 92-95%).



F.e. and conversion to **chiral α,β-dihydroxycarboxylic acid amides or esters** without loss of enantiopurity s. T. Misaki, G. Takimoto, T. Sugimura, J. Am. Chem. Soc. *2010*, *132* (18), 6286-7 [DOI: 10.1021/ja101216x].

Acetone cyanohydrin s. under Oxovanadium(IV) salalen complex *$Me_2C(OH)CN$*

Chiral α-aminocarboxylic acid esters or amphiphilic 4-acoxyproline derivs. ←
Organocatalyzed asym. aldol condensation in water CHO → CH(OH)C-CO
s. *68*, 259s*72*; asym. synthesis of *L*- or *D*-erythrose and -threose derivs. with chiral, face-selective α-aminocarboxylic acid esters as catalyst (e.g. *L*-prolinate, *L*-alaninate and *L*-leucinate) s. L. Burroughs, M.E. Vale, J.A.R. Gilks, H. Forintos, C.J. Hayes, P.A. Clarke, Chem. Commun. *2010, 46* (26), 4776-8 [DOI: 10.1039/c0cc00613k]; with amphiphilic isosteviol-based 4-acoxy-(S)-proline derivs. (at 1 mol%) s. Y.-J. An, Y.-X. Zhang, Y. Wu, Z.-M. Liu, C. Pi, J.-C. Tao, Tetrahedron: Asym. *2010, 21* (6), 688-94 [DOI: 10.1016/j.tetasy.2010.04.019]; with chiral α-subst. 2-picolyl-amines, notably for the diastereoselective asym. aldol condensation of functionalized cyclic ketones with electron-diverse ar. aldehydes, s. T.C. Nugent, M.N. Umar, A. Bibi, Org. Biomol. Chem. *2010, 8* (18), 4085-9 [DOI: 10.1039/c0ob00049c]; *heterogeneous* conversion with recyclable aerogel microspheres of the biopolymer chitosan (from crab shells) s. A. Ricci, L. Bernardi, C. Gioia, S. Vierucci, M. Robitzer, F. Quignard, Chem. Commun. *2010, 46* (34), 6288-90 [DOI: 10.1039/c0cc01502d].

Chiral α-guanidinocarboxylic acid esters/triphenylphosphine ←
Cocatalyzed asym. Baylis-Hillman reaction s. *58*, 233s*78* CHO → CH(OH)C(=CH_2)CO

3,3′-Dinaphthyl-2,2′-biphenols s. under Ti(OPr-i)$_4$ ←
Trifluoroacetic acid s. under Trimethylsilyl triflate *CF_3COOH*

Chiral 2-tert-aminothioureas ←
Organocatalyzed asym. aldol condensation s. *58*, 245s*78* CHO → CH(OH)C-CO

4,4-Dibromo-2,6-di-tert-butyl-2,5-cyclohexadienone/(S)-2,6-bis[diphenyl(trimethylsiloxy)-methyl]-4,5-dihydro-3H-dinaphtho[2,1-c;1′,2′-e]azepine s. under Mg ←
1-Trimethylsilylpropyne s. under P_4-Phosphazene base *$Me_3SiC{\equiv}CMe$*
Trimethylsilyl cyanide s. under Chiral titanium(IV) salen complex *Me_3SiCN*

Titanium tetraisopropoxide/quinidine or desmethoxyquinidine/3,3′-dinaphthyl-2,2′-biphenols ← *Chiral titanium(IV) salan complexes* *[Ti(IV)]**
Asym. synthesis of α-siloxynitriles from oxo compds. CO → C(OSi≤)CN
s. *43*, 576s*76*; from aldehydes with chiral tetradentate titanium(IV) salan [reduced salen] complexes s. C. Lv, M. Wu, S. Wang, C. Xia, W. Sun, Tetrahedron: Asym. *2010, 21* (15), 1869-73 [DOI: 10.1016/j.tetasy.2010.05.050]; from aldehydes or ketones with chiral titanium(IV) complexes prepared *in situ* from Ti(OPr-*i*)$_4$, quinidine or desmethoxyquinidine and an achiral 3,3′-dinaphthyl-2,2′-biphenol, **also** asym. synthesis of **cyanohydrin carbonates** (cf. *63*, 253s*78*) and Strecker synthesis of chiral α-tosylaminonitriles (cf. *58*, 261s*78*) s. J. Wang, W. Wang, W. Li, X. Hu, K. Shen, C. Tan, X. Liu, X. Feng, Chem. Eur. J. *2009, 15* (43), 11642-59 [DOI: 10.1002/chem.200900936]; from aldehydes, *heterogeneous* conversion with cerium-based homochiral metal-organic frameworks, also asym. aldol condensation with chiral cadmium-based analogs, s. D. Dang, P. Wu, C. He, Z. Xie, C. Duan, J. Am. Chem. Soc. *2010, 132* (41), 14321-3 [DOI: 10.1021/ja101208s].

Chiral titanium(IV) salen complex/trimethylsilyl cyanide *[Ti(IV)]*/Me$_3$SiCN*
Asym. synthesis of cyanohydrins from aldehydes CHO → CH(OH)CN
update s. *43*, 576s*74*; under titanium(IV) catalysis with a chiral norbornane-derived salen as ligand s. Z.-C. Lin, C. Chen, J. Chin. Chem. Soc. *2010, 57* (4A), 726-37; from aliphatic and aromatic aldehydes with an oxovanadium(IV) salalen complex and acetone cyanohydrin as cyanide source s. Y. Sakai, J. Mitote, K. Matsumoto, T. Katsuki, Chem. Commun. *2010, 46* (31), 5787-9 [DOI: 10.1039/c0cc00588f]; safe, molar-scale method of preparing acetone cyanohydrin under continuous flow in a microreactor s. T.S.A. Heugebaert, B.I. Roman, A. De Blieck, C.V. Stevens, Tetrahedron Lett. *2010, 51* (32), 4189-91 [DOI: 10.1016/j.tetlet.2010.06.004].

Triphenylphosphine s. under MgI$_2$ and Chiral α-guanidinocarboxylic acid esters *Ph$_3$P*
1,2-((R,R)-2,5-Diphenylphospholano)ethane s. under [(MeCN)$_4$Cu]PF$_6$ *(R,R)-Ph-BPE*

P$_4$-Phosphazene base/1-trimethylsilylpropyne *t-BuP$_4$/Me$_3$SiC≡CMe*
Metal-free deprotonative functionalization of 5-membered heteroarenes ←

287.

The first example is reported of the *organocatalyzed* [metal-free!] deprotonative functionalization of heteroarenes without generating organometallic aromatic species. **E: Heteroarylcarbinols from oxo compds**. Benzothiazole (0.3 mmol), DMF (0.6 ml), and 1-trimethylsilylpropyne (0.45 mmol) added to benzophenone (0.36 mmol), the mixture treated dropwise with *t*-BuP$_4$ in *n*-hexane (1 *M*; 0.03 mmol) at -40°, warmed to room temp., stirred for 24 h, quenched with satd. aq. NH$_4$Cl, extracted with ethyl acetate, dried, concentrated, the residue placed in a round-bottomed flask, 2 *M* aq. NaOH (2 ml) and methanol (0.5 ml) added at 0°, stirred for 1 h at 0° to effect desilylation, quenched with satd. aq. NH$_4$Cl, and worked up with purification by chromatography on silica gel → product. Y 84%. The silylating agent was employed to activate the catalytic cycle in order to regenerate the base, the initial product being the silyl ether of the carbinol. Reaction was also applied to the regioselective functionalization of benzoxazole, ethyl thiophene-1-carboxylate and 1-cyanofuran by reaction with benzophenone, pivaldehyde or chalcone (there being no 1,4-addition with the latter). F.e. and comparison of silylated activators, also **deuteriation** with DMSO-d$_6$ as deuteriating agent, s. Y. Hirono, K. Kobayashi, M. Yonemoto, Y. Kondo, Chem. Commun. *2010, 46* (40), 7623-4 [DOI: 10.1039/c0cc03106b].

Chiral N-phosphoryl-1,2-diamines s. under R$_2$Zn ←

Chiral H_8-BINOL-based 1,1′-binaphthyl-2,2′-diyl hydrogen phosphates ←
Organo-Brønsted acid-catalyzed asym. Friedel-Crafts reaction s. *71*, 271s*78* H → C(OH)<

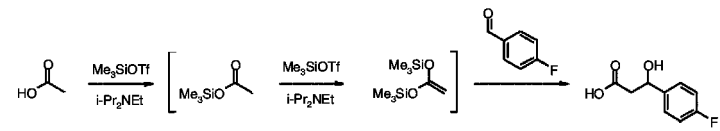
Organo-Brønsted acid-catalyzed asym. aldol condensation CHO → CH(OH)C-CO
s. *58*, 245s*78*

Oxovanadium(IV) salalen complex/acetone cyanohydrin *[O=V(IV)]*/$Me_2C(OH)CN$*
Asym. synthesis of cyanohydrins from aldehydes s. *43*, 576s*78* CHO → CH(OH)CN

Sulfonamides s. under Camphorsulfonamide-based (S)-prolinamide ←

Trimethylsilyl triflate/ethyldiisopropylamine/trifluoroacetic acid ←
β-Hydroxycarboxylic acids from [non-enolizable] aldehydes CHO → CH(OH)C-COOH
via aldol-type condensation

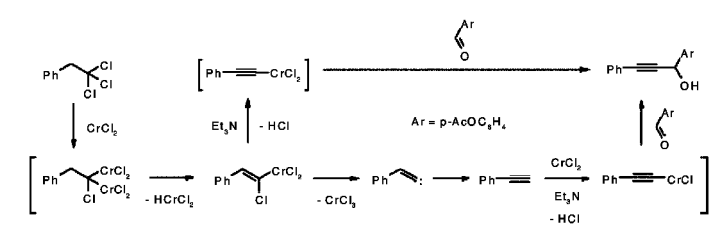
288.



with addition of two C-atoms. Acetic acid (0.996 mmol), *i*-Pr_2NEt (2.5 eq.), *p*-fluorobenzaldehyde (1.4 eq.) and trimethylsilyl triflate (2.21 eq.) added to methylene chloride (5 ml) under N_2 [note: addition of trimethylsilyl triflate produces a mild exotherm], the mixture stirred at room temp. (the colorless soln. becoming pale yellow), after 2 h the mixture added to ethanol (95%; 10 ml) and trifluoroacetic acid (5-10 drops), concentrated by rotary evaporation, and the residue subjected to flash chromatography → product. Y 91%. Good results were obtained from benzaldehydes bearing electron-donating or -withdrawing groups (apart from *p*-nitrobenzaldehyde which generally gave <50% conversion), naphthaldehydes and 2-furyl or 2-thienyl analogs (seven examples; Y 66-91%); while cinnamaldehyde gave a moderate yield (45%), results were better with α-methylcinnamaldehyde (71%). Reaction is believed to proceed via trimethylsilyl acetate formation, followed by disilyl ketene acetal formation and trimethylsilyl triflate-catalyzed Mukaiyama aldol-type reaction. In accord with this mechanism, similar results were obtained from trimethylsilyl acetate with 1.5 eq. *i*-Pr_2NEt (eleven examples; Y 71-93%, as well as 54% from cinnamaldehyde and 56% from *p*-nitrobenzaldehyde) or from tetra-*n*-butylammonium acetate with 1.8 eq. *i*-Pr_2NEt (Y 78%). No aldol adducts were obtained from phenylacetic acid or isobutyric acid, while propionic acid reacted sluggishly with *i*-Pr_2NEt as base (50% conversion overnight) but afforded a 72% yield with less-hindered 2,6-lutidine; butyric acid gave a 67% yield under similar conditions. F.e.s. C.W. Downey, M.W. Johnson, D.H. Lawrence, A.S. Fleisher, K.J. Tracy, J. Org. Chem. *2010*, *75* (15), 5351-4 [DOI: 10.1021/jo100828c].

Chromium(II) chloride/triethylamine *$CrCl_2/Et_3N$*
Generation of chromium(II/III) acetylides from 1,1,1-trichlorides ←

289.



A mixture of chromium(II) and chromium(III) acetylides can be simply generated by reduction of 1,1,1-trichlorides, and have been used in an efficient **synthesis of 2-acetylenealcohols from**

aldehydes. **E:** *p*-Acetoxybenzaldehyde (1 mmol), $CrCl_2$ (6 eq.) and triethylamine (10 eq.) added under an inert atmosphere to a soln. of the startg. trichloroalkane (1 mmol) in THF (15 ml), the mixture stirred overnight at room temp. for 10 h, quenched with 1 *N* HCl (5 ml), and worked up with purification by chromatography on silica gel → product. Y 72% (with 10% of the corresponding (Z)-2-chloroalk-2-en-1-ol). It is thought that the intermediate chromium acetylides are formed via initial generation of an unstable 1-chloro-1,1-bis(chromium) carbenoid which undergoes *syn*-β-elimination to give a more stable chromium(III) vinylene carbenoid; this develops in a divergent manner: through elimination of HCl to give a chromium(III) acetylide and, predominantly, via Fritsch-Buttenberg-Wiechell rearrangement, to give the corresponding chromium(II) acetylide as the principal nucleophile for addition to the aldehyde. Reaction is applicable to electron-diverse aromatic aldehydes (notably possessing Br, CN, AcO, MeO and F on the benzene ring) as well as enals. Reaction with enolizable aliphatic aldehydes, however, was low-yielding. F.e. (ten; Y 56-90%) s. D. Kashinath, S. Tisserand, N. Puli, J.R. Falck, R. Baati, Eur. J. Org. Chem. *2010* (10), 1869-74 [DOI: 10.1002/ejoc.200901476].

Dicarbonylmanganese η^2-(α,β-acetylenecarbonyl compds.) s. under KOBu-t *[Mn]*

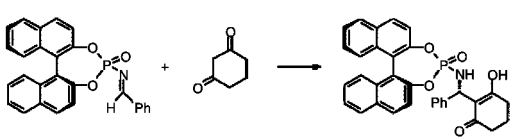
(Sparteine)nickel(II) chloride/triethylamine ←
((S)-2,2′-Bis(diphenylphosphino)-1,1′-binaphthyl)ruthenium(III) complexes *[Ru(III)]**
Catalytic asym. aldol condensation s. *37*, 630s*78* CHO → CH(OH)C-CO

Chiral palladium(II) or platinum(II) di(phosphine) complexes
Asym. carbonyl-ene reaction s. *56*, 242s*78* CHO → CH(OH)C-C=C

Addition to Nitrogen and Carbon CC ⇓ NC

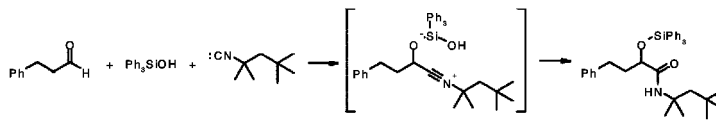
Without additional reagents *w.a.r.*
Mannich reaction C=NPO(OR)$_2$ → C(NHPO(OR)$_2$)C-CO
of chiral BINOL-based N-phosphorylimines
with asym. induction

290.

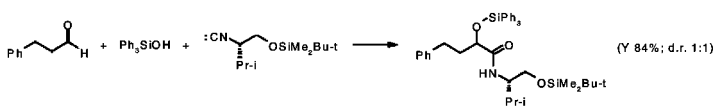


Chiral β′-(phosphorylamino)-β-diketones. A soln. of the startg. BINOL-based N-phosphoryimine (0.2 mmol) and 1,3-cyclohexanedione (1.2 eq.) in methylene chloride stirred at room temp. with 4 Å molecular sieves (100 mg) for 6 h *in the absence of base* → product. Y 92% (d.r. >99:1). The procedure was applied to the addition of 1,3-cyclohexanedione and acetylacetone to a range of N-phosphorylimines derived from benzaldimines (nine examples; Y 78-96%) with high diastereoselectivity (d.r. 87:13 to >99:1) irrespective of the electronic nature of ring substituents. There was no reaction, however, with the N-phosphorylimine based on acetophenone, while reaction with diethyl malonate required the addition of K_2CO_3 (1 eq.) for an efficient conversion (one example; Y 100%; d.r. 83:17). Diastereoselectivities were very high in methylene chloride, toluene and acetonitrile, but both yield and diastereoselectivities were lower in ether, THF, benzene and ethyl acetate. The temperature was also critical, there being no reaction at all at -78°. F.e., also cleavage of the chiral ligand from the diethyl malonate adduct to give the corresponding N-protected aminomalonate, and preparation of the N-phosphorylimines, s. H. Sun, T. Rajale, Y. Pan, G. Li, Tetrahedron Lett. *2010, 51* (33), 4403-7 [DOI: 10.1016/j.tetlet.2010.06.072].

α-Siloxycarboxylic acid amides from aldehydes and isonitriles CHO → CH(OSi≤)C(O)N≤
O-Silylative Passerini reaction

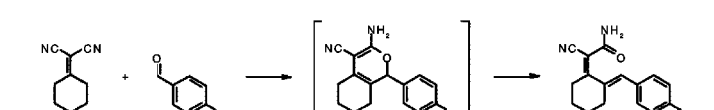


291.



tert-Octyl isocyanide (1.5 eq.) in toluene (0.5 ml) added at room temp. to a soln. of 3-phenylpropionaldehyde (0.5 mmol) and triphenylsilanol (1.5 eq.) in toluene (0.5 ml), the mixture stirred at 110° for 17-48 h (TLC), solvent removed under reduced pressure, and the residue purified by preparative TLC → 4-phenyl-N-(2,4,4-trimethylpentan-2-yl)-2-(triphenylsilyloxy)butanamide. Y 87% (90% with 2 eq. each of isonitrile and silanol). The method is applicable to a variety of aldehydes (cinnamaldehyde and aromatic ones, especially those bearing electron-donating groups, showing low activity, however) and isonitriles (incl. aliphatic or aromatic ones bearing electron-donating or -withdrawing groups); chiral isonitriles derived from amino acids gave high yields but no asym. induction was observed. Yields were low with trialkylsilanols, the Lewis acidity of the silicon atom being crucial. Polar solvents and cyclic ethers were less effective than aromatic solvents or dichloroethane. Direct O-alkylative Passerini reaction under In(III) catalysis cf. *76*, 294. F.e. (twelve; Y 15%, 37-89%) s. T. Soeta, Y. Kojima, Y. Ukaji, K. Inomata, Org. Lett. *2010*, *12* (19), 4341-3 [DOI: 10.1021/ol101763w]; α-(aryloxy)-analogs from electron-deficient phenols (or hetaryl analogs) by **O-arylative Passerini reaction** via irreversible Smiles rearrangement of intermediate iminoester adducts, also α-(arylamino)carboxylic acid amides, cf. L. El Kaim, M. Gizolme, L. Grimaud, J. Oble, J. Org. Chem. *2007*, *72* (11), 4169-80 [DOI: 10.1021/jo070202e]; Org. Lett. *2006*, *8* (22), 5021-3 [DOI: 10.1021/ol0617502].

Triethylamine *Et_3N*
2,4-Dienecarboxylic acid amides CHO → CH=C-C=C-C(O)NH_2
from α,β-ethylenenitriles and aldehydes under mild conditions



292.

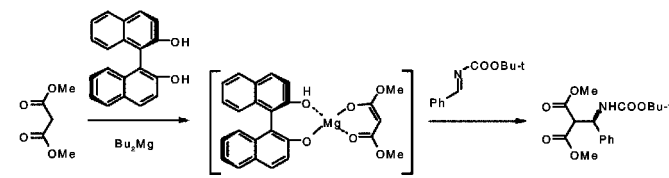
5-Aryl-2-cyano-2,4-dienecarboxylic acid amides. A mixture of cyclohexylidenemalononitrile (1.5 eq.), 4-chlorobenzaldehyde (1 mmol) and Et_3N (1 eq.) in ethylene glycol (7 ml) stirred at 40° for 40 min, the mixture cooled to room temp. when reaction complete by TLC, diluted with acid water (10 ml), the resulting precipitate filtered, and subjected to chromatographic purification over silica gel → (2Z,4E)-product. Y 78% (single diastereomer). This method is simple and quick and avoids the use of isocyanates and transition metal catalysts. It is applicable to a variety of alkylidenemalononitriles and aromatic aldehydes (eleven examples; Y 70-85%) with excellent diastereoselectivity, but failed with aliphatic aldehydes. Reaction is believed to proceed via vinylogous aldol condensation, intramolecular nucleophilic addition/isomerization and electrocyclic ring opening. F.e.s. T.H. Babu, S. Pawar, D. Muralidharan, P.T. Perumal, Synlett *2010* (14), 2125-9 [DOI: 10.1055/s-0030-1258522].

Chiral aminoalcohols s. under Et_2AlCN ←
4-Phenylpyridine N-oxide s. under Chiral manganese(III) salen complexes ←

Chiral copper(I) 1-tert-butylthio-2-(diphenylphosphino)ferrocene complexes/triethylamine ←
Asym. synthesis of differentially-protected *syn*-α,β-diaminocarboxylic acid esters ←
by Mannich reaction s. *69*, 284s*78*

Magnesium (R)-1,1′-bi-2-naphthoxide *Bu_2Mg/(R)-BINOL*
N-Protected β-aminomalonic acid esters from aldimines ←
by magnesium(II)-catalyzed asym. Mannich reaction with malonic acid esters

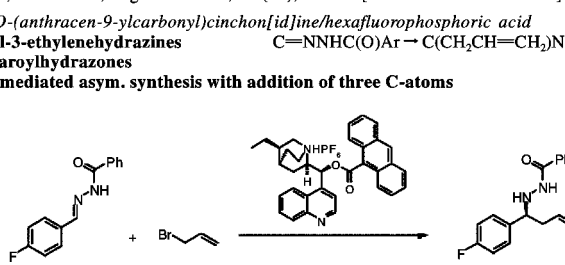
293.



Toluene (3 ml) added to a well-dried Schlenk tube charged with (R)-1,1′-bi-2-naphthol (0.025 mmol) and well-dried $MgSO_4$ (100 mg) under N_2, the suspension stirred at -20° for 5 min, di-*n*-butylmagnesium (1 *M* in heptanes; 0.025 mmol) added, stirring continued at -20° for 5 min, dimethyl malonate (0.55 mmol) and the startg. aldimine (0.5 mmol) added to the formed magnesium (R)-1,1′-bi-2-naphthoxide, stirred again at -20° for 3 h, the mixture diluted with 10% w/w HCl/methanol (2 ml) at -20°, water and ethyl acetate added after 10 min, and worked up with purification by chromatography on silica gel → (R)-dimethyl 2-[(*tert*-butoxycarbonylamino)(phenyl)methyl]-malonate. Y >99% (e.e. 92%). The *in situ*-generated reagent serves as a *cooperative* acid-base catalyst, activating both the aldimine and the malonate (the latter by intermediate formation of a BINOL-complexed magnesium(II) enolate). The corresponding chiral lithium BINOL-ate has previously been shown to be effective for the asym. Mannich reaction with β-diketones and β-keto-amides, but not so with less reactive, poorly acidic malonates where intermediate formation of an enolate is disadvantaged. High yields and enantioselectivity (sixteen examples; Y 88 to >99%; e.e. 81-97%) were recorded for the addition of a range of dialkyl malonates (incl. α-halogenomalonates) to N-Boc-protected aromatic or heteroaromatic aldimines (notably possessing electron-withdrawing or -donating groups on the benzene ring). The catalyst loading (as little as 2.5 mol% being required) is also lower than that ordinarily used in such Mannich reactions, and the reaction time is relatively short. F.e. and application on the 2 g scale s. M. Hatano, T. Horibe, K. Ishihara, Org. Lett. *2010*, *12* (15), 3502-5 [DOI: 10.1021/ol101353r].

Indium/O-(anthracen-9-ylcarbonyl)cinchon[id]ine/hexafluorophosphoric acid ←
N′-Aroyl-3-ethylenehydrazines $C{=}NNHC(O)Ar \rightarrow C(CH_2CH{=}CH_2)NHNHC(O)Ar$
from N-aroylhydrazones
Indium-mediated asym. synthesis with addition of three C-atoms

294.



A mixture of the tert. ammonium hexafluorophosphate (0.3 eq.) and startg. N-benzoylhydrazone (0.45 mmol) in methanol (4 ml) stirred at room temp. under argon for 10 min, allyl bromide (3 eq.) and In powder (3 eq.) added, the mixture stirred under argon at room temp. for 10 h, diluted with methylene chloride, then washed with satd. $NaHCO_3$, dried ($MgSO_4$), filtered, solvent

evaporated, and the residue purified by flash chromatography on silica gel → (S)-product. Y 94% (e.e. 99%). The method gives exceptionally high enantioselectivity without requiring a low temperature and is more general than that using (R)-3,3′-bis(trifluoromethyl)-1,1′-bi-2-naphthol (*69*, 288), being applicable to ar. aldehyde hydrazones bearing *m*- or *p*-groups as well as those bearing *o*-substituents (eleven examples; Y 86-94%; e.e. 98-99%), with functional groups such as chloro, bromo, nitro, keto, amide, methoxy and, notably, free hydroxyl tolerated. Hydrazones derived from aliphatic aldehydes afforded lower yields and enantioselectivity (two examples; Y 80%, 95%; e.e. 80%, 86%). The pseudoenantiomer of the promoter provided products with reversed chiralities (six ar. examples: Y 88-92%, e.e. 96-99%; one aliphatic example: Y 81%, e.e. 78%). Both chiral promoters may be recovered after workup in >95% yield. It is believed that the promoter interacts with the N-benzoylhydrazone via hydrogen bonding and π-π interaction. F.e. and optimization s. S.J. Kim, D.O. Jang, J. Am. Chem. Soc. *2010*, *132* (35), 12168-9 [DOI: 10.1021/ja1035336]; with tuneable chiral 3,3′-bis(perfluoroalkylsulfonyl)-BINOLs cf. R. Kargbo, Y. Takahashi, S. Bhor, G.R. Cook, G.C. Lloyd-Jones, I.R. Shepperson, ibid. *2007*, *129* (13), 3846-7 [DOI: 10.1021/ja070742t]; with chiral 2-(sulfinylamino)ureas s. K.L. Tan, E.N. Jacobsen, Angew. Chem., Int. Ed. *2007*, *46* (8), 1315-7 [DOI: 10.1002/anie.200603354].

Diethylaluminum cyanide/chiral aminoalcohols or 1,1′-bi-2-naphthols ←
Ytterbium(III) triflate/chiral bis(Δ^2-oxazolines)/ionic liquid-based silica/trimethylsilyl cyanide ←

Asym. Strecker reaction s. *58*, 261s*78* CH=NR → CH(NHR)CN

2(S)-[Di-n-hexyl(trimethylsiloxy)methyl]-4(R)-hydroxypyrrolidine/p-nitrobenzoic acid ←
Chiral 2-aminoureas ←

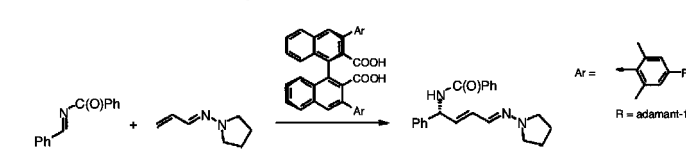
Organocatalyzed asym. Mannich reaction CH(=N-) → CH(NH-)C-CO

with N-protected imines, update, s. *63*, 266s*76*; *anti*-selectivity with aromatic N-sulfonylimines using 2(S)-[di-*n*-hexyl(trimethylsiloxy)methyl]-4(R)-hydroxypyrrolidine as catalyst in the presence of *p*-nitrobenzoic acid as hydrogen-bonding Brønsted acid s. E. Gómez-Bengoa, M. Maestro, A. Mielgo, I. Otazo, C. Palomo, I. Velilla, Chem. Eur. J. *2010*, *16* (18), 5333-42 [DOI: 10.1002/chem.200903537]; chiral *anti*-β-(sulfonylamino)thiolic acid esters from phenylthiolacetic acid esters with a cinchona alkaloid-based 2-amino-urea or -thiourea as catalyst under proximity-assisted soft enolization s. M.C. Kohler, J.M. Yost, M.R. Garnsey, D.M. Coltart, Org. Lett. *2010*, *12* (15), 3376-9 [DOI: 10.1021/ol101152b]; asym. Mannich reaction of fluoromalonic acid esters with N-Boc-protected aldimines using chiral 2-aminothioureas as catalyst s. J.H. Lee, D.Y. Kim, Synthesis *2010* (11), 1860-4 [DOI: 10.1055/s-0029-1218736]; reaction with α-acyllactones using rosin-derived 2-aminothioureas as catalyst s. X. Jiang, D. Fu, G. Zhang, Y. Cao, L. Liu, J. Song, R. Wang, Chem. Commun. *2010*, *46* (24), 4294-6 [DOI: 10.1039/c000621a].

Chiral bis(Δ^2-oxazolines) s. under Yb(OTf)$_3$ ←
Chiral N-(o-hydroxybenzyl)-2-aminoalcohols s. under Partially-hydrolyzed titanium(IV) alkoxides ←
Chiral 1,1′-bi-2-naphthols s. under Et$_2$AlCN *BINOLs*

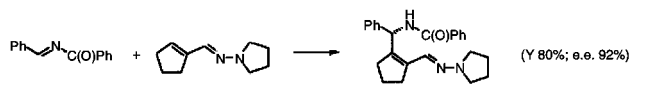
(R)-3,3′-Bis(4-adamant-1-yl-2,6-dimethylphenyl)-1,1′-binaphthyl-2,2′-dicarboxylic acid ←
Asym. synthesis of γ-aroylamino-α,β-ethylenehydrazones from N-aroylaldimines and α,β-ethylenehydrazones ←

295.

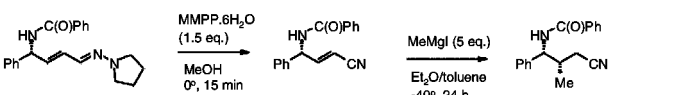


α,β-Ethylenealdehyde hydrazones exhibit nucleophilic character at C1 and C3 with highly electrophilic reactants as a result of electron-donation from the N,N-dialkylamino group. This has now been exploited in an axially-chiral dicarboxylic acid-catalyzed addition to imines. **E:** (R)-3,3′-Bis(4-adamant-1-yl-2,6-dimethylphenyl)-1,1′-binaphthyl-2,2′-dicarboxylic acid

(10 mol%), the startg. N-benzoylimine (0.1 mmol) and 1,2-dichloroethane (1 ml) added to powdered 4 Å molecular sieves (50 mg; previously flame-dried under vacuum), the mixture cooled to -35°, startg. N,N-dialkylhydrazone (0.12 mmol) added, the mixture stirred for 48 h at -35°, treated with satd. $NaHCO_3$, extracted with methylene chloride, the combined organic layers dried (Na_2SO_4), concentrated under vacuum, and the residue purified by chromatography on silica gel → product. Y 87% (E/Z 3.3:1; e.e. (E): 91%, e.e. (Z): 87%). The optimal conditions for addition of aldehyde hydrazones to N-Boc-imines (cf. *70*, 291s*74*) were ineffective for these vinylogs. The method is applicable to a variety of ar. aldimines with electron-donating or -withdrawing groups being tolerated (seven examples; Y 72-87%; E/Z 2.3:1 to 4.1:1; e.e. (E): 90-93%, e.e. (Z): 87-93%). Stereoselectivity was reduced with a methyl or isopropyl group at C2, and the enantioselectivity of the (Z)-isomers was moderate (Y 83%, 77%; E/Z 1.2:1, 1.5:1; e.e. (E): 90%, 89%, e.e. (Z): 63%, 71%, respectively). Introduction of a C3-substituent generally led to lower reactivity and formation of two regioisomers, an exception being the cyclopentenecarboxaldehyde-derived hydrazone which displayed good regioselectivity (six examples; C3/C1 adduct 3.1:1 to 14:1; Y of C3 adduct 72-82% by ^1H NMR; e.e. 85-92%) apart from in reaction with the *o*-tolualdehyde-derived imine (C3/C1 adduct 0.7:1; Y of C3 adduct 39% by ^1H NMR; e.e. 84%).



The products may be oxidized readily to chiral γ-aroylamino-α,β-ethylenenitriles with Mg-monoperoxyphthalate [MMPP·$6H_2O$] and then transformed to **chiral γ-(aroylamino)nitriles**.



F.e., also Z→E-isomerization (with acetic acid at room temp.), s. T. Hashimoto, H. Kimura, K. Maruoka, Angew. Chem., Int. Ed. *2010*, *49* (38), 6844-7 [DOI: 10.1002/anie.201003600].

Chiral 2-aminothioureas ←

Organocatalyzed asym. Mannich reaction s. *63*, 266s*78* CH(=N-) → CH(NH-)C-CO

Ionic liquid-based silica s. under Yb(OTf)$_3$ ←

Trimethylsilyl cyanide s. under Yb(OTf)$_3$, Partially-hydrolyzed titanium(IV) alkoxides Me$_3$SiCN and Chiral manganese(III) salen complexes

Partially-hydrolyzed titanium(IV) alkoxides/chiral N-(o-hydroxybenzyl)-2-aminoalcohols/ trimethylsilyl cyanide ←

Asym. Strecker reaction CH=NR → CH(NHR)CN

with Ti(OPr-*i*)$_4$ and a chiral 2,2′-biphenol as ligand cf. *58*, 261s*76* and with added quinidine or desmethoxyquinidine s. *58*, 261s*78* (p. 203); rapid procedure, with near-perfect enantioselectivity, by addition of HCN to N-protected imines with a partially hydrolyzed titanium(IV) alkoxide and a chiral N-(*o*-hydroxybenzyl)-2-aminoalcohol as ligand in the presence of Me_3SiCN (10-25 mol%) s. B. Ramalingam, A.M. Seayad, L. Chuanzhao, M. Garland, K. Yoshinaga, M. Wadamoto, T. Nagata, C.L.L. Chai, Adv. Synth. Catal. *2010, 352* (13), 2153-8 [DOI: 10.1002/adsc.201000462]; *heterogeneous* procedure by asym. addition of Me_3SiCN with recyclable Yb(OTf)$_3$/pybox immobilized in a novel self-assembled ionic liquid [organic-inorganic] hybrid silica phase s. B. Karimi, A. Maleki, D. Elhamifar, J.H. Clark, A.J. Hunt, Chem. Commun. *2010, 46* (37), 6947-9 [DOI: 10.1039/c0cc01426e]; with chiral mono- or di-meric manganese(III) salen complexes for asym. addition to N-benzylimines in the presence of 4-phenylpyridine N-oxide s. N.-u.H. Khan, S. Saravanan, R.I. Kureshy, S.H.R. Abdi, H.C. Bajaj, Tetrahedron: Asym. *2010, 21* (17), 2076-80 [DOI: 10.1016/j.tetasy.2010.07.003]; asym. addition of Et_2AlCN to N-(diamino-phosphoryl)imines in the presence of chiral BINOLs or aminoalcohols, with facile cleavage and recovery of the

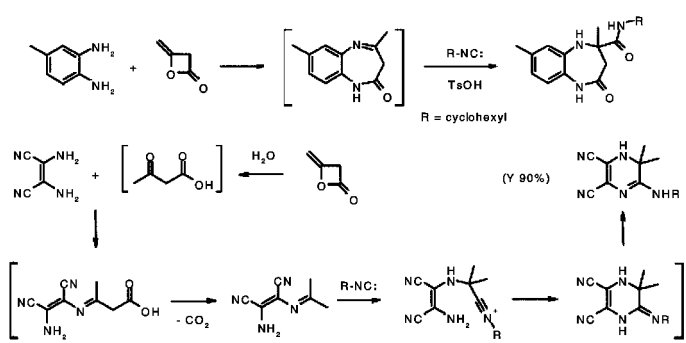
N-phosphoryl group, s. P. Kaur, S. Pindi, W. Wever, T. Rajale, G. Li, Chem. Commun. *2010, 46* (24), 4330-2 [DOI: 10.1039/c0cc00287a].

Chiral zirconium(IV) 1,1′-bi-2-naphthoxide complexes *[Zr(IV)]**
Catalytic asym. Mannich reaction CH=N- → CH(NH-)C-CO
with Trost's chiral binuclear zinc complex, N-protected *syn*-ß-amino-α-hydroxyketones from N-(*p*-methoxyphenyl)aldimines, cf. *64*, 249; with a chiral Brønsted basic zirconium(IV) 1,1′-bi-2-naphthoxide as catalyst [prepared from $Zr(OBu\text{-}t)_4$ and a chiral 3,3′-disubst. BINOL deriv.] for the asym. Mannich reaction of malonates with PMP-protected ethyl iminoacetate s. S. Kobayashi, M.M. Salter, Y. Yamazaki, Y. Yamashita, Chem. Asian J. *2010, 5* (3), 493-5 [DOI: 10.1002/asia.200900524]; of cyclic β-keto-esters with N-Boc-protected aldimines using a chiral cationic 1,1′-binaphthyl-based C_2-symmetric bis(aqua)palladium(II) N-heterocyclic carbene complex as catalyst, reversal of face selectivity by comparison with chiral palladium phosphine complexes, s. Z. Liu, M. Shi, Organometallics *2010, 29* (12), 2831-4 [DOI: 10.1021/om100331z]; asym. synthesis of differentially-protected *syn*-α,β-diaminocarboxylic acid esters from N-(8-quinolyl)-sulfonylimines and alkylideneaminoacetic acid esters with a copper(I) Fesulphos complex and Et_3N (cf. *69*, 284s*76*) s. J. Hernández-Toribio, R.G. Arrayás, J.C. Carretero, Chem. Eur. J. *2010, 16* (4), 1153-7 [DOI: 10.1002/chem.200902258]; asym. synthesis of 3-aminoaspartic acid monoesters from chiral nickel(II)-complexed alkylideneaminoacetic acid esters with asym. induction using DBU as base s. J. Wang, D. Lin, J. Shi, X. Ding, L. Zhang, H. Jiang, H. Liu, Synthesis *2010* (7), 1205-8 [DOI: 10.1055/s-0029-1219275].

Chiral 3,3′-diaryl-1,1′-binaphthyl-2,2′-diyl N-triflylphosphoramidate ←
Organo-Brønsted acid-catalyzed asym. aza-Friedel-Crafts reaction H → CH(NH-)R
s. *75*, 306s*78*

Cinchon[id]ine-derived tert. ammonium hexafluorophosphate s. under In ←

p-Toluenesulfonic acid *TsOH*
4,5-Dihydro-1*H*-1,5-benzodiazepin-2(3*H*)-one-4-carboxylic acid amides ○
from *o*-diamines, isonitriles and diketene
Regioselective 3-component synthesis



296.

in one-pot. A soln. of 2-amino-4-methylaniline (1 mmol) and diketene (1 eq.) in acetonitrile (3 ml) stirred for 4 h at room temp., cyclohexyl isocyanide (1 eq.) and *p*-TsOH·H_2O (1 eq.) added, the mixture stirred until reaction complete (TLC; 1 h), the precipitate filtered off, washed with water, and purified by recrystallization → N-cyclohexyl-2,3,4,5-tetrahydro-2,8-dimethyl-4-oxo-1*H*-benzo[*b*][1,4]diazepine-2-carboxamide. Y 90%. The procedure was applicable to aliphatic, alicyclic and ar. isonitriles, reacting with *o*-phenylenediamines optionally subst. with electron-

donating or -withdrawing groups (e.g. alkyl, acyl, halogen), regioselectivity dictated solely by the comparative electronegativity of the ar. amine groups (reversed by replacing Me with COPh, for example) (fourteen examples; Y 75-92%). Reaction proceeds via the intermediate 4-methyl-1*H*-1,5-benzodiazepin-2(3*H*)-one, which may be isolated in high yield after the first step or by attempting the reaction in the absence of *p*-TsOH. Reaction takes a different course when 2,3-diaminomaleonitrile is used in place of *o*-diamines, affording **3-amino-5,6-dicyano-1,2-dihydropyrazines** (five examples; Y 85-90%) via initial diketene hydrolysis, catalyzed by traces of water. F.e.s. A. Shaabani, A. Maleki, F. Hajishaabanha, H. Mofakham, M. Seyyedhamzeh, M. Mahyari, S.W. Ng, J. Comb. Chem. *2010, 12* (1), 186-90 [DOI: 10.1021/cc900125a].

Chiral manganese(III) salen complexes/4-phenylpyridine N-oxide/trimethylsilyl cyanide ←
Asym. Strecker reaction s. *58,* 261s*78* CH=NR → CH(NHR)CN

Chiral cationic 1,1′-binaphthyl-based bis(aqua)palladium(II) N-heterocyclic carbene complexes *[Pd(II)]**
Catalytic asym. Mannich reaction s. *64,* 249s*78* CH=NBoc → CH(NHBoc)C-CO

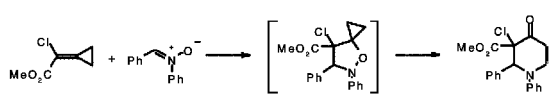
Addition to Carbon-Carbon Bonds CC ⇓ CC

Without additional reagents *w.a.r.*
3-Component ring closures ○
via zwitterionic addition of isonitriles to acetylenedicarboxylic acid esters
s. *61,* 267s*75*; synthesis of 5-aryl-2-imino-2,5-dihydrofuran-3,4-dicarboxylic acid esters with added water s. A. Ramazani, A. Rezaei, A.T. Mahyari, M. Rouhani, M. Khoobi, Helv. Chim. Acta *2010, 93* (10), 2033-6 [DOI: 10.1002/hlca.201000057]; highly functionalized 4*H*-pyrano[3,2-*d*]-isoxazoles s. A.A. Esmaeili, R. Hosseinabadi, A. Habibi, Synlett *2010* (10), 1477-80 [DOI: 10.1055/s-0029-1220072]; 2-*sec*-amino-5-vinylfuran-3,4-dicarboxylic acid esters from α,β-ethylenealdehydes in PEG-400 s. B.V.S. Reddy, D. Somashekar, A.M. Reddy, J.S. Yadav, B. Sridhar, Synthesis *2010* (12), 2069-74 [DOI: 10.1055/s-0029-1218762]; highly functionalized γ-spiroiminolactones from benzofuran-2,3-dione derivs. s. A.A. Esmacili, H. Vesalipoor, ibid. *2009* (10), 1635-8 [DOI: 10.1055/s-0028-1088042]; 5-imino-2,3,5,8-tetrahydropyrazolo[1,2-*a*]pyridazin-1-one derivs. s. B. Qian, M.-J. Fan, Y.-X. Xie, L.-Y. Wu, Y. Shi, Y.-M. Liang, ibid. *2009* (10), 1689-93 [DOI: 10.1055/s-0028-1088070]; diastereoselective synthesis of 4-phosphoranylidene-3,4'-bis-(2,5-dioxotetrahydro-1*H*-pyrrole-3-carboxylates) in the presence of trifluoroacetic acid s. A. Alizadeh, S. Rostamnia, L.-G. Zhu, Tetrahedron Lett. *2010, 51* (36), 4750-4 [DOI: 10.1016/j.tetlet.2010.07.027].

Hetero-Diels-Alder reaction of Δ¹-azirines and 1-alkoxy-3-siloxy-1,3-dienes
s. *78,* 486

3-Chloro-4-piperidone-3-carboxylic acid esters ○
from α-chloro-α-cyclopropylideneacetic acid esters and nitrones

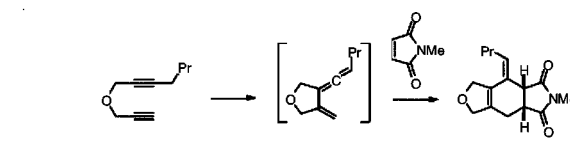
297.



A soln. of methyl 2-chlorocyclopropylideneacetate (0.252 mmol) and N-phenylbenzylidenenitrone (2 eq.) in chloroform (1 ml) stirred at room temp. for 5 d, concentrated *in vacuo*, and purified by flash chromatography on silica → methyl 3-chloro-4-oxo-1,2-diphenylpiperidine-3-carboxylate. Y 40%. Previous work, utilizing cyclic nitrones, had identified an alternative and exclusive rearrangement of intermediate 1-chloro-2-oxa-3-azabicyclo[3.2.0]heptane-5-carboxylic acid esters

to 3,4-dihydropyrid-2-one-5-carboxylic acid esters [s. C. Zorn et al., J. Org. Chem. *1999*, *64* (3), 755-63 [DOI: 10.1021/jo981366l]]. In this work, the presence of an N-aryl substituent on the nitrone promoted the 'normal' rearrangement via presumed stabilization of a diradical intermediate, affording only piperid-4-ones with retention of chlorine, albeit in moderate yield (five examples; Y 38-45%). Interestingly, treatment of methyl (Z)-2-chlorospiropentylideneacetate under these conditions afforded ca. 1:1 mixtures of the two isomeric pyridones (two examples; Y 66-75%) but an electron-rich N-4-methoxyphenylnitrone gave only a low yield of the alternative product (17%). F.e.s. S. Cicchi, J. Revuelta, I. Objartel, A. de Meijere, A. Brandi, Synlett *2010* (13), 1939-42 [DOI: 10.1055/s-0030-1258136]; enantiopure indolizinones by cascade ring enlargements of 4'-chlorospiro[cyclopropane-1,5'-isoxazolidines] s. J. Revuelta, S. Cicchi, C. Faggi, S.I. Kozhushkov, A. de Meijere, A. Brandi, J. Org. Chem. *2006*, *71* (6), 2417-23 [DOI: 10.1021/jo052564x].

3-Alkylidenecyclohexene ring from diynes and ethylene derivs. via diastereoselective intramolecular ene reaction-Diels-Alder reaction ○



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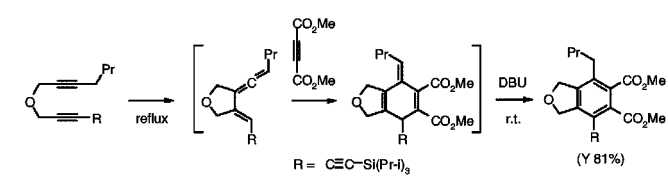
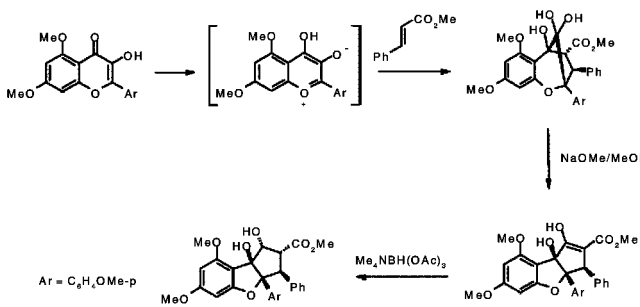


Formal, *metal-free* [2+2+2]-cycloaddition may be carried out via two pericyclic processes, intramolecular *propargylic* ene reaction of a 1,6-diyne (which may contain a heteroatom) to generate a highly reactive exocyclic 1,2,4-triene [vinylallene] in an *s-cis*-conformation, followed by inter- or intra-molecular Diels-Alder reaction with *1 equivalent* of an alkene (or alkyne). **E:** A soln. of startg. diyne (0.67 mmol) and N-methylmaleimide (1 eq.) in toluene (6.7 ml) under degassed argon stirred at 160° in a sealed tube for 21 h, allowed to cool to room temp., concentrated, and the resulting pale yellow oil subjected to chromatography on silica gel → (Z)-*cis*-4-butylidene-6-methyl-4,4a,7a,8-tetrahydro-1*H*-furo[3,4-*f*]isoindole-5,7(3*H*,6*H*)-dione. Y 94% (Z/E 91:9 by ^{1}H NMR). For ene reactions involving unactivated alkynes as enophiles temperatures of 150-160° were required, while those bearing electron-withdrawing groups may be performed in refluxing toluene. For reactions with methyl vinyl ketone, methyl acrylate or butynone, yields were slightly better in the presence of BHT as radical inhibitor and reaction proceeded with good regioselectivity. The diyne tether may possess an N-tosyl or disulfonylmethylene group in place of oxygen. With alkynes as dienophiles the intermediate isotoluene-type products are isomerized to the **benzene ring** on treatment with DBU (10 mol%) at room temp. It is believed that the mechanisms of several related fully intramolecular transformations involve analogous pericyclic cascades rather than the diradical-mediated pathways previously proposed. F.e. (from alkenes: ten, Y 52-93%; from alkynes: three, Y 40-81%) s. J.M. Robinson, T. Sakai, K. Okano, T. Kitawaki, R.L. Danheiser, J. Am. Chem. Soc. *2010*, *132* (32), 11039-41 [DOI: 10.1021/ja1053829].

Irradiation [s.a. under Chiral (1,5-cyclooctadiene)(1-neomenthylindenyl)cobalt(I)] ///
3a-Aryl-1,8b-dihydroxy-2,3,3a,8b-tetrahydro-1*H*-cyclopenta[*b*]benzofurans ○
from 3-hydroxyflavones and ethylene derivs.
via biomimetic photochemical [3+2]-cycloaddition-rearrangement



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The scope of a biomimetic approach to aglain-forbaglin-rocaglamide classes of natural products having anticancer properties, involving photogeneration of oxidobenzopyryliums via excited-state intramolecular proton transfer [ESIPT] of 3-hydroxyflavones, has been evaluated. **E:** A Pyrex test tube was charged with startg. 3-hydroxyflavone (0.49 mmol) and methyl cinnamate (5 eq.) in ethanol-free chloroform/*2,2,2-trifluoroethanol* (7:3; 16 ml), degassed with argon for 10 min, the mixture stirred and irradiated in a photobox using an ethylene glycol-cooled Hanovia 450 W medium pressure mercury lamp through a uranium filter ($\lambda > 330$ nm) at 0° for 12 h, the crude material concentrated under vacuum, and the resulting oil directly chromatographed on silica gel → intermediate adduct (Y 55%), 0.12 mmol of which in methanol (4 ml) under an inert atmosphere treated with a soln. of freshly prepared NaOMe in methanol (0.3 *M*; 2.5 eq.) at room temp., the soln. stirred for 30 min at 60°, methanol removed under vacuum, the crude mixture quenched with satd. NH_4Cl soln. and HCl (1 *M*), extracted with ethyl acetate, washed with brine (10 ml), dried over Na_2SO_4, filtered, and concentrated *in vacuo* → intermediate crude yellow oil (Y ca. 100%), 0.12 mmol of which as a soln. in acetonitrile (3 ml) at 0° under inert atmosphere treated successively with acetic acid (10 eq.) and $Me_4NBH(OAc)_3$ (6 eq.), the resulting yellow soln. stirred for 18 h at 0° to room temp., then quenched with satd. NH_4Cl soln., extracted with ethyl acetate, washed with satd. $NaHCO_3$, dried (Na_2SO_4), filtered, concentrated *in vacuo*, and purified by flash chromatography → product (Y 62%; d.r. 5:1). The cyclopentabenzofurans may also be obtained by a pinacol-type rearrangement [a) Me_3SiOTf/Et_3N; b) HCl/methanol; c) $Me_4NBH(OAc)_3$] as an alternative to the base-mediated α-ketol [acyloin] shift, allowing access to additional rocaglate derivs. F.e.s. S.P. Roche, R. Cencic, J. Pelletier, J.A. Porco Jr., Angew. Chem., Int. Ed. *2010*, *49* (36), 6533-8 [DOI: 10.1002/anie.201003212]; total synthesis of (-)-silvestrol via an asym. variant using a TADDOL deriv. as chiral Brønsted acid s. B. Gerard, R. Cencic, J. Pelletier, J.A. Porco Jr., ibid. *2007*, *46* (41), 7831-4 [DOI: 10.1002/anie.200702707]; also asym. syntheses of rocaglamide and rocaglaol s. B. Gerard, S. Sangji, D. O'Leary, J.A. Porco Jr., J. Am. Chem. Soc. *2006*, *128* (24), 7754-6 [DOI: 10.1021/ja062621j]; synthesis of (±)-methyl rocaglate s. B. Gerard, G. Jones II, J.A. Porco Jr., ibid. *2004*, *126* (42), 13620-1 [DOI: 10.1021/ja044798o].

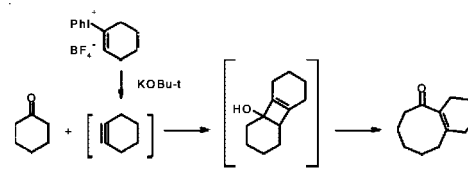
Microwaves s. under CuBr, L-Proline and $CpCo(CO)_2$ [\\\\]

Potassium tert-butoxide *KOBu-t*

Bicyclo[n.4.0]alk-(n+2)-en-2-ones from cyclic ketones

Ring expansion by two C-atoms via [2+2]-cycloaddition with cyclohexyne

300.

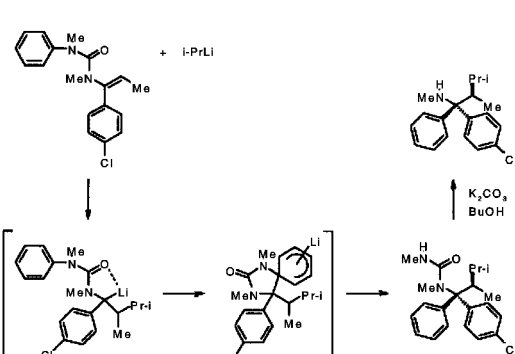


under mild conditions. A soln. of K-*tert*-butoxide (2.5 eq.) in **THF** (5 ml) added over 5 min to a soln. of cyclohexanone (0.5 mmol) and cyclohex-1-enyl(phenyl)iodonium fluoroborate (1.5 eq.) in **THF** (20 ml) at -78°, the mixture stirred for 30 min, warmed to room temp. over 25 min, quenched with phosphate buffer (pH 7), extracted with ethyl acetate, and purified by chromatography on silica → 1,2,3,4,7,8,9,10-octahydrobenzo[8]annulen-5(6*H*)-one. Y 70% (plus 6% of the intermediate cycloadduct). In this novel formal cycloinsertion, strong base and mild conditions were required for generation of the intermediate cyclohexyne (cf. 1,2-cyclohexadiene) which underwent [2+2]-cycloaddition/ring expansion with C5-C8 cyclic ketones, affording the corresponding n-6 bicyclic enones (nine examples; Y 51-76%) in the presence of benzyl ether and acetal functionality. Deconjugated ketone by-products, formed in most cases (exclusively in the case of cyclooctanone), were converted to conjugated isomers with NaOMe/MeOH. In two examples, the initial cyclobutenol [2+2]-cycloadducts were isolated (characterized by X-ray analysis in one case) and converted to the anticipated ring-expanded products by treatment with base at room temp. F.e.s. C.M. Gampe, S. Boulos, E.M. Carreira, Angew. Chem., Int. Ed. *2010*, *49* (24), 4092-5 [DOI: 10.1002/anie.201001137].

Organolithium compds. *RLi*

Regio- and diastereo-selective synthesis of β-branched sec. benzylamines from N-subst. N′-aryleneureas via carbolithiation-1,4-N→C-aryl migration

301.



An *umpolung* of eneurea reactivity, based on *nucleophilic* attack at the β-position, is the basis of a new regio- and diastereo-selective synthesis of highly branched sec. amines. **E: β-Branched**

sec. benzhydrylamines. Isopropyllithium (2 eq.; 0.7 *M* in pentane) added slowly to a soln. of the startg. vinylurea (0.102 g) in dry THF (0.3 *M*) at -40°, quenched after 4 h with methanol and NH_4Cl, and worked up with purification by chromatography on silica gel → 1-[(1S*,2S*)-1-(4-chlorophenyl)-2,3-dimethyl-1-phenylbutyl]-1,3-dimethylurea (Y 81%), 0.056 g of which dissolved in *n*-butanol (0.03 *M*), treated with K_2CO_3 (1 eq. w/w), refluxed for 2.5 h, and worked up with purification by chromatography on silica gel → (1S*,2R*)-1-(4-chlorophenyl)-N,2,3-trimethyl-1-phenylbutan-1-amine (Y 67%). Good to excellent yields were recorded for the addition of *n*- or *sec*-alkyl-, alkenyl- and aryl-lithiums to a range of α-styrylureas possessing an electron-withdrawing or -donating group on the benzene ring with a migrating phenyl, *m*-methoxyphenyl or *p*-methoxyphenyl group at the urea terminus (ten examples; 1st step: Y 54-81%; 2nd step: Y 66-75%). With biphenyl substitution at the urea terminus, however, there was generally no aryl migration, reaction stopping by proton quench after the initial carbolithiation (six examples; Y 60-85%). Both the carbolithiation and migration are stereospecific, the latter step taking place by stereoretentive attack of the incipient benzylic carbanion on the aryl ring at the terminus prior to C-N cleavage. F.e.s. J. Clayden, M. Donnard, J. Lefranc, A. Minassi, D.J. Tetlow, J. Am. Chem. Soc. *2010*, *132* (19), 6624-5 [DOI: 10.1021/ja1007992].

n-Butyllithium *BuLi*
β-Acylamino-α,β-ethyleneketones from allenyllithium compds., nitriles and carboxylic acids ○
en route to pyrimidine N-oxides s. *78*, 175

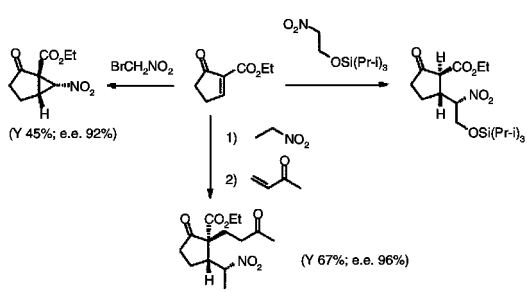
Lithium L-phenylalaninate ←
Catalytic asym. Michael addition of aldehydes to 1-nitroethylene derivs. C=C → CHC(R)
s. *49*, 635s*78*

Chiral diamines or Pyrrolidin-2(S)-ylglycol benzyl ether or Cinchona-based prim. amines ←
Organocatalyzed asym. Michael addition s. *62*, 282s*78*

Chiral N-isopropyl-2,2′-bipyrrolidines ←
Organocatalyzed asym. Friedel-Crafts reaction of indoles
with electron-deficient ethylene derivs. s. *67*, 336s*78*

Chiral polycyclic diaminoglycols or supported variants s. under CuOTf ←

Quinine ←
Organocatalyzed asym. Michael addition of aliphatic nitro compds. to cyclic α,β-ethylene-β′-ketocarboxylic acid esters



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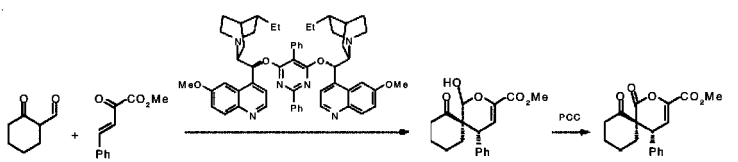
2-(Triisopropylsiloxy)nitroethane (3 eq.) added to a soln. of ethyl cyclopent-2-enone-2-carboxylate (0.35 mmol) and quinine (10 mol%) in toluene (3.5 ml) at -20°, the mixture left *without stirring* until substrate consumed (TLC; 3 d), and the mixture purified directly by flash chromatography on silica → product. Y 90% (d.r. 20:1; e.e. 98%). In the presence of quinine as catalyst, nitroalkanes

underwent 1,4-addition to the 2-subst. cyclopentenone in a highly diastereo- and enantio-selective fashion (six examples; Y 90-96%; d.r. 5:1 to 40:1; e.e. 88-98%), in the presence of ester and silyl ether functionality. Addition of bromonitromethane resulted in further reaction to afford a [3.1.0]-bicyclic (Y 45%; d.r. 25:1; e.e. 92%), while the cyclohexenone analog reacted with somewhat reduced stereoselectivity (two examples; Y 84-87%; d.r. 2:1; e.e. 76-87%), and the β-diketone analog, 2-acetylcyclopent-2-enone, gave only moderate enantioselectivity (Y 90%; e.e. 45%). Further development included addition of methyl vinyl ketone as a third component enabling one-pot asym. synthesis of **2-γ-keto-3-α-nitrocyclopentanones** (six examples; Y 67-85%; d.r. >10:1; e.e. 93 to >97%). F.e. and optimization s. S. Piovesana, D.M.S. Schietroma, L.G. Tulli, M.R. Monaco, M. Bella, Chem. Commun. *2010*, *46* (28), 5160-2 [DOI: 10.1039/c003296d].

4,6-Bis(9-O-dihydroquin[id]ine)-2,5-diphenylpyrimidine *(DHQD)$_2$PYR*
6-Hydroxy-5,6-dihydro-4*H*-pyran-2-carboxylic acid esters from β,γ-ethylene-α-ketocarboxylic acid esters and aldehydes Organocatalyzed asym. Michael addition-lactolization

303.

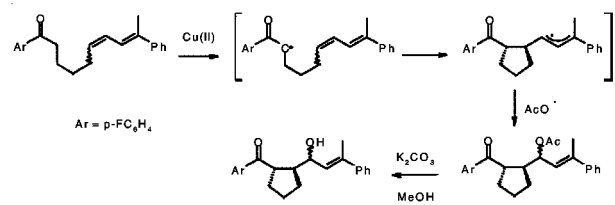


Chiral 3,4-dihydro-3-spiro-2-pyrone-6-carboxylic via 5-spiro-6-hydroxy-5,6-dihydro-4*H*-pyran-2-carboxylic acid esters. Startg. aldehyde (2 eq.) and β,γ-ethylene-α-keto ester (0.2 mmol) dissolved in a toluene/*tert*-butanol mixture (10/1; 2 ml) at -20° under N_2, $(DHQD)_2PYR$ (10 mol%) added, the mixture stirred at this temp. for 48 h (TLC), quenched with satd. aq. $NaHCO_3$, extracted with ethyl acetate, washed with brine, the organic layer dried ($MgSO_4$), concentrated under reduced pressure, and the oily residue purified chromatographically → methyl 1-hydroxy-7-oxo-5-phenyl-2-oxaspiro[5.5]undec-3-ene-3-carboxylate (Y 89%; ratio of anomers 8:1 by ^1H NMR), in methylene chloride (5 ml) treated with pyridinium chlorochromate (0.3 mmol), the mixture heated at reflux for several hours, cooled to room temp., diluted with ether, quickly passed through a short pad of diatomite with ether as eluent, concentrated under vacuum, and purified chromatographically → product (e.e. 95%). The method is effective with aromatic unsatd. α-keto esters having either electron-donating or -withdrawing groups, reactivity being higher for the latter, and for heteroaromatic analogs. The aldehyde may be attached to 5- to 7-membered rings (incl. tetrahydro-4-pyrone and γ-lactone derivs.) or may be an acyclic β-aldehydo ester. F.e. (fourteen; Y 62-99%; e.e. after oxidation 66-95%) s. W. Yao, L. Pan, Y. Wu, C. Ma, Org. Lett. *2010*, *12* (10), 2422-5 [DOI: 10.1021/ol1007873]; **chiral 5,6-fused 2-hydroxy-3,4-dihydro-2*H*-pyran-2-carboxylic acid esters** from cyclic enols, especially 4-hydroxycoumarin derivs., with a tyrosine-derived chiral 2-*tert*-aminothiourea s. X.-K. Chen, C.-W. Zheng, S.-L. Zhao, Z. Chai, Y.-Q. Yang, G. Zhao, W.-G. Cao, Adv. Synth. Catal. *2010*, *352* (10), 1648-52 [DOI: 10.1002/adsc.201000045]; with a series of chiral bifunctional organocatalysts, especially Takemoto's catalyst, s. J.-j. Wang, J.-h. Lao, Z.-p. Hu, R.-J. Lu, S.-z. Nie, Q.-s. Du, M. Yan, ARKIVOC *2010* (ix), 229-43; **chiral** α,γ-disubst. or β-subst. **δ-carbalkoxy-δ-lactones** from aldehydes with a diarylprolinol ether as catalyst followed by oxidation with Dess-Martin periodinane (or PCC) and hydrogenation over Pd-C s. D. Xu, Y. Zhang, D. Ma, Tetrahedron Lett. *2010*, *51* (29), 3827-9 [DOI: 10.1016/j.tetlet.2010.05.077].

Chiral cyclic bis(N-oxides) s. under Sc(OTf)$_3$ and Yb(OTf)$_3$ ←
Copper(II) acetate s.a. under R$_2$Zn *Cu(OAc)$_2$*

Copper(II) acetate/sodium acetate *$Cu(OAc)_2$/NaOAc*
2-(1-Acoxyallyl)cyclopentyl ketones from 6,8-dienones ○
via copper(II)-promoted radical ring closure-regioselective acoxylation

304.



DMSO (3 ml) added to a mixture of startg. dienone (0.3 mmol), $Cu(OAc)_2$ (2.5 eq.) and NaOAc (2.5 eq.) under argon in a Schlenk tube, the mixture stirred at 80° until reaction complete (TLC; 8 h), cooled, diluted with water, extracted with ethyl acetate, solvents removed *in vacuo*, the residue dissolved in methanol (2.5 ml), K_2CO_3 (1.5 eq.) added, the mixture stirred at room temp. for 1 h, concentrated, and purified by flash chromatography on silica → 1-[2-(4-fluorobenzoyl)cyclopent-1-yl]-3-phenylbut-2-enol. Y 56% (regioselectivity 95:5; d.r. 2:1). This simple 5-*exo*-cyclization uses readily available substrates, inexpensive oxidant, generates three contiguous stereocenters and was also effective using $NaHCO_3$ or amines as base. Acetoxylation occurred predominantly adjacent to the new C-C bond but diastereoselectivity was generally modest (thirteen examples; Y 39-82%; regioselectivity 75:25 to 97:3; d.r. 1:1 to 3.7:1). Stereochemistry was confirmed in one case using X-ray methods. F.e. and optimization s. Y. Wang, H. Du, J. Org. Chem. *2010, 75* (10), 3503-6 [DOI: 10.1021/jo100413p].

Copper(I) thiophene-2-carboxylate s. under Mg *CuOCOTh*

Silver acetate/chiral ferrocenyl-phosphines or -di(phosphines) *[Ag(I)]**
Pyrrolidines from ethylene derivs. and azomethines
Asym. 1,3-dipolar cycloaddition
under silver catalysis s. *67*, 301s*76*; with AgOAc and a chiral 5-*tert*-butylthio-1,2,3-triazole-functionalized ferrocenylphosphine [ThioClickFerrophos] as ligand for *endo*-selective cycloaddition to methyl (benzylideneamino)acetates (e.e. up to >99%) s. K. Shimizu, K. Ogata, S.-i. Fukuzawa, Tetrahedron Lett. *2010, 51* (38), 5068-70 [DOI: 10.1016/j.tetlet.2010.07.085]; with TaniaPhos as ligand for *endo*-selective cycloaddition to (alkylideneamino)acetonitriles s. R. Robles-Machín, I. Alonso, J. Adrio, J.C. Carretero, Chem. Eur. J. *2010, 16* (18), 5286-91 [DOI: 10.1002/chem.200903443]; base-free, *endo*-selective cycloaddition of α-(alkylideneamino)carboxylic acid esters to maleimides and *trans*-1,2-bis(phenylsulfonyl)ethylene with chiral [2,2′-bis(diphenylphosphino)-1,1′-binaphthyl]gold(I) trifluoroacetates s. M. Martín-Rodríguez, C. Nájera, J.M. Sansano, F.-L. Wu, Tetrahedron: Asym. *2010, 21* (9-10), 1184-6 [DOI: 10.1016/j.tetasy.2010.06.011]; *metal-free* cycloaddition of chiral *meso*-hydrobenzoin-derived acrylic acid esters with asym. induction s. K. Bica, P. Gaertner, ibid. *21* (6), 641-6 [DOI: 10.1016/j.tetasy.2010.04.010]; application of recyclable cellulose- and starch-hydrogen sulfates for heterogeneous, diversity-oriented, diastereoselective 1,3-dipolar cycloaddition under mild conditions s. A. Kumar, G. Gupta, S. Srivastava, J. Comb. Chem. *2010, 12* (4), 458-62 [DOI: 10.1021/cc100007a].

Copper(II) bis(Δ^2-oxazoline) complexes *[Cu(II)]**
Asym. Diels-Alder reaction
under copper catalysis s. *46*, 662s*75*; with novel bis(Δ^2-oxazolin-4-yl)methanes as ligand s. D. Frain, F. Kirby, P. McArdle, P. O'Leary, Tetrahedron Lett. *2010, 51* (30), 4103-6 [DOI: 10.1016/j.tetlet.2010.05.135]; asym. cycloaddition of (R)-camphor- and acetone-derived α,β-ethylene-α′-hydroxyketones to dienes *less reactive* than cyclopentadiene, and subsequent manipulation of

the products by oxidative C-cleavage of the ketol residue, also under Brønsted acid catalysis, s. P. Bañuelos, J.M. García, E. Gómez-Bengoa, A. Herrero, J.M. Odriozola, M. Oiarbide, C. Palomo, J. Razkin, J. Org. Chem. *2010, 75* (5), 1458-73 [DOI: 10.1021/jo9023039]; generation of tunable copper(II)-DNA complexes as potential supramolecular catalysts for asym. Diels-Alder reaction s. S. Roe, D.J. Ritson, T. Garner, M. Searle, J.E. Moses, Chem. Commun. *2010, 46* (24), 4309-11 [DOI: 10.1039/c0cc00194e]; **under organocatalysis** with chiral camphor-based N-aminosultams for asym. cycloaddition with enones, with isolation of the intermediate hydrazonium ion, s. Q. Li, W.-Y. Wong, W.-H. Chan, A.W.M. Lee, Adv. Synth. Catal. *2010, 352* (13), 2142-6 [DOI: 10.1002/adsc.201000438]; with a chiral oxazolidine·CF_3COOH catalyst for preparing chiral isoquinuclidines by cycloaddition of enals to N-protected 1,2-dihydropyridines (e.e. up to >99%) s. H. Nakano, K. Osone, M. Takeshita, E. Kwon, C. Seki, H. Matsuyama, N. Takano, Y. Kohari, Chem. Commun. *2010, 46* (26), 4827-9 [DOI: 10.1039/c0cc00110d].

Chiral copper(I) phosphine or di(phosphine) complexes s. under R_3Al *[Cu(I)]**

Copper(I) triflate/chiral polycyclic diaminoglycols or supported variants ←
Copper(II) triflate/chiral bis(Δ^2-oxazolines) *Cu(OTf)$_2$/box*
Asym. Friedel-Crafts reaction of indoles with electron-deficient ethylene derivs. C=C → CHC(R)

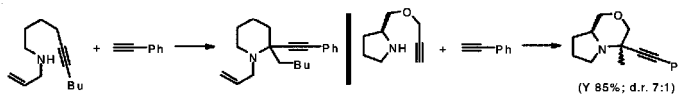
under copper(II) catalysis s. *67*, 336s*75*; with CuOTf and a chiral polycyclic diaminoglycol as ligand, also reversal of face-selectivity using an insoluble supported variant, s. H.Y. Kim, S. Kim, K. Oh, Angew. Chem., Int. Ed. *2010, 49* (26), 4476-8 [DOI: 10.1002/anie.201001484]; with $Cu(OTf)_2$ and a chiral fluoren-9-ylidenemalonate-derived bis(Δ^2-oxazoline) as ligand s. J. Li, H.-L. Chen, L. Liu, B. Fu, Molecules *2010, 15* (12), 8582-92 [DOI: 10.3390/molecules15128582]; with chiral, recyclable, dendrimer-immobilized, diphenylamine-linked bis(Δ^2-oxazolines) as ligand s. H. Liu, D.-M. Du, Eur. J. Org. Chem. *2010* (11), 2121-31 [DOI: 10.1002/ejoc.200901434]; with $Zn(OTf)_2$ and diphenylamine-linked bis(Δ^2-oxazolines) as ligand s. H. Liu, D.-M. Du, Adv. Synth. Catal. *2010, 352* (7), 1113-8 [DOI: 10.1002/adsc.201000111]; reaction of indoles and pyrrole with chalcones using $Sc(OTf)_3$/chiral cyclic bis(N-oxides) as catalyst s. W. Wang, X. Liu, W. Cao, J. Wang, L. Lin, X. Feng, Chem. Eur. J. *2010, 16* (5), 1664-9 [DOI: 10.1002/chem.200902355]; reaction of indoles with α,β-ethylene-α-hydroxyketones using an iron(III) salt and a 1,1′-binaphthyl-2,2′-diyl phosphate as Brønsted acid catalyst s. L. Yang, Q. Zhu, S. Guo, B. Qian, C. Xia, H. Huang, ibid. 1638-45 [DOI: 10.1002/chem.200902705]; reaction of activated benzenes with methyl (E)-2-oxo-4-aryl-3-butenoates using $Sc(OTf)_3$/Pybox s. G. Faita, M. Mella, M. Toscanini, G. Desimoni, Tetrahedron *2010, 66* (16), 3024-9 [DOI: 10.1016/j.tet.2010.02.054]; **organocatalyzed asym. Friedel-Crafts reaction** of indoles (with enals) using a chiral N-isopropyl-2,2′-bipyrrolidine as catalyst s. S. Jin, C. Li, Y. Ma, Y. Kan, Y.J. Zhang, W. Zhang, Org. Biomol. Chem. *2010, 8* (17), 4011-5 [DOI: 10.1039/c0ob00016g]; with planar-chiral paracyclophane-based N-[3,5-bis(trifluoromethyl)phenyl]thioureas s. J.F. Schneider, F.C. Falk, R. Fröhlich, J. Paradies, Eur. J. Org. Chem. *2010* (11), 2121-31 [DOI: 10.1002/ejoc.200901353]; asym. addition to trifluoromethyl α,β-ethyleneketones **under organo-Brønsted acid catalysis** with a chiral 3,3′-disubst. 1,1′-binaphthyl-2,2′-diyl hydrogen phosphate as catalyst s. Z.-k. Pei, Y. Zheng, J. Nie, J.-A. Ma, Tetrahedron Lett. *2010, 51* (35), 4658-61 [DOI: 10.1016/j.tetlet.2010.06.132]; asym. addition to β,γ-ethylene-α-ketophosphonic acid esters with the same organocatalyst s. P. Bachu, T. Akiyama, Chem. Commun. *2010, 46* (23), 4112-4 [DOI: 10.1039/c000862a]; with chiral 5,5′-dichlorobiphenyl-2,2′-diyl hydrogen phosphates or hexaalkylated biphenyl-2,2′-diyl N-triflylthionophosphoramidates, also asym. hydrophosphonylation of imines (cf. *67*, 242s*75*), s. E.G. Gutierrez, E.J. Moorhead, E.H. Smith, V. Lin, L.K.G. Ackerman, C.E. Knezevic, V. Sun, S. Grant, A.G. Wenzel, Eur. J. Org. Chem. *2010* (16), 3027-31 [DOI: 10.1002/ejoc.201000070]; asym. addition of the phenol, sesamol, to nitroalkenes with a chiral *cinchona*-based 2-*tert*-aminothiourea as catalyst s. H. Zhang, Y.-H. Liao, W.-C. Yuan, X.-M. Zhang, ibid. (17), 3215-8 [DOI: 10.1002/ejoc.201000271]; asym. addition of pyrroles to enals with chiral 5-benzylimidazolidine-4-thiones as organocatalyst s. X. Liang, J. Fan, F. Shi, W. Su, Tetrahedron Lett. *2010, 51* (18), 2505-7 [DOI: 10.1016/j.tetlet.2010.02.160].

Copper(II) triflate s. under R_2Zn *Cu(OTf)$_2$*
Copper(I) thiophenoxide s. under R_2Zn *CuSPh*

Copper(I) bromide s.a. under R_2Zn *CuBr*

Copper(I) bromide/microwaves *CuBr/[\\\\]*

Cyclic 2-acetyleneamines from acetyleneamines and terminal acetylene derivs. via copper(I)-catalyzed cycloisomerization-addition ○



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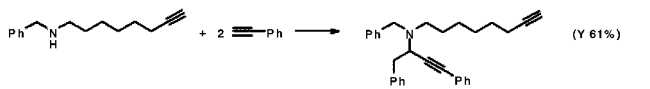


1,2-Disubst. 2-(alk-1-ynyl)piperidines. CuBr (5 mol%) added to a stirred soln. of N-allyl-5-decyn-1-amine (0.25 mmol) and phenylacetylene (4 eq.) in dioxane (1 ml), the mixture heated by microwaves under argon at 100° for 0.5 h, concentrated *in vacuo*, and purified by flash chromatography → 1-allyl-2-pentyl-2-(phenylethynyl)piperidine. Y 98%. The authors introduce the concept of cyclization triggered reactions, wherein initial cycloisomerization of an acetyleneamine affords a reactive enamine that undergoes further addition of a second alkyne moiety. The method was applied successfully to the prepn. of 5-7 membered N-heterocyclics via exclusive double addition at the *same carbon atom* for second alkyne components terminated with alkyl, silyl, and aryl functionality (thirteen examples; Y 85-99%), with an N-methyliminodiacetic acid (MIDA) boronate losing the boronate moiety to afford a terminal 2-acetylpyrrolidine (Y 89%). The reaction failed for an acetyleneamine carrying a $SiMe_3$ terminus and also for attempted prepn. of 3- and 4-membered rings, while the 8-membered ring precursor, a 7-acetyleneamine, underwent *intermolecular double addition* to the second alkyne component (Y 61%). Chiral N-1-phenylethylpent-4-ynamine effected only modest induction (d.r. 1:1.3) but (S)-2-propargyloxymethylpyrrolidine was more diastereoselective (Y 85%; d.r. 7:1). F.e., optimization and substrate prepn. s. J. Han, B. Xu, G.B. Hammond, J. Am. Chem. Soc. *2010, 132* (3), 916-7 [DOI: 10.1021/ja908883n].

Chiral (1,2-diamine)chloro(hydroxo)copper(II) complexes ←

Catalytic asym. Michael addition C=C → CHC(R)

cf. *49*, 657s*75*; *47*, 654s*75*; of α-keto-esters to nitroalkenes with chiral (1,2-diamine)chloro-(hydroxo)copper(II) complexes, *anti*-selectivity, s. A. Nakamura, S. Lectard, R. Shimizu, Y. Hamashima, M. Sodeoka, Tetrahedron: Asym. *2010, 21* (13-14), 1682-7 [DOI: 10.1016/j.tetasy.2010.04.009]; addition of malonates to β,γ-ethylene-α-ketocarboxylic acid esters with $Yb(OTf)_3$/chiral cyclic bis(N-oxides) s. L. Zhou, L. Lin, W. Wang, J. Ji, X. Liu, X. Feng, Chem. Commun. *2010, 46* (20), 3601-3 [DOI: 10.1039/c002208j]; addition of 4-hydroxycoumarins to enones with $FeCl_3$/chiral prim. amines, incl. synthesis of Warfarin, s. H.-M. Yang, Y.-H. Gao, L. Li, Z.-Y. Jiang, G.-Q. Lai, C.-G. Xia, L.-W. Xu, Tetrahedron Lett. *2010, 51* (29), 3836-9 [DOI: 10.1016/j.tetlet.2010.05.074]; addition of β-dicarbonyl compds. to 3-nitro-2*H*-chromenes with chiral bis(1,2-diamine)dibromonickel(II) complexes s. W.-Y. Chen, L. Ouyang, R.-Y. Chen, X.-S. Li, ibid. *51* (30), 3972-4 [DOI: 10.1016/j.tetlet.2010.05.111]; addition of α-ketoanilides to nitroalkenes with chiral dinuclear nickel(II) Schiff base complexes s. Y. Xu, S. Matsunaga, M. Shibasaki, Org. Lett. *2010, 12* (14), 3246-9 [DOI: 10.1021/ol101185p]; addition of aldehydes with lithium *L*-phenylalaninate (cf. *49*, 635) s. M. Yoshida, A. Sato, S. Hara, Org. Biomol. Chem. *2010, 8* (13), 3031-6 [DOI: 10.1039/c003940c].

Copper(II) chloride/silver hexafluoroantimonate *$CuCl_2/AgSbF_6$*

[2+2]-Cycloaddition with acetylene derivs. □

under Ru(II) catalysis cf. *60*, 288; with ynesulfonylamines using $CuCl_2/AgSbF_6$ as catalyst s. H. Li, R.P. Hsung, K.A. DeKorver, Y. Wei, Org. Lett. *2010, 12* (17), 3780-3 [DOI: 10.1021/ol101418d];

cycloaddition of alkynes to alkenes using hindered cationic gold(I) complexes s. V. López-Carrillo, A.M. Echavarren, J. Am. Chem. Soc. *2010, 132* (27), 9292-4 [DOI: 10.1021/ja104177w]; perfectly regioselective cycloaddition of ynones or ynoates to trialkoxy(siloxy)ethylenes as precursors of cyclobutenediones using Me_3Al as catalyst (or under thermal conditions) s. S. Iwata, T. Hamura, K. Suzuki, Chem. Commun. *2010, 46* (29), 5316-8 [DOI: 10.1039/c0cc00883d].

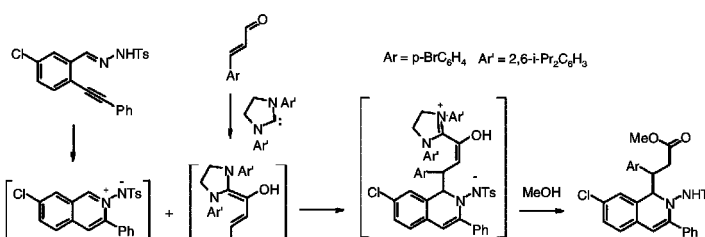
Silver hexafluoroantimonate s. under $PtCl_2$ *$AgSbF_6$*

Silver triflate s.a. under $[Rh(CO)_2Cl]_2$ *AgOTf*

Silver triflate/1,3-bis(2,6-diisopropylphenyl)-Δ^2-imidazolinium chloride/cesium carbonate ←

β-(2-Tosylamino-1,2-dihydroisoquinolin-1-yl)carboxylic acid esters ○
from *o*-acetylene-N-tosylhydrazones and α,β-ethylenealdehydes
via silver(I)/N-heterocyclic carbene-cocatalyzed ring closure

306.

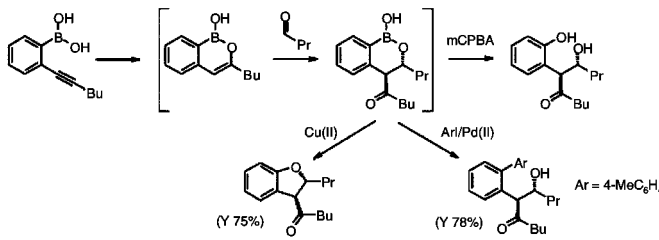


The first example of an umpolung reaction involving a hydrazide is reported, reaction taking place **via** the previously described **isoquinolinium N-tosylimides** (cf. *76*, 265, 466). **E: β-Aryl-β-(3-aryl-2-tosylamino-1,2-dihydroisoquinolin-1-yl)carboxylic acid esters.** A mixture of startg. N′-(*o*-alkynylbenzylidene)hydrazide (0.2 mmol) and AgOTf (5 mol%) in 1,2-dichloroethane (1 ml) stirred at 50° for 1 h under N_2, startg. enal (1.2 eq.), IPr·HCl (5 mol%), Cs_2CO_3 (25 mol%), THF (1.8 ml) and methanol (0.2 ml) added, the mixture stirred at 50° until reaction complete by TLC (generally 12-15 h), the solvent removed under vacuum, and the residue purified by flash chromatography on silica gel → methyl 3-[7-chloro-2-(4-methylphenylsulfonamido)-3-phenyl-1,2-dihydroisoquinolin-1-yl]-3-(*p*-bromophenyl)propanoate. Y 92% (*anti*/*syn* >20:1). The reaction was successful with a series of cinnamaldehydes (which may bear ar. bromine or methoxy groups) or a pyrid-3-yl-analog but alkyl-subst. acroleins gave complicated mixtures. The alkyne group may have an aryl terminating group but there was no reaction with cyclopropyl or *n*-butyl. Use of other alcohols in place of methanol gave little or no product. *syn*-δ,ε-Ethylene-γ-(sulfonylamino)carboxylic acid esters cf. *77*, 410. F.e. (sixteen; Y 54-94%; *anti*/*syn* 3.5:1 to >20:1) and optimization s. Z. Chen, X. Yu, J. Wu, Chem. Commun. *2010, 46* (34), 6356-8 [DOI: 10.1039/c0cc01207f]; **δ-nitrocarboxylic acid esters** from α,β-ethylenealdehydes and 1-nitroethylene derivs. via diastereoselective N-heterocyclic carbene-catalyzed 1,4-addition using 1,3-dimesityl-Δ^2-imidazolinium chloride (15 mol%) and K_2CO_3 (20 mol%) in THF/methanol (9:1) s. V. Nair, C.R. Sinu, B.P. Babu, V. Varghese, A. Jose, E. Suresh, Org. Lett. *2009, 11* (24), 5570-3 [DOI: 10.1021/ol901918x]; **α-isoquinolinium-2-yl-β-(sulfonylimino)succinic acid esters** from dimethyl acetylenedicarboxylate using AgOTf/NaOAc, also 4-bromo-derivs. using Br_2/NaOAc, and 6-iodopyrazolo[5,1-*a*]isoquinoline-1,2-dicarboxylic acid esters using I_2/NaOAc, s. Z. Chen, Q. Ding, X. Yu, J. Wu, Adv. Synth. Catal. *2009, 351* (10), 1692-8 [DOI: 10.1002/adsc.200900131]; 6-subst. pyrazolo[5,1-*a*]isoquinolines from terminal acetylene derivs. with Br_2 then AgOTf/DBU followed by Pd-catalyzed coupling with boronic acids s. Z. Chen, M. Su, X. Yu, J. Wu, Org. Biomol. Chem. *2009, 7* (22), 4641-6 [DOI: 10.1039/b914265g]; 2-*prim*-amino-1-(indol-3-yl)isoquinolinium triflates from indoles using AgOTf/$Dy(OTf)_3$ s. X. Yu, X. Yang, J. Wu, ibid. (21), 4526-30 [DOI: 10.1039/b913409c]; pyrazolo[5,1-*a*]isoquinolines from enoxysilanes with AgOTf/Na_2CO_3 s. X. Yu, Z. Chen, X. Yang, J. Wu, J. Comb. Chem. *2010, 12* (3), 374-8 [DOI: 10.1021/cc1000314].

Hindered cationic gold(I) complexes *[Au(I)]*
[2+2]-Cycloaddition with acetylene derivs. s. *60*, 288s*78* □

(Triphenylphosphine)gold(I) triflimide/m-chloroperoxybenzoic acid *$(Ph_3P)AuNTf_2/ArCO_2OH$* ←
α-(*o*-Hydroxyaryl)-β-hydroxyketones from *o*-acetyleneboronic acids via stereoselective gold-catalyzed aldol-type condensation with cyclic boron enolates

307.

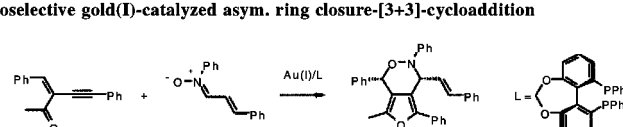


in one-pot. Butyraldehyde (2 eq.) and $[(Ph_3P)AuNTf_2]_2$·PhMe (1 mol%) added to a soln. of 2-(hex-1-ynyl)phenylboronic acid (0.45 mmol) in methylene chloride-d_2 (0.5 ml) at room temp., the mixture stirred for 2 h, diluted with ether, filtered through silica, concentrated, the residue (*anti/syn* 4:1) dissolved in methylene chloride (4 ml), cooled to 0°, *m*CPBA (1.2 eq.) added, the mixture allowed to reach room temp., stirred for a further 30 min, quenched with water, extracted with methylene chloride, washed with satd. aq. $NaHCO_3$, water and brine, concentrated, and purified by flash chromatography → 7-hydroxy-6-(2-hydroxyphenyl)decan-5-one. Y 91% (*anti/syn* 4:1). Boron enolates, formed from unactivated *o*-alkynylphenylboronic acids under exceptionally mild conditions, underwent *in situ* aldol reaction with aldehydes (*incl. acetaldehyde*) with variable stereoselectivity (*anti/syn* 80:20 to 45:55). The crude products, which were often prone to retro-aldol reaction, were transformed via loss of boron to ***o*-β-hydroxybiaryls** (Suzuki coupling), phenols/acetates (by oxidation as above) and **3-acyl-2,3-dihydrobenzofurans** (Chan-Lam coupling) with little change in the diastereomeric ratio (eleven examples; Y 65-99%). F.e. and substrate prepn. s. C. Körner, P. Starkov, T.D. Sheppard, J. Am. Chem. Soc. *2010*, *132* (17), 5968-9 [DOI: 10.1021/ja102129c].

Chiral [2,2′-bis(diphenylphosphino)-1,1′-binaphthyl]gold(I) trifluoroacetates *[Au(I)]**
Pyrrolidines from ethylene derivs. and azomethines ○
Asym. 1,3-dipolar cycloaddition s. *67*, 301s*78*

Gold(I) chloride-dimethyl sulfide/silver triflate/(R)-6,6′-methylenedioxy-2,2′-bis(diphenyl-phosphino)-1,1′-binaphthyl ←
3,4-Dihydro-1*H*-furo[3,4-*d*][1,2]oxazines from 2-acyl-1,3-enynes and nitrones Regioselective gold(I)-catalyzed asym. ring closure-[3+3]-cycloaddition

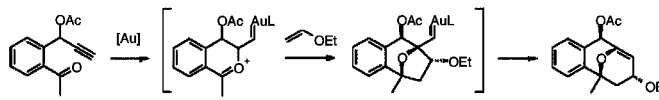
308.



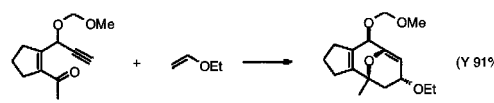
An asym. variant of *76*, 306 is reported. **E:** A soln. of (R)-C1-TunePhos (2.5 mol%) and $AuCl·SMe_2$ (5 mol%) in methylene chloride stirred at room temp. for 12 h, concentrated *in vacuo*, a soln. of AgOTf (2.5 mol%) in 1,2-dichloroethane (1 ml) added, the mixture stirred at -10° for 15 min, solns. of startg. ketone (0.4 mmol) and nitrone (1.1 eq.) in 1,2-dichloroethane (3 ml) added, the mixture stirred until reaction complete (TLC; 1-12 h), concentrated *in vacuo*, and purified by flash chromatography on silica → (1S,4R)-7-methyl-1,3,5-triphenyl-4-styryl-3,4-dihydro-1*H*-furo-

[3,4-*d*][1,2]oxazine. Y 97% (e.e. 97%). The cycloaddition was successful, scaleable (to 5 mmol at 0.2 mol% catalyst loading) and highly enantioselective, for nitrones derived from ar. aldehydes and acylenynes carrying ar. or branched alkene groups at alkene and alkyne termini. Linear alkyl/alkene termini, however, gave poor enantioselectivity, which was not improved with alternative ligands, but cyclic α-alkynyl-enones were generally good substrates (sixteen examples; Y 61-99%; e.e. 92-99%). Absolute configuration was confirmed by X-ray analysis of representative products. F.e., optimization and hydrogenolysis (H_2/Pd) of the oxazine ring (Y 88%) without loss of chirality s. F. Liu, D. Qian, L. Li, X. Zhao, J. Zhang, Angew. Chem., Int. Ed. *2010*, *49* (37), 6669-72 [DOI: 10.1002/anie.201003136].

[o-Biphenylyl(di-tert-butyl)phosphine]gold(I) chloride/silver triflimide ←
***anti*-Bredt 4-alkoxy-3,4-dihydro-2*H*-pyran ring** ○
from acetyleneoxo compds. and enolethers

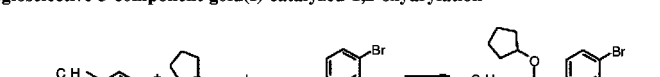


309.



A highly diastereoselective formal [4+2]-cycloaddition on an *s-trans*-heterodiene has been reported via an initial [3+2]-cycloaddition of an α-carbonyl ylid followed by ring expansion. **E: 6-Oxy-3-alkoxy-9-oxabicyclo[3.3.1]nona-4,7-diene ring**. A soln. of [(*o*-biphenyl)(*t*-Bu)$_2$P]AuCl (3 mol%) and AgNTf$_2$ (3 mol%) in dry methylene chloride (2 ml) stirred at 25° for 10 min under N_2 before addition of a soln. of 1-(2-acetylphenyl)prop-2-yn-1-yl acetate (0.3 mmol) and ethyl vinyl ether (3 eq.) in methylene chloride (1 ml), the mixture stirred for another 2.5 h, filtered over a short silica bed, solvent removed under reduced pressure, and the crude product eluted through a silica gel column → product. Y 76% (single diastereomer). This method, which was applied to seventeen further examples (Y 42-95%; all as single diastereomers), provides easy access to bioactive benzo-fused 6-functionalized 9-oxabicyclo[3.3.1]nonenes exhibiting activity in the central nervous system and HIV-1 inhibitory effects. The oxy group, incl. OMOM, OAc, OBn or OBu-*n*, is essential and is believed to facilitate 6-*exo-dig* cyclization via an electron-withdrawing effect on the alkyne (rather than by metal coordination). The benzene ring may bear chloro, fluoro or methoxy groups and the method is also applicable to non-aromatic 2,5-enyn-als or -ones (nine examples; Y 63-91%). F.e.s. T.-M. Teng, A. Das, D.B. Huple, R.-S. Liu, J. Am. Chem. Soc. *2010*, *132* (36), 12565-7 [DOI: 10.1021/ja106493h].

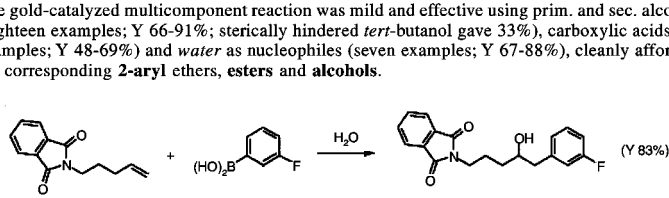
[Bis(diphenylphosphino)methane]bis[gold(I) bromide]/N'-chloromethyl-N-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(fluoroborate) ←
2-Arylalcohol O-derivs. C=C → C(OR)C(Ar)
from terminal ethylene derivs., arylboronic acids and O-nucleophiles
Regioselective 3-component gold(I)-catalyzed 1,2-oxyarylation



310.

2-Arylethers. 1-Octene (0.1 mmol), 4-bromobenzeneboronic acid (1 eq.) and dppm(AuBr)$_2$ (5 mol%) dissolved in acetonitrile/cyclopentanol (9:1; 1 ml) at room temp., Selectfluor (2 eq.)

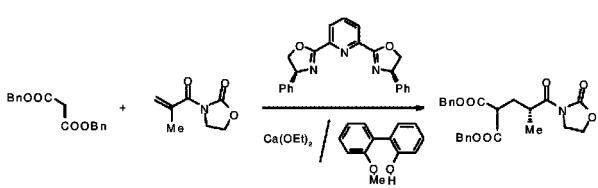
added in one portion, the mixture stirred at 50°, additional boronic acid (1 eq.) and catalyst (2.5 mol%) added after 2 h, stirring continued for 12 h, the mixture cooled to room temp., quenched with satd. aq. $Na_2S_2O_3$, extracted with ether, washed with brine, concentrated *in vacuo*, and purified by flash chromatography on silica → 1-(4-bromophenyl)-2-cyclopentyloxyoctane. Y 76%. This rare gold-catalyzed multicomponent reaction was mild and effective using prim. and sec. alcohols (eighteen examples; Y 66-91%; sterically hindered *tert*-butanol gave 33%), carboxylic acids (six examples; Y 48-69%) and *water* as nucleophiles (seven examples; Y 67-88%), cleanly affording the corresponding **2-aryl** ethers, **esters** and **alcohols**.



Arylboronic acid components containing electron-withdrawing and mild electron-releasing groups (e.g. methyl) were compatible. F.e., alkene prepn. and optimization s. A.D. Melhado, W.E. Brenzovich Jr, A.D. Lackner, F.D. Toste, J. Am. Chem. Soc. *2010*, *132* (26), 8885-7 [DOI: 10.1021/ja1034123].

Calcium ethoxide/chiral bis(Δ²-oxazolines)/2,2′-biphenol monomethyl ether ←
Asym. Michael addition of malonic acid esters C=C → CHC(R)
via catalytic protonation of calcium enolates

311.



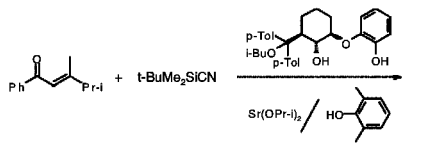
Cyclopentyl methyl ether (0.5 ml) added under argon (in a glove box) to a dry tube charged with $Ca(OEt)_2$ (0.02 mmol), (S,S)-Ph-PyBox (0.022 mmol) and 2,2′-biphenol monomethyl ether (0.02 mmol), stirred at room temp. for 2 h, ethanol (0.4 mmol) added, the soln. cooled to -20°, the startg. Michael acceptor (0.2 mmol) added as a soln. in cyclopentyl methyl ether (0.5 ml), treated slowly with dibenzyl malonate (0.28 mmol) in the same solvent (0.5 ml) over 10 h via syringe pump, stirring continued for 48 h, quenched with satd. aq. NH_4Cl, and worked up with purification by preparative thin-layer chromatography → product. Y 90% (e.e. 95%). High yields and high enantioselectivities were recorded for the asym. Michael addition of *dibenzyl* malonate to a range of α-alkyl-, α-allyl- and α-propargyl-subst. N-acryloyl-2-oxazolidones (nine examples; Y 77-97%; e.e. 93-96%), but racemic products (or those having very low enantioselectivities) were obtained with *prim-*, *sec-* and *tert*-alkyl-malonates. The substitution of the chiral PyBox ligand, the nature of the calcium alkoxide and the temperature had a significant effect on enantioselectivity, which was optimized with ethanol as additive in cyclopentyl methyl ether. Reaction involves *catalytic* generation of enolates, rigidified by coordination to calcium and the ligand, thereby presenting an effective chiral environment for the subsequent, rate-determining asym. protonation with the achiral phenol. F.e. and gram-scale application s. T. Poisson, Y. Yamashita, S. Kobayashi, J. Am. Chem. Soc. *2010*, *132* (23), 7890-2 [DOI: 10.1021/ja102555a]; addition of Δ²-5-oxazolones to enoates with $Ca(OEt)_2$/Pybox, also conversion to chiral α-alkylated glutamic acids, s. T. Tsubogo, Y. Kano, K. Ikemoto, Y. Yamashita, S. Kobayashi, Tetrahedron: Asym. *2010*, *21* (9-10), 1221-5 [DOI: 10.1016/j.tetasy.2010.03.004].

Strontium isopropoxide/(1R,2R,6S)-6-[di-p-tolyl(2-methyl-1-propyloxy)methyl]-2-(2-hydroxy-phenoxy)cyclohexanol/2,6-dimethylphenol/tert-butyldimethylsilyl cyanide ←

β-Cyanocarbonyl from α,β-ethylenecarbonyl compds. C=C → CHC(CN)

Generation of β-quaternary centers by strontium-catalyzed asym. 1,4-addition

312.

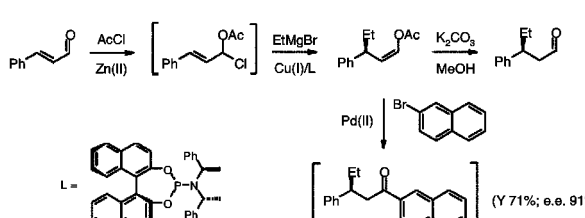


With the aid of a highly active strontium complex, a *general* procedure has evolved for the catalytic 1,4-addition of cyanide ion to β-subst. α,β-ethylenecarbonyl compds. to generate chiral β-quaternary carbon centers in high yield and enantioselectivity at catalyst loadings as low as 0.5 mol%. **E: Chiral β-subst. β-cyanoketones.** $Sr(OPr\text{-}i)_2$ (0.1 *M* soln. in THF; 50 μl; 5 μmol) added at room temp. to a soln. of (1R,2R,6S)-6-[di-*p*-tolyl(2-methyl-1-propyloxy)methyl]-2-(2-hydroxy-phenoxy)cyclohexanol (8.3 μmol) in THF (500 μl), the solvent evaporated, the resulting pre-catalyst dried under reduced pressure (<5 mmHg) for 1 h, toluene (1 ml) added, the mixture stirred for 30 min at room temp., the catalyst soln. (100 μl) transferred to a reaction vessel using a gas-tight syringe, the startg. (E)-enone (0.1 mmol) added, followed by a soln. prepared by mixing *tert*-butyldimethylsilyl cyanide (0.2 mmol) and 2,6-dimethylphenol (0.2 mmol) in toluene (0.1 ml) at room temp. for 20 min, stirred at room temp. for 16 h, the mixture directly loaded onto a silica gel column in a well-ventilated hood (*caution*! highly toxic HCN is generated), and purified by flash chromatography → product. Y 100% (e.e. 97%). The key catalytic species is believed to be a *high-order* (3:5) Sr/ligand complex, the Lewis basic ether group of the ligand being largely responsible for the high enantioselectivity. The procedure is applicable to a wide range of aryl- or alkyl-subst. enones (fifteen examples; Y 70-100%; e.e. 89-99%) and N-(α,β-ethyleneacyl)pyrroles (six examples; Y 73-100%; e.e. 96-99%), (E)- and (Z)-isomers producing opposing enantiomers. One of the substrates was a tetrasubst. enone (methyl 2-methylcyclohexenyl ketone) which gave, initially, a 1:1 mixture of diastereoisomers, convertible to a single diastereoisomer on treatment with methanolic NaOMe (d.r. <20:1; e.e. 99%). A related chiral gadolinium(II) complex gave low yields and low enantioselectivity. F.e. and comparison of ligands s. Y. Tanaka, M. Kanai, M. Shibasaki, J. Am. Chem. Soc. *2010*, *132* (26), 8862-3 [DOI: 10.1021/ja1035286].

Magnesium/copper(I) thiophene-2-carboxylate/chiral 1,1′-binaphthyl-2,2′-diyl phosphoramidite/zinc chloride ←

Copper-catalyzed asym. 1,4-addition to α,β-ethylenealdehydes via enol acetates C=C → CHC(R)

313.



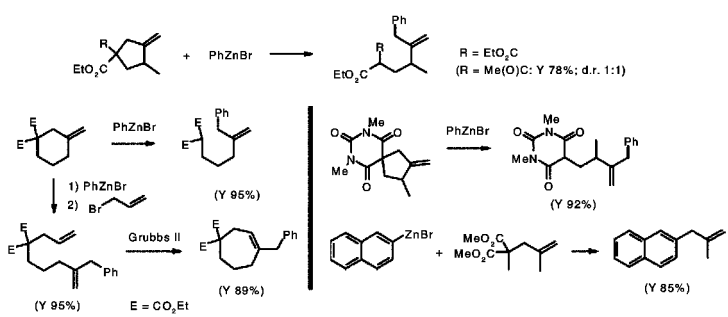
Chiral β-alkylaldehydes. Cinnamaldehyde (0.5 mmol) added dropwise to a soln. of acetyl chloride (1 eq.) and freshly fused $ZnCl_2$ (1.5 mol%) in methylene chloride (1 ml) at -10°, the soln. added

to a soln. of Cu(I)-thiophene-2-carboxylate (5 mol%) and chiral phosphoramidite ligand (5.5 mol%) in the same solvent (2 ml) (previously stirred at room temp. for 30 min) under N_2 at -78°, the mixture stirred for 5 min, a soln. of ethylmagnesium bromide (1.2 eq.) in ether/methylene chloride added dropwise over 6 h via syringe pump, the mixture stirred for a further 4 h, quenched with methanol, K_2CO_3 (5 eq.) added, the mixture stirred for 1 h, quenched with satd. aq. NH_4Cl, warmed to room temp., extracted with ether, concentrated *in vacuo*, and purified by flash chromatography on silica → (S)-3-phenylpentanal. Y 89% (γ/α 99:1; e.e. 92%). A series of acrolein derivs. (terminated with phenyl, 2-furyl, 4-methoxyphenyl or methyl) reacted efficiently with prim. alkyl Grignard reagents via *in situ* generation of an α-chloroallyl acetate, with selectivity generally high (seven examples; Y 69-89%; γ/α 98:2-99:1; Z/E 2:1 to 18:1; e.e. 90-94%). Isobutylmagnesium bromide gave high regioselectivity but enantioselectivity was low (Y 85%; γ/α 97:3; Z/E 12:1; e.e. 48%), while methylmagnesium bromide gave low yield and reduced regio- and enantioselectivity. The enol acetate products could be isolated or hydrolyzed quantitatively *in situ* to the corresponding aldehydes. A number of other ligands were effective for the initial alkylation step but were incompatible with the final hydrolysis. The product enol acetates were also shown to be useful partners for Pd(II)-catalyzed cross-coupling reactions with ar. bromides. F.e. and optimization s. M. Fañanás-Mastral, B.L. Feringa, J. Am. Chem. Soc. *2010*, *132* (38), 13152-3 [DOI: 10.1021/ja105585y].

Zinc/bis(1,5-cyclooctadiene)nickel(0)/triphenylphosphine ←
Zinc/nickel(II) acetoacetonate/triphenylphosphine or dibromobis(triphenylphosphine)-nickel(II)/magnesium bromide ←

Nickel-catalyzed arylative ring opening C
of cyclic γ-methylene-α-dicarbonyl compds. with arylzinc compds.

314.



ε-Aryl-δ-methylene-α-dicarboxylic acid esters. Toluene (3 ml) added to a mixture of $Ni(cod)_2$ (5 mol%) and triphenylphosphine (10 mol%) under argon, the resulting suspension stirred for 10 min at room temp., diethyl 4-methyl-3-methylenecyclopentane-1,1-dicarboxylate (0.5 mmol) added, followed by phenylzinc bromide [prepared from $ZnBr_2$ (2 eq.) in dry THF (1 ml) and phenylmagnesium bromide (2 eq.; 1 *M* in THF)], the mixture allowed to warm to 60° and stirred for 8 h, quenched with satd. aq. NH_4Cl (3 ml), extracted then concentrated *in vacuo*, and the crude oil purified on silica gel → product. Y 96% [Y 89% using PhZnI·LiCl and $NiBr_2(PPh_3)_2$ or $Ni(acac)_2/2PPh_3$ with $MgBr_2$ (2 eq.) as additive; Y 11% without $MgBr_2$]. $MgBr_2$, either formed *in situ* under the first set of conditions or as an additive, is believed to promote sp^3C-sp^3C bond cleavage by Lewis acid activation of the dicarboxylate (or by promoting transmetalation between nickel and organozinc complexes). The method is also applicable to arylzinc iodide-LiCl complexes bearing methyl, methoxy, fluorine or ester groups, while the α-allyldicarbonyl compds. may also be based on Meldrum's acid, a cyclic diamide or a β-keto ester (eight examples; Y 59-93%); a methylenecyclohexane deriv. also participated (Y 95%). An alkenylzinc iodide-LiCl complex

was also reactive (Y 66%) but benzylzinc bromide gave a low yield (28% by NMR). Reaction failed with mono-activated methylenecyclopentanes. The method was extended to **arylative ring opening-α-substitution** with electrophiles such as AcOD, MeI or activated halides (six examples; Y 54-96%) allowing a methylenecyclohexane to cycloheptene ring expansion after ring-closing metathesis. **Allylarenes** may also be obtained from acyclic allylmalonates (three examples; Y 85-100%), albeit with low regioselectivity for a crotyl deriv. F.e.s. Y. Sumida, H. Yorimitsu, K. Oshima, Org. Lett. *2010*, *12* (10), 2254-7 [DOI: 10.1021/ol100599c].

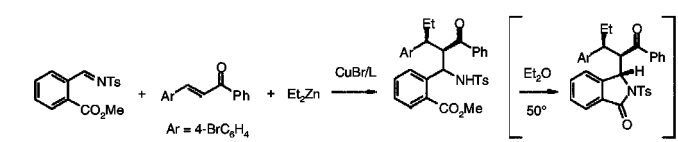
Organomagnesium salts s. under Cobalt(II) phosphine or di(phosphine) complexes *RMgX*

Dialkylzinc compds./copper(II) triflate/sodium 2(R)-[o-(diphenylphosphino)-benzylideneamino]-3,3-dimethylbutyrate *R_2Zn/[Cu(II)]**

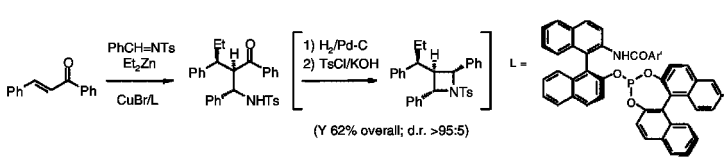
Asym. 1,6-addition s. *52*, 297s*78* C=C → CHC(R)

Dialkylzinc compds./copper(I) bromide/chiral 1,1′-binaphthyl-2,2′-diyl 2′-acylamino-1,1′-binaphthyl-2-yl phosphites ←

β-(Sulfonylamino)ketones from α,β-ethyleneketones and N-sulfonylimines via copper(I)-catalyzed asym. 1,4-addition-Mannich reaction ←



315.



in one pot. Startg. chalcone (0.5 mmol), N-tosylaldimine (1.2 eq.) and catalyst soln. [freshly prepared from CuBr (1 mol%) and chiral phosphite ligand (1.2 mol%) in methylene chloride (1 ml) at 40° for 30 min] added to a flame-dried Schlenk tube under N_2, solvent removed *in vacuo*, anhydrous ether (2 ml) added, the mixture stirred at room temp. for 10 min, cooled to -20°, a soln. of diethylzinc (1.5 eq.) in toluene (0.7 ml) added slowly, the mixture stirred for 12 h, diluted with ether, washed with 1 *M* aq. HCl and brine, concentrated *in vacuo*, and purified by flash chromatography on silica → methyl 2-[(1S,2R,3S)-2-benzoyl-3-(4-bromophenyl)-1-(4-methylphenylsulfonamido)pentyl]benzoate. Y 88% (d.r. 70:30; e.e. 95%). This efficient tandem sequence gave products containing three contiguous stereocenters with high diastereo- and enantio-selectivity for electron-diverse chalcones and N-tosyl/nosyl-imines (twenty-two examples; Y 66-96%; d.r. 67:33 to 95:5; e.e. 87-95%). An aliphatic imine gave good stereoselectivity at relatively low yield (72%) while a fur-2-ylaldimine gave lowest diastereoselectivity (67:33), and N-alkyl/aryl imines were unreactive. The products are useful intermediates for the one-pot synthesis of chiral **3-β-keto-N-sulfonyl-1(3*H*)-isoindolones** (two examples; Y 71-73%; d.r. 67:33 to 78:22; e.e. 86-95%) and also for **N-sulfonylazetidines** via ketone reduction (Pd/H_2) and cyclization with TsCl (two examples; Y 62-65% for 3 steps; d.r. >95:5). F.e. and optimization s. S. Guo, Y. Xie, X. Hu, C. Xia, H. Huang, Angew. Chem., Int. Ed. *2010*, *49* (15), 2728-31 [DOI: 10.1002/anie.200907320].

Dialkylzinc/copper(II) acetate/chiral bis(phosphoromonoamidites) $R_2Zn/[Cu(II)]$*
Dialkylzinc/copper(I) thiophenoxide/(R)-6,6′-dibromo-1,1′-bi-2-naphthol/dicyclohexyl(methyl)amine $R_2Zn/[Cu(I)]$*
Dialkylzinc/nickel(II) acetoacetonate/S-chiral 2-(aziridin-1-ylmethyl)phenyl 2-(hydroxymethyl)phenyl sulfoxides ←

Asym. 1,4-addition C=C → CHC(R)

of dialkylzinc under copper catalysis s. *52,* 297s*75*; asym. addition to cyclic enones, chalcone and nitroalkenes with CuSPh/(R)-6,6′-dibromo-BINOL/Cy_2NMe s. S. Gou, Z. Ye, L. Shi, D. Qing, W. Zhang, Y. Wang, Appl. Organomet. Chem. *2010, 24* (7), 517-22 [DOI: 10.1002/aoc.1651]; via a *multinuclear* copper(I)/zinc complex based on chiral 3,3′-bis(diarylphosphino)-1,1′-bi-2-naphthols as ligand s. K. Endo, M. Ogawa, T. Shibata, Angew. Chem., Int. Ed. *2010, 49* (13), 2410-3 [DOI: 10.1002/anie.200906839]; asym. addition to enones and nitroalkenes with *atropos* bis(phosphoromonoamidites) based on the D_2-symmetric biphenyl backbone s. H. Zhang, F. Fang, F. Xie, H. Yu, G. Yang, W. Zhang, Tetrahedron Lett. *2010, 51* (22), 3119-22 [DOI: 10.1016/j.tetlet.2010.04.033]; asym. 1,4-addition to 1,4-benzoquinone mono(cyclic acetals), and aromatization of the corresponding cyclic mercaptals, s. M. Welker, S. Woodward, L.F. Veiros, M.J. Calhorda, Chem. Eur. J. *2010, 16* (19), 5620-9 [DOI: 10.1002/chem.200903310]; asym. addition to acyclic and cyclic enones with Ni(acac)$_2$ and *tridentate* S-chiral 2-(aziridin-1-yl-methyl)phenyl 2-(hydroxymethyl)phenyl sulfoxides as ligand cf. M. Rachwalski, S. Lesniak, P. Kielbasinski, Tetrahedron: Asym. *2010, 21* (15), 1890-2 [DOI: 10.1016/j.tetasy.2010.05.053]; asym. 1,6-addition to cyclic 2,4-dienones with Cu(OTf)$_2$ and Na-2(R)-[*o*-(diphenylphosphino)-benzylideneamino]-3,3-dimethylbutyrate as ligand cf. J. Wencel-Delord, A. Alexakis, C. Crvisy, M. Mauduit, Org. Lett. *2010, 12* (19), 4335-7 [DOI: 10.1021/ol1017382].

Zinc triflate/chiral bis(Δ^2-oxazolines) $Zn(OTf)_2$/*box*

Asym. Friedel-Crafts reaction of indoles

with electron-deficient ethylene derivs. s. *67,* 336s*78*

Magnesium bromide s. under Zn $MgBr_2$
Zinc chloride s. under Mg $ZnCl_2$

Triorganoalanes/chiral copper(I) phosphine or di(phosphine) complexes or chiral rhodium(I) di(phosphine) complexes $R_3Al/[Cu]$* *or* $[Rh]$*

Asym. 1,4-addition of triorganoalanes

to enones under Cu-catalysis cf. *52,* 297s*69*; chiral β-quaternary cyclic β-vinylketones by asym. 1,4-addition of enalanes to cyclic enones with Cu(I)-thiophene-1-carboxylate [CuTC] and the chiral monophosphine, SimplePhos, as ligand s. D. Müller, C. Hawner, M. Tissot, L. Palais, A. Alexakis, Synlett *2010* (11), 1694-8 [DOI: 10.1055/s-0029-1219958]; asym. 1,4-addition of trialkylalanes to 1-nitro-1,3-dienes and -1,3-enynes with CuTC and a chiral ferrocenyldi(phosphine) as ligand (e.e. 91-95%), also asym. 1,6-addition under fine-tuning, s. M. Tissot, D. Müller, S. Belot, A. Alexakis, Org. Lett. *2010, 12* (12), 2770-3 [DOI: 10.1021/ol100849j]; chiral β-quaternary β-arylketones by asym. 1,4-addition of aryl(dimethyl)alanes to enones with [Rh(cod)Cl]$_2$/(R)-BINAP (e.e. up to >99%) s. C. Hawner, D. Müller, L. Gremaud, A. Felouat, S. Woodward, A. Alexakis, Angew. Chem., Int. Ed. *2010, 49* (42), 7769-72 [DOI: 10.1002/anie.201003300].

Trimethylaluminum (s.a. under Nickel N-heterocyclic carbene complexes) Me_3Al

Regioselective [2+2]-cycloaddition with α,β-acetylenecarbonyl compds. □

to trialkoxy(siloxy)ethylenes *en route* to cyclobutenediones s. *60,* 288s*78*

o-Nitrobenzeneboronic acid *o*-$NO_2C_6H_4B(OH)_2$

1,3-Dipolar cycloaddition with acetylene derivs. ○

review, s. *24,* 900s*28*; general procedure for 1,3-dipolar cycloaddition with α,β-acetylenecarboxylic acids under mild conditions using *o*-nitrobenzeneboronic acid as catalyst s. H. Zheng, R. McDonald, D.G. Hall, Chem. Eur. J. *2010, 16* (18), 5454-60 [DOI: 10.1002/chem.200903484

Bis(pinacolato)diboron s. under Ni(cod)$_2$ $(RO)_2BB(OR)_2$
Mesoporous aluminosilicates s. under Iron ←

Montmorillonite *clay*

Heterogeneous Friedel-Crafts reaction of indoles C=C → CHC(R)

with electron-deficient ethylene derivs. without solvent s. *11,* 770s*78*

Indium(III) bromide *$InBr_3$*
3-Vinylindoles from indoles and acetylene derivs. C≡C → CH=C(Ar)
by regio- and stereo-selective hydroarylation s. *59*, 311s*78*

1-Ethyl-3-methylimidazolium tetrachloroindate(III) *[emim][$InCl_4$]*
Regioselective hydroarylation of ethylene derivs. C=C → CHC(Ar)
with phenols s. *27*, 686s*78*

Ionic liquid-tagged ytterbium(III) sulfonates ←
Friedel-Crafts reaction of indoles with electron-deficient ethylene derivs. C=C → CHC(R)
s. *11*, 770s*76*; with nitroalkenes using a recyclable ionic liquid-tagged ytterbium(III) sulfonate as catalyst in ethanol s. W. Shen, L. Wang, J. Tang, Z. Qian, X. Tong, Chin. J. Chem. *2010, 28* (3), 443-8 [DOI: 10.1002/cjoc.201090094]; also reaction of pyrroles with montmorillonite K10 under solventless conditions s. L.-T. An, L.-L. Zhang, J.-P. Zou, G.-L. Zhang, Synth. Commun. *2010, 40* (13), 1978-84 [DOI: 10.1080/00397910903219344]; synthesis of (S)- and (R)-2-methyltryptophan-containing peptides s. L. Gentilucci, L. Cerisoli, R. De Marco, A. Tolomelli, Tetrahedron Lett. *2010, 51* (19), 2576-9 [DOI: 10.1016/j.tetlet.2010.03.017]; diastereoselective reaction of indoles with hormone-type steroidal enones with $RuCl_3{\cdot}nH_2O$ s. K. Tabatabaeian, M. Mamaghani, N. Mahmoodi, A. Khorshidi, Synth. Commun. *2010, 40* (11), 1677-84 [DOI: 10.1080/00397910903161678]; reaction of electron-deficient perfluoroarenes with acrylic acid derivs. using hydroxo[*o*-bis(diphenylphosphino)benzene]rhodium(I) complexes cf. Z.-M. Sun, J. Zhang, R.S. Manan, P. Zhao, J. Am. Chem. Soc. *2010, 132* (20), 6935-7 [DOI: 10.1021/ja102575d].

Scandium(III) triflate/chiral cyclic bis(N-oxides) or bis(Δ^2-oxazolines) ←
Asym. Friedel-Crafts reaction of indoles C=C → CHC(R)
with electron-deficient ethylene derivs. s. *67*, 336s*78*

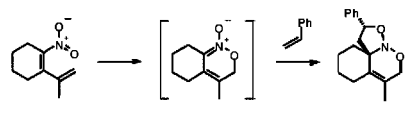
Ytterbium(III) triflate/chiral cyclic bis(N-oxides) ←
Catalytic asym. Michael addition s. *47*, 654s*78*; *49*, 657s*78*

Samarium diiodide/methanol or tert-butanol *SmI_2/ROH*
Cyclic alcohols from unsatd. oxo compds. ○
Samarium(II)-mediated reductive ring closure
s. *41*, 621s*46*; cyclopropanols from aryl- or cyano-subst. β,γ-ethyleneoxo compds. with SmI_2/*t*-BuOH, diastereoselectivity, s. M. Martin-Fontecha, A.R. Agarrabeitia, M.J. Ortiz, D. Armesto, Org. Lett. *2010, 12* (18), 4082-5 [DOI: 10.1021/ol101666m]; linearly condensed 2,6-*syn*-2,3-*trans*- and 2,6-*syn*-2,3-*cis*-tetrahydropyran-3-ols via ring closure of aldehyde-functionalized (E)- and (Z)-β-alkoxyvinyl sulfones with methanol as proton source s. T. Kimura, T. Nakata, Tetrahedron: Asym. *2010, 21* (11-12), 1389-95 [DOI: 10.1016/j.tetasy.2010.04.066]; *all-cis*-annelated A-ring aromatic steroidal 14-α-hydroxysteroids by ring closure of γ-naphthyl-β-diketones, diastereoselectivity, s. U.K. Wefelscheid, H.-U. Reissig, Tetrahedron: Asym. *2010, 21* (11-12), 1601-10 [DOI: 10.1016/j.tetasy.2010.04.036]; 5-*exo-trig*- to 8-*exo-trig* cyclization of (indol-1-yl)- and (pyrrol-1-yl)ketones to give tri- and tetra-cyclic N-condensed indolines and Δ^2-pyrrolines as single diastereoisomers s. C. Beemelmanns, V. Blot, S. Gross, D. Lentz, H.-U. Reissig, Eur. J. Org. Chem. *2010* (14), 2716-32 [DOI: 10.1002/ejoc.200901455].

1,4-Cyclohexadiene s. under Chiral titanocene dichloride ←
Methanol or tert-butanol s. under SmI_2 *ROH*

p-Quinol monomethyl ether/sodium hydrogen carbonate *p-$MeOC_6H_4OH$/$NaHCO_3$*
2,9-Dioxa-1-azabicyclo[4.3.0]non-4-enes from 1-nitro-1,3-dienes and ethylene derivs.
6π-Electrocyclization-1,3-dipolar cycloaddition

316.



2-(2-Propenyl)-1-nitrocyclohexene (0.2 mmol) added via syringe in one portion to a mixture of $NaHCO_3$ (1.2 eq.), hydroquinone monomethyl ether (0.4 eq.), dry dichloroethane (3 ml) and

styrene (3 ml), the mixture stirred vigorously at 90° until reaction complete (TLC; 12-36 h), concentrated *in vacuo*, and purified by flash chromatography on silica → product. Y 88% (exclusively *exo*). In this novel transformation, 6π-electrocyclization of a series of 1-nitro-2-vinylcyclohexenes and trapping of the intermediate cyclic nitronate with electron-diverse dipolarophiles gave synthetically useful tricyclic nitrosoacetals, generally with high diastereoselectivity (fifteen examples; Y 60-91%). The highly conjugated 2-styryl analog was unreactive (presumed due to its stability). The hydroquinone additive is thought to stabilize the nitrodiene substrate, while addition of base is required to scavenge for traces of acid. The nitrodiene substrates were readily available from 2-(ethylthio)nitrocyclohexene and zinc cuprates derived from vinyl halides (six examples; Y 53-88%; the substrate derived from 1-bromo-2-methylpropene cyclized spontaneously to the nitronate on SiO_2 in 86% yield). F.e. and transformations of the products s. G.S. Creech, O. Kwon, J. Am. Chem. Soc. *2010, 132* (26), 8876-7 [DOI: 10.1021/ja1038819].

Benzyltriethylammonium cyanide s. under N'-Chloromethyl-N-fluoro-1,4-diazonia- $BnEt_3NCN$ bicyclo[2.2.2]octane bis(fluoroborate)

*Chiral squaramides or Tripeptide amides/N-methylmorpholine or Chiral 2-[diaryl- ←
(siloxy)methyl]pyrrolidines or ionic-tagged variants*

Organocatalyzed asym. Michael addition C=C → CHC(R)

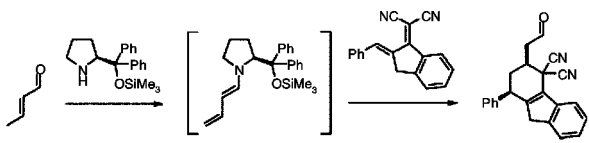
update s. *62,* 282s*75,77*; **of aldehydes** to 1-nitroethylene derivs. with a tripeptide amide (1 mol%) and N-methylmorpholine s. M. Wiesner, H. Wennemers, Synthesis *2010* (9), 1568-71 [DOI: 10.1055/s-0029-1218651]; synthesis of chiral δ-aldehydo-β-(trifluoromethyl)- from (2,2,2-trifluoroethylidene)-malonates, also α-carbalkoxy-β-(trifluoromethyl-δ-lactones, with 2(S)-[diphenyl(trimethylsiloxy)methyl]pyrrolidine s. L. Wen, Q. Shen, L. Lu, Org. Lett. *2010, 12* (20), 4655-7 [DOI: 10.1021/ol101894h]; asym. addition of α-functionalized aldehydes to α,β-ethylenesulfones with a 2-(pyrrolidin-2(S)-yl)imidazolidine as catalyst s. A. Quintard, A. Alexakis, Chem. Commun. *2010, 46* (23), 4085-7 [DOI: 10.1039/c000326c]; *in water* with a tricyclic [indoline-condensed] 2(S)-pyrrolidinecarboxylic acid/DMAP as catalyst s. J. Xiao, Y.-L. Liu, T.-P. Loh, Synlett *2010* (13), 2029-32 [DOI: 10.1055/s-0030-1258483]; asym. addition of isobutyraldehyde to 1-nitroethylene derivs. with a 2-*prim*-aminothiourea [1-((1R,2R)-2-amino-1,2-diphenylethyl)-3-benzylthiourea] as catalyst s. T. He, Q. Gu, X.-Y. Wu, Tetrahedron *2010, 66* (17), 3195-8 [DOI: 10.1016/j.tet.2010.02.069]; addition of other α-subst. aldehydes to β-nitrostyrenes (and heterocyclic analogs) with a chiral 2-(prolylamino)thiourea as catalyst cf. J.-F. Bai, X.-Y. Xu, Q.-C. Huang, L. Peng, L.-X. Wang, Tetrahedron Lett. *2010, 51* (21), 2803-5 [DOI: 10.1016/j.tetlet.2010.03.039]; with a quinine-based 2-*prim*-aminothiourea and DABCO as catalyst s. J.-R. Chen, Y.-Q. Zou, L. Fu, F. Ren, F. Tan, W.-J. Xiao, Tetrahedron *2010, 66* (29), 5367-72 [DOI: 10.1016/j.tet.2010.05.056]; addition of α-subst. aldehydes to maleimides with a chiral 2-*prim*-aminothiourea-benzoic acid salt s. F. Yu, Z. Jin, H. Huang, T. Ye, X. Liang, J. Ye, Org. Biomol. Chem. *2010, 8* (20), 4767-4 [DOI: 10.1039/c0ob00154f]; addition of nitrophenylacetonitriles **to α,β-ethylenealdehydes** with a chiral 2(S)-[diaryl(trimethylsiloxy)methyl]pyrrolidine as catalyst s. M.B. Cid, S. Duce, S. Morales, E. Rodrigo, J.L. García Ruano, Org. Lett. *2010, 12* (16), 3586-9 [DOI: 10.1021/ol101178u]; addition of β-ketosulfones s. J. Alemán, V. Marcos, L. Marzo, J.L. García Ruano, Eur. J. Org. Chem. *2010* (23), 4482-91 [DOI: 10.1002/ejoc.201000502]; with a recyclable ionic liquid-tagged 2(S or R)-[diaryl(siloxy)methyl]pyrrolidine as immobilized catalyst in 96% aq. methanol s. O.V. Maltsev, A.S. Kucherenko, I.P. Beletskaya, V.A. Tartakovsky, S.G. Zlotin, ibid. *2010* (15), 2927-33 [DOI: 10.1002/ejoc.201000239]; combinatorial preparation and screening of chiral (2S)-pyrrolidinyl-based organocatalysts for addition to enals s. I. Fleischer, A. Pfaltz, Chem. Eur. J. *2010, 16* (1), 95-9 [DOI: 10.1002/chem.200902449]; addition of nitro compds. **to α,β-ethyleneketones** with chiral *prim-sec*-diamines s. Y.-Q. Yang, X.-K. Chen, H. Xiao, W. Liu, G. Zhao, Chem. Commun. *2010, 46* (23), 4130-2 [DOI: 10.1039/c002552f]; addition of malonates *in water* with the same organocatalysts and added TFA cf. Z. Mao, Y. Jia, W. Li, R. Wang, J. Org. Chem. *2010, 75* (21), 7428-30 [DOI: 10.1021/jo101188m]; addition of 3-subst. oxindoles and 3(2*H*)-benzofuranones to cyclic enones with a cinchona-based prim. amine (9-amino-9-deoxy-*epi*-cinchonine) as catalyst s. F. Pesciaioli, X. Tian, G. Bencivenni, G. Bartoli, P. Melchiorre, Synlett *2010* (11), 1704-8 [DOI: 10.1055/s-0029-1219955]; addition of nitroacetic acid esters *in water* with the same organocatalyst and added benzoic acid s. H.W. Moon, D.Y. Kim, Tetrahedron Lett. *2010, 51* (21), 2906-8 [DOI: 10.1016/j.tetlet.2010.03.105]; in xylene with added (+)-camphorsulfonic acid cf. C. Liu, Y. Lu, Org. Lett. *2010, 12* (10), 2278-81 [DOI: 10.1021/ol1006407];

addition of malonates *under microwave irradiation without solvent* with L-proline/piperidine as catalyst s. A. Procopio, A. De Nino, M. Nardi, M. Oliverio, R. Paonessa, R. Pasceri, Synlett *2010* (12), 1849-53 [DOI: 10.1055/s-0030-1258126]; addition of 3-subst. 2(3*H*)-benzofuranones to chalcones with a chiral trifluoromethylated 2-*tert*-aminothiourea as catalyst s. X. Li, Z. Xi, S. Luo, J.-P. Cheng, Adv. Synth. Catal. *2010, 352* (7), 1097-101 [DOI: 10.1002/adsc.201000106]; of anthrone with 9-[N′-[3,5-bis(trifluoromethyl)phenyl]thioureido]-9-deoxy-*epi*-quinine as catalyst s. C. Wu, W. Li, J. Yang, X. Liang, J. Ye, Org. Biomol. Chem. *2010, 8* (14), 3244-50 [DOI: 10.1039/b927421a]; addition of nitromethane and malononitrile to aryl 2,4-dienones with the corresponding hydroquinine-based thiourea or the parent 9-*prim*-amino-9-deoxy deriv. (with added TFA) as catalyst s. C.G. Oliva, A.M.S. Silva, D.I.S.P. Resende, F.A.A. Paz, J.A.S. Cavaleiro, Eur. J. Org. Chem. *2010* (18), 3449-58 [DOI: 10.1002/ejoc.201000273]; addition of nitromethane, f. examples, s. C.G. Oliva, A.M.S. Silva, F.A.A. Paz, J.A.S. Cavaleiro, Synlett *2010* (7), 1123-7 [DOI: 10.1055/s-0029-1219576]; addition of 4-hydroxycoumarins and 4-hydroxy-2-pyrone to β,γ-ethylene-α-ketocarboxylic acid esters with chiral squaramides as catalyst s. D.-Q. Xu, Y.-F. Wang, W. Zhang, S.-P. Luo, A.-G. Zhong, A.-B. Xia, Z.-Y. Xu, Chem. Eur. J. *2010, 16* (14), 4177-80 [DOI: 10.1002/chem.201000094]; addition of 2-hydroxy-1,4-naphthoquinone s. Y.-F. Wang, W. Zhang, S.-P. Luo, G.-C. Zhang, A.-B. Xia, X.-S. Xu, D.-Q. Xu, Eur. J. Org. Chem. *2010* (26), 4981-5 [DOI: 10.1002/ejoc.201000885]; addition of cyclic β-dicarbonyl compds. with Takemoto's chiral 2-aminothiourea as catalyst cf. J.-j. Wang, J.-h. Lao, Z.-p. Hu, R.-J. Lu, S.-z. Nie, Q.-s. Du, M. Yan, ARKIVOC *2010* (ix) 229-43; addition of cyclohexanone **to 1-nitroethylene derivs.** with pyrrolidin-2(S)-ylglycol benzyl ethers as catalyst s. D. Díez, A.B. Antón, J. Peña, P. García, N.M. Garrido, I.S. Marcos, F. Sanz, P. Basabe, J.G. Urones, Tetrahedron: Asym. *2010, 21* (7), 786-93 [DOI: 10.1016/j.tetasy.2010.05.005]; addition of unprotected 3-subst. oxindoles with quinidine or quinidine-derived thioureas s. M. Ding, F. Zhou, Z.-Q. Qian, J. Zhou, Org. Biomol. Chem. *2010, 8* (13), 2912-4 [DOI: 10.1039/c004037a]; addition of β-diketones and β-keto-esters with ephedrine- and pseudoephedrine-derived 2-*tert*-aminothioureas s. A.M. Flock, A. Krebs, C. Bolm, Synlett *2010* (8), 1219-22 [DOI: 10.1055/s-0029-1219582]; addition of malonates to 3-nitro-2*H*-chromenes s. S.-z. Nie, Z.-p. Hu, Y.-n. Xuan, J.-j. Wang, X.-m. Li, M. Yan, Tetrahedron: Asym. *2010, 21* (16), 2055-9 [DOI: 10.1016/j.tetasy.2010.07.015]; addition of 2-arylcyclopentanones with a chiral 2-*tert*-amino-2′-(sulfonylamino)thiourea as catalyst s. X.-Q. Dong, H.-L. Teng, M.-C. Tong, H. Huang, H.-Y. Tao, C.-J. Wang, Chem. Commun. *2010, 46* (36), 6840-2 [DOI: 10.1039/c0cc01987a]; addition of ketones to 1-nitro-1,3-dienes with a chiral α-thioureidocarboxylic acid 2-(pyrrolidin-2(S)-ylmethylthio)imidazole salt s. Z.-B. Li, S.-P. Luo, Y. Guo, A.-B. Xia, D.-Q. Xu, Org. Biomol. Chem. *2010, 8* (11), 2505-8 [DOI: 10.1039/c002197k]; addition of acetone with chiral N-tosyl-1,2-diamines as catalyst s. L. Peng, X.-Y. Xu, L.-L. Wang, J. Huang, J.-F. Bai, Q.-C. Huang, L.-X. Wang, Eur. J. Org. Chem. *2010* (10), 1849-53 [DOI: 10.1002/ejoc.200901509] (correction s. ibid. *2010* (15), 2978 [DOI: 10.1002/ejoc.201000424]); addition to β-nitrostyrenes *in brine* with chiral N-(pyrrolidin-2(S)-ylmethyl)-*o*-tosylaminobenzamides as catalyst (with added benzoic acid) s. S. Saha, S. Seth, J.N. Moorthy, Tetrahedron Lett. *2010, 51* (40), 5281-6 [DOI: 10.1016/j.tetlet.2010.07.164]; addition of ketones with chiral cyclic β-aminophosphonic acid monoesters as catalyst s. T. Widianti, Y. Hiraga, S. Kojima, M. Abe, Tetrahedron: Asym. *2010, 21* (15), 1861-8 [DOI: 10.1016/j.tetasy.2010.05.049]; f. catalysts s. L.-J. Wang, F.-F. Hu, Bull. Korean Chem. Soc. *2010, 31* (5), 1280-2 [DOI: 10.5012/bkcs.2010.31.5.1280]; addition of 3-subst. oxindoles to maleimides with chiral 2-*tert*-aminothioureas s. Y.-H. Liao, X.-L. Liu, Z.-J. Wu, L.-F. Cun, X.-M. Zhang, W.-C. Yuan, Org. Lett. *2010, 12* (13), 2896-9 [DOI: 10.1021/ol100822k]; addition of anthrones s. A. Zea, G. Valero, A.-N.R. Alba, A. Moyano, R. Rios, Adv. Synth. Catal. *2010, 352* (7), 1102-6 [DOI: 10.1002/adsc.201000031]; addition of ketones with a chiral N-(2,6-dichlorobenzenesulfonyl)-1,2-diphenylethylenediamine·benzoic acid salt s. F. Yu, X. Sun, Z. Jin, S. Wen, X. Liang, J. Ye, Chem. Commun. *2010, 46* (25), 4589-91 [DOI: 10.1039/c0cc00774a]; addition of Δ^2-5-oxazolones to 1,1-bis(phenylsulfonyl)ethylene with chiral 2-*tert*-aminothioureas as catalyst, also conversion to chiral α-quaternary α-acylaminocarboxylic acids s. A.-N.R. Alba, X. Companyó, G. Valero, A. Moyano, R. Rios, Chem. Eur. J. *2010, 16* (18), 5354-61 [DOI: 10.1002/chem.200903025]; addition to *cis*-1,2-bis(phenylsulfonyl)ethylene with Takemoto's catalyst s. N. Bravo, A.-N.R. Alba, G. Valero, X. Companyó, A. Moyano, R. Rios, New J. Chem. *2010, 34* (9), 1816-20 [DOI: 10.1039/c0nj00321b]; synthesis of chiral 2-*tert*-aminoguanidines for asym. Michael addition s. K. Thai, M. Gravel, Tetrahedron: Asym. *2010, 21* (6), 751-5 [DOI: 10.1016/j.tetasy.2010.04.033]; **vinylogous asym. Michael addition** of

2(5*H*)-furanone to enones with a chiral N-tosyltri-*prim*-amine as catalyst and added N-Boc-L-proline s. H. Huang, F. Yu, Z. Jin, W. Li, W. Wu, X. Liang, J. Ye, Chem. Commun. *2010, 46* (32), 5957-9 [DOI: 10.1039/c0cc01054e].

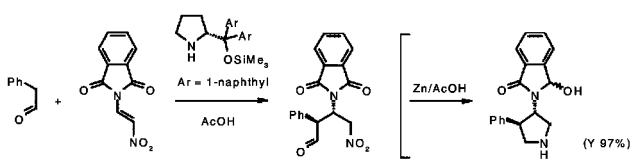
2(S)-[Diphenyl(trimethylsiloxy)methyl]pyrrolidine/benzoic acid ←
Cyclohex-3-enylacetaldehydes from electron-deficient 1,3-dienes via organocatalyzed asym. Diels-Alder reaction ○

317.

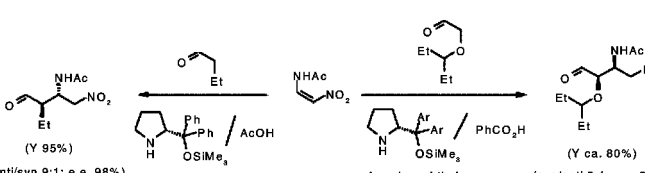


Chiral 2-functionalized 2-cyanocyclohex-3-enylacetaldehydes. A mixture of crotonaldehyde (2 eq.), startg. diene (0.2 mmol), chiral prolinol deriv. (10 mol%) and benzoic acid (10 mol%) in 1,4-dioxane (1 ml) stirred at 25° for 24-48 h, concentrated *in vacuo*, and purified by flash chromatography on silica → product. Y 80% (d.r. 89:11; e.e. 91%). This novel all-carbon cycloaddition of electron-deficient dienes and crotonaldehyde requires the presence of a carboxylic acid additive and provides a route to polyfunctional cyclohexenes with high diastereo- and enantiocontrol (twenty-two examples; Y 43-80%) with lowest yields observed for dienes carrying both β- and γ-hydrogens. F.e., optimization and product transformations, s. J.-L. Li, T.-R. Kang, S.-L. Zhou, R. Li, L. Wu, Y.-C. Chen, Angew. Chem., Int. Ed. *2010, 49* (36), 6418-20 [DOI: 10.1002/anie.201002912].

2(R)-[Diphenyl(trimethylsiloxy)methyl]pyrrolidine/acetic acid ←
2(R)-[Dinaphth-1-yl(trimethylsiloxy)methyl]pyrrolidine/acetic or benzoic acid ←
β-Acylamino-γ-nitroaldehydes from 2-nitroenacylamines and aldehydes via organocatalyzed asym. Michael addition C=C → CHC(R)



318.

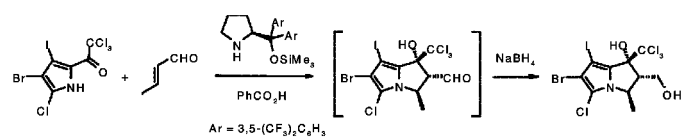


Phenylacetaldehyde (2 eq.) and acetic acid (10 mol%) added to a suspension of chiral catalyst (10 mol%), (E)-N-2-nitrovinylphthalimide (0.2 mmol) and 4 Å molecular sieves (powder; 50 mg)

in anhydrous chloroform (0.4 ml) at -10°, the mixture stirred until startg. m. consumed (NMR), and purified directly by chromatography on silica → product. Y 99% (*syn/anti* 26:1; e.e. 97%). Diastereo- and enantio-selective Michael addition to the protected (E)-2-amino-1-nitroethylene was effective for a number of α-aliphatic (incl. unsaturated) and α-aryl acetaldehydes (thirteen examples; Y 87-99%; *syn/anti* 3:1 to 26:1; e.e. 88-99%). The analogous (Z)-2-acetylamino-1-nitroethylene was also a suitable substrate, while a series of aliphatic aldehydes afforded mainly *anti*-adducts (five examples; Y 80-98%; *anti/syn* 3:1 to 9:1; e.e. 93-98%). The aldehyde-ether, 2-pentyl-2-yloxyacetaldehyde, afforded a *syn*-adduct with stereochemistry (2S,3R) not predicted by the commonly accepted transition state model, however. The products serve as precursors to **chiral 3-(acylamino)pyrrolidines** via nitro group reduction and intramolecular condensation (eleven examples; Y 66-99%). F.e.s. S. Zhu, S. Yu, Y. Wang, D. Ma, Angew. Chem., Int. Ed. *2010*, *49* (27), 4656-60 [DOI: 10.1002/anie.201001644].

(S)-2-[Bis[3,5-bis(trifluoromethyl)phenyl](trimethylsiloxy)methyl]pyrrolidine/benzoic acid ←
2,3-Dihydro-1*H*-pyrrolizin-1-ols from 2-acylpyrroles and α,β-ethylenealdehydes ○
via organocatalyzed asym. Michael addition-intramolecular aldol condensation

319.



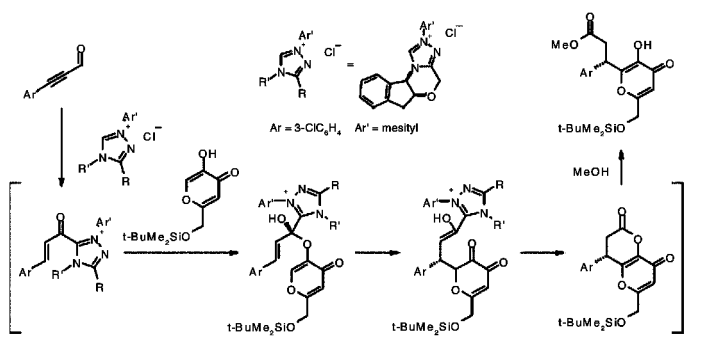
Crotonaldehyde (2 eq.) added in one portion to a soln. of startg. pyrrole, (S)-prolinol-deriv. (20 mol%) and benzoic acid (40 mol%) in toluene (0.1 *M*), the mixture stirred at -10° for 18 h, worked up by *in situ* reduction of the initially-formed aldehyde with $NaBH_4$ (1 eq.) in ethanol (0.1 *M*), the mixture adsorbed onto silica gel by evaporation of the solvent, and purified by chromatography on silica gel → product. Y 71% (d.r. >20:1; e.e. 92%). The procedure, producing three consecutive stereogenic centers, was successful for a range of pyrrole derivs., tolerating cyano, nitro, bromo, chloro, iodo, trichloromethyl and trifluoromethyl groups (nine examples; Y 60-81%; d.r. >20:1; e.e. 90-96%). Longer chain enals (tolerating ether, ester, chloro, silyl ether, N-Cbz and N-Boc substituents on the chain) were also successful substrates (eleven examples; Y 46%, 62-81%; d.r. >20:1; e.e. 91-98%). Key to the success of the transformation is that the NH of the pyrrole is acidic enough to be deprotonated by carboxylate anion acting as base, enabling the resulting pyrrole anions to act as novel nucleophiles in the initial conjugate addition. F.e., optimization and a proposed mechanism, s. J.-Y. Bae, H.-J. Lee, S.-H. Youn, S.-H. Kwon, C.-W. Cho, Org. Lett. *2010*, *12* (19), 4352-5 [DOI: 10.1021/ol101811c].

1,3-Bis(2,6-diisopropylphenyl)imidazolium chloride/potassium tert-butoxide s. under ←
Ni(cod)$_2$
1,3-Bis(2,6-diisopropylphenyl)-Δ^2-imidazolinium chloride/cesium carbonate s. under AgOTf ←
1,3-Bis(2,6-diisopropylphenyl)imidazol-2-ylidene s. under Ni(cod)$_2$ *NHC*
Chiral bis(Δ^2-oxazolines) s. under Cu(OTf)$_2$, Ca(OEt)$_2$ and Zn(OTf)$_2$ *box*

Chiral oxazolidine hydrotrifluoroacetates ←
Organocatalyzed asym. Diels-Alder reaction s. *46*, 662s*78*

Chiral condensed triazolium chlorides ←
γ,δ-Ethylene-δ-hydroxycarboxylic acid esters ←
from enols and α,β-acetylenealdehydes via 3,4-dihydro-2-pyrone ring
Asym. conversion with a chiral base-free generated N-heterocyclic carbene as catalyst

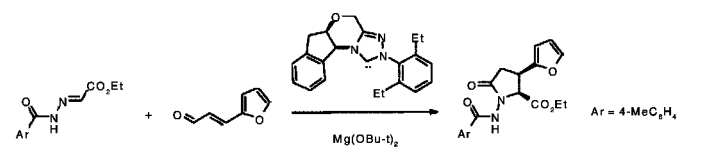
320.



2-(*tert*-Butyldimethylsilyloxymethyl)-5-hydroxy-4*H*-pyran-4-one (0.4 mmol), chiral triazolium precatalyst (10 mol%), toluene (4 ml) and 3-(3-chlorophenyl)propynal (1.5 eq.) added sequentially to a dry flask, the flask sealed with a polyethylene cap, the soln. stirred at 40° for 24 h, diluted with ethyl acetate, quenched with satd. aq. NH_4Cl, extracted with ethyl acetate, concentrated *in vacuo*, the residue dissolved in methanol (5 ml), the soln. stirred for 6 h, concentrated *in vacuo*, and purified by flash chromatography → methyl (S)-3-[6-(*tert*-butyldimethylsilyloxymethyl)-3-hydroxy-4-oxo-4*H*-pyran-2-yl]-3-(3-chlorophenyl)propanoate. Y 87% (e.e. 99%). The authors suggest that the chloride counterion acts as a base, providing activation of the catalyst (as an N-heterocyclic carbene), thereby generating an acyl azolium species from the ynal. Reaction with the enol and subsequent Claisen rearrangement of the generated hemiacetal ultimately provide somewhat unstable dihydropyranones, in this case, which were isolated via methanolysis. Kojic acid derivs. as enol source, reacted efficiently with 3-aryl/alkyl-propynals (twelve examples; Y 78-98%; e.e. 92-99%), and a pyruvate was also effective (in the presence of amine to generate the enol), affording a stable dihydropyranone (Y 74%; e.e. 99%), but phenolic compds. gave reduced enantioselectivity (e.g. 2-naphthol; Y 79%; e.e. 68%). F.e. and optimization s. J. Kaeobamrung, J. Mahatthananchai, P. Zheng, J.W. Bode, J. Am. Chem. Soc. *2010*, *132* (26), 8810-2 [DOI: 10.1021/ja103631u].

Chiral condensed triazolium chlorides/1,5,7-triazabicyclo[4.4.0]dec-5-ene/magnesium tert-butoxide ←
1-Acylamino-2-pyrrolidones from N-acylhydrazones and α,β-ethylenealdehydes ○
[3+2]-Cycloaddition under cooperative catalysis with a N-heterocyclic carbene and Lewis acid

321.



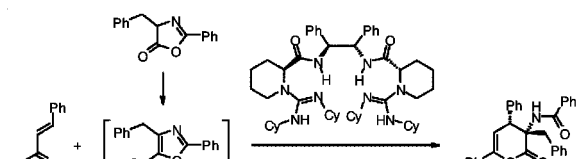
Chiral 1-aroylamino-2-pyrrolidone-5-carboxylic acid derivs. Startg. hydrazone (0.273 mmol), chiral catalyst (5 mol%) and Mg-*tert*-butoxide (5 mol%) added to a vial in a dry-box under N_2,

the vial sealed, THF (1.1 ml) added, the white suspension stirred at 60° for 15-20 min, 3-fur-2-yl-acrolein (1.5 eq.) and 1,5,7-triazabicyclo[4.4.0]dec-5-ene (10 mol%) added to the clear yellow soln., stirring continued until reaction complete (TLC; 24 h), the mixture diluted with methylene chloride, washed with aq. NH_4Cl, concentrated *in vacuo*, and purified by flash chromatography on Biotage SP-1 → ethyl 4-fur-2-yl-1-(4-toluoylamino)pyrrolid-2-one-5-carboxylate. Y 71% (d.r. 12:1; e.e. 98%). This novel formal [3+2]-cycloaddition involves activation of both nucleophilic and electrophilic components via two distinct catalytic cycles (carbene and Lewis acid respectively). The method was successful with electron-diverse N′-aroyl-glyoxal-derived hydrazones (ar. aldehyde-derived analogs were not reactive), reacting with (het)ar. and aliphatic derived enals (twenty examples; Y 60-85%; d.r. 5:1 to 20:1; e.e. 85-98%) in the presence of halo, ester, ether and silyl ether functionality. F.e., optimization and conversion to pyroglutamic acid derivs. s. D.E.A. Raup, B. Cardinal-David, D. Holte, K.A. Scheidt, Nature Chem. *2010*, *2* (9), 766-71 [DOI: 10.1038/nchem.727].

Chiral 2-tert-aminoguanidines ←
Organocatalyzed asym. Michael addition s. *62*, 282s*78* C=C → CHC(R)

C_2-Symmetric chiral bis(guanidine) ←
3-Acylamino-3,4-dihydro-2-pyrones OC
from α,β-ethyleneketones and Δ^2-5-oxazolones
via organocatalyzed asym. hetero-Diels-Alder reaction

322.

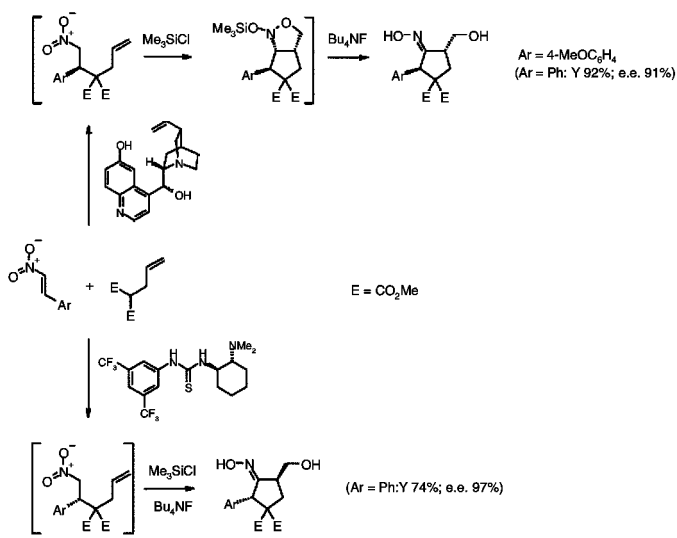


A rare example of chalcones (or heteroaryl analogs) acting as heterodienes in catalytic asymmetric inverse-electron-demand hetero-Diels-Alder reactions is reported using novel C_2-symmetric chiral bis(guanidine) catalysts, affording δ-enollactones having α-quaternary-β-tertiary stereocenters from azlactones. **E: Chiral 3-subst. 3-acylamino-4,6-diaryl-3,4-dihydro-2-pyrones**. Startg. azlactone (0.1 mmol) in THF/chloroform (1:1; 0.3 ml) added slowly at -20° to a stirred soln. of chalcone (2 eq.) and chiral (S,S)-1,2-diphenylethylenediamine-based bis(guanidine) catalyst (10 mol%) in THF/chloroform (1:1; 0.7 ml), stirred for 72 h (TLC monitoring), the residue directly purified by chromatography on silica gel to afford pure cycloadduct and a mixture of cycloadduct and Michael adduct, then the mixture purified by chromatography on silica gel for a second time → (3S,4R)-cycloadduct. Y 73% (single diastereomer; e.e. 96%) plus 8% Michael adduct. The method is applicable to electron-deficient or -rich chalcones, the former exhibiting higher reactivity, while a variety of azlactones may also be used, regardless of the electronic nature or steric hindrance of the 2-substituent. A bifunctionally activated transition state is proposed, hydrogen bonding from the amide activating the chalcone, while the azlactone is enolized by the guanidine and hydrogen bonded to both the guanidine and the second amide group. F.e. (thirty-one; Y 40-88%; e.e. 89-99%) s. S. Dong, X. Liu, X. Chen, F. Mei, Y. Zhang, B. Gao, L. Lin, X. Feng, J. Am. Chem. Soc. *2010*, *132* (31), 10650-1 [DOI: 10.1021/ja1046928].

Polymer-based 3,6-bis(9-O-[dihydro]quinidine)pyridazine ←
Heterogeneous asym. dimerization of ketenes ←
Chiral β-ketohydroxamic acid esters s. *78*, 436

Cupreidine or (R,R)-N-[3,5-bis(trifluoromethyl)phenyl]-N′-[2-(dimethylamino)cyclohexyl]-thiourea/trimethylsilyl chloride/triethylamine/tetra-n-butylammonium fluoride ←

3-Hydroximino-4-α-hydroxycyclopentane-1,1-dicarboxylic acid esters from α-allylmalonic acid esters and 1-nitroethylene derivs. Organocatalyzed asym. Michael addition-intramolecular [3+2]-cycloaddition-fragmentation ○



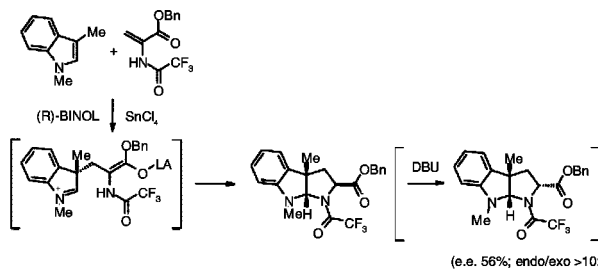
323.

in one pot. Cupreidine (10 mol%) added to a stirred soln. of 2-(4-methoxyphenyl)-1-nitroethylene (1 mmol) and dimethyl 2-allylmalonate (2 eq.) in THF (2 ml) at room temp., the mixture stirred for 2 d, cooled to -30°, Me_3SiCl (3 eq.) and triethylamine (3 eq.) added sequentially, warmed to room temp. over ca. 1 h, the mixture stirred for 18 h, quenched with *n*-Bu_4NF (2 eq.) in THF (2 ml), stirred at room temp. for 10 min, diluted with water, extracted with ether, washed with satd. aq. NH_4Cl, concentrated, and purified by flash chromatography → dimethyl (2R,3E,4R)-3-(hydroxyimino)-4-(hydroxymethyl)-2-(4-methoxyphenyl)cyclopentane-1,1-dicarboxylate. Y 73% (e.e. 97%). The Michael addition-cycloaddition-fragmentation sequence was accomplished for electron-diverse 2-(het)aryl-1-nitroethylenes and 2-allylmalonates (incl. 2- and 3-methyl derivs.) with cupreidine [O-desmethylquinidine], or a complementary chiral 2-*tert*-aminothiourea catalyst, providing enantiomeric products with good chirality transfer for 2 or 3 stereocenters (seventeen examples; Y 57-99%; e.e. 88-98%). Lowest yield was obtained from an electron-rich trimethoxyphenylnitroethylene. Alternative use of aq. HCl in the fragmentation step afforded a known isoxazoline in one case with retention of stereochemistry. Absolute structure was confirmed by X-ray analysis. F.e.s. W. Raimondi, G. Lettieri, J.-P. Dulcère, D. Bonne, J. Rodriguez, Chem. Commun. *2010*, *46* (38), 7247-9 [DOI: 10.1039/c0cc01940b].

2,2′-Biphenol monomethyl ether s. under Ca(OEt)₂ ←

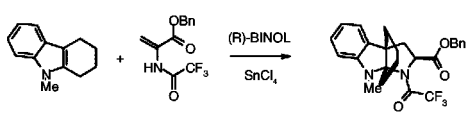
(R)-1,1′-Bi-2-naphthol/tin(IV) chloride *(R)-BINOL/$SnCl_4$*

1-Acyl-2-amino-5-carbalkoxypyrrolidine ring
from cyclic enamines and α-acylaminoacrylic acid esters
Asym. [3+2]-cycloaddition via Michael addition-intramolecular iminium ion trapping



(e.e. 56%; endo/exo >10:1)

324.



(Y 65%; d.r. >18:1; e.e. 86%)

Chiral 1-trifluoroacetyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole-2-carboxylic acid benzyl esters. 1,3-Dimethyl-1*H*-indole (0.15 mmol), benzyl 2-trifluoroacetamidoacrylate (1 eq.) and (R)-BINOL (0.2 eq.) added to a flame-dried flask under N_2, followed by dry methylene chloride (1.5 ml) and $SnCl_4$ (1.2 eq.; 1 *M* in methylene chloride), stirred at room temp. for 5.5 h, quenched by dilution with acetonitrile (1 ml) and 1 *M* HCl (1 ml), followed by addition of water (5 ml), the aq. layer extracted with ethyl acetate, washed with either satd. aq. $NaHCO_3$ or 1 *M* aq. NaOH, the aq. layer back-extracted with ethyl acetate, the combined organic layers dried (Na_2SO_4), filtered, concentrated, then the crude residue purified by flash chromatography → product. Y 86% (d.r. 4:1; e.e. *exo* 94%, e.e. *endo* 91%). This method should facilitate the total synthesis of an important class of biologically active natural products. Indoles bearing electron-donating or -withdrawing groups at the 5-position react with high enantioselectivity but yields were somewhat lower with electron-poor groups. The 3-position tolerates more functionalized groups such as 2-*tert*-butyldimethylsiloxyethyl or 2-phenylethyl, while N-methyl-1,2,3,4-tetrahydrocarbazole is also a suitable substrate, affording the aza-propellane core found in vincorine or minfiensine. F.e. (nine; Y 51-93%; d.r. 3:1 to >18:1; e.e. 86-94%), optimization and epimerization to the *ent-endo* deriv. with DBU (excess in CD_2Cl_2) s. L.M. Repka, J. Ni, S.E. Reisman, J. Am. Chem. Soc. *2010*, *132* (41), 14418-20 [DOI: 10.1021/ja107328g]; diastereospecific variant with $ZrCl_4$, incl. application to (±)-esermethole, s. S. Lucarini, F. Bartoccini, F. Battistoni, G. Diamantini, G. Piersanti, M. Righi, G. Spadoni, Org. Lett. *2010*, *12* (17), 3844-7 [DOI: 10.1021/ol101527j].

(R)-6,6′-Dibromo-1,1′-bi-2-naphthol s. under R_2Zn ←

(1R,2R,6S)-6-Di-p-tolyl(2-methyl-1-propyloxy)methyl-2-(2-hydroxyphenoxy)cyclohexanol/2,6-dimethylphenol s. under $Sr(OPr\text{-}i)_2$ ←

Formic acid s. under $Ru(CO)H_2(PPh_3)_3$ *HCOOH*

Acetic acid s. under $Rh(acac)(CH_2{=}CH_2)_2$ *AcOH*

Pivalic acid s. under $[Cp^*Rh(MeCN)_3][SbF_6]_2$ *t-BuCOOH*

Chiral α-acylaminocarboxylic acids or L-Proline/piperidine/microwaves or Tricyclic (S)-prolines/4-dimethylaminopyridine ←
Organocatalyzed asym. Michael addition s. *62*, 282s*78* C=C → CHC(R)

Trifluoroacetic acid s. under μ-Chlorine-bridged ruthenium(II) complex and $PdCl_2(MeCN)_2$ CF_3COOH

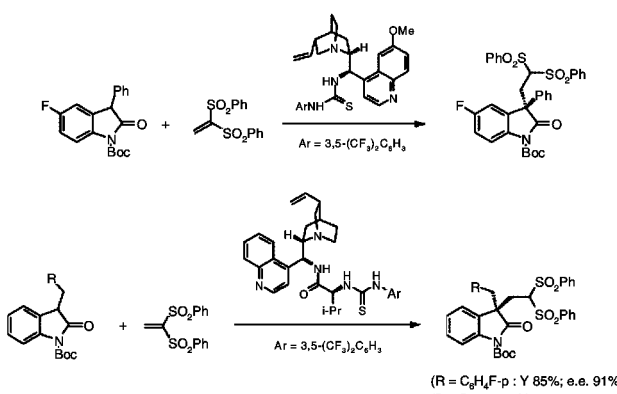
m-Chloroperoxybenzoic acid s. under $(Ph_3P)AuNTf_2$ $ArCO_3OH$

S-Chiral 2-(aziridin-1-ylmethyl)phenyl 2-(hydroxymethyl)phenyl sulfoxides s. under R_2ZnAr_2SO

Chiral 2-tert-aminothioureas (s.a. under Cupreidine) ←
Chiral α-thioureidocarboxylic acid salts ←
Organocatalyzed asym. Michael addition s. *62*, 282s*78*

Planar-chiral paracyclophane-based N-[3,5-bis(trifluoromethyl)phenyl]thioureas ←
Organocatalyzed asym. Friedel-Crafts reaction of indoles
with electron-deficient ethylene derivs. s. *67*, 336s*78*

Cinchona alkaloid-derived aminothiourea or α-thioureidocarboxylic acid amides ←
Organocatalyzed asym. Michael reaction with oxindoles
Chiral 3-(2,2-disulfonylethyl)oxindoles



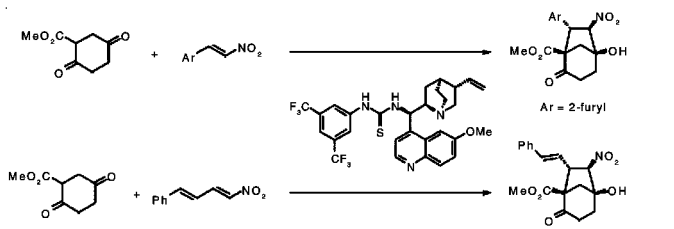
325.

(R = C_6H_4F-p : Y 85%; e.e. 91%)
(R = Pr-n : Y 76%; e.e. 80%)

1,1-Bis(benzenesulfonyl)ethylene (0.05 mmol) added to a mixture of *tert*-butyl 5-fluoro-2-oxo-3-phenylindoline-1-carboxylate (1.2 eq.) and chiral quinine-based thiourea catalyst (20 mol%) in anhydrous toluene (0.4 ml) in a sealed vial at -78°, the mixture stirred for 12 h, concentrated *in vacuo*, and purified chromatographically → *tert*-butyl (R)-3-[2,2-bis(phenylsulfonyl)ethyl]-5-fluoro-2-oxo-3-phenylindoline-1-carboxylate. Y 94% (e.e. 93%). The illustrated catalyst was extremely effective for the conjugate addition of 3-arylated oxindoles (ten examples; Y 92-98%; e.e. 90-99%) but gave lower yield (76%) and poor enantioselectivity (e.e. 28%) for a 3-benzyl deriv. Catalyst development, incorporating an amino acid bridge between cinchonidine and thiourea moieties, produced an effective trifunctional catalyst for conjugate addition of 3-benzyl and 3-*n*-alkyl derivs. to afford 3,3-dialkyloxindoles (seven examples; Y 72-88%; e.e. 77-91%). Interestingly, the Boc protecting group appeared to be crucial for high enantioselectivity, since an unprotected 3-aryloxindole gave a racemic product. F.e., optimization and further elaboration of the products s. Q. Zhu, Y. Lu, Angew. Chem., Int. Ed. *2010*, *49* (42), 7753-6 [DOI: 10.1002/anie.201003837].

Cinchona alkaloid-derived aminothiourea ←
6-Nitrobicyclo[3.2.1]octan-5-ol-2-one-1-carboxylic acid esters from 1-nitroethylenes via organocatalyzed asym. Michael addition-intramolecular Henry reaction ○

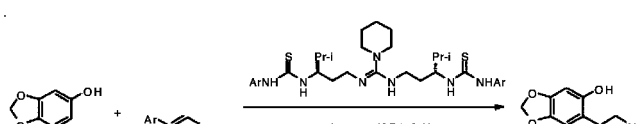
326.



Chiral thiourea catalyst (5 mol%) added to a soln. of methyl 2,5-dioxocyclohexanecarboxylate (2 eq.) and startg. nitroalkene (0.1 mmol) in benzonitrile (0.5 ml) at room temp., the resulting mixture stirred vigorously until reaction complete (TLC/NMR; 6 h), and purified by flash chromatography on silica gel → (1R,5S,6R,7S)-methyl 7-(furan-3-yl)-5-hydroxy-6-nitro-2-oxobicyclo[3.2.1]octane-1-carboxylate. Y 84% (d.r. >99:1; e.e. 92%). This novel domino reaction affords bicyclo[3.2.1]-octane derivs. with four new stereogenic centers, incl. two quaternary ones, and is applicable to a range of electron-diverse β-nitrostyrenes (twelve examples, incl. naphthyl and hetar. analogs) in high yield (77-93%) and with high diastereo- and enantio-selectivity (d.r. >99:1; e.e. 90-96%). Extension to a nitrodiene (illustrated) gave a single adduct (Y 76%; d.r. >99:1; e.e. 86%), with no evidence of attack at the δ-position. Lower catalyst loadings led to longer reaction times but, notably, the reaction was unaffected by changes in reaction temperature (4° to room temp.); the polar benzonitrile was the optimal solvent, affording highest enantioselectivities while maintaining the activity of the catalyst. F.e., incl. theoretical DFT calculations supporting a proposed novel dual catalytic activation model s. B. Tan, Y. Lu, X. Zeng, P.J. Chua, G. Zhong, Org. Lett. *2010, 12* (12), 2682-5 [DOI: 10.1021/ol1007795]; correction s. ibid. 2892 [DOI: 10.1021/ol101179s]; **chiral 7-nitrobicyclo[3.2.1]octan-1-ol-8-ones** from 1,2-cyclohexandiones (e.e. 92-99%) cf. D. Ding, C.-G. Zhao, Q. Guo, H. Arman, Tetrahedron *2010, 66* (25), 4423-7 [DOI: 10.1016/j.tet.2010.04.044].

Chiral bis(thioureido)guanidines ←
Entropy-controlled catalytic asym. Friedel-Crafts reaction of phenols using conformationally flexible chiral bis(thioureido)guanidines as organocatalysts CHC(Ar)

327.



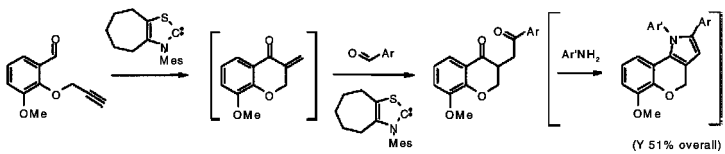
β-Nitrostyrene (0.1 mmol) added to a soln. of chiral bis(thioureido)guanidine catalyst (5 mol%) and sesamol (1 eq.) in toluene (4 ml) at 20°, the mixture stirred for 9 h, quenched with satd. aq. NH_4Cl, extracted with ethyl acetate, and purified by flash chromatography → (-)-(S)-4,5-methylenedioxy-2-(2-nitro-1-phenylethyl)phenol. Y 97% (e.e. 91%). Extensive catalyst development identified an α-branched substituent on the chiral spacer and a 6-membered ring containing the

guanidine moiety as key requirements for high enantioselectivity. A series of phenols and naphthols were alkylated efficiently with electron-diverse 2-(het)aryl- and 2-alkyl-1-nitroethylene derivs. in the presence of the optimized catalyst (fourteen examples; Y 66-99%; e.e. 82-94%). Absolute stereochemistry was determined in one case by X-ray analysis of a deriv. F.e., optimization and catalyst prepn., s. Y. Sohtome, B. Shin, N. Horitsugi, R. Takagi, K. Noguchi, K. Nagasawa, Angew. Chem., Int. Ed. *2010*, *49* (40), 7299-303 [DOI: 10.1002/anie.201003172].

Chiral 5-benzylimidazolidine-4-thiones ←
Organocatalyzed asym. Friedel-Crafts reaction of pyrroles C=C → CHC(R)
with electron-deficient ethylene derivs. s. *67*, 336s*78*

N-Mesityl-4,5-pentamethylenethiazolium perchlorate/potassium carbonate ←
3-β-Ketochroman-4-ones from *o*-propargyloxyaldehydes and aldehydes ○
N-Heterocyclic carbene-(NHC)-catalyzed intramolecular hydroacylation-Stetter reaction

328.



Ar = 4-ClC$_6$H$_4$ Ar' = 4-MeC$_6$H$_4$

in one-pot. N-Mesityl-4,5-pentamethylenethiazolium perchlorate (5 mol%) and dry K_2CO_3 (10 mol%) added to 2-propargyloxy-3-methoxybenzaldehyde (1 mmol) under argon, a soln. of 4-chlorobenzaldehyde (1 eq.) in **THF** (2 ml) added, the mixture stirred at 70° for 2 h, cooled, and purified by flash chromatography on silica → 3-[2-(4-chlorophenyl)-2-oxoethyl]-8-methoxychroman-4-one. Y 96%. Initial experiments demonstrated cyclization of unactivated 2-propargyloxybenzaldehydes to **3-benzylidenechroman-4-ones** (eight examples; Y 72-95%) and a single example of a **1,2-dihydro-4-quinolone** analog (Y 63%) using the illustrated carbene catalyst. In subsequent experiments the enones were trapped *in situ* with electron-diverse (het)ar. and aliphatic aldehydes to afford the title products (twenty-four examples; Y 65-96%) in the presence of ether, ester, halo, *allyloxy* and alkyne functionality, with formation of the usual Stetter by-products suppressed by use of the particular NHC. In a further development, the γ-diketone moiety of the product was trapped with toluidine, in one case, to afford a **benzopyranopyrrole** in a one-pot three step sequence (Y 51%). F.e.s. A.T. Biju, N.E. Wurz, F. Glorius, J. Am. Chem. Soc. *2010*, *132* (17), 5970-1 [DOI: 10.1021/ja102130s].

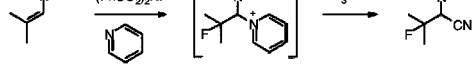
N′-Chloromethyl-N-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(fluoroborate) ←
s.a. under dppm(AuBr)$_2$

N′-Chloromethyl-N-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(fluoroborate)/ ←
benzyltriethylammonium cyanide

N′-Chloromethyl-N-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(fluoroborate) or ←
N-fluorobenzenesulfonimide/pyridine or triethylamine/trimethylsilyl cyanide

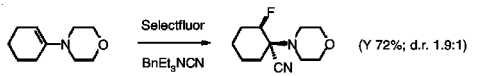
α-Amino-β-fluoronitriles from enamines C=C(N<) → C(F)C(N<)CN

329.



A novel fluorocyanation is reported using convenient reagents. **E:** Pyridine (1.2 eq.) and startg. enamine (0.35 mmol) added successively to a soln. of trimethylsilyl cyanide (1.5 eq.) and N-fluorobenzenesulfonimide (1.1 eq.) in dry acetonitrile (1.4 ml) at 0° under argon, the mixture stirred for

1 h at 0°, quenched with satd. aq. $NaHCO_3$, diluted with an excess of water, extracted with ether, washed with brine, filtered through Na_2SO_4, concentrated, azeotropically dried with acetonitrile, and the residue purified by flash chromatography → product. Y 89%. Four further examples of β,β-disubst. enamines gave reasonable yields (60-87%) in the presence of NFSI or Selectfluor and pyridine or triethylamine. For enamines containing a β-hydrogen, Selectfluor/benzyltriethylammonium cyanide was more effective (four examples; Y 42-87%), the β,β-difluoro-deriv. being the major product using trimethylsilyl cyanide.



F.e.s. A.D. Dilman, P.A. Belyakov, M.I. Struchkova, D.E. Arkhipov, A.A. Korlyukov, V.A. Tartakovsky, J. Org. Chem. *2010*, *75* (15), 5367-70 [DOI: 10.1021/jo1008993].

Trimethylsilyl cyanide s. under N′-Chloromethyl-N-fluoro-1,4-diazoniabicyclo-[2.2.2]octane bis(fluoroborate) *Me_3SiCN*

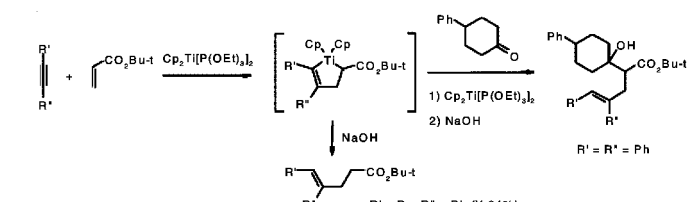
tert-Butyldimethylsilyl cyanide s. under Sr(OPr-i)₂ *t-$BuMe_2SiCN$*

Trimethylsilyl chloride s. under Cupreidine *Me_3SiCl*

Titanocene dichloride/magnesium/triethyl phosphite *$Cp_2TiCl_2/Mg/(EtO)_3P$*

α-Allyl-β-hydroxycarboxylic acid esters from acetylene derivs. and acrylic acid esters via coupling of titanacyclopent-2-ene-5-carboxylic acid esters with oxo compds. ←

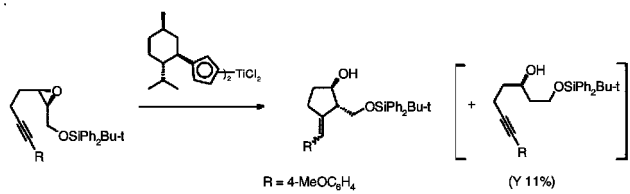
330.



A soln. of diphenylacetylene (1 mmol) in THF (2 ml) added to a soln. of $Cp_2Ti[P(OEt)_3]_2$ [prepared by reaction of $P(OEt)_3$ (2 mmol), Mg turnings (1.1 mmol), finely powdered 4 Å molecular sieves (100 mg) and Cp_2TiCl_2 (1 mmol) in THF (2 ml) at room temp. for 3 h], stirred for 1 h, a THF (2 ml) soln. of *tert*-butyl acrylate (2 mmol) added dropwise over 5 min, the resulting mixture stirred for a further 3 h, filtered, the filtrate purified by chromatography on alumina under N_2, the resulting dark red powder washed with hexanes, and dried *in vacuo* → intermediate titanacycle (Y 61%), a soln. of which (0.5 mmol) in THF (2 ml) added to a soln. of $Cp_2Ti[P(OEt)_3]_2$ (0.5 mmol) in THF (2 ml) at room temp., stirred for 1 h, a soln. of 4-phenylcyclohexanone (1 mmol) in THF (2 ml) added, the resulting mixture stirred for 2 h, quenched with 1 *M* NaOH (20 ml), filtered through Celite, extracted with methylene chloride, the extracts dried (Na_2SO_4), concentrated, and the residue purified chromatographically → *tert*-butyl (Z)-2-(1-hydroxy-4-phenylcyclohexyl)-4,5-diphenylpent-4-enoate. Y 88%. Reaction afforded exclusively (Z)-products with both aldehydes and ketones (five examples; Y 45-88%; d.r. 62:38 to 82:18 for three unsym. ketones). The intermediate titanacycle was inactive towards carbonyl compds. in the absence of the Ti(II) complex, although the role of the latter is unclear. Titanacycles from a variety of alternative internal alkynes (alkyl- and/or [het]aryl-subst.) were too unstable to be isolated, but afforded **(Z)-γ,δ-ethylenecarboxylic acid esters** on quenching with aq. NaOH (six examples; Y 54-74%), regioselectivity of unsym. examples being controlled by heteroatom coordination to Ti. A one-pot, 3-component procedure obviated the need to isolate the intermediate titanacycles (two examples; Y 58%, 61%). F.e.s. S. Oishi, K. Ohomika, A. Tsubouchi, T. Takeda, Chem. Lett. *2010*, *39* (7), 723-4 [DOI: 10.1246/cl.2010.723].

Chiral titanocene dichloride/manganese/2,4,6-collidine/1,4-cyclohexadiene ←
Exocyclic 3-ethylenealcohols from acetyleneepoxides C○
Catalytic asym. radical ring closure via regiodivergent epoxide opening

331.



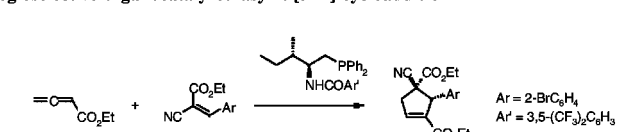
R = 4-MeOC$_6$H$_4$ (Y 11%)

It has been demonstrated for the first time that the diastereoselectivity of cyclizations of acyclic radicals can be controlled catalytically. **E: 3-Alkylidenecyclopentanols**. A dry Schlenk flask, charged with 2,4,6-collidine hydrochloride (1.5 eq.) under argon, gently heated under vacuum until the contents started to sublime slightly, Kagan's complex (10 mol%), Mn powder (2 eq.) and THF (3 ml) added, the mixture stirred for 30 min (color change from red to green), (2S,3R)-1-*tert*-butyldiphenylsilyloxy-7-(4-methoxyphenyl)-2,3-epoxyhept-6-yne (e.r. 93:7; 1 mmol) and 1,4-cyclohexadiene (4.35 eq.) added sequentially, the resulting mixture stirred for 72 h, quenched by addition of phosphate buffer (4 ml), extracted with methylene chloride, the extracts washed with brine, dried over $MgSO_4$, filtered, concentrated under vacuum, and the residue purified by chromatography on silica gel → (1R,2S)-2-(*tert*-butyldiphenylsilyloxymethyl)-3-(4-methoxybenzylidene)cyclopentanol. Y 68% (d.r. 97:3; e.r. >99:1; *E*/*Z* ca. 1:1), along with 11% of a linear alcohol resulting from regioisomeric epoxide ring opening. The combination of Kagan's catalyst and the bulky *tert*-butyldiphenylsilyl protecting group (compared with using Cp_2TiCl_2 and/or the less bulky *tert*-butyldimethylsilyl group) helped to promote the desired regioselective homolytic epoxide ring cleavage, followed by exclusive 5-*exo* radical cyclization with the alkyne (which may be terminal or variously substituted). Twelve examples afforded cyclopentanol derivs. in yields of 25-68%, along with significant amounts of linear alcohol by-products (Y 11-47%; major products in five cases); diastereoselectivity (d.r. 91:9 to 97:3) was high in all cases, however. F.e.s. A. Gansäuer, L. Shi, M. Otte, J. Am. Chem. Soc. *2010*, *132* (34), 11858-9 [DOI: 10.1021/ja105023y].

Tin(IV) chloride s. under (R)-1,1'-Bi-2-naphthol *$SnCl_4$*
Tert. phosphines s. under Zn, Ni(cod)$_2$ and Pd(dba)$_2$ *⩾P*
Tris(trimethylsilyl)phosphine s. under Ni(cod)$_2$ *$(Me_3Si)_3P$*

(S,S)-[2-[3,5-Bis(trifluoromethyl)benzamido]-3-methylpentyl]diphenylphosphine ←
Cyclopentene-1-carboxylic acid esters from electron-deficient ethylene derivs. via regioselective organocatalyzed asym. [3+2]-cycloaddition ○

332.

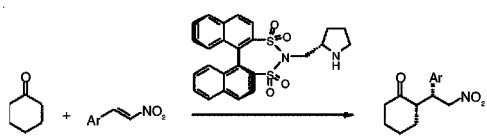


under mild conditions. Ethyl 2,3-butadienoate (2 eq.) added via syringe to a soln. of ethyl 2-(2-bromobenzylidene)cyanoacetate (0.1 mmol) and chiral phosphine catalyst (10 mol%) in toluene (1 ml), the mixture stirred vigorously at room temp. for 1 h, and purified directly by chromatography on silica → ethyl 5-(2-bromophenyl)-4-ethoxycarbonyl-4-cyanocyclopentene-1-carboxylate. Y 99% (e.e. 97%). A series of chiral N-acyl-β-aminophosphines, readily available from inexpensive amino alcohols, were evaluated as catalysts in this novel asym. cycloaddition, with substrates

sterically hindered at the β-carbon and carrying electron-deficient β-benzamides affording the highest enantioselectivities. A series of electron-diverse malononitrile/cyanoacetate condensates of (het)ar. aldehydes (alkylidene analogs were unsuitable) reacted efficiently with a terminal allenoate to afford single regioisomers (twenty-one examples; Y 79-99%; e.e. 80-97%), with highest enantioselectivities observed for *o*-subst. substrates. The reaction was also applicable to an internal allenoate but enantioselectivity was somewhat reduced (four examples; Y 92-99%; d.r. 4:1 to 6:1; e.e. 70-82%). F.e., optimization and 1,2-dihydroxylation of products (two examples; Y 74%, 97%; d.r. 19:1) s. H. Xiao, Z. Chai, C.-W. Zheng, Y.-Q. Yang, W. Liu, J.-K. Zhang, G. Zhao, Angew. Chem., Int. Ed. *2010*, *49* (26), 4467-70 [DOI: 10.1002/anie.201000446].

Sodium 2(R)-[o-(diphenylphosphino)benzylideneamino]-3,3-dimethylbutyrate s. under R_2Zn ←
Chiral di(phosphines) s. under $AuCl\text{-}SMe_2/AgOTf$, $[Rh(cod)_2]BF_4$, $Rh(acac)(CH_2{=}CH_2)_2$ and $[Rh(CO)_2Cl]_2$ ←
(R,R)-2-Isopropoxy-1-methyl-3-phenylbenz[d][1,3]azaphospholine s. under $Rh(acac)(CO)_2$ ←
Chiral cyclic β-aminophosphonic acid monoesters ←
Organocatalyzed asym. Michael addition s. *62*, 282s*78* C=C → CHC(R)
Chiral phosphoramidites s. under Mg and $Ni(cod)_2$ ←
Chiral bis(phosphoromonoamidites) s. under R_2Zn ←
Chiral 1,1′-binaphthyl-2,2′-diyl 2′-acylamino-1,1′-binaphthyl-2-yl phosphites s. under R_2Zn ←
Chiral 3,3′-disubst. 1,1′-binaphthyl-2,2′-diyl hydrogen phosphate or Chiral 5,5′-dichloro-biphenyl-2,2′-diyl hydrogen phosphates or Chiral hexaalkylated biphenyl-2,2′-diyl N-triflylthionophosphoramidates ←
Organo-Brønsted acid-catalyzed asym. Friedel-Crafts reaction of indoles with electron-deficient ethylene derivs. s. *67*, 336s*78*
Niobium trichloride *$NbCl_5$*
[2+2+2]-Cycloaddition s. *33*, 658s*78* ○
Chiral N-sulfonyl-1,2-diamines or Chiral N-tosyltri-prim-amines or Chiral o-(tosyl-amino)benzamides or Chiral 2-tert-amino-2′-(sulfonylamino)thioureas ←
Organocatalyzed asym. Michael addition s. *62*, 282s*78* C=C → CHC(R)
Chiral camphor-based N-aminosultams ←
Asym. Diels-Alder reaction s. *46*, 662s*78* ○
N-[[(S)-Pyrrolidin-2-yl]methyl]-(S)-1,1′-binaphthyl-2,2′-disulfonimide/benzoic acid ←
Organocatalyzed asym. Michael addition of ketones to 1-nitroethylene derivs. C=C → CHC(R)

333.



L-Proline-derived *chiral N-pyrrolidin-2-ylmethyl-1,1′-binaphthyl-2,2′-disulfonimides and -disulfonamides* are efficient catalysts for the enantio- and diastereo-selective Michael addition of ketones to 1-nitroethylene derivs. **E:** A soln. of N-[[(S)-pyrrolidin-2-yl]methyl]-(S)-1,1′-binaphthyl-2,2′-disulfonimide (0.013 mmol) and cyclohexanone (0.1 mmol) in methylene chloride (0.2 ml) stirred at room temp. for 30 min, benzoic acid (0.013 mmol) added, stirring continued for 15 min, the startg. nitroalkene (0.13 mmol) added at 0°, and worked up after 24 h with purification by chromatography on silica gel → product. Y 87% (*syn/anti* >99:1; e.e. 96%). Both enantio- and diastereo-selectivity were very high for the Michael addition of cyclohexanone to a range of β-nitrostyrenes bearing electron-donating or -withdrawing groups on the benzene ring

(ten examples; *syn/anti* 98:2 to >99:1; e.e. 93-96%), although chemical yields were lower with substrates possessing electron-donating groups. Nitroalkenes derived from aliphatic aldehydes, however, were poor substrates, as were cyclopentanone and acetone as nucleophile. Enantioselectivity was slightly lower with chiral N-[[(S)-pyrrolidin-2-yl]methyl]-(S)-1,1′-binaphthyl-2,2′-disulfonamides, and the choice of carboxylic acid as cocatalyst was critical (benzoic acid being optimal). Reaction is presumed to involve initial acid-catalyzed formation of an enamine by condensation of the ketone with the organocatalyst, followed by *re*-face attack on the nitroalkene (the oxygen atom of the sulfonimide and the carboxylic acid orientating the nitro group through hydrogen bonding). F.e. and preparation of the reagents s. S. Ban, D.-M. Du, H. Liu, W. Yang, Eur. J. Org. Chem. *2010* (27), 5160-4 [DOI: 10.1002/ejoc.201000818].

p-Toluenesulfonic acid s. under Rh(acac)(CO)$_2$ *TsOH*
Tetra-n-butylammonium fluoride s. under Cupreidine *Bu$_4$NF*
Manganese s. under Chiral titanocene dichloride *Mn*

Iron-containing mesoporous aluminosilicate ←
Regioselective hydro[hetero]arylation of ethylene derivs. s. *49*, 679s*78* C=C → CHC(Ar)

Chiral cyclopentadienyliron complexes s.a. [[Bis-η^5-(4′R,5′R)-(Sp)-2-(4′,5′-diphenyl-1′-tosyl-Δ^2-imidazolin-2′-yl)cyclopentadienyl)]iron(II) 1-C,3′-N dipalladium(II)]-triflate acetonitrile complex ←
1,1′-Bis(diphenylphosphino)ferrocene s. under Cp(π-allyl)Pd *dppf*
Chiral ferrocenyl-phosphines or -di(phosphines) s. under AgOAc and PtCl$_2$ ←

Chiral iron(III) 1,1′-binaphthyl-2,2′-diyl phosphates ←
Asym. Friedel-Crafts reaction of indoles C=C → CHC(R)
with electron-deficient ethylene derivs. s. *67*, 336s*78*

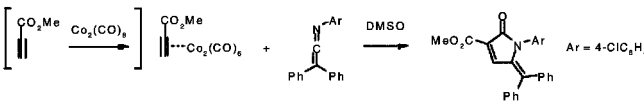
Iron(III) chloride/chiral prim. amines ←
Catalytic asym. Michael addition s. *49*, 657s*78*; *47*, 654s*78*

Chiral (1,5-cyclooctadiene)(1-neomenthylindenyl)cobalt(I)/irradiation *[Co(I)]*/hν*
1-Aryl-5,6,7,8-tetrahydroquinolines by asym. [2+2+2]-cycloaddition s. *33*, 658s*78* ○

Dicarbonyl(cyclopentadienyl)cobalt(I)/microwaves ←
Transition metal-catalyzed [2+2+2]-cycloaddition
[dihydro]benzene ring s. *33*, 658s*73*, and pyridine ring s. *37*, 674s*74*; synthesis of allocolchicine analogs with a pyridine C-ring using $CpCo(CO)_2$ under microwaves s. N. Nicolaus, H.-G. Schmalz, Synlett *2010* (14), 2071-4 [DOI: 10.1055/s-0030-1258512]; asym. synthesis of axially chiral 1-aryl-5,6,7,8-tetrahydroquinolines with chiral (1,5-cyclooctadiene)(1-neomenthylindenyl)-cobalt(I) under photoirradiation s. M. Hapke, K. Kral, C. Fischer, A. Spannenberg, A. Gutnov, D. Redkin, B. Heller, J. Org. Chem. *2010, 75* (12), 3993-4003 [DOI: 10.1021/jo100122d]; fused oligocycles and extension to enantiomerically pure (6aR,10aR)-dihydroanthracyclinones s. C. Aubert, V. Gandon, S. Han, B.M. Johnson, M. Malacria, S. Schömenauer, K.P.C. Vollhardt, G.D. Whitener, Synthesis *2010* (13), 2179-200 [DOI: 10.1055/s-0029-1220007]; diastereoselective synthesis of 3,5-diacylcyclohexenes from an alkyne and two enone molecules with Ni(0) [$Ni(cod)_2$/Cyp_2P] as catalyst s. S. Ogoshi, A. Nishimura, M. Ohashi, Org. Lett. *2010, 12* (15), 3450-2 [DOI: 10.1021/ol101264r]; coupling of alkynes with diynes and trimerization of alkynes with 2nd generation Grubbs′ catalyst or Hoveyda-Grubbs′ catalyst s. Á. Mallagaray, S. Medina, G. Domínguez, J. Pérez-Castells, Synlett *2010* (14), 2114-8 [DOI: 10.1055/s-0030-1258521]; regiodivergent, ligand-controlled coupling of alkyl-subst. methyl propiolates with enynes using rhodium(I) mono- or di-(phosphine) complexes s. P.A. Evans, J.R. Sawyer, P.A. Inglesby, Angew. Chem., Int. Ed. *2010, 49* (33), 5746-9 [DOI: 10.1002/anie.201002117]; synthesis of ar. selenides by coupling yneselenides with two acetylenedicarboxylate molecules using $PdCl_2(PPh_3)_2$, also bimolecular coupling to give 1-organoseleno-1,3-enynes with $Pd(OAc)_2$/(*o*-tol)$_3$P/K_2CO_3, s. T. Mitamura, A. Ogawa, Tetrahedron Lett. *2010, 51* (27), 3538-41 [DOI: 10.1016/j.tetlet.2010.04.125]; 5-ω-alkenyl-1,3-cyclohexadienes from terminal alkynes and dienes with $NbCl_3$ s. Y. Obora, Y. Satoh, Y. Ishii, J. Org. Chem. *2010, 75* (17), 6046-9 [DOI: 10.1021/jo101229u].

Dicobalt octacarbonyl/dimethyl sulfoxide $Co_2(CO)_8$/DMSO
5-Ene-Δ^3-2-pyrrolones from ketenimines and acetylenedicobalt hexacarbonyl complexes by Pauson-Khand-type reaction ○

334.



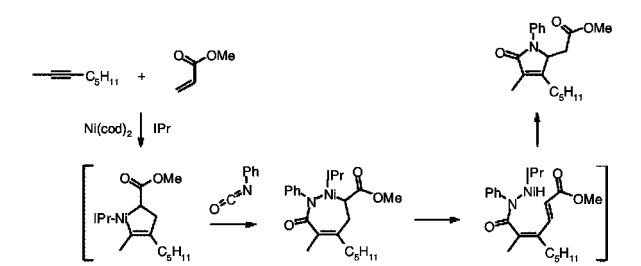
3-Subst. 1-aryl-5-(diarylmethylene)-Δ^3-2-pyrrolones. A mixture of methyl propiolate dicobalt hexacarbonyl complex (0.303 mmol), startg. C,C,N-triarylketenimine (1.2 eq.), dimethyl sulfoxide (5 eq.) and toluene (5 ml) heated at 115° for 2 h, concentrated to dryness, and the residue purified by chromatography on silica gel → product. Y 43%. This novel reaction was suitable for *thermally stable* C,C,N-triarylketenimines, affording γ-methylene-γ-lactams in moderate to good yields (43-77%; thirteen examples); reaction of a C-H ketenimine failed, probably due to isomerization or polymerization under the conditions. Chloro, methyl or methoxy substituents were tolerated on the N-aryl group, while the terminal acetylene could alternatively be aryl-, alkyl-, or hydroxyalkyl-subst. The reaction did not proceed in the absence of a promoter (even on prolonged heating), DMSO giving optimum results of several screened, incl. DMF, MeCN, Me_2S, NMO and $(PhO)_3P$. F.e.s. T. Saito, K. Sugizaki, H. Osada, N. Kutsumura, T. Otani, Heterocycles *2010*, *80* (1), 207-11 [DOI: 10.3987/com-09-s(s)62].

Cobalt(II) phosphine or di(phosphine) complexes/organomagnesium salts ←
Regio- and stereo-selective hydroarylation C≡C → CH=C(Ar)
of acetylene derivs. s. *59*, 311s*78*

Bis(1,5-cyclooctadiene)nickel(0) s.a. under Zn ←

Bis(1,5-cyclooctadiene)nickel(0)/1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene ←
Δ^3-2-Pyrrolone-5-acetic acid esters ○
from acetylene derivs., acrylic acid esters and isocyanates
Nickel-catalyzed [2+2+1]-cycloaddition

335.



Phenyl isocyanate (0.25 mmol), 2-octyne (4 eq.) and methyl acrylate (1 eq.) added to a soln. of $Ni(cod)_2$ (10 mol%) and 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene [IPr] (10 mol%) in 1,4-dioxane (1 ml) in a dry box, the mixture stirred at 100° in a sealed tube under argon for 5 h, cooled to room temp., filtered through a silica gel pad, concentrated *in vacuo*, and the residue purified by flash chromatography on silica gel → methyl 2-(4-methyl-5-oxo-3-pentyl-1-phenyl-2,5-dihydro-1*H*-pyrrol-2-yl)acetate. Y 63%. Use of tert. phosphine ligands in place of the hindered N-heterocyclic carbene ligand was not effective, leading instead to 2-pyridones via [2+2+2]-cycloaddition. The method is applicable to alkyl- or aryl-subst. alkynes, but reaction failed with terminal alkynes, presumably due to rapid oligomerization. The aryl isocyanate may bear electron-

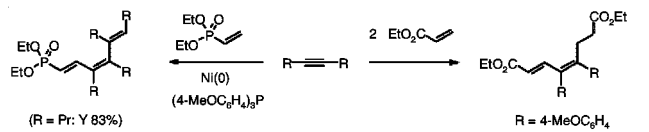
donating or -withdrawing groups but yields were low with cyclohexyl or isopropyl isocyanate (24%, 29% respectively). The steric environment of the alkyne and acrylate dictated the regioselectivity while the isocyanate had no influence. It is believed reaction takes place via oxidative cyclization of nickel(0) with the alkyne and acrylate to afford a nickelacyclopentene (in which the steric repulsion between the IPr ligand and the alkyne are minimized), followed by isocyanate insertion, β-hydride elimination and reductive elimination. F.e. (thirteen; Y 28%, 45-72%; regioisomeric ratio 1:1 to 10:1) and optimization s. T. Ozawa, H. Horie, T. Kurahashi, S. Matsubara, Chem. Commun. *2010*, *46* (42), 8055-7 [DOI: 10.1039/c0cc02613a].

Bis(1,5-cyclooctadiene)nickel(0)/1,3-bis(2,6-diisopropylphenyl)imidazolium chloride/ potassium tert-butoxide or tert. phosphines ←

1,3-Dienes or 1,3,5-trienes from ethylene and acetylene derivs. ←

Regio- and stereo-selective nickel(0)-catalyzed cotrimerization

336.



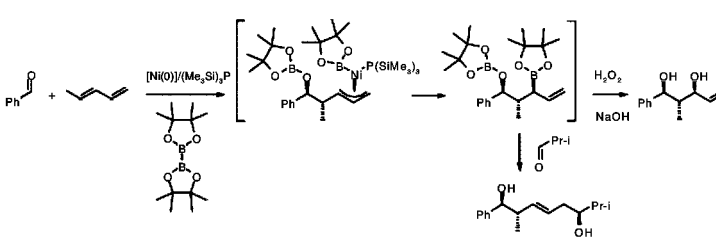
1,3-Dienes. Ethyl acrylate (2 eq.) and bis(4-methoxyphenyl)acetylene (0.5 mmol) added to a soln. of $Ni(cod)_2$ (5 mol%), 1,3-bis(2,6-diisopropylphenyl)imidazolium chloride (10 mol%) and K-*tert*-butoxide (11 mol%) in 1,4-dioxane (2 ml) in a dry box, the mixture heated at 100° for 24 h, cooled to room temp., filtered through silica, concentrated *in vacuo*, and purified by flash chromatography on silica → diethyl (2E,4Z)-4,5-bis(4-methoxyphenyl)-2,4-octadienedioate. Y 82%. Use of the sterically hindered N-heterocyclic carbene ligand favored 2:1 trimerization of acrylate esters and internal alkynes to afford 1,3-dienes as major products, with unsymmetrical alkynes affording 1:1 mixtures of regioisomers (eight examples; Y 49-82%). Low yields were obtained for bis(4-fluorophenyl)acetylene (30%) and sterically hindered 2,2-dimethylpent-3-yne (Y 24%; 3:1 isomer mixture), however. 1,3,5-Trienes, formed as by-products in some cases (up to 23% yield), were obtained exclusively by replacing the bulky NHC with a triaryl- or tricyclohexylphosphine ligand (nine examples; Y 60-94%). This alternative 1:2 trimerization of alkenes and acetylenes was effective with acrylates, acrylamides and vinyl phosphonates, but acrylonitrile gave only 22% yield. F.e. and optimization s. H. Horie, T. Kurahashi, S. Matsubara, Chem. Commun. *2010*, *46* (38), 7229-31 [DOI: 10.1039/c0cc01754j].

Bis(1,5-cyclooctadiene)nickel(0)/tris(trimethylsilyl)phosphine/bis(pinacolato)diboron ←

4-Ene-1,3-diols from aldehydes and 1,3-dienes ←

via ligand-dependent regio- and stereo-selective O,C-diborylation

337.

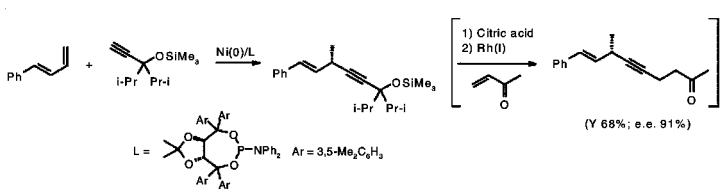


While nickel-catalyzed borylative coupling of aldehydes and 1,3-dienes in the presence of tricyclohexylphosphine leads to 2-ene-1,5-diols (s. *75*, 341), polyketide-like 4-ene-1,3-diols having

three contiguous stereocenters are obtained with *tris(trimethylsilyl)phosphine* as ligand. It is believed electronic rather than steric effects are responsible for this ligand-dependent regioselectivity, the large cone angle of the latter ligand, combined with its ability to act as an electron acceptor, facilitating reductive elimination without allyl isomerization of the intermediate nickel π-allyl complex. **E:** An oven-dried scintillation vial charged with $Ni(cod)_2$ (10 mol%), $(Me_3Si)_3P$ (15 mol%) [*caution!* highly pyrophoric], and THF (5 ml; 0.2 *M*) in a dry box under argon, after stirring for 5 min, benzaldehyde (1 mmol), *trans*-1,3-pentadiene (3 eq.) and bis(pinacolato)diboron (3 eq.) added sequentially, the vial sealed with a polypropylene cap then removed from the dry box, the mixture stirred at room temp. for 12 h, cooled to 0° (ice-water bath), NaOH (3 *M*; 4 ml) and 30% H_2O_2 (3 ml) added dropwise with caution, the mixture stirred at room temp. for 10 h, cooled to 0°, quenched with satd. aq. $Na_2S_2O_3$, extracted with ethyl acetate, dried (Na_2SO_4), filtered, solvent evaporated *in vacuo*, and the residue purified by silica gel chromatography → (1S*,2S*,3S*)-2-methyl-1-phenylpent-4-ene-1,3-diol. Y 67% (d.r. >20:1). The method is effective for aromatic, heteroaromatic or [linear or branched] aliphatic aldehydes (ten further examples; Y 37-73%; d.r. >20:1), while a simple α-chiral aldehyde reacted with Felkin selectivity (Felkin/anti-Felkin selectivity 6:1). Quenching the diborylated intermediate with isobutanal instead of H_2O_2/NaOH led to the corresponding **3-ene-1,6-diol** as a single regioisomer (Y 68%; d.r. >20:1). F.e.s. H.Y. Cho, J.P. Morken, J. Am. Chem. Soc. *2010*, *132* (22), 7576-7 [DOI: 10.1021/ja101513d].

Bis(1,5-cyclooctadiene)nickel(0)/chiral TADDOL-derived phosphoramidite ←
Nickel(0)-catalyzed asym. synthesis of 6-*tert*-siloxy-1,4-enynes from 1,3-dienes and siloxy-2-acetylenes C=C → CHC-C≡C

338.



trans-1-Phenyl-1,3-butadiene (0.3 mmol) and THF (0.1 ml) added sequentially to a stirred mixture of $[Ni(cod)_2]$ (10 mol%) and (R,R)-TADDOL-derived phosphoramidite ligand (11 mol%) under N_2 at room temp., startg. propargyl silyl ether (1.5 eq.) added via syringe pump over *82-90 h*, the mixture filtered through silica, concentrated, and purified chromatographically → product. Y 63% (e.e. 91%). Use of the phosphoramidite ligand coupled with slow addition of the alkyne were essential to minimize formation of alkyne dimerization products and, while both trimethylsilyl and phenyldimethylsilyl propargyl ethers were effective, replacing the propargylic *sec*-alkyl groups with Me or H gave none of the diene-alkyne coupled products. The reaction was successful with electron-diverse 1-aryl-*trans*-1,3-butadienes (nine examples; Y 41-68%; e.e. 90-92%), with *cis*-analogs giving mainly alkyne dimerization products. Desilylation with citric acid (Y 97%) and rhodium catalyzed conjugate addition to methyl vinyl ketone gave a **chiral 1-en-4-yn-8-one** (Y 70%), *via C-C bond cleavage*, with complete retention of stereochemistry (single example). F.e. and ligand optimization s. M. Shirakura, M. Suginome, Angew. Chem., Int. Ed. *2010*, *49* (22), 3827-9 [DOI: 10.1002/anie.201001188].

Nickel(II) acetoacetonate s. under Zn and R_2Zn *$Ni(acac)_2$*

Nickel(0) N-heterocyclic carbene complexes ←
Regioselective hydro[hetero]arylation of ethylene derivs. s. *49*, 679s*78* C=C → CHC(Ar)

Nickel N-heterocyclic carbene complexes/trimethylaluminum ←
Regio- and stereo-selective hydroarylation C≡C → CH=C(Ar)
of acetylene derivs. s. *59*, 311s*78*

Chiral bis(1,2-diamine)dibromonickel(II) complexes or Chiral dinuclear nickel(II) Schiff base complexes [Ni]
Catalytic asym. Michael addition C=C → CHC(R)
s. *49*, 657s*78*; *47*, 654s*78*

Dibromobis(triphenylphosphine)nickel(II) s. under Zn ←

Carbonyl(dihydrido)tris(triphenylphosphine)ruthenium(II)/formic acid ←
Regioselective hydro[hetero]arylation of ethylene derivs. s. *49*, 679s*78* C=C → CHC(Ar)

Ruthenium N-heterocyclic carbene complexes ←
Transition metal-catalyzed [2+2+2]-cycloaddition s. *33*, 658s*78* ○

μ-Chlorine-bridged ruthenium(II) complex/trifluoroacetic acid ←
Regio- and stereo-selective hydroarylation C≡C → CH=C(Ar)
of acetylene derivs. s. *59*, 311s*78*

Ruthenium trichloride *$RuCl_3$*
Regioselective hydroarylation of ethylene derivs. C=C → CHC(Ar)
under Ru-catalysis s. *49*, 679; mild hydroarylation of olefins with aryl ketones using $RuCl_3$, also hydroalkylation with Michael acceptors (cf. *49*, 640), s. M.-O. Simon, J.-P. Genet, S. Darses, Org. Lett. *2010, 12* (13), 3038-41 [DOI: 10.1021/ol101038c]; hydroarylation of terminal olefins with sec. benzyl alcohols (at the *ortho* site) with $RuH_2(CO)(PPh_3)_3$/formic acid, also with simultaneous oxidation of the hydroxyl group (in the absence of formic acid), s. A.J.A. Watson, A.C. Maxwell, J.M.J. Williams, ibid. *12* (17), 3856-9 [DOI: 10.1021/ol101548a]; hydroarylation of styrenes with phenols *under heterogeneous conditions* with recyclable iron-containing mesoporous aluminosilicate (MCM-41) s. S. Haldar, S. Koner, J. Org. Chem. *2010, 75* (17), 6005-8 [DOI: 10.1021/jo100803y]; of alkenes with phenols or catechol in a chloroindate(III) ionic liquid [[emim]$InCl_4$] s. H.Q.N. Gunaratne, T.J. Lotz, K.R. Seddon, New J. Chem. *2010, 34* (9), 1821-4 [DOI: 10.1039/c0nj00301h]; regiospecific hydropyridylation (at the 4-position) of terminal alkenes and styrenes with a nickel(0) N-heterocyclic carbene complex and MAD as Lewis acid, also addition to alkynes, s. Y. Nakao, Y. Yamada, N. Kashihara, T. Hiyama, J. Am. Chem. Soc. *2010, 132* (39), 13666-8 [DOI: 10.1021/ja106514b]; hydroarylation of styrenes with azoles (at the 2-position) using a nickel(0) N-heterocyclic carbene complex s. Y. Nakao, N. Kashihara, K.S. Kanyiva, T. Hiyama, Angew. Chem., Int. Ed. *2010, 49* (26), 4451-4 [DOI: 10.1002/anie.201001470].

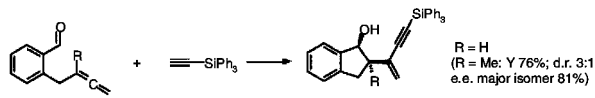
Friedel-Crafts reaction of indoles C=C → CHC(R)
with steroidal α,β-ethyleneketones s. *11*, 770s*78*

Tris(acetonitrile)(pentamethylcyclopentadienyl)rhodium(III) bis(hexafluoroantimonate)/pivalic acid ←
Regio- and stereo-selective hydroarylation of acetylene derivs. C≡C → CH=C(Ar)
under Pt-catalysis cf. *59*, 311s*72*; of internal alkynes with [Cp*$Rh(MeCN)_3$][SbF_6]$_2$/pivalic acid in isopropyl acetate s. D.J. Schipper, M. Hutchinson, K. Fagnou, J. Am. Chem. Soc. *2010, 132* (20), 6910-1 [DOI: 10.1021/ja103080d]; **N-directed hydroarylation** of 2-arylpyridines and ar. aldimines using a cobalt(II) phosphine complex/organomagnesium salt under chelation control s. K. Gao, P.-S. Lee, T. Fujita, N. Yoshikai, ibid. *132* (35), 12249-51 [DOI: 10.1021/ja106814p]; addition of azoles (at the 2-position) using a cobalt(II) di(phosphine) complex cf. Z. Ding, N. Yoshikai, Org. Lett. *2010, 12* (18), 4180-3 [DOI: 10.1021/ol101777x]; addition of indoles (at the 3 position) to internal and internal alkynes with $InBr_3$, E/Z-selectivity, s. G. Bhaskar, C. Saikumar, P.T. Perumal, Tetrahedron Lett. *2010, 51* (23), 3141-5 [DOI: 10.1016/j.tetlet.2010.04.036]; unprecedented formation of 3-(1-methylalkyl)indoles by addition of indoles to internal alkynes *in water* with [RuCl(μ-Cl)(η^3:η^3-$C_{10}H_{16}$)]$_2$/TFA cf. V. Cadierno, J. Francos, J. Gimeno, Chem. Commun. *2010, 46* (23), 4175-7 [DOI: 10.1039/c002804e]; hydroarylation of internal alkynes with pyridines (at the 4-position) with Ni(cod)$_2$ and an amino-functionalized imidazol-2-ylidene as ligand in the presence of $AlMe_3$ s. C.-C. Tsai, W.-C. Shih, C.-H. Fang, C.-Y. Li, T.-G. Ong, G.P.A. Yap, J. Am. Chem. Soc. *2010, 132* (34), 11887-9 [DOI: 10.1021/ja1061246]; regio- and stereo-selective formation of 4,4-diarylbut-2(E)-enoates by hydroarylation of γ-aryl-α-allene-carboxylic acid esters with electron-rich arenes using $PdCl_2(MeCN)_2$/TFA s. Z. Fang, C. Fu, S. Ma, Chem. Eur. J. *2010, 16* (13), 3910-3 [DOI: 10.1002/chem.200903012].

Acetoacetonatobis(ethylene)rhodium(I)/(S)-2,3;2′,3′-bis(methylenedioxy)-6,6′-bis(diphenylphosphino)biphenyl/acetic acid ←

Asym. synthesis of 2-(1,3-enyn-2-yl)-1-indanols from *o*-α-allenylaldehydes ○

339.

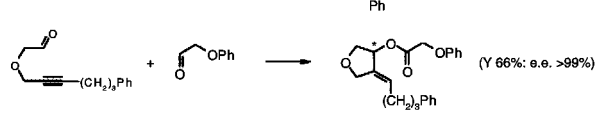


1,4-Dioxane (0.4 ml) added to a mixture of Rh(acac)(CH_2=CH_2)$_2$ (5 mol%) and (S)-SegPhos (6 mol%) in a screw cap test tube under N_2, the mixture stirred at room temp. for 10 min, (triphenylsilyl)acetylene (0.2 mmol), 2-(buta-2,3-dienyl)benzaldehyde (2 eq.) and acetic acid (5 mol%) added, the tube capped tightly, the mixture stirred at 80° for 24 h, concentrated under vacuum, and the residue subjected to chromatography on silica gel → (1S,2R)-2-[4-(triphenylsilyl)but-1-en-3-yn-2-yl]indan-1-ol. Y 80% (e.e. 99%). This method gives high yields (50-87%; eight examples) and high regio- and enantio-selectivities (95-99% e.e.) from allenylaldehydes, which may possess ar. fluorine or methoxy groups, and silylethynes, arylethynes or propargyl ethers. An aldehyde bearing a 1,1-disubst. allene group gave an indanol with an all-carbon quaternary stereocenter in 76% yield and 81% e.e., although the diastereoselectivity was moderate (*cis/trans* 3:1). It is believed that the acetic acid facilitates formation of an alkynylrhodium species, while acac prevents isomerization of the indanol to an indanone. F.e.s. X.-X. Guo, T. Sawano, T. Nishimura, T. Hayashi, Tetrahedron: Asym. *2010*, *21* (13-14), 1730-6 [DOI: 10.1016/j.tetasy.2010.04.039].

Bis(1,5-cyclooctadiene)rhodium(I) fluoroborate/(R)-2,2′-bis(diphenylphosphino)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl ←

Rhodium(I)-catalyzed asym. reductive ring closure of N- and O-tethered δ,ε-acetylenealdehydes

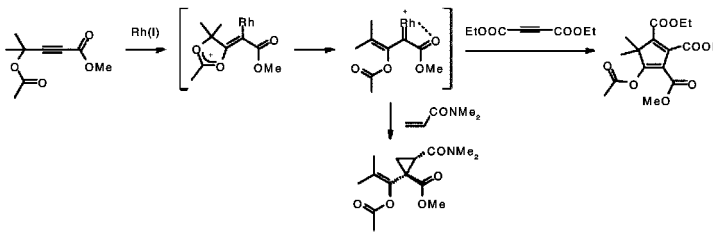
340.



Chiral 3-acoxy-4-alkylidene-N-tosylpyrrolidines under mild conditions. A soln. of (R)-H_8-BINAP (10 mol%) and [Rh(cod)$_2$]BF_4 (10 mol%) in methylene chloride (2 ml) stirred at room temp. under H_2 in a Schlenk tube for 1 h, concentrated to dryness, redissolved in methylene chloride (0.5 ml), a soln. of startg. alkynal (0.2 mmol) in the same solvent (1.5 ml) added dropwise at room temp., stirred for 16 h, concentrated, and purified by preparative TLC → (+)-4-benzylidene-1-tosylpyrrolidin-3-yl [3-phenylprop-2-ynyl-(tosyl)amino]acetate. Y 83% (e.e. >99%). Homo-coupling of two molecules of alkyl or phenyl terminated 5-alkynals carrying N-tosyl or oxygen tethers afforded the corresponding pyrrolidine or chiral **3-acoxy-4-alkylidene-tetrahydrofurans** with high enantioselectivity (six examples; Y 72-83%; e.e. 98 to >99%). Further development utilized 2 eq. of a second aldehyde (benzyloxy-, phenoxy- or N-benzyltosylamino-acetaldehyde) to afford cross-coupled products (eight examples; Y 49-66%; e.e. 98 to >99%), but attempted preparation of a carbocyclic analog was unsuccessful. Absolute stereochemistry was determined to be (S) in one case using a dispersion method. F.e., substrate prepn. and optimization s. R. Tanaka, K. Noguchi, K. Tanaka, J. Am. Chem. Soc. *2010*, *132* (4), 1238-9 [DOI: 10.1021/ja9104655].

Bis(1,5-cyclooctadiene)rhodium(I) hexafluoroantimonate *$[Rh(cod)_2]SbF_6$*
Rhodium-catalyzed cycloaddition with α,β-acetylene-γ-acoxycarboxylic acid esters

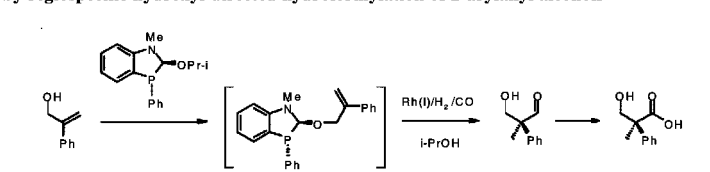
341.



4-Acoxycyclopentadiene-1,2,3-tricarboxylic from acetylenedicarboxylic acid esters. A soln. of $[Rh(cod)_2]SbF_6$ (5 mol%), the startg. propargyl ester (0.5 mmol) and diethyl acetylenedicarboxylate (2 eq.) in methylene chloride (1 ml) stirred at room temp. for 72 h, the resulting mixture concentrated, and purified by preparative TLC → 4-acetoxy-5,5-dimethylcyclopenta-1,3-diene-1,2,3-tricarboxylic acid 1,2-diethyl 3-methyl ester. Y 81%. Reaction is presumed to involve initial activation of the alkyne residue by rhodium(I), followed by **carbalkoxy-directed 1,2-acoxy group migration** with generation of a rhodium carbenoid, which undergoes **[3+2]-cycloaddition** with the acetylenedicarboxylate (ten examples; Y 50-90%). On the other hand, with N,N-disubst. acrylamides the carbenoid simply undergoes **[2+1]-cycloaddition** to give the corresponding **1-(α-acoxyvinyl)-2-carbamylcyclopropane-1-carboxylic acid esters** with *perfect* diastereoselectivity (eight examples; Y 43-77%). [3+2]-Cycloaddition took place with a number of tertiary propargyl esters, while a secondary ester gave the isomerized 3-acoxycyclopentadiene-1,2,5-tricarboxylate. [2+1]-Cycloaddition, however, was more limited: there was no reaction with a secondary propargyl ester, and a cyclohexane analog gave a low product yield (11%). F.e. and comparison with other rhodium and iridium catalysts (all of which were less efficient) s. Y. Shibata, K. Noguchi, K. Tanaka, J. Am. Chem. Soc. *2010*, *132* (23), 7896-8 [DOI: 10.1021/ja102418h].

Acetoacetonato(dicarbonyl)rhodium(I)/2-isopropoxy-1-methyl-3-phenylbenz[d]-[1,3]azaphospholine/p-toluenesulfonic acid ←
Generation of quaternary hydrocarbon groups C=C → CHC-CHO
by regiospecific hydroxyl-directed hydroformylation of 2-arylallyl alcohols

342.



under mild conditions. 2-Isopropoxy-1-methyl-3-phenylbenz[*d*][1,3]azaphospholine serves as a *catalytic* 'scaffolding' ligand for the hydroformylation of 2-arylallyl alcohols, affording, for the first time, branched [quaternary] aldehydes in excellent yield. **E:** The startg. allyl alcohol (0.6 mmol) added to a glass reaction vial placed in an Endeavor vessel, the latter sealed and purged with N_2, a soln. of acetoacetonato(dicarbonyl)rhodium(I) (4 mol%), (R,R)-2-isopropoxy-1-methyl-3-phenylbenz[*d*][1,3]azaphospholine (20 mol%), *p*-toluenesulfonic acid (0.2 mol%) and benzene (to a total volume of 4 ml) injected into the system, followed by a further amount of benzene (2 ml) to wash the injection port, the vessel purged with N_2, heated with stirring to 45° for 10 min,

stirring stopped, charged with 400 psi H_2/CO, stirring re-initiated, the pressure/temp. maintained for 12 h, the system vented to ambient pressure and cooled to ambient temp., and the formed aldehyde isolated more conveniently as the carboxylic acid [by stirring the crude aldehyde overnight at room temp. in *tert*-butanol with $NaClO_2$ (80%; 4 eq.) and NaH_2PO_4 (4 eq.) in water in the presence of 2-methyl-2-butene (10 eq.), followed by work-up and acidification with 10% HCl and brine in ethyl acetate prior to chromatographic purification] → 3-hydroxy-2-methyl-2-phenylpropanoic acid. Y 73% (branched/linear 97:3). The catalytic directing group binds to the central metal while reversibly bonded to the substrate [as the allyl ether], thereby accelerating the reaction intramolecularly at low temp. and providing a 'scaffold' to direct hydroformylation towards formation of the branched isomer. With triphenylphosphine as ligand *only the linear isomer is formed.* The procedure tolerates either electron-withdrawing (e.g. CN, COOR, Br, Cl) or [in slightly lower yield] electron-donating groups on the aromatic ring, but the *o*-methyl deriv. was unreactive, presumably because of steric hindrance. The yield was poor (49%) and regioselectivity lower (branched/linear 76:24) with a 2-alkylallyl alcohol. F.e. (thirteen; Y 60-85%; branched/linear 94:6 to >98:2) s. X. Sun, K. Frimpong, K.L. Tan, J. Am. Chem. Soc. *2010, 132* (34), 11841-3 [DOI: 10.1021/ja1036226].

Rhodium(I) phosphine or phosphite complexes or dendritic or supported variants *[Rh(I)]*
Hydroformylation C=C → CHC-CHO
update s. *4,* 667s*75*; highly regioselective hydroformylation of terminal alkenes *at high temp.* with 2,2′,6,6′-tetrakis(diarylphosphino)biphenyls as a new class of tetra(phosphines) as ligand s. S. Yu, X. Zhang, Y. Yan, C. Cai, L. Dai, X. Zhang, Chem. Eur. J. *2010, 16* (16), 4938-43 [DOI: 10.1002/chem.200903109]; with a remarkably active covalently-bonded mesoporous silica-supported 1,9-bis(diphenylphosphino)-5*H*-dibenz[1,4]oxazine as ligand s. F. Marras, J. Wang, M.-O. Coppens, J.N.H. Reek, Chem. Commun. *2010, 46* (35), 6587-9 [DOI: 10.1039/c0cc00924e]; with 1-diphenylphosphino-1′-dimesitylborylferrocene and related *o*-phenylene-bridged systems as *amphiphilic* ligand s. M.W.P. Bebbington, S. Bontemps, G. Bouhadir, M.J. Hanton, R.P. Tooze, H. van Rensburg, D. Bourissou, New J. Chem. *2010, 34* (8), 1556-9 [DOI: 10.1039/c0nj00117a]; with tunable hexacationic dendriphos ligands with large dendritic shells s. D.J.M. Snelders, K. Kunna, C. Müller, D. Vogt, G. van Koten, R.J.M.K. Gebbink, Tetrahedron: Asym. *2010, 21* (11-12), 1411-20 [DOI: 10.1016/j.tetasy.2010.04.037]; regioselective (up to 41:1 linear/branched isomers) hydroformylation of β,γ-unsatd. carboxylic acids with enzyme-like monodentate phosphine ligands bearing guanidine receptors (for the carboxylate residue) facilitating *secondary substrate-ligand* interaction s. T. Šmejkal, D. Gribkov, J. Geier, M. Keller, B. Breit, Chem. Eur. J. *2010, 16* (8), 2470-8 [DOI: 10.1002/chem.200902553]; **under solvent-free conditions** with highly active calixarene-based hemispherical bis(phosphite) ligands for completely linear-directed hydroformylation of terminal alkenes s. L. Monnereau, D. Sémeril, D. Matt, Eur. J. Org. Chem. *2010* (16), 3068-73 [DOI: 10.1002/ejoc.201000245]; selective hydroformylation of long-chain alkenes in olefinic mixtures by *catalytic supercritical fluid extraction* based on differential solubility in $scCO_2$ s. T.J. Koch, S.L. Desset, W. Leitner, Green Chem. *2010, 12* (10), 1719-21 [DOI: 10.1039/c0gc00299b]; **under continuous flow** in a nanofiltration reactor with a bulky, rigid and robust silsesquioxane-modified triphenylphosphine ligand permitting homogeneous catalyst recycling s. M. Janssen, J. Wilting, C. Müller, D. Vogt, Angew. Chem., Int. Ed. *2010, 49* (42), 7738-41 [DOI: 10.1002/anie.201001926]; *platinum(II)-catalyzed* regioselective hydroformylation of terminal [giving aldehydes] and internal alkenes **in aq. micellar medium** with readily recyclable bis(aqua)[1,1′-bis(diphenylphosphino)ferrocene]platinum(II) bis(triflate) as catalyst in the presence of a surfactant s. M. Gottardo, A. Scarso, S. Paganelli, G. Strukul, Adv. Synth. Catal. *2010, 352* (13), 2251-62 [DOI: 10.1002/adsc.201000341].

Rhodium(I) phosphine complexes *[Rh(I)]*
Transition metal-catalyzed [2+2+2]-cycloaddition ○
Regiodivergent, ligand-controlled coupling of alkyl-subst. methyl propiolates with enynes s. *33,* 658s*78*

Rhodium(I) di(phosphine) complexes *[Rh(I)]*

Pauson-Khand reaction ○

without carbon monoxide s. *40,* 475s*73*; with acetylated aldoses as source of CO for intramolecular Pauson-Khand reaction with enynes using $[RhCl(cod)]_2$/BINAP as catalyst s. K. Ikeda, T. Morimoto, K. Kakiuchi, J. Org. Chem. *2010, 75* (18), 6279-82 [DOI: 10.1021/jo1012288]; with prim. alcohols as source of CO using $[Rh(CO)Cl(dppp)]_2$ as catalyst s. J.H. Park, Y. Cho, Y.K. Chung, Angew. Chem., Int. Ed. *2010, 49* (30), 5138-41 [DOI: 10.1002/anie.201001246]; **asym. Pauson-Khand reaction** (cf. *68,* 325s*75*) with $[Rh(CO)_2Cl]_2$/AgOTf and (S)-2,2′-dimethoxy-6,6′-bis[3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino]biphenyl as ligand for reaction with O-, N- and $(EtO_2C)_2C$-tethered enynes (notably terminally-substituted by aryl at the alkyne site) s. D.E. Kim, V. Ratovelomanana-Vidal, N. Jeong, Adv. Synth. Catal. *2010, 352* (11-12), 2032-40 [DOI: 10.1002/adsc.201000221].

Chiral rhodium(I) di(phosphine) complexes s. under R_3Al *[Rh(I)]**

Chiral rhodium(I) aminophosphine, phosphoromonoamidite, phosphine-phosphoro-monoamidite, 1,3,2-diazaphospholane or 2-alkoxy-2,3-dihydro-1,3-benzazaphosphole complexes *[Rh(I)]**

Asym. hydroformylation C=C → CHC-CHO

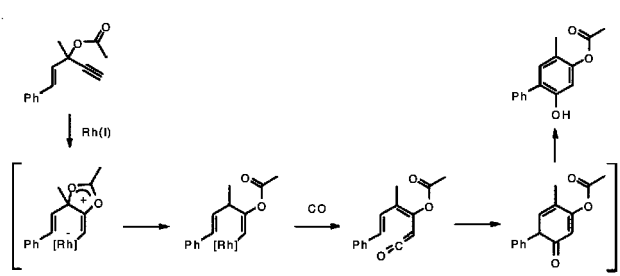
s. *49,* 683s*75*; with chiral biaryl-based phosphoromonoamidites and aminophosphines as ligand for asym. hydroformylatiion of styrenes and heterocyclic olefins (with moderate enantioselectivity) s. J. Mazuela, O. Pàmies, M. Diéguez, L. Palais, S. Rosset, A. Alexakis, Tetrahedron: Asym. *2010, 21* (17), 2153-7 [DOI: 10.1016/j.tetasy.2010.07.005]; with modular chiral N-(2′-diphenylphosphino-1,1′-binaphth-2-yl)-1,1′-binaphthyl-2,2′-diyl phosphoramidites for the regioselective asym. hydroformylation of styrenes, vinyl acetate and allyl cyanide, structure-selectivity relationships, s. X. Zhang, B. Cao, Y. Yan, S. Yu, B. Ji, X. Zhang, Chem. Eur. J. *2010, 16* (3), 871-7 [DOI: 10.1002/chem.200902238]; asym. hydroformylation of N-allylamides, allyl ethers and allylsilanes to give chiral α-branched β-functionalized aldehydes with the phosphine-phosphoromonoamidite, YanPhos, as ligand (e.e. 92-99%) s. X. Zhang, B. Cao, S. Yu, X. Zhang, Angew. Chem., Int. Ed. *2010, 49* (24), 4047-50 [DOI: 10.1002/anie.201000955]; chiral N-protected β-aminoaldehydes with a chiral N-condensed 2-alkoxy-2,3-dihydro-1,3-benzazaphosphole *as scaffolding ligand* (e.e. up to 93%) s. A.D. Worthy, C.L. Joe, T.E. Lightburn, K.L. Tan, J. Am. Chem. Soc. *2010, 132* (42), 14757-9 [DOI: 10.1021/ja107433h]; regioselective asym. hydroformylation of N-protected enamines, allylamines and allyl ethers to give the corresponding chiral functionalized aldehydes (e.e. 89-99%) using a chiral 1,3,2-diazaphospholane as ligand s. R.I. McDonald, G.W. Wong, R.P. Neupane, S.S. Stahl, C.R. Landis, ibid. *2010, 132* (40), 14027-9 [DOI: 10.1021/ja106674n].

Dicarbonyl(chloro)rhodium(I) dimer *$[Rh(CO)_2Cl]_2$*

Resorcinol monoesters from 3-acoxy-1,4-enynes and carbon monoxide ○

Rhodium(I)-catalyzed carbonylative [4+1]-cycloaddition

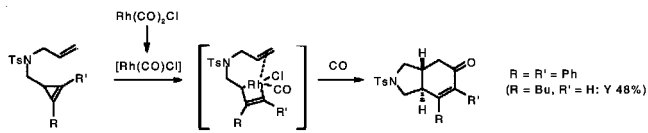
343.



A mixture of (E)-3-methyl-1-phenylpent-1-en-4-yn-3-yl acetate (E/Z 1:0.22; 0.53 mmol), $[RhCl(CO)_2]_2$ (2.5 mol%) and methylene chloride (10 ml) heated at 80° under CO (80 atm.) in a

stainless steel autoclave for 5 h, cooled to room temp., and purified by flash chromatography on silica → 5-acetoxy-4-methyl-2-phenylphenol. Y 68%. This efficient synthesis was successful for 1-aryl and 1-alkyl 1,4-enynyl acetates and pivalates (a 2-Me group was tolerated) affording mono- and di-subst. resorcinol derivs. via a 1,2-acoxy shift (ten examples; Y 53-76%), with a 1-H enyne affording a mixture of resorcinol (37%) and cyclopentenone (19%) derivs. (the latter were formed preferentially using gold or platinum catalysis). At lower pressures of CO (20 or 50 atm.) the yields were somewhat reduced. The proposed ketene intermediate was trapped with methanol in one case to afford the expected methyl 3,5-dienoate as a by-product. F.e. and optimization s. C. Brancour, T. Fukuyama, Y. Ohta, I. Ryu, A.-L. Dhimane, L. Fensterbank, M. Malacria, Chem. Commun. *2010*, *46* (30), 5470-2 [DOI: 10.1039/c0cc00747a].

2-Cyclohexenone ring from 3-(alkenyl)cyclopropenes via stereospecific carbonylative [3+2+1]-cycloaddition ○◎



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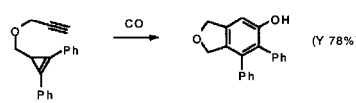
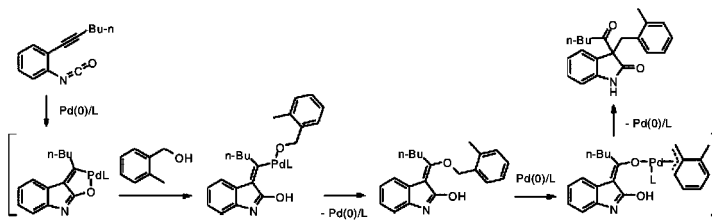


Homologous Pauson-Khand-type reaction. 1,2-Dichloroethane (5 ml) added by syringe to a degassed mixture of startg. alkenylcyclopropene (0.12 mmol) and $[Rh(CO)_2Cl]_2$ (5 mol%) under CO, the mixture heated to 80° until reaction complete by TLC (12 h), cooled to room temp., solvent removed under vacuum, and the residue purified chromatographically → 6,7-diphenyl-2-tosyl-2,3,3a,4-tetrahydro-1*H*-isoindol-5(7a*H*)-one. Y 89%. Eight further examples gave yields of 36-76%, incl. tetrahydroisobenzofuranone and hydrindenone analogs, all with *trans* configuration at the junction; the presence of a methyl group on the alkene resulted in lower yield, whereas reaction was faster with two alkyl groups on the cyclopropene than with phenyl. A single product was obtained from an unsymmetrically-subst. cyclopropene (Y 48%) via regioselective insertion of rhodium into the less substituted C-C bond. Alkynyl-derivs. reacted to give analogs containing the **phenol ring** (seven examples; Y 55%, 70-90%). An allenyl analog gave a moderate yield (28%) with most of the starting material recovered. F.e.s. C. Li, H. Zhang, J. Feng, Y. Zhang, J. Wang, Org. Lett. *2010*, *12* (13), 3082-5 [DOI: 10.1021/ol101091r]; **4-vinylcyclohexanone ring** from 1-alkenyl-1-vinylcyclopropanes with $[Rh(CO)_2Cl]_2$, **also 4-vinyl-2-cyclohexenone ring** from 1-alkynyl-1-vinylcyclopropanes, incl. application to the furanoid sesquiterpene natural product, α-agarofuran, s. L. Jiao, M. Lin, L.-G. Zhuo, Z.-X. Yu, ibid. (11), 2528-31 [DOI: 10.1021/ol100625e].

Dicarbonyl(chloro)rhodium(I) dimer/(S)-2,2′-dimethoxy-6,6′-bis[3,5-di-tert-butyl-4-methoxyphenyl)phosphino]biphenyl/silver triflate ←
Asym. Pauson-Khand reaction s. *68*, 325s*78* ○

π-Allyl(cyclopentadienyl)palladium(II)/1,1′-bis(diphenylphosphino)ferrocene ←
3-Acyl-3-benzyloxindoles from *o*-acetyleneisocyanates and benzyl alcohols ○
via palladium-catalyzed ring closure-1,3-O→C-benzyl migration



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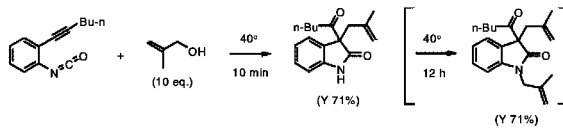
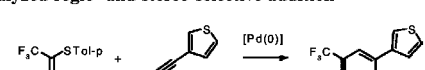


A soln. of startg. isocyanate (0.2 mmol) and 2-methylbenzyl alcohol (3 eq.) in dry toluene (2 ml) added via syringe to a mixture of CpPd(π-allyl) (5 mol%) and dppf (5 mol%) in a septum-sealed flask under argon, the resulting mixture heated with stirring at 80° for 12 h, cooled to room temp., passed through a pad of Florisil (with ethyl acetate), the filtrate concentrated under reduced pressure, and the residue purified by gel permeation chromatography → product. Y 73%. Nine examples (incl. (het)ar. terminated alkynes and electron-diverse ring substitution on the benzyl alcohol, and a 3-pyridyl analog) afforded yields of 63-76%. A single asym. example, using (S,S)-f-Binaphane as chiral ligand, was only moderately successful (Y 61%; e.e. 38%). Crossover experiments supported the intermediacy of an (η^3-benzyl)palladium(II) complex, itself formed from an intermediate 3-[1-(benzyloxy)alkylidene]oxindole, which was the major product using $Pd_2(dba)_3$ as catalyst. Similarly, formation of **3-acyl-3-allyloxindoles from** *o*-acetyleneisocyanates **and 2-ethylenealcohols** (eight examples; Y 56-79%) was facile, reaction completing in 10 min at 40° to give (E)-products (from either (E)- or (Z)-allyl alcohols), with substitution occurring at the least hindered site. Prolonged reaction (12 h) with excess allyl alcohol (10-20 eq.) afforded **1,3-diallyl derivs.** (three examples; Y 70-71%). F.e.s. T. Toyoshima, Y. Mikano, T. Miura, M. Murakami, Org. Lett. *2010*, *12* (20), 4584-7 [DOI: 10.1021/ol101892b].

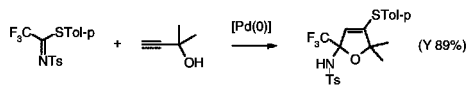
Bis(dibenzylideneacetone)palladium(0)/triphenylphosphine *Pd(dba)$_2$/Ph$_3$P*
α,β-Ethylene-β-(organothio)azomethines C(SR)=C-C=N
from acetylene derivs. and thioiminoesters
Palladium(0)-catalyzed regio- and stereo-selective addition

346.



The first synthesis of 4-thio-1-aza-1,3-dienes is reported via an uprecedented addition reaction to alkynes, which includes a rare catalytic introduction of an imino group. The presence of a trifluoromethyl group adjacent to the imine appears essential for a successful outcome, phenyl giving low yields and no reaction occurring with phenethyl. **E:** A soln. of $Pd(dba)_2$ (5 mol%), Ph_3P (1 eq.), startg. thioiminoester (0.5 mmol) and 3-ethynylthiophene (1.2-6 eq.) in 1,2-dichloro-

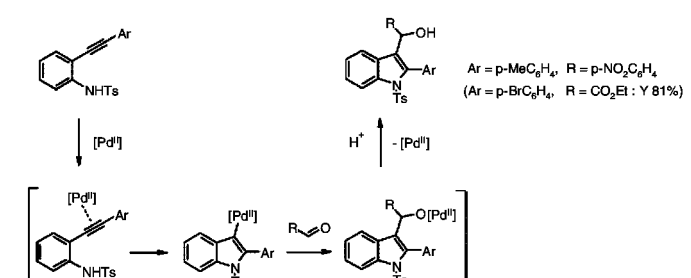
ethane (0.5 ml) stirred under N_2 at 80° for 1 h, the mixture filtered through Celite, evaporated to dryness, and the residue purified by TLC → product. Y 83% (Z/E >99:1). Reaction was successful for trifluoroacetyl thioiminoesters bearing electron-diverse N- and S-aryl substituents (or S-benzyl in one case), reacting with terminal alkynes to afford *cis*-addition products in yields of 74-95% (ca. ten examples; Z/E 82:18 to >99:1). Ethyl phenylpropiolate was a good substrate (with microwave heating at 100°) but other internal alkynes gave poor yields (14-51%; two examples) even at elevated temps. (160-180°). Chloro, ester, acetal and hydroxyl groups were all tolerated under the conditions. An adduct derived from an N-tosyl analog underwent facile *cis/trans* isomerization under the conditions, cyclizing with a pendant hydroxyl group to afford a 2,5-dihydrofuran deriv.



F.e., incl. prepn. of startg. thioiminoesters and a plausible mechanism involving insertion of Pd into the imine-sulfur bond, s. Y. Minami, H. Kuniyasu, A. Sanagawa, N. Kambe, Org. Lett. *2010*, *12* (17), 3744-7 [DOI: 10.1021/ol101289k].

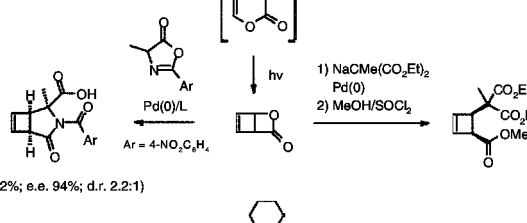
Bis(aquo)(2,2′-bipyridyl)palladium(II) triflate *$Pd(bpy)(H_2O)_2(OTf)_2$*

3-α-Hydroxy-1-tosylindoles from *o*-acetylenetosylamines and activated aldehydes under cationic palladium(II) catalysis ○



Startg. alkyne deriv. (0.1 mmol) and 4-nitrobenzaldehyde (*2 eq.*) added to a dried Schlenk tube charged with $Pd(bpy)(H_2O)_2(OTf)_2$ (2 mol%) and dioxane (1 ml), the mixture stirred at 60° until reaction complete (TLC; overnight), concentrated under reduced pressure, and purified by flash chromatography on silica gel → product. Y 78%. This efficient synthesis proceeds without the need for a redox system and was successful for a range of *ar. terminated* 2-alkynyl *N-tosyl* anilides (optionally carrying Me, Cl or F substituents on the benzene ring), reacting with activated aldehydes (electron-deficient ar. aldehydes or ethyl glyoxylate) to afford 2,3-disubst. indoles in yields of 49-93%. Reaction was unsuccessful with alkyl-terminated alkynes, with benzaldehyde, electron-rich ar. aldehydes or ketones, or by replacing N-tosyl with N-trifluoroacetyl or N-mesyl (except for a single ethyl glyoxylate example; Y 51%). Although the major by-products were 3-H indoles, mechanistic experiments suggested a tandem reaction rather than a one-pot, two-step cyclization/ Friedel-Crafts process. Other Pd(II) catalysts, particularly neutral Pd species, such as $Pd(OAc)_2$ or $PdCl_2(MeCN)_2$, were less effective than those possessing cationic character. F.e.s. X. Han, X. Lu, Org. Lett. *2010*, *12* (15), 3336-9 [DOI: 10.1021/ol1011086].

Tetrakis(triphenylphosphine)palladium(0)/sodium hydride *$Pd(PPh_3)_4/NaH$*
4-Functionalized cyclobut-2-enecarboxylic acid derivs. from 2-pyrone via nucleophilic cleavage of photochemically-generated 2-oxabicyclo[2.2.0]hex-5-en-3-one



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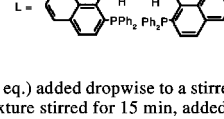
(Y 62%; e.e. 94%; d.r. 2.2:1)



Diethyl 2-methylmalonate (2.2 eq.) added dropwise to a stirred suspension of NaH (2 eq.) in THF (0.8 ml) at room temp., the mixture stirred for 15 min, added to a soln. of $Pd(PPh_3)_4$ (5 mol%) in THF (0.8 ml) under argon at 0°, stirred for 5 min, a soln. of 2-oxabicyclo[2.2.0]hex-5-en-3-one [0.1 mmol; prepared via photolysis (450 W) of 2-pyrone at -10° for 24-36 h] in ether (0.4 ml) added slowly, stirred for 30-40 min, quenched with water, warmed to room temp., washed with ether, slowly acidified with 1.2 *N* aq. HCl (pH ~2), extracted with ethyl acetate, concentrated *in vacuo*, dissolved in methanol (1 ml), $SOCl_2$ (1.5 eq.) added at 0°, warmed to room temp., stirred for 16 h, quenched with water, extracted with methylene chloride, concentrated *in vacuo*, and purified by flash chromatography on silica → diethyl 2-[*cis*-4-(methoxycarbonyl)cyclobut-2-enyl]-2-methylmalonate. Y 80%. A stock soln. of the bicyclic lactone [*caution!* potentially explosive] was found to be stable at a 0.1-0.2 *M* concentration at 4° for several weeks and, on treatment with active methylene derivs., reacted efficiently to provide a novel and convenient route to single diastereomers of functionalized *cis*-cyclobutenes from commercially available 2-pyrone (twelve examples; Y 46-90%), with products conveniently isolated as methyl esters. Surprisingly, treatment of the bicyclic lactone with 4-subst. 2-aryl-Δ^2-oxazol-5-ones proceeded via apparent ring-opening/recyclization of the expected adducts to afford **2-subst. 3-aroyl-3-azabicyclo[3.2.0]hept-6-en-4-one-2-carboxylic acids** (ten examples; Y 26-68%; d.r. 88:12 to >95:5), and preliminary experiments using chiral ligands afforded chiral derivs. (two examples; Y 50-62%; e.e. 84-94%). F.e., optimization and further reactions of products s. F. Frébault, M. Luparia, M.T. Oliveira, R. Goddard, N. Maulide, Angew. Chem., Int. Ed. *2010*, *49* (33), 5672-6 [DOI: 10.1002/anie.201000911].

Bis(acetonitrile)dichloropalladium(II)/trifluoroacetic acid *$PdCl_2(MeCN)_2/CF_3COOH$*
Regio- and stereo-selective hydroarylation of acetylene derivs. C≡C → CH=C(Ar)
s. *59*, 311s*78*

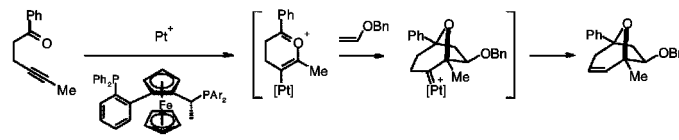
Dichlorobis(triphenylphosphine)palladium(II) *$PdCl_2(PPh_3)_2$*
Transition metal-catalyzed [2+2+2]-cycloaddition
Ar. selenides from yneselenides s. *33*, 658s*78*

[[Bis-η^5-(4′R,5′R)-(Sp)-2-(4′,5′-diphenyl-1′-tosyl-Δ^2-imidazolin-2′-yl)cyclopenta-dienyl)]iron(II) 1-C,3′-N dipalladium(II)]-triflate acetonitrile complex/sodium acetate *[Pd(II)]**
Asym. Michael addition of *in situ*-prepared Δ^2-5-oxazolones C=C → CHC(R)
to α,β-ethyleneketones s. *78*, 418

Bis(aqua)[1,1′-bis(diphenylphosphino)ferrocene]platinum(II) bis(triflate) *[Pt(II)]*
Regioselective hydroformylation in aq. micellar medium s. *4*, 667s*78* C=C → CHC-CHO

Platinum(II) chloride/(S)-2[o-(diphenylphosphino)phenyl]-1-[(1R)-(di-3,5-xylyl-phosphino)ethyl]ferrocene/silver hexafluoroantimonate ←
7-Alkoxy-8-oxabicyclo[3.2.1]oct-2-enes from γ,δ-acetyleneketones and enolethers via platinum-catalyzed asym. [3+2]-cycloaddition to 5-metallo-3,4-dihydropyrylium ylids ○

349.



The first example is reported of a catalytic asym. cycloaddition of a metal-containing carbonyl ylid generated from a γ,δ-acetyleneketone. **E:** 4 Å Molecular sieves (80 mg) heated by a heat-gun under reduced pressure in a flask, the $PtCl_2$·Walphos complex (10 mol%; prepared by stirring equivalent amounts of $PtCl_2$ and the Walphos ligand in methylene chloride at room temp. for 40 min before removing the solvent and drying) and $AgSbF_6$ (10 mol%) added under argon, followed by a soln. of the startg. ynone (0.075 mmol) and vinyl ether (10 eq.) in methylene chloride (1.5 ml), the mixture stirred at room temp. for 16.5 h, filtered through a short pad of Celite, the solvent removed from the filtrate under reduced pressure, and the residue purified by silica gel chromatography → (1S,5R,7R)-7-benzyloxy-1-methyl-5-phenyl-8-oxabicyclo[3.2.1]oct-2-ene. Y 70% (e.e. 91%). High enantioselectivity was recorded for the reaction of benzyl, *p*-methoxybenzyl and silyl vinyl ethers with alkyne-functionalized alkyl or aryl ketones (eleven examples; e.e. 89-97%), yields being high (68-89%) for substrates possessing a methyl group at the alkyne terminus, but only moderate (50-65%) with butyl, benzyloxymethyl and vinyl substitution at this site. Enantioselectivity was consistently high with Walphos ligands, but low with other classical chiral di(phosphine) ligands (e.g. (R)-BINAP, (R)-SegPhos, JosiPhos). It is also significant that reaction is only efficient with *monocationic* platinum di(phosphine) complexes. F.e. and intramolecular variant (one example; Y 90%; e.e. 90%) s. K. Ishida, H. Kusama, N. Iwasawa, J. Am. Chem. Soc. *2010*, *132* (26), 8842-3 [DOI: 10.1021/ja102391t].

Rearrangement ∩

Hydrogen/Carbon Type CC ∩ HC

Microwaves s. under (Phenanthroline)bis(triphenylphosphine)copper(I) nitrate [\\\\]

Sodium hydroxide/9-cyanophenanthrene/irradiation ←
1,8-Diazabicyclo[5.4.0]undec-7-ene *DBU*
Cycloisomerization of ethylene derivs. ○
by sensitized photoisomerization s. *22*, 735; 5- to 7-membered carbocyclics by cycloisomerization of styrenes *o*-substituted by a chain possessing an electron-withdrawing group with NaOH as base and 9-cyanophenanthrene as sensitizer, diastereoselectivity, s. M. Ohashi, K. Nakatani, H. Maeda, K. Mizuno, Tetrahedron Lett. *2010*, *51* (42), 5537-9 [DOI: 10.1016/j.tetlet.2010.07.165]; β′-keto-β-nitroaryl-γ-lactones by diastereoselective cycloisomerization of nitrocinnamyl β-keto-carboxylic acid esters with DBU s. H. He, L.-X. Dai, S.-L. You, Org. Biomol. Chem. *2010*, *8* (14), 3207-10 [DOI: 10.1039/b924770j].

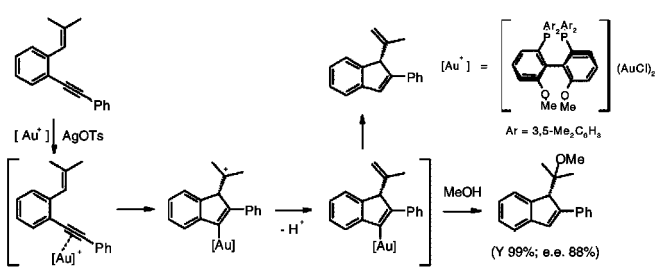
1,8-Diazabicyclo[5.4.0]undec-7-ene *DBU*
2,6,7,7a-Tetrahydroisoindolones from 5-(α,β-ethyleneacylamino)-1,3-enynes
s. *78*, 439

Chiral copper(II) bis- or tris-(Δ^2-oxazoline) complexes *[Cu(II)]**
Asym. Nazarov cyclization ○
with a chiral copper(I) bis(Δ^2-oxazoline) complex cf. *67*, 339; chiral 7-oxa-4,5,6,7-tetrahydro-1-indanones with $Cu(Barf)_2$ and a chiral tris(Δ^2-oxazoline) [TOX] as ligand s. P. Cao, C. Deng, Y.-Y. Zhou, X.-L. Sun, J.-C. Zheng, Z. Xie, Y. Tang, Angew. Chem., Int. Ed. *2010*, *49* (26), 4463-6 [DOI: 10.1002/anie.200907266]; with chiral bis(Δ^2-oxazolines) s. *78*, 223.

(Phenanthroline)bis(triphenylphosphine)copper(I) nitrate/microwaves *[Cu(I)]/[\\\\]*
Catalytic cycloisomerization of acetylenecarbonyl compds.
Conia-ene cycloisomerization of acetylene-β-dicarbonyl compds. with CuOTf/$AgBF_4$ cf. *67*, 340s*75*; geoselective synthesis of 2-alkylidenecyclopentane-1,1-dicarbonyl compds. with (phenanthroline)bis(triphenylphosphine)copper(I) nitrate under microwave irradiation s. S. Montel, D. Bouyssi, G. Balme, Adv. Synth. Catal. *2010*, *352* (13), 2315-20 [DOI: 10.1002/adsc.201000351]; 5-membered carbo- and hetero-cyclics by cycloisomerization of tethered α-subst. acetylene-aldehydes with $InCl_3$/N-isopropylcyclohexylamine s. B. Montaignac, M.R. Vitale, V. Michelet, V. Ratovelomanana-Vidal, Org. Lett. *2010*, *12* (11), 2582-5 [DOI: 10.1021/ol100729t].

[(R)-2,2′-Bis(di-3,5-xylylphosphino)-6,6′-dimethoxybiphenyl]bis(gold(I) chloride)/ silver tosylate ←
1-Vinylindenes from *o*-(alk-1-ynyl)styrenes
Gold(I)-catalyzed asym. cycloisomerization under mild conditions

350.



AgOTs (10 mol%) added to a soln. of [(R)-2,2′-bis(di-3,5-xylylphosphino)-6,6′-dimethoxybiphenyl]bis(gold(I) chloride) (5 mol%) in dry methylene chloride, stirred for 5-10 min, cooled to -30°, a soln. of the startg. *o*-(alk-1-ynyl)styrene (0.3 mmol) in dry methylene chloride added, stirring continued until TLC (or GC-MS analysis) indicated consumption of the substrate (3-4 d), the mixture diluted with hexanes, filtered through a pad of silica gel, solvent removed, and the crude residue purified by flash chromatography on silica gel → product. Y 81% (e.e. 82%). This is the first instance of a metal-catalyzed 5-*endo-dig*-cyclization of an *o*-(alk-1-ynyl)styrene, such treatment normally yielding naphthalene derivs. High yields and high enantioselectivity were recorded for the reaction of a wide range of *β,β-disubst.* styrene derivs. possessing a [het]aryl group at the alkyne terminus (six examples; Y 81-96%; e.e. 68-86%), but enantioselectivity was low with a terminally alkyl-subst. deriv. Reaction is presumed to involve initial activation of the alkyne residue, followed by 5-*endo-dig*-cyclization to give an indenyl carbocation (stabilized by the *two* connected alkyl groups) prior to generation of a vinylgold species and protodemetalation. **Chiral 1-α-hydroxy- or 1-α-alkoxy-indenes** were obtained under the same conditions (with added AgOTs or $AgSbF_6$) by interception of the intermediate indenyl carbocation with water or alcohols (prim. or sec.), respectively (seventeen examples; Y 72-99%; e.e. 28%, 30%; 75-92%). F.e. and comparison of catalysts and chiral ligands s. A. Martínez, P. García-García, M.A. Fernández-Rodríguez, F. Rodríguez, R. Sanz, Angew. Chem., Int. Ed. *2010*, *49* (27), 4633-7 [DOI: 10.1002/anie.201001089].

Indium(III) triflate $In(OTf)_3$

Intramolecular hydroarylation of ethylene derivs.

with $Gd(OTf)_3$ cf. *25*, 527*s75*; tetralins and chromans with $In(OTf)_3$ s. K. Xie, S. Wang, P. Li, X. Li, Z. Yang, X. An, C.-C. Guo, Z. Tan, Tetrahedron Lett. *2010*, *51* (33), 4466-9 [DOI: 10.1016/j.tetlet.2010.06.091]; polycyclic pyridines and quinolines with a fused 5-membered ring in the presence of a rhodium(I) phosphine complex s. S. Yotphan, R.G. Bergman, J.A. Ellman, Org. Lett. *2010*, *12* (13), 2978-81 [DOI: 10.1021/ol101002b]; 1,4-dihydronaphthalene-2-carboxylic acid esters and homologs by intramolecular hydroarylation of α-allenecarboxylic acid esters with $PtCl_2$/AgOTf s. J. Mo, P.H. Lee, ibid. *12* (11), 2570-3 [DOI: 10.1021/ol1007857].

Indium(III) chloride/N-isopropylcyclohexylamine $InCl_3$/*i*-$PrNHC_6H_{11}$

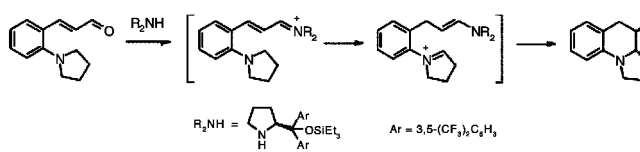
Catalytic cycloisomerization of acetylenealdehydes s. *67*, 340*s78*

2(S)-[Bis[3,5-bis(trifluoromethyl)phenyl](tert-butyldimethylsiloxy)methyl]pyrrolidine/(-)-camphorsulfonic acid ←

N-Subst. 1,2,3,4-tetrahydroquinoline-3-carboxaldehydes from *o-tert*-aminocinnamaldehydes

Organocatalyzed asym. cycloisomerization via 1,5-hydride transfer

351.



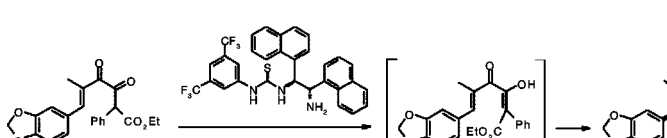
The first example of an organocatalyzed intramolecular redox reaction is reported, illustrated here by the asym. synthesis of 1,2,3,4-tetrahydroquinoline-3-carboxaldehydes from *o-tert*-aminocinnamaldehydes. **E:** 2(S)-[Bis[3,5-bis(trifluoromethyl)phenyl](*tert*-butyldimethylsiloxy)methyl]-pyrrolidine (0.03 mmol) added to a stirred soln. of the startg. aldehyde (0.1 mmol) in 1,1,2-trichloroethane (0.2 ml), the mixture cooled to 0°, (1R)-10-camphorsulfonic acid (0.03 mmol) added, stirred for 9 d at 20°, diluted with satd. NH_4Cl soln., extracted with ethyl acetate, dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography to isolate the two diastereoisomers (formed in 90:10 ratio) → (3aS,4R)-1,2,3,3a,4,5-hexahydropyrrolo[1,2-*a*]quinoline-4-carbaldehyde (major isomer). Y 57% (e.e. 91%). Moderate chemical yields and high diastereo- and enantioselectivity were recorded for the synthesis of a range of chiral N-condensed 1,2,3,4-tetrahydroquinoline-3-carboxaldehydes (nine examples; Y 37-75%; d.r. 69:31 to 100:0; e.e. 85-99%). This novel intramolecular C-H bond functionalization is presumed to involve initial formation of an iminium ion, followed by a 1,5-hydride shift prior to 6-*endo*-cyclization with elimination of the catalyst. F.e. and comparison of organocatalysts s. Y.K. Kang, S.M. Kim, D.Y. Kim, J. Am. Chem. Soc. *2010*, *132* (34), 11847-9 [DOI: 10.1021/ja103786c].

Chiral bis(Δ²-oxazolines) s. under Fe(OTf)₂ *box*

Chiral 2-prim-aminothioureas ←

Organocatalyzed asym. Nazarov cyclization under mild conditions

352.



Chiral 3-hydroxycyclopent-3-en-2-onecarboxylic acid esters. A soln. of the *bifunctional* 2-*prim*-aminothiourea catalyst (0.1 *M* in toluene; 0.031 mmol) added under N_2 to a stirred soln. of (E)-ethyl

6-(benzo[*d*][1,3]dioxol-5-yl)-2-phenyl-5-methyl-3,4-dioxohex-5-enoate (0.157 mmol) in dry toluene (1.263 ml), stirred at room temp. in a Teflon-sealed flask for 7 d, and the mixture purified directly by chromatography on silica → (1S,2S)-ethyl 2-(benzo[*d*][1,3]dioxol-5-yl)-1-phenyl-4-hydroxy-3-methyl-5-oxocyclopent-3-enecarboxylate. Y 95% (e.r. 92.5:7.5). Two adjacent chiral carbon centers, one tertiary and the other quaternary, are simply forged in good yield with high enantioselectivity (thirteen examples; Y 42-96%; e.r. 90:10 to 98.5:1.5). The carbalkoxy group and the aryl group at C_6 of the diketo-ester, however, are critically important, the former being required to stabilize the intermediate (E)-enol and thereby provide complementary polarization at the two carbon termini to facilitate the subsequent conrotatory ring closure. The bifunctional 2-aminothiourea is also important, the Brønsted acidic thiourea residue activating the keto group at C_3 while the Lewis basic amine residue activates the enolic hydroxyl group (in each case via hydrogen bonding). F.e.s. A.K. Basak, N. Shimada, W.F. Bow, D.A. Vicic, M.A. Tius, J. Am. Chem. Soc. *2010*, *132* (24), 8266-7 [DOI: 10.1021/ja103028r].

(-)-Camphorsulfonic acid s. under 2(S)-[Bis[bis(3,5-trifluoromethyl)phenyl]-(tert-butyldimethylsiloxy)methyl]pyrrolidine — *RSO_3H*

Tetra-n-butylammonium fluoride — *Bu_4NF*
1,5-Dihydro- from 1,7-dihydro-4-azepinones s. *78*, 486 ←

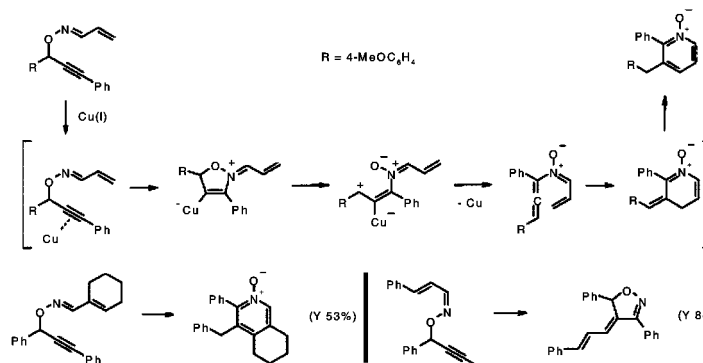
Iron(II) triflate or perchlorate or cobalt(II) perchlorate/chiral bis(Δ^2-oxazolines) ←
Asym. Nazarov cyclization s. *78*, 223 ○

Oxygen/Carbon Type — CC ∩ OC

Chiral N-[4-(dimethylamino)-2-pyridylcarbonyl]-2-aminoalcohols s. under [CpRu(MeCN)$_3$]PF$_6$ ←

Tris(triphenylphosphine)copper(I) bromide/triphenylphosphine — *$(Ph_3P)_3CuBr/Ph_3P$*
Pyridine N-oxides from α,β-ethylene-O-propargyloximes via copper-catalyzed [2.3]-sigmatropic rearrangement-6π-3-azatriene electrocyclization ○

353.



DMSO (0.8 ml) added to a mixture of (E)-acrylaldehyde O-[1-(4-methoxyphenyl)-3-phenylprop-2-yn-1-yl]oxime (0.4 mmol), $(Ph_3P)_2CuBr$ (10 mol%) and Ph_3P (10 mol%) in a pressure vial under argon, the mixture stirred at 120° for 3 h, passed through a pad of silica gel (with chloroform), solvents removed *in vacuo*, and the residue purified by flash chromatography on silica gel → 3-(4-methoxybenzyl)-2-phenylpyridine N-oxide. Y 86%. Fourteen examples afforded yields of

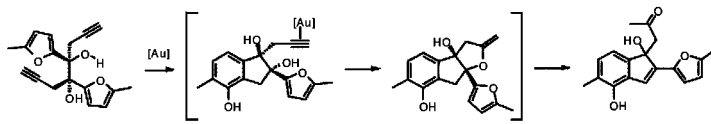
44-87%. Yields were adversely affected by bulky alkyl groups (Y 0% with *tert*-butyl) or electron-withdrawing aryl groups on the alkyne terminus and also by alkyl groups (Y 47% with *n*-propyl) or electron-withdrawing ar. groups (Y 0% with *p*-trifluoromethylphenyl) at the propargylic position. Small alkyl group substitution was tolerated on the alkene moiety, with a cyclohex-1-ene-carboxaldehyde oxime deriv. affording a **5,6,7,8-tetrahydroisoquinoline N-oxide** in moderate yield (53%). The (E) geometry of the oxime moiety was critical to the success of the reaction, with a (Z) isomer affording a 4-allylidene-Δ^2-isoxazoline deriv. in high yield (84%). F.e., optimization and a proposed mechanism s. I. Nakamura, D. Zhang, M. Terada, J. Am. Chem. Soc. *2010*, *132* (23), 7884-6 [DOI: 10.1021/ja102436z].

Gold(III) chloride $AuCl_3$

2-(2-Furyl)-1-β-keto-1,4-indenediols

from 4,5-bis(2-furyl)-1,7-diyne-4,5-diols under gold catalysis

354.



A soln. of *anti*-4,5-bis(5-methylfuran-2-yl)octa-1,7-diyne-4,5-diol (179 μmol) in methylene chloride-d2 (0.7 ml) treated with $AuCl_3$ (5 mol%) in acetonitrile-d3 under N_2, after 5 min (monitored by ^1H NMR) the solvent removed *in vacuo*, and the residue purified by chromatography on silica gel → 1-[1,4-dihydroxy-5-methyl-2-(5-methylfuran-2-yl)-1*H*-inden-1-yl]propan-2-one. Y 92%. Two further examples from *anti*-isomers both proceeded in 95% yield. The *syn*-diastereomer was completely converted to oligomeric/polymeric material, and conversion of *syn*/*anti*-mixtures gave 36-95% yields (five examples). It is assumed for the *anti*-isomer that an intramolecular hydrogen bridge between one furan ring and distal hydroxyl group stabilizes a conformation in which the other furyl group is placed close to the alkyne, facilitating the first cycloisomerization; the intermediate may then undergo cycloisomerization to an exocyclic enolether, which then ring opens to the ketone. Reaction in $CDCl_3$ was not selective and other gold catalysts were less effective. F.e. and prepn. of the startg. m. from furfurals s. A.S.K. Hashmi, M. Wölfle, F. Ata, W. Frey, F. Rominger, Synthesis *2010* (13), 2297-307 [DOI: 10.1055/s-0029-1218800]; **2-propargyl-2,8-tetralindiols** from 4-(2-furan-2-ylethyl)-1,6-diyn-4-ols cf. A.S.K. Hashmi, M. Hamzic, F. Rominger, J.W. Bats, Chem. Eur. J. *2009*, *15* (48), 13318-22 [DOI: 10.1002/chem.200901695]; application of acyclic gold(I) diaminocarbene complexes (prepared from gold(I) isonitrile complexes and prim. and sym. sec. amines) to gold-catalyzed phenol synthesis (cf. *40*, 486s*71*,*75*) and to hydration of acetylene derivs. s. A.S.K. Hashmi, T. Hengst, C. Lothschütz, F. Rominger, Adv. Synth. Catal. *2010*, *352* (7), 1315-37 [DOI: 10.1002/adsc.201000126].

Triphenyl borate s. under [CpRu(MeCN)$_3$]PF$_6$ $(PhO)_3B$

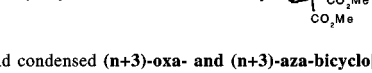
Scandium(III) triflate $Sc(OTf)_3$

2,5-Bridged tetrahydrofuran- or pyrrolidine-3,3-dicarboxylic acid esters

by regioselective Lewis acid-catalyzed intramolecular [3+2]-cycloaddition

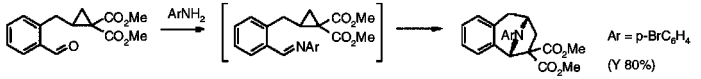
of cyclopropane-1,1-dicarboxylic acid esters to carbonyl or imino groups, respectively

355.



A series of isolated and condensed **(n+3)-oxa- and (n+3)-aza-bicyclo[n.2.1]alkanes** has been secured for the first time by intramolecular [3+2]-cycloaddition of cyclopropane-1,1-dicarboxylic acid esters to carbonyl or imino groups, respectively. **E:** $Sc(OTf)_3$ (20 mol%) added to a soln. of dimethyl 2-(2-formylbenzyl)cyclopropane-1,1-dicarboxylate (0.29 mmol) in dichloroethane (4 ml) at room temp. under argon, stirred for 2 h, filtered through Celite, concentrated under reduced

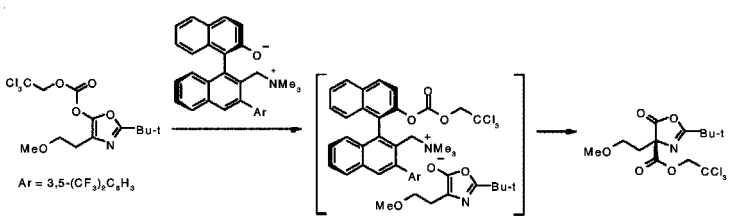
pressure, and the residue purified chromatographically → 12-oxatricyclo[7.2.1.$0^{2,7}$]dodeca-2(7),3,5-triene-11,11-dicarboxylic acid dimethyl ester. Y 90%. Tri- and tetra-cyclic products were normally obtained in very high yield (68-96%), but formation of simple, uncondensed bridged bicyclics was low-yielding (27-47%); other Lewis acids [Yb(OTf)$_3$ and $SnCl_4$] were more efficient in certain cases (seventeen examples in all). Aza-analogs were obtained similarly, in one pot, by reaction of formyl-functionalized cyclopropane-1,1-dicarboxylic acid esters with aromatic or aliphatic amines via the corresponding aldimines (eight examples; Y 55-84%).



Reaction of a chiral substrate (e.e. 90%) proceeded with asym. induction (e.e. 97% for the product). F.e. and application to the synthesis of the compact core of platensimycin s. S. Xing, W. Pan, C. Liu, J. Ren, Z. Wang, Angew. Chem., Int. Ed. *2010*, *49* (18), 3215-8 [DOI: 10.1002/anie.201000563].

Chiral 2-ammoniomethyl-2′-oxidobi-1,1′-naphthyl betaines ←
Δ^2-5-Oxazolone-4-carboxylic acid esters from oxazol-5-yl carbonates ∩
Asym. Steglich reaction with chiral oxidoammonium betaines as ionic nucleophilic catalysts

356.



Chiral Δ^2-5-oxazolone-4-carboxylic acid 2,2,2-trichloroethyl esters. A soln. of startg. oxazole (0.25 mmol) in dioxane (1.5 ml) added dropwise over 15 min to a mixture of chiral betaine catalyst (2 mol%) and 4 Å molecular sieves (100 mg) in the same solvent (1 ml) at 25° under argon, the mixture stirred for a further 10 min, quenched with 0.5 *M* trifluoroacetic acid in toluene, filtered, concentrated *in vacuo*, and purified by chromatography on silica → (S)-2-*tert*-butyl-4-(2-methoxyethyl)-4-(2,2,2-trichloroethoxycarbonyl)oxazol-5-one. Y 91% (e.e. 94%). This novel use of the betaine was extremely effective for a series of amino acid-derived oxazole derivs. (the bulky valine-derived substrate required heating at 40°), affording the corresponding oxazolones in high yields and with high enantioselectivity (ten examples; Y 91-99%; e.e. 94-97%). Enantioselectivity was critically dependent on maintaining a low substrate concentration, consistent with observations that the proposed intramolecular onium salt (detected by ESI/MS in one case) could react by both intra- (high e.e.) and inter-molecular (low e.e.) routes. F.e. and optimization s. D. Uraguchi, K. Koshimoto, S. Miyake, T. Ooi, Angew. Chem., Int. Ed. *2010*, *49* (32), 5567-9 [DOI: 10.1002/anie.201002315].

Triphenylphosphine s. under $(Ph_3P)_3CuBr$ *Ph_3P*

Tris(acetonitrile)(cyclopentadienyl)ruthenium(II) hexafluorophosphate/chiral N-[4-(dimethylamino)-2-pyridylcarbonyl]-2-aminoalcohols/triphenyl borate *[Ru(II)]**
Catalyzed asym. Claisen rearrangement of allyl enolethers ∩
under palladium catalysis cf. *62*, 320s*75*; *under cocatalysis* with [CpRu(MeCN)$_3$]PF_6 and a chiral N-[4-(dimethylamino)-2-pyridylcarbonyl]-2-aminoalcohol as ligand with triphenyl borate as Lewis acid s. M.E. Geherty, R.D. Dura, S.G. Nelson, J. Am. Chem. Soc. *2010*, *132* (34), 11875-7 [DOI: 10.1021/ja1039314].

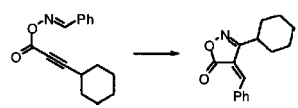
Platinum(II) chloride/(S)-2[o-(diphenylphosphino)phenyl]-1-[(1R)-(di-3,5-xylyl-phosphino)ethyl]ferrocene/silver hexafluoroantimonate ←
7-Alkoxy-8-oxabicyclo[3.2.1]oct-2-ene ring ○
via platinum-catalyzed asym. intramolecular [3+2]-cycloaddition to 5-metallo-3,4-dihydropyrylium ylids s. *78*, 349

Nitrogen/Carbon Type CC ∩ NC

Irradiation s. under $CpCo(CO)_2$ ///
Microwaves s. under Rhodium(I) complexes [\\\\]

(Triphenylphosphine)gold(I) triflimide *$[(Ph_3P)Au]NTf_2$*
4-Arylidene-Δ²-isoxazol-5-ones from ar. O-(α,β-acetyleneacyl)aldoximes via arylidene group transfer ○

357.



Acetonitrile (1 ml) added to a mixture of (E)-benzaldehyde O-(3-cyclohexylpropioloyl)oxime (0.2 mmol) and $[(Ph_3P)Au]NTf_2$ (5 mol%), stirred at room temp. until reaction complete (TLC; 4.5 h), filtered through a silica gel plug (with methylene chloride and ethyl acetate), the filtrate evaporated to dryness, and the residue purified by GPC → (Z)-4-benzylidene-3-cyclohexylisoxazol-5(4*H*)-one. Y 93% (Z/E >99:1). The reaction, involving a novel, formal 1,3-migration of an arylidene group, is applicable to a variety of O-propioloylbenzaldoxime derivs. in which the alkyne moiety may be terminated with alkyl or ar. groups and the benzaldoxime aromatic ring may be substituted by electron-donating or -withdrawing groups, with yields significantly depressed for the latter (ten examples; Y 50%, 69%, 78-94%; Z/E 92:8 to >99:1). Reaction was also successful with a ketoxime deriv. (Y 87%), but a single alkylidene analog suffered decomposition. Crossover experiments afforded an insight into the mechanism and firmly established the arylidene group transfer to be an *intermolecular* process. F.e.s. I. Nakamura, M. Okamoto, M. Terada, Org. Lett. *2010*, *12* (11), 2453-5 [DOI: 10.1021/ol100581m].

Scandium(III) triflate *$Sc(OTf)_3$*
2,5-Bridged tetrahydrofuran-3,3-dicarboxylic acid esters ○◎
via regioselective Lewis acid-catalyzed intramolecular [3+2]-cycloaddition s. *78*, 355

Cyclopentadienylcobalt(I) dicarbonyl/irradiation *$CpCo(CO)_2$////*
Rhodium(I) complexes/microwaves *[Rh(I)]/[\\\\]*
Polycyclic pyridines by intramolecular [2+2+2]-cycloaddition ○
5,6,7,8-tetrahydroquinolines cf. *37*, 674s*70*; octahydrophenanthridines by intramolecular cycloaddition of diyne-α-siloxynitriles with $CpCo(CO)_2$ under irradiation s. A. Meißner, U. Groth, Synlett *2010* (7), 1051-4 [DOI: 10.1055/s-0029-1219572]; tricyclic pyridines and similarly condensed 2,2′-bipyridyls from tethered cyanodiynes, rapid procedure with a rhodium(I) complex under microwave irradiation s. L. Garcia, A. Pla-Quintana, A. Roglans, T. Parella, Eur. J. Org. Chem. *2010* (18), 3407-15 [DOI: 10.1002/ejoc.200901318]; metal-free, formal intramolecular [2+2+2]-cycloaddition via a pericyclic cascade mechanism cf. T. Sakai, R.L. Danheiser, J. Am. Chem. Soc. *2010*, *132* (38), 13203-5 [DOI: 10.1021/ja106901u].

Carbon/Carbon Type CC ∩ CC

Irradiation [s.a. under $AlBr_3$, Chiral bridged lactams and $[Ru(bpy)_3](PF_6)_2$] ///
Photochemical intramolecular [2+2]-cycloaddition □○
s. *22*, 761; rapid, controllable method (re: time, temperature and wavelength) in a *flow-based* photoreactor (LOPHTOR) s. A. Vasudevan, C. Villamil, J. Trumbull, J. Olson, D. Sutherland, J. Pan, S. Djuric, Tetrahedron Lett. *2010*, *51* (31), 4007-9 [DOI: 10.1016/j.tetlet.2010.05.119]; intra-

molecular cycloaddition of *electron-rich* olefins under sun-light irradiation with tris(2,2′-bipyridyl)ruthenium(II) bis(hexafluorophosphate) s. M.A. Ischay, Z. Lu, T.P. Yoon, J. Am. Chem. Soc. *2010*, *132* (25), 8572-4 [DOI: 10.1021/ja103934y]; **photochemical asym. intramolecular [2+2]-cycloaddition** of 3-(ω′-alkenyl)- and 3-(ω′-alkenyloxy)-subst. 5,6-dihydro-2-pyridones with a chiral bridged lactam as template s. D. Albrecht, F. Vogt, T. Bach, Chem. Eur. J. *2010*, *16* (14), 4284-96 [DOI: 10.1002/chem.200902616]; photochemical Lewis acid-catalyzed asym. intramolecular cycloaddition of coumarins with $AlBr_3$ complexed ionically with a chiral N-condensed 1,3,2-oxazaborolidine s. H. Guo, E. Herdtweck, T. Bach, Angew. Chem., Int. Ed. *2010*, *49* (42), 7782-5 [DOI: 10.1002/anie.201003619].

Chlorogold(I) N-heterocyclic carbene complexes/silver hexafluoroantimonate ←
Effect of π-acceptor properties of N-heterocyclic carbene ligands ←
on the chemoselectivity of gold(I)-catalyzed reactions

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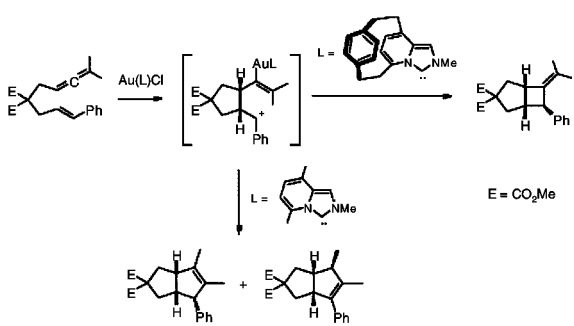
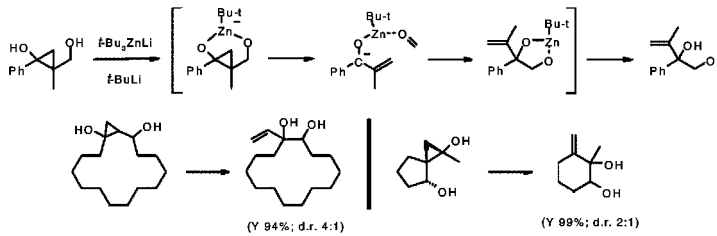


It has been demonstrated for the first time that the course of a gold(I)-catalyzed reaction can be determined largely by the *π-acceptor* properties of NHC ligands, which hitherto have been studied solely from the point of view of their σ-donating characteristics. **E:** A soln. of ([2](1,4)-benzeno-[2](5,8)-2-methylimidazo[1,5-*a*]pyridin-3-ylidenephane)gold(I) chloride (5 mmol) in methylene chloride (0.75 ml) added to a soln. of $AgSbF_6$ (5 mmol) in the same solvent (0.75 ml) at -5°, the mixture stirred for 5 min, a soln. of dimethyl 2-cinnamyl-2-(4-methylpenta-2,3-dienyl)malonate (0.1 mmol) in methylene chloride (1.5 ml) added, stirred at -5° until reaction complete (GC-MS), treated with triethylamine (0.05 ml), the mixture filtered through a short pad of silica, and the filtrate and washings worked up with purification by flash chromatography → [2+2]-adduct. Y 71%. Here, DFT calculations showed that the NHC ligand had an E_σ value of -5.00 and an E_π value of -1.14. However, with 2-mesityl-5,8-dimethylimidazo[1,5-*a*]pyridin-3-ylidene as ligand (having an almost identical E_σ value but a *significantly lower* E_π *energy* of -0.63), the course of the reaction changes completely: the product being a mixture of isomeric bicyclo[3.3.0]oct-2-enes (Y 63%) formed via a formal [3+2] pathway with methyl group migration. The differing reactivity is interpreted in terms of the stabilizing effect of the two ligands on the intermediate cationic species. This divergent reactivity was also demonstrated in two other gold(I)-catalyzed conversions, an essential finding being that it can be much easier to tune the π-acceptor properties of NHC ligands than to alter their σ-donating qualities by similar margins. F.e. and comparison of ligands s. M. Alcarazo, T. Stork, A. Anoop, W. Thiel, A. Fürstner, Angew. Chem., Int. Ed. *2010*, *49* (14), 2542-6 [DOI: 10.1002/anie.200907194].

Lithium tri-tert-butylzincate/tert-butyllithium or Zinc chloride/tert-butyllithium ←
3-Ene-1,2-diols from 2-α-hydroxycyclopropanols C
via zincate-mediated rearrangement



A soln. of *tert*-butyllithium (3 eq.) in pentane (1.9 ml) added to a soln. of 2-hydroxymethyl-2-methyl-1-phenylcyclopropanol (1 mmol) in THF (8 ml) at 0°, the mixture stirred for 10 min, freshly prepared *t*-Bu_3ZnLi (20 mol%) in THF added, the mixture refluxed for 24 h, quenched with satd. aq. NH_4Cl, extracted with ethyl acetate, washed with brine, concentrated *in vacuo*, and purified by chromatography on silica → 3-methylene-2-phenylbutane-1,2-diol. Y 89%. This novel rearrangement, promoted by *t*-BuLi/$ZnCl_2$ (3:1; a 2:1 ratio gave a complex mixture), or by using catalytic *t*-Bu_3ZnLi with *t*-BuLi (2 eq.), appears general for prim. and sec. 2-α-hydroxycyclopropanols (six examples; Y 78-98%), giving modest diastereoselectivity (2:1 to 3:1) with sec. alcohols. Analogous tert. 2-α-hydroxycyclopropanols, however, were less suitable substrates, affording significant amounts of ketone by-products (sole products in one case), resulting from C-C bond cleavage. Where the hydroxyalkylcyclopropanol moiety formed part of a macrocyclic ring, a ring-contracted 1,2-diol was formed (Y 94%; d.r. 4:1), while a spirocyclic substrate gave a ring-expanded analog (Y 99%; d.r. 2:1). A 2-α-(sulfonylamino)cyclopropanol was also a suitable substrate, affording the corresponding **2-ethylene-2′-(sulfonylamino)alcohol** as a single (unspecified) diastereomer (Y 81%). F.e. and optimization s. K. Nomura, S. Matsubara, Chem. Eur. J. *2010*, *16* (2), 703-8 [DOI: 10.1002/chem.200901054].

Dimethylaluminum chloride s. under Chiral nickel(0) phosphine complexes *Me_2AlCl*

Aluminum bromide/chiral N-condensed 1,3,2-oxazaborolidine/irradiation ←
Photochemical Lewis acid-catalyzed asym. intramolecular [2+2]-cycloaddition □○
s. *22*, 761s*78*

Chiral bridged lactams/irradiation ←
Photochemical asym. intramolecular [2+2]-cycloaddition
of 3-(ω′-alkenyl)- or 3-(ω′-alkenyloxy)-5,6-dihydro-2-pyridones s. *22*, 761s*78*

Chiral 1,1′-binaphthyl-2,2′-diyl phosphoramidite/N,N′-dimethyltrimethyleneurea ←
s. under Pd(dba)$_2$

Chiral nickel(0) phosphine complexes/dimethylaluminum chloride *[Ni(0)]/Me_2AlCl*
Asym. intramolecular carbocyanation of ethylene derivs. ○
s. *74*, 405; chiral 3-subst. 3-cyanomethylindolines with the chiral phosphino-Δ^2-oxazoline, (S,S)-*i*-Pr-Foxap or (S)-*i*-Pr-Phox, as ligand s. J.-C. Hsieh, S. Ebata, Y. Nakao, T. Hiyama, Synlett *2010* (11), 1709-11 [DOI: 10.1055/s-0029-1219964]; chiral 3-subst. 3-cyanomethyloxindoles with Pd(dba)$_2$ and a chiral 1,1′-binaphthyl-2,2′-diyl phosphoramidite as ligand in the presence of DMPU s. Y. Yasui, H. Kamisaki, T. Ishida, Y. Takemoto, Tetrahedron *2010*, *66* (11), 1980-9 [DOI: 10.1016/j.tet.2010.01.073].

Tris(2,2′-bipyridyl)ruthenium(II) bis(hexafluorophosphate)/irradiation *[Ru(bpy)$_3$](PF$_6$)$_2$/hν*
Photochemical intramolecular [2+2]-cycloaddition □○
with electron-rich ethylene derivs. s. *22*, 761s*78*

Dichloro(1,3-dimesitylimidazolidin-2-ylidene)(benzylidene)(tricyclohexylphosphine)- [Ru(II)] ruthenium(II)
Ring-closing ene-yne metathesis ○
s. *50*, 443s*76*; selenabicyclic 2-azetidinones s. D.B. Bankar, M. Koketsu, Eur. J. Org. Chem. *2010* (14), 2742-5 [DOI: 10.1002/ejoc.201000055]; 6- and 7-membered α-vinyl-α,β-ethylenelactolides s. D.A. Lanfranchi, C. Bour, B. Boff, G. Hanquet, Eur. J. Org. Chem. *2010* (27), 5232-47 [DOI: 10.1002/ejoc.201000305]; 2-alkoxy-3-vinyl-2,5-dihydrofurans s. S. Vuong, M.M. Rodriguez-Fernandez, B. Renoux, C. Len, Carbohydr. Res. *2010*, *345* (2), 324-9 [DOI: 10.1016/j.carres.2009.09.023]; 3,3-difluoro-4-vinyl-5,6-dihydro-2-pyridones and conversion to hexahydro-3-quinolone derivs. by subsequent Diels-Alder reaction, also via cross-metathesis-ene-yne metathesis, s. S. Arimitsu, G.B. Hammond, Beilstein J. Org. Chem. *2010*, *6*, No. 48 [DOI: 10.3762/bjoc.6.48].

Bis(dibenzylideneacetone)palladium(0)/chiral 1,1′-binaphthyl-2,2′-diyl phosphoramidite/ N,N′-dimethyltrimethyleneurea ←
Asym. intramolecular carbocyanation of ethylene derivs. s. *74*, 405s*78*

Exchange ↓↑

Hydrogen ↑ CC ↓↑ H

Electrolysis ϟ
Anodic α-cyanation of tert. amines s. *47*, 715s*78* H → CN

Lithium tert-butoxide s. under CuCN, $Cu(OTf)_2$ and $NiBr_2$ *LiOBu-t*
Sodium cyanide s. under CuCN and Polymer-based iron(II) phthalocyanines *NaCN*
Cesium fluoride s. under $Zn(CN)_2$ *CsF*
Ammonia s. under $POCl_3$ *NH_3*
Phenanthroline s. under CuCN and $Cu(OTf)_2$ *phen*
Copper(II) acetate [s.a. under $[Cp^*RhCl_2]_2$] *$Cu(OAc)_2$*
N-Subst. pyrazoles from enamines and nitriles ○
Copper(II)-mediated oxidative ring closure

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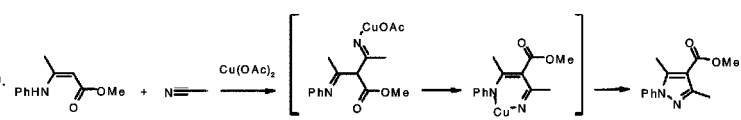


While N-arylenamino-esters afford indole-3-carboxylic acid esters via intramolecular oxidative ring closure in DMF (cf. *74*, 543), **pyrazole-4-carboxylic acid esters** are obtained in an excess of an aliphatic or aromatic nitrile (the addition of palladium(II) as cocatalyst and base or acid not being required). **E:** (Z)-Methyl 3-(phenylamino)but-2-enoate (1 mmol) and $Cu(OAc)_2$ (1.5 eq.) added to an oven-dried screw-capped vial, followed by the liquid nitrile (1.5 ml; 14-29 eq.), the vial closed, the mixture stirred vigorously at room temp. until the solids well suspended, then placed into a preheated metal block (110°), stirred at that temp. for 24 h, cooled to room temp., diluted with ethyl acetate, the mixture briefly stirred at room temp. to suspend the metallic precipitate, filtered through a short pad of silica and Celite, the solid washed thoroughly with ethyl acetate, the combined filtrates concentrated *in vacuo*, the crude product dissolved in methylene chloride, adsorbed on silica, and purified chromatographically → product. Y 80% [Y 81% with 3 eq. $Cu(OAc)_2$ in 3 ml nitrile at 120° for 14-24 h]. This method, which features a novel, mild, N-N coupling, is regioselective and avoids the use of carcinogenic hydrazines. Reaction may be conducted under argon or air; however, use of catalytic amounts of copper(II) salts in the presence of a reoxidant such as air was not satisfactory. The enamines may bear a variety of N-substituents, incl. *o*-, *p*- or *m*-subst. electron-rich or -poor aryl groups, notably allowing the formation of

N-mesityl- (Y 83%, 92%) and N-(2,6-diisopropylphenyl)-pyrazoles (Y 35%); an N-phenethyl-deriv. was also formed (Y 58%). F.e. (twenty-six; Y 39-90%), bis(pyrazolyl)arenes (Y 70%, 73%), and a 4-acyl-deriv. from an enaminone (Y 43%), also one pot synthesis **from β-keto-esters and prim. amines** with added $InBr_3$ (Y 73%, 78%), s. J.J. Neumann, M. Suri, F. Glorius, Angew. Chem., Int. Ed. *2010*, *49* (42), 7790-4 [DOI: 10.1002/anie.201002389].

Silver acetate s. under Pd(OAc)$_2$ *AgOAc*

Copper(I) cyanide/palladium(II) acetate/copper(II) bromide *CuCN/Pd(OAc)$_2$/CuBr$_2$*
Copper(I) cyanide/phenanthroline/iodine/sodium cyanide/lithium tert-butoxide ←
Ar. cyanation H → CN
with CuCN/Pd(OAc)$_2$/$CuBr_2$ cf. *3*, 600s*76*; 3-cyanation of indoles s. B.V.S. Reddy, Z. Begum, Y.J. Reddy, J.S. Yadav, Tetrahedron Lett. *2010*, *51* (25), 3334-6 [DOI: 10.1016/j.tetlet.2010.04.086]; 2-cyanation of azoles and cyanation of azulene with CuCN/phenanthroline/I_2/NaCN/LiOBu-*t* s. H.-Q. Do, O. Daugulis, Org. Lett. *2010*, *12* (11), 2517-9 [DOI: 10.1021/ol100772u].

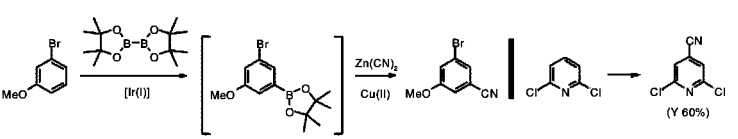
Copper(II) nitrate s. under Zn(CN)$_2$ *Cu(NO$_3$)$_2$*

Copper(II) triflate/1,10-phenanthroline/lithium tert-butoxide/oxygen *Cu(OTf)$_2$/phen/LiOBu-t/O$_2$*
Polyfluoroarylacetylenes H → C≡CR
from polyfluoroarenes and terminal acetylene derivs. s. *71*, 337s*78*

Copper(I) chloride/sodium carbonate/oxygen *CuCl/Na$_2$CO$_3$/O$_2$*
Copper(I) iodide/2,3-dichloro-5,6-dicyanoquinone/chloroformic acid esters *CuI/DDQ/ROCOCl*
Arylacetylenes from terminal acetylene derivs. and arenes
under copper catalysis s. *71*, 337s*77*; 2-(alk-1-ynyl)pyridines from pyridines with CuI/DDQ in the presence of a chloroformic acid ester s. R.E. Beveridge, B.A. Arndtsen, Synthesis *2010* (6), 1000-8 [DOI: 10.1055/s-0029-1218632]; polyfluoroarylacetylenes with Cu(OTf)$_2$/1,10-phenanthroline/LiOBu-*t* under O_2, also 2-(alk-1-ynyl)azoles under nickel catalysis with $NiBr_2$-diglyme/4,4′-di-*tert*-butyl-2,2′-bipyridyl/LiOBu-*t*/O_2 s. N. Matsuyama, M. Kitahara, K. Hirano, T. Satoh, M. Miura, Org. Lett. *2010*, *12* (10), 2358-61 [DOI: 10.1021/ol100699g]; 2-(alk-1-ynyl)-1,3,4-oxadiazoles and -oxazoles with CuCl/Na_2CO_3 under O_2 s. M. Kitahara, K. Hirano, H. Tsurugi, T. Satoh, M. Miura, Chem. Eur. J. *2010*, *16* (6), 1772-5 [DOI: 10.1002/chem.200902916]; 2-(alk-1-ynyl)indoles with K_2PdCl_4/Cs_2CO_3/pivalic acid under O_2 s. L. Yang, L. Zhao, C.-J. Li, Chem. Commun. *2010*, *46* (23), 4184-6 [DOI: 10.1039/c0cc00014k].

Copper(II) bromide s. under CuCN *CuBr$_2$*
Silver nitrate s. under Pd(OCOCF$_3$)$_2$ *AgNO$_3$*
*Silver hexafluoroantimonate s. under [Cp*RhCl$_2$]$_2$* *AgSbF$_6$*
Silver triflate s. under PtCl$_2$ *AgOTf*

Zinc cyanide/copper(II) nitrate/cesium fluoride/cyclooctadiene(methoxy)iridium(I) dimer/ bis(pinacolato)diboron/di-tert-butylpyridine ←
Copper-mediated *m*-cyanation via iridium-catalyzed *m*-borylation H → B(OR)$_2$ → CN



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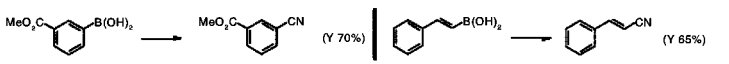
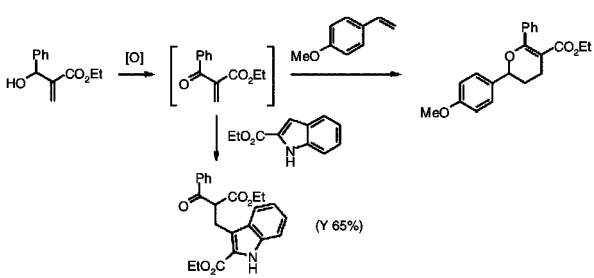


in one pot. 3-Bromoanisole (0.5 mmol), bis(pinacolato)diboron (0.375 mmol) and a stock soln. containing [Ir(cod)(OMe)]$_2$ (0.5 μmol) and di-*tert*-butylpyridine (1 μmol) in THF (1 ml) combined in a vial under N_2, the vial sealed, the mixture heated at 80° for 16 h (method cf. *64*, 219), the red

soln. cooled to room temp., volatiles removed under reduced pressure, the residue taken up in methanol (2.5 ml), $Cu(NO_3)_2 \cdot 3H_2O$ (1 mmol), $Zn(CN)_2$ (1.5 mmol), CsF (0.5 mmol) and water (1 ml) added sequentially, the vessel sealed, the resulting green suspension stirred vigorously at 100° for 3-6 h (GC-MS), cooled to room temp., quenched with satd. aq. NH_4Cl (4 ml), extracted with ethyl acetate, the extracts washed with brine, dried (Na_2SO_4), evaporated, and the residue purified by chromatography on silica gel → 3-bromo-5-methoxybenzonitrile. Y 67%. The procedure was successful for a variety of 1,3-di- and 1,2,3-tri-subst. arenes (incl. pyridine derivs.) containing halide, ketone, ester, amide, acetal and ether functionalities (thirteen examples; Y 51-67%); a variety of protected anilines were poor substrates, however. Electron-diverse arylboronic acids (incl. a pyridyl example) also proved to be suitable substrates for the cyanation step, affording ar. nitriles in yields of 61-70% (eight examples); styrenylboronic acid afforded 3-phenylacrylonitrile analogously, in 65% yield. F.e. and optimization of the cyanation reaction s. C.W. Liskey, X. Liao, J.F. Hartwig, J. Am. Chem. Soc. *2010*, *132* (33), 11389-91 [DOI: 10.1021/ja104442v].

Bis(pinacolato)diboron s. under $Zn(CN)_2$ — $(RO)_2BB(OR)_2$
Benzoquinone/N-acetylvaline s. under $Pd(OAc)_2$ — ←
Dimethylformamide s. under $POCl_3$ — *DMF*
(2R,5R)-2-tert-Butyl-3,5-dimethyl-4-imidazolidone s. under Tris(phenanthroline)iron(III) hexafluoroantimonate — ←
tert-Butyl hydroperoxide s. under $Pd(OAc)_2$ — *t-BuOOH*
Pivalic acid s. under K_2PdCl_4 — *t-BuCOOH*
o-Iodoxybenzoic acid — $ArIO_2$

Oxidative generation of β-keto-α-methylene- from β-hydroxy-α-methylene-carboxylic acid esters in water and catalyst-free trapping with nucleophiles under mild conditions ←



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by hetero-Diels-Alder reaction with ethylene derivs. *p*-Methoxystyrene (0.4 mmol), the startg. Baylis-Hillman adduct (0.3 mmol), water (1 g) and *o*-iodoxybenzoic acid (IBX; 0.4 mmol) mixed under air, stirred for 3 h at 90°, extracted with ethyl acetate, concentrated under reduced pressure, and worked up with purification by preparative TLC → 3-ethoxycarbonyl-2-phenyl-6-(4-methoxyphenyl)-5,6-dihydropyran. Y 57%. With water as both medium and activator of the Diels-Alder reaction, the procedure is mild, eco-friendly and widely applicable to the reaction of aliphatic or electron-diverse β-[het]aryl-β-hydroxy-α-methylenecarboxylic acid esters with a range of olefins (electron-diverse styrenes and enolethers) in moderate to good yield (fifteen examples; Y 39-80%). Such *oxidative* generation of β-keto-α-methylenecarboxylic acid esters is considered superior to the established *in situ* Knoevenagel route by condensation of β-ketocarboxylic acid esters with formaldehyde, where the initial condensation may be difficult and require excess of the keto-ester, and where complications may arise through undesirable reaction of the nucleophiles with formaldehyde. A further advantage of the method is that the reduced oxidant (*o*-iodobenzoic acid) is easily recovered by precipitation and can be simply re-oxidized to IBX. The generated

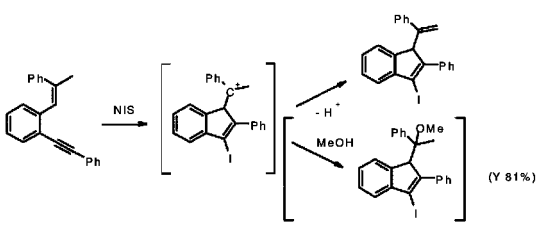
β-keto-α-methylenecarboxylic acid esters were **also** trapped **by Michael addition** with β-keto-esters (seven examples; Y 67-81%), indoles (six examples; Y 59-72%), and even benzamide (one example; Y 63%). Other solvents (organic and ionic liquid) gave lower yields. F.e.s. J.-N. Tan, H. Li, Y. Gu, Green Chem. *2010*, *12* (10), 1772-3 [DOI: 10.1039/c0gc00274g].

Phenyl iodoso(hydroxy)tosylate/trimethylsilyl bromide *PhI(OH)OTs/Me$_3$SiBr*
Oxidative dimerization of 3-subst. thiophenes s. *27*, 761s*78* 2 ArH → Ar-Ar

2,3-Dichloro-5,6-dicyanoquinone (s.a. under CuI) *DDQ*
Metal-free oxidative cross-coupling ⩾CH + HC⩽ → ⩾C-C⩽
of allylic or benzylic carbon-hydrogen bonds with active methylene groups s. *73*, 355s*78*

N-Bromo- or N-Iodo-succinimide *NBS or NIS*
3-Halogeno-1-vinylindenes from *o*-(alk-1-ynyl)styrenes ○
via halogenocarbocyclization

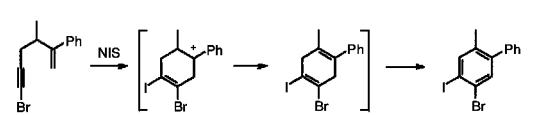
363.



N-Iodosuccinimide (3 eq.) added to a soln. of the startg. *o*-(alkynyl)styrene (1 mmol) in methylene chloride (4 ml) in a vial, the vial sealed and protected from light, the mixture refluxed until startg. m. consumed (TLC; 4.5 h), quenched with satd. aq. $Na_2S_2O_3$, extracted with methylene chloride, concentrated *in vacuo*, and purified by flash chromatography on silica → 3-iodo-2-phenyl-1-(1-phenylvinyl)-1*H*-indene. Y 81%. This novel example of a 5-*endo*-*dig* cyclization is apparently driven by formation of a stabilized carbocation that eliminates a proton to afford 3-iodo/bromo-derivs. with NIS (fourteen examples; Y 55-92%) or NBS (two examples; Y 65%, 74%), respectively. The reaction failed for terminal alkynes, while substrates lacking a β-styryl substituent gave complex mixtures. Halocyclization was also achieved with I_2, but yields were reduced due to side-product formation, while in the presence of excess methanol, the intermediate carbocation was trapped to afford **1-α-alkoxy-3-iodoindenes** (six examples; Y 58-81%). F.e., substrate prepn., optimization and conversion of products to **2,3-diarylindenes** via Suzuki-type coupling (three examples; Y 77-90%) s. R. Sanz, A. Martínez, P. García-García, M.A. Fernández-Rodríguez, M.A. Rashid, F. Rodríguez, Chem. Commun. *2010*, *46* (39), 7427-9 [DOI: 10.1039/c0cc02590a].

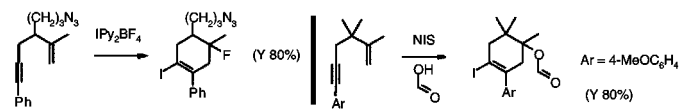
N-Iodosuccinimide *NIS*
Metal-free halogenocarbocyclization of 1,5-enynes

364.



Iodoarene ring. N-Iodosuccinimide (3 eq.) added to a soln. of 6-bromo-3-methyl-2-phenylhex-1-en-5-yne (0.05 mmol) in methylene chloride (1 ml) in a vial, the vial sealed and protected from light, stirred at 50° under air until reaction complete (TLC; 5 h), quenched with satd. aq. $Na_2S_2O_3$, extracted with methylene chloride, washed with brine, concentrated *in vacuo*, and purified by flash chromatography on silica → 5-bromo-4-iodo-2-methylbiphenyl. Y 90%. This iodocyclization/aromatization is apparently general for H, alkyl, (het)ar. and bromo terminated 1,5-enynes, using

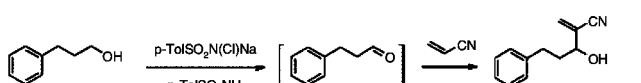
NIS as iodonium source (I_2 gave complex mixtures). The presence of a β-ethylene substituent is essential (apparently to stabilize a carbocation intermediate), with the reaction affording tri-, tetra- and penta-subst. iodo-benzenes and -naphthalenes (twenty-three examples; Y 44-96%) in the presence of silyl ether, nitro, ester, halo, azide and additional alkyne functionality (low yields (9%, 13%) were obtained with alcohol and aldehyde derivs.). Where aromatization was blocked by *gem*-disubstitution, a **1-iodo-1,3-cyclohexadiene** was obtained (Y 93%), while short exposure (1-2 h) to I_2/K_3PO_4 gave **1-iodo-1,4-cyclohexadienes** (four examples; Y 75-99%), and bis(pyridine)-iodonium fluoroborate afforded **1-iodo-4-fluorocyclohexenes** (seven examples; Y 33-85%). In a final development, halogenocarbocyclization (with NIS) in the presence of the O-nucleophile, formic acid, trapped the intermediate carbocation to produce **1-iodo-4-formyloxycyclohexenes** (two examples; Y 53%, 80%).



F.e.s. B. Crone, S.F. Kirsch, K.-D. Umland, Angew. Chem., Int. Ed. *2010*, *49* (27), 4661-4 [DOI: 10.1002/anie.201001113].

Chloramine-T/triethylenediamine — *Chloramine-T/DABCO*
β-Hydroxy-α-methylenecarbonyl compds. — CHOH → C(OH)C=CH_2
from α-methylenecarbonyl compds. and prim. alcohols
Oxidative Baylis-Hillman reaction with *in situ*-generated aldehydes

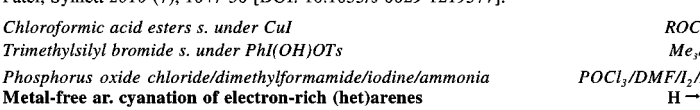
365.



A mixture of 3-phenylpropan-1-ol (5 mmol), Chloramine-T (1 eq.), DABCO (1 eq.) and SiO_2 (200 mg) in dioxane/water (1:1; 3 ml) stirred at room temp. until substrate consumed (TLC; 6-24 h), acrylonitrile (3 eq.) added, the mixture stirred until reaction complete (TLC; 32 h), concentrated *in vacuo*, extracted with ethyl acetate, evaporated to dryness, and the crude product purified by chromatography on silica → 2-cyano-3-hydroxy-5-phenylpent-1-ene. Y 85%. Generation of the required aldehydes *in situ* provides convenient and efficient access to Morita-Baylis-Hillman adducts from stable, less volatile and less toxic prim. alcohols. Electron-diverse benzylic and linear aliphatic alcohols were good substrates with acrylonitrile or acrylate esters (sixteen examples; Y 70-87%). *p*-Toluenesulfonamide, formed as a by-product of oxidation, was recovered and recycled via oxidation with NaOCl. F.e. and optimization s. L.D.S. Yadav, V.P. Srivastava, R. Patel, Synlett *2010* (7), 1047-50 [DOI: 10.1055/s-0029-1219577].

Chloroformic acid esters s. under CuI — *ROCOCl*
Trimethylsilyl bromide s. under PhI(OH)OTs — *Me_3SiBr*
Phosphorus oxide chloride/dimethylformamide/iodine/ammonia — *$POCl_3/DMF/I_2/NH_3$*
Metal-free ar. cyanation of electron-rich (het)arenes — H → CN

366.



in one pot. $POCl_3$ (1.1 eq.) and DMF (4 eq.) added to 1,5-dimethoxynaphthalene (6 mmol) at 0°, the mixture stirred at 80° for 4 h, I_2 (2 eq.) and aq. NH_3 (28-30%; 12 ml) added, the mixture stirred

at room temp. for 3 h, quenched with satd. aq. Na_2SO_3, extracted with chloroform, and concentrated → 4-cyano-1,5-dimethoxynaphthalene. Y 91%. This experimentally simple and environmentally benign synthesis of (het)ar. nitriles uses inexpensive and readily available reagents. Electron-rich benzenes, naphthalenes, phenanthrenes, indoles, furans and thiophenes gave single products (twelve examples; Y 59-99%; N-benzylpyrrole gave a 3:1 mixture of 3- and 2-cyano derivs. in 87% yield) with low yields obtained for thiophene (45%), 2-bromothiophene (13%), benzofuran (12%) and benzothiophene (0%). F.e.s. S. Ushijima, H. Togo, Synlett *2010* (7), 1067-70 [DOI: 10.1055/s-0029-1219575].

*Oxygen or air s. under Cu(OTf)$_2$, CuCl, MeSO$_3$H, Fe, Chiral iron(III) salan complexes, NiBr$_2$, [Cp*RhCl$_2$]$_2$, Pd(OAc)$_2$ and K$_2$PdCl$_4$* O_2

Hydrogen peroxide s. under Polymer-based iron(II) phthalocyanines H_2O_2

Methanesulfonic acid/oxygen $MeSO_3H/O_2$

Metal-free oxidative cross-coupling ⩾CH + HC⩽ → ⩾C-C⩽

of benzylic carbon-hydrogen bonds with active methylene groups s. *73*, 355s*78*

Phosphomolybdovanadate s. under Pd(OAc)$_2$ ←

Iodine s. under CuCN and POCl$_3$ I_2

Sodium hypochlorite/sodium hydroxide *NaOCl/NaOH*

Oxidative dimerization of phenols 2 ArH → Ar-Ar

with NaOH/lauric acid/H_2O_2 cf. *31*, 719s*65*; eco-friendly procedure for the oxidative dimerization of phenols and naphthols with aq. NaOCl and 4% aq. NaOH s. R. Neelamegam, M.T. Palatnik, J. Fraser-Rini, M. Slifstein, A. Abi-Dargham, B. Easwaramoorthy, Tetrahedron Lett. *2010*, *51* (18), 2497-9 [DOI: 10.1016/j.tetlet.2010.02.173].

Iron nanoparticles/oxygen *Fe/O$_2$*

2-Nitro-*tert*-amines ⩾CH + HC⩽ → ⩾C-C⩽

from tert. amines and aliphatic nitro compds. s. *74*, 409s*78*

Polymer-based iron(II) phthalocyanines/sodium cyanide/hydrogen peroxide ←

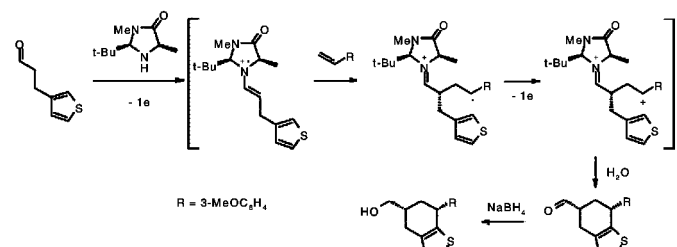
α-Cyanation of tert. amines H → CN

under iron catalysis s. *47*, 715s*76*; *heterogeneous* conversion with a recyclable polymer-based iron(II) phthalocyanine in the presence of $NaCN/H_2O_2$ s. S. Singhal, S.L. Jain, B. Sain, Adv. Synth. Catal. *2010*, *352* (8), 1338-44 [DOI: 10.1002/adsc.201000007]; diastereoselective anodic 1-cyanation of 2-subst. 1,2,3,4-tetrahydroisoquinoline alkaloids s. F. Louafi, J.-P. Hurvois, A. Chibani, T. Roisnel, J. Org. Chem. *2010*, *75* (16), 5721-4 [DOI: 10.1021/jo100714y].

Tris(1,10-phenanthroline)iron(III) hexafluoroantimonate/(2R,5R)-2-tert-butyl-3,5-dimethyl-4-imidazolidone/disodium hydrogen phosphate ←

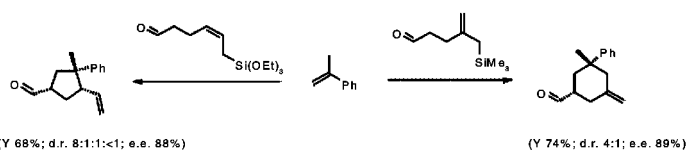
Fused 4-formylcyclohexene ring from β-[het]arylaldehydes and ethylene derivs. via asym. organo-SOMO [4+2] cascade cycloaddition ○

367.



An argon-degassed mixture of (2R,5R)-2-*tert*-butyl-3,5-dimethylimidazolid-4-one trifluoroacetic acid salt (0.2 eq.), 3-methoxystyrene (3 eq.), 3-(thiophen-3-yl)propanal (0.4 mmol), $Fe(phen)_3(SbF_6)_3$

(2.5 eq.), Na_2HPO_4 (1 eq.) and THF (5.3 ml) in an oven-dried round-bottom flask stirred at -20° for 12 h, diluted with ether, passed through a plug of silica gel (with ether), concentrated, dissolved in methylene chloride/ethanol (4:1; 10 ml), and treated with $NaBH_4$ (2 eq.) → [(5R,7R)-4,5,6,7-tetrahydro-7-(3-methoxyphenyl)benzo[*b*]thiophen-5-yl]methanol. Y 90% (d.r. 19:1; e.e. 94%). This novel, radical-mediated cascade olefin addition/Friedel-Crafts reaction is applicable to a range of electron-rich β-[het]arylaldehydes, reacting with electron-diverse styrenes (incl. α-subst. and hetar. analogs) to afford aryl-fused cyclohexenes in high yield (69-90%; fourteen examples) and with high enantio- and diastereo-selectivity (e.e. 88-94%; d.r. 4:1 to >20:1). Reaction was successfully extended to a diene (2,4-dimethylpenta-1,3-diene), albeit with reduced enantioselectivity (e.e. 70%); and use of allylsilanes as carbogenic π-nucleophiles in place of [het]aryl groups gave rise to [3+2] or [4+2] cascade cycloadditions, affording **chiral 3-vinylcyclopentane- or 3-methylenecyclohexane-carboxaldehydes**, respectively, in decent yields and with good enantio- and diastereoselectivities (desilylation occurring with added KF).

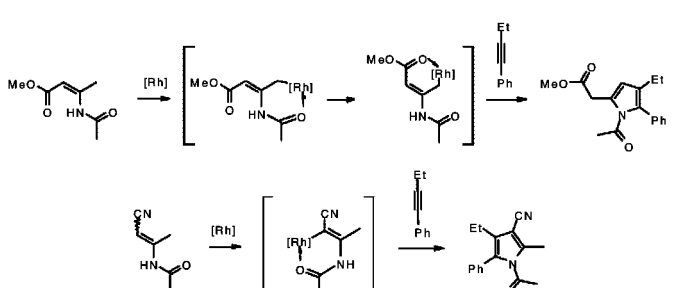


F.e.s. N.T. Jui, E.C.Y. Lee, D.W.C. MacMillan, J. Am. Chem. Soc. *2010*, *132* (29), 10015-7 [DOI: 10.1021/ja104313x].

Chiral iron(III) salan complexes/air *[Fe(III)]/O_2*
Sym. 1,1′-bi-2-naphthols by asym. aerobic dimerization 2 ArH → Ar-Ar
s. *61*, 321s*75*; synthesis of C_1-*symmetric* BINOLs s. H. Egami, K. Matsumoto, T. Oguma, T. Kunisu, T. Katsuki, J. Am. Chem. Soc. *2010*, *132* (39), 13633-5 [DOI: 10.1021/ja105442m].

Nickel(II) bromide/4,4′-di-tert-butyl-2,2′-bipyridyl/lithium tert-butoxide/oxygen ←
2-(Alk-1-ynyl)azoles from azoles and terminal acetylene derivs. s. *71*, 337s*78* H → C≡CR

Dichloro(pentamethylcyclopentadienyl)rhodium(III) dimer/copper(II) acetate/ silver hexafluoroantimonate ←
N-Acylpyrroles from enacylamines and acetylene derivs. ○



368.

Rhodium(III)-catalyzed N-heterocyclic ring closure by oxidative coupling with [unactivated] alkynes (cf. *75*, 376) has now been extended to pyrrole formation from enacylamines via allylic sp^3 or vinylic sp^2 C-H activation. **E: N-Acylpyrrole-2-acetic acid esters via allylic sp^3 C-H activation.** $[Cp^*RhCl_2]_2$ (2.5 mol%), $AgSbF_6$ (10 mol%) and anhydrous $Cu(OAc)_2$ (2.1 eq.) added

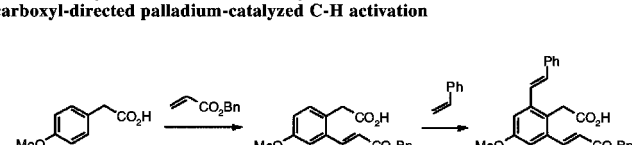
to a flame-dried sealed tube fitted with a J. Young Teflon valve in a glovebox, the vessel evacuated and backfilled with argon 3 times, startg. N-acetylenamine (1.3 eq.), 1-phenyl-1-butyne (1 mmol) and dry DCE (5 ml) added under argon, the tube closed, lowered into a preheated oil bath at 120°, then stirred for 16 h, cooled to room temp., the mixture diluted with ethyl acetate (15 ml), filtered through a short pad of silica, the solid washed with ethyl acetate, the combined filtrates concentrated under reduced pressure, and the residue purified by flash chromatography on silica → product. Y 60% (single regioisomer). The N-acetyl group on the enamine appears essential, other groups such as trifluoroacetyl, benzoyl, Boc, phenyl or methyl resulting in <5% yield. Formation of a pentasubst. pyrrole required a higher temp. (140° for 24 h) and higher catalyst loading, while affording only a moderate yield (31%). A variety of internal alkynes bearing electron-neutral, electron-deficient or electron-rich aromatic or heteroaromatic groups were coupled successfully (nineteen examples; Y 34-81%), with groups such as bromide, chloride, and ester tolerated. Ester-activated alkynes or propargylic alcohol derivs. did not afford the corresponding pyrrole, however, possibly due to poisoning of the catalyst by chelation. Replacement of the enamine ester by a keto group failed, suggesting chelation by the ester is crucial for the reaction. Supporting this, it was found that **N-acyl-3-cyanopyrroles** may be obtained **from β-acylamino-α,β-ethylenenitriles via vinylic sp² C-H activation** (two examples; Y 70%, 72%). F.e.s. S. Rakshit, F.W. Patureau, F. Glorius, J. Am. Chem. Soc. *2010*, *132* (28), 9585-7 [DOI: 10.1021/ja104305s]; **4-acylpyrrole-2,3-dicarboxylic acid esters** from acetylenedicarboxylic acid esters and β-enamino-ketones or -esters with CuI/O_2 cf. R.-L. Yan, J. Luo, C.-X. Wang, C.-W. Ma, G.-S. Huang, Y.-M. Liang, J. Org. Chem. *2010*, *75* (15), 5395-7 [DOI: 10.1021/jo101022k].

Dichloro(pentamethylcyclopentadienyl)rhodium(III) dimer/copper(II) acetate/silver hexafluoroantimonate/oxygen ←
Stereoselective oxidative *o*-vinylation of acetanilides s. *69*, 369s*78* H → C=C

Palladium(II) acetate s.a. under CuCN $Pd(OAc)_2$

Palladium(II) acetate/potassium hydrogen carbonate/benzoquinone/oxygen or oxygen/N-acetylvaline ←
Sequential *o*-vinylation with activated ethylene derivs. via carboxyl-directed palladium-catalyzed C-H activation

369.



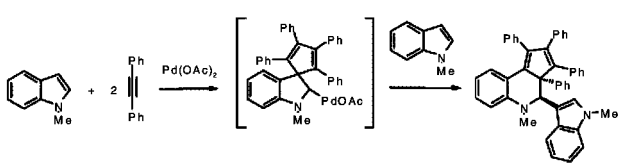
***o,o′*-Divinylarylacetic acids**. A mixture of 4-methoxyphenylacetic acid (0.5 mmol), $Pd(OAc)_2$ (5 mol%), $KHCO_3$ (2 eq.), benzoquinone (10 mol%), benzyl acrylate (2 eq.) and *tert*-amyl alcohol (2.5 ml) stirred under O_2 (balloon) at room temp. for 5 min then at 90° for 48 h, cooled to 0°, quenched with 2 *M* aq. HCl, extracted with ethyl acetate, concentrated *in vacuo*, purified chromatographically, the resulting benzyl cinnamate deriv. (Y 70%) dissolved in *tert*-amyl alcohol (2.5 ml), $Pd(OAc)_2$ (5 mol%), $KHCO_3$ (2 eq.), N-acetylvaline (10 mol%) and styrene (2 eq.) added, the mixture stirred under O_2 at 90° for 6 h, and worked up as before → 2-(2-benzyloxycarbonyl-vinyl)-4-methoxy-6-styrylphenylacetic acid. Y 71%. Initial experiments identified reactive ligands that would promote bis-*o*-vinylation of phenylacetic and hydrocinnamic acids with acrylates and styrene (twenty-three examples; Y 59-96%; naphth-1-ylacetic gave a *2,8-bis-vinyl* deriv. in 35% yield). Using ligands of varying reactivity gave rise to a method for sequential *o*-vinylation with different coupling partners (styrenes and acrylates) (three examples; Y 71-94%); interestingly, reaction with 1-hexene in the second step afforded the *non-conjugated* 2-hexenyl deriv. (formal C-H allylation; Y 23%). In a final development, hydrogenation of a divinylarene product allowed introduction of a *third vinyl group* (Y 35%). F.e. and optimization s. K.M. Engle, D.-H. Wang, J.-Q. Yu, Angew. Chem., Int. Ed. *2010*, *49* (35), 6169-73 [DOI: 10.1002/anie.201002077].

Palladium(II) acetate/silver acetate $Pd(OAc)_2/AgOAc$
Palladium(II) acetate/phosphomolybdovanadate/oxygen ←
Regioselective oxidative ar. vinylation H → C=C
of thiophenes and furans s. *69*, 369s*76*; 5-vinylation of 2-subst. oxazoles and thiazoles s. M. Miyasaka, K. Hirano, T. Satoh, M. Miura, J. Org. Chem. *2010*, *75* (15), 5421-4 [DOI: 10.1021/jo101214y]; cinnamonitriles from acrylonitriles and benzenes with $Pd(OAc)_2$/phosphomolybdovanadate under O_2 s. Y. Obora, Y. Okabe, Y. Ishii, Org. Biomol. Chem. *2010*, *8* (18), 4071-3 [DOI: 10.1039/c0ob00176g]; *trans*-selective *o*-vinylation of unactivated acetanilides with $[RhCp^*Cl_2]_2$/$AgSbF_6$ and $Cu(OAc)_2$ as stoichiometric oxidant or with $Cu(OAc)_2$ as catalyst under air s. F.W. Patureau, F. Glorius, J. Am. Chem. Soc. *2010*, *132* (29), 9982-3 [DOI: 10.1021/ja103834b].

Palladium(II) acetate/tert-butyl hydroperoxide $Pd(OAc)_2$/*t-BuOOH*
Oxidative C-acylation with aldehydes H → Ac
aerobic C-acylation of N-heteroarenes with $Co(acac)_2$/$Co(acac)_3$/N-hydroxyphthalimide/trifluoroacetic acid cf. *26*, 775s*65*; **directed *o*-acylation** of aryl ketoximes with $Pd(OAc)_2$/*tert*-butyl hydroperoxide s. C.-W. Chan, Z. Zhou, A.S.C. Chan, W.-Y. Yu, Org. Lett. *2010*, *12* (17), 3926-9 [DOI: 10.1021/ol101618u]; pyridine-directed *o*-acylation (e.g. of benzo[*h*]quinolines) under solvent-free conditions s. O. Baslé, J. Bidange, Q. Shuai, C.-J. Li, Adv. Synth. Catal *2010*, *352* (7), 1145-9 [DOI: 10.1002/adsc.200900874].

Palladium(II) acetate/oxygen $Pd(OAc)_2/O_2$
4-(Indol-3-yl)-4,5-dihydro-3a*H*-cyclopenta[*c*]quinolines from two indole molecules and two acetylene deriv. molecules

370.



N-Methylindole (0.2 mmol), diphenylacetylene (2.5 eq.) and $Pd(OAc)_2$ (10 mol%) added to a Schlenk tube, the tube purged 3 times with O_2 (1 atm.), followed by addition of acetonitrile/acetic acid (1:1; 1 ml), the mixture stirred at room temp. under O_2 (1 atm.) for 36 h (TLC), quenched with water, extracted with ethyl acetate, the combined organic phases washed with satd. $NaHCO_3$ soln., dried ($MgSO_4$), filtered, evaporated under vacuum, and the crude product purified by chromatography on silica gel → 5-methyl-4-(1-methyl-1*H*-indol-3-yl)-1,2,3,3a-tetraphenyl-4,5-dihydro-3a*H*-cyclopenta[*c*]quinoline. Y 78% (59% under air). Only 9-methyl-1,2,3,4-tetraphenyl-9*H*-carbazole was obtained in 4:1 DMA/pivalic acid (Y 41%). The method is applicable to both aryl- and alkyl-subst. internal acetylenes, while the indole may be N-unsubst. or carry N-2-hydroxyethyl or N-benzyl instead of N-methyl and be substituted on the benzene ring by functions such as halogen, nitro or nitrile. Mechanistically, two possible routes are proposed, both involving an intermediate spirocyclopentadiene. F.e. (thirteen; Y 33-83%) s. Z. Shi, B. Zhang, Y. Cui, N. Jiao, Angew. Chem., Int. Ed. *2010*, *49* (24), 4036-41 [DOI: 10.1002/anie.201001237].

Palladium(II) trifluoroacetate/silver nitrate $Pd(OCOCF_3)_2/AgNO_3$
Oxidative dimerization of arenes 2 ArH → Ar-Ar
under ruthenium catalysis cf. *27*, 761s*73*; synthesis of sym. 3,3′-biindoles from protected or unprotected indoles with $Pd(OCOCF_3)_2/AgNO_3$ s. Y. Li, W.-H. Wang, S.-D. Yang, B.-J. Li, C. Feng, Z.-J. Shi, Chem. Commun. *2010*, *46* (25), 4553-5 [DOI: 10.1039/c0cc00486c]; head-to-tail bithiophenes from 3-subst. thiophenes with hypervalent iodine(III) reagents, e.g. phenyl iodoso(hydroxy)tosylate, and Me_3SiBr s. K. Morimoto, N. Yamaoka, C. Ogawa, T. Nakae, H. Fujioka, T. Dohi, Y. Kita, Org. Lett. *2010*, *12* (17), 3804-7 [DOI: 10.1021/ol101498r].

Potassium tetrachloropalladate(II)/cesium carbonate/pivalic acid/oxygen ←
2-(Alk-1-ynyl)indoles from indoles and terminal acetylene derivs. s. *71*, 337s*78* H → C≡CR

Cyclooctadiene(methoxy)iridium(I) dimer s. under Zn(CN)$_2$ *[(cod)Ir(OMe)]$_2$*

Platinum(II) chloride *$PtCl_2$*

Formation of functionalized sp^3 carbon-carbon bonds by oxidative cross-coupling ⩾CH + HC⩽ → ⩾C-C⩽

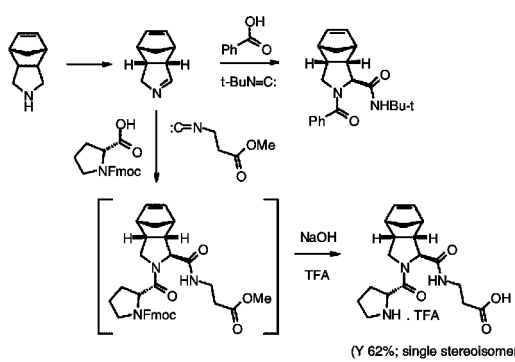
2-nitro-*tert*-amines from tert. amines and aliphatic nitro compds. with CuBr under O_2 cf. *72*, 491; *dehydrogenative* cross-coupling of tert. amines with active methylene groups (e.g. nitro compds., malonates, ketoesters) with $PtCl_2$ in the *absence* of oxidant s. X.-Z. Shu, Y.-F. Yang, X.-F. Xia, K.-G. Ji, X.-Y. Liu, Y.-M. Liang, Org. Biomol. Chem. *2010*, *8* (18), 4077-9 [DOI: 10.1039/c0ob00261e]; with magnetically recoverable iron nanoparticles under O_2 (cf. *74*, 409) s. T. Zeng, G. Song, A. Moores, C.-J. Li, Synlett *2010* (13), 2002-8 [DOI: 10.1055/s-0030-1258128]; oxidative coupling of allylic or benzylic carbon-hydrogen bonds with active methylene groups under *metal-free* conditions with DDQ (cf. *73*, 355) s. D. Ramesh, U. Ramulu, S. Rajaram, P. Prabhakar, Y. Venkateswarlu, Tetrahedron Lett. *2010*, *51* (37), 4898-903 [DOI: 10.1016/j.tetlet.2010.07.080]; alternative procedure by metal-free oxidative coupling of benzylic carbon-hydrogen bonds using methanesulfonic acid as catalyst under O_2 s. Á. Pintér, A. Sud, D. Sureshkumar, M. Klussmann, Angew. Chem., Int. Ed. *2010*, *49* (29), 5004-7 [DOI: 10.1002/anie.201000711].

Platinum(II) chloride/silver triflate *$PtCl_2$/AgOTf*

Intramolecular hydroarylation of α-allenecarboxylic acid esters s. *25*, *527s78* ○

Via intermediates *v.i.*

1-Acylpyrrolidine-2-carboxylic acid amides from *meso*-pyrrolidines, isonitriles and carboxylic acids via oxidative enzymatic desymmetrization and Ugi-type 3-component synthesis ←



371.

(Y 62%; single stereoisomer)

Biocatalytic oxidative desymmetrization of 3,4-disubst. pyrrolidines (cf. *77*, 390) has been combined with Ugi-type 3-component synthesis to afford otherwise hard-to-access **3,4-disubst. (S)-N-acylprolinamides and prolyl peptides** of interest in medicinal chemistry, especially for novel hepatitis C drugs. **E:** A soln. of startg. amine (1 mmol) in K-phosphate buffer (100 m*M*; 30 ml; pH 8) adjusted to pH 8 with NaOH then added to freeze-dried MAO-N D5 *E. Coli* cells (2.5 g), previously rehydrated for 30 min in K-phosphate buffer (100 m*M*; 20 ml; pH 8) at 37°, after 16-17 h the reaction stopped (conversion >95%), worked up by centrifugation at 4000 rpm and 4° until the supernatant had clarified (40-60 min), the pH of the supernatant adjusted to 10-11 by addition of aq. NaOH, the supernatant extracted with *tert*-butyl methyl ether or methylene chloride, the combined organic phases dried (Na_2SO_4), and concentrated by rotary evaporation → intermediate pyrroline (Y 84%; e.e. >99%), 0.7 mmol of which dissolved in methylene chloride (2 ml) followed by addition of startg. carboxylic acid (0.93 mmol) and isocyanide (0.93 mmol),

the mixture stirred for 24 h at room temp., methylene chloride (8 ml) added, the mixture washed with Na_2CO_3 soln., dried ($MgSO_4$), filtered, and concentrated → product (Y 82%; d.r. >99:1; e.e. >99%). Reaction proceeds with excellent diastereoselectivity under mild conditions. F.e. (thirteen; Y 71-83%; d.r. 92:8 to >99:1; e.e. 94 to >99%) and from optically pure acids or isonitriles, also application of the products as Wennemers-type organocatalysts (cf. *62*, 282s77), s. A. Znabet, E. Ruijter, F.J.J. de Kanter, V. Köhler, M. Helliwell, N.J. Turner, R.V.A. Orru, Angew. Chem., Int. Ed. *2010*, *49* (31), 5289-92 [DOI: 10.1002/anie.201001592]; application of biocatalytic desymmetrization and two multicomponent reactions to the synthesis of the hepatitis C drug, telaprevir, s. A. Znabet, M.M. Polak, E. Janssen, F.J.J. de Kanter, N.J. Turner, R.V.A. Orru, E. Ruijter, Chem. Commun. *2010*, *46* (42), 7918-20 [DOI: 10.1039/c0cc02823a]; sequential oxidative enzymatic desymmetrization-Ugi-type reaction-double ring closure s. *78*, 420.

Oxygen ↑ CC ↓↑ O

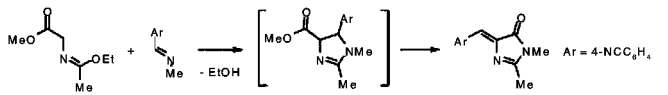
Without additional reagents *w.a.r.*

Ugi-type 4-component synthesis of α-arylaminocarboxylic acid amides via Smiles rearrangement ←

s. *70*, 356; in water (at 90°) instead of methanol (or toluene), incl. reaction with pyrimidinols, s. L. El Kaïm, L. Grimaud, S.R. Purumandla, Tetrahedron Lett. *2010*, *51* (38), 4962-4 [DOI: 10.1016/j.tetlet.2010.07.058].

4-Arylidene-Δ²-5-imidazolones from ar. aldimines via [3+2]-cyclocondensation with methyl 2-(1-ethoxyethylideneamino)acetate ○

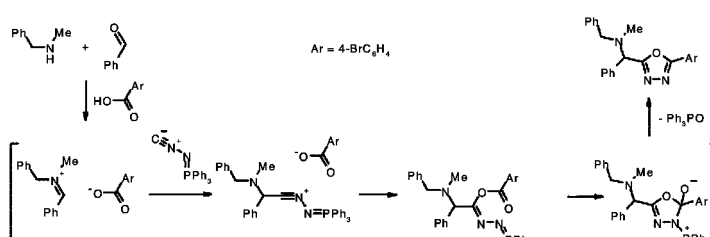
372.



under mild conditions. A mixture of N-methyl-4-cyanobenzaldimine (1 mmol) and methyl 2-(1-ethoxyethylideneamino)acetate (1.1 eq.) in ethanol (1 ml) stirred at room temp. overnight, and filtered → 4-(4-cyanobenzylidene)-1,2-dimethylimidazol-5-one. Y 96%. A diverse range of Schiff bases (from commercially available aldehydes and amines) cyclized with the stabilized imine ylid under the experimentally simple conditions (fifty-seven examples; Y 44-99%). F.e. and detailed spectroscopic data for the products s. A. Baldridge, J. Kowalik, L.M. Tolbert, Synthesis *2010* (14), 2424-36 [DOI: 10.1055/s-0029-1218796].

4-Component synthesis of 2-α-*tert*-amino-1,3,4-oxadiazoles from aldehydes, carboxylic acids, sec. amines and triphenylphosphine N-isocyanimine via Ugi condensation-intramolecular aza-Wittig synthesis

373.

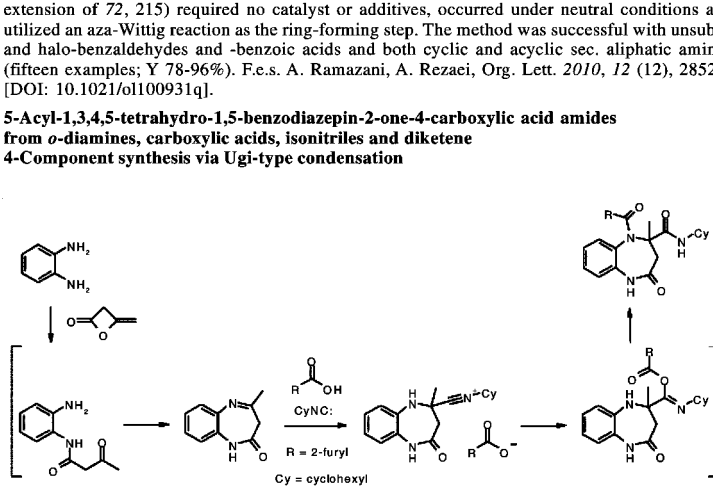


under mild conditions. A soln. of 4-bromobenzoic acid (1 mmol) in methylene chloride (5 ml) added dropwise to a stirred soln. of benzyl(methyl)amine (1 eq.), benzaldehyde (1 eq.) and tri-

phenylphosphine N-isocyanimine (1 eq.) in the same solvent (5 ml) at room temp. over 15 min, the mixture stirred for 2 h, concentrated *in vacuo*, and purified by flash chromatography on silica → N-benzyl-1-[5-(4-bromophenyl)-1,3,4-oxadiazol-2-yl]-N-methyl-1-phenylmethanamine. Y 87%. This novel and experimentally simple synthesis of 2,5-disubst. 1,3,4-oxadiazoles (an extension of *72*, 215) required no catalyst or additives, occurred under neutral conditions and utilized an aza-Wittig reaction as the ring-forming step. The method was successful with unsubst. and halo-benzaldehydes and -benzoic acids and both cyclic and acyclic sec. aliphatic amines (fifteen examples; Y 78-96%). F.e.s. A. Ramazani, A. Rezaei, Org. Lett. *2010*, *12* (12), 2852-5 [DOI: 10.1021/ol100931q].

5-Acyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2-one-4-carboxylic acid amides from *o*-diamines, carboxylic acids, isonitriles and diketene 4-Component synthesis via Ugi-type condensation ○

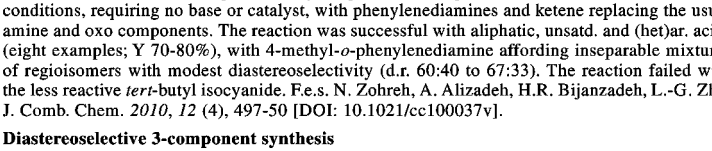
374.



A soln. of *o*-phenylenediamine (2 mmol) and diketene (1 eq.) in methylene chloride (2 ml) stirred at room temp. for 15 min, a soln. of 2-furoic acid (1 eq.) and cyclohexyl isocyanide (1 eq.) in toluene (3 ml) added, the mixture stirred under reflux (100-120°) until reaction complete (TLC; 8 h), solvent removed *in vacuo*, and the residue purified by chromatograpy on silica → N^2-cyclohexyl-1-(2-furylcarbonyl)-2-methyl-4-oxo-2,3,4,5-tetrahydro-1*H*-1,5-benzodiazepine-2-carboxamide. Y 77%. This efficient and experimentally simple multi-component reaction occurs under neutral conditions, requiring no base or catalyst, with phenylenediamines and ketene replacing the usual amine and oxo components. The reaction was successful with aliphatic, unsatd. and (het)ar. acids (eight examples; Y 70-80%), with 4-methyl-*o*-phenylenediamine affording inseparable mixtures of regioisomers with modest diastereoselectivity (d.r. 60:40 to 67:33). The reaction failed with the less reactive *tert*-butyl isocyanide. F.e.s. N. Zohreh, A. Alizadeh, H.R. Bijanzadeh, L.-G. Zhu, J. Comb. Chem. *2010*, *12* (4), 497-50 [DOI: 10.1021/cc100037v].

Diastereoselective 3-component synthesis of 6-amino-7-hydroxymethyl-3-azabicyclo[3.2.0]heptanes from α,β-ethylenealdehydes and sec. amines ○

375.

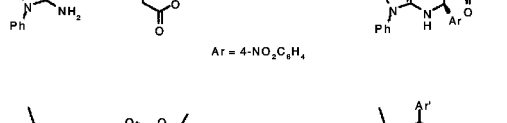


in one pot. Diethylamine (2 eq.) and ethyl 4-(benzylamino)crotonate (0.2 mmol) added to a mixture of 4-methoxycinnamaldehyde (2 eq.) and 4 Å molecular sieves in anhydrous methylene

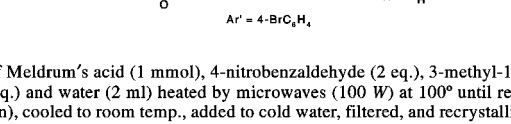
chloride (1 ml), the mixture stirred at room temp. for 42 h, concentrated *in vacuo*, $LiAlH_4$ (2 eq.) in anhydrous THF (1 ml) added, the mixture stirred for 3 h, cooled to 0°, quenched with water and 4 *M* aq. NaOH, and purified by chromatography on silica → (3-benzyl-7-*exo*-diethylamino-2-*exo*-*p*-methoxyphenyl-3-azabicyclo[3.2.0]hept-6-*endo*-yl)methanol. Y 66% (d.r. 24:1). In this efficient multi-component reaction the use of anhydrous conditions and 2-fold excess of amine and aldehyde components was essential for minimization of a pyrrolidine by-product (formed in <5% yield under these conditions but significant using stoichiometric reactants or alternative solvents). The initially formed product, although isolable, was relatively unstable and products were hence reduced to the stable alcohols *in situ* (seven examples; Y 52-73%), with diethylamine and pyrrolidine giving predominantly 2-*exo*-derivs. (d.r. 7:1 to 45:1) while dimethylamine gave an all-*cis*-configuration (2-*endo*) with 6-*exo*/*endo* ratios of 5:1 to 6.5:1. 2-Nitrocinnamaldehyde gave the highest diastereoselectivity (65:1), which was determined on the crude ester product due to incompatibility with $LiAlH_4$. Preliminary attempts at development of an asymmetric version were unsuccessful. F.e. and optimization s. K. Kriis, K. Ausmees, T. Pehk, M. Lopp, T. Kanger, Org. Lett. *2010*, *12* (10), 2230-3 [DOI: 10.1021/ol1005714].

Microwaves [s.a. under Et_3N, Triethylenediamine, CuBr, CuI, Montmorillonite, $AlCl_3$, $[Bu_4N]CN$, NH_4OAc, NH_4VO_3, 1-Methylimidazolium hydrogen sulfate and $FeCl_3$] [\\\\]
Hantzsch synthesis of sym. N-aryl-1,4-dihydropyridines in water s. *47*, 727s*78* ○

1,2,3,4-Tetrahydropyridine ring from cyclic enamines and two aldehyde molecules 3-Component (4 molecule) synthesis in water under microwave irradiation



376.



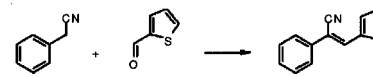
A mixture of Meldrum's acid (1 mmol), 4-nitrobenzaldehyde (2 eq.), 3-methyl-1-phenylpyrazol-5-amine (1 eq.) and water (2 ml) heated by microwaves (100 *W*) at 100° until reaction complete (TLC; 12 min), cooled to room temp., added to cold water, filtered, and recrystallized → 4′,6′-bis-(4-nitrophenyl)-2,2,3′-trimethyl-1′-phenyl-1′,4′,6′,7′-tetrahydrospiro[1,3]dioxane-5,5′-pyrazolo-[3,4-*b*]pyridine-4,6-dione. Y 86%. Two molecules of electron-diverse (het)ar. aldehydes underwent ring closure with the illustrated pyrazole or the analogous 3-methylisoxazol-5-amine and one molecule of Meldrum's acid to afford spirocyclic tetrahydropyridines within 9-13 min (sixteen examples; Y 77-86%), with structure confirmed by X-ray crystallography in one case. Interestingly, the corresponding N-H or N-Me pyrazoles incorporated only one molecule of aldehyde to afford **4-aryl-1,4,5,7-tetrahydropyrazolo[3,4-*b*]pyrid-6-ones**, with a similar range of aldehydes, within 6-9 min (ten examples; Y 88-93%). F.e.s. N. Ma, B. Jiang, G. Zhang, S.-J. Tu, W. Wever, G. Li, Green Chem. *2010*, *12* (8), 1357-61 [DOI: 10.1039/c0gc00073f].

Cesium oxide- or aminopropylsilyl-modified mesoporous silica ←
Heterogeneous Knoevenagel condensation with solid bases s. *46*, 713s*78* CO → C=C

Heterogeneous Claisen-Schmidt reaction s. *47*, 710s*78*

Sodium hydroxide/1,12-bis(dodecyldimethylammonio)dodecane dibromide ←
Phase transfer-catalyzed Knoevenagel condensation in water CHO → CH=C

377.



of ar. aldehydes under mild conditions. 2-Thienylcarboxaldehyde (1 mmol) and benzyl cyanide (1 eq.) added to a soln. of NaOH (1 eq.) and 1,12-bis(dodecyldimethylammonio)dodecane dibromide (2.5 mol%) in water (20 ml), the mixture sonicated at 25° until reaction complete (TLC; 10 min), the precipitate filtered off, and recrystallized → (Z)-2-phenyl-3-(thien-2-yl)acrylonitrile. Y 90%. A series of dicationic quaternary salts, readily available from inexpensive 1,ω-dihaloalkanes, gave higher yields than monocationic tetrabutylammonium bromide, with the best results obtained for the longest alkane (C12) spacer. The use of ultrasound produced a significant increase in reaction rate in the condensation of electron-diverse ar. aldehydes with benzyl cyanide or 3,3-dimethylbutan-2-one (nine examples; Y 67-99%; *p*-tolualdehyde gave 40% and 55%, respectively). F.e., catalyst prepn. and optimization s. I. Essen, C. Yolacan, F. Aydogan, Bull. Korean Chem. Soc. *2010*, *31* (8), 2289-92 [DOI: 10.5012/bkcs.2010.31.8.2289].

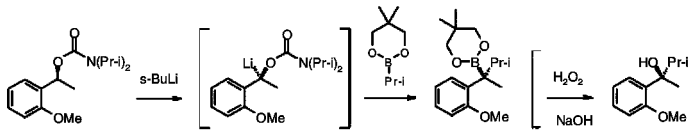
Sodium or potassium tert-butoxide *NaOBu-t or KOBu-t*
Base-catalyzed Biginelli synthesis s. *55*, 337*s78* ○

n-Butyllithium s.a. under Ti(OPr-i)$_4$ and ClTi(OPr-i)$_3$ *BuLi*

n-Butyllithium/bis(diisopropylamino)boryl chloride *BuLi/(i-Pr$_2$N)$_2$BCl*
α,β-Ethylenenitriles from aldehydes CHO → CH=CHCN
with LiOR cf. *11*, 821; (Z)-α,β-ethylenenitriles from acetonitrile with *n*-BuLi/bis(diisopropylamino)boryl chloride via the α-(diaminoboryl)acetonitrile carbanion s. T. Tomioka, Y. Takahashi, T.G. Vaughan, T. Yanase, Org. Lett. *2010*, *12* (10), 2171-3 [DOI: 10.1021/ol100534s].

sec-Butyllithium *s-BuLi*
***tert*-Benzylboronic acid esters** CH(OCON≤) → C(R)B(OR′)$_2$
from sec. benzyl carbamates and alkylboronic acid esters

378.



(Y 92% overall)

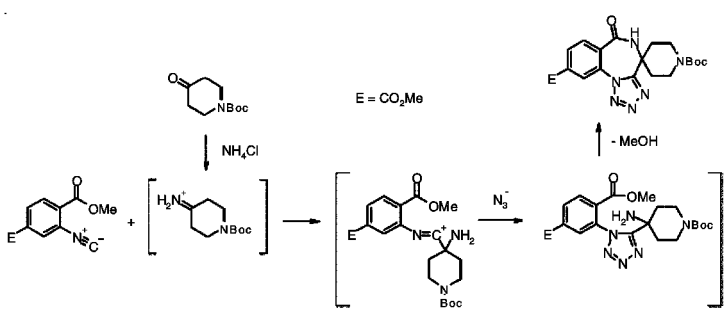
via lithiation with retention of chirality. *sec*-Butyllithium (1.1 eq.) in cyclohexane/hexane (92:8; 0.43 ml) added dropwise over 5 min to a vigorously stirred soln. of (S)-1-(2-methoxyphenyl)ethyl N,N-diisopropylcarbamate (0.5 mmol) in anhydrous ether (2 ml) at -75°, the mixture stirred for 20 min, neopentyl isopropylboronate (1.5 eq.) added dropwise over 5 min, the mixture stirred for 1 h, then at ambient temp. for 16 h, cooled to 0-5°, 1 *M* aq. KH_2PO_4 added with vigorous stirring [*caution!* gas evolution], the mixture stirred at room temp. for 10 min, extracted with ether, washed with water and brine, concentrated *in vacuo*, and purified chromatographically → (S)-2-[2-(2-methoxyphenyl)-3-methylbut-2-yl]-5,5-tetramethyl-1,3,2-dioxaborinane. Y 89% (e.e. 96%). A previous method for preparation of pinacolboronate analogs [s. J.L. Stymiest, V. Bagutski, R.M. French, V.K. Aggarwal, Nature *2008*, *456* (7223), 778-82 [DOI: 10.1038/nature07592]] gave only moderate chirality transfer for sterically demanding substrates, attributed to dissociation of an intermediate ate-complex to the lithiated carbamate, which is prone to racemization. In addition, efficient oxidation of the products to tert. alcohols was only achieved after a solvent change. Use of the less sterically hindered neopentyl boronate derivs. not only eliminated the dissociation but allowed **chiral tert. benzyl alcohols** to be isolated in a one-pot procedure (with

retention of stereochemistry) via conventional oxidative work-up, without requirement for solvent exchange (eleven examples; Y 48-98% as the alcohols; e.e. 96-99%). Furthermore, improvement in preparation of pinacolatoborane analogs was achieved in the presence of a Lewis acid ($MgBr_2$/MeOH), giving excellent enantioselectivity for all eighteen examples (Y 61-93%; e.e. 96-99%). F.e. and substrate prepn. s. V. Bagutski, R.M. French, V.K. Aggarwal, Angew. Chem., Int. Ed. *2010*, *49* (30), 5142-5 [DOI: 10.1002/anie.201001371]; chiral 2-subst. sec. alcohols from 1-lithiated carbamates and boronic acid esters cf. J.L. Stymiest, G. Dutheuil, A. Mahmood, V.K. Aggarwal, ibid. *2007*, *46* (39), 7491-4 [DOI: 10.1002/anie.200702146].

Sodium bis(trimethylsilyl)amide s. under Triethylenediamine $NaN(SiMe_3)_2$
Sodium acetate s. under AgOAc $NaOAc$

Sodium azide/ammonium chloride NaN_3/NH_4Cl
4,5-Dihydro-6*H*-tetrazolo[1,5-*a*][1,4]benzodiazepin-6-ones ○
from *o*-isocyanocarboxylic acid esters and ketones
Double ring closure via Ugi-type condensation-1,3-dipolar cycloaddition

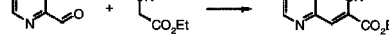
379.



under mild conditions. A soln. of N-Boc-4-piperidone (1 mmol), NaN_3 (1.2 eq.), NH_4Cl (1.2 eq.) and dimethyl 2-isocyanoterephthalate (1 eq.) in water/methanol (1:3; 15 ml) stirred vigorously until isonitrile consumed (TLC; 27 h), the precipitate filtered off, and dried in air → 1-*tert*-butyl-9′-methyl 6′-oxo-5′,6′-dihydro-1*H*-spiro[piperidine-4,4′-tetrazolo[1,5-*a*][1,4]benzodiazepine]-1,9′-dicarboxylate. Y 61%. This novel and experimentally simple synthesis of heteroannulated tetrazoles was successful with cyclic and acyclic ketones (nineteen examples; Y 32-81%) in the presence of ester, halo and carbamate functionality, with structures confirmed by X-ray analysis in one case. The use of aliphatic aldehydes in place of ketones gave no isolable products, while methylamine hydrochloride in place of NH_4Cl afforded only the initially-formed tetrazole, which could not be cyclized. F.e.s. R.S. Borisov, A.I. Polyakov, L.A. Medvedeva, V.N. Khrustalev, N.I. Guranova, L.G. Voskressensky, Org. Lett. *2010*, *12* (17), 3894-7 [DOI: 10.1021/ol101590w].

Poly(N-methyl-4-vinylpyridinium hydroxide)-mesoporous silica composite ←
Knoevenagel condensation with a highly active solid hydroxide base CO → C=C

380.



in water. A mixture of pyridine-2-carbaldehyde (2 mmol), ethyl cyanoacetate (1 eq.) and polymeric catalyst (120 mg) in water (10 ml) stirred vigorously at 95° until reaction complete (TLC; 5 min), cooled to 10°, filtered, the solid extracted with hot ethanol, and recrystallized → ethyl 2-cyano-3-(pyrid-2-yl)propenoate. Y 99%. The mesoporous silica-supported catalyst provided an experimentally simple and effective method for the selective condensation of electron-diverse

(het)ar. aldehydes and cyanoacetate, with reactions complete within 5-35 min (eight examples; Y 70-99%). The catalyst was recycled four times without loss in reactivity. F.e. and catalyst prepn. and characterization s. R.J. Kalbasi, M. Kolahdoozan, A. Massah, K. Shahabian, Bull. Korean Chem. Soc. *2010, 31* (9), 2618-26 [DOI: 10.5012/bkcs.2010.31.9.2618].

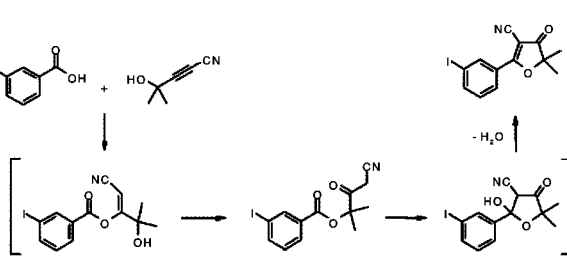
Ion exchanger IRA-400 (hydroxide) or Piperidine ←
3-Component synthesis of the 2-amino-3-cyano-4*H*-pyran ring ○

s. *61*, 340s*67*; 4*H*-benzo[*b*]pyran derivs. with the solid quaternary ammonium base, IRA-400 (hydroxide), in water s. M.M. Khodaei, K. Bahrami, A. Farrokhi, Synth. Commun. *2010, 40* (10), 1492-9 [DOI: 10.1080/00397910903097336]; 6-[chloro(fluoro)pyrid-3-yl]-derivs. with piperidine s. Z. Ye, R. Xu, X. Shao, X. Xu, Z. Li, Tetrahedron Lett. *2010, 51* (38), 4991-4 [DOI: 10.1016/j.tetlet.2010.07.065]; pyrano[2,3-*d*]pyrimidine derivs. with zinc L-prolinate s. M.M. Heravi, A. Ghods, K. Bakhtiari, F. Derikvand, Synth. Commun. *2010, 40* (13), 1927-31 [DOI: 10.1080/00397910903174390]; coumarin-condensed 4-spiro-4*H*-pyran derivs. with alum s. A.R. Karimi, F. Sedaghatpour, Synthesis *2010* (10), 1731-5 [DOI: 10.1055/s-0029-1219748]; f. coumarin-fused tricyclics with hexamethylenetetramine as catalyst s. H.-J. Wang, J. Lu, Z.-H. Zhang, Monatsh. Chem. *2010, 141* (10), 1107-12 [DOI: 10.1007/s00706-010-0383-4]; microwave-assisted conversion s. A.F. Mahmoud, F.F.A. El-Latif, A.M. Ahmed, Chin. J. Chem. *2010, 28* (1), 91-6 [DOI: 10.1002/cjoc.201090041]; spiro[4*H*-pyran-3,3′-oxindole] derivs. in water with L-proline s. Y. Li, H. Chen, C. Shi, D. Shi, S. Ji, J. Comb. Chem. *2010, 12* (2), 231-7 [DOI: 10.1021/cc9001185]; **organocatalyzed asym. synthesis** of spiro[4*H*-pyran-3,3′-oxindole] derivs. under mild conditions with cupreine as organocatalyst s. W.-B. Chen, Z.-J. Wu, Q.-L. Pei, L.-F. Cun, X.-M. Zhang, W.-C. Yuan, Org. Lett. *2010, 12* (14), 3132-5 [DOI: 10.1021/ol1009224].

Piperidine $(CH_2)_5NH$
4-Aryl-3-carbamyl-3,4-dihydro-2-pyridone-5-carboxylic acid esters
from ar. aldehydes – 3-Component synthesis s. *78*, 541

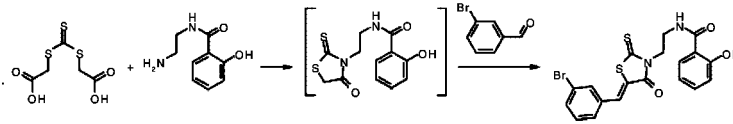
Triethylamine Et_3N
4-Cyano-3(2*H*)-furanones from α,β-acetylene-γ-hydroxynitriles and carboxylic acids

381.



5-Aryl-4-cyano-3(2*H*)-furanones. Triethylamine (1 eq.) added dropwise over 1 min to a soln. of 3-iodobenzoic acid (1 mmol) and 1-cyano-3-hydroxy-3-methylbut-1-yne (1 eq.) in acetonitrile (6 ml), the resulting mixture stirred at 20-25° for 48 h, solvent removed *in vacuo*, and the residue purified by recrystallization from ether → 2-(3-iodophenyl)-5,5-dimethyl-4-oxo-4,5-dihydro-3-furancarbonitrile. Y 80%. This mild, transition metal-free domino reaction is applicable to a range of arylcarboxylic acids, reacting with tert. propargyl alcohol derivs. to afford the title compds. in yields of 67-86% (ten examples). Reaction proceeds **via** intermediate **α′-acoxy-α-cyanoketones**, which may be isolated and cyclized on further treatment with triethylamine. With sterically-hindered arylcarboxylic acids, such as *o*-toluic acid, the acoxycyanoketones are formed as major products (3:1) under the standard conditions. Aliphatic acids afford mixtures of the expected 3(2*H*)-furanones along with intermediate keto-esters (1-2:1), indicating potential for further optimization. F.e.s. B.A. Trofimov, O.A. Shemyakina, A.G. Mal'kina, I.A. Ushakov, O.N. Kazheva, G.G. Alexandrov, O.A. Dyachenko, Org. Lett. *2010, 12* (14), 3200-3 [DOI: 10.1021/ol1011532].

Triethylamine/microwaves *Et_3N/[\\\\]*
(Z)-5-Arylidenerhodanines from prim. amines and ar. aldehydes via Holmberg reaction-Knoevenagel condensation under microwave irradiation

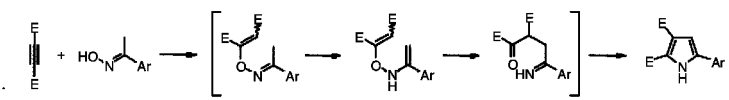
382. 

Triethylamine (1 eq.) and startg. amine (1 eq.) added to a soln. of bis(carboxymethyl) trithiocarbonate (1 eq.) in DME (1 ml), heated at 90° under microwave irradiation for 10 min, 3-bromobenzaldehyde (1 eq.) added, the mixture heated at 110° under microwave irradiation for 5 min, evaporated to dryness, methanol added, and the precipitate collected → product. Y 69%. This multi-component synthesis is fast, efficient and inexpensive and avoids the use of toxic carbon disulfide. It is applicable to a variety of amines, incl. phenethyl, benzyl, propargyl and aliphatic ones, and to ar. or hetar. aldehydes. F.e. (eleven; Y 31-64%; purity generally >99%) incl. reaction of a masked aldehyde, aminoacetaldehyde diethyl acetal, s. M. Radi, L. Botta, G. Casaluce, M. Bernardini, M. Botta, J. Comb. Chem. *2010, 12* (1), 200-5 [DOI: 10.1021/cc9001789].

1(S)-Benzyl-N²-methylethylenediamine/N-(carbo-tert-butoxy)-D-phenylglycine or 9-prim-Amino-9-deoxycinchona alkaloids ←
2-Cyclohexenones from α,β-ethyleneketones and oxo compds. by organocatalyzed asym. Michael addition-intramolecular aldol condensation
with (S,S)-1,2-diaminocyclohexane/(S,S)-cyclohexane-1,2-dicarboxylic acid/KOH cf. *77*, 402; highly functionalized chiral 2-cyclohexenones with 1(S)-benzyl-N²-methylethylenediamine/N-(carbo-*tert*-butoxy)-*D*-phenylglycine s. Y.-Q. Yang, Z. Chai, H.-F. Wang, X.-K. Chen, H.-F. Cui, C.-W. Zheng, H. Xiao, P. Li, G. Zhao, Chem. Eur. J. *2009, 15* (48), 13295-8 [DOI: 10.1002/chem.200901541]; chiral 3-spirooxindole derivs. with 9-*prim*-amino-9-deoxycinchona alkaloids s. L.-L. Wang, L. Peng, J.-F. Bai, Q.-C. Huang, X.-Y. Xu, L.-X. Wang, Chem. Commun. *2010, 46* (42), 8064-6 [DOI: 10.1039/c0cc03032e]; 4,4-disubst. 2-cyclohexenones from α-subst. aldehydes with N′-[*p*-(carbododecyloxy)benzenesulfonyl]-(S)-prolinamide/benzylamine s. H. Yang, R.G. Carter, Org. Lett. *2010, 12* (13), 3108-11 [DOI: 10.1021/ol1011955].

Cupreine ←
Organocatalyzed asym. 3-component synthesis of the 2-amino-3-cyano-4*H*-pyran ring
s. *61*, 340s*78*

Triethylenediamine/microwaves *DABCO/[\\\\]*
Pyrroles from oximes and electron-deficient acetylene derivs. via regioselective thermal rearrangement of O-vinyloximes under microwave irradiation

383. 

Ar = 4-BrC_6H_4 E = CO_2Me

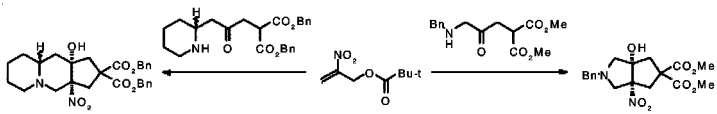
in one pot. Dimethyl acetylenedicarboxylate (1 eq.) added to a soln. of DABCO (10 mol%) and (E)-1-(4-bromophenyl)ethanone oxime (0.9 mmol) in dry toluene (2.5 ml), the mixture heated by microwaves at 80° for 5 min then at 170° for 45 min, concentrated *in vacuo*, and purified by flash chromatography on silica → dimethyl 5-(4-bromophenyl)-1*H*-pyrrole-2,3-dicarboxylate. Y 67%. This novel and experimentally simple method avoids the use of strong bases and allows direct synthesis of di-, tri- and tetra-subst. pyrroles (ten examples; Y 39-70%) from oximes. The method

was successful with (het)aryl methyl and benzyl ketoximes and also with cyclohexanone oxime but failed for phenyl-ethyl, acyclic aliphatic ketoximes and aldoximes (presumed due to instability in the thermal step). The initial addition was catalyzed effectively by DMAP, Ph_3P and DABCO, with the latter being the reagent of choice due to ease of work-up. In some cases products were isolated as N-Boc derivs. via addition of di-*tert*-butyl dicarbonate to the crude mixture following irradiation. F.e., optimization and substrate prepn. s. S. Ngwerume, J.E. Camp, J. Org. Chem. *2010*, *75* (18), 6271-4 [DOI: 10.1021/jo1011448].

Triethylenediamine/sodium bis(trimethylsilyl)amide *DABCO/NaN(SiMe$_3$)$_2$*

Stereospecific double ring closures
of 2-nitroallyl pivalate and keto-functionalized dinucleophiles

384.



(Y 33%)

5-Nitro-3-azabicyclo[3.3.0]octan-1-ols. A soln. of 2-nitroallyl pivalate (1.1 eq.) in THF (0.2 ml) added to a soln. of DABCO (3 eq.) in THF (1 ml) at -78°, the clear yellow soln. stirred for 15 min, a suspension of startg. ketone (0.061 mmol) in THF (1 ml) added, the mixture stirred for 1 h, diluted with THF (37.8 ml), a soln. of NaN($SiMe_3$)$_2$ (2 eq.) in toluene (0.2 ml) added, the mixture warmed to 0° over 4 h, stirred at room temp. for 12 h, concentrated *in vacuo*, suspended in ethyl acetate, washed with satd. aq. Na_2CO_3, concentrated, and purified chromatographically → *cis*-N-benzyl-7,7-bis(methoxycarbonyl)-1-hydroxy-5-nitro-3-azabicyclo[3.3.0]octane. Y 70%. The *cis*-fused product was thermodynamically favored in this case. The methodology appears to be generally applicable to cyclization of ketones containing two α or β nucleophilic centers, with the formation of 3 new bonds. Examples of N- and C-based nucleophilic centers are described in syntheses of 5,5-, 5,6- and 6,6-bicyclics, all affording *cis*-fused products exclusively (six examples; Y 31-83%). F.e. and substrate prepn. s. B.D. Chandler, J.T. Roland, Y. Li, E.J. Sorensen, Org. Lett. *2010*, *12* (12), 2746-9 [DOI: 10.1021/ol100845z].

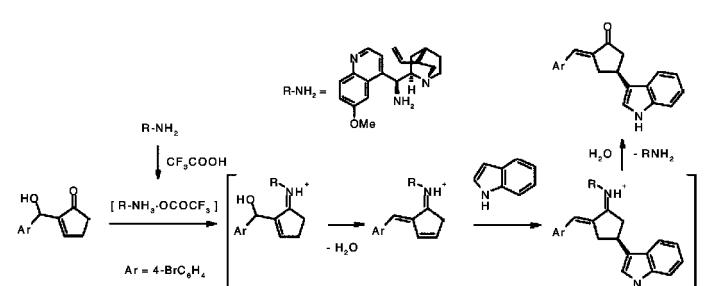
Nitrogen-doped carbon [pyridine-fused polyarene networks] ←

Heterogeneous Knoevenagel condensation with solid bases s. *46*, 713s*78* CO → C=C

9-Amino-9-deoxy-epi-quinine/trifluoroacetic acid ←

Regioselective organocatalyzed asym. 3-homoallylation of indoles ←
with cyclic 2-ethylenealcohols

385.

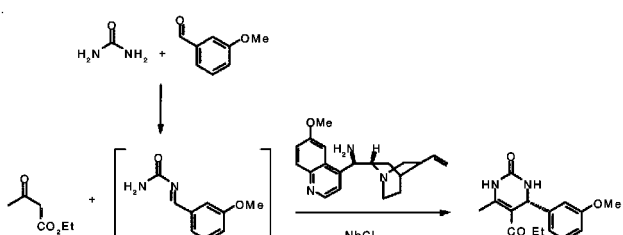


Chiral 2-benzylidene-4-(indol-3-yl)cyclopentanones. 9-Amino-9-deoxy-*epi*-quinine (10 mol%) added to a soln. of α-hydroxy-2-(4-bromobenzyl)cyclopent-2-enone (2 eq.) and indole (0.2 mmol)

in isopropyl acetate/THF (1:1; 2 ml), the soln. stirred for 5 min, trifluoroacetic acid (20 mol%) added, the mixture heated at 30° until reaction complete (TLC; 5 d), and purified by chromatography on silica → (S)-2-(4-bromobenzylidene)-4-indol-3-ylcyclopentanone. Y 88% (e.e. 93%). This novel iminium-assisted direct nucleophilic substitution of readily available Morita-Baylis-Hillman adducts unexpectedly demonstrated δ-selectivity, with careful optimization affording the unexpected regioisomers as sole products (fifteen examples; Y 68-92%; e.e. 79-83%), and with an acid co-catalyst essential for high enantioselectivity. The reaction was tolerant of 5- and 6-substituents on the indole ring but methylation of indole NH resulted in significant reduction in enantioselectivity (Y 70%; e.e. 47%) as did the presence of a bulky 2-phenyl substituent (Y 85%; e.e. 57%), while 2-methylindole gave a 35:65 mixture of γ/δ adducts (Y 83%; e.e. 93%). Structures were confirmed by X-ray crystallography in one case. F.e. and optimization s. Z. Qiao, Z. Shafiq, L. Liu, Z.-B. Yu, Q.-Y. Zheng, D. Wang, Y.-J. Chen, Angew. Chem., Int. Ed. *2010*, *49* (40), 7294-8 [DOI: 10.1002/anie.201003131].

9-Amino-9-deoxyquinine/niobium pentachloride ←
Asym. Biginelli synthesis under cooperative catalysis ○
with a chiral organocatalyst and a Lewis acid under mild conditions

386.



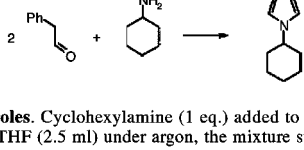
A chiral quinine-based primary amine and $NbCl_5$ act *synergistically* in a cooperative asym. Biginelli synthesis with yields up to 99% and enantioselectivity up to 84% (or 99%). **E:** A catalytic amount of 9-amino-9-deoxyquinine (10 mol%) and $NbCl_5$ (10 mol%) added to a vial containing the startg. aldehyde (1 mmol), urea (1.2 eq.) and ethyl acetoacetate (5 eq.) in dioxane (2 ml), stirred vigorously at room temp. for 16 h, followed by aq. work-up, extraction with ethyl acetate, and purification by chromatography on silica gel → product. Y 88% (e.e. 84%). The procedure is applicable to a range of aromatic aldehydes, enantioselectivity being highest with substrates possessing electron-withdrawing groups (nine examples; Y 48-99%; e.e. 43-84%). Interestingly, the enantioselectivity was improved (up to 99%) by adopting an alternative *non-chromatographic* work-up (simply by precipitating the product with small amounts of ethanol and water). Conversions were poor in the absence of the Lewis acid, and reaction failed with other metal salts (based on In(III), Li, Mg, Zn, Ce(III), Ni(II) and Ag(I)), while enantioselectivity was lower with Fe(III) and Sb(III) salts. A dual activation pathway is envisaged: the keto-ester reacting with the chiral amine to give an enamine which is activated by the Lewis acid through coordination prior to asym. addition to *in situ*-generated N-arylideneurea and ring closure. cf. *70*, 370s77. F.e.s. Y.-F. Cai, H.-M. Yang, L. Li, K.-Z. Jiang, G.-Q. Lai, J.-X. Jiang, L.-W. Xu, Eur. J. Org. Chem. *2010* (26), 4986-90 [DOI: 10.1002/ejoc.201000894]; with HCl as cocatalyst (e.e. up to 78%) s. D. Ding, C.-G. Zhao, ibid. *2010* (20), 3802-5 [DOI: 10.1002/ejoc.201000448].

Chiral cyclic bis(N-oxides) s. under $Sc(OTf)_3$ ←

Silver acetate/sodium acetate *AgOAc/NaOAc*

Pyrroles from two aldehyde molecules and prim. amines
Silver(I)-mediated oxidative ring closure

387.



Sym. 1,3,4-trisubst. pyrroles. Cyclohexylamine (1 eq.) added to a soln. of phenylacetaldehyde (0.5 mmol) in anhydrous THF (2.5 ml) under argon, the mixture stirred at room temp. for 0.5 h, AgOAc (2 eq.) and NaOAc (2 eq.) added sequentially, the soln. heated at 60° for 8 h, cooled to room temp., filtered through Celite, concentrated *in vacuo*, and purified chromatographically → 1-cyclohexyl-3,4-diphenyl-1*H*-pyrrole. Y 80%. This experimentally simple procedure uses equimolar quantities of aliphatic aldehydes and electron-rich/neutral anilines or aliphatic amines to afford 1,3,4-trisubst. pyrroles (eighteen examples; Y 55-80%) in the presence of alkyl chloride, Boc-amines and ethers, and is tolerant of bulky amine components. An NH analog, 3,4-diphenylpyrrole, was prepared using NH_3 (balloon) as amine component (Y 25%). Reactions with two different aldehydes were unselective, affording mixtures of all three possible pyrrole derivs. The method was applied to the rapid synthesis of purpurone (Y 59%). F.e. and optimization s. Q. Li, A. Fan, Z. Lu, Y. Cui, W. Lin, Y. Jia, Org. Lett. *2010, 12* (18), 4066-9 [DOI: 10.1021/ol101644g].

Copper(II) nitrate *$Cu(NO_3)_2$*

Catalytic Biginelli synthesis

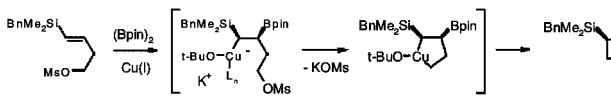
update s. *55*, 337s*77*; with $Cu(NO_3)_2 \cdot 3H_2O$ without solvent s. D.-C. Wang, H.-M. Guo, G.-R. Qu, Synth. Commun. *2010, 40* (8), 1115-22 [DOI: 10.1080/00397910903043009]; under *heterogeneous* conditions with HBF_4-SiO_2 s. V.T. Kamble, D.B. Muley, S.T. Atkore, S.D. Dakore, Chin. J. Chem. *2010, 28* (3), 388-92 [DOI: 10.1002/cjoc.201090084]; solvent-free, inexpensive method with $AlCl_3 \cdot 6H_2O$ under microwaves s. D. Kumar, J.S. Sandhu, Indian J. Chem. *2010, 49B* (3), 360-3; rapid method with yttrium(III) acetate hydrate s. G. Aridoss, Y.T. Jeong, Bull. Korean Chem. Soc. *2010, 31* (4), 863-8 [DOI: 10.5012/bkcs.2010.31.04.863]; with readily recyclable $Ce(SO_4)_2$-SiO_2 s. W. Pei, Q. Wang, Synth. Commun. *2010, 40* (8), 1209-15 [DOI: 10.1080/00397910903061076]; with the acidic ionic liquid, [bmim]HSO_4, as catalyst under microwaves s. V. Singh, S. Kaur, R. Ratti, G.L. Kad, J. Singh, Indian J. Chem. *2010, 49B* (5), 611-6; *in water* with thiamine hydrochloride under ultrasonication s. P.G. Mandhane, R.S. Joshi, D.R. Nagargoje, C.H. Gill, Tetrahedron Lett. *2010, 51* (23), 3138-40 [DOI: 10.1016/j.tetlet.2010.04.037]; with thiamine in ethanol or neat cf. M. Lei, L. Ma, L. Hu, Monatsh. Chem. *2010, 141* (9), 1005-8 [DOI: 10.1007/s00706-010-0357-6]; condensation with acyl pyruvates using Me_3SiCl s. S.V. Ryabukhin, A.S. Plaskon, S.S. Bondarenko, E.N. Ostapchuk, O.O. Grygorenko, O.V. Shishkin, A.A. Tolmachev, Tetrahedron Lett. *2010, 51* (32), 4229-32 [DOI: 10.1016/j.tetlet.2010.06.032]; solvent-free method with NH_4VO_3 under microwaves s. K.S. Niralwad, B.B. Shingate, M.S. Shingare, ibid. *2010, 51* (28), 3616-8 [DOI: 10.1016/j.tetlet.2010.04.118]; with vanadium hydrogen sulfate s. F. Shirini, A. Yahyazadeh, M. Abedini, D.I. Langroodi, Bull. Korean Chem. Soc. *2010, 31* (6), 1715-8 [DOI: 10.5012/bkcs.2010.31.6.1715]; solvent-free method with $NaHSO_4$ s. Q. Cheng, Q. Wang, X. Xu, M. Ruan, H. Yao, X. Yang, J. Heterocycl. Chem. *2010, 47* (3), 624-8 [DOI: 10.1002/jhet.368]; without solvent using $H_6P_2W_{18}O_{62} \cdot 18H_2O$ s. M.M. Heravi, F. Derikvand, L. Ranjbar, F.F. Bamoharram, Synth. Commun. *2010, 40* (9), 1256-63 [DOI: 10.1080/00397910903062272]; solvent-free *base-catalyzed* procedure with NaOBu-*t* under microwaves s. I.T. Phucho, A, Nongpiur, R. Nongrum, R.L. Nongkhlaw, Indian J. Chem. *2010, 49B* (3), 346-50; 4,5,6-triaryl-3,4-dihydro-2(1*H*)-pyrimidin-ones and -ethiones with a little KOBu-*t* in ethanol s. M.M. Heravi, F. Derikvand, L. Ranjbar, F.F. Bamoharram, Synth. Commun. *2010, 40* (9), 1256-63 [DOI: 10.1080/00397910903062272]; **Biginelli synthesis with acylals** using $FeCl_3 \cdot 6H_2O$ without solvent under microwaves cf. M.M. Majd, K. Saidi, H. Khabazzadeh, Phosphorus, Sulfur Silicon Relat. Elem. *2010, 185* (2), 325-9 [DOI: 10.1080/10426500902796931].

Copper(I) triflate/chiral bis(Δ^2-imidazolines) *[Cu(I)]**
Asym. 3-component synthesis of 2-acetyleneamines s. *63*, 356s*78* CO → C(N≤)C≡C

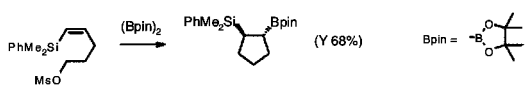
Copper(II) triflate s. under NH_4OAc *$Cu(OTf)_2$*
Copper(II) chloride s. under i-Bu_2AlH *$CuCl_2$*

Copper(II) sulfate/p-toluenesulfonic acid *$CuSO_4$/TsOH*
N-Condensed imidazole ring ○
from cyclic amidines, terminal acetylene derivs. and aldehydes
imidazo[1,2-*a*]pyridines with CuCl/$Cu(OTf)_2$ cf. *77*, 404; with $CuSO_4$/TsOH s. P. Liu, L.-s. Fang, X. Lei, G.-q. Lin, Tetrahedron Lett. *2010*, *51* (35), 4605-8 [DOI: 10.1016/j.tetlet.2010.05.139].

Copper(I) chloride/1,3-bis(diphenylphosphino)propane/potassium tert-butoxide ←
Cyclobutaneboronic acid esters from sulfonyloxy-3-ethylenes □
Stereospecific copper(I)-catalyzed ring closure



388.



***cis*-2-Silylcyclobutaneboronic acid esters**. A soln. of *t*-BuOK (1 eq.) in THF (0.5 ml) added to a mixture of CuCl (5 mol%), dppp (5 mol%) and bis(pinacolato)diboron (2 eq.) under argon in a sealed vial, the mixture stirred for 30 min at room temp., startg. homoallylic methanesulfonate (0.5 mmol; E/Z 96:4) added, the mixture stirred vigorously until reaction complete (GC or TLC; 48 h), the viscous soln. filtered through silica, concentrated *in vacuo*, and purified by flash chromatography on silica → *cis*-1-[dimethyl(benzyl)silyl]-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclobutane. Y 81% (*cis/trans* 96:4). This novel stereospecific tandem boronation/cyclization was successful for homoallylic sulfonates terminated with silane or electron-neutral/rich aryl functionality (ten examples; Y 60-89%), (E)-isomers affording *cis*-products and (Z)-isomers affording *trans*-derivs. Electron-poor aryl derivs. gave low yields (two examples; 28%, 39%), however, while alkyl terminated analogs were unreactive. The presence of Cu(I), ligand and base (1 eq.) and the use of vigorous stirring were essential for success, and the reaction occurred without detection of regioisomeric products. The method was extended to the preparation of cyclopentanes (two examples; Y 68%, 78%) but cyclohexane analogs were only formed in trace amounts. F.e., substrate prepn. and product derivatization s. H. Ito, T. Toyoda, M. Sawamura, J. Am. Chem. Soc. *2010*, *132* (17), 5990-2 [DOI: 10.1021/ja101793a].

Copper(I) bromide/microwaves *CuBr/[\\\\\]*
Copper(I) iodide/microwaves or polyethylene glycol *CuI/[\\\\\] or PEG*
Copper(II)-exchanged molecular sieves *[Cu(II)]*
Gold nanoparticles-in-mesoporous carbon nitride *Au-MCN*
3-Component synthesis of 2-acetyleneamines CO → C(N≤)C≡C
update s. *66*, 353s*76*; from ketones with CuI under microwave irradiation s. O.P. Pereshivko, V.A. Peshkov, E.V. Van der Eycken, Org. Lett. *2010*, *12* (11), 2638-41 [DOI: 10.1021/ol1008312]; from aldehydes s. J.B. Bariwal, D.S. Ermolat'ev, E.V. Van der Eycken, Chem. Eur. J. *2010*, *16* (11), 3281-4 [DOI: 10.1002/chem.200903143]; from aldehydes with CuI in PEG for improved recovery of the catalyst s. Q. Zhang, J.-X. Chen, W.-X. Gao, J.-C. Ding, H.-Y. Wu, Appl. Organomet. Chem. *2010*, *24* (11), 809-12 [DOI: 10.1002/aoc.1707]; *heterogeneous* procedure with copper(II)-exchanged 4 Å molecular sieves s. A. Fodor, Á. Kiss, N. Debreczeni, Z. Hell, I. Gresits, Org. Biomol. Chem. *2010*, *8* (20), 4575-81 [DOI: 10.1039/c0ob00224k]; with gold nanoparticles in the channels of mesoporous carbon nitride s. K.K.R. Datta, B.V.S. Reddy, K. Ariga, A. Vinu, Angew. Chem., Int. Ed. *2010*, *49* (34), 5961-5 [DOI: 10.1002/anie.201001699]; diversity-oriented

synthesis of benzo-condensed 2-(alk-1-ynyl)-N-heterocyclics by *intramolecular* conversion with CuBr under microwaves s. J.B. Bariwal, D.S. Ermolat'ev, T.N. Glasnov, K. Van Hecke, V.P. Mehta, L. Van Meervelt, C.O. Kappe, E.V. Van der Eycken, Org. Lett. *2010, 12* (12), 2774-7 [DOI: 10.1021/ol1008729]; with $NiCl_2$ s. S. Samai, G.C. Nandi, M.S. Singh, Tetrahedron Lett. *2010, 51* (42), 5555-8 [DOI: 10.1016/j.tetlet.2010.08.043]; **asym. 3-component synthesis** from ar. aldehydes (cf. *63*, 356s*71*) with [CuOTf]-toluene and a chiral bis(Δ^2-imidazoline) as ligand (pybim) s. S. Nakamura, M. Ohara, Y. Nakamura, N. Shibata, T. Toru, Chem. Eur. J. *2010, 16* (8), 2360-2 [DOI: 10.1002/chem.200903550].

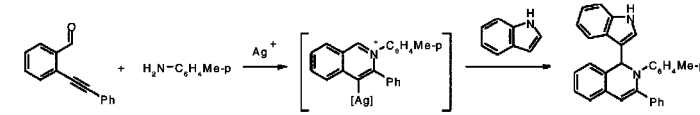
Chiral binuclear (1,3,4-triarylimidazolidin-2-ylidene)silver(I) complex s. under i-Bu_2AlH ←

Silver triflate/sodium sulfate *AgOTf/Na_2SO_4*

3-Component ring closures of *o*-acetylenealdehydes

1-(Indol-3-yl)-1,2-dihydroisoquinolines from indoles and prim. amines

389.



via 4-metalloisoquinolinium salts. Indole (2 eq.) and AgOTf (5 mol%) added to a mixture of startg. 2-alkynylbenzaldehyde (0.5 mmol), amine (1 eq.), and Na_2SO_4 (2 eq.) in acetonitrile (2 ml), the mixture stirred vigorously at room temp. until reaction complete, diluted with ethyl acetate, quenched with water, the organic layer washed with brine, dried (Na_2SO_4), concentrated *in vacuo*, and the residue purified by chromatography on silica gel → 1-(1*H*-indol-3-yl)-3-phenyl-2-*p*-tolyl-1,2-dihydroisoquinoline. Y 90%. The method is applicable to a variety of indoles (bearing electron-donating or -withdrawing groups on the aromatic ring), anilines or alkyl amines, and 2-alkynylbenzaldehydes (which may possess an electron-withdrawing group on the aromatic backbone). Similar results were obtained with CuI, $Cu(OTf)_2$ or $Pd(OAc)_2$ as catalysts, but 1,1,1-arylbis(indolyl)methanes were obtained with Lewis acids such as $FeCl_3$, $Zn(OTf)_2$, $Yb(OTf)_3$, $Bi(OTf)_3$ or $Dy(OTf)_3$. F.e. (twenty-six; Y 37-93%) s. X. Yu, J. Wu, J. Comb. Chem. *2010, 12* (2), 238-44 [DOI: 10.1021/cc9001263]; **(Z)-1-ene-2,2-dicyano-3-(indol-1-yl)indans** from indoles and malononitrile with Cs_2CO_3/Na_2SO_4/pyridine in acetonitrile s. G. Qiu, Q. Ding, Y. Peng, J. Wu, Tetrahedron Lett. *2010, 51* (33), 4391-4 [DOI: 10.1016/j.tetlet.2010.06.065]; **1-methyleneindans** from *o*-ethynylaldehydes and active methylene groups with *L*-proline/CuI/*i*-Pr_2NEt and Hantzsch ester as hydride source, **also 4-aryl-1,2,3-triazoles** with BnN_3 in place of the base, s. D.B. Ramachary, R. Mondal, C. Venkaiah, Eur. J. Org. Chem. *2010* (17), 3205-10 [DOI: 10.1002/ejoc.201000220].

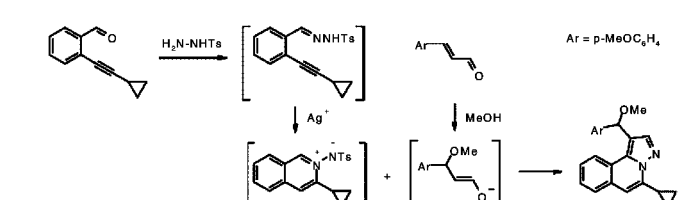
Silver triflate/tosylhydrazine/potassium hydroxide *AgOTf/TsNHNH$_2$/KOH*

1-α-Alkoxypyrazolo[5,1-*a*]isoquinolines

from *o*-acetylenealdehydes and α,β-ethyleneoxo compds.

Silver-catalyzed 4-component double ring closure via isoquinolinium N-tosylimides

390.



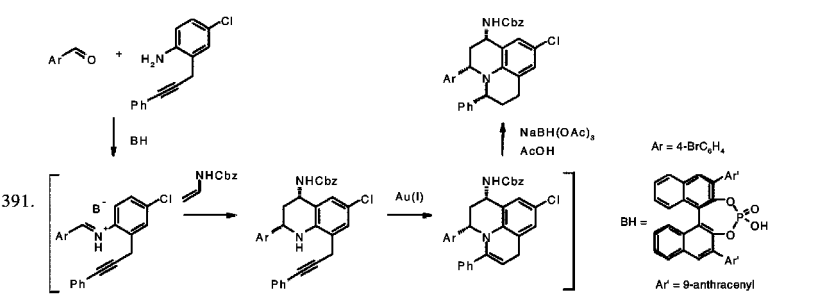
An alternative course for reaction of *o*-acetylene-N-tosylhydrazones, α,β-ethylenealdehydes (or enones) and alcohols has been investigated in the *absence* of an N-heterocyclic carbene (cf. *78*,

306), reaction being of greater generality, being applicable to alkynylaldehyde derivs. bearing cyclopropyl, butyl or aryl groups. **E:** A mixture of startg. 2-alkynylbenzaldehyde (0.2 mmol) and tosylhydrazine (0.2 mmol) in 1,2-dichloroethane (1 ml) stirred at room temp. for 1 h, the formed tosylhydrazone treated with AgOTf (5 mol%), the mixture stirred at 70° for 3 h, cooled to room temp., startg. α,β-ethyleneoxo compd. (1.2 eq.), methanol (0.1 ml) and KOH (3 eq.) added, the mixture stirred at room temp. under air until completion of reaction by TLC, the mixture quenched with water, extracted with methylene chloride, dried (Na_2SO_4), the solvent removed under vacuum, and the residue purified by flash chromatography on silica gel → 5-cyclopropyl-1-[methoxy-(4-methoxyphenyl)methyl]pyrazolo[5,1-*a*]isoquinoline. Y 78%. Preliminary results indicate that some of these products display promise as CDC25B, TC-PTP and PTP1B inhibitors. F.e. (twenty-three; Y 51-93%) s. Z. Chen, J. Wu, Org. Lett. *2010*, *12* (21), 4856-9 [DOI: 10.1021/ol101988q]; pyrazolo[5,1-*a*]isoquinolines from *o*-acetylene-N-tosylhydrazones and terminal acetylene derivs. cf. *76*, 466; **3-component synthesis of pyrazolo[5,1-*a*]isoquinolines** from *o*-acetylenealdehydes, oxo compds. and sulfonylhydrazines with $AgOTf/K_3PO_4$ s. X. Yu, S. Ye, J. Wu, Adv. Synth. Catal. *2010*, *352* (11-12), 2050-6 [DOI: 10.1002/adsc.201000176]; pyrazolo-[5,1-*a*]isoquinoline-1-carbonyl compds. from α,β-ethylenecarbonyl compds. (with AgOTf) s. S. Ye, X. Yang, J. Wu, Chem. Commun. *2010*, *46* (29), 5238-40 [DOI: 10.1039/c0cc00905a].

[o-Biphenylyl(di-tert-butyl)phosphine]methylgold(I)/chiral 3,3′-bis(9-anthracenyl)-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate ←

1-Carbobenzoxyamino-1,2,3,5,6,7-hexahydropyrido[3,2,1-*ij*]quinolines from *o*-propargylamines and aldehydes ○

Asym. 3-component synthesis via organo-Brønsted acid-catalyzed hetero-Diels-Alder reaction-gold(I)-catalyzed intramolecular hydroamination

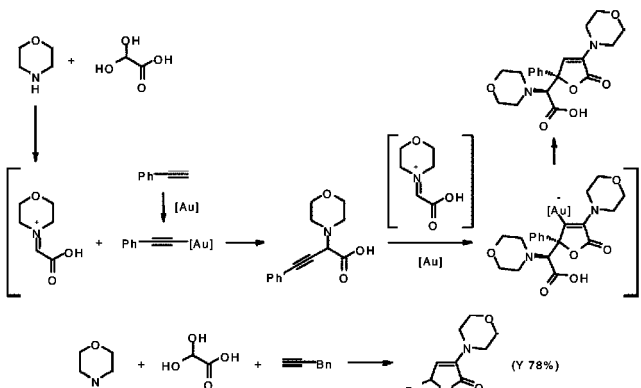


in one pot. A soln. of 4-chloro-2-(3-phenylprop-2-ynyl)aniline (0.1 mmol) in methylene chloride (0.4 ml) added to a mixture of 4-bromobenzaldehyde (1.05 eq.), chiral phosphate diester catalyst (15 mol%) and 3 Å molecular sieves (100 mg) under argon, the mixture stirred for 10 min, cooled to -40°, gold catalyst (10 mol%) in the same solvent (0.2 ml) added via syringe, a soln. of benzyl vinylcarbamate (3 eq.) in the same solvent (0.4 ml) added, the mixture stirred for 12 h, warmed to 25°, stirred for 12 h, cooled to 0°, acetic acid (0.1 ml) and $NaBH(OAc)_3$ (100 mg) added, the mixture stirred for 24 h, diluted with ethyl acetate, filtered through silica, washed with satd. aq. $NaHCO_3$, concentrated, and purified by chromatography on silica → benzyl (1S,3S,5R)-3-(4-bromophenyl)-9-chloro-5-phenyl-1,2,3,5,6,7-hexahydropyrido[3,2,1-*ij*]quinolin-1-ylcarbamate. Y 82% (d.r. 3.1:1; e.e. >99% for both diastereomers). This highly enantioselective, multi-component reaction was successful for arene-terminated *o*-propargylamines (phenyl, naphth-2-yl, 4-fluorophenyl) and electron-diverse (het)ar. aldehydes, affording diastereomeric mixtures of julolidine derivs. (fourteen examples; Y 63-85%; e.e. 92 to >99%; d.r. 3.1:1 to 10.5:1; 3-methoxybenzaldehyde gave a single diastereomer in 63% yield). The aliphatic aldehyde, 3-phenylpropanal, also reacted with high enantioselectivity (e.e. 96%), but in slightly lower yield (59%; d.r. 47:12).

The initial products, being somewhat unstable, were isolated following *in situ* reduction. Absolute stereochemistry was confirmed in one case by X-ray crystallography. F.e., optimization and catalyst prepn. s. C. Wang, Z.-Y. Han, H.-W. Luo, L.-Z. Gong, Org. Lett. *2010*, *12* (10), 2266-9 [DOI: 10.1021/ol1006086].

Gold(III) bromide $AuBr_3$
α,δ-Di-*tert*-amino-γ-aryl-γ-adipolactones
from ethynylarenes, sec. amines and glyoxylic acid
3-Component (5 molecule) synthesis via β,γ-acetylene-α-*tert*-aminocarboxylic acids

392.

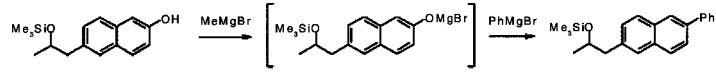


in one pot under sequential gold(III) catalysis. A soln. of ethynylbenzene (1 mmol), morpholine (2 eq.) and glyoxylic acid hydrate (2 eq.) in methanol treated with $AuBr_3$ (5 mol%) at room temp. until reaction complete → product. Y 68% (d.r. 1.8:1). The procedure is applicable to a range of ethynylarenes and acyclic or cyclic sec. amines (nine examples; Y 40-76%; d.r. 1:3.1 to 3.5:1), the reaction involving *two* catalytic cycles under the influence of the *same* gold catalyst: initially, after activation of the acetylene bond, the three components couple to give an intermediate β,γ-acetylene-α-*tert*-aminocarboxylic acid which then undergoes an unprecedented gold-catalyzed *endo-dig*-cyclization to the product via electrophilic trapping of a second molecule of immonioacetic acid (initially generated in the first cycle); reaction is then terminated via a deprotonation-protonation sequence or a 1,2-hydride shift. The method is limited, however, to ethynylarenes, aliphatic terminal acetylene derivs. giving the corresponding **3-*tert*-amino-2(5*H*)-furanones** (eleven examples; Y 38-78%) via addition of a proton in the second cycle. The proposed mechanism is substantiated by the isolation of the intermediate β,γ-acetylene-α-*tert*-aminocarboxylic acid (in one instance), which was predictably converted to the product on treatment with $AuBr_3$. Hydroxyl and isolated alkyne groups on the startg. ethynylbenzenes were tolerated. F.e. and comparison of catalysts s. Q. Zhang, M. Cheng, X. Hu, B.-G. Li, J.-X. Ji, J. Am. Chem. Soc. *2010*, *132* (21), 7256-7 [DOI: 10.1021/ja101804p].

Calcium triflimide/tetra-n-butylammonium hexafluorophosphate $Ca(NTf_2)_2/Bu_4NPF_6$
Friedel-Crafts alkylation with activated alcohols s. *43*, 703s*78* H → R

Magnesium *Mg*
4-Acyl-Δ³-oxazolines from Δ³-oxazoline-4-carboxylic acid esters COOR → C(O)R′
s. 78, 165

Magnesium/methylmagnesium bromide/nickel(II) fluoride/tricyclohexylphosphine ←
Biaryls from halogenomagnesium aroxides and arylmagnesium halides Ar-Ar′
Nickel(II)-catalyzed cross-coupling

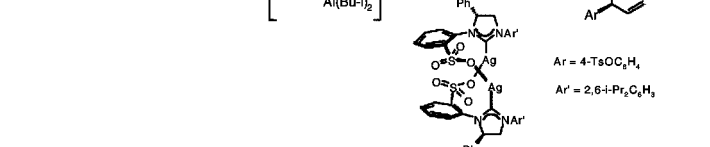
393. 

Methylmagnesium bromide (1.2 eq.) added via syringe to a mixture of 6-(2-trimethylsiloxyprop-1-yl)-2-naphthol (0.2 mmol), NiF_2 (10 mol%) and tricyclohexylphosphine (40 mol%) in **THF** (0.25 ml) at room temp., the mixture stirred for 5 min, phenylmagnesium bromide (2 eq.) added, solvent removed *in vacuo*, toluene (0.375 ml) added, the mixture stirred for 5 min, diisopropyl ether (0.125 ml) added, stirred for 10 min, then heated at 120° under N_2 for 24 h, cooled, quenched with ethanol, filtered through silica, concentrated, and purified by chromatography on silica → 2-phenyl-6-(2-trimethylsiloxyprop-1-yl)naphthalene. Y 89%. *in situ*-Generation of the magnesium naphthoxide (using inexpensive MeMgBr) provided activation for the C-O bond in this novel and efficient cross-coupling of naphthols with ar. Grignard reagents (twelve examples; Y 67-92%). The method was compatible with silyl ether, alkene, *tert*-butyl ether and pyrrole functionality and also tolerated a single *o*-substituent, but mesityl Grignard reagent gave a somewhat reduced yield (67%). *The method was not effective for simple phenol derivs.* F.e. and optimization s. D.-G. Yu, B.-J. Li, S.-F. Zheng, B.-T. Guan, B.-Q. Wang, Z.-J. Shi, Angew. Chem., Int. Ed. *2010, 49* (27), 4566-70 [DOI: 10.1002/anie.200907359].

Zinc oxide s. under $CeCl_3$ *ZnO*
Methylmagnesium bromide s. under Mg *MeMgBr*
Cyclopentylmagnesium chloride s. under $Ti(OPr\text{-}i)_4$ and $ClTi(OPr\text{-}i)_3$ *c-C_5H_9MgCl*

Zinc L-prolinate ←
3-Component synthesis of the 2-amino-3-cyano-4*H*-pyran ring s. *61*, 340s*78* ○

Diisobutylaluminum hydride/copper(II) chloride/chiral binuclear (1,3,4-triaryl-imidazolidin-2-ylidene)silver(I) complex ←
Asym. synthesis of 2-silyl-1,4-dienes C≡C → CH=C-C-C=C
from silylacetylenes and 2-ethylenephosphoric acid esters under cooperative catalysis

394. 

via regio- and stereo-selective hydroalumination. *i*-Bu_2AlH (1.5 eq.) added via syringe to a soln. of phenylethynyltrimethylsilane (1.5 eq.) in hexanes (3.75 ml) at 0° under N_2, the mixture stirred at 55° for 2 h, the vinylaluminum reagent added to a blue soln. of the catalyst [prepared by mixing the silver(I) N-heterocyclic carbene complex (1 mol%), $CuCl_2 \cdot 2H_2O$ (2 mol%) and **THF** (2.4 ml) at 22° under N_2] at -78°, startg. allyl phosphate (0.2 mmol) added, the mixture warmed to -15°, stirred for 6 h, quenched with satd. aq. Rochelle's salt soln., stirred for 1 h at 22°, extracted with ether, filtered through $MgSO_4$, concentrated *in vacuo*, and purified by chromatography on silica → (S,E)-1-phenyl-3-(4-tosyloxyphenyl)-2-trimethylsilyl-1,4-pentadiene. Y >98% (d.r. >98:2; e.e. 98%). This general and efficient reaction involves initial highly stereoselective hydroalumination (>98% selectivity) of the alkynylsilane. The generated (E)-α-silylvinylaluminum

compds. underwent enantio- and regio-selective copper(II)-catalyzed allylation with electron-diverse allyl phosphates (eleven examples; Y 82 to >98%; d.r. >98:2; e.e. 95 to >98%) in the presence of halo, nitro, ether and sulfonate functionality. A complementary series of products was obtained via the (Z)-α-silylvinylaluminum compds. (generated with >98% selectivity by hydroalumination *in the presence of THF*) using a similar catalyst (ten examples; Y 61-86%; d.r. >98:2; e.e. 94-96%). The method was used in the first enantioselective synthesis of nyasol, a naturally occurring chiral 1,4-diene. F.e.s. K. Akiyama, F. Gao, A.H. Hoveyda, Angew. Chem., Int. Ed. *2010, 49* (2), 419-23 [DOI: 10.1002/anie.200905223].

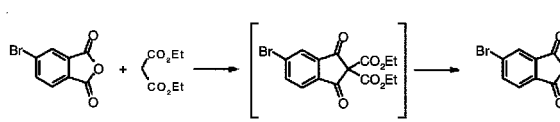
Pentafluorophenylboronic acid $C_6F_5B(OH)_2$
Friedel-Crafts alkylation with activated alcohols H → R

allylation with 2-ethylenealcohols using pentafluorophenylboronic acid cf. *43*, 703s*77*; benzylation using pentafluorophenylboronic acid to produce di-, tri- and tetra-[hetero]arylmethanes from electron-rich [hetero]arenes s. J.A. McCubbin, O.V. Krokhin, Tetrahedron Lett. *2010, 51* (18), 2447-9 [DOI: 10.1016/j.tetlet.2010.02.151]; alkylation of electron-rich arenes with sec. and tert. benzyl, allyl or propargyl alcohols using $Ca(NTf_2)_2/Bu_4NPF_6$ under very mild conditions s. M. Niggemann, M.J. Meel, Angew. Chem., Int. Ed. *2010, 49* (21), 3684-7 [DOI: 10.1002/anie.200907227]; diastereoselective (*trans*-selective) synthesis of 2-subst. 1-aryltetralins with $AlCl_3$ s. M. Davoust, J.A. Kitching, M.J. Fleming, M. Lautens, Chem. Eur. J. *2010, 16* (1), 50-4 [DOI: 10.1002/chem.200902694]; 3-propargylation of indoles with tertiary propargyl alcohols using $CeCl_3/ZnO$ s. C.C. Silveira, S.R. Mendes, L. Wolf, G.M. Martins, Tetrahedron Lett. *2010, 51* (34), 4560-2 [DOI: 10.1016/j.tetlet.2010.06.112]; benzylation with molybdenum or tungsten nitride or carbide nanoparticles, also comparison with other early transition metal nitrides and carbides, s. W. Yao, P. Makowski, C. Giordano, F. Goettmann, Chem. Eur. J. *2009, 15* (44), 11999-2004 [DOI: 10.1002/chem.200901496]; regiospecific 3-allylation of indoles with allyl alcohols using cationic ruthenium(IV) *o*-(diphenylphosphino)benzenesulfonate complexes (cf. *69*, 393s*70*) s. B. Sundararaju, M. Achard, B. Demerseman, L. Toupet, G.V.M. Sharma, C. Bruneau, Angew. Chem., Int. Ed. *2010, 49* (15), 2782-5 [DOI: 10.1002/anie.200907034].

Boric acid H_3BO_3
Sym. 1,1-bis(indol-3-yl)alkanes from oxo compds. s. *5*, 549s*78* CO → CAr_2

Montmorillonite/microwaves ←
Indan-1,3-diones from phthalic anhydrides ←
via indan-1,3-dione-2,2-dicarboxylic acid esters

395.



A mixture of 4-bromophthalic anhydride (2 mmol), diethyl malonate (1.1 eq.) and montmorillonite KSF clay (1 g) placed in a quartz tube, the latter subjected to microwaves in a Synthewave 402 (Prolabo, France) single-mode focused microwave reactor for 8 min at 130° (monitored temp.) with continuous rotation, cooled to room temp., extracted with methylene chloride, the montmorillonite clay filtered off, the filtrate concentrated *in vacuo*, the resulting red precipitate washed with distilled water, dissolved in 8% NaOH (30 ml), filtered, the filtrate acidified with a hot soln. of concd. HCl (15 ml) in water (75 ml) at 70-80°, kept at about 70° until decarboxylation ceased (10 min), solids filtered off, dried, and recrystallized twice → 5-bromoindan-1,3-dione. Y 82%. The procedure is safe, mild, economical, highly selective, rapid, simple in operation, and avoids handling strong acids or bases and corrosive or toxic reagents. It is also moderate- to good-yielding (54-79%; thirteen examples) and the catalyst can be easily retrieved and reused without significant loss of activity. F.e.s. O. Marvi, M. Giahi, Bull. Korean Chem. Soc. *2009, 30* (12), 2918-20 [DOI: 10.5012/bkcs.2009.30.12.2918].

Mesoporous indium(III)-exchange zeolite ←
Heterogeneous Knoevenagel condensation s. *46*, 713s*78* CO → C=C

Aluminum potassium sulfate $AlK(SO_4)_2$
3-Component synthesis of the 2-amino-3-cyano-4*H*-pyran ring s. *61*, 340s*78* ○

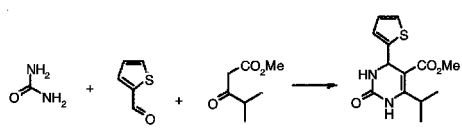
Bis(diisopropylamino)boryl chloride s. under BuLi $(i\text{-}Pr_2N)_2BCl$

Boron fluoride BF_3
Hetero-Diels-Alder reaction with *in situ*-generated N-arylaldimines
s. *52*, 363s*73*; *trans*-fused 5*H*-chromeno[2,3-*c*]acridine derivs. with BF_3-etherate s. B.V.S. Reddy, A. Antony, J.S. Yadav, Tetrahedron Lett. *2010, 51* (23), 3071-4 [DOI: 10.1016/j.tetlet.2010.04.018]; *cis*-fused pyrano- and furano-quinoline derivs. with $Sm(OTf)_3$ s. A.V. Narsaiah, A.R. Reddy, B.V.S. Reddy, J.S. Yadav, Synth. Commun. *2010, 40* (12), 1750-7 [DOI: 10.1080/00397910903161736]; benzo[*f*]quinoline derivs. and naphthalene analogs with I_2 as catalyst s. X.-S. Wang, J. Zhou, M.-Y. Yin, K. Yang, S.-J. Tu, J. Comb. Chem. *2010, 12* (2), 266-9 [DOI: 10.1021/cc900165j]; **asym. hetero-Diels-Alder reaction** (cf. *75*, 403) with cyclopentadiene using $Sc(OTf)_3$ and a chiral cyclic bis(N-oxide) s. M. Xie, X. Chen, Y. Zhu, B. Gao, L. Lin, X. Liu, X. Feng, Angew. Chem., Int. Ed. *2010, 49* (22), 3799-802 [DOI: 10.1002/anie.201000590]; tetrahydro-γ-carbolines from 2-vinylindoles with 3,5-dinitrobenzoic acid [DNBA] s. H.-G. Cheng, C.-B. Chen, F. Tan, N.-J. Chang, J.-R. Chen, W.-J. Xiao, Eur. J. Org. Chem. *2010* (26), 4976-80 [DOI: 10.1002/ejoc.201000853].

Ammonium fluoroborate s. under Thiolate-bridged diruthenium(II) complex NH_4BF_4

Hexakis(aqua)aluminum fluoroborate $[Al(H_2O)_6](BF_4)_3$
Hexakis(aqua)aluminum fluoroborate ←
as a mild, recyclable, non-hygroscopic Lewis acid catalyst

396.



Biginelli synthesis. Urea (1.5 eq.), methyl 4-methyl-3-oxopentanoate (1 eq.) and $[Al(H_2O)_6](BF_4)_3$ (10 mol%) added to a soln. of freshly distilled thiophene-2-carbaldehyde (*200 mmol*) in acetonitrile (250 ml), the mixture stirred under reflux for 20 h, concentrated *in vacuo*, and recrystallized → 5-methoxycarbonyl-6-isopropyl-4-thien-2-yl-3,4-dihydro-2-pyrimidinone. Y 90%. The novel aluminum salt was an excellent acid catalyst for the Biginelli reaction of (het)ar. aldehydes, enabling synthesis of a range of 3,4-dihydropyrimidin-2-ones incorporating acid-sensitive and sterically-hindered functionality (seventeen examples; Y 80-95%). Significantly improved yields were observed in some cases using freshly distilled aldehydes and the method was routinely used for the preparation of multigram quantities of product. In tests the catalyst was superior to a number of alternatives, could be recycled four times without loss in efficiency and when used at 50 mol% loading gave improvements in yield (from 80% to 98% in a test example). F.e., optimization and catalyst prepn. s. M. Litvic, I. Vecenaj, Z.M. Ladišic, M. Lovric, V. Vinkovic, M. Filipan-Litvic, Tetrahedron *2010, 66* (19), 3463-71 [DOI: 10.1016/j.tet.2010.03.024].

Fluoroboric acid-silica gel HBF_4-SiO_2
Catalytic Biginelli synthesis s. *55*, 337s*78* ○

Aluminum chloride $AlCl_3$
Friedel-Crafts alkylation with activated alcohols H → R
trans-2-Subst. 1-aryltetralins s. *43*, 703s*78*

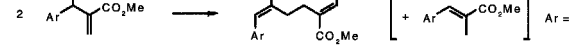
Aluminum chloride/microwaves $AlCl_3$/[\\\\]
Catalytic Biginelli synthesis s. *55*, 337s*78*

Aluminum chloride/N-fluorobenzenesulfonimide $AlCl_3/(PhSO_2)_2NF$
Knoevenagel condensation-fluorinative Nazarov cyclization
2-Fluoro-1-indanone-2-carboxylic acid esters s. *78*, 223

1-Butyl-3-methylimidazolium tetrachloroindate s. under [Bu$_4$N]CN *[bmim][InCl$_4$]*

Samarium/iodine/ethyl chloroacetate/bismuth(III) chloride *$Sm/I_2/ClCH_2COOEt/BiCl_3$*
Sym. 1,5-dienes from 2-ethylenealcohols C=C-C-C-C=C
Samarium-promoted reductive self-coupling of Baylis-Hillman adducts

397.



Sym. 1,6-diaryl-1,5-diene-2,5-dicarboxylic acid esters. $BiCl_3$ (5 mol%), I_2 (5 mol%) and startg. Baylis-Hillman adduct (1 mmol) added to a stirred mixture of Sm powder (1.5 eq.) and ethyl chloroacetate (2 eq.) in THF (15 ml), the mixture heated under reflux until reaction complete (ca. 3 h), quenched with 1 *M* HCl, extracted with ethyl acetate, the extracts washed with brine, dried (Na_2SO_4), filtered, solvents removed *in vacuo,* and the residue purified by chromatography on silica gel → (E,E)-product. Y 65% (along with 26% methyl α-methyl-4-bromocinnamate). A range of Baylis-Hillman adducts, tolerating electron-donating or -withdrawing groups on the aromatic ring, afforded corresponding 1,5-dienes with exclusive (E,E) selectivity (seven examples; Y 48-65%), accompanied in all cases by significant amounts (22-32%) of (E)-cinnamate reduction products. Iodine appears to activate the metallic samarium, while the presence of a Lewis acid ($BiCl_3$ optimal) appears to facilitate elimination of the hydroxyl group; the presence of ethyl chloroacetate is crucial to the success of the reaction although its role is unclear. Metallic Sm is preferred to SmI_2 as reductant, since it is relatively inexpensive and stable to air. F.e.s. H. Bian, J. Li, C. Li, G. Wang, Z. Duan, X. Jia, Synlett *2010* (9), 1412-4 [DOI: 10.1055/s-0029-1219808].

Ammonium cerium(IV) nitrate *CAN*
3-Component synthesis of 2-chromenes from phenols ○
2-amino-2-chromenes from aldehydes and nitriles cf. *61*, 340s*75*; polycyclic 2-chromenes from 2-naphthol with CAN, also cyclocondensation with β-diketones or a second 2-naphthol molecule, s. A. Kumar, S. Sharma, R.A. Maurya, J. Sarkar, J. Comb. Chem. *2010, 12* (1), 20-4 [DOI: 10.1021/cc900143h]; benzo[*c*]xanthene derivs. with proline hydrotriflate s. J. Li, L. Lu, W. Su, Tetrahedron Lett. *2010, 51* (18), 2434-7 [DOI: 10.1016/j.tetlet.2010.02.149]; tetracyclics with TsOH without solvent under sonication s. J. Li, J. Li, J. Fang, W. Su, Synth. Commun. *2010, 40* (7), 1029-39 [DOI: 10.1080/00397910903029966]; alternative solvent-free method under *heterogeneous* conditions with recyclable $HClO_4$-silica s. L.-P. Mo, H.-L. Chen, J. Chin. Chem. Soc. *2010, 57* (2), 157-61.

Ammonium cerium(IV) nitrate/polyethylene glycol *CAN/PEG*
Hantzsch synthesis of sym. N-aryl-1,4-dihydropyridines s. *47*, 727s*78*

Yttrium(III) acetate *$Y(OAc)_3$*
Cerium(IV) sulfate-silica (s.a. under NH_4OAc) *$Ce(SO_4)_2$-SiO_2*
Catalytic Biginelli synthesis s. *55*, 337s*78*

Scandium(III) triflate *$Sc(OTf)_3$*
2,5-Bridged pyrrolidine-3,3-dicarboxylic acid esters
via regioselective Lewis acid-catalyzed intramolecular [3+2]-cycloaddition s. *78*, 355

Scandium(III) triflate/chiral cyclic bis(N-oxides) *[Sc(III)]**
Asym. hetero-Diels-Alder reaction with *in situ*-generated N-arylaldimines s. *75*, 403s*78*

Samarium(III) triflate *$Sm(OTf)_3$*
Hetero-Diels-Alder reaction with *in situ*-generated N-arylaldimines
cis-Fused pyrano- and furano-quinoline derivs. s. *52*, 363s*78*

Cerium(III) chloride/zinc oxide *$CeCl_3/ZnO$*
Friedel-Crafts 3-propargylation of indoles with tert. propargyl alcohols H → C-C≡C
s. *43*, 703s*78*

Polyethylene glycol s. under CuI and Ammonium cerium(IV) nitrate *PEG*

Ammonium acetate/copper(II) triflate/microwaves $NH_4OAc/Cu(OTf)_2/[\backslash\backslash\backslash\backslash]$
Ammonium acetate/3-ethyl-1-vinylimidazolium iodide ←
4-Component Hantzsch 1,4-dihydropyridine synthesis ○
unsym. N-unsubst. 1,4-dihydropyridines, update s. *68,* 368s*76*; with $Cu(OTf)_2$ (2 mol%) in ethanol under microwaves s. K.K. Pasunooti, C.N. Jensen, H. Chai, M.L. Leow, D.-W. Zhang, X.-W. Liu, J. Comb. Chem. *2010, 12* (4), 577-81 [DOI: 10.1021/cc100060s]; with a little 3-ethyl-1-vinylimidazolium iodide as ionic liquid s. J.P. Nirmal, P.V. Dadhaniya, M.P. Patel, R.G. Patel, Indian J. Chem. *2010, 49B* (5), 587-92; N-aryl derivs. from anilines with the Preyssler-type heteropolyacid, $H_{14}NaP_5W_{30}O_{110}$, in ethanol or without solvent s. M.M. Heravi, F. Derikvand, L. Ranjbar, F.F. Bamoharram, Synth. Commun. *2010, 40* (9), 1256-63 [DOI: 10.1080/00397910903062272]; combinatorial synthesis of tricyclic 4-aryl-1*H*-thiopyrano[3,4-*b*]pyrid-5-one derivs. s. C.-S. Yao, C.-H. Wang, B. Jiang, S.-J. Tu, J. Comb. Chem. *2010, 12* (4), 472-5 [DOI: 10.1021/cc100017f].

Ammonium acetate/cerium(IV) sulfate-silica $NH_4OAc/Ce(SO_4)_2$-SiO_2
Ammonium acetate/L-proline NH_4OAc/Pro-OH
Hantzsch synthesis of sym. 1,4-dihydropyridines
sym. N-unsubst. 1,4-dihydropyridines, update s. *47,* 727s*76*; mild procedure with L-proline under ultrasonication s. S. Guo, Y. Yuan, Chin. J. Chem. *2010, 28* (5), 811-7 [DOI: 10.1002/cjoc.201090151]; rapid, solvent-free method with $Ce(SO_4)_2$-SiO_2 s. W. Pei, Q. Wang, X. Li, L. Sun, ibid. *2010, 28* (3), 483-6 [DOI: 10.1002/cjoc.201090101]; N-aryl-derivs. from anilines with CAN in recoverable, non-toxic PEG s. M. Kidwai, D. Bhatnagar, Tetrahedron Lett. *2010, 51* (20), 2700-3 [DOI: 10.1016/j.tetlet.2010.03.033]; uncatalyzed conversion in water under microwaves s. Z.-Q. Tang, Y. Chen, C.-N. Liu, K.-Y. Cai, S.-J. Tu, J. Heterocycl. Chem. *2010, 47* (2), 363-7 [DOI: 10.1002/jhet.322].

Tetra-n-butylammonium cyanide/1-butyl-3-methylimidazolium tetrachloroindate/microwaves ←
Nitriles from (m)ethoxymethyl ethers $OCH_2OR \rightarrow CN$
with a Lewis acidic ionic liquid as catalyst under microwave irradiation s. *78,* 226

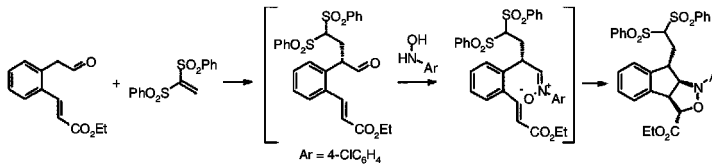
2-Hydroxyethylammonium formate or Lipase ←
Knoevenagel condensation $CO \rightarrow C{=}C$
s. *46,* 713s*74*; with 2-hydroxyethylammonium formate as task-specific ionic liquid for condensation with rhodanine s. A. Alizadeh, M.M. Khodaei, A. Eshghi, Can. J. Chem. *2010, 88* (6), 514-8 [DOI: 10.1139/v10-011]; with a weakly basic diphenylphosphinite-functionalized imidazolium ionic liquid as both solvent and catalyst s. H. Valizadeh, H. Gholipour, Synth. Commun. *2010, 40* (10), 1477-85 [DOI: 10.1080/00397910903097310]; with porcine pancreatic lipase for condensation of ar. aldehydes with methyl cyanoacetate in alcoholic medium (with trans-esterification) s. Y.-F. Lai, H. Zheng, S.-J. Chai, P.-F. Zhang, X.-Z. Chen, Green Chem. *2010, 12* (11), 1917-8 [DOI: 10.1039/c004547k]; under *heterogeneous* conditions with recyclable indium(III)-exchange mesoporous zeolite (AlMCM-41) s. S.S. Katkar, M.K. Lande, B.R. Arbad, S.B. Rathod, Bull. Korean Chem. Soc. *2010, 31* (5), 1301-4 [DOI: 10.5012/bkcs.2010.31.5.1301]; with tunable, nitrogen-doped carbon (prepared by ammoxidation of commercial carbon black and activated carbon) as solid base s. N. Kan-nari, S. Okamura, S.-i. Fujita, J.-i. Ozaki, M. Arai, Adv. Synth. Catal. *2010, 352* (9), 1476-84 [DOI: 10.1002/adsc.201000029]; with cesium oxide- or aminopropylsilyl-modified mesoporous silica (Si-MCM-41) as solid base for both Knoevenagel and Claisen-Schmidt condensation (cf. *47,* 710s*76*) cf. L. Martins, W. Hölderich, P. Hammer, D. Cardoso, J. Catal. *2010, 271* (2), 220-7 [DOI: 10.1016/j.jcat.2010.01.015].

Hexamethylenetetramine ←
3-Component synthesis of the 2-amino-3-cyano-4*H*-pyran ring s. *61,* 340s*78* ○

N-Phenylacetamide s. under $Re(CO)_5Br$ *PhNHAc*

2(S)-[Diphenyl(trimethylsiloxy)methyl]pyrrolidine ←
8-[2,2-Bis(sulfonyl)ethyl]-3,3a,8,8a-tetrahydro-1*H*-indeno[2,1-*c*]isoxazoles ○
from *o*-vinylarylacetaldehydes by 3-component synthesis
via organocatalyzed asym. Michael addition-intramolecular 1,3-dipolar cycloaddition

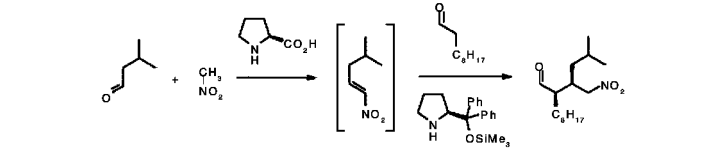
398.



in one pot. Startg. aldehyde (1.5 eq.) added to a stirred mixture of 2(S)-[diphenyl(trimethylsiloxy)-methyl]pyrrolidine (20 mol%), 1,1-bis(phenylsulfonyl)ethylene (0.1 mmol) and toluene (0.6 ml) at -20°, the mixture stirred until reaction complete (TLC; 24 h), N-(4-chlorophenyl)hydroxylamine (1.5 eq.) added, the mixture stirred at room temp. for 3 h, and purified chromatographically → (3S,3aS,8S,8aR)-ethyl 8-[2,2-bis(phenylsulfonyl)ethyl]-1-(4-chlorophenyl)-3,3a,8,8a-tetrahydro-1*H*-indeno[2,1-*c*]isoxazole-3-carboxylate. Y 92% (e.e. 98%). This efficient reaction generates four contiguous stereocenters for a series of electron-diverse N-arylhydroxylamines and δ,ε-unsaturated aldehydes (incl. the linear aliphatic, methyl (E)-7-oxohept-2-enoate), affording products as single diastereomers with high enantioselectivity (eleven examples; Y 90-98%; e.e. 92-99%). The intermediate Michael adducts (isolated in one case with e.e. of 97%), appeared to control the formation of the remaining stereocenters. Absolute stereochemistry was determined by X-ray analysis in one case. F.e., optimization and reactions of the products s. P.J. Chua, B. Tan, L. Yang, X. Zeng, D. Zhu, G. Zhong, Chem. Commun. *2010*, *46* (40), 7611-3 [DOI: 10.1039/c0cc01577f].

2(S)-[Diphenyl(trimethylsiloxy)methyl]pyrrolidine/lauric acid/L-proline ←
γ-Nitroaldehydes from two different aldehyde molecules and nitromethane ←
Polarity-directed organocatalyzed asym. Knoevenagel condensation-Michael addition
in a 2-phase medium

399.

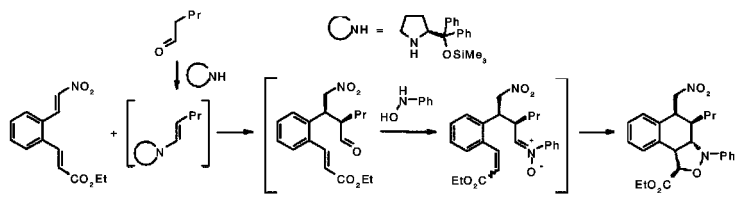


Phosphate buffer soln. (1 ml; pH 7.5) added to a mixture of 2(S)-[diphenyl(trimethylsiloxy)methyl]-pyrrolidine (1 mol%), *L*-proline (40 mol%) and lauric acid (20 mol%), the cloudy mixture stirred at room temp. for a few min, nitromethane (3 eq.) added via syringe, the mixture stirred for a few min, decanal (1 mmol) and 3-methylbutanal (1 eq.) added, the mixture stirred vigorously until reaction complete (GC/MS; 16 h), extracted with methylene chloride, concentrated, and purified chromatographically → (R,R)-2-(4-methyl-1-nitropent-2-yl)decanal. Y 77% (d.r. 16:1; e.e. >90%). In this two-step sequence, initial condensation, catalyzed by *L*-proline, occurs in the aq. phase with subsequent siloxymethylpyrrolidine-catalyzed addition occurring in the organic phase. Selectivity is therefore controlled by the relative hydrophobicity of the aldehyde components (cf. reactivity), the most effective approach being optimization of the condensation step (thereby removing the least hydrophobic aldehyde), with both aldehydes being added at the same time (seven examples; Y 40-77%; d.r. 10:1 to 16:1; e.e. >90%). The illustrated example affords the highest yield, as sterically-hindered 3-methylbutanal is not only the most polar aldehyde but also

the least reactive in the addition step. F.e. and optimization s. S.T. Scroggins, Y. Chi, J.M.J. Fréchet, Angew. Chem., Int. Ed. *2010*, *49* (13), 2393-6 [DOI: 10.1002/anie.200902945].

2(S)-[Diphenyl(trimethylsiloxy)methyl]pyrrolidine/benzoic acid ←
Asym. 3-component synthesis ○
of 5-nitromethyl-1,3,3a,4,5,9b-hexahydronaphtho[2,1-*c*]isoxazoles
from *o*-vinyl-β-nitrostyrenes, aldehydes and hydroxylamines
via organocatalyzed asym. Michael addition-intramolecular 1,3-dipolar cycloaddition

400.



in water. Highly functionalized 1,2,3,4-tetrahydronaphthalenes with 5 new contiguous chiral centers have been synthesized efficiently with extraordinarily high diastereo- and enantioselectivity in water by a new, one-pot, 3-component coupling. **E:** Valeraldehyde (3 eq.) added to a suspension of 2(S)-[diphenyl(trimethylsiloxy)methyl]pyrrolidine (2 mol%), benzoic acid (20 mol%), and the startg. nitroolefin (0.2 mmol) in water (*1 ml*) at room temp., N-hydroxyphenylamine (4 eq.) added when the nitroolefin had been consumed, the mixture stirred for a further 3 h (TLC monitoring), and worked up with purification by flash chromatography on silica gel → ethyl (1R,3aS,4R,5S,9bR)-5-(nitromethyl)-3-phenyl-4-propyl-1,3,3a,4,5,9b-hexahydronaphtho[2,1-*c*]isoxazole-1-carboxylate. Y 73% (e.e. >99%). Water serves not only as an eco-friendly solvent but also enhances reactivity and stereoselectivity as well as being involved in the catalytic cycle by hydrolyzing the intermediate iminium ion prior to condensation with the hydroxylamine. Significantly, the organocatalyst is stable in the acidic medium for at least a couple of hours, with reaction taking place in a concentrated organic phase through hydrophobic interactions. The proposed mechanism is based on initial organocatalyzed asym. Michael addition of the aldehyde to the nitroolefin, followed by acid-catalyzed hydrolysis to liberate the aldehyde function, condensation with the hydroxylamine to generate a nitrone *in situ*, and terminating by classical intramolecular 1,3-di-polar cycloaddition. The procedure is applicable to a range of aliphatic aldehydes and phenyl-acetaldehyde, as well as other hydroxylamines (fifteen examples; Y 48-83%; d.r. 95:5 to 99:1; e.e. >99% in *all* instances). F.e. and comparison of organocatalysts and acidic additives s. B. Tan, D. Zhu, L. Zhang, P.J. Chua, X. Zeng, G. Zhong, Chem. Eur. J. *2010*, *16* (12), 3842-8 [DOI: 10.1002/chem.200902932].

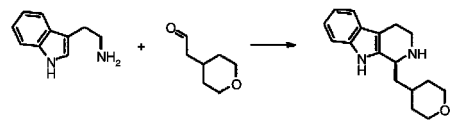
2(S)-[Bis[3,5-bis(trifluoromethyl)phenyl](trimethylsiloxy)methyl]pyrrolidine ←
s. under Thiolate-bridged diruthenium(II) complex
Chiral bis(Δ^2-imidazolines) s. under CuOTf ←
Imidazolium salts s.a. under NH_4OAc, Phosphinite..., Sulfur-tethered diaryl- ←
bismuthonium fluoroborates and 1-Methyl-3-(4-sulfobutyl)imidazolium...

1,3-Dibutylimidazolium bromide or 1-Methoxyethyl-3-methylimidazolium trifluoroacetate ←
2,3-Dihydro-1*H*-1,5-benzodiazepines from *o*-diamines and two ketone molecules
with SmI_2 cf. *50*, 471s*70*; 1-ribosyl derivs. in various imidazolium ionic liquids, e.g. 1,3-dibutylimidazolium bromide, s. A.K. Yadav, M. Kumar, T. Yadav, R. Jain, Indian J. Chem. *2010*, *49B* (4), 461-8; in 1-methoxyethyl-3-methylimidazolium trifluoroacetate cf. R. Jain, T. Yadav, M. Kumar, A.K. Yadav, J. Heterocycl. Chem. *2010*, *47* (3), 603-10 [DOI: 10.1002/jhet.365]; *heterogeneous* catalytic procedure with recyclable MoO_3-SiO_2 s. K.D. Parghi, R.V. Jayaram, Catal. Commun. *2010*, *11* (15), 1205-10 [DOI: 10.1016/j.catcom.2010.07.008].

1-(Pyrrolidin-2(S)-ylmethyl)-3-butylbenzimidazolium bromide/phthalic acid ←
Asym. α-alkylation with activated alcohols s. *22*, 782s*78* H → R

Strictosidine synthase ←
1,2,3,4-Tetrahydro-9*H*-pyrid[3,4-*b*]indoles from aldehydes ○
via enzymatic asym. Pictet-Spengler reaction

401.



A mixture of tetrahydropyran-4-ylacetaldehyde (1 *mM*), tryptamine (1 *mM*) and *Ophiorrhiza pumila* strictosidine synthase (0.2 mol%) incubated in phosphate buffer (pH 7) and analyzed by GC/MS → product. Y unspecified. The cloned enzyme, while having a strong preference for the natural substrate, showed a broader acceptance with respect to the aldehyde component compared to enzymes from other sources. Linear and branched aliphatic, aromatic and the illustrated tetrahydropyran-derived aldehyde were accepted substrates (nine examples) with absolute configuration at C3 confirmed to be identical to that for the natural substrate. F.e. and spectroscopic data for products s. P. Bernhardt, A.R. Usera, S.E. O'Connor, Tetrahedron Lett. *2010*, *51* (33), 4400-2 [DOI: 10.1016/j.tetlet.2010.06.075].

Ethyl chloroacetate s. under Sm/I$_2$ *ClCH$_2$COOEt*

3,5-Dinitrobenzoic acid *ArCOOH*
Hetero-Diels-Alder reaction with *in situ*-generated N-arylaldimines
1,2,3,4-Tetrahydro-5*H*-pyrid[4,3-*b*]indoles from 2-vinylindoles s. *52*, 363s*78*

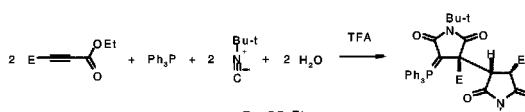
N-(Carbo-tert-butoxy)-D-phenylglycine s. under 1(S)-Benzyl-N²-methylethylenediamine ←

L-Proline [s.a. under NH$_4$OAc and 2-[Diphenyl(trimethylsiloxy)methyl]pyrrolidine] ←
3-Component synthesis of the 2-amino-3-cyano-4*H*-pyran ring s. *61*, 340s*78*

4-(tert-Butyldimethylsiloxy)-(S)-proline ←
Asym. Friedländer quinoline synthesis
update s. *65*, 334s*77*; in a mixture of water and the acidic ionic liquid, 1-methyl-3-(4-sulfobutyl)imidazolium triflate, s. J. Akbari, A. Heydari, H.R. Kalhor, S.A. Kohan, J. Comb. Chem. *2010*, *12* (1), 137-40 [DOI: 10.1021/cc9001313]; 1,8-naphthyridines by aza-Friedländer synthesis with KI$_3$ s. K. Mogilaiah, K.S. Kumar, N.V. Reddy, Indian J. Chem. *2010*, *49B* (2), 253-5; asym. Friedländer synthesis under enamine catalysis with 4-(*tert*-butyldimethylsiloxy)-(S)-proline s. L. Li, D. Seidel, Org. Lett. *2010*, *12* (21), 5064-7 [DOI: 10.1021/ol1023932].

Trifluoroacetic acid (s.a. under 9-Amino-9-deoxy-epi-quinine) *CF$_3$COOH*
4-Component (7 molecule) synthesis
of 3-phosphoranylidene-2,2′-bis(succinimides)
from isonitriles and α,β-acetylenecarboxylic acid esters

402.



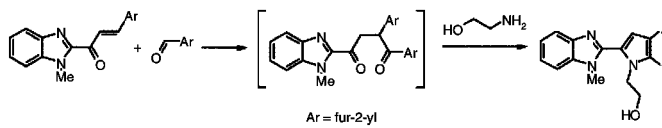
in one pot. A soln. of *tert*-butyl isocyanide (2 eq.) and triphenylphosphine (1 mmol) in methylene chloride (4 ml) added dropwise over 10 min to a stirred soln. of diethyl acetylenedicarboxylate (2 eq.), water (2 eq.) and trifluoroacetic acid (TFA; 2 eq.) in the same solvent (5 ml) at room temp., the mixture stirred for 24 h, concentrated *in vacuo*, and purified by chromatography on silica → diethyl 1,1′-di-*tert*-butyl-4-triphenylphosphoranylidene-3,3′-bis(2,5-dioxotetrahydro-1*H*-

pyrrole)-3,4′-dicarboxylate. Y 95%. Initial treatment of triphenylphosphine-acetylenedicarboxylate adducts with isocyanides was expected to afford 2-aminofurans, and the formation of bis-pyrrolidine derivs. was attributed to traces of water in the TFA. The reaction requires stoichiometric amounts of TFA as a proton source, appears general for aliphatic isocyanides and occurs in a number of common solvents (methylene chloride proving optimal), giving products as single diastereomers (five examples; Y 79-95%). Variation in temperature (-10° to reflux) affords the same products in varying yields. Structures were confirmed by X-ray analysis in one case. F.e.s. A. Alizadeh, S. Rostamnia, L.-G. Zhu, Tetrahedron Lett. *2010*, *51* (36), 4750-4 [DOI: 10.1016/j.tetlet.2010.07.027].

3-Ethyl-5-(2-hydroxyethyl)-4-methylthiazolium bromide/1,8-diazabicyclo[5.4.0]-undec-7-ene/acetic acid or p-toluenesulfonic acid or hydrogen chloride ←

Pyrroles from aldehydes, α,β-ethyleneketones and prim. amines via Stetter reaction-Paal-Knorr reaction ○

403.

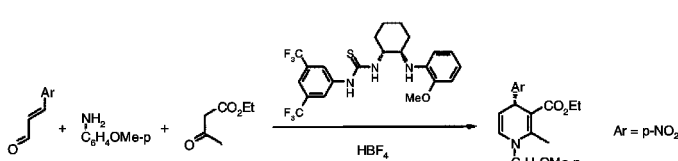


in one-pot. A soln. of 1-(1-methylbenzimidazol-2-yl)-3-fur-2-ylpropenone (1 eq.), furfural (1.5 eq.), 3-ethyl-5-(2-hydroxyethyl)-4-methylthiazolium bromide (25 mol%) and DBU (30 mol%) in methanol (10 ml) heated under reflux until substrate consumed (TLC; 1-8 h), ethanolamine (2 eq.) and acetic acid (3 eq.) added, the mixture refluxed for 1-3 h, diluted with methylene chloride, washed with water, concentrated *in vacuo*, and purified by chromatography on silica → 4,5-difur-2-yl-1-(2-hydroxyethyl)-2-(1-methylbenzimidazol-2-yl)pyrrole. Y 85%. This efficient procedure utilized a neutral organocatalyst to generate γ-diketones from (het)ar. and aliphatic 1-(benzimidazol-2-yl)propenones and aldehydes, which were cyclized *in situ* by Paal-Knorr reaction with ar. and aliphatic prim. amines (incl. ammonia) to afford multi-substituted pyrroles (twelve examples; Y 56-85%). Hydrochloric and *p*-toluenesulfonic acids were also suitable for the final condensation step. F.e. and optimization s. X. Jing, X. Pan, Z. Li, X. Bi, C. Yan, H. Zhu, Synth. Commun. *2009*, *39* (21), 3833-44 [DOI: 10.1080/00397910902838952].

Chiral 2-aminothioureas/Brønsted acids ←

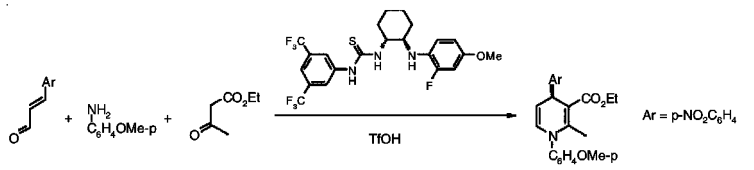
Asym. synthesis of 1,4-dihydropyridines from α,β-ethylenealdehydes and ketones Effect of Brønsted acids on the face selectivity of asym. organocatalysis with chiral 2-*sec*-aminothioureas

404.



By using different Brønsted acids, such as difluoroacetic acid, triflic acid or HBF_4, with the same (or similar) bifunctional thiourea, either enantiomer of 4-subst. 1,4-dihydropyridines can be prepared from the same starting materials, both the Brønsted acid and bifunctional thiourea co-catalysts being important for determining the enantioselectivity and sense of chirality. **E: Chiral 4-subst. 1,4-dihydropyridine-3-carboxylic acid esters**. 4-Nitrocinnamaldehyde (0.15 mmol) and 4-methoxyaniline (0.1 mmol) added at room temp. to a mixture of the chiral aminothiourea (10 mol%) and HBF_4 (10 mol%) in toluene (1 ml) under argon, stirred at the same temp. for 30 min, ethyl acetoacetate (2 eq.) added, stirring continued until reaction complete (72 h), the mixture

concentrated *in vacuo*, and the residue purified by silica gel chromatography → (R)-product. Y 52% (e.c. 69%). The (S)-isomer was obtained in 50% e.e. (Y 82%) using an analogous thiourea and *triflic acid* after 48 h.



F.e. and catalysts, **also from enamines** (e.e. up to 80%), s. K. Yoshida, T. Inokuma, K. Takasu, Y. Takemoto, Molecules *2010, 15* (11), 8305-26 [DOI: 10.3390/molecules15118305].

N-Fluorobenzenesulfonimide s. under $AlCl_3$ *$(PhSO_2)_2NF$*
Benzoyl chloride s. under $K_4Fe(CN)_6$ *PhCOCl*

Bromo(dimethyl)sulfonium bromide *$[Me_2SBr]Br$*
3-Component Mannich reaction CHO → CH(NHR)C-CO
with $CeCl_3$ cf. *68*, 361s*77*; from aromatic aldehydes and anilines with bromo(dimethyl)sulfonium bromide s. M. Shailaja, A. Manjula, B.V. Rao, Indian J. Chem. *2010, 49B* (4), 482-6; with benzyltriethylammonium chloride in water s. X.-S. Wang, J. Zhou, K. Yang, Q. Li, Synth. Commun. *2010, 40* (7), 964-72 [DOI: 10.1080/00397910903029859].

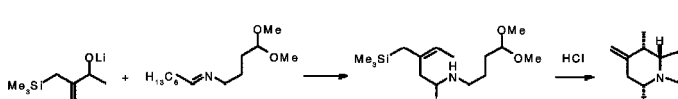
Silica s. under HBF_4, $Ce(SO_4)_2$, Trifluoromethanesulfonic acid, Sulfuric acid, MoO_3 and $HClO_4$ *SiO_2*
Mesoporous silica s. under Cesium oxide, Poly(4-methyl vinylpyridinium hydroxide) and Sulfonic acid... ←

Trimethylsilyl cyanide (s.a. under o-Tol_3P) *Me_3SiCN*
3-Amino-3-cyanooxindoles from isatins CO → C(N≤)CN
by uncatalyzed Strecker reaction s. *52*, 449s*78*

Trimethylsilyl cyanide/silica-bonded thiosulfuric acid S-monoester or iron(III) chloride or mesoporous silica-supported cobalt(II) Schiff base complex or tetranuclear palladium(II) bis(imidazol-2-ylidene) complexes or potassium tetrachloropalladate(II) ←
α-Aminonitriles from oxo compds. s. *52*, 449s*78*

Titanium tetraisopropoxide/n-butyllithium *$Ti(OPr\text{-}i)_4/BuLi$*
Regioselective reductive coupling of (alkylideneamino)acetals with 3-hydroxy-2-methylenesilanes and subsequent stereoselective double ring closure ○

405.

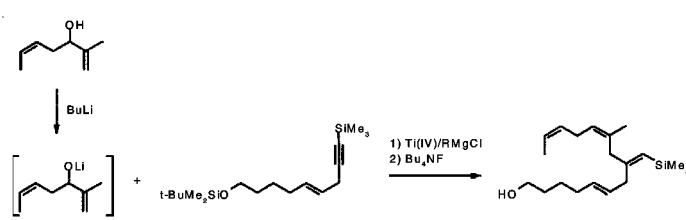


7-Methyleneindolizidines. A soln. of BuLi (4 eq.) in hexanes (4 ml) added over 2 min to a soln. of $Ti(OPr\text{-}i)_4$ (2 eq.) in dry ether (10 ml) at -78° under argon, the mixture stirred for 10 min, a soln.

of startg. imine (2 eq.) in the same solvent added via syringe, the mixture stirred for 30 min, the yellow soln. warmed to room temp. over 30 min, the resulting red soln. cooled to -78°, Li-3-methylene-4-trimethylsilylbut-2-oxide (freshly prepared from the alcohol and BuLi; 1 mmol) in THF (4 ml) added via cannula, the mixture warmed slowly to room temp., stirred for 16 h, diluted with ether, quenched with satd. aq. $NaHCO_3$, stirred for 1 h, extracted with ether, and purified by chromatography on silica → intermediate homoallylic amine (Y 70%), dissolved in THF (5 ml), 1 *M* aq. HCl (1 ml) added at room temp. under argon, the mixture stirred for 16 h, neutralized with powdered K_2CO_3, extracted with ether, concentrated *in vacuo*, and purified by chromatography on silica → (5R*,8S*,8aS*)-5-hexyl-8-methyl-7-methyleneoctahydroindolizine (Y 95%). This novel, convergent and stereoselective route involves regioselective reductive coupling of the imine at C-3 of the sec. allylic alcohol to afford homoallylic amines (six examples; Y 55-70%; E/Z >20:1), with the synthetically useful allylsilane moiety remaining intact. Subsequent hydrolysis of the masked aldehyde gave simple and polycyclic 7-methyleneindolizidines and **8-methylenequinolizidines** via double ring closure (Y 75-95%; d.r. >20:1). Note that, while a *tert.* allylic analog showed similar regioselective coupling with an imine (Y 70%), a *prim. analog reacted at C-2 of the allylic alcohol moiety* to afford a 2-trimethylsilyl-1,3-aminoalcohol (Y 75%). F.e.s. D. Yang, G.C. Micalizio, J. Am. Chem. Soc. *2009*, *131* (48), 17548-9 [DOI: 10.1021/ja908504z].

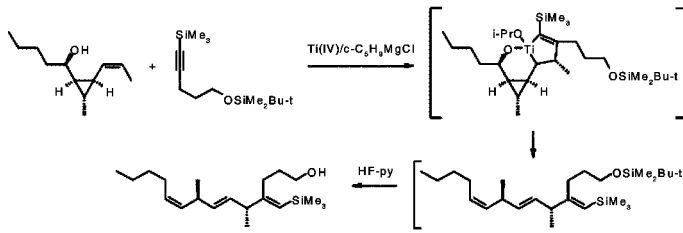
Titanium tetraisopropoxide/cyclopentylmagnesium chloride/n-butyllithium ←
1,4,7-Trienes from acetylene derivs. and 1,5-dien-3-ols C(OH)C=C → C=C-C-C=CH
Chemo-, regio- and stereo-selective reductive cross-coupling

406.



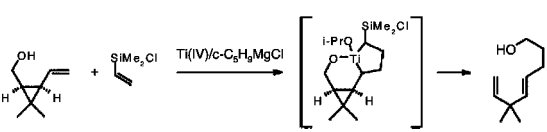
$Ti(OPr\text{-}i)_4$ (2.7 eq.) added via syringe to a stirred soln. of startg. enyne (2.5 eq.) in toluene (15 ml), the soln. cooled to -78°, a soln. of cyclopentylmagnesium chloride (5.5 eq.) in ether (1.64 ml) added via syringe, the mixture warmed to -35° over 30 min, stirred for 1 h, cooled to -78°, a soln. of Li-(5Z)-2-methyl-1,5-heptadien-3-oxide [freshly prepared from the alcohol (0.601 mmol) and butyllithium (1.1 eq.)] in THF (1.5 ml), added dropwise via cannula to the brown soln., the mixture warmed to 0° over 5 h, stirred for 1 h, quenched with satd. aq. NH_4Cl, stirred rapidly, ether added, filtered through silica, extracted with ether, the extracts concentrated *in vacuo*, purified by chromatography on silica, the product dissolved in THF (4 ml), cooled to -10°, Bu_4NF (2.5 eq.) in the same solvent (1.5 ml) added dropwise, the mixture stirred until reaction complete (TLC; 1 h), quenched with satd. aq. NH_4Cl, extracted with ether, concentrated *in vacuo*, and purified by chromatography on silica → (5E,8E,10Z,13Z)-10-methyl-8-[(trimethylsilyl)methylene]pentadeca-5,10,13-trien-1-ol. Y 51% (single isomer). A series of 1,5-dien-3-ols, containing substituents at *both alkenes*, reacted exclusively with sym. and unsym. alkynes at the allylic alcohol moiety to afford 'skipped' triene derivs. as single isomers (nine examples; Y 51-76%), with silyl ether products conveniently deprotected to the corresponding alcohols. The presence of the substrate alcohol was essential for control of both regio- and stereo-selectivity. F.e. and optimization s. P.S. Diez, G.C. Micalizio, J. Am. Chem. Soc. *2010*, *132* (28), 9576-8 [DOI: 10.1021/ja103836h].

Chlorotitanium triisopropoxide/cyclopentylmagnesium chloride/n-butyllithium ⊣
Regio- and stereo-specific synthesis of 1,4,7-trienes ⊂
from 2-vinylcyclopropylcarbinols and acetylene derivs.



407.

Skipped trienes [1,4,7-trienes], familiar naturally in polyunsaturated fatty acids and many complex antibiotics and bio-molecules, have been prepared simply and *directly* in one step via *stereospecific reductive coupling* of 2-vinylcyclopropylcarbinols with acetylene derivs., thereby generating three stereodefined alkene residues and optionally introducing stereogenic centers at the central positions. **E: (1,4,7-Trien)ols.** Cyclopentylmagnesium chloride (4-5 eq.) added via syringe to a soln. of the startg. alkyne (2 eq.) and $ClTi(OPr\text{-}i)_3$ (2-2.5 eq.; 1 *M* in hexanes) in toluene (0.1 *M*) at -78°, the mixture warmed to -30°, stirred for 1 h (becoming deep brown in color), a soln. of the startg. Li-alkoxide [prepared by adding *n*-BuLi (1.2 eq.) via syringe to a soln. of the vinylcyclopropylcarbinol (1 mmol) in ether (0.3 *M*) at -78° and warming to 0° over 20 min] added by cannula to the formed titanium complex at -70°, the mixture slowly warmed to room temp. over 2-3 h, treated with 1 *M* HCl (ca. 5 ml/mmol of the vinylcyclopropane) with rapid stirring, worked up after dilution with ethyl acetate, filtration and purification by flash column chromatography, then isolated after O-de-*tert*-butyldimethylsilylation [by treatment with HF·pyridine in acetonitrile/methylene chloride (5 ml; 1:1) at 0°] → product. Y 34% (after purification by flash chromatography; Y 82% based on recovered startg. m.). **4,7-Dienols** (possessing a terminal mono-, 1,1-di-, 1,2-di- or tri-subst. alkene residue) were prepared similarly by replacing the alkyne component by dimethyl(vinyl)silyl chloride, followed by standard oxidation of the silyl group to the prim. alcohol (eight examples; Y 42-61%).



(Y 58%; E/Z 20:1)
(Y 82% based on recovered startg. m.)

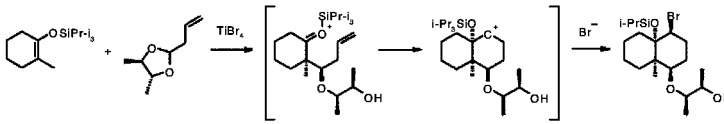
Coupling is presumed to take place via alkoxide-mediated formation of a tricyclic titanacyclopent(e,a)ne which is consistent with the intimate relationship between the relative stereochemistry of the cyclopropane deriv. and the olefin geometry. F.e., also oxidation of the trienols to the corresponding **(1,4,7-triene)-carboxylic acids** (three examples; Y 53-57%), and preparation of the startg. vinylcyclopropyl-carbinols from allyl diazoacetates or 2,4-dienols, s. T.K. Macklin, G.C. Micalizio, Nature Chem. *2010*, *2* (8), 638-43 [DOI: 10.1038/nchem.665].

Trimethylsilyl chloride (s.a. under Tungstophosphoric acid) *Me_3SiCl*
Catalytic Biginelli synthesis s. *55*, 337s*78* ○

Titanium tetrabromide *$TiBr_4$*

4-Functionalized 3-siloxycyclohexyl ethers from enoxysilanes and acetals via aldol-type condensation-Prins cyclization with asym. induction

408.



One-pot procedure under mild conditions. A soln. of startg. silyl enol ether (1.2 eq.) and acetal (0.5 mmol) in methylene chloride (3 ml) added to a soln. of $TiBr_4$ (2 eq.) in the same solvent at -78°, the mixture stirred for 30 min, quenched with satd. aq. $NaHCO_3$, extracted with methylene chloride, concentrated *in vacuo*, and purified by chromatography on silica → product. Y 85% (d.r. 75:25; e.e. >98%). This highly efficient cascade [Mukaiyama] **aldol-type reaction-Prins reaction** uses inexpensive and readily available substrates, affording products as separable mixtures of two diastereomers (at C-1) from an achiral diethyl acetal (six examples; Y 75-92%; d.r. 63:37 to 79:21) or the illustrated chiral acetal (five examples; Y 76-90%; d.r. 57:43 to 75:25; e.e. >98%). Absolute stereochemistry was confirmed in one case by X-ray analysis. Use of a more labile trimethylsilyl enol ether gave only the Mukaiyama-aldol product (Y 70%). F.e.s. H. Li, T.-P. Loh, Org. Lett. *2010*, *12* (12), 2679-81 [DOI: 10.1021/ol100937r].

Mesoporous carbon nitride s. under Au *MCN*

Tosylhydrazine s. under AgOTf *$TsNHNH_2$*

Tricyclohexylphosphine s. under Mg *Cy_3P*

Dicyclohexyl(phenyl)phosphine s. under Ni(cod)$_2$ *Cy_2PPh*

Tri-o-tolylphosphine/triethylsilyl triflate/trimethylsilyl cyanide *$o\text{-}Tol_3P/Et_3SiOTf/Me_3SiCN$*

α-Alkoxynitriles from acetals via 1-alkoxyphosphonium salts $C(OR)_2 \rightarrow C(OR)CN$

s. *78*, 242

1,3-Bis(diphenylphosphino)propane s. under CuCl and [(cinnamyl)PdCl]$_2$ *dppp*

Phosphinite-functionalized imidazolium ionic liquids ←

Knoevenagel condensation s. *46*, 713s*78* $CO \rightarrow C{=}C$

Triphenyl phosphite s. under Ni(cod)$_2$ *$(PhO)_3P$*

Chiral 3,3′-bis(9-anthracenyl)-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate s. under [o-Biphenylyl(di-tert-butyl)phosphine]methylgold(I) ←

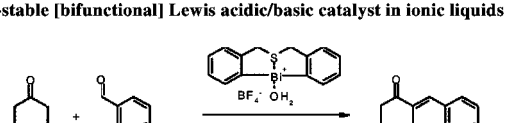
Tetra-n-butylammonium hexafluorophosphate s. under Ca(NTf$_2$)$_2$ *Bu_4NPF_6*

Arsenic trioxide s. under Pd(PPh$_3$)$_4$ *As_2O_3*

Sulfur-tethered diarylbismuthonium fluoroborates/n-propylamine/1-n-butyl-3-methylimidazolium fluoroborate ←

(E)-α,β-Ethyleneketones from ketones and aldehydes using an air-stable [bifunctional] Lewis acidic/basic catalyst in ionic liquids

409.



under mild conditions. A homogeneous mixture of catalyst (1 mol%), 4-trifluoromethylbenzaldehyde (20 mmol), *n*-propylamine (1 eq.), cyclohexanone (3 eq.) and [bmim]BF_4 (1 ml) stirred until reaction complete (TLC; 6 h), and the upper layer purified chromatographically → (E)-2-(4-trifluoromethylbenzylidene)cyclohexanone. Y 100% (E/Z 100:0). The novel, stable

catalyst is completely miscible with water and polar media and, as the condensation progresses, becomes concentrated in the lower layer of water (produced during the reaction) and ionic liquid, from which it is easily separated and recycled. Electron-diverse (het)ar. and enolizable aliphatic aldehydes reacted cleanly with cyclic ketones, β-diketones and β-keto-esters, affording (E)-isomers exclusively (eleven examples; Y 93-100%). F.e. and optimization s. R. Qiu, Y. Qiu, S. Yin, X. Song, Z. Meng, X. Xu, X. Zhang, S. Luo, C.-T. Au, W.-Y. Wong, Green Chem. *2010*, *12* (10), 1767-71 [DOI: 10.1039/c004940a].

Bismuth(III) chloride s. under Sm/I$_2$ *BiCl*$_3$

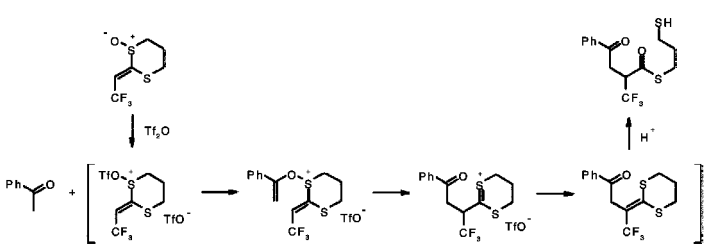
Ammonium vanadate/microwaves NH_4VO_3/[\\\\]
Vanadium hydrogen sulfate ←
Catalytic Biginelli synthesis s. *55*, 337*s78* ○

Niobium pentachloride s. under 9-Amino-9-deoxyquinine *NbCl*$_5$

N′-[p-(Carbododecyloxy)benzenesulfonyl]-(S)-prolinamide/benzylamine/molecular sieves ←
2-Cyclohexenones from α,β-ethyleneketones and aldehydes
by organocatalyzed asym. Michael addition-intramolecular aldol condensation s. *77*, 402*s78*

Trifluoromethanesulfonic anhydride *Tf*$_2O$
β-Keto(trifluoromethyl)ketene mercaptals from ketones ←
Pummerer-type synthesis with addition of three C-atoms

410.



and subsequent hydrolysis to α-trifluoromethyl-γ-ketothiolic acid esters. Trifluoromethanesulfonic anhydride (0.4 mmol) added to a soln. of acetophenone (0.4 mmol) in nitroethane (2 ml) containing 2-(2,2,2-trifluoroethylidene)-1,3-dithiane 1-oxide (0.2 mmol) under argon at -78°, stirred for 30 min at -40°, the mixture poured into satd. aq. $NaHCO_3$, extracted with chloroform, the organic layer dried, concentrated *in vacuo*, the residue dissolved in methanol (2 ml) and water (1 ml), aq. HCl (11 *M*; 2 mmol) added, heated at reflux for 2 h, and worked up with purification by chromatography on silica gel → S-(3-mercaptopropyl) 4-oxo-4-phenyl-(2-trifluoromethyl)-butanethioate. Y 73%. Although Pummerer reactions with ketones have not been reported, in this instance coupling is effected via preferential activation of the sulfoxide residue over the keto group, followed by nucleophilic attack at the generated cationic sulfur atom to give a vinyl(vinyloxy)sulfonium species, which undergoes a rapid [3.3]-sigmatropic rearrangement at low temp. to give the β-ketoketene mercaptal. This mechanistic proposition is borne out by DFT calculations, which underline the importance of the negative trifluoromethyl (or heptafluoropropyl) group in facilitating the reaction: significantly, with substrates bearing a methyl or phenyl group in place of trifluoromethyl, a complex mixture of products was obtained. The procedure is applicable to the coupling of a range of ketones (aryl ketones, acyclic ketones, β-diketones, 1-tetralone) and reaction supports a diverse range of substituents on the aromatic ring of the aryl ketones (although reaction with *o*-subst. derivs. was slower and lower yielding). An acyclic ketene mercaptal S-oxide also participated in the reaction, but the yield of thiolic ester was moderate (one example; Y 50%). F.e. (thirteen; Y 40-81%) and conversion of the products to trifluoromethyl-substituted azoles s. T. Kobatake, S. Yoshida, H. Yorimitsu, K. Oshima, Angew. Chem., Int. Ed. *2010*, *49* (13), 2340-3 [DOI: 10.1002/anie.200906774].

Triethylsilyl triflate s. under o-Tol$_3$P *Et_3SiOTf*

Sodium hydrogen sulfate *$NaHSO_4$*

1-Methylimidazolium hydrogen sulfate/microwaves *$[Hmim]HSO_4$/[\\\\]*

Catalytic Biginelli synthesis s. *55*, 337s*78* ○

1-Methyl-3-(4-sulfobutyl)imidazolium triflate ←

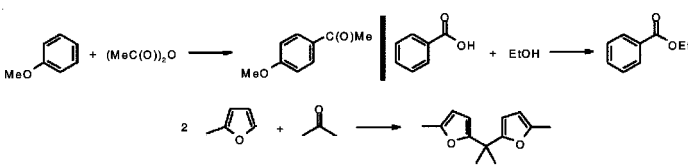
Friedländer quinoline synthesis

update s. *65*, 334s*77*; in a mixture of water and the acidic ionic liquid, 1-methyl-3-(4-sulfobutyl)-imidazolium triflate, s. J. Akbari, A. Heydari, H.R. Kalhor, S.A. Kohan, J. Comb. Chem. *2010, 12* (1), 137-40 [DOI: 10.1021/cc9001313]; 1,8-naphthyridines by aza-Friedländer synthesis with KI_3 s. K. Mogilaiah, K.S. Kumar, N.V. Reddy, Indian J. Chem. *2010, 49B* (2), 253-5; **asym. Friedländer synthesis** under enamine catalysis with 4-(*tert*-butyldimethylsiloxy)-(S)-proline s. L. Li, D. Seidel, Org. Lett. *2010, 12* (21), 5064-7 [DOI: 10.1021/ol1023932].

Poly(vinylsulfonic acid)-on-polystyrene ←

Syntheses using a polymer-grafted poly(vinylsulfonic acid) as solid acid catalyst ←

411.



Heterogeneous Friedel-Crafts acylation. A mixture of anisole (10 mmol), acetic anhydride (1 eq.) and high-density polymeric sulfonic acid catalyst (200 mg) heated at 90° for 1 h → 4-methoxyacetophenone. Y unspecified (regioselectivity 98%). The heterogeneous acid catalyst, while not as active as analogous homogeneous acids, was often superior to other solid catalysts; furthermore, it was stable, recyclable and effective for Friedel-Crafts acylation, esterification and condensation reactions, and remained active even in the presence of generated water. F.e. and prepn. of the catalyst s. T. Okayasu, K. Saito, H. Nishide, M.T.W. Hearn, Green Chem. *2010, 12* (11), 1981-9 [DOI: 10.1039/c0gc00241k]; esterification s.a. idem., Chem. Commun. *2009* (31), 4708-10 [DOI: 10.1039/b823177j].

Sulfonic acid-functionalized mesoporous silica ←

Sym. 1,1-bis(indol-3-yl)alkanes from oxo compds. $CO \rightarrow CAr_2$

update s. *5*, 549s*75*; with propylsulfonic acid-functionalized mesoporous silica (SBA-15) s. M.A. Naik, D. Sachdev, A. Dubey, Catal. Commun. *2010, 11* (14), 1148-53 [DOI: 10.1016/j.catcom.2010.06.004]; solvent-free method with benzyltriphenylphosphonium tribromide (from aldehydes) s. F. Shirini, M.S. Langroodi, M. Abedini, Chin. Chem. Lett. *2010, 21* (11), 1342-5 [DOI: 10.1016/j.cclet.2010.05.028]; with [Fe(III)(salophen)]Cl in molten tetra-*n*-butylammonium bromide s. S. Saeidnia, I. Sheikhshoaie, Chin. J. Chem. *2010, 28* (4), 601-4 [DOI: 10.1002/cjoc.201090119]; inexpensive, solvent-free method with boric acid s. J.S. Yadav, M.K. Gupta, R. Jain, N.N. Yadav, B.V.S. Reddy, Monatsh. Chem. *2010, 141* (9), 1001-4 [DOI: 10.1007/s00706-010-0355-8]; **1,1-bis-(2-pyrrolyl)alkanes** from aldehydes with recyclable silica-supported H_2SO_4 under heterogeneous conditions s. Y. Zhang, J. Liang, Z. Shang, Chin. J. Chem. *2010, 28* (2), 259-62 [DOI: 10.1002/cjoc.201090063]; with I_2 as catalyst s. P.-A. Faugeras, B. Boëns, P.-H. Elchinger, J. Vergnaud, K. Teste, R. Zerrouki, Tetrahedron Lett. *2010, 51* (35), 4630-2 [DOI: 10.1016/j.tetlet.2010.06.122].

Trimethylsilyl triflate *Me_3SiOTf*

Trifluoromethanesulfonic acid-silica gel *$TfOH\text{-}SiO_2$*

α-Alkylation with activated alcohols $H \rightarrow R$

s. *22*, 782s*72*; **α-benzylation** of β-dicarbonyl compds. and 4-hydroxycoumarin with Me_3SiOTf under mild conditions s. P. Theerthagiri, A. Lalitha, Tetrahedron Lett. *2010, 51* (41), 5454-8 [DOI: 10.1016/j.tetlet.2010.08.019]; f. synthesis of 3-alkyl-4-hydroxycoumarins (incl. warfarin derivs.) cf. M. Rueping, B.J. Nachtsheim, E. Sugiono, Synlett *2010* (10), 1549-53 [DOI: 10.1055/

s-0029-1219936]; **α-allylation** of N-sulfonyliminoesters with allyl alcohols using $Pd(PPh_3)_4/As_2O_3$ s. R. Matsubara, K. Masuda, J. Nakano, S. Kobayashi, Chem. Commun. *2010, 46* (45), 8662-4 [DOI: 10.1039/c0cc03067h]; **α-propargylation** with S- and Se-functionalized propargyl alcohols under scandium(III) catalysis in nitromethane/water s. K. Ohta, T. Kobayashi, G. Tanabe, O. Muraoka, M. Yoshimatsu, Chem. Pharm. Bull. *2010, 58* (9), 1180-6 [DOI: 10.1248/cpb.58.1180]; general, heterogeneous procedure with recyclable triflic acid absorbed on silica gel without solvent or in nitromethane/water s. P.N. Liu, F. Xia, Q.W. Wang, Y.J. Ren, J.Q. Chen, Green Chem. *2010, 12* (6), 1049-55 [DOI: 10.1039/b926142g]; **asym. α-alkylation** of cyclic ketones with phthalic acid and the chiral ionic liquid, 1-(pyrrolidin-2(S)-ylmethyl)-3-butylbenzimidazolium bromide, as catalyst, also with desymmetrization, s. L. Zhang, L. Cui, X. Li, J. Li, S. Luo, J.-P. Cheng, Chem. Eur. J. *2010, 16* (7), 2045-9 [DOI: 10.1002/chem.200902509].

Triethylsilyl triflate s. under Ni(cod)$_2$ *Et_3SiOTf*

Proline hydrotriflate *Pro-OH·HOTf*
3-Component synthesis of 2-chromenes from phenols ○
Benzo[*c*]xanthene derivs. s. *61*, 340s*78*

p-Toluenesulfonic acid (s.a. under $CuSO_4$) *TsOH*
3-Component synthesis of 2-chromenes from phenols
under sonication in the absence of solvent s. *61*, 340s*78*

Sodium dodecyl sulfate s. under Phosphomolybdic acid *$NaOSO_2OC_{12}H_{25}$*

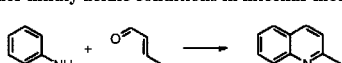
Sulfuric acid-silica ←
Sym. 1,1-bis(indol-3-yl)alkanes from oxo compds. s. *5*, 549s*78* $CO \rightarrow CAr_2$

Silica-bonded thiosulfuric acid S-monoester s. under Me_3SiCN ←

Molybdenum trioxide-silica *MoO_3-SiO_2*
2,3-Dihydro-1*H*-1,5-benzodiazepines from *o*-diamines and two ketone molecules ○
s. *50*, 471s*78*

Molybdophosphoric acid/sodium dodecyl sulfate *$H_3PMo_{12}O_{40}/NaOSO_2OC_{12}H_{25}$*
Quinolines from anilines and α,β-ethyleneoxo compds.
One-pot conversion under mildly acidic conditions in micellar medium

412.



Aniline (0.1 mol) added to a soln. of molybdophosphoric acid (0.001 mol) in water (8 ml) containing sodium dodecyl sulfate (0.001 mol), crotonaldehyde (0.15 mol) added with toluene (10 ml), the mixture stirred vigorously at 80° for 1 h, the lower layer separated and basified with aq. $NaHCO_3$ soln., and worked up with purification by chromatography on silica gel → product. Y 91%. The procedure is simple, efficient, eco-friendly and high-yielding for the condensation of electron-diverse anilines with crotonaldehyde or methyl vinyl ketone (eighteen examples; Y 79-97%). The rate of reaction and yields are higher in the micellar medium than in toluene, in which reaction requires a more elevated temp. (110°) over 2 h. The product is associated (by solvation) with the catalyst in the aq. phase, from which each is isolated via extraction of the product with ethyl acetate (the catalyst thereby being separated simply and may be used in a second run with no loss of activity). Reaction is presumed to involve initial Michael addition of the aniline to the unsatd. oxo compd., followed by cyclization. F.e.s. A. Chaskar, V. Padalkar, K. Phatangare, B. Langi, C. Shah, Synth. Commun. *2010, 40* (15), 2336-40 [DOI: 10.1080/00397910903245141].

Sodium phosphotungstate *$H_{14}NaP_5W_{30}O_{110}$*
4-Component Hantzsch synthesis of N-aryl-1,4-dihydropyridines s. *68*, 368s*78*

Tungstophosphoric acid/trimethylsilyl chloride *$H_3PW_{12}O_{40}/Me_3SiCl$*
Catalytic Biginelli synthesis s. *55*, 337s*78*

Iodine (s.a. under Sm) *I_2*
Sym. 1,1-bis(indol-3-yl)alkanes or 1,1-bis(2-pyrrolyl)alkanes $CO \rightarrow CAr_2$
from oxo compds. s. *5*, 549s*78*

Hetero-Diels-Alder reaction with *in situ*-generated N-arylaldimines s. *52*, 363s*78* ○

Perchloric acid-silica $HClO_4$-SiO_2

3-Component synthesis of 2-chromenes from phenols
under heterogeneous conditions in the absence of solvent s. *61*, 340s*78*

Ammonium chloride s. under NaN_3 NH_4Cl

Thiamine hydrochloride ←

Catalytic Biginelli synthesis s. *55*, 337s*78*

Tetra-n-butylammonium bromide s. under Chloroiron(III) salophen complex Bu_4NBr

Benzyltriethylammonium chloride $BnEt_3NCl$

3-Component Mannich reaction in water s. *68*, 361s*78* CHO → CH(NHR)C-CO

1,12-Bis(dodecyldimethylammonio)dodecane dibromide s. under NaOH ←

Potassium triiodide KI_3

1,8-Naphthyridines by aza-Friedländer synthesis s. *65*, 334s*78* ○

Benzyltriphenylphosphonium tribromide $[BnPPh_3]Br_3$

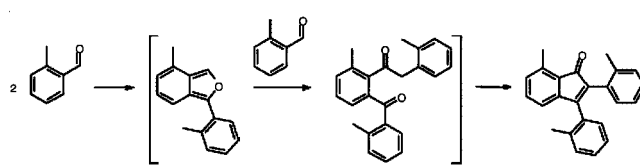
Sym. 1,1-bis(indol-3-yl)alkanes or 1,1-bis(2-pyrrolyl)alkanes CO → CAr_2
from oxo compds. s. *5*, 549s*78*

(Pentacarbonyl)rhenium(I) bromide/N-phenylacetamide $Re(CO)_5Br/PhNHAc$

2,3-Diaryl-1-indenones from three ar. aldehyde molecules ○

Rhenium-catalyzed dehydrative trimerization via C-H activation

413.



A soln. of 2-methylbenzaldehyde in toluene treated with $ReBr(CO)_5$ (5 mol%) and N-phenylacetamide (5 mol%) at 180° under argon for 24 h → 7-methyl-2,3-bis(2-methylphenyl)-1-indenone. Y 98%. The reaction was general for electron-diverse ar. aldehydes, tolerating methoxy, methyl, trifluoromethyl, methoxycarbonyl and bromo groups in the *p*-position (five examples; Y 77-98%) as well as the *o*-methyl deriv. (illustrated), and the analogous *m*-methylbenzaldehyde was highly regioselective (>11:1) in favor of the 6-methylinden-1-one deriv. via preferential C-H activation at the least-hindered site (Y 97%). No indenone analogs were obtained from thiophene-2-carbaldehyde, pyridine-4-carbaldehyde, *trans*-2-decenal or *trans*-cinnamaldehyde, however. Mechanistic experiments suggested that reaction proceeded via the illustrated isobenzofuran and diketone intermediates. F.e.s. Y. Kuninobu, T. Matsuki, K. Takai, Org. Lett. *2010*, *12* (13), 2948-50 [DOI: 10.1021/ol100947p].

Iron complexes s. under Chiral ferrocenylbis(palladacyclic Δ^2-imidazoline) complexes *[Fe]*

Potassium hexacyanoferrate(II)/benzoyl chloride $K_4Fe(CN)_6/PhCOCl$

α-Aminonitriles from oxo compds. CO → C(N≤)CN

update s. *52*, 449s*77*; eco-friendly procedure from aldehydes or ketones with $K_4[Fe(CN)_6]$ with benzoyl chloride as promoter s. Z. Li, Y. Ma, J. Xu, J. Shi, H. Cai, Tetrahedron Lett. *2010*, *51* (30), 3922-6 [DOI: 10.1016/j.tetlet.2010.05.088]; rapid procedure from aldehydes with Me_3SiCN and $FeCl_3$ *without* solvent s. M.M. Heravi, M. Ebrahimzadeh, H.A. Oskooie, B. Baghernejad, Chin. J. Chem. *2010*, *28* (3), 480-2 [DOI: 10.1002/cjoc.201090100]; *heterogeneous* procedure from aldehydes or ketones with a recyclable cobalt(II) Schiff base complex supported on mesoporous SBA-15 *without* solvent s. F. Rajabi, S. Ghiassian, M.R. Saidi, Green Chem. *2010*, *12* (8), 1349-52 [DOI: 10.1039/c0gc00047g]; f. heterogeneous procedure from ketones within the *tetranuclear* hollow spheres (500 nm) created supramolecularly from palladium(II) bis(imidazol-2-ylidene)

complexes s. J. Choi, H.Y. Yang, H.J. Kim, S.U. Son, Angew. Chem., Int. Ed. *2010, 49* (42), 7718-22 [DOI: 10.1002/anie.201003101]; from aldehydes *in water* with K_2PdCl_4 s. B. Karmakar, J. Banerji, Tetrahedron Lett. *2010, 51* (20), 2748-50 [DOI: 10.1016/j.tetlet.2010.03.059]; heterogeneous procedure from aldehydes with a recyclable, covalently linked, silica-bonded thiosulfuric acid S-monoester s. K. Niknam, D. Saberi, M.N. Sefat, ibid. *2010, 51* (22), 2959-62 [DOI: 10.1016/j.tetlet.2010.03.093]; *uncatalyzed* procedure for the cyanoamination of isatins in methanol, also asym. variant (e.e. up to 74%) with a cinchona-based phosphinamide, s. Y.-L. Liu, F. Zhou, J.-J. Cao, C.-B. Ji, M. Ding, J. Zhou, Org. Biomol. Chem. *2010, 8* (17), 3847-50 [DOI: 10.1039/c0ob00174k].

Chloroiron(III) salophen complex/tetra-n-butylammonium bromide *[Fe(III)]/Bu$_4$NBr*
Sym. 1,1-bis(indol-3-yl)alkanes from oxo compds. s. *5,* 549s*78* $CO \rightarrow CAr_2$

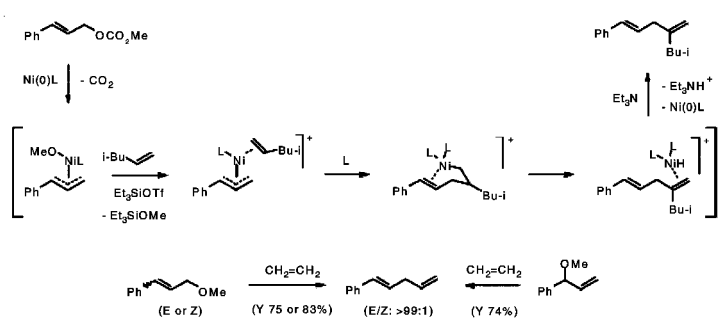
Iron(III) chloride s.a. under Me$_3$SiCN *FeCl$_3$*

Iron(III) chloride/microwaves *FeCl$_3$/[\\\\\]*
Catalytic Biginelli synthesis with acylals in the absence of solvent s. *55,* 337s*78* ○

Mesoporous silica-supported cobalt(II) Schiff base complex s. under Me$_3$SiCN ←

Bis(1,5-cyclooctadiene)nickel(0)/dicyclohexyl(phenyl)phosphine/triphenyl phosphite/triethylsilyl triflate/triethylamine ←
Nickel-catalyzed synthesis of terminal 1,4-dienes from [unactivated] terminal ethylene derivs. and 2-ethylenealcohol O-derivs. $CH{=}CH_2 \rightarrow C(C{-}C{=}C){=}CH_2$

414.



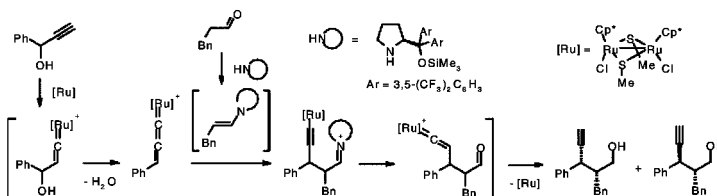
The first catalytic intermolecular process for the direct allylation of non-conjugated, non-strained simple alkenes is reported. **E:** Cinnamyl methyl carbonate (0.5 mmol) added to a soln. of Ni(cod)$_2$ (20 mol%) and Cy_2PPh (20 mol%) in toluene (0.5 ml) under argon, the mixture stirred at room temp. for 30 min, $(PhO)_3P$ (20 mol%), triethylamine (6 eq.), 4-methyl-1-pentene (5 eq.) and triethylsilyl triflate (1.75 eq.) added in that order, the resulting mixture stirred for 21 h, filtered through a silica gel plug (with hexane/ethyl acetate), solvents removed under reduced pressure, and the crude mixture purified by chromatography on silica gel → (E)-(6-methyl-4-methylenehept-1-enyl)benzene. Y 87%. Six examples, using a variety of terminal aliphatic alkenes (tolerating silyl ether substituents) afforded yields of 64-87% (lowest for the hindered vinylcyclohexane); opposite regioselectivity was observed for styrene, albeit in only 25% yield. Allylation of ethylene itself could be accomplished using allyl ethers, carbonates, acetates, *chlorides*, silyl ethers and even allyl alcohols, although methyl ether and methyl carbonate derivs. were optimal (eleven examples; Y 57%, 71-97%, with lowest yield obtained for a substrate having a methyl-subst. allylic double bond). E/Z (83:17 to >99:1) and linear/branched (95:5 to >99:1) selectivity were generally very high. F.e., optimization, a mechanistic proposal, and gram-scale reactions s. R. Matsubara, T.F. Jamison, J. Am. Chem. Soc. *2010, 132* (20), 6880-1 [DOI: 10.1021/ja101186p].

Nickel(II) fluoride s. under Mg *NiF$_2$*

Cationic ruthenium(IV) o-(diphenylphosphino)benzenesulfonate complexes *[Ru(IV)]*
Regiospecific 3-allylation of indoles with 2-ethylenealcohols s. *69*, 393s*78* H → C-C=C

Thiolate-bridged diruthenium(II) complex/ammonium fluoroborate/2(S)-[bis[3,5-bis-(trifluoromethyl)phenyl](trimethylsiloxy)methyl]pyrrolidine ←
Asym. α-propargylation of aldehydes with 2-acetylenealcohols under cooperative catalysis with a chiral organocatalyst and a transition metal complex H → C-C≡CH

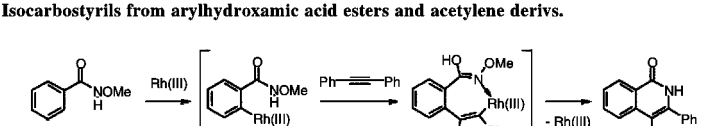
415.



The novel concept of cooperative catalysis with a chiral organocatalyst and a transition metal complex is illustrated in the asym. α-propargylation of aldehydes (products being isolated after *in situ* reduction to the more stable **chiral 4-acetylene-*prim*-alcohols**). **E:** Anhydrous toluene (2 ml) added under N_2 to a mixture of $[Cp^*RuCl(\mu^2\text{-}SMe)]_2$ (5 mol%) and NH_4BF_4 (10 mol%), stirred at room temp. for 15 min, a soln. of 1-phenyl-2-propyn-1-ol (0.2 mmol) in anhydrous toluene (4 ml) added to the mixture, followed successively by 2(S)-[bis[3,5-bis(trifluoromethyl)-phenyl](trimethylsiloxy)methyl]pyrrolidine (5 mol%) and 3-phenylpropanal (3 eq.), kept at room temp. for 90 h, cooled to 0°, ethanol (6 ml) and $NaBH_4$ (3 eq.) added, stirring continued at 0° for 1 h, quenched with water, and worked up with purification by chromatography on silica gel → 2-benzyl-3-phenyl-4-pentyn-1-ol. Y 89% [as a 2.2:1 mixture of *syn*- and *anti*-isomers (e.e. 96% and 89%, respectively)]. Reaction is presumed to involve a dual catalytic cycle: the aldehyde condenses initially with the chiral sec. amine to give the corresponding enamine, which serves as a nucleophile on asym. addition to the allenylidene complex formed by dehydrative activation of the propargyl alcohol with the ruthenium catalyst; the generated alk-1-ynylruthenium complex is then hydrolyzed to liberate the organocatalyst and further converted to the product with elimination of the ruthenium catalyst. The fact that reaction does not take place with internal alkynes is in keeping with the proposed formation of an intermediate allenylidene complex. α-Substitution of the propargyl alcohol by aryl is mandatory, but the aldehyde may be aliphatic or substituted at the β-site by aryl (sixteen examples; Y 80-93%; *syn/anti* 1.7:1 to 3.3:1; e.e. *syn*-isomer 88-99%; e.e. *anti*-isomer 52-95%). The propargyl alcohol may be substituted on the aromatic ring by an electron-withdrawing or -donating group, while *o*-substitution enhances the enantioselectivity. F.e.s. M. Ikeda, Y. Miyake, Y. Nishibayashi, Angew. Chem., Int. Ed. *2010*, *49* (40), 7289-93 [DOI: 10.1002/anie.201002591].

*Dichloro(pentamethylcyclopentadienyl)rhodium(III) dimer/cesium acetate [Cp*RhCl$_2$]$_2$/CsOAc*
Isocarbostyrils from arylhydroxamic acid esters and acetylene derivs. ○

416.



Methanol added to a test-tube containing the startg. hydroxamic acid ester (30 mmol; 1 *M*), tolan (1.1 eq.), $[Cp^*RhCl_2]_2$ (2.5 mol%) and CsOAc (30 mol%) (with no particular precautions to exclude oxygen or moisture), the mixture stirred at 60° for 16 h, diluted with methylene chloride, the mixture transferred to a round-bottom flask, silica added, volatiles evaporated under reduced

pressure, and the residue worked up with purification by flash chromatography on silica gel → 3,4-diphenylisoquinolin-1(2*H*)-one. Y 90%. The procedure is mild, insensitive to air and moisture, and, significantly, does *not* require an external oxidant. It is applicable in good to high yield (48-90%; twelve examples) to the coupling of electron-diverse arylhydroxamic acid esters with both sym. and unsym. internal alkynes, aryl(alkyl)alkynes reacting regioselectively with the alkyl group being installed at the 3-position of the formed ring. *m*-Subst. arylhydroxamic acid esters also reacted regioselectively, ring closure taking place at the less hindered site. The N-O bond is effectively used as an instrument for C-N bond formation and catalyst release: initially it serves as a directing group for the initial reversible *o*-rhodation, which is then followed by insertion of the alkyne to give a 7-membered azarhodacyclic prior to concerted (or synchronous) C-N bond formation and N-O bond cleavage. Notably, this copper-free method is also applicable to pyridyl-subst. alkynes. F.e.s. N. Guimond, C. Gouliaras, K. Fagnou, J. Am. Chem. Soc. *2010*, *132* (20), 6908-9 [DOI: 10.1021/ja102571b].

Palladium(II) acetate/phosphines/potassium carbonate/microwaves ←
2- or 5-Arylation of oxazoles with [het]aryl triflates H → Ar
Solvent- and ligand-dependent regioselectivity s. *77*, 421s*78*

Tetranuclear palladium(II) bis(imidazol-2-ylidene) complexes s. under Me_3SiCN ←

Chiral palladium 2,2′-bipyridyl, 2-(acylamino)chalcogenide, β-tert-aminosulfoxide or β-iminodisulfide complexes *[Pd]**

Chiral palladium phosphine, di(phosphine), phosphinite, bis(phosphinite), phosphite or phosphaalkene-Δ^2-oxazoline complexes *[Pd]**

Palladium-catalyzed asym. α-allylation H → C-C=C

s. *48*, 772s*70*, *73*; with chiral ferrocene-fused 2,2′-bipyridyls (isolated or condensed) as sole ligand s. A. Mroczek, G. Erre, R. Taras, S. Gladiali, Tetrahedron: Asym. *2010*, *21* (15), 1921-7 [DOI: 10.1016/j.tetasy.2010.06.015]; with readily recoverable chiral *fluorous* 2-(acylamino)-chalcogenides s. J.A. Sehnem, P. Milani, V. Nascimento, L.H. Andrade, L. Dorneles, A.L. Braga, ibid. *2010*, *21* (8), 997-1003 [DOI: 10.1016/j.tetasy.2010.05.015]; with cinchona-based β-*tert*-aminosulfoxides [9-phenylsulfinyl-9-deoxy-*epi*-cinchonidine and -quinidine] s. E. Wojaczynska, M. Zielinska-Blajet, I. Turowska-Tyrk, J. Skarzewski, ibid. *2010*, *21* (7), 853-8 [DOI: 10.1016/j.tetasy.2010.04.032]; with chiral conformationally rigid and congested 'roofed' β-iminodisulfides s. H. Matsunaga, R. Tokuda, M. Nakajima, T. Ishizuka, Chem. Pharm. Bull. *2010*, *58* (10), 1419-21 [DOI: 10.1248/cpb.58.1419]; with chiral monodentate dinaphthophosphepines [BINEPINES] as ligand s. E. Alberico, S. Gladiali, R. Taras, K. Junge, M. Beller, Tetrahedron: Asym. *2010*, *21* (11-12), 1406-10 [DOI: 10.1016/j.tetasy.2010.04.031]; with chiral [5]-ferrocenophane di-(phosphines), regio- and enantio-selectivity, s. R. Šebesta, A. Škvorcová, B. Horváth, ibid. *21* (15), 1910-5 [DOI: 10.1016/j.tetasy.2010.05.054]; with stereodynamic di(phosphines) and di-(phosphinites) based on 2,2′-biphosphole s. M. Gouygou, J.-C. Daran, E. Robé, C. Ortéga, C.R. Chim. *2010*, *13* (8-9), 1054-62 [DOI: 10.1016/j.crci.2010.03.003]; with atropisomeric 1-[*o*-(diphenylphosphino)phenyl]indoles s. T. Mino, S. Komatsu, K. Wakui, H. Yamada, H. Saotome, M. Sakamoto, T. Fujita, Tetrahedron: Asym. *2010*, *21* (6), 711-8 [DOI: 10.1016/j.tetasy.2010.03.039]; with chiral quaternary ammonium-tagged 1-(diphenylphosphino)-2-[α-(benzylideneamino)alkyl]ferrocenes s. H. Yuan, Z. Zhou, J. Xiao, L. Liang, L. Dai, ibid. *2010*, *21* (15), 1874-84 [DOI: 10.1016/j.tetasy.2010.05.047]; with related chiral imidate-functionalized ferrocenylphosphines for a broadly applicable procedure s. T. Noël, K. Bert, E. Van der Eycken, J. Van der Eycken, Eur. J. Org. Chem. *2010* (21), 4056-61 [DOI: 10.1002/ejoc.201000238]; with chiral cyclic β-(diphenylphosphino)-sulfoximines s. F. Lemasson, H.-J. Gais, J. Runsink, G. Raabe, ibid. *2010* (11), 2157-75 [DOI: 10.1002/ejoc.200901462]; with chiral 4,5-dihydro-N-[*o*-(diphenylphosphino)benzylidene]-3*H*-dinaphth[2,1-*c*;1′,2′-*e*]azepines s. M. Widhalm, M. Abraham, V.B. Arion, S. Saarsalu, U. Maeorg, Tetrahedron: Asym. *2010*, *21* (16), 1971-82 [DOI: 10.1016/j.tetasy.2010.05.031]; with chiral oxazole- or thiazole-functionalized biphenyl-2,2′-diyl phosphites as ligand s. J. Mazuela, A. Paptchikhine, P. Tolstoy, O. Pàmies, M. Diéguez, P.G. Andersson, Chem. Eur. J. *2010*, *16* (2), 620-38 [DOI: 10.1002/chem.200901842]; with carbohydrate-based 2-(benzylideneamino)phosphinites s. C. Shen, H. Xia, H. Zheng, P. Zhang, X. Chen, Tetrahedron: Asym. *2010*, *21* (15), 1936-41 [DOI: 10.1016/j.tetasy.2010.06.037]; with chiral phosphaalkene-Δ^2-oxazolines as ligand s. J. Dugal-Tessier, G.R. Dake, D.P. Gates, Org. Lett. *2010*, *12* (20), 4667-9 [DOI: 10.1021/ol1020652].

Tetrakis(triphenylphosphine)palladium(0)/arsenic trioxide $Pd(PPh_3)_4/As_2O_3$

α-Allylation of N-sulfonyliminoesters with allyl alcohols s. *48*, 772s*78* H → C-C=C

Chiral palladium(II) biphenyl-2,2′-diyl Δ²-oxazolin-4-ylmethyl phosphite complexes *[Pd(II)]**

Asym. Heck reaction with unsatd. triflates ←

with aryl triflates cf. *46*, 738s*67,68*; of aryl or vinyl triflates with various ethylene derivs. under microwave or thermal conditions with chiral palladium(II) biphenyl-2,2′-diyl Δ²-oxazolin-4-ylmethyl phosphite complexes s. J. Mazuela, O. Pàmies, M. Diéguez, Chem. Eur. J. *2010, 16* (11), 3434-40 [DOI: 10.1002/chem.200902777].

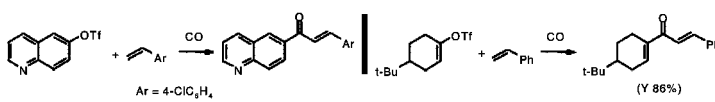
Bis(cinnamylpalladium chloride)/1,3-bis(diphenylphosphino)propane/triethylamine ←

α,β-Ethyleneketones C=CH + TfOR → C=C-C(O)R

from ethylene derivs. and unsatd. triflates

via palladium(II)-catalyzed carbonylative Heck coupling

417.



Chalcones from (het)aryl triflates. Quinolin-6-yl triflate (1 mmol), 4-chlorostyrene (6 eq.), triethylamine (2 eq.) and toluene (0.5 ml) added via syringe to a mixture of $[(cinnamyl)PdCl]_2$ (1 mol%) and dppp (2 mol%) in a steel autoclave under argon, the mixture pressurized with CO (10 atm.), heated at 100° for 20 h, cooled, vented, diluted with water, extracted with ether, washed with brine, concentrated, and purified by chromatography on silica → 6-(4-chlorocinnamoyl)-quinoline. Y 73%. This first example of a carbonylative Heck reaction (scalable to 10 mmol) was successful for (het)aryl and alkenyl triflates cross-coupling with styrene derivs., with electronic-diversity tolerated in both components (twenty-three examples; Y 40-95%) and yields generally lower for alkenyl triflates. A single (unoptimized) one-pot preparation of chalcones from a phenol precursor was also demonstrated (Y 50%). F.e. and optimization s. X.-F. Wu, H. Neumann, M. Beller, Angew. Chem., Int. Ed. *2010, 49* (31), 5284-8 [DOI: 10.1002/anie.201002155].

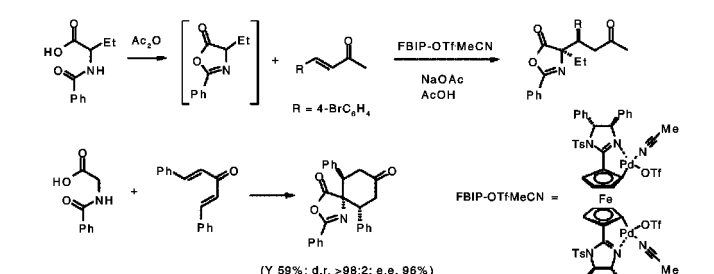
Potassium tetrachloropalladate(II) s. under Me_3SiCN K_2PdCl_4

Chiral ferrocenylbis(palladacyclic Δ²-imidazoline) complexes/ sodium acetate/acetic acid/acetic anhydride *[Pd(II)]*/NaOAc/AcOH/Ac_2O*

4-γ-Keto-Δ²-5-oxazolones from α-(acylamino)carboxylic acids and α,β-ethyleneketones ○

via palladium-catalyzed asym. Michael addition

418.



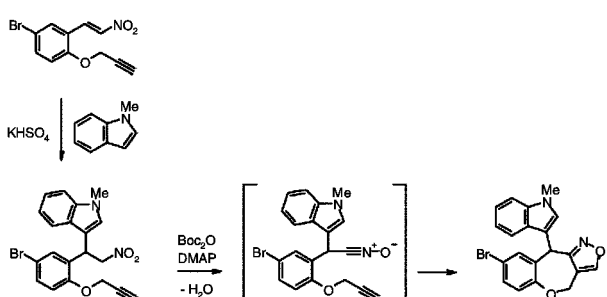
trans-4-(4-Bromophenyl)but-3-en-2-one (2 eq.) added to *rac*-N-benzoyl-2-aminobutyric acid at 8°, followed by addition of stock solns. of NaOAc (10 mol%) in acetic acid/acetic anhydride (7:3; 125 μl) and [[bis-η^5-(4′R,5′R)-(S_p)-2-(4′,5′-diphenyl-1′-tosyl-Δ²-imidazolin-2′-yl)cyclopenta-

dienyl)]iron(II) 1-C,3′-N dipalladium(II)]-triflate acetonitrile complex [FBIP-OTf·MeCN] (2 mol%) in the same solvent system (200 μl), the resulting slurry stirred (450 rpm) at 30° for 23 h, cooled to room temp., and purified directly by chromatography on silica gel → (R)-4-[(R)-1-(4-bromophenyl)-3-oxobutyl]-4-ethyl-2-phenyloxazol-5(4*H*)-one. Y 88% (e.e. 92%; d.r. >98:2). This simple procedure, involving cooperative activation by a soft bimetallic catalyst, a hard Brønsted acid and a hard Brønsted base, was used to prepare a range of highly enantioenriched, diastereomerically pure masked α-amino acids, having adjacent quaternary and tertiary stereocenters, from simple racemic N-benzoyl amino acids (sixteen examples; Y 41-95%; d.r. >98:2; e.e. 76-99%). Reaction is thought to occur via initial acetic anhydride-promoted azlactone formation (via a mixed anhydride), followed by coordination to both Pd centers of the catalyst, deprotonation by NaOAc acting as base, and activation by acetic acid towards Michael addition to the enone. Poor results (yield and/or e.e.) are obtained using alternative solvent systems, with the use of pure acetic acid having the single greatest positive effect on enantioselectivity. F.e. and optimization using azlactones as startg. m. s. M. Weber, S. Jautze, W. Frey, R. Peters, J. Am. Chem. Soc. *2010*, *132* (35), 12222-5 [DOI: 10.1021/ja106088v].

Chiral iridium(I) 1,1′-binaphthyl-2,2′-diyl phosphoramidite σ-complex/sodium salt *[Ir]*/Na⁺*
α-Allylation with acoxy-2-ethylenes H → C-C=C
Kinetic asym. transformation with retention of the double bond s. *78*, 116

Via intermediates *v.i.*
Isoxazole ring from 1-nitroenynes ○
via Friedel-Crafts reaction intramolecular 1,3-dipolar cycloaddition

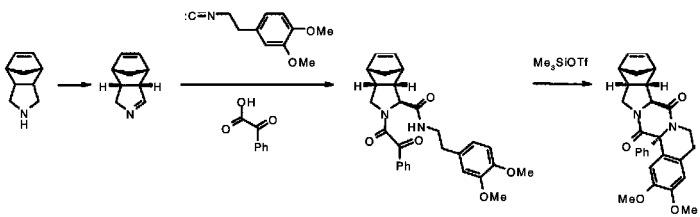
419.



4-(Indol-3-yl)-4*H*,10*H*-isoxazolo[4,3-*c*]benzoxepanes. $KHSO_4$ (30 mol%) added to a soln. of 5-bromo-2-propargyloxy-β-nitrostyrene (1.74 mmol) in water (10 ml), the mixture stirred for 5 min, N-methylindole (1 eq.) added, the mixture stirred until reaction complete (TLC; 3-5 h), extracted with ethyl acetate, concentrated, and purified chromatographically → intermediate adduct (Y 90%), 1 mmol of which dissolved in toluene (5 ml), DMAP (20 mol%) added, the soln. stirred at 90° during addition of di-*tert*-butyl dicarbonate (2.5 eq.) over 30 min, stirring continued for 2 h, the mixture concentrated *in vacuo*, and purified chromatographically → 6-bromo-4-(1-methyl-1*H*-indol-3-yl)-4*H*,10*H*-2,9-dioxa-3-azabenzo[*f*]azulene. Y 85%. Fourteen Michael adducts prepared from *o*-propargyloxy-β-nitrostyrenes and 1- or 2-subst. indoles (Y 55-92%) underwent dehydration and intramolecular nitrile oxide cycloaddition on heating with $(Boc)_2O$/DMAP to afford isoxazolo[4,3-*c*]benzoxepanes, with N-H indoles isolated as N-Boc derivs. (Y 72-96%). The reaction was successful with terminal and internal alkynes. Structures were confirmed by X-ray crystallography in one case. F.e. and optimization s. K. Ramachandiran, K. Karthikeyan, D. Muralidharan, P.T. Perumal, Tetrahedron Lett. *2010*, *51* (22), 3006-9 [DOI: 10.1016/j.tetlet.2010.04.001].

Sequential oxidative enzymatic desymmetrization-Ugi-type reaction-double ring closure of *meso*-pyrrolidines, α-ketocarboxylic acids and ω-(het)arylisonitriles with asym. induction

420.



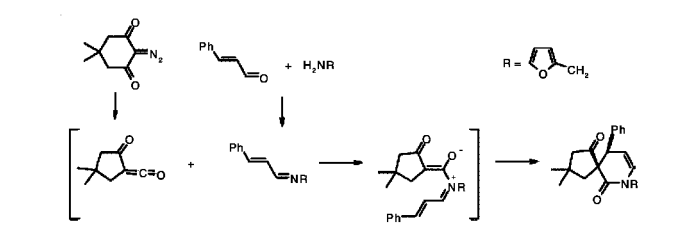
Oxidative enzymatic desymmetrization of 3,4-disubst. pyrrolidines (*77*, 390) has been combined with Ugi and Pictet-Spengler-type reactions for the asym. synthesis of unusual alkaloid-like compounds containing piperazine-2,5-diones fused to 5-membered rings. **E:** Startg. chiral amine (1 mmol) treated according to *78*, 371 → intermediate pyrroline, 0.7 mmol of which dissolved in methylene chloride (2 ml) followed by addition of startg. α-ketocarboxylic acid (1.3 eq.) and isocyanide (1.3 eq.), the mixture stirred for 24 h at room temp., methylene chloride (8 ml) added, the mixture washed with Na_2CO_3 soln., dried ($MgSO_4$), filtered, and concentrated *in vacuo* → intermediate Ugi adduct (isolable in 72% yield; d.r. >99:1), 0.25 mmol of which dissolved in dry methylene chloride (300 ml), cooled to -10°, treated dropwise with trimethylsilyl triflate (1.1-1.3 eq.) in dry methylene chloride (5 ml) over 5 h with stirring, the mixture allowed to warm to room temp., stirred for another 11 h, filtered, washed with $NaHCO_3$, dried ($MgSO_4$), filtered, concentrated *in vacuo*, the crude product subjected to column chromatography on silica, concentrated *in vacuo*, the pure oily compd. dissolved in methylene chloride/hexane, and concentrated to afford a solid → product (Y 72%; d.r. >99:1). The Ugi product from phenylglyoxylic acid and 3,4-dimethoxybenzyl isocyanide required harsher conditions [trifluoroacetic anhydride (1 eq.) in 1:1 trifluoroacetic acid/ methylene chloride] for cyclization (1st step: Y 79%; 2nd step: Y 60%, d.r. >99:1). F.e. (four; 1st step: Y 48-77%; 2nd step: Y 71-92%, d.r. 57:43 to >99:1) s. A. Znabet, J. Zonneveld, E. Janssen, F.J.J. De Kanter, M. Helliwell, N.J. Turner, E. Ruijter, R.V.A. Orru, Chem. Commun. *2010*, *46* (41), 7706-8 [DOI: 10.1039/c0cc02938f].

Nitrogen ↑ CC ↓↑ N

Microwaves [\\\\]

3-Component synthesis of 3-α-keto-3,4-dihydro-3-spiro-2-pyridones from cyclic α-diazo-β-diketones, α,β-ethylenealdehydes and prim. amines via Wolff rearrangement-[4+2]-cycloaddition

421.



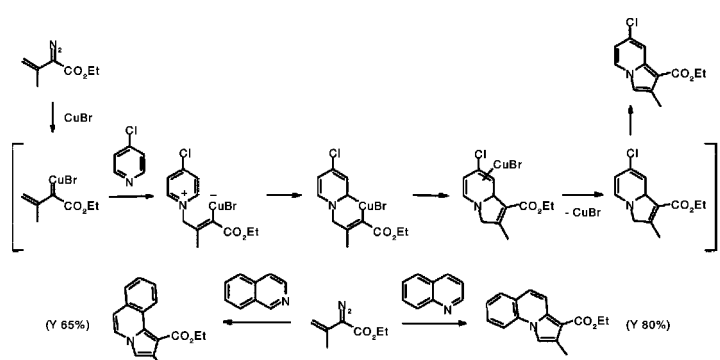
A soln. of the startg. diazo compd., amine (1 eq.) and aldehyde (1 eq.) in anhydrous toluene (2-3 ml; ca. 0.4 *M*) introduced into a microwave tube under argon, the tube sealed and subjected

to microwave irradiation with stirring at 140° for 15 min in a CEM Discover 1-300W or Anton-Paar Monowave 300 system (after a ramp up time of 2 min), the mixture cooled to 50° under an airflow, concentrated, and directly purified by flash chromatography → product. Y 70%. Reaction is presumed to involve initial Wolff rearrangement of the cyclic α-diazo-β-diketones followed by an unprecedented [4+2]-cycloaddition of the formed **α-ketoketenes *as dienophile*** with *in situ*-generated α,β-ethylenealdimines in a 6π-electrocyclization. In order to avoid undesirable addition of water (liberated on aldimine formation) to the α-ketoketene, an efficient *stepwise* protocol was also designed based on initial formation of the aldimine in toluene under microwave irradiation (at 140°), followed by elimination of all volatiles (incl. water) before addition of the diazo compd. and continued irradiation. The procedures are effective with both 6- and 7-membered diazodiketones and a range of alkylamines (incl. benzylamines, heterocyclic analogs and allylamines) as well as enals possessing isolated alkene groups. Anilines, however, failed to react although a complementary approach with the latter was developed based on a one-pot aza-Wittig-Wolff rearrangement-[4+2]-cycloaddition (five examples; Y 21-75%). F.e. (sixteen in all; Y 24-95%) s. M. Presset, Y. Coquerel, J. Rodriguez, Org. Lett. *2010*, *12* (18), 4212-5 [DOI: 10.1021/ol101938r].

Chiral cyclic bis(N-oxides) s. under Sc(OTf)$_3$ ←

Copper(I) bromide *CuBr*

Indolizines from pyridines and α,β-ethylenediazo compds.
Copper(I)-catalyzed [3+2]-cycloaddition



422.

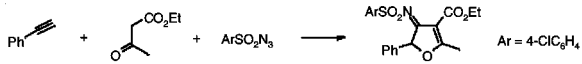
The first metal-catalyzed cyclization of a π-deficient heterocyclic system with alkenyldiazo compds. is reported, affording air- and light-sensitive indolizine derivs. in moderate to good yields following chromatographic purification. **E:** CuBr (5 mol%) added to a soln. of 4-chloropyridine (0.5 mmol) and ethyl 2-diazo-3-methylbut-3-enoate (1 eq.) in methylene chloride (5 ml), the mixture stirred at room temp., with protection from light, until reaction complete (TLC; 4-14 h), solvent removed under reduced pressure, and the residue purified by flash chromatography on a short, light-shielded column of deoxygenated silica gel → ethyl 7-chloro-2-methylindolizine-1-carboxylate. Y 74%. Sixteen examples afforded yields of 37-85%, tolerating a range of 4- or 3,5-substitution on the pyridine ring, vinyl or strongly electron-donating substituents (e.g. tosyloxy, methoxy or dimethylamino) being detrimental, affording poor yields or complex mixtures; α-substitution on the diazo compd. was particularly beneficial to the outcome. Regioselectivity for unsym. 3-subst. pyridines was highly dependent on the nature of the substituent, electron-withdrawing substituents (NO_2, CN, CO_2Me) favoring cyclization at the remote C-atom (100:1 to 3:1; Y 54-73%), while electron-donating substituents (Cl, F, Me) favored cyclization at the adjacent C-atom (1.5:1 to 7:1; Y 45-60%), in keeping with the proposed mechanism. Reaction was also

successful with benzo-fused pyridines, with quinolines and isoquinolines affording **pyrrolo[1,2-*a*]-quinolines** and **pyrrolo[2,1-*a*]isoquinolines** in good yield (50-80%; three examples), while phenanthridine gave a pyrrolo[1,2-*f*]phenanthridine (Y 30%). F.e.s. J. Barluenga, G. Lonzi, L. Riesgo, L.A. López, M. Tomás, J. Am. Chem. Soc. *2010*, *132* (38), 13200-2 [DOI: 10.1021/ja106751t].

Copper(I) iodide/triethylamine *CuI/Et$_3$N*

4-Sulfonylimino-4,5-dihydrofuran-3-carboxylic acid esters from β-ketocarboxylic acid esters, acetylene derivs. and sulfonic acid azides Copper(I)-catalyzed 3-component ring closure

423.

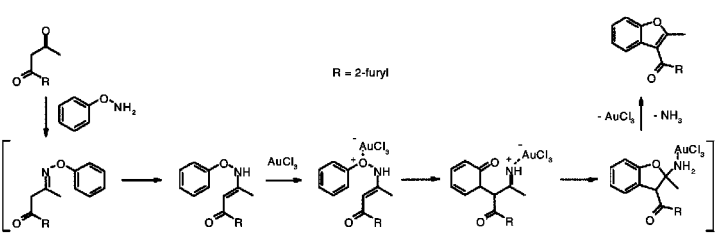


in one pot. Triethylamine (2 ml) added slowly via syringe to a stirred mixture of CuI (10 mol%), 4-chlorobenzenesulfonyl azide (1.2 eq.), phenylacetylene (1 mmol) and ethyl acetoacetate (3 eq.) in anhydrous THF (5 ml) under N_2 at 40°, the mixture stirred in a sealed tube for 8 h, concentrated *in vacuo*, extracted with methylene chloride, and purified by flash chromatography on silica → ethyl 4-(4-chlorophenylsulfonylimino)-2-methyl-5-phenyl-4,5-dihydrofuran-3-carboxylate. Y 82%. This novel and efficient cyclization was successful for electron-diverse arenesulfonyl azides and acyl- or aroyl-acetates (fourteen examples; Y 75-88%) but variations in the terminal acetylene component (aryl- or alkyl- acetylenes) or use of β-diketones resulted in no reaction. Structures were confirmed by X-ray analysis in one case. F.e. and optimization s. Y. Shang, K. Ju, X. He, J. Hu, S. Yu, M. Zhang, K. Liao, L. Wang, P. Zhang, J. Org. Chem. *2010*, *75* (16), 5743-5 [DOI: 10.1021/jo1010075].

Gold(III) chloride/silver hexafluoroantimonate *$AuCl_3$/$AgSbF_6$*

Benzofuran-3-carbonyl compds. from aroxylamines and β-ketocarbonyl compds.

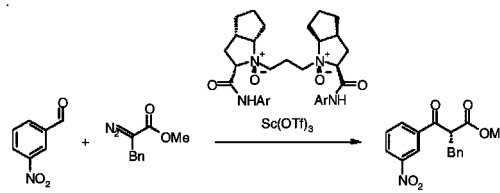
424.



in one pot. A soln. of O-phenylhydroxylamine (1 mmol) and startg. β-diketone (1.2 eq.) in nitromethane (1 ml) added to a soln. (previously stirred at room temp. for 5 min) of $AuCl_3$ (3 mol%) and $AgSbF_6$ (9 mol%) in the same solvent (2 ml) in a glovebox, the resulting mixture heated at 90° for 3 h, cooled to room temp., diluted with methylene chloride, filtered through Celite, solvent evaporated under reduced pressure, and the residue purified by chromatography on silica gel → furan-2-yl(2-methylbenzofuran-3-yl)methanone. Y 87% (single regioisomer). This facile, mild, gold(III)-catalyzed condensation-rearrangement-ring closure avoids the use of toxic CO gas, multistep reactions and high catalyst loadings, and employs readily-available starting materials (having wide functional group tolerance on either substrate), to afford title compds. in moderate to good yields (36-93%; twenty-five examples), with best results obtained from aliphatic or mono-(het)aryl β-diketones. β-Ketoesters and diaryl β-diketones afforded only moderate yields, however, while simple ketones (e.g. acetophenone or cyclohexanone) gave none of the desired products. Regioselectivity was excellent for alkyl aryl β-diketones, but poor for their unsym. dialkyl counterparts (e.g. hexane-2,4-dione). F.e. and optimization s. Y. Liu, J. Qian, S. Lou, Z. Xu, J. Org. Chem. *2010*, *75* (18), 6300-3 [DOI: 10.1021/jo101357d].

Zinc s. under (dppe)CoI_2 *Zn*
Zinc triflate s. under $Rh_2(OAc)_4$ *$Zn(OTf)_2$*
Zinc iodide s. under (dppe)CoI_2 *ZnI_2*
Triphenyl borate s. under Chiral biphenanthrols *$(PhO)_3B$*
Scandium(III) triflate/chiral cyclic bis(N-oxides) *[Sc(III)]**
Asym. Lewis acid-catalyzed synthesis of α-aroylcarboxylic acid esters from ar. aldehydes and α-diazocarboxylic acid esters $C{=}N_2 \rightarrow CHC(O)Ar$

425.



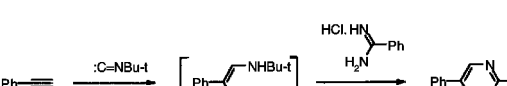
under mild conditions. A mixture of 3 Å molecular sieves (10 mg) and catalyst (*0.05 mol%*) in methylene chloride (0.2 ml) stirred at 35° under N_2 for 1 h, 3-nitrobenzaldehyde (1 mmol) and methyl 3-phenyl-2-diazopropanoate (1 eq.) added at -20°, the mixture stirred until substrates consumed, and purified by flash filtration through a thin layer of silica gel → methyl 2-benzyl-3-(3-nitrophenyl)-3-oxopropanoate. Y 93% (e.e. 96%). This novel, efficient, scalable (to 5 mmol) and clean asym. version of the Roskamp reaction was successful for a range of electron-diverse (het)ar. aldehydes, incl. sterically challenging substrates (twenty-six examples; Y 85-99%; e.e. 87-98%). Enantiomeric excess was determined after rapid filtration, as products were prone to racemization on silica, while quoted yields were determined after conventional chromatography during which significant racemization occurred (e.e. 29-92%). Absolute stereochemistry was determined by conversion to known compds. in one case. The catalyst was prepared by mixing $Sc(OTf)_3$ (1.2 eq.) and ligand in THF and was stable in soln. for at least one month. F.e., substrate prepn., optimization and reduction of products to **chiral β-hydroxycarboxylic acid esters or 1,3-diols** s. W. Li, J. Wang, X. Hu, K. Shen, W. Wang, Y. Chu, L. Lin, X. Liu, X. Feng, J. Am. Chem. Soc. *2010*, *132* (25), 8532-3 [DOI: 10.1021/ja102832f].

Chiral bis(Δ^2-oxazolines) s. under $Rh_2(OAc)_4$ *box*
tert-Butyl isocyanide s. under [Bis(pyrrol-2-ylmethyl)methylamine-N′,N′-diyl]-bis(dimethylaminato)titanium(IV) *t-BuNC*

Chiral biphenanthrols/triphenyl borate ←
Asym. synthesis of 2-acylaziridines
from diazomethyl ketones and aldimines s. *78*, 485

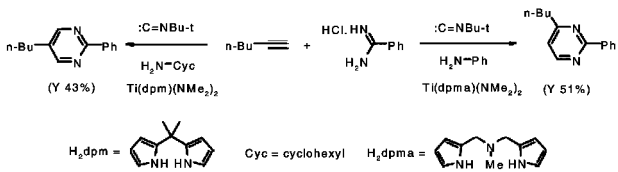
[Bis(pyrrol-2-ylmethyl)methylamine-N′,N′-diyl]bis(dimethylaminato)titanium(IV)/tert-butyl isocyanide/cyclohexylamine or aniline ←
Pyrimidines from acetylene derivs. and *tert*-butyl isocyanide via condensation of intermediate vinylogous amidines with amidines ○

426.



Titanium-catalyzed 3-component synthesis of vinylogous amidines (*65*, 283) has been elaborated to afford pyrimidines (which may bear substituents in the 2-, 4- and/or 5-positions) by further reaction with amidines **in one pot** (with loss of NBu-*t* from the isonitrile and the prim. amine).

E: Cyclohexylamine (1 eq.), Ti(dpma)$(NMe_2)_2$ (10 mol%), phenylacetylene (5 mmol), *tert*-butyl isonitrile (1.5 eq.) and dry toluene (10 ml) added to a pressure tube in a glove box under N_2, the tube sealed with a Teflon screw cap, taken out of the dry box, heated at 100° with vigorous stirring for 24 h (monitored by GC-FID), the pressure tube cooled to room temp., volatiles removed under reduced pressure, benzamidine hydrochloride (7.5 mmol) in *tert*-amyl alcohol (10 ml) added, heated to 150° for 24 h, *tert*-amyl alcohol removed under reduced pressure, the crude product dissolved in methylene chloride, washed with water, the organic layer dried (Na_2SO_4), concentrated on a rotary evaporator, and the residue purified by chromatography on silica → 2,5-diphenylpyrimidine. Y 51%. Although yields are moderate (17-51%; sixteen examples), the method is simple and is applicable to internal or terminal acetylenes, incl. heteroaromatic alkynes and enynes, and to a variety of amidines (or guanidine or isothioureas). It shows high regioselectivity: with arylacetylenes, 5-arylpyrimidines are favored electronically, while with 1-hexyne, for example, the regioselectivity can be controlled by choice of catalyst.

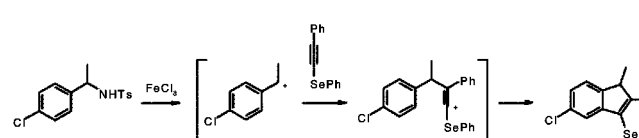


F.e. and with aniline in place of cyclohexylamine s. S. Majumder, A.L. Odom, Tetrahedron *2010*, *66* (17), 3152-8 [DOI: 10.1016/j.tet.2010.02.066].

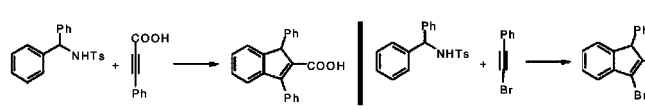
p-Toluenesulfonic acid s. under $Rh_2(OAc)_4$ *TsOH*

Hydrogen chloride *HCl*
Benzofurans from ketones s. *78*, 95 ○

Iron(III) chloride *$FeCl_3$*
Indenes from N-tosylbenzylamines and acetylene derivs.
Regioselective ring closure



427.

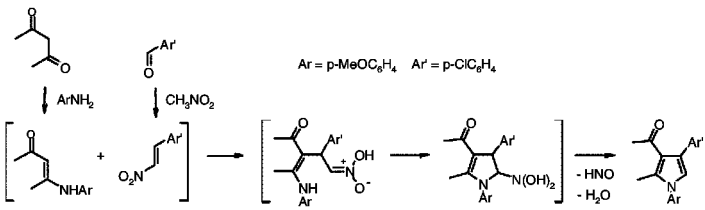


3-(Organoseleno)indenes. Startg. alkyne (1.2 eq.) and $FeCl_3$ (10 mol%) added to a soln. of N-benzylic sulfonamide (0.2 mmol) in dry nitromethane (2 ml), the mixture stirred at 80° for 24 h (TLC), cooled to room temp., and purified by silica gel chromatography → product. Y 81%. This method uses an inexpensive catalyst with a broad range of readily accessible N-benzylic sulfonamides (avoiding formation of hydrogen halides as by-products) and disubst. acetylenes (diarylacetylenes bearing electron-donating or -withdrawing groups, aryl-alkyl-derivs.,

α,β-acetylenecarbonyl compds., α,β-acetylenehalides or alkynyl chalcogenides); there was no reaction with terminal acetylenes, however. Reaction of phenylethynyl(trimethyl)silane with diphenylacetylene afforded 1,3,3-triphenylprop-1-yne instead of an indene, supporting the proposal that reaction involves cationic intermediates. F.e. (twenty-nine; Y 43-83%) and optimization s. C.-R. Liu, F.-L. Yang, Y.-Z. Jin, X.-T. Ma, D.-J. Cheng, N. Li, S.-K. Tian, Org. Lett. *2010*, *12* (17), 3832-5 [DOI: 10.1021/ol101524w].

4-Component synthesis of pyrrol-3-ylcarbonyl compds. from β-ketocarbonyl compds., aldehydes, prim. amines and aliphatic nitro compds. ○

428.

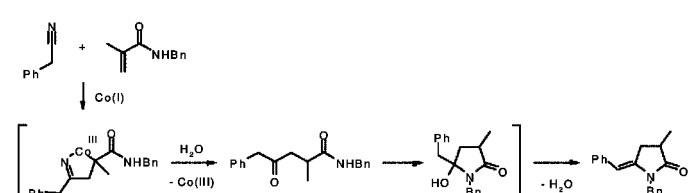


in the absence of solvent. Anhydrous $FeCl_3$ (0.1 mmol) added to a stirred soln. of *p*-anisidine (1.5 mmol), *p*-chlorobenzaldehyde (1 mmol) and acetylacetone (1 mmol) in nitromethane (1 ml), the mixture heated to reflux slowly for 7 h, cooled to room temp., excess solvent removed under vacuum, and the residue purified directly by chromatography on silica gel → 1-[4-(4-chlorophenyl)-1-(4-methoxyphenyl)-2-methyl-1*H*-pyrrol-3-yl]ethanone. Y 56%. The procedure is simple, eco-friendly, inexpensive and generally applicable in moderate to very good yield to the coupling of electron-diverse aromatic or aliphatic aldehydes and electron-diverse anilines or aliphatic prim. amines with β-diketones or β-ketocarboxylic acid esters in nitro-methane or -ethane (thirty-six examples; Y 44-85%). Other iron salts, $InCl_3$, $Yb(OTf)_3$, and Brønsted acids (HCl, TsOH, CF_3SO_3H) were less effective, as was reaction in organic solvents. A variety of functional groups were tolerated (e.g. OMe, Cl, Br, F, CN, keto), as well as heteroaryl groups, but one limitation is that anilines with strongly electron-withdrawing groups (e.g. NO_2) gave unsatisfactory yields. Reaction is presumed to involve initial Lewis acid-catalyzed enamine formation from the aldehyde and prim. amine, followed by its Michael-type addition to *in situ*-generated nitroalkene prior to ring closure with expulsion of HNO and water. F.e.s. S. Maiti, S. Biswas, U. Jana, J. Org. Chem. *2010*, *75* (5), 1674-83 [DOI: 10.1021/jo902661y].

Chiral cobalt(II) porphyrin complexes *[Co(II)]** ▽
Asym. cyclopropanation of ethylene derivs. with diazo compds. s. *23*, 819s*78*

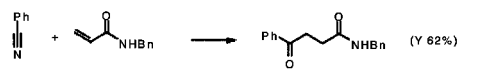
Diiodo[1,2-bis(diphenylphosphino)ethane]cobalt(II)/zinc/zinc iodide/water ←
Regioselective cobalt(II)-catalyzed synthesis of (E)-5-alkylidene-2-pyrrolidones from α-methylenecarboxylic acid amides and nitriles ○

429.



Phenylacetonitrile (2.5 eq.), N-benzyl-2-methylacrylamide (1 mmol) and water (1 eq.) added sequentially to a nitrogen-purged sealed tube containing CoI_2(dppe) (10 mol%), Zn powder (1.5 eq.)

and ZnI_2 (20 mol%), the mixture stirred at 80° for 12 h, filtered through a Celite pad (with methylene chloride), the filtrate concentrated, and the residue purified by chromatography on silica gel → (5E)-1-benzyl-5-benzylidene-3-methylpyrrolidin-2-one. Y 66%. This atom- and step-economical method afforded exclusively *(E)*-5-alkylidene-2-pyrrolidones (eighteen examples, Y 58-91%) from acetonitriles (incl. a variety of α-alkyl and α-[het]aryl derivs.) and N-alkyl or N-aryl acrylamides (with or without an α-alkyl substituent). Mechanistically, reaction proceeds via zinc-promoted reduction of Co(II) to Co(I), which combines regioselectively with both nitrile and alkene moieties to form an intermediate cobaltaazacyclopentene, subsequent hydrolysis and cyclocondensation of which affords the product. Interestingly, reductive coupling of *benzonitrile* with N-benzylacrylamide proceeds to give a linear product which fails to undergo keto-amide cyclization, demonstrating the need for α protons on the nitrile component.

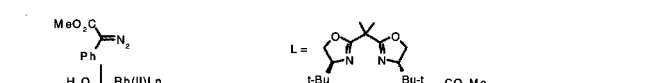


F.e.s. Y.-C. Wong, K. Parthasarathy, C.-H. Cheng, J. Am. Chem. Soc. *2009*, *131* (51), 18252-3 [DOI: 10.1021/ja9088296].

Chiral aqua(carbonyl)chlorobis(Δ^2-oxazoline)ruthenium(II) complexes *[Ru(II)]**
Chiral ruthenium(II) or rhodium(I or II) complexes *[Ru(II)]* or [Rh(I or II)]**
Asym. cyclopropanation of ethylene derivs. with diazo compds. ▽
with chiral rhodium(I) complexes s. *23*, 819s*77*; asym. cyclopropanation with dimethyl diazomalonate using a chiral chlororhodium(I) diene complex based on a *tridentate* bis(amide)-functionalized tetrafluorobenzene-condensed norbornadiene as ligand s. T. Nishimura, Y. Maeda, T. Hayashi, Angew. Chem., Int. Ed. *2010, 49* (40), 7324-7 [DOI: 10.1002/anie.201003775]; using a chiral dirhodium(II) tetracarboxylate based on N-(*tert*-butylphenylsulfonyl)-4-hydroxyproline s. H.T. Bonge, M. Kaboli, T. Hansen, Tetrahedron Lett. *2010, 51* (41), 5375-7 [DOI: 10.1016/j.tetlet.2010.07.115]; using chiral dirhodium(II) tetracarboxylates based on *functionalized* 1,8-naphthaloyl-(S)-*tert*-leucinate (e.g. the 4-bromo deriv.) s. A. Ghanem, M.G. Gardiner, R.M. Williamson, P. Müller, Chem. Eur. J. *2010, 16* (11), 3291-5 [DOI: 10.1002/chem.200903231]; chiral *trans*-cyclopropanes by reaction with *tert*-butyl diazoacetate using a chiral aqua(carbonyl)-chlorobis(Δ^2-oxazoline)ruthenium(II) complex s. J.-i. Ito, S. Ujiie, H. Nishiyama, ibid. *16* (17), 4986-90 [DOI: 10.1002/chem.200903514]; asym. cyclopropanation with cyano(diazo)acetic acid esters using the D_2-symmetric cobalt(II) porphyrin complexes, 3,5-di-*tert*-butyl-ChenPhyrin, s. S. Zhu, X. Xu, J.A. Perman, X.P. Zhang, J. Am. Chem. Soc. *2010, 132* (37), 12796-9 [DOI: 10.1021/ja1056246].

Rhodium(II) acetate/zinc triflate/chiral bis(Δ^2-oxazolines)/p-toluenesulfonic acid ←
Asym. synthesis of α-hydroxy-δ-ketocarboxylic acid esters from α,β-ethyleneketones, α-diazocarboxylic acid esters and water $C{=}N_2 \rightarrow C(OH)C\text{-}CHCO$

430.



under cooperative catalysis. Methylene chloride (1 ml; containing *0.05 wt% water*) added via a septum to $Zn(OTf)_2$ (0.03 mmol) and (S)-*t*-Bu-Box (0.036 mmol) in a flame-dried vial, the mixture stirred for 1 h at 25°, a soln. of 3-(4-bromophenyl)-1-(1-methyl-1*H*-imidazol-2-yl)prop-2-en-1-one (0.1 mmol), $Rh_2(OAc)_4$ (0.0022 mmol) and *p*-toluenesulfonic acid (0.042 mmol) in the same solvent (2 ml) added, stirring continued for 5 min at room temp., cooled to -8°, stirred for 10 min at this temp., methyl phenyldiazoacetate (0.25 mmol) in methylene chloride (1 ml) added, stirred

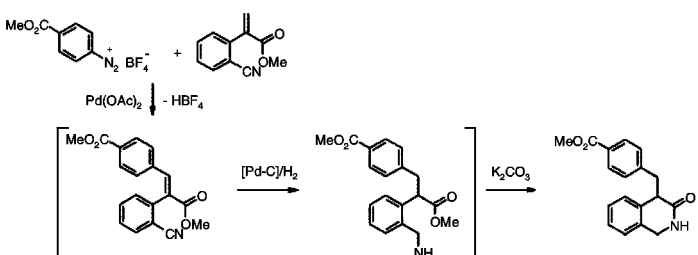
at -8° for 6-12 h (TLC monitoring), the soln. concentrated under reduced pressure, and worked up with purification by flash chromatography on silica gel → product. Y 78% (d.r. 97:3; e.e. 96%). Water is the third key component of the reaction, the amount of which is critical. Reaction is high-yielding with high enantioselectivity for the coupling of a range of methyl aryl(diazo)-acetates with cinnamyl 2-imidazolyl ketones, supporting both electron-donating and -withdrawing groups on the aromatic ring of both partners (sixteen examples; Y 60-86%; e.e. 85-99%). Reaction is presumed to involve initial generation of a highly nucleophilic oxonium ylid formed by complexation of the initially generated rhodium carbenoid with a water molecule; this then undergoes zinc-catalyzed asym. 1,4-addition to the enone in the same pot to secure the *quaternary* chiral center. $Sc(OTf)_3$ and $Yb(OTf)_3$ also served as Lewis acid, but Mg and Cu(II) salts were ineffective; TsOH was the most effective Brønsted acid, increasing the rate and selectivity of the reaction. F.e. and preliminary study with initial coupling of rhodium(II) with benzyl alcohol s. X.-Y. Guan, L.-P. Yang, W. Hu, Angew. Chem., Int. Ed. *2010*, *49* (12), 2190-2 [DOI: 10.1002/anie.200904905].

Palladium(II) acetate/carbon/potassium carbonate $Pd(OAc)_2/C/K_2CO_3$

4-Benzyl-1,2-dihydro-3(4*H*)-isoquinolones ○

from α-(*o*-cyanoaryl)acrylic acid esters and diazonium fluoroborates

via homogeneous Heck arylation-heterogeneous hydrogenation-lactamization



431.

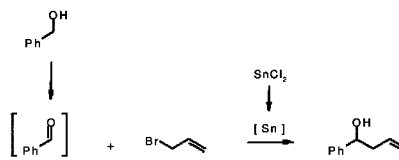
A palladium(II)-catalyzed *homogeneous* reaction [Heck-type arylation] has been combined sequentially in one pot with a *heterogeneous* hydrogenation and cyclization, the intermediate hydrogenation being facilitated by a palladium(0) catalyst generated *in situ* after the first stage. **E:** Startg. acrylate (1 mmol) and $Pd(OAc)_2$ (5 mol%) added to a soln. of the startg. diazonium fluoroborate (1.2 mmol) in methanol (5 ml), stirred for 12 h at 40°, charcoal (110 mg) added, stirring continued under a H_2 balloon (1 atm.) for 24 h at 50°, cooled to room temp., K_2CO_3 (2 mmol) added in one portion, the heterogeneous mixture stirred for 2 h, filtered, and purified by flash chromatography → product. Y 89%. After the initial Heck arylation, palladium-carbon is formed *in situ* and catalyzes hydrogenation of both the double bond and the cyano groups prior to base-catalyzed lactam formation. The procedure is mild, simple, eco-friendly, ligand- and additive-free, and highly efficient, as *only one* palladium source is required; it is also generally applicable to a range of diazonium fluoroborates possessing electron-withdrawing or -donating groups in the *o*-, *m*- or *p*-position (eight examples; Y 46-89%). Interestingly, reaction is also catalyzed by fluoroboric acid, formed *in situ* after the Heck arylation, which activates the cyano group towards hydrogenation. Furthermore, the generated palladium-carbon is easily removed by filtration, and proved active in other contexts, e.g. in Suzuki biaryl coupling, hydrogenation of alkyne groups and hydrogenative O-debenzylation. F.e.s. J. Laudien, E. Fouquet, C. Zakri, F.-X. Felpin, Synlett *2010* (10), 1539-43 [DOI: 10.1055/s-0029-1219926].

Halogen ↑ CC ↓↑ Hal

Irradiation s. under (2R,5S)-5-Benzyl-2,3-dimethyl-4-imidazolidone ///

Electrolysis/tin(II) chloride ϟ/$SnCl_2$
Barbier-type synthesis of 3-ethylenealcohols from *in situ*-generated oxo compds. under paired electrolysis CHOH → C(OH)C-C=C

432.



Electrosynthesis of homoallylic alcohols may now be carried out directly from alcohols by a tandem reaction in one pot. Thus, alcohols undergo oxidation to the corresponding aldehydes (or ketones) on the surface of a platinum anode in the absence of chemical oxidants, with concomitant reduction of $SnCl_2$ to Sn on a graphite cathode. The *in situ* generated oxo compds. and Sn then react with allyl bromide in solution. This method reduces energy waste by making use of the counter electrode. **E: 1-Aryl-3-ethylene-*sec*-alcohols**. A mixture of $SnCl_2$ (0.5 eq.), benzyl alcohol (2 mmol), allyl bromide (1.5 eq.), and aq. KNO_3 soln. (0.5 *M*; 6 ml) added to an undivided cell equipped with a Pt anode, graphite rod cathode and saturated calomel electrode (SCE) as reference electrode, the cell sealed with film, the mixture electrolyzed at a constant current of 20 mA at room temp. (25±1°) with stirring for 6 h, diluted with ethyl acetate, solvent removed by rotary evaporation, the residue purified by chromatography on silica gel, and the product dried under high vacuum for at least 0.5 h → 1-phenylbut-3-en-1-ol. Y 91%. The method is applicable to a variety of benzyl alcohols bearing electron-donating or -withdrawing groups (seven examples; Y 82-96%), although a moderate yield was obtained for the *p*-nitro deriv. (40%) and *o*-substitution lowered the yield (two examples, Y 50%, 70%; 1-naphthyl deriv.: Y 62%). The 2-thienyl deriv. also gave a low yield (34%). For solid alcohols acetonitrile was added to aid solubility. 1-Phenylethanol underwent oxidation but gave no allylation product, while aliphatic prim. or sec. alcohols worked well (phenethyl alcohol: Y 70%; cyclohexanol: Y 80%). Crotyl bromide gave the γ-product (Y 82%). F.e.s. L. Zhang, Z. Zha, Z. Zhang, Y. Li, Z. Wang, Chem. Commun. *2010*, *46* (38), 7196-8 [DOI: 10.1039/c0cc01964j]; s.a. L. Zhang, Z. Zha, Z. Wang, Synlett *2010* (13), 1915-8 [DOI: 10.1055/s-0030-1258504].

Microwaves s. under Zn, Ph_3P, 1-Methyl-3-[2-(diphenylphosphinoxy)propyl]-imidazolium hexafluorophosphate, $Mo(CO)_6$, Pd-C and $Pd(OAc)_2$ [\\\\]

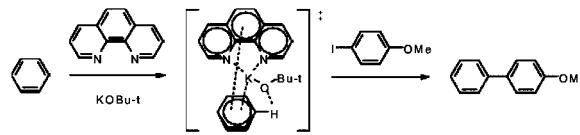
Sodium hydride *NaH*
α-Alkylation H → R
of β-ketocarboxylic acid esters s. *13*, 795; **α-methylation-^{11}C** of arylacetic acid esters s. M. Takashima-Hirano, M. Shukuri, T. Takashima, M. Goto, Y. Wada, Y. Watanabe, H. Onoe, H. Doi, M. Suzuki, Chem. Eur. J. *2010*, *16* (14), 4250-8 [DOI: 10.1002/chem.200903044].

Potassium hydroxide *KOH*
2-Arylthiophene ring from *o*-halogenaldehydes and benzyl mercaptans s. *78*, 246 ○

Cesium hydroxide/chiral quaternary ammonium bromides *CsOH/[R_4N]*Br*
Deconjugative asym. α-alkylation of 1,3-enyne-2-carboxylic acid esters s. *23*, 832s*78* ←

Potassium tert-butoxide/1,10-phenanthroline *KOBu-t/phen*
Organocatalyzed synthesis of biaryls from ar. halides and arenes Ar-Ar′

433.



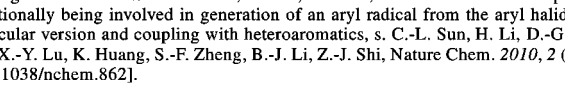
The first *organocatalyzed* synthesis of biaryls by direct coupling of aryl halides with arenes via C-H bond activation is reported. **E:** *t*-BuOK (0.4 mmol) added [in a glove box] to *p*-iodoanisole (0.2 mmol) and *1,10-phenanthroline* (20 mol%) in a dry Schlenk tube, benzene (2 ml) added, the mixture stirred in a sealed tube under N_2 at 100° for 24 h, cooled to room temp., filtered through a short plug of silica gel, washed with copious quantities of ethyl acetate, the combined organic phase concentrated under vacuum, and the residue purified by flash chromatography on silica gel → product. Y 83% (Y 86% from *p*-bromoanisole with 40 mol% catalyst). Significantly, no late transition metal or noble metal is required, so the procedure is relatively inexpensive, eco-friendly, waste-free and uncomplicated by metallic impurities. The procedure is applicable to aryl iodides or bromides possessing a wide range of functionality, yields being highest with substrates possessing electron-donating groups (notably MeO), while aryl chlorides and fluorides were notably unreactive (ca. forty examples; Y 26-89%). Some electron-deficient aryl iodides, however, were poor substrates, although the corresponding aryl bromides were reactive (with 40 mol% catalyst). Several arenes, incl. hindered mesitylene, participated in the coupling, enhancement of C-H acidity dramatically improving efficiency, but electron-deficient arenes (e.g. benzonitrile and ethyl benzoate) generally showed poor reactivity. Substituted 1,10-phenanthrolines also catalyzed the coupling but there was no reaction with DMEDA, suggesting that C-H activation involves interaction of the two nitrogen atoms of the catalyst and K^+ with the arene through π,π-stacking as well as ion-π-interactions; overall, however, a radical mechanism is proposed, the base additionally being involved in generation of an aryl radical from the aryl halide. F.e., also intramolecular version and coupling with heteroaromatics, s. C.-L. Sun, H. Li, D.-G. Yu, M. Yu, X. Zhou, X.-Y. Lu, K. Huang, S.-F. Zheng, B.-J. Li, Z.-J. Shi, Nature Chem. *2010*, *2* (12), 1044-9 [DOI: 10.1038/nchem.862].

Potassium tert-butoxide/chiral trans-3,4-dihydro-3,4-diaryldibenzo[c,g]phenanthrene-3,4-diols ←
Asym. α-benzylation of α-(alkylideneamino)carboxylic acid esters s. *23*, 832s*78* H → Bn

n-Butyllithium/dimethylformamide/ammonia/iodine *BuLi/DMF/NH_3/I_2*
Ar. nitriles from halides s. *29*, 845s*78* Hal → CN

Lithium bis(trimethylsilyl)amide [s.a. under $FeCl_3$] *LiN($SiMe_3$)$_2$*
α-Difluoroiodomethylation of carbonyl compds. with trifluoromethyl iodide via lithium enolates H → CF_2I

434.



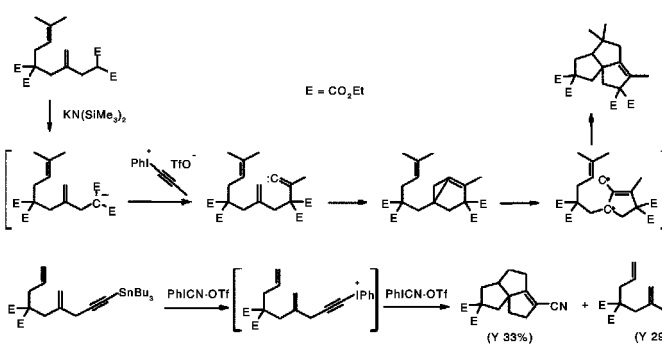
Remarkably, α-alkylation of lithium enolates with trifluoromethyl iodide results in *cleavage of the C-F bond* to give α-difluoroiodomethyl derivs., rather than cleavage of the weaker C-I bond to give the anticipated α-trifluoromethyl derivs.; and, just as surprisingly, no transition metal catalyst is required! **E:** Lithium bis(trimethylsilyl)amide (0.575 mmol) added at room temp. to a soln. of 3-benzyldihydrofuran-2-one (0.5 mmol) in THF (1 ml), gaseous trifluoromethyl iodide (5 mmol) introduced at -78°, stirred for 4 h at room temp., quenched by acetic acid (5 *M* soln. in THF) at room temp., and worked up with purification by chromatography on silica gel → 3-benzyl-

3-(difluoroiodomethyl)dihydrofuran-2-one. Y 71%. Reaction is applicable to a variety of carbonyl compds. (lactones, cyclic and acyclic ketones, esters and N-tosyllactams; seven examples; Y 32-72%), but relatively electron-rich lactams, e.g. N-(carbo-*tert*-butoxy)lactams, underwent classical α-trifluoromethylation. The nature of the amide base is critical, good yields also being reported with Li-bis[dimethyl(phenyl)silyl]amide and Li-2,2,6,6-tetramethylpiperidide, and via formation of the amine-free Li-enolates prepared **from enoxysilanes** and *n*-butyllithium. Mechanistically, reaction is thought to involve a 6-electron pericyclic process whereby a C-F bond is weakened via coordination of a fluorine atom to lithium. With the less sterically demanding Li-diisopropylamide, however, there was no reaction, as coordination of lithium to amide nitrogen and an NH-π interaction in the initially formed enolate prevents such Li-F coordination. α-Difluoroiodomethylation was also effected with two equivalents of the base, reaction in this case proceeding through an open-chain dimer formed by both O-Li-N and N-Li-F coordination. F.e. and application to the synthesis of the racemic iododifluoromethyl analog of ibuprofen s. K. Mikami, Y. Tomita, Y. Itoh, Angew. Chem., Int. Ed. *2010*, *49* (22), 3819-22 [DOI: 10.1002/anie.201000435].

Potassium bis(trimethylsilyl)amide $KN(SiMe_3)_2$

Angular triquinanes from 1,6-dienes via intramolecular [3+2]-cycloaddition

435.



A soln. of $KN(SiMe_3)_2$ (1 eq.) in toluene (0.15 ml) added to a stirred soln. of startg. diene (0.0749 mmol) in THF (10 ml) at 0°, the mixture stirred for 30 min, warmed to room temp., a soln. of 1-propynyl(phenyl)iodonium triflate (1.23 eq.) in THF (10 ml) added over 1.5 h via cannula, the mixture stirred for 2 h, quenched with satd. aq. $NaHCO_3$, extracted with ethyl acetate, concentrated *in vacuo*, and purified by flash chromatography on silica → (8aS)-tetraethyl 4,4,6-trimethyl-3,3a,4,5-tetrahydrocyclopenta[*c*]pentalene-2,2,7,7(1*H*,8*H*)-tetracarboxylate. Y 38%. This novel method proceeds via formation of a trimethylenemethane-diyl moiety and appears general (six examples; Y 28-40%) for varied substitution patterns on the terminal alkene (in contrast to analogous prepn. of *linear triquinanes*, s. *66*, 485). A phenyl terminated deriv. however, afforded an unexpected isomeric by-product (Y 16%). The reaction is limited to the simple propynyl-iodonium salt due to facile side-reactions of its derivatives, and appears restricted to carbon-tethered substrates (an O-tethered analog was unreactive). In a further development, substrates incorporating the alkynyliodonium moiety were treated with nucleophiles to afford ca. 1:1 mixtures of triquinanes and simple substitution products of the alkyne (three examples; Y 37-82%). F.e. and substrate prepn. s. H.-Y. Lee, Y. Jung, Y. Yoon, B.G. Kim, Y. Kim, Org. Lett. *2010*, *12* (11), 2672-4 [DOI: 10.1021/ol100907t].

Potassium carbonate/chiral quaternary ammonium chlorides $K_2CO_3/[R_4N]^*Cl$

Asym. α-alkylation H → R

under phase transfer catalysis s. *23*, 832s*39*; synthesis of N-(β-glycosyl)asparagines via reaction of ethyl nitroacetate with per-O-acetylated N-(β-glycosyl)iodoacetamides with N-(9-anthracenyl-

methyl)cinchoninium chloride as phase transfer catalyst and K_2CO_3 as base s. K.J.V. Paul, L. Sahoo, D. Loganathan, Tetrahedron Lett. *2010, 51* (43), 5713-7 [DOI: 10.1016/j.tetlet.2010.08.072]; asym. α-alkylation of α-benzoyloxy-β-keto-esters with a chiral spirocyclic quaternary ammonium salt as catalyst *en route* to chiral α,β-dihydroxycarboxylic acid esters s. T. Hashimoto, K. Sasaki, K. Fukumoto, Y. Murase, N. Abe, T. Ooi, K. Maruoka, Chem. Asian J. *2010, 5* (3), 562-70 [DOI: 10.1002/asia.200900344]; deconjugative asym. α-alkylation of 1,3-enyne-2-carboxylic acid esters with CsOH and a chiral N,N-disubst. 4,5-dihydro-3*H*-dinaphth[2,1-*c*;1′,2′-*e*]azepinium bromide as catalyst s. T. Hashimoto, K. Sakata, K. Maruoka, Adv. Synth. Catal. *2010, 352* (10), 1653-6 [DOI: 10.1002/adsc.201000179]; asym. α-benzylation of α-(alkylideneamino)carboxylic acid esters with *t*-BuOK and a chiral *trans*-3,4-dihydro-3,4-diaryldibenzo[*c,g*]phenanthrene-3,4-diol as chiral source s. M. Kitamura, D. Kitahara, T. Okauchi, Synlett *2010* (14), 2097-100 [DOI: 10.1055/s-0030-1258520].

Cesium carbonate Cs_2CO_3

α-Arylation of α-(benzothiazol-2-ylsulfonyl)carbonyl compds. s. *78*, 462 H → Ar

Potassium iodide s. under Co(OAc)$_2$ or CoCl$_2$ *KI*

Sodium iodide s. under Chloro[2,2′-bis(dimethylamino)diphenylaminato]nickel(II) *NaI*

Ammonia s. under BuLi NH_3

Tetra-n-butylammonium hydroxide s. under Pd nanoparticles Bu_4NOH

Triethylamine Et_3N

1,1-Dichloro-1,9b-dihydroazeto[2,1-*c*][1,3]benzothiazin-2-ones from 2*H*-1,3-benzothiazines ☐N

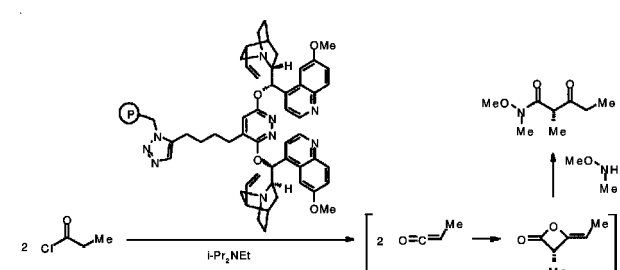
en route to 2*H*-1,3-benzothiazine 1,1-dioxides s. *78*, 41

Ethyldiisopropylamine/polymer-based 3,6-bis(9-O-[dihydro]quinidine)pyridazine ←

Heterogeneous asym. dimerization of ketenes CHC(O)C-C(O)N(R)(OR′)

Chiral β-ketohydroxamic acid esters

436.

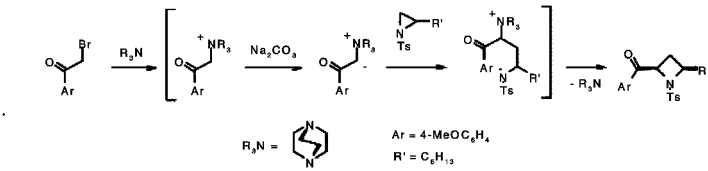


A convenient, easily scaled up route to polystyrene-supported quinidine and hydroquinidine ethers having high alkaloid loadings has been reported via 'click' chemistry, which obviates the need for chromatographic purification. These catalysts have been tested in the first heterogeneous asym. organocatalyzed dimerization of ketenes prepared *in situ* **from carboxylic acid chlorides** (cf. *66*, 383). **E:** A flask fitted with a medium porosity glass frit and stopcock side arm charged under N_2 with the Merrifield resin-supported organocatalyst (2.5 mol%) and dry methylene chloride (10 ml), followed by ethyldiisopropylamine (1 eq.) and startg. acid chloride (1 mmol), the flask closed under N_2, kept on an orbital shaking platform at room temp. for 6 h, the mixture filtered through the enclosed frit, the combined filtrates treated under N_2 with HN(OMe)Me (0.5 eq.) and 2-pyridone (5 mol%), the soln. stirred at room temp. for 2 h, worked-up, and filtered through silica gel → product. Y 60% (e.e. 97%). The catalyst displays good substrate compatibility and may be recycled 20 times with little loss of efficiency. F.e. (two; Y 56%, 61%; e.e. 97%) and catalysts s. R.P. Jumde, A. Mandoli, F. De Lorenzi, D. Pini, P. Salvadori, Adv. Synth. Catal. *2010, 352* (9), 1434-40 [DOI: 10.1002/adsc.201000165].

Triethylenediamine/sodium carbonate/silica gel *DABCO/Na_2CO_3/SiO_2*

2-Acyl-N-tosylazetidines from N-tosylaziridines and α-bromoketones
Diastereoselective heterogeneous ring expansion in water
via 2-ketoammonium ylids

437.



in one pot. A mixture of 4-methoxyphenacyl bromide (1 eq.), DABCO (40 mol%), 2-hexyl-N-tosylaziridine (1 mmol), Na_2CO_3 (1.5 eq.) and silica gel (60-120 mesh; 1 g) in water (5 ml) stirred at 80° until reaction complete (TLC; 23 h), filtered through Celite, acidified with 1 *M* aq. HCl (5 ml), extracted with ethyl acetate, washed with satd. aq. $NaHCO_3$, concentrated *in vacuo*, and purified by chromatography on silica → *cis*-2-hexyl-4-(4-methoxybenzoyl)-N-tosylazetidine. Y 78% (*cis/trans* 89:11). This novel and environmentally-friendly ring expansion is catalyzed by several tert. amines, generating nitrogen ylids *in situ*, with little reaction taking place in the absence of silica or at room temp. Electron-diverse phenacyl bromides reacted effectively with 2-alkyl- or 2-aryl-aziridines to afford ***cis*-2-aroyl-N-tosylazetidine** with high selectivity (89-95%; fifteen examples; Y 77-86%). F.e.s. Garima, V.P. Srivastava, L.D.S. Yadav, Green Chem. *2010*, *12* (8), 1460-5 [DOI: 10.1039/c004736h].

Copper(I) oxide/4,5-bis(diphenylphosphino)-9,9-dimethylxanthene/cesium carbonate ←

Palladium-free Sonogashira coupling C≡CH → C≡CR

s. *66*, 384s*77*; with ar. iodides using Cu_2O/XantPhos/Cs_2CO_3 for coupling sterically demanding substrates s. C.-H. Lin, Y.-J. Wang, C.-F. Lee, Eur. J. Org. Chem. *2010* (23), 4368-71 [DOI: 10.1002/ejoc.201000653]; at low catalyst loading under copper(I) catalysis in the presence of a large excess of a diamine cf. E. Zuidema, C. Bolm, Chem. Eur. J. *2010*, *16* (14), 4181-5 [DOI: 10.1002/chem.201000344].

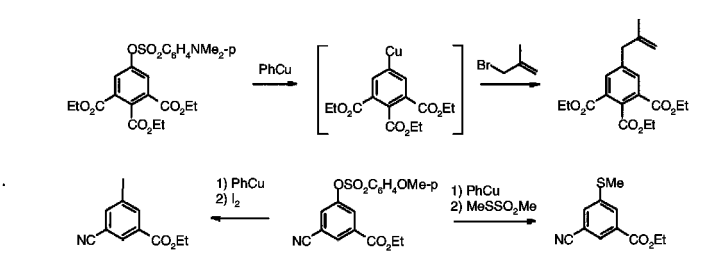
Silver(I) oxide s. under Pd(OAc)₂ *Ag_2O*

Phenylcopper/cobalt(II) acetoacetonate/4-fluorostyrene/tetra-n-butylammonium iodide ←

Cobalt-catalyzed cross-coupling $ArOSO_2Ar'$ → [ArCu] → ArR

of electron-deficient aryl sulfonates via arylcopper(I) compds.

438.



Bu_4NI (1 eq.), startg. aryl sulfonate (1 mmol), $Co(acac)_2$ (20 mol%), 4-fluorostyrene (50 mol%) and dry *N,N'-dimethyl-N,N'-propyleneurea* (2.2 ml) added to a soln. of phenylcopper [freshly

prepared from PhMgCl (3 eq.) and CuCN·2LiCl (3.6 eq.)] in THF (3.6 ml) at -20° under argon, the mixture stirred at 25° until startg. m. consumed (GC), the mixture cooled to -20°, 2-methyl-3-bromoprop-1-ene (2 eq.) added, the mixture stirred at -20° for 30 min and at 25° for 2 h, quenched with aq. NH_4Cl/NH_3, extracted with ether and ethyl acetate, concentrated *in vacuo*, and purified by chromatography on silica → triethyl 5-(2-methylprop-2-en-1-yl)benzene-1,2,3-tricarboxylate. Y 72%. In this novel method, use of benzenesulfonate esters containing electron-donating *para* substituents (OMe, NMe_2) minimized the formation of cross-coupled products to afford arylcopper species; these were trapped with carbon-, sulfur- and iodine-based electrophiles to afford relatively inaccessible tri- and tetra-subst. arenes (twenty examples; Y 53-78%) in the presence of nitrile, ester and aldehyde functionality. F.e. and substrate prepn. s. C.J. Rohbogner, C.R. Diène, T.J. Korn, P. Knochel, Angew. Chem., Int. Ed. *2010*, *49* (10), 1874-7 [DOI: 10.1002/anie.200905379].

Copper(I) tert-butoxide s. under Mg — *CuOBu-t*

Silver carbonate s. under Pd(OAc)$_2$ — *Ag_2CO_3*

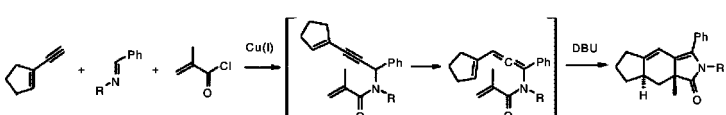
Silver acetate s. under Pd nanoparticles — *AgOAc*

Copper(I) bromide s. under Mg — *CuBr*

Copper(I) iodide s.a. under Mg, Chloro[2,2′-bis(dimethylamino)diphenylaminato]-nickel(II), Pd(OAc)$_2$, Pd$_2$(dba)$_3$, Nanosized MCM-41-anchored (2,2′-bipyridyl)palladium complexes, Palladium phosphine complexes and supported variants, [(cinnamyl)PdCl]$_2$ and PdCl$_2$(PPh$_3$)$_2$ — *CuI*

Copper(I) iodide/triethylamine/1,8-diazabicyclo[5.4.0]undec-7-ene — *CuI/Et$_3$N/DBU*

Copper-catalyzed diastereoselective 3-component synthesis of 2,6,7,7a-tetrahydroisoindol-1-ones from 1,3-enynes, aldimines and α,β-ethylenecarboxylic acid chlorides ○



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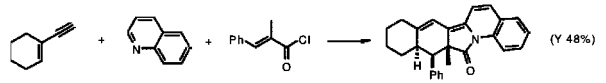


in one-pot. 1-Ethynylcyclopent-1-ene (1.2 eq.), N-benzylidene-4-methylbenzenamine (0.5 mmol), methacryloyl chloride (1.2 eq.), and triethylamine (1.5 eq.) added sequentially to a suspension of CuI (10 mol%) in acetonitrile (5 ml), the mixture stirred under N_2 at room temp. for 1 h, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; *3 eq.*) added, stirring continued for a further 12 h, filtered, concentrated, and the residue purified by flash chromatography on silica gel → product. Y 80%. The procedure was applicable to a wide variety of substrates in which the enyne, imine or enoic acid chloride could be variously substituted with H, alkyl or (het)aryl groups, affording tetrahydroisoindolone derivs. with up to three stereogenic centers (eleven examples; Y 41%, 55-92%). Reaction proceeds **via** isolable intermediate **5-(α,β-ethyleneacylamino)-1,3-enynes** which, on treatment with DBU, undergo propargyl-allenyl isomerization, followed by intramolecular [4+2]-cycloaddition. Weaker bases (Et_3N, K_2CO_3) failed to effect the isomerization step, while use of a stronger base (*t*-BuOK) gave rise to unidentified product mixtures. The imine component could be successfully replaced with quinoline or isoquinoline, affording polycyclic products in moderate to good yield (48-77%; three examples). F.e.s. J. Cao, X. Huang, Org. Lett. *2010*, *12* (21), 5048-51 [DOI: 10.1021/ol102235t].

Copper(I) iodide·ferrocenyltri(phosphines) s. under Bis(allylpalladium chloride) ←
Silver(I) salts s. under Zn *Ag(I)*

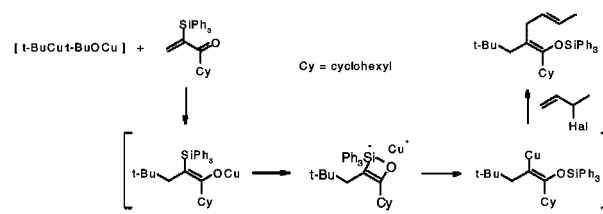
Calcium oxide *CaO*
Arndt-Eistert synthesis of diazomethyl ketones C(O)Hal → $C(O)CHN_2$
s. 2, 707; improved procedure with CaO requiring a *minimal* amount of diazomethane s. V. Pace, G. Verniest, J.-V. Sinisterra, A.R. Alcántara, N. De Kimpe, J. Org. Chem. *2010, 75* (16), 5760-3 [DOI: 10.1021/jo101105g].

Magnesium [s.a. under Fe(OTf)$_3$] *Mg*
Ketones from carboxylic acid esters COOR → C(O)R′
4-Acyl-oxazoles via -oxazolines s. *78*, 165

Magnesium/copper(I) bromide/1(S)-(dicyclohexylphosphino)-2-[2(R)-(dicyclohexyl-phosphino)phenyl](dimethylamino)methyl]ferrocene or chiral TADDOL-based o-(diphenylphosphino)phenyl phosphites *Mg/[L]**
Magnesium/(S,S)-1-(o-hydroxybenzyl)-3-mesityl-4,5-diphenylimidazolidin-2-ylidene ←
Regioselective asym. synthesis of ethylene derivs. from β,γ-ethylenehalides C(R)C=C
under copper(I) catalysis s. *62*, 381s*70*; asym. synthesis of 3-ethylenetosylamines with CuBr and TaniaPhos as chiral ligand s. J.F. Teichert, S. Zhang, A.W. van Zijl, J.W. Slaa, A.J. Minnaard, B.L. Feringa, Org. Lett. *2010, 12* (20), 4658-60 [DOI: 10.1021/ol101944j]; of chiral α-subst. allylarenes from cinnamyl chlorides with chiral TADDOL-based *o*-(diphenylphosphino)phenyl phosphites as ligand s. W. Lölsberg, S. Ye, H.-G. Schmalz, Adv. Synth. Catal. *2010, 352* (11-12), 2023-31 [DOI: 10.1002/adsc.201000213]; *copper-free* method with (S,S)-1-(*o*-hydroxybenzyl)-3-mesityl-4,5-diphenylimidazolidin-2-ylidene as ligand s. O. Jackowski, A. Alexakis, Angew. Chem., Int. Ed. *2010, 49* (19), 3346-50 [DOI: 10.1002/anie.201000577].

Magnesium/copper(I) iodide/copper(I) tert-butoxide *Mg/CuI/CuOBu-t*
Regio- and stereo-selective 3-component synthesis of enoxysilanes from α,β-ethylene-α-silylketones, organocopper compds. and halides ←

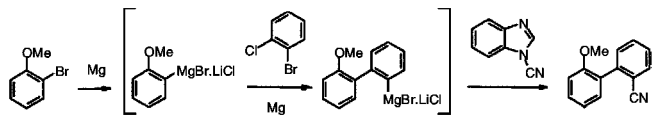
440.



tert-Butylmagnesium bromide (1.2 eq.) in THF (0.77 ml) added to a suspension of CuI (1.2 eq.) in THF (1.5 ml) at 0° under argon, the mixture stirred for 30 min, Cu-*tert*-butoxide [freshly prepared from Li-*tert*-butoxide (1.2 eq.) and CuI (1.2 eq.)] in THF (1.5 ml) added via cannula, stirred for 30 min, a soln. of startg. ketone (0.6 mmol) in THF (1.5 ml) added, the resulting mixture stirred for 2 h, DMF (6 ml) added, heated at 50° for 30 min, a soln. of the 3-halobut-1-ene (3 eq.) in DMF (3 ml) added, stirred for a further 4 h, quenched with 3.5% aq. NH_3, extracted with ether, washed with water, concentrated *in vacuo*, and purified chromatographically → (1E,4E)-1-cyclohexyl-2-(2,2-dimethylprop-1-yl)-1-triphenylsiloxy-1,4-hexadiene. Y 91%. This novel method appears general for α-silylvinyl ketones, with key rearrangement of the initial copper enolate *occurring critically in DMF*, before final quenching with allyl, benzyl, methyl or dimethylphenylsilyl halides. Stereoselectivity (93-100%; 87% for MeI) was controlled by a cyclic silyl ether intermediate (fourteen examples; Y 64-91%). F.e.s. A. Tsubouchi, S. Enatsu, R. Kanno, T. Takeda, Angew. Chem., Int. Ed. *2010, 49* (39), 7089-91 [DOI: 10.1002/anie.201003152].

Magnesium/N-cyanobenzimidazole ←
Ar. nitriles from ar. bromides via arylmagnesium bromides Br → CN

441.



The development of an electrophilic cyanation process is reported that is applicable to electron-diverse (het)aryl Grignard reagents under mild conditions (fourteen examples; Y 61-86%) in the presence of vinyl, tert. amine, ether, chloro and trifluoromethyl functionality. The method has been used in a novel **3-component synthesis of *o*-cyanobiaryls** starting from ar. bromides and *o*-chlorobromides. **E:** A freshly prepared soln. of 2-methoxyphenylmagnesium bromide·LiCl (1.05 eq.) in THF (2 ml) added via septum to a stirred mixture of Mg (1.1 eq.) and THF (1 ml) under argon, a portion (0.1 ml) of a soln. of 2-chlorobromobenzene (2 mmol) in THF (1 ml) added with vigorous stirring at room temp. to initiate the reaction and the remainder added over 15 min at 60°, the mixture stirred for 1 h, added via syringe pump to a soln. of N-cyanobenzimidazole (1.5 eq.) in THF (3 ml) at 0° over 45 min, stirred for 2 h, quenched with satd. aq. NH_4Cl, extracted with ether, and purified chromatographically → 2-(2-methoxyphenyl)benzonitrile. Y 62%. F.c. (seven; Y 54-71%) and optimization s. P. Anbarasan, H. Neumann, M. Beller, Chem. Eur. J. *2010*, *16* (16), 4725-8 [DOI: 10.1002/chem.201000086].

Magnesium/iron(III) acetoacetonate or anionic iron(II) N-heterocyclic carbene complexes ←
Magnesium/palladium N-heterocyclic carbene or phosphine or *Mg/[Pd]*
sec-phosphine oxide or chlorophosphine complexes
Cross-coupling with Grignard compds. [Kumada coupling] RMgHal + R′Hal → R-R′
update s. *26*, 875s*77*; cross-coupling of arylmagnesium bromides *with unactivated alkyl chlorides* (bearing β-hydrogens) in the presence of $Pd(OAc)_2$ and air-stable *sec*-phosphine oxides [e.g. *tert*-butyl-(1-phenyl-2-indolyl)phosphine oxide] or aryl(*tert*-butyl)chlorophosphines [e.g. 2-[*tert*-butyl-(chloro)phosphino]-2′,6′-dimethoxybiphenyl] s. L. Ackermann, A.R. Kapdi, C. Schulzke, Org. Lett. *2010*, *12* (10), 2298-301 [DOI: 10.1021/ol100658y]; coupling with allyl halides (or protected allyl alcohols) with added $Fe(acac)_3$ s. M. Mayer, W.M. Czaplik, A.J. von Wangelin, Adv. Synth. Catal. *2010*, *352* (13), 2147-52 [DOI: 10.1002/adsc.201000228]; with alkyl halides, e.g. cyclohexyl bromide, in the presence of a highly active *anionic* iron(II) N-heterocyclic carbene complex, [[Fe(IPr)Br_3](HIPr)·C_7H_8], s. H.-h. Gao, C.-h. Yan, X.-P. Tao, Y. Xia, H.-M. Sun, Q. Shen, Y. Zhang, Organometallics *2010*, *29* (18), 4189-92 [DOI: 10.1021/om100482w]; coupling of alkyl- and cyclopropyl-magnesium bromides with ar. bromides mediated by $Pd(OAc)_2$/*t*-Bu_3P/$ZnBr_2$ as catalytic system s. C. Shu, K. Sidhu, L. Zhang, X.-j. Wang, D. Krishnamurthy, C.H. Senanayake, J. Org. Chem. *2010*, *75* (19), 6677-80 [DOI: 10.1021/jo100983c]; low-temp. coupling of polychlorinated acenes with methylmagnesium bromide and sterically demanding Grignards (substituting *all* chlorine atoms) with dichloro(3-chloropyridine)[1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene]palladium(II) as catalyst s. E. Yagodkin, C.J. Douglas, Tetrahedron Lett. *2010*, *51* (23), 3037-40 [DOI: 10.1016/j.tetlet.2010.03.121]; N-directed coupling of dichlorinated benzo-condensed N-heteroarenes with Grignards using $PdCl_2(PCy_3)_2$ as catalyst s. H. Konishi, T. Itoh, K. Manabe, Chem. Pharm. Bull. *2010*, *58* (9), 1255-8; **Kumada diaryl coupling** (cf. *32*, 828s*70*) of *o*-subst. ar. chlorides with hindered arylmagnesium bromides using an imidazol-2-ylidene-ligated cyclopalladated ferrocenylimine as catalyst s. G. Ren, X. Cui, Y. Wu, Eur. J. Org. Chem. *2010* (12), 2372-8 [DOI: 10.1002/ejoc.200901495]; synthesis of 2-arylpyridines with an air- and moisture-stable acetatopalladium(II) bis(*sec*-phosphine) complex as catalyst s. L. Ackermann, H.K. Potukuchi, A.R. Kapdi, C. Schulzke, Chem. Eur. J. *2010*, *16* (11), 3300-3 [DOI: 10.1002/chem.201000032].

Magnesium/tri-o-tolylphosphine/triethylsilyl triflate *Mg/o-Tol_3P/Et_3SiOTf*
Synthesis of ethers from acetals via 1-alkoxyphosphonium salts $C(OR)_2$ → C(OR)CN
s. *78*, 242

Zinc s.a. under Ph_3P and $Pd(OAc)_2$ *Zn*

Zinc/silver(I) salt *Zn/Ag(I)*

Zinc/nickel-carbon/microwaves or Zinc/nickel(I) complex *Zn/Ni-C[\\\\] or Zn/Ni(I)*

Zinc/palladium N-heterocyclic carbene or phosphine complexes *Zn/[Pd]*

Negishi coupling R-R′

update s. *38,* 836s*76*; coupling of 6-iodopurine bases and nucleosides with diisopropoxyphosphinylmethylzinc bromide with added $Pd(PPh_3)_4$ (cf. *56,* 385s*70*) s. Z. Hasník, R. Pohl, M. Hocek, Tetrahedron Lett. *2010, 51* (18), 2464-6 [DOI: 10.1016/j.tetlet.2010.02.167]; coupling of functionalized [het]aryl or alkenyl iodides or bromides with alkylzinc halides under nickel catalysis via an alkylnickel(I) complex s. V.B. Phapale, M. Guisán-Ceinos, E. Buñuel, D.J. Cárdenas, Chem. Eur. J. *2009, 15* (46), 12681-8 [DOI: 10.1002/chem.200901913]; *alkyl-alkyl* Negishi coupling (cf. *58,* 374s*69*) with a palladium(0) 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene complex and 1:1 LiBr/*n*-BuZnBr via a presumed higher-order alkyl(tribromo)zincate s. G.T. Achonduh, N. Hadei, C. Valente, S. Avola, C.J. O'Brien, M.G. Organ, Chem. Commun. *2010, 46* (23), 4109-11 [DOI: 10.1039/c002759f]; generation of *quaternary carbon centers* by coupling benzyl- or allylzinc halides with *tert*-alkyl bromides or 1,1-dibromides in the presence of a silver(I) salt s. Y. Mitamura, Y. Asada, K. Murakami, H. Someya, H. Yorimitsu, K. Oshima, Chem. Asian J. *2010, 5* (6), 1487-93 [DOI: 10.1002/asia.201000068]; preparation (and coupling) of functionalized alkyl-zinc halides ($RZnX{\cdot}MgX_2{\cdot}LiX$) from alkyl bromides with $Mg/ZnCl_2/LiCl$ s. T.D. Blümke, F.M. Piller, P. Knochel, Chem. Commun. *2010, 46* (23), 4082-4 [DOI: 10.1039/c001845g]; **Negishi diaryl coupling** (cf. *38,* 836s*70,76*) with bromoanilines under catalysis with $Pd(dba)_2$/RuPhos with isopropyl iodide as accelerator s. M. Kienle, P. Knochel, Org. Lett. *2010, 12* (12), 2702-5 [DOI: 10.1021/ol1007026]; synthesis of 5-aryl- and 5-heteroaryl-2-furaldehydes with $Pd(PPh_3)_4$ as catalyst s. S.-H. Kim, R.D. Rieke, Tetrahedron Lett. *2010, 51* (19), 2657-9 [DOI: 10.1016/j.tetlet.2010.03.035]; low-temp. synthesis of highly functionalized *tetra-o-subst.* biaryls with dichloro(3-chloropyridine)[1,3-bis(2,6-diisopentyl)imidazol-2-ylidene]palladium(II) as catalyst s. S. Çalimsiz, M. Sayah, D. Mallik, M.G. Organ, Angew. Chem., Int. Ed. *2010, 49* (11), 2014-7 [DOI: 10.1002/anie.200906811]; *heterogeneous* biaryl synthesis under microwave irradiation with Ni-carbon/triphenylphosphine under *vigorous* stirring for efficient mass transfer, also f. reactions with other supported catalysts, s. M. Irfan, M. Fuchs, T.N. Glasnov, C.O. Kappe, Chem. Eur. J. *2009, 15* (43), 11608-18 [DOI: 10.1002/chem.200902044]; preparation (and coupling) of functionalized 2- and 3-pyridylzinc bromides s. S.-H. Kim, R.D. Rieke, Tetrahedron *2010, 66* (17), 3135-46 [DOI: 10.1016/j.tet.2010.02.061]; preparation of [het]arylzinc chlorides with sensitive functionality s. T. Bresser, M. Mosrin, G. Monzon, P. Knochel, J. Org. Chem. *2010, 75* (14), 4686-95 [DOI: 10.1021/jo100884u]; *t*-Bu-P_4-promoted synthesis of arylzinc compds. from aryl iodides with $ZnEt_2$ s. H. Naka, K. Ito, M. Ueno, K. Kobayashi, Y. Kondo, New J. Chem. *2010, 34* (8), 1700-6 [DOI: 10.1039/c0nj00202j]; Negishi-type coupling of alkenyl with alkyl halides *in water* in the presence of Zn/TMEDA and a $PdCl_2(Amphos)_2$ with PTS as amphiphilic surfactant s. A. Krasovskiy, C. Duplais, B.H. Lipshutz, Org. Lett. *2010, 12* (21), 4742-4 [DOI: 10.1021/ol101885t].

Zinc cyanide s. under $Pd(OAc)_2$ *$Zn(CN)_2$*

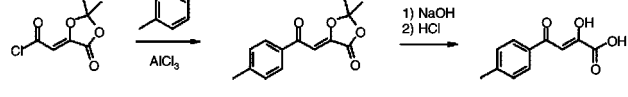
Indium s. under Ph_3P *In*

Silver fluoroborate s. under $Pd(OAc)_2$ *$AgBF_4$*

Aluminum chloride/sodium hydroxide/hydrogen chloride *$AlCl_3$/NaOH/HCl*

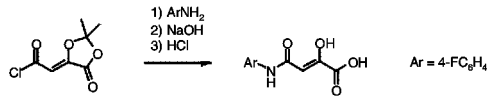
Syntheses with (Z)-2,2-dimethyl-5-carboxymethylene-1,3-dioxolan-4-one or its chlorocarbonyl deriv. as protected 2-hydroxyfumaric acid derivs. ←

442.



α,γ-Diketocarboxylic acids. (Z)-2,2-Dimethyl-5-chlorocarbonylmethylene-1,3-dioxolan-4-one treated with $AlCl_3$ in toluene → (Z)-2,2-dimethyl-5-[(4-methylbenzoyl)methylene]-1,3-dioxolan-

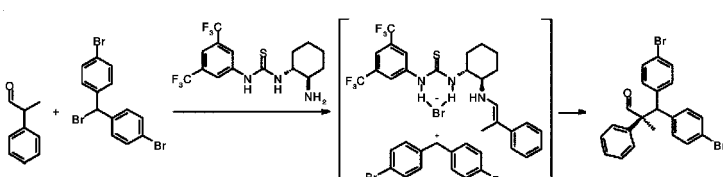
4-one (Y 61%), the product treated with 1 *M* aq. NaOH at 0°, and acidified with aq. HCl → 2-hydroxy-3-(4-methylbenzoyl)propenoic acid. Y 88%. (Z)-2,2-Dimethyl-5-carboxymethylene-1,3-dioxolan-4-one is a novel, stable and versatile synthon for the α,γ-diketoacid moiety. Treatment of the acid chloride under Friedel-Crafts conditions, or with arylstannanes in the presence of a palladium(II) catalyst afforded the corresponding ketones (four examples; Y 61-75%) which were deprotected to 3-aroyl-2-hydroxyprop-2-enoic acids (Y 48-95%). Conventional carboxylic acid chemistry on the acid chloride or free acid gave ester and amide derivs. of the carboxymethyl-dioxolanone (seven examples; Y 73-95%) which were similarly unmasked to **2-hydroxyfumaric acid esters or monoamides** (Y 55-100%).



F.e., substrate prepn. from the corresponding carboxymethyl-analog and selective transformation of the dioxolanone moiety s. J. Banville, G. Bouthillier, S. Plamondon, R. Remillard, N.A. Meanwell, A. Martel, M.A. Walker, Tetrahedron Lett. *2010*, *51* (24), 3170-3 [DOI: 10.1016/j.tetlet.2010.04.032].

Graphene s. under Palladium(II) N-heterocyclic carbene complex ←
3,3-Dimethylbut-1-ene s. under $IrH_5(i\text{-}Pr_3P)_2$ *CH_2=CHBu-t*
Norbornene s. under $Pd(OAc)_2$ ←
Glucose s. under Pd nanoparticles ←
Dimethylformamide s. under BuLi *DMF*
(S,S)-1-(o-Hydroxybenzyl)-3-mesityl-4,5-diphenylimidazolidin-2-ylidene s. under Mg *[NHC]**
(2R,5S)-5-Benzyl-2,3-dimethyl-4-imidazolidone/tris(2-phenylpyridinato-C2,N)iridium(III)/2,6-lutidine hydrobromide or hydrotriflate/irradiation ←
Asym. organocatalyzed asym. α-benzylation of aldehydes s. *78*, 443 H → C-Ar
N-Cyanobenzimidazole s. under Mg ←
Chiral trans-3,4-dihydro-3,4-diaryldibenzo[c,g]phenanthrene-3,4-diols s. under KOBu-t ←
Chiral 2-prim-aminothioureas/triethylamine/acetic acid ←
Organocatalyzed asym. α-benzhydrylation of aldehydes with benzhydryl bromides H → CH(Ar)(Ar′)

443.



Chiral 2-*prim*-aminothioureas have now been used as H-bond donor catalysts to promote S_N1 reactions via anion binding involving carbocations that are *not* heteroatom-stabilized. **E: Chiral α,β,β-triarylaldehydes**. 4,4′-Dibromobenzhydryl bromide (2 eq.) added to a flame-dried Schlenk flask under N_2, the flask sealed with a rubber septum, evacuated and backfilled with N_2 4 times, 2-phenylpropionaldehyde (0.375 mmol), acetic acid (10 mol%), Et_3N (1 eq.), and toluene (7.5 ml) added, the rubber septum replaced with a glass stopper under positive N_2 flow, the mixture degassed (3 freeze-pump-thaw cycles), the glass stopper replaced with a rubber septum, 6 ml of this stock

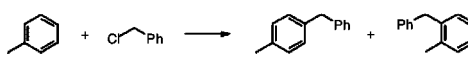
soln. (0.29 mmol aldehyde, 0.58 mmol bromide) added to a flame-dried Schlenk flask containing the chiral thiourea catalyst (20 mol%) under N_2, previously treated with degassed, deionized water (1 eq.), with care taken to wash the water from the side of the flask, the rubber septum replaced with a glass stopper under positive N_2 flow, the Schlenk flask sealed, the reaction stirred at room temp. for 72 h, treated with 1 *N* aq. HCl (3 ml), stirred for 15 min, extracted with methylene chloride, dried (Na_2SO_4), concentrated under reduced pressure, and the residue purified by flash chromatography → product. Y 61% (e.e. 91%). The presence of a prim. amino group on the organocatalyst was essential, while more elaborate aminothioureas bearing additional stereochemical elements afforded no advantage. Catalyst structure-activity studies, kinetic isotope effects, linear free-energy relationship studies, and competition experiments all provide evidence for a stepwise, S_N1 mechanism. F.e. (one isolated as the aldehyde: Y 60%, e.e. 90%; seven isolated as the alcohol after reduction with $NaBH_4$: Y 52-70%, e.e. 85-94%) s. A.R. Brown, W.-H. Kuo, E.N. Jacobsen, J. Am. Chem. Soc. *2010*, *132* (27), 9286-8 [DOI: 10.1021/ja103618r]; **asym. α-benzylation** with (2R,5S)-5-benzyl-2,3-dimethyl-4-imidazolidone as organocatalyst and tris-(2-phenylpyridinato-C2,N)iridium(III) [fac-Ir(ppy)$_3$]/2,6-lutidine hydrotriflate (or 2,6-lutidine if starting from basic substrates as their HBr salts) as photoredox catalyst under irradiation by a household fluorescent light s. H.-W. Shih, M.N. Van der Wal, R.L. Grange, D.W.C. MacMillan, ibid. *132* (39), 13600-3 [DOI: 10.1021/ja106593m]; **asym. α-trifluoromethylation or α-perfluoroalkylation** (non-photolytic method cf. *77*, 456) s. D.A. Nagib, M.E. Scott, D.W.C. MacMillan, ibid. *2009*, *131* (31), 10875-7 [DOI: 10.1021/ja9053338].

4-Fluorostyrene s. under PhCu — *ArCH=CH$_2$*

Silica s. under Triethylenediamine — *SiO$_2$*

Protonated titanate nanotubes ←

Protonated titanate nanotubes as solid acid catalysts — H → C-Ar



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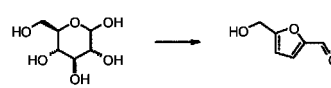


Friedel-Crafts benzylation. A mixture of catalyst (200 mg), toluene (5 eq.) and benzyl chloride (20 mmol) heated at 27° under argon, and the reaction monitored by GC → benzyltoluenes. Y 90% (*o/p* ca 1:1). The solid, recyclable catalyst (obtained by hydrothermal treatment of TiO_2 in basic soln.) was significantly more reactive than other solid catalysts at low temp., with the yield of benzyltoluene reaching 90% after 3 h at 27° (turnover of ca. 320) and 97.2% at 100°. The catalyst was shown to contain both Lewis and Brønsted acid sites but removal of the Brønsted acid sites (via cation exchange with NaOH) produced a catalyst that was only active at higher temps. (100°). The catalyst also effected conversion of glucose or fructose to 5-hydroxymethylfurfural in water at 120°. F.e. and catalyst prepn. s. M. Kitano, K. Nakajima, J.N. Kondo, S. Hayashi, M. Hara, J. Am. Chem. Soc. *2010*, *132* (19), 6622-3 [DOI: 10.1021/ja100435w].

Chlorobis(cyclopentadienyl)hydridozirconium(IV) s. under IrH$_5$(i-Pr$_3$P)$_2$ — *Cp$_2$ZrHCl*

Tin(II) chloride s. under Electrolysis — *SnCl$_2$*

Tert. phosphines and di(phosphines) s.a. under Cu$_2$O, Mg, Ni(cod)$_2$, FeCl$_3$, Pd(OAc)$_2$, Pd$_2$(dba)$_3$, Nanosized MCM-41-anchored (2,2'-bipyridyl)palladium complexes and [(cinnamyl)PdCl]$_2$ — *R$_3$P*

Triphenylphosphine/zinc — *Ph$_3$P/Zn*

Triphenylphosphine/indium/microwaves — *Ph$_3$P/In/[\\\\\]*

Polymer-based triarylphosphines/tert. amines — *Ⓟ-PAr$_2$/⩾N*

α,β-Ethylene- from α-halogeno-carbonyl compds. and aldehydes — CHO → CH=C-CO

via *in situ*-Wittig synthesis with Bu_3P/Zn, (E)-enoates, cf. *44*, 805; solvent-free synthesis of N-unsubst. α,β-ethylenecarboxylic acid amides with Ph_3P/Zn s. S. Feng, Z. Zhang, S. Jiang, X.

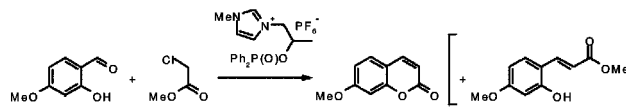
Yu, J. Chem. Res. *2010, 34* (7), 382-4 [DOI: 10.3184/030823410x520741]; unsatd. N,N-diethylamides with Ph_3P/In under microwaves s. S. Feng, Z. Zhang, S. Jiang, X. Yu, ibid. *34* (7), 392-4 [DOI: 10.3184/030823410X520750]; with a new polymer-based triarylphosphine, Rasta Resin-PPh_3, with benzyldiethylamine as base for a chromatography-free synthesis of α,β-ethylenic ketones, esters and amides s. P.S.-W. Leung, Y. Teng, P.H. Toy, Org. Lett. *2010, 12* (21), 4996-9 [DOI: 10.1021/ol1021614]; with triethylamine as base s. P.S.-W. Leung, Y. Teng, P.H. Toy, Synlett *2010* (13), 1997-2001 [DOI: 10.1055/s-0030-1258130].

2-(Dicyclohexylphosphinomethyl)-1,3-bis(2,6-diisopropylphenyl)imidazolium iodide ←
s. under Bis(cinnamylpalladium chloride)

1-Methyl-3-[2-(diphenylphosphinyloxy)propyl]imidazolium hexafluorophosphate/ ←
sodium methoxide/microwaves

Coumarins or (E)-cinnamic acid esters ○
from *o*-hydroxyaldehydes or ar. aldehydes and chloroacetic acid esters
via *in situ*-Horner synthesis mediated by a phosphinite-functionalized ionic liquid

445.

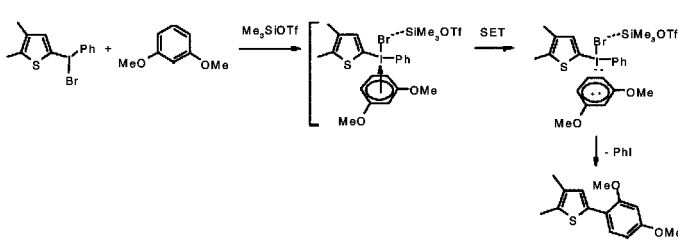


2-Hydroxy-4-methoxybenzaldehyde (1 mmol), methyl chloroacetate (1.5 eq.) and Na-methoxide (1.2 eq.) added to freshly prepared ionic liquid (2 ml) in a Teflon microwave vessel, the vessel capped, the mixture heated by microwaves (400 *W*) at 100° until reaction complete (TLC; 11 min), cooled, extracted with ether, concentrated *in vacuo*, and purified by flash chromatography on silica → 7-methoxycoumarin. Y 81% (as an 86:14 mixture with the uncyclized cinnamate). The combination of microwaves and environmentally benign ionic liquid (as solvent and reagent) promoted rapid condensation and cyclization of salicylaldehyde derivs. to afford coumarins (five examples; Y 79-83%) as ca. 4:1 mixtures with intermediate cinnamate esters. Rates of reaction were 60-70 fold faster than for conventional heating, and yields were also significantly higher. Electron-diverse benzaldehydes lacking the *o*-hydroxy group afforded cinnamates with good (E)-selectivity (eight examples; Y 79-87%; E/Z 78:22 to 88:12). F.e. and optimization s. H. Valizadeh, A. Shockravi, Synth. Commun. *2009, 39* (24), 4341-9 [DOI: 10.1080/00397910902898650].

Triphenyl phosphite s. under Ni(cod)$_2$ *$(PhO)_3P$*
Chiral TADDOL-based o-(diphenylphosphino)phenyl phosphites s. under Mg ←

Trimethylsilyl triflate *Me_3SiOTf*
Arylheteroarenes from aryl(heteroaryl)iodonium bromides and electron-rich arenes Ar-Ar′
***ipso*-Substitution via oxidation by single electron transfer**

446.



Trimethylsilyl triflate (2 eq.) added to a stirred soln. of 4,5-dimethyl-2-thienyl(phenyl)iodonium bromide (0.2 mmol) and 1,3-dimethoxybenzene (3 eq.) in 1,1,1,3,3,3-hexafluoropropan-2-ol (8 ml)

at room temp. under N_2, the homogeneous mixture stirred for an additional 3 h with TLC monitoring, satd. aq. $NaHCO_3$ added, the aq. phase extracted, and worked up with purification by chromatography on silica gel → 5-(2,4-dimethoxyphenyl)-2,3-dimethylthiophene. Y 77%. This is the first example of carbon-carbon bond formation between the *ipso* carbon atom of a heteroaromatic ring in iodonium salts with an unfunctionalized aromatic nucleophile. Reaction is thought to involve a unique SET mechanism, taking advantage of the oxidizing ability of the silyl triflate-activated iodonium salt: initially, a charge transfer complex is formed between the two reactants, separating into a radical anion and cation by single electron transfer prior to the heteroaryl transfer. The procedure is applicable to the coupling of a variety of 2-thienyl-, 2-furyl- and 2-pyrrolyl-(phenyl)iodonium bromides with 1,3-dimethoxybenzene and other electron-rich aromatics of similar oxidation potential (thirteen examples; Y 50-81%). Significant, also, is the fact that no regioisomeric products were formed. F.e. and functional group tolerance, also comparison of Lewis- and Brønsted-acidic additives, s. T. Dohi, M. Ito, N. Yamaoka, K. Morimoto, H. Fujioka, Y. Kita, Angew. Chem., Int. Ed. *2010*, *49* (19), 3334-7 [DOI: 10.1002/anie.200907281].

Triethylsilyl triflate s.under Mg and Ni(cod)₂ — *Et_3SiOTf*
Sulfuric acid s. under Pd(OAc)₂ — *H_2SO_4*

Molybdenum hexacarbonyl/microwaves — *$Mo(CO)_6$/[\\\\]*
Molybdenum-catalyzed carbonylation of halides s. *12*, 867s*78* — Hal → C(O)X

Iodine s. under BuLi — *I_2*
Tetra-n-butylammonium iodide s. under PhCu — *Bu_4NI*
Chiral quaternary ammonium chlorides s. under K_2CO_3 — *$[R_4N]^*Cl$*
Chiral quaternary ammonium bromides s. under CsOH — *$[R_4N]^*Br$*
Iron(III) acetoacetonate s. under Mg — *$Fe(acac)_3$*
Anionic iron(II) N-heterocyclic carbene complexes s. under Mg — *[Fe(II)]*
1(S)-(Dicyclohexylphosphino)-2-[2(R)-(dicyclohexylphosphino)phenyl](dimethylamino)methyl]ferrocene s. under Mg — ←
Ferrocenyltri(phosphines) s. under Bis(allylpalladium chloride) — ←

Iron(III) triflate/magnesium — *$Fe(OTf)_3/Mg$*
Sym. biaryls from ar. halides s. *34*, 825s*78* — 2 ArHal → Ar-Ar

Iron(III) chloride/N,N′-dimethylethylenediamine/lithium bis(trimethylsilyl)amide — ←
Biaryls from ar. halides — Ar-Ar′
and aryllithium compds. with added piperidine cf. *14*, 852; and arenes at relatively low temp. with $FeCl_3$/DMEDA/$LiN(SiMe_3)_2$ s. W. Liu, H. Cao, A. Lei, Angew. Chem., Int. Ed. *2010*, *49* (11), 2004-8 [DOI: 10.1002/anie.200906870].

Iron(III) chloride/triphenylphosphine/potassium phosphate — *$FeCl_3/Ph_3P/K_3PO_4$*
Iron-catalyzed Sonogashira coupling s. *74*, 478s*78* — C≡CH → C≡CR

Cobalt nanoparticles s. under Palladium(II) N-heterocyclic carbene complex — *Co*
Cobalt(II) acetoacetonate s. under PhCu — *$Co(acac)_2$*

Cobalt(II) acetate or chloride/potassium iodide/sodium acetate — *$Co(OAc)_2$ or $CoCl_2$/KI/NaOAc*
Cobalt(II)-catalyzed carbonylation of alkyl chlorides s. *12*, 867s*78* — Cl → C(O)X

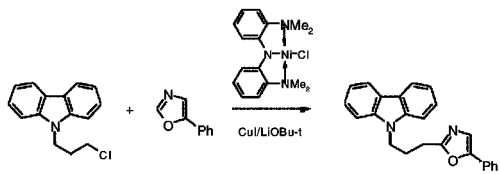
Nickel-carbon s. under Zn — *Ni-C*
Nickel(I) complex s. under Zn — *[Ni(I)]*

Bis(1,5-cyclooctadiene)nickel(0)/dicyclohexyl(phenyl)phosphine/triphenyl phosphite triethylsilyl triflate/triethylamine — ←
Nickel-catalyzed synthesis of terminal 1,4-dienes — CH=CH_2 → C(C-C=C)=CH_2
from [unactivated] terminal ethylene derivs. and β,γ-ethylenechlorides s. *78*, 414

Chloro[2,2′-bis(dimethylamino)diphenylaminato]nickel(II)/copper(I) iodide/ lithium tert-butoxide/sodium iodide ←

o-Alkylation of 5-membered heteroarenes under transition metal catalysis H → R

447.



The first direct, transition metal-catalyzed C-alkylation of heteroarenes via C-H bond activation is reported. **E:** A mixture of chloro[2,2′-bis(dimethylamino)diphenylaminato]nickel(II) (5 mol%), CuI (5 mol%), *t*-BuOLi (1.4 eq.), the startg. alkyl halide (1.2 eq.) and heteroarene (1.5 mmol) diluted with dioxane (5 ml) in a vial, NaI (20 mol%) added, the mixture heated under N_2 during 16 h at 140°, cooled to room temp., quenched with water and 1 *M* HCl, and worked up with purification by flash chromatography on silica gel → product. Y 74%. The procedure is simple, straightforward, inexpensive, high-yielding and generally applicable to the *o*-alkylation [i.e. adjacent to ring hetero atom] of a wide range of electron-rich and -poor 5-membered heteroarenes (benzoxazoles, oxazoles, benzothiazoles, thiazoles, indole, thiophenes, benzo[*b*]thiophenes and furans) with non-activated alkyl iodides, bromides and chlorides, incl. those *with β-hydrogen* atoms (twenty-five examples; Y 44-86%). This is a useful alternative to classical, but more limited, methods based on the generation of organometallic species. Although CuI is not strictly necessary, yields are higher in its presence by dint, presumably, of facilitating transmetalation of the intermediate anionic heteroarene to nickel. Mechanistically, reaction is assumed to follow the same course as direct arylation and alkynylation of heteroarenes, the nickel(I) precatalyst generating active nickel(0) particles *in situ*. The procedure tolerates a wide range of functionality in both coupling partners, e.g. ethers, olefins, esters, NBoc groups, thioethers, nitriles, acetals, ketones and, significantly, [hetero]aromatic halogen which remains intact for subsequent manipulation. There is one important limitation, however: *sec*-alkyl halides are unreactive. F.e. and comparison of nickel complexes and bases s. O. Vechorkin, V. Proust, X. Hu, Angew. Chem., Int. Ed. *2010*, *49* (17), 3061-4 [DOI: 10.1002/anie.200907040].

Ruthenium phosphine complexes and supported variants *[Ru]*

Dichloro(p-cymene)ruthenium(II) dimer/potassium pivalate/potassium carbonate ←

N-Directed ruthenium-catalyzed *o*-arylation of aryl-N-heteroarenes Ar-Ar′

s. *73*, 419s*76*; of 2-arylpyridines with electron-diverse ar. chlorides using an efficient (η^6-*p*-cymene)-dichloro[(1,2-diarylvinyl)phosphine]ruthenium(II) complex s. B. Yu, X. Yan, S. Wang, N. Tang, C. Xi, Organometallics *2010, 29* (14), 3222-6 [DOI: 10.1021/om100407q]; with [het]ar. chlorides *in water* using $[(RuCl_2(p\text{-cymene})]_2$/K-pivalate/$K_2CO_3$ without surfactant s. P.B. Arockiam, C. Fischmeister, C. Bruneau, P.H. Dixneuf, Angew. Chem., Int. Ed. *2010, 49* (37), 6629-32 [DOI: 10.1002/anie.201002870]; 10-arylation of benzo[*h*]quinolines with ar. chlorides using $RuCl_3 \cdot xH_2O$/ Ph_3P/Na_2CO_3 s. N. Luo, Z. Yu, Chem. Eur. J. *2010, 16* (9), 787-91 [DOI: 10.1002/chem.200902612]; under *heterogeneous* conditions with a recyclable ruthenium phosphine complex-on-cerium dioxide s. H. Miura, K. Wada, S. Hosokawa, M. Inoue, ibid. *16* (14), 4186-9 [DOI: 10.1002/chem.200903564]; *o*-arylation of 4-aryl-1,2,3-triazoles with ar. chlorides s. L. Ackermann, P. Novák, R. Vicente, V. Pirovano, H.K. Potukuchi, Synthesis *2010* (13), 2245-53 [DOI: 10.1055/s-0029-1220010].

Palladium nanoparticles, complexes, and supported or polymer-based variants *[Pd]*

Heck arylation H → Ar

update s. *27*, 871s*77*; with *in situ*-generated palladium *nanoparticles* in PEG-400 s. W. Han, N. Liu, C. Liu, Z.L. Jin, Chin. Chem. Lett. *2010, 21* (12), 1411-6 [DOI: 10.1016/j.cclet.2010.06.019];

with reusable, reductively generated *carbon nanotube-supported* palladium nanoparticles (Pd/CR-CTN) s. Y. Zhang, W. Chu, L. Xie, W. Sun, Chin. J. Chem. *2010, 28* (6), 879-83 [DOI: 10.1002/cjoc.201090165]; with $Pd(dba)_2$-on-carbon nanotubes (0.2 mol%) with K_3PO_4 as base s. Y. Jo, J.Y. Kim, I.-K. Oh, H.C. Choi, S. Lee, Bull. Korean Chem. Soc. *2010, 31* (6), 1735-8 [DOI: 10.5012/bkcs.2010.31.6.1735]; with reductively generated poly(1,8-diaminonaphthalene)-stabilized palladium nanoparticles s. R.U. Islam, M.J. Witcomb, M.S. Scurrell, W. Van Otterlo, K. Mallick, Catal. Commun. *2010, 12* (2), 116-21 [DOI: 10.1016/j.catcom.2010.08.005]; with palladium/zirconium oxide nanocomposites formed by electrochemical deposition of palladium nanoparticles on nanostructured ZrO_2 powders stabilized by tetraalkylammonium hydroxide for Heck, Ullmann and Suzuki reactions *in water* s. A. Monopoli, A. Nacci, V. Calò, F. Ciminale, P. Cotugno, A. Mangone, L.C. Giannossa, P. Azzone, N. Cioffi, Molecules *2010, 15* (7), 4511-25 [DOI: 10.3390/molecules15074511]; with reusable palladium-on-shell powder s. Y.-M. Shen, Y.-J. Du, M.-F. Zeng, D. Zhi, S.-X. Zhao, L.-M. Rong, S.-Q. Lv, L. Du, C.-Z. Qi, Appl. Organomet. Chem. *2010, 24* (9), 631-5 [DOI: 10.1002/aoc.1657]; tetraalkylammonium-free Heck coupling with strongly deactivated ar. chlorides using *macrocyclic* dinuclear Schiff base or porphyrin complexes for *controlled release* and capture of palladium s. C. Röhlich, K. Köhler, Adv. Synth. Catal. *2010, 352* (13), 2263-74 [DOI: 10.1002/adsc.201000458]; s.a. C. Röhlich, K. Köhler, Chem. Eur. J. *2010, 16* (8), 2363-5 [DOI: 10.1002/chem.200903331]; with $[(allyl)PdCl]_2$ and the tetra(phosphine), N,N,N′,N′-tetrakis(diphenylphosphinomethyl)-1,2-ethylenediamine, as ligand at low (0.1 mol%) catalyst loading s. X.-J. Yu, R. Zhou, Y. Zhang, H.-Y. Fu, R.-X. Li, H. Chen, X.-J. Li, Catal. Commun. *2010, 12* (3), 222-5 [DOI: 10.1016/j.catcom.2010.07.007]; with a monomeric cyclopalladated benzylamine complex ligated to (4-methoxybenzoylmethylene)triphenylphosphorane under microwave irradiation for reaction with ar. chlorides, bromides or iodides s. A.R. Hajipour, K. Karami, G. Tavakoli, Appl. Organomet. Chem. *2010, 24* (11), 798-804 [DOI: 10.1002/aoc.1705]; coupling with activated or unactivated [het]ar. bromides *in water* under microwaves with a benzimidazole-based cyclopallad(II)ated oxime complex (TOF up to 420,000), also Suzuki coupling, s. K.M. Dawood, M.M. El-Deftar, ARKIVOC *2010* (ix), 319-30; with a palladium(II) phosphine complex ligated to a tridentate thiosemicarbazone based on salicylaldehyde (at 0.1 to 1 mol%) s. G. Xie, P. Chellan, J. Mao, K. Chibale, G.S. Smith, Adv. Synth. Catal. *2010, 352* (10), 1641-7 [DOI: 10.1002/adsc.201000218]; with amide-functionalized palladium-(0) or -(II) bis(imidazol-2-ylidene) complexes in Bu_4NBr as *ionic liquid* for coupling activated or deactivated ar. chlorides and bromides with NaOAc as base s. J.-Y. Lee, P.-Y. Cheng, Y.-H. Tsai, G.-R. Lin, S.-P. Liu, M.-H. Sie, H.M. Lee, Organometallics *2010, 29* (17), 3901-11 [DOI: 10.1021/om1006402]; under *heterogeneous* conditions with a reusable *polymer-based* palladium phosphine complex based on *tert*-butyl(benzyl)phenylphosphine at low loading (0.04 mol%) s. C. Diebold, S. Schweizer, J.-M. Becht, C. Le Drian, Org. Biomol. Chem. *2010, 8* (21), 4834-6 [DOI: 10.1039/c0ob00523a]; with recoverable polymer-based aldimine-type cyclopalladated complexes (TOF 12,600 h^{-1}) s. Y-x. Liu, Z.-w. Ma, J. Jia, C.-c. Wang, M.-l. Huang, J.-c. Tao, Appl. Organomet. Chem. *2010, 24* (9), 646-9 [DOI: 10.1002/aoc.1662]; with polymer-based ketimine-type cyclopalladated complexes s. Y. Liu, J. Jia, H. Tan, Y. Sun, J. Tao, Chin. J. Chem. *2010, 28* (6), 967-73 [DOI: 10.1002/cjoc.201090179]; with *magnetically retrievable* macroporous poly(GMA-EGDMA-DVB)-type, microsphere-supported palladium complexes s. D.Z. Yuan, Q.Y. Zhang, J.B. Dou, Chin. Chem. Lett. *2010, 21* (9), 1062-6 [DOI: 10.1016/j.cclet.2010.04.025]; with recyclable (15 times!), non-leaching, surface-supported palladium(II) complexes-on-gold nanoparticles (TOF up to 4.87 x 10^4) s. J.-N. Young, T.-C. Chang, S.-C. Tsai, L. Yang, S.J. Yu, J. Catal. *2010, 272* (2), 253-61 [DOI: 10.1016/j.jcat.2010.04.005]; scalable (by a factor of *50*) Heck reactions *in an integrated microreactor under continuous flow* s. J.P. McMullen, M.T. Stone, S.L. Buchwald, K.F. Jensen, Angew. Chem., Int. Ed. *2010, 49* (39), 7076-80 [DOI: 10.1002/anie.201002590].

Palladium nanoparticles/tetra-n-butylammonium hydroxide/glucose ←
Sym. biaryls from ar. halides 2 ArHal → Ar-Ar

under palladium catalysis s. *34*, 825s*70*; homocoupling of ar. bromides and chlorides *in water* with colloidal palladium nanoparticles in the presence of Bu_4NOH as base, surfactant and phase transfer catalyst with glucose as reductant s. A. Monopoli, V. Calò, F. Ciminale, P. Cotugno, C. Angelici, N. Cioffi, A. Nacci, J. Org. Chem. *2010, 75* (11), 3908-11 [DOI: 10.1021/jo1005729];

from ar. bromides with $Fe(OTf)_3$/Mg s. Y.-Y. Zhang, J.-D. Lin, X.-L. Xu, J.-H. Li, Synth. Commun. *2010, 40* (17), 2556-63 [DOI: 10.1080/00397910903289230]; fluorinated 2,2′-bis(anisoles) from the corresponding ar. iodides with freshly activated copper(0) powder s. R. Francke, G. Schnakenburg, S.R. Waldvogel, Org. Lett. *2010, 12* (19), 4288-91 [DOI: 10.1021/ol101698a].

Palladium nanoparticles/silver acetate *Pd/AgOAc*
2-[Het]arylation of benzothiazoles s. *77,* 466s*78* Ar-Ar′

Palladium-carbon nanoparticles or Palladium complexes and supported variants *Pd-C*
Copper-free Sonogashira coupling C≡CH → C≡CR
update s. *63,* 411s*77*; *heterogeneous* conversion with recyclable, *large* nanoparticulate size samples of palladium-carbon ('UC Pd') s. C. Duplais, A.J. Forman, B.A. Baker, B.H. Lipshutz, Chem. Eur. J. *2010, 16* (11), 3366-71 [DOI: 10.1002/chem.200902471]; *in water* under copper- and phosphine-free conditions with a recyclable poly(N-vinylcarbazole)-anchored cyclopallad(II)ated complex based on 3,6-dibenzaldimino-N-vinylcarbazole monomer, also Suzuki coupling, s. M. Islam, P. Mondal, A.S. Roy, K. Tuhina, Synthesis *2010* (14), 2399-406 [DOI: 10.1055/s-0029-1218776]; with a recyclable polymer-supported palladium(II) N,N-bis(naphthylideneimino)diethylenetriamine complex/Et_3N under aerobic conditions s. M. Bakherad, A.H. Amin, A. Keivanloo, B. Bahramian, M. Raeissi, Tetrahedron Lett. *2010, 51* (43), 5653-6 [DOI: 10.1016/j.tetlet.2010.07.011]; *by ball milling* with $Pd(OAc)_2$ or $Pd(PPh_3)_4$ as catalyst and DABCO as base with SiO_2 or Al_2O_3 as grinding auxiliary s. R. Thorwirth, A. Stolle, B. Ondruschka, Green Chem. *2010, 12* (6), 985-91 [DOI: 10.1039/c000674b]; with $Pd(PPh_3)_4$ and AuI/dppe (cf. *66,* 384s*75*) s. T. Lauterbach, M. Livendahl, A. Rosellón, P. Espinet, A.M. Echavarren, Org. Lett. *2010, 12* (13), 3006-9 [DOI: 10.1021/ol101012n]; under copper-, palladium- and amine-free conditions with $FeCl_3/Ph_3P/K_3PO_4$ for coupling with a wide variety of ar. iodides (cf. *74,* 478) s. D.N. Sawant, P.J. Tambade, Y.S. Wagh, B.M. Bhanage, Tetrahedron Lett. *2010, 51* (20), 2758-61 [DOI: 10.1016/j.tetlet.2010.03.063].

Palladium-carbon/1,8-diazabicyclo[5.4.0]undec-7-ene/microwaves *Pd-C/DBU/[\\\\]*
(Dioxygen)palladium(II) phosphine complexes/hydrogen *[Pd(II)]/H_2*
Transition metal-catalyzed carbonylation of halides Hal → C(O)X
under palladium catalysis s. *12,* 867s*70*; arylcarboxylic acid esters and amides (incl. heteroaromatic compds.) under *ligand-free, heterogeneous* conditions with Pd-C/DBU under microwaves s. J. Salvadori, E. Balducci, S. Zaza, E. Petricci, M. Taddei, J. Org. Chem. *2010, 75* (6), 1841-7 [DOI: 10.1021/jo9021315]; arylcarboxylic acid esters from ar. bromides with palladium(0) generated *in situ* from air-stable (dioxygen)palladium(II) phosphine complexes of the type $Pd(O_2)L_2$ (L = Ad_2PBu-*n*) under CO/H_2 s. A.G. Sergeev, H. Neumann, A. Spannenberg, M. Beller, Organometallics *2010, 29* (15), 3368-73 [DOI: 10.1021/om1003418]; (Z)-α-chloro-α,β-ethylenecarboxylic acid esters from dichloromethylene compds. under palladium(0) catalysis s. M. Arthuis, A. Lecup, E. Roulland, Chem. Commun. *2010, 46* (41), 7810-12 [DOI: 10.1039/c0cc02517h]; N-aroylureas from [het]ar. bromides or chlorides with $Mo(CO)_6$ under microwaves s. D. Liptrot, L. Alcaraz, B. Roberts, Adv. Synth. Catal. *2010, 352* (13), 2183-8 [DOI: 10.1002/adsc.201000395]; N-aroylsulfamides s. idem., Tetrahedron Lett. *2010, 51* (40), 5341-3 [DOI: 10.1016/j.tetlet.2010.08.009]; further O- and N-nucleophiles, also with tetraethylammonium pentacarbonyl(chloro)molybdate, s. B. Roberts, D. Liptrot, L. Alcaraz, T. Luker, M.J. Stocks, Org. Lett. *2010, 12* (19), 4280-3 [DOI: 10.1021/ol1016965]; carbonylation of benzyl chloride with cobalt(II) 6-methoxybenzothiazole-2-carboxylate·$(DMF)_2$ s. B. Zhang, J. Li, W. Chen, Y. Wang, Z. Shi, Chin. J. Chem. *2010, 28* (1), 111-4 [DOI: 10.1002/cjoc.201090023]; photocatalyzed carbonylation of alkyl chlorides with $Co(OAc)_2$ or $CoCl_2$ and KI/NaOAc s. Y.P. Jia, Y.N. Cui, J.M. Yin, G.Y. Zhou, S.M. Li, D.B. Gao, X.S. Wang, Chin. Chem. Lett. *2010, 21* (9), 1033-6 [DOI: 10.1016/j.cclet.2010.04.027].

Palladium(II) acetate/triethylenediamine *$Pd(OAc)_2$/DABCO*
Copper-free Sonogashira coupling by ball milling s. *63,* 411s*78* C≡CH → C≡CR

Palladium(II) acetate/silver(I) oxide/trifluoroacetic acid $Pd(OAc)_2/Ag_2O/CF_3COOH$
9-Phenanthrones from α-subst. acylophenones and ar. halides via palladium-catalyzed dual C-H activation-enolate cyclization

448.

Trifluoroacetic acid (2 ml), startg. aryl ketone (1 mmol) and 4-nitro-iodobenzene (3 eq.) added to a nitrogen-purged mixture of $Pd(OAc)_2$ (1 mol%) and Ag_2O (1 eq.) in a sealed tube, the resulting mixture stirred at 120° for 20 h, filtered through a Celite pad (with methylene chloride), the filtrate concentrated *in vacuo*, and the residue purified by chromatography on silica gel → 3′-chloro-7′-nitro-10′H-spiro[cyclohexane-1,9′-phenanthren]-10′-one. Y 72%. Nine examples, with electron-deficient ar. iodides (nitro- or carbethoxy-subst.), similarly afforded phenanthrone derivs. in yields of 60-78%, tolerating bromo or chloro groups on the aromatic ring of the ketone. α-Unsubst. acylophenones, however, simply undergo arylation without subsequent cyclization to afford ***o*-acylbiaryls** (eleven examples; Y 52%, 63-92% for electron-deficient ar. iodides, but only 20% and 23% for iodobenzene and iodoanisole, respectively). The role of Ag_2O is not entirely clear, but it probably acts as a base, a halide-scavenger and an oxidant (Pd(IV) → Pd(II)). F.e. and a proposed mechanism s. P. Gandeepan, K. Parthasarathy, C.-H. Cheng, J. Am. Chem. Soc. *2010*, *132* (25), 8569-71 [DOI: 10.1021/ja1026248].

Palladium(II) acetate/silver carbonate $Pd(OAc)_2/Ag_2CO_3$
Umpolung biaryl synthesis Hal → Ar

449.

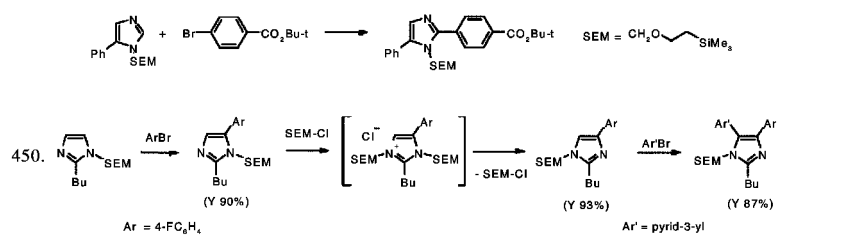
R = Ph: Y 94%
(R = OEt: Y 88%)
(R = NMe_2: Y 87%)
(R = Me: Y 51%)
(R = OH: Y 42%)
(R = H: Y 74%)

An umpolung version of biaryl synthesis *from unactivated arenes* is reported, involving the application of carbonyl as directing group on the *ar. halide* to facilitate oxidative addition of palladium. **E: Biaryl-2-carbonyl compds. from *o*-bromocarbonyl compds. and arenes**. $Pd(OAc)_2$ (5 mol%) and Ag_2CO_3 (0.51 eq.) added to a microwave vial, startg. aryl halide (0.5 mmol) in benzene (25 eq.) added via syringe, the vial then rinsed with benzene (3 x 25 eq.), the vial sealed with a Teflon cap, stirred at 125° for 16-20 h, cooled, filtered through a silica plug (1:1 ether/hexanes), the combined soln. concentrated, and the crude mixture purified chromatographically → product. Y 94%. This *phosphine-free* palladium-catalyzed direct arylation is facile and high yielding. The ar. bromide or iodide (not chloride) can be prepared readily via directed *o*-metalation from inexpensive starting materials. A range of directing groups may be employed, yields increasing with greater Lewis basicity of the group, so that phenyl ketones are more effective than esters, and amides are quite effective. *o*-Bromobenzoic acid underwent full conversion but the product was isolated in only 42% yield, believed to be due to decarboxylation, with the resulting biphenyl

being removed during purification. The scope of the reaction was explored with *o*-bromo-esters (yields being higher in the presence of groups such as ar. nitro or fluorine than with methoxy) and a variety of arenes (eleven examples; Y 27%, 30%, 43-94%). F.e.s. J.J. Mousseau, F. Vallée, M.M. Lorion, A.B. Charette, J. Am. Chem. Soc. *2010*, *132* (41), 14412-4 [DOI: 10.1021/ja107541w].

Palladium(II) acetate/silver fluoroborate/microwaves $Pd(OAc)_2/AgBF_4/[\backslash\backslash\backslash\backslash]$
2-Arylation of peptidyl tryptophan residues s. *57*, 376s*78* Ar-Ar′

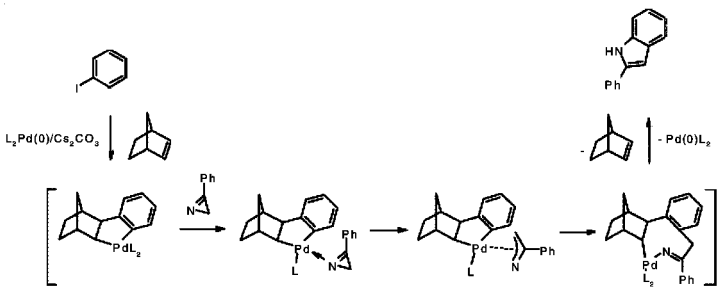
Palladium(II) acetate/di-1-adamantyl(butyl)phosphine/sodium tert-butoxide ←
Regioselective palladium-catalyzed arylation H → Ar
of N-[2-(trimethylsilyl)ethoxymethyl]imidazoles



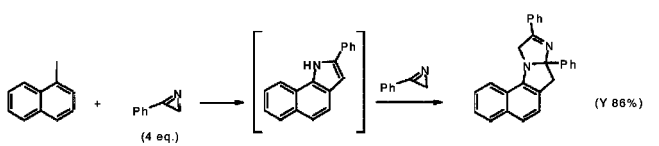
$Pd(OAc)_2$ (5 mol%), di-1-adamantyl(butyl)phosphine (7.5 mol%) and Na-*tert*-butoxide (2 eq.) added to a soln. of 5-phenyl-1-[2-(trimethylsilyl)ethoxymethyl]imidazole (0.5 mmol) and *tert*-butyl 4-bromobenzoate (1.5 eq.) in toluene (0.25 ml) under argon, the reaction vial sealed with a Teflon cap, the mixture stirred at 100° for 24 h, cooled, and purified chromatographically → 2-(4-*tert*-butoxycarbonylphenyl)-5-phenyl-1-[2-(trimethylsilyl)ethoxymethyl]imidazole. Y 70%. A detailed methodology is described for general and experimentally simple **sequential arylation** of 2-(trimethylsilyl)ethoxymethyl (SEM)-protected imidazoles using inexpensive (het)ar. halides (cf. *57*, 376s*66*,*71*). Arylation of 1-SEM-imidazole occurs initially at the more reactive 5-position (six examples; Y 59-72%), with subsequent arylation affording **1-SEM-2,5-diarylimidazoles** (six examples; Y 45-88%). In a further crucial development, 2-subst. 1-SEM-5-arylimidazoles were isomerized to the more reactive 4-aryl isomers via a one-pot quaternization/dequaternization sequence with a second molecule of SEM-Cl (also with benzyl bromide or methyl triflate), affording **1,2-disubst. 4,5-diarylimidazoles**. Five 2-subst. 1-SEM-imidazoles (subst. = phenyl, butyl, piperid-1-yl) were also converted to 4,5-diaryl derivs. via a 5-arylation (Y 65-90%), isomerization (Y 74-93%), arylation (Y 71-88%) sequence. F.e. incl. synthesis of a 1-methyl-2,4,5-triarylimidazole s. J.M. Joo, B.B. Touré, D. Sames, J. Org. Chem. *2010*, *75* (15), 4911-20 [DOI: 10.1021/jo100727j].

Palladium(II) acetate/2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl/sulfuric acid/ zinc/zinc cyanide ←
Ar. nitriles from halides Hal → CN
under palladium catalysis s. *29*, 845s*70*; from [hetero]aryl chlorides with 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl as ligand s. M. Shevlin, Tetrahedron Lett. *2010*, *51* (37), 4833-6 [DOI: 10.1016/j.tetlet.2010.07.045]; from electron-diverse ar. chlorides and bromides with 2-(di-*tert*-butylphosphino)-1,1′-binaphthyl as ligand s. B. Wang, R. Zhao, B.-C. Chen, B. Balasubramanian, ARKIVOC *2010* (vi), 47-52; alternative uncatalyzed procedure from ar. bromides or iodides via Hal-Li exchange with *n*-BuLi, followed by oxidative ammoniation of the intermediate DMF adducts with NH_3/I_2 cf. S. Ushijima, H. Togo, Synlett *2010* (10), 1562-6 [DOI: 10.1055/s-0029-1219935].

Palladium(II) acetate/tri-m-chlorophenylphosphine/norbornene/cesium carbonate ←
Indoles from ar. iodides and Δ^1-azirines
by norbornene-mediated palladium-catalyzed annelation ○



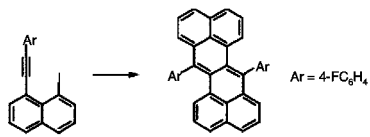
451.



Cleavage of the highly strained azirine ring is the driving force behind a new palladium-catalyzed indole synthesis. **E:** A flame-dried flask containing the startg. aryl iodide (0.2 mmol), $Pd(OAc)_2$ (10 mol%), *electron-deficient* tri-*m*-chlorophenylphosphine (25 mol%), Cs_2CO_3 (3 eq.) and norbornene (2 eq.) purged with argon for 1 min and maintained under an atm. of argon, the mixture diluted with dry acetonitrile (2 ml), stirred at room temp. for 10 min, heated to 110° in an oil bath, a stock soln. of the startg. 2*H*-azirine (0.1 *M*; 2 ml) added slowly via syringe pump over 16 h, allowed to cool to room temp., diluted with ethyl acetate, filtered through a plug of silica, and the filtrate and washings worked up with purification by chromatography on silica gel → product. Y 95%. The procedure is applicable to a number of ar. iodides (e.g. possessing MeO, Me, Cl, CF_3 or NHAc groups) and 2-aryl-Δ^1-azirines tolerating electron-withdrawing or -donating groups on the benzene ring, even at the *ortho* site (twelve examples; Y 54-95%), but reaction with 2-alkyl- and 2-acyl-Δ^1-azirines resulted in disappearance of the azirine and recovery of the aryl iodide. Vinyl azides were used as the starting point where the azirine is highly reactive. With excess of the azirine (4 eq.), however, the corresponding **9,9a-dihydro-3*H*-imidazo[1,2-*a*]indoles** were obtained in one pot in limited cases by subsequent [3+2]-cycloaddition of a second molecule of the azirine on the initially formed indole (three examples; Y 41-86%). The indole system is presumed to be formed via norbornene-mediated C-H bond functionalization to give a cyclopalladated complex, which captures the azirine prior to palladium-mediated ring opening to give 1,3-dipole equivalent, this then inserts into the palladacyclic ring and the catalytic cycle continues with sequential elimination of norbornene and palladium(0) to give the product. F.e.s. D.A. Candito, M. Lautens, Org. Lett. *2010*, *12* (15), 3312-5 [DOI: 10.1021/ol100975b].

Palladium(II) acetate/tri-2-furylphosphine/silver carbonate $Pd(OAc)_2/(2\text{-furyl})_3P/Ag_2CO_3$
Dibenzo[*de,mn*]naphthacenes [zethrenes] from 1-(alk-1-ynyl)-8-iodonaphthalenes via palladium(II)-catalyzed cyclodimerization ○

452.



A mixture of 1-(4-fluorophenylethynyl)-8-iodonaphthalene (0.5 mmol), tri-2-furylphosphine (15 mol%), Ag_2CO_3 (1 eq.), $Pd(OAc)_2$ (5 mol%) and *o*-xylene (5 ml) heated in a sealed tube under N_2 at 130° for 36 h, cooled, filtered through Celite, concentrated *in vacuo*, and purified by chromatography on silica → 7,14-bis(4-fluorophenyl)dibenzo[*de,mn*]naphthacene. Y 56%. This simple method for the preparation of an unusual class of aromatics gave moderate yields for aryl-terminated 8-iodonaphthalene-1-acetylenes, with yields sensitive to steric and electronic factors (thirteen examples; Y 24-73%). Low or zero yields were obtained for 9-anthracenyl (14%), N-ethyl-carbazolyl (16%), *n*-butyl (20%), *tert*-butyl (0%) and phenylethynyl (0%) terminators, while the trimethylsilylalkyne deriv. afforded the parent hexacycle (Y 20%) via *in situ* desilylation. Structures were confirmed by X-ray analysis in one case. F.e. and optimization s. T.-C. Wu, C.-H. Chen, D. Hibi, A. Shimizu, Y. Tobe, Y.-T. Wu, Angew. Chem., Int. Ed. *2010*, *49* (39), 7059-62 [DOI: 10.1002/anie.201001929].

Palladium(II) acetate/water-soluble triarylphosphine/copper(I) iodide/triethylamine ←
Nanosized MCM-41-anchored (2,2′-bipyridyl)palladium complexes/copper(I) iodide/triphenylphosphine ←
Palladium phosphine complexes and supported variants/copper(I) iodide ←
Sonogashira coupling C≡CH → C≡CR

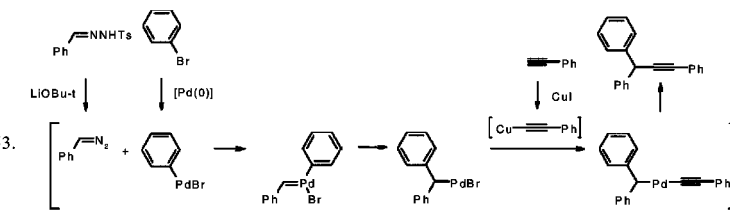
update s. *27*, 851s*77*; with $[(allyl)PdCl]_2$ and CuI·ferrocenyltri(phosphine) adducts at low catalyst loading for coupling of demanding aryl halides, e.g. electron-poor ar. chlorides, and study of ligand exchange between Cu and Pd, s. M. Beaupérin, A. Job, H. Cattey, S. Royer, P. Meunier, J.-C. Hierso, Organometallics *2010, 29* (12), 2815-22 [DOI: 10.1021/om1003336]; coupling of unprotected halogenonucleosides *in aq. medium* with $Pd(OAc)_2$, *water-soluble* trisodium tris(2,4-dimethyl-5-sulfonatophenyl)phosphine as ligand and CuI/Et_3N s. J.H. Cho, C.D. Prickett, K.H. Shaughnessy, Eur. J. Org. Chem. *2010* (19), 3678-83 [DOI: 10.1002/ejoc.201000313]; coupling of [het]ar. halides under *heterogeneous* conditions with recyclable nanosized MCM-41-anchored (2,2′-bipyridyl)palladium complexes at very low loading (0.01 mol%) in the presence of CuI/Ph_3P s. B.-N. Lin, S.-H. Huang, W.-Y. Wu, C.-Y. Mou, F.-Y. Tsai, Molecules *2010, 15* (12), 9157-73 [DOI: 10.3390/molecules15129157]; with various commercial samples of Pd-C, comparative study of this and other Pd-catalyzed conversions, s. A. Komáromi, F. Szabó, Z. Novák, Tetrahedron Lett. *2010, 51* (41), 5411-4 [DOI: 10.1016/j.tetlet.2010.07.170]; with $PdCl_2(PPh_3)_2/CuI$ under microwaves for the *double* Sonogashira coupling of 3,4-diiodopyrazoles s. H. Ichikawa, H. Ohfune, Y. Usami, Heterocycles *2010, 81* (7), 1651-9 [DOI: 10.3987/com-10-11950]; synthesis of *exo*-glycal-type 1,3-enynes s. A.M. Gómez, A. Barrio, A. Pedregosa, C. Uriel, S. Valverde, J.C. López, Eur. J. Org. Chem. *2010* (15), 2910-20 [DOI: 10.1002/ejoc.201000170]; of alkyne-linked (1→6)-C-disaccharides s. D.C. Koester, M. Leibeling, R. Neufeld, D.B. Werz, Org. Lett. *2010, 12* (17), 3934-7 [DOI: 10.1021/ol101625p]; of 2,4-enyne-1,6-diols s. X. Zhang, Z. Lu, C. Fu, S. Ma, J. Org. Chem. *2010, 75* (8), 2589-98 [DOI: 10.1021/jo100146p].

Tris(dibenzylideneacetone)dipalladium/tri-tert-butylphosphine-fluoroboric acid/dicyclohexl(methyl)amine ←
N-Protected 3-arylpyrroles from *trans*-γ-amino-α,β-ethyleneketones ○
s. *78*, 203

Tris(dibenzylideneacetone)dipalladium/2-dicyclohexylphosphino-2′,4′,6′-triisopropyl-biphenyl/copper(I) iodide/lithium tert-butoxide ←

Palladium-catalyzed 3-component synthesis of 1,1-diaryl-2-acetylenes C≡C-CH(Ar)(Ar′) **from terminal acetylene derivs., ar. N-tosylhydrazones and ar. bromides**

453.



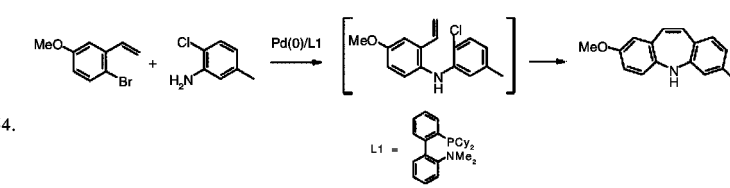
$Pd_2(dba)_3$ (2.5 mol%), 2-(dicyclohexylphosphino)-2′,4′,6′-triisopropylbiphenyl (10 mol%), CuI (7.5 mol%), *t*-BuOLi (3.5 eq.) and benzaldehyde N-tosylhydrazone (0.2 mmol) suspended in toluene (0.8 ml) in a Schlenk tube under N_2, bromobenzene (1.1 eq.) and phenylacetylene (1.1 eq.) added, the resulting soln. stirred at 90° for 1 h, after cooling to room temp., the mixture filtered through silica gel, eluting with hexane and methylene chloride, volatiles removed *in vacuo*, and the crude residue purified by chromatography on silica gel → product. Y 81%. The use of bromide as the halide component was essential, phenyl iodide or chloride affording the Sonogashira product mainly in 55% or 21% yield, respectively; *o*-substituents reduced the yield. A wide range of substituents are tolerated on the alkyne (but not ester) and on the aromatic moiety of the N-tosylhydrazone. It is proposed that a diazo species is generated *in situ* from the tosylhydrazone in the presence of base; decomposition by the arylpalladium species formed by oxidative addition of Pd(0) to the ar. bromide affords a palladium carbene, migratory insertion of an aryl group to the carbenic carbene gives a benzhydrylpalladium species, which undergoes transmetalation of the Cu-acetylide, and finally reductive elimination, affording the product with regeneration of the palladium catalyst. F.e. (twenty-one; Y 21%, 41-84%) s. L. Zhou, F. Ye, Y. Zhang, J. Wang, J. Am. Chem. Soc. *2010*, *132* (39), 13590-1 [DOI: 10.1021/ja105762n].

Tris(dibenzylideneacetone)dipalladium/2-(dicyclohexylphosphino)-2′-(dimethylamino)-biphenyl/sodium tert-butoxide ←

Dibenzo-fused N-heterocyclics ○

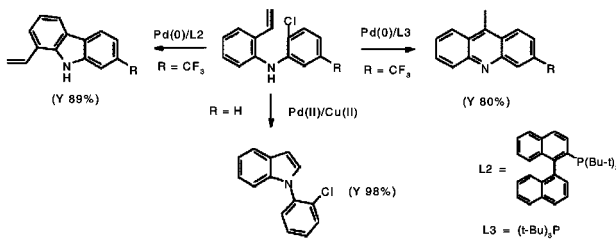
via ligand-controlled palladium-catalyzed ring closures of *o*-(chloroarylamino)styrenes

454.



***5H*-Dibenz[*b,f*]azepines in one pot.** A soln. of 2-bromo-5-methoxystyrene (1 mmol) in dioxane (1 ml) added to a mixture of 2-(dicyclohexylphosphino)-2′-(dimethylamino)biphenyl (2.25 mol%), $Pd_2(dba)_3$ (0.75 mol%), NaOBu-*t* (3 eq.) and 2-chloro-5-methylaniline (1.1 eq.) in an oven-dried Schlenk tube under argon, the mixture stirred at 110° until reaction complete (GC; 24 h), and purified by chromatography on Biotage SP4 → 2-methoxy-7-methyl-5*H*-dibenzo[*b,f*]azepine. Y 92%. Initial palladium-catalyzed coupling of *o*-chloroanilines and *o*-bromostyrenes afforded

stable ***o*-(arylamino)styrenes** which were isolated from reactions using *2-dicyclohexylphosphino-2′,4′,6′-triisopropyl-3,5-dimethoxybiphenyl* as ligand. Subsequent palladium-catalyzed ring closure demonstrated remarkable ligand control, with various phosphines selectively affording a 5*H*-dibenz-[*b,f*]azepine (7-*endo*) (one example; Y 99%), **9-methylacridines** (6-*exo*) (six examples; Y 78-98%) or **1-vinyl-9*H*-carbazoles** (six examples; Y 78-94%). Utilization of the illustrated biphenylphosphine ligand allowed the dibenz-azepines and -azepinones (and some aza- and diaza- analogs) to be synthesized efficiently in a one-pot process (fourteen examples; Y 65-99%). In a further development, intermediate *o*-(arylamino)styrenes were cyclized to **N-arylindoles** via treatment with $Pd(OAc)_2$/$Cu(OAc)_2$ (three examples; Y 87-98%).



F.e.s. D. Tsvelikhovsky, S.L. Buchwald, J. Am. Chem. Soc. *2010, 132* (40), 14048-51 [DOI: 10.1021/ja107511g].

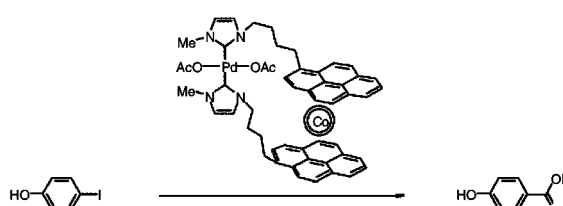
Palladium N-heterocyclic carbene complexes s.a. under Mg and Zn *[Pd]*

Graphene-coated cobalt nanoparticle-supported palladium(II) N-heterocyclic carbene complex ←

Arylcarboxylic acids from ar. halides in water Hal → COOH

Carbonylation using a magnetically-retrievable nanoparticle-supported palladium(II) N-heterocyclic carbene complex as 'boomerang' catalyst

455.



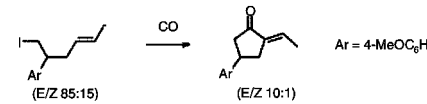
A method is reported for the reversible immobilization of pyrene-tagged palladium N-heterocyclic carbene complexes on highly magnetic, graphene-coated cobalt nanoparticles through π-π stacking interactions, such noncovalent grafting being strongly temperature dependent in polar solvents, such as water, giving rise to a 'boomerang'-type catalyst that dissociates from the heterogeneous support into the homogeneous phase at elevated temperatures. **E:** 4-Iodophenol (0.5 mmol) and K_2CO_3 (0.75 eq.) added to a suspension of Co/C-supported catalyst [2 mol%; prepared from 1-methyl-3-[4-(pyren-1-yl)butyl]-1*H*-imidazol-3-ium bromide, $Pd(OAc)_2$ and Co@C nanoparticles] in

Millipore water (5 ml) in a Schlenk tube, the tube evacuated and filled with CO from a balloon 4 times, stirred at 100° for 10 h (TLC), the catalyst separated from the reaction mixture at room temp. by magnetic decantation, washed with 10% NaOH soln., the extracts treated with dil. HCl until acidic to litmus, extracted with ethyl acetate, dried ($MgSO_4$), and the solvent evaporated → 4-hydroxybenzoic acid. Y 95% (Y 88% after the 16th run). The catalyst was quantitatively recycled with only a small decrease in activity after the 10th run and leaching of palladium into the product phase was negligible. Five further examples with ar. bromides or iodides bearing phenolic or carboxy groups afforded yields of 75-89% for the 11th to 15th runs. F.e.s. S. Wittmann, A. Schätz, R.N. Grass, W.J. Stark, O. Reiser, Angew. Chem., Int. Ed. *2010, 49* (10), 1867-70 [DOI: 10.1002/anie.200906166].

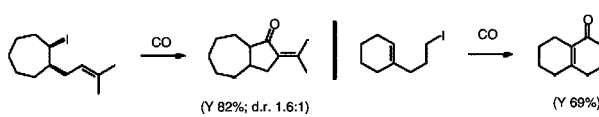
Palladium phosphine complexes (s.a. under Mg and Zn) ←
Palladium-catalyzed coupling of aryl halides with 5-membered heteroarenes Ar-Ar′
s. *57,* 376s*70,75*; arylation with ar. chlorides using an air-stable, robust complex prepared from $Pd(OAc)_2$ and a *tridentate* phosphine ligand in the presence of KOAc/Bu_4NBr at low catalyst loading s. D. Roy, S. Mom, M. Beaupérin, H. Doucet, J.-C. Hierso, Angew. Chem., Int. Ed. *2010, 49* (37), 6650-4 [DOI: 10.1002/anie.201002987]; with $Pd(PBu\text{-}t_3)_2$/LiOBu-t s. S. Tamba, Y. Okubo, S. Tanaka, D. Monguchi, A. Mori, J. Org. Chem. *2010, 75* (20), 6998-7001 [DOI: 10.1021/jo101433g]; 2-, 4- and 5-arylation of a wide range of heteroaromatics under palladium catalysis *in eco-friendly diethyl carbonate* s. J.J. Dong, J. Roger, C. Verrier, T. Martin, R. Le Goff, C. Hoarau, H. Doucet, Green Chem. *2010, 12* (11), 2053-63 [DOI: 10.1039/c0gc00229a]; arylation of condensed 5-membered heteroarenes with ar. iodides using a palladium(0) complex based on the *electron-deficient* 2-[bis[*p*-(trifluoromethyl)phenyl]phosphino]-2′,6′-dimethoxybiphenyl as ligand s. O. René, K. Fagnou, Adv. Synth. Catal. *2010, 352* (13), 2116-20 [DOI: 10.1002/adsc.201000397]; 5-arylation of furfurylamine derivs. and thiophene analogs with ar. bromides using a *phosphine-free* palladium complex s. J. Roger, H. Doucet, Eur. J. Org. Chem. *2010* (23), 4412-5 [DOI: 10.1002/ejoc.201000358]; 5-arylation of 4-chloropyrazoles with $Pd(OAc)_2$/Bu_4NOAc/isobutyric acid and DavePhos as ligand (with automated reaction screening) s. C. Mateos, J. Mendiola, M. Carpintero, J.M. Mínguez, Org. Lett. *2010, 12* (21), 4924-7 [DOI: 10.1021/ol1020898]; 2- or 5-arylation of 3-*prim*-aminothiophenes with (allyl)PdCl(dppb)/KOAc s. F. Derridj, J. Roger, S. Djebbar, H. Doucet, ibid. *2010, 12* (19), 4320-3 [DOI: 10.1021/ol101758w]; ligand- and solvent-dependent 2- or 5-arylation of oxazoles **with** a wide range of [het]aryl halides or **triflates** (cf. *77,* 421) using $Pd(OAc)_2$/phosphine/K_2CO_3 under microwaves s. N.A. Strotman, H.R. Chobanian, Y. Guo, J. He, J.E. Wilson, ibid. *12* (16), 3578-81 [DOI: 10.1021/ol1011778]; 2-[het]arylation of benzothiazoles with [het]aryl iodides under ligand-free conditions with palladium nanoparticles/AgOAc (cf. *77,* 466) s. D. Saha, L. Adak, B.C. Ranu, Tetrahedron Lett. *2010, 51* (42), 5624-7 [DOI: 10.1016/j.tetlet.2010.08.063]; 2-arylation of tryptophan residues in Trp-containing peptides with ar. iodides *in water* with $Pd(OAc)_2$/$AgBF_4$ under microwave irradiation s. J. Ruiz-Rodríguez, F. Albericio, R. Lavilla, Chem. Eur. J. *2010, 16* (4), 1124-7 [DOI: 10.1002/chem.200902676]; C_6-[het]arylation of imidazo[1,2-*b*][1,2,4,5]tetrazines with a palladium phosphine complex under microwave irradiation s. L. Pellegatti, E. Vedrenne, J.-M. Leger, C. Jarry, S. Routier, J. Comb. Chem. *2010, 12* (4), 604-8 [DOI: 10.1021/cc1000456].

Palladium phosphine complexes ←
Intramolecular aminopalladation-Heck arylation ○
s. *48,* 830s*70*; regio- and stereo-selective synthesis of (E)-3-arylidene-3,4-dihydro-2*H*-1,4-benzoxazines s. C. Chowdhury, K. Brahma, S. Mukherjee, A.K. Sasmal, Tetrahedron Lett. *2010, 51* (21), 2859-61 [DOI: 10.1016/j.tetlet.2010.03.081]; of the 1-functionalized 2-arylindolizine ring s. D. Chernyak, C. Skontos, V. Gevorgyan, Org. Lett. *2010, 12* (14), 3242-5 [DOI: 10.1021/ol1011949]; of *trans*-5-benzylpyrrolidin-2-ylcarbinols via intramolecular aminopalladation of 2-oxazolidones with $[(allyl)PdCl]_2$/RuPhos/NaOBu-*t* s. G.S. Lemen, J.P. Wolfe, ibid. *12* (10), 2322-5 [DOI: 10.1021/ol1006828]; of 3-arylindoles from *o*-(trifluoroacetylamino)arylacetylenes and diazonium salts with $Pd(PPh_3)_4$/Bu_4NI/K_2CO_3 (CC↓↑C; cf *54,* 479) s. S. Cacchi, G. Fabrizi, A. Goggiamani, A. Perboni, A. Sferrazza, P. Stabile, ibid. *2010, 12* (14), 3279-81 [DOI: 10.1021/ol101321g].

Tetrakis(triphenylphosphine)palladium(0)/ethyldiisopropylamine $Pd(PPh_3)_4/i\text{-}Pr_2NEt$
Cyclic α,β-ethyleneketones from ethyleneiodides ○
via intramolecular carbonylative Heck-type reaction



456.



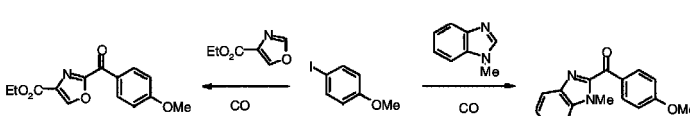
A rare example of a palladium-catalyzed Heck-type cyclization, involving unactivated alkyl iodides with β-hydrogens, is reported, affording a range of mono- and bi-cyclic carbocycles via CO-insertion. **E: 2-Alkylidenecyclopentanones**. In a glovebox, startg. alkyl iodide (0.474 mmol; E/Z 85:15), $Pd(PPh_3)_4$ (10 mol%), *i*-Pr_2NEt (2 eq.) and toluene (0.5 *M*) combined in a 20 ml Parr reactor, the reactor sealed and purged with CO at 150 psi, then pressurized to 735 psi, the reaction vessel heated at 130° (oil bath temp.) for 12 h, allowed to cool to room temp., vented, the mixture extracted with ether, washed with brine, dried ($MgSO_4$), concentrated *in vacuo*, and purified by flash chromatography on silica → 2-ethylidene-4-(4-methoxyphenyl)cyclopentanone. Y 77% (E/Z 10:1). Eight examples afforded cyclopentanone or cyclohexanone derivs. (incl. fused and spiro-cyclic products) in yields of 55-91%. Other Pd-catalysts were less effective, as were inorganic bases (e.g. Cs_2CO_3) or polar solvents (possibly due to competing formation of phosphonium salt by-products). The mechanism was not elucidated, but addition of a radical trap (TEMPO) indicated the involvement of carbon-centered radicals. F.e.s. K.S. Bloome, E.J. Alexanian, J. Am. Chem. Soc. *2010*, *132* (37), 12823-5 [DOI: 10.1021/ja1053913].

Palladium sec-phosphine oxide or chlorophosphine complexes s. under Mg *[Pd]*

Bis(allylpalladium chloride)/copper(I) iodide·ferrocenyltri(phosphines) ←
Sonogashira coupling s. *27*, 851s*78* C≡CH → C≡CR

Bis(cinnamylpalladium chloride)/copper(I) iodide/1,3-bis(diphenylphosphino)propane/ ←
1,8-diazabicyclo[5.4.0]undec-7-ene
Aryl azolyl ketones from azoles and ar. iodides H → C(O)Ar
Palladium(II)-catalyzed carbonylative cross-coupling

457.



4-Iodoanisole (1 mmol), DBU (1 eq.) and DMF (2 ml) added via syringe to a mixture of 1-methylbenzimidazole (1.5 eq.), $[(cinnamyl)PdCl]_2$ (5 mol%), dppp (10 mol%) and CuI (1.5 eq.) under argon, the mixture heated in an autoclave under CO (40 bar) at 120° for 30 h, cooled to room temp., vented, diluted with water, extracted with ethyl acetate, concentrated *in vacuo*, and purified

by chromatography on silica → 2-(4-methoxybenzoyl)-1-methylbenzimidazole. Y 56%. This novel carbonylative C-H activation was successful for electron-diverse (het)ar. iodides reacting with oxazole, thiazole and *imidazole* derivs. (twenty-five examples; Y 54-71%), with yields somewhat lower for sterically hindered 2-iodotoluene (40%) and 4-bromoiodobenzene (45%). Use of the bidentate ligand appears crucial to the reaction (Ph_3P gave mainly a non-carbonylated coupled product), while ar. bromides were almost inactive under these conditions. F.e. and optimization s. X.-F. Wu, P. Anbarasan, H. Neumann, M. Beller, Angew. Chem., Int. Ed. *2010*, *49* (40), 7316-9 [DOI: 10.1002/anie.201003895].

Bis(cinnamylpalladium chloride)/2-(dicyclohexylphosphinomethyl)-1,3-bis(2,6-di-isopropylphenyl)imidazolium iodide/cesium carbonate ←

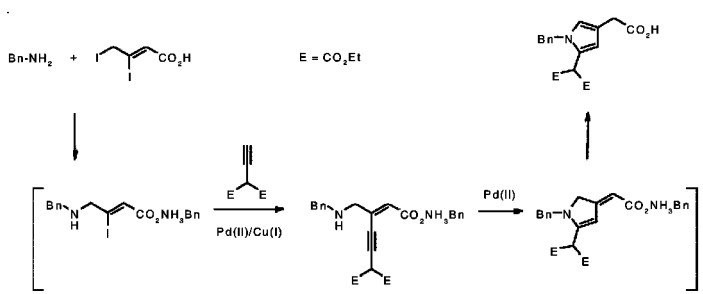
Sonogashira coupling C≡CH → C≡CAr

with 2-phosphinomethyl-1,3-bis(2,6-diisopropylphenyl)imidazolium iodides as readily recyclable, hindered ligands s. *78*, 96

Dichlorobis(triphenylphosphine)palladium(II)/copper(I) iodide $PdCl_2(PPh_3)_2$/CuI

Palladium(II)-catalyzed 3-component synthesis of pyrrole-3-acetic acids from α,β-ethylene-β,γ-diiodocarboxylic acids, terminal acetylene derivs. and prim. amines ○

458.



in one pot. A mixture of startg. alkyne (2.2 eq.), benzylamine (5 eq.) and CuI (10 mol%) in DMF (2 ml) stirred at -80° under argon for 15 min, (E)-3,4-diiodobut-2-enoic acid (2.5 mmol) and $PdCl_2(PPh_3)_2$ (5 mol%) added at 0°, the mixture stirred at room temp. for 18 h, quenched with satd. aq. NH_4Cl, extracted with ether, the aq. layer acidified at 0° with 1 *M* aq. HCl, extracted with ether, the combined organic phases concentrated *in vacuo*, and purified by flash chromatography on silica → diethyl 2-(1-benzyl-4-carboxymethyl-1*H*-pyrrol-2-ylmethyl)malonate. Y 48%. This novel sequential N-allylation-Sonogashira coupling-cycloisomerization required careful optimization to minimize products formed by competing lactonization. Prim. ar. and aliphatic amines and a variety of terminal alkynes reacted with the readily available diiodobutenoic acid to afford 1,2,4-tri- and 1,3-di-subst. pyrroles generally in moderate yields (fourteen examples; Y 10-61%) with silyl and germyl groups lost during the acidic work-up. Ester, ether, thioether and acetal groups were tolerated but the reaction failed with ethyl propiolate. F.e., optimization and substrate prepn. s. S. Lamandé-Langle, M. Abarbri, J. Thibonnet, A. Duchêne, J.-L. Parrain, Chem. Commun. *2010*, *46* (28), 5157-9 [DOI: 10.1039/c0cc00500b].

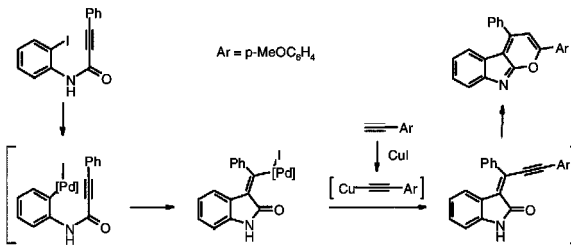
Dichlorobis(triphenylphosphine)palladium(II)/copper(I) iodide/triethylamine ←

Pyrano[2,3-*b*]indoles ○

from α,β-acetylenecarboxylic acid *o*-iodoanilides and acetylene derivs.

Double ring closure

459.



Startg. N-(*o*-iodophenyl)alkynylamide (1 mmol), CuI (5 mol%), and $PdCl_2(PPh_3)_2$ (5 mol%) dissolved in a mixture of dry THF (5 ml) and dry triethylamine (5 ml) in an argon-flushed oven-dried screw-cap vessel, after stirring for 5 min, 4-methoxyphenylacetylene (1.1 eq.) added, the mixture stirred at room temp. for 36 h, then heated to 85° for 48 h, cooled to room temp., solvents removed *in vacuo*, the residue chromatographed on silica gel, then crystallized from methylene chloride/*n*-hexane → product. Y 54%. Although yields are moderate (nine further examples; Y 15-41%), this Pd-Cu-catalyzed insertion-coupling-cycloisomerization gives flexible access to novel **2,4-diarylpyrano[2,3-*b*]indoles** which, unusually, can act as metal-selective luminescence sensors. F.e.s. J. Schönhaber, W. Frank, T.J.J. Müller, Org. Lett. *2010*, *12* (18), 4122-5 [DOI: 10.1021/ol101709p]; spirocyclizations cf. *68*, 419; s.a. D.M. D'Souza, A. Kiel, D.-P. Herten, F. Rominger, T.J.J. Müller, Chem. Eur. J. *2008*, *14* (2), 529-47 [DOI: 10.1002/chem.200700759].

Tris(2-phenylpyridinato-C2,N)iridium(III) s. under (2R,5S)-5-Benzyl-2,3-dimethyl-4-imidazolidone *[Ir(III)]*

Pentahydridobis(triisopropylphosphine)iridium(V)/3,3-dimethylbut-1-ene/chlorobis(cyclopentadienyl)hydridozirconium(IV) ←

Terminal functionalization of hydrocarbons H → R

via regioselective hydrozirconation of terminal ethylene derivs. s. *78*, 224

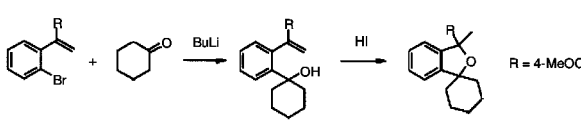
Via intermediates *v. i.*

***o,o'*-Dioxybiaryls from *o*-bromophenols and phenols** ←

via aryloxy(*o*-bromoaryloxy)silanes s. *78*, 539

Phthalans [1,3-dihydroisobenzofurans] from *o*-bromostyrenes and oxo compds. via acid-catalyzed cycloisomerization of *o*-vinylbenzyl alcohols ○

460.



One drop of concd. HI added to a soln. of 1-[2-[1-(4-methoxyphenyl)ethenyl]phenyl]cyclohexanol (1.3 mmol) [prepared in 78% yield by sequential treatment of 1-bromo-2-[1-(4-methoxyphenyl)-ethenyl]benzene with *n*-BuLi and cyclohexanone] in acetonitrile (9 ml) at 0°, quenched with satd. aq. $NaHCO_3$ after 5 min, extracted with ether (following removal of acetonitrile by evaporation), the extracts dried (Na_2SO_4), concentrated, and the residue purified by preparative TLC on silica gel → 3'-(4-methoxyphenyl)-3'-methyl-3'*H*-spiro(cyclohexane-1,1'-isobenzofuran). Y 61%. The

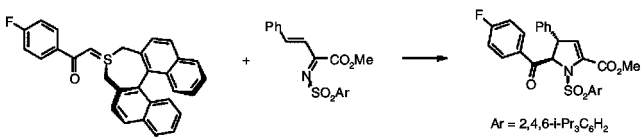
cyclization was successful for the preparation of 1,1,3-tri- and 1,1,3,3-tetra-subst. phthalans (eleven examples; Y 33-65%), with lowest yields (33%, 36%) obtained for the former (sec. alcohols as substrates) or for β-subst. styrenes (39%, 43%). Startg. benzylic alcohols were obtained from *o*-bromostyrenes and oxo compds. (via *o*-lithiostyrenes) in moderate yield (50-78%). Although yields are not high, the procedure offers a convenient method for the synthesis of this class of compd., which is more generally applicable than those published previously. F.e.s. K. Kobayashi, K. Shikata, Y. Fujii, S. Fukamachi, M. Tanmatsu, H. Konishi, Heterocycles *2010*, *81* (6), 1459-66 [DOI: 10.3987/com-10-11947]; synthesis of **phthalans from *o*-vinylbenzyl alcohols via** intramolecular iodoetherification with I_2, followed by reduction of the intermediate **1-(iodomethyl)-phthalans** with *n*-Bu_3SnH s. K. Kobayashi, K. Shikata, S. Fukamachi, H. Konishi, ibid. *2008*, *75* (3), 599-609 [DOI: 10.3987/com-07-11244].

Sulfur ↑ CC ↓↑ S

Without additional reagents *w.a.r.*

N-Sulfonyl-Δ²-pyrrolines from α,β-ethylene-N-sulfonylimines and sulfonium ylids ○

461.



In the presence of an N-sulfonyl group the kinetic preference for formation of aziridines from α,β-ethyleneimines and sulfur ylids can be overcome via electronic rather than steric effects, allowing unprecedented [4+1]-annelation with high chemo- and stereo-selectivity. **E: 5-Acyl-N-sulfonyl-Δ²-pyrroline-2-carboxylic acid esters with asym. induction**. A soln. of startg. unsatd. tosylimine (0.2 mmol) and toluene/methylene chloride (9:1; 20 ml) stirred at -80° for 0.5 h, startg. chiral sulfur ylid added, stirring continued for 48 h at the same temp., the mixture allowed to warm slowly to room temp., when reaction complete by TLC the solvent removed under reduced pressure, and the crude residue purified by flash chromatography on silica gel → (4S,5R)-methyl 5-(4-fluorobenzoyl)-4-phenyl-1-(2,4,6-triisopropylphenylsulfonyl)-4,5-dihydro-1*H*-pyrrole-2-carboxylate. Y 90% (d.r. > 95:5, e.e. 98%). Increasing the size of the ester, electron deficiency of the protecting group, solvent polarity, or concentration offered no advantage, whereas increasing the steric bulk of the sulfonyl group from tosyl to 2,4,6-triisopropylphenylsulfonyl resulted in a substantial improvement in enantioselectivity (from 87% to 98% e.e. for the 5-benzoyl-4-phenyl-deriv.). The chiral BINOL-derived sulfide auxiliary is cheap, readily available and recoverable. The derived sulfur ylids may carry electron-rich, electron-neutral, or electron-deficient substituents on the aroyl rings (Y 88-98%; d.r. >95:5; e.e. 95-98%), or be stabilized by thien-2-ylcarbonyl, cinnamoyl or 3-phenylpropanoyl groups, while the α-imino-esters may bear electronically-diverse aryl, styryl or furan-2-yl groups in the γ-position. F.e. (twenty; Y 83-99%; d.r. >95:5; e.e. 82-98%) and optimization s. L.-Q. Lu, J.-J. Zhang, F. Li, Y. Cheng, J. An, J.-R. Chen, W.-J. Xiao, Angew. Chem., Int. Ed. *2010*, *49* (26), 4495-8 [DOI: 10.1002/anie.201000755].

Microwaves s. under $PdCl_2(PPh_3)_2$ [\\\\]

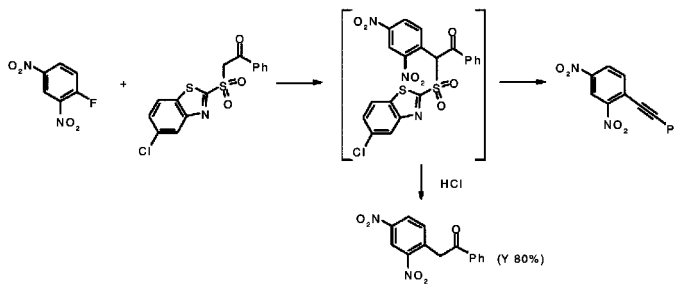
Potassium carbonate K_2CO_3

Arylacetylenes ArF → Ar-C≡C

from ar. fluorides and benzothiazol-2-ylsulfonylmethyl ketones

Transition metal-free formal Sonogashira coupling via α-arylation

462.

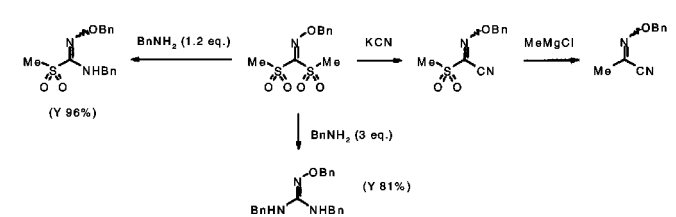


in one pot. A mixture of startg. benzothiazol-2-ylsulfonylmethyl ketone (0.2 mmol) and 2,4-dinitrofluorobenzene (2.2 eq.) in acetone (1 ml) treated with K_2CO_3 (1.2 eq.), the mixture stirred vigorously at 65° until TLC or NMR analysis indicated consumption of the startg. sulfone (typically 12-72 h), concentrated under reduced pressure, and purified by flash chromatography on silica gel → 2,4-dinitro-1-(phenylethynyl)benzene. Y 71% (51% from the non-chlorinated benzothiazolyl analog). This truly transition metal-free method is applicable to a variety of electron-deficient ar. fluorides bearing nitro, cyano and/or keto groups in the *o*- and *p*-positions, while the benzothiazol-2-ylsulfonylmethyl ketone may be aryl or alkyl (Me, *i*-Pr or *t*-Bu) substituted (eighteen examples; Y 49-86%; mostly from non-chlorinated benzothiazolyl analogs). A milder two-step procedure was also investigated, using Cs_2CO_3 in acetone at 4° for the arylation and $NaHCO_3$ in acetone at 45° for the elimination (thirteen examples; Y 42-74%). **α-Aryl-ketones** (fifteen examples; Y 58-86%) **or -carboxylic acid esters** (four examples; Y 39-77%) were also prepared by α-arylation using Cs_2CO_3 in acetone at room temp. or 4° then desulfonylation using HCl (1 *N* aq.). F.e.s. B. Prüger, G.E. Hofmeister, C.B. Jacobsen, D.G. Alberg, M. Nielsen, K.A. Jørgensen, Chem. Eur. J. *2010*, *16* (12), 3783-90 [DOI: 10.1002/chem.200902911].

Potassium cyanide *KCN*

Replacement of sulfonyl groups in 1,1-alkoximinosulfones by nucleophiles ←

463.

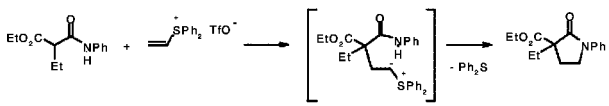


Sequential nucleophilic substitution of bis(methanesulfonyl)-O-benzyloxime. A soln. of bis(methanesulfonyl)-O-benzyloxime (0.2 mmol) in THF (1 ml) treated with KCN (1.2 eq.), stirred for 2 h at room temp., diluted with ethyl acetate, quenched with satd. aq. NH_4Cl soln., the phases

separated, the aq. layer further extracted with ethyl acetate, the combined organic layer dried ($MgSO_4$), filtered, evaporated under reduced pressure, and the crude residue purified chromatographically → N-(benzyloxy)(methylsulfonyl)methanimidoyl cyanide (Y 90%), treated with methylmagnesium chloride (1.2 eq.) in THF at -78° for 2 h → 2-benzyloxyiminopropionitrile (Y 93%). Reaction of this phosgene equivalent with 1.2 eq. benzylamine in THF at room temp. for 2 h afforded the corresponding N-alkoxy(sulfonyl)formamidine (Y 96%), while reaction with 3 eq. of the amine under the same conditions afforded the N-alkoxyguanidine (Y 81%). In eight further examples monosubstitution was effected with NaOMe, NaN_3, LiSPh, a Li-acetylide, PhMgBr, Li-enolates or $NaP(O)(OEt)_2$ (Y 70-89%). Twelve examples of reactions of 1-benzenesulfonyl-1-benzyloxyimino-3-phenylpropane are also reported (Y 79-99%) with nucleophiles including organolithium compds. (lithium diorganocuprates giving lower yields); the sulfonyl group is less readily displaced compared to the phosgene equivalent since there was no reaction with benzylamine, and use of lithium benzylamide was required. F.e.s. S. Kim, N.A.B. Kamaldin, S. Kang, S. Kim, Chem. Commun. *2010, 46* (41), 7822-4 [DOI: 10.1039/c0cc02081h]; **alkoximes from** 1,1-alkoximinosulfones and **ethylene derivs.** with 1,1,2,2-tetramethyl-1,2-ethanediamino-N,N′-bis(3,5-di-*tert*-butylsalicylidene)cobalt(II)/$PhSiH_3$, **also α-alkoximinonitriles**, s. B. Gaspar, E.M. Carreira, J. Am. Chem. Soc. *2009, 131* (37), 13214-5 [DOI: 10.1021/ja904856k].

1,8-Diazabicyclo[5.4.0]undec-7-ene *DBU*
2-Pyrrolidone-3-carboxylic acid esters ○
from malonamic acid esters and enesulfonium salts

464.



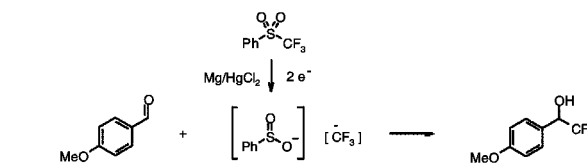
Ethyl 2-(phenylcarbamoyl)butanoate (1 mmol), DBU (2 mmol), and methylene chloride (2 ml) charged into an oven-dried flask, a soln. of diphenyl(vinyl)sulfonium triflate (1.5 mmol) in the same solvent (3 ml) added dropwise at room temp., the mixture allowed to react at the same temp. for 6 h, solvent removed under vacuum, and the residue purified on a silica gel column → product. Y 93%. The procedure is very mild, unlike many established 2-pyrrolidone syntheses which require high temp., acidic reagents or expensive transition metals; it is also based on readily available substrates and is generally applicable to the coupling of electron-diverse N-arylmalonamic acid esters, as well as N-heteroaryl-, N-acyl-, N-tosyl- and N-benzyl-derivs., with vinyl- and 2-arylvinyl-(diphenyl)sulfonium triflates (ten examples; Y 41-98%). A cyanoacetanilide reacted similarly to give the 3-cyano-2-pyrrolidone (Y 85%), but an N-alkylmalonamate gave a cyclopropane deriv. instead, while acetanilide itself gave the corresponding 2-acetoxyamine. The choice of base is critical, NaH giving lower yields, while triethylamine gave a mixture of 2-pyrrolidone and isomeric iminolactone. Reaction is presumed to involve base-catalyzed Michael-type addition of the malonamate to the enesulfonium salt to generate a sulfur ylid, which undergoes intramolecular attack by nitrogen with displacement of diphenyl sulfide. F.e.s. C. Xie, D. Han, Y. Hub, J. Liu, T. Xie, Tetrahedron Lett. *2010, 51* (40), 5238-41 [DOI: 10.1016/j.tetlet.2010.07.108].

Copper(I) iodide s. under $PdCl_2(PPh_3)_2$ *CuI*

Magnesium *Mg*
Replacement of sulfonyl groups in 1,1-alkoximinosulfones by nucleophiles ←
Sequential nucleophilic substitution of bis(methanesulfonyl)-O-benzyloxime s. *78*, 463

Magnesium/mercury(II) chloride *Mg/HgCl$_2$*
2,2,2-Trifluoroalcohols from aldehydes CHO → CH(OH)CF$_3$
Synthesis with addition of one C-atom

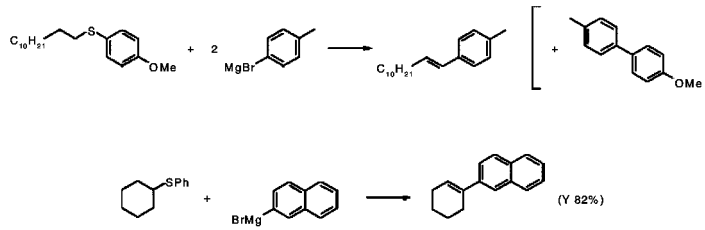
465.



Conditions for reductive nucleophilic trifluoromethylation of non-enolizable or enolizable aldehydes with phenyl trifluoromethyl sulfone have been reported, using magnesium activated by mercury(II) chloride in a highly polar solvent, which facilitates the electron-transfer process and stabilizes the anionic intermediate. **E:** Phenyl trifluoromethyl sulfone (2 eq.) and *p*-anisaldehyde (0.5 mmol) in DMF (2 ml) added dropwise to a suspension of $HgCl_2$ (6 mol%) and Mg (2 eq.) in DMF (2 ml) at -15°, the mixture allowed to warm to room temp., and, upon disappearance of Mg (ca. 2 h), the reaction quenched with 3 *N* HCl (1.5 ml), extracted with ether, the combined organic phase washed with brine, dried ($MgSO_4$), filtered, concentrated under vacuum, and the residue purified by silica gel chromatography → product. Y 88%. A variety of ar. aldehydes reacted in moderate to good yields (55-82%; six examples), yields being lower with strong electron-withdrawing groups on the aromatic ring (28-60%; four examples), while dihydrocinnamaldehyde gave a 45% yield (higher than the yield obtained via alkoxide-induced nucleophilic trifluoromethylation; cf. *44*, 577*s66*). Reaction failed with reducing agents such as Mg alone, Al, Zn or SmI_2. In the absence of aldehyde, DMF reacted to afford fluoral hydrate in 77% yield. F.e.s. Y. Zhao, J. Zhu, C. Ni, J. Hu, Synthesis *2010* (11), 1899-904 [DOI: 10.1055/s-0029-1218752].

Magnesium/bis(1,5-cyclooctadiene)nickel(0)/1,3-bis(2,6-diisopropylphenyl)-imidazolidine hydrochloride ←
Nickel(0)-catalyzed synthesis of styrenes CHCH(SAr) → C=C(Ar′)
from ar. thioethers and arylmagnesium bromides

466.

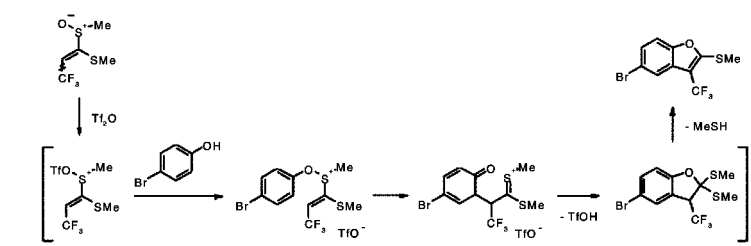


p-Tolylmagnesium bromide (3 eq.) added to a soln. of $Ni(cod)_2$ (2 mol%) and 1,3-bis(2,6-diisopropylphenyl)imidazolidine hydrochloride (4 mol%) in THF at 0°, the mixture stirred at this temp. for 10 min, dodecyl *p*-anisyl sulfide (10 mmol) added, stirred at 0° for a further 10 min, then at 60° for 6 h, cooled to room temp., quenched with satd. aq. NH_4Cl, extracted with ether, filtered through a pad of Na_2SO_4 and Florisil, solvent removed *in vacuo*, and the residue purified by chromatography on silica gel → 1-(4-methylphenyl)-1-dodecene. Y 90% (E/Z 95:5). Similar results were obtained from a range of linear prim. alkyl, or sym. sec. cycloalkyl, ar. sulfides and

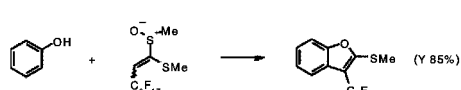
aryl Grignards (incl. naphthyl analogs), affording styrene derivs. in good yield (75-93%; ca. twelve examples), with high stereoselectivity (E/Z 94:6 to 100:0). *o*-Subst. ar. Grignards gave low yields, however, and regioselectivity was poor with a non-symmetrical sec. alkyl sulfide; low E/Z selectivity (43:57) was observed for the formation of a trisubst. olefin. In all cases, geminal diarylation by-products were observed (generally only 1-3%, but 37% in the case of 8-phenylthio-1,4-dioxaspiro[4.5]decane as substrate). Other Ni-catalysts were less effective, as were less-bulky NHC ligands; use of phosphine ligands improved the yields of the biaryl side-products, but did not promote the desired coupling. A mechanism is proposed, based on experimental observations, literature precedent and DFT calculations, in which the initial step is the oxidative addition of an alkyl aryl sulfide to a nickel(0) species to afford an arylnickel(II) intermediate; the bulkiness of the NHC ligand is thought to suppress a conventional biaryl coupling pathway. F.e.s. K. Ishizuka, H. Seike, T. Hatakeyama, M. Nakamura, J. Am. Chem. Soc. *2010*, *132* (38), 13117-9 [DOI: 10.1021/ja104155f].

1,3-Bis(2,6-diisopropylphenyl)imidazolidine hydrochloride s. under Mg — *SIPr·HCl*
Acetic acid s. under $PdCl_2(PPh_3)_2$ — *AcOH*
Phenylsilane s. under 1,1,2,2-Tetramethyl-1,2-ethanediamino-N,N′-bis(3,5-di-tert-butylsalicylidene)cobalt(II) — $PhSiH_3$

Trifluoromethanesulfonic anhydride — Tf_2O
2-Alkylthio-3-(trifluoromethyl)benzofurans from phenols via extended Pummerer reaction with dimethyl trifluoromethylketene mercaptal monoxide



467.



Trifluoromethanesulfonic anhydride (2 eq.) added to a soln. of 4-bromophenol (0.4 mmol) and dimethyl trifluoromethylketene dithioacetal monoxide (2 eq.) in methylene chloride (4 ml) at -78° under argon, the mixture stirred at 40° for 30 min, poured into satd. aq. $NaHCO_3$, extracted with methylene chloride, and purified by chromatography on silica gel → 5-bromo-2-methylthio-3-trifluoromethylbenzo[*b*]furan. Y 76%. Five further *p*-subst. (*n*-Bu, Bpin, CN, CF_3, CO_2Et) phenols reacted similarly to afford corresponding products in yields of 64-89%; a *p*-methoxy analog was too reactive to undergo the desired transformation (even at -40°), giving only its triflate as major by-product; notably, the *p*-(pinacolato)boryl analog is stable, however, and can serve as a

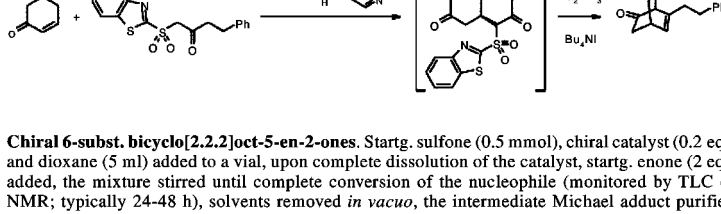
p-methoxyphenol equivalent. Apart from *m*-cresol (67:33; Y 70%), regioselectivity for *m*-subst. (*t*-Bu, MeO, CF_3) phenols was very high (>99:1; three examples; Y 55-76%), favoring cyclization at the least-hindered site. *o*-Cresol gave a yield of 51%, and both 1- and 2-naphthol were suitable substrates, affording tricyclics, regioselectively, in yields of 52% and 74%, respectively. The highly electron-withdrawing trifluoromethyl group is critical to the success of the transformation and, while it could not be successfully replaced by methyl or phenyl, a heptadecafluorooctyl analog gave rise to 2-methylthio-3-heptadecafluorooctylbenzo[*b*]furan in high yield (85%). F.e. and derivatization of the products via transformation of the 2-methylthio group s. T. Kobatake, D. Fujino, S. Yoshida, H. Yorimitsu, K. Oshima, J. Am. Chem. Soc. *2010*, *132* (34), 11838-40 [DOI: 10.1021/ja1030134].

9-Amino-9-deoxy-epi-quinine/trifluoroacetic acid/sodium carbonate/tetra-n-butyl-ammonium iodide ←

3-Cyclohexenone ring ○

from cyclic α,β-ethyleneketones and benzothiazol-2-ylsulfonylmethyl ketones via organocatalyzed asym. Michael addition-intramolecular aldol condensation-Smiles rearrangement

468.



Chiral 6-subst. bicyclo[2.2.2]oct-5-en-2-ones. Startg. sulfone (0.5 mmol), chiral catalyst (0.2 eq.) and dioxane (5 ml) added to a vial, upon complete dissolution of the catalyst, startg. enone (2 eq.) added, the mixture stirred until complete conversion of the nucleophile (monitored by TLC or NMR; typically 24-48 h), solvents removed *in vacuo*, the intermediate Michael adduct purified on a short pad of Iatrobeads, re-dissolved in a 1:1 mixture of toluene and satd. aq. Na_2CO_3 soln. (10 ml), treated with tetra-*n*-butylammonium iodide (1.2 eq.), the biphasic suspension stirred vigorously at 45° for 24 h, then diluted with water (10 ml), extracted with ethyl acetate, the combined organic phases dried ($MgSO_4$), concentrated *in vacuo*, and purified by flash chromatography on Iatrobeads → (1S,4S)-6-phenethylbicyclo[2.2.2]oct-5-en-2-one. Y 58% (e.e. 95%). These conditions are applicable to the synthesis of 6-aryl-derivs. (five examples; Y 44-59%; e.e. 91-97%) as well as 6-alkyl-derivs. and to a bicyclo[2.2.1]heptenone (Y 44%; e.e. 60%) but not a bicyclo[3.2.2]-nonenone, the 3-alkynylheptenone being isolated instead (Y 51%; e.e. 98%). Reaction of 5,5-dimethyl-2-cyclohexenone unexpectedly gave 5-(benzo[*d*]thiazol-2-yloxy)bicyclo[2.2.2]octan-2-ones (two examples; Y 54%, 59%; d.r. 95:5, 1:1). F.e. and mechanisms for aryl- and alkyl-subst. derivs. s. N. Holub, H. Jiang, M.W. Paixão, C. Tiberi, K.A. Jørgensen, Chem. Eur. J. *2010*, *16* (14), 4337-46 [DOI: 10.1002/chem.200903274]; **chiral cyclic γ,δ-acetyleneketones, 4-ethylene-alcohols or 1,5-diketones** from cyclic α,β-ethyleneketones via organocatalyzed asym. Michael addition of benzothiazol-2-ylsulfonylmethyl ketones (cf. *76*, 468) s. M.W. Paixão, N. Holub, C. Vila, M. Nielsen, K.A. Jørgensen, Angew. Chem., Int. Ed. *2009*, *48* (40), 7338-42 [DOI: 10.1002/anie.200903790].

1,1,2,2-Tetramethyl-1,2-ethanediamino-N,N′-bis(3,5-di-tert-butylsalicylidene)cobalt(II)/phenylsilane ←

Alkoximes from 1,1-alkoximinosulfones C(=NOR)SO_2R′ → C(=NOR)C-CH

and ethylene derivs. s. *78*, 463

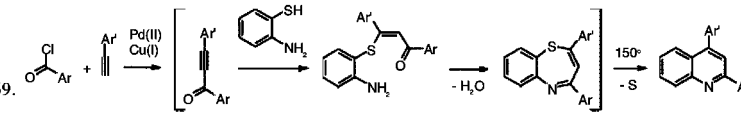
Bis(1,5-cyclooctadiene)nickel(0) s. under Mg *Ni(cod)$_2$*

Dichlorobis(triphenylphosphine)palladium(II)/copper(I) iodide/triethylamine/acetic acid/ microwaves ←

2,4-Disubst. quinolines ○

from *o*-aminomercaptans, terminal acetylene derivs. and carboxylic acid chlorides via microwave-assisted sulfur extrusion from 1,5-benzothiazepines

469.



Ar = 4-ClC$_6$H$_4$ Ar' = 4-NO$_2$C$_6$H$_4$

4-Chlorobenzoyl chloride (1 mmol), 4-nitrophenylacetylene (1 eq.) and triethylamine (1.05 eq.) added to a soln. of $PdCl_2(PPh_3)_2$ (2 mol%) and CuI (4 mol%) in **THF** (4 ml) under N_2 at room temp., the mixture stirred for 1 h, 2-aminothiophenol (1.1 eq.), glacial acetic acid (0.5 ml) and isopropanol (0.5 ml) added sequentially, the mixture heated by microwaves at 150° for 1 h, cooled, concentrated *in vacuo*, and purified chromatographically → 2-(4-chlorophenyl)-4-(4-nitrophenyl)quinoline. Y 72%. This Sonogashira coupling-Michael addition-cyclocondensation-sulfur extrusion sequence provides experimentally simple, versatile and *regiospecific* synthesis of 2,4-di- and 2,4,7-tri-subst. quinolines, with complete extrusion of sulfur being crucial for obtaining pure products. The method was successful for electron-diverse (het)aroyl chlorides and aryl- (or silyl-) acetylenes but failed with aliphatic acyl chlorides (seventeen examples; Y 45-72%). Structures were confirmed by X-ray analysis in one case. F.e. and DFT-computational examination of the extrusion process s. S. Rotzoll, B. Willy, J. Schönhaber, F. Rominger, T.J.J. Müller, Eur. J. Org. Chem. *2010* (18), 3516-24 [DOI: 10.1002/ejoc.201000212].

Via intermediates *v.i.*

(Z)-5-Arylidenerhodanines from prim. amines and ar. aldehydes

via Holmberg reaction-Knoevenagel condensation under microwave irradiation s. *78*, 382

Remaining Elements ↑ CC ↓↑ Rem

Without additional reagents *w.a.r.*

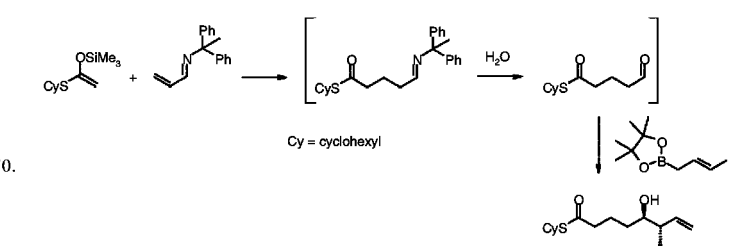
Uncatalyzed aldol-type condensation CHO → CH(OH)C-CO

with peptide- and -protein N-terminal aldehydes in water s. *44*, 875s*78*

***anti*-ζ,η-Ethylene-δ-hydroxythiolic acid esters** ←

from O-silyl ketene S,O-acetals, β,γ-ethyleneboronic acid esters and N-allylidene(1,1-diphenylethyl)amine as acrolein equivalent

470.



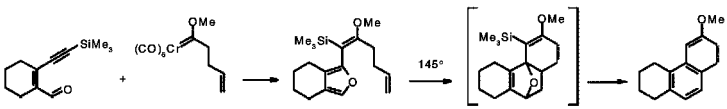
Cy = cyclohexyl

3-Component synthesis in one pot. Solns. of 1-cyclohexylthio-1-trimethylsilyloxyethene (2 eq.) in methylene chloride (1 ml), 2-(E)-crotonyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.1 eq.)

in the same solvent (1 ml) and water (2.8 eq.) added sequentially to a soln. of N-allylidene(1,1-diphenylethyl)amine (0.2 mmol) in the same solvent (1 ml) at -78° under argon, the mixture warmed to room temp. during 15.5 h, quenched with 2 *M* aq. HCl, extracted with ethyl acetate, washed with brine, concentrated *in vacuo*, and purified chromatographically → *anti*-S-cyclohexyl 5-hydroxy-6-methyloct-7-enethioate. Y 67% (*anti/syn* >99:1). Analogous **anti-ζ,η-ethylene-δ-hydroxycarboxylic acid esters** were obtained from O-silyl O-alkyl keteneacetals. The reaction proceeds via 1,4-addition of the silyl ester to the allylideneamine, imine hydrolysis and subsequent 1,2-addition of allylboronate, and was highly diastereoselective in the 1,2-addition step only. 1-Ethoxy-, 1-benzyloxy- and methyl-subst. 1-cyclohexylthio-1-trimethylsilyloxyethylenes were also effective components (thirteen examples; Y 52-81%; d.r. 94:6 to >99:1), with analogs (OPh, SEt, OCy, SPh) giving low yields (0-17%). F.e. and optimization s. M. Shimizu, M. Kawanishi, I. Mizota, I. Hachiya, Org. Lett. *2010*, *12* (16), 3571-3 [DOI: 10.1021/ol101061t].

3-Alkoxy-1,2-dihydronaphthalene ring ○
from 2,4-enynals and chromium γ,δ-ethylene(alkoxy)carbene complexes
via dehydrative intramolecular [4+2]-cycloaddition of 2-(1,5-dienyl)furans

471.



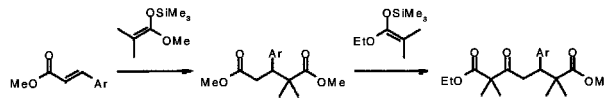
A soln. of startg. chromium carbene complex (1.35 eq.) in dioxane (5 ml) added dropwise over 5 min to a soln. of startg. enynal (1 mmol) in the same solvent (20 ml) at 85° under N_2, the mixture stirred for 10 h, cooled to room temp., filtered through Celite, concentrated *in vacuo*, DMF (15 ml) added, the soln. heated at 145° for 7 h, cooled, diluted with hexane, washed with water, concentrated *in vacuo*, and purified chromatographically → 1,2,3,4,7,8-hexahydro-6-methoxyphenanthrene. Y 60% (plus 5% of the 1,2,3,4-tetrahydro-deriv.). Initial coupling of internal and terminal 2,4-enynals with suitable chromium carbene complexes afforded furan derivs. carrying a 1,5-dienyl moiety at the 2-position (nine examples; Y unspecified) which were resistant to direct Diels-Alder cycloaddition (prolonged heating or high temps. resulting in slow decomposition). Calculations suggested that, while direct Diels-Alder cycloaddition was unfavorable, tandem cycloaddition and dehydration was energetically feasible. Net [5+5]-cycloaddition to the dihydronaphthalene moiety was achieved using a high boiling and polar solvent to facilitate dehydration (two examples; Y 60-64%). The role of the trimethylsilyl group (lost during the cyclodehydration step) was not discussed. F.e.s. R.K. Patti, S. Duan, A. Camacho-Davila, K. Waynant, K.A. Dunn, J.W. Herndon, Tetrahedron Lett. *2010*, *51* (28), 3682-4 [DOI: 10.1016/j.tetlet.2010.05.049].

Microwaves [s.a. under Nanoferrite-anchored glutathione, $Sn(OTf)_2$, $Mn(OAc)_3$ and Na_2PdCl_4] [\\\\]
Petasis reaction $B(OH)_2 \rightarrow CH(N<)R$
s. *48*, 856s*70*; rapid procedure *without solvent under microwaves* with simplified work-up s. P. Nun, J. Martinez, F. Lamaty, Synthesis *2010* (12), 2063-8 [DOI: 10.1055/s-0029-1218727]; improved catalyst-free reaction with 2-pyridinecarboxaldehydes s. H. Mandai, K. Murota, T. Sakai, Tetrahedron Lett. *2010*, *51* (36), 4779-82 [DOI: 10.1016/j.tetlet.2010.07.039]; synthesis of N-protected α-hydrazinocarboxylic acids s. S. Neogi, A. Roy, D. Naskar, J. Comb. Chem. *2010*, *12* (1), 75-83 [DOI: 10.1021/cc900092x].

Sodium hydroxide *NaOH*
Wittig synthesis $CO \rightarrow C{=}C$
s. *13*, 820; by segmented fluid flow under ultrasonication, with a study of the effect of bases (e.g. NaOH), aldehydes, phosphonium salts, solvents, phase transfer catalysts and flow parameters, s. M. Riccaboni, E. La Porta, A. Martorana, R. Attanasio, Tetrahedron *2010*, *66* (23), 4032-9 [DOI: 10.1016/j.tet.2010.04.031].

β-Keto-ε-dicarboxylic acid esters ←
from α,β-ethylenecarboxylic acid esters
and two different O-silyl O-alkyl keteneacetal molecules
via sequential Michael-type addition-Claisen condensation

472.



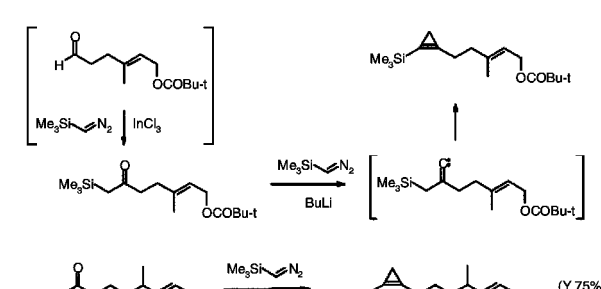
Ar = 4-MeOC$_6$H$_4$

in one pot. Startg. ketene silyl acetal (1.2 eq.) added to a stirred mixture of methyl 4-methoxycinnamate (0.5 mmol), powdered NaOH (40 mol%) and DMF (0.1 ml) at 20-25° under argon, the mixture stirred for 1.5 h, the second ketene silyl acetal (2 eq.) added, stirred for 2 h, 1 *M* methanolic HCl added, stirred for 0.5 h, quenched with water, extracted with ether, concentrated, and purified chromatographically → 1-ethyl 7-methyl 3-oxo-5-(4-methoxyphenyl)-2,2,6,6-tetramethylheptane-1,7-dioate. Y 70%. This mild, one-pot synthesis of relatively inaccessible and differentially functionalized 1,3,7-tricarbonyl compds. was successful for electron-diverse cinnamate esters reacting with single or different ketene silyl acetal molecules (eighteen examples; Y 48-85%). Yields were somewhat lower for aliphatic (crotonate) esters (35-57%; three examples). The reaction was also carried out sequentially, using LiOH optimally for the initial Mukaiyama-Michael-type step (eighteen examples; Y 56-98%), and NaOH for subsequent crossed Claisen condensation (twelve examples; Y 64-98%). F.e.s. H. Tamagaki, Y. Nawate, R. Nagase, Y. Tanabe, Chem. Commun. *2010*, *46* (32), 5930-2 [DOI: 10.1039/c0cc01110j].

n-Butyllithium *BuLi*
α-(Difluoroiodomethyl)carbonyl compds. from enoxysilanes C(OSi≤)=C → C(O)CF$_2$I
via lithium enolates s. *78*, 434

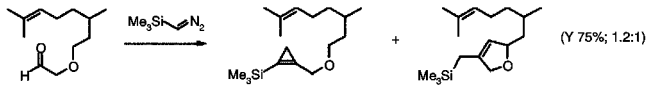
1-Silylcyclopropenes from aldehydes via silylmethyl ketones ▽

473.



Alkylidenecarbenes, derived from a variety of α-silylketones on treatment with lithiated trimethylsilyldiazomethane, demonstrated preferential intramolecular Cα-Si over Cγ-Si bond insertion, affording 1-silylcyclopropenes rather than the anticipated 1-(silylmethyl)cyclopentene derivs. Unsaturation (alkene, alkyne and aryl) is tolerated at the γ position, as well as oxa and alkyl substitution. Only in the case of 3-oxa-aldehydes, in which the Cγ-H bond is strongly activated, are the anticipated dihydrofurans observed at all, and even then only as minor products. **E:** *n*-Butyllithium (2.5 *M* in hexanes; 1.3 eq.) added dropwise to a soln. of trimethylsilyldiazomethane (2 *M* in ether; 1.2 eq.) in THF (2 ml) at -78° under N_2, the mixture stirred at that temp. for 30 min, a soln. of the crude startg. α-trimethylsilylketone (1 mmol) [prepared by treatment of the aldehyde

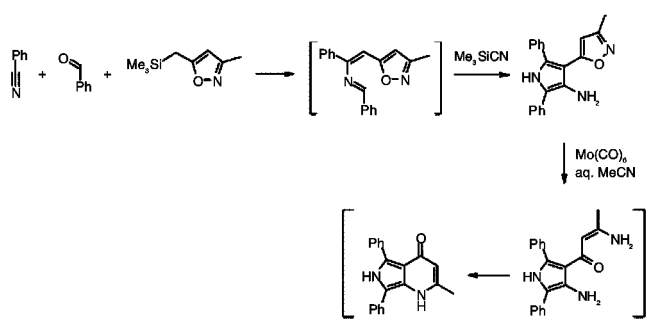
precursor with trimethylsilyldiazomethane and $InCl_3$ in methylene chloride at room temp., followed by removal of volatiles under reduced pressure following completion of reaction] in THF (1 ml) added dropwise, the resulting mixture warmed to room temp., quenched with satd. aq. NH_4Cl, dried over $MgSO_4$, filtered through a short plug of silica gel, concentrated, and the residue purified by chromatography on silica gel → product. Y 75%. Twelve examples afforded yields of 51-82%; five examples using 3-oxa-aldehydes as substrates afforded cyclopropene/dihydrofuran mixtures (1.2:1 to 3.2:1; Y 69-84%), the ratio of which being determined by intricate electronic and steric factors and defying prediction by the simple additive effect of contributing factors.



F.e.s. J. Li, C. Sun, D. Lee, J. Am. Chem. Soc. *2010*, *132* (19), 6640-1 [DOI: 10.1021/ja101998w].

n-Butyllithium/ytterbium(III) triflate/trimethylsilyl cyanide *BuLi/Yb(OTf)$_3$/Me$_3$SiCN*

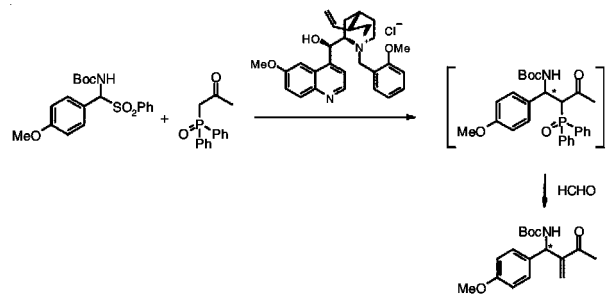
4-Component synthesis of 3-aminopyrroles from nitriles, aldehydes and silanes via ring closure of enazomethines with trimethylsilyl cyanide



474.

in one pot. A soln. of butyllithium (1.1 eq.) in hexane (1.5 ml) added to a soln. of 3-methyl-5-trimethylsilylmethylisoxazole (2 mmol) in THF (5 ml) at -70°, the mixture stirred for 1 h, benzonitrile (1 eq.) added by syringe, the soln. stirred at -70° for 1 h, then at room temp. for 1 h, re-cooled to -70°, benzaldehyde (1 eq.) added, the mixture stirred for 1 h, then at room temp. for 1 h, trimethylsilyl cyanide (1.2 eq.) and $Yb(OTf)_3$ (5 mol%) added, the mixture stirred for 24 h, quenched with satd. aq. $NaHCO_3$, extracted with chloroform, concentrated *in vacuo*, and purified chromatographically → 3-amino-2,5-diphenyl-4-(3-methylisoxazol-5-yl)pyrrole. Y 53%. This novel and experimentally simple procedure involves initial 3-component synthesis of 2-azadienes (eleven examples; Y 30-69%) which were subsequently cyclized by treatment with the nitrile source in the presence of $Yb(OTf)_3$ (other common Lewis acids were significantly less effective) to afford trisubst. 3-aminopyrroles (ten examples; Y 51-87%; an α-pyrid-3-yl deriv. gave 30%). In two cases the 3-aminopyrroles were obtained efficiently in a one-pot process (Y 41-53%). In a further development, reductive cleavage of the isoxazole was accompanied by unexpected and efficient recyclization to **1,6-dihydropyrrolo[3,4-*b*]pyrid-4-ones** (three examples; Y 88-99%). F.e., optimization and substrate prepn. s. T. Sasada, T. Sawada, R. Ikeda, N. Sakai, T. Konakahara, Eur. J. Org. Chem. *2010* (22), 4237-44 [DOI: 10.1002/ejoc.201000241].

Potassium phosphate/N-(o-methoxybenzyl)quininium chloride ←
N-Protected β-amino-α-methyleneketones ←
from α-aminosulfones and β-ketophosphine oxides
via organocatalyzed asym. Mannich-type reaction-Wittig methylenation



475.

in one pot. Aq. K_3PO_4 (50% w/w; 5 eq.) added in one portion to a mixture of startg. amidosulfone (0.2 mmol), diphenylphosphinylacetone (1.1 eq.) and chiral catalyst (10 mol%) in toluene/methylene chloride (7:3; 1 ml) at -20°, the biphasic mixture stirred vigorously for 60 h, aq. formaldehyde (37% w/w; 5 eq.) and additional aq. K_3PO_4 (20 eq.) added, the mixture stirred at 45° for 4 h, extracted with toluene, and purified chromatographically → (-)-*tert*-butyl 1-(4-methoxyphenyl)-2-methylene-3-oxobutylcarbamate. Y 69% (e.e. 98%). This novel and efficient synthesis of chiral aza-Morita-Baylis-Hillmann adducts required development of the Mannich donor component, with the phosphine oxide proving a better directing group than diethyl phosphonate, and ester or nitrile groups in place of the ketone moiety giving only moderate enantioselectivity (ten examples; Y 42-89%; e.e. 80-98%). The illustrated catalyst was the best of five N-(*o*-subst. benzyl)quininium salts tested, with the *o*-substituents thought to impart beneficial rigidity to the catalyst structure. F.e. and optimization s. S. Mazzotta, L. Gramigna, L. Bernardi, A. Ricci, Org. Process Res. Dev. *2010, 14* (3), 687-9 [DOI: 10.1021/op1000308].

Fluoride ion F^-
***o*-Annelation with arynes** ○

update s. *68*, 464s*70*; acridines from *o*-aminoketones s. D.C. Rogness, R.C. Larock, J. Org. Chem. *2010, 75* (7), 2289-95 [DOI: 10.1021/jo1000687]; 4-chromanones from α,β-acetylenecarboxylic acids, and xanthones from *o*-halogenocarboxylic acids, s. A.V. Dubrovskiy, R.C. Larock, Org. Lett. *2010, 12* (14), 3117-9 [DOI: 10.1021/ol101017z]; indole-2-carboxylic from α-azido-α,β-ethylenecarboxylic acid esters with Ph_3P/CsF under air s. D. Hong, Z. Chen, X. Lin, Y. Wang, ibid. *12* (20), 4608-11 [DOI: 10.1021/ol101934v]; 6-acyl-6*H*-benzo[*c*]chromenes from α-(*o*-iodoaryloxy)ketones under Pd-catalysis with $Pd(OAc)_2/Ph_3P$/CsF s. R.-J. Li, S.-F. Pi, Y. Liang, Z.-Q. Wang, R.-J. Song, G.-X. Chen, J.-H. Li, Chem. Commun. *2010, 46* (43), 8183-5 [DOI: 10.1039/c0cc02720k]; 2-alkylidene-1-indanones from 2-ethylenecarbonic acid esters by catalytic **carbonylative *o*-annelation** with $PdCl_2/(o\text{-Tol})_3P$/CsF s. S.-F. Pi, X.-H. Yang, X.-C. Huang, Y. Liang, G.-N. Yang, X.-H. Zhang, J.-H. Li, J. Org. Chem. *2010, 75* (10), 3484-7 [DOI: 10.1021/jo1003828]; isoquinolines from 3,4-pyridynes via nickel(0) phosphine-catalyzed [2+2+2]-cycloaddition s. T. Iwayama, Y. Sato, Heterocycles *2010, 80* (2), 917-24 [DOI: 10.3987/com-09-s(s)126]; improved synthesis of the benzyne precursor, 2-(trimethylsilyl)phenyl triflate, s. D.J. Atkinson, J. Sperry, M.A. Brimble, Synthesis *2010* (6), 911-3 [DOI: 10.1055/s-0029-1218631]; novel generation of benzynes from 2-pyrones and silylacetyleneboronic acid esters via conversion of *o*-silylboronates (cf. *22*, 877s*71*) to *o*-silyltriflates s. J.D. Kirkham, P.M. Delaney, G.J. Ellames, E.C. Row, J.P.A. Harrity, Chem. Commun. *2010, 46* (28), 5154-6 [DOI: 10.1039/c0cc01345e]; indazoles s. *78*, 519.

Potassium fluoride s.a. under CuI and [(allyl)PdCl]$_2$ *KF*

Potassium fluoride/benzoyl peroxide *KF/(PhCOO)$_2$*
Transition metal-free oxidative trifluoromethylation of tert. amines H → CF$_3$
with trifluoromethyl(trimethyl)silane – 1-Trifluoromethyl-1,2,3,4-tetrahydroisoquinolines s. *78*, 476

Cesium fluoride s. under [Rh(cod)(OH)]$_2$ and Pd(OAc)$_2$ *CsF*
Potassium hydrogen fluoride s. under [RhCl(H$_2$C=CH$_2$)$_2$]$_2$ *KHF$_2$*
Lithium chloride s. under Ti(OPr-i)$_4$ *LiCl*
Chiral 2-aminoalcohols s. under Et$_2$Zn ←

1,8-Diazabicyclo[5.4.0]undec-7-ene *DBU*
Horner synthesis CO → C=C
s. *39*, 854s*48*; enhanced (E)-selectivity in the synthesis of enoates under *solvent-free* conditions s. K. Ando, K. Yamada, Tetrahedron Lett. *2010, 51* (25), 3297-9 [DOI: 10.1016/j.tetlet.2010.04.072]; (Z)-β-arylcinnamic acid esters from bis(2,2,2-trifluoroethoxy)phosphinylacetic acid esters with Sn(OTf)$_2$/N-ethylpiperidine under microwaves s. D. Rossi, A.C. Baraglia, M. Serra, O. Azzolina, S. Collina, Molecules *2010, 15* (9), 5928-42 [DOI: 10.3390/molecules15095928]; carbohydrate α,β-ethylenesulfonic acid esters from 3-ulosides s. L. Franchini, F. Compostella, D. Colombo, L. Panza, F. Ronchetti, J. Org. Chem. *2010, 75* (15), 5363-6 [DOI: 10.1021/jo1008788]; synthesis of chiral N-protected *syn-* or *anti*-δ-alkoxy-γ-hydrazino-α,β-(E)-ethylene-carboxylic acid esters s. V. Jha, N.B. Kondekar, P. Kumar, Org. Lett. *2010, 12* (12), 2762-5 [DOI: 10.1021/ol100856u].

1,10-Phenanthroline s. under CuI *1,10-phen*
(-)-Sparteine s. under Pd[(-)-sparteine]Cl$_2$ ←

Chiral 1,2-bis(nitrones)/N,N′-dimethyl-N,N′-propyleneurea ←
Asym. synthesis of 3-ethylenealcohols from aldehydes CHO → CH(OH)C-C=C
and 2-ethylene(trichloro)silanes with chiral N-oxides s. *55*, 433s*69*; with chiral 1,2-bis(nitrones) as Lewis base with N,N′-dimethyl-N,N′-propyleneurea s. Y.S. Oh, S. Kotani, M. Sugiura, M. Nakajima, Tetrahedron: Asym. *2010, 21* (15), 1833-5 [DOI: 10.1016/j.tetasy.2010.05.048]; from electron-poor aldehydes with chiral aryl methyl sulfoxides as activator (cf. *55*, 433s*75*) s. V. De Sio, A. Massa, A. Scettri, Org. Biomol. Chem. *2010, 8* (13), 3055-9 [DOI: 10.1039/c002988b]; with chiral imino- and amino-sulfoxides s. V. De Sio, M.R. Acocella, R. Villano, A. Scettri, Tetrahedron: Asym. *2010, 21* (11-12), 1432-5 [DOI: 10.1016/j.tetasy.2010.04.015]; with BINAPO for the synthesis of chiral 2-functionalized *anti*-3-ethylenealcohols s. A.V. Malkov, C. MacDonald, P. Kocovský, ibid. *21* (9-10), 1173-5 [DOI: 10.1016/j.tetasy.2010.03.026]; asym. allylstannylation with triallylstannyl bromide using a mixture of L-proline and -prolinol s. G.-h. Chen, L.-y. Liu, X.-n. Wei, W.-x. Chang, J. Li, Chem. Lett. *2010, 39* (9), 1013-8 [DOI: 10.1246/cl.2010.1013].

Silver oxide *Ag$_2$O*
3-Ethylenealcohols from oxo compds. and 2-ethylenestannanes CO → C(OH)C-C=C
from ketones with In(OTf)$_3$ cf. *36*, 879s*70*; from aldehydes with recoverable Ag$_2$O in aq. medium s. M. Ueno, A. Tanoue, S. Kobayashi, Chem. Lett. *2010, 39* (6), 652-3 [DOI: 10.1246/cl.2010.652]; with (alaninato)bis(triethylenediamine)dicadmium tris(perchlorate) monohydrate in aq. media, regio- and diastereo-selectivity, s. D. Deng, P. Liu, B. Ji, L. Wang, W. Fu, Tetrahedron Lett. *2010, 51* (42), 5567-70 [DOI: 10.1016/j.tetlet.2010.08.047]; N-protected *syn*-3-allyl-3-hydroxyoxindoles from isatins and chiral 2-ethylenestannanes with asym. induction using BF$_3$ as Lewis acid s. D.J. Vyas, R. Fröhlich, M. Oestreich, J. Org. Chem. *2010, 75* (19), 6720-3 [DOI: 10.1021/jo101420e].

Copper(II) hexafluoroacetoacetonate s. under Pd(OAc)$_2$ *Cu(CH(COCF$_3$)$_2$)$_2$*
Silver carbonate s. under Pd(OAc)$_2$ *Ag$_2$CO$_3$*

Copper(I) acetate/hydrogen chloride *CuOAc/HCl*
β-Aryl-α,β-ethylenelactones from siloxy-α,β-acetylenecarboxylic acid esters ○
and arylboronic acids s. *77*, 508s*78*

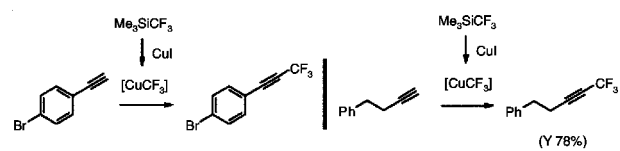
Copper(II) isobutyrate/chiral 3,3′-di-tert-butyl-4,4′-dimethoxy-2,2′-bi-[1,3-benzoxaphospholine]/lithium tert-butoxide ←
Chiral 3,7,1-dioxazabicyclo[3.3.0]octane-tethered copper(I) bis(phosphine) complexes ←
Catalytic asym. allylboration of oxo compds. s. *33*, 865s*78* CO → C(OH)C-C=C

Copper(II) triflate/chiral N-(o-sec-amino)sulfoximines ←
Asym. vinylogous aldol-type condensation s. *66*, *452s78* ←

Copper(I) chloride/chiral 3-aryl-1-(2-hydroxyalkyl)-Δ²-imidazolinium salts/potassium tert-butoxide ←
Asym. synthesis of 3-aryl-3-hydroxyoxindoles from isatins CO → C(OH)Ar
and arylboronic acid esters s. *65*, 437s*78*

Copper(I) iodide/1,10-phenanthroline/potassium fluoride *CuI/1,10-phen/KF*
Copper-mediated trifluoromethylation of terminal acetylene derivs. with trifluoromethyl(trimethyl)silane C≡CH → C≡C-CF_3

476.

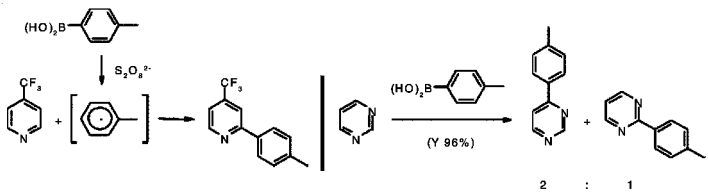


CuI (100 mol%), 1,10-phenanthroline (100 mol%) and KF (5 eq.) introduced into a reaction tube under an inert atmosphere, the tube evacuated and refilled with air (3 times), DMF (1 ml) added, the mixture stirred at room temp. for 15 min, trifluoromethyl(trimethyl)silane (5 eq.) added by syringe, the resulting mixture heated to 100° before addition of a soln. of 4-bromophenylethyne (0.2 mmol) in DMF (1 ml) by syringe-pump over 4 h (under 1 atm. air), stirring continued at 100° for a further 2 h, allowed to cool to room temp., quenched with ice-cold water, extracted with ether, and purified by chromatography on silica gel → 1-(4-bromophenyl)-2-(trifluoromethyl)-ethyne. Y 71%. This relatively straightforward procedure, avoiding Pd-catalysts and the need to pre-prepare alkynyl-metal reagents, was suitable for the trifluoromethylation of a range of electron-diverse (het)ar. (incl. naphthyl) and alkyl acetylenes in moderate to high yield (47-91%; eighteen examples), tolerating a range of functionality, incl. dimethylamino, methoxy, nitro, ester, chloro, fluoro and bromo groups. Careful optimization, including the use of 1,10-phenanthroline as copper chelating ligand, helped to increase yields by suppressing diyne formation via competing homocoupling. The process is thought to involve formation of intermediate Cu(II) or Cu(III) species but the mechanism was not elucidated. Surprisingly, replacement of the aerial atmosphere by O_2 resulted in complete inhibition of the reaction, possibly due to rapid oxidative quenching of the reactive $CuCF_3$ species. F.e. and 10 mmol scale-up s. L. Chu, F.-L. Qing, J. Am. Chem. Soc. *2010*, *132* (21), 7262-3 [DOI: 10.1021/ja102175w]; **(trifluoromethyl)arenes** from ar. chlorides and trifluoromethyl(triethyl)silane under Pd catalysis [[(allyl)PdCl]$_2$/BrettPhos/KF] s. E.J. Cho, T.D. Senecal, T. Kinzel, Y. Zhang, D.A. Watson, S.L. Buchwald, Science *2010*, *328* (5986), 1679-81 [DOI: 10.1126/science.1190524]; **transition metal-free oxidative trifluoromethylation** of tert. amines with trifluoromethyl(trimethyl)silane using KF/benzoyl peroxide, especially for **1-trifluoromethyl-1,2,3,4-tetrahydroisoquinolines**, s. L. Chu, F.-L. Qing, Chem. Commun. *2010*, *46* (34), 6285-7 [DOI: 10.1039/c0cc01073a].

Copper(II) chloride s. under $PdCl_2(PhCN)_2$ *$CuCl_2$*

Silver nitrate/potassium persulfate/trifluoroacetic acid $AgNO_3/K_2S_2O_8/CF_3COOH$
Silver-catalyzed direct arylation of electron-deficient heteroarenes with arylboronic acids H → Ar

477.

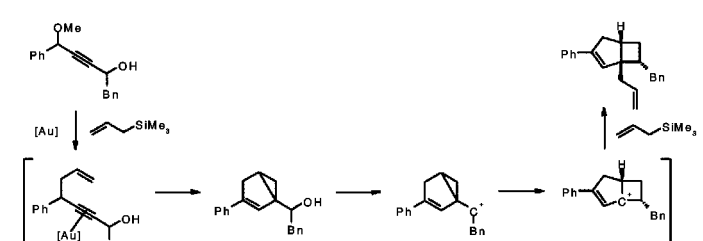


under mild conditions. Trifluoroacetic acid (1 eq.), 4-methylbenzeneboronic acid (1.5 eq.), water (0.75 ml), aq. $AgNO_3$ (0.1 *M*; 20 mol%) and $K_2S_2O_8$ (3 eq.) added sequentially to a soln. of 4-trifluoromethylpyridine (0.25 mmol) in methylene chloride (1.25 ml), the soln. stirred vigorously at room temp. for 6 h (TLC) with additional solid $AgNO_3$ (20 mol%) and $K_2S_2O_8$ (3 eq.) added after 3 h, diluted with methylene chloride, washed with 5% aq. $NaHCO_3$ (or 2 *M* aq. NaOH), concentrated *in vacuo*, and purified by chromatography on silica → 2-(4-tolyl)-4-trifluoromethylpyridine. Y 81%. This experimentally simple and scalable arylation uses inexpensive reagents and has broad functional group tolerance for electron-diverse arylboronic acids, generally affording mixtures of regioisomers in variable yields consistent with a radical process. Pyridines, pyrimidines, pyrazines and their benzo-analogs were generally good substrates (twenty examples; Y 43-96%) with lower yields obtained for pyrazine (30%), isoquinoline (33%), imidazole (28%) and with 2-methyl-, 2-methoxy- and 4-trifluoromethyl-benzeneboronic acids (21-37%), while indole, 2-chloropyrazine and 1,3,5-triazine were unreactive (Y 0-5%). Quinine was also mono-arylated under these conditions (Y 40%) without need for protection, while a 2-hetaryl-1,3-dioxolane was partially cleaved to the corresponding 2-hydroxyethyl ester. F.e.s. I.B. Seiple, S. Su, R.A. Rodriguez, R. Gianatassio, Y. Fujiwara, A.L. Sobel, P.S. Baran, J. Am. Chem. Soc. *2010*, *132* (38), 13194-6 [DOI: 10.1021/ja1066459].

(Triphenylphosphine)gold(I) triflimide/m-chloroperoxybenzoic acid $(Ph_3P)AuNTf_2/ArCO_2OH$
Stereoselective gold-catalyzed aldol-type condensation with cyclic boron enolates ←
s. *78*, 307

(Triphenylphosphine)gold(I) chloride/silver triflimide $(Ph_3P)AuCl/AgNTf_2$
Stereospecific gold(I)-catalyzed synthesis of 1-allylbicyclo[3.2.0]hept-2-enes from 2-acetylene-1,4-diol monoethers via regiospecific double nucleophilic allylation with allyl(trimethyl)silane ○

478.



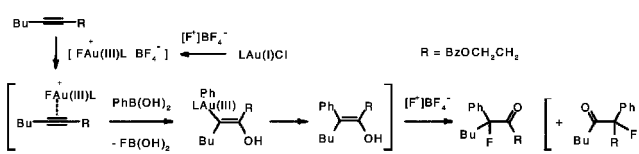
A soln. of $(Ph_3P)AuCl$ (5 mol%) and $AgNTf_2$ (5 mol%) in methylene chloride (2 ml) stirred at 25° for 10 min, a soln. of 1,5-diphenyl-1-methoxypent-2-yn-4-ol (0.35 mmol) and allyl(trimethyl)silane

(4 eq.) in the same solvent (1.5 ml) added, the mixture stirred for 6 h, filtered through Celite, and purified by chromatography on silica → 1-allyl-7-benzyl-3-phenylbicyclo[3.2.0]hept-2-ene. Y 91% (d.r. >30:1). This novel [3+2]/[2+2]-cycloannulation, promoted by a *single catalyst*, was effective for (het)ar. substituents at the propargylic ether- and H or alkyl (incl. benzyl) at the propargylic alcohol-centers. Products were formed with high diastereoselectivity via regioselective allylation, cycloisomerization of the 1,5-enyne intermediate and ring expansion of the generated bicyclo[3.1.0]hexene with a second molecule of allylsilane (fifteen examples; Y 53-94%; d.r. 12:1 to >30:1). A substrate containing 4-methoxyphenyl at the propargylic alcohol afforded a mixture of 1-allyl- (Y 53%; d.r. >30:1) and 1-methoxy-derivs. (Y 36%; d.r. >30:1) of the isomeric bicycloheptene. Variations in the two oxy substituents gave products in reduced yields. The proposed mechanism is based on labelling experiments and isolation of a bicyclo[3.1.0]hexene intermediate. F.e. and optimization s. C.-Y. Yang, C.-D. Wang, S.-F. Tian, R.-S. Liu, Adv. Synth. Catal. *2010*, *352* (10), 1605-9 [DOI: 10.1002/adsc.201000201].

(Triphenylphosphine)gold(I) chloride/N′-chloromethyl-N-fluoro-1,4-diazoniabicyclo-[2.2.2]octane bis(fluoroborate) ←

Regioselective synthesis of α-functionalized α-arylketones from acetylene derivs. and arylboronic acids via activation of the triple bond with cationic fluorogold(III) species C≡C → C(Ar)(F)CO

479.



While cationic gold(I) species happily hydrate acetylene derivs. to give the corresponding ketones, *in situ*-generated cationic fluorogold(III) species are more effective at activating the triple bond while at the same time offering the possibility of producing α-functionalized ketones in one pot. This is illustrated in a new **synthesis of α-fluoroketones** via transmetalation of the initially formed vinyl(fluoro)gold(III) intermediate with boronic acids. **E:** Selectfluor (2.5 eq.) added to a soln. of the startg. alkyne (0.4 mmol), $(Ph_3P)AuCl$ (5 mol%) and phenylboronic acid (2 eq.) in acetonitrile/water (20:1; 3 ml), stirred at room temp. for 18 h, the mixture quenched with satd. NH_4Cl soln., and worked up with purification by flash chromatography on silica gel → product. Y 88% (as a 6.7:1 mixture of regioisomers). The procedure was applied to a variety of functionalized or non-functionalized alkynes and arylboronic acids in good yield with regioselectivities in the range 2.1:1 to 6.7:1 (twelve examples; Y 47-90%). The key step in the conversion is generation of the active fluorogold(III) species by initial oxidation of gold(I) with Selectfluor; this activates the triple bond towards hydration followed by F→aryl exchange on gold through transmetalation with the boronic acid prior to reductive elimination (with regeneration of gold(I)) and subsequent α-fluorination of the formed enol. The driving force for the transmetalation is the formation of the strong F-B bond in the displaced $FB(OH)_2$. Other gold salts and transition metal reagents were less effective or inactive. F.e. and study of the Au(I)→Au(III) conversion by X-ray photoelectron spectroscopy s. W. Wang, J. Jasinski, G.B. Hammond, B. Xu, Angew. Chem., Int. Ed. *2010*, *49* (40), 7247-52 [DOI: 10.1002/anie.201003593].

[Bis(diphenylphosphino)methane]bis[gold(I) bromide]/N′-chloromethyl-N-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(fluoroborate) ←

2-Arylalcohol O-derivs. C=C → C(OR)C(Ar)

from terminal ethylene derivs., arylboronic acids and O-nucleophiles – Regioselective 3-component gold(I)-catalyzed 1,2-oxyarylation s. *78*, 310

(Alaninato)bis(triethylenediamine)dicadmium tris(perchlorate) *[Cd(II)]*

3-Ethylenealcohols from aldehydes CO → C(OH)C-C=C

and 2-ethylenestannanes s. *36*, 879s*78*

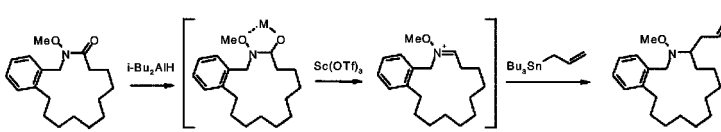
p-Nitrophenoxymagnesium iodide *p-$NO_2C_6H_4OMgI$*
Lewis base-catalyzed aldol-type condensation s. *44,* 875*s78* CHO → CH(OH)C-CO

Diethylzinc/alcohols *Et_2Zn/ROH*
Allylboration of oxo compds. CO → C(OH)C-C=C
with ethanolamine cf. *33,* 865; regioselective allylboration of ketones with B-allylpinacolboronates using zinc alkoxide as catalyst (generated from Et_2Zn/ROH) s. K.R. Fandrick, D.R. Fandrick, J.J. Gao, J.T. Reeves, Z. Tan, W. Li, J.J. Song, B. Lu, N.K. Yee, C.H. Senanayake, Org. Lett. *2010, 12* (17), 3748-51 [DOI: 10.1021/ol101301s]; with indium(III) bis(trimethylsilyl)amide as catalyst, regio- and diastereo-selectivity with retention of free hydroxyl and amino groups, s. M. Yamaguchi, N. Morita, U. Schneider, S. Kobayashi, Adv. Synth. Catal. *2010, 352* (9), 1461-5 [DOI: 10.1002/adsc.201000097]; allylboration of aldehydes and ketones with B-allyl- and B-crotyl-1,3,2-dioxazaborolidines *under Brønsted acid activation* with trifluoroacetic acid, diastereoselectivity, s. M.K. Reilly, S.D. Rychnovsky, Org. Lett. *2010, 12* (21), 4892-5 [DOI: 10.1021/ol1020515].

Diethylzinc/chiral 2-aminoalcohols or N-prolyl-2-amino-3-hydroxyselenides ←
Asym. 1,2-addition of arylboronic acids to oxo compds. CO → C(OH)Ar
asym. synthesis of diarylcarbinols with chiral 2-aminoalcohols as ligand s. *65,* 437*s70*; with chiral chalcogen-functionalized peptides and N-prolyl derivs., e.g. chiral N-prolyl-2-amino-3-hydroxyselenides, s. R.S. Schwab, L.C. Soares, L. Dornelles, O.E.D. Rodrigues, M.W. Paixão, M. Godoi, A.L. Braga, Eur. J. Org. Chem. *2010* (19), 3574-8 [DOI: 10.1002/ejoc.201000237]; with carbohydrate-based 2-aminoalcohols s. A.D. Wouters, G.H.G. Trossini, H.A. Stefani, D.S. Lüdtke, ibid. *2010* (12), 2351-6 [DOI: 10.1002/ejoc.201000113]; under rhodium catalysis with $[RhCl(CH_2{=}CH_2)_2]_2$ and (R)-2′-(diphenylphosphino)-1,1′-binaphthyl-2-yl[bis(trifluoromethyl)]-carbinol as ligand with NaOBu-*t* as base s. S. Morikawa, K. Michigami, H. Amii, Org. Lett. *2010, 12* (11), 2520-3 [DOI: 10.1021/ol100697a]; chiral N-protected 3-aryl-3-hydroxyoxindoles from isatins (cf. *65,* 437*s71*) and arylboronic acid esters with CuCl/KOBu-*t* and a chiral 3-aryl-1-(2-hydroxyalkyl)-Δ^2-imidazolinium salt as ligand s. R. Shintani, K. Takatsu, T. Hayashi, Chem. Commun. *2010, 46* (36), 6822-4 [DOI: 10.1039/c0cc01635g].

Magnesium bromide s. under Dichloro[1,2-bis(diarylphosphino)benzene]iron(II) complex *$MgBr_2$*

Diisobutylaluminum hydride/scandium(III) triflate *i-$Bu_2AlH/Sc(OTf)_3$*
Synthesis of alkoxylamines from hydroxamic acid esters via Lewis acid-promoted nucleophilic addition C(O)N-OR → CH(R′)N-OR



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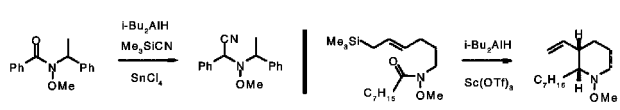
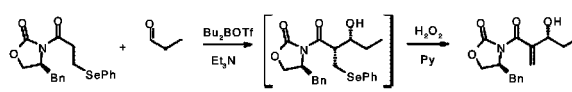


3-Ethylenealkoxylamines. A soln. of *i*-Bu_2AlH (1.35 eq.) in toluene (0.11 ml) added dropwise to a soln. of startg. N-methoxyamide (0.0813 mmol) in methylene chloride (1 ml) at -78°, the soln. stirred for 30 min, allyltributyltin (3 eq.) and $Sc(OTf)_3$ (1.3 eq.) added, the soln. stirred for 30 min, warmed to room temp., stirred for 1.5 h, quenched with satd. aq. K,Na-tartrate, stirred for 1 h, extracted with ethyl acetate, washed with brine, concentrated, and purified by chromatography on silica → 3-allyl-2-methoxy-2,3,4,5,6,7,8,9,10,11,12,13-dodecahydro-1*H*-benzo[*c*][1]azacyclo-

pentadecine. Y 90%. This procedure does not require preactivation of the Weinreb amide and generates an N-methoxyiminium ion *in situ* which undergoes addition with organometallic reagents, allyltributylstannane and trimethylsilyl cyanide, promoted optimally by $Sc(OTf)_3$ and $SnCl_4$, respectively. Both linear and branched N-alkylhydroxamates (incl. the illustrated macrocyclic analogs) were suitable substrates (Y 65-92%), with the branched chain hydroxamates affording moderate diastereoselectivity (ca. 4:1) in the presence of $SnCl_4$. A single intramolecular example afforded a 2-subst. 1-alkoxy-3-vinylpiperidine, with the unusual *cis* isomer predominating (Y 88%; d.r. 5:1). F.e., optimization and substrate prepn. s. K. Shirokane, Y. Kurosaki, T. Sato, N. Chida, Angew. Chem., Int. Ed. *2010*, *49* (36), 6369-72 [DOI: 10.1002/anie.201001127].

Indium(III) bis(trimethylsilyl)amide — *$In[N(SiMe_3)_2]_3$*
Catalytic allylboration of ketones s. *33*, 865s*78* — $CO \rightarrow C(OH)C\text{-}C{=}C$

Di-n-butylborinyl triflate/triethylamine/hydrogen peroxide/pyridine ←
β-Hydroxy-α-methylenecarboxylic acid 2-oxazolidonides from aldehydes ←
Synthesis with addition of three C-atoms via eliminative aldol condensation with asym. induction



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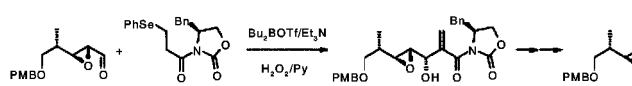


(Y 79%)

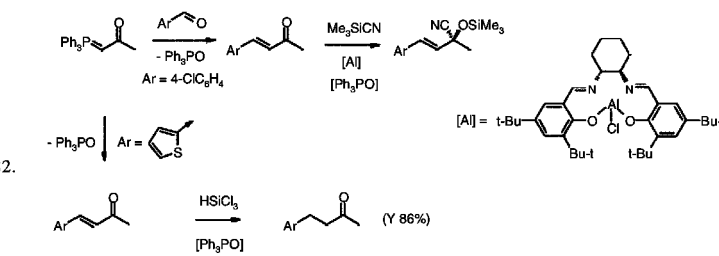
An alternative to the Baylis-Hillman reaction is reported which proceeds with high diastereoselectivity but does not require a large excess of the aldehyde component. **E:** A stirred soln. of 4(S)-benzyl-3-[β-(phenylselenyl)propionyl]-2-oxazolidone (1 mmol) in methylene chloride (5 ml) at -78° treated with a soln. of Bu_2BOTf in methylene chloride (1 *M*; 1.2-1.5 eq.), stirring continued for 10 min, triethylamine (1.8-2.15 eq.) added dropwise, the mixture stirred at -78° for 75 min then at 0° for 15 min before being re-cooled to -78°, propionaldehyde (1.1-1.25 eq.; freshly distilled) added dropwise, the mixture stirred for 6 h, allowed to warm to -10° (or stirred overnight at room temp. without diminished yield in most instances), quenched with satd. NH_4Cl soln., diluted with methylene chloride, the organic phase separated, the aq. phase extracted with methylene chloride, the combined organic layers cooled to 0°, treated with pyridine (2 eq.) followed by aq. H_2O_2 (3.1 eq.; 50 wt%), stirred vigorously with monitoring by TLC [if oxidation did not go to completion an additional aliquot of aq. H_2O_2 (1.5 eq.; 50 wt%) added], when reaction complete the mixture poured into the remaining aq. phase, the organic phase separated, the aq. phase extracted three times with methylene chloride, the combined organic layers dried (Na_2SO_4), filtered, concentrated under reduced pressure, and the residue purified chromatographically → product. Y 93% (single diastereomer). The method is applicable to a variety of aliphatic (bearing olefin or silyl ether groups) or (het)aromatic aldehydes (eight examples; Y generally 76-88%, 56% from sterically demanding pivaldehyde and isolated as the TBS ether), all giving single diastereomers; acrolein gave a multitude of side-products however. Under such mild oxidative conditions there was no pyridine N-oxide formation with 3-pyridinecarboxaldehyde as substrate. F.e. and application to the synthesis of the C(15)-C(21) fragment of tedanolide C, an epoxypolyhydroxyketo-macrolactone marine natural product having anti-cancer activity (Y 79% for the aldol reaction-elimination sequence), s. R. Barth, W.R. Roush, Org. Lett. *2010*, *12* (10), 2342-5 [DOI: 10.1021/ol1006955].

Boric acid s. under $[Rh(cod)OH]_2$ — *H_3BO_3*

Boron fluoride [s.a. under Polymer-based palladium(II) N-heterocyclic carbene complex] BF_3
Asym. allylboration CO → C(OH)C-C=C
with B-allyldiisocampheylboranes cf. *33,* 865s*50*; chiral 3(E)-ethylenealcohols from aldehydes and cyclic B-allylisocampheyl-2,3-boronates with BF_3 s. M. Chen, W.R. Roush, Org. Lett. *2010, 12* (12), 2706-9 [DOI: 10.1021/ol1007444]; chiral 3-ethylenealcohols from B-allylpinacol boronates under asym. organo-Brønsted acid catalysis with (R)-3,3′-bis(2,4,6-triisopropylphenyl)-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate s. P. Jain, J.C. Antilla, J. Am. Chem. Soc. *2010, 132* (34), 11884-6 [DOI: 10.1021/ja104956s]; asym. allylboration of ketones under copper(I) catalysis with a chiral 3,7,1-dioxazabicyclo[3.3.0]octane-tethered copper(I) bis(phosphine) complex, **also asym. propargylboration** (cf. *75*, 265), s. S.-L. Shi, L.-W. Xu, K. Oisaki, M. Kanai, M. Shibasaki, ibid. *132* (19), 6638-9 [DOI: 10.1021/ja101948s]; asym. propargylboration of aldehydes with Cu(II)-isobutyrate/LiOBu-*t* and chiral 3,3′-di-*tert*-butyl-4,4′-dimethoxy-2,2′-bi[1,3-benzoxaphospholine] as ligand s. D.R. Fandrick, K.R. Fandrick, J.T. Reeves, Z. Tan, W. Tang, A.G. Capacci, S. Rodriguez, J.J. Song, H. Lee, N.K. Yee, C.H. Senanayake, ibid. *2010, 132* (22), 7600-1 [DOI: 10.1021/ja103312x].

Fluoroboric acid s. under $PdCl_2(NH_3)_2$ HBF_4

Chiral chloroaluminum(III) salicylidene complex *[Al(salen)Cl]**
Lewis base-cocatalyzed reactions with triphenylphosphine oxide generated *in situ* by Wittig synthesis ←

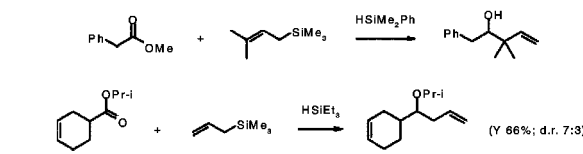


482.

Wittig synthesis-asym. cyanosilylation in one pot. A mixture of startg. phosphorane (0.5 mmol), 4-chlorobenzaldehyde (1 eq.) and anhydrous methylene chloride (1 ml) heated in a sealed tube at 80° under N_2 for 20 h, cooled to room temp., chiral catalyst (10 mol%) added, the mixture stirred for 0.5 h, cooled to -30°, trimethylsilyl cyanide (2 eq.) added, stirred vigorously for 48 h, and purified chromatographically → (S)-4-(4-chlorophenyl)-2-methyl-2-trimethylsiloxybut-3-enenitrile. Y 93% (e.e. 93%). This atom economical method uses the by-product, Ph_3PO, produced from initial Wittig reaction of electron-diverse ar. aldehydes, to catalyze subsequent cyanosilylation (nine examples; Y 84-97%; e.e. 86-93%) with lower enantioselectivity obtained for sterically-hindered 2-chlorobenzaldehyde (Y 71%; e.e. 68%), 2-thienylcarboxaldehyde (Y 97%; e.e. 65%) and isobutanal (Y 66%; e.e. 75%). In control experiments, no cyanosilylation occurred in the absence of Ph_3PO. The strategy was also applied to a **Wittig synthesis-reduction** sequence, with the generated Ph_3PO efficiently catalyzing reduction of the initial enone (seventeen examples; Y 70-98%) in the presence of ketone, nitro, halogen and terminal alkene functionality, but a pyruvate-derived phosphorane gave a complex mixture. F.e. and optimization s. J.-J. Cao, F. Zhou, J. Zhou, Angew. Chem., Int. Ed. *2010, 49* (29), 4976-80 [DOI: 10.1002/anie.201000896].

Indium(III) iodide/organosilicon hydrides *InI_3/≡SiH*
3-Ethylenealcohols COOR → CH(OH)C-C=C
from carboxylic acid esters and 2-ethylenesilanes
Indium(III)-catalyzed regiospecific reductive allylation

483.



under mild conditions. A soln. of dimethyl(phenyl)silane (2 eq.) in methylene chloride (2 ml) added *via syringe pump* to a mixture of InI_3 (5 mol%), methyl phenylacetate (1 mmol) and 3,3-dimethylprop-2-en-1-yl(trimethyl)silane (2 eq.) in the same solvent (1 ml) at room temp., the mixture stirred for 10 min, quenched with Bu_4NF, added to 1 *M* aq. HCl, extracted with ether, concentrated *in vacuo*, and purified chromatographically → 3,3-dimethyl-5-phenylpent-1-en-4-ol. Y 72% (plus 9% 2-phenylethyl alcohol). Slow addition of hydrosilanes to esters was essential to minimize ester reduction in this regioselective hydroallylation. Chemoselective elimination of the alkoxy moiety in the presence of nitrile, alkene, alkyne, nitro, halo and ether functionality was favored by use of methyl esters and relatively bulky hydrosilanes (seventeen examples; Y 20-90%), with low yields obtained for ar. or bulky carboxylic acid esters. The use of bulkier esters and smaller silanes (e.g. $HSiEt_3$) favored elimination of the oxygen moiety to afford **alkoxy-3-ethylenes** (five examples; Y 41-66%). Lactones also reacted under these latter conditions without cleavage of the ring to afford **2-allyl-O-heterocyclics** (two examples; Y 49-78%). Note NMR yields of the crude products were up to 30% higher than the isolated yields, and diastereoselectivity was modest (<7:3). F.e. and optimization s. Y. Nishimoto, Y. Inamoto, T. Saito, M. Yasuda, A. Baba, Eur. J. Org. Chem. *2010* (18), 3382-6 [DOI: 10.1002/ejoc.201000475].

Chiral tris(aqua)lanthanide(III) α-aminocarboxylic acid ester complexes *[Ln(III)]**
Asym. aldol-type condensation in aq. medium s. *44*, 871s*78* CHO → CH(OH)C-CO

Scandium(III) triflate s. under i-Bu_2AlH *$Sc(OTf)_3$*
Ytterbium(III) triflate s. under BuLi *$Yb(OTf)_3$*
Alcohols s. under $NiBr_2$·diglyme and Pd[(-)-sparteine]Cl_2 *ROH*
p-Benzoquinone s. under $Pd(OAc)_2$ *BQ*
N,N′-Dimethyl-N,N′-propyleneurea s. under Chiral 1,2-bis(nitrones) *DMPU*
N-Carbethoxy-2-ethoxy-1,2-dihydroquinoline s. under $Pd(PPh_3)_4$ *EEDQ*
(1R,4R,7R)-7-Isopropyl-5-methylbicyclo[2.2.2]octa-2,5-diene-2-carboxylic acid [(1S,2S)-2-(2,5-dimethylpyrrol-1-yl)cyclohexyl]amide s. under [RhCl(H_2C=CH_2)$_2$]$_2$ ←
Chiral 3-aryl-1-(2-hydroxyalkyl)-Δ²-imidazolinium salts/potassium tert-butoxide s. under CuCl ←
(R)-1,1′-Bi-2-naphthol s. under Ti(OPr-i)$_4$ *(R)-BINOL*
L-Proline/L-prolinol ←
Asym. synthesis of 3-ethylenealcohols from aldehydes s. *55*, 433s*78* CHO → CH(OH)C-C=C

Trifluoroacetic acid (s.a. under $AgNO_3$) *CF_3COOH*
Allylboration of oxo compds. with B-allyl-1,3,2-dioxazaborolidines CO → C(OH)C-C=C
under Brønsted acid activation s. *33*, 865s*78*

Chiral O-monoacyltartaric acids ←
Organocatalyzed asym. 1,4-addition C=C → CHC(R)
of aryl- and α,β-ethylene-boronic acids s. *55*, 452s*78*

Nanoferrite-anchored glutathione/microwaves ←
Sym. biaryls from arylboronic acids under organocatalysis s. *53*, 471s*78* Ar-Ar

Chiral N-prolyl-2-amino-3-hydroxyselenides s. under Et_2Zn ←

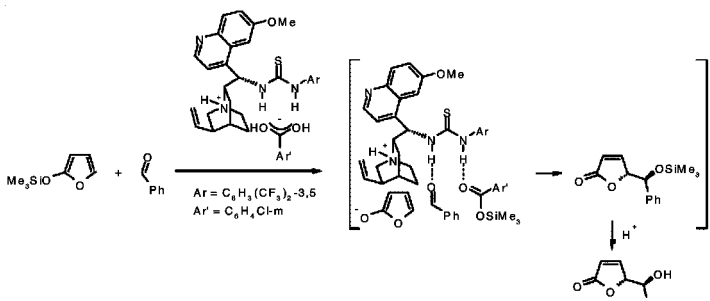
Chiral sulfoxides ←

Asym. synthesis of 3-ethylenealcohols from aldehydes s. *55*, 433s*78* CHO → CH(OH)C-C=C

Chiral cinchona-based 2-aminothiourea·m-chlorobenzoic acid ←

5-α-Hydroxy-2(5*H*)-furanones from 2-siloxyfurans and aldehydes via organocatalyzed asym. vinylogous aldol-type reaction ←

484.



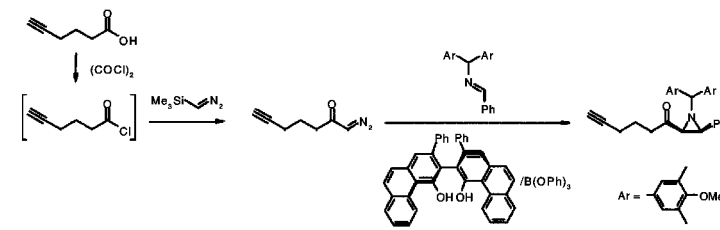
An efficient *anti*-selective asymmetric vinylogous aldol reaction is reported of unprecedented scope with respect to both starting 2-trimethylsilyloxyfurans and aldehydes. The chiral organocatalyst is a salt readily prepared from a cinchona alkaloid-based aminothiourea and a carboxylate salt, in which the carboxylate binds to the thiourea moiety *through hydrogen bonding interactions* instead of forming a tight ion pair with the quinuclidinium cation. **E:** Benzaldehyde (0.25 mmol) added to a soln. of chiral thiourea catalyst (10 mol%) in methylene chloride/ether (1:1; 0.25 ml), the mixture cooled to -20°, stirred for 15 min at that temp., 2-(trimethylsilyloxy)furan (1.5 eq.) added, the mixture kept at the same temp. with stirring for 96 h, diluted with THF (1 ml), treated with 1 *N* HCl (1 ml), allowed to warm to room temp., stirred for 15 min, neutralized with satd. $NaHCO_3$ soln., extracted with ethyl acetate, the combined organic phase washed with water, dried (Na_2SO_4), concentrated, the crude mixture passed through a short plug of silica gel (for removal of the catalyst), washing with ethyl acetate, the eluent concentrated *in vacuo*, and the residue subjected to flash chromatography on silica gel → 5-[hydroxy(phenyl)methyl]furan-2(5*H*)-one. Y 94% (*anti/syn* 95:5; e.e. 95%). The method is applicable to reaction of 2-(trimethylsilyloxy)furan with a range of ar. (seven examples; Y 75%, 93-98%; *anti/syn* 94:6 to 96:4; e.e. 90-95%), hetaryl (three examples; Y 71-98%; *anti/syn* 84:16 to 92:8; e.e. 91-93%), styryl (one example; Y 74%; *anti/syn* 81:19; e.e. 86%) or, notably, aliphatic (four examples; Y 47-76%; *anti/syn* 72:28 to 82:18; e.e. 80-93%) aldehydes; furthermore, 3-, 5- or 3,5-di-subst. 2-(trimethylsilyloxy)furans react with benzaldehyde or dihydrocinnamaldehyde in 81-94% e.e. (Y 62-75%; d.r. 80:20 to 96:4; five examples). It is believed the hydrogen-bonded carboxylate reacts with the siloxyfuran to afford trimethylsilyl *m*-chlorobenzoate and the 2-furoxy anion (which interacts with the protonated quinuclidine), while releasing a thiourea NH that activates the aldehyde by hydrogen bonding; the furoxy anion and the aldehyde then combine, the carboxylate facilitating the silyl transfer to the aldolate product. F.e.s. R.P. Singh, B.M. Foxman, L. Deng, J. Am. Chem. Soc. *2010*, *132* (28), 9558-60 [DOI: 10.1021/ja103331t]; with a cinchona alkaloid-based 2-aminothiourea (e.e. up to 91%) s. N. Zhu, B.-C. Ma, Y. Zhang, W. Wang, Adv. Synth. Catal. *2010*, *352* (8), 1291-5 [DOI: 10.1002/adsc.201000099]; with Denmark's chiral bisphosphoramide/$SiCl_4$/*i*-Pr_2NEt as Lewis base-Lewis acid catalyst, **also chiral Δ^3-2-pyrrolone analogs**, s. C. Curti, B. Ranieri, L. Battistini, G. Rassu, V. Zambrano, G. Pelosi, G. Casiraghi, F. Zanardi, ibid. *352* (11-12), 2011-22 [DOI: 10.1002/adsc.201000189].

N'-Chloromethyl-N-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(fluoroborate) *Selectfluor*
s. under (Ph$_3$P)AuCl and [Bis(diphenylphosphino)methane]bis[gold(I) bromide]

Oxalyl chloride *(COCl)$_2$*

Asym. synthesis of 2-acylaziridines
from carboxylic acids, aldimines and diazo(trimethylsilyl)methane
via diazomethyl ketones

485.



Oxalyl chloride (1.5 eq.) added slowly to a soln. of hex-5-ynoic acid (15 mmol) in dry methylene chloride (15 ml) at room temp., the mixture stirred for 1 h, concentrated *in vacuo*, the residue dissolved in acetonitrile (75 ml), trimethylsilyldiazomethane (1.1 eq.) added at 0°, the mixture stirred for 24 h, concentrated *in vacuo*, and purified chromatographically → intermediate α-diazoketone (Y 66%), 1.2 mmol of which added to a soln. of chiral catalyst [5 mol%; freshly prepared from the chiral biphenanthrol (5 mol%), triphenyl borate (20 mol%) and water (5 mol%)] and N-[bis(4-methoxy-3,5-dimethylphenyl)methyl]benzaldimine (1 mmol) in dry toluene (2 ml) under argon, the mixture stirred at room temp. for 24 h, diluted with hexanes, concentrated *in vacuo*, and purified chromatographically → 1-[(2R,3R)-1-[bis(4-methoxy-3,5-dimethylphenyl)methyl]-3-phenylaziridin-2-yl]hex-5-yn-1-one (Y 89%; e.e. 99%). Diazoketone formation (via this variant of the Shiori modification of the Arndt-Eistert synthesis; cf. *36*, 824) from aliphatic acids (seven examples; Y 52-82%) and subsequent aziridination with N-protected imines in the presence of chiral bis(arenol) ligands afforded *cis*-aziridines (d.r. at least 50:1) with high enantioselectivity (e.e. 87-99%; thirty examples; Y 58-95%). Tolerated groups included alkyl bromide, ester, alkene, alkyne, acetal and phthalimide. The N-protecting group was removed in one case using triflic acid/anisole/0° (Y 84%). F.e., optimization and reactions of the aziridines s. H. Ren, W.D. Wulff, Org. Lett. *2010*, *12* (21), 4908-11 [DOI: 10.1021/ol102064b].

Organosilicon hydrides s. under InI$_3$ *≥SiH*

Silica *SiO$_2$*

1,7-Dihydro-4-azepinones from Δ^1-azirines and 1-alkoxy-3-siloxy-1,3-dienes

486.

(Y 100% by NMR)

in one-pot. 1-Methoxy-3-trimethylsilyloxypenta-1,3-diene (7.5 mmol) added to a soln. of ethyl 2*H*-azirine-3-carboxylate [generated by heating a mixture of ethyl 2-azidoacrylate (10 mmol) in

methylene chloride (150 ml) in a sealed tube at 150° and cooling] at 23°, the orange soln. heated at 80° for 40 min, cooled to 23°, silica gel (10 g) added, the mixture stirred for 18 h, filtered, concentrated *in vacuo*, and purified chromatographically → 6-ethoxycarbonyl-5-methyl-1,7-dihydro-4-azepinone. Y 51%. The reaction involves silica-induced ring expansion of the initial adduct (which could be isolated in 59% yield). The 5-H derivative was similarly prepared in 45% overall yield. The products were found to undergo facile isomerization to their **1,5-dihydro-derivs.** under basic conditions, with tetra-*n*-butylammonium fluoride giving 100% conversion in both cases. F.e.s. G.G. Dubinina, W.Y. Yoshida, W.J. Chain, Tetrahedron Lett. *2010, 51* (40), 5325-7 [DOI: 10.1016/j.tetlet.2010.08.003].

Trimethylsilyl cyanide s. under BuLi *Me_3SiCN*

Titanium tetraisopropoxide/(R)-1,1′-bi-2-naphthol/water/lithium chloride *[Ti(IV)]*/LiCl*
Asym. vinylogous aldol-type condensation ←
under cooperative Lewis acid catalysis s. *66*, *452s78*

Dichlorotitanium diisopropoxide *$TiCl_2(OPr\text{-}i)_2$*
Vinylogous aldol-type condensation ←
with 2-siloxypyrroles s. *53*, 453s*61*; *anti*-selective condensation with 3-alkylidene-6-siloxy-5-silyl-3*H*-1,3-dioxins using $TiCl_2(OPr\text{-}i)_2$ s. T. Yoshinari, K. Ohmori, K. Suzuki, Chem. Lett. *2010, 39* (10), 1042-4 [DOI: 10.1246/cl.2010.1042]; under neutral Lewis base catalysis for coupling with aldehydes or activated ketones s. A. Scettri, V. De Sio, R. Villano, P. Manzo, M.R. Acocella, Tetrahedron Lett. *2010, 51* (28), 3658-61 [DOI: 10.1016/j.tetlet.2010.05.016]; diastereoselective condensation with 2-siloxyfurans (cf. *37*, 911) under *heterogeneous* conditions with reusable silica-sulfuric acid s. G. Sabitha, M.N. Prasad, M. Ramesh, J.S. Yadav, Monatsh. Chem. *2010, 141* (11), 1245-8 [DOI: 10.1007/s00706-010-0388-z]; **asym. vinylogous aldol-type condensation** (cf. *66*, 452s*74*) with $Cu(OTf)_2$ and chiral N-(*o-sec*-aminoaryl)sulfoximines as ligand s. M. Frings, I. Atodiresei, Y. Wang, J. Runsink, G. Raabe, C. Bolm, Chem. Eur. J. *2010, 16* (15), 4577-87 [DOI: 10.1002/chem.200903077]; f. chiral sulfoximines for asym. coupling of 1-amino-1-siloxy-1,3-dienes s. M. Frings, D. Goedert, C. Bolm, Chem. Commun. *2010, 46* (30), 5497-9 [DOI: 10.1039/c0cc00996b]; asym. coupling of Brassard's diene *under cooperative Lewis acid catalysis* with a binuclear chiral titanium(IV) complex formed from $Ti(OPr\text{-}i)_4$/(R)-BINOL/water as strong Lewis acid and LiCl as weak Lewis acid s. G. Wang, J. Zhao, Y. Zhou, B. Wang, J. Qu, J. Org. Chem. *2010, 75* (15), 5326-9 [DOI: 10.1021/jo100674f].

Silicon tetrachloride s. under Chiral bisphosphoramides *$SiCl_4$*

Titanium tetrachloride *$TiCl_4$*
Phenol ring from 1,3-disiloxy-1,3-dienes ○
update s. *36*, 885s*75*; polysubst. *p*-hydroxybiphenyls from 3-arylacetylacetones s. I. Ullah, M. Sher, R.A. Khera, A. Ali, M. Nawaz, M. Shkoor, I. Iqbal, M. Imran, A. Villinger, C. Fischer, P. Langer, Tetrahedron *2010, 66* (21), 3824-35 [DOI: 10.1016/j.tet.2010.03.054]; 3-hydroxyphthalic and 2-hydroxyterephthalic acid esters from α,β-ethylene-γ-keto-α-siloxycarboxylic acid esters s. M. Shkoor, O. Fatunsin, A. Riahi, M. Lubbe, S. Reim, M. Sher, A. Villinger, C. Fischer, P. Langer, Eur. J. Org. Chem. *2010* (19), 3732-42 [DOI: 10.1002/ejoc.200901373]; 5-chlorosalicylic acid esters from β-alkoxy-α-chloro-α,β-ethylenecarboxylic acid esters s. O. Fatunsin, M. Shkoor, S.-M.T. Toguem, A. Riahi, O.O. Aiyelaagbe, E.T. Akintayo, C. Fischer, P. Langer, Synlett *2010* (13), 1963-5 [DOI: 10.1055/s-0030-1258488]; 5-phosphonylsalicylic acid esters s. O. Fatunsin, M. Shkoor, A. Riahi, P. Langer, ibid. *2010* (10), 1525-7 [DOI: 10.1055/s-0029-1219950]; 5-β-chlorosalicylic acid esters from 4-acyl-2,3-dihydrofurans s. M. Lau, M. Sher, A. Villinger, C. Fischer, P. Langer, Eur. J. Org. Chem. *2010* (19), 3743-53 [DOI: 10.1002/ejoc.201000158]; 9-hydroxybenzo[*c*]chromen-6-ones from 4-coumarin-3-carboxaldehydes s. O. Fatunsin, V.O. Iaroshenko, S. Dudkin, S. Mkrtchyan, A. Villinger, P. Langer, Tetrahedron Lett. *2010, 51* (36), 4693-5 [DOI: 10.1016/j.tetlet.2010.06.138]; 3-hydroxy-9,10-dihydrophenanthrenes from 4-aroyl-2,3-dihydrofurans s. M. Lau, M. Sher, A. Villinger, C. Fischer, P. Langer, Eur. J. Org. Chem. *2010* (26), 5118-27 [DOI: 10.1002/ejoc.201000451]; synthesis of the first 1-trifluoromethyl-1,3-disiloxy-1,3-diene s. S. Büttner, F. Bendrath, P. Langer, Tetrahedron Lett. *2010, 51* (39), 5106-8 [DOI: 10.1016/j.tetlet.2010.05.082].

Fluorous distannoxanes ←
Aldol-type condensation CHO → CH(OH)C-CO
with $BiCl_3$ cf. *44*, 875; with fluorous distannoxanes *in a fluorous/organic biphase medium* for facile recovery of catalyst and product, also 3-ethylenealcohols from aldehydes and tetraallyltin (cf. *36*, 879s*78*), s. A. Orita, S. Tanabe, T. Ono, J. Otera, Adv. Synth. Catal. *2010, 352* (9), 1419-23 [DOI: 10.1002/adsc.201000130]; from aldehydes in an automated continuous flow reactor under solvent-free conditions with Amberlite IRA-900 (fluoride) s. F. Fringuelli, D. Lanari, F. Pizzo, L. Vaccaro, Green Chem. *2010, 12* (7), 1301-5 [DOI: 10.1039/c004461j]; β-hydroxyketones under Lewis base catalysis with *p*-nitrophenoxymagnesium iodide s. X. Zhang, J. Shi, S. Hu, J. Chem. Res. *2010*, *34* (5), 263-5 [DOI: 10.3184/030823410X12733354109885]; catalyst-free condensation with peptide or protein N-terminal aldehydes in water s. J. Alam, T.H. Keller, T.-P. Loh, J. Am. Chem. Soc. *2010, 132* (28), 9546-8 [DOI: 10.1021/ja102733a]; **asym. aldol-type condensation** (cf. *44*, 871s*70*) with chiral tris(aqua)lanthanide(III) α-aminocarboxylic acid ester complexes *in aq. medium* s. Y. Mei, P. Dissanayake, M.J. Allen, ibid. *132* (37), 12871-3 [DOI: 10.1021/ja107197p]; with a chiral 1,1′-binaphthyl-2,2′-diyl N-triflylthionophosphoramidate **under organo-Brønsted acid catalysis** (cf. *47*, 885s*70*) s. C.H. Cheon, H. Yamamoto, Org. Lett. *2010, 12* (11), 2476-9 [DOI: 10.1021/ol100233t].

Tin(II) triflate/N-ethylpiperidine/microwaves $Sn(OTf)_2/EtN(CH_2)_5$/[\\\\]
Horner synthesis of (Z)-β-arylcinnamic acid esters s. *39*, 854s*78* CO → C=C

Tert. phosphines and di(phosphines) s. under $NiCl_2$, [Rh(cod)(OH)]$_2$, [Rh(cod)Cl]$_2$, $Pd(OAc)_2$ and [(allyl)PdCl]$_2$ ⩾P
2-(Dicyclohexylphosphinomethyl)-1,3-bis(2,6-diisopropylphenyl)imidazolium iodide s. under Bis(cinnamylpalladium chloride) ←
(R)-2′-(Diphenylphosphino)-1,1′-binaphthyl-2-yl[bis(trifluoromethyl)]carbinol s. under [RhCl(H_2C=CH_2)$_2$]$_2$ ←
3-[o-(Dicyclohexylphosphino)phenyl]-2,4-dimethoxybenzenesulfonic acid sodium salt s. under Na_2PdCl_4 ←
Chiral 1,1′-binaphthyl-2,2′-phosphoramidite complexes s. under (π-allyl)Pd(Cp) ←
Chiral bisphosphoramides/silicon tetrachloride/ethyldiisopropylamine ←
5-α-Hydroxy-2(5*H*)-furanones from 2-siloxyfurans and aldehydes ←
via organocatalyzed asym. vinylogous aldol-type reaction – Also chiral 5-α-hydroxy-Δ^3-2-pyrrolones from 2-siloxypyrroles s. *78*, 484

Chiral 1,1′-binaphthyl-2,2′-diyl N-triflylthionophosphoramidates ←
Organo-Brønsted acid-catalyzed aldol-type condensation s. *47*, 885s*78* CH(OH)C-CO

3-tert-Butyl-4-(2,6-dimethoxyphenyl)-1,3-benzoxaphospholine s. under $Pd_2(dba)_3$ ←
Chiral 3,3′-di-tert-butyl-4,4′-dimethoxy-2,2′-bi[1,3-benzoxaphospholine] s. under Cu(OCOR)$_2$ ←
Triphenyl phosphite s. under $Pd(OAc)_2$ $(PhO)_3P$

(R)-3,3′-Bis(2,4,6-triisopropylphenyl)-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate ←
Organo-Brønsted acid-catalyzed asym. allylboration s. *33*, 865s*78* CO → C(OH)C-C=C

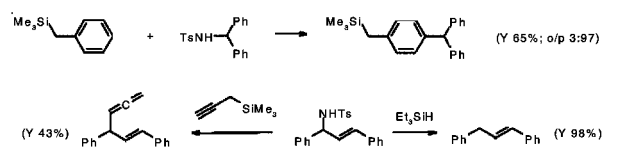
Hydrogen peroxide s. under Bu_2BOTf H_2O_2

Triflimide Tf_2NH
Regiospecific synthesis of homoallylarenes from N-tosylbenzylamines and 2-ethylenesilanes with allyl shift NHTs → C-C=C

487.

1-Phenylprop-1-en-3-yl(trimethyl)silane (2 eq.) and triflimide (10 mol%) added to a soln. of startg. sulfonamide (0.2 mmol) in methylene chloride (0.3 ml) at room temp., the mixture stirred until reaction complete (TLC; 12 h), and the product purified by chromatography on silica → 4-(4-methoxyphenyl)-3-phenylbut-1-ene. Y 75%. A series of N-bis- and N-mono-benzylic

sulfonamides underwent unprecedented and regioselective coupling (via initial formation of a benzylic cation) with allylic silanes (ten examples; Y 70-97%), with 4-chlorobenzylic (52%) and propargylic sulfonamides (45%) affording somewhat lower yields. The silane nucleophile was required in excess (2 eq.) to minimize alkylation of products by the sulfonamide substrate. Use of a propargylic silane as nucleophile afforded the corresponding allene product (Y 43%), whereas a benzylic silane underwent regioselective Friedel-Crafts benzylation with the silane remaining intact (Y 65%; *o:p* 3:97). In a further development, **replacement of benzylic tosylamino groups by hydrogen** was achieved with triethylsilane (six examples; Y 71-99%) in the presence of alkene and alkyne moieties.



F.e. and optimization s. B.-L. Yang, S.-K. Tian, Chem. Commun. *2010*, *46* (33), 6180-2 [DOI: 10.1039/c0cc00765j].

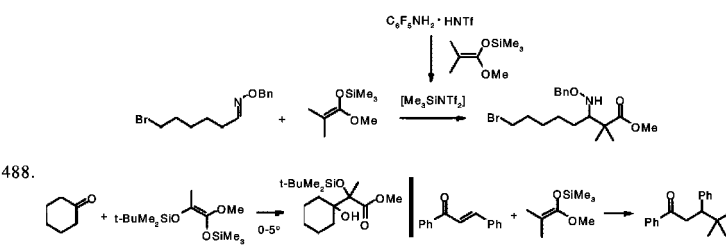
Pentafluoroaniline·triflimide $C_6F_5NH_2{\cdot}HNTf_2$

β-Alkoxylaminocarboxylic acid esters C=NOR → C(NHOR)C-COOR

from O-alkylaldoximes and O-silyl O-alkyl keteneacetals

Mannich-type reaction with *in situ*-generated N-trimethylsilyltriflimide as catalyst

488.



under mild conditions. O-(Benzyl)-6-bromohexanaldoxime (1 mmol) and startg. ketene silyl acetal (1.5 eq.) added sequentially to a stirred soln. of pentafluorophenylammonium triflimide (5 mol%) in toluene (0.5 ml) at -50° under argon, the mixture stirred for 1 h, quenched with water, extracted with ether, concentrated, and purified chromatographically → methyl 3-benzyloxyamino-8-bromo-2,2-dimethyloctanoate. Y 86%. *in situ*-Generation of catalytic N-trimethylsilyltriflimide provides a general method for the little studied Mannich reaction of oxime ethers, affording novel β-alkoxyamino-esters (twenty examples; Y 65-99%) in the presence of silyl ether, halo and ester functionality. Diastereoselectivity, however, was generally poor (d.r. <4:1) and *syn/anti* ratios were not assigned. The catalyst was also successfully applied to the preparation of relatively inaccessible **β-hydroxycarboxylic acid esters** (twenty-four examples; Y 57-98%) from ketones *(incl. enolizable ketones which are prone to form enol silyl ethers)* by [Mukaiyama] aldol-type condensation (cf. *44*, 875s*78*). α,β-Unsaturated ketones, however, gave **δ-ketocarboxylic acid esters** by Michael-type addition under these conditions (four examples; Y 57-90%). F.e. and optimization s. R. Nagase, J. Osada, H. Tamagaki, Y. Tanabe, Adv. Synth. Catal. *2010*, *352* (7), 1128-34 [DOI: 10.1002/adsc.200900869].

Chiral N-(o-sec-amino)sulfoximines s. under Cu(OTf)$_2$ ←

Trimethylsilyl triflate/ethyldiisopropylamine/trifluoroacetic acid ←
β-Hydroxycarboxylic acids from [non-enolizable] aldehydes CHO → CH(OH)C-COOH
via aldol-type condensation s. *78*, 288

Silica-sulfuric acid *SiO_2-OSO_3H*
Diastereoselective vinylogous aldol-type condensation ←
with 2-siloxyfurans under *heterogeneous* conditions s. *37*, 911s*78*

Potassium persulfate s. under AgNO$_3$ *$K_2S_2O_8$*
Tetra-n-butylammonium fluoride s. under Pd$_2$(dba)$_3$ and Silica-supported palladium phosphine complex *Bu_4NF*

Amberlite IRA-900 (fluoride) ←
Aldol-type condensation CHO → CH(OH)C-CO
in an automated continuous flow reactor s. *44*, 875s*78*

N-(o-Methoxybenzyl)quininium chloride s. under K$_3$PO$_4$ ←
4,4′-Bis(trimethylammoniomethyl)-2,2′-bipyridyl dibromide s. under PdCl$_2$(NH$_3$)$_2$ ←

Manganese(III) acetate/microwaves *$Mn(OAc)_3$/[\\\\]*
Biaryls from arylboron compds. and arenes Ar-Ar′
under iron(III) catalysis cf. *74*, 516; with Mn(OAc)$_3$ under microwave irradiation s. S.K. Guchhait, M. Kashyap, S. Saraf, Synthesis *2010* (7), 1166-70 [DOI: 10.1055/s-0029-1219234]; ***o*-arylation** of arylcarboxylic acid esters with arylboronic acid esters using RuH$_2$(CO)(PPh$_3$)$_3$ in refluxing pinacolone s. K. Kitazawa, M. Kotani, T. Kochi, M. Langeloth, F. Kakiuchi, J. Organomet. Chem. *2010, 695* (8), 1163-7 [DOI: 10.1016/j.jorganchem.2010.01.022]; *o*-arylation of pyrrole and pyridine under iron(III) catalysis s. J. Wen, S. Qin, L.-F. Ma, L. Dong, J. Zhang, S.-S. Liu, Y.-S. Duan, S.-Y. Chen, C.-W. Hu, X.-Q. Yu, Org. Lett. *2010, 12* (12), 2694-7 [DOI: 10.1021/ol100838m]; *o*-arylation of 2-phenoxypyridines with potassium aryl(trifluoro)borates using Pd(OAc)$_2$/Ag$_2$CO$_3$/*p*-benzoquinone s. J.-H. Chu, P.-S. Lin, M.-J. Wu, Organometallics *2010, 29* (18), 4058-65 [DOI: 10.1021/om100494p].

Nanoferrite s. under Glutathione ←

Tris(1,10-phenanthroline)iron(III) hexafluoroantimonate/(2R,5R)-2-tert-butyl-3,5-dimethyl-4-imidazolidone/disodium hydrogen phosphate/potassium fluoride ←
3-Vinylcyclopentane- or 3-methylenecyclohexane-carboxaldehydes ○
from ethylene derivs. via asym. organo-SOMO [4+2] cascade cycloaddition s. *78*, 367

1,1′-Bis(diphenylphosphino)ferrocene s. under Pd(OAc)$_2$ *dppf*

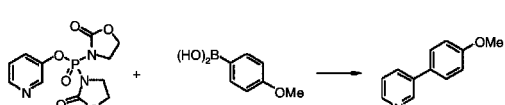
Dichloro[1,2-bis(diarylphosphino)benzene]iron(II) complex/magnesium bromide ←
Iron-catalyzed Suzuki coupling of lithium arylborates with alkyl halides s. *64*, 453s*78* Ar-R

Pincer-type pyridine-tethered nickel(II) bis(benzimidazol-2-ylidene) complexes *[Ni(II)]*
Nickel-catalyzed Suzuki biaryl coupling s. *51*, 453s*78* Ar-Ar′

Nickel(0) phosphine complexes *[Ni(0)]*
Isoquinolines from 3,4-pyridynes via [2+2+2]-cycloaddition s. *68*, 464s*78* ○

Nickel(II) chloride/1,3-bis(diphenylphosphino)propane/potassium carbonate ←
Nickel-catalyzed Suzuki coupling ArOH → Ar-Ar′
with aryl phosphorobis(2-oxazolidon-3-idates)

489.



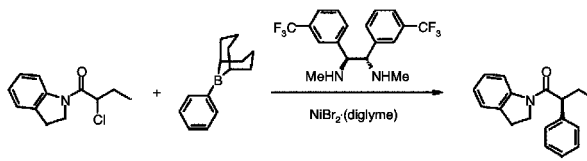
A mixture of NiCl$_2$ (10 mol%) and dppp (20 mol%) in dry dioxane (2 ml) stirred at 100° under N$_2$ for 3 h, cooled, pyrid-3-yl phosphorobis(2-oxazolidon-3-idate) (0.5 mmol), 4-methoxyphenyl-

boronic acid (2 eq.), anhydrous K_2CO_3 (4 eq.) and dry dioxane (4 ml) added, the mixture stirred at 100° until reaction complete (TLC; 16-24 h), added to water, extracted with methylene chloride, concentrated *in vacuo*, and purified chromatographically → 3-(4-methoxyphenyl)pyridine. Y 85%. This novel Suzuki-Miyaura reaction uses bis(2-oxo-3-oxazolidinyl)-phosphinyl (BOP) as an effective activator of the phenol C-O bond, allowing efficient coupling in the presence of relatively inexpensive and stable nickel-based catalysts. The method was effective for electron diverse (het)aryl-BOP and boronic acid derivs. (twenty-two examples; Y 75-96%) in the presence of ester, ketone, *nitrile*, tert. amine, fluoro and ether functionality. Sterically-hindered *o*-tolyl-BOP gave a reduced yield (46%). F.e. and optimization s. Y.-L. Zhao, Y. Li, Y. Li, L.-X. Gao, F.-S. Han, Chem. Eur. J. *2010*, *16* (17), 4991-4 [DOI: 10.1002/chem.201000420].

Nickel(II) bromide·diglyme/potassium tert-butoxide/isobutanol ←
Nickel(II) bromide·diglyme/chiral 1,2-diamine/potassium tert-butoxide/isobutanol or n-hexanol ←

Nickel-catalyzed Suzuki coupling with 9-subst. 9-borabicyclo[3.3.1]nonanes Hal → R
Asym. synthesis of α-aryl- from α-chloro- or -bromo-carboxylic acid amides

490.



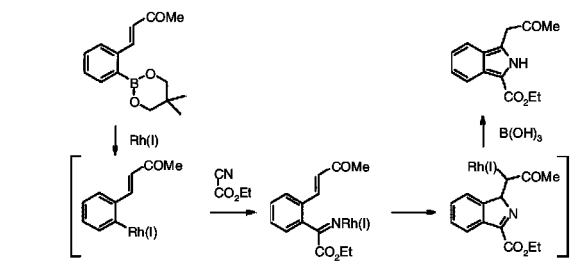
$NiBr_2$·diglyme (8 mol%), (S,S)-N,N′-dimethyl-1,2-bis(*m*-trifluoromethylphenyl)-1,2-ethylenediamine (10 mol%), 2-chloro-1-(indolin-1-yl)butan-1-one (0.5 mmol) and toluene (2.5 ml) added to a flask in a glovebox under N_2, KOBu-*t* (1.3 eq.), isobutanol (1.5 eq.), 9-phenyl-9-borabicyclo[3.3.1]nonane (1.5 eq.) and toluene (2.5 ml) added sequentially to a vial, the flask and the vial each capped with a rubber septum, the two mixtures stirred for 10 min, the vessels removed from the glovebox, placed in a -5° bath, each stirred for 10 min, the soln. in the vial then transferred by syringe to the slurry in the flask, under N_2, the resulting mixture stirred at -5° for 24 h (turning orange after a few min), washed with satd. Na_2CO_3 soln., the aq. phase extracted with ethyl acetate, the organic layers washed with brine, dried (Na_2SO_4), concentrated, and the residue purified by flash chromatography → 1-(indolin-1-yl)-2-phenylbutan-1-one. Y 81% (e.e. 93%). The same product was obtained in 88% yield (e.e. 91%) from the corresponding bromide. This method, using commercially available reagents and applicable on the gram scale, represents the first enantioselective arylation of α-haloamides or α-chlorocarbonyl compds. and the first asym. Suzuki reactions of activated alkyl electrophiles or arylboron reagents. Eight further examples proceeded in yields of 70-88% and enantiomeric excesses of 84-94%, with functional groups such as olefin or silyl ether, as well as β-branching, tolerated on the alkyl side chain of the haloamide, and an electron-withdrawing or -donating group in the *m*- or *p*-position tolerated on the arylboron compd. F.e. and conversion of the product to chiral α-arylcarboxylic acids (with DDQ then LiOH/H_2O_2) or 2-arylalcohols ($LiBH_3NH_2$) s. P.M. Lundin, G.C. Fu, J. Am. Chem. Soc. *2010*, *132* (32), 11027-9 [DOI: 10.1021/ja105148g]; asym. alkyl-alkyl Suzuki coupling of 2-carbamyloxyhalides and B-alkyl-9-borabicyclo[3.3.1]nonanes (with N,N′-dimethyl-1,2-diphenyl-1,2-ethylenediamine as the ligand and *n*-hexanol as additive) s. N.A. Owston, G.C. Fu, ibid. *132* (34), 11908-9 [DOI: 10.1021/ja105924f]; general method for alkyl-alkyl Suzuki coupling of prim. or sec. halides, especially unactivated sec. chlorides, in the absence of diamine s. Z. Lu, G.C. Fu, Angew. Chem., Int. Ed. *2010*, *49* (37), 6676-8 [DOI: 10.1002/anie.201003272].

Carbonyl(dihydrido)tris(triphenylphosphine)ruthenium(II) $RuH_2(CO)(PPh_3)_3$
o-Arylation of arylcarboxylic acid esters with arylboronic acid esters s. *74*, 516s*78* Ar-Ar′

(1,5-Cyclooctadiene)bis(2-methylallyl)ruthenium(II)/sodium tert-butoxide *[Ru(II)]/NaOBu-t*
Ruthenium-catalyzed Suzuki biaryl coupling s. *37*, 902s*78*

1,5-Cyclooctadiene(hydroxo)rhodium(I) dimer/boric acid *$[Rh(cod)OH]_2/H_3BO_3$*
α-(1-Carbalkoxy-2*H*-isoindol-3-yl)carbonyl compds.
from (E)-β-(*o*-borylaryl)-α,β-ethylenecarbonyl compds. and cyanoformic acid esters

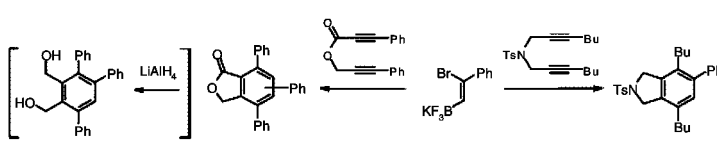
491.



A soln. of ethyl cyanoformate (0.9 mmol) in N-methyl-2-pyrrolidone (0.3 ml) added to a mixture of the startg. benzalacetone deriv. (0.3 mmol), boric acid (0.9 mmol) and $[Rh(OH)(cod)]_2$ (2.5 mol%) under argon, stirred at room temp. for 30 min and then at 80° for 3 h, cooled, diluted with ethyl acetate/toluene (2:1; 5 ml) and water (2 ml), and the aq. layer worked up with purification by preparative TLC → product. Y 75%. The procedure is applicable to a range of *o*-borylbenzalacetone derivs. and chalcone analogs (nine examples; Y 26%; 46-76%), reaction being enhanced by substrates with electron-donating groups on the aromatic ring, but yields being lower with those possessing electron-withdrawing chlorine (Y 26-46%). *o*-Borylcinnamic acid esters reacted similarly in 1,3-dimethyl-2-imidazolidone at 120° (four examples; Y 50-62%), but cyclooctadiene (10 eq.) was required as added ligand to prevent deterioration of the rhodium catalyst. Reaction is thought to involve initial generation of an arylrhodium species which adds across the cyano group of the cyanoformate, followed by *exo*-mode intramolecular Michael addition and prototropic shift. Yields were also good with isopropyl and isobutyl cyanoformate, but lower with methyl cyanoformate. F.e.s. H. Shimizu, T. Igarashi, M. Murakami, Bull. Korean Chem. Soc. *2010, 31* (6), 1461-2 [DOI: 10.5012/bkcs.2010.31.6.1461]; **asym. synthesis of indenes** from *o*-ethyleneboronic acid esters and [internal] acetylene derivs. (cf. *68*, 461) with $Pd(OTf)_2 \cdot 2H_2O/2,3{:}2',3'$-bis-(isopropylidenedioxy)-6,6′-bis(di-*p*-tolylphosphino)biphenyl, chiral α-indenylketones, s. F. Zhou, M. Yang, X. Lu, Org. Lett. *2009*, *11* (6), 1405-8 [DOI: 10.1021/ol9001015].

1,5-Cyclooctadiene(hydroxo)rhodium(I) dimer/triphenylphosphine/cesium fluoride ←
Benzene ring from diynes and potassium (Z)-2-bromovinyl(trifluoro)borates

492.



(Y 90%) (Y 51%; 4,5,7/4,6,7-Ph_3 2.5:1)

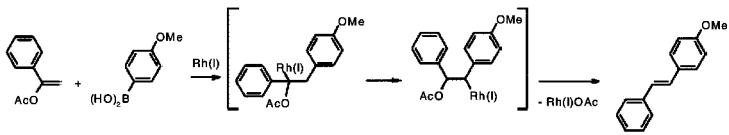
Startg. 1,6-diyne (0.3 mmol), K-(Z)-(1-bromo-2-styryl)trifluoroborate (3 eq.), $[Rh(OH)(cod)]_2$ (5 mol%), triphenylphosphine (20 mol%) and CsF (3 eq.) added to 1,4-dioxane/water (20:1; 3 ml) in a Schlenk tube, the mixture stirred at 100° until reaction complete (TLC; 2 h), cooled to room temp., volatiles removed *in vacuo,* and the residue purified chromatographically → N-tosyl-4,7-dibutyl-5-phenylisoindoline. Y 88%. Crucial to the success of this novel rhodium(I)-catalyzed formal [2+2+2]-cycloaddition route to polysubst. benzenes is the use of a bromovinylborate as 2-C fragment, which contains both nucleophilic (vinyl borate) and electrophilic (vinyl bromide) centers.

The reaction appears general for internal 1,6-diynes tethered by N-, O- and C-based fragments (incl. a lactone tether) (nine examples; Y 40-88%), with a terminal alkyne deriv. giving low yield (20%) presumed due to unfavorable interaction with the rhodium catalyst. Regioselectivity for unsymmetrical diynes was modest (2:1 to 2.5:1). F.e., optimization, a gram-scale synthesis of bromovinylborates, and further reactions of the products s. X. Fang, J. Sun, X. Tong, Chem. Commun. *2010*, *46* (21), 3800-2 [DOI: 10.1039/c001830a].

Acetato(1,5-cyclooctadiene)rhodium(I) dimer/1,5-cyclooctadiene/potassium phosphate/ diisopropylamine ←

***trans*-Stilbenes from α-acoxystyrenes and arylboronic acids** C(OAc)=CH → CH=C(Ar)
Rhodium(I)-catalyzed *cine*-substitution

493.



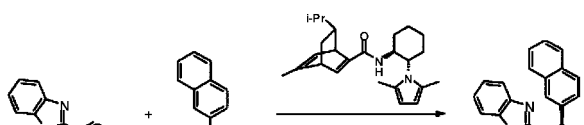
$[Rh(OAc)(cod)]_2$ (7.6 μmol), *p*-methoxyphenylboronic acid (0.75 mmol) and K_3PO_4 (1.5 mmol) placed in a screw-capped vial inside a nitrogen-filled drybox, diluted with toluene (2 ml), the vial sealed with a screw cap, removed from the drybox, *1,5-cyclooctadiene* (30 μmol), 1-phenylethenyl acetate (0.49 mmol) and diisopropylamine (0.5 mmol) added with stirring via a micro-syringe at room temp., the mixture stirred at 100° for 24 h, poured into ethyl acetate, filtered through a Celite pad, the filtrate evaporated under reduced pressure, and the residue purified chromatographically → (E)-1-(4-methoxyphenyl)-2-phenylethene. Y 70%. This is the first example of a *cine*-substitution of an enolester. Reaction was performed with a range of ring-substituted α-acetoxystyrenes and arylboronic acids, although electron-deficient B-aryl-1,3,2-dioxaborolanes were preferred over the corresponding arylboronic acids in order to suppress decomposition of the enolester to acetophenone. The regioselectivity is strongly influenced synergistically by the steric repulsion between the two aryl groups and the electronic character of the aryl group of the enolester, complete regioselectivity being effected with electron-deficient substrates. It is also critically dependent on the choice of 1,5-cyclooctadiene for coordination to rhodium which accelerates the initial formation of a reactive arylrhodium (preferably with diisopropylamine as additive). Carborhodation of the enolester then takes place, followed, it is presumed, by β-hydride elimination, a 1,2-rhodium shift and finally β-oxygen elimination. F.e.s. J.-Y. Yu, R. Shimizu, R. Kuwano, Angew. Chem., Int. Ed. *2010*, *49* (36), 6396-9 [DOI: 10.1002/anie.201002745].

Chiral fluorous rhodium(I) di(phosphine) complex or cationic bis(alkene)- coordinated rhodium(I) bis(phosphoromonoamidite) complexes *[Rh(I)]**
Asym. 1,4-addition of arylboronic acids s. *55*, 452s*78* C=C → CHC(Ar)

Chlorobis(ethylene)rhodium(I) dimer/(1R,4R,7R)-7-isopropyl-5-methylbicyclo-[2.2.2]octa-2,5-diene-2-carboxylic acid [(1S,2S)-2-(2,5-dimethylpyrrol-1-yl)-cyclohexyl]amide/potassium hydroxide ←

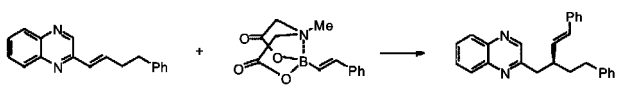
Rhodium(I)-catalyzed asym. 1,4-addition of arylboronic acids to *o*-vinyl-N-heteroarenes

494.



A soln. of $[RhCl(CH_2{=}CH_2)_2]_2$ (2.5 mol%) and chiral ligand (6 mol%) in dioxane (1 ml) in a sealed microwave vial stirred at room temp. for 15 min, a soln. of 2-(2-phenylethenyl)benzoxazole

(0.5 mmol), 2-naphthylboronic acid (2.4 eq.) and KOH (2.5 eq.) in dioxane/water (5:1; 1.5 ml) added via cannula, the mixture heated with microwaves at 80° for 30 min, cooled to room temp., filtered through a short plug of silica (with chloroform), the filtrate concentrated *in vacuo*, and the residue purified by chromatography on silica gel → 2-[(R)-2-naphthalen-2-yl-2-phenylethyl]-benzoxazole. Y 78% (e.e. 93%). The reaction was successful for arylboronic acids (optionally bearing methyl, chloro, fluoro or alkoxy substituents), reacting with π-deficient (quinoline, quinoxaline, pyrimidine) or π-excessive (benzoxazole, 4,5-diphenyloxazole, 3-phenyl-1,2,4-oxadiazole) (E)-alkenylheteroarenes, β-subst. with either an aryl or alkyl group (fourteen examples; Y 56%, 64-91%; e.e. 89-98%). A 2-alkenyl-pyridine and -thiazole were poor substrates (Y <30%), whose lower reactivity was attributed to the loss of aromatic stabilization accompanying the formation of an intermediate aza-π-allylrhodium species. Conventional heating also appeared to be successful, requiring lower catalyst (1.5 mol%) and ligand (3.6 mol%) loading. Attempted extension of the procedure to alkenylboronic acids was largely unsuccessful, although a more stable N-methyliminodiacetic acid (MIDA) alkenylboronate deriv. showed promising results.



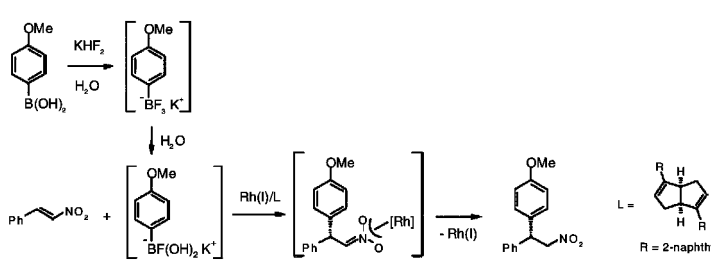
(Y 58%; e.e. 61%)

F.e., catalyst prepn., optimization and a proposed mechanism s. G. Pattison, G. Piraux, H.W. Lam, J. Am. Chem. Soc. *2010*, *132* (41), 14373-5 [DOI: 10.1021/ja106809p].

Chlorobis(ethylene)rhodium(I) dimer/chiral bicyclo[3.3.0]octa-2,6-diene/ potassium hydrogen fluoride *[Rh(I)]*/KHF$_2$*

Asym. 1,4-addition of arylboronic acids to terminal 1-nitroethylene derivs. C=C → CHC(Ar)

495.



The first general, highly enantioselective asym. 1,4-addition of boronic acids to *α-unsubst.* 1-nitroethylene derivs. is reported, courtesy of rhodium catalysis with C_2-symmetric chiral bicyclo[3.3.0]octa-2,6-dienes as ligand. **E:** A mixture of $[RhCl(CH_2{=}CH_2)_2]_2$ (0.007 mmol), the chiral bicyclo[3.3.0]octa-2,6-diene ligand (0.023 mmol) and the startg. arylboronic acid (0.75 mmol) in toluene (1 ml) stirred under N_2 at 60° for 30 min, the startg. nitroalkene (0.5 mmol) in toluene (1 ml) and aq. KHF_2 (3 *M*; 0.5 ml) added successively, heated under reflux at 100° for 4-7 h, the reaction cooled to room temp., water added, and worked up with purification by chromatography on silica gel → (R)-product. Y 96% (e.e. 78%). The procedure is applicable to the coupling of electron-diverse β-nitrostyrenes and aliphatic analogs with a range of arylboronic acids, highest enantioselectivities being recorded with sterically hindered and electron-deficient substrates (seventeen examples; Y 85-99%; e.e. 78-97%). Enantioselectivity was low, however, with the linear nitroolefin, 1-nitrohexene (e.e. 61%). Acidic KHF_2 ensures the excellent catalyst regeneration in 10:1 toluene/water, while at the same time converts the boronic acid *in situ* into the corresponding

organo(fluoro)borate as the effective arylating agent. Several chiral bicyclo[3.3.0]octa-2,6-dienes were effective as ligand, the hindered 2,6-bis(2-naphthyl) deriv. being the most satisfactory. The mechanism of conversion was not established but it is thought that hydrolysis of the organo-(trifluoro)borate before arylation may be involved. F.e. and comparison of bases and solvents s. Z.-Q. Wang, C.-G. Feng, S.-S. Zhang, M.-H. Xu, G.-Q. Lin, Angew. Chem., Int. Ed. *2010, 49* (33), 5780-3 [DOI: 10.1002/anie.201001883].

Chlorobis(ethylene)rhodium(I) dimer/(R)-2′-(diphenylphosphino)-1,1′-binaphthyl-2-yl[bis(trifluoromethyl)]carbinol/sodium tert-butoxide *[Rh(I)]*/NaOBu-t*

Asym. synthesis of diarylcarbinols from ar. aldehydes CO → C(OH)Ar

and arylboronic acids s. *65,* 437*s78*

Chiral chloro(diene)rhodium(I) complexes *[Rh(I)]**

Asym. 1,2-addition of arylboron compds. to N-protected imines C=N- → C(NH-)Ar

update s. *68,* 458*s75*; asym. addition of arylboronic acids to N-tosylaldimines with $[RhCl(CH_2{=}CH_2)_2]_2$ and a chiral monosubst. C_1-symmetric dicyclopentadiene as ligand in the presence of KHF_2 s. C. Shao, H.-J. Yu, N.-Y. Wu, C.-G. Feng, G.-Q. Lin, Org. Lett. *2010, 12* (17), 3820-3 [DOI: 10.1021/ol101531r]; asym. addition to N-sulfamylaldimines with chiral 3,3′-diaryl-2,2′-divinyl-1,1′-binaphthyls as ligand s. Z. Cao, H. Du, ibid. *12* (11), 2602-5 [DOI: 10.1021/ol1008087]; asym. addition of sodium tetraarylborates to N-tosylketimines with a chiral 2,5-diarylnorbornadiene as ligand s. R. Shintani, M. Takeda, T. Tsuji, T. Hayashi, J. Am. Chem. Soc. *2010, 132* (38), 13168-9 [DOI: 10.1021/ja106114q]; asym. 1,2-addition to 3-pyrazolidone azomethine imides with chiral norbornadiene-2-carboxylic acid esters as ligand s. R. Shintani, Y.-T. Soh, T. Hayashi, Org. Lett. *2010, 12* (18), 4106-9 [DOI: 10.1021/ol101700v].

Chloro(cyclooctadiene)rhodium(I) dimer/1,4-bis(diphenylphosphino)butane *[Rh(cod)Cl]$_2$/dppb*

Ring closures via 1,2(4)-addition of arylboron compds. ○

3-arylphthalides from *o*-aldehydocarboxylic acid esters and arylboronic acids under palladium catalysis cf. *77,* 508; from *o*-dialdehydes with $[Rh(cod)Cl]_2$/dppb via intramolecular esterification, also 3-vinylphthalides, s. Z. Ye, G. Lv, W. Wang, M. Zhang, J. Cheng, Angew. Chem., Int. Ed. *2010, 49* (21), 3671-4 [DOI: 10.1002/anie.201000302]; with $PdCl_2$/tris(1-naphthyl)phosphine/K_2CO_3 cf. Z. Ye, P. Qian, G. Lv, F. Luo, J. Cheng, J. Org. Chem. *2010, 75* (17), 6043-5 [DOI: 10.1021/jo101203b]; 1,3-diarylisobenzofurans from *o*-aroylaldehydes under rhodium or palladium catalysis s. J. Jacq, B. Bessières, C. Einhorn, J. Einhorn, Org. Biomol. Chem. *2010, 8* (21), 4927-33 [DOI: 10.1039/c0ob00110d]; β-subst. lactones and lactams from hydroxy- and amino-functionalized enoates, respectively, via 1,4-addition of organoboroxines under rhodium(I) catalysis s. J.O. Park, S.W. Youn, Org. Lett. *2010, 12* (10), 2258-61 [DOI: 10.1021/ol100610v]; β-aryl-α,β-ethylenelactones from siloxy-functionalized α,β-acetylenecarboxylic acid esters with CuOAc/HCl s. Y. Yamamoto, N. Kirai, Heterocycles *2010, 80* (1), 269-79 [DOI: 10.3987/com-09-s(s)8].

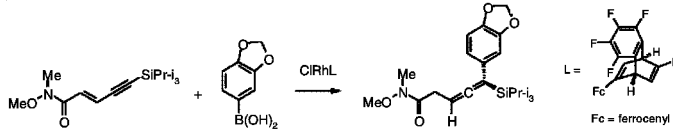
Chiral chloro[bis(ferrocenyl)tetrafluorobarrelene]rhodium(I) complexes/potassium phosphate ←

δ-Aryl-β-allene-δ-silylcarboxylic acid amides C=C-C≡C → CHC=C=C(Ar)

from 5-silyl-2,4-enynecarboxylic acid amides

via rhodium(I)-catalyzed asym. 1,6-addition of arylboronic acids

496.



Chiral δ-aryl-β-allene-δ-silylhydroxamic acid esters. Startg. enynamide (0.2 mmol) added to a soln. of chiral rhodium catalyst (5 mol%), 3,4-(methylenedioxy)benzeneboronic acid (2 eq.) and K_3PO_4 (20 mol%) in dioxane/water (10:1; 1.1 ml), the mixture stirred at 50°, cooled to room temp., quenched with aq. NH_3, stirred for 10 min, extracted with ether, filtered through silica gel, and purified chromatographically → (S)-N-methoxy-N-methyl-5-[3,4-(methylenedioxy)phenyl]-

5-triisopropylsilylpenta-3,4-dienamide. Y 87% (e.e. 96%). The amide group promotes regioselective 1,6-addition of electron-diverse arylboronic acids to the enyne moiety (a *tert*-butyl ester analog gave a 1:1 mixture of 1,4- and 1,6-adducts) to afford chiral 3,4-dienamides with high enantioselectivity (thirteen examples; Y 70-89%; e.e. 94-99%). Traces of the isomeric 2,4-dienamides (1-5%) were also observed. The (S)-configuration of products was confirmed by X-ray analysis of a deriv. in one case. A model was proposed to rationalize the observed enantioselectivity. F.e., optimization and substrate prepn. s. T. Nishimura, H. Makino, M. Nagaosa, T. Hayashi, J. Am. Chem. Soc. *2010*, *132* (37), 12865-7 [DOI: 10.1021/ja1066509].

Protein-stabilized palladium nanoparticles *[Pd(0)]*
Sym. biaryls from arylboronic acids Ar-Ar
update s. *53*, 471s*75*; with palladium nanoparticles stabilized within the protein cavity of a thermostable Dps protein for homocoupling of arylboronic acids or potassium aryl(trifluoro)borates (cf. *57*, 438s*75*) *in water* under air s. A. Prastaro, P. Ceci, E. Chiancone, A. Boffi, G. Fabrizi, S. Cacchi, Tetrahedron Lett. *2010, 51* (18), 2550-2 [DOI: 10.1016/j.tetlet.2010.03.015]; under microwave-assisted palladium catalysis in silica matrices for homocoupling of 1-pyreneboronic acid s. Y. Kajiwara, A. Nagai, Y. Chujo, Chem. Lett. *2010, 39* (5), 480-1 [DOI: 10.1246/cl.2010.480]; *under organocatalysis* with a magnetically separable nanoferrite-anchored glutathione catalyst for biaryl coupling in water under microwave irradiation s. R. Luque, B. Baruwati, R.S. Varma, Green Chem. *2010, 12* (9), 1540-3 [DOI: 10.1039/c0gc00083c].

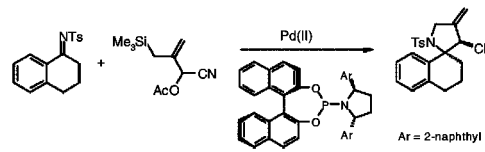
Palladium nanoparticles, complexes or supported/immobilized variants *[Pd]*
Suzuki coupling $B(OH)_2 \rightarrow R$
update s. *37*, 902s*77*; *64*, 448s*75*; using a *nanoreactor* composed of highly active palladium nanoparticles inside mesoporous silica hollow spheres s. Z. Chen, Z.-M. Cui, F. Niu, L. Jiang, W.-G. Song, Chem. Commun. *2010, 46* (35), 6524-6 [DOI: 10.1039/c0cc01786h]; with sustainable palladium nanoparticles formed as clusters from palladium acetate immobilized as a supported ionic liquid catalyst in a nanosilica dendrimer, notably for coupling *o*-subst. ar. bromides or triflates s. H. Hagiwara, H. Sasaki, N. Tsubokawa, T. Hoshi, T. Suzuki, T. Tsuda, S. Kuwabata, Synlett *2010* (13), 1990-6 [DOI: 10.1055/s-0029-1219816]; with recyclable palladium supported on a perfluoroalkylated polymer s. N. Audic, P.W. Dyer, E.G. Hope, A.M. Stuart, S. Suhard, Adv. Synth. Catal. *2010, 352* (13), 2241-50 [DOI: 10.1002/adsc.201000196]; with palladium-on-alumina, and a notable study of various parameters on palladium leaching therefrom s. S.S. Soomro, F.L. Ansari, K. Chatziapostolou, K. Köhler, J. Catal. *2010, 273* (2), 138-46 [DOI: 10.1016/j.jcat.2010.05.007]; with recyclable palladium supported on sulfur-modifed gold (SAPD) having high activity and extremely low leaching characteristic s. N. Hoshiya, M. Shimoda, H. Yoshikawa, Y. Yamashita, S. Shuto, M. Arisawa, J. Am. Chem. Soc. *2010, 132* (21), 7270-2 [DOI: 10.1021/ja9100084]; with magnetically recoverable [up to 25 times!] dendronic palladium di(phosphine) complexes grafted onto core-shell superparamagnetic nanoparticles (γ-Fe_2O_3/polymer) s. D. Rosario-Amorin, X. Wang, M. Gaboyard, R. Clérac, S. Nlate, K. Heuzé, Chem. Eur. J. *2009, 15* (46), 12636-43 [DOI: 10.1002/chem.200901866]; with air-stable 1,7-bis(diphenylphosphino)-indole as ligand s. R. Ghosh, N.N. Adarsh, A. Sarkar, J. Org. Chem. *2010, 75* (15), 5320-2 [DOI: 10.1021/jo100643j]; with highly active, stable dichlorobis(aminophosphine)palladium(II) complexes releasing palladium nanoparticles *in situ* s. J.L. Bolliger, C.M. Frech, Chem. Eur. J. *2010, 16* (13), 4075-81 [DOI: 10.1002/chem.200903309]; with phosphirano[1,2-*c*][1,2,3]diazaphospholes as ligand s. S. Maurer, C. Burkhart, G. Maas, Eur. J. Org. Chem. *2010* (13), 2504-11 [DOI: 10.1002/ejoc.201000102]; with an *o*-aminobiphenyl-type *o*-palladated phosphine [XPhos] complex for the rapid coupling of polyfluorinated aryl- and 2-heteroaryl-boronic acids s. T. Kinzel, Y. Zhang, S.L. Buchwald, J. Am. Chem. Soc. *2010, 132* (40), 14073-5 [DOI: 10.1021/ja1073799]; with thermally-stable benzylamine-type *o*-palladated complexes s. K. Karami, M.M. Salah, Appl. Organomet. Chem. *2010, 24* (11), 828-32 [DOI: 10.1002/aoc.1713]; with thiophene-based oxime-type *o*-palladated di(phosphine) complexes for coupling deactivated ar. chlorides s. M.S. Subhas, S.S. Racharlawar, B. Sridhar, P.K. Kennady, P.R. Likhar, M.L. Kantam, S.K. Bhargava, Org. Biomol. Chem. *2010, 8* (13), 3001-6 [DOI: 10.1039/b927367k]; with air- and moisture-resistant selenium-functionalized benzylamine-type *o*-palladated complexes, liberating $Pd_{17}Se_{15}$ nanoparticles *in situ* s. G.K. Rao, A. Kumar, J. Ahmed, A.K. Singh, Chem. Commun. *2010, 46* (32), 5954-6 [DOI: 10.1039/c0cc01075h]; with ionic liquid-tagged salicylaldehyde Schiff bases as ligand s. B. Li,

Y.-Q. Li, J. Zheng, ARKIVOC *2010* (ix), 163-70; with a palladium(II) cyclobutene-1,2-bis-(imidazol-2-ylidene) complex for coupling at room temp. s. A. Rahimi, A. Schmidt, Synlett *2010* (9), 1327-30 [DOI: 10.1055/s-0029-1219824]; with dichlorobis(1,2,3-triazol-4-ylidene)-palladium(II) complexes as catalyst for coupling *o*-subst. ar. chlorides s. T. Nakamura, K. Ogata, S.-i. Fukuzawa, Chem. Lett. *2010, 39* (9), 920-2 [DOI: 10.1246/cl.2010.920]; with palladium azopyridine complexes within quartz slide multilayers releasing soluble palladium catalytic species s. S. Gao, Z. Zheng, J. Lü, R. Cao, Chem. Commun. *2010, 46* (40), 7584-6 [DOI: 10.1039/c0cc01986k]; with robust palladium pyridylmethylamine complexes s. M.-A. Gunawan, C. Qiao, I. Abrunhosa-Thomas, B. Puget, J.-P. Roblin, D. Prim, Y. Troin, Tetrahedron Lett. *2010, 51* (41), 5392-4 [DOI: 10.1016/j.tetlet.2010.07.151]; Suzuki coupling *in water* with palladium nanoparticles deposited in an ionic liquid s. Y. Oda, K. Hirano, K. Yoshii, S. Kuwabata, T. Torimoto, M. Miura, Chem. Lett. *2010, 39* (10), 1069-71 [DOI: 10.1246/cl.2010.1069]; with water-soluble starch-stabilized palladium nanoparticles s. S. Liu, Q. Zhou, H. Jiang, Chin. J. Chem. *2010, 28* (1), 589-93 [DOI: 10.1002/cjoc.201090117]; with water-soluble palladium nanoparticles stabilized by PEG-tagged 1,3,5-tris(1,2,3-triazol-4-yl)benzene s. N. Mejías, R. Pleixats, A. Shafir, M. Medio-Simón, G. Asensio, Eur. J. Org. Chem. *2010* (26), 5090-9 [DOI: 10.1002/ejoc.201000671]; in aq. media with highly active, recyclable silica gel-supported (β-ketoiminato)(triphenylphosphine)-palladium(II) complexes (Pd@SiO_2) for coupling heteroaryl chlorides at low catalyst loading, also Stille and Sonogashira coupling, s. D.-H. Lee, J.-Y. Jung, M.-J. Jin, Green Chem. *2010, 12* (11), 2024-9 [DOI: 10.1039/c0gc00251h]; coupling ar. chlorides in aq. medium with a palladium catalyst supported on a metal-organic framework (MIL-101), also Ullmann homocoupling, s. B. Yuan, Y. Pan, Y. Li, B. Yin, H. Jiang, Angew. Chem., Int. Ed. *2010, 49* (24), 4054-8 [DOI: 10.1002/anie.201000576]; with water-soluble Pd,Au-nanoparticles stabilized by PEG-tethered phosphine-functionalized zwitterionic imidiazolium sulfonates s. T. Akiyama, C. Ibata, H. Fujihara, Heterocycles *2010, 80* (2), 925-31 [DOI: 10.3987/com-09-s(s)128]; in water at room temperature with Stilbazo [stilbene-4,4′-bis[(1-azo)-3,4-dihydroxybenzene]-2,2′-disulfonic acid diammonium salt] as ligand s. Y.-Y. Peng, J. Liu, X. Lei, Z. Yin, Green Chem. *2010, 12* (6), 1072-5 [DOI: 10.1039/c000739k]; with water-tolerant $Pd_2(dba)_3$/tri-*tert*-butylphosphine·fluoroboric acid/KF·$2H_2O$ s. S. Lou, G.C. Fu, Adv. Synth. Catal. *2010, 352* (11-12), 2081-4 [DOI: 10.1002/adsc.201000267]; microwave-assisted coupling of 4-(halogenophenyl)thiazoles in water with a dichloro(benzimidazol-2-ylketoxime)palladium(II) complex s. K.M. Dawood, M.M. El-Deftar, Synthesis *2010* (6), 1030-8 [DOI: 10.1055/s-0029-1218662]; in aq. medium with a phosphine-free palladium(II) salen complex for biaryl coupling s. S.R Borhade, S.B Waghmode, Indian J. Chem. *2010, 49B* (5), 565-72; in water with a chloropalladium(II) 1-(1,2,3-triazol-4-yl)imidazol-2-ylidene complex s. S. Gu, H. Xu, N. Zhang, W. Chen, Chem. Asian J. *2010, 5* (7), 1677-86 [DOI: 10.1002/asia.201000071]; *ligand-free* coupling *in PEG-300* with $Pd_2(dba)_3/K_2CO_3$ at very low catalyst loading (0.01 mol%) s. A. da Conceição Silva, J.D. Senra, L.C.S. Aguiar, A.B.C. Simas, A.L.F. de Souza, L.F.B. Malta, O.A.C. Antunes, Tetrahedron Lett. *2010, 51* (30), 3883-5 [DOI: 10.1016/j.tetlet.2010.04.092]; *in supercritical carbon dioxide* with a reusable palladium phosphine complex anchored inside mesoporous SBA-15 s. X. Feng, M. Yan, T. Zhang, Y. Liu, M. Bao, Green Chem. *2010, 12* (10), 1758-66 [DOI: 10.1039/c004250a]; biaryl coupling *with potassium aryl(trifluoro)borates* (cf. *70*, 467s75) releasing arylboronic acids *in situ* on hydrolysis s. M. Butters, J.N. Harvey, J. Jover, A.J.J. Lennox, G.C. Lloyd-Jones, P.M. Murray, Angew. Chem., Int. Ed. *2010, 49* (30), 5156-60 [DOI: 10.1002/anie.201001522]; ligand-free coupling *'on water'* with sodium aryl(trihydroxy)borates s. B. Basu, K. Biswas, S. Kundu, S. Ghosh, Green Chem. *2010, 12* (10), 1734-8 [DOI: 10.1039/c0gc00122h]; with shelf-stable *o*-(aziridinio)aryl(difluoro)-borate inner salts s. R. Luisi, A. Giovine, S. Florio, Chem. Eur. J. *2010, 16* (9), 2683-7 [DOI: 10.1002/chem.200902056]; biaryl coupling *with hindered aryl(dimesityl)boranes* s. N. Wang, Z.M. Hudson, S. Wang, Organometallics *2010, 29* (18), 4007-11 [DOI: 10.1021/om1006903]; *ruthenium-catalyzed* Suzuki biaryl coupling with (1,5-cyclooctadiene)bis(2-methylallyl)-ruthenium(II)/NaOBu-*t* or CsOH s. M. Kawatsura, K. Kamesaki, M. Yamamoto, S. Hayase, T. Itoh, Chem. Lett. *2010, 39* (10), 1050-1 [DOI: 10.1246/cl.2010.1050]; *under nickel catalysis* (cf. *51*, 453s77) with pincer-type pyridine-tethered nickel(II) bis(benzimidazol-2-ylidene) complexes for coupling less-activated ar. halides or sulfonates s. T. Tu, H. Mao, C. Herbert, M. Xu, K.H. Dötz, Chem. Commun. *2010, 46* (41), 7796-8 [DOI: 10.1039/c0cc03107k]; Suzuki coupling of *o*-carbamyloxyboronic acid esters with Pd(PPh_3)$_4$/Na_2CO_3, also nickel(II)-catalyzed [Nakamura-type] coupling with ar. bromides s. *78*, 260.

(π-Allyl)(cyclopentadienyl)palladium(II)/chiral 1,1′-binaphthyl-2,2′-diyl phosphoramidite complexes [Pd(II)]*

Asym. synthesis of 3-cyano-4-methylene-1-tosylpyrrolidines from N-tosylketimines and 1-cyano-2-[(trimethylsilyl)methyl]allyl acetate ○

497.



A mixture of startg. imine (1 eq.), 1-cyano-2-[(trimethylsilyl)methyl]allyl acetate (1.5 eq.), (π-allyl)Pd(Cp) (5 mol%) and chiral phosphoramidite ligand (10 mol%) in toluene (0.2 *M*) stirred at 4° for 2-4 h → product. Y 99% (d.r. >20:1; e.e. >99%). The masked trimethylenemethane deriv. underwent cycloaddition with diverse N-tosylimines with high enantio- and diastereo-selectivity (twelve examples; Y 77-99%; d.r. 5:1 to >20:1; e.e. generally 95 to >99%). A 2-furyl substituent was tolerated on the imine component but gave reduced enantioselectivity (Y 99%; d.r. 15:1; e.e. 81%), while other N-subst. imines were unreactive (benzyl, 4-methoxyphenyl, methoxy) or gave complex mixtures (diphenylphosphoryl). Absolute configuration of products was determined by X-ray analysis in one case. F.e. and optimization s. B.M. Trost, S.M. Silverman, J. Am. Chem. Soc. *2010, 132* (24), 8238-40 [DOI: 10.1021/ja102102d].

Palladium(II) acetate/phenanthroline/boric acid/oxygen ←

α-Aryl-α,β-ethylenecarbonyl from α-diazocarbonyl compds. and arylboronic acids C=C(Ar)CO

with $Pd(PPh_3)_4$/*i*-Pr_2NH/benzoquinone cf. *73*, 486; with $Pd(OAc)_2$/phenanthroline/$B(OH)_3$ (50 mol%) under O_2 as sole reoxidant, (E)-α,β-diarylacrylic acid esters, s. Y.-T. Tsoi, Z. Zhou, A.S.C. Chan, W.-Y. Yu, Org. Lett. *2010, 12* (20), 4506-9 [DOI: 10.1021/ol1017961].

Palladium(II) acetate/silver carbonate/p-benzoquinone $Pd(OAc)_2/Ag_2CO_3/BQ$

***o*-Arylation of 2-phenoxypyridines with potassium aryl(trifluoro)borates** *74*, 516*s78* Ar-Ar′

Palladium(II) acetate/triphenylphosphine/cesium fluoride $Pd(OAc)_2/Ph_3P/CsF$

6-Acyl-6*H*-benzo[*c*]chromenes from arynes and α-(*o*-iodoaryloxy)ketones s. *68*, 464*s78* ○

Palladium(II) acetate/triphenyl phosphite/cesium carbonate or Bis(ammonia)-dichloropalladium(II)/4,4′-bis(trimethylammoniomethyl)-2,2′-bipyridyl dibromide/fluoroboric acid or Chiral 1,1′-binaphthyl-based bis(benzimidazol-2-ylidene)(dicarboxylato)palladium(II) complexes [Pd(II)]

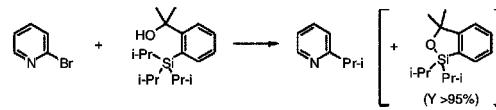
1,4-Addition of arylboronic acids C=C → CHC(Ar)

under palladium catalysis s. *62*, 449*s70*; synthesis of α-acylamino-β-arylcarboxylic acid esters with $Pd(OAc)_2$/$(PhO)_3P$/Cs_2CO_3, also β-vinyl analogs, s. D. Ray, A.M. Nyong, A. Natarajan, Tetrahedron Lett. *2010, 51* (19), 2655-6 [DOI: 10.1016/j.tetlet.2010.03.034]; 1,4-addition to enones with reusable $Pd(NH_3)_2Cl_2$ and 4,4′-bis(trimethylammoniomethyl)-2,2′-bipyridyl dibromide/fluoroboric acid as catalyst system *in water* (pH 1) s. S.-H. Huang, T.-M. Wu, F.-Y. Tsai, Appl. Organomet. Chem. *2010, 24* (9), 619-24 [DOI: 10.1002/aoc.1654]; **asym. 1,4-addition** (cf. *55*, 452*s70*) to α,β-unsatd. lactones (incl. coumarins) with a chiral fluorous rhodium(I) di(phosphine) complex [(R)-MeO-F_{12}-BIPHEP] s. T. Korenaga, R. Maenishi, K. Osaki, T. Sakai, Heterocycles *2010, 80* (1), 157-62 [DOI: 10.3987/com-09-s(s)40]; asym. 1,4-addition to enones with chiral cationic bis(alkene)-coordinated rhodium(I) bis(phosphoromonoamidite) complexes s. E. Drinkel, A. Briceño, R. Dorta, R. Dorta, Organometallics *2010, 29* (11), 2503-14 [DOI: 10.1021/om100248u]; asym. addition to N-carbalkoxy-2,3-dihydro-4(1*H*)-pyridones with chiral 1,1′-binaphthyl-based bis(benzimidazol-2-ylidene)(dicarboxylato)palladium(II) complexes s. Q. Xu, R. Zhang, T. Zhang, M. Shi, J. Org. Chem. *2010, 75* (11), 3935-7 [DOI: 10.1021/jo1006224]; **organocatalyzed asym. 1,4-addition** of aryl- and vinyl-boronic acids to enones with chiral O-monoacyltartaric acids s. M. Sugiura, M. Tokudomi, M. Nakajima, Chem. Commun. *2010, 46* (41), 7799-800 [DOI: 10.1039/c0cc03076g].

Palladium(II) acetate/1,1′-bis(diphenylphosphino)ferrocene/copper(II) hexafluoroacetoacetonate/potassium phosphate ←

Alkylarenes from ar. halides and trialkyl[*o*-(2-hydroxyprop-2-yl)phenyl]silanes under fluoride-free conditions Hal → R

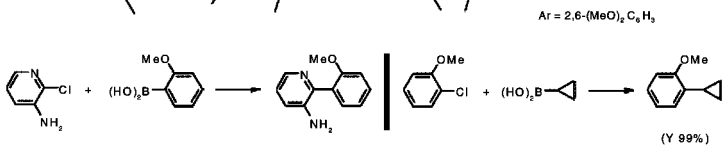
498.



2-Bromopyridine (1 mmol) and *tert*-butanol (1-2 ml) added sequentially via syringe to a mixture of K_3PO_4 (2.5 eq.), Cu(II)-hexafluoroacetoacetonate (3 mol%), dppf (4.2 mol%), $Pd(OAc)_2$ (1 mol%) and 2-[2-(triisopropylsilyl)phenyl]propan-2-ol (1.3 eq.) under argon in a vial, the vial sealed, the mixture stirred at 50° for 3 h, filtered through silica, concentrated *in vacuo*, and purified by chromatography on silica → 2-isopropylpyridine. Y 82% (isopropyl/*n*-propyl 20:1). This reaction appears remarkably versatile for coupling of prim. and sec. alkyl moieties with electron-diverse chloro- and bromo-(het)arenes (thirty-four examples; Y 53-98%) in the presence of alkene, alcohol, ester, nitro, nitrile, ether, ketone, aldehyde and silyl ether functionality. For coupling of sec. alkyl, butyl/functionalized prim. alkyl [using the appropriate alkyl(*diisopropyl*)-arylsilane], the presence of the copper catalyst was essential to avoid competing O-arylation, but was not required for methylation (using the trimethylarylsilane). The cyclic silyl ether by-product, isolated in near quantitative yield in most cases, was readily converted to the *o*-(trialkylsilyl)benzyl alcohol by treatment with alkyllithiums. It is noteworthy that the analogous prim. alcohol, 2-trimethylsilylbenzyl alcohol, effected mainly dehalogenation of 4-chlorobenzonitrile under these conditions (Y 75%), with 4-methylbenzonitrile obtained in <5% yield. F.e. and optimization s. Y. Nakao, M. Takeda, T. Matsumoto, T. Hiyama, Angew. Chem., Int. Ed. *2010, 49* (26), 4447-50 [DOI: 10.1002/anie.201000816].

Tris(dibenzylideneacetone)dipalladium/3-tert-butyl-4-(2,6-dimethoxyphenyl)-1,3-benzoxaphospholine/potassium phosphate ←

Suzuki coupling using 4-aryl-1,3-benzoxaphospholines as ligands $ArB(OH,R)_2$ → Ar-Ar′



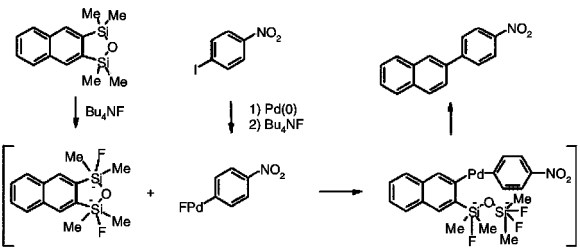
499.

with hindered substrates. A mixture of startg. arylboronate (1.5 eq.), K_3PO_4 (3 eq.), $Pd_2(dba)_3$ (1 mol%), benzoxaphospholine ligand (2 mol%) and mesityl bromide (1 mmol) in toluene/water (2:1; 3 ml) stirred at 100° for 24 h under N_2, cooled to room temp., extracted with methylene chloride, concentrated, and purified by chromatography on silica → 4-mesityl-3,5-dimethylisoxazole. Y 89%. A series of novel sterically-hindered phosphine ligands provided versatile, general and efficient homogeneous catalysis for the Suzuki-Miyaura synthesis of sterically hindered di-, tri- and tetra-*o*-subst. bi(het)aryls (twenty-four examples; Y 74-99%). The method was effective for coupling of aryl chlorides, bromides and triflates with (het)aryl-, alkyl- and vinyl-boronic acids and their pinacol esters. The air-stable ligands can be prepared in kilogram quantities from

commercially available substrates. F.e.s. W. Tang, A.G. Capacci, X. Wei, W. Li, A. White, N.D. Patel, J. Savoie, J.J. Gao, S. Rodriguez, B. Qu, N. Haddad, B.Z. Lu, D. Krishnamurthy, N.K. Yee, C.H. Senanayake, Angew. Chem., Int. Ed. *2010*, *49* (34), 5879-83 [DOI: 10.1002/anie.201002404].

Tris(dibenzylideneacetone)dipalladium/tetra-n-butylammonium fluoride $Pd_2(dba)_3/Bu_4NF$
2-Arylnaphthalenes from ar. halides and naphth[2,3-*c*][1,2,5]oxadisiloles ArHal → Ar-Ar′

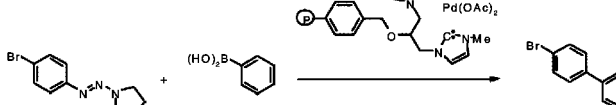
500.



under mild conditions. Tetra-*n*-butylammonium fluoride (6 eq.) in THF (6 ml) added to a mixture of naphth[2,3-*c*][1,2,5]oxadisilole (1 mmol), $Pd_2(dba)_3$ (5 mol%), and 4-nitrophenyl iodide (2 eq.) under N_2, the mixture stirred at 35° for 24 h, concentrated *in vacuo*, and purified chromatographically → 2-(4-nitrophenyl)naphthalene. Y 95%. Novel use of the oxadisilole as coupling partner was most effective for electron-poor ar. iodides (six examples; Y 58-95%; no reaction occurred with 4-methoxy- or 2,4-dinitro derivs.), while ar. bromides gave lower yields (29-54%; four examples). Variations in reaction conditions were unable to suppress homo-coupling of the ar. halides, which were major products at 80° (no cross-coupled products detected). F.e. and optimization s. H. Ding, Y. Chen, W. Cao, K. Wu, J. Chen, A.W.M. Lee, Synth. Commun. *2010*, *40* (7), 984-91 [DOI: 10.1080/00397910903029883].

Polymer-based palladium(II) bis(imidazol-2-ylidene) complexes/boron fluoride ←
Suzuki biaryl coupling with ar. triazenes Ar-N=NN≤ → Ar-Ar′

501.

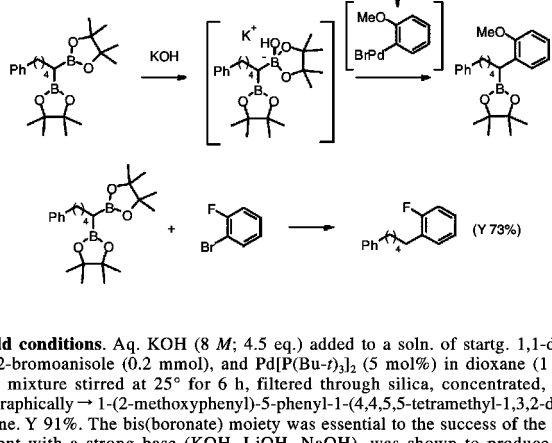


BF_3-etherate (1 eq.) added dropwise to a mixture of supported catalyst (1 mol%), startg. aryltriazene (0.5 mmol) and benzeneboronic acid (2 eq.) in dioxane (5 ml) at room temp. under argon, the mixture stirred for 12 h, filtered, concentrated *in vacuo*, and purified chromatographically → 4-bromobiphenyl. Y 71%. The supported catalyst showed good selectivity in the presence of aryl halides in this coupling of electron diverse ar. triazenes (as surrogate diazonium salts) and arylboronic acids (fifteen examples; Y 66-96%). The catalyst [for prepn. s. T. Kang et al., *37*, 902s*70*] was simply recycled via filtration, washing and drying and yields were only marginally reduced after 4 cycles (92% → 88%; 78% after 8 cycles). No reaction occurred in the absence of a Lewis acid. F.e. and optimization s. G. Nan, F. Ren, M. Luo, Beilstein J. Org. Chem. *2010*, *6*, No. 70 [DOI: 10.3762/bjoc.6.70].

Palladium N-heterocyclic carbene or phosphine complexes *[Pd]*
Suzuki coupling with alkyl halides R-R′

alkylarenes s. *64*, 453s*70*; with a rationally-designed, acetanilide-type *o*-palladated imidazol-2-ylidene complex for a *generalized* coupling of arylboronic acids with alkyl bromides, also biaryl coupling with ar. chlorides, and coupling of the latter or alkyl bromides **with B-alkyl-9-borabicyclo[3.3.1]nonanes** (cf. *67*, 459) s. G.-R. Peh, E.A.B. Kantchev, J.-C. Er, J.Y. Ying, Chem. Eur. J. *2010, 16* (13), 4010-7 [DOI: 10.1002/chem.200902842]; synthesis of aryl(fluoro)acetic from bromo(fluoro)acetic acid esters with $Pd(OAc)_2/Ph_3P/K_3PO_4$ s. C. Guo, X. Yue, F.-L. Qing, Synthesis *2010* (11), 1837-44 [DOI: 10.1055/s-0029-1218740]; Suzuki coupling of Li-arylborates with prim. or sec. halides *under iron catalysis* with a dichloro[1,2-bis(diarylphosphino)benzene]iron(II) complex/$MgBr_2$ s. T. Hatakeyama, T. Hashimoto, Y. Kondo, Y. Fujiwara, H. Seike, H. Takaya, Y. Tamada, T. Ono, M. Nakamura, J. Am. Chem. Soc. *2010, 132* (31), 10674-6 [DOI: 10.1021/ja103973a]; coupling of ar. chlorides **with** amide-functionalized **potassium alkyl(trifluoro)-borates** s. G.A. Molander, I. Shin, L. Jean-Gérard, Org. Lett. *2010, 12* (19), 4384-7 [DOI: 10.1021/ol101865e]; with potassium acylaminomethyl(trifluoro)borates s. G.A. Molander, M.-A. Hiebel, ibid. *12* (21), 4876-9 [DOI: 10.1021/ol102039c]; synthesis of N-protected diarylmethylamines from ar. halides and N-protected α-aminobenzylboronic acid esters with *inversion* of configuration s. T. Ohmura, T. Awano, M. Suginome, J. Am. Chem. Soc. *2010, 132* (38), 13191-3 [DOI: 10.1021/ja106632j].

Bis(tri-tert-butylphosphine)palladium(0)/potassium hydroxide *$Pd[P(Bu\text{-}t)_3]_2/KOH$*
α-Arylboronic acid esters $C[B(OR)_2]_2 \rightarrow C[B(OR)_2]Ar$
from ar. bromides and 1,1-diboronic acid esters



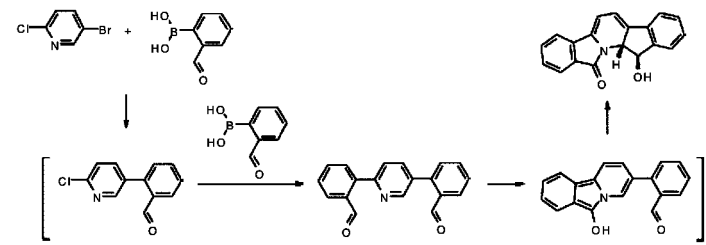
502.

under mild conditions. Aq. KOH (8 *M*; 4.5 eq.) added to a soln. of startg. 1,1-diborylalkane (1.5 eq.), 2-bromoanisole (0.2 mmol), and $Pd[P(Bu\text{-}t)_3]_2$ (5 mol%) in dioxane (1 ml) at room temp., the mixture stirred at 25° for 6 h, filtered through silica, concentrated, and purified chromatographically → 1-(2-methoxyphenyl)-5-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentane. Y 91%. The bis(boronate) moiety was essential to the success of the reaction and, on treatment with a strong base (KOH, LiOH, NaOH), was shown to produce monoborate intermediates which were not formed by monoboryl-alkanes under these conditions. The intermediate promoted rapid transmetalation and stabilization of a probable alkyl-palladium species, allowing arylation under mild conditions, thereby avoiding typical side-reactions associated with Suzuki-Miyaura coupling. The method was successful with electron-rich ar. bromides (incl. *o*-subst. derivs.), with mono-arylated products generally isolated as boronates

(seventeen examples; Y 53-95%) or oxidized (H_2O_2) to the corresponding benzylic alcohols (two examples; Y 42%, 65%). While 4-fluorobromobenzene reacted cleanly under these conditions, the 2- and 3-isomers apparently suffered concomitant protodeboration (Y 73% and 65% respectively). The analogous 1,1-borylsilyl- or 1,2-diboryl-alkanes did not react under these conditions. F.e. and one-pot arylation-oxidation to **sec. benzyl alcohols** (nineteen examples; Y 42-91%) s. K. Endo, T. Ohkubo, M. Hirokami, T. Shibata, J. Am. Chem. Soc. *2010*, *132* (32), 11033-5 [DOI: 10.1021/ja105176v].

Tetrakis(triphenylphosphine)palladium(0)/sodium carbonate $Pd(PPh_3)_4/Na_2CO_3$
7-Hydroxy-6a,7-dihydroindeno[3,2-*b*]isoindolo[1,2-*f*]pyrid-5-ones ○
from 5-bromo-2-chloro- or 2-bromo-5-iodo-pyridines and two *o*-borylaldehyde molecules
Palladium-catalyzed regio- and diastereo-selective double annelation

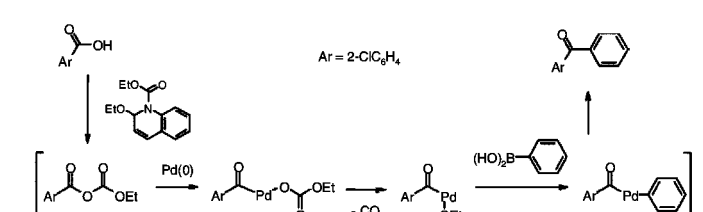
503.



Degassed solns. of *o*-formylbenzeneboronic acid (2.5 eq.) in methanol (5 ml) and Na_2CO_3 (5 eq.) in water (5 ml) added successively to a degassed toluene soln. (10 ml) containing $Pd(PPh_3)_4$ (10 mol%) and 5-bromo-2-chloropyridine (1 mmol), after heating for 12 h at 100°, the mixture cooled to room temp., extracted with ethyl acetate, dried ($MgSO_4$), concentrated, and the residue purified by chromatography on silica gel → product. Y 57% (single *trans* isomer). Eight further examples, in which the pyridine may be 4-, 6- or 4,6-di-substituted and the boronic acid may have methoxy, fluorine or *tert*-amino groups on the aromatic ring, gave yields of 12%, 17% and 31-60%. 2,5-Dibromopyridine did not afford the desired pentacyclic product, indicating that the C5 then C2 order of reactivity toward palladium is crucial. The postulated intermediate dialdehyde appears to undergo rapid intramolecular attack of the formyl group by pyridine nitrogen, followed by isomerization and intramolecular trapping of the second formyl group. F.e.s. Z.e.a. Chamas, O. Dietz, E. Aubert, Y. Fort, V. Mamane, Org. Biomol. Chem. *2010*, *8* (21), 4815-8 [DOI: 10.1039/c0ob00390e].

Tetrakis(triphenylphosphine)palladium(0)/N-carbethoxy-2-ethoxy-1,2-dihydroquinoline ←
Aryl ketones from carboxylic acids and arylboronic acids COOH → C(O)Ar

504.

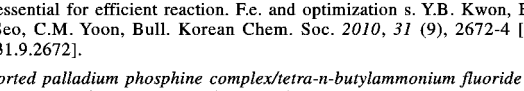


Phenylboronic acid (1.2 eq.) added to a soln. of 2-chlorobenzoic acid (0.66 mmol), EEDQ (1.5 eq.), $Pd(PPh_3)_4$ (3 mol%) and water (2.5 eq.) in DMF (1 ml) under argon, the mixture stirred at 60°

until reaction complete (TLC; 15 h), quenched with water, extracted with ethyl acetate, concentrated, and purified chromatographically → 2-chlorobenzophenone. Y 84%. Ketone formation was general, efficient and experimentally simple for electron-diverse arylcarboxylic acids and (het)arylboronic acids, and also for less reactive aliphatic carboxylic acids (using *2.5 eq.* boronic acid due to competing homocoupling) (sixteen examples; Y 73-99%). Some sterically-hindered *o*-subst. benzoic acids required heating at higher temp. (80°). Activation of the carboxylic acid occurs via mixed anhydride formation (detected by TLC), with the presence of water (2.5 eq.) being essential for efficient reaction. F.e. and optimization s. Y.B. Kwon, B.R. Choi, S.H. Lee, J.-s. Seo, C.M. Yoon, Bull. Korean Chem. Soc. *2010*, *31* (9), 2672-4 [DOI: 10.5012/bkcs.2010.31.9.2672].

Silica-supported palladium phosphine complex/tetra-n-butylammonium fluoride [Pd(0)]/Bu_4NF
Biaryls from ar. bromides and aryl(trialkoxy)silanes ArBr → Ar-Ar′

505.

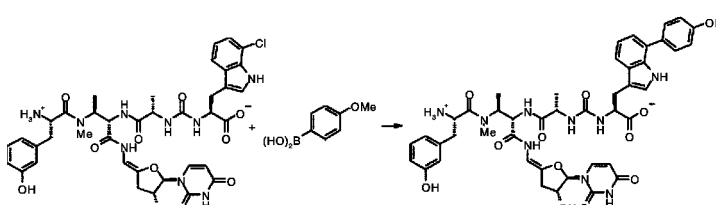


under continuous flow. Solns. of methyl 4-bromobenzoate (14 mmol) in xylene (48 ml) and triethoxy(phenyl)silane (3 eq.) and Bu_4NF (2 eq.) in the same solvent (36 ml) passed over a packed catalyst bed at 0.025 ml/min and 0.035 ml/min respectively for 3 h at 120°, and the eluate purified chromatographically → methyl 4-phenylbenzoate. Y 99%. The air and moisture stable catalyst [prepared from silica, chloro(diphenyl)phosphine and $Pd(acac)_2$] was most effective with a particle size of 70-270 mesh and catalyzed coupling of the silane with electron-diverse ar. bromides under continuous flow (four examples; Y 78-99%) **or under batch conditions** (eight examples; Y 92-100%). 2-Bromopyridine and 2-bromothiophene were less efficient coupling partners, giving conversions of 32-75% (Y 15-43%). In the batch process, catalyst recycling showed reduction in yield on the third run, while under continuous conditions the catalyst was effective for 40 h, allowing prepn. of up to 12 mmol of product. F.e.s. G.-R. Yang, G. Bae, J.-H. Choe, S.-W Lee, K.-H. Song, Bull. Korean Chem. Soc. *2010*, *31* (1), 250-2 [DOI: 10.5012/bkcs.2010.31.01.250].

Palladium(II) triflate/chiral 2,3:2′,3′-bis(isopropylidenedioxy)-6,6′-bis(di-p-tolylphosphino)biphenyl ←
Asym. synthesis of indenes from *o*-ethyleneboronic acid esters and acetylene derivs. ○
Chiral α-indenylketones s. *78*, 491; *68*, 461s*78*

Sodium tetrachloropalladate/3-[o-(dicyclohexylphosphino)phenyl]-2,4-dimethoxybenzenesulfonic acid sodium salt/potassium carbonate/microwaves ←
Suzuki biaryl coupling Cl → Ar
with peptidyl 7-chlorotryptophan residues in aq. media

506.



under mild conditions. A soln. of chloropacidamycin (0.001 mmol), Na_2PdCl_4 (5 mol%), water-soluble SPhos (12.5 mol%), K_2CO_3 (5 eq.), and 4-methoxybenzeneboronic acid (1.1 eq.) in water/acetonitrile (5:1; 0.7 ml) stirred at 80° under microwave irradiation (150 *W*) for 1 h, cooled, diluted with water, neutralized with 10% aq. HCl, washed with ethyl acetate, and the aq. layer evaporated to dryness → product. Y 67%. Introduction of a halogenase gene (prnA) into

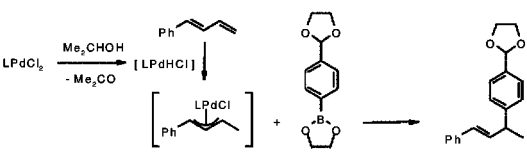
Streptomyces coeruleorubidus allowed biosynthesis of the unnatural halometabolite substrate, thereby providing a handle for further modification. Cross-coupling of the functionalized and thermally unstable substrate under Suzuki-Miyaura conditions was achieved using microwave irradiation in >95% conversion and moderate yields, even for unreactive (het)arylboronic acids (four examples; Y 33-67%). The reaction was also successful using crude product extracts from the biosynthesis. F.e., optimization and substrate prepn. s. A.D. Roy, S. Grüschow, N. Cairns, R.J.M. Goss, J. Am. Chem. Soc. *2010*, *132* (35), 12243-5 [DOI: 10.1021/ja1060406].

Bis(π-allylpalladium chloride)/2-(dicyclohexylphosphino)-2′,4′,6′-triisopropyl-3,6-dimethoxybiphenyl/potassium fluoride ←
(Trifluoromethyl)arenes from ar. chlorides Cl → CF_3
and trifluoromethyl(triethyl)silane s. *78*, 476

Bis(cinnamylpalladium chloride)/2-(dicyclohexylphosphinomethyl)-1,3-bis(2,6-di-isopropylphenyl)imidazolium iodide/cesium carbonate ←
Suzuki coupling Ar-R
with 2-phosphinomethyl-1,3-bis(2,6-diisopropylphenyl)imidazolium iodides as readily recyclable, hindered ligands s. *78*, 96

Dichloro((-)-sparteine)palladium(II)/(-)-sparteine/potassium tert-butoxide/isopropanol ←
Regiospecific palladium-catalyzed 1,2-hydroarylation of 1,3-dienes with arylboronic acid esters under aerobic conditions C=C → CHC(Ar)
(π-Allyl)chloro(hydrido)palladium(II) complexes as intermediates

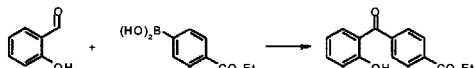
507.



Allylarenes. A soln. of K-*tert*-butoxide (0.5 mol%) in isopropanol (0.05 ml) added to a mixture of Pd[(-)-sparteine]Cl_2 (0.75 mol%), (-)-sparteine (20 mol%), (E)-1-phenyl-1,3-butadiene (0.5 mmol) and startg. boronic acid ester (3 eq.) in the same solvent (5 ml) under O_2 (balloon), the mixture stirred vigorously at 75° for 8 h, solvent removed *in vacuo*, water added, the mixture stirred for 10 min, extracted with ether, washed with brine, and purified by chromatography on silica → (E)-3-[4-(1,3-dioxolan-2-yl)phenyl]-1-phenylbut-1-ene. Y 80%. This novel approach to hydroarylation, using diverse arylboronates, was tolerant of a range of functional groups (incl. ester, nitrile, silyl ether, acetal), affording the 1,2-addition products with >99% selectivity (fourteen examples; Y 60-90%). The proposed mechanism, involving generation of a palladium hydride and hydride insertion to form a π-allyl complex, was supported by experimental evidence. F.e., optimization and substrate prepn. s. L. Liao, M.S. Sigman, J. Am. Chem. Soc. *2010*, *132* (30), 10209-11 [DOI: 10.1021/ja105010t].

Bis(benzonitrile)dichloropalladium(II)/copper(II) chloride/sodium hydrogen carbonate ←
***o*-Hydroxybenzophenones from *o*-hydroxyaldehydes and arylboronic acids** CHO → C(O)Ar

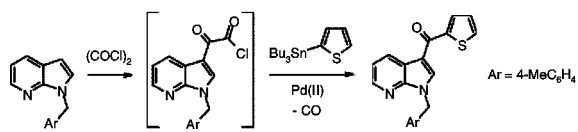
508.



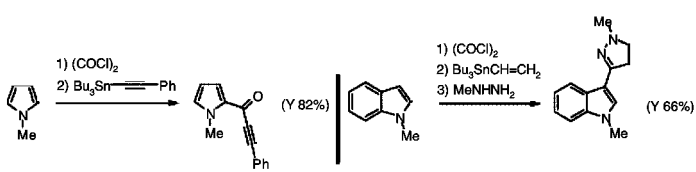
A mixture of salicylaldehyde (0.5 mmol), 4-ethoxycarbonylbenzeneboronic acid (1.7 eq.), $PdCl_2(PhCN)_2$ (5 mol%), $CuCl_2$ (10 mol%) and $NaHCO_3$ (2-3 eq.) in DMF (2 ml) stirred at 60° under O_2 (1 atm.) for 7 h → 4-ethoxycarbonyl-2′-hydroxybenzophenone. Y 74%. This mild and efficient formal arylation of aldehyde C-H was generally applicable to salicylaldehyde derivs. and electron-diverse arylboronic acids (incl. electron-deficient derivs. prone to homocoupling or protodeborylation) (twenty-nine examples; Y 54-96%) in the presence of halo, ether, nitro, ester,

sulfonate, alkene, diazo and aldehyde functionality (on the boronic acid component). A 2,6-diformylphenol gave the bis-arylated product (Y 68%). Yields were reduced when the O_2 atmosphere was replaced with air, or with excess or without $CuCl_2$. F.e. and optimization s. F. Weng, C. Wang, B. Xu, Tetrahedron Lett. *2010*, *51* (19), 2593-6 [DOI: 10.1016/j.tetlet.2010.02.166].

Dichlorobis(triphenylphosphine)palladium(II)/triethylamine $PdCl_2(PPh_3)_2/Et_3N$
Regiospecific acylation of pyrroles H → C(O)R
via decarbonylative Stille coupling of pyrrolylglyoxylic acid chlorides with unsatd. stannanes in one-pot



509.



3-Acyl[aza]indole derivs. Oxalyl chloride (1 eq.) added dropwise to a soln. of 1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-*b*]pyridine (5 mmol) in anhydrous dimethoxyethane (25 ml) at 0° under argon, the mixture warmed to room temp., stirred for 4 h, $PdCl_2(PPh_3)_2$ (5 mol%), anhydrous triethylamine (2 eq.) and tributyl(thiophen-2-yl)stannane (1 eq.) added sequentially, the mixture stirred at 60° [*caution*: CO evolution] until reaction complete (TLC; 1 h), cooled to room temp., methanol (25 ml) and KOH (2 eq.) added, the mixture stirred for 20 h, diluted with water, extracted with methylene chloride, concentrated *in vacuo*, and purified chromatographically → [1-(4-methoxybenzyl)-1*H*-pyrrolo[2,3-*b*]pyridin-3-yl](thiophen-2-yl)methanone. Y 62%. This novel and experimentally simple synthesis of 3-acyl-indoles and -azaindoles involves initial glyoxylation at the electronically-rich 3-position and subsequent decarbonylative Stille coupling using (het)aryl-, vinyl- or alkynyl-(tributyl)stannanes (seven examples; Y 58-81%). Similar treatment of N-methylpyrrole afforded **2-acylpyrroles** (four examples; Y 81-88%) with acylation occurring at the 3-position for 1,2,5-trimethylpyrrole (Y 57%). The use of 1 eq. of triethylamine was required to remove HCl produced during the first step, with a further 1 eq. suppressing the formation of non-decarbonylated Stille products (detected by TLC). The final treatment with KOH was found to be the most effective method for removal of tin residues. The method was extended to a 4-component synthesis of a 3-(Δ^2-pyrazolin-3-yl)indole (Y 66%) by *in situ* treatment of a 3-acryloylindole product with $MeNHNH_2$. F.e.s. B.O.A. Tasch, E. Merkul, W. Frank, T.J.J. Müller, Synthesis *2010* (13), 2139-46 [DOI: 10.1055/s-0029-1218802].

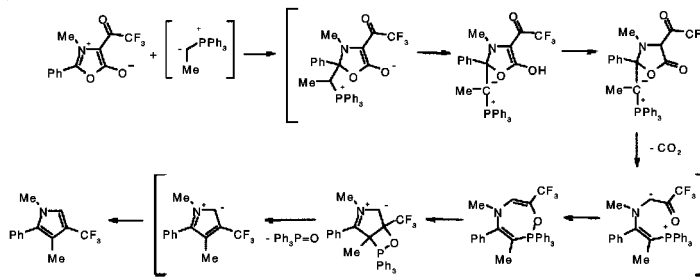
Carbon ↑ CC ↓↑ C

Without additional reagents *w.a.r.*
Benzene ring from 2-pyrones and acetylene derivs. ←
o-Silylboronic acid esters s. *22*, 877s*78*

Microwaves s. under $Sc(OTf)_3$ and $Pd(OCOCF_3)_2$ [\\\\]

n-Butyllithium/acetic acid or hexafluoroisopropanol *BuLi/AcOH or $(F_3C)_2CHOH$*
3-(Trifluoromethyl)pyrroles ←
from 4-(trifluoroacetyl)-5-hydroxyoxazolium betaines and alkylidenephosphoranes

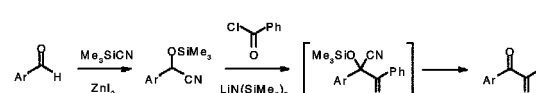
510.



n-Butyllithium (1.1 mmol) added to a stirred suspension of ethylphosphonium bromide (1.2 mmol) in THF (2 ml) at -20° under argon, the mixture stirred at room temp. for 30 min, a soln. of 4-trifluoroacetyl-3-methyl-2-phenyl-1,3-oxazolium-5-olate (0.5 mmol) in THF (3 ml) added at -20°, allowed to warm to room temp., stirred for 10 h, acetic acid (2 ml) added, heated at 80° for a further 10 h, quenched with 10% aq. Na_2CO_3, extracted with ethyl acetate, and purified by chromatography on silica gel → 4-trifluoromethyl-1,3-dimethyl-2-phenyl-1*H*-pyrrole. Y 87%. Reaction was particularly successful with linear alkylphosphonium ylids, affording 1,2-di- and 1,2,3-tri-subst. 4-trifluoromethylpyrrole derivs. in yields of 53-90% (ca. ten examples). Branched alkyl-, aryl-subst. or α-functionalized (OMe, SMe, $SiMe_3$) phosphonium ylids were less successful (five examples; Y 6-47%), however, presumably due to a combination of steric and electronic effects. Low yields and significant quantities of polar by-products were formed in the absence of an additive; acetic acid and hexafluoroisopropanol gave optimum results from a number screened, the additive possibly helping to promote the decarboxylation step. F.e.s. R. Saijo, Y. Hagimoto, M. Kawase, Org. Lett. *2010*, *12* (21), 4776-9 [DOI: 10.1021/ol1018689].

Lithium bis(trimethylsilyl)amide/potassium carbonate *$LiN(SiMe_3)_2/K_2CO_3$*
α-Diketones $RCH(OSi\in)CN \rightarrow RC(O)C(O)R'$
from α-siloxynitriles and carboxylic acid chlorides

511.



Ar = m-MeOC$_6$H$_4$

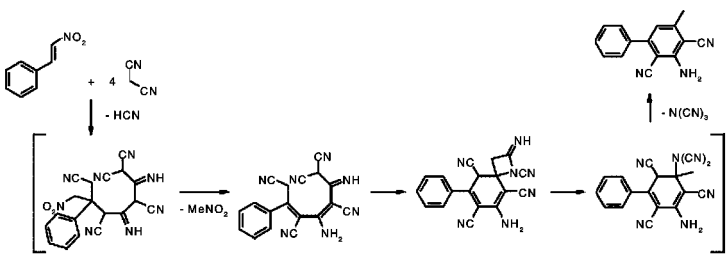
n-Butyllithium (2.5 *M* in hexanes; 4.25 mmol) added to a soln. of hexamethyldisilazane (4.67 mmol) in THF at 0°, the mixture cooled to -78° after 5 min, cannulated into a soln. of 3-methoxy-α-[(trimethylsilyl)oxy]benzeneacetonitrile (4.25 mmol) in THF (15 ml) at -78°, after a further 30 min the soln. cannulated into benzoyl chloride (5.1 mmol) in THF (15 ml) at the same temp., left for 30 min, warmed to 0° in an ice bath for 15 min, quenched with 10% aq. K_2CO_3 (40 ml), extracted with ether, and worked up with purification by flash chromatography → (3-methoxyphenyl)phenylethanedione. Y 90%. This is part of a 2-step conversion **from aldehydes**, which are converted to the substrates by classical cyanosilylation with Me_3SiCN/ZnI_2. This cross-benzoin-like condensation is simple, reliable, rapid, inexpensive, based on readily available substrates,

and is high-yielding for the synthesis of unsym. α-diketones by the overall coupling of aromatic (incl. 2-thienyl) aldehydes or cyclohexanecarboxaldehydes with aromatic (or 2-thienyl) carboxylic acid chlorides or cyclohexanecarbonyl chloride (nine examples of the second step; Y 65-94%). There was no reaction, however, with pyridine derivs. F.e.s. P. Nowak, D. Malwitz, D.C. Cole, Synth. Commun. *2010*, *40* (14), 2164-71 [DOI: 10.1080/00397910903219575].

Sodium carbonate Na_2CO_3

3-Aminobiaryl-2,4-dicarbonitriles
from β-nitrostyrenes and four malononitrile molecules

512.

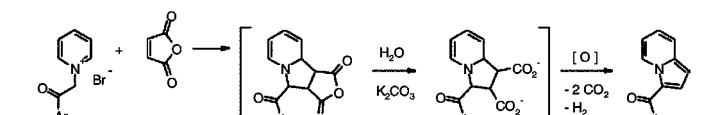


A mixture of β-nitrostyrene (1 mmol), malononitrile (*4.5 mmol*) and Na_2CO_3 (3 mmol) in 80% ethanol (4 ml) stirred at room temp. for 4 h, the resulting white precipitate removed by filtration, and recrystallized → 2,6-dicyano-5-methyl-3-phenylaniline. Y 85%. This direct route to multisubst. donor/acceptor biphenyls is mild, inexpensive and based on readily available substrates. A possible mechanism for the reaction (involving *12 intermediates*) is proposed, a key feature being elimination of nitroalkane (confirmed by the fact that the same products were obtained from β-methyl-β-nitrostyrenes). F.e.s. M. Adib, B. Mohammadi, S. Ansari, H.R. Bijanzadeh, L.-G. Zhu, Synthesis *2010* (9), 1526-30 [DOI: 10.1055/s-0029-1218717].

Potassium carbonate/tetrakis(pyridine)cobalt(II) dichromate $K_2CO_3/Py_4Co(HCrO_4)_2$

3-Acylindolizines from 1-β-ketopyridinium salts
via regioselective 1,3-dipolar cycloaddition with maleic anhydride
and oxidative bisdecarboxylation

513.



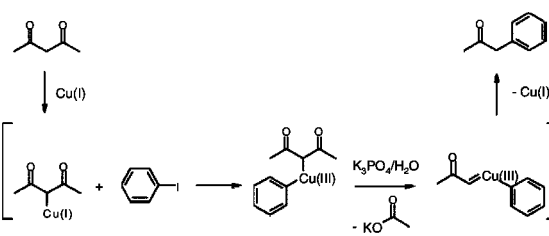
A novel approach to 1,2-unsubst. 3-functionalized indolizines, as well as benzo-fused analogs, is reported, such compounds having interesting biological properties, but not being readily accessible via the Tschitschibabin reaction or previous cycloaddition methods (e.g. requiring substrates such as nitroketene mercaptals). **E:** A stirred mixture of startg. 1-phenacylpyridinium salt (1 mmol), maleic anhydride (2 eq.), $Py_4Co(HCrO_4)_2$ (1 g) and K_2CO_3 (3.5 eq.) in DMF (15 ml) heated at 90° under N_2 for 3 h (TLC), solvent removed under reduced pressure, and the residue purified by flash chromatography on silica gel → 3-(*p*-chlorobenzoyl)indolizine. Y 78% (71% with freshly-prepared MnO_2 as oxidant). The method was applied to five further examples of 3-aroylindolizines

(Y 68-83%), which may carry alkoxy, fluorine or chlorine on the aroyl group, and to 1-acylpyrrolo-[1,2-*a*]quinolines (six examples; Y 73-89%) or -[2,1-*a*]isoquinolines (eight examples; Y 67-92%) from analogous quinolinium or isoquinolinium ylids; a 3-cyanopyrrolo[2,1-*a*]isoquinoline was also prepared (Y 63%). MnO_2 is less convenient to use as oxidant and gave lower yields (Y 65%, 66%). F.e.s. Y. Liu, Y. Zhang, Y.-M. Shen, H.-W. Hu, J.-H. Xu, Org. Biomol. Chem. *2010*, *8* (10), 2449-56 [DOI: 10.1039/c000277a].

Potassium fluoride s. under $SiCl_4$ *KF*
Silver oxide s. under $Pd(OAc)_2$ and $PdCl_2(PhCN)_2$ *Ag_2O*
Silver carbonate s. under $Pd(OAc)_2$ and $PdCl_2$ *Ag_2CO_3*
Copper(II) acetate s. under $Pd(OAc)_2$ *$Cu(OAc)_2$*

Copper(I) iodide/potassium phosphate *CuI/K_3PO_4*
α-Arylketones from ar. halides and β-diketones C(O)R → Ar
Copper(I)-catalyzed C-deacylative α-arylation

514.



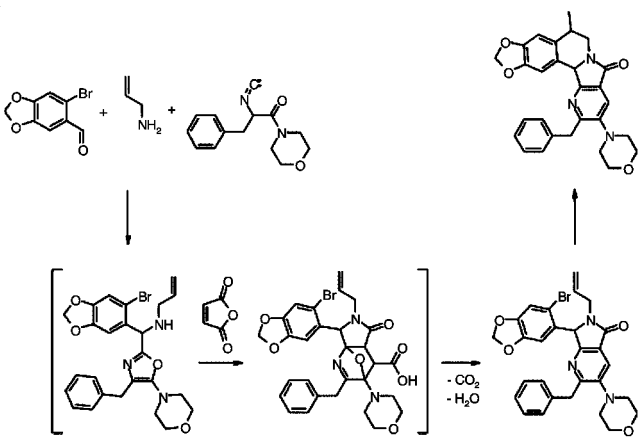
A mixture of iodobenzene (1 mmol), acetylacetone (3 mmol), CuI (10 mol%) and $K_3PO_4 \cdot 3H_2O$ (3 mmol) in DMSO (3 ml) stirred under N_2 at 90° for 20 h, quenched with dil. HCl (2 ml; 2 *M*), extracted with ethyl acetate, dried, and worked up with purification by flash chromatography on silica gel → 1-phenylpropan-2-one. Y 75%. The procedure is simple, mild, practical, ligand-free, complementary to existing methods, and generally applicable to the coupling of electron-diverse ar. iodides or bromides (bearing, for example, Me, *i*-Pr, MeO, Cl, F, COOH, COOR, NO_2 or Ph groups at the *m*- or *p*-position), with a number of aliphatic β-diketones (incl. α-alkyl derivs.) as well as β-diketones substituted by an aryl group at one of the terminal positions of the 1,3-dione residue (ca. twenty-five examples; Y 35-89%). There was no reaction, however, with *o*-subst. ar. iodides nor with 1,3-diphenylpropane-1,3-dione and α-aryl derivs. Significantly, there was also no reaction under anhydrous conditions, the water in the system being critically important in assisting the unprecedented activation of the cleaved C-C bond. A mechanism for the reaction, based on initial oxidative addition of the aryl iodide to Cu(I), has been proposed. F.e., regioselectivity, and comparison of copper catalysts s. C. He, S. Guo, L. Huang, A. Lei, J. Am. Chem. Soc. *2010*, *132* (24), 8273-5 [DOI: 10.1021/ja1033777].

Zinc/nickel phosphine complexes *Zn/[Ni(II)]*
Allylarenes from allylmalonic acid esters s. *78*, 314 $C(COOR)_2$ → Ar

Sodium tetrahydridoborate s. under EtCOOH *$NaBH_4$*

Scandium(III) triflate/microwaves *Sc(OTf)$_3$/[\\\\]*

9-Amino-5,11b-dihydro-6*H*-6a,11-diazabenzo[*c*]fluoren-7-ones from *o*-bromoaldehydes, α-isocyanocarboxylic acid amides and allylamine 4-Component triple ring closure via Diels-Alder reaction-lactamization-dehydration-decarboxylation of 2-(α-allylamino-*o*-bromobenzyl)-5-aminooxazoles with maleic anhydride and radical ring closure of 6-allyl-3-amino-7-(*o*-bromophenyl)-6,7-dihydropyrrolo[3,4-*b*]pyridin-5-ones

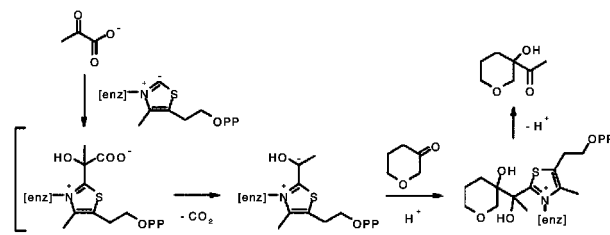


515.

A mixture of allylamine (1.1 eq.) and startg. *o*-bromobenzaldehyde (0.315 mmol) in benzene (1 ml) in a sealed CEM Discover™ microwave reaction tube irradiated at 50° (4 W) for 5 min, treated with $Sc(OTf)_3$ (3 mol%), irradiation continued at 50° (4 W) for 5 min, the α-isocyanoamide (1.3 eq.) added, the soln. irradiated at 80° (180 W) for 15 min, maleic anhydride (1.3 eq.) added then irradiated at 60° (4 W) for 15 min, and the crude product purified by silica gel column chromatography → intermediate 6-allyl-2-benzyl-7-(2-bromophenyl)-6,7-dihydro-3-morpholinopyrrolo[3,4-*b*]pyridin-5-one (Y 84%), 0.091 mmol of which was placed in a sealed CEM Discover™ microwave reaction tube, a soln. of Bu_3SnH (4 eq.) and 1,1′-azobis(cyclohexanecarbonitrile) [ACHN] (0.5 eq.) in benzene (1 ml) added in three portions at 30 min intervals, microwave irradiation resumed at 138° (280 W), solvent removed under reduced pressure, and the crude product purified by silica gel column chromatography → 10-benzyl-5-methyl-9-morpholin-4-yl-5,11b-dihydro-6*H*-1,3-dioxa-6a,11-diazaindeno[5,6-*c*]fluoren-7-one (Y 85%). This provides a rapid, efficient, atom-economical route to aza-analogs of nuevamine from readily available starting materials. Three further examples produced the pyrrolopyridinone in 30-80% yield and the diazabenzo[*c*]fluorenones in 40-85% yield, yields being lower in the presence of a phenolic group. The intermediate oxazole was isolated in one case in 82% yield. The final ring closure was unsuccessful under intramolecular Heck conditions. F.e. and one pot procedure (Y 72%) s. A. Zamudio-Medina, M.C. García-González, J. Padilla, E. González-Zamora, Tetrahedron Lett. *2010*, *51* (37), 4837-9 [DOI: 10.1016/j.tetlet.2010.07.047].

Norbornene s. under $Pd(OAc)_2$ ←

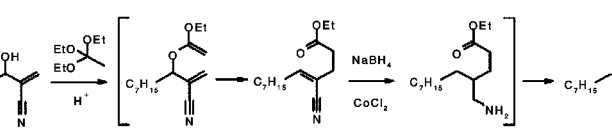
Flavoenzyme (YerE) ←
α-*tert*-Hydroxyketones from ketones $CO \rightarrow C(OH)C(O)Me$
Enzymatic asym. synthesis with addition of two C-atoms

516. 

The first examples are reported of the asym. synthesis of α-*tert*-hydroxyketones by enzymatic decarboxylative carboligation *with simple and functionalized, non-carbohydrate, ketones.* **E:** Sodium pyruvate (50 mmol) and the thiamine diphosphate-dependent flavoenzyme, YerE, from a *Yersinia pseudotuberculosis* sp. [as the overexpressed C-terminal His-tagged protein (450-800 mg crude protein)] in K-phosphate buffer (50 mmol; pH 8) containing $MgCl_2 \cdot 6H_2O$ (3 mmol), thiamine diphosphate (0.1 mmol) and FAD (0.01 mmol) added to the startg. acceptor ketone (20 mmol) in *tert*-butyl methyl ether (2-2.5 ml; 5% of the reaction volume), the temp. adjusted to 25° under slow stirring, and worked up after 20-25 h with purification by silica gel chromatography → product. Y 34% (97% conversion; e.e. 84%). The procedure is generally applicable to a wide range of cyclic and acyclic ketones, incl. α-aryloxy- and α-acoxy-ketones (six examples; Y 9-34%; e.e. 63-96%). However, the enantioselectivity was low with cyclohexanone, 2-tetralone, an α-(arylthio)ketone and 1,2-cyclohexanedione (0-22% e.e.), and only moderate (30%) with α- and β-keto-esters. There was no reaction at all with aryl, α,β-unsatd. or α-branched ketones. F.e. and regioselective carboligation with an unsym. diketone s. P. Lehwald, M. Richter, C. Röhr, H. Liu, M. Müller, Angew. Chem., Int. Ed. *2010*, *49* (13), 2389-2 [DOI: 10.1002/anie.200906181].

tert-Butyl hydroperoxide s. under $Rh(acac)(CO)_2$ *t-BuOOH*
Formic acid s. under $Pd(OCOCF_3)_2$ *HCOOH*
Acetic acid or hexafluoroisopropanol s. under BuLi *AcOH or* $(F_3C)_2CHOH$
Propanoic acid/cobalt(II) chloride/sodium tetrahydridoborate $EtCOOH/CoCl_2/NaBH_4$

2-Piperidones from β-hydroxy-α-methylenenitriles and orthocarboxylic acid esters ○
via Johnson-Claisen rearrangement-reductive ring closure

517. 

in one pot. A mixture of 2-cyano-3-hydroxydec-1-ene (1 mmol), ethyl orthoacetate (1 ml) and propanoic acid (3 drops) stirred at 145° for 2 h, concentrated *in vacuo*, the residue diluted with methanol (8 ml), $CoCl_2 \cdot 6H_2O$ (2 eq.) added, the soln. cooled to 0°, $NaBH_4$ (5 eq.) added in three portions over 15 min [*caution:* H_2 evolution], the mixture stirred for 30 min (black precipitate), concentrated *in vacuo*, quenched with 4 *M* aq. HCl, extracted with ethyl acetate, washed with water, and purified by chromatography on silica → 5-octylpiperidin-2-one. Y 65%. This operationally simple procedure utilizes readily available Baylis-Hillman alcohols (derived from ar. and aliphatic aldehydes and acrylonitrile) in reaction with ortho-acetate or -propanoate esters

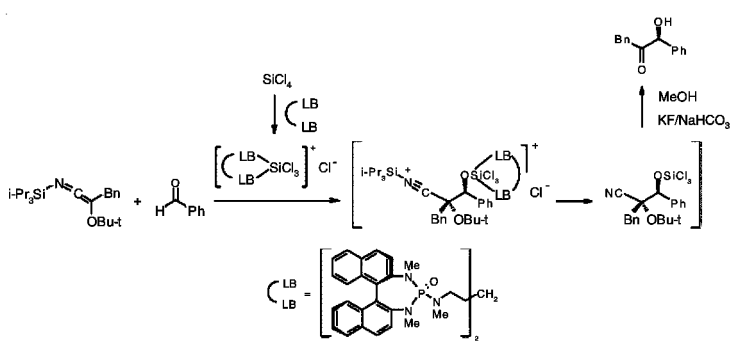
to afford intermediate (4Z)-4-cyano-4-alkenoates, which undergo reductive cyclization to 5- or 3,5-di-subst. 2-piperidones (nine examples; Y 53-65%). Structures were confirmed by X-ray analysis in two cases. F.e.s. D. Basavaiah, R.J. Reddy, D.V. Lenin, Helv. Chim. Acta *2010*, *93* (6), 1180-6 [DOI: 10.1002/hlca.200900352].

Benzoic acid s. under $Pd(OAc)_2$ *PhCOOH*

Silicon tetrachloride/chiral bis[N,N′-(1,1′-binaphthyl-2,2′-diyl)phosphoric acid triamides]/ ethyldiisopropylamine/potassium fluoride/sodium hydrogen carbonate ←

Asym. syntheses with N-silyl-1-alkoxyketenimines as acyl carbanion equivalents ←

518.



N-Silyl-1-alkoxyketenimines [readily prepared by treatment of protected cyanohydrins with silyl chlorides in the presence of $KN(SiMe_3)_2$] are stable and isolable representatives of a new class of compd. which serve as *aliphatic* **acyl carbanion equivalents**, notably for the **asym. synthesis of α-hydroxyketones from aldehydes** (cross-benzoin condensation) with high enantioselectivity. **E:** A flame-dried Schlenk flask charged with the (R,R)-bis[N,N′-(1,1′-binaphthyl-2,2′-diyl)-phosphoric acid triamide] (0.025 mmol), benzaldehyde (1 mmol) and anhydrous methylene chloride (5 ml; 0.2 *M* in aldehyde) under argon, the soln. cooled to -78° (internal), ethyldiisopropylamine (0.2 mmol) and $SiCl_4$ (1.1 mmol) added via syringe, stirred for 5 min at -78°, a 1.66 *M* soln. of the startg. N-silyl(alkoxy)keteneimine (1.4 mmol) in anhydrous methylene chloride (0.84 ml) added dropwise via syringe, stirring continued for 2 h at -78°, diluted with methanol (3.3 mmol), the quenched mixture stirred for 30 min at -78°, warmed to 0°, stirred again for 1.5 h before being transferred to a stirred, satd. aq. soln. of $NaHCO_3$ (10 ml) and KF (10 ml), the 2-phase mixture stirred vigorously for 2 h at room temp., filtered through a pad of Celite, and worked up with purification by chromatography on silica gel → product. Y 84% (after recrystallization; e.e. >99%). The procedure is applicable to electron-diverse and hindered ar. aldehydes in high yield and with very high enantioselectivity (six examples; Y 75-84%; e.e. 98 to >99%). The intermediate **chiral α-alkoxy-β-hydroxynitriles** were also isolated (prior to the aq. $KF/NaHCO_3$ hydrolysis) with exceptionally high diastereoselectivity (twelve examples; Y 84-95%; d.r. 96:4 to 99:1; e.e. >99% in all but one case). These products were readily elaborated by manipulation of the cyano group to give **chiral O-protected α,β-dihydroxy-aldehydes and -ketones** with retention of stereochemistry. A mechanism for the key 1,2-addition is proposed, based on Lewis base-activation of $SiCl_4$ by the bis(phosphorotriamide) to give a chiral trichlorosilyl cation of enhanced Lewis acidity for coordination to the aldehydic carbonyl group prior to attack by the nucleophilic silylketenimine. F.e.s. S.E. Denmark, T.W. Wilson, Nature Chem. *2010*, *2* (11), 937-43 [DOI: 10.1038/nchem.857].

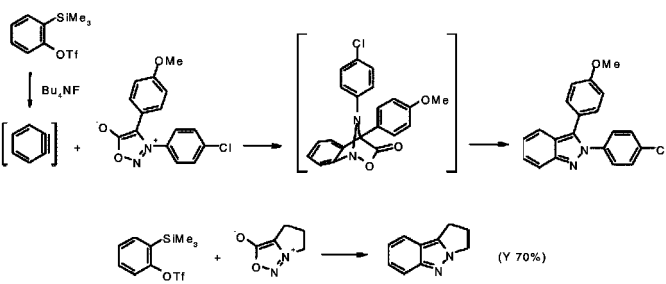
Triphenylphosphine s. under $Pd(OAc)_2$ and $PdCl_2$ *Ph_3P*

4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene s. under $Pd_2(dba)_3$ *XantPhos*

Chiral bis[N,N′-(1,1′-binaphthyl-2,2′-diyl)phosphoric acid triamides] s. under $SiCl_4$ ←

Oxygen s. under Pd(OAc)$_2$ O_2
Persulfate s. under Pd(OCOCF$_3$)$_2$ and PdCl$_2$(PhCN)$_2$ $S_2O_8^{2-}$
Dichromate s. under K$_2$CO$_3$ ←
Tetra-n-butylammonium fluoride Bu_4NF
2*H*-Indazoles from benzynes and sydnones C○
Regiospecific 1,3-dipolar cycloaddition-decarboxylative cycloreversion

519.



under mild conditions. Startg. *o*-silylaryl triflate (1.2 eq.) and sydnone (0.4 mmol) added sequentially to an oven-dried round-bottom flask, THF (4 ml if solid Bu_4NF used, 3.4 ml if Bu_4NF soln. used) added, the mixture stirred until homogeneous, treated with solid Bu_4NF (1.6 eq.) in one portion (or 0.6 ml of a 1 *M* soln. in THF, dropwise), the flask sealed with a septum, an N_2-balloon attached (for ventilation of CO_2), the mixture stirred at room temp. overnight, poured into satd. aq. $NaHCO_3$, extracted with ethyl acetate, the combined extracts washed with brine, dried ($MgSO_4$), filtered, evaporated, and the residue purified chromatographically → 2-(4-chlorophenyl)-3-(4-methoxyphenyl)-2*H*-indazole. Y 93%. CsF in acetonitrile was less effective for this reaction than Bu_4NF in THF (or acetonitrile). The method was applied to reaction of *o*-trimethylsilylphenyl triflate with eleven further sydnones which may bear hydrogen, alkyl, aryl, hetaryl, alk-1-ynyl or vinyl groups in the 4-position and an N-aryl group or be 3,4-fused (Y 63-95%), and to four substituted *o*-silyltriflates (Y 33%, 93-97%), a 1:1 mixture of regioisomers being obtained with an unsymmetrical aryne precursor that is neither electronically nor sterically biased. N-Unsubst. pyrazoles from sydnones cf. *27*, 900s*76*. F.e.s. C. Wu, Y. Fang, R.C. Larock, F. Shi, Org. Lett. *2010*, *12* (10), 2234-7 [DOI: 10.1021/ol100586r]; **1*H*-indazoles from 1,1-halogenohydrazones** with CsF/18-crown-6 s. C. Spiteri, S. Keeling, J.E. Moses, ibid. *12* (15), 3368-71 [DOI: 10.1021/ol101150t].

Tetra-n-butylammonium bromide s. under Pd(OAc)$_2$ Bu_4NBr
Tetra-n-butylammonium iodide s. under Pd(PPh$_3$)$_4$ Bu_4NI
Tetrakis(pyridine)cobalt(II) dichromate s. under K$_2$CO$_3$ $Py_4Co(HCrO_4)_2$
Cobalt(II) chloride s. under EtCOOH $CoCl_2$
Nickel phosphine complexes s. under Zn *[Ni(II)]*

Ruthenium carbene complexes and supported variants *[Ru(II)]*
Cross metathesis of ethylene derivs. C=C
update s. *49*, 932s*77*; with Grubbs-Hoveyda Type II complex confined within the nanocages of SBA-1 for improved recyclability s. H. Yang, Z. Ma, Y. Wang, Y. Wang, L. Fang, Chem. Commun. *2010*, *46* (45), 8659-61 [DOI: 10.1039/c0cc03227a]; with tailored, covalently-bonded, hybrid meso-structured, silica-supported ruthenium imidazol-2-ylidene complexes s. I. Karamé, M. Boualleg, J.-M. Camus, T.K. Maishal, J. Alauzun, J.-M. Basset, C. Copéret, R.J.P. Corriu, E. Jeanneau, A. Mehdi, C. Reyé, L. Veyre, C. Thieuleux, Chem. Eur. J. *2009*, *15* (44), 11820-3 [DOI: 10.1002/chem.200901752]; *solid-phase* cross-metathesis, notably with microwave enhancement,

s. A.A. Poeylaut-Palena, E.G. Mata, Org. Biomol. Chem. *2010, 8* (17), 3947-56 [DOI: 10.1039/c004729e]; synthesis of chiral ene-1,3-diboronic acid esters by cross-metathesis of β,γ-ethylene- and α,β-ethylene-boronic acid esters *en route* to chiral (Z)-1,2-*anti*-2,5-*anti*-triol monosilyl ethers s. S.A.M. Winbush, W.R. Roush, Org. Lett. *2010, 12* (19), 4344-7 [DOI: 10.1021/ol101789g]; synthesis of shape-persistent arylenevinylene macrocycles s. Y. Jin, A. Zhang, Y. Huang, W. Zhang, Chem. Commun. *2010, 46* (43), 8258-60 [DOI: 10.1039/c0cc02941f]; α,β-ethyleneketones from terminal ethylene derivs. and methyl vinyl ketone with Grubbs-Hoveyda Type II complex *en route* to α-methylamines s. F. Poulhès, R. Sylvain, P. Perfetti, M.P. Bertrand, G. Gil, S. Gastaldi, Synthesis *2010* (8), 1334-8 [DOI: 10.1055/s-0029-1218672]; *trans*-γ-amino-α,β-ethyleneketones from α,β-ethyleneketones and 2-ethyleneamines *en route* to N-protected pyrroles s. *78*, 203.

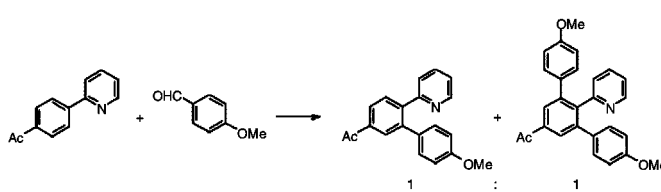
6-Nitro-2-spiro-3-chromene-tagged o-isopropoxybenzylidene(dichloro)ruthenium imidazolidin-2-ylidene complex *[Ru]*

Cross-metathesis C=C

with a simplified catalyst recovery by light-controlled phase switching s. *78*, 543

Acetoacetonato(dicarbonyl)rhodium(I)/tert-butyl hydroperoxide *$Rh(acac)(CO)_2$/t-BuOOH*

Rhodium-catalyzed directed arylation of 2-arylpyridines by oxidative decarbonylative cross-coupling with ar. aldehydes ArH + Ar′CHO → Ar-Ar′



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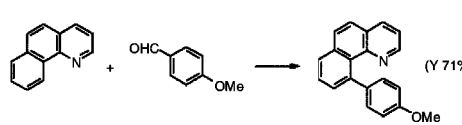
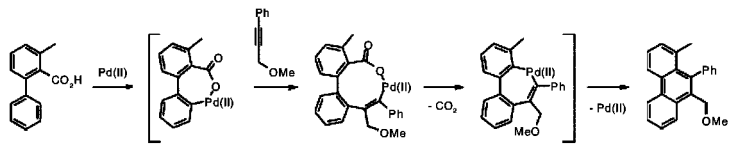


***o*-(2-Pyridyl)biaryls**. 4-(2-Pyridyl)acetophenone (0.2 mmol), 4-methoxybenzaldehyde (3 eq.), *tert*-butyl hydroperoxide (2.5 eq.) and chlorobenzene (0.4 ml) added to $Rh(acac)(CO)_2$ (10 mol%) under argon, the mixture heated at 150° for 24 h, with stirring, cooled to room temp., diluted with ethyl acetate, washed with aq. $NaHCO_3$, worked up, and purified by chromatography on silica gel → 3-(4-methoxyphenyl)-4-(2-pyridyl)acetophenone and 3,5-bis(4-methoxyphenyl)-4-(2-pyridyl)-acetophenone (1:1; Y 83%). Reaction tolerated a range of benzaldehyde derivs. (optionally subst. with methoxy, methyl, phenyl, cyano, ester, chloro, fluoro or bromo groups), with electron-rich substrates affording highest yields (the yield from 4-tolualdehyde (63%) being compromised by partial oxidation of the methyl group). Efficiency of the reaction was unaffected by substituents (Ac, Cl, Me) on the phenyl ring of the 2-arylpyridine. In all cases (with the exception of the illustrated *o*-subst. example), mixtures of mono- and bis-arylated products (10:5-10:18) were obtained. Choice of solvent was critical, with chlorobenzene proving optimal; *tert*-butyl hydroperoxide was used in preference to dicumyl peroxide due to the higher cost of the latter, coupled with the difficulties in removing 2-phenylpropan-2-ol. F.e. (fifteen; Y 56%, 64-87%), and a tentative mechanism s. Q. Shuai, L. Yang, X. Guo, O. Baslé, J. Am. Chem. Soc. *2010, 132* (35), 12212-3 [DOI: 10.1021/ja105396b]; **Pd-catalyzed decarboxylative acylation** of 2-arylpyridines with α-ketocarboxylic acids using $PdCl_2(PhCN)_2/Ag_2O/K_2S_2O_8$ in dioxane/AcOH/DMSO (cf. *77*, 526) s. M. Li, H. Ge, Org. Lett. *2010, 12* (15), 3464-7 [DOI: 10.1021/ol1012857];

Pd-catalyzed decarboxylative *o*-acylation of acetanilides with α-ketocarboxylic acids using $Pd(OCOCF_3)_2/(NH_4)_2S_2O_8$ in diglyme s. P. Fang, M. Li, H. Ge, J. Am. Chem. Soc. *2010*, *132* (34), 11898-9 [DOI: 10.1021/ja105245f].

Palladium(II) acetate/acridine/silver carbonate *[Pd(II)]*
Palladium(II) acetate/1,10-phenanthroline/benzoic acid/copper(II) acetate/ potassium hydrogen phosphate/tetra-n-butylammonium bromide ←
Phenanthrenes from *o*-carboxybiaryls and acetylene derivs. ○

521.



Dry DMF (5 ml) and 3-methoxy-1-phenylprop-1-yne (2 eq.) added to a mixture of $Pd(OAc)_2$ (10 mol%), acridine (0.5 eq.), Ag_2CO_3 (3 eq.) and 2-methyl-6-phenylbenzoic acid (0.5 mmol) in a flame-dried flask under argon, the resulting mixture stirred at 140° for 14 h, cooled to room temp., diluted with ethyl acetate, filtered through a short pad of silica, the filtrate concentrated *in vacuo*, the residue pre-adsorbed onto silica gel, and purified by flash chromatography → 9-(methoxymethyl)-1-methyl-10-phenylphenanthrene. Y 45% (regioselectivity 20:1). 2-Phenylbenzoic acid (and its methyl or methoxy derivs.) reacted smoothly under the conditions with a wide range of disubst. alkynes, tolerating nitro, chloro, fluoro, methoxy, ester and silyl ether functionality (ca. sixteen examples; Y 40-81%), with high regioselectivity (10:1-20:1) obtained from unsym. alkynes. 2-Naphthylbenzoic acids were also suitable substrates, affording benzo[*c*]phenanthrene and benzo[*a*]anthracene derivs. in yields of 60% and 66%, respectively (two examples). Acridine was found to be optimal from a number of pyridine ligands screened. F.e. and mechanistic considerations s. C. Wang, S. Rakshit, F. Glorius, J. Am. Chem. Soc. *2010*, *132* (40), 14006-8 [DOI: 10.1021/ja106130r]; **triphenylenes** from arylcarboxylic acids by Pd-catalyzed decarboxylative cyclotrimerization with $Pd(OAc)_2$/1,10-phenanthroline/benzoic acid/$Cu(OAc)_2$/K_2HPO_4/Bu_4NBr s. A.A. Cant, L. Roberts, M.F. Greaney, Chem. Commun. *2010*, *46* (45), 8671-3 [DOI: 10.1039/c0cc02547j].

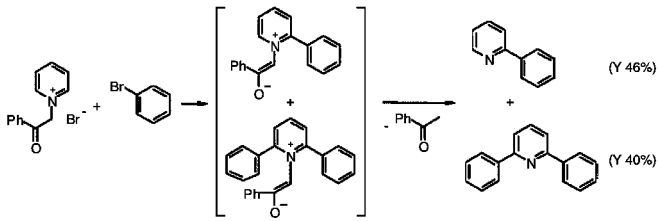
Palladium(II) acetate/silver oxide/potassium acetate *$Pd(OAc)_2/Ag_2O/KOAc$*
Arylacetylenes C≡C-COOH → C≡C-Ar
from α,β-acetylenecarboxylic acids and arylboronic acids
Palladium(II)-catalyzed decarboxylative cross-coupling

522.

under mild conditions. 4-Methoxybenzeneboronic acid (0.2 mmol), 4-bromophenylpropynoic acid (1.2 eq.), $Pd(OAc)_2$ (5 mol%), Ag_2O (1.5 eq.), KOAc (1.5 eq.), 4 Å molecular sieves (100 mg) and methylene chloride (1 ml) added sequentially to a flask, the mixture stirred vigorously at room temp. for 12 h, diluted with methylene chloride, filtered through Celite, concentrated *in vacuo*, and purified chromatographically → 1-bromo-4-[2-(4-methoxyphenyl)ethynyl]benzene. Y 89%. This novel, mild and efficient cross-coupling was successful with electron-diverse arylboronic acids and both aromatic and aliphatic carboxylic acids at catalyst loadings as low as 1 mol% (twenty-three examples; Y 70-99%) in the presence of nitro, ether, halo, nitrile, ketone and cyclopropane functionality. Low yields were obtained with sterically-hindered mesityleneboronic acid (41%) and 2-butynoic acid (50%). Copper salts were ineffective catalysts in this reaction. F.e. and optimization s. C. Feng, T.-P. Loh, Chem. Commun. *2010*, *46* (26), 4779-81 [DOI: 10.1039/c0cc00403k].

Palladium(II) acetate/triphenylphosphine/potassium carbonate $Pd(OAc)_2/Ph_3P/K_2CO_3$
2-Arylpyridines or 2,6-diarylpyridines
from N-phenacylpyridinium salts and ar. bromides

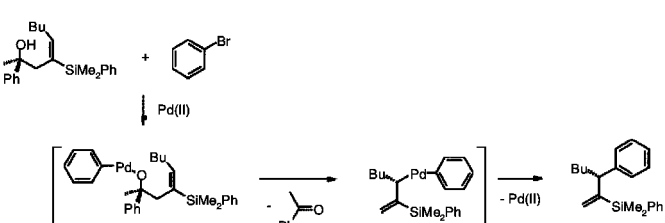
523.



A novel palladium-catalyzed direct *o*-arylation of pyridinium salts is reported in which the activating N-phenacyl group automatically departs, thereby avoiding an additional step for its cleavage. **E:** A mixture of N-phenacylpyridinium bromide (3 eq.), $Pd(OAc)_2$ (0.05 eq.), Ph_3P (0.15 eq.) and K_2CO_3 (4 eq.) in toluene (5 ml) stirred for 5 min at room temp. under N_2, bromobenzene (1 mmol) added, the mixture heated to reflux for 12 h, cooled to room temp., the solid removed by filtration, the solvent removed, and the crude product purified by chromatography on silica gel → 2-phenylpyridine (Y 46%) and 2,6-diphenylpyridine (Y 40%). Attempts to improve the selectivity for mono- vs. di-arylation by using different phenacyl groups (such as *o*-methyl or *p*-nitro-derivs.) was unsuccessful; however, using a *10:1* ratio of pyridinium salt to bromobenzene gave a 64% yield of 2-phenylpyridine (and 31% of the 2,6-diphenyl-deriv.), while a *1:4* ratio gave a 50% yield of 2,6-diphenylpyridine (and 12% of the 2-phenyl-deriv.). Iodobenzene gave similar results to bromobenzene, but chlorobenzene could not be used. 2-Arylpyridines were obtained exclusively, however, using ar. bromides having strong electron-withdrawing (NO_2, CO_2Me) or bulky substituents (four examples; Y 62-80%). DMF, DMSO, acetonitrile or toluene were all suitable solvents, but workup was more convenient with the latter. Strongly chelating ligands such as dppe or dppp were unsuitable, as were tert. amines (which may not be able to effect the enolization required to remove the phenacyl group) or strong bases such as NaOH, NaOBu-*t* or Cs_2CO_3 (which may effect nucleophilic substitution before arylation). F.e. (seven; monoaryl-deriv.: Y 35-49%; diaryl-deriv.: Y 32-40%) s. J. Xu, G. Cheng, D. Su, Y. Liu, X. Wang, Y. Hu, Chem. Eur. J. *2009*, *15* (47), 13105-10 [DOI: 10.1002/chem.200901399].

Palladium(II) acetate/triphenylphosphine/cesium carbonate $Pd(OAc)_2/Ph_3P/Cs_2CO_3$
Synthesis of allylarenes from ar. halides and 3-ethylene-*tert*-alcohols ArHal → Ar-C-C=C
Regioselective arylative retroallylation with asym. induction

524.



Chiral 1,2-disubst. allylarenes. Triphenylphosphine (20 mol%; 0.5 *M* toluene soln.) added to a Schlenk flask containing dry Cs_2CO_3 (1.5 eq.) and $Pd(OAc)_2$ (5 mol%) under argon, toluene

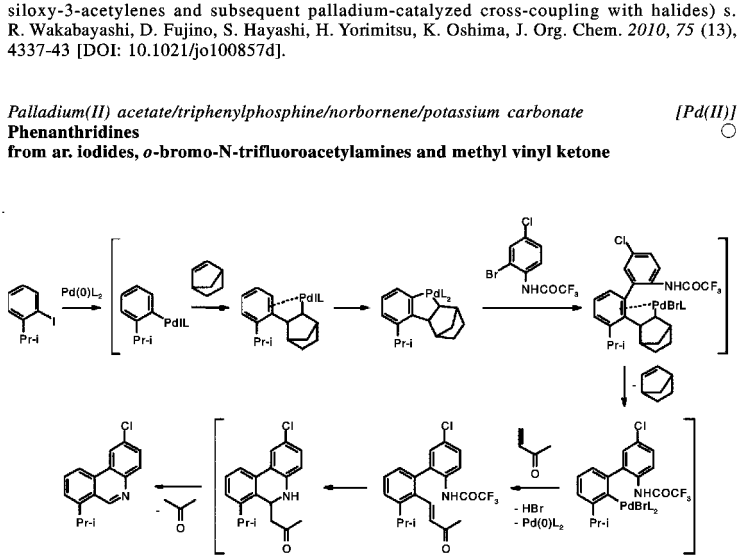
(0.4 ml), (S)-(E)-4-dimethylphenylsilyl-2-phenyl-4-nonen-2-ol (0.4 mmol; e.e. 94%) and bromobenzene (1.5 eq.) added sequentially at room temp., the resulting mixture heated at reflux for 24 h, cooled to room temp., water (20 ml) added, and worked up with purification by chromatography on silica gel → (R)-2-dimethylphenylsilyl-3-phenyl-1-heptene. Y 77% (e.e. 83%). Reaction is presumed to take place via an arylpalladium(II) homoallyloxide, followed by intramolecular approach of palladium to the *Si*-face of the alkene residue to give the corresponding (S)-allyl(aryl)palladium(II) prior to reductive elimination. High levels of chirality transfer were recorded (four examples; Y 72-84%; e.e. 77-92%). This followed a preliminary study of the racemic conversion which demonstrated that the method is applicable to a range of electron-diverse aryl bromides and the hindered 1-bromonaphthalene, as well as chlorobenzene and ethyl *p*-chlorobenzoate and 3-iodopyridine (ca. twenty examples in all; Y 35%, 67-89%). However, the yields decreased with increase in steric hindrance around the hydroxyl group of the homoallyl alcohols. F.e. and synthesis of the latter **from epoxides** (via intramolecular silylation of hydrosiloxy-3-acetylenes and subsequent palladium-catalyzed cross-coupling with halides) s. R. Wakabayashi, D. Fujino, S. Hayashi, H. Yorimitsu, K. Oshima, J. Org. Chem. *2010, 75* (13), 4337-43 [DOI: 10.1021/jo100857d].

Palladium(II) acetate/triphenylphosphine/norbornene/potassium carbonate *[Pd(II)]*

Phenanthridines

from ar. iodides, *o*-bromo-N-trifluoroacetylamines and methyl vinyl ketone

525.

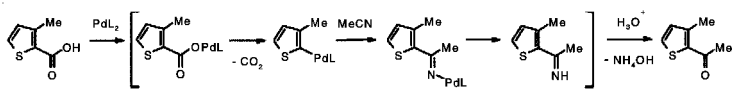


in one pot. K_2CO_3 (2.25 eq.) added to a mixture of $Pd(OAc)_2$ (5 mol%), triphenylphosphine (10 mol%), norbornene (1 eq.), *o*-iodoisopropylbenzene (1.1 eq.), 2-bromo-4-chloro-N-trifluoroacetylaniline (0.88 mmol) and methyl vinyl ketone (4 eq.) in DMF (20 ml), the mixture stirred at 105° for 24 h, cooled to room temp., diluted with ethyl acetate, washed with brine, concentrated *in vacuo*, and purified chromatographically → 2-chloro-7-isopropylphenanthridine. Y 93%. This experimentally simple 3-component synthesis, via palladium-catalyzed biaryl coupling-Heck coupling-intramolecular Michael addition-retro-Mannich reaction, uses readily available ar. iodide and 2-bromo-N-trifluoroacetylaniline derivs., and gave best results with methyl vinyl ketone as the one-carbon component (cf. methyl acrylate). A series of mono-, di- and tri-subst. phenanthridines were prepared, with by-product formation arising from Heck coupling of the ar. iodide and methyl vinyl ketone leading to recovery of the ar. bromide component in some cases (fourteen examples; Y 40-93%). F.e. and optimization s. N. Della Ca', E. Motti, A. Mega, M. Catellani, Adv. Synth. Catal. *2010, 352* (9), 1451-4 [DOI: 10.1002/adsc.201000114].

Palladium(II) acetate/oxygen $Pd(OAc)_2/O_2$
Decarboxylative Heck arylation C=CH → C=C(Ar)
cinnamic acid esters under rhodium(I) catalysis cf. *77*, 42; under palladium catalysis with $Pd(OAc)_2$ or $Pd(OAc)_2$/1,3-bis(2,6-diisopropylimidazol-2-ylidene) for coupling electron-rich or electron-deficient benzoic acids, respectively, *with oxygen* as terminal oxidant s. Z. Fu, S. Huang, W. Su, M. Hong, Org. Lett. *2010, 12* (21), 4992-5 [DOI: 10.1021/ol102158n].

Palladium(II) trifluoroacetate/6-methyl-2,2′-bipyridyl/formic acid/microwaves ←
(Het)aryl ketones from (het)arylcarboxylic acids and nitriles COOH + NCR → C(O)R
Palladium(II)-catalyzed decarboxylative acylation

526.

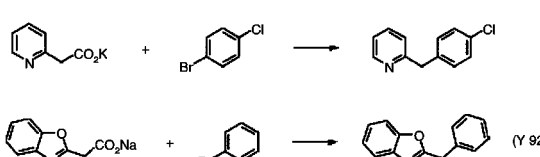


A mixture of 3-methylthiophene-2-carboxylic acid (0.5 mmol), $Pd(OCOCF_3)_2$ (8 mol%), 6-methyl-2,2′-bipyridyl (9.6 mol%), water (0.2 ml), and acetonitrile (2 ml) in a capped vial under air heated by microwaves at 130° for 1 h, formic acid (1 ml) added, heated at 100° for 1 h, concentrated, and purified chromatographically → 2-acetyl-3-methylthiophene. Y 84%. This novel method allows rapid synthesis of ketones from *o*-functionalized carboxylic acids of pyridine, thiophene or benzene and inexpensive nitriles, with CO_2 and NH_4OH being the only by-products. The method generally gave good results for alkyl cyanides (Me, Et, Pr and Bn) reacting with carboxylic acids carrying at least one electron-releasing group (sixteen examples; Y 51-94%), with low yields obtained from 2-methoxy-3-carboxynaphthalene (20%) and 2,5-dimethoxybenzoic acid (26%), or by using benzonitrile as acyl source (20%). In most cases, reactions were performed under different conditions to achieve optimum results. An ESI/MS study of the reaction identified key intermediates. F.e. and optimization s. J. Lindh, P.J.R. Sjöberg, M. Larhed, Angew. Chem., Int. Ed. *2010, 49* (42), 7733-7 [DOI: 10.1002/anie.201003009].

Palladium(II) trifluoroacetate/ammonium persulfate $Pd(OCOCF_3)_2/(NH_4)_2S_2O_8$
Palladium-catalyzed decarboxylative *o*-acylation with α-ketocarboxylic acids H → C(O)R
of 2-acetanilides s. *77*, 526s78; *78*, 520

Tris(dibenzylideneacetone)dipalladium/4,5-bis(diphenylphosphino)-9,9-dimethylxanthene/ sodium or potassium salt ←
2-Benzyl-N-heteroarenes $CH_2COOH → CH_2Ar$
from N-heteroarene-2-acetic acids and ar. halides
N-Directed palladium-catalyzed decarboxylative cross-coupling

527.



p-Chlorobromobenzene (0.3 mmol) and diglyme (0.6 ml) added via syringe under a counter flow of argon to a dried Schlenk tube charged with $Pd_2(dba)_3$ (0.5 mol%), XantPhos and K-pyridyl-2-acetate (0.36 mmol), the tube sealed with a screw cap, stirred at room temp. for 10 min, connected to a Schlenk line full of argon, stirred in a preheated oil bath (150°) for 24 h, the mixture cooled to room temp., diluted with ethyl acetate, filtered through a short silica gel column to remove the deposition, and the filtrate worked up with purification by chromatography on silica gel → product. Y 70%. The procedure is applicable to the coupling of a wide range of N-heteroarene-2-acetic acids (pyridine, quinoline, pyrazine, benzoxazole and benzothiazole derivs.) with electron-diverse aryl bromides, activated aryl chlorides **or with aryl triflates** (ca. forty-five examples; Y 56-98%).

There was no reaction, however, with [unactivated] chlorobenzene, nor with 2-(3-pyridyl)-, 2-(4-pyridyl)- or 2-phenyl-acetic acid, indicating that the nitrogen atom and the *o*-substitution are critically important factors in the reaction. This was further substantiated theoretically by DFT calculations, which confirm that nitrogen is coordinated to palladium(II) in the transition state. F.e.s. R. Shang, Z.-W. Yang, Y. Wang, S.-L. Zhang, L. Liu, J. Am. Chem. Soc. *2010*, *132* (41), 14391-3 [DOI: 10.1021/ja107103b].

Tetrakis(triphenylphosphine)palladium(0)/tetra-n-butylammonium iodide/potassium carbonate $Pd(PPh_3)_4/Bu_4NI/K_2CO_3$

3-Arylindoles from *o*-(trifluoroacetylamino)arylacetylenes and diazonium salts ○

s. *54*, 479s*78*

Palladium(II) chloride/triphenylphosphine/silver carbonate $PdCl_2/Ph_3P/Ag_2CO_3$

Decarboxylative cross-coupling of [hetero]arylcarboxylic acids with [hetero]arenes Ar-Ar′

2-(azolyl)oxazoles with $Pd(OAc)_2$/1,2-bis(dicyclohexylphosphino)ethane/$CuCO_3$ s. *77*, 526; 4-[hetero]-aryl-oxazoles and -thiazoles from the corresponding oxazole- and thiazole-carboxylic acids with $PdCl_2/Ph_3P/Ag_2CO_3$ s. F. Zhang, M.F. Greaney, Org. Lett. *2010*, *12* (21), 4745-7 [DOI: 10.1021/ol1019597].

Bis(benzonitrile)dichloropalladium(II)/silver oxide/potassium persulfate ←

Palladium-catalyzed decarboxylative acylation with α-ketocarboxylic acids H → C(O)R

of 2-arylpyridines s. *77*, 526s*78*; *78*, 520

Dichlorobis(triphenylphosphine)palladium(II)/triethylamine $PdCl_2(PPh_3)_2/Et_3N$

Acylation of the pyrrole ring

via one pot glyoxylation-decarbonylative Stille coupling s. *78*, 509

Dichlorobis(tri-o-tolylphosphine)palladium/tri-n-butyltin methoxide $PdCl_2(PAr_3)_2/Bu_3SnOMe$

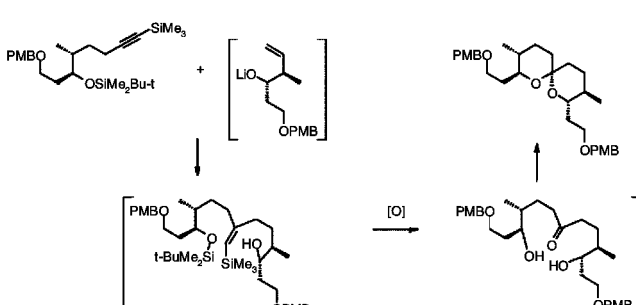
Aryl ketones from enol acetates and ar. bromides C=C(OAc) → CHC(O)Ar

Chiral β-subst. aryl ketones s. *78*, 313

Via intermediates *v.i.*

1,7-Dioxaspiro[5.5]undecanes from 6-(siloxy)silylacetylenes and 3-ethylenealcohols via oxidative C-cleavage ○

528.



A soln. of startg. silylacetylene (2.5 eq.) in toluene treated with $Ti(OPr\text{-}i)_4$ (2.5 eq.) at room temp., cooled to -78°, cyclopentylmagnesium chloride (1.9 *M* in ether; 5 eq.) added dropwise, the soln. allowed to warm slowly to -30° over 1 h, stirred at -30° for 2 h, cooled to -78°, a soln. of Li-alkoxide [generated by addition of *n*-BuLi (2.5 *M* in hexanes; 1.1 eq.) to startg. homoallylic alcohol (0.08 mmol) in ether (0.8 ml) at -78°, then warmed to 0°, and stirred for 10 min] added dropwise via syringe (using an additional 0.2 ml ether to aid the transfer), the soln. allowed to warm slowly to -30°, stirred at this temp. until completion by TLC, quenched with HCl (1 *N*),

worked up (cf. *78*, 406), the crude intermediate passed through a short silica plug (eluting with hexanes/ethyl acetate), dissolved in *tert*-butanol (0.5 ml), treated sequentially with pyridine (0.12 mmol), OsO_4 (4% aq.; 0.0024 mmol) and $NaIO_4$ (0.5 *M* aq.; 0.12 mmol) at room temp, stirred for 16 h, quenched with brine, extracted with ethyl acetate, the organic layer dried ($MgSO_4$), concentrated, the crude material dissolved in methylene chloride/methanol (2:1; 1 ml), treated with a little TsOH at room temp., the soln. stirred for 12 h, diluted with ethyl acetate (5 ml), washed with satd. $NaHCO_3$ (5 ml) and brine (5 ml), dried ($MgSO_4$), concentrated, and subjected to column chromatography → (2S,3R,6R,8S,9R)-2,8-bis[2-(4-methoxybenzyloxy)ethyl]-3,9-dimethyl-1,7-dioxaspiro[5.5]undecane. Y 52% overall. The startg. chiral **6-(siloxy)silylacetylenes** are prepared **from siloxy-3-ethylenes** with addition of two C-atoms by hydroboration with BBN, mono-oxidation of the resulting tert. borane with trimethylamine N-oxide, addition of Li-trimethylsilylacetylide, then iodine-induced 1,2-alkyl migration and base-induced (NaOH) elimination (six examples; Y 72-86%). This provides a highly convergent and concise entry to stereodefined spiroketals, as an alternative to aldol condensation. F.e. (three; Y 32-48% overall) and isolation of intermediate **chiral 5-silylmethylene-1,9-diol monosilyl ethers** (six; Y 22%, 74-88%) s. D.P. Canterbury, G.C. Micalizio, J. Am. Chem. Soc. *2010*, *132* (22), 7602-4 [DOI: 10.1021/ja102888f].

Elimination ⇑

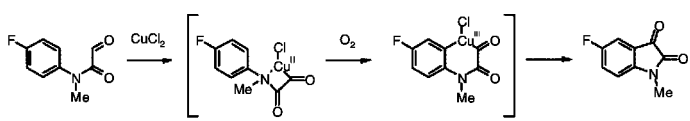
Hydrogen ↑ CC ⇑ H

Copper(II) chloride/oxygen $CuCl_2/O_2$

N-Subst. isatins from N-subst. glyoxylic acid anilides

Copper(II)-catalyzed ring closure using molecular oxygen as oxidant

529.



A mixture of 2-oxo-N-(4-fluorophenyl)acetamide (0.2 mmol), $CuCl_2$ (10 mol%) and anhydrous THF (3 ml) stirred at 100° under O_2 (1 atm.) until substrate consumed (TLC/GC; 12 h), cooled to room temp., diluted with ether, washed with brine, concentrated *in vacuo*, and purified by chromatography on silica gel → 5-fluoro-1-methylindoline-2,3-dione. Y 74%. This novel transition metal-catalyzed oxidative cyclization appears general, at catalyst loadings of 2-10 mol%, for cyclization of electron-diverse substrates. Yields of 56-90% were obtained for substrates bearing electron-releasing or mildly electron-withdrawing substituents (twelve examples), while those containing strongly electron-withdrawing *p*-CF_3 or *p*-Ac groups gave reduced yields of 30% and 50%, respectively. *m*-Subst. derivs. gave mixtures of 3- and 6-subst. products (1:1.6), while the NH-isatin was only obtained in trace amounts. Experimental evidence excludes the possibility of chelation controlled C-H activation or free-radical processes and was rationalized via formation of intermediate copper complexes. A copper complex was isolated from a reaction performed under argon but was unstable, decomposing to the isatin in 91% yield. F.e. and optimization s. B.-X. Tang, R.-J. Song, C.-Y. Wu, Y. Liu, M.-B. Zhou, W.-T. Wei, G.-B. Deng, D.-L. Yin, J.-H. Li, J. Am. Chem. Soc. *2010*, *132* (26), 8900-2 [DOI: 10.1021/ja103426d].

Activated carbon/oxygen C/O_2

Dehydrogenative aromatization of N-heterocyclics s. *14*, 901s*78* ←

Ethylene s. under Pd-C $CH_2{=}CH_2$

o-Iodoxybenzoic acid $ArIO_2$

Carbazoles by dehydrogenative aromatization s. *14*, 901s*78* ←

Phenyl iodosoacetate s. under $Pd(OAc)_2$ *$PhI(OAc)_2$*

2,3-Dichloro-5,6-dicyanoquinone/manganese dioxide *DDQ/MnO_2*
Dehydrogenation ←
with 2,3-dichloro-5,6-dicyanoquinone and manganese dioxide as reoxidant s. *78*, 542

N-Bromosuccinimide/potassium carbonate *NBS/K_2CO_3*
Oxazoles from Δ^3-oxazolines ←
Oxazole-4-carbonyl compds. s. *78*, 165

Oxygen or air s. under $CuCl_2$, Activated carbon and $Pd(OAc)_2$ *O_2*

Bromine·triethylenediamine *$DABCO·Br_2$*
Dehydrogenative aromatization of 5-membered N-heteroarenes s. *14*, 901s*78* ←

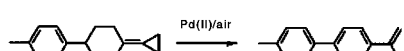
Manganese dioxide s. under 2,3-Dichloro-5,6-dicyanoquinone *MnO_2*

Palladium-carbon/ethylene *$Pd\text{-}C/CH_2{=}CH_2$*
Dehydrogenative aromatization of N-heterocyclics ←
with Pd-C s. *14*, 901; dehydrogenation of subst. 1,2,3,4-tetrahydro-quinolines, -isoquinolines and -carbazoles with Pd-C/ethylene or activated carbon/O_2 s. T. Tanaka, K.-i. Okunaga, M. Hayashi, Tetrahedron Lett. *2010, 51* (35), 4633-5 [DOI: 10.1016/j.tetlet.2010.06.118]; room-temperature aromatization of tetrahydro-β-carbolines with *o*-iodoxybenzoic acid, and application to alkaloid synthesis, s. J.D. Panarese, S.P. Waters, Org. Lett. *2010, 12* (18), 4086-9 [DOI: 10.1021/ol101688x]; pyrazoles and oxazoles from Δ^2-pyrazolines and -oxazolines, respectively, with bromine·triethylenediamine s. D. Azarifar, K. Khosravi, R.-A. Veisi, ARKIVOC *2010* (ix), 178-84.

Palladium(II) acetate/phenyl iodosoacetate *$Pd(OAc)_2/PhI(OAc)_2$*
1′-Tosylspiro[indoline-3,3′-pyrrolidin]-2-ones ○
via stereoselective intramolecular carboacoxylation-N-alkylation s. *78*, 81

Palladium(II) acetate/air *$Pd(OAc)_2/O_2$*
Isopropenylarenes from cyclopropylidenecyclohexanes ○
via palladium(II)-catalyzed oxidative aromatization

530.



***p*-Isopropenylbiaryls**. $Pd(OAc)_2$ (50 mol%) added to a soln. of 4-(4-methylphenyl)cyclohexylidenecyclopropane (0.2 mmol) in toluene (2 ml), the mixture stirred at 100° under air until reaction complete (TLC; 10 h), concentrated *in vacuo*, and purified chromatographically → 4-methyl-4′-prop-2-enylbiphenyl. Y 75%. This effective tandem C-H and C-C activation was shown (by deuterium labelling) to involve intramolecular hydrogen transfer from cyclohexyl to cyclopropane. The reaction was successful with electron-diverse 4-arylcyclohexylidenecyclopropanes (ten examples; Y 54-75%), with electron-poor substrates giving lowest yields, while isomeric 2- and 3-aryl-isomers gave complex mixtures, presumed due to steric effects. The high catalyst loading was essential for optimum yield and was not improved at higher loadings, while use of argon or oxygen atmospheres gave low yields or complex mixtures. F.e. and optimization s. M. Jiang, Y. Wei, M. Shi, Eur. J. Org. Chem. *2010* (17), 3307-11 [DOI: 10.1002/ejoc.201000299].

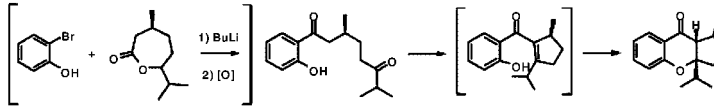
Oxygen ↑ CC ⇑ O

Triethylamine *Et_3N*
4-Cyano-3(2*H*)-furanones from α-acoxy-α′-cyanoketones s. *78*, 381 ○

Pyrrolidine $(CH_2)_4NH$

1,2.3,3a-Tetrahydrocyclopenta[*b*]chrom-9(9a*H*)-ones from *o*-hydroxyaryl 1,6-diketones ○
via diastereoselective organocatalyzed intramolecular aldol condensation-Michael addition

531.



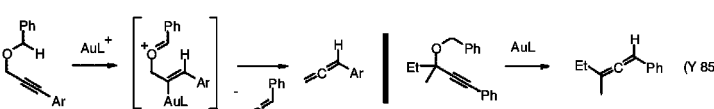
with asym. induction. Pyrrolidine (15 mol%) added to a soln. of 1-(2-hydroxyphenyl)-3,7-dimethyl-1,6-octanedione (0.45 mmol) in methanol (5 ml), the mixture stirred at 50° until reaction complete (TLC; 24 h), concentrated *in vacuo*, and purified chromatographically → (1S,3aR,9aR)-1,2,3,3a-tetrahydro-3a-isopropyl-1-methylcyclopenta[*b*]chromen-9(9a*H*)-one. Y 85%. In this synthesis of *cis*-fused chromones from 1,6-diketones, bulky isopropyl terminated derivs. gave single diastereomers (two examples; Y 85-86%), whereas a series of n,6-dimethyl-1,6-diketone derivs. gave mixtures of diastereomers, with the 3,6-dimethyl deriv. giving highest diastereoselectivity (d.r. 9:1; Y 88%) compared to 4,6- (d.r. 2:1; Y 82%) and 5,6-dimethyl isomers (d.r. 5:1; Y 87%), with the unsubst. *cis* analog isolated in 87% yield. Interestingly, in one case, heating either diastereomer with pyrrolidine (or triethylamine) afforded the original mixture of diastereomers in the same thermodynamic ratio via a recyclization process. F.e. and prepn. of startg. 1,6-diketones by one of two routes (2-4 steps) from *o*-bromophenol s. J.D. Butler, W.E. Conrad, M.W. Lodewyk, J.C. Fettinger, D.J. Tantillo, M.J. Kurth, Org. Lett. *2010, 12* (15), 3410-3 [DOI: 10.1021/ol101221c].

Supported silver nanoparticles/alcohols or carbon monoxide *Ag/ROH or CO*
Supported gold nanoparticles/alcohols *Au/ROH*
Ethylene derivs. from epoxides ▽ → C=C

heterogeneous conversion with $AgNO_3/Al_2O_3$ cf. *43,* 925; with supported Au or Ag nanoparticles using alcohols as reductant s. T. Mitsudome, A. Noujima, Y. Mikami, T. Mizugaki, K. Jitsukawa, K. Kaneda, Angew. Chem., Int. Ed. *2010, 49* (32), 5545-8 [DOI: 10.1002/anie.201001055]; with hydrotalcite-supported Ag nanoparticles (Ag/HT) using CO/H_2O as reductant for the deoxygenation of styrene oxides s. Y. Mikami, A. Noujima, T. Mitsudome, T. Mizugaki, K. Jitsukawa, K. Kaneda, Tetrahedron Lett. *2010, 51* (41), 5466-8 [DOI: 10.1016/j.tetlet.2010.08.031]; multistep conversion via epoxide ring opening with 2-mercaptobenzothiazole, followed by oxidation of the resulting 2-hydroxymercaptan to the sulfone and elimination, s. F.-L. Wu, B.P. Ross, R.P. McGeary, Eur. J. Org. Chem. *2010* (10), 1989-98 [DOI: 10.1002/ejoc.200901264].

(Acetonitrile)[dicyclohexyl(2,4,6-triisopropylbiphenyl-2′-yl)phosphine]gold(I) ←
hexafluoroantimonate
Allenes from benzyloxy-2-acetylenes C(OBn)C≡C → C=C=CH
via gold(I)-catalyzed 1,5-hydride shift and loss of benzaldehyde

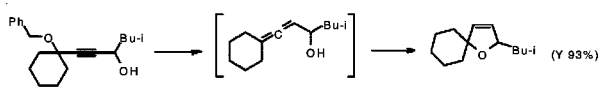
532.



Ar = 3-$CF_3C_6H_4$

under mild conditions. [Au(MeCN)(XPhos)]SbF_6 (4 mol%) added to a soln. of startg. propargyl ether (0.1 mmol) in dry chloroform (0.5 ml), the mixture heated at 60°, concentrated, and purified by flash chromatography on silica → 1-(propa-1,2-dienyl)-3-(trifluoromethyl)benzene. Y 84%. This apparently general transformation is rapid for readily available prim. (60°/0.5-1 h) and sec./tert. (20°/1-3 h) terminal and internal benzyl propargyl ethers, affording mono-, di- and tri-subst. allenes (twenty-one examples; Y 57-98%) in the presence of silyl ether, ester, nitrile, ether and

halo functionality. Tert. progargylic derivs. were particularly reactive, and in competitive experiments were converted exclusively in the presence of sec. analogs, while competition between sec. and prim. sites gave a ca. 6:1 mixture in favor of the sec. derived product. Deuterium-labelling experiments established initial 1,5-hydride transfer from the *benzylic C-H* with subsequent fragmentation affording a mixture of product and benzaldehyde.



F.e., optimization and trapping of the allenes *in situ* with nucleophiles to afford **2,5-dihydrofurans** (two examples; Y 90%, 93%), a 2-ethyleneether (Y 78%) and a cyclopentadiene (Y 66% as the N-phenylmaleimide cycloadduct) s. B. Bolte, Y. Odabachian, F. Gagosz, J. Am. Chem. Soc. *2010, 132* (21), 7294-6 [DOI: 10.1021/ja1020469].

Alcohols s. under Ag, Au and $Re_2(CO)_{10}$ *ROH*

Carbon monoxide s. under Ag *CO*

Triphenylphosphine s. under $Pd(dba)_2$ Ph_3P

Dirhenium decacarbonyl/alcohols/oxygen $Re_2(CO)_{10}/ROH/O_2$

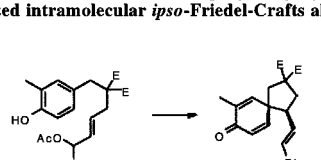
Ethylene derivs. from glycols C(OH)C(OH) → C=C

with Cp^*ReO_3/Ph_3P cf. *52*, 482; from terminal and internal glycols with a readily available low-valent rhenium carbonyl complex [$Re_2(CO)_{10}$] and a simple alcohol as a reducing agent under O_2 s. E. Arceo, J.A. Ellman, R.G. Bergman, J. Am. Chem. Soc. *2010, 132* (33), 11408-9 [DOI: 10.1021/ja103436v].

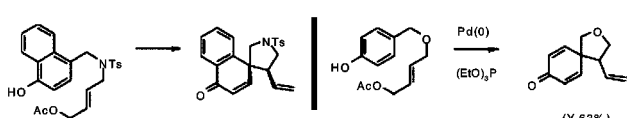
Bis(dibenzylideneacetone)palladium(0)/triphenylphosphine $Pd(dba)_2/Ph_3P$

7-Vinylspiro[5.n]alka-2,5-dien-4-ones from ω-(*p*-hydroxyaryl)-1-acoxy-2-ethylenes ○

Palladium(0)-catalyzed intramolecular *ipso*-Friedel-Crafts allylation

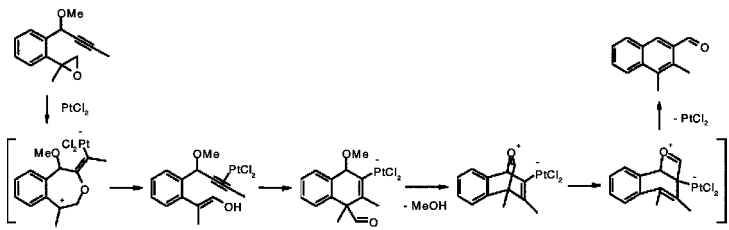


533.

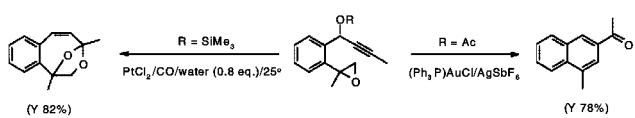


1-Vinylspiro[4.5]cyclodeca-6,9-dien-8-ones. A soln. of startg. allylic acetate (0.3 mmol), $Pd(dba)_2$ (5 mol%) and triphenylphosphine (12 mol%) in methylene chloride (1.5 ml) stirred at room temp. for 6 h, quenched with satd. aq. NH_4Cl, extracted with ethyl acetate, washed with brine, concentrated *in vacuo*, and purified chromatographically → product. Y 97% (d.r. 13.4:1). This novel and experimentally simple spirocyclization gave good results at catalyst loadings as low as 1 mol%, with malonate-, dimethyl acetal- and N-tosyl-tethered allylic acetates derived from prim. and sec. alcohols (twelve examples; Y 87-94%). A single O-tethered example required use of triethyl phosphite as ligand (Y 63%). Diastereoselectivity varied with substituents on the phenol ring, from 1.1:1 for a methyl substituent α to the ring junction to 13.4:1 for the illustrated β-methyl isomer. F.e. and optimization s. T. Nemoto, Y. Ishige, M. Yoshida, Y. Kohno, M. Kanematsu, Y. Hamada, Org. Lett. *2010, 12* (21), 5020-3 [DOI: 10.1021/ol102190s].

Platinum(II) chloride $PtCl_2$
2-Acylnaphthalenes from 1-(*o*-epoxyaryl)alkoxy-2-acetylenes via platinum-catalyzed 1,3-acyl group migration-cycloaromatization



534.



Naphthalene-2-carboxaldehydes. Dry dichloroethane (1 ml) added to a long tube containing $PtCl_2$ (0.03 mmol), a dichloroethane soln. (3 ml) of startg. epoxide (0.46 mmol) added, the resulting suspension stirred at 80° for 40 min under CO, the soln. concentrated, and eluted through a silica column with hexane → 3,4-dimethyl-2-naphthaldehyde. Y 91%. The method was applied to sixteen further examples, incl. mono-, 1,1-di- and 1,1,2-tri-subst. epoxy-derivs., affording the corresponding aldehydes or ketones in yields of 68-89%. Control experiments and deuterium-labelling studies established the mechanism proceeded as outlined via a π-alkyne-assisted epoxy-enol rearrangement. It was also observed that the chemoselectivity of cyclization of such 2-acetylenealcohol derivs. was sensitive to the catalyst and the oxy functionality, a bicyclic ketal being obtained from the O-trimethylsilyl-deriv. under Pt-catalysis in the presence of water (0.8 eq.) and 3-acetyl-1-methylnaphthalene being obtained from the O-acetyl-deriv. under gold catalysis (Y 78%). F.e.s. R. Chaudhuri, A. Das, H.-Y. Liao, R.-S. Liu, Chem. Commun. *2010*, *46* (25), 4601-3 [DOI: 10.1039/c002660c]; 3-arylated **1-alkoxynaphthalenes** from 1-(*o*-vinylaryl)alkoxy-2-acetylenes via retro-cyclopropanation under gold catalysis with (acetonitrile)[(2-biphenyl)di-*tert*-butylphosphine]gold(I) hexafluoroantimonate s. C.R. Solorio-Alvarado, A.M. Echavarren, J. Am. Chem. Soc. *2010*, *132* (34), 11881-3 [DOI: 10.1021/ja104743k].

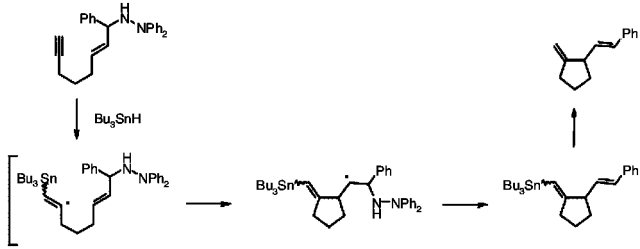
Via intermediates *v.i.*
Ethylene derivs. from epoxides via 2-benzothiazolyl β-hydroxysulfones
s. *43*, 925s*78*

Nitrogen ↑ CC ⇑ N

Potassium phosphate K_3PO_4
Ring closures via intramolecular nucleophilic displacement
of N-aryl-N-sulfonylamines s. *78*, 124

Tri-n-butyltin hydride/azodiisobutyronitrile/silica *$Bu_3SnH/AIBN/SiO_2$*
Radical ring closures with hydrazines
2-Methylene-1-vinylcyclopentanes from 2,7-enynehydrazines

535.



The use of hydrazinyl moieties as radical leaving groups has been described for the first time. **E:** A mixture of startg. 2,7-enynehydrazine (0.191 mmol), AIBN (30 mol%), tri-*n*-butyltin hydride (1.2 eq.) and benzene (4.5 ml) heated under reflux, with stirring, for 3 h, solvent removed under reduced pressure, and the residue purified by flash chromatography on silica gel → product. Y 60% (E/Z 96:4). A series of optimization experiments on similar model compds. established that the illustrated N,N-diphenylhydrazine afforded highest yields and stereoselectivity. Lower yields were obtained using dialkyl- or aralkyl-hydrazines, and reaction was completely suppressed with a dibenzyl analog. Yields were also dramatically affected by the nature of the α-substituent, with the greater steric hindrance of the phenyl group [compared with *n*-butyl (Y 37%) or methyl (Y 22%)] promoting radical elimination rather than radical quenching via H-abstraction from the tin hydride. F.e.s. S. Kobayashi, H. Hirao, T. Kawauchi, I. Ryu, Heterocycles *2010, 80* (2), 879-85 [DOI: 10.3987/com-09-s(s)115].

Rhodium(II) acetate *$Rh_2(OAc)_4$*
Chiral polymer-based rhodium(II) carboxylates *[Rh(II)]**
Intramolecular carbene insertion into carbon-hydrogen bonds with diazo compds.
s. *38,* 954s*50*; 1,5- and the rare *1,7-insertion* with readily cleavable *alkoxylamine-tethered* diazo compds. s. J. Wang, B. Stefane, D. Jaber, J.A.I. Smith, C. Vickery, M. Diop, H.O. Sintim, Angew. Chem., Int. Ed. *2010, 49* (23), 3964-8 [DOI: 10.1002/anie.201000160]; **asym. intramolecular carbene insertion** (cf. *47,* 955s*50*) with a chiral, recyclable (*100-fold*!) polymer-based dirhodium(II) tetracarboxylate [based on $[Rh_2(S\text{-}PTTL)_4]$, where PTTL = N-phthaloyl-*tert*-leucinate] with low leaching characteristics (0.28 ppm) s. K. Takeda, T. Oohara, M. Anada, H. Nambu, S. Hashimoto, ibid. *2010, 49* (39), 6979-83 [DOI: 10.1002/anie.201003730].

Halogen ↑ CC ⇑ Hal

Microwaves s. under Bu_3SnH [\\\\]
Silver carbonate s. under $Pd(OAc)_2$ *Ag_2CO_3*

Tri-n-butyltin hydride/triethylborane/oxygen or azodiisobutyronitrile *$Bu_3SnH/Et_3B/O_2$ or AIBN*
Hexabutyldistannane/boron fluoride *$(Bu_3Sn)_2/BF_3$*
Radical ring closures of unsatd. halides
ring closures of ethylenehalides s. *29,* 970s*50*; regioselective synthesis of azocan-2-ones via 8-*endo*-cyclization of α-carbamyl radicals with hexabutyldistannane *under Lewis acid catalysis* [e.g. with BF_3 or $Mg(ClO_4)_2$] to control stereoselectivity s. X. Fang, K. Liu, C. Li, J. Am. Chem. Soc. *2010, 132* (7), 2274-83 [DOI: 10.1021/ja9082649]; bicyclic carbocycles via radical ring closure of alkyne-functionalized cyclic α-halogenoketones (cf. *38,* 965) with $Bu_3SnH/Et_3B/O_2$ s. C. Prakash, G.G. Rajeshwaran, A.K. Mohanakrishnan, Synth. Commun. *2010, 40* (14), 2097-107 [DOI: 10.1080/00397910903219484]; 7- and 8-membered benzo-condensed sultams via aryl

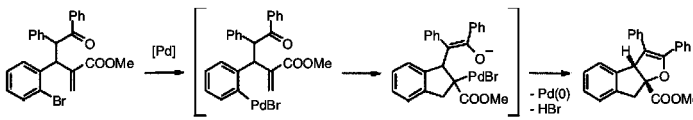
radicals (cf. *43*, 957s50) with Bu_3SnH/AIBN s. D. Biswas, L. Samp, A.K. Ganguly, Tetrahedron Lett. *2010, 51* (20), 2681-4 [DOI: 10.1016/j.tetlet.2010.03.089].

Tri-n-butyltin hydride/1,1′-azobis(cyclohexanecarbonitrile)/microwaves $Bu_3SnH/RN{=}NR/[\backslash\backslash\backslash\backslash]$
9-Amino-5,11b-dihydro-6*H*-6a,11-diazabenzo[*c*]fluoren-7-ones ○
via radical ring closure of 6-allyl-3-amino-7-(*o*-bromophenyl)-6,7-dihydropyrrolo[3,4-*b*]pyridin-5-ones s. *78*, 515

Tris(pentafluorophenyl)phosphine s. under $Pd(OAc)_2$ Ar_3P

Palladium(II) acetate/triphenylphosphine/cesium carbonate $Pd(OAc)_2/Ph_3P/Cs_2CO_3$
8,8a-Dihydro-3a*H*-indeno[2,1-*b*]furans from β-(*o*-bromoaryl)-γ-methyleneketones via regioselective intramolecular carbopalladation

536.



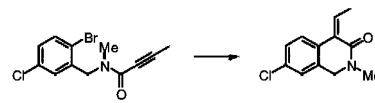
***cis*-8,8a-Dihydro-3a*H*-indeno[2,1-*b*]furan-8a-carboxylic acid esters.** A mixture of startg. γ-methyleneketone (1 mmol), $Pd(OAc)_2$ (10 mol%), Ph_3P (20 mol%) and Cs_2CO_3 (2 eq.) in toluene (3 ml) heated to reflux for 1 h, then subjected to aq. workup and chromatographic purification → product. Y 57%. This intramolecular 5-*endo*-*trig*-carbopalladation-intramolecular O-alkylation appears to be the first example of enolate O-alkylation with a $C(sp^3)$-bound palladium intermediate. The starting materials are readily prepared from *o*-bromoaldehydes via Baylis-Hillman reaction, deoxybromination and α-allylation of ketones. Yields of indenofurans were generally good to high (four examples; Y 42%, 74-81%; 35% for a pentacycle derived from 1-tetralone) for adducts derived from acrylates but lower, with formation of intractable side-products, for those derived from acrylonitrile (five examples; Y 26-41%, 62%). F.e.s. E.S. Kim, K.H. Kim, S. Park, J.N. Kim, Tetrahedron Lett. *2010, 51* (35), 4648-52 [DOI: 10.1016/j.tetlet.2010.06.127]; **benzofulvenes** from 2-(*o*-bromoaryl)acoxy-3-ethylenes, derived from Baylis-Hillman adducts of *o*-bromobenzaldehyde, via intramolecular Heck reaction-elimination using $Pd(OAc)_2/Ph_3P/Et_3N$ in refluxing acetonitrile s. K.H. Kim, S.H. Kim, B.R. Park, J.N. Kim, ibid. *51* (26), 3368-71 [DOI: 10.1016/j.tetlet.2010.04.110].

Palladium(II) acetate/tris(pentafluorophenyl)phosphine/silver carbonate/ potassium phosphate ←
***o,o′*-Diacoxybiaryls from aryloxy(*o*-bromoaryloxy)silanes** s. *78*, 539 ←

Tris(dibenzylideneacetone)dipalladium/tert. phosphines/sodium tert-butoxide ←
Dibenzo-fuzed N-heterocyclics from (*o*-chloroarylamino)styrenes ○
via ligand-controlled palladium-catalyzed ring closure – 5*H*-Dibenzo[*b*,*f*]azepines – 1-Vinyl-9*H*-carbazoles s. *78*, 454

Tetrakis(triphenylphosphine)palladium(0)/sodium formate $Pd(PPh_3)_4/HCOONa$
4-Alkylidene-1,4-dihydro-3(2*H*)-isoquinolones from N-*o*-bromobenzyl-α,β-acetylenecarboxylic acid amides via intramolecular reductive Heck reaction

537.



A soln. of startg. propynamide (0.4 mmol) in water/DMF (1:3; 6 ml) added to a mixture of $Pd(PPh_3)_4$ (3 mol%) and $HCOONa{\cdot}2H_2O$ (1.5 eq.) under N_2, the mixture heated at 100° for 3 h, cooled, diluted with methylene chloride, washed with brine, concentrated *in vacuo*, and purified

chromatographically → (Z)-7-chloro-4-ethylidene-2-methyl-1,4-dihydroisoquinolin-3-one. Y 82%. Electron-diverse N-2-bromobenzylpropynamides (prepared in two steps from commercially available 2-bromobenzaldehydes, prim. amines and 3-subst. propynoic acids) cyclized efficiently to the corresponding 4-alkylidene-1,4-dihydroisoquinolin-3-ones (eighteen examples; Y 69-85%). Methyl terminated propynamides gave marginally better yields than phenyl or *o*-tolyl analogs, presumed due to steric reasons. The products showed strong antiproliferative properties against several tumor lines. F.e., optimization and substrate prepn. s. T. Ma, W. Chen, G. Zhang, Y. Yu, J. Comb. Chem. *2010*, *12* (4), 488-90 [DOI: 10.1021/cc100021t].

Sulfur ↑ CC ⇑ S

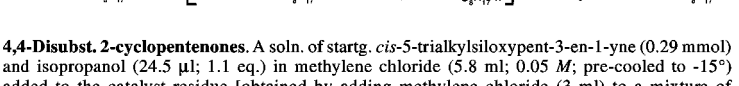
Sodium hydrogen carbonate $NaHCO_3$
Arylacetylenes Ar-C≡C
from aryl benzothiazol-2-ylsulfonylmethyl ketones s. *78*, 462

Remaining Elements ↑ CC ⇑ Rem

Without additional reagents *w.a.r.*
3-Alkoxy-1,2-dihydronaphthalene ring ○
via dehydrative intramolecular [4+2]-cycloaddition of 2-(1-silyl-1,5-dienyl)furans s. *78*, 471

[Tris(pentafluorophenyl)phosphine]gold(I) chloride/silver hexafluoroantimonate/ isopropanol ←
2-Cyclopentenones from (Z)-5-siloxy-3,1-enynes

538.



4,4-Disubst. 2-cyclopentenones. A soln. of startg. *cis*-5-trialkylsiloxypent-3-en-1-yne (0.29 mmol) and isopropanol (24.5 µl; 1.1 eq.) in methylene chloride (5.8 ml; 0.05 *M*; pre-cooled to -15°) added to the catalyst residue [obtained by adding methylene chloride (3 ml) to a mixture of $[(C_6F_5)_3P]AuCl$ (5 mol%) and $AgSbF_6$ (2.5 mol%), stirring for 10 min, filtering through a pad of Celite then concentrating, drying the residue over high vacuum for 2 h, then cooling to -15°], after stirring at room temp. for 10 min, the yellow mixture passed through a pad of Celite, concentrated, and the residual oil purified by flash chromatography on silica gel → product. Y 93%. The same product was obtained in 94% yield using $(Ph_3P)AuCl$ and $AgSbF_6$ at higher catalyst loading (10 mol% and 5 mol%) at higher temp. for a longer time (room temp. for 1 h). Nine further examples from acyclic or cyclic siloxyenynes afforded yields of 44-97%, a cation-stabilizing group such as aryl or vinyl being essential; the yields were considerably reduced with an electron-donating group such as *p*-methoxy on aryl, while poorer conversion was observed with a more electron-withdrawing *p*-fluorophenyl group (Y 73% after 7 h). The method was also applied to the racemic synthesis of a key intermediate of cuparenone, yields being considerably higher via formation and desilylation of a 2-silyl-2-cyclopentenone. F.e.s. S.E. An, J. Jeong, B. Baskar, J. Lee, J. Seo, Y.H. Rhee, Chem. Eur. J. *2009*, *15* (44), 11837-41 [DOI: 10.1002/chem.200901824]; **4-cycloheptenones** from 3-siloxy-1,6-enynes via gold-catalyzed siloxycyclization-[3.3]-sigmatropic rearrangement, **also 8-alkylidenebicyclo[4.3.0]nonan-2-ones** from 2-propargyl-1-siloxy-1-vinylcyclopentanes via carbocyclization and pinacol rearrangement, effect of triarylphosphine ligand and substitution pattern of substrate on reaction course, s. B. Baskar, H.J. Bae, S.E. An, J.Y. Cheong, Y.H. Rhee, A. Duschek, S.F. Kirsch, Org. Lett. *2008*, *10* (12), 2605-7 [DOI: 10.1021/ol8008733].

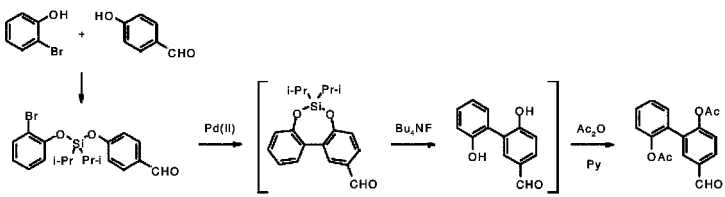
Diisobutylaluminum hydride/scandium(III) triflate $i\text{-}Bu_2AlH/Sc(OTf)_3$
Cyclic 3-ethylenealkoxylamines from (2-ethylenesilyl)hydroxamic acid esters
s. *78*, 480

Silica gel *SiO_2*
1,7-Dihydro-4-azepinones from 2-alkoxy-4-siloxyazabicyclo[4.1.0]hept-3-enes
s. *78*, 486

Hydrogen chloride *HCl*
7-Methyleneindolizidine and 8-methylenequinolizidine ring
via desilylative double ring closure s. *78*, 405

Palladium(II) acetate/tris(pentafluorophenyl)phosphine/silver carbonate/ potassium phosphate/tetra-n-butylammonium fluoride ←
o,o'-Diacoxybiaryls from *o*-bromophenols and phenols via aryloxy(*o*-bromoaryloxy)silanes ←

539.

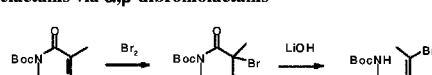


An oven dried 2.5 ml Wheaton vial charged with (2-bromophenoxy)diisopropyl(4-formylphenoxy)silane [(0.5 mmol) prepd. by stepwise silylation of *o*-bromophenol with *i*-Pr_2SiHCl/imidazole, chlorination of the resulting silane with trichloroisocyanuric acid, followed by reaction of the resulting chlorosilane with *p*-formylphenol], $Pd(OAc)_2$ (10 mol%), $(C_6F_5)_3P$ (20 mol%), K_3PO_4 (2 eq.), Ag_2CO_3 (1 eq.), 3 Å molecular sieves (100 mg) and anhydrous mesitylene (1 ml) under argon, the mixture stirred at 140° for 5 h, cooled to room temp., filtered through Celite, concentrated, the residue treated with *n*-Bu_4NF (2 eq.; 1 *M* soln. in THF), with stirring, at room temp. for 2 h, acetic anhydride (10 eq.) and pyridine (10 eq.) added, the mixture stirred overnight at room temp., diluted with water (100 ml), extracted with ether, and purified by flash chromatography on silica gel → 2,2′-diacetoxy-4-formylbiphenyl. Y 74%. Stepwise, or 'semi-one-pot' procedures may be used to isolate the intermediates at each stage, if required, the bis-phenols being converted to bis-acetates for ease of purification. This mild, general and efficient method is particularly useful for the synthesis of a wide range of *unsym.* biphenols, bearing a variety of functional groups (OMe, F, Cl, CF_3, CHO, NO_2, Br) on either ring (fourteen examples; Y 51-86%); *m*-substitution gives rise to product mixtures, with regioselectivity (1:1.2 to 9:1) determined by both steric and electronic factors. Use of 1- or 2-naphthols as substrates permits the preparation of unsym. phenol-naphthol or **binaphthol** derivs. in good yield (61-96%; eleven examples). Extensive optimization demonstrated that the bulky, electron-deficient monodentate ligand, $(C_6F_5)_3P$, in conjunction with a non-polar solvent, almost completely suppressed competing reductive debromination reactions. F.e.s. C. Huang, V. Gevorgyan, Org. Lett. *2010*, *12* (10), 2442-5 [DOI: 10.1021/ol100924n].

Carbon ↑ CC ⇑ C

Lithium hydroxide *LiOH*
N-Protected (E)-ω-amino-α,β-ethylenebromides from α,β-ethylenelactams via α,β-dibromolactams

540.



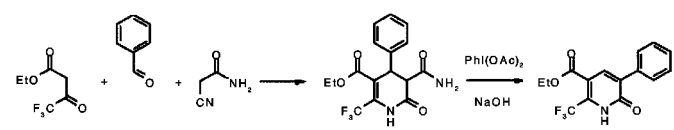
Bromine (4 ml) in methylene chloride (2 *M*) added over 10 min at -10° to a soln. of the startg. N-Boc-lactam (2.4 mmol) in the same solvent (2 ml), the mixture poured after 30 min into satd.

$NaHSO_3$ (aq.) and ice with the aid of ethyl acetate (*caution*: the quenching process is quite exothermic), and the organic layer worked up with chromatographic purification → intermediate dibromide (Y 85%), 1.1 mmol of which was charged into a flask, DMF/water (4:1; 3 ml) and LiOH hydrate (3 eq.) added at 0°, warmed to room temp. for 1 h, and the mixture directly chromatographed → product (Y 78%). Good overall yields were obtained from 5- to 7-membered lactams (four examples; 1st step: Y 72-85%; 2nd step: Y 69-81%). The second step involves **stereoselective decarboxylative ring opening**, the C-C bond of the intermediate dibromide rotating for *anti*-coplanar alignment of the departing carboxylate and bromide groups prior to elimination. F.e.s. S.-I. Jung, N.T. Tam, C.-G. Cho, Bull. Korean Chem. Soc. *2009*, *30* (12), 2863-4 [DOI: 10.5012/bkcs.2009.30.12.2863]; **(E)-(ω-1)-ethylene-ω,1-bromhydrins from α,β-ethylenelactones via α,β-dibromolactones** s. C.-G. Cho, W.-S. Kim, A.B. Smith III, Org. Lett. *2005*, *7* (16), 3569-72 [DOI: 10.1021/ol051376q].

(Acetonitrile)[(2-biphenyl)di-tert-butylphosphine]gold(I) hexafluoroantimonate *[Au]*
1-Alkoxynaphthalenes via retro-cyclopropanation s. *78*, 534

Phenyl iodosoacetate/sodium hydroxide *$PhI(OAc)_2$/NaOH*
3-Component synthesis of 3-aryl-2-pyridone-5-carboxylic acid esters from ar. aldehydes via oxidative 1,2-aryl migration in 4-aryl-3-carbamyl-3,4-dihydro-2-pyridone-5-carboxylic acid esters

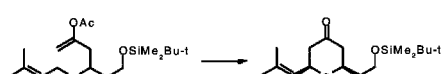
541.



3-Aryl-6-trifluoromethyl-2-pyridone-5-carboxylic acid esters. A mixture of benzaldehyde (1.5 mmol), cyanoacetamide (1 eq.), ethyl 4,4,4-trifluoro-3-oxobutanoate (1 eq.) and piperidine (0.25 eq.) in ethanol (15 ml) refluxed for 2 h, the solvent evaporated, and the residue purified by chromatography on silica gel → ethyl 5-carbamoyl-6-oxo-4-phenyl-2-(trifluoromethyl)-1,4,5,6-tetrahydropyridine-3-carboxylate (Y 69%), 1 mmol of which in ethanol (10 ml) containing NaOH (2.5 eq.) treated with phenyl iodosoacetate (1.5 eq.) with stirring, the mixture heated to reflux for 2 h, solvent removed by rotary evaporation, the residue dissolved in water (20 ml), neutralized with dil. HCl, extracted with ethyl acetate, the organic layer dried (Na_2SO_4), and the residue isolated and purified by chromatography on silica gel → ethyl 6-oxo-5-phenyl-2-(trifluoromethyl)-1,6-dihydropyridine-3-carboxylate (Y 83%). The method was applied to a range of electron-diverse ar. aldehydes, the presence of substituents appearing to have little effect on reactivity in the first step (ten examples giving yields of 63-93%; *o*-nitrobenzaldehyde or furfural requiring prolonged reaction times at room temp. to afford only 27% or 33% yield, respectively, however; Y 63% for a 6-methyl-deriv.). Substituents were also well tolerated for the aryl migration, although there was a steric effect (five examples, Y 73-82%; 11% and 43% for *o*-chloro- and *o*-methoxyphenyl-derivs.; Y 89% for a 6-methyl-deriv.). Treatment of the intermediate 4-phenyl-3,4-dihydro-2-pyridone with $PhI(OAc)_2$ in the *absence* of base afforded the 3-(carbethoxyamino)-3,4-dihydro-4-phenyl-deriv. (Y 89%). F.e.s. H. Yi, L. Song, W. Wang, J. Liu, S. Zhu, H. Deng, M. Shao, Chem. Commun. *2010*, *46* (37), 6941-3 [DOI: 10.1039/c0cc01815e].

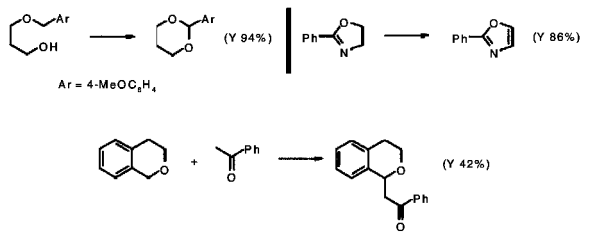
2,3-Dichloro-5,6-dicyanoquinone/manganese dioxide/2,6-dichloropyridine ←
Catalytic oxidations with 2,3-dichloro-5,6-dicyanoquinone and manganese dioxide as reoxidant ←

542.



Tetrahydro-4-pyrones from 3′-alkoxyenolesters. A suspension of startg. homoallyl ether (0.12 mmol), 2,6-dichloropyridine (1.9 eq.), MnO_2 (5.8 eq.) and 4 Å molecular sieves (60 mg) in

anhydrous nitromethane (1.2 ml) stirred at room temp. for 15 min, DDQ (5 mol%) added, stirred until reaction complete (TLC; 48 h) with addition of further DDQ (5 mol%) after 10 and 24 h, quenched with triethylamine, concentrated, and purified chromatographically → *cis*-2-[2-(*tert*-butyldimethylsilyloxy)ethyl]-6-(2-methylprop-1-en-1-yl)dihydro-2*H*-pyran-4(3*H*)-one. Y 79%. The use of MnO_2 as an inexpensive, non-acidic and environmentally benign reoxidant for DDQ produced a system that was as effective as DDQ alone, albeit at a reduced reaction rate, with tetrahydropyrones isolated by simple filtration and chromatography (nine examples; Y 68-92%), in the presence of silyl ether, electron-rich alkene and prim. alcohol functionality. The system was also effective for cleavage of 4-methoxybenzyl ethers (Y 90%), cyclization of a mono-benzyl-1,3-propanediol to a 2-aryl-1,3-dioxane (Y 94%), dehydrogenation of 1,4-dihydronaphthalene (Y 96%) and 2-phenyl-2-oxazoline (Y 86%), and prepn. of 2-benzoylmethylisochroman via oxidative coupling of isochroman and acetophenone (Y 42%).



Attempted biaryl formation from an electron-rich toluene was unsuccessful, however, attributed to deactivation of MnO_2 under the strongly acidic conditions ($MeSO_3H$) employed. F.e.s. L. Liu, P.E. Floreancig, Org. Lett. *2010, 12* (20), 4686-9 [DOI: 10.1021/ol102078v].

Ruthenium(II) indenylidene, imidazol[idin]-2-ylidene or bis(imidazol[idin]-2-ylidene) [Ru(II)] complexes

Ring-closing metathesis ○

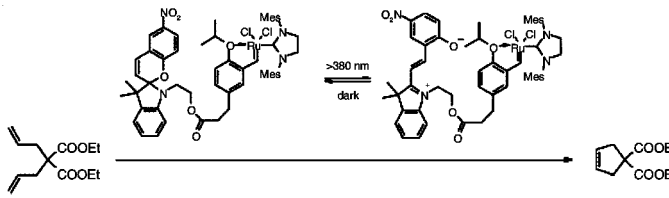
update s. *49,* 985s*77*; with dichloro(3-phenyl-1-indenylidene)(9-isobutylphosphabicyclo[3.3.1]-nonane)(1,3-dimesitylimidazolidin-2-ylidene)ruthenium(II) as an effective 2nd generation catalyst for ring-closing metathesis and cross-metathesis (cf. *49,* 932s*78*) s. X. Sauvage, G. Zaragoza, A. Demonceau, L. Delaude, Adv. Synth. Catal. *2010, 352* (11-12), 1934-8 [DOI: 10.1002/adsc.201000207]; with *in situ*-generated dichloro(tricyclohexylphosphine)(5,7-dimethoxy-3-phenyl-1-indenylidene)ruthenium(II) for the synthesis of 5- to 7-membered disubst. cycloalkenes s. L.R. Jimenez, B.J. Gallon, Y. Schrodi, Organometallics *2010, 29* (16), 3471-3 [DOI: 10.1021/om1005929]; ring-closing metathesis of *hindered* olefins with benzylidene(dichloro)(4,5-dichloro-imidazol-2-ylidene)(1,3-dimesitylimidazolidin-2-ylidene)ruthenium(II) complexes having both an *electron-deficient* NHC ligand and a conventional NHC ligand (at 0.2 to 0.5 mol% loadings), also preparation of fluorophor-tagged analogs for mechanistic studies, s. V. Sashuk, L.H. Peeck, H. Plenio, Chem. Eur. J. *2010, 16* (13), 3983-93 [DOI: 10.1002/chem.200903275]; with related (indenylidene)ruthenium(II) complexes with mixed NHC ligands s. X. Bantreil, R.A.M. Randall, A.M.Z. Slawin, S.P. Nolan, Organometallics *2010, 29* (13), 3007-11 [DOI: 10.1021/om100310f]; with aminocarbonyl-containing 'boomerang'-type catalysts (cf. *58*, 497) for preparing 10-membered lactones s. D.K. Mohapatra, R. Somaiah, M.M. Rao, F. Caijo, M. Mauduit, J.S. Yadav, Synlett *2010* (8), 1223-6 [DOI: 10.1055/s-0029-1219807]; ring-closing metathesis *in eco-friendly glycerol under microwave irradiation* s. N. Bakhrou, F. Lamaty, J. Martinez, E. Colacino, Tetrahedron Lett. *2010, 51* (30), 3935-7 [DOI: 10.1016/j.tetlet.2010.05.101]; synthesis of N-benzyl-amino(hydroxymethyl)cyclopentitols by ring-closing metathesis s. J. Prasada Rao, B. Venkateswara Rao, J. Lakshmi swarnalatha, ibid. *51* (23), 3083-7 [DOI: 10.1016/j.tetlet.2010.04.011]; cycloheptenes via ring-closing metathesis s. *78*, 314.

6-Nitro-2-spiro-3-chromene-tagged o-isopropoxybenzylidene(dichloro)ruthenium imidazolidin-2-ylidene complex [Ru]

Ring-closing metathesis ○

with a simplified catalyst recovery by light-controlled phase switching

543.



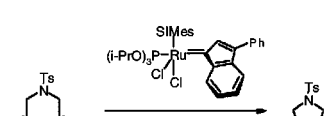
The use of a *light-controlled phase tag* to separate homogeneous catalysts from reaction products is reported, it being possible to switch such phase tags between a neutral (lipophilic) phase and a charged (lipophobic) phase, the photoreaction resulting in drastic changes in the polarity and solubility of the catalyst. **E:** A soln. of diethyl diallylmalonate in methylene chloride containing (R/S)-SP-tagged ruthenium carbene complex (0.5 mol%) allowed to react at 30-35° for 1 h, solvent removed under vacuum, cyclohexane and a glycol/methanol mixture (2:1) added, the system irradiated with light (to transform the (R/S)-SP tag into the *trans*-ME tag, which completely shifted into the lower, glycol/methanol layer) and the product isolated from the cyclohexane layer → diethyl cyclopent-3-ene-1,1-dicarboxylate. Y 95% (with 96% recovery of the catalyst after addition of methylene chloride to the glycol/methanol layer, storage of the biphasic mixture in the dark for 3-5 min causing reversion to the neutral (R/S)-SP form, which then shifted back to the lower, methylene chloride layer). This method avoids the problems associated with solid- or polymer-based catalysts and does not require use of expensive ionic liquid or fluorous solvents, nor oxidizing or reducing agents (as for ionic liquid-, fluorous- or ferrocene-tagged catalysts). As the tag is an organic group it does not affect the catalytic activity of the Ru-carbene complex. It is applicable to a wide range of substrates, forming 5- to 7-membered rings which may contain N-, O- or S-heteroatoms (ten examples; Y 85-97%). It is also applicable to intramolecular ene-yne metathesis (Y 80%) and cross-methathesis (Y 85%). F.e.s. G. Liu, J. Wang, Angew. Chem., Int. Ed. *2010*, *49* (26), 4425-9 [DOI: 10.1002/anie.200906034].

cis-Dichloro(triisopropyl phosphite)(1,3-dimesitylimidazolidin-2-ylidene)(3-phenyl-inden-1-ylidene)ruthenium(II) [Ru(II)]

Ring-closing metathesis

with (trialkyl phosphite)ruthenium N-heterocyclic carbene complexes

544.



Ruthenium(II) complexes possessing *both trialkyl phosphite and NHC ligands* are highly efficient for ring closing metathesis at catalyst loadings *as low as 200 ppm*, and display a much better longevity than established metathesis catalysts, the inexpensive, strongly π-acidic trialkyl phosphite acting synergistically with the σ-donor NHC ligand. **E:** The startg. diene (0.25 mmol), *cis*-dichloro(triisopropyl phosphite)(1,3-dimesitylimidazolidin-2-ylidene)(3-phenylinden-1-ylidene)-ruthenium(II) *(0.02 mol%;* from a stock soln. of 2.2 mg in 2 ml of toluene) and toluene (0.5 ml) introduced into a vial (kept in a glovebox), the mixture stirred outside the glovebox at 120° for

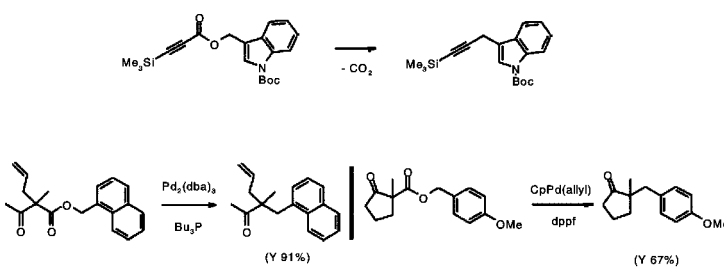
15 h, the solvent evaporated, and the residue worked up with purification by flash chromatography on silica gel → product. Y 84%. This robust ruthenium complex is applicable to the preparation of *di-, tri- and tetra-subst.* cyclic ethylene derivs., offering complete conversions at catalyst loadings of 0.02 to 0.1 mol%, and is clearly superior to established ruthenium complexes for the conversion of **hindered compounds**. The described, thermodynamically-stable *cis*-complex is in equilibrium with the kinetic *trans*-isomer which is transformed into the former by a non-dissociative mechanism on heating; the *trans*-isomer itself is also an excellent metathesis catalyst *at room temp.*, although yields were uniformly lower (52-82%) than those recorded for the *cis*-isomer at elevated temp. (seven examples; Y 74 to >99%). F.e. and solventless procedure, also one example each of ring-closing metathesis of enynes and cross-metathesis, s. X. Bantreil, T.E. Schmid, R.A.M. Randall, A.M.Z. Slawin, C.S.J. Cazin, Chem. Commun. *2010, 46* (38), 7115-7 [DOI: 10.1039/c0cc02448a].

Tetrakis(triphenylphosphine)palladium(0) $Pd(PPh_3)_4$

Decarboxylative α-allylation COOC-C=C-C → C-C=C

nitro-3-ethylene derivs. cf. *36,* 990s*77*; chiral α-quaternary homoallyl sulfones from sulfonylacetic acid allyl esters with *retention* of configuration s. J.D. Weaver, B.J. Ka, D.K. Morris, W. Thompson, J.A. Tunge, J. Am. Chem. Soc. *2010, 132* (35), 12179-81 [DOI: 10.1021/ja104196x].

Palladium-catalyzed intramolecular decarboxylative coupling of propiolic or β-ketocarboxylic acid benzyl or heteroarylmethyl esters under mild, base-free conditions ←



545.

3-Propargylindoles. A soln. of $Pd(PPh_3)_4$ (5 mol%) in toluene (5 ml) added under argon to the startg. propiolic ester (1 mmol), the mixture stirred at 110° for 7 h, cooled to room temp., concentrated *in vacuo*, and the residue purified by flash chromatography on silica gel → *tert*-butyl 3-[3-(trimethylsilyl)prop-2-ynyl]-1*H*-indole-1-carboxylate. Y 85%. Reaction was successful for a variety of propiolic acid benzylic esters (incl. hetar. analogs and an α-phenyl deriv.), *having extended aromatic conjugation*, wherein the acetylene group may be terminated with alkyl, aryl or trimethylsilyl (but not H) (seventeen examples; Y 30%, 74-93%). Analogous benzylic esters of β-ketoacids similarly underwent decarboxylative coupling to afford **β-(het)arylketones** (fifteen examples; Y 51-95%), notably allowing the preparation of hindered all-carbon quaternary centers, with $Pd_2(dba)_3/Bu_3P$ affording optimal results in such cases. Parent benzyl esters failed to undergo the reaction, although a single *p*-methoxybenzyl β-ketoester was successful, presumably due to the strongly electron-donating methoxy substituent providing sufficient stabilization for the putative π-benzyl intermediate. This method allows the preparation of medicinally relevant heterocyclics without the use of organometallics. F.e.s. R.R.P. Torregrosa, Y. Ariyarathna, K. Chattopadhyay, J. Am. Chem. Soc. *2010, 132* (27), 9280-2 [DOI: 10.1021/ja1035557].

Formation of Electron Pair on Sulfur

Elimination ⇑

Oxygen ↑ EIS ⇑ O

Potassium tetrahydridoborate/hafnium tetrachloride *$KBH_4/HfCl_4$*
N-Benzyltriethylenediammonium bromide/sulfuric acid-silica ←
Thioethers from sulfoxides $\geqslant SO \rightarrow \geqslant S$
with $Mo(CO)_6$ cf. *52*, 495s*73*; mild, efficient and general procedure with $KBH_4/HfCl_4$ s. J. Zhang, X. Gao, C. Zhang, C. Zhang, J. Luan, D. Zhao, Synth. Commun. *2010, 40* (12), 1794-801 [DOI: 10.1080/00397910903161819]; solvent-free method with N-benzyltriethylenediammonium bromide in the presence of sulfuric acid-on-silica s. S.A. Pourmousavi, P. Salehi, Phosphorus, Sulfur Silicon Relat. Elem. *2010, 185* (4), 803-7 [DOI: 10.1080/10426500902994312].

Heteropolar Bond

Uptake ⇓

Addition to Nitrogen Het ⇓ N

Without additional reagents *w.a.r.*
Microwaves [\\\\]
N-Quaternization $\geqslant N \rightarrow \geqslant N^+R$
s. *1*, 786; polymer-based synthesis of tert. methylamines, incl. tropane derivs., via quaternization of Wang resin-supported amines with methyl iodide s. M. Sienkiewicz, R. Lazny, J. Comb. Chem. *2010, 12* (1), 5-8 [DOI: 10.1021/cc900108p]; quaternization of N-mesitylimidazole (cf. *30*, 701s*67*) under microwave irradiation s. B.J. Truscott, R. Klein, P.T. Kaye, Tetrahedron Lett. *2010, 51* (38), 5041-3 [DOI: 10.1016/j.tetlet.2010.07.097]; synthesis of sym. and unsym. viologens by quaternization of 4,4′-bipyridyls s. M. Lamberto, E.E. Rastede, J. Decker, F.M. Raymo, ibid. *2010, 51* (42), 5618-20 [DOI: 10.1016/j.tetlet.2010.08.070].

Addition to Remaining Elements Het ⇓ Rem

Quaternary methylphosphonium salts from tert. phosphines s. *78*, 261 $\geqslant P \rightarrow \geqslant P^+Me$

Resolutions Res

Without additional reagents *w.a.r.*
Determination of absolute configuration ←
update s. *5*, 666s*75*; with ^{13}C NMR spectroscopy as a general tool for the assignment of the abs. configuration of a wide range of compds. (alcohols, amines, carboxylic acids, thiols, cyanohydrins, *sec,sec*-diols and *sec,sec*-aminoalcohols, derivatized with appropriate chiral auxiliaries) s. I. Louzao, J.M. Seco, E. Quiñoá, R. Riguera, Chem. Commun. *2010, 46* (42), 7903-5 [DOI: 10.1039/c0cc02774j]; through the DFT simulation of optical rotation, a *caveat*, s. G. Mazzeo, E. Giorgio, R. Zanasi, N. Berova, C. Rosini, J. Org. Chem. *2010, 75* (13), 4600-3 [DOI: 10.1021/jo100401w]; application of a highly reliable criterion for the assignment of absolute stereochemistry of chiral alcohols based on the IR spectra of their CFTA esters s. K. Omata, K. Kotani, K. Kabuto, T. Fujiwara, Y. Takeuchi, Chem. Commun. *2010, 46* (20), 3610-2 [DOI: 10.1039/b926793j]; ^1H NMR determination of the abs. configuration of sec. alcohols derivatized with chiral tetrahydro-

1,4-epoxynaphthalene-1-carboxylic acid s. S. Sungsuwan, N. Ruangsupapichart, S. Prabpai, P. Kongsaeree, T. Thongpanchang, Tetrahedron Lett. *2010, 51* (38), 4965-7 [DOI: 10.1016/j.tetlet.2010.07.062]; of 1-aryl-2-propanols using 1,1′-binaphthyl-2,2′-diyl-based phosphoroselenoyl chlorides as chiral derivatizing agents s. T. Murai, H. Tsuji, S. Imaizumi, T. Maruyama, Chem. Lett. *2010, 39* (5), 524-6 [DOI: 10.1246/cl.2010.524]; of 1,2,3-triols by ^{1}H NMR of their tris(α-methoxy-α-phenylacetic acid esters) s. F. Freire, E. Lallana, E. Quiñoá, R. Riguera, Chem. Eur. J. *2009, 15* (44), 11963-75 [DOI: 10.1002/chem.200901505]; NMR determinations of the abs. configuration of α-chiral prim. amines via derivatization with 2′-methoxy-1,1′-binaphthalene-8-carbaldehyde s. H. Fukui, Y. Fukushi, Org. Lett. *2010, 12* (12), 2856-9 [DOI: 10.1021/ol100951s]; chiral discrimination of α-chiral amines as their ammonium salts in the confined space of C_3-symmetric cage-like receptors s. S. Sambasivan, S.-G. Kim, S.M. Choi, Y.M. Rhee, K.H. Ahn, ibid. *12* (19), 4228-31 [DOI: 10.1021/ol1015527]; enantioselective recognition and NMR analysis of protected amines with 3,5-dinitrobenzoyl-derived 1-naphthylethyl amide as chiral solvating agent s. D.P. Iwaniuk, C. Wolf, J. Org. Chem. *2010, 75* (19), 6724-7 [DOI: 10.1021/jo101426a]; chiral recognition of amines and amino acid derivs. using chiral ruthenium Halterman porphyrins in organic solvents and water s. I. Nicolas, S. Chevance, P. Le Maux, G. Simonneaux, Tetrahedron: Asym. *2010, 21* (13-14), 1788-92 [DOI: 10.1016/j.tetasy.2010.05.026]; chiral recognition of 2-aminoalcohols and conversion of *L*- to *D*-amino acids s. H. Jung, R. Nandhakumar, H.-J. Yoon, S.-g. Lee, K.M. Kim, Bull. Korean Chem. Soc. *2010, 31* (5), 1289-94 [DOI: 10.5012/bkcs.2010.31.5.1289]; determination of the abs. configurations of bicyclo[3.1.0]hexane derivs. via electronic CD, optical rotation dispersion, vibrational CD spectroscopy and DFT calculations s. G. Yang, J. Li, Y. Liu, T.L. Lowary, Y. Xu, Org. Biomol. Chem. *2010, 8* (16), 3777-83 [DOI: 10.1039/c002655g]; of pentacoordinate chiral phosphorus compounds in solution by using vibrational CD Spectroscopy and DFT calculations s. G. Yang, Y. Xu, J. Hou, H. Zhang, Y. Zhao, Chem. Eur. J. *2010, 16* (8), 2518-27 [DOI: 10.1002/chem.200902501]; enantiodifferentiation of carbohydrates by TOCSY NMR using amino acids as chiral ligands s. F. Fernández-Trillo, E. Fernandez-Megia, R. Riguera, J. Org. Chem. *2010, 75* (11), 3878-81 [DOI: 10.1021/jo1004263]; direct assignment of the relative configuration in 1,3,n-methyl-branched carbon chains by ^{1}H NMR s. Y. Schmidt, B. Breit, Org. Lett. *2010, 12* (10), 2218-21 [DOI: 10.1021/ol1005399].

Chromatography, Liquid-liquid extraction or Sublimation ←

Separation of enantiomers by physical means ←

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Sodium azide/halohydrin dehalogenase *NaN_3/dehalogenase*
Kinetic resolution of 1,1-disubst. epoxides by enzymatic azidolysis s. *78*, 133 ←

Potassium fluoride/chiral 3,3′-diiodo-1,1′-bi-2-naphthol-based polyethers *[F^-]**
Kinetic resolution by asym. O-desilylation ←
with a chiral polyether-complexed ['naked'] fluoride ion s. *78*, 1

N-Cyclohexyl-(R,R)-cyclohexane-1,2-diamine monotrifluoroacetate ←
Kinetic resolution of 2-cinnamoyl-Δ^1-azirines by aza-Nazarov cyclization s. *78*, 142 ←

1,4-Dihydropyridines/(R)-3,3′-bis(2,4,6-triisopropylphenyl)-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate ←
Transfer-hydrogenative N-alkylation with α-subst. ketones with dynamic kinetic resolution ←
s. *78*, 160

4-Dimethylaminopyridine/(R,R)-N-[3,5-bis(trifluoromethyl)benzoyl]-N′-[3,5-bis(trifluoromethyl)thiobenzoyl]cyclohexane-1,2-diamine ←
Kinetic resolution by N-benzoylation $NH_2 \rightarrow NHCOPh$
of 2-acetylene-*prim*-amines or α-subst. prim. benzylamines under cooperative nucleophilic catalysis and anion-binding organocatalysis s. *78*, 161

Alcohol dehydrogenase/formate dehydrogenase s. under Acetonitrile[o-(methylaminomethyl)phenyl](pentamethylcyclopentadienyl)iridium(III) hexafluorophosphate ←
Halohydrin dehalogenase s. under NaN_3 *dehalogenase*
Immobilized lipase s.a. under Tris(triphenylsilyl) vanadate ←

Immobilized lipase/butyltrimethylammonium triflamide coated zeolite ←
Dynamic kinetic resolution of sec. benzyl alcohols $OH \rightarrow OCOR$
via heterogeneous enzymatic transesterification under continuous flow conditions s. *78*, 108

2,2-Dimethyl-6-chlorocyclohexanone s. under Acetonitrile[o-(methylaminomethyl)phenyl](pentamethylcyclopentadienyl)iridium(III) hexafluorophosphate ←

Chiral 4,8,8-trimethyl-2-phenyl-2-phosphabicyclo[3.3.0]octane/(R,R)-3-(1-acetoxy-2-benzoylamino-3,3-dimethylbutyl)-4-(dimethylamino)pyridine/triethylamine ←
Dual-organocatalyzed parallel kinetic resolution of sec. alcohols via O-acylation $OH \rightarrow OAc$
s. *78*, 85

(R)-3,3′-Bis(2,4,6-triisopropylphenyl)-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate s. under1,4-Dihydropyridines ←

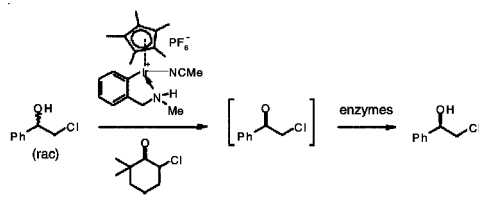
Tris(triphenylsilyl) vanadate or polymer-based vanadyl phosphonate/immobilized lipase ←
Dynamic kinetic resolution of 2-ethylenealcohols ←
via racemizing allyl shift-enzymatic O-acylation s. *78*, 111

Chiral ruthenium(II) complexes *[Ru(II)]**
Kinetic resolution by asym. homogeneous hydrogenation ←
of α-chloro-β-keto-carboxylic or -phosphonic acid esters s. *67*, 22s*78*

Acetonitrile[o-(methylaminomethyl)phenyl](pentamethylcyclopentadienyl)iridium(III) hexafluorophosphate/2,2-dimethyl-6-chlorocyclohexanone/alcohol dehydrogenase/ formate dehydrogenase/sodium formate ←

Deracemization of 1,2-chlorohydrins ←
via iridium(III)-catalyzed transfer-dehydrogenation-enzymatic asym. reduction

546.



Mutually compatible [orthogonal] iridium(III) and an alcohol dehydrogenase effect a one-pot deracemization of 1,2-chlorhydrins via a unique oxidation-reduction sequence. **E:** Solns. of the alcohol dehydrogenase (ADH-A) from *Rhodococcus ruber* (500 U; 500 µl; pH 7.5; 50 m*M*), formate dehydrogenase (FDH) (140 µl; 30 U), Na-formate (260 m*M*) and NADH (110 µl; final concentration 1 m*M*) in Tris-HCl buffer mixed together, a soln. of the iridacyclic complex (5 mol%) in toluene poured onto the aq. phase, followed by a soln. of 2,2-dimethyl-6-chloro-cyclohexanone (10 eq.) in the same solvent, the startg. sec. alcohol (33 µmol) added, the mixture shaken on a rotary plate at 120 rpm for 16 h at 30° under argon, extracted with ethyl acetate, the organic layer separated from the aq. phase by centrifugation, dried, and worked up → product (as a >999:1 mixture of alcohol and intermediate ketone; e.e. 40%). The *hindered* ketone, 2,2-dimethyl-6-chloro-cyclohexanone, was selected as H-acceptor for the initial iridium-catalyzed dehydrogenation as it was resistant to reduction by the enzyme; by the same token, the formate/FDH system was chosen as the reducing agent for the bioreduction as formate is compatible with the iridium catalyst. Although enantioselectivity was only moderate (three examples; e.e. 6%, 29%, 40%), proof of principle has been demonstrated, anticipating that the future application of a matched chiral iridium catalyst will significantly improve the deracemization. F.e.s. F.G. Mutti, A. Orthaber, J.H. Schrittwieser, J.G. de Vries, R. Pietschnig, W. Kroutil, Chem. Commun. *2010*, *46* (42), 8046-8 [DOI: 10.1039/c0cc02813d].

Reviews

This is a collection of reviews gathered from the literature during the six months up to and including April 2011, arranged in the following sections:

1 **General**

2 **Asymmetric catalysis – chiral ligands, organocatalysts ...**

3 **Chirality – dynamic kinetic resolution, physical separation of enantiomers, electronic effects, autocatalysis**

4 **Transition metal catalysis – general methods, Groups 8-10, Re, Au**

5 **Catalytic C-H activation and functionalization; catalytic C-C cross-coupling**

6 **Catalysis – multicatalysis, cooperative catalysis, photocatalysis, heterogeneous catalysis; solid catalysts and supports, metal-organic framework**

7 **Biocatalysis, enzymes ...**

8 **Heterocyclic chemistry – general methods; N-, O-, S-heterocyclics ..., condensed heterocyclics**

9 **Natural product synthesis – general aspects, alkaloids, terpenes, ... antibiotics, pharmacologically active compounds, drug discovery**

10 **Peptide chemistry, peptidomimetics, proteins**

11 **Carbohydrate chemistry – glycosylation, carbohydrate reactions, oligosaccharides**

12 **Nucleic acids, oligonucleotides, DNA**

13 **Carbocyclic chemistry**

14 **Aromatic chemistry**

15 **Name reactions, standard transformations – Heck, Stille ..., cycloaddition, 1,4-addition, 1,2-addition, ammoxidation, epoxidation, halogenation, ... metathesis ...**

16 **Multicomponent, tandem, cascade reactions; combinatorial ...**

17 **Functional group chemistry**

18 **Syntheses with organometallics; carbenes and carbene complexes**

19 **Reagents, auxiliaries**

20 **Methodology – electrochemistry, microwave irradiation, sonochemistry, continuous flow, media ...**

21 **Miscellaneous**

1 General

Aiming for the ideal synthesis, T. Gaich, P.S. Baran, J. Org. Chem. *2010, 75* (14), 4657-73; lesser-known enabling technologies for organic synthesis, M. O'Brien, R. Denton, S.V. Ley, Synthesis *2011* (8), 1157-92.

2 Asymmetric catalysis – chiral ligands, organocatalysts ...

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3 Chirality – dynamic kinetic resolution, physical separation of enantiomers, electronic effects, autocatalysis

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4 Transition metal catalysis – general methods, Groups 8-10, Re, Au

(for transition metal-catalyzed C-H activation and C-C cross-coupling s. under Section 5; for Heck and Stille chemistry, transition metal-catalyzed cycloaddition, 1,4-addition, 1,2-addition, metathesis ... s. under Section 15).

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7 Biocatalysis, enzymes ...

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(s.a. under Section 15 for heterocyclic synthesis by cycloaddition)

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9 Natural product synthesis – general aspects, alkaloids, terpenes, ... antibiotics, pharmacologically active compounds, drug discovery

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17 Functional group chemistry

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19 Reagents, auxiliaries, ...

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21 Miscellaneous

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Hydrogenated and functionalized ring systems are indexed by the conventional reversal, e.g. '**Pyridines, aryl-**', the only important exception to the rule being alkylideneisocyclics which are indexed as such, e.g. '**Alkylidenecyclopentanes**'.

As from Volume *51*, '**Epoxides**' has been used in place of 'Oxido compds.'; '**Thiiranes**' in place of 'Sulfido compds.'; '**Diels-Alder reaction**' in place of 'Diene synthesis'; and '**Benzo[*b*]thiophenes**' in place of 'Thianaphthenes'.

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