CATALYSIS BY METAL COMPLEXES 34

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Ruthenium Oxidation Complexes

Their Uses as Homogenous Organic Catalysts

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VOLUME 34:
RUTHENIUM OXIDATION COMPLEXES

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ISBN 978-1-4020-9376-0 e-ISBN 978-1-4020-9378-4
DOI 10.1007/978-1-4020-9378-4
Springer Dordrecht New York Heidelberg London

Library of Congress Control Number: 2010935300

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

Preface

This book is concerned with the application of ruthenium complexes as catalysts for useful organic oxidations.

Ruthenium was the last of the platinum-group elements to be discovered, and has perhaps the most interesting and challenging chemistry of the six. In this book just one major aspect is covered: its ability, mainly by virtue of its remarkably wide range of oxidation states which exist in its many complexes (from +8 to −2 inclusive) to effect useful and efficient oxidations of organic substrates.

Emphasis has been placed on useful organic oxidations, particularly on the catalytic production of natural products or pharmaceuticals and of the oxidation of important organic functional groups such as alcohols, alkenes, alkynes, amines and heteroatomic functionalities. The book is not directed solely at organic chemists. It is hoped that the inorganic, organometallic and coordination chemist will draw from it useful information, particularly from Chapter 1. The coverage of this very large subject can not claim to be entirely comprehensive, but it is hoped that all the main references, including some from 2010, have been covered.

The first chapter concerns the chemistry of the oxidation catalysts, some 250 of these, arranged in decreasing order of the metal oxidation state (VIII) to (0). Preparations, structural and spectroscopic characteristics are briefly described, followed by a summary of their catalytic oxidation properties for organic substrates, with a brief appendix on practical matters with four important oxidants. The subsequent four chapters concentrate on oxidations of specific organic groups, first for alcohols, then alkenes, arenes, alkynes, alkanes, amines and other substrates with hetero atoms. Frequent cross-references between the five chapters are provided.

I would like to thank my good friend Brian James of the University of British Columbia (UBC), who suggested some years ago that I write a book of this type and who has carefully read and trenchantly criticised large sections of it. From Imperial College I am deeply indebted to Ed Smith who has read all of it and pointed out a number of errors and inconsistencies, and Ed Marshall who has drawn all the figures. I am very grateful to Steve Ley from Cambridge who has read the section on TPAP, the reagent which he, I and our co-workers developed. Any remaining errors and omissions are entirely my responsibility. All the cited references have of course been consulted and, though most are from online sources, it

is a pleasure to thank the librarians of Imperial College, the Science Museum and the Royal Society of Chemistry libraries, and of course of the British Library. Finally, I am deeply grateful to my wife Anne (and in earlier years to my daughters Helen and Miranda) for her forbearance during the long time this book has taken to compile.

Contents

Abbreviations

Abbreviations which are commonly used in the book are listed here: each is defined when it first occurs in the text, but not subsequently; those used once only are not listed here. Wherever possible internationally known abbreviations (e.g. bpy, py, etc.) are used, but in some cases the usage of the authors of the papers cited have been used.

acac	Acetylacetonate mono-anion (2,4-pentanedionate mono-anion)
atm	Atmospheres (pressure)
aq.	In aqueous solution, or aquated
BHT	2,6-di-*tert*-Butyl-4-methylphenol
B.M.	Bohr magnetons
Bmim	1-Butyl-3-methylimidazolium mono-cation
Bn	Benzyl, $C_6H_5CH_2$
Boc	*tert*-Butoxycarbonyl
bpy	2,2′-Bipyridyl
BDTAC	Benzyldimethyltetradecylammonium chloride
BTBAC	Benzyltributylammonium chloride
BTEAC	Benzyltriethylammonium chloride, $(PhCH_2NEt_3)Cl.H_2O$
Bu	Butyl
^{t}Bu	*tert*-Butyl
Bz	Benzoyl, C_6H_5CO
Ch.	Chapter
CHP	Cumene hydroperoxide
cinc	Cinchomeronate (3,4-pyridinedicarboxylate dianion)
COD	Cyclo-octa-1,5-diene
Cp	π-C_5H_5 Mono-anion
Cp*	η^5-C_5Me_5 Mono-anion
Cl_2bpy	6,6′-Dichloro-2,2′-bipyridyl
Cl_2pyNO	2,6-Dichloropyridine-*N*-oxide
DCE	1,2-Dichloroethane
DDAB	Didecyldimethylammonium bromide
DFT	Density function theoretical (calculations)

DMF	Dimethylformamide
dmg	Dimethylglyoxime mono-anion
dmp	2,9-Dimethyl-1,10-phenanthroline
DMSO, dmso	Dimethylsulfoxide (upper case for solvent, lower-for ligand)
dpae	1,2-bis-(Diphenylarsino)ethane
dppe	1,2-bis(Diphenylphosphino)ethane
dppp	1,3-bis(Diphenylphosphino)propane
dppm	bis(Diphenylphosphino)methane
ε	Molar extinction coefficient,/ $dm^3\ mol^{-1}\ cm^{-1}$
EDTA	Ethylenediaminetetra-acetate tetra-anion $EDTA^{4-}$ (acid is H_4EDTA; Fig. 1.33)
e.e.	Enantiomeric excess
emim	1-Ethyl-3-methy l-1H-imidazolium mono-cation
ESR	Electron spin resonance
Et	Ethyl
EtOAc	Ethyl acetate
h	Hours
Hx	*n*-Hexyl
IR	Infrared
M	Molar
MCPBA	Metachloroperbenzoic acid or 3-chloroperbenzoic acid
Me	Methyl
mech.	Mechanism
Me_2CO	Acetone
MTCAC	Methyltricaprylammonium chloride
μ_{eff}	Magnetic moment in Bohr Magnetons at room temperature
(N)	Nitride (N^{3-}) ligand
napy	1, 8-Naphthyridine
$\upsilon^{as}(Ru(O)_2)$	Asymmetric IR or Raman stretching vibration of an RuO_2 unit
$\upsilon^{s}(Ru(O)_2)$	Symmetric IR or Raman stretching vibration of an RuO_2 unit
υ (Ru=(O))	Stretching vibration of an Ru=O unit
nic	Nicotinate dianion
NMO	N-methylmorpholine-*N*-oxide
n.o.	Not observed
(O)	Oxo (O^{2-}) ligand
OAc	Acetate
OEP	2,3,7,8,12,13,17,18-Octaethylporphyrinate dianion
ox	Oxalate, $(C_2O_4)^{2-}$
Oxone®	$2KHSO_5.\ KHSO_4.K_2SO_4$
Pc	4,4,′4,′′′4′′′′-Tetrasulfophthalocyaninate dianion
PCB	Polychlorinated biphenyls

PDTA	Propylenediamine tetra-acetate tetra-anion, $PDTA^{4-}$
Ph	Phenyl, C_6H_5
phen	1,10-Phenanthroline
pic	Picolinate (2-pyridinecarboxylate dianion)
PMS	Powdered (4 Å) molecular sieves
PNAO	Poly-*N*-methylmorpholine-*N*-oxide
PPN	$(Ph_3P)_2N)^+$
Pr	Propyl
^{i}Pr	Isopropyl
py	Pyridine
pydic	Pyridine-2,6-dicarboxylic acid
pyNO	Pyridine *N*-oxide
PS-TPAP	Polymer-supported TPAP
R	Raman spectrum
RT	Room temperature
SB	Schiff's base
SCE	Standard calomel electrode
stoich.	Stoicheiometric
Tet-Me_6	*N, N, N′, N′,* 3, 6-Hexamethyl-3,6-diazaoctane-1,8-diamine
TBAP	Tetra-*n*-butylammonium perruthenate, $(^nBu_4N)[RuO_4]$
TBHP	*tert*-Butylhydroperoxide, ^{t}BuOOH
TCCA	Trichloroisocyanuric acid
TDCPP	*meso*-5,10,15,20-*tetrakis*(2,6-Dichlorophenyl)porphyrin dianion
TEMPO	2,2′,6,6′-Tetramethylpiperidine-N-oxyl radical (Fig. 1.40)
$TFPPCl_8$	Octachloro*tetrakis*(pentafluorophenyl)porphyrinate dianion
TGA	Thermal gravimetric analysis
THF	Tetrahydrofuran
TMC	Tetramethyl-tetra-azacyclotetradecane (Fig. 1.29)
TMEA	*N,N,N′,N′*- Tetramethyl-1,2-diaminoethane
tmeda	*N, N, N′, N′*-tetramethylethylenediamine
TMP	*meso*-5,10,15,20-Tetramesityl(porphyrinate) dianion (Fig. 1.24)
TMPZNO	Tetramethylpyrazine-*N,N′* dioxide
tmtacn	1,4,7-Trimethyl-1,4,7-triazacyclononane (Fig. 1.30)
tpa	Tris(2-pyridylmethyl)amine)
TPAP	Tetra-*n*-propylammonium perruthenate, $(^nPr_4N)[RuO_4]$
TPAP/NMO	Oxidising mixture of TPAP and NMO
TPAPORM	TPAP doped on ormosil silica glass
TPP	*meso*-5,10,15,20-Tetraphenyl(porphyrin)ate dianion
Troc	Trichloroethoxycarbonyl
TTP	Tetramesitylporphyrinate dianion
tpy	2,2′:6′,2″-Terpyridine
UV	Ultra-violet (irradiation)
v	Volts

Chapter 1
The Chemistry of Ruthenium Oxidation Complexes

Abstract This chapter introduces the topic and scope of the book and principally concerns the basic preparation, physical and chemical properties of Ru-based oxidation catalysts, then summarising the catalytic oxidations which they accomplish. More detail on these is given in the succeeding four chapters. The major oxidants RuO_4 (1.2.1), perruthenate $[RuO_4]^-$ (1.3.1) – mainly TPAP, $(^nPr_4N)[RuO_4]$, ruthenate $[RuO_4]^{2-}$ (1.4.1), trans-$Ru(O)_2$(TMP) (1.4.2.5), $RuCl_2(PPh_3)_3$ (1.9.3) and cis-$RuCl_2(dmso)_4$ (1.9.4) are covered in some detail, but many other catalysts are also discussed. In some cases brief comments are made on the mechanisms involved when data on these are given in the cited papers. There is also an Appendix (1.11) which gives brief details on the preparation of four ruthenium oxidation catalysts and selected model oxidations using them.

1.1 Overview and Introduction

This chapter is essentially a review of those ruthenium complexes which have been used as oxidation catalysts for organic substrates, emphasis being placed on such species which have been chemically well-defined and are effective catalysts. Of all the ruthenium oxidants dealt with here those which have the greatest diversity of use are RuO_4, $[RuO_4]^-$, $[RuO_4]^{2-}$, the tetramesityl porphyrinato (TMP) complex *trans*-$Ru(O)_2$(TMP), $RuCl_2(PPh_3)_3$, and *cis*-$RuCl_2(dmso)_4$. Many other catalysts are covered, and the uses of two principal starting materials, $RuO_2.nH_2O$ and $RuCl_3.nH_2O$ as precursors for a number of catalysts, discussed.

The material is arranged under the formal oxidation state of the ruthenium in the complexes, in descending order within each category, *viz.* Ru(VIII) to Ru(0). Individual complexes within each oxidation state are covered and for each, wherever possible, references to preparation, structural and basic physico-chemical data are given. The arrangement of complexes within each oxidation state broadly follows the sequence of donor atoms used in the book: O, N, P, As, Sb, S, C. Within each formulation ligands determining the oxidation state are placed first (e.g. (O), (N), F, Cl, Br, I, (acac) etc.), e.g. *cis*-$RuCl_2(phen)_2$) rather than *cis*-$Ru(phen)_2Cl_2$.

W.P. Griffith, *Ruthenium Oxidation Complexes*, Catalysis by Metal Complexes 34,
DOI 10.1007/978-1-4020-9378-4_1,

In general ligands are listed in order of increasing denticity within a complex, e.g. $[Ru(H_2O)(bpy)(tpy)]^{2+}$ rather than $[Ru(tpy)(H_2O)(bpy)]^{2+}$.

Oxidations of organic substrates by these species are then briefly considered for classes of organic substrates. Both in this and in subsequent chapters these are arranged in the order: alcohols (including carbohydrates), alkenes, arenes, alkynes, alkanes, amines, amides, ethers, sulfides, phosphines, arsines and stibines; and finally miscellaneous oxidations not covered in preceding sections. Tables of typical oxidations are given in Chapters 2–5; within these tables oxidation products are arranged alphabetically in the central column. In a few cases stoicheiometric oxidants are covered where it is likely that such reactions might be rendered catalytic; occasionally species which show potential catalytic or stoicheiometric oxidative properties are mentioned. Electrocatalytic oxidations are covered but not heterogeneous catalysis not patented procedures, though a few instances of supported catalysis are mentioned. Since the book concentrates on practical usage of the catalysts, the coverage of reaction mechanisms is deliberately light, though references are given wherever possible.

At the head of most of the oxidation sections in Chapters 2–5 a very simplified overall equation is given for the specified set of reactions, its purpose being merely to indicate the notional overall stoicheiometry of the reaction. In these [O] indicates the input of one oxygen atom, 2[O] of two, etc. from the oxidant; there being no mechanistic implications in these simplistic equations. For oxidations of a given organic substrate to the organic product the relation between a Ru starting material (assumed in this case to be an oxoruthenate) is generalised as $Ru^{N}O_x$ with $Ru^{N+2}O_{x+1}$ (two-electron oxidation) or $Ru^{N+4}O_{x+2}$ (four-electron oxidation) as the likely catalyst or catalyst precursor. In Fig. 1.1 the example given is of $Ru^{IV}O_2$ and its four-electron oxidation product $Ru^{VIII}O_4$.

In this and subsequent chapters the rubric:

Starting Ru material/co-oxidant/solvent/temperature (if not ambient) is used. Thus Fig. 1.1 would be written in the text as RuO_2/aq. $Na(IO_4)$, meaning that RuO_4 is generated *in situ* from $RuO_2.nH_2O$ and aqueous sodium periodate (only non-ambient temperatures would appear in the rubric). Biphasic solvent mixtures with water are denoted as water-solvent.

Most of the Ru(VIII) to Ru(IV) complexes featured are oxoruthenates; although those of Ru(III), (II) – e.g. $RuCl_2(PPh_3)_3$ – and Ru(0) do not lie in this category,

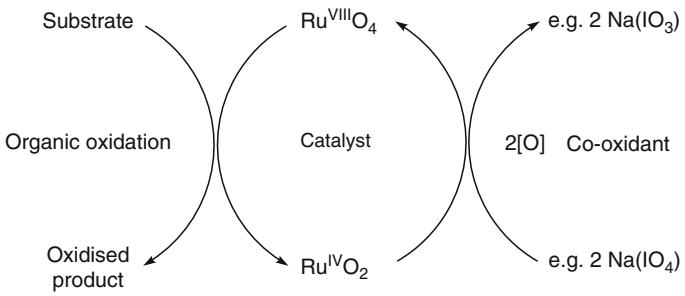

Fig. 1.1 Simple scheme for oxoruthenate oxidation catalysis

oxoruthenates may well be intermediates in their oxidation reactions. The modern convention of bracketing co-ordinated oxo ligands O_2^{2-} as (O) is followed except for the homoleptic RuO_4, $[RuO_4]^-$, $[RuO_4]^{2-}$ species, RuO_2 and polyoxometalates. The precursors mainly used in ruthenium oxidation catalysis are the hydrated dioxide $RuO_2.nH_2O$ and particularly the hydrated trichloride $RuCl_3.nH_2O$; for brevity throughout the text these are referred to simply as RuO_2 and $RuCl_3$. Such reactions are much more effective if carried out with the hydrated materials than with the anhydrous forms.

In a work of this length the use of abbreviations is essential. If an abbreviation is used in one paragraph only (as is the case for some complex ligands) it is defined in that paragraph alone.

1.1.1 Discovery of Ruthenium

Ruthenium was the last of the six platinum group metals to be isolated, and was discovered in Kazan (now capital of the Tatarstan Republic, Russian Federation) by Karl Karlovich Klaus[1] (1796–1864) in 1844. The original papers were published in Russian journals which are difficult to obtain now, but were published in Western Europe in 1845 [1, 2] with a summary in English [3]. Klaus made the metal by reduction of RuO_2 with H_2 and named it Ruthenium in honour of his native land (*Ruthenia*, Latin for Russia); there are short biographies of him [4, 5].

Gottfried Wilhelm Osann (1797–1866) discovered what he thought was a new element in 1827 and named it 'Ruthenium' but his claim is generally discounted [6, 7] though he still has some supporters [8]. Klaus was the first to make RuO_4, *trans*-$K_2[Ru(OH)_2(O)_3]$ (which he regarded as $K_2[RuO_4].H_2O$), RuO_2 and $RuCl_3$, all essential players in Ru oxidation chemistry. He assigned to ruthenium an atomic weight of 102.4 based on the $Na_3[RuCl_6]/H_2$ reaction [9], later raising this to 104 [10]. The modern IUPAC recommended value for Ru is 101.07(2) [11], and its atomic number is 44.

1.1.2 Oxidation States in Ruthenium Complexes

Ruthenium and osmium are unique amongst all known metallic elements in three respects. Firstly they alone form octavalent homoleptic oxo complexes, RuO_4 and OsO_4. Secondly, complexes of these metals containing one of the eleven oxidation states theoretically available to transition metals are known, from M(VIII) to M(-II) inclusive (M=Ru, Os), corresponding to electron configurations of d^0 to d^{10}. Good σ-donors such as F^-, O^{2-} and N^{3-} stabilise higher oxidation states while effective π-acceptors such as CO and NO^+ stabilise low oxidation states. The oxo ligand O^{2-}, the complexes of which concern us in this book, stabilises five oxidation states of Ru (VIII) to (IV) inclusive as a terminal ligand and four (VI to III) inclusive as a bridging

[1] K. K. Klaus appears as C. Claus in the early German publications, which are cited here since they are more accessible than the Russian originals.

ligand. It is this very wide range of oxidation states, mostly of course in conjunction with suitable co-ligands, and a generally favourable balance of kinetic lability and stability which allows so much oxidation chemistry to be carried out with ruthenium. By choosing suitable co-ligands it is possible to change the redox characteristics of the ruthenium centre and so in effect to adjust the oxidation properties of the catalyst.

1.1.3 Reviews on Ruthenium Complexes in Oxidation Reactions

There is no previous review or book of the type presented here, but there are some very useful reviews on its general chemistry. The two classic volumes by Gmelin in 1970 [12] and in 1938 [13] are invaluable for the early work, as are the magisterial bibliographies by Howe covering the period 1844–1950 [14–16]. The Seddons' admirably comprehensive book on the element, *The Chemistry of Ruthenium*, covers material up to 1983 [6] and the author's book *The Chemistry of the Rarer Platinum Metals (Os, Ru, Ir and Rh)* does so to 1967 [17]; less comprehensive but still useful is Simon Cotton's *Chemistry of Precious Metals* [18]. There are reviews on higher [19–21] and lower [22] oxidation state complexes of the element. The *Encyclopedia of Inorganic Chemistry* has useful articles on its coordination and organometallic chemistry respectively [23, 24].

There is no single publication covering oxidations by ruthenium[2] complexes as presented in this book. However there are some fairly general reviews, and also more specific ones which will be mentioned in the relevant parts of the text. Here we list only those which apply to Ru oxidants in general: [25–27]; biomimetic Ru oxidations [28, 29]; a book on *Ruthenium in Organic Synthesis* has a chapter on oxidations [30]; a review on large-scale oxidations in the pharmaceutical industry include some Ru-catalysed examples [31]. There are broad reviews on Ru complexes in organic synthesis [32]; on Ru oxo complexes as organic oxidants [33–36]; reviews on platinum-group metal oxidations including Ru [37–40]; oxidations by Ru porphyrin species [41–47] and by Ru macrocyclic complexes [48]. There are also reviews as part of more general treatments of oxidation by metal-oxo species [49–51]; on 'green' oxidations involving O_2 and H_2O_2 [52] and on O_2 [47, 52–54] as co-oxidants. For reviews on RuO_4 *cf.* 1.2.1 below and for TPAP *cf.* 2.1.2.

1.1.4 Reviews on Oxidations of Organic Substrates by Ru Complexes

These are included in the following chapters but are grouped together here. They include oxidations of *alcohols* in Ch. 2, a prime target for Ru-catalysed oxidations

[2] Henceforth in most cases abbreviated as Ru.

[19, 25–27, 29, 30, 35, 53–60]. In Ch. 3 are considered *alkenes* for which Ru complexes are active in epoxidation reactions [27, 30, 35, 60–62], including asymmetric epoxidations [44, 63]; *cis*-dihydroxylations [64–67]; ketohydroxylations [28, 64, 66, 67]; alkene cleavage reactions [38, 50, 65, 68, 69, 71], *arenes* [27, 28], and *alkynes* [60, 65, 70, 71]. In Ch. 4 Ru-catalysed oxidations of *alkanes* are covered: [19, 27, 30, 51, 72]. Finally in Ch. 5 oxidation of a series of heteroatomic substrates is considered: *amines* [27, 28, 30, 32, 42, 73, 74]; *β-lactams and amides* [27, 30]; *ethers* [35, 47]; *sulfides* [42, 46, 47]; *phosphines, arsines and stibines* [46, 47], and finally those few substrates which do not fall under the categories above.

1.1.5 Syntheses of Natural Products or Pharmaceuticals by Ru Catalysts

Many biologically important materials have been synthesised by using Ru catalysts as part of multi-step syntheses. The catalyst used is indicated in parentheses. These include essential steps in synthesis of the phytohormone Abscisic acid (TPAP) [75]; the marine eicosanoid Agardhilactone (TPAP) [76]; the sugar D-allose (RuO_4); Fig. 2.13, [77]; the hormone *d*-Aldosterone (RuO_4) [78, 79]; the antitumour styryllactone (+)-Altholactone (TPAP) [80]; the macrolide Altohyrtin A (TPAP) [81]; the quassinoid (±)-Amarolide (RuO_4) [82]; the fragrance (−)-Ambrox® (RuO_4 and $[RuO_4]^-$) (Fig. 3.20) [83]; the marine macrolide Amphidinolide T1 (TPAP) [84]; the immunosuppressive agent Antascomicin B (TPAP) [85]; the marine natural product Antheliolide A (TPAP) [86]; the plant hormone (±)-Antheridiogen (A_{An}, 2) ($[RuO_4]^{2-}$) [87]; the non-proteinogenic amino acid Anticapsin (TPAP) (Fig. 2.7) [88, 89]; the cytotoxic benzolactone enamide Apicularen A (TPAP) [90]; the sugar D-Arcanose (RuO_4) [91]; the anti-malarial agent Arteether (TPAP; Fig. 2.4) [92]; the AChE inhibitor (+)-Arisugacin A and B (TPAP) [93]; the eunicellin Astrogorgin (TPAP) [94]; the anti-parasitic Avermectin-B1a (TPAP; Fig. 2.6, 1.11) [95–97]; the antifeedant and growth-disruption agent Azadirachtin (TPAP) [98–100]; the alkaloid (+)-Batzelladine A (TPAP; Fig. 1.13) [101]; the antibiotic Biphenomycin B (RuO_4) [102]; the antibiotic (−)-Borrelidin (TPAP) [103]; the neurotoxin Brevetoxin B (TPAP) [104, 105]; the limonoid Calodendrolide (TPAP) Fig. 2.8) [106]; the pheromone *R*-γ-Caprolactone (RuO_4) [107]; the nutritional supplement L-Carnitine (RuO_4) [108]; the antiviral Castanospermine and 1-Epicastanospermine (TPAP) [109]; the vinca alkaloid (+)-Catharanthine (TPAP) [110]; the sesquiterpene (−)-Ceratopicanol (RuO_4, TPAP) [111]; the sugar L-Cladinose (RuO_4) [112, 113]; the antitumour agent *ent*-Clavilactone B (TPAP) [114]; the synthase inhibitor (−)-CP-263,114 (TPAP) [115]; the biologically active sequiterpene (−)-Diversifolin (TPAP) [116]; the sesquiterpene isoDrimeninol ($[RuO_2Cl_3]^-$) [117]; the agonist Dysiherbaine (TPAP) [118]; the marine anti-tumour agent Eleutherobin (TPAP) [119]; the analgesic (±)-Epibatidine (TPAP) [120]; the anti-growth factor 2-Epibotcinolide (TPAP) [121]; the cytotoxic (−)-7-Epicylindrospermopsin (TPAP) [122]; the carbohydrate 1-*epi*Hyantocidin (TPAP) [123]; the alkaloid (±)-Epimaritidine (TPAP) [124]; the cytotoxic antitumour

agent Epothilone C (TPAP) [125]; the antileukemic agents (−)-Eriolangin and (−)-Eriolanin (TPAP) [126]; the spirobicyclic sesquiterpene (±)-Erythrodiene (TPAP) [127]; the enzyme inhibitor (+)-Fagomine (TPAP) [128]; the cytotoxic Fasicularin (TPAP) [129]; the anti-inflammatory Flurbiprofen (RuO_4) [130]; the limonoid Fraxinellone (TPAP) [131]; the polycyclopropane antibiotic FR-900848 (RuO_4) [132]; the plasmodial pigment Fuligorubin A (TPAP) [133]; the biologically active amino sugars Furanodictines A and B (TPAP) [134]; the antibiotic carbasugars Gabosine I and Gabosine G (TPAP) [135]; the antifungal Gambieric acids A and C (TPAP) [136]; the ether toxin Gambierol (TPAP) [137]; the growth factor Gibberellic acid ($[RuO_4]^{2-}$) [138]; the anti-cancer agent (+)-Goniodiol (TPAP) [139, 140]; the cytotoxic Gymnocin-A (TPAP) [141]; the steroidal phytohormone (22*S*, 23*S*)-28-Homobrassinolide (Fig. 3.5) (RuO_4) [142]; the acetogenin 10-Hydroxyasimicin (TPAP [143]; the xenicane diterpene 4-Hydroxydictyolactone (TPAP) [144]; the antibiotic *dl*-Indolizomycin (TPAP) [145]; the carbohydrate *allo*-Inositol (Fig. 3.3) (RuO_4) [146]; the antitumour agent Irisquinone (TPAP) (Fig. 2.3) [147]; the alkaloid (+)-Laccarin (RuO_4) [148]; the alkaloid (±)-Lapidilectine B (TPAP) [149]; the colony-stimulating factor Leustroducsin B (TPAP) [150]; the pheromone (±)-Lineatin (RuO_4) [151]; the antiparasitic spiroketal macrolides (+)-Milbemycin α_1 (TPAP) [152] and (+)-Milbemycin β_1 (TPAP) [153]; the cytotoxic sponge alkaloids Motopuramines A and B (TPAP) [154]; the acetogenin Muricatetrocin C (TPAP) [155]; the sugar L-Mycarose (RuO_4) [112, 113]; the pathogenetic agent Mycocerosic acid (RuO_4) [156]; the glutamate receptor Neodysiherbaine (TPAP) [157]; the antiviral nucleoside (−)-Neplanocin A (TPAP) [158]; the sesquiterpene Nortrilobolide (TPAP) [159]; the marine alkaloid Norzoanthamine (TPAP) [160]; the phosphatase inhibitor Okadaic acid (TPAP) [161]; the triterpene (+)-α-Onocerin (RuO_4) [162]; the eunicellin Ophirin B (TPAP) [94]; the antiviral (−)-Oseltamivir (RuO_4) [163, 164]; the anticarcinogen Ovalicin (TPAP) [165]; the alkaloid (±)-Oxomaritidine (TPAP) [166]; the biologically active diterpene Phonactin A (TPAP) [167]; the cytotoxic agent Phorboxazole (TPAP) [168]; the macrolide Prelactone B (TPAP) [169]; the antibacterial agent Pseudomonic acid C (TPAP) [170]; the sugar D-Psicose (RuO_4) [171]; the immunoadjuvant QS-21A_{api} (TPAP) [172]; the lipophilic maacrolide Rapamycin (TPAP) [173], *cf* 1.11, [174], (RuO_4) [175]; the antigenic diterpene (+)-Resiniferatoxin (TPAP) [176]; the antitumour macrolide (+)-Rhizoxin D (TPAP) [177]; the spiroketal ionophore antibiotic Routiennocin (TPAP) [178, 179]; the metabolites Salicylihalamines A and B (TPAP) [180]; the anti-tumour stablising agents Sarcodictyins A and B (TPAP) [181]; the polypropionate Siphonarienolone (TPAP) [182]; the microbial metabolite (+)-SCH 351448 (TPAP) [183]; the antitumour *cis*-Solamin (RuO_4, TPAP) [184]; the heliobactericidal (+)-Spirolaxine methyl ether (TPAP) [185]; the antimicrobial Squalamine (RuO_4) [186]; the anticancer drug Taxol® (TPAP) [187, 188]; the antibiotic and antiparasitic Tetronasin (TPAP) [189, 190]; the antiviral Tamiflu ((−)-Oseltamivir) (RuO_4) [163, 164]; the antitumour Tetronolide (TPAP) [191]; the coagulation protein Thrombin (RuO_4) [192]; the antibiotic (+)-Tetronomycin (TPAP) [193]; the SERCA inhibitors Thapsigargins (TPAP) [194–196]; the sesquiterpene Thapsivillosin F and Trilobolide (TPAP) [159]; the antitumour agent Tonantzitlolone (TPAP) [197]; the sesquiterpene Trilobolide (TPAP) [159];

the naturally occurring toxin Verrucarin A (RuO_4) [198]; the therapeutic hypercholesterolemia agent Zaragozic acid A (TPAP) [199], and the cholesterol biosynthesis inhibitor 1233A (TPAP) [200].

1.2 Ru(VIII) Complexes

The chemistry of Ru(VIII) is dominated by that of the tetroxide, RuO_4.

1.2.1 Ruthenium Tetroxide, RuO_4

This was the first oxidant of Ru to be discovered and is still one of the most important and versatile. The coverage here and in subsequent chapters of organic oxidations by this reagent does not claim to be fully comprehensive but it is hoped that most of the major applications have been included. It is perhaps the most celebrated compound of Ru as an oxidant, although it does in general lack selectivity in its oxidation reactions. Its CAS number is **20427-56-9**.

It is extensively used as an oxidant, mainly catalytically. There are good reviews on its oxidative properties: [12, 34–36, 39, 60, 64, 201–203]. Rylander's historic paper [71], Courtney [60] and Gore's [35] reviews, though early, are highly recommended, as is the article by Lee and van der Engh in 1973 which gives good experimental details for a number of organic oxidations by RuO_4 [203].

1.2.2 Preparation

Although Klaus discovered Ru in 1844 [1] it was not until 1860 that he isolated (and analysed) the volatile tetroxide, by passing Cl_2 into a solution of $Na_2[RuO_4]$ [10]. It is usually prepared *in situ* from a convenient Ru compound such as the trichloride or dioxide with a suitable oxidant, a procedure used in all but the earliest organic oxidations using RuO_4. The pure compound was made by boiling aqueous $RuCl_3$ with $Na(BrO_3)$ and HCl and the vapour condensed in an ice-cooled container [204]; from Ru(IV) or Ru(VI) species distilled with $K_2(S_2O_8)$ [205]; or from Cl_2 with aqueous $K_2[RuO_4]$ [203].

However, none of the oxidations described in this book requires the use of solid RuO_4. It is generated in solution, normally in a biphasic system from a lower oxidation state compound such as $RuO_2.nH_2O$ or $RuCl_3.nH_2O$[3], and a co-oxidant replenishes the RuO_4 reduced by the organic substrate (1.2.6).

[3] The hydrates $RuO_2.nH_2O$ or $RuCl_3.nH_2O$ are much more reactive than the anhydrous materials and are always used as such for oxidation catalysis. For brevity in this book, however, they will simply be referred to as RuO_2 and $RuCl_3$ respectively.

1.2.3 Physical Properties

These have been comprehensively reviewed: [6, 12, 17]. There is only one form of the solid [206] despite early claims that there were two. It is pale yellow and, like OsO_4, has a substantial vapour pressure at room temperatures; it melts at 25.4 ± 0.1°C [206], boiling at 129.6 ± 0.2°C [207]. Its density is 3.28 g/cm^3; the solubility in water at 0°C is 1.7% and 2.11% at 50°C, but it is very soluble in those organic solvents with which it does not react such as CCl_4 [6].

1.2.3.1 X-ray and Electron Diffraction Studies

The X-ray crystal structure of the solid shows that there are two crystal modifications, one cubic and one monoclinic, but within both forms the molecule is tetrahedral with Ru=(O) 1.695(3) Å [208]**.** Electron diffraction measurements on the vapour show the molecule to be tetrahedral with an Ru=(O) distance of 1.705(8) Å [209]. Similarity of the profiles of the Raman spectra of the solid, liquid and aqueous solution suggest that the molecule has tetrahedral symmetry in all three phases (Fig. 1.3) [210]. Aqueous solutions of RuO_4 are stable only at pH below 7 [211, 212].

1.2.3.2 Electronic and Vibrational Spectra

The electronic spectra of RuO_4, $[RuO_4]^-$ and $[RuO_4]^{2-}$ in aqueous solution of the appropriate pH are shown in Fig. 1.2 (in which the 385 and 320 nm. maxima are labelled I and II respectively) and the peaks listed in Table 1.1.

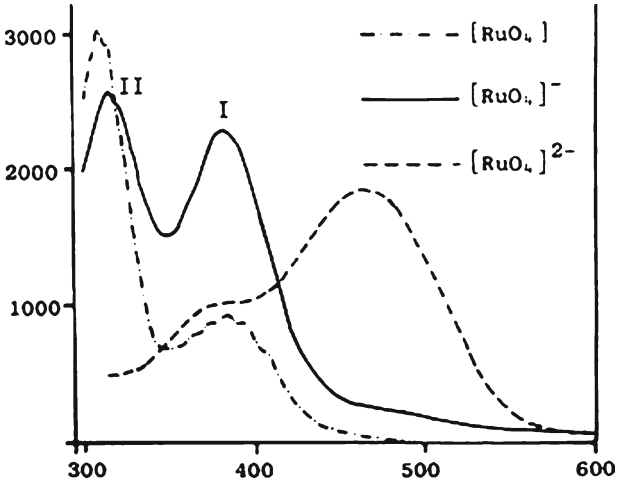

Fig. 1.2 Electronic spectra of RuO_4, $[RuO_4]^-$ and $[RuO_4]^{2-}$ in aqueous media [6] (Reproduced from the author and by Elsevier Ltd. With permission)

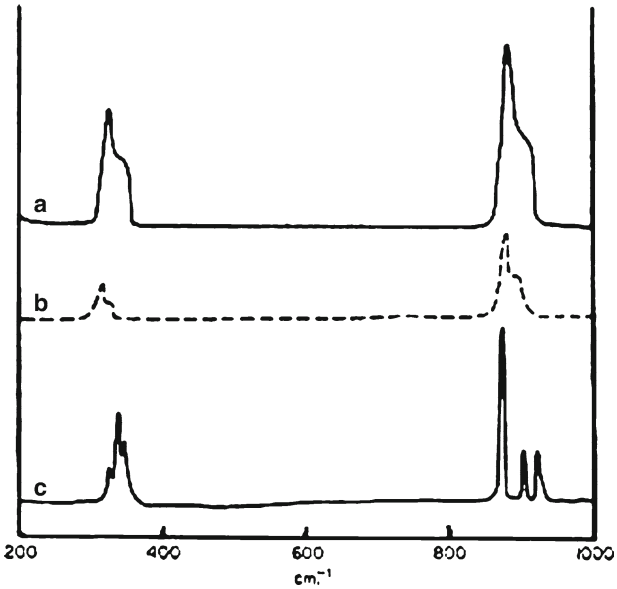

Fig. 1.3 Raman spectra of RuO_4 (**a**) pure liq.; (**b**) 5% aqueous soln.; (**c**) solid [210] (Reproduced from The Royal Society of Chemistry. With permission from [210])

Table 1.1 Electronic spectra[a] of RuO_4, $[RuO_4]^-$ and $[RuO_4]^{2-}$ in water [215]

RuO_4	310 (2960)[a]	385 (930)	–
$[RuO_4]^-$	310 (2445)	385 (2275)	460 (283)
$[RuO_4]^{2-}$	–	385 (1030)	460 (1820)

[a] λ in nm; ε in $dm^3M^{-1}cm^{-1}$

Table 1.2 Raman spectra[a] of RuO_4 (a) pure liquid; (b) 5% aqueous solution; (c) solid [210]

Fundamentals	$\nu_1(A_1)$	$\nu_2(E)$	$\nu_3(F_2)$	$\nu_4(F_2)$	Ref.
RuO_4					
Liquid	882[a]	323	914	334	[210]
Aq. soln.	883	318	921	332	[210]
Solid	881	324	922, 906	336,330	[210]
$[RuO_4]^-$					
K[RuO_4] solid	830	339	846	312	[226]
TPAP/CH_2Cl_2	844 (R^b)		843 (IR)	235 (IR)	[475]
$[RuO_4]^{2-}$					
$[RuO_4]^{2-}$/aq. KOH	807	291	828	291	[536]

[a] υ (cm^{-1})

[b] Polarised in Raman spectrum

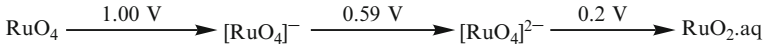

Fig. 1.4 Potential diagram for RuO_4-$[RuO_4]^-$-$[RuO_4]^{2-}$-RuO_2.aq [25, 227]

Other values of the wavelength λ and molar extinction coefficient ε have been given, e.g. in refs. [213] and [214] but differ little from the classic results of Connick and Hurley [215]. Such data can help in establishing which oxoruthenate species are present in oxidising solutions [212, 216]. A speciation diagram for RuO_4, $[RuO_4]^-$ and $[RuO_4]^{2-}$ based on electronic spectra has been given [217].

Raman spectra of RuO_4 in solid, liquid and aqueous solution phases were measured, all consistent with T_d symmetry for the molecule in these environments [210]; solid, liquid, vapour [218], solid, liquid [219], solid, liquid, vapour and for the normal and ^{18}O-substituted form of the liquid and vapour [220]. The Raman spectrum of the pure liquid (a) is very similar in profile to that of the aqueous solution (b) and of the solid (c), suggesting retention of tetrahedral symmetry in the solution (Fig. 1.3) [210]. As with electronic spectra, the Raman spectrum in particular can be useful for establishing the presence of RuO_4 in catalyst solutions [216, 221, 222].

IR spectra have been reported of isotopomers of RuO_4 with ^{16}O and ^{18}O in argon matrices [223]. Force-field calculations were made on the molecule [220, 224–226].

1.2.3.3 Electrochemical and Thermodynamic Data

The potential diagram for RuO_4 – $[RuO_4]^-$ – $[RuO_4]^{2-}$ – RuO_2.aq has been given [25], based on classic polarographic work of 1954 [227] (Fig. 1.4):

Other electrochemical data on RuO_4 have been obtained [228–230]. A Pourbaix (E-pH) diagram was given for RuO_4, $[Ru_4O_6]^{5+}$, $[Ru_4O_6]^{4+}$, $[RuO_4]^-$, RuO_2, Ru^{3+}, $Ru(OH)^{2+}$ and Ru^{2+} [231]. Thermodynamic data on RuO_4 and other Ru species were summarised [230, 232, 233], and reviewed [234]. Static electric dipole polarisabilities of RuO_4, OsO_4 and HsO_4 were calculated [235].

1.2.4 Analysis and Toxicity

The simplest method is probably colorimetric, based on its electronic spectrum [215]. It can also be determined gravimetrically by addition of diphenylsulfide or ethanol to a solution of RuO_4; this gives RuO_2 which is then reduced to the metal [236]. Alternatively addition of 2-propanol to a solution of RuO_4 solution generates $RuO_2.nH_2O$ [237].

Although it has been said [236] that RuO_4 is less harmful to the eyes than is OsO_4, nevertheless great care should always be taken in handling it. The high vapour pressure of the solid under ambient conditions makes it very dangerous

to the eyes and mucous membranes. It explodes above 100°C and can also explode when mixed with a variety of substances, e.g. HI, ethanol, diethylether, ammonia and a number of organic materials [238]. There are no oxidations in this book involving solid RuO_4, although frequent reference is made to its use in dilute solution. Nevertheless RuO_4 solutions, however weak, and indeed all Ru-containing materials, should be handled with care. Safety aspects of reactions involving RuO_4 generated from $RuCl_3$/TBHP/water-cyclohexane have been examined [186].

1.2.5 RuO_4 as an Organic Oxidant

As mentioned in 1.2.1 above, there are several reviews on the properties of RuO_4 as an oxidant in organic chemistry, both as a stoicheiometric but also as a catalytic reagent [12, 34–36, 39, 60, 64, 201–203]. It is one of the most important and versatile of Ru oxidants. In the first few years after its properties in the field were realised it was often used for oxidation of alcohol groups in carbohydrates, but its versatility as an oxidant quickly became apparent and its use was extended to a variety of other reactions, notably to alkene cleavage and, more recently, to the *cis*-dihydroxylation and ketohydroxylation of alkenes.

The properties of RuO_4 as an oxidant for organic substrates were first investigated by Djerassi and Engle in 1953 [236]. The use of OsO_4 as a selective oxidant had by then been recognised, both as a stoicheiometric and as a catalytic reagent, but RuO_4 is, by virtue of its position in the Periodic Table, a much fiercer oxidant. It was found that phenanthrene was converted to 9,10-phenanthrenequinone with a little 9,10-dihydrophenanthrene-9,10-diol, and a number of sulfides to mixtures of sulfoxides and sulfones [236]. In 1958 Berkowitz and Rylander carried out more systematic investigations using stoicheiometric RuO_4/H_2O, showing that it oxidised primary alcohols to aldehydes or carboxylic acids, aldehydes to acids, secondary alcohols to ketones, diols to the diones; alkenes were cleaved to acids and ethers to esters, amides to imides; benzene and pyridine were oxidised to intractable products [204]. The first use of RuO_4 as a catalyst seems to have been by Pappo and Becker, who in 1956 generated it *in situ* for oxidation of cholest-4-en-3-one (1) by the unusual mixture $RuO_2/Pb(OAc)_4$/aq. AcOH and also effected alkyne oxidation of 1,2-bis(1-acetoxycyclohexyl)ethyne (2) to a diketone: minimal experimental details were given. Fig. 1.5 shows two of the four oxidations accomplished by Pappo and Becker [239].

The publication used [239] is relatively obscure, and it was a paper of 1959 which really established the RuO_2/aq. $Na(IO_4)/CCl_4$ system[4] for production of RuO_4

[4] As indicated in 1.1 above, this takes the form: Ru starting material/co-oxidant/solvent; temperatures are only indicated if not ambient. For brevity RuO_2 and $RuCl_3$ denote the *hydrates* $RuO_2.nH_2O$ and $RuCl_3.nH_2O$.

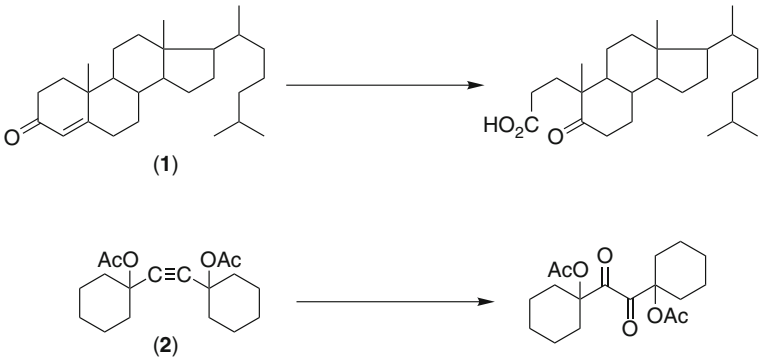

Fig. 1.5 The first catalytic oxidations by RuO_4 [239]

[240]. Although reference is often made (e.g. [241]) to Nakata's publication of 1963 as the standard procedure for this method, his use of it was more stoicheiometric than catalytic; however, Nakata was one of the first to use CCl_4 as a solvent for RuO_4 [237].

1.2.6 Co-oxidants and Solvents for RuO_4 Oxidations

Common procedures for making RuO_4 *in situ* generally use hydrated RuO_2 or $RuCl_3$ as starting materials. The dioxide RuO_2 is said to be preferable to $RuCl_3$ since oxidised chloro impurities are not formed and it may react faster than $RuCl_3$ [242]); hydrated rather than anhydrous RuO_2 should be used [243, 244].

1.2.6.1 Co-oxidants

Sodium periodate $Na(IO_4)$ (occasionally called sodium metaperiodate) is the commonest co-oxidant, e.g. as RuO_2/aq. $Na(IO_4)/CCl_4$ [240], RuO_2/aq. $Na(IO_4)$/EtOAc-CH_3CN [146], $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN [51]; *cf.* also 1.11. Very occasionally iodide from the reduced $(IO_4)^-$ can become incorporated into the organic reaction product (Fig. 3.21) [245]. Potassium periodate, as $RuCl_3$/aq. $K(IO_4)$/(BTEAC)/$CHCl_3$ is said to generate $[RuO_4]^-$ [246], but RuO_4 is probably the major product [213]. The low solubility of $K(IO_4)$ in water is disadvantageous, although it has been claimed that its use in oxidations of carbohydrates by RuO_4 renders over -oxidation less likely [247]. Periodic acid, $IO(OH)_5$, has long been known as a useful co-oxidant [248] and is becoming more popular, e.g. as in $RuCl_3$/aq. $IO(OH)_5/CCl_4$-CH_3CN [221, 249], or $RuCl_3$/aq. $IO(OH)_5/C_6H_{12}$ [216]; it is however a strong acid and this could affect some substrates. Bromate is an effective co-oxidant, e.g. $RuCl_3/Na(BrO_3)$/aq. HCl/CCl_4 [250], more so with ultrasound [242, 251]. Sodium bromate is much cheaper than $Na(IO_4)$, is equally efficient for

generating RuO_4 [252], has a lower molecular weight and is more soluble in water. Chlorite and bromite as $RuCl_3$/$Na(ClO_2)$ or $Na(BrO_2)$/aq. NaOH are less effective than the hypochlorite reagent $RuCl_3$/Na(ClO)/aq. NaOH [253].

Caro's acid has been used to generate RuO_4 from RuO_2/aq. 0.02M H_2SO_5 [254]. Caroate, as Oxone®, $2KHSO_5.KHSO_4.K_2SO_4$, better formulated as $K_5(HSO_5)_2(HSO_4)(SO_4)$, has been used as $RuCl_3$/Oxone®/aq.$Na(HCO_3)$ [255] and is increasingly popular. Hypochlorite is normally used essentially as household bleach, an aqueous basic solution of Na(ClO), and was first used for Ru oxidations in 1970 as $RuCl_3$/1.5M aq. Na(ClO) [256]. It may, depending on pH, give $[RuO_4]^-$ as well as RuO_4; in fact $[RuO_4]^-$ may prevail in basic solutions [217, 222]. Rarely-used co-oxidants to generate RuO_4 include lead tetra-acetate in RuO_2/$Pb(OAc)_4$/aq. AcOH [239]; peracetic acid in RuO_2/aq. $CH_3CO_3H/AcOH/CH_2Cl_2$ [257]; chlorate in $[Ru\{PW_{11}(O)_{39}\}]^{3-}$/aq. $K(ClO_3)$/50°C [258]; permanganate in RuO_2/aq. $K[MnO_4]$ or cerium(IV), as RuO_2/aq. $Ce(SO_4)_2.nH_2O$, both at low pH [242], though it is not entirely clear whether RuO_4 is the sole product in the latter case [222]. A simple procedure for RuO_4 generation is to bubble O_3/O_2 from an ozoniser into suspended RuO_2 or aqueous $RuCl_3$ [259].

Co-oxidants which do not generate RuO_4 include ferricyanide – despite occasional claims to the contrary, RuO_4 can not be generated from $RuCl_3$/$[Fe(CN)_6]^{3-}$/aq. base [212]. Persulfate, $(S_2O_8)^{2-}$ surprisingly does not oxidise RuO_2 to RuO_4 under ambient conditions [244], although it does do so with Ru sponge or RuO_2/aq. $K_2(S_2O_8)$/100°C [205].

1.2.6.2 Solvents

Owing to the very reactive nature of RuO_4 relatively few solvents are suitable for its reactions. It is soluble in water to the extent of some 2% and is stable in such solutions, but reacts violently with diethyl ether, benzene and pyridine [236]. It has often been used catalytically in a biphasic system, with the co-oxidant in the aqueous layer. Under these circumstances the RuO_2 formed from reduction of RuO_4 by the substrate is re-oxidised at the organic – aqueous interface, so that oxidations with such systems can be much enhanced by stirring, shaking or sonication. In some cases (e.g. oxidation of alkenes) it may be necessary to cool the reactants below room temperature, but in most cases ambient temperatures suffice, as indeed they do for the vast majority of organic oxidations catalysed by Ru complexes.

By far the most commonly used – though not the most environmentally friendly – solvent is CCl_4 (or more usually water-CCl_4). In a classic paper Sharpless et al. showed that oxidation reactions of RuO_4 (and other some Ru-based oxidants) were accelerated by addition of a little acetonitrile to the conventional water-CCl_4 biphasic mixture. It was suggested that the CH_3CN might function as a mild donor stabilising a lower oxidation state carboxylato Ru species which could be involved in the catalytic process [260]. A comparative study of CCl_4, acetone, ethyl acetate, cyclohexane and acetone for cleavage of alkenes and alkynes by $RuCl_3$/aq. $IO(OH)_5$/solvent showed that cyclohexane was the most effective [216]. Other solvents sometimes

used include CH_2Cl_2, $CHCl_3$, CH_3CN, EtOAc, and water itself is a particularly useful medium for carbohydrate oxidations.

1.2.7 Oxidations Effected by RuO_4

This account is not comprehensive, but gives some idea of the range of oxidations which can be accomplished with this versatile reagent; fuller details of more successful or useful oxidations are given in the appropriate chapters. Although when first used it was most noted for its oxidations of carbohydrates, a principal application for it now is as a catalyst for alkene cleavage and, increasingly, as a *cis*-dihydroxylation reagent for alkenes. There are several total syntheses of natural products which involve RuO_4 in one or more steps (1.1.5).

1.2.7.1 Alcohols (Ch. 2, Tables 2.1–2.3)

The first oxidation of alcohols was by stoicheiometric (hereafter abbreviated as stoich.) RuO_4/H_2O, reported in 1958, showing that primary alcohols were rapidly oxidised to aldehydes or carboxylic acids, whereas secondary alcohols gave ketones [204]. The first catalytic use of RuO_4, generated from $RuO_2/Na(IO_4)$/aq. $Na(HCO_3)/CCl_4$, was for oxidation of secondary alcohol groups on carbohydrates to ketones (Table 2.3) [261]. Carbohydrate oxidation was an important area for RuO_4-based oxidations, but is less used these days although there has been a recent resurgence of interest in it [262]. In most cases the oxidations are of secondary alcohols to ketones on carbohydrate rings [60, 263].

Primary Alcohols to Aldehydes (Table 2.1)

The two-electron oxidation of primary alcohols RCH_2OH to aldehydes RCHO is rarer with RuO_4 than is the four-electron process to RCOOH (2.1, 2.4.1.1; Table 2.1). Examples include the reagents $RuCl_3$/aq. $Na(BrO_3)/(^nBu_4N)Br/CH_2Cl_2$ [264], RuO_2/aq. $Na(IO_4)/CCl_4$ [265], the electrochemical systems $RuCl_3$/aq. NaCl-CCl_4/Pt anode (Table 2.1) [266] and RuO_2/aq. NaCl-$Na(H_2PO_4)$ @ pH 4/Pt electrodes (Tables 2.1–2.4) [267].

Oxidations to acids are more common with RuO_4 (2.2, 2.4.1; Table 2.1) and include: $RuCl_3$/TCCA/$(^nBu_4N)Br$/aq. $K_2(CO_3)/CH_3CN$ (Fig. 2.14, Table 2.1) [268]; $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN [260]; $RuCl_3$/aq. $Na(IO_4)/CCl_4$ (Table 2.1) [265]; $RuCl_3$/aq. NaCl/CCl_4/Pt anode [266], and RuO_2/aq. NaCl @ pH 7/Pt electrodes (Table 2.1) [267]. Epoxy 2-3-alcohols $R^1R^1C(O)CHCH_2OH$ were oxidised by $RuCl_3$/aq. $IO(OH)_5/CCl_4$-CH_3CN to the 2,3-epoxy acids $R^1R^1C(O)CHCOOH$ [260, 269].

Secondary Alcohols to Ketones (2.3; Table 2.2)

Early work used stoich. RuO_4/H_2O [204] or RuO_4/CCl_4 to oxidise steroidal alcohols [203], [237] while RuO_4/Freon-11 was used for oxidation of norborneol to norcamphor [270], but most subsequent work has used catalytically generated RuO_4. Examples include $RuCl_3$/aq. Na(ClO) (for desethermuscarine, *cf.* Fig. 2.5) [271], RuO_2/aq. $Na(IO_4)/CCl_4$ (hydroxylactones to ketolactones) (Fig. 2.9) [272]; *cf.* also [273, 274]. The system $RuCl_3$/TCCA/(^{n}Bu$_4$N)Br/aq. $K_2(CO_3)/CH_3CN$ effected several such oxidations (Fig. 2.14) [268], as did $RuCl_3$ or RuO_2/aq. $Na(IO_4)/CCl_4$ (Table 2.2) [265]. Oxidation of octan-2-ol by RuO_2/aq. $Na(BrO_3)/CCl_4$ was studied with respect to mixing speeds and sonication [242, 251]. A stage in the industrial preparation of the inhibitor thrombin used $RuCl_3$/aq. $Na(BrO_3)/CH_3CN$ [192]. Oxidative cleavage of monocyclic and bicyclic allylic alcohols to keto acids and di-acids respectively was effected by $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN [275].

Conversion by stoich. RuO_4/CCl_4 of cyclobutanol to cyclobutanone with no acyclic by-products suggested that the reaction proceeds through two 2-electron steps, involving hydride transfer and initial formation of $[HRu^{VI}O_4]^-$:

$$R^1R^2CH(OH) + RuO_4 \rightarrow R^1R^2C^+(OH) + [HRuO_4]^- \quad (1.1)$$

$$R^1R^2C^+(OH) + [HRuO_4]^- \rightarrow R^1R^2CO + H_2RuO_4 \quad (1.2)$$

The absence of any acyclic products from the reaction of cyclobutanol with RuO_4 suggests that clean two-electron steps are involved [276]. Kinetic data for the oxidation of 2-propanol to acetone by RuO_4/aq. $HClO_4$ indicated that at moderate acidities the rate-determining step involves hydride abstraction, while at very high acid concentrations carbonium ions may be formed [277].

For large-scale oxidations of secondary alcohols and of carbohydrates by RuO_4 *cf.* 2.3.7.

Carbohydrates (2.4; Table 2.3)

Early work with RuO_4-assisted oxidations was much concerned with alcohol functions in carbohydrates, and there are early but illuminating reviews on such reactions [60, 263].

There are a few examples of primary alcohol group oxidation in carbohydrates to carboxylic acids (2.4.1.1, 2.4.1.2). Glucopyranosides were oxidised by $RuCl_3$/$Na(BrO_3)$/water @ pH 4.5 to glucuronic acids (Fig. 2.12); kinetic studies suggested involvement of a hydride-transfer mechanism [278]. Other examples included oxidation of the 5′ hydroxy group of 2′,3′-*O*-isopropylideneadenosine to the corresponding 5′-carboxylic acid (Fig. 2.10) by $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN [279], of a galactopyranose to aldehyde and acid by RuO_2/aq. $Na(IO_4)$/(BTEAC)/$K_2(CO_3)/CHCl_3$ [246] and electrochemically by RuO_2/CCl_4/water @ pH 4/Pt anode [267].

For secondary alcohol groups in carbohydrates, although the use of $Na(IO_4)$ as co-oxidant with RuO_2 or $RuCl_3$ is common for generating RuO_4 in these reactions, use of the sparingly soluble $K(IO_4)$ as co-oxidant is said to reduce over-oxidation [91, 171, 247, 280].

In Table 2.3 a *threose* and several *furanoses* are listed first (products are alphabetically arranged in the second column); in the first column some 'large-scale' oxidations of substrates (≥1 g) are included. The effective oxidant in most cases is RuO_4, although a few involve $[RuO_4]^-$ or $[RuO_4]^{2-}$. Oxidations by stoich. RuO_4/CCl_4 were used in early work (Table 2.3) [281–286] (Fig. 2.13) shows one of the first pyranoses so oxidised [287]). Several catalytic procedures were also used: $RuCl_3$/TCCA/aq. ($^nBu_4N$)Br/CH_3CN (Fig. 2.14, Table 2.3) [268]; RuO_2/$Na(IO_4)$/-(BTEAC)/aq. $K_2(CO_3)$/$CHCl_3$ [246], RuO_2/$K(IO_4)$/aq. $K_2(CO_3)$/($PhCH_2NEt_3$)Cl)/$CHCl_3$ [288]; RuO_2/CCl_4/water @ pH 4/Pt anode (Table 2.3) [267]; RuO_2/$K(IO_4)$/aq. $K_2(CO_3)$/$CHCl_3$ (Fig. 2.13) [77], RuO_2/$Na(IO_4)$/aq. $Na(HCO_3)$/CCl_4 or -$CHCl_3$ [289], RuO_2/aq. $Na(IO_4)$/$Na(HCO_3)$/CCl_4 [247, 290], RuO_2/aq. $Na(IO_4)$/CCl_4 [261].

Pyranoses were oxidised by RuO_4 with stoich. RuO_4/CCl_4: (Table 2.3) [112, 263, 291–296]. As with furanoses, catalytic methods later held sway, e.g. RuO_2/$K(IO_4)$/aq. $K_2(CO_3)$/EtOAc [280], RuO_2/aq. $Na(IO_4)$/CCl_4 [261]; RuO_2/$K(IO_4)$/aq. $K_2(CO_3)$/$CHCl_3$ [91, 171, 203, 247]; RuO_2/aq. Na(ClO)/$CHCl_3$ [243]. Oxidation of kraft pulp cellulose by $RuCl_3$ or RuO_2/Na(ClO)/water or 0.02M aq. $H_2(SO_5)$ gave oxycellulose [254]. Oxidation of methyl-4,6-*O*-benzylidene-2-deoxy-α-D-*lyxo*-hexopyranoside by RuO_2/$K(IO_4)$/aq. $K_2(CO_3)$/$CHCl_3$ formed part of a synthesis of D-arcanose [91] and oxidation by the same reagent of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose formed part of a synthesis of D-allose [77]. Syntheses of L-mycarose and L-cladinose [112, 113] involved oxidations of methyl 4,6-*O*-benzylidene-2-deoxy-α-L-*arabino*-hexopyranoside by RuO_2/aq. $Na(IO_4)$/$CHCl_3$ [112], or by stoich. RuO_4/CCl_4 [244]. Selective synthesis of natural and non-natural carbohydrates was accomplished using an oxidative fragmentation pathway (a) at pH 4–6; or a dehydrogenation dihydroxylation cyclisation (b) at pH >7 or <4 (Fig. 3.15, 3.1.3.3) [262]. A step in the synthesis of D-psicose involved oxidation of 1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranose (Fig. 2.18) by RuO_2/$K(IO_4)$/aq. $K_2(CO_3)$/$CHCl_3$ [171].

For large-scale oxidations of carbohydrates by RuO_4 *cf.* 2.3.7**.**

Diols (2.5; Table 2.4)

Nakata showed that stoich. RuO_4/CCl_4 oxidised steroidal diols to the corresponding ketones [237]; electrogenerated RuO_4 from RuO_2/aq. NaCl/$Na(H_2PO_4)$ @ pH 4/Pt electrodes converted diols to lactones and keto acids (Tables 2.1–2.4) [267] and $RuCl_3$/aq. $IO(OH)_5$/CCl_4-CH_3CN oxidised 3-(benzyloxy)-1,2-octanediol to the acid (Tables 3.4, 3.5) [107]. A diol was converted to a lactone by stoicheiometric oxidation with RuO_4/CCl_4 as part of the total synthesis of the quassinoid (±)-amarolide [82].

1.2.7.2 Alkenes (3.1, 3.2; Tables 3.1–3.3, 3.6)

There is a rich chemistry of alkene and alkyne oxidation by RuO_4. The main application lies in alkene cleavage, but there is growing interest in *cis*-dihydroxylation by the reagent. In the sections below we first consider oxidations which do not sever the C=C bond (epoxidation, *cis*-dihydroxylation, ketohydroxylation), and then alkene cleavage reactions.

Epoxidation and cis-Dihydroxylation of Alkenes (3.1.1, 3.1.2; Tables 3.1, 3.2)

Little epoxidation catalysis has been accomplished with RuO_4 since it is a prime alkene cleavage reagent, but RuO_2/aq. $Na(IO_4)$/acetone/70°C epoxidised some $\Delta^{7,9(11)}$ conjugated sterols. (Fig. 3.1) [297, 298]. It is clear that RuO_4 should be capable, like OsO_4, of effecting this and related reactions, and its development for this purpose is potentially a very important area. On cost grounds *cis*-dihydroxylation reactions catalysed by RuO_4 may well become competitive with those effected by OsO_4, though stringent reaction conditions need to be used because RuO_4 is so much more powerful an oxidant. Reactions are much faster than for OsO_4, but so-called 'flash dihydroxylations' in which low temperatures are used have been developed and are the subject of much current research. They have been reviewed [64–67], and a discussion presented of the factors affecting whether *cis*-dihydroxylation or ketohydroxylation of alkenes occurs [66]. Examples of *cis*-dihydroxylation and ketohydroxylation effected by RuO_4 are given in Table 3.2.

The first observation of the *cis*-dihydroxylation reaction with RuO_4 was made by Sharpless et al. in 1976, who noted that *E* and *Z*-cyclododecene were oxidised by stoich. RuO_4/EtOAc/−78°C to the *threo* and *erythro* diols [299]. Later $RuCl_3$/aq. $Na(IO_4)$/EtOAc-CH_3CN/0°C was used and reaction conditions optimised for many alkenes [300]; a useful paper with good practical examples discusses the scope and limitations of the procedure (Table 3.2) [301]. Later oxidations were done with stoich. RuO_4/aq. acetone/−70°C [302]; the same reagent converted Δ^2, $\Delta^{2,4}$ and $\Delta^{4,6}$ steroids to *cis*–diols, ketones or acids [303], while RuO_2/aq. $Na(IO_4)$/acetone gave diones and acids [304].

Brönsted acid-containing systems, e.g. $RuCl_3$/aq. $Na(IO_4)$/$CeCl_3.7H_2O$/EtOAc-CH_3CN/0°C (Table 3.2) [305] effected stereoselective *cis*-dihydroxylation of glycols (Fig. 3.2); exclusive formation of *cis*-diols was observed depending on the stereochemistry of substituents present in the substrates [306]. The system was also used to *cis*-dihydroxylate a substituted cyclo-octenone as part of a total synthesis of pentopyranose derivatives [307], and $RuCl_3$/aq. $Na(IO_4)$/aq. H_2SO_4/EtOAc-CH_3CN/0°C was used for *cis*-dihydroxylation of several alkenes (Table 3.2) [308, 309], with the nature of the solvent on the efficacy of the reaction also being assessed [310]. Directions were given for both a small-scale and large-scale (18 g of product) preparation of the cyclitol (1) from $RuCl_3$/aq. $Na(IO_4)$/CH_3CN-

EtOAc/0°C to give the diol (2) (Fig. 3.3), a precursor of *allo*-inositol [146]. *Cis*-dihydroxylation of 1,6-dienes with subsequent cyclisation was catalysed by $RuCl_3$/aq. $Na(IO_4)/CH_3CN$-EtOAc/0°C (Fig. 3.13) [311].

Terminal alkene groups in nucleosides (1) were oxidised to diols (2) by $RuCl_3$/aq. $Na(IO_4)/CH_3CN$-EtOAc/0°C (Fig. 3.4) [312], and formation of the phytohormone (22*S*, 23*S*)-28-homobrassinolide achieved via *cis*-dihydroxylation of the dienone (Fig. 3.5) with $RuCl_3$/aq. $Na(IO_4)$/acetone-CH_3CN-EtOAc/6°C [142]. *Cis*-dihydroxylation of C_{60}- and C_{70}-fullerenes by stoich. RuO_4/CCl_4-1,2,4-trichlorobenzene gave the diols 1,2-$C_{60}(OH)_2$, 1,2-$C_{70}(OH)_2$ and 5,6-$C_{70}(OH)_2$ [313]. Asymmetric *cis*-dihydroxylation of α,β-unsaturated carbonyl compounds was achieved with $RuCl_3$/aq. $Na(IO_4)/CH_3CN$-EtOAc using N-enoyl sultams as chiral auxiliaries [314]. Two *cis*-dihydroxylation reactions of alkenes by RuO_2/aq. $Na(IO_4)$/EtOAc-CH_3CN/4°C were steps in the synthesis of the antiviral drug (−)-oseltamvir ('tamiflu') [164].

Density function (DFT) calculations suggest that the *cis*-dihydroxylation of alkenes following a (3+2) pathway is favoured by some 92 kJ/mol over the (2+2) path [315]. Earlier DFT calculations on possible diastereomeric osmaoxetane intermediates, using Ru as a model rather than Os, were made [316, 317]. Quantum chemical calculations were used to show why alkenes are normally cleaved by RuO_4 while they are *cis*-dihydroxylated by OsO_4 [318].

Alkene Ketohydroxylations (3.1.3, Table 3.2)

The term 'ketohydroxylation' was coined for this reaction [319, 320] and the subject has been reviewed and the scope and limitations of the procedure discussed [64, 66, 67, 319]. Factors affecting whether *cis*-dihydroxylation or ketohydroxylation of alkenes occurs were discussed [66].

Early ketohydroxylations were those of β-allenic esters $R^1R^2C{=}C{=}CHCHR^3COOEt$ to the αα′dihydroxyketones $R^1R^2C(OH)COCC(OH)CHR^3COOEt$ by flash oxidation with $RuCl_3$/aq. $Na(IO_4)/CH_3CN$-EtOAc/0°C (Fig. 3.7) [321]. The system $RuCl_3$/Oxone®/aq. $Na(HCO_3)/CH_3CN$-EtOAc oxidised alkenes to a wide range of symmetric and unsymmetrical α-hydroxyketones (Table 3.2) [67, 310, 320]. Reaction of (−)-α-pinene with stoich. RuO_4/CCl_4 gave a keto-aldehyde, while RuO_4/acetone yielded an α-ketol as the main product. A Ru(VI) diester is probably involved. Such an intermediate was isolated and both ^1H and ^{13}C NMR data suggest the structure such as that shown in Fig. 3.8. An X-ray crystal structure was carried out of the osmium analogue [322] (see also Fig. 1.31 [323]). Several chiral alkenes were oxidised to give symmetrical and unsymmetrical α-hydroxyketones (Table 3.2) [255].

In Fig. 1.6 a simplified mechanism for *cis*-dihyroxylation of alkenes and ketohydroxylation of $R^1CH{=}CHR^2$ by $RuCl_3$/Oxone®/aq. $Na(HCO_3)$/EtOAc-CH_3CN is shown. The *cis*-dihydroxylation route involves (3 + 2) cycloaddition of RuO_4 to the alkene giving a Ru(VI) ester (**1**) which is oxidised by $(HSO_5)^-$ to the Ru(VIII) ester (**2**). Reversible nucleophilic addition of water to (**2**) gives the diol $R^1CH(OH)CH(OH)R^2$ (**3**). Ketohydroxylation ensues when the activated Ru(VIII) ester

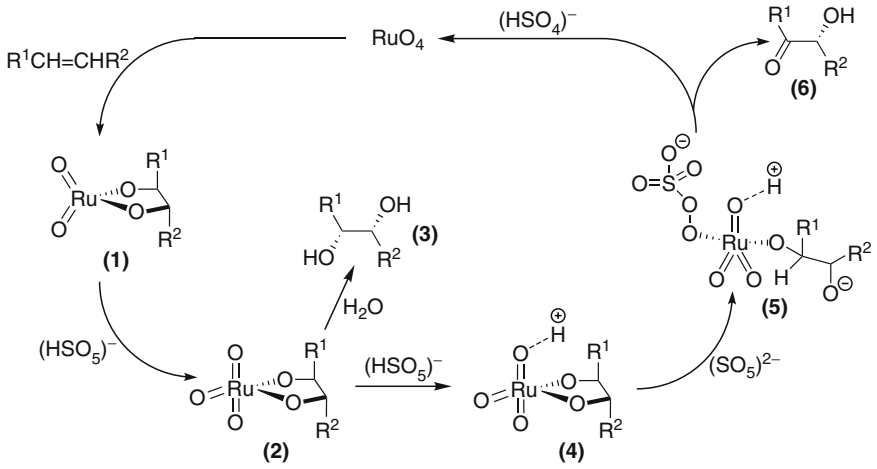

Fig. 1.6 Proposed simplified mechanism for alkene *cis*- and ketohydroxylation by RuO_4 with Oxone® (Adapted from [67, 255])

(**2**) reacts with more $(HSO_5)^-$ to give (**4**) which, with $(SO_5)^{2-}$, gives the coordinated peroxosulfate (**5**) collapsing to the α-hydroxyketone $R^1COCH(OH)R^2$ (**6**) and regenerating RuO_4 [255]; see also [67, 319].

A few other oxidations involve no C=C bond cleavage. *Cis*-9-octadecene gave 9.10-diketo-octadecane with RuO_2/aq. Na(ClO)/($^nBu_4N$)Br/CH_2Cl_2 [324], while cyclo-octene was oxidised by $RuCl_3$/aq. Na(IO_4)/DCE to 8-oxo-octanal [325]. Oxidation of Δ^2-, $\Delta^{2,4}$- and $\Delta^{4,6}$- steroids using RuO_2/aq. Na(IO_4)/acetone gave *cis*-diols, diones and acids [303] while RuO_2/aq. Na(IO_4)/CH_2Cl_2-CH_3CN oxidised 2,3-dichlorodecene to decane-2,3-dione [326].

Alkene Cleavage to Aldehydes, Ketones or Acids (3.2; Tables 3.3, 3.6)

This is one of the most important applications for RuO_4. Oxidative cleavage of alkenes and alkynes by a variety of reagents has been reviewed [30, 35, 50, 60, 68–71]. The gentler cleavage reactions of alkenes to aldehydes or ketones are considered first (Table 3.3), then the commoner cases of cleavage to carboxylic acids (Table 3.6).

The earliest paper on alkene cleavage catalysed by RuO_4 (from RuO_2/Na(IO_4)/aq. AcOH) demonstrated oxidation of cholesten-3-one and hexahydroindene to the corresponding carboxylic acids (Fig. 1.5 (1)) [239]; better experimental data were given for the use of RuO_2/aq. Na(IO_4)/acetone [327]. Early examples of aldehyde formation from alkenes by stoich. RuO_4/H_2O were reported [204, 328] (Table 3.3) [329]. The system $RuCl_3$/Oxone®/aq. Na(HCO_3)/CH_3CN or $RuCl_3$/aq. Na(IO_4)/DCE oxidised symmetrical stilbenes, trisubstituted aryl alkenes and styrene to the corresponding aldehydes (Table 3.3, Fig. 3.17) [325]. A mono-fluorinated

alkene was oxidised to the corresponding ketone by $RuCl_3$/aq. $Na(IO_4)/C_6H_{12}$-CH_3CN. Hydrolysis of the CF_2 unit to C=O did not occur; in contrast, neutral aq. $KMnO_4$ under phase transfer conditions produced no ketone but caused extensive hydrolysis (*cf.* 1.11) [330].

A total synthesis of (−)-ceratopicanol involved two Ru-catalysed oxidations: cleavage of an isopropylidene side-chain in a bicyclic enone to a diquinane dione with $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN, and the TPAP/NMO oxidation of a diol to a γ-lactone [111]. Cleavage of enolic alkenes to the corresponding ketones was effected by RuO_2/aq. $Na(IO_4)/CCl_4$ [331]; RuO_2/aq. $Na(IO_4)$/EtOAc-CF_3COOH converted 3β-acetoxy-28-hydroxy-18-lupene to acid and dione (Table 3.3) [332]. The alkene side-chain in marine odourants was oxidised by $RuCl_3$/aq. $Na(IO_4)/CCl_4$) (Table 3.3; Fig. 3.16) [333], and the sesquiterpene (+)-longifolene was oxidised to longicamphenolone by $RuCl_3$/aq. $Na(IO_4)/CHCl_3$-CH_3CN (Table 3.3) [51, 334].

Alkene cleavage to acids is the commonest reactions of alkenes with RuO_4**.** Early examples included the cleavage of sodium undecylenate to sebacic acid by RuO_2/aq. $Na(ClO)/CH_2Cl_2$ [335]. Many alkenes $R^1CX{=}CYR^2$ were oxidised to R^1COOH and/or R^2COOH with RuO_2/aq. $Na(IO_4)/CH_2Cl_2$-CH_3CN or with RuO_2/aq. Na(ClO) (Table 3.6) [326]. Hypochlorite was first used as a co-oxidant in Ru chemistry, *inter alia*, for cleavage of cyclohexene to adipic acid by $RuCl_3$/aq. Na(ClO) (Table 3.6) [256]. Oleic acid and methyl oleate were cleaved by stoich. RuO_4/CCl_4 to $Me(CH_2)_7COOH$ and $MeOOC(CH_2)_7COOH$ [211]; oxidative cleavage of monocyclic and bicyclic allylic alcohols to keto acids and di-acids respectively was accomplished with $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN (Table 3.6) [275]. Alkenes were cleaved to carboxylic acids by $RuCl_3$/aq. $IO(OH)_5/CH_3CN$-cyclohexane (Table 3.6) [216], and norbornene oxidised by RuO_2 or $RuCl_3$/aq. $Na(IO_4)/CHCl_3$ to *cis*-1,3-cyclopentane-dicarboxylic acid [336]. A simple procedure using $RuCl_3$/aq. $Na(IO_4)$/EtOAc-CH_3CN cleaved unsaturated acids and cyclic alkenes to acids (Tables 3.4, 3.6) [337]. Oxidation of linear alkenes (e.g. 1-pentadecene to myristic acid) by RuO_2 or $RuCl_3$/aq. Na(ClO)/(^{n}Bu_4N)Br/CH_2Cl_2 was carried out [324], and conjugated and cross-conjugated steroidal alkenes converted to ketones or acids effected bu RuO_2/aq. $Na(IO_4)$/acetone (Table 3.6) [338]. Oxidation of diethyl 2-allyl-2-hydroxypentanedioate by $RuCl_3$/aq. $Na(IO_4)$/CH_3CN-EtOAc gave triethyl homocitrate and the lactone [339]. The system RuO_2/aq. $Na(IO_4)$/acetone oxidised barbituric acid derivatives [340], and the fragrance (−)-Ambrox® was made by oxidation of (−)-sclareol with $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN/40°C (Fig. 3.20) [83]. Ultrasonic irradiation was used to oxidise oleic and other olefinic acids with $RuCl_3$/aq. $Na(IO_4)$/Aliquat®; Ru(VI) diesters were thought to be intermediates [341]. As part of a total synthesis of (+)-α-onocerin a (diphenylethylene)-acetoxy-ketone was oxidised to the corresponding acetoxyketoacid by RuO_2/aq. $Na(IO_4)$/acetone [162].

Oxidation of a number of substituted ethenylcyclopropanes to propanecarboxylic acids was achieved with $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN (Fig. 3.19) [342], while perfluoro alkenes were cleaved by RuO_2/aq. $IO(OH)_5$, Na(ClO) or CH_3COOOH/Freon 113 to carboxylic acids [343]; anthocyanidins, flavones, chal-

cones and coumarins were similarly cleaved by RuO_2/aq. $Na(IO_4)$/AcOH (Table 3.6) [344]. An unusual incorporation of iodine from $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN was noted in its oxidation of a terminal alkene (Fig. 3.21) [245].

Early work on the mechanisms of alkene cleavage by RuO_4 has been briefly reviewed [50]. In the oxidation of 1,5-dienes to *cis*-tetrahydrofurandiols by RuO_2/aq. $Na(IO_4)$/EtOAc-acetone it is likely that there is cyclo-addition of RuO_4 to one double bond of two 1,5-diene molecules to give a Ru(IV) diester; this is oxidised by $Na(IO_4)$ to a Ru(VI) diester, which is then hydrolysed to the organic product (Fig. 3.12) [345], and indeed Ru(VI) diesters $RuO(O_2R)_2$ have been isolated (Fig. 1.31) [323, 346] .

Kinetic studies on oxidation of methylcinnamates to benzoic acid by stoich. RuO_4/CCl_4 suggest that the first step may involve formation of a radical-cation perruthenate species to a cyclic Ru(VI) diester, which then oxidatively decomposes to two carbonyl groups; isotope and substituent effects are consistent with this scheme [347]. Kinetics of oxidation by stoich. RuO_4/CCl_4-CH_3CN of styrene and substituted styrenes to benzoic acids suggest that electron-donating groups (e.g. *p*-methoxy) slow the reaction rates while electron-withdrawing groups (e.g. *m*-nitro) increase the rate constants. The first step is envisaged as a concerted pericycloaddition (k_1) followed by a decomposition process (k_2) to aldehydes which are then oxidised further to acids [347, 348] (Fig. 1.7).

See also the discussion below on the cleavage of *trans*-cinnamate to benzoic acid by $[RuO_4]^{2-}$ (1.4.1.4, Fig. 1.16) [349, 350].

Oxidative Cyclisation of Alkenes (3.1, 3.3)

Cyclisation of geraniol- and nerol-1,5-dienes was effected by RuO_2/aq. $Na(IO_4)$/CH_3CN-EtOAc/0°C (Fig. 3.11) [351] and by $RuCl_3$/aq. $Na(IO_4)/CH_2Cl_2$-CH_3CN [260]. In the synthesis of *cis*-solamin, RuO_4 (generated from $RuCl_3/Na(IO_4)$/wet SiO_2) was used for oxidative cyclisation of a 1,3-diene, *cf.* 3.2.2.2) [184]. Isoprenoid polyenes underwent oxidative polycyclisation to tetrahydrofurans with RuO_2/aq. $Na(IO_4)/CH_3CN$-EtOAc [352–355]; squalene gave the *cis-threo-cis-threo-trans-threo-trans-threo-trans* penta-tetrahydrofuranyl diol product (Fig. 3.14) [354, 355]. A cascade of ring-closing steps with Ru(VI) diester intermediates was proposed, closure of each THF ring occurring via a *syn*-addition of two oxygen atoms in a [3 + 2] cycloaddition to each of the six double bonds of squalene (see

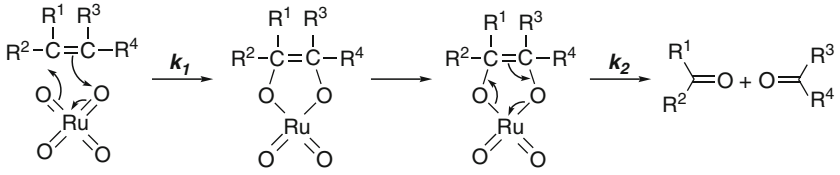

Fig. 1.7 Possible mechanism for alkene cleavage by RuO_4 for methyl cinnamates [347, 348]

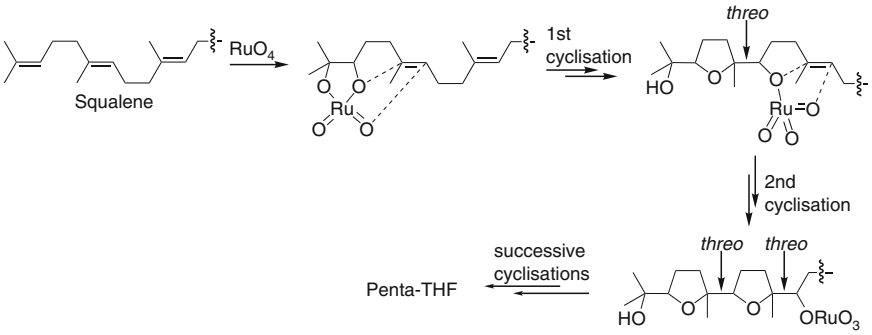

Fig. 1.8 Possible mechanism for polycyclisation of squalene with RuO_4 [352]

Fig. 1.8 for the first two ring-closing steps), giving first a mono-THF, then a bis-THF intermediate and finally the penta-tetrahydrofuranyl diol product (penta-THF in Fig. 1.8) [352].

1.2.7.3 Arenes (3.3; Tables 3.5, 3.6)

The first example of arene oxidation by RuO_4 was Djerassi and Engle's demonstration that stoich. RuO_4/CCl_4 oxidised phenanthrene to 9,10-phenanthrenequinone [236].

Oxidation of single phenyl rings was effected by $RuCl_3$ or RuO_2/aq. $Na(IO_4)$/CCl_4/60°C, e.g. phenylcyclohexane to cyclohexanecarboxylic acid (Table 3.5) [265] and the destruction of the two phenyl rings by RuO_4/aq. $Na(IO_4)$/acetone in a synthesis of 19-hydroxy-10-*iso*testosterone (Fig. 3.18; 3.2.2.1) [356]. Chemoselective oxidation of phenyl and *p*-methoxyphenyl groups attached to tetrahydropyran rings to carboxylic acids was effected by $RuCl_3$/aq. $IO(OH)_5$/CCl_4-CH_3CN (Fig. 3.22) [249]. Oxidation of a number of substrates in which phenyl groups were converted to carboxylic acids was described (Tables 3.4 and 3.5) using $RuCl_3$/aq. $IO(OH)_5/CCl_4$-CH_3CN; such oxidations were intermediate processes in a synthesis of the pheromone *R*-γ-caprolactone [107]. Pentachlorophenol and other chlorophenyls, once used as wood preservatives, were oxidatively destroyed by $RuCl_3$/Na(ClO)/0.1M aq. NaOH or $RuCl_3/K_2(S_2O_8)$/aq. 0.1M NaOH/60°C. Under these conditions $Na(IO_4)$ was relatively ineffectual [357]; presumably a mixture of RuO_4 and $[RuO_4]^-$ is involved. Polychlorinated biphenyls (PCBs) were destroyed using $RuCl_3$/Na(ClO) giving CO_2 [358] or by stoich. RuO_4/CCl_4 [359]. Oxidation of a tetralin derivative to (+)dimethyl-*tert*-butylsuccinate was effected by RuO_2/aq. $Na(IO_4)$/acetone (Table 3.5) [360]. Oxidation of 2,6-dichlorophenoxide to 2,6-dichlorobenzoquinone and of arylfurans to arylcarboxylic acids by $RuCl_3$/aq. Na(ClO)/CCl_4) probably proceeds via free radicals, observed by ESR measurements (Tables 3.4 and 3.5) [361]. The system $RuCl_3$/aq. H_2O_2/(DDAB)/80°C oxidised alkylaromatic compounds, e.g. ethylbenzene to acetophenone (Table 3.5) [362].

Several polycyclic arenes (Table 3.5) were oxidised to a variety of products by $RuCl_3$/$Na(IO_4)$/aq. EtOAc-CH_3CN (Table 3.6) [337]; $RuCl_3$/aq. $Na(IO_4)$/H_2SO_4/EtOAc-CH_3CN/0°C [308]; $RuCl_3$/aq. $Na(IO_4)$/CH_3CN-EtOAc/6°C [142]; $RuCl_3$/aq. $Na(IO_4)$/CCl_4-CH_3CN [248], and *cis*-dihydroxylated by $RuCl_3$/$Na(IO_4)$/aq. $Na(HCO_3)$EtOAc-CH_3CN/5°C [301]. Oxidation of α- and β-naphthols with $RuCl_3$/aq. Na(ClO) gave phthalic acids [363], while naphthalenes and substituted naphthalenes with RuO_2/aq. Na(ClO)/CCl_4 gave mainly phthalic acids (Table 3.5) [364, 365]. Several aromatic polycyclic steroids were selectively degraded by RuO_2/aq. $Na(IO_4)$/acetone [366], and degradation of phenylcyclohexane and of β-phenylpropionic acid was effected by $RuCl_3$/aq. Na(ClO) (Table 3.5) [256]. Oxidation of a quinone by $RuCl_3$/aq. $Na(IO_4)$/acetone-CH_3CN-EtOAc/6°C gave a diol during the part-synthesis of lactonamycin [367]. Quinolines (**1**) were oxidised to diacids (**2**) by RuO_2/aq. Na(ClO)/CCl_4 (Fig. 3.23) [368]. A wide range of arenes was oxidised by $RuCl_3.nH_2O$/aq. $Na(IO_4)$/CH_2Cl_2-CH_3CN assisted by ultrasound: thus naphthalene gave phthaladehyde and pyrene gave pyrene-4,5-dione. A mechanism was outlined for the oxidation of chrysene involving Ru(VI) esters [369]. The trifluoroactate group protects aromatic rings against oxidation by RuO_4 generated from RuO_2/aq. $Na(IO_4)$/CCl_4. Thus isoeugenyl trifluoroacetate gave vanillin and vanillic acid (Tables 3.4 and 3.6) [370].

Kinetics of naphthalene and substituted naphthalenes oxidation by stoich. RuO_4/CCl_4 to phthalic acids suggest an initial second-order reaction giving a complex with a naphthalene-O-Ru(VI) bond, followed by a slower decomposition of this intermediate involving C–H bond cleavage [371].

1.2.7.4 Alkynes (3.4; Table 3.6)

Oxidative cleavage of alkynes by a variety of reagents has been reviewed [35, 60, 70, 71]. In most cases the CC bond is broken, but in some cases α-diketones are formed instead of, or in addition to, carboxylic acids. Examples of both types of reaction are given in Tables 3.3 and 3.6.

An early paper described the use of RuO_2/aq. Na(ClO) for conversion of alkynes R^1CCR^2 (R^1=R^2=Ph, Bu and Pr) to the corresponding α-diketones and carboxylic acids [372]. Alkynes were oxidised to 1,2-diketones by $RuCl_3$/$Na(IO_4)$/aq. $Na(HCO_3)$/$Mg(SO_4)$/CH_3CN-CCl_4 [373], or by RuO_4 electro-generated by RuO_2/saturated aq. NaCl @ pH 4/0°C/Pt electrodes giving diones or acids (Table 3.3) [374]. Acetylenic amides derived from diethylamine and proline gave the corresponding amide-diones with RuO_2/aq. $Na(IO_4)$/CCl_4-CH_3CN, in a step used in the synthesis of rapamycin [175]. Oxidation of ynamides gave α-keto-imides with RuO_2/aq. $Na(IO_4)$/CH_2Cl_2-CH_3CN [375] while alkynes were converted to carboxylic acids at room temperatures by $RuCl_3$/aq. $IO(OH)_5$/CH_3CN-C_6H_{12} [216] or $RuCl_3$/aq. $IO(OH)_5$/CCl_4-CH_3CN [221]. With $RuCl_2(PPh_3)_3$/PhIO/CH_2Cl_2 terminal alkynes gave carboxylic acids (Table 3.6) while disubstituted alkynes gave α-diketones; other catalysts for this are $RuCl_2(PPh_3)_3$, $RuCl_2(CO)_2(PPh_3)_2$ and $Ru_3(CO)_{12}$) [376].

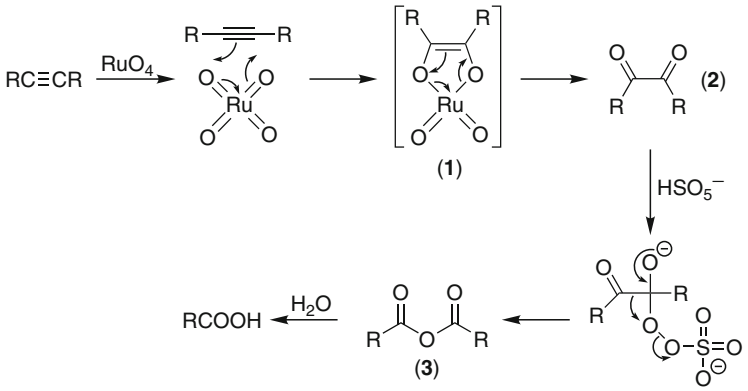

Fig. 1.9 Possible mechanism for cleavage by RuO_4 of alkynes to diones and carboxylic acids [377]

For oxidation of terminal and internal alkynes to carboxylic acids by RuO_2/Oxone®/$Na(HCO_3)$/aq. CH_3CN-EtOAc (Table 3.4) a mechanism was proposed in which $C_3H_7CCC_3H_7$ is oxidised by RuO_4 to the dione via a Ru(VI) diester (**1**), with the resulting dione (**2**) then undergoing Baeyer-Villiger oxidation by HSO_5^- to give an acid anhydride (**3**) which was hydrolysed to the acid (Fig. 1.9; R=$^nC_3H_7$) [377].

1.2.7.5 Alkanes (4.1, 4.2; Table 4.1)

Amongst Ru complexes the tetroxide is the best able to effect C–H bond activation, though some other Ru-containing reagents will do this. Some of the oxidations with Ru-based catalysts have been with adamantane as a substrate: its common oxidation products are shown in Fig. 4.2.

CH_n (n = 1 to 3) groups (4.1, 4.2, 4.3, Table 4.1)

In principle the simplest oxidations of a single C–H bond are those in the conversion of aldehydes RCHO to acids RCOOH (Table 4.1), effected by the electro-oxidative anodic systems $RuCl_3$/aq. NaCl-CCl_4/Pt-Ti anode [266] and RuO_2/aq. NaCl @ pH 7/CCl_4/Pt [267]. An early RuO_4-catalysed oxidation of a methylene group adjacent to cyclopropane rings to give a keto group (Fig. 4.1; Table 4.1) was effected by $RuCl_3$/aq. $Na(IO_4)$/CCl_4-CH_3CN; it was suggested that the cyclopropane ring may facilitate abstraction of a hydrogen radical by RuO_4 from the methylene group adjacent to the ring [378]. The same reagent converted Grundmann's ketone to the 25-hydroxyketone by oxidations of a **–CH_2–** unit [379], while oxidation of CH_2 groups in aromatic steroids gave ketones with RuO_2/aq. $Na(IO_4)$/acetone [380]. The system $RuCl_3$/aq. Na(ClO)/aq. ($^nBu_4N$)HSO_4 @ pH 9 oxidised methyl side-chains in aromatic compounds to acids; at pH 9 the main oxidising species would be RuO_4 (at pH > 9, where $[RuO_4]^-$ or $[RuO_4]^{2-}$ could be present, no such oxidation occured) [381].

Cyclic Alkanes (4.1.4, Table 4.1).

Adamantane (Fig. 4.2) is a commonly used test substrate for alkane oxidation. Some of the first RuO_4 – catalysed alkane oxidations were of cyclopentane, cyclohexane, cycloheptane and cyclo-octane to give mixtures of the corresponding ketones and acids by RuO_2/aq. Na(ClO) or $Na(IO_4)$ (Table 4.1) [382], while RuO_2/aq. $Na(IO_4)$/acetone oxidised perhydroboraphenalene to the corresponding triketone [383]. Cedranes were oxidised by $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN; e.g. epicedrane was hydroxylated regioselectively with retention of configuration to 8α-cedranolol (Fig. 4.4). A concerted mechanism in which the C-H bond is polarised by the electrophilic RuO_4 was postulated, this giving a partial positive charge on the carbon atom [384]. Oxidation with $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN/60°C of bridged polycyclic alkanes gave the alcohol and ketolactone: a concerted oxidation mechanism rather than one involving carbocations may be involved [385]. C*is*- and *trans*-pinane were oxidatively fragmented by $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN to several products but no alcohols. It was suggested that two mechanisms were involved, one involving a concerted attack pathway [386]. Oxidation of several cyclic alkanes (Table 4.1) by RuO_2/aq. $Na(IO_4)/CCl_4$-CH_3CN was accomplished; a carbocation intermediate may have been involved [387].

Second-order kinetics for oxidation of adamantane and other hydrocarbons by stoich. RuO_4/aq. acetone or /aq. CCl_4-CH_3CN were demonstrated; there is a large deuterium isotope effect, a small enthalpy and a large negative entropy of activation. A two-step mechanism was proposed: a pre-equilibrium reaction in which (for the alkene RH), RH + RuO_4 gives RH....RuO_4 which, in a rate-determining concerted reaction, yields R-O-RuO_2(OH) which is then aquated to form R(OH) [388] (Fig. 1.10) [389, 390].

During synthesis of the hormone *d*-aldosterone, 20,21-dihydroxy-11β,18-epoxy-5α-pregnan-3-one diacetate was oxidised to the 3-oxo acid by stoich. RuO_4/CCl_4 [78, 79]. Oxidation of a substituted pyrrolidine to a pyroglutamate, part of the total synthesis of the antibiotic biphenomycin B, was effected by RuO_2/aq. $Na(IO_4)$/EtOAc [102]. Oxidation of a number of Δ-5 steroids to enones was effected by $RuCl_3$/TBHP/cyclohexane [391]; safety aspects of these large-scale reactions were examined, as in the preparation of the antibacterial squalamine [186].

Epoxide ring-opening of functionalised norbornanes can be achieved with $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN/60°C to give diketones or keto-ethers (Fig. 4.5)

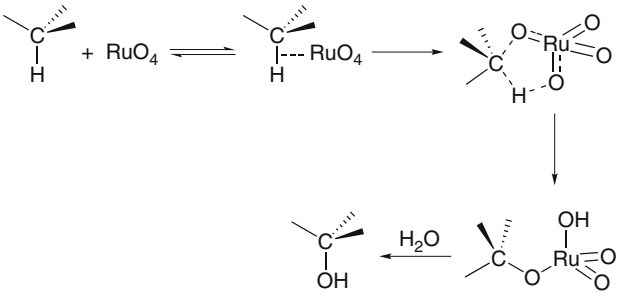

Fig. 1.10 Proposed mechanism for alkane oxidation by RuO_4 [389, 390]

[392]. The system $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN oxidised substituted epoxides containing bicyclic [2.2.1] heptane skeletons (e.g. *exo*-2,3-epoxynorbornanes) to the corresponding diketo compounds [393]. Several co-oxidants ($(IO_4)^-$, H_2O_2, Oxone®, $(ClO)^-$, $(BrO_2)^-$, $(S_2O_8)^{2-}$) were used for 2,3-epoxynorbornane oxidation, and only $(BrO_2)^-$ was ineffective [394]. As part of a study on coal oxidation (5.6.3), $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN was used for oxidation of a number of model alkanes and naphthalenes (Tables 3.4, 3.5). A large-scale oxidation of (+)-dihydrocholesterol to the ketone used RuO_2/aq. $K(IO_4)$/(BTEAC)/$K_2(CO_3)$/$CHCl_3$ (2.3.7) [288]. The reagent $RuCl_3$/aq. $Na(IO_4)$/EtOAc-MeCN achieved mild C-H oxyfunctionalisation of cyclic steroidal ethers (Fig. 4.3) [252].

There is early work on the use of RuO_4 to oxidise hydrocarbons in coals, e.g. by $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN [248, 395] and by $RuCl_3$/aq. $Na(IO_4)/CCl_4$ [396, 397] (5.6.3).

C–C Linkages (4.2; Table 4.1)

Optically pure D- and L-glyceric acids were made by cleavage of vicinal diols or of α-hydroxy acids by $RuCl_3$/aq. Na(ClO) pH 8 (Fig. 4.6) [398]. The system $RuCl_3$/aq. $Na(IO_4)/CH_3CN$-CCl_4 oxidised $PhCMeCH(OH)CH_2OH$ to PhCMeCOOH [260], and $RuCl_3$/aq. Na(ClO)/0°C converted 1,2-dihydroxycyclohexane to adipic acid [35, 256].

1.2.7.6 Amines[5] (5.1, Table 5.1)

Protecting groups are needed for the few oxidations reported for primary and secondary amines, but there is a substantial chemistry of oxidation by RuO_4 of tertiary amines and of amides

The reagent RuO_2/aq. $Na(IO_4)$/EtOAc oxidised RCH_2NH_2 to $RCONH_2$ via the protected RCH_2NH-Boc derivative to RCONH-Boc; hydrolysis then gave $RCONH_2$ [399]**.** Electrocatalytic oxidation of *N*-protected secondary amines (piperidines and proline esters) was effected by RuO_2/aq. NaCl/acetone/Pt anode [400]; RuO_2/aq. $Na(IO_4)$/EtOAc converted L-α,ω-diamino acids bearing urethane-type protecting groups to L-ω-carbamoyl-α-damino acids [401, 402]. Such oxidation of *N*-Boc-piperidines by RuO_2/aq. $Na(IO_4)$/EtOAc formed a step in the synthesis of the nutritional supplement L-carnitine [108]**.** Cyanation of tertiary amines $RNMe_2$ to the corresponding α-aminonitriles RNCH(CN)Me was catalysed by $RuCl_3$/Na(CN)/CH_3OH-AcOH/60°C. Rates of reaction and isotope effects were measured and a catalytic cycle involving iminium-ion ruthenium hydride complex was invoked [403]**.**

Optically active *N*-ethyl and *N*-benzylpiperidine gave the 2,6-diones with RuO_2/aq. $Na(IO_4)/CCl_4$ (Table 5.1) [404, 405]. Regiospecific oxidations of 2-substituted -

[5] Oxidation of primary and secondary amines and of amides may be considered either as amine/amide or as alkane oxidations; for convenience they are considered here and in 5.1.1, 5.1.2, cross-referenced in Ch. 4.

N-acetyl pyrrolidines and -piperidines to the corresponding diones or ketones were similarly effected [405, 406], as were conversions of diacetyl and dibenzyl piperazines to diketo compounds by the same system (Table 5.1) [407]. Methylene groups adjacent to the N atom in tertiary polycyclic amines were oxidised by RuO_2/aq. $Na(IO_4)/CCl_4$ (Fig. 5.5) [408]**.** A large-scale oxidation of 1,4-bis(2-phenylethyl) piperazine to the dione was made by RuO_2/aq. $Na(IO_4)$/EtOAc [409], and RuO_2/aq. $Na(IO_4)/CCl_4$ converted dialkyl or diaryl N^6,N^6-dimethyladenosines to the corresponding monoamido derivatives (Fig. 5.4) [410].

For oxidation of *N*-acylalkylamines $R^1CH_2NH(COR^2)$ to the *N*-acylalkylimides $R^1CONH(COR^2)$ by RuO_2/aq. $Na(IO_4)$/EtOAc *cf.* 5.2.3 [411].

1.2.7.7 Amides (5.2; Table 5.1)

The first reported stoicheiometric Ru-assisted oxidation of an amide was the conversion of γ-butyrolactam to succinimide by RuO_4/H_2O [204]. The reagent RuO_2/aq. $Na(IO_4)/CCl_4$ or EtOAc-CH_3CN oxidised *N*-acylated cyclic α-amino acid esters to the corresponding lactams for a variety of R^1 and R^2 groups (Fig. 5.6) [412]. Oxidation of L-proline esters to L-pyroglutamic acids was accomplished with RuO_2/aq. $Na(IO_4)$/EtOAc [413, 414], as was the first chemical conversion of L-proline to L-glutamic acid [414]. The same reagent oxidised *N*-alkyllactams to *N*-acyllactams and *NH*-lactams (Fig. 5.7) [415]. Protected proline methyl esters were converted by $RuCl_3$/aq. $Na(IO_4)$/EtOAc or CCl_4-CH_3CN to the corresponding pyrrolidin-5-ones; other protected substituted proline esters were similarly oxidised (X=H, OCOMe, OSO_2Me); *cf.* Fig. 5.9 [416]. With RuO_2/aq. $Na(IO_4)/CHCl_3$ acylated amines gave lactams and/or imides [417].

Oxidation of protected pyrrolidones to γ-lactams was accomplished with RuO_2/aq. $Na(IO_4)$/EtOAc (Fig. 5.10) [418], and the anorexigen drug *trans*-phendimetrazine was oxidised by $RuCl_3$/aq. $Na(IO_4)/CCl_4$ [419]. Oxidation of 1-formyl, 1-acetyl and 1-benzoyl-perhydro-azepines and -azocines to the corresponding N-acyllactams were accomplished with RuO_2/aq. $Na(IO_4)/CCl_4$ (Fig. 5.10) [420], and with RuO_2/aq. $Na(IO_4)$/EtOAc, 3,4-dihydroisoquinolin-1(*2H*)-ones gave *iso*quinolin-1,3,4(*2H*)-triones [421]. Oxidation of 3,4-dihydroisoquinolin-1(*2H*)-ones by RuO_2/aq. $Na(IO_4)$/EtOAc gave the corresponding isoquinolin-1,3,4(*2H*)-triones [421]. The antiviral drug (−)-oseltamvir ('tamiflu') was made via an intermediate amide to imide oxidation with RuO_2/aq. $Na(IO_4)/CH_2Cl_2$ [163].

For oxidation of ynamides by RuO_2/aq. $Na(IO_4)/CH_2Cl_2$-CH_3CN to α-ketoimides *cf.* 3.4.1.1 [375].

1.2.7.8 Ethers (5.3; Table 5.2)

The reagent most commonly used for oxidation of ethers is RuO_4, and esters or lactones are the main products; early results are well summarized by Gore [35]. The first such oxidation of an ether was in 1958 when *n*-butylether gave *n*-butyl-*n*-

butyrate with stoich. RuO_4/H_2O [204]; stoich. RuO_4/CCl_4 or catalytic RuO_2/aq. $Na(IO_4)/CCl_4$ oxidised ethers to esters or lactones [422].

Catalytic oxidation of ethers to esters or lactones was also accomplished with RuO_2/aq. Na(ClO) [423, 424]**.** Benzyl ethers of primary, secondary and tertiary alcohols were oxidised to the corresponding esters by RuO_2/aq. $Na(IO_4)/CCl_4$-CH_3CN [425]; addition of CH_3CN to the solvent with $RuCl_3$/aq. $Na(IO_4)/CCl_4$ substantially improved yields in ether oxidations [260]. Benzyl-alkyl, dialkyl, cyclic and acyclic ethers were oxidised to esters or lactones by $RuCl_3$/aq. Na(ClO) or $Ca(ClO)_2/CH_2Cl_2$ A one-electron transfer mechanism was suggested [426] in which RuO_4 or $[RuO_4]^-$ could be the effective oxidants. The furan ring in 3-alkyl-4(2-furyl)-4-oxobutanenitriles was converted by $RuCl_3$/aq. $K(IO_4)/CH_2Cl_2$-CH_3CN to the corresponding 2-alkyl-3-cyanopropanoate esters $MeO(CO)C(H)RCH_2CN$); this recent use of $K(IO_4)$ is unusual, $Na(IO_4)$ being much more water-soluble [427] (Fig. 5.15).

Oxidation by $RuCl_3$/aq. $Na(IO_4)/CCl_4$ of an ether to a dione formed part of the synthesis of the pheromone (±)-lineatin (Fig. 5.13) [151]. A substituted furan ring was oxidised by $RuCl_3$ /aq. $K(IO_4)/CH_2Cl_2$-CH_3CN to the corresponding propanoic acid (Fig. 5.15). Oxidation of cyclocholestan-6β-yl ethers by RuO_2/aq. $Na(IO_4)$/acetone-CCl_4 gave formate or acetate esters; kinetics of the oxidation of 3α,5α-cyclocholestan-6β-yl methylether to 3α,5α-cyclocholestan-6-one were investigated [428]. Oxidative cleavage of β-hydroxyethers was accomplished by $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN (Fig. 5.14) [429]. Hydride abstraction was suggested as the rate-determining step for the oxidation of THF to γ-butyrolactone by stoich. RuO_4/aq. $HClO_4$. The observed isotope effect suggested that the α-C-H bond is cleaved, and that a carbonium ion and a Ru(VI) species $[Ru(O)_3(OH)]^-$ give the product with subsequent formation of 'H_3RuO_3' (presumably $RuO_2.H_2O$) [430]. Kinetics, solvent, variation of substituent and kinetic deuterium isotope effects were studied for oxidation by stoich. RuO_4/acetone or water-CCl_4/CH_3CN of substituted 4-benzylmethylethers to methyl benzoates. The reaction is second-order, with associated complex deuterium isotope effects. A concerted S_E2-type reaction was proposed with $PhCH_2O$-coordinating to Ru giving an ether-RuO_3H intermediate (Fig. 1.11) [388, 431].

1.2.7.9 Sulfides, Sulfoxides and Sulfites (5.4; Table 5.2)

In 1953 Djerassi and Engle showed that stoich. RuO_4/CCl_4 oxidised several sulfides to the corresponding sulfones [236]. Sulfilimines ($R^1R^2S{=}NR^3$) were oxidised to sulfoximes $R^1R^2S(=O){=}NR^3$ by RuO_2/aq. $Na(IO_4)/CH_2Cl_2$ [432]; oxidation of thianthrene-5-oxide with RuO_2/aq. $Na(IO_4)/CCl_4$/0°C gave thianthrene-5,5-dioxide. Comparisons were made between the behaviour of RuO_4, CrO_2Cl_2 and $[MnO_4]^-$ for these reactions, and O-atom transfer with a possible intermediacy of $[RuO_4]^-$ was postulated [433]. Oxidations of RSPh to the sulfoxides and sulfones by stoich. RuO_4/aq. CH_3CN were studied; a concerted mechanism may be involved for these and for similar oxidations by $[RuO_4]^-$ and $[RuO_4]^{2-}$ (Fig. 1.12) [434].

The reagent $RuCl_3$/aq. $Na(IO_4)/CH_3CN$ also oxidised sulfoxides to sulfones (Table 5.2) [435], and oxidations of β-sulfidecarboxylic acids to the corresponding

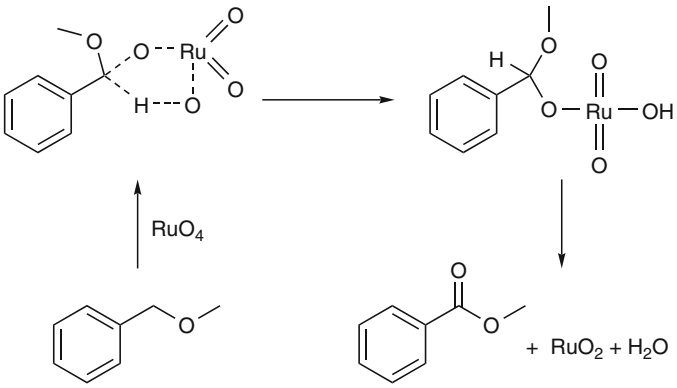

Fig. 1.11 Reaction scheme for stoicheiometric oxidation of ethers to esters by RuO_4 [388]

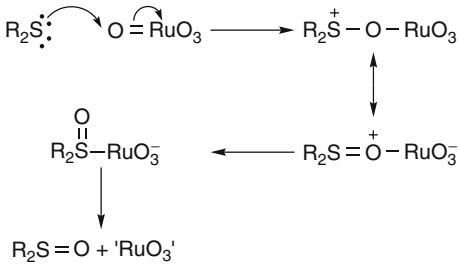

Fig. 1.12 Reaction scheme for stoich. oxidation of. R_2S to R_2SO by RuO_4 [434]

sulfones were carried out with $RuCl_3$/aq. $IO(OH)_5$ (Fig. 5.16) [436]. Conversion of a wide variety of N-sulfonylsulfilimines $R^1R^2S{=}NS(O)_2R^3$ to the corresponding sulfoximines $R^1R^2S(O){=}NS(O)_2R^3$ was effected with RuO_2/aq. CH_3CO_3H/CH_2Cl_2 [257].

Oxidation of cyclic sulfites to sulfates was accomplished with $RuCl_3$/aq. $Na(IO_4)$/CH_3CN-CCl_4/0°C and a large-scale oxidation of *D*-mannitol-1,2:5,6-diacetonide-2,3-cyclic sulfite to the sulfate described (Fig. 5.17) [437]. The system RuO_2/aq. $Na(IO_4)$/$CHCl_3$ converted cyclic sulfite diesters to the sulfates (Fig. 5.18) [438]. Oxidations of thiophene and alkyl- and aryl-substituted thiophenes by $RuCl_3$/aq. Na(ClO) were compared with similar reactions effected by stoich. $[MnO_4]^-$ [439].

1.2.7.10 Oxidations Which may Involve RuO_4 in Solution

There are numerous reports of kinetic investigations of Ru-catalysed oxidations in which the nature of the active catalyst or catalyst precursor is unclear; some work has been done in this area using electronic (Fig. 1.2) and/or Raman spectroscopy (Fig. 1.3) [212, 222]. Some oxidations thought to involve RuO_4 probably involve $[RuO_4]^-$ or indeed even $[RuO_4]^{2-}$ instead, depending on the pH of the reactions (particularly likely when hypochlorite is used as a co-oxidant) [212, 222]. Under

some circumstances RuO_4 may have a short-lived existence at pH 14 in solutions containing $(ClO)^-$ despite formation of $[RuO_4]^{2-}$. Although $[RuO_4]^{2-}$ would be expected to preponderate at this high pH, it is more rapidly oxidised by $(ClO)^-$ to RuO_4 than is the latter reduced to $[RuO_4]^{2-}$ by OH^- [217]. It is clear that $[Fe(CN)_6]^{3-}$ does not oxidise Ru(III) compounds to RuO_4 [212].

1.2.8 Other Ru(VIII) Complexes

$Ru(O)_4(py)_2$ is said to be the brown product of reaction of RuO_4 in CCl_4 with pyridine [440]; it is diamagnetic and its IR and electronic spectra were reported [441]. The complex could be of interest as a potential oxidation catalyst if it does indeed exist, but it is probably a Ru(VI) species $Ru_2(O)_6(py)_4$ (1.4.2.3) [241, 442]. It was also reformulated as $Ru^{VI}(O)_2(OH)_2(py)_2$ [443].

$[Ru(O)_3(phen)]_2O$ and **$Ru(O)_4(bpy).3H_2O$** These formulae were proposed for the products of reaction of RuO_4 with 1,10-phenanthroline (phen) or 2,2′-bipyridyl (bpy) in CCl_4 They are diamagnetic, and their electronic and IR spectra were measured [444, 445]. With methanol they give a variety of Ru(VI) and Ru(IV) complexes [444]. By analogy with '$Ru(O)_4(py)_2$', though, they may be better formulated as $Ru_2(O)_6(L)_2$ (L=bpy, phen).

$[Ru(O)_4(OH)_2]^{2-}$ was suggested as an intermediate in oxidations of alcohols or diols by RuO_4 in the presence of alkaline $[Fe(CN)_6]^{3-}$ [446, 447]. However this seems dubious since $[Fe(CN)_6]^{3-}$ does not produce Ru(VIII) in solution [212].

'$[HRu(O)_5]^-$' (presumably $[Ru(OH)(O)_4]^-$ or $[Ru(OH)(O)_4(H_2O)]^-$) has been suggested as an intermediate in the oxidation of cyclic alcohols by Ru species in the presence of bromate (BrO_3^-) as co-oxidant [448].

1.3 Ru(VII) Complexes

Just as Ru(VIII) chemistry is dominated by RuO_4, Ru(VII) chemistry is dominated by salts of the perruthenate ion, $[RuO_4]^-$, particularly TPAP, $(^nPr_4N)[RuO_4]$. Another similarity between RuO_4 and $[RuO_4]^-$ in solution is their reluctance to expand their coordination spheres beyond tetrahedral. The principal salts are listed first. There are few Ru(VII) complexes apart from $[RuO_4]^-$.

1.3.1 Perruthenates, TPAP and $[RuO_4]^-$

Although perruthenates contains no peroxo ligands (like permanganates and perrhenates) the name is a well-established one and will be used here.

1.3.2 Preparation

K[RuO_4] This dark green salt was first prepared by Deville and Debray by treatment of an aqueous solution of $[RuO_4]^{2-}$ with Cl_2 [449]. In later work a melt of $RuCl_3$, KNO_3 and KOH was extracted by water and Cl_2 at 0°C passed through the $[RuO_4]^{2-}$ so formed to give the salt [450]. Single crystals were made from RuO_4 vapour with $[RuO_4]^{2-}$ in aqueous KOH [451].

(^{n}Pr_4N)[RuO_4] (TPAP) and **(^{n}Bu_4N)[RuO_4]** (TBAP) The acronyms TPAP and TBAP were coined in 1987 [452]. The most frequently used is TPAP (CAS number **114615-82-6**); very occasionally it is called the Griffith, Ley or Griffith-Ley reagent, but here TPAP is used throughout.

The complexes were first made from K[RuO_4] and (^{n}Pr_4N)Cl [452] or (^{n}Bu_4N)Cl [453]. The simplest preparation is to add (^{n}Pr_4N)OH or (^{n}Bu_4N)OH to $RuCl_3$ or RuO_2/Na(BrO_3)/aq. M $Na_2(CO_3)$ [213, 452]. Other preparations of TPAP include reaction of K_3[Ru(ox)$_3$] and Na(BrO_3) in aq. M $Na_2(CO_3)$ with (^{n}Pr_4N)Cl [454] or from RuO_4 vapour, aq. M $K_2(CO_3)$ and (^{n}Pr_4N)Cl [455].

(PPh_4)[RuO_4] and (PPN)[RuO_4] (PPN=$(Ph_3P)_2N)^+$). The former was made by passing RuO_4 vapour into aqueous M $K_2(CO_3)$ with (PPh_4)Cl [456], and the latter in similar fashion with (PPN)Cl [455].

Supported TPAP. Although the use of supported (or 'heterogenised') TPAP is strictly not within the purview of this work, remarkable advances have been made in supporting TPAP and using it as an oxidant for alcohols, and selected examples are given here [457–461]. Polymer-supported perruthenate (PSP) is made from Amberlyst IR-27 ion-exchange resin with aqueous K[RuO_4] [461], and similarly with poly(*N*-isoprpoylacrylamide) [462] or polymer-supported 1-vinyl-3-butylimidazolium chloride [463]. Other systems include TPAP on mesoporous MCM-41 silicate (TPAP-MCM41) [464], TPAPSIL (TPAP-doped ormosil sol-gels) [457, 465–468] and TPAP with silica-supported ionic liquids [469]. A polymer-supported *N*-oxide PNAO (based on ArgoGel-NH_2 oxidised by MCBA) functioned as the co-oxidant [470], and a mobile microreactor with TPAP supported on Al_2O_3/O_2/mesitylene/75°C was used to oxidise benzyl alcohol to benzaldehyde [471].

1.3.2.1 Preparations of $[RuO_4]^-$ in Aqueous Base

Procedures include the use of: $RuCl_3$/Na(BrO_3/aq. M $Na_2(CO_3)$ [450], $RuCl_3$/(O_3+O_2)/aq. borax buffer @ pH 10 [259], K_3[Ru(ox)$_3$]/Na(BrO_3/aq. M $Na_2(CO_3)$ [454], RuO_4/aq. 0.01M $Na_3(PO_4)$/Na(ClO) (where a little Ru metal stabilises the solution) [215], and from $[RuO_4]^{2-}$/$K_2(S_2O_8)$/aq. 0.01 M KOH/100°C [214].

1.3.3 Physical Properties

1.3.3.1 X-ray Studies

The X-ray crystal structure of $K[RuO_4]$ shows the salt to have the scheelite ($CaWO_4$) structure with a slightly flattened tetrahedral anion (mean Ru=(O) 1.79 Å) [451]. A single crystal X-ray structure of TPAP shows this to contain the expected tetrahedral anion [472].

1.3.3.2 Electronic, Vibrational and ESR Spectra

Electronic spectra have been measured for the green solution in aqueous base from 250–600 nm [212–215, 222] (1.2.3; Table 1.1, Fig. 1.2) and reproduced [215, 222]. As is the case for RuO_4 and $[RuO_4]^{2-}$ the distinctive electronic spectrum of perruthenate in solution is useful for distinguishing its presence [212, 215, 222]. Potential modulated reflectance spectroscopy (PMRS) was used to identify $[RuO_4]^-$ and $[RuO_4]^{2-}$ in alkaline aqueous solutions during anodic oxidation of Ru electrodeposited on Pt from $[Ru_2(\mu\text{-}N)Cl_8(H_2O)_2]^{3-}$ [228]. A speciation diagram based on electronic spectra for RuO_4-$[RuO_4]^-$-$[RuO_4]^{2-}$ has been given for aqueous solutions at different pH [217].

The IR spectra of $K[RuO_4]$ and $Na[RuO_4]$ have been measured [210, 453, 473], as well as the Raman spectrum of $K[RuO_4]$ [210, 226] and TBAP [453] (1.2.3; Table 1.2). Force constants for $[RuO_4]^-$ were calculated [225, 226]. ESR spectra of $R[RuO_4]$ ($R={}^nPr_4N$, PPN, PPh_4) in frozen glasses in CH_2Cl_2 at 90 K were measured and are consistent with near-tetrahedral symmetry; in aqueous solution the spectrum suggests the presence of a species such as $[Ru^{VII}(O)_4(OH)_2]^{3-}$ [456]. Similarly, ESR spectra of $[RuO_4]^-$ in frozen (−135° and −160°C) aq. M NaOH solutions were interpreted as arising from $[Ru(O)_4(OH)_2]^{3-}$ with an elongated octahedral structure [474].

1.3.3.3 Electrochemical and Thermodynamic Data

For an electrode potential diagram see 1.2.3 and Fig. 1.4; data are given in [215, 227, 475]. The reversibility of polarographic waves for $RuO_4/[RuO_4]^-$ and $[RuO_4]^-/[RuO_4]^{2-}$ suggests that all three species have the same tetrahedral structures in solution [227]. A Pourbaix (E-pH) diagram has been produced covering, amongst other species, $[RuO_4]^-$ [231]. Thermodynamic data were presented for $[RuO_4]^-$ [230, 476]. Kinetics of the decomposition of $[RuO_4]^-$ in aqueous base to RuO_4 and $[RuO_4]^{2-}$ were measured spectrophotometrically; a mechanism in which H_2O_2 is formed as an intermediate was proposed, and a possible expansion of the coordination sphere of $[RuO_4]^-$ to $[Ru^{VII}(O)_4(OH)_2]^{3-}$ was considered [477].

1.3.4 TPAP and $[RuO_4]^-$ as Organic Oxidants

There are several reviews on the properties of TPAP as a catalytic oxidant in organic chemistry, [57, 59, 450, 458, 459, 478].

In aqueous base $[RuO_4]^-$ is quite a fierce oxidant, oxidising primary alcohols to carboxylic acids and secondary alcohols to ketones, and cleaving C=C double bonds in unsaturated alcohols. By contrast TPAP, which is used under non-aqueous, anhydrous conditions (powdered molecular sieves (PMS)) help the reaction by removing the water formed) is gentler, tolerating a wide variety of functional groups including olefinic double bonds. Although the stoicheiometric systems TBAP/acetone or CH_2Cl_2 oxidise primary alcohols to aldehydes and secondary alcohols to ketones without competing double-bond cleavage [40, 453], it was the discovery in 1987 that these systems could be made catalytic by using NMO as a co-oxidant that made TPAP (which is somewhat easier to prepare than TBAP) one of the most useful of all organic oxidation catalysts [452].

1.3.4.1 Co-oxidants and Solvents for TPAP and $[RuO_4]^-$ Oxidations

For TPAP or TBAP by far the commonest co-oxidant is N-methylmorpholine-*N*-oxide (NMO). For aqueous $[RuO_4]^-$ bromate is effective, as in $RuCl_3$/$Na(BrO_3)$/aq. M $Na_2(CO_3)$ [213]; hypochlorite (ClO^-) also generates $[RuO_4]^-$ rather than RuO_4 or $[RuO_4]^{2-}$, depending on the pH of the solution, e.g. as RuO_2/ or $RuCl_3$/aq. Na(ClO) [212, 217]. Bismuthate can be used as RuO_2/ or $RuCl_3$/$Na(BiO_3)$/aq. M $Na_2(CO_3)$ for generation of $[RuO_4]^-$, but is less effective than $(BrO_3)^-$ because of the low solubility of $Na(BiO_3)$ [213]. Periodate, $(IO_4)^-$ has been used as $RuCl_3$/aq. $K(IO_4)$/(BTEAC) to generate aqueous $[RuO_4]^-$ [246], but RuO_4 is probably the major product [213].

The commonest solvent for TPAP in organic oxidations is CH_2Cl_2 (DCM), normally in conjunction with 4 Å powdered molecular sieves (PMS) to remove water formed during the oxidation. Addition of CH_3CN, as in many Ru-catalysed oxidations, makes reactions with TPAP/NMO more effective [59], and occasionally CH_3CN is used as the only solvent [159]. Ionic liquids, e.g. [emim](PF_6)/PMS [479] and [bmim](BF_4)/PMS [480] have been used with TPAP/NMO. It has also been used in supercritical CO_2 [457].

1.3.4.2 Alcohols: Oxidation by TPAP and aq. $[RuO_4]^-$ (Tables 2.1–2.4)

The reagent TPAP/NMO/PMS/CH_2Cl_2 or CH_2Cl_2-CH_3CN (Tables 2.1 and 2.2) oxidises primary alcohols to aldehydes and secondary alcohols to ketones. Most labile functional groups such as double bonds, halides, enones, cyclopropanes, acetyls, peroxides and catechols, indoles, esters, tetrahydropyranyl and silyl ethers, epoxides and most protecting groups are unaffected by TPAP reagents [57, 59, 458]. The use of TPAP is now so common in synthetic organic chemistry that it can

be quite difficult to elicit modern references on the subject, so some of the material here is quite early, when conditions for its use were being optimized.

Primary Alcohols to Aldehydes (2.1; Table 2.1)

TPAP has been used as TPAP/NMO/PMS/CH_2Cl_2 in many instances for the oxidation of primary alcohols to aldehydes, but TPAP/NMO/PMS/CH_3CN and TPAP/NMO/PMS/CH_2Cl_2-CH_3CN are increasingly used (2.1.2 and Table 2.1). As TPAP/NMO/CH_2Cl_2/PMS it is more effective at oxidising primary than secondary alcohols: a 1:1 mixture of $Me(CH_2)_7OH$ with $Me(CH_2)_3CH(OH)(CH_2)_2Me$ gave 85% of $Me(CH_2)_6CHO$ and 15% of $Me(CH_2)_3CO(CH_2)_2Me$ [481].

In Fig. 2.1 preferential oxidation by this system of a primary over a secondary alcohol group is shown [482], while Fig. 2.2 illustrates oxidation of a primary long-chain alcohol by TPAP/NMO/PMS/CH_2Cl_2 with retention of its epoxy linkage [59]. The tolerance of this reagent to epoxy linkages is shown in other instances, e.g. with allylic alcohols [483] and secondary alcohols [145]; also by TPAP/NMO/PMS/CH_2Cl_2-CH_3CN (Fig. 2.7) [89, 200]. Tolerance of TPAP/NMO/PMS/CH_2Cl_2 to a triple bond was shown in the preparation of 2-propargyloxy-cyclopentanone [484].

Some reactions with TPAP have been carried out in ionic liquids, e.g. TPAP/NMO/[bmim](BF_4) ($bmim^+$=1-butyl-3-methylimidazolium) converted primary alcohols to aldehydes and secondary alcohols to ketones [480] as did TPAP/NMO or Me_3NO/[emim](PF_6) ($emim^+$=1-ethyl-3-methyl-1*H*-imidazolium cation – the use of such reagents allows recovery of TPAP) [479]. Systems such as TPAP/PMS/O_2/CH_2Cl_2 were used for oxidation of primary and secondary alcohols [485]. Various forms of supported TPAP, in essence 'heterogenised' catalysts, were used to oxidise primary alcohols to aldehydes (see below for natural products). Stoicheiometric PSP/CH_2Cl_2 oxidised a number of primary alcohols to aldehydes [486, 487] as did stoich. PSP/CH_3CN-THF (Table 2.1) [166], and catalytically as PSP/O_2/toluene/75°C [488]. The systems Si-TPAP/O_2/toluene/80°C also oxidised such systems [464]. Oxidations of both primary alcohols to aldehydes and of secondary alcohols to ketones were effected by PSP/NMO or Me_3NO/CH_2Cl_2 [461]; TPAPSIL/PMS/H_2O_2/ether [467]; Si-TPAP/O_2/toluene/75°C [468], and the polymer supported co-oxidant *N*-oxide PNAO/TPAP/CH_2Cl_2 [470]**.** Two bimetallic systems, TPAP/Cu_2Cl_2/O_2/2-aminopyridine/PMS/CH_2Cl_2 [489], and TPAP/CuCl(phen)/O_2/1,2-bis(ethoxy-carbonyl)-hydrazine/toluene/75°C [490] oxidised primary and secondary alcohols. A mobile microreactor using TPAP/NMO/CH_3CN or TPAPAl_2O_3/O_2/mesitylene/75°C oxidised benzyl alcohol [471].

Several natural products and pharmaceuticals have been made in which a TPAP-catalysed oxidation of a primary alcohol to aldehyde step occurs, and these are listed in 2.1.3: abscisic acid, altohyrtin A, (+)-arisugacin A, 14-[2H]-arteether (Fig. 2.4), astrogorgin, avermectin-B1a (Fig. 2.6), (+)-batzelladine A (Fig. 1.13), brevetoxin B, (+)-catharanthin, (±)-epibatidine, 2-epibotcinolide, (−)-7-epicylindrospermopsin, (±)-epimaritidine, epothilone C, irisquinone (Fig. 2.3), gambieric

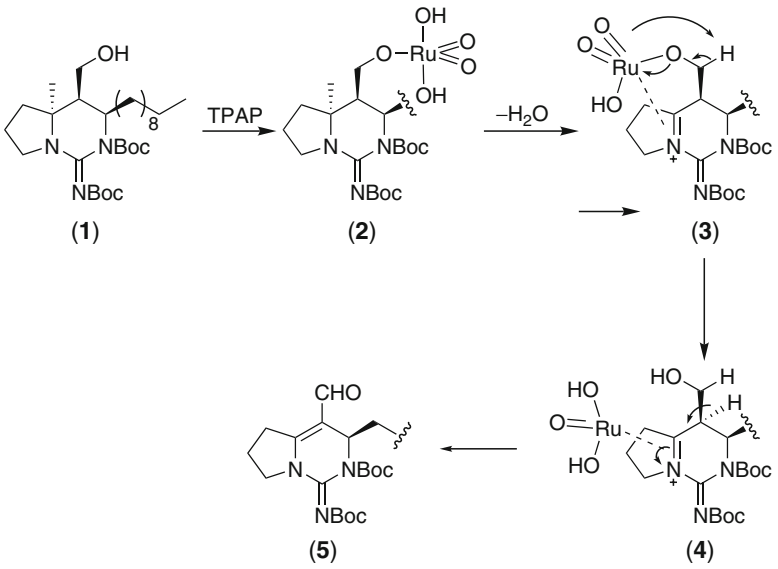

Fig. 1.13 Possible cycle for a TPAP oxidation step in the synthesis of (+)-batzelladine A [101]

acids A and C, gambierol, gymnocin-A, 10-hydroxyasimicin, leustroducsin B, (+)-milbemycin α_1, (+)-milbemycin-β_1, motopuramines A and B, nortrilobolide, norzoanthamine, okadaic acid, ophirin B, ±-oxomaritidine, prelactone B, routiennocin, salicylihalamines A and B, sarcodictyins A and B, siphonarienolone, taxol®, tetronasin, tetronolide, (+)-tetronomycin, thapsigargin, thapsivillosin F, trilobolide and 1233A.

There is a primary alcohol-to-aldehyde step in the synthesis of (+)-batzelladine A, and it was suggested that the oxidation of the primary alcohol (**1**) with TPAP/NMO/PMS/CH_2Cl_2 proceeds through an iminium-Ru alkoxide complex (**2**), rearranging as in (**3**)–(**4**) to give the aldehyde (**5**) (Fig. 1.13) [101] (a similar mechanism was proposed for the Ru-catalysed oxidative cyanation of tertiary amines [403] ; *cf.* 5.1.3.4, Fig. 5.3).

Primary Alcohols to Carboxylic Acids (2.2; Table 2.1)

There are few reported oxidations of this type with TPAP in organic solvents, one of the advantages of the reagent being that the alcohol-to-aldehyde oxidation rarely proceeds further. One natural product which did involve such a step is antascomicin B using TPAP/NMO/PMS/CH_2Cl_2 [85]. In aqueous base however $[RuO_4]^-$ is a much more powerful oxidant than TPAP in organic media, perhaps because oxidation of aldehydes to carboxylic acids may proceed via an aldehyde hydrate, the formation of which is inhibited by the molecular sieves used in catalytic TPAP systems.

Primary alcohols were oxidised to carboxylic acids by stoich. $K[RuO_4]$/aq. M NaOH [450], but $[RuO_4]^-$ in base is conveniently generated *in situ* from $RuCl_3$ or RuO_2/$Na(BrO_3)$/aq. M $Na_2(CO_3)$,and this oxidised benzylic alcohols to the acids in high yield, while the olefinic linkage in cinnamic acid was severed to give benzoic acid (Table 2.1). The reagent ($RuCl_3$/$Na(BrO_3)$/Aliquat®/aq. $Na_2(CO_3)$/DCE gave aldehydes rather than acids) [213]. Although it has been claimed that RuO_2/$Na(IO_4)$/aq. base gave $[RuO_4]^-$ (a system used to oxidise carbohydrates) [246]), electronic spectra suggest that RuO_4 rather than $[RuO_4]^-$ was present in such solutions [213]. Oxidations of 1-octanol to 1-octanal, octanoic acid and octyl octanoate, and of 2-octanol to 2-octanone were made using TPAP/Na(ClO)/aq. $Na(HCO_3)$/EtOAc (Fig. 2.18) [491]. A step in the synthesis of (+)-SCH351448 involved oxidation of a primary alcohol to an acid [183].

Secondary Alcohols to Ketones (2.3; Tables 2.2 and 2.3)

As with primary alcohols TPAP/NMO/CH_2Cl_2/PMS is a favoured reagent for secondary alcohol to ketone oxidations (for a partial listing of such oxidations see 2.3) but TPAP/NMO/PMS/CH_3CN and TPAP/NMO/PMS/CH_2Cl_2-CH_3CN are increasingly used. Sonication was used for oxidations using TPAP/NMO/PMS/CH_2Cl_2 [492]. Homopropargylic alcohols were oxidised to allenic ketones by TPAP/NMO/PMS/CH_2Cl_2 [493], and there are other examples of oxidation of allylic alcohols to enones using this system [494, 495]; also for vinyl oxiranes [496]. The supported reagent Si-TPAP/O_2/toluene or supercritical CO_2/75°C oxidised secondary alcohols to ketones [466]; for oxidations using supported TPAP for primary and secondary alcohols *cf.* 2.1.2. Isomerisation of allylic alcohols by TPAP/2-undecanol/C_6H_5F following their oxidation by TPAP/O_2/C_6H_5F was noted, e.g. of 1-phenylprop-2-enol to propiophenone; intermediacy of a Ru(III) species was proposed [497].

Several syntheses and natural products or pharmaceuticals involving the conversion of secondary alcohols to ketones using TPAP have been reported, and are listed in 2.3.3: (+)-altholactone, amphidinolide T1, antheliolide A, anticapsin (Fig. 2.7), (+)-arisugacin A and B, avermectin-B1a (Fig. 2.6), azadirachtin, calodendrolide (Fig. 2.8), (−)-CP-263,114, dysiherbaine, (±)-erythrodiene, fasicularin, fraxinellone, fuligorubin A, gambieric acids A and C, gambierol, (+)-goniodiol, gymnocin-A, *dl*-indolizomycin, (±)-lapidilectine B, (+)-milbemycin-β_1, muricatetrocin C, neodysiherbaine, nortrilobolide, norzoanthamine, ovalicin, phorboxazole, pseudomonic acid C, rapamycin, (+)-resiniferatoxin, (+)-rhizoxin D, (+)-spirolaxine methyl ether, taxol®, thapsigargins, thapsivillosin F, tonantzitlolone, trilobolide and zaragozic acid.

Some lactol-to-lactone oxidations were effected by TPAP/NMO/PMS/CH_2Cl_2 [498, 499], or TPAP/NMO/PMS/CH_3CN [159]. The system $RuCl_3$ or RuO_2/$Na(BrO_3)$/aq. M $Na_2(CO_3)$ generates $[RuO_4]^-$ in aqueous solution and oxidised secondary alcohols to ketones in high yield (Table 2.2) [213]. Kinetics of the oxidation of benzhydrol and 9-fluorenol by TPAP/NMO/CH_3CN/30°C were measured.

The oxidation is first order with respect to catalyst and alcohol, while the order with respect to NMO is fractional. A rate expression was derived and formation of a catalyst substrate complex proposed [500]. Oxidation of 2-propanol to acetone (and other secondary alcohols) by stoich. TPAP/CH_2Cl_2 may be auto-catalytic; the initial reduction product (RuO_2) may form an adduct $[RuO_4.nRuO_2]^-$ with $[RuO_4]^-$. The initially slow rate of oxidation by TPAP accelerated sharply as the concentration of product built up and then decreased near the end of the reaction because of the lower concentration of reactants, giving a bell-shaped curve typical of autocatalytic reactions [501].

Carbohydrates (2.4; Table 2.3)

Far fewer examples have been reported of carbohydrate oxidations with TPAP than with RuO_4. Some involve $[RuO_4]^-$ in aqueous solution, e.g. oxidation of ethyl and octyl α-D-glucopyranosides to glucuronic acids (Fig. 2.12) by $[RuO_4]^-$ from $RuCl_3$/$Na(BrO_3)$/aq. $Na_2(CO_3)$ @ pH 10 [278]. Reactions in organic media include oxidations of primary alcohol groups in glycopyranosides by TPAP/NMO/PMS/CH_2Cl_2 *en route* to natural products (castanospermine and 1-epicastanospermin) [109]**.** A step in the synthesis of D-psicose involved oxidation by TPAP/aq. Na(ClO) @ pH 9.5/ Me^{t}BuO of a secondary alcohol in a fructopyranose to a ketone (Fig. 2.18) [491]; of a lactol to a lactone in a ribopentafuranoside by TPAP/NMO/PMS/CH_2Cl_2 [499], and of a secondary alcohol in a fucopyranose by TPAP/NMO/PMS/CH_3CN to a fuco-1,5-lactone (Fig. 2.17) [502].

Diols (2.5; Table 2.4)

The system $RuCl_3$/$Na(BrO_3)$/aq. M Na_2CO_3 [213] converted diols to acids while TPAP/NMO/PMS/CH_3CN oxidised diols to lactones [119]; TPAP/NMO/PMS/ CH_2Cl_2 was used for diol to dione conversion for sensitive steroidal alcohols [503]. The reagent TPAP/NMO/PMS/CH_2Cl_2 oxidised primary-secondary 1,4- and 1,5-diols to lactones (Fig. 2.19) [481].

Several natural products and pharmaceuticals have been made in which a TPAP-catalysed oxidation of a primary alcohol to aldehyde step occurs, and these are listed in 2.1.3. They include agardhilactone, (−)-ceratopicanol, eleutherobin, (−)-eriolangin, (−)-eriolanin, okadaic acid, QS-21A_{api}, *cis*- rapamycin, solamin and taxol® syntheses.

Miscellaneous Oxidations of Alcohols by TPAP

The dehydrogenative coupling of primary alcohols to indoylamides was effected by TPAP/NMO/PMS/CH_3CN, e.g. of 3-phenyl-1-propanol with pratosine and hippadine [504]**.**

1.3.4.3 Alkenes and Alkanes: Oxidation by aq. $[RuO_4]^-$ (3.2; 4.1; Table 4.1)

Oxidation of cyclopentene to glutaric acid by $RuCl_3$/aq. Na(ClO)/CCl_4 or CH_2Cl_2 was much improved by addition of CH_3CN and by NaOH (presumably leading to formation of $[RuO_4]^-$ as the effective oxidant, though this was not established directly). Other co-oxidants ($Na(ClO_2)$, $Na(BrO_2)$, $Na(BrO_3)$ and $Na(IO_4)$) were less effective than Na(ClO) [253]. Oleic acid and methyl oleate were cleaved by stoich. $[RuO_4]^-$/aq. base giving $Me(CH_2)_7COOH$ and $HOOC(CH_2)_7COOH$ [211]. Rate constants were measured for the oxidation of crotonate, cinnamate, substituted crotonates and cinnamates by stoich. $[RuO_4]^-$/aq. NaOH and their behaviour contrasted with that of $[MnO_4]^-$. The initial step is probably formation of a cyclic Ru(V) ester $[RuO_2(O_2R)]^-$ which then reacts with more $[RuO_4]^-$ to give ruthenate ($[RuO_4]^{2-}$) and a Ru(VI) ester $[RuO_2(O_2R)]^-$ [505]. The fragrance (−)-ambrox® was made by oxidation of the intermediate (+)-sclareol with $[RuO_4]^-$, produced from $RuCl_3$/$Ca(ClO)_2$/aq. ($^nBu_4N$)Br/CCl_4-CH_3CN (Fig. 3.20) [83].

The $RuCl_3$/$K_2(S_2O_8)$/aq. M KOH system oxidised aldehydes RCHO to acids RCOOH [213, 450] as did $RuCl_3$/$Na_2(BrO_3)$/aq. M $Na_2(CO_3)$ [213].

1.3.4.4 Amines; Oxidation by TPAP and aq. $[RuO_4]^-$ (3.2, Ch. 4: 4.1)[6]

Secondary amines were oxidised by TPAP/NMO/PMS/CH_3CN to the corresponding imines (Fig. 5.1, Table 5.1) [506], cyclic amines to imines [507] and *N,N*-disubstituted hydroxylamines to the corresponding nitrones (Table 5.1) [508]. Dihydroxyimidazolidine derivatives were oxidised to nitronyl nitroxide radicals by TPAP/NMO/CH_2Cl_2 (Fig. 5.2) [509]; TPAP/O_2/TFE or CH_2Cl_2/PMS (TFE=2,2,2-trifluoroethanol) oxidised *N,N*-disubstituted hydroxylamines $R^1CH_2N(OH)R^2$ to the corresponding nitrones $R^1CH{=}N^+(R^2)O^-$ [510]. Stoicheiometric PSP/CH_2Cl_2 converted secondary hydroxylamines $R^1N(OH)CH_2R^2$ to nitrones $R^1N^+(O^-){=}CHR^2$ [511]. Carbohydrate azido-lactones were oxidosed to bicyclic amines (from N_3R to HN=R) by TPAP/NMO/PMS/CH_3CN as part of a synthesis of 1-*epi*hyantocidin from D-ribose [123], while dehydrogenative coupling of primary alcohols to indoylamides was effected by TPAP/NMO/PMS/CH_3CN [504].

1.3.4.5 Ethers, sulfides and miscellaneous substrates: oxidation by TPAP and aq. $[RuO_4]^-$ (5.3, 5.4, 5.6; Table 5.2)

The systems TPAP/aq. Na(ClO) @ pH 9.5/CH_2Cl_2 oxidised ethers to esters or lactones (Table 5.2) [423, 424]; it was however suggested that RuO_4 was generated [424].

[6] Oxidation of primary and secondary amines and of amides may be considered either as amine/amide or as alkane oxidations; for convenience they are considered here and in Ch. 5, cf. 5.1, 5.2, cross-referenced in Ch. 4.

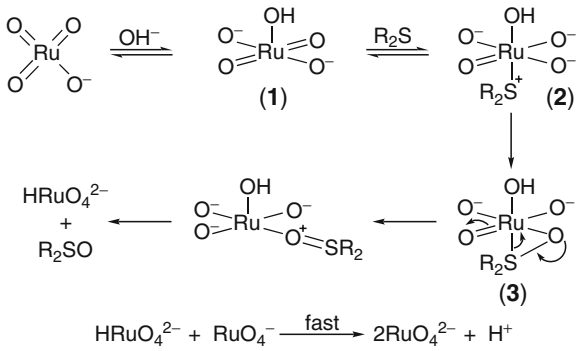

Fig. 1.14 Reaction scheme for oxidation of R_2S to R_2SO by $[RuO_4]^-$ [513]

Benzyl-alkyl, dialkyl, cyclic and acyclic ethers were converted to esters or lactones by RuO_4 or $[RuO_4]^-$ ($RuCl_3$/aq. Na(ClO) or $Ca(ClO)_2/CH_2Cl_2$). It was not stated whether RuO_4 or $[RuO_4]^-$ was the effective oxidant, but oxidation of *p*-methoxybenzylmethyl ether apparently involved a one-electron transfer process, which might be more likely to occur with $[RuO_4]^-$ [426].

The reagent TPAP/NMO/PMS/CH_3CN)/40°C is an effective chemoselective catalyst for conversion of sulfides to sulfoxides without competing double-bond cleavage (Table 5.2) [512]. In oxidations of RCH_2SPh to give RCH_2PhSO and RCH_2PhSO_2 by stoich. K[RuO_4]/water-CH_3CN and TPAP/CH_2Cl_2 a concerted mechanism may be involved with RuO_4 (Fig. 1.12) [434]. Kinetics of the oxidation of alkyl- and arylthioacetates $RSCH_2COO^-$ to the corresponding sulfoxides and sulfones by stoich. $[RuO_4]^-$/aq. 0.5M NaOH suggested that initial expansion of the coordination shell to $[Ru(O)_4(OH)]^{2-}$ (**1**) may be followed by coordination from the sulfur lone-pair to Ru (**2**) and oxo-atom transfer (**3**), with final formation of $[RuO_4]^{2-}$ from the hypothetical $[HRu(O)_4]^{2-}$ (Fig. 1.14) [513]**.**

Primary nitro compounds RNO_2 were oxidised to RCOOH (the Nef reaction; e.g. nitroethane to acetic acid) $[RuO_4]^-$ from $RuCl_3/(BrO_3)^-$/aq. M $Na_2(CO_3)$; activated primary alkyl halides RCl to RCOOH and secondary alkyl halides were similarly oxidised to ketones [213]. Secondary nitro compounds were converted to ketones by TPAP/NMO/PMS/$K_2(CO_3)/CH_3CN$ (*cf.* 5.6.4, Fig. 5.19) [514]. As part of the total synthesis of the natural product (±)-erythrodiene a nitro-alcohol intermediate was converted to the diketone by TPAP/NMO/PMS/CH_2Cl_2 [127].

1.3.4.6 Oxidations Which May Involve $[RuO_4]^-$ in Solution

There are some reports of kinetic investigations of Ru-catalysed oxidations in which the nature of the active catalyst or catalyst precursor is unclear but which may be predominantly $[RuO_4]^-$. Two papers used electronic or Raman spectroscopy to identify such species [212], [222]. Examples in which $[RuO_4]^-$ has been shown to be the active species or catalyst precursor in the oxidation of secondary alcohols to ketones include

$RuCl_3$/aq. $Na(BrO_3)$/($^nBu_4N$)Br/CH_2Cl_2 (Table 2.2) [264] and in the oxidation of secondary alcohols to ketones by $RuCl_3$/aq. $Na(BrO_3)$/ $Na_2(HPO_4)$/Aliquat®/$CHCl_3$ (Table 2.2) [515]. The system $RuCl_3$/$Na(BrO_3)$/aq. $Na_2(CO_3)$ @ pH 9.8 oxidised various forms of cellulose [516]; $[RuO_4]^-$ is probably the effective oxidant.

1.3.5 Other Ru(VII) Species

$[Ru(O)_4(OH)]^{2-}$ ESR spectra of $[RuO_4]^-$ in aqueous base suggest that this species may be present, having a flattened monocapped tetrahedral structure with a long Ru-O(OH) bond, or a bi-capped tetrahedron $[Ru(O)_4(OH)_2]^{3-}$ [456]. It has however also been suggested that such an ESR signal could arise from $[Ru(O)_4(OH)_2]^{3-}$ [474].

$[Ru(O)_4(OH)_2]^{3-}$ may be an intermediate in the alkaline decomposition of $[RuO_4]^-$ in aq. base [477], responsible for the ESR signal observed for basic solutions of $[RuO_4]^-$ [474].

$[Ru(O)_2(H_2IO_6)_2]^{3-}$ (perhaps better formulated as $[Ru(O)_2\{IO_4(OH)_2\}_2]^{3-}$) has been postulated as one of the products of reactions of $[RuO_4]^{2-}$ with IO_4^- in base [517].

1.4 Ru(VI) Complexes

Many oxo-Ru(VI) complexes are known, there having been much development in this field over the last decade. Most are octahedral, containing *trans*-dioxo ligands, but a few are *cis*, e.g. $[Ru(O)_2Cl_3]^-$ and $[Ru(O)_2(OCOR)Cl_2]^-$. The barium and potassium salts *trans*-$Ba[Ru(OH)_2(O)_3]$ and *trans*-$K_2[Ru(OH)_2(O)_3]$ contain trigonal bipyramidal anions in which the three oxo ligands are mutually *cis*, an unusual arrangement, and the sodium salt contains chains of RuO_5 trigonal bipyramids. An interesting area, as yet little investigated, is the comparison of oxidative reactivities of *cis* and *trans* oxoruthenates(VI). Simple *d*-orbital overlap considerations suggest that dioxo complexes with no d electrons (d^0) will be *trans* while d^2 complexes will be *cis* [518–521]. Calculations showed that such *cis*-complexes are favoured over the *trans* isomers if the electron donating capacity of the metal is increased (similar calculations were made for *cis*-dioxo complexes of Os and Re) [522]. Che and Yam have written a useful review of the structural, spectroscopic and electrochemical properties of oxoruthenate (VI) complexes with a representative compilation of kinetic parameters of their oxidation reactions with alcohols, alkanes and alkenes [20], and the author has reviewed the use of Ru(VI) complexes as oxidation catalysts for alcohols [40].

The next section concerns oxoruthenates with O-donor ligands (oxo, hydroxo, carboxylato) first, followed by halo donors and finally a substantial section on the rapidly growing area of N-donor complexes.

1.4.1 Ruthenates, $[RuO_4]^{2-}$

The balance of evidence (electrochemical and Raman data, *cf.* 1.2.2; Figs. 1.2, 1.3; Tables 1.1 and 1.2) suggests that ruthenate is likely to be the tetrahedral anion $[RuO_4]^{2-}$ in solution, so this formulation is used in the text. In the solid state the anion can be either $[RuO_4]^{2-}$ or, more commonly, *trans*-$[Ru(OH)_2(O)_3]^{2-}$.

1.4.1.1 Preparation

Potassium ruthenate, *trans*-$K_2[Ru(OH)_2(O)_3]$ The deep red potassium salt was first made by Klaus in 1844 (published in 1845) [1, 2]. It was later made by fusion of Ru metal with KOH and KNO_3 followed by extraction with water and crystallization, methods used also by subsequent workers [456, 523]. A dark green form which contains tetrahedral $[RuO_4]^{2-}$ (see below) was made by fusion of RuO_2 with KO_2 at 780°C for 45 days [524]. MO orbital energy levels for the anion were calculated using the Wolfsberg-Helmholtz method [523].

Sodium ruthenate, $Na_2[RuO_4]$ was prepared from RuO_2 and Na_2O_2 at 800–900°C [525].

$Rb_2[RuO_4]$ is dark green, made by fusion of RuO_2 and '$RbO_{1.6}$' (*sic*) at 780°C over a 45-day period [524].

$Cs_2[RuO_4]$ This dark green salt was prepared from Cs_2O_2 and RuO_2 in a 2.2:1 ratio at 800°C under argon [526].

$CsK_5[RuO_5][RuO_4]$ This dark green salt is made by heating to 750°C a mixture of $KO_{1.2}$, $CsO_{1.2}$ and RuO_2 [527].

Barium ruthenate, *trans*-$Ba[Ru(OH)_2(O)_3]$, sometimes formulated as $Ba[RuO_4].H_2O$, is made by addition of a barium salt to an alkaline solution of $Na_2[RuO_4]$ [450, 528]; it is brick-red and insoluble in water.

The salt is a useful starting material for other Ru(VI) complexes; thus with pyridine and RCOOH (R=CH_3, C_2H_5, C_3H_7, Me_2CH and C_6H_5) *trans*-$Ru^{VI}(O)_2(py)_2(OCOR)_2$ complexes are formed [529].

1.4.1.2 $[RuO_4]^{2-}$ in Aqueous Base

Preparations of this include reaction of $RuCl_3$ [213] or $K_3[Ru(ox)_3]$ [454] with $K_2(S_2O_8)$ in aq. M KOH or by ozonolysis of RuO_2 in aq. M KOH [259]; from RuO_4 in CCl_4 in aqueous M NaOH [211, 530] or KOH [276]; from *trans*-$Cs_2[Ru(O)_2Cl_4]$ and $K_2(S_2O_8)$ in 2M aq. KOH [214]; or from $[RuO_4]^-$ with H_2O_2 in M aqueous NaOH [215].

The ion is stable at high pH only. At pH > 12 (in 0.05 aq. M [OH^-]) there is a mixture of $[RuO_4]^-$ and $[RuO_4]^{2-}$ in solution; below 0.005M [OH^-] RuO_4 is stable; above 0.1 M [OH^-] essentially pure $[RuO_4]^{2-}$ is present [212]. A speciation diagram for RuO_4 – $[RuO_4]^-$ – $[RuO_4]^{2-}$ has been given [217]; disproportionation of $[RuO_4]^{2-}$ to $[RuO_4]^-$ and $RuO_2.nH_2O$ in aqueous alkali was studied [215]. Kinetics of the oxidative dissolution of RuO_2 by O_3 to give $[RuO_4]^{2-}$ and $[RuO_4]^-$ were measured: formation of $[RuO_4]^{2-}$ is the first step followed by autocatalytic reactions giving $[RuO_4]^-$ [531]; there is similar work with $[Ru(NO)(OH)_5]^{2-}/O_3$/aq. NaOH [532].

The reversibility of the $[RuO_4]^-$ – $[RuO_4]^{2-}$ couple (*cf.* 1.4.1.3) and the Raman spectrum of ruthenate in aqueous base suggest that it is tetrahedral, $[RuO_4]^{2-}$, in solution. Thus, unlike RuO_4 and $[RuO_4]^-$, ruthenate changes the structure of its anion from that of the trigonal bipyramidal *trans*-$[Ru(OH)_2(O)_3]^{2-}$ in the solid potassium and barium salts to tetrahedral $[RuO_4]^{2-}$ in solution. There is evidence from electronic spectra of potassium ruthenate doped into K_2CrO_4 and K_2SeO_4 and of barium ruthenate doped into $BaSO_4$, $BaCrO_4$ and $BaSeO_4$ that, in that these environments at least, the Ru is tetrahedrally coordinated [533].

1.4.1.3 Physical Properties

X-ray Studies

Two X-ray crystal structure analyses show potassium ruthenate to be *trans*-$K_2[Ru(OH)_2(O)_3]$ [523, 534] (identical in chemical analytical terms to Klaus' original formulation of it as $K_2[RuO_4].H_2O$). The anion is trigonal bipyramidal (Fig. 1.15) with the two hydroxo ligands in the *trans* position (Ru-(OH) distances 2.028(2) and 2.040(2) Å.). The three equatorial Ru=(O) distances are 1.763(2), 1.760(2) and 1.741(2) Å with the axial O atoms of the hydroxo ligands at 2.028(2) and 2.040(2) Å. The anion has slightly distorted D_{3h} symmetry: the (O)=Ru=(O) angle of the apical hydroxo ligands is 177.3(1)° rather than the idealised 180°, and the three equatorial (O)=Ru=(O) angles are not 120° but close to those at 120.3(1), 116.9(1) and 122.8(1)° [523, 526]. An X-ray crystal structure of $K_2[RuO_4]$ made by fusion of RuO_2 and KO_2 at 780°C shows the salt to be of the β-K_2SO_4 type; the anions are isolated tetrahedral (Ru=(O) varying between 1.740 and 1.690 Å, no standard deviations quoted); $Rb_2[RuO_4]$ was also studied and the Ru=(O) distances lie between 1.773 and 1.666 Å) [524].

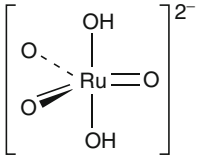

Fig. 1.15 Structure of the anion of *trans*-$K_2[Ru(OH)_2(O)_3]$ [523]

The X-ray structure of $Na_2[RuO_4]$ shows the anion to contain RuO_4 chains of two non-equivalent RuO_5 trigonal bipyramids within the unit cell; these share axial corners, with Ru-(O_{ax}) distances of *ca.* 2.00 Å (axial) and Ru=(O) 1.76 Å (equatorial), the Ru-(O_{ax})-Ru angle in the …Ru-O_{ax}-Ru-O_{ax}-Ru… chain being 125° [525]. The X-ray crystal structure of $Cs_2[RuO_4]$ shows the salt to be of the β-K_2SO_4 type; the anions are isolated tetrahedral (Ru=(O) varying between 1.737 and 1.766 Å with no standard deviations quoted) [524]. In $CsK_5[RuO_5][RuO_4]$ the X-ray crystal structure shows that there is a 50:50 assemblage of anions which are tetrahedral and trigonal bipyramidal: in the former the mean Ru–(O) distance is 1.75 Å, and in the latter the mean Ru-(O) axial distances are 1.93 Å and the equatorial 1.80 Å [527]. In *trans*-$Ba[Ru(OH)_2(O)_3]$ the X-ray structure shows the anion to be trigonal bipyramidal as in the potassium salt, and atomic dimensions are close to those of the latter. There are two equatorial Ru=(O) distances of 1.759 and one of 1.751 Å, and the axial Ru-(OH) distances are 2.036 Å. The three (O)=Ru=(O) angles are 120.8°, 118.4° and 118.4° and the angle between the two oxygen (hydroxo) ligands is 177.8° [528].

Electronic, Vibrational and ESR Spectra (*cf.* also 1.2.3)

Ruthenate is unusual in that it appears to undergo a change of structure from the solid state to aqueous solution; as indicated above, RuO_4 and $[RuO_4]^-$ retain their tetrahedral structures in the solid and solution states. Potassium and barium ruthenates contain the *trans*-$[Ru(OH)_2O_3]^{2-}$ anion, while $Cs_2[RuO_4]$ is tetrahedral.

Electronic spectra (Table 1.1, Fig. 1.2) have been measured for the orange solutions of $(RuO_4]^{2-}$ in aqueous base from 250–600 nm. [212–215, 222], and reproduced [215, 222]. There are two at 460 and 385 nm. [212, 213, 222] or three bands in the visible-UV region, at 460, 385 and 317 nm [214, 215]. These appear to be at the same positions as those for $[RuO_4]^-$ but the intensities and hence the general outline of the two spectra are very different. Woodhead and Fletcher reviewed the published molar extinction coefficients and their optimum values / dm (mol^{-1} cm^{-1}) are 1710 for the 460 nm. band, 831 for the 385 nm. band and 301 for the 317 nm. band – the latter band was not observed by some workers [214]. The distinctive electronic spectrum of ruthenate in solution is useful for distinguishing between it, $[RuO_4]^-$ and RuO_4 [212, 222]. Measurements of the electronic spectra of potassium ruthenate doped in K_2CrO_4 and K_2SeO_4 and of barium ruthenate doped into $BaSO_4$, $BaCrO_4$, and $BaSeO_4$ (in all cases the anions of these host materials are tetrahedral) indicate that in that these environments at least the Ru is tetrahedrally coordinated. Based on this evidence it has been suggested that $[RuO_4]^{2-}$ in aqueous solution is tetrahedral $[RuO_4]^{2-}$ rather than *trans*-$[Ru(OH)_2(O)_3]^{2-}$ [533, 535]. Potential modulated reflectance spectroscopy (PMRS) was used to identify $[RuO_4]^-$ and $[RuO_4]^{2-}$ in alkaline aqueous solutions during anodic oxidation of Ru electrodeposited on platinum from $[Ru_2(N)Cl_8(H_2O)_2]^{3-}$ [228].

The IR and Raman spectra of *trans*-$Ba[Ru(OH)_2(O)_3]$ and of *trans*-$K_2[Ru(OH)_2(O)_3]$ [40, 536] have been measured and assigned, as have those of their deuterated forms

[536]. In aqueous base however the Raman spectrum of $[RuO_4]^{2-}$ is very simple and has a different profile from those of the solid potassium and barium salts (Table 1.2).

The ESR spectrum of powdered *trans*-$Na_2[Ru(OH)_2(O)_3]$ showed two broad, overlapping bands at g 2.04 and 1.98 at room temperature [456], relatively close to the g_{eff} of 2.0 and 2.05 found by Carrington et al. of at 20 K [537]. The magnetic susceptibility of solid *trans*-$K_2[Ru(OH)_2(O)_3]$ from 80–370 K follows the Curie-Weiss law with $\mu_{eff} = 2.721(3)$ B.M. and a θ value of −9.6 K with g = 1.923 assuming that S = 1 [523]. Magnetic susceptibility measurements on $K_2[RuO_4]$ down to 60K show that the salt obeys the Curie-Weiss law (θ −30K) with a magnetic moment μ_{eff} of 2.68 B.M. The magnetic susceptibility of $Rb_2[RuO_4]$ was measured down to 60K and also obeys the Curie-Weiss law (θ −19 K); the magnetic moment μ_{eff} is again 2.68 B.M. [524]. The molar magnetic susceptibility χ_M of $Na_2[RuO_4]$ has a maximum at 74 K and the salt is a magnetic semiconductor at all temperatures [525].

Electrochemical and Thermodynamic Data; Analysis of $[RuO_4]^{2-}$

For an electrode potential diagram *cf.* 1.2.3, Fig. 1.4. The $[RuO_4]^{-}/[RuO_4]^{2-}$ couple has been determined potentiometrically as +0.59 V. at 25°C from pH 11.5 to 12.6 [215], in good agreement with data from polarographic measurements [227]. It is reversible polarographically and independent of hydroxide concentration [227], suggesting that $[RuO_4]^{2-}$ is tetrahedral in solution, as is $[RuO_4]^{-}$. Eichner studied the equilibria between RuO_4, $[RuO_4]^{-}$ and $[RuO_4]^{2-}$ electrochemically and as a function of pH [538].

Thermodynamic data for salts of the ruthenate anion have been accumulated [230, 476, 539]. The simplest analytical procedure for ruthenate is colorimetric, based on the use of its electronic spectrum [215].

1.4.1.4 $[RuO_4]^{2-}$ As an Organic Oxidant

As with RuO_4 and $[RuO_4]^{-}$, ruthenate was first investigated as a stoicheiometric oxidant and then used catalytically, $[RuO_4]^{2-}$ being generated *in situ* by a suitable co-oxidant. It suffers by being usable only in strong aqueous base; water is a cheap but limiting solvent, and the alkali necessary to keep $[RuO_4]^{2-}$ stable is inimical to many organic substrates, representing a severe restriction on its utility as an oxidant. The reagent is self-indicating: the orange colour of ruthenate changes to black (probably colloidal RuO_2) on addition of substrate, the orange colour reappearing when the oxidation is complete [213, 540].

Persulfate is the most commonly used oxidant for ruthenate. It was first noted in 1952 that $[RuO_4]^{2-}$ could be generated from powdered Ru and $K_2(S_2O_8)$ in boiling 4M aq. NaOH [215], but now is normally made from $RuCl_3/Na_2(S_2O_8)$ or $K_2(S_2O_8)$/aq. M NaOH [213], or from $RuCl_3$ or $RuO_2/Na(BrO_3)$/aq. M NaOH [213]. Although expensive and environmentally unfriendly, $RuCl_3$ or $RuO_2/[Fe(CN)_6]^{3-}/$

aq. M NaOH has been used on a preparative scale for oxidation of primary alcohols to carboxylic acids and secondary alcohols to ketones [212]. No solvents other than water (normally as aqueous base) has yet been found effective for oxidations by alkali-metal ruthenates, although *trans*-Ba[$Ru(OH)_2(O)_3$] can be used in acetic or trifluoroacetic acids as a suspension.

Primary and Secondary Alcohols (Tables 2.1 and 2.2)

The system $[RuO_4]^{2-}$/aq. M NaOH was first shown in 1972 to function as a stoicheiometric oxidant: primary alcohols were oxidised to carboxylic acids and secondary alcohols to ketones; it is a more vigorous oxidant than ferrate, $[FeO_4]^{2-}$ [530]. Its first catalytic use dates from 1979, when, following a report that it can be generated from Ru powder/$K_2(S_2O_8)$/aq. 4M NaOH/100°C [541], the room-temperature system $RuCl_3/K_2(S_2O_8)$/aq. M KOH was developed [540] and its use extended with $RuCl_3/Na_2(S_2O_8)$ or $K_2(S_2O_8)$/aq. M NaOH [213, 450]. Oxidations of primary alcohols to acids and of secondary alcohols to ketones were carried out with $RuCl_3/Na_2(S_2O_8)$ or $K_2(S_2O_8)$/M aq. KOH or NaOH; $RuCl_3/K_2(S_2O_8)$/Aliquat®/aq. M KOH/DCE oxidised primary alcohols to aldehydes (Tables 2.1 and 2.2) [213]. However the reagents attacked allylic double bonds (e.g. allyl and crotyl alcohols gave acrylic and β-methacrylic acids in low yields only) [450]. Another system involving $[RuO_4]^{2-}$ for oxidation of primary alcohols to carboxylic acids and secondary alcohols to ketones is $RuCl_3/[Fe(CN_6]^{3-}$/aq. M NaOH [212]. Oxidation of allylic and benzylic alcohols by $[RuO_4]^{2-}$/aq. $K_2(S_2O_8)$/Adogen®/CH_2Cl_2 gave aldehydes or ketones, while diols gave hydroxyketones (Tables 2.2 and 2.4) [542]. Stoicheiometric *trans*-Ba[$Ru(OH)_2(O)_3$]/CH_2Cl_2 oxidised alcohols to aldehydes and ketones [450], while *trans*-Ba[$Ru(OH)_2(O)_3$]/($^nBu_4N$)IO_4/CH_2Cl_2 converted cyclohexanol to cyclohexanone [543].

Kinetic studies of the oxidation by stoich. $[RuO_4]^{2-}$/aq. M NaOH of 2-propanol and cyclobutanol were made; the high yield of cyclobutanone from the reaction suggested that it functions as a one-step, two-electron oxidant [544]. Kinetics of the oxidation by stoich. $[RuO_4]^{2-}$/aq. base of cyclobutanol with its high conversion to cyclobutanone and the absence of acyclic products from oxidations effected by stoich. RuO_4/CCl_4 suggests that the reaction proceeds through two-electron steps, as for RuO_4 (1.2.7.1.1 [276]. A suggestion [545] that oxidation reactions by $[RuO_4]^{2-}$ are initiated by traces of $[RuO_4]^-$ was refuted [450, 544]**.** Kinetics of the oxidation of 2-propanol, mandelic acid and substituted mandelic acids by $[RuO_4]^-$ and $[RuO_4]^{2-}$/aq. base show striking similarities between the reactions of both oxidants (concavity of Hammett plots, primary deuterium isotope effects, small enthalpies of activation and large negative entropies of activation). It was suggested that $RCH_2(OH)$ forms an adduct $[RC(OH).RuO_3(OH)]^{2-}$ with ruthenate a rate-limiting decomposition of this by homolytic cleavage of the Ru-C bond ensues [546].

The systems $RuCl_3/K_2(S_2O_8)$/aq. M KOH [213, 450] oxidised diols to acids and $[RuO_4]^{2-}$/aq. $K_2(S_2O_8)$/Adogen®/CH_2Cl_2 converted diols to ketones (Table 2.4) [542]. Oxidation of purine and pyrimidine nucleosides of AZT by $RuCl_3/K_2(S_2O_8)$/aq. M KOH gave the corresponding 5′-carboxylic acid derivatives (Fig. 2.11).

It was implied that RuO_4 was involved [547], but under the conditions used it is likely that ruthenate, $[RuO_4]^{2-}$, was the oxidant. Oxidation of methyl-α-D-glucopyranoside (MGP) and octyl-α-D-glucopyranoside (OGP) to the corresponding α-D-glucuronic acids (Fig. 2.11) was accomplished with $RuCl_3$/$Na(BrO_3)$/aq. M NaOH [278], and some protected ribo-, fructo- and glucofuranoses converted by $[RuO_4]^{2-}$/aq. $Na(IO_4)$ to uronic acids [548]. Corey et al. used stoich. $[RuO_4]^{2-}$/aq. M NaOH to oxidise a hydroxy acid to a ketone as part of the total synthesis of gibberellic acid [138]. Primary alcohol groups in several protected ribo-, fructo- and glucofuranoses were converted to the corresponding uronic acids by $RuCl_3/K_2(S_2O_8)$/aq. M KOH [548].

Alkenes and Alkanes

Kinetic studies were made on the cleavage of *trans*-cinnamate to benzoic acid by stoich. $[RuO_4]^{2-}$/aq. 1.7M NaOH/85°C; isotope effects and activation parameters were determined. Formation of an alkene-$[RuO_4]^{2-}$ cyclic Ru(IV) ester (1), oxidation of this with more ruthenate to the cyclic Ru(VI) ester (2) and oxidative decomposition of this via (3) to aldehydes R^1CHO and R^2CHO was suggested. The aldehydes are subsequently oxidised to R^1COOH and R^2COOH by more $[RuO_4]^{2-}$ (not shown in the Scheme) (Fig. 1.16) [349, 350].

Alkanes (e.g. adamantane, cyclohexane, toluene) were oxidised to alcohols and cyclohexanol to cyclohexanone by stoich. *trans*-$Ba[Ru(OH)_2(O)_3]$/AcOH, a reaction

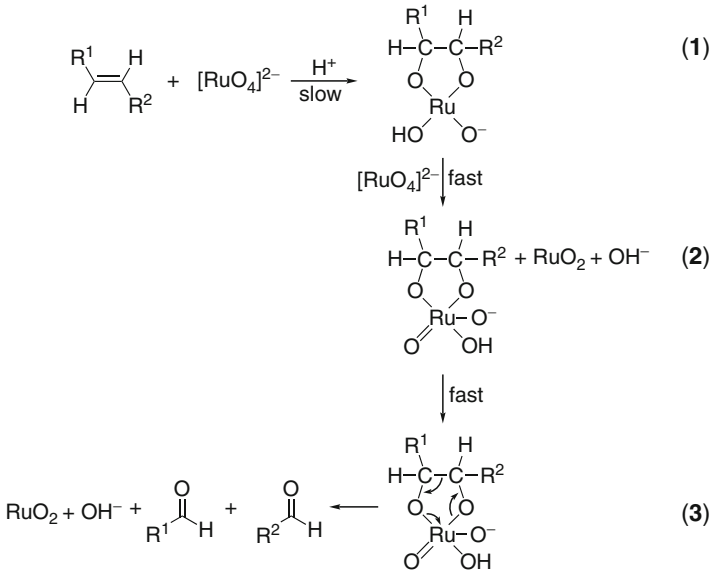

Fig. 1.16 Reaction scheme for stoicheiometric cleavage of unsaturated acids by $[RuO_4]^{2-}$ [349, 350]

enhanced by addition of Lewis acids such as $ZnCl_2$ and $AlCl_3$. The active oxidant may be $Ba[Ru(O)_2(OAc)_4].3H_2O$ [543].

Amines, Sulfides and Miscellaneous Substrates (5.1, 5.4, 5.6; Table 5.1)

The reagent stoich. $[RuO_4]^{2-}$/aq. M KOH oxidised benzylamine to benzonitrile [530], and conversion of RCH_2NH_2 to RCN was effected with $[RuO_4]^{2-}$ from $RuCl_3$/$K_2(S_2O_8)$/aq. M KOH [450, 540, 549]: an intermediate species such as $[Ru(OH)_2(O)_3(NH_2CH_2R)]^{2-}$ may be involved [549]**.** Oxidations of RSPh (R=Ph, MeOPh and $((MeO)_3Ph)$ to the sulfoxides and sulfones by stoich. $[RuO_4]^{2-}$/aq. NaOH/CH_3CN were studied; a concerted mechanism may be involved (Fig. 1.12) [434].

Primary nitro compounds RNO_2 were oxidised to RCOOH (the Nef reaction, e.g. nitroethane to acetic acid, nitrohexane to hexanoic acid) by $RuCl_3/(BrO_3)^-$/aq. M $Na_2(CO_3)$, activated primary alkyl halides RCl to RCOOH and secondary alkyl halides to ketones [213]. Corey used $RuCl_3/K_2(S_2O_8)$/aq. base @ pH 14 to oxidise a carbon-bearing nitro group to a carbonyl function as part of a total synthesis of antheridiogen (A_{An}, 2) [87].

The reagents $RuCl_3/Na(BrO_3)^-$/aq. M $Na_2(CO_3)$ and $RuCl_3/K_2(S_2O_8)$/aq. M KOH oxidised activated primary alkyl halides RX to carboxylic acids and secondary alkyl halides to ketones, e.g. 1-bromophenylethane to acetophenone [213]. Stoicheiometrically *trans*-$Ba[Ru(OH)_2(O)_3]/CF_3COOH/(bpy)/CH_2Cl_2$ oxidised alkanes (e.g. cyclohexane, adamantane, *n*-hexane, ethane) to ketones or acids, perhaps via $Ru^{VI}(O)_2(bpy)(CF_3C(O)O)_2$ [550].

1.4.1.5 Oxidations Which May Involve $[RuO_4]^{2-}$ in Solution

As mentioned above for RuO_4 (1.2.7.10) and $[RuO_4]^-$ (1.3.4.6) there are reports of Ru-catalysed oxidations for which the nature of the active catalyst or catalyst precursor is unclear but is probably predominantly $[RuO_4]^{2-}$. Electronic and Raman spectroscopy have been used to establish the nature of the catalytic species, but incorrectly *trans*-$[Ru(OH)_2(O)_3]^{2-}$ rather than $[RuO_4]^{2-}$ was the formula ascribed to the ruthenate solute [212, 222]. Examples in which $[RuO_4]^{2-}$ is the catalytic species include oxidations of nucleosides by $RuCl_3/K_2(S_2O_8)$/aq. M KOH (Fig. 2.11) [547], and of primary alcohols oxidised to aldehydes $RuCl_3$ or $RuO_2/Na(ClO)$/aq. base [551].

1.4.2 Ru(VI) Complexes Containing Dioxo Moieties

Many Ru(VI) dioxo complexes are known, the great majority of them having a *trans* arrangement of the oxo ligands with a few being *cis* [518] (*cf.* 1.4). Cundari and

Drago have made MO calculations which suggest that, under some circumstances, a *cis* dioxo configuration may be energetically slightly more favourable than the *trans* [521].

1.4.2.1 Dioxo Complexes with Carboxylato, Periodato and Tellurato Ligands

This first section on Ru(VI) dioxo complexes complexes concentrates on those with other O-donor ligands: periodate, tellurate and carboxylates. There is a review on ruthenium acetato complexes [552].

***Trans*-$Na_6[Ru(O)_2\{(IO_5(OH)\}_2].18H_2O$** This deep red complex, originally formulated as $Na_6[Ru(IO_6)_2(OH)_2].nH_2O$ [553], was made from $RuCl_3$ and $Na(IO_4)$ in aqueous NaOH, and *trans*-$K_6[Ru(O)_2\{(IO_5(OH)\}_2].6H_2O$ from $RuCl_3$, K(ClO), KOH and $IO(OH)_5$. The mixed salt *trans*-$NaK_5[Ru(O)_2\{(IO_5(OH)\}_2].8H_2O$ was obtained from RuO_2 in NaOH with K(ClO) and $IO(OH)_5$. The X-ray crystal structure (Fig. 1.17) of the mixed salt shows the anion to contain *trans* oxo ligands coordinated to the metal (Ru=(O) 1.732(8) Å) with two bidentate $\{I^{VII}O_5(OH)\}^{4-}$ ligands (mean Ru-O 2.01(1) Å, mean terminal I=(O) 1.82 Å, mean bridging I–O 1.95 Å). One of the I–O bonds on each side of the molecule at 1.990(9) Å carries the protons of the two hydroxo groups. Vibrational spectra of *trans*-$Na_6[Ru(O)_2\{(IO_5(OH)\}_2].18H_2O$ show $\upsilon^s(Ru(O)_2)$ at 806 cm^{-1} (Raman) and $\upsilon^{as}(Ru(O)_2)$ at 820 cm^{-1} (IR) [554].

The complex is unusual in being a 'double oxidant', in that both the periodato ligands (containing I(VII)) and the Ru(VI) each function as two-electron oxidants to organic substrates, making the molecule an overall six-electron oxidant. Thus, from a micture of *trans*-$Na_6[Ru(O)_2\{(IO_5(OH)\}_2].18H_2O$ and benzyl alcohol both $Na(I^VO_3)$ and $Ru^{IV}O_2.nH_2O$ were isolated as the inorganic reduction products [554].

The catalytic system *trans*-$[Ru(O)_2\{(IO_5(OH)\}_2]^{6-}$/K($IO_4$)/aq. KOH or aq. Aliquat® converted primary alcohols [554, 555] and primary activated alkyl halides [555] to carboxylic acids, while secondary alcohols [554, 555], and secondary alkyl halides were oxidised to ketones [555]. As with catalytic oxidations by aqueous $[RuO_4]^-$ double bond cleavage occurs [555].

***Trans*-$Na_6[Ru(O)_2\{TeO_4(OH)_2\}_2].13H_2O$** This yellow species is made from $[RuO_4]^{2-}$ in aqueous NaOH with $Te(OH)_6$. The vibrational spectra of *trans*-$K_6[Ru(O)_2\{TeO_4(OH)\}_2].4H_2O$ show $\nu^s(Ru(O)_2)$ at 817 cm^{-1} (Raman) and the asymmetric stretch $\nu^{as}(Ru(O)_2)$ at 825 cm^{-1} (IR). It functions as a two-electron

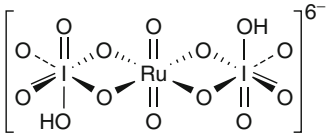

Fig. 1.17 Structure of the anion in *trans*-$NaK_5[Ru(O)_2\{(IO_5(OH)\}_2].8H_2O$ [554]

oxidant (unlike the periodato complex this is not a double oxidant and the tellurato ligand has no apparent oxidative function). As stoich. *trans*-$[Ru(O)_2\{TeO_4(OH)_2\}_2]^{6-}$/water it oxidised benzylic alcohols to carboxylic acids and secondary alcohols to ketones but does not function as a catalyst [554].

***Trans*-Ba[Ru(O)$_2$(OAc)$_4$].3H$_2$O** This dark green material may be the species formed by reaction of *trans*-$Ba[Ru(OH)_2(O)_3]$ with AcOH. Stoicheiometric *trans*-$Ba[Ru(OH)_2(O)_3]$/AcOH/CH_2Cl_2 oxidised alkanes to alcohols and cyclohexanol to cyclohexanone while *trans*-$Ba[Ru(OH)_2(O)_3]$/(^{n}Bu$_4$N)IO$_4$/AcOH/CH_2Cl_2 effected the latter reaction catalytically [543].

***Cis*-(PPh$_4$)[Ru(O)$_2$Cl$_2$(OAc)]** This green complex is made from RuO_4 vapour or RuO_4/CCl_4 and $(PPh_4)Cl$ in glacial AcOH. The compound first obtained from these procedures is *cis*-$(PPh_4)[Ru(O)_2Cl_2(OAc)].2AcOH$, but the acetic acid of crystallisation can be removed by recrystallisation. The X-ray crystal structure (Fig. 1.18) shows the anion to have a distorted octahedral configuration with *cis* oxo ligands (mean Ru=(O) 1.68 Å, (O)=Ru=(O) angle of 120(1)°). Since the acetato group is symmetrically side-bonded the anion would be an essentially undistorted trigonal bipyramid if the coordination point of the acetato ligand were supposed to be the mid-point of its two O-donor atoms. The mean Ru-O (acetato) distance is 2.17 Å with an O-Ru-O angle of 60.6°, and the Ru–Cl distances are 2.38(1) Å. The complex is diamagnetic and its ^{1}H spectrum was measured. Raman and IR spectra of the solid and solutions in CH_2Cl_2 are similar, suggesting retention of the structure in solution ($\upsilon_s(Ru(O)_2)$ lies in the Raman at 872 cm^{-1} (solid) and at 866 cm^{-1} (solution), while $\nu_{as}(Ru(O)_2)$ is at 889 cm^{-1} and at 886 cm^{-1} for solid and solution respectively) [556].

With $(PPh_4)Cl$, *trans*-$(PPh_4)_2[Ru(O)_2Cl_4]$ is formed, while pyridine (py) gives $[Ru(py)_4Cl_2]Cl_2$. The α-hydroxycarboxylic acids $HOOC.C(OH)R^1R^2$ (R^1R^2=Me$_2$, Et$_2$, EtMe or PhMe) give diamagnetic complexes which are thought to be (PPh_4)-$[Ru^{IV}(OH)(H_2O)(OOC.C(O)R^1R^2)]$ [557].

As stoich. *cis*-$[Ru(O)_2Cl_2(OAc)]^-$/CH_3CN and catalytically as $[Ru(O)_2$-$Cl_2(OAc)]^-$NMO/PMS/CH_3CN it oxidised primary alcohols to aldehydes and secondary alcohols to ketones; as with TPAP double bonds were not attacked [556]. Earlier work suggested that the system oxidised activated primary halides to the aldehydes but it was subsequently established that NMO/CH_3CN/PMS effects this reaction stoicheiometrically [558]. The reagent $[Ru(O)_2Cl_2(OAc)]^-$/NMO/PMS/CH_3CN oxidised sulfides to sulfoxides and sulfones (Table 5.2), and phosphines to phosphine oxides [556, 559]. Kinetics of the oxidation of benzhydrol and 1-phenylethanol by *cis*-$[Ru(O)_2Cl_2(OAc)]^-$/NMO/CH_2Cl_2/30°C were measured, a rate expression derived and formation of a catalyst substrate complex proposed [500].

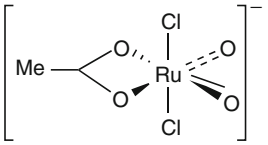

Fig. 1.18 Structure of the anion in *cis*-(PPh_4) $[Ru(O)_2Cl_2(OAc)]$ [556]

***Cis*-$(PPh_4)[Ru(O)_2Cl_2(OCOR)]$** (R=Et, Pr, CHF_2) These are made from RuO_4 vapour, $(PPh_4)Cl$ and propionic or butyric acids; the difluoroacetato complex is made from RuO_4 in CCl_4 with the acid and $(PPh_4)Cl$ in CH_3CN. The appearance in the IR of two bands suggests a *cis* disposition of the oxo ligands, assigned to $\nu^s(Ru(O)_2)$ and $\nu^{as}(Ru(O)_2)$; these lie at 916 and 864 cm^{-1} (R=Et); 891 and 878 cm^{-1} (Pr) and 891 and 878 cm^{-1} (CHF_2) [557]. The reagents *cis*-$[Ru(O)_2Cl_2(OR)]$/NMO/CH_2Cl_2 (R=Me, CHF_2) oxidised primary alcohols to aldehydes and secondary alcohols to ketones [557, 559].

For *trans*-$Ru(O)_2(OCOR)_2(py)_2$ (R = Me, Et, Pr, $(CH_3)_2CH$, C_6H_5) *cf.* 1.4.2.3.

1.4.2.2 Dioxo Complexes with Halogeno Donors

In this section the *trans*-dioxo species *trans*-$[Ru(O)_2X_4]^{2-}$ and $[Ru(O)_2X_3]^-$ (X=Cl, Br) are covered.

***Trans* $R_2[Ru(O)_2Cl_4]$** (R=$(PPh_4)^+$ and $\{Ph_2P)_2N\}^+$) were made from $[RuO_4]^{2-}$ in aqueous base with the cation and HCl; the salts are red, and electronic spectra were measured. The X-ray crystal structure of $\{Ph_2P)_2N\}_2[Ru(O)_2Cl_4]$ confirms that the anion has a *trans* structure (Ru=(O) 1.709(4) Å, two Ru–Cl bonds at 2.388(2) and two at 2.394(2) Å) [560]. The pyridinium salt $(pyH)_2[Ru(O)_2Cl_4]$, salts of substituted pyridines $(R\text{-}py)_2[Ru(O)_2Cl_4]$, (R-py=4-*tert*-butyl-pyridine, 3,4-dimethylpyridine); $(bpyH)^+$ and $(phenH)^+$ salts were similarly made in concentrated HCl with RuO_4 vapour. Vibrational spectra of the (pyH) salt show $\nu^s(Ru(O)_2)$ at 840 cm^{-1} (Raman) and $\nu^{as}(Ru(O)_2)$ at 824 cm^{-1} (IR) [561]. In organic solvents the red *trans*-$[Ru(O)_2Cl_4]^{2-}$ dissociates to the green $[Ru(O)_2Cl_3]^-$, and the dissociation constant K for

$$\left[Ru(O)_2Cl_3\right]^- + Cl^- \leftrightarrow trans-\left[Ru(O)_2Cl_4\right]^{2-} \qquad (1.3)$$

was determined spectrophotometrically as 5.3×10^{-3}M in CH_2Cl_2 [560]. The red 4-*tert*-butylpyridinium salt *trans* $(4\text{-}^t\text{Bu-pyH})_2[Ru(O)_2Cl_4]$ in solution exists with its $[Ru(O)_2Cl_3]^-$ partner in the equilibrium [561]:

$$(4-{}^t\text{Bu}-\text{pyH})\ [Ru(O)_2Cl_3(4-{}^t\text{Bu}-\text{py})] + HCl \leftrightarrow trans-(4-{}^t\text{Bu}-\text{pyH})_2[Ru(O)_2Cl_4] \qquad (1.4)$$

The system $(4\text{-}^t\text{Bu-pyH})_2[Ru(O)_2Cl_4]$/NMO/PMS/$CH_2Cl_2$ catalysed the oxidation of primary alcohols to aldehydes and of secondary alcohols to ketones: like TPAP (Tables 2.1 and 2.2), such oxidations did not attack double bonds. As stoich. *trans*-$(PPh_4)_2[Ru(O)_2Cl_4]^{2-}$/$CH_3CN$ it is a two electron oxidant for alcohols [561]. For *trans*-$[Ru(O)_2Cl_4]^{2-}$ in solution the effective oxidant or oxidant precursor is $[Ru(O)_2Cl_3]^-$, and this species is coordinatively unsaturated. That this is the case is suggested by the observation that addition of extra Cl^- (as $(PPh_4)Cl$) to the green $[Ru(O)_2Cl_3]^-$ in solution (Eq. 1.4) generating the red *trans*-$[Ru(O)_2Cl_4]^{2-}$, a markedly less effective catalytic oxidant for alcohols than $[Ru(O)_2Cl_3]^-$ [561].

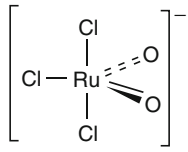

Fig. 1.19 Structure of the anion in $\{(Ph_2P)_2N)\}$ $[Ru(O)_2Cl_3]$ [560]

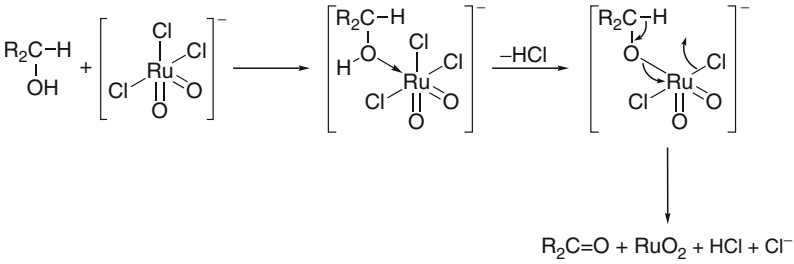

Fig. 1.20 A possible reaction sequence for oxidations by $[Ru(O)_2Cl_3]^-$ [33]

$R[Ru(O)_2Cl_3]$ (R=(PPh_4) [450], $(AsPh_4)$). The emerald-green salts [450, 560] are made from the cation in HCl with aqueous basic $[RuO_4]^{2-}$. The $(Et_4N)^+$, $(Me_4N)^+$ and $\{Ph_2P)_2N\}^+$ salts are prepared from RuO_4 in CCl_4 with HCl and the cation [560]. The X-ray crystal structure of $\{Ph_2P)_2N\}[Ru(O)_2Cl_3]$ shows the anion to be essentially trigonal bipyramidal, the two oxo ligands lying in the equatorial plane (Ru=(O) 1.658(5) and 1.768(8) Å, (O)=Ru=(O) angle 127.1(6)°) with the chloro ligands axial (Cl-Ru-Cl axial angle 174.5(3)°; Cl axial – equatorial angle 90.3(2)° and 94.5(3)°). There is some disorder in the structure with two slightly different anions in the unit cell (Fig. 1.19). The crystal structure of $(PPh_4)[Ru(O)_2Cl_3]$ is disordered and it was concluded that the anions have an approximate 6:6 occupancy of trigonal bipyramidal: square-based pyramidal structures. The salt is diamagnetic. The electronic spectrum of $Ru(O)_2Cl_3]^-$ was measured (for the equilibrium with *trans*-$[Ru(O)_2Cl_4]^{2-}$ *cf.* Eq. 1.3) [560]. The IR spectrum of $(PPh_4)_2[Ru(O)_2Cl_3]$ shows two $\nu^{as}(Ru(O)_2)$ stretches at 892 and 879 cm^{-1}, consistent with a *cis* arrangement of oxo ligands [561].

The reagent stoich. $(PPh_4)[Ru(O)_2Cl_3]/CH_2Cl_2$ oxidised a wide variety of primary alcohols to aldehydes and secondary alcohols to ketones without competing double-bond cleavage [450], and was used to convert drimanediol to isodrimeninol [117]. It is not clear why $[Ru(O)_2Cl_3]^-$ reacts differently towards unsaturated alcohols and unsaturated hydrocarbons: possibly the different solvents used or a rate difference in reaction with the hydroxyl groups on the alcohols may account for this.

The system $[Ru(O)_2Cl_3]^-$/NMO/PMS/CH_2Cl_2 oxidised primary alcohols to aldehydes and secondary alcohols to ketones without competing double-bond cleavage [561]. A possible outline reaction path has been proposed for oxidation of secondary alcohols by stoich. $[Ru(O)_2Cl_3]^-$ (Fig. 1.20) [33].

Cyclohexene was oxidisesd by stoich. $(Ph_4P)[Ru(O)_2Cl_3]/CH_3CN$ to give cyclohexene oxide, 2-cyclohexenone, 2-chlorocyclohexanone and cyclohexene

chlorohydrin. As stoich. $[Ru(O)_2Cl_3]^-/CH_3CN$ it quantitatively oxidised Ph_3P to Ph_3PO [560].

$(AsPh_4)[Ru(O)_2Cl_3(OPPh_3)]$ This red material is prepared from RuO_4 vapour and PPh_3 in HCl and the cation; the IR spectrum suggests that the oxo ligands are *trans* ($\nu^{as}(Ru(O)_2)$ lies at 824 cm^{-1} in the IR). As $[Ru(O)_2Cl_3(OPPh_3)]^-$/NMO/PMS/CH_2Cl_2 it is comparable with $[Ru(O)_2Cl_3]^-$/NMO/CH_2Cl_2 as an oxidant of primary alcohols to aldehydes and secondary alcohols to ketones without competing double-bond cleavage [561].

***Trans*-$[Ru(O)_2Br_4]^{2-}$** and **$[Ru(O)_2Br_3]^-$** Red-brown salts of $[Ru(O)_2Br_4]^{2-}$ with a variety of cations (PPh_4^+, *trans*-$(Me_2NH(CH_2)_2BHMe_2)^{2+}$, *trans*-$(Me_2NH(C_2H_4)_2BHMe_2)^{2+}$) are isolated by reaction of RuO_4 vapour with the cation in HBr [561]; $Cs_2[Ru(O)_2Br_4]$ has been made from CsBr in HBr with RuO_4 [562] and the olive-green $(PPh_4)[Ru(O)_2Br_3]$ from $[RuO_4]^{2-}$ and PPh_4Br with HBr. The IR spectrum of $(Ph_4P)_2[Ru(O)_2Br_4]$ shows $\nu^{as}(Ru(O)_2)$ at 839 cm^{-1} while that of $(PPh_4)[Ru(O)_2Br_3]$ has two IR stretches $\nu^{as}(Ru(O)_2)$ at 888 and 876 cm^{-1}, consistent with a *cis* arrangement of oxo ligands [561]. The system *trans*-$[Ru(O)_2Br_4]^{2-}$/NMO/PMS/CH_2Cl_2 oxidised primary alcohols to aldehydes and secondary alcohols to ketones, being slightly more effective than $(PPh_4)_2[Ru(O)_2Cl_4]$ in this respect but less so than $[Ru(O)_2Cl_3]^-$ [561].

For $[Ru(O)_2(py)Cl_3]^-$ and *trans*-$Ru(O)_2(OCOR)_2(py)_2$ *cf.* 1.4.2.3 below.

1.4.2.3 Ru(VI) Dioxo Complexes with Monodentate N-Donors

Pyridine and substituted pyridine species such as *trans*-$[Ru(O)_2(py)_4]^{2+}$, $Ru(O)_2(py)_2X_2$ and $Ru_2(O)_6(py)_4$ are covered here. The pyridine species are unusual in that some are aerobic catalysts (albeit inefficient ones) for the oxidation of alcohols. The oxoruthenate(VI) complexes so far considered are two electron oxidants, the metal being reduced to Ru(IV); the (py) complexes however, and probably those of (bpy) and (phen), are effectively four electron oxidants, being reduced to Ru(II). This probably arises from the strong π-acceptor properties of these N-donor ligands, which will prefer a d^6 metal configuration to maximise metal-to-ligand back bonding.

Reactions of of high oxidation state osmium and Ru polypyridyl complexes have been reviewed [43].

***Trans*-$[Ru(O)_2(py)_4]^{2+}$** This, as the yellow PF_6^- or BF_4^- salt, is made by adding $H(PF_6)$ or $H(BF_4)$ to $[RuO_4]^{2-}$ in aqueous base in the presence of pyridine. Vibrational spectra suggest a *trans*-arrangement of the oxo ligands; electronic spectra in DMSO and CH_3CN were recorded of the yellow, diamagnetic salts [442]. Stoicheiometrically *trans*-$[Ru(O)_2(py)_4]^{2+}/CH_2Cl_2$ is a four-electron oxidant of primary alcohols to aldehydes and of secondary alcohols to ketones without competing double-bond cleavage; similar reactions were accomplished catalytically with *trans*-$[Ru(O)_2(py)_4]^{2+}$/NMO or $(^nBu_4N)IO_4/CH_2Cl_2$ [442]. In common with a number of other oxo-Ru(VI) pyridine complexes *trans*-$[Ru(O)_2(py)_4]^{2+}/O_2$/PMS/CH_3CN oxidised primary and secondary alcohols, but with low turnovers [241]; CH_3CN is known to accelerate

Ru-catalysed oxidations [221, 260], and O_2 has a susbtantial solubility in CH_3CN. It seems likely that a μ-oxo dimer such as $[(py)_4(OH)Ru^{IV}(\mu\text{-}O)Ru^{IV}(OH)(py)_4]^{4+}$ could be formed which is inert to further oxidation and so terminates the catalytic reaction (a similar situation is found with some oxo-Ru(VI) porphyrin complexes). Another possibility is that unreactive polymeric Ru species are formed [241].

***Trans*-[Ru(O)$_2$(R-py)$_4$](BF$_4$)$_2$** (R-py=nicotinic acid, pyridine-2-carboxylate (picolinate, pic), *iso*nicotinamide, pyridine-3-carboxylate (nicotinate, nic), and pyridine-3,4-dicarboxylate (cinchonomeronate, cinc) are made from $[RuO_4]^{2-}$ and the ligand with $H(BF_4)$. The complexes are diamagnetic; vibrational spectra were measured [241].

***Trans*-Ru(O)$_2$X$_2$(py)$_2$** (X=Cl, Br) The yellow chloro complex is made by reaction of pyridine and HCl neutralised to pH 7 with $Na_2(CO_3)$ followed by addition of a solution of RuO_4 in CCl_4 [562] or from $[RuO_4]^{2-}$, pyridine and HCl or HBr. Their vibrational and electronic spectra of these diamagnetic salts were measured. With pyridine the complexes give *trans*-$Ru^{II}X_2(py)_4$. As *trans*-$Ru(O)_2(py)_2X_2$/NMO or (^{n}Bu$_4$N)IO$_4$/PMS/CH_2Cl_2 both oxidised alcohols but their utility for this is limited due to their low solubilities in organic solvents [442].

***Trans*-Ru(O)$_2$Cl$_2$(R-py)$_2$** (R=4-^{t}Bu-py, 4-Cl-py) The yellow-green 4-*tert*-butylpyridine complex is made from $[RuO_4]^{2-}$ in base with pyridine and HCl, while the more stable 4-chloropyridine analogue is prepared by passing RuO_4 vapour into a solution of 4-chloropyridinium hydrochloride in water. They are diamagnetic; vibrational spectra of $Ru(O)_2Cl_2(4\text{-}^tBu\text{-}py)_2.H_2O$ show $\upsilon^s(Ru(O)_2)$ at 858 cm^{-1} (Raman) and $\upsilon^{as}(Ru(O)_2)$ at 842 cm^{-1} (IR) [241].

***Trans*(R-pyH)[Ru(O)$_2$Cl$_3$(py)]** (R-py=4-*tert*-butylpyridine, 4-chloropyridine, 3-methylpyridine and 3,4-dimethylpyridine). The diamagnetic complexes are made by passing RuO_4 vapour into a solution of (R-py) in HCl [241]. The 4-*tert*-butylpyridine complex is probably formed in solution when *trans*-$(4\text{-}^tBu\text{-}py)_2[Ru(O)_2Cl_4]$ is dissolved in CH_2Cl_2, the equilibrium

$$\left(4-{}^{t}\,\mathrm{Bu}-\mathrm{pyH}\right)\left[\mathrm{Ru}\left(\mathrm{O}\right)_2\left(4-{}^{t}\,\mathrm{Bu}-\mathrm{py}\right)\mathrm{Cl}_3\right]+\mathrm{HCl}\leftrightarrow \textit{trans}-\left(4-{}^{t}\,\mathrm{Bu}-\mathrm{pyH}\right)_2\left[\mathrm{Ru}\left(\mathrm{O}\right)_2\mathrm{Cl}_4\right] \quad (1.5)$$

having been shown to exist in such solutions by electronic spectroscopy [561]. The system *trans*-$[Ru(O)_2Cl_3(4\text{-}^tBu\text{-}py)]^-$/NMO/PMS/$CH_2Cl_2$ is a less effective oxidant for alcohols than $[Ru(O)_2Cl_3]^-$, perhaps because the pyridine ligand does not dissociate in solution and thus leave a vacant coordination site [561].

Ru$_2$(O)$_6$(py)$_4$.3.5H$_2$O Deep red-purple crystals of this material are made by passing RuO_4 vapour into an ice-cold solution of pyridine in water [241]. The anhydrous material is made by passing RuO_4 vapour into aqueous pyridine, by slow addition of (pyH)Cl to a solution of $[RuO_4]^{2-}$ or by careful addition of $H(BF_4)$ to a basic aqueous solution of $[RuO_4]^{2-}$ with pyridine [442]. It is likely that the previously claimed $Ru(O)_4(py)_2$ [440] and *trans*-$Ru(O)_2(py)_2(OH)_2$ [443] are in fact $Ru_2(O)_6(py)_4$ [241, 442]. The X-ray crystal structure of the hydrate (Fig. 1.21)

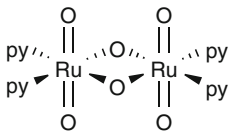

Fig. 1.21 X-ray structure of $Ru_2(O)_6(py)_4.3.5H_2O$ [241]

shows the complex to be centrosymmetric with a planar $Ru_2(O)_2$ bridge (Ru-(O) 1.93(1) Å), Ru-(O)-Ru angle 100.0(5)°; the Ru ….. Ru distance is 2.948(2) Å but there is unlikely to be direct Ru – Ru interaction. The terminal Ru=(O) distance is 1.73(1) Å with an (O)-Ru-(O) angle of 160.5(4)°; this deviation from linearity probably arises from repulsion between the π cloud around the oxo ligands and the tightly bound $Ru_2(O)_2$ unit since the oxo atoms are bent away from this unit and towards the pyridine rings. The latter (mean Ru-N 2.20(1) Å) are pitched with respect to each other so as to minimise steric repulsions. The complex is diamagnetic and its vibrational spectra show $\upsilon^s(Ru(O)_2)$ at 810 cm^{-1} (Raman) and $\upsilon^{as}(Ru(O)_2)$ at 826 cm^{-1} (IR) [241].

Like *trans*-$[Ru(O)_2(py)_4]^{2+}$, stoich. $Ru_2(O)_6(py)_4/CH_2Cl_2$ is a four-electron oxidant towards alcohols (four electrons per metal or eight electrons per dimer unit), converting primary alcohols to aldehydes and secondary alcohols to ketones without attacking double bonds. The nature of the Ru(II) species thus formed is unclear, though reaction of $Ru_2(O)_6(py)_4$ with HCl gives $(pyH)_3[RuCl_3]_3$ (formerly believed to be $Ru(py)_2Cl_4$) [442]. Like *trans*-$[RuO_2(py)_4]^{2+}$ the system $Ru_2(O)_6(py)_4$/NMO/PMS/CH_2Cl_2 oxidised primary alcohols to aldehydes and secondary alcohols to ketones; ($^nBu_4N)IO_4$ was a less effective co-oxidant [241, 442]. As $Ru_2(O)_6(py)_4/O_2$/PMS/CH_3CN it effected such oxidations aerobically but with low turnovers: the latter increased slightly with $Cu(OAc)_2$ at 50°C. The use of O_2 at 5 atmospheres' pressure did not increase turnover numbers [241].

$Ru_2(O)_6(R\text{-}py)_4$ (R-py=4-*tert*butyl pyridine (4-^{t}Bu-py), pyridine-3-carboxylate (nicotinate, nic), pyridine-4-carboxylate (isonicotinate, isonic) and pyridine-3,4-dicarboxylate (cinchonomeronate, cinc) are made from (R-py) in CCl_4 with RuO_4 vapour; the products are brown-green and of low solubility: the 4-*tert*-butylpyridine complex is dark red. The vibrational spectra of $Ru_2(O)_6(4\text{-}^t\text{Bu-py})_4$ show $\upsilon^s(Ru(O)_2)$ at 822 cm^{-1} (Raman) and $\upsilon^{as}(Ru(O)_2)$ at 815 cm^{-1} (Raman) [241].

***Trans*-$Ru(O)_2(OC(O)R)_2(py)_2$** (R=Me, Et, ^{n}Pr, ^{i}Pr, C_6H_5). These are made from a suspension of *trans*-$Ba[Ru(OH)_2(O)_3]$ and the appropriate acid with pyridine. The complexes are orange; the 4-methylpyridine complex *trans*-$Ru(O)_2$(4MeO-py)$(OC(O)CH_3)$ was also prepared. The X-ray crystal structure of *trans*-$Ru(O)_2(OC(O)Et)_2(py)_2$ shows that the two oxo ligands are *trans* (Ru=(O) 1.726(1) Å) with an (O)=Ru=(O) angle of 180°); the two pyridine molecules are *trans* (Ru-N 2.100(2) Å), as they also are in the two η^1- monodentate acetato ligands (Ru–O 2.052(1) Å) (Fig. 1.22). Infrared, electronic and ^{1}H NMR spectra were measured [529].

The reagent stoich. *trans*-$Ru(O)_2(OAc)_2(py)_2/CH_3CN$ oxidised Ph_3P to Ph_3PO giving what may be $Ru^{IV}(O)(OAc)(py)_2$ or a μ-oxo bridged polymer. Linear and cyclic alkenes were epoxidised with additional by-products; hydrocarbons and

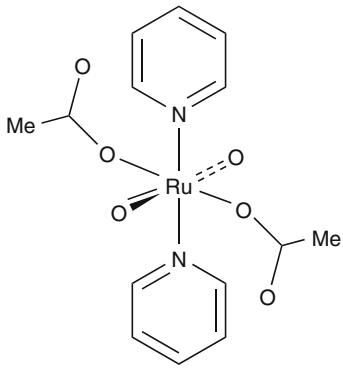

Fig. 1.22 X-ray of *trans*-$Ru(O)_2(OCOEt)_2(py)_2$ [529]

ethers were oxidised (e.g. THF to γ-butyrolactone, toluene to benzaldehyde). With the sterically hindered 2,6-di-*tert*-butylphenol a mixture of 2,6-di-*tert*-butyl-*p*-benzoquinone and 3,3′,5,5′-tetra-*tert*-butyl-diphenolquinone was formed [529].

***Trans*-$Ru(O)_2(OH)_2(py)_2$** On the basis of vibrational spectra ($\upsilon^s(Ru(O)_2)$ at 850 cm^{-1} in the Raman and $\upsilon^{as}(Ru(O)_2)$ at 790 cm^{-1} in the IR) this green species was assigned this formula [443]; it may however be $Ru_2(O)_6(py)_4$ [442]. It was made from RuO_4 and pyridine in CCl_4 by the method of Koda who formulated it as $Ru(O)_4(py)_2$ [440].

1.4.2.4 Dioxo Complexes with Bidentate and Terdentate N-Donors

This section concentrates on (bpy) and (tpy) complexes: *trans*-$Ru(O)_2X_2(bpy)$ (X=Cl, Br, carboxylate); *trans*-$[Ru(O)_2(bpy)_2]^{2+}$ and species with substituted (bpy) ligands; the unusual periodato and tellurato oxidants *trans*-$Ru(O)_2(bpy)\{IO_3(OH)_3\}$ and *trans*-$Ru(O)_2(bpy)\{TeO_2(OH)_4\}$, and the (tpy) complex *trans*-$[Ru(O)_2(H_2O)(tpy)](ClO_4)_2$.

***Trans*-$Ru(O)_2Cl_2(bpy)$** This is made by reaction of a mixture of (bpy) with HCl neutralised with $Na_2(CO_3)$ and RuO_4 in CCl_4 [562, 450]. It is yellow, and as stoich. *trans*-$Ru(O)_2Cl_2(bpy)/CH_2Cl_2$ oxidised alcohols to aldehydes and ketones [450].

***Trans*-$Ru(O)_2(CF_3COO)_2(bpy)$** may be a product of reaction of *trans*-$Ba[Ru(OH)_2(O)_3]$ in CF_3COOH in the presence of (bpy) in CH_2Cl_2; addition of HCl to the mixture yields *trans*-$Ru(O)_2Cl_2(bpy)$. The reaction mixture before addition of HCl stoicheiometrically oxidised alkanes: thus propane (3 atm) gave propan-2-one, while benzene gave 1,4-benzoquinone [550].

***Trans*-$[Ru(O)_2(bpy)_2](ClO_4)_2$** This yellow species is made by oxidation of $[Ru(OH)(H_2O)(bpy)_2]^{2+}$ with cerium(IV). It is diamagnetic; infrared (υ^{as} $(Ru(O)_2)$ 850 cm^{-1}) and electronic spectra were measured together with cyclic voltammetric data [563]. Kinetics of oxidations of primary alcohols to aldehydes and of secondary alcohols to ketones by stoich. *trans*-$[Ru(O)_2(bpy)_2]^{2+}$/water or CH_3CN were measured and the second-order rate constants compared with those for a number of *trans*-$[Ru(O)_2(L)]^{2+}$ complexes (L=macrocyclic ligand, *cf.* 1.4.2.6). Kinetic isotope effects for oxidation of toluene, ethylbenzene, cumene and THF by stoich. *trans*-$[Ru(O)_2(bpy)_2]^{2+}/CH_3CN$

were measured as were activation parameters for such reactions by *trans*-[$Ru(O)_2(bpy)_2$]$^{2+}$, and the results obtained compared with those for other macrocyclic complexes of *trans*-[$Ru(O)_2(L)$]$^{2+}$. A hydrogen-atom abstraction mechanism was suggested for oxidation of C-H bonds by the complexes [564].

***cis*-[$Ru(O)_2(Cl_2bpy)_2$](ClO_4)$_2$** (Cl_2bpy=6,6′-dichloro-2,2′-bipyridyl). This is made by oxidising *cis*-[$Ru^{II}(H_2O)_2(Cl_2bpy)_2$]$^{2+}$ with cerium(IV) and Na(ClO_4). The IR $\upsilon^{as}(Ru(O)_2)$ bands lie at 840 and 791 cm^{-1}; electronic spectra and electrochemical properties were measured [565, 566]. As stoich. *cis*-[$Ru(O)_2(Cl_2bpy)_2$]$^{2+}$/CH_3CN it oxidised cyclohexane to cyclohexanone, THF to butyrolactone, styrene to benzaldehyde and styrene oxide, and norbornene to *exo*-2, 3-epoxynorbornane in HCl and CH_3CN [566].

***Trans*-[$Ru(O)_2$(bpy){$IO_3(OH)_3$}].1.5H_2O** is made from RuO_4 in aqueous Na(IO_4) with (bpy) in 1:1 aqueous acetone [567]; *cf.* also 1.11. The X-ray crystal structure of the orange-yellow complex shows it to be octahedral; the Ru=(O) distances are 1.731(5) Å with an (O)=Ru=(O) angle of 167.3(2)° (Fig. 1.23). This *trans*-$Ru(O)_2$ moiety is bent away from the {$IO_3(OH)_3$}$^{2-}$ ligand, rather similar to the effect noted above for $Ru_2(O)_6(py)_4$. The tight RuO_2I unit between the metal and the {$IO_3(OH)_3$}$^{2-}$ ligand is planar (Ru–O 1.99(4) Å, I–O 1.91(4) Å). The one doubly-bonded (I=O) distance is 1.801(4) Å, while the three I–O(OH) distances are 1.90 Å. Vibrational spectra of *trans*-$Ru(O)_2$(bpy){$IO_3(OH)_3$}.1.5H_2O show $\upsilon^{s}(Ru(O)_2)$ at 797 cm^{-1} (Raman) and the asymmetric stretch $\upsilon^{as}(Ru(O)_2)$ at 817 cm^{-1} (IR) [568].

Stoicheiometrically *trans*-$Ru(O)_2$(bpy){$IO_3(OH)_3$}/water-CH_2Cl_2 is a "double oxidant" (like *trans*-[$Ru(O)_2${$(IO_5(OH)$}$_2$]$^{6-}$) in that both the Ru centre – functioning as a four-electron oxidant – and the periodate ligands, functioning as two-electron oxidants giving iodate, IO_3^-, are involved. Thus it is an overall six-electron oxidant, one mole of the complex oxidising three moles of cyclo-octene [567]. The system *trans*-$Ru(O)_2$(bpy){$IO_3(OH)_3$}/aq. Na(IO_4)/CH_2Cl_2/2°C oxidised primary alcohols to aldehydes and secondary alcohols to ketones. As *trans*-$Ru(O)_2$(bpy){$IO_3(OH)_3$}/aq. Na(IO_4)/CH_2Cl_2/2°C it stereoselectively epoxidised a wide variety of alkenes (Table 3.1; 1.11) [567, 568] and, as *trans*-$Ru(O)_2$(bpy){$IO_3(OH)_3$}/aq. Na(IO_4)/CH_2Cl_2/80°C, converted linear and cyclic alkanes to alcohols, aldehydes or ketones, but *trans*-[$Ru(H_2O)_2(bpy)_2$]$^{2+}$/TBHP/water-C_6H_6 gave better yields [567].

***Trans*-[$Ru(O)_2$(bpy){$TeO_2(OH)_4$}]** This green material is made from RuO_4 in aqueous Na(IO_4) with $Te(OH)_6$ in 1:1 aqueous acetone. The structure is probably (Fig. 1.24):

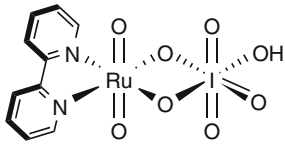

Fig. 1.23 X-ray of $Ru(O)_2$(bpy){$IO_3(OH)_3$}1.5H_2O [568]

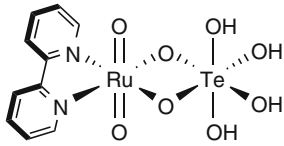

Fig. 1.24 Likely structure of *trans*-$Ru(O)_2$(bpy){$TeO_2(OH)_4$} [567]

The vibrational spectra of the complex show that $\upsilon^{s}(Ru(O)_2)$ lies at 815 cm^{-1} (Raman) and $\upsilon^{as}(Ru(O)_2)$ at 821 cm^{-1} (IR) [567]. Stoicheiometrically the complex functions as a four-electron oxidant, Ru(VI) being reduced to Ru(II) by organic substrates. As *trans*-$Ru(O)_2(bpy)\{TeO_2(OH)_4\}$/aq. $Na(IO_4)/CH_2Cl_2$/2°C it oxidised alcohols in much the same way as $Ru(O)_2(bpy)\{IO_3(OH)_3\}$ [567].

***Trans*-$[Ru(O)_2(dmbpy)_2](ClO_4)_2$** (dmbpy=5,5′-dimethyl-2,2′-bipyridyl) is a diamagnetic material, made by oxidation of *trans*-$[Ru(OH)(H_2O)(dmbpy)_2](ClO_4)_2$ with $(NH_4)_2[Ce(NO_3)_6]$. As stoich. *trans*-$[Ru(O)_2(dmbpy)_2]^{2+}/CH_3CN$, it oxidised alcohols to aldehydes and ketones, THF to γ-butyrolactone; oxidation of saturated alkanes occurs preferentially at the tertiary C–H bond. The mechanisms of the oxidations of alcohols and cyclohexane were investigated by kinetic and isotopic labelling studies [569].

***Cis*-$[Ru(O)_2(dmp)_2](PF_6)_2$** (dmp=2,9-dimethyl-1,10-phenanthroline) is made *in situ* from *cis*-$[Ru(H_2O)_2(dmp)_2](PF_6)_2$ and H_2O_2 [570] or cerium(IV) [571]. It is orange-yellow, and the IR spectrum showed bands at 839 and 787 cm^{-1} assigned to υ(Ru=(O), suggesting a *cis*-arrangement of the oxo ligands [571]. It is probably involved in the epoxidation by *cis*-$[Ru(dmp)_2(H_2O)_2]^{2+}/O_2$(3 atm)/$CH_3CN$/65–75°C of norbornene, cyclo-octene and *trans*-β-methylstyrene, and as *cis*-$[Ru(dmp)_2(H_2O)_2]^{2+}$/aq. H_2O_2/CH_3CN/65–75°C catalysed the hydroxylation of cyclohexane and adamantane. An atom-transfer mechanism was suggested [570]. It may also be the active species in the hydroxylation of methane by *cis*-$[Ru(dmphen)_2(S)_2]^{2+}$/aq. H_2O_2/75°C (S = CH_3CN or H_2O) under 4 atm pressure of CH_4; MeOH and HCHO were formed, while ethane under similar conditions gave EtOH and CH_3CHO [572].

***Trans*-$[Ru(O)_2(H_2O)(tpy)](ClO_4)_2$** (tpy=2,2′:6′,2′,2″-terpyridine). This yellow, explosive material is made from $[Ru(H_2O)(ox)(tpy)].2H_2O$, $HClO_4$ and cerium(IV) [573]. The X-ray crystal structure shows that the *trans*-oxo ligands (Ru=(O) 1.661 Å, (O)=Ru=(O) angle 171.3°) are slightly bent away from the terpyridyl ligand [574]. Vibrational spectra of the complex show $\upsilon^{s}(Ru(O)_2)$ at 834 cm^{-1} (Raman) and $\upsilon^{as}(Ru(O)_2)$ at 841 cm^{-1} (IR). Resonance Raman, electronic and ^1H NMR spectra and cyclic voltammograms were measured [573]. As stoich. *trans*-$[Ru(O)_2(H_2O)(tpy)]^{2+}/CH_3CN$ it converted PPh_3 and the chelating diphosphines $Ph_2P(CH_2)_nPPh_2$ (n=1 (dppm) and n=2 (dppe)) to their oxides; kinetics of the reaction were studied, which probably occurs via Ru (VI) to Ru(IV) and Ru(IV) to Ru(II) steps [574]**.** Kinetics and mechanism of the oxidation of benzyl alcohol by stoich. $[Ru(O)_2(H_2O)(tpy)]^{2+}$ or by *trans*-$[Ru(O)_2(CH_3CN)(tpy)]^{2+}$/water or CH_3CN to benzaldehyde were studied. From ^{18}O studies it seems that there is O-atom transfer from the Ru=(^{18}O) ligand in *trans*-$[Ru(O)_2(CH_3CN)(tpy)]^{2+}$ and formation of an intermediate $[Ru(O)(CH_3CN)(tpy)]^{2+}$ to give, finally, $[Ru(CH_3CN)_2\{(OH)_2CHPh\}(tpy)]^{2+}$, with a first step involving coordination of benzyl alcohol to a Ru(VI) centre [575].

***Trans*-$[Ru(O)_2(TMEA)](ClO_4)_2$** (TMEA=*N,N,N′,N′*-tetramethyl-1,2-diaminoethane) is made by oxidation of *trans*-$[Ru(TMEA)Cl_2]Cl$ and silver-*p*-sulfonate with H_2O_2. Electronic spectra in perchloric acid and also in CH_3CN were recorded; the IR spectrum showed ν(Ru=(O)) at 860 cm^{-1}. As *trans*-$[Ru(O)_2(TMEA)]^{2+}/O_2/CH_3CN$/28°C it oxidised benzyl alcohol to benzaldehyde [576].

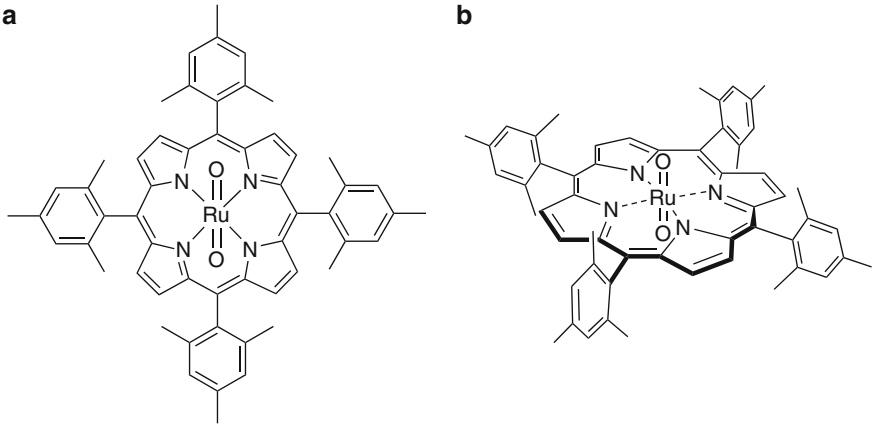

Fig. 1.25 *Trans*-Ru(O)$_2$TMP (**a**) 'flat' representation; (**b**) showing orthogonal pitching of methyl rings [584]

1.4.2.5 Dioxo Complexes with Porphyrin Donors

Oxidations with Ru porphyrin complexes, both catalytic and stoicheiometric, have been reviewed [42, 45–47], as has the relatively fledgling subject of asymmetric oxidations catalysed by Ru porphyrin complexes [44].

***Trans*-Ru(O)$_2$(TMP)** (TMP=*meso*-5,10,15,20-tetramesityl(porphyrin) dianion) This is made by oxidation of Ru(CO)(TMP) with MCPBA [577–579] or with PhIO [580]; also from Ru(MeCN)$_2$(TMP) and O_2 in C_6H_6 [580, 581] or from Ru(TMP) in $C_6{}^2H_6$ [582]. Spectra (IR, ^{1}H NMR and electronic) were measured: in the IR υ^{as}(Ru(O)$_2$) lies at 821 cm^{-1}, shifting to 785 cm^{-1} in the ^{18}O-substituted complex; cyclic voltammetric data were also presented [580]. The complex was probably formed as a by-product of the decomposition of cyclohexyl hydroperoxide catalysed by Ru(CO)(TMP) [577].

The orthogonal pitching of the mesityl rings (Fig. 1.25) may inhibit formation of μ-oxo dimers (likely to inhibit catalytic oxidations) which can be formed by flat porphyrin rings in their metal complexes, e.g. (TPP) ligands [583].

There is an extensive oxidation chemistry of *trans*-Ru(O)$_2$(TMP) and this has been reviewed [42, 45–47].

Alcohols

Alcohols were oxidised by stoich. *trans*-Ru(O)$_2$(TMP)/C_6H_6 or catalytically as *trans*-Ru(O)$_2$(TMP)/O_2/C_6H_6 [581, 585]. Thus, *trans*-Ru(O)$_2$(TMP)/C_6H_6 oxidised 2-propanol to acetone via formation of Ru^{IV}(TMP)(OCHMe$_2$)$_2$, which was characterised crystallographically. The oxidation of 2-propanol may take place via hydrogen transfer [585]:

$$trans-Ru^{VI}(O)_2(TMP)+Me_2CH(OH)\rightarrow Ru^{IV}(OH)_2(TMP)+Me_2CO \quad (1.6)$$

$$Ru^{IV}(TMP)(OH)_2+2Me_2CH(OH)\rightarrow Ru^{IV}(OCHMe_2)_2(TMP)+2H_2O \quad (1.7)$$

Allylic β-unsaturated,alcohols (geraniol, 3-phenyl-2-propenol) were efficiently oxidised to the aldehydes by *trans*-$Ru(O)_2$(TMP)/(lutidine-*N*-oxide)/C_6H_6 [586]. As *trans*-$Ru(O)_2$(TMP)/(Cl_2pyNO)/C_6H_6/24h it oxidised cyclohexanol to cyclohexanone [587].

Alkenes and Alkanes

Some typical epoxidations are listed in Table 3.1. The first Ru-catalysed epoxidation was reported in 1983 by James et al., in which $RuBr(PPh_3)$(OEP)/PhIO/CH_2Cl_2 was used to epoxidise styrene, norbornene and *cis*-stilbene in low yields; *trans*-stilbene was not oxidised [588]. It was later noted that *trans*-$Ru(O)_2$(TMP)/O_2/C_6H_6 aerobically oxidised cyclic alkenes, and a catalytic cycle involving $Ru^{IV}O$(TMP) was proposed, in which there is disproportionation of Ru(O)(TMP) to Ru(TMP) and *trans*-$Ru(O)_2$(TMP), the latter epoxidising the alkene and the former being oxidised back to the latter by O_2 (Fig. 1.26) [46, 583]. Stilbene, *trans*-styrene and norbornene were efficiently epoxidised by *trans*-$Ru(O)_2$(TMP)/(Cl_2pyNO)/C_6H_6 [589], as was epoxidation of *exo*-norbornenes catalysed by *trans*-$Ru(O)_2$(TMP)/O_2/C_6H_6 [590].

Epoxidation of propene and oct-1-ene was effected with *trans*-$Ru(O)_2$(TMP)/O_2(1 atm)/water-CH_2Cl_2. After some 40 turnovers in a day, the deactivated form of the complex, Ru(CO)(TMP).H_2O was detected (*vide infra*). Use of (1-(^{13}C)-oct-1-ene suggest that, in part at least, the carbon atom of the Ru(CO)(TMP) formed derives from the first C atom of the octene [591]. For styrene epoxidation by *trans*-$Ru(O)_2$(TMP)/(LNO)/C_6H (LNO=N-oxides of 2,3,5,6-tetramethylpyrazine, acridine, 2-methylquinoline and 3,6-dichloropyridazine) the mono- and bis-*N*-oxides of tetramethylpyrazine were the most effective co-oxidants [586].

The unusual system *trans*-$Ru(O)_2$(TMP)/N_2O(10 atm)/fluorobenzene epoxidised linear alkenes, cholesteryl acetate and the *tert*-butyldimethylsilyl ether of citronellol [592]; cholest-5-ene-3-one was oxidised to the 6α and 6β alcohols and the enedione by *trans*-$Ru(O)_2$(TMP)/O_2/C_6H_6 (Table 3.2) [593]. With terpenes the 6,7-double bonds were selectively epoxidised by *trans*-$Ru(O)_2$(TMP)/

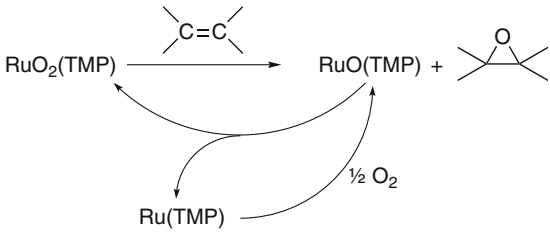

Fig. 1.26 Catalytic cycle for aerobic alkene epoxidation by *trans*-$Ru(O)_2$(TMP) [46, 583]

2,6-lutidine-*N*-oxide/C_6H_6. In $H_2{}^{18}O$ for this system and also with *trans*-Ru(O)$_2$(TMP)/O_2/C_6H_6 some ^{18}O appeared in the epoxide, suggesting that the *N*-oxide and aerobic systems involve different intermediates [594]. The efficacies of *trans*-Ru(O)$_2$(TMP)/(pyNO)/C_6H_6 (pyNO=2,6-Me_2 or 2,6-Cl_2 pyridine-*N*-oxide) for epoxidation of styrene, substituted styrenes, *cis* and *trans*-stilbene and *l*-carvone was compared with those for other Ru porphyrin complexes, e.g. Ru(CO)(TMP) and Ru(CO)(TPP), and other metal porphyrin complexes. Only the Ru-containing complexes showed significant activity (Table 3.1) [595].

The system *trans*-Ru(O)$_2$(TMP)/O_2/C_6H_6 catalysed the β-stereospecific epoxidation of the acetic esters of cholesterol, 3-epicholesterol, isocholesterol and its 7β-epimer (Table 3.1); reasons for this stereospecificity were discussed [596]. The system *trans*- Ru(O)$_2$(TMP)/O_2/C_6H_6/50°C/24 h dehydrogenated primary and secondary amines [597, 598]; epoxidation of (Z)-17-ethylideneandrostane with the same system gave three isomeric unsaturated steroids [578]. Oxidation of cholesteryl acetate to its 5β, 6β epoxide by *trans*-Ru(O)$_2$(TMP)/O_2/C_6H_6 (or by Ru(CO)(TMP)/MCPBA/C_6H_6) was studied kinetically: the system is gradually inactivated by protic impurities, probably by proton transfer from weakly acidic alcohol functions to the basic oxo ligands of the catalyst [599–601]. In the asymmetric epoxidation of ring-substituted styrenes by *trans*-Ru(O)$_2$(TMP)/PhIO or Cl_2pyO/C_6H_6 the alkene probably approaches the Ru=O bond [602]. As *trans*-Ru(O)$_2$(TMP)/HCl or HBr(Cl_2pyNO)/aq. C_6H_6/24 h. it catalysed oxidation of adamantane to adamant-1-ol and ethylbenzene to acetophenone [587].

Amines, Sulfides, Phosphines, Arsines and Stibines

Kinetics and mechanisms of oxidation of amines by Ru porphyrin complexes (particularly TMP species) have been reviewed [42]. *Trans*-Ru(O)$_2$(TMP)/O_2/C_6H_6/50°C/24h oxidised primary and secondary amines; in the oxidation of benzylamine *trans*-Ru(NH_2)$_2$$CH_2$Ph)$_2$(TMP) was isolated and characterised crystallographically. A mechanism involving a two-electron oxidation of benzylamine to *N*-benzylideneamine by *trans*-Ru(O)$_2$(TMP) was proposed with concomitant reduction of the latter to Ru^{IV}(O)(TMP). This disproportionates to *trans*-Ru^{VI}(O)$_2$(TMP) and Ru^{II}(TMP); the latter regenerates Ru^{IV}(O)(TMP) with O_2, while the second two-electron oxidation of the imine to the aldehyde is effected by *trans*-Ru(O)$_2$(TMP) [597], (Table 5.1) [598]**.**

Kinetics and mechanisms of oxidation of sulfides to sulfoxides and sulfones by Ru porphyrin complexes (particularly TMP species) have been reviewed [42, 46]. Diethylsulfide was oxidised to Et_2SO by *trans*-Ru(O)$_2$(TMP)/O_2/65°C and to Et_2SO_2 at 100°C [589], and *trans*-Ru(O)$_2$(TMP)/lutidine-*N*-oxide/benzene/80°C oxidised PhMeS and benzyl sulfide to the sulfoxides and sulfones [586]. Kinetic data for O-atom transfer in the oxidation by *trans*-Ru(O)$_2$(TMP)/O_2/C_6H_6 of alkyl thioethers R_2S to the sulfoxides R_2SO were measured. *Trans*-Ru(O)$_2$(TMP)/C_6H_6 may react with R_2S in a slow step to give Ru^{IV}(O)(OSR_2)(TMP) which in a fast step reacts with more R_2S yielding Ru(OSR_2)$_2$(TMP); in both the OSR_2 ligands are O-bonded to the metal.

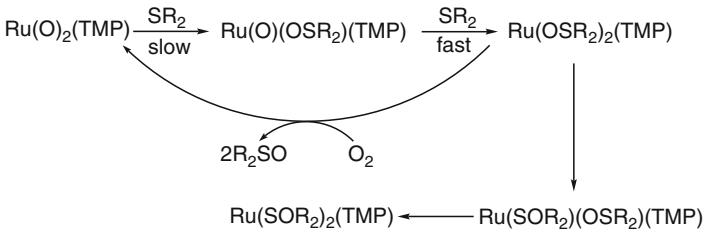

Fig. 1.27 Reaction scheme for oxidation of sulfides to sulfoxides catalysed by Ru(TMP) complexes [603]

The latter is the effective catalyst; reaction of O_2 with it liberates free sulfoxide, but there is also slow conversion of $Ru^{IV}(O)(OSR_2)_2(TMP)$ to the more substitution-inert (S-bonded) $Ru(SOR_2)(OSR_2)(TMP)$ and $Ru(SOR_2)_2(TMP)$ leading to loss of catalytic activity [47, 581], (Fig. 1.27) [603].

Kinetics and mechanisms of oxidation of phosphines to phosphine oxides by Ru porphyrin complexes, particularly (TMP) species, have been reviewed [42, 46]. Stoicheiometrically *trans*-$Ru(O)_2(TMP)/C_6H_6$ oxidised Ph_3P to Ph_3PO via a 2-electron step to Ru(O)(TMP); two moles of PPh_3 with the latter gave Ph_3PO and $Ru(PPh_3)$ (TMP) [604]. Kinetics of the oxidation of LR_3 (L=P, R=(p-XC_6H_4) with X=OMe, H, F, Cl, CF_3; $AsPh_3$ and $SbPh_3$) to the corresponding oxides by stoich. *trans*-$RuO_2(TMP)/C_6H_6$ were studied. A mechanism involving formation of $Ru^{IV}(O)(OLR_3)(TMP)$ followed by its disproportionation to *trans*-$Ru(O)_2(TMP)$ and $Ru^{II}(LR_3)(TMP)$ was proposed. Kinetic data were measured for oxidation of P(p-$XC_6H_4)_3$ (X=H, CH_3, CF_3, OMe, F, Cl) to P(p-$XC_6H_4)_3O$ catalysed by *trans*-$Ru(O)_2(TMP)/O_2/C_6H_6$ [605].

***Trans*-[Ru(O)$_2$(TMP$^{\cdot}$)]$^+$** (cation radical) Oxidation of *trans*-$Ru(O)_2(TMP)$ with phenoxathiin hexachloroantimonate gives the complex as a porphyrin cation radical; ESR and electronic spectra were measured. Stoicheiometric *trans*-$[Ru(O)_2(TMP^{\cdot})]^+/CH_2Cl_2/-45°C$ epoxidised norbornene and *cis*- and *trans*-stilbene, while Ph_2S gave Ph_2SO and Ph_2SO_2 [579].

***Trans*-Ru(O)$_2$(TPP)** (TPP=*meso*-5,10,15,20-tetraphenylporphyrinate dianion) is made from Ru(CO)(MeOH)(TPP) and MCPBA; IR, electronic and ^1H NMR spectra were recorded. Kinetics of the oxidation of alkanes, aromatic hydrocarbons and epoxidation of cyclo-octene, norbornene, and styrene, *cis* and *trans*-stilbene were measured for stoich. *trans*-$Ru(O)_2(TPP)/C_6H_6$. Second-order rate constants were evaluated, and Hammett plots for the epoxidation of substituted styrenes obtained for stoich. *trans*-$Ru(O)_2(TPP)/CH_2Cl_2$ [606].

***Trans*-Ru(O)$_2$(R-TPP)** (R-TPP=*p*-substituted tetraphenylporphyrinate dianions; R=Cl, Me, MeO) These purple materials are made by reaction of Ru(CO)(MeOH)(R-TPP) and MCPBA. Electronic and ^1H NMR spectra were recorded. Kinetics of their epoxidation of alkenes and saturated alkanes by stoich. *trans*-$Ru(O)_2(R\text{-}TPP)/CH_2Cl_2$ were measured; second-order rate constants were measured. A continuum of transition states is probably involved [606].

***Trans*-Ru(O)$_2$(TDCPP)** (TDCPP=*meso*-5,10,15,20-tetrakis(2,6-dichlorophenyl) porphyrinate di-anion, sometimes called OCP) is made by oxidation of Ru(CO)(TDCPP) with MCPBA [577], or, *in situ*, from Ru(CH$_3$CN)$_2$(TDCPP) in C$_6$H$_6$ with O$_2$ or MCPBA [581]. The IR, electronic and ^{1}H NMR spectra of the purple complex were measured [577]. The system *trans*-Ru(O)$_2$(TDCPP)/O$_2$/C$_6$H$_6$ epoxidised norbornene, though not as efficiently as *trans*-Ru(O)$_2$(TMP)/O$_2$/C$_6$H$_6$ [581, 590].

***Trans*-Ru(O)$_2$(OEP)** (OEP=2,3,7,8,12,13,17,18-octaethylporphyrin dianion). This deep purple material is made from Ru^{II}(CO)(CH$_3$OH)(OEP) and MCPBA. It is diamagnetic, and its IR, electronic and ^{1}H NMR spectra were recorded as were its cyclic voltammetric properties. In the IR spectrum ν^{as}(Ru(O)$_2$) lies at 820 cm^{-1} [607]. Stoicheiometric *trans*-Ru(O)$_2$(OEP)/CH$_2$Cl$_2$ epoxidised norbornene, styrene, *cis* and *trans*- stilbene giving the μ-oxo reduction product (OH)(OEP)Ru^{IV}(μ-O) Ru^{IV}(OH)(OEP) [607]. As *trans*-Ru(O)$_2$(OEP)/O$_2$/C$_6$H$_6$ it oxidised Et$_2$S to Et$_2$SO and Et$_2$SO$_2$ [47, 581].

***Trans*-[Ru(O)$_2$(OEP$^{\cdot}$)]$^+$** (cation radical) Oxidation of *trans*-Ru(O)$_2$(OEP) with phenoxathiin hexachloroantimonate gives the complex as a porphyrin cation radical; electronic and ESR spectra were measured. As stoich. *trans*-[Ru(O)$_2$(OEP$^{\cdot}$)]$^+$/ CH$_2$Cl$_2$ it epoxidised norbornene and *cis*- and *trans*-stilbene, while Ph$_2$S gave Ph$_2$SO and Ph$_2$SO$_2$ [579].

***Trans*-Ru(O)$_2$(pfp)** (pfp=5,10,15,20-*tetrakis*[*o*-((2-methoxy-2-phenyl-3,3,3-trifluoropropanoyl)-amino)phenyl]porphyrin). These optically active picket-fence α,β,α,β and α,α,β,β porphyrin complexes are made by oxidation with MCPBA of the appropriate isomers of Ru(CO)(THF)(pfp); IR, electronic and ^{1}H NMR spectra of the red-purple species were recorded (ν^{as}(Ru(O)$_2$) 823 cm^{-1}), and the X-ray crystal structure of Ru(CO)(THF))(pfp) (α,β,α,β) was determined [608]. The system stoich. *trans*-RuO$_2$(pfp)/CH$_2$Cl$_2$ oxidised racemic phosphines to the corresponding phosphine oxides. A mechanism was proposed in which either the *R* or the *S* isomer of the phosphine is attacked to give Ru^{IV}(O)(pfp) and phosphine oxide; more phosphine reacts with the Ru^{IV}(O)(pfp) which then oxidises more phosphine. There is clear evidence of weak chiral recognition during the oxygen-atom transfer process [608, 609]. The stereoselectivity was explained by differences in the reactivity of the complexes towards the *R* and *S* isomers of the phosphines [42].

***Trans*-Ru(O)$_2$(hpp)** (hpp=5,10,15,20-*tetrakis*(2-hydroxyphenyl)porphyrin encumbered with four chiral threitol units) is made by oxidation of Ru^{II}(CO)(EtOH)(hpp) with MCPBA, and is dark purple. As stoich. *trans*-Ru(O)$_2$(hpp)/pyrazole/C$_6$H$_6$ or catalytically as TBHP/C$_6$H$_6$ *trans*-Ru(O)$_2$(hpp)/(Cl$_2$pyNO) or O$_2$ (9 atm)/pyrazole/ C$_6$H$_6$ it epoxidised aromatic alkenes with good e.e. values [610, 611].

***Trans*-Ru(O)$_2$(por*)** (H$_2$por*=5,10,15,20-*tetrakis*-[(1*S*.4*R*,5*R*,8*S*)-1,2,3,4,5,6,7,8-octahydro-1,4:-5,8-dimethanoanthracen-9-yl]porphyrin), a D$_4$ porphyrinato species, was made from Ru(CO)(EtOH)(por*) and MCPBA. It is dark purple and diamagnetic: electronic, ^{1}H and ^{13}C NMR spectra were recorded. The X-ray crystal structure shows the Ru=(O) bonds to be *trans* (Ru=(O) 1.74(1) Å, with an (O)=Ru=(O) angle of 175.4° (Fig. 1.28); the IR υ^{as}(Ru(O)$_2$) lies at 822 cm^{-1} [612].

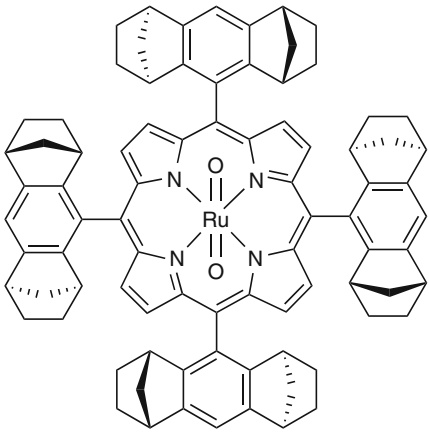

Fig. 1.28 Likely structure of *trans*-$Ru(O)_2$(por*) [612]

The stoicheiometric reagent *trans*-$Ru(O)_2$(por*)/CH_2Cl_2 epoxidised several alkenes with good e.e.; while *trans*-$Ru(O)_2$(por*)/PhIO/CH_2Cl_2 epoxidised styrene to the (*R*) oxide, and *cis*-β-methylstyrene to (1*R*,2*S*)-*cis*-β-methylstyrene oxide with an e.e. of 91% [613]; *trans*-$Ru(O)_2$(por*)/O_2 (8 atm)/CH_2Cl_2 also asymmetrically epoxidised alkenes [612]. Second order rate constants for a number of such reactions were measured, as were Hammett plots for oxidation of *para*-substituted styrenes. Oxygen-atom transfer via the unstable Ru^{IV}(O)(por*) was suggested [613, 614].

***Trans*-$Ru(O)_2$(chir-TPP)** (chir-TPP=(*R*)-*trans*-1,2-dimethoxycyclohexane)$_4$-TPP and (*R*)-*trans*-1,2-diethoxycyclohexane)$_4$-TPP) These homochiral porphyrins are made from *meso*-tetrakis(2,6-dihydroxyphenyl)porphyrin and (1*R*,2*R*)-*trans*-1,2-bis(hydroxymethyl)-cyclohexane) or (1*R*,-2*R*)-*trans*-1,2-bis(hydroxyethyl)cyclohexane), the products reacted with $Ru_3(CO)_{12}$ to give Ru(CO)(chir-TPP), then oxidised with MCPBA. The IR, electronic and ^{1}H NMR spectra of the hydroxyethyl complex were measured. Epoxidations by *trans*-$Ru(O)_2$(chir-TPP)/(Cl_2pyNO)/C_6H_6 of styrene and substituted styrenes and 1,2-dihydronaphthalene gave the epoxides in good yields and with good turnovers, with e.e. of up to 35%. Reactivity and enantioselectivity are strongly dependent on the central cyclohexane position [615].

1.4.2.6 Dioxo Complexes with Macrocyclic Donors

Mechanisms of oxidations of inorganic and organic substrates by macrocyclic complexes containing the *trans*-$Ru^{VI}(O)_2$ unit have been reviewed [48].

***Trans*-[$Ru(O)_2$(R-TMC)](ClO_4)$_2$** These are complexes of the macrocyclic tertiary amines 14-TMC (1,4,8,11-tetramethyl-1,4,8,11-tetra-azacyclotetradecane (**a**); 15-TMC (1,4,8,12-tetramethyl-1,4,-8,12-tetra-azapentadecane (**b**); and 16-TMC (1,5,9,13-tetramethyl-1,5,9,13-tetra-azacyclohexa-decane (**c**) (Fig. 1.29) [576].

The complexes are made, usually as yellow perchlorates, by reaction of *trans*-[$RuCl_2$(R-TMC)]Cl, Ag($MeC_6H_4SO_3$) and aq. H_2O_2 with $HClO_4$ [576, 616]. X-ray

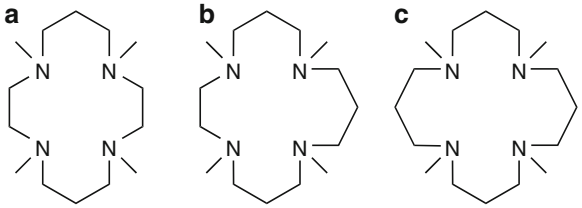

Fig. 1.29 Structures of TMC macrocyclic ligands [576]

data confirmed the *trans* configuration in *trans*-$[Ru(O)_2(14\text{-TMC})](ClO_4)_2$ (Ru=(O) 1.765(5) Å) [576]. For *trans*-$[Ru(O)_2(15\text{-TMC})](ClO_4)_2$ (Ru=(O) 1.718(5) Å) and *trans*-$[Ru(O)_2(16\text{-TMC})](ClO_4)_2$ (Ru=(O) 1.705(7); Cyclic voltammetric, electronic and IR spectroscopic studies were made; υ^{as} $(Ru(O)_2)$ lie at 850, 855 and 860 cm^{-1} for the three complexes respectively [617].

Stoicheiometric *trans*-$[Ru(O)_2(14\text{-TMC})]/CH_3CN/50°C$ oxidised alcohols (benzyl to benzaldehyde, 2-propanol to acetone); cyclohexene gave 2-cyclohexene-1-one and toluene yielded benzyl alcohol and benzaldehyde. The system *trans*-$[Ru(O)_2(14\text{-TMC})]^{2+}/O_2/CH_3CN/50°C/17h$ converted benzyl alcohol to benzaldehyde and oxidised cyclohexane and toluene [576]. Possible mechanisms for the oxidation of benzhydrol and 2-propanol by stoich. *trans*-$[Ru(O)_2(14\text{-TMC})]^{2+}/CH_3CN$ were considered: primary deuterium isotope effects indicate that cleavage of the α-C-H bond is rate-limiting. A 2+2(C-H+Ru=(O)) addition reaction or a reaction initiated by ligand formation through interaction of the highest HOMO of the alcohol with the LUMO of the complex may be involved [616]. Kinetics and mechanism of the oxidation of hydroquinone to p-benzoquinone (and of substituted hydroquinones) by stoich. *trans*-$[Ru(O)_2(14\text{-TMC})]^{2+}/CH_3CN$ suggest that a species such as $[Ru^{IV}(O)(CH_3XCN)(14\text{-TMC})]^{2+}$ is involved [618].

***Trans*-$[Ru(O)_2(dpt)](ClO_4)_2$** (dpt=*N,N´*-dimethyl-6,7,8,9,10,11,17,18-octahydro-5*H*-dibenzo[*en*][4,8,12]-dioxa-diaza-cyclopentadecane; *N,N´*-dimethyl-*N,N´*-bis (2-pyridylmethyl)propylenediamine; *meso*-2,3,7,11,-12-pentamethyl-3,7,11,17-tetraazabicyclo[11.3.1]-heptadeca-1(17),13,15-triene; 1,4,8,-11-tetra-methyl-1,4,8,11-tetraaza-cyclotetradecane) are made by oxidation of $[RuCl_2(dpt)]^+$ with H_2O_2 and $Ag(p\text{-}MeC_6H_4SO_3)$. The Ru^{VI}/Ru^{IV} redox potentials were measured and related to the rates of stoicheiometric oxidation of alcohols. Oxidations by stoich. *trans*-$[Ru(O)_2(dpt)]^{2+}$/water or CH_3CN of benzyl alcohol and propan-2-ol were accompanied by large α-C-H bond isotope effects, suggesting association of the Ru=(O) and the α-CH bond in the transition state [564]. As *trans*-$[Ru(O)_2(dpt)]^{2+}/CH_3CN/UV>330$ nm it photo-oxidised norbornene to exo-2,3-epoxynorbornane, cyclohexene to cyclohexen-2-one and cyclohexen-2-ol, *trans*-stilbene to *trans*-stilbene oxide, Ph_2S to the sulfoxide and propan-2-ol to acetone [619].

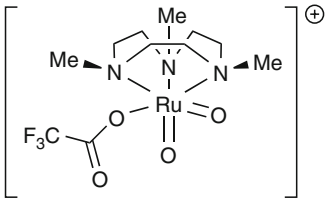

Fig. 1.30 Structure of the cation in *cis*-$[Ru(O)_2(CF_3COO)(tmtacn)](ClO_4)$ [622]

***Cis*-$[Ru(O)_2(tet\text{-}Me_6)](ClO_4)_2$** (tet-$Me_6$=*N,N,N′,N′*,3,6-hexamethyl-3,6-diazaoctane-1,8-diamine) is a yellow diamagnetic material made by reaction of *cis*-$[RuCl_2(tet\text{-}Me_6)](ClO_4)$, cerium(IV) and silver toluene-*p*-sulphonate. The X-ray crystal structure shows that the Ru=(O) distances are 1.795(9) Å and the (O)=Ru=(O) angle 112.0(4)°. Two IR bands in the Ru=O stretching region at 859 cm^{-1} and 874 cm^{-1} are assigned to $\nu^{as}(Ru(O)_2)$ and $\nu^{s}(Ru(O)_2)$. Electronic spectra and electrochemical properties were measured [620]. As stoich. *cis*-$[Ru(O)_2(tet\text{-}Me_6)]^{2+}/CH_3CN$ it oxidised cyclo-hexanol, -pentanol and -butanol to ketones, alkenes (styrene, *cis*- and *trans*-stilbenes, styrene, norbornene, cyclo-octene, cyclohexene) to mixtures of epoxides and cleavage products; alkanes (toluene, ethylbenzene, cumene, adamantane, 2,3-dimethylbutane) gave alcohols and ketones. For alkene oxidations it was suggested that a radical pathway was involved, with an electrophilic attack of an Ru=O moiety on the olefinic double bond [620, 621].

***Cis*-$[Ru(O)_2(CF_3COO)(tmtacn)](ClO_4)$** (tmtacn=1,4,7-trimethyl-1,4,7-triazacyclononane; in [622] this is called Cn in [623], but the more usual abbreviation (tmtacn) is used here). The light green complex is made by oxidation of $Ru^{III}(CF_3COO)_3(tmtacn).H_2O$ with $(NH_4)_2[Ce^{IV}(NO_3)_6]$. The X-ray crystal structure shows the oxo ligands to be *cis* (mean Ru=(O) 1.716(9) Å, with an (O)=Ru=(O) angle of 118.3(4)°) (Fig. 1.30). The IR, electronic and mass spectra were recorded; the IR spectrum shows two bands, at 842 and 856 cm^{-1}, assigned to $\nu^{as}(Ru(O)_2)$ and $\nu^{s}(Ru(O)_2)$ respectively [622].

Stoicheiometric *cis*-$[Ru(O)_2(CF_3COO)(tmtacn)]^+/CH_3CN$ epoxidised alkenes, and as *cis*-$[Ru(O)_2(CF_3COO)(tmtacn)]^+$/PhIO or TBHP/$CH_2Cl_2$ epoxidised cyclo-octene and -hexene, norbornene, *cis*-and *trans*-stilbene, styrene, and oxidised alkynes (diphenylacetylene to benzil). Cyclohexane gave cyclohexanone, and Me_2S gave the sulfoxide and sulfone. Much better turnovers were accomplished with TBHP rather than PhIO as the co-oxidant [624]. Kinetics of oxidation by stoich. *cis*-$[Ru(O)_2(CF_3COO)(tmtacn)]^+/CF_3COOH\text{-}CH_3CN$ of alkyl- or aryl-silylacetylenes to diketones were measured; with the alkyne *bis*-trimethysilylacetylene $[Ru^{IV}(CF_3COO)\{OC_2(SiMe_3)_2O\}(tmtacn)](ClO_4)$ was obtained and its X-ray crystal structure determined. The *cis*-$Ru(O)_2$ moiety of the starting complex may directly bind to the two acetylenic carbon atoms forming a five-membered planar metallacycle, so that the compound can be envisaged as a [3 + 2] cyclo-adduct of the starting complex and the acetylene [622].

1.4.3 Ru(VI) Complexes Containing Mono-Oxo or Nitride Donors

$Ru(O)(O_2R)_2$ (R=7,8-didehydrocholesteryl acetate and cholesteryl acetate). These esters were isolated from RuO_4 (as RuO_2/aq. $Na(IO_4)$/acetone) and R, and were shown by ^1H and ^{13}C NMR and mass spectrometry to be Ru(VI) diesters similar to those obtained from the alkenes R with OsO_4. Their isolation, despite the absence of X-ray structural studies, suggests that such diesters could be involved in reactions of RuO_4, as indeed they are in the corresponding reactions with OsO_4. In each case a pair of isomeric diesters was formed (Fig. 1.31) [323, 346].

Formation of a Ru(VI) diester was proposed as an intermediate in the reaction of (−)-α-pinene with RuO_4 (Fig. 3.8) [322].

Ru(O)(PHAB) (H_4PHAB=1,2-*bis*(2,2-diphenyl-2-hydroxy-ethaneimido)benzene) is made by oxidation with cerium(IV) of ($^nPr_4N$)[Ru(O)(PHAB)]. It is diamagnetic, and square pyramidal with the oxo ligand in the axial position (Ru=(O) 1.661(1), Ru-N 1.92(2) Å), with the Ru atom sitting 0.70 Å above the basal plane. The IR spectrum shows ν(Ru=(O)) at 926 cm^{-1}, shifting to 887 cm^{-1} on ^{18}O-substitution. As Ru(O)(PHAB)/O_2/CH_2Cl_2 it oxidised PPh_3 to Ph_3PO, and as stoich. Ru(O)(PHAB)/CH_2Cl_2 converted benzyl alcohol to benzaldehyde [625].

(PPh_4)[Ru(N)$Me_2(\mu_2$-O)$_2$Pd(−)(sparteine)] This red heterobiometallic complex is made from (PPh_4)[Ru^{VI}(N)$(OH)_2Me_2$] and Pd($OSiMe_3$)(−)-sparteine), and the IR υRu(N) stretch lies at 1070 cm^{-1}. The system Ru(N)$Me_2(\mu_2$-O)$_2$Pd(−)(sparteine)]$^-$/O_2/C_6H_5Cl/PMS/100°C oxidised primary alcohols to aldehydes and secondary alcohols to ketones [626].

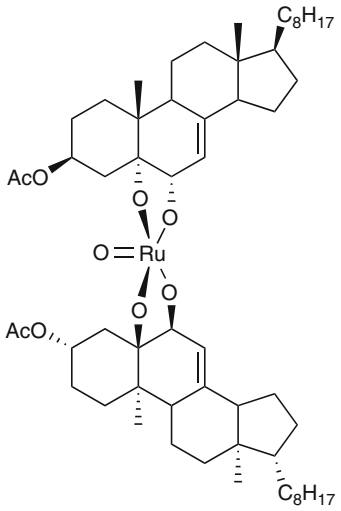

Fig. 1.31 Likely structure of diester formed from RuO_4 and 7,8-didehydrocholesteryl acetate [323]

1.5 Ru(V) Complexes

Relatively few oxoruthenate(V) complexes were known, but there has recently been more activity in this area. Che and Yam have reviewed complexes in this category [20]. All of the complexes in this section contain a single oxo ligand.

(^{n}Pr$_4$N)[Ru(O)(O$_2$C(O)CR^{1}R^2)$_2$] (R^{1}R^2=Me$_2$, Et$_2$, EtMe, PhMe) are made from TPAP and the appropriate α-hydroxycarboxylic acid in acetone [455]. The X-ray crystal structure of the 2-ethyl-2hydroxybutyrato complex (^{n}Pr$_4$N)[Ru(O)(O$_2$C(O)CEt$_2$)$_2$] shows it to have a trigonal bipyramidal structure with the oxo ligand in the equatorial position (Ru=(O) 1.697(5) Å), the other equatorial positions being occupied by oxygen atoms from the C(O)Et$_2$ groups (Fig. 1.32) [627].

The complex (^{n}Pr$_4$N)[Ru(O)(O$_2$C(O)CEt$_2$)$_2$] is paramagnetic (μ_{eff} 1.70 B.M at room temperature); the ESR spectrum was measured in the solid and in a CH$_2$Cl$_2$-CH$_3$OH glass. The IR spectrum shows ν(Ru=(O)) at 900 cm^{-1} [627]. Spectra (IR, ESR) were also measured for (^{n}Pr$_4$N)[Ru(O)(O$_2$COCEtMe)$_2$], (Ph$_3$P)$_2$N)[Ru(O)(O$_2$COCEt$_2$)$_2$], (^{n}Pr$_4$N)[Ru(O)(O$_2$C(O)CMe$_2$)$_2$] and (^{n}Pr$_4$N)[Ru(O)(O$_2$C(O)PhMe)$_2$] [455]. These complexes are remarkably unreactive: stoich. [RuO(O$_2$C(O)CEt$_2$)$_2$]$^-$/CH$_3$CN very slowly oxidised activated (benzylic) alcohols to ketones, and even as [Ru(O)(O$_2$C(O)CEt$_2$)$_2$]$^-$/NMO/CH$_3$CN they were poor catalytic oxidants for alcohols [627].

K[Ru(O)(EDTA)].3H$_2$O (EDTA=(ethylenediamine tetra-acetate)$^{4-}$). The chemistry of Ru-EDTA complexes has been reviewed [628]. This complex is made by reaction

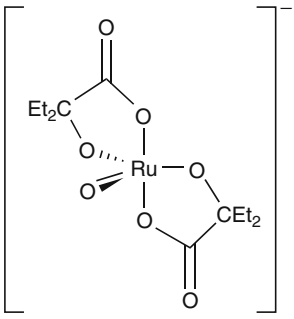

Fig. 1.32 Structure of (^{n}Pr$_4$N)[Ru(O)(O$_2$C(O)CR^{1}R^2)$_2$] [627]

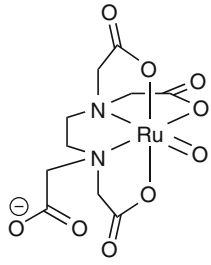

Fig. 1.33 Likely structure of [Ru^V(O)(EDTA)]$^-$ [631]

of PhIO with K[Ru^{III}(EDTA.H)Cl] in a water-dioxane mixture. It is greenish-yellow and paramagnetic (μ_{eff} 1.98 B.M. at 298K), and probably has the structure shown in Fig. 1.33. An IR band at 890 cm^{-1} shifts to 850 cm^{-1} on ^{18}O-substitution and so is likely to arise from ν(Ru=(O); the ESR spectrum of the complex was measured [629].

Kinetics of oxidation of $Ru^{III}(H_2O)$(EDTA-H) to [Ru(O)(EDTA)]$^-$/aq. Na(ClO) [630] and by aq. $(HSO_5)^-$ [631] were measured. Rates and activation energies for epoxidation of cyclohexene, styrene, *cis*- and *trans*-stilbene by [Ru(O)(EDTA)]$^-$/aq. Na(ClO)/30°C were determined, as were those for oxidation of cyclohexane to cyclohexanol and cyclohexanone [632] and for epoxidation of cyclohexene and cyclo-octene by [Ru(H_2O)(EDTA)]$^-$/$(HSO_5)^-$/water [631]. Stoicheiometric [Ru(O)(EDTA)]$^-$/water-dioxane oxidised cyclohexane and toluene to cyclohexanol and benzaldehyde; kinetics of the reaction were measured and discussed [629]. Involvement of stoich. [Ru(O)(EDTA)]$^-$ and [Ru(O)(PDTA)]$^-$/water-dioxane in the oxidation of toluene were studied, and rates and activation parameters determined [633]. Kinetics of the oxidation of diethylamine to ethylamine and acetaldehyde, and of triethylamine to diethylamine and acetaldehyde by stoich. [Ru(O)(EDTA)]$^-$/water were determined. Mechanisms were proposed involving a hydride shift from the α-carbon of the substrate to the oxo ligand [634]. Kinetics of the oxidation by [Ru(H_2O)(EDTA)]$^-$/aq. Na(ClO) of Ph_3P to Ph_3PO were studied; [Ru(O)(EDTA)]$^-$ is probably an intermediate [630].

K[Ru(O)(PDTA)].3H_2O and **Ru(O)(HEDTA)** (PDTA=(propylenediaminetetraacetate)$^{4-}$) are made by oxidation of K[Ru^{III}Cl(PDTA.H)] or K[Ru^{III}Cl(EDTA.H)] with PhIO; electronic and ESR spectra were recorded. Rates and activation energies for epoxidation by stoich. Ru(O)(PDTA)]$^-$ or Ru(O)(HEDTA)/water-dioxane of cyclo-alkanes were measured, as were those for oxidation of cyclohexane to cyclohexanol and cyclohexanone [632].

[Ru(O)(H_2O)$_3$$Cl_2$]($PF_6$) is made by electrochemical oxidation of [$RuCl_2(H_2O_4)$]$^+$ with $(Bu_4N)PF_6$. Epoxidation of cyclohexene and *cis*- and *trans*-stilbene was effected electro-catalytically by [Ru(O)$Cl_2(H_2O)_3$]$^+$/water-dioxane/Pt anode [632]. It may be involved as part of an electrocatalytic [Ru^{III}{$SiW_{11}(H_2O)O_{39}$}]$^{5-}$/[Ru^{V}O{$SiW_{11}O_{39}$}]$^{5-}$ cycle in which alkenes are cleaved [635].

[Ru(O)(N_4O)](ClO_4)$_2$ (N_4O^- =bis(2-(2-pyridyl)ethyl)(2-hydroxy-2-(2-pyridyl)ethyl)amine mono-anion) is made as a brown-green solid by oxidation of [$Ru^{III}(H_2O)$(N_4O)]$(ClO_4)_2$ with $(NH_4)_2[Ce(NO_3)_6]$ [636], or by electro-oxidation from [Ru(H_2O)(N_4O)]$^{2+}$ [637]. The IR ν(Ru=(O) stretch lies at 872 cm^{-1}, and electronic spectra and electrochemical data were measured. The magnetic moment μ_{eff} at 300K is 2.29 B.M. [636].

As stoich. [Ru(O)((N_4O)]$^{2+}$/CH_3CN it oxidised primary alcohols to aldehydes, secondary alcohols to ketones, alkenes to aldehydes, tetrahydrofuran to γ-butyrolactone. Styrene, *cis*- and *trans*-stilbenes gave benzaldehyde and adamantane gave 1-adamantol exclusively, while cyclohexanol gave cyclohexanone, suggesting that the complex is an effective oxidant for unactivated C-H bonds [636]. Immobilisation of the catalyst within Nafion films on a basal plane pyrolitic graphite electrode was achieved, but the

oxidations in $CF_3C(O)OH$ of benzyl alcohol were kinetically slow and the catalyst degraded during the course of alcohol oxidation [637]. Kinetics and isotope effects of the oxidation of primary and secondary alcohols by stoich. $[Ru(O)((N_4O)]^{2+}$/0.1 M aq. $HClO_4$ were studied, rate laws calculated and second-order rate constants determined [638]. Kinetics of oxidation of alkanes by stoich. $[Ru(O)((N_4O)]^{2+}/CH_3CN$-THF were studied: H-atom abstraction is probably involved [638], [639].

Ru(O)Cl(dmg)$_2$ (dmg=dimethylglyoximato mono-anion). This is prepared from $K[Ru^{III}Cl_2(dmg)_2]$ and PhIO; IR (ν(Ru=O) 835 cm^{-1}), electronic spectra and cyclic voltammetric data were recorded. The magnetic moment is 3.9 B.M. It may be involved as an intermediate in the catalytic epoxidation of cyclohexene by $RuCl_2(dmg)_2$/PhIO/water [640].

(^{n}Pr$_4$N)[Ru(O)(PHAB)] (H_4PHAB=1,2-*bis*(2,2-diphenyl-2-hydroxy-ethanamido) benzene) is made from (^{n}Pr$_4$N)[RuO_4] and the ligand. It has a distorted trigonal pyramidal structure. The oxo ligand is apical (Ru=(O) 1.702(3), Ru-N 1.95(2) Å), with the N_2O_2 donor atoms of the PHAB ligand being significantly distorted from planarity. The IR spectrum shows ν(Ru=(O)) at 885 cm^{-1}, shifting to 841 cm^{-1} on ^{18}O substitution. It is paramagnetic (μ_{eff} 2.0 B.M. at 298K); ESR data were measured. Extended Hückel calculations suggest that a d^3 metal-oxo structure will, in the absence of significant ligand strain, prefer a trigonal bipyramidal over a square-based pyramidal structure, as observed in these cases. As $[Ru(O)(PHAB)]^-/O_2/CH_2Cl_2$ it catalysed the oxidation of PPh_3 to Ph_3PO, and stoich. $[Ru(O)(PHAB)]^-/CH_2Cl_2$ oxidised benzyl alcohol to benzaldehyde [625].

***Trans*-[Ru(O)$_2$(R-TMC)](ClO$_4$)** These are complexes of the macrocyclic tertiary amines listed under *trans*-$[Ru(O)_2(R\text{-}TMC)](ClO_4)_2$ (Fig. 1.29). The 14-TMC complex is yellow; the 15-TMC and 16-TMC complexes were not isolated, but were made by electro reduction of *trans*-$[Ru^{VI}(O)_2(R\text{-}TMC)]^{2+}$. Their oxidative properties were not studied [576].

***Trans*-[Ru(O)(X)(14-TMC)]$^{2+}$** (Cl^-, NCO^-, N_3^-) are made by electrogeneration from the corresponding tetravalent complexes *trans*-$[Ru(O)(X)(14\text{-}TMC)]^{2+}$. Electrocatalytic oxidation of benzyl alcohol to benzaldehyde with *trans*-$[Ru(O)(X)(14\text{-}TMC)]^{2+}/CH_3CN$/Pt-C electrodes was studied [641].

1.6 Ru(IV) Complexes

Of the Ru(IV) complexes recorded here most are mono-oxo species which, despite the strong axial distortion brought about by the terminal oxo ligand, are probably all paramagnetic. Semi-empirical molecular orbital calculations (INDO/1) for epoxidations effected by oxo-Ru(IV) complexes have been reported (a non-concerted [1 + 2] pathway was preferred) [642], [643] and for alcohol oxidations by octahedral species containing an $Ru^{IV}(O)^{2+}$ unit [644]. The reactivity of high oxidation-state polypyridyl complexes of osmium and Ru, with particular emphasis on Ru(IV) and Os(IV) oxo species, has been reviewed [43].

The structural, spectroscopic and electrochemical properties of oxoruthenate (IV) complexes have been summarised, and a representative compilation of kinetic parameters for their oxidation reactions with alcohols, alkanes and alkenes presented [20].

This account starts with the most important of Ru(IV) compounds, ruthenium dioxide.

1.6.1 Ruthenium Dioxide, RuO_2 and $RuO_2.nH_2O$

This, and its rather ill-characterised hydrates $RuO_2.nH_2O$ ($n \approx 3$), was first mentioned by Klaus in 1844 [1] and more fully described by him in 1860 [10]. The hydrate $RuO_2.nH_2O$ is one of the most useful of Ru compounds, of comparable importance with that of $RuCl_3.nH_2O$ as a starting material for oxoruthenate catalysts.

Anhydrous RuO_2 has a tetragonal rutile structure with a slightly distorted octahedral structure, there being two sets of Ru-O distances at 1.917(8) and 1.999(8) Å [645] and has an extensive chemistry as a heterogeneous oxidation catalyst, a topic beyond the scope of this book. It is rarely used as a precursor for Ru oxidations, the hydrated form $RuO_2.nH_2O$ (for brevity written below simply as RuO_2) being much more effective in this respect. A procedure for converting "inactive" RuO_2 (presumably the anhydrous form) to the hydrated RuO_2 used in catalytic oxidations has been described [243].

The toxicology of RuO_2 has been summarised: it may give off toxic RuO_4 vapour when heated, and is poisonous by inhalation and mildly so by ingestion [238]. Thermodynamic data have been given for anhydrous and hydrated RuO_2 [230].

The black hydrated material ($n \sim 3$–4) is made by hydrolysis in air of an aqueous solution of $RuCl_3$. A number of thermal gravimetric analyses (TGA) and differential thermal gravimetric analyses (DTGA) have been made on it [646], and there are thermodynamic data for anhydrous and hydrated RuO_2 [230]. A Pourbaix (E-pH) diagram was constructed for, amongst other species, $RuO_2.2H_2O$ [231]. The potential diagram for RuO_4 – $[RuO_4]^-$ – $[RuO_4]^{2-}$ – RuO_2.aq was given [25], based on the classic polarographic work of 1954 (Fig. 1.4, 1.2.3), [227]. Kinetics of the oxidative dissolution of RuO_2 by ozone to give $[RuO_4]^{2-}$ and $[RuO_4]^-$ were studied: formation of $[RuO_4]^{2-}$ is the first step followed by autocatalytic reactions giving $[RuO_4]^-$ [531]. A rather similar sequence is followed when $[Ru(NO)(OH)_5]^{2-}$ is ozonised in aqueous base [532].

Hydrated RuO_2 is often used to generate RuO_4, $[RuO_4]^-$ or $[RuO_4]^{2-}$ using co-oxidants such as periodate or bromate. There are many examples in this and subsequent chapters of the use of $RuO_2.nH_2O$ as starting material with co-oxidants such as $Na(IO_4)$ for organic oxidations. Surprisingly, RuO_2 was found to be inactive as an oxidation catalyst as $RuO_2.nH_2O$/NMO/acetone or DMF [647]. Oxidation of benzyl alcohol to benzaldehyde was effected with RuO_2 or $RuCl_3$/(^{n}Bu$_4$N)Cl/aq. H_2O_2/CH_2Cl_2/60°C [648].

1.6.2 Ru(IV) Complexes with O- or N-Donors

$[Ru\{PW_{11}(O)_{39}\}]^{3-}$ No formula is given for this species in papers relating to it. It is made in solution from aqueous $Na_7[\{PW_{11}(O)_{39}\}].nH_2O$ and '$K_2[Ru(OH)Cl_5]$' (presumably $K_4[Ru_2(O)Cl_{10}]$). The electronic absorption spectrum was measured [258]. The system $[Ru\{PW_{11}(O)_{39}\}]^{3-}$/aq. $K(ClO_3)$/50°C oxidised primary alcohols and aldehydes to carboxylic acids [258, 649] and $[Ru\{PW_{11}(O)_{39}\}]^{3-}$/TBHP/$CH_3CN$/60°C epoxidised *trans*-stilbene [650].

$Cs_9[Ru_4O_5(OH)(H_2O)_4\{\gamma\text{-}PW_{10}O_{36}\}_2].17H_2O$ Strictly this lies outside the terms of reference of this book as it has so far only been used as a water oxidant. It is made from $[\{\gamma\text{-}PW_{10}O_{36}\}]^{7-}$ in aqueous $RuCl_3$ at pH 6 in air. The X-ray crystal structure was determined and cyclic voltammetric properties were measured. The system $[Ru_4O_5(OH)(H_2O)_4\{\gamma\text{-}PW_{10}O_{36}\}_2]^{9-}$/$[Ru(bpy)_3]^{2+}$/aq. $Na_2(S_2O_8)$ @ pH 5.8/UV oxidised water to O_2 [651].

***Trans*-$[Ru(O)Cl(py)_4]ClO_4$** is made from *trans*-$[Ru(NO)Cl(py)_4](ClO_4)_2$ and Na(ClO). The X-ray crystal structure shows a long Ru=(O) bond length of 1.862(8) Å, and the complex has a magnetic moment of 2.92 B.M. As stoich. *trans*-$[Ru(O)Cl(py)_4]^+$/CH_3CN it oxidised Ph_3P to Ph_3PO [652].

***Cis*-$[Ru(O)(py)(bpy)_2](ClO_4)_2$** is made by oxidation of $[Ru(H_2O)(py)(bpy)_2]^{2+}$ with cerium(IV) [653] or Br_2 gas [654], and is light green and paramagnetic; electronic spectra and electrochemical data were given. The IR spectrum shows ν(Ru=(O) at 792 cm^{-1} [653] or at 798 cm^{-1}, shifting to 755 cm^{-1} on ^{18}O-substitution [654].

Much work has been carried out with this species, and although the majority of the oxidations studied with it of a variety of organic substrates were stoicheiometric rather than catalytic, investigation of the mechanisms involved has been illuminating for an understanding of Ru oxidation chemistry. The many possible pathways of organic oxidations by $[Ru(O)(py)(bpy)_2]^{2+}$ have been reviewed [43].

Kinetics of the oxidation of primary and secondary alcohols by stoich. *cis*-$[Ru(O)(py)(bpy)_2]^{2+}$/water or CH_3CN were studied, large k_H/k_D effects observed and a two-electron hydride transfer mechanism proposed [655]. The system *cis*-$[Ru(O)(py)(bpy)_2]^{2+}$/aq. Na(ClO)/(BDTAC)/CH_2Cl_2 catalysed alkene epoxidations. With stoich. $[Ru(O)(py)(bpy)_2]^{2+}$/CH_3CN epoxidation of styrene and of *cis*-and *trans*-stilbene occurred and kinetic data were measured: O-insertion into the C=C bond may occur, followed by solvolysis of the bound epoxide [656]. Kinetics of the oxidation of cyclohexene, cyclohexen-1-ol and indene to the ketonic products 2-cyclohexen-1-one and indenone by stoich. *cis*-$[Ru(O)(py)(bpy)_2]^{2+}$/CH_3CN were studied, kinetic isotope effects measured and complex mechanisms suggested involving Ru(III) and Ru(II) intermediates; in the latter case transfer of ^{18}O from the $[Ru(^{18}O)(py)(bpy)_2]^{2+}$ to the epoxide occurs [657]. Mechanisms of epoxidation of *cis*- and *trans*-stilbene, styrene and norbornene by stoich. *cis*-$[Ru(O)(py)(bpy)_2]^{2+}$/CH_3CN were considered in a comprehensive paper. Labelling with ^{18}O shows that the oxygen atom in the epoxide derives from the oxo ligand in the complex, and Ru(II) and Ru(III) epoxide complexes may be involved [658]. The mechanism of the oxidation

of cyclohexene oxidation to 2-cyclohexen-1-ol by stoich. $[Ru(O)(py)(bpy)_2]^{2+}$/CH_3CN was discussed [659].

Kinetic studies on oxidations of hydroquinone, 2-chlorohydroquinones and 2,6-dichlorohydroquinone to the quinones by stoich. $[Ru(O)(py)(bpy)_2]^{2+}$/water indicated that a proton-coupled electron transfer mechanism may operate [660]. Transfer of ^{18}O from $[Ru(^{18}O)(py)(bpy)_2]^{2+}$ to the product in oxidation of phenol to *p*-benzoquinone by stoich. $[Ru(O)(py)(bpy)_2]^{2+}$/CH_3CN was quantitative. It is likely that electrophilic attack on the aromatic ring occurs [661], and that there are multiple electron oxidations of phenols to *o*- and *p*-benzoquinone and alkylated phenol derivatives by stoich. $[RuO(py)(bpy)_2]^{2+}$/CH_3CN [659, 661]. Kinetic studies suggested that, in the oxidation by *cis*-$[Ru(O)(py)(bpy)_2]^{2+}$/Pt electrode of Me_2S to Me_2SO and then to Me_2SO_2, an oxo ligand is transferred from the complex to the substrate at each stage; $[Ru^{II}(CH_3CN)(py)(bpy)_2]^{2+}$ may be an intermediate [662]. Kinetics of the oxidation of Ph_3P to Ph_3PO by stoich. *cis*-$[Ru(^{18}O)(py)(bpy)_2]^{2+}$/$CH_3CN$ were measured: it is likely that there is a two-electron oxygen transfer mechanism, with quantitative transfer of (^{18}O) from the ^{18}O-labelled complex to the phosphine, via $[Ru^{II}(OPPh_3)(py)(bpy)_2]^{2+}$ which then reacts with CH_3CN to give PPh_3O and $[Ru^{II}(CH_3CN)(py)(bpy)_2]^{2+}$ [663].

Thymidine-specific depyrimidination of DNA by this and other Ru(IV) oxo complexes, e.g. electrocatalytically by $[Ru(O)(py)(bpy)_2]^{2+}$/aq. formate buffer was studied and related to their Ru(IV)/Ru(II) redox potentials [664]. Oxidation of formate and of formic acid to CO_2 by stoich. *cis*-$[Ru(O)(py)(bpy)_2]^{2+}$/water was studied kinetically, and a two-electron hydride transfer mechanism proposed [665].

***Cis*-Λ-[Ru(O)(py)(bpy)$_2$](ClO$_4$)$_2$** is made from *cis*-$[Ru(py)_2(bpy)_2]Cl_2$ resolved with disodium-*(O,O′*-dibenzoyl-(*R,R*)-tartrate, and the resulting salt converted to *cis*-Λ-$[Ru(H_2O)(py)(bpy)_2](ClO_4)_2$ and oxidised by cerium(IV). The system stoich. *cis*-Λ-$[Ru(O)(py)(bpy)_2]^{2+}$/water-CH_3CN oxidised methyl-*p*-tolyl sulfide to (R)-methyl-*p*-tolyl sulfoxide [666].

***cis*-[Ru(O)(H$_2$O)(dmp)$_2$](PF$_6$)$_2$** This sterically crowded species is orange-yellow and is made from *cis*-$[Ru(H_2O)_2(dmp)_2](PF_6)_2$ and H_2O_2 [570] or cerium(IV); in the IR ν(Ru=(O) lies at 792 cm^{-1} [571]. The system *cis*-$[Ru(O)(H_2O)(dmp)_2]^{2+}$/$O_2$(1.3 atm)/$CH_3CN$/55°C epoxidised norbornene, cyclohexene and *trans*-β-methylstyrene [571], and the species is probably involved, via *cis*-$[Ru(CH_3CN)_2(dmp)_2]^{2+}$/$O_2$(3 atm)/$CH_3CN$/75°C, in the alkene epoxidation [570].

***Trans*-[Ru(O)(bpy)(tpy)](ClO$_4$)$_2$** This light green salt is made from $[Ru(H_2O)(bpy)(tpy)]^{2+}$ and Br_2; electronic spectra and cyclic voltammograms were recorded. Much mechanistic work has been carried out with this species, often in parallel with studies on *cis*-$[Ru(O)(py)(bpy)_2]^{2+}$, mainly by Meyer *et al*. and principally with stoicheiometric oxidations [667].

Kinetic parameters for the oxidation by stoich. $[Ru(H_2O)(bpy)(tpy)]^{2+}$/water @ pH 7 of a number of carbohydrates and nucleotides were measured and are consistent with carbohydrate oxidation at the 1′ position [668]. Electrocatalytic oxidations of 2-propanol to acetone, ethanol and acetaldehyde to acetate, *p*-xylene and *p*-phthalate to terephthalate, cyclohexene to 2-cyclohexen-1-one and toluene to benzoate with the couple $[Ru(O)(bpy)(tpy)]^{2+}$/$[Ru^{II}(H_2O)(bpy)(tpy)]^{2+}$/water @ pH

7–9/Pt electrodes were described [669]. The electrochemical system [Ru(H_2O)(bpy)(tpy)]$^{2+}$/water @ pH 6.8/Pt electrodes oxidised primary alcohols to aldehydes and carboxylic acids, aldehydes to acids, secondary alcohols to ketones, and C-H bonds adjacent to aromatic groups (e.g. 4-methylbenzoate to terephthalic acid and toluene to benzoate). It functions as a two-electron oxidant via a 'shuttle' mechanism, without one-electron pathways which might lead to the formation of radicals; *trans*-[Ru(O)(bpy)(tpy)]$^{2+}$ is probably involved [670]. Mechanistic studies were also made on stoich. *trans*-[Ru(O)(bpy)(tpy)]$^{2+}$/CH_3CN for oxidation of 2-propanol to acetone; a concerted hydride transfer from the α-CH bond of 2-propanol is probably involved [654]. As *trans*-[Ru(O)(bpy)(tpy)]$^{2+}$/aq. Na(ClO)/(BDTAC)/CH_2Cl_2 the reagent epoxidised styrene, *cis*- and *trans*- stilbene (although only a trace in the case of *cis*-stilbene); for a possible mechanism see *cis*-[Ru(O)(py)$(bpy)_2$]$(ClO_4)_2$ [656]. Stoicheiometrically *trans*-[Ru(O)(bpy)(tpy)]$^{2+}$/water cleaved DNA, and was used electro-catalytically at 0.8 v. (vs. SCE) for this purpose [671].

Kinetics of oxidation of toluene and cumene to the corresponding α-hydroxy compounds by stoich. *trans*-[Ru(O)(bpy)(tpy)]$^{2+}$/CH_3CN were reported; a two-electron hydride-ion transfer step may be involved [672]. Electro-oxidation of side-chains in alkylaromatics by [Ru(O)(bpy)(tpy)]$^{2+}$ (generated electrochemically *in situ* from [Ru(OH)(bpy)(tpy)]$^{2+}$/^{t}BuOH/water @ pH 6.8/Pt electrodes/50°C) was effected: toluene gave benzoic acid and ethylbenzene gave acetophenone (Table 4.1) [673].

[Ru(O)(pic)(tpy)](ClO_4) (pic=picolinate mono-anion) is made from [Ru(O)(pic)(tpy)]$^{2+}$ and $(NH_4)_2[Ce(NO_3)_6]$ [674, 675]. It is yellow and paramagnetic (μ 2.85 B.M.); IR and electronic spectra were measured. As stoich. [Ru(O)(pic)(tpy)]$^+$/CH_3CN it epoxidised cyclic alkenes. Kinetic measurements and Hammett plots suggest the involvement of a carbon-centred radical intermediate [674]. With stoich. [Ru(O)(pic)(tpy)]$^+$/water kinetics of oxidation of phenol to *p*-quinone were studied; a [Ru^{II}(quinone)(pic)(tpy)]$^+$ intermediate may be involved [675].

***Trans*-[Ru(O)$(Cl_2$bpy)(tpy)]$(ClO_4)_2$** and **[Ru(O)(tmeda)(tpy)]$(ClO_4)_2$** (tmeda = *N,N,N′,N′*-tetramethylethylenediamine) are made by oxidation of the corresponding Ru(II) aqua complexes with cerium(IV). The kinetics of their non-stereospecific, stoicheiometric epoxidation of aromatic alkenes in CH_3CN were studied, and the rates compared with those of oxidations effected by other Ru(IV) oxo complexes with N-donors [676]. The system [Ru(O)(tmeda)(tpy)]$^{2+}$/water/Pt anode electro-oxidatively cleaved DNA [677].

[Ru(O)(biqn)(tmtacn)]$(ClO_4)_2$ and **[Ru(O)(diopy)(tmtacn)]$(ClO_4)_2$** (biqn=C_2 symmetric 1,1′-biisoquinoline, diopy=(*R,R*)-3,3′-(1,2-dimethylethylenedioxy)-2,2′-bipyridine) are made from [RuCl(L)(tmtacn)]$^{2+}$ (L=biqn, diopy) and $(NH_4)_2[Ce(NO_3)_6]$ with Li(ClO_4). Electronic and IR spectra were measured (ν(Ru=(O) bands lie at 760 and 795 cm^{-1} respectively). The (diopy) complex is paramagnetic with μ_{eff} 2.88 B.M. As stoich. [Ru(O)(biqn)(tmtacn)]$^{2+}$ and [Ru(O)(diopy)(tmtacn)]$^{2+}$/CH_3CN they oxidised alkenes (styrene, *cis* and *trans*-β-methylstyrenes, *trans*-stilbene, norbornene, cyclohexene) to mixtures of aldehydes and epoxides. Contrary to expectation the (diopy) complex did not effect enantioselective epoxidations except with *trans*-stilbene, for which a moderate e.e. of 33% was observed [623].

[Ru(OH)$_3$(phen)]$_2$(O) is said to be formed when '[Ru(O)$_3$(phen)]$_2$O' (1.2.8) is treated with methanol; **Ru(O)$_2$(bpy)$_2$.3H$_2$O** and **Ru(O)$_2$(phen)$_2$** from 'Ru(O)$_4$(py)$_2$' and '[Ru(O)$_3$(phen)]$_2$(O)' with the appropriate ligands; **Ru(O)$_2$(phen)(bpy).3H$_2$O** from 'Ru(O)$_4$(bpy' and (phen). All these complexes lack full characterisation, although electronic spectra and polarographic data were recorded [444].

[Ru(H$_2$O)(pp)(bpp)](ClO$_4$)$_2$ (bpp={2, 6-bis(*N*-pyrazolyl)pyridine}or {2, 6-bis(3, 5-dimethyl-*N*-pyrazolyl)pyridine}; pp=2,2′-bipyridyl or 4, 4′-dimethyl-2,2′-bipyridyl) are made from Ru(pp)Cl$_3$ and (bpp) with AgClO$_4$; electronic spectra and cyclic voltammograms were recorded. As [Ru(H$_2$O)(bpy)(bpp)]$^{2+}$/Na(ClO)/(BDTAC)/aq. CH$_2$Cl$_2$/pH 10.5 it oxidised styrene, cyclohexene and cyclo-octene to mixtures of the epoxide and aldehyde, probably via [Ru^{IV}(O)(bpy)(bpp)]$^{2+}$ [678].

[Ru(O)(R$_2$-dppi)(tpy)]$^{2+}$ (R$_2$-dppi=R$_2$-3,6-bis(6-chloropyrid-2-yl)pyridazine with R=H, Me, Cl) is probably the species generated by cyclic voltammetric oxidation of [Ru(H$_2$O)(R$_2$-dppi)(tpy)]$^{2+}$. The reagents [Ru(O)(R$_2$-dppi)(tpy)]^2/water @ pH 7 electrochemically oxidised benzyl alcohol to benzaldehyde. Second-order rate constants were determined and a mechanism proposed which involves pre-association of the substrate with the Ru(IV) complex [679].

[Ru(O)(bpy)(thm)]X$_2$ (X=(PF$_6$)$^-$, (ClO$_4$)$^-$; (thm)=2,6-bis[(4*S*,7*R*)-7,8,8-trimethyl-4,5,6,7-tetra-hydro-4,7-methanoindazol-2-yl]pyridine). This chiral complex is made from the C$_2$ chiral tridentate imine, RuCl$_3$ and (bpy) followed by oxidation with MCPBA. The perchlorate has an IR ν(Ru=(O) band at 788 cm^{-1}. As stoich. [RuO(bpy)(thm)]$^{2+}$/CH$_3$CN it asymmetrically epoxidised styrene and its 3-nitro, 4-chloro and *cis*-β-methyl derivatives with e.e. of some 30% [680].

[Ru(O)Cl(bpy)(ppz*)](ClO$_4$)$_2$ and **[Ru(O)Cl(Cl$_2$bpy)(ppz*)](ClO$_4$)$_2$** (ppz*=2,6-bis-[(4*S*,7*R*)-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methanoindazol-2-yl]pyridine, Cl$_2$bpy=6,6′-dichloro-2,2′-bipyridyl) are made from RuCl$_3$(ppz*) and (bpy); their electronic spectra were measured. As stoich. (complex)/CH$_3$CN they epoxidised aromatic alkenes, with styrene and *cis*- and *trans*-methylstyrene achieving modest e.e. values of up to 59%. It was suggested that the ligand dissymmetry together with the bipyridyl ligand creates a "pocket" around the Ru=(O) unit leading to enantiofacial discrimination via non-bonding interactions [676].

Ru(O)(TMP) is made from *trans*-Ru(O)$_2$(TMP) with PPh$_3$; or from O$_2$ and Ru(MeCN)$_2$(TMP). It is paramagnetic with a magnetic moment of 2.4 B.M. in solution, and the ν(Ru=(O) stretch lies at 823 cm^{-1}, shifting to 782 cm^{-1} in Ru(^{18}O)(TMP) [604]. Its likely involvement in the stoicheiometric and aerobically catalysed epoxidations of alkenes by *trans*-Ru(O)$_2$(TMP) was noted [583].

Ru(OH)$_2$(TMP) is made from Ru(CO)(TMP) and MCPBA. It forms air-stable violet crystals and is paramagnetic with μ_{eff} 2.7 B.M. and in the IR ν(R=(O)) lies at 760 cm^{-1}. The reagent Ru(OH)$_2$(TMP)/O$_2$(4 atm)/C$_6$H$_6$ epoxidised norbornene; it was suggested that this dihydroxy species is present in equilibrium with Ru(O)(TMP) in solution and that the latter is the effective catalyst [590].

$RuCl_2$(TMP), as $RuCl_2$(TMP)/(Cl_2pyNO)/$CDCl_3$, oxidised alkenes RCH_2=CH to the aldehydes RCH_2CHO. Oxidation of 1,3-dienes gave the unsaturated aldehyde – thus 1-phenyl-1,3-butadiene gave the β, γ-unsaturated aldehyde 4-phenylbut-3-enal (styrylacetaldehyde); $RuCl_2$(TDCPP) also effected these reactions [584].

Ru(O)($OEP^{+\cdot}$)Br is made from RuBr(PPh_3)(OEP) and PhIO. It is green, and its ESR spectrum shows a *g* value of 2.0 suggesting that it may contain a radical cation. As stoich. Ru(O)($OEP^{+\cdot}$)Br/CH_2Cl_2 it oxidised Ph_3P to PPh_3O [588].

$RuCl_2$(TDCPP) as $RuCl_2$(TDCPP)/(Cl_2pyNO)/$CDCl_3$ oxidised terminal alkenes RCH_2=CH to the aldehydes RCH_2CHO; 1,3-dienes gave the unsaturated aldehydes; $RuCl_2$(TMP) was also effective as a catalyst [584].

***Trans*-[Ru(O)X(R-TMC)]$(PF_6)_2$** (R-TMC=14-, 15-, and 16-TMC, the macrocyclic tertiary amine ligands in Fig. 1.29; X=Cl^-, NCO^-, N_3^-, CH_3CN) are made from *trans*-[Ru$(O)_2$(R-TMC)]$(PF_6)_2$ and PPh_3 and X^- or CH_3CN [576]. The X-ray crystal structure of *trans*-[Ru(O)Cl(14-TMC)]$(ClO_4)_2$ shows an Ru=(O) distance of 1.765(5) Å and Ru-Cl 2.505(3) Å, the oxo ligand being *trans* to N-bonded cyanato for X=NCO [576, 681]. Cyclic voltammetric with electronic and IR spectral data were recorded; in the IR ν(Ru=(O) lies near 815 cm^{-1}. Like most oxoruthenates(IV) they are paramagnetic (μ_{eff} 2.70–2.95 B.M.) [576, 681]. Electro-oxidation of $[Ru(O)X(14\text{-}TMC)]^+$ (X = Cl^-, NCO^-, N_3^-) gives the Ru(V) species *trans*-[Ru(O)X(14-TMC)]$^{2+}$ which has electro-oxidation catalytic properties (*cf.* 1.5) [641]. The reagents stoich. *trans*-$[Ru(O)X(R\text{-}TMC)]^{2+}$/PhCHO and *trans*-$[Ru(O)X(R\text{-}TMC)]^{2+}$/$O_2$/PhCHO oxidised benzyl alcohol to benzaldehyde [576].

[Ru(O)(bpy)(tmtacn)]$(ClO_4)_2$ (tmtacn=1,4,7-trimethyl-1,4,7-triazacyclononane, Fig. 1.30) is made from [Ru(H_2O)(bpy)(tmtacn)]$(ClO_4)_2$ and $(NH_4)_2[Ce(NO_3)_6]$, and the X-ray crystal structure reported. The molecule is octahedral with the oxo ligand (Ru=(O) 1.815(6) Å *trans* to an N atom of the (tmtacn)); the mean Ru-N distance is 2.14 Å. Electronic spectra and cyclic voltammetric data were given. The crystal structure of $[Ru^{II}(H_2O)(bpy)(tmtacn)](ClO_4)_2$ was determined [682].

As stoich. $[Ru(O)(bpy)(tmtacn)]^+$/CH_3CN it functioned as a "competent" *(sic)* epoxidant for alkenes, though the products were often contaminated with by-products (e.g. *trans*-stilbene gave *trans*-stilbene oxide and benzaldehyde; *cis*-stilbene gave *cis*- and *trans*- epoxides). Kinetics of the epoxidation of norbornene and styrene were reported, with activation parameters measured and discussed [682]. Kinetics of its non-stereospecific, stoicheiometric epoxidation of aromatic alkenes in CH_3CN were studied, and the rates compared with those of oxidations effected by other Ru(IV) oxo complexes with N-donors, e. g. $[Ru(O)(tmeda)(tpy)]^{2+}$, *trans*-$[Ru(O)(Cl_2bpy)(tpy)]^{2+}$ and $[Ru(O)Cl(bpy)(ppz^*)]^{2+}$ [676].

[Ru(O)(H_2O)(ddd)]$(ClO_4)_2.2H_2O$ (ddd=1,12-dimethyl-3,4:9,10-1,12-diaza-5,8-dioxacyclo-penta-decane) was made from controlled potential oxidation of $[Ru(OH)(H_2O)(ddd)]^{2+}$. The X-ray crystal structure showed the Ru=(O) bond length to be 1.739(2) Å, a short Ru=(O) distance for such a Ru(IV) species; the *trans* aqua ligand is at 2.199(3) Å. Electronic and IR spectra were measured (the IR

ν(Ru=(O)) stretch is at 845 cm^{-1}) as well as cyclic voltammetric data. As *trans*-$[Ru(O)_2(ddd)]^{2+}$/PhIO/acetone it converted alkenes to epoxides and other species. The effective oxidant is probably *trans*-$[Ru(O)_2(ddd)]^{2+}$ [683].

$[Ru(O)(PR_3)(bpy)_2](ClO_4)_2$ (PR_3=PPh_3, $P(p\text{-}C_6H_4OCH_3)_3$, $P(p\text{-}C_6H_4CH_3)_3$, $P(p\text{-}C_6H_4F)_3$, $P(C_6H_5)(p\text{-}C_6H_4CF_3)_2$, $P(p\text{-}C_6H_4CF_3)_3$). The complexes with (R=Et, Ph) are made from *cis*-$RuCl_2(bpy)_2$ and PR_3; for the PEt_3 complex ν(Ru=(O) lies at 790 cm^{-1} [684].

Primary alcohols were oxidised to aldehydes by stoich. $[Ru(O)(PPh_3)(bpy)_2]^{2+}$ and $[Ru(O)(PEt_3)(bpy)_2]^{2+}$/water or CH_3CN, with rate constants depending on the hydrophobicity of the alcohols and phosphines and the nature of the solvent [685]. Oxidation of *N, N*-dimethylaniline to *N*-methylaniline and formaldehyde was effected by $[Ru(H_2O)((PPh_3)(bpy)_2]^{2+}/O_2/\alpha,\alpha,\alpha$-trifluorotoluene, while *p*-substituted *N,N*-dimethylanilines (R=H, Me, Cl) were oxidised to the corresponding *N*-methylanilines by stoich. $[Ru(O)(PR_3)(bpy)_2]^{2+}/CH_3CN$ (R=Ph, Et) and rate constants determined [686]. Several sulfides were oxidised to sulfoxides and sulfoxides to sulfones by stoich. $[Ru(O)(PR_3)(bpy)_2]^{2+}/CH_3CN$. Kinetics and kinetic isotope effects were measured, and it was proposed that the rate-determining step for thioanisole was primarily a single electron-transfer while that for MePhSO arose primarily from an S_N2 mechanism [687]. Stoicheiometric $[Ru(O)(PEt_3)(bpy)_2]^{2+}$/water oxidised Ph_3P to Ph_3PO [684].

$[Ru(O)(ER_3)(bpy)_2]^{2+}$ (R=Me, Et; E=P, As). These are made by oxidation of *cis*-$[Ru(H_2O)_2(ER_3)(bpy)_2]^{2+}$ with cerium(IV) [688]. As stoich. $[Ru(O)(ER_3)(bpy)_2]^{2+}/CH_3CN$-$CH_2Cl_2$ they converted alcohols to aldehydes and ketones, the rates of oxidation depending, amongst other factors, on the hydrophilicity of the alcohols [689]. Kinetics of the oxidation of primary and secondary alcohols by stoich. $[Ru(O)(PPh_3)(bpy)_2]^{2+}$/water or CH_2Cl_2 were measured and variations in the rates of oxidation with the nature of the phosphine noted [688].

1.7 Ru(III) Complexes

In general Ru(III), having a d^5 configuration, does not form complexes containing terminal oxo ligands, but there are a few μ-oxo bridged polymeric species. Some Ru(III) complexes are precursors for oxidation catalysis, predominantly $RuCl_3$. In general it is supposed that the co-oxidant produces either an oxo or a peroxo-Ru complex which is the active intermediate. A Pourbaix (E-pH) diagram includes, amongst other species, Ru^{3+} and $Ru(OH)^{2+}$ [231].

1.7.1 Ru(III) Complexes with O-Donors

Ruthenium has a considerable propensity to form polynuclear complexes, particularly with carboxylate ligands which as bridging ligands span the Ru centres, sometimes accompanied by a bridging oxo ligand. Preparation and properties of bi- and tri-nuclear acetato complexes of Ru have been reviewed [552].

$[Ru_3(\mu\text{-}O)(L)_3(OCOR)_6]^+$ complexes (R=Me, Et; L=H_2O, PPh_3; anions not specified) are made by reaction of $RuCl_3$ and acetic or propionic acids with water or PPh_3 [690].

The system $[Ru_3(\mu\text{-}O)(H_2O)_3(OC(O)Et)_6]^+/O_2$(1.3 atm)/water/65°C (no solvent specified) oxidised primary and secondary aliphatic alcohols to aldehydes and ketones; mixed-oxidation state species may be involved, with H_2O_2 playing a possible rôle in the mechanism [690]. The system $[Ru_3(\mu\text{-}O)(H_2O)_3(OAc)_6]^+$/aq. NaCl @ pH 7/$CCl_4$/Pt electrodes, perhaps electro-generating RuO_4, oxidised cyclohexylmethanol and 4-*tert*butylcyclohexanol to the acid and ketone respectively [267]. Although $[Ru_3(\mu\text{-}O)(H_2O)_3(OAc)_6]^+$/aq. $Na(IO_4)/CCl_4$ is inactive as a catalyst, after addition of a little CH_3CN it oxidised 1-octene to pentanoic acid. It may be that, for oxidations by RuO_4 of alcohols or alkenes, lower-valent carboxylato complexes are formed impeding further oxidations, and that CH_3CN competes as a ligand for such intermediates thereby enhancing the oxidations (Tables 3.3 and 3.6) [260]. Methylphenols were oxidised to the corresponding *p*-benzoquinones by $RuCl_3$ or $[Ru_3(\mu\text{-}O)(H_2O)_3(OAc)_6]^+$/aq. H_2O_2/AcOH (Table 3.5) [691].

$[Ru_3(\mu\text{-}O)(Et_2O)_3(pfb))_6](pfb)$ (pfb=perfluorobutyrate) is made from perfluorobutyric acid and its anhydride with $[Ru_3(\mu\text{-}O)(H_2O)_3(OC(O)Et)_6]^+$. As $[Ru_3(\mu\text{-}O)(Et_2O)_3(pfb))_6]^+/O_2$ (1.3 atm)/CH_3CN/65°C it epoxidised cyclohexene and norbornene but gradually degraded during this procedure. A suggested mechanism involved generation of a hydrocarbon radical, then reaction of this with O_2 to give a hydroperoxide and a subsequent Haber-Weiss decomposition [692]. A similar system oxidised cyclohexane and methylcyclohexane to the hexanols and hexanones [693].

$[Ru(OH)(H_2O)_5]^{2+}$ may be the active intermediate in the oxidation of L-alanine to acetaldehyde and bicarbonate by $RuCl_3/[Ag^{III}\{IO(OH)_5\}_2]^{5-}$/aq. HCl [694].

Ru(acac)$_3$ (acac=acetylacetonate). Oxidative dehydrogenation of α-hydroxy esters $R^1CH(OH)COOR^2$ to the keto-ester $R^1(CO)C(O)OR^2$ (R^1=Me, R^2=OAc) was effected by $Ru(acac)_3$/TBHP/C_6H_6, and the reaction was also catalysed by $RuCl_3$, $RuBr_3$ and $RuCl_2(PPh_3)_3$ [695]. The system $Ru(acac)_3/O_2/C_6H_6$/60°C oxidised cyclohexene to the epoxide, 2-cyclo-hexen-1-one and 2-cyclo-hexen-1-ol; c*is*- and *trans*-$RuCl_2(CO)_2(PPh_3)_2$, $RuCl_2(PPh_3)_3$ and $RuBr_2(PPh_3)_3$ also catalyses the reaction [696]. The reagent $Ru(acac)_3/O_2/Me_2CHCHO$/DCE catalysed epoxidation of *trans*-2-octene and of (*R*)-(+)-limonene [697].

$[Ru\{SiW_{11}(H_2O)(O)_{39}\}]^{5-}$ is made by reaction of $RuCl_3$ and $K_8[\{SiW_{11}(O)_{39}\}]$; IR, electronic and ESR spectra and cyclic voltammograms were measured [698]. As $[Ru\{SiW_{11}(H_2O)(O)_{39}\}]^{5-}$/co-ox/water/65°C (co-ox=$Na(IO_4)$, $(HSO_5)^-$, PhIO or TBHP) in the form of the $(^nHx_4N)^+$ salt it epoxidised styrene, cyclohexene and 1-octene; the nature of the products depended on the nature of the co-oxidant; it also oxidised, with the same co-oxidants, adamantane and cyclohexane [699]. A Ru(IV) heteropoly species may be involved as an intermediate [698, 699]. It was used as part of an ingenious electrocatalytic system for the cleavage of alkenes to aldehydes. In the biphasic system $(^nBu_4N)_5[Ru\{SiW_{11}(H_2O)(O)_{39}\}]$/aq. $Na(IO_3)/CH_2Cl_2$/Pb/PbO_2 anode the anode converts IO_3^- to IO_4^- which oxidises $[\{Ru^{III}\{SiW11(H_2O)(O)_{39}\}]^{5-}$ to $[Ru^V(O)\{SiW_{11}(O)_{39}\}]^5$, and so the catalytic $[Ru^{III}\{SiW_{11}(H_2O)(O)_{39}\}]^{5-}/[Ru^V(O)$

$\{SiW_{11}(O)_{39}\}]^{5-}$ couple is brought into play. Thus 3,4-methylenedioxy-1-(1-propenyl) benzene was oxidised to 3,4-methylenedioxy-benzaldehyde [635].

'$Na_{11}[WZnRu_2(OH)(H_2O)_2\{ZnW_9(O)_{34})_2\}].42H_2O$' was said to have been made by reaction of *cis*-$RuCl_2(dmso)_4$ and $Na_{12}[WZn_3(H_2O)_2]\{ZnW_9(O)_{34}\}_2\}.46H_2O$. The X-ray crystal structure of this "sandwich" type of polyoxometalate was briefly reported, the anion containing a WRuZnRu ring between two $\{ZnW_9(O)_{34}\}$ units; ESR, IR, electronic spectra and cyclic voltammetric data were recorded [700, 701]

However, comprehensive later work suggest that the material was probably the Ru-free $Na_{12}[WZn_3(H_2O)_2\{ZnW_9O_{34}\}].13H_2O$ contaminated with some *cis*-$RuCl_2(dmso)_4$ $13H_2O$ [702]. A number of oxidations reactions were earlier reported for $[WZnRu_2(OH)(H_2O)_2\{ZnW_9(O)_{34})\}]^{11-}$, abbreviated here as (complex), *viz.* (complex)**/-**(MTCAC)/TBHP or aq. H_2O_2 (alcohols to aldehydes and ketones, vicinal diols to α-ketols, alkenes to epoxides [703]; hydroxylation of adamantane by (complex)/O_2/aq. (MTCAC)/DCE/80°C [701, 704, 705]. Mechanisms were proposed [701, 704] for (complex)/TBHP/water-DCE/(MTCAC)/75°C for alkane oxidations, and alkene epoxidations by (complex)/aq. H_2O_2/(MTCAC)/DCE) [700] and (complex)/O_2/DCE/80°C [706]. It seems likely that the adamantane hydroxylation at least was caused by traces of *cis*-$RuCl_2(dmso)_4$ together with Ru-free $[WZn_3(H_2O)_2\{ZnW_9(O)_{34})_2\}]^{12-}$ [702].

α-$K_5[Ru\{Si(H_2O)W_{11}(O)_{39}\}]$, α-$K_4[Ru\{P(H_2O)W_{11}(O)_{39}\}]$ and **$K_7[Ru\{P_2(H_2O)W_{17}(O)_{61}\}]$** were used, as $(^nBu_4N)^+$ salts, as complex/aq. $Na(IO_4)$/DCE/60°C to effect oxidative cleavage of styrene to benzaldehyde and benzoic acid. Kinetic studies and activation parameters were determined [707]. The system α-$(^nHx_4N)_5[Ru\{Si(H_2O)W_{11}(O)_{39}\}]^{5-}$/TBHP/$C_6H_6$ oxidised cyclohexane, *n*-heptane, *n*-decane and ethylbenzene to alcohols and ketones [708].

$(^nBu_4N)_4[Ru\{PW_{11}(H_2O)(O)_{39}\}]$ This lacunary polyoxotungstoruthenate is made by reaction of $[Ru(H_2O)_6]^{2+}$ with $[\{PW_{11}(O)_{39}\}]^{7-}$; electronic and ^{31}P NMR spectra were recorded and several salts of the anion isolated. It can be electrolytically reduced to $[Ru^{II}\{PW_{11}(H_2O)\}]^{5-}$ or oxidised to $[Ru^{IV}(O)\{PW_{11}(O)_{39}\}]^{5-}$ and $[Ru^{V}(O)\{PW_{11}(O)_{39}\}]^{4-}$ [709].

Catalytic activities of $[Ru\{PW_{11}(H_2O)(O)_{39}\}]^{4-}$/$O_2$/$CH_3CN$/80°C and of $[Ru\{PMo_{11}(H_2O)(O)_{39}\}]^{4-}$/$O_2$/$CH_3CN$ were compared. The tungsten complex did not catalyse the aerobic oxidation of cumene and 1-octene to cumyl alcohol and 1-octene oxide while the Mo analogue did so; the tungsten complex underwent structural change with O_2 to an inert form, while its molybdenum analogue did not [710]. As $(^nBu_4N)_4[Ru\{PW_{11}(H_2O)(O)_{39}\}]$/PhIO/$CH_3CN$/60°C *trans*-stilbene was epoxidised, and with $[Ru\{PW_{11}(H_2O)(O)_{39}\}]^{4-}$/DMSO/graphite anode, electrolytic oxidation of Me_2S gave DMSO [709].

$(^nBu_4N)_4[Ru(H_2O)\{PMo_{11}(O)_{39}\}]$ is made from $(^nBu_4N)_4H_3[\{PMo_{11}(O)_{39}\}]$ and $RuCl_3$ [711] and its IR, electronic, ^{31}P NMR spectra and cyclic voltammograms measured [710]. The system $[Ru\{P(H_2O)Mo_{11}(O)_{39}\}]^{4-}$/$O_2$/$CH_3CN$/80°C slowly catalysed the epoxidation of cyclohexene, cumene and 1-octene [711]. Unlike $[Ru\{P(H_2O)W_{11}(O)_{39}\}]^{4-}$/$O_2$/$CH_3CN$/80°C the Mo system showed no structural change during catalysis, oxidizing cumene and 1-octene to cumyl alcohol and 1-octene oxide [710].

1.7.2 Ruthenium Trichloride, $RuCl_3$ and $RuCl_3.nH_2O$

The anhydrous form is rarely if ever used for catalysis, as is the case with anhydrous RuO_2. It exists in two modifications. The black α-form is made by heating β-$RuCl_3$ to 600°C *in vacuo*, and has the laminar α-$TiCl_3$ structure also found in $CrCl_3$ and $FeCl_3$ with a distorted octahedral structure (Ru–Cl distance 2.40 Å). The brown β-form has the β-$TiCl_3$ structure with linear polymers of $RuCl_3$ units, the metal atoms having distorted octahedral coordination (Ru–Ru 2.68 Å, Ru–Cl 2.30(7) and 2.39(7) Å). Infrared spectra and magnetic susceptibility data were recorded for both forms [712]. The toxicological properties of $RuCl_3$ have been listed: it may give off toxic RuO_4 when heated, and is mildly toxic by intraperitoneal routes [238].

The hydrate is the commonest of Ru compounds, forming black, hygroscopic crystals, and is the most important precursor for other Ru oxidation catalysts apart from being a catalyst in its own right. It was mentioned by Klaus in 1844 [1] and more fully described by him in 1860 [10]. Its use as a catalyst [201] and its general uses have both been briefly reviewed [713]. For most commercial samples $n \approx 3$, but the material is not normally a single compound; it may contain chloro, chlorohydroxo and chloro-oxo Ru(IV) and Ru(III) species, and sometimes can even contain nitrosyl chloro complexes of Ru(II) [6, 713]. It is best used in the hydrated form – it is often found to be difficult to react when anhydrous. Both it and RuO_2 are the reagents most often used either in their own right as starting materials for oxidation catalysis or, more frequently, as precursors for other catalysts such as RuO_4, $[RuO_4]^-$ or $[RuO_4]^{2-}$. In many of the preparations of catalysts mentioned in this book it was stated by several authors that '$RuCl_3$' was used as a starting material; in most such cases we have substituted the hydrate, since almost certainly it was this rather than the anhydrous material that was used.

In the section below on oxidations catalysed by $RuCl_3$ only those are mentioned which are *not* likely to involve RuO_4; many examples have been given above (1.2.7) in which $RuCl_3$/aq. $Na(IO_4)$, for example, was used to generate RuO_4. Such reactions are not repeated here.

1.7.2.1 Alcohols

Oxidation of benzyl alcohol to benzaldehyde was effected by $RuCl_3$ or RuO_2/($^nBu_4N$)Cl/aq. H_2O_2/CH_2Cl_2/60°C [648], and geraniol and nerol were oxidised to the aldehydes by $RuCl_3$ or $K_2[Ru(H_2O)Cl_5]$/aq. $H_2O_2/(R_4N^+)$/60°C (R_4N^+=unspecified quaternary cation) [714]. The system $RuCl_3$/aq. $Na_2(CO_3).1½H_2O_2$/Adogen®/83°C oxidised 1-indanol to 1-indanone [715], while $RuCl_2(PPh_3)_3$/1-dodecene/aq. KOH/dioxane/100°C oxidised secondary alcohols to ketones [716], and $RuCl_3$/aq. H_2O_2/AcOH/80°C converted cyclohexanol to cyclohxanone [717]. Oxidation of α-hydroxy esters $R^1CH(OH)R^2$ to the ketones R^1COR^2 was effected by $RuCl_3$/TBHP/C_6H_6; the reaction was also catalysed by $RuCl_2(PPh_3)_3$ and $RuH_2(PPh_3)_4$. Cyanohydrins

$R^1CH(OH)(CN)$ were oxidised by the same systems to acylcyanides $R^1CO(CN)$ (2.3.4) [695, 718], though $RuCl_2(PPh_3)_3$/TBHP/C_6H_6 is more effective [719]. The system $RuCl_3$/aq. H_2O_2/(DDAB)/DCE converted 1-phenylethanol to acetophenone and the intermediacy of a Ru(IV) oxo species suggested [720]; secondary alcohols were oxidised to ketones by $RuCl_3$/CH_3CO_3H or MCPBA/EtOAc; Ru(V) oxo species may be involved [721]. Bimetallic $RuCl_3$-$Co(OAc)_2.4H_2O$/O_2/CH_3CHO converted secondary alcohols to ketones and also oxidised alkanes. It was suggested that peracetic acid with acetaldehyde is formed by a cobalt-mediated radical chain with O_2, the $RuCl_3$ then effects the oxidation with the peracid via a Ru(V) oxo intermediate [722]. Kinetics of oxidation of cyclohexanol to cyclohexanone by $RuCl_3$ or $[RuCl_6]^{3-}$/aq. $[Fe(CN)_6]^{3-}$ @ pH 11.9 suggest that reduction of Ru(III) follows hydride-transfer from the alcohol, $[Fe(CN)_6]^{3-}$ then re-oxidising the Ru [723].

The system $RuCl_3$/O_2/water/90°C oxidised primary aldehydes to alcohols and secondary alcohols to ketones [724]; $RuCl_3$/NMO/acetone also effected such reactions ($RuCl_2(PPh_3)_3$ and $Ru_3(CO)_{12}$ were also used as catalysts) (Tables 2.1 and 2.2) [647]. In one of the few kinetic studies on a catalytic rather than a stoicheiometric system, oxidations of ethanol, propanol, butanol, pentanol, hexanol, 2-propanol, benzyl, *p*-chlorobenzyl and *p*-methylbenzyl alcohols to aldehydes or ketones catalysed by $RuCl_3$/NMO/DMF were studied. Structure-reactivity comparisons were made and activation parameters determined; a rate-determining formation of $Ru^V(O)Cl_3(OHCH_2R)$ was proposed [725]. Oxidation of a number of 1,2 diols, mainly benzylic, to the corresponding 1,2-diketones was accomplished using $RuCl_3$/bromamine-T/water @ pH 8.4/acetone: thus hydrobenzoin gave benzil [726]. Kinetics of the oxidation of galactose to galactonic acid and of cyclopentanol to cyclopentaonone by $RuCl_3$Na(BrO_3)/$Hg(OAc)_2$/aq. NaOH were studied: $RuCl_2(OH)(H_2O)_3$ and $[RuCl_3(OH)(H_2O)]^-$ respectively were suggested as the reactive intermediates [727].

1.7.2.2 Alkenes, Arenes, Alkynes

The system $RuCl_3$/(pydic)/H_2O_2/^{t}AmOH (pydic=pyridine-2,6-dicarboxylic acid) epoxidised several cyclic and linear alkenes (Table 3.1); (pydic) was the most effective of a variety of other pyridine carboxylic acids [728]. Kinetics of epoxidation of cyclo-octene, styrene and *trans*-stilbene by $RuCl_3$/EDTA/ascorbate/O_2/water @ pH 2.5/30°C were measured [729]: the system was regarded as a model for peroxidase systems. Kinetic data and rate laws were derived for it [730], and similarly for *cis*-cyclo-octene epoxidation (analogues of the Udenfriend system) [731]. Kinetics of the epoxidation of cyclohexene by $RuCl_3$/O_2/aq. EtOH/30°C were measured [732]. The system $RuCl_3$/O_2/Me_2CHCHO/DCE epoxidised *trans*-2-octene; $Ru(acac)_3$ similarly catalysed this oxidation [697], while $RuCl_3$/PhIO/CH_3CN epoxidised norbornene and cyclo-octene, -heptene, -hexene, -pentene (Table 3.1). The intermediacy of a Ru(V) oxo species was invoked, and its ESR and IR spectra measured (in the latter case the appearance of the IR υ(Ru=(O) at 810 cm^{-1} was noted) [733]. Kinetic and activation energy parameters were obtained for the epoxidation of

cyclohexene by $RuCl_3$/EDTA/O_2/water, both in the presence and absence of ascorbic acid [734].

Efficient epoxidation of a variety of linear and cyclic alkenes by $RuCl_3$/aq. $Na(IO_4)$/(bpy)/CH_2Cl_2/0–5°C/15 h was observed [735]; 5-methyl- or 3,4,7,8-tetramethyl-phenanthroline can replace (bpy) [736]. The active species when (bpy) is present is probably *trans*-$Ru(O)_2(bpy)\{IO_3(OH)_3\}$ [567, 568]. Competition between epoxidation and cleavage of *trans*-stilbene with bidentate ligands (pyridine, oxazoline, oxazolidine and thiophene), containing two different nitrogen heterocycles either linked or separated by a spacer together with $RuCl_3$/aq. $Na(IO_4)$/CH_2Cl_2/2°C was reported [737].

Asymmetric alkene epoxidation was achieved by using a mixture of $RuCl_3$/(oxal)/aq. phosphate buffer @ pH 8/4°C (oxal=chiral oxalamides). One of the most effective was the *N,N′*-bis-[2-(4,5-dihydro-oxazol-2-yl)phenyl]oxalamide derivative in epoxidising *trans*-stilbene, giving >99% conversion with e.e. values up to 62%. The reactions were stereospecific for (*E*)- and (*Z*)-alkenes [738, 739]. A somewhat similar system using $RuCl_3$/(pyoxal)/aq. $Na(IO_4)$/CH_2Cl_2/0°C (pyoxal=chiral 2-pyridyl oxazolines) gave e.e. values of up to 21% for epoxidation of 1-phenylcyclohexene and for *trans*-stilbene [740]. A fluorous pyridine benzimidazolic ligand (pyben) together with $RuCl_3$/(pyben)/O_2/Me_2CHCHO+$C_8F_{17}Br$+C_6H_5Cl/40°C epoxidised linear and cyclic alkenes, though the complex involved was seemingly not identified [741].

Cis-dihydroxylation without reduction of the alkene linkage occurred when cyclic unsaturated carbonyl and carboxylic acids were oxidised by $RuCl_3$/aq. CH_3CO_3H/CH_2Cl_2-CH_3CN to the corresponding α-oxo-ene-diols (Fig. 3.6) [742]. Alkenes reacted with $RuCl_3$/aq. CH_3CO_3H/CH_3CN-CH_2Cl_2 gave α-ketols (Fig. 3.9, Table 3.2) [743]. Ketohydroxylation of the allyl acetate (**1**) by $RuCl_3$/aq. CH_3CO_3H/CH_3CN-CH_2Cl_2 gave a precursor of 4-demethoxyadriamycinone ((**2**) in Fig. 3.10) [744].

The systems $RuCl_3$ or $RuCl_2(PPh_3)_3$/TBHP/EtOAc-C_6H_6 converted *p*-phenols to *p*-quinones [745], and $RuCl_3$/aq. Oxone®/CH_2Cl_2 destroyed the benzyl ring in alkylbenzenes to give CO_2 and water; *cis*-$RuCl_2(dmso)_4$, $RuCl_2(PPh_3)_3$, $K_5[Ru(H_2O)\{PW_{11}O_{39}\}]$ and $[RuCl(dpp)_2](PF_6)$ were also used [746]. Methylphenols were oxidised to the corresponding *p*-benzoquinones by $RuCl_3$ or $[Ru_3(O)(OAc)_6(H_2O)_3]^+$/aq. H_2O_2/AcOH (Table 3.4) [691]. Several 2-naphthols were oxidatively coupled by $RuCl_3$/O_2/[bmim](PF_6) to binaphthols [747], and $RuCl_3$/$(NH_4)_2[Cr_2O_7]$/aq. $HClO_4$/CH_3CN oxidised 2-methylnaphthalene to 2-methyl-1,4-naphthoquinone. Apparently RuO_4 is not produced: it was suggested that the reaction occurred through the enhanced oxidation of water [748]. The system $RuCl_3$/aq. H_2O_2/AcOH/80°C oxidised anthracene and phenanthrene to the quinones (Table 3.5) [717], and $RuCl_3$/aq. $Na(IO_4)$/CH_2Cl_2-CH_3CN oxidised pyrenes and 2,7-substituted pyrenes to the pyrene 4,5-diones or 4,5,9,10-tetraones [749].

Alkynyl amines $R^1CCNR^2R^3$ were oxidised to α-keto amides $R(CO)CO)NR^1R^2$ with $RuCl_2(PPh_3)_3$/PhIO/CH_2Cl_2 (RuO_4, *trans*-$RuCl_2(CO)_2(PPh_3)_2$ and $Ru_3(CO)_{12}$ can also be used). The same system oxidised alkynyl ethers R^1CCOR^2 to α-keto esters $R^1CO(COOR^2)$ [750]. The bimetallic $RuCl_3$/MoO_3/(DDAB)/aq. H_2O_2/^{t}BuOH/80°C cleaved linear and cyclic alkenes to acids, e.g. oleic to azelaic

acid [751], while $RuCl_2(PPh_3)_2$/PhIO/CH_2Cl_2 oxidatively cleaved disubstituted alkynes to α-diketones and terminal alkynes to carboxylic acids (Table 3.6) ($RuCl_2(PPh_3)_3$, $RuCl_2(CO)_2(PPh_3)_2$ and $Ru_3(CO)_{12}$ were also effective) [376].

1.7.2.3 Alkanes, Amines, Amides, Sulfides

The reagent $RuCl_3$/aq. H_2O_2/AcOH/80°C oxidised several benzaldehydes to the corresponding carboxylic acids [717]. With $RuCl_3$/TBHP/C_6H_6 nitriles RCH_2CN were converted to acyl cyanides [752], and side-chains of alkylaromatic compounds were oxidised by $RuCl_3$/aq. H_2O_2/(DDAB)/80°C to aldehydes, ketones or alcohols (Table 4.1) [362].

Oxidation of cyclo-octane and adamantane was effected by $RuCl_3/O_2$/heptanal/CH_2Cl_2 [753]; and that of cyclohexane by $RuCl_3$/EDTA/O_2/water, both in the presence and absence of the ascorbic acid [734], while the system $RuCl_3/CH_3CO_3H/CF_3C(O)OH$-$CH_2Cl_2$ oxidised several alkanes to ketones and alcohols [754]. Although later work suggested that such oxidations could be effected in the absence of $RuCl_3$, e.g. by CF_3COOH/H_2O_2 [755] this was disputed [756]. Oxidation by $RuCl_3/CH_3CO_3H/CF_3COOH$-$CH_2Cl_2$ of alkanes gave trifluoroacetates and ketones (Table 4.1); kinetic measurements were made and a Ru(V) oxo intermediate postulated [756].

The reagent $RuCl_3/O_2$/water-toluene/100°C oxidised primary amines (benzylamine, *n*-butylamine) to nitriles, and 2-aminoalkanes to imines [757], while oxidation of aniline by $RuCl_3$/aq. H_2O_2/(DDAB)/DCE/90°C gave nitrobenzene and azoxybenzene [758]. Kinetics of the oxidation of β-alanine to acetaldehyde and MeCN by $RuCl_3$/N-bromophthalimide/aq. $Hg(OAc)_2$/AcOH were studied; $RuCl_2(OH)(H_2O)_3$ is probably the active catalyst [759]. Sulfanilic acid was oxidised to *N*-hydroxylaminobenzene-4-sulfonic acid by $RuCl_3$/aq. chloramine-T; kinetic measurements were made [760]. Tertiary amines $R^1R^2R^3N$ were converted by $RuCl_3$/aq. bromamine-T/CH_3CN/80°C to $R^1R^2R^3NO$ [761] and $RuCl_3$ or $K_2[Ru(H_2O)Cl_5]/O_2$/DCE also effected this (Table 5.1); formation of a Ru(V) oxo complex followed by oxo-transfer from this to the substrate was suggested [762]. Kinetics of the oxidation of isatins to anthranilic acids by $RuCl_3$/bromamine-T/aq. HCl were studied [763]. The α-methoxylation of tertiary methylamines $R^1R^2NCH_3$ to α-methoxymethylamines $CH_3R^1R^2NCH_2OCH_3$ was effected by $RuCl_3$/aq. H_2O_2/CH_3OH; an Ru(V) intermediate may be involved [764]. Cyanation of tertiary amines $RNMe_2$ to the corresponding α-aminonitriles RNCH(CN)Me was catalysed by $RuCl_3$/Na(CN)/CH_3OH-AcOH/60°C (R=Ph, *m*-MeC_6H_4, *p*-MeC_6H_4, *p*-BrC_6H_4 or *p*-$PhOC_6H_4$). Thus *N,N*-dimethylaniline gave *N*-methyl-*N*-phenylaminoacetonitrile in 93% yield after 2 h (Fig. 5.3). Kinetics were measured; an iminium-ion Ru hydrido complex may be involved) [403]. An outline mechanism was proposed involving a Ru(V) mono-oxo intermediate (see also Fig. 1.13) for an analogous mechanism with TPAP oxidation of alcohols [101, 403]). Acetoxylation of β-lactams by $RuCl_3/O_2$/MeOH-MeCHO-EtOAc/40°C gave the corresponding 4–acyloxy-β-lactams (Fig. 5.8) [765, 766]. It was surmised that acetaldehyde reacts with O_2

under Ru catalysis to give peracetic acid which then gives an oxo-Ru(V) species [765]. Methylene groups adjacent to tertiary amines in N,C-protected short glycine-containing peptides were selectively oxidised at the C^{α} position of glycine by $RuCl_3/CH_3CO_3H$/AcOH-EtOAc. A Ru(V) oxo intermediate was proposed with a cytochrome P-450 type of mechanism [767]. The oxidation of the drug gabapentin (neurotin) to 1-(hydroxymethyl)cyclohexane acetic acid by $RuCl_3/[Ag^{III}\{IO(OH)_5\}_2]^{5-}$/water were studied; the active intermediate is probably $[Ru(OH)(H_2O)_5]^{2+}$ [768]. Both Et_2S and Bu_2^nS were oxidised by $RuCl_3/O_2$/EtOH/100°C to the sulfoxides and a little sulfone [769].

1.7.3 $RuBr_3$ and Halo-Aqua Complexes

$RuBr_3$ (no degree of hydration indicated) as $RuBr_3$/TBHP/C_6H_6 oxidised MeCH(OH)COOEt to Me(CO)C(O)OEt [695].

$[RuCl_3(OH)(H_2O)_4]^-$ may be the parent species active in the oxidation by $RuCl_3$/*N*-bromophthalimide/aq. $HClO_4$/35°C of glycine to CO_2 and HCN; $[RuCl_3(OBr)(OH)_2]^{3-}$ may be an intermediate [770].

$[RuCl_2(H_2O)_4]^+$ This species was made from $RuCl_3$ in HCl from pH 0.4–2.0. Kinetic studies suggest that in the epoxidation by $[RuCl_2(H_2O)_4]^+/O_2$/water-dioxane of cyclo-octene and -hexene; homolytic cleavage of the O-O bond plays an essential part [771, 772], and that this is so for similar oxidation of alkanes (e.g. of cyclohexane to cyclohexanol) [771].

1.7.4 Ru(III) Complexes with Chelating O-, N-Donors

Structures and reactivities of Ru complexes with EDTA have been reviewed [628].

$K[Ru(H_2O)(EDTA)]$, $Ru(H_2O)(EDTA.H)$ and **$K[RuCl(EDTA.H)]$** $K[Ru(H_2O)(EDTA)]$ is made in solution by reaction of $K_2[Ru(H_2O)Cl_5]$ and $EDTA.H_4$ or by aquation of $K[RuCl(EDTA.H)].2H_2O$, though there seems to be some uncertainty as to whether the species in solution is $[Ru(H_2O)(EDTA)]^-$, $[RuCl(EDTA.H)]^-$ or $Ru(H_2O)(EDTA.H)$. The complex $Ru(H_2O)(EDTA.H)$ is made by hydrolysis of $K[RuCl(EDTA.H)]$ and AgCl. The X-ray crystal of $Ru(H_2O)(EDTA.H)$ shows it to have an octahedral structure with the aqua ligand *trans* to one of the nitrogen ligands of EDTA (the Ru-O(H_2O) bond is quite long at 2.127(3) Å). The mean Ru – N distance is 2.08(1) Å) and the mean Ru – O(EDTA) distance is 2.03(1) Å. Thus the EDTA is pentadentate with one free carboxylate group (Fig. 1.34) [772].

These complexes, either as $[Ru(H_2O)(EDTA)]^-$, $Ru(H_2O)(EDTA.H)$ or even mixtures of $RuCl_3$ and $EDTA.H_4$, are ubiquitous oxidation catalysts, and a number of kinetic and mechanistic studies on a variety of oxidations with them as starting

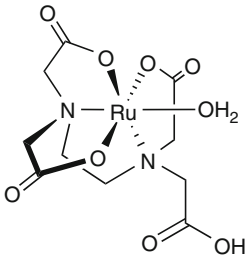

Fig. 1.34 Structure of $Ru(H_2O)(EDTA.H)$ [772]

materials have been reported, mainly in extensive work by Taqui Khan et al. Some of their results have been reviewed [771].

Most of the work reported with these complexes has been concerned with kinetic measurements and suggestions of possible mechanisms. The $[Ru(H_2O)(EDTA)]^-$/aq. H_2O_2/ascorbate/dioxane system was used for the oxidation of cyclohexanol to *cis*-1,3-cyclohexanediol and regarded as a model for peroxidase systems: kinetic data and rate laws were derived [773]. Kinetic data were recorded for the following systems: $[Ru(H_2O)(EDTA)]^-/O_2$/aq. ascorbate/dioxane/30°C (an analogue of the Udenfriend system; cyclohexanol oxidation) [731]; $[Ru(H_2O)(EDTA)]^-/O_2$/water (alkanes and epoxidation of cyclic alkenes – $[Ru^V(O)(EDTA)]^-$ may be involved) [774]; $[Ru(H_2O)(EDTA)]^-/O_2$/water-dioxane (epoxidation of styrenes – a metallo-oxetane intermediate was postulated) [775]; $[Ru(H_2O)(EDTA)]^-$/aq. H_2O_2/dioxane (ascorbic acid to dehydroascorbic acid and of cyclohexanol to cyclohexanone) [776]; $[RuCl(EDTA.H]^-/O_2$/water-dioxane/37–62°C (epoxidation of cyclo-octene) [777]; $[Ru(H_2O)(EDTA)]^-/(HSO_5)^-$/water (epoxidation of cyclohexene and cyclo-octene: $[Ru^V(O)(EDTA)]^-$ is probably involved) [631]; $[Ru(H_2O)(EDTA)]^-/O_2$/water @ pH 1.75 – 2.75/dioxane/35°C (adamantane oxidation with and without ascorbic acid) [731, 778]; $[Ru(H_2O)(EDTA)]^-/O_2$/water: $[Ru^V(O)(EDTA)]^-$ may be involved [774]; $[Ru(H_2O)(EDTA)]^-/O_2$/aq. cetyltrimethylammonium bromide/dioxane (cyclohexane) [779]; $[Ru(H_2O)(EDTA)]^-/O_2$/water/25–45°C (diethylamine, triethylamine) [780]; $[Ru(H_2O)(EDTA)]^-$/aq. Na(ClO) (PPh_3 to PPh_3O, may involve $[Ru^V(O)(EDTA)]^-$) [630]; $[Ru(H_2O)(EDTA)]^-$/(pyNO)/water/25–45°C (Me_2S to DMSO – intermediacy of a peroxo-Ru(IV) species $[Ru(O_2)(Me_2S)(EDTA)]^{2-}$ was proposed) [781, 782]; $[Ru(H_2O)(EDTA)]^-$/aq. Na(ClO) (PPh_3 to PPh_3O – $[Ru^V(O)(EDTA)]^-$ may be involved) [630]; while for $[Ru(H_2O)(EDTA)]^-/O_2$/water (PPh_3 to PPh_3O) a peroxo-Ru(IV) intermediate may participate [774]**.**

For **Ru(NO)(EDTA)** and other Ru nitrosyl complexes see Ru(II), [783].

Ru(hedta) and **Ru{$(CH_3)_2$edda}** ($hedta^{3-}$=*N*-hydroxyethylethylenediaminetriaceta te, $(CH_3)_2$edda=*N,N′*-dimethylethylenediamine-*N,N′*-diacetate) are made by reaction of $K_2[Ru(H_2O)Cl_5]$ with the ligands followed by aquation of the products. The system complex/aq. TBHP/CH_2Cl_2 epoxidised *cis* and *trans*-stilbenes; the *cis*-isomer is sparingly water-soluble and the oxidation was judged to be essentially heterogeneous. *Trans*-stilbene gave the *cis*-epoxide in high yield but no *trans* isomer, rationalised by the suggestion of the existence of an acyclic pathway which has both free radical and carbocation character, allowing for isomerisation of *cis*-stilbene to the *trans*-epoxide involving the intermediacy of $Ru^{III}(O)$(hedta) [784].

1.7.5 Ru(III) Complexes with N-Donors

Thermodynamic and theoretical investigations on (bpy) and (tpy) complexes have been reviewed [785].

$RuCl_3(CH_3CN)_3$ is made from $RuCl_3$ with H_2 and CH_3CN; it is brick-red. The X-ray crystal structure of $RuCl_3(CH_3CN)_3.4CH_3CN$ shows a *mer*-octahedral geometry. The electrochemistry of the complex was studied as were IR and mass spectra. As $RuCl_3(CH_3CN)_3$/aq. $Li(ClO_4)$/Pt electrodes it oxidised tetralin to tetralone [786]. .

$K[RuCl_2(H\text{-}dmg)_2]$ and **$K[RuCl_2(H\text{-}dpg)_2]$** (dmg and dpg=monoanions of dimethyl-glyoxime and diphenylglyoxime) are made from $K_2[Ru(H_2O)Cl_5]$ and the ligands. As [complex]/PhIO/water they epoxidised cyclohexene, probably via a $Ru^V(O)Cl(H\text{-}L)_2$ species [640].

$[RuCl_2(bpy)_2](PF_6)$ is made by reaction of *cis*-$RuCl_2(bpy)_2$ with $Na_2(S_2O_8)$; it is deep orange [787]. The X-ray crystal structure of *cis*-$[RuCl_2(bpy)_2]Cl$ has been reported (mean Ru-Cl 2.325(2) Å, mean Ru-N 2.05(1) Å), Cl-Ru-Cl angle 93.7(1)°) [788]. As $[RuCl_2(bpy)_2]^+$/TBHP/CH_2Cl_2 it oxidised primary alcohols to aldehydes, secondary alcohols to ketones, di-*tert*-butylcatechol to the *o*-benzoquinone and alkanes to ketones, e. g. ethylbenzene to acetophenone and fluorene to fluorenone [787].

$[Ru(H_2O)(bpy)(amp)]^+$ (H_2amp=*N*-(2-hydroxyphenyl)salicyldimine) is made from $RuCl_3$, the ligand and (bpy); electronic spectra were measured [789]. The reagent $[Ru(H_2O)(bpy)(amp)]^+$/TBHP/(BTBAC)/C_6H_6 oxidised benzene to phenol and benzoquinone, while phenol was oxidised to benzoquinone. The intermediate species is likely to be $[Ru^V(O)(bpy)(amp)]^+$ [789].

$RuCl(bpy)(amp).H_2O$ is made in similar fashion to $[Ru(H_2O)(bpy)(amp)]^+$; its magnetic moment μ_{eff} is 1.98 B.M. As RuCl(bpy)(amp)/TBHP/aq. ($PhCH_2\{N(CH_2)_3Me\}_3$)Cl/CH_2Cl_2 it epoxidised cyclohexene and *cis* and *trans*-stilbene [790].

$[Ru(acac)_2(bpy)](PF_6)$ and **$RuCl_2(bac)(bpy)$** (bac=benzoylacetone) are made by heating the ligands in water-methanol with $RuCl_3$(bpy). Infrared, TGA, cyclic voltammetric and conductivity data were measured; the magnetic moments μ_{eff} of the complexes were 1.92 and 1.87 B.M. The system $[Ru(acac)_2(bpy)]^+$ or $RuCl_2$(bac)(bpy)/TBHP/C_6H_6 catalysed the oxidation of primary alcohols to aldehydes, secondary alcohols to ketones, primary amines to nitriles and the alkanes diphenylmethane and fluorene to the carbonyls (Table 4.1) [791] .

RuCl(en)(DPA), RuCl(bpy)(DPA) and **RuCl(phen)(DPA)** (DPA=2,6-dipicolinic acid) are made by reaction of $RuCl_3$, the diamine and DPA in ethanol under reflux. The IR spectra and magnetic moments (μ_{eff} 1.84, 1.79 and 1.78 B.M. respectively) were measured. As RuCl(bpy)(DPA) and RuCl(phen)(DPA)/PhIO or TBHP/water-dioxane they epoxidised styrene and norbornene and oxidised cyclohexane to cyclohexanol and cyclohexanone. A Ru^V(O)Cl(diamine)(DPA) species may be involved [792].

$RuCl_3$(Hmpi) (Hmpi=1,3-bis(4-methyl-2-pyridylimino)isoindoline) is made from (Hmpi) and $RuCl_3$. As $RuCl_3$(Hmpi)/O_2/2,6-lutidine or Na(OEt)/25–90°C it oxidised ethanol, 1-propanol and 1-butanol to the aldehydes and 2-propanol and 2-butanol to the ketones. A Ru(IV) alkoxo complex may be formed (e.g. $Ru^{IV}Cl_2(mpi)(OC_2H_5)$), which then reacts with another mole of ethanol to give $Ru^{II}Cl_2(Hmpi)(C_2H_5OH)$ and CH_3CCHO [793].

$[Ru_2(OH)Cl(H_2O)_4(napy)_2](ClO_4)_4$ (napy=1, 8-naphthyridine) is made from $Ru_2(napy)_2Cl_4$ and $AgClO_4$ in acetone [794, 795]. The X-ray crystal structure shows the two Ru atoms to be bridged by the chloro and hydroxo ligands, with two bridging naphthyridine ligands (Fig. 1.35).

The system $[Ru_2(OH)Cl(H_2O)_4(napy)_2]^{4-}$/aq. $Na(BrO_3)$/Me_2CHCHO/DCE/60°C converted primary alcohols to aldehydes and acids and secondary alcohols to ketones, and *trans*-stilbene was epoxidised by $[Ru_2(OH)Cl(napy)_2(H_2O)_4]^{4-}$/$O_2$/$Me_2CHCHO$/water-DCE/40°C [794] and by $[Ru_2(OH)Cl(napy)_2(H_2O)_4]^{4-}$/aq. $Na(IO_4)$ or $Na(BrO_3)$/Me_2CHCHO/DCE/40°C [795].

K[$RuCl_2$(saloph)] (saloph=*bis*(salicylaldehyde)*o*-phenylenediamine) is made from $K_2[Ru(H_2O)Cl_5]$ and the ligand. As $[RuCl_2(saloph)]^-$/O_2/water-dioxane it oxidised cyclohexane and adamantane. The intermediacy of Ru(IV) and Ru(V) complexes was proposed [796].

$[Ru(H_2O)(bpy)(cpsd)]^+$, $Ru(H_2O)(pic)(bpy)(cppc)$ (cpsd, cppc=tridentate Schiff base dianions *N*-(2-carboxyphenyl)salicylaldiminate and *N*-2-carboxyphenylpyridine-2-carboxal-diminate; pic=picolinate) are made from the Schiff base ligand and $RuCl_3$ in base with (bpy) or with picolinic acid. They are paramagnetic (μ_{eff} 1.95 B.M.); electronic, IR and cyclic voltammetric data were obtained. As (complex)/TBHP/$(PhCH_2\{N(CH_2)_3Me\}_3)Cl/CH_2Cl_2$ they oxidised cyclohexene to a mixture of products and some alkanes to mixtures of alcohols and aldehyde; Na(ClO), $K(HSO_5)$ and pyNO were also used as co-oxidants. Kinetic data were obtained; Ru(V) oxo intermediates may be involved [797].

$RuCl(H_2O)(csb)_2$ (csb=chiral Schiff base derived from dehydroacetic acid and 1*S*,2*S*-(+)-cyclohexanediamine, 1*R*,2*R*(−)-1,2-diphenylethylenediamine and *S*-(+)1,2-diaminopropane) are made from $RuCl_3$ and the ligands; the IR, ^1H and ^{13}C

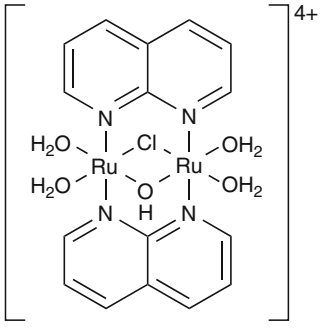

Fig. 1.35 Structure of the cation in $[Ru_2(OH)Cl(H_2O)_4(napy)_2](ClO_4)_4$ [795]

NMR spectra were measured. As $RuCl(H_2O)(csb)_2/O_2/Me_2CHCHO/CH_2Cl_2/4°C$ it asymmetrically epoxidised styrene and substituted styrenes with e.e. of up to 30% [798]. Complexes with (csb′=1*R*,2*R*(−)1,2-diaminocyclohexane with 3-acetyl-4-hydroxy-6-methyl-2-pyrone and salicylaldehyde, 5-chloro-5-methoxy, 5-methoxy and 5-nitrosalicyladehyde) asymmetrically epoxidised styrene as $RuCl(H_2O)(csb')_2$/PhIO/CH_3CN [799].

$[RuCl_2$(picphen)]Cl (picphen=*bis*(picolinaldehyde)-*o*-phenylenedi-imine) is made by condensation of picolinaldehyde and *o*-phenylenediamine) and the resulting Schiff base then treated with $RuCl_3$ in ethanol. Kinetics were followed of the oxidation of secondary alcohols (benzhydrol, 1-phenylethanol and α-tetralol) to the corresponding ketones by $[RuCl_2(picphen)]^+$/NMO or $Tl(OAc)_3$/water/30°C. The intermediacy of a Ru(V) oxo species was suggested [800].

$RuCl_2$(Hcbx)(cbx) (Hcbx=*N*-2′-chlorophenyl-2-pyridine-carboxamide). This red-brown material is made from the ligand and $RuCl_3$, and its X-ray crystal structure determined (Fig. 1.36). The system $RuCl_2(Hcbx)(cbx)/O_2$/*iso*butyraldehyde/DCE epoxidised a number of cyclic alkenes efficiently at room temperatures (Table 3.1). Addition of the radical trap 2,6-di-*tert*-butyl-4-methylphenol stopped epoxidation reactions altogether, suggesting that a mechanism involving radicals is involved [801].

$[Ru(CF_3COO)_2(H_2O)$(tmtacn)](CF_3COO) (tmtacn=1,4,7-trimethyl-1,4,7-triazacyclo-nonane, Fig. 1.30) is made from $RuCl_3$(tmtacn) with $Ag(CF_3COO)$, and its electronic spectrum was measured [802, 803]. The X-ray crystal structure shows a distorted octahedral geometry with two *cis* η^1-bound trifluoroacetato ligands; (tmtacn) coordinates facially to Ru [802]. As $[Ru(CF_3COO)_2(H_2O)(tmtacn)]^+$/TBHP/DCE it oxidised primary alcohols to aldehydes and secondary alcohols to ketones. Kinetic studies on oxidation of benzyl alcohol were made and a radical mechanism suggested in preference to one involving oxo-Ru intermediates [804]. Immobilised on silica gel as $[Ru(CF_3COO)_2(H_2O)(tmtacn)]^+/SiO_2$/TBHP/DCE-$CH_2Cl_2$ it oxidised alcohols and epoxidised alkenes [802], while $[Ru(CF_3COO)_2(H_2O)(tmtacn)]^+$/TBHP/$CH_2Cl_2$ epoxidised cyclic alkenes (Table 3.1). A heterolytic O–O cleavage mechanism was suggested involving an alkylperoxo-Ru(VI) intermediate [803]. The same reagent oxidised several anisoles to *p*- benzoquinone monoketals – thus 2-methoxyanisole gave 3,4-dimethoxy-4-*tert*-butoxy-2,5-cyclohexadienone (Fig. 3.24) [805].

$[RuCl_2$(tpa)](ClO_4) (tpa=tris(2-pyridylmethyl)amine) is made from the tripodal (tpa) ligand with $K_2[Ru(H_2O)Cl_5]$ and $Na(ClO_4)$; the X-ray crystal structure of the complex shows the two chloro ligands to occupy *cis* positions in a distorted

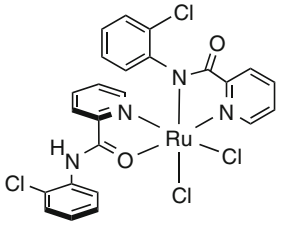

Fig. 1.36 Structure of the carboxamide epoxidation catalyst $RuCl_2(Hcbx)(cbx)$ [801]

octahedron around the metal. As $[RuCl_2(tpa)]^+$/MCPBA/CH_3CN it oxidised cyclohexane, while adamantane gave 1- and 2-adamantanol and adamantanone. An oxo-Ru(V) intermediate may be involved [806].

1.7.6 Ru(III) Complexes with -P, -As, -Sb and -S Donors

For polyoxometalate complexes containing phosphorus, e.g. $[Ru\{PW_{11}(H_2O)(O)_{39}\}]^{4-}$, *cf.* 1.7.1**.**

$RuCl_2(acac)(PPh_3)_2$ is made by reaction of $RuCl_2(PPh_3)_3$ with acetylacetone. It is green: IR, electronic spectra and cyclic voltammetric data were measured. The system $RuCl_2(acac)(PPh_3)_2$/NMO/CH_2Cl_2 oxidised primary alcohols (benzyl, cinnamyl) to aldehydes and secondary alcohols (cyclohexanol, benzhydrol, benzoin) to ketones [807].

$RuCl_2(AsPh_3)_2(lq)$ (lq=lawsone, i.e. 2-hydroxyl-1,4-naphthoquinone) [808] and 8-hydroxyquinoline [809]) are made from $RuCl_3(AsPh_3)_2(CH_3OH)$ and the ligand. As $RuCl_2(AsPh_3)_2(lq)$/NMO/CH_2Cl_2 they oxidised primary alcohols to aldehydes and secondary alcohols to ketones [808, 809].

$RuCl_2(PPh_3)_2(am)$ (am=one of twelve co-ordinated amides, e.g. 2-(anilinocarbonyl)benzoic acid) complexes are made from the ligand and $RuCl_2(PPh_3)_3$. As $RuCl_2(PPh_3)_2(am)$/aq. H_2O_2 they oxidised a primary alcohol group to an aldehyde in the drug pyridoxine, and a primary and secondary alcohol group to aldehyde and ketone respectively in the drug albuterol [810].

$RuX(EPh_3)(bSB)_2$ (X=Cl or Br; E=P or As; bSB=bidentate Schiff bases derived from 1-methyl-1-mesityl-3-(2-chloro-1-oxoethyl)cyclobutane and 1-(2-hydroxybenzylidene-thiosemi-carbazide or 1-(2-hydroxy-5-bromobenzylidene)thiosemicarbazide). The pale yellow or green complexes are made from $RuX_3(EPh_3)_3$ with the ligands; IR, electronic and ESR spectra with cyclic voltammetric and TGA data were measured. As $RuX(EPh_3)(bSB)_2$/NMO/C_2H_5OH-CH_2Cl_2 they oxidised benzyl and cinnamyl alcohols to the aldehydes and cyclohexanol to cyclohexanone [811].

$RuBr(PPh_3)(OEP)$ is made from $Ru(PPh_3)_2(OEP)$ and Br_2. As $RuBr(PPh_3)(OEP)$/PhIO/CH_2Cl_2 it epoxidised styrene, norbornene and *cis*-stilbene to their epoxides, but *trans*-stilbene was not oxidised [588]. The reagent $RuBr(PPh_3)(OEP)$/PhIO/CH_2Cl_2 oxidised cyclohexane and cyclohexene to a mixture of products [812].

$Ru(OH)(PPh_3)(salen)$ is made from $Ru(NO)Cl_3(PPh_3)_2$, (salen=*N,N′*-ethan-1,2-bis-(salicyliden-amine) and ethyldi-*iso*propylamine in EtOH. As $Ru(OH)(PPh_3)$(salen)/O_2/CH_2Cl_2 or $CHCl_3$ it preferentially oxidised primary alcohols to aldehydes while 1-phenyl-1,*n* diols (*n* = 2 to 5) were oxidised by $Ru(PPh_3)(OH)(salen)$/O_2/$CHCl_3$ to lactols or the *n*-hydroxyaldehyde [813].

$RuX_2(EPh_3)(tSB)$ (X=Cl, Br; E=P, As; tSB=tridentate Schiff base made from antipyrine and salicylaldehyde, *o*-vanillin, *o*-phenylenediamine) are made from the

ligands and $RuCl_3$. Magnetic, ESR, NMR, IR and electronic spectral data were recorded. The reagent $RuX_2(EPh_3)(tSB)/O_2/CH_2Cl_2$ oxidised primary and secondary alcohols to aldehydes and ketones [814].

$RuBr_2(AsPh_3)_2(HPhb)$ and **$RuBr_2(AsPh_3)_2(Hdhb)$** (HPhb or Hdhb=mono-anions of Schiff bases formed by condensation of 2,3-dihydroxybenzaldehyde and aniline or its *o*-or *p*-substituted derivatives) are made from $RuBr_3(AsPh_3)_2(CH_3OH)$ and the ligand; they are paramagnetic with magnetic moments μ_{eff} near 2.2 B.M. As $RuBr_2(AsPh_3)_2$(HPhb) or $RuBr_2(AsPh_3)_2$(Hdhb)/NMO/CH_2Cl_2 they oxidised primary alcohols to aldehydes, secondary alcohols to ketones and 3, 5-di(*tert*-butyl) catechol) to the corresponding *o*-benzoquinone [815].

$[RuCl_2(dppe](BF_4)$ and **$[RuCl_2(dppp)](BF_4)$** (dppe=1,2-(diphenylphosphino)ethane, dppp=1,2-(diphenylphosphino)propane) are made from $RuCl_3$ and the ligands in the presence of $(NO)BF_4$. The system $[RuCl_2(dppe]^+$, $[RuCl_2(dppp)]^+$/PhIO or $K(HSO_5)$/(BDTAC)/CH_2Cl_2 oxidised adamantane, cyclo-octane and cyclohexane to alcohols and ketones. The same results were obtained with $[RuCl(dppp)_2]^+$ as catalyst [816].

***mer*-$RuCl_3(dmso)_2(MePhSMe)$** and ***mer*-$RuCl_3((dmso)(MePhSMe)_2$** are made from *mer*-$RuCl_3(dmso)_3$ and methyl-*p*-tolylsulfide. As (complex)/O_2(7 atm)/CH_3OH/80°C they oxidised methyl-*p*-tolylsulfide to the sulfoxide, being slightly more efficient in this respect than *cis*- or *trans*-$RuCl_2(dmso)_4$. The reaction was also catalysed by $K_2[Ru(H_2O)Cl_5]$ [817].

1.8 Ru(II–III) Complexes

$Ru_2(OAc)_4Cl$ The reagent $Ru_2(OAc)_4Cl/O_2$/toluene/50°C oxidised secondary amines $R^1CH_2NHR^2$ to imines $R^1CH{=}NR^2$ and converted 1,2,3,4-tetrahydroisoquinoline to 3,4-dihydroisoquinoline and isoquinoline. The system is far superior to other catalysts such as RuO_2, $RuCl_3$, and $RuCl_2(PPh_3)_3$ (Table 5.1). The amines may coordinate to $Ru_2(OAc)_4Cl$ giving a complex from which β-hydride elimination occurs; insertion of O_2 gives a hydroperoxide which, with secondary amines, gives the imine, H_2O_2 and the starting complex [818].

$Ru_2(\mu\text{-}OAc)_3(\mu\text{-}CO_3)$ The reagent $Ru_2(OAc)_3(CO_3)/O_2$/water-toluene/80°C oxidised a number of primary alcohols to aldehydes and secondary alcohols to ketones; formation of an alkoxyruthenium complex followed by β-hydride elimination was suggested. The reactions were also catalysed by $[Ru_2(\mu\text{-}OAc)_4](OAc)$ [819].

1.9 Ru(II) Complexes

Many Ru(II) complexes function as oxidation catalysts, particularly effective being $RuCl_2(PPh_3)_3$ and *cis*-$RuCl_2(dmso)_4$. In most cases the nature of the active intermediate is not known, but oxo-Ru(IV) species are likely to be involved in many cases.

1.9.1 Ru(II) Complexes with O- and N-Donors

$Ru_2(OAc)_2(py)_4$ is made as orange crystals from $Ru_3(O)(OCOR)_6(py)_3$ and Zn; the single-crystal X-ray structure was reported. As $Ru_2(OAc)_2(py)_4$/Zn/O_2/(py)/AcOH it oxidised cyclohexane to cyclohexanol and cyclohexanone in low yield [820].

$[Ru(C_7F_{15}C(O)CH_2C(O)C_7F_{15})_3]^-$, a substituted (acac) complex, is made from the 1,3-diketone $C_7F_{15}COCH_2COC_7F_{15}$ with $RuCl_3$ (quoted as 'RuCl$_2$' in the paper) in ethanol with K(HCO_3). In biphasic solvents $[Ru(C_7F_{15}C(O)CH_2C(O)C_7F_{15})_3]^-$/perfluorodecalin-toluene/O_2 (1 atm)/65°C oxidised aldehydes to ketones, disubstituted alkenes (cyclo-octene, norbornene) to epoxides and sulfides to sulfoxides or sulfones [821, 822].

$K_5[Ru(H_2O)\{PW_{11}(O)_{39}\}].15H_2O$ is made from $K_7[Ru\{PW_{11}(O)_{39}\}].15H_2O$ and *cis*-$RuCl_2(dmso)_4$ The system $[Ru(H_2O)\{PW_{11}(O)_{39}\}]^{5-}$/aq. Na(ClO) or TBHP/$CH_2Cl_2$ oxidised cyclic alkanes to alcohols (also effected by *cis*-$RuCl_2(dmso)_4$); reaction rates were measured [823]. The reagent $[Ru(H_2O)\{PW_{11}(O)_{39}\}]^{5-}$/aq. Oxone®/$CH_2Cl_2$ catalysed the oxidative fission of the benzyl ring in alkylbenzenes (ethylbenzene, benzaldehyde, benzoic acid, benzonitrile, benzyl chloride and bromide), the rings giving CO_2 and water; $RuCl_3$, *cis*-$RuCl_2(dmso)_4$, $RuCl_2(PPh_3)_3$, and $[RuCl(dpp)_2](PF_6)$ were also effective [746]. An unformulated species which may contain $[Ru^{II}(H_2O)\{PW_{11}(O)_{39}\}]^{5-}$ made from $H_3\{PW_{11}O_{40}\}.nH_2O$, $RuCl_3$ and HCl with O_2 at 80°C for styrene and 50°C for other cyclic alkenes gave a mixture of aldehydes and epoxide [824].

$[Ru\{PW_{11}(O)_{39}\}(dmso)]^{5-}$ is made from $K_7[\{PW_{11}O_{39}\}]$ with aqueous *cis*-$RuCl_2(dmso)_4$ under microwave irradiation; IR, ^{183}W and ^{99}Ru NMR spectra were recorded. With $[Ru\{PW_{11}(O)_{39}\}(dmso)]^{5-}$/aq. Na($IO_4$) cyclo-octene gave suberic acid, while with $[Ru\{PW_{11}(O)_{39}\}(dmso)]^{5-}$/aq. Oxone®/^{n}Bu($HSO_4$)/DCE/50°C adamantane gave 1-adamantanol and 1-chloroadamantane as the main products [825]. No information was given on the nature of the effective catalyst – it is likely that some RuO_4 at least would have been generated.

Ru(NO)Cl(salen^{chir}) is made by reaction of $Ru(NO)Cl_3.nH_2O$ with (salen^{chir}), the latter made by condensation of (R)-3-formyl-2-hydroxy-2′-phenyl-1,1′-binaphthyl with (1*S* ,2*S)*-1,2-diamino-cyclohexane. The X-ray crystal structure of the acetonitrile adduct shows the Ru-N-O unit to be essentially linear (Ru-N 1.862(6)Å, N-O 0.971(8) Å, with the Ru-N-O angle at 176.0(9)°), so that the nitrosyl ligand may be regarded as NO^+ and the formal oxidation state of the Ru as (II) [826].

Primary alcohols were oxidised to aldehydes and (less readily) secondary alcohols to ketones by Ru(NO)Cl(salen^{chir})/O_2//UV (incandescent or halogen lamp). In competitive experiments between 1- and 2-decanol or benzyl alcohols only the primary alcohol was oxidised [827]. With Ru(NO)Cl(salen^{chir})/(Cl_2pyNO) or TMPNO or O_2/C_6H_6/UV (TMPNO=tetra-methylpyridine-*N,N*′-oxide) racemic secondary alcohols were asymmetrically oxidised to ketones [828]. A Ru(NO)(salen^{chir}) complex was used as Ru(NO)Cl(salen^{chir})/O_2/UV/C_6H_5Cl to oxidise racemic secondary alcohols to the ketones; in the presence of 1,3-bis(*p*-bromophenyl)propane-1,3-dione e.e. of 55–99% were achieved [829]. Chiral Ru(NO)Cl(salen^{chir}) complexes were made

from $RuCl_3(NO)(PPh_3)_2$ with (1*S*,2*S*)-1,2-dimethyl-1,2-cyclohexanediammonium dimandelate and (a*S*)-3-formyl-2-hydroxy-2′-(4-biphenyl)-1,1′-binaphthyl. As the system $Ru(NO)Cl(salen^{chir})/O_2/CHCl_3$/UV it oxidatively desymmetrized *meso*-diols giving optically active lactols and lactones. Kinetic isotope effects were studied and a catalytic cycle for the process proposed [830].

The system $Ru(NO)Cl(salen^{chir})$/TMPZNO/dioxane/UV (TMPZNO=tetramethylpyrazine-*N,N′* dioxide, UV= halogen or incandescent lamp) epoxidised conjugated alkenes (Table 3.1). Good yields were obtained of epoxides with high e.e. values (80–97%) and the reactions were highly stereospecific, *cis*- and *trans*-alkenes giving *cis*- and *trans*- epoxides. An oxo-Ru complex is probably involved [826]. Asymmetric epoxidation of conjugated alkenes were done in sunlight through a window or in incandescent light with $Ru(NO)Cl(salen^{chir})/(Cl_2pyNO)$/UV or O_2/CH_2Cl_2//UV/4°C; e.e. values of up to 98% were obtained in some cases [831].

Ru(NO)(EDTA) is made from K[RuCl(EDTA.H)] and NOCl, and was characterised by IR, ESR and electronic spectroscopy. The system $Ru(NO)(EDTA)/O_2$ or PhIO/aq. EtOH oxidised 1-hexene to 2-hexanone and epoxidised cyclohexene; kinetic data were measured and ^{18}O-substitution shows that the oxygen atom in the products derives from the $^{18}O_2$ [783].

***Cis*-$RuCl_2(bpy)_2$** is not a versatile catalyst in its own right but is a useful starting material for other Ru (bpy) complexes, many of which are good catalysts. It is made by reaction of $RuCl_3$, LiCl and (bpy) in ethanol [788], or from $RuCl_3$, LiCl, (bpy), glucose and ascorbic acid in ethylene glycol [832]. Its X-ray crystal structure shows the *cis* arrangement of chloro ligands (mean Ru-Cl 2.426(1) Å), mean Ru-N 2.01(1) Å), Cl-Ru-Cl angle 89.16(13)° [788]. The system *cis*-$RuCl_2(bpy)_2$/aq. H_2O_2/^{t}BuOH or 1,2-dimethoxyethane stereospecifically epoxidised oleic acid to 9, 10-epoxyoctadecanoic acid, possibly via an oxo-Ru(IV) species [833], and *cis*-$RuCl_2(bpy)_2$/aq. $Na(IO_4)/CH_2Cl_2$/2°C epoxidised several alkenes, though not as effectively as did *trans*-$Ru(O)_2(bpy)\{IO_3(OH)_3\}$/aq. $Na(IO_4)/CH_2Cl_2$/2°C [567].

***Trans*-$[Ru(H_2O)_2(bpy)_2](PF_6)_2.H_2O$** is made from $RuCl_2(bpy)_2$ and $NH_4(PF_6)$ in water. With aq. $Na(IO_4)/CH_2Cl_2$/2°C it epoxidised a variety of alkenes to much the same extent as did *trans*-$Ru(O)_2(bpy)\{IO_3(OH)_3\}$/aq. $Na(IO_4)/CH_2Cl_2$/2°C, and as *trans*-$[Ru(H_2O)_2(bpy)_2]^{2+}$/TBHP/ water-C_6H_6 it oxidised linear (pentane, hexane, heptane, octane) and cyclic alkanes (adamantane, cyclo-pentane, -hexane, -heptane, -octane) to alcohols, aldehydes or ketones [567].

***Cis*-$RuCl_2(phen)_2$** is made as black crystals by reaction of $RuCl_3$ with (phen). As *cis*-$RuCl_2(phen)_2$/aq. H_2O_2/^{t}BuOH or 1,2-dimethoxyethane it stereospecifically epoxidised oleic acid to 9, 10-epoxyoctadecanoic acid [833] The reagent *cis*-$RuCl_2(phen)_2$/aq. $Li(ClO)/CH_2Cl_2$ oxidised dipropylether to propylpropionate, tetrahydropyran to δ-valerolactone, adamantane to adamantan-1-ol and adamantanone, and octan-2-ol to octan-2-one [834].

***Cis*-$[Ru(H_2O)(py)(bpy)_2](ClO4)_2$,** as *cis*-$[Ru(H_2O)(py)(bpy)_2]^{2+}$/aq. $Na(ClO)/(BDTAC)/CH_2Cl_2$ oxidised benzyl alcohol to benzaldehyde. Comparative rate studies were made; an oxo-Ru(IV) complex is probably involved [835].

***Cis*-[Ru(H$_2$O)$_2$(Cl$_2$bpy)$_2$]$^{2+}$** is made from $RuCl_3$ with the ligand and silver toluene-*p*-sulfonate; with $(NH_4)_2[Ce(NO_3)_6]$ it gives *cis*-$[Ru(O)_2(Cl_2bpy)_2]^{2+}$. As *cis*-$[Ru(H_2O)_2(Cl_2bpy)_2]^{2+}$/$CF_3COOH$/Pt electrodes it oxidised methanol, ethanol and 2-propanol to formaldehyde, acetaldehyde and acetone respectively, while cyclobutanol gave cyclobutanone and THF gave γ-butyrolactone. The complex was incorporated into Nafion coatings on electrode surfaces for oxidations [565]. The system *cis*-$[Ru(H_2O)_2(Cl_2bpy)_2]^{2+}$/TBHP/acetone oxidised cyclohexane, hexane and heptane to a mixture of the alcohols and ketones [836], while *cis*-$[Ru(H_2O)_2(Cl_2bpy)_2]^{2+}$/$CF_3COOH$/glassy carbon electrode oxidised methanol and ethanol to the aldehydes and 2-propanol and cyclobutanol to the ketones [565].

[Ru(acac)(bpy)$_2$](PF$_6$) is made from $RuCl_2(bpy)_2$, acetylacetone and $(NH_4)PF_6$. It is dark brown; IR and electronic spectra, TGA and cyclic voltammetry were measured. As $[Ru(acac)(bpy)_2]^+$/TBHP/CH_2Cl_2 it oxidised primary alcohols to aldehydes, secondary alcohols to ketones, di-tert-butylcatechol to the *o*-benzoquinone and alkanes to ketones, e. g. ethylbenzene was converted to acetophenone and fluorene to fluorenone [787].

***Cis*-[Ru(H$_2$O)$_2$(dmp)$_2$](PF$_6$)$_2$** and ***cis*-[Ru(CH$_3$CN)$_2$(dmp)$_2$](PF$_6$)$_2$** (dmp=2,9-dimethyl-1,10-phenanthroline). These sterically-hindered complexes are made from *cis*-$RuCl_2(dmp)_2$ with water or CH_3CN and $H(PF_6)$, and are red-brown and orange respectively [570]. The system *cis*-$[Ru(H_2O)_2(dmp)_2]^{2+}$/aq. H_2O_2/CH_3CN/55°C oxidised primary allylic alcohols to aldehydes [837], while *cis*-$[Ru(H_2O)_2(dmp)_2]^{2+}$/aq. H_2O_2/CH_3CN epoxidised alkenes; the pH dependence of peroxide activation by *cis*-$[Ru(H_2O)_2(dmp)_2]^{2+}$ was studied [838]. The reagent *cis*-$[Ru(H_2O)_2(dmp)_2]^{2+}$/aq. H_2O_2/CH_3CN/55°C oxidised alkenes and dienes to aldehydes or ketones (Table 3.3) [837], and the same system at 75°C hydroxylated alkanes. Radical intermediates and formation of high-oxidation state Ru oxo complexes was invoked [570].

***Cis*-[Ru(H$_2$O)(^{t}Bupy)(bpy)$_2$]ClO$_4$)$_2$** (^{t}Bupy=*p*-^{t}butylpyridine) as *cis*-$[Ru(H_2O)(^tBupy)(bpy)]^{2+}$/aq. Na(ClO)/(BDTAC)/$CH_2Cl_2$ oxidised benzyl alcohol to benzaldehyde, probably via *cis*-$[Ru^{IV}(O)(^tBupy)(bpy)]^{2+}$ [835].

[Ru(H$_2$O)(bpy)(tpy)]$^{2+}$ and **[Ru(H$_2$O)(phen)(tpy)]$^{2+}$** were used as electro-oxidants for conversion of primary and secondary alcohols to aldehydes and ketones, and for diols (as were *cis*- and *trans*-$[Ru(H_2O)_2(bpy)_2]^{2+}$ and $[Ru(H_2O)(py)(bpy)_2]^{2+}$) as [complex]/water @ pH 1-6.8/Pt electrodes [839].

[Ru(NH$_3$)(sq)(tpy)](ClO$_4$) (the ligand sq=3,5-di-*tert*-1,2-benzosemiquinone) is made from Ru(OAc)(sq)(tpy) with $HClO_4$ and then ammonia in THF. Cyclic voltammetry of oxidation to $[Ru(sq))NH_3)(tpy)]^{2+}$ was measured as were their electronic spectra; $[Ru(NH_3)(sq)(tpy)]^{n+}$ (n=1, 2)/water/carbon-Pt electrodes oxidised 2-propanol to acetone [840].

RuCl$_2$(pap)$_2$ (pap=2(phenylazo)pyridine; the α, β and γ isomers were used) is made from $RuCl_3$ and the ligand. As $RuCl_2(pap)_2$/aq. $Na(IO_4)$/CH_2Cl_2 the complexes epoxidised *trans*-stilbene to the oxide with benzaldehyde as the sole side-product. The *cis*-β and *trans*-γ isomers of the complex gave the best yields, while the most stable isomer, the *cis*-α, was less effective [841].

Ru(tpy)(pydic), Ru(R_2-pybox)(pydic), Ru(R_2-pyboxazine)(pydic) (pydic=pyridine-2,6-dicarb-xylate; R_2-pybox=*N,N,N,N*-pyridine-2.6-bisoxazolines – chiral bis(oxazolinyl)-pyridines with R=Pr^i, Ph; R_2-pyboxazine=*N,N,N,N*-pyridine-2,6-bisoxazines), made from $[Ru(p\text{-cymene})Cl_2]_2$ and the ligands; Ru(tpy)(pydic) is dark violet and most of the others are green (Fig. 1.37) [842, 843]. The X-ray crystal structures of four of these were determined: [2,6-bis-[(4*R*,5*S*)-4,5-diphenyl-4,5-dihydro-oxazol-2-yl]pyridine](pyridine-2,6-dicarboxylate)-Ru (Fig. 1.37 (a); and its (4*R*,5*R*) analogue; [2,6-bis-(4*S*)-4-*iso*propyl-4,5-dihydro-oxazol-2-yl]-pyridine](pyridine-2,6-dicarboxylate-Ru and [2,6-bis-[(4*S*)-4-phenyl-5,6-dihydro-4*H*-[1,3]-oxazinyl]pyridine](pyridine-2,6-dicarb-oxylate)-Ru (Fig. 1.37 (b)). Electronic and ^{1}H NMR spectra were recorded [844].

The Ru(tpy)(pydic)/PhI$(OAc)_2$/CH_2Cl_2 system epoxidised *trans*-stilbene; TBHP or O_2 were also used as co-oxidants. Asymmetric epoxidations of *trans*-stilbene were similarly achieved by Ru(R_2-pybox)(pydic)(/PhI$(OAc)_2$/toluene with e.e. values from 40% to 80% [842, 843, 845]. The reagents Ru(pybox)(pydic) or Ru(R_2-pyboxazine)(pydic)/aq. H_2O_2/^{t}AmOH epoxidised mono-, 1,1-di-, *cis* and *trans*-1,2-di, tri- and tetra-substituted alkenes with a variety of functional groups with high yields and e.e. For the latter system kinetics and kinetic isotope effects were measured, and DFT calculations suggested that *N*-oxide intermediates were involved rather than the oxo-Ru intermediates often invoked for porphyrin-catalysed epoxidations [846]. The reagent Ru(pydic)(R_2-pybox)/TBHP/^{t}BuOH or ^{t}AmOH effected the asymmetric epoxidation of *trans*-stilbene: particularly effective was Ru(*S*,S-Ph_2-pybox)(pydic), both for yields and e.e. values [847].

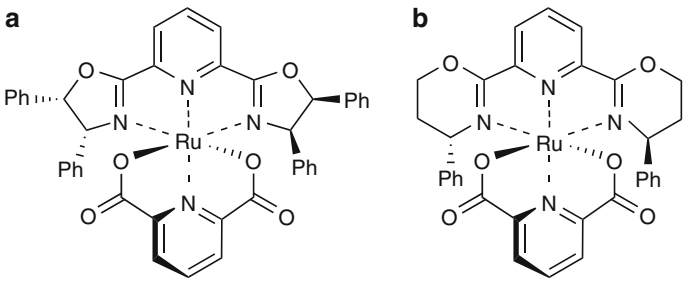

Fig. 1.37 Structure of complexes of (**a**) Ru(pydic)(Ph_2-pybox) and (**b**) Ru(pydic)(Ph_2-pyboxazine) [844]

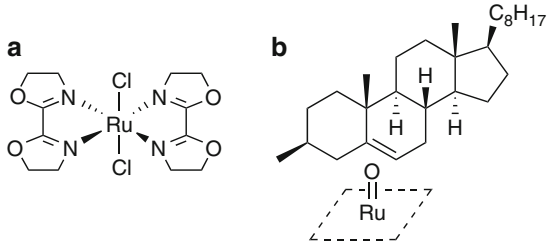

Fig. 1.38 Structure of $RuCl_2(biox)_2$ (**a**) and its reaction with cholesteryl substrates (**b**) [851]

$RuX_2(R_2$-pybox)(C_2H_4) is made from R_2-pybox (Fig. 1.37b) and $[RuX_2(p\text{-cymene})]_2$ with ethylene; in these Ph is replaced by R=^{i}Pr with X=Cl, or R=Ph with X=Br. The system $RuX_2(R_2$-pybox$)(C_2H_4)$/PhI$(OAc)_2$/MgO/CH_2Cl_2 oxidised sulfamate esters to cyclic imines [848].

***Fac*-[Ru(H_2O)(dpzp)(tppm)]$(PF_6)_2$**(dpzp=di(pyrazol-1-yl)propane;tppm=tris(pyrid-2-yl)methoxymethane). This complex of a 'heteroscorpionate' ligand is made from $RuCl_3$ and (tppm) giving $RuCl_3$(tppm), which was then treated with (dpzp), NEt_3 and $(PF_6)^-$. Its X-ray crystal structure was determined. As *fac*-$[Ru(H_2O)(dpzp)(tppm)]^{2+}$/$O_2$/*o*-$C_6H_4Cl_2$ it oxidised methyl-*p*-tolyl sulfide to the sulfoxide. The nature of the ligands has a profound effect on the reaction rate of oxidation of the substrate; $[Ru^{IV}(O)(dpzp)(tppm)]^{2+}$ is probably an intermediate [849].

[Ru(N4py)]Cl and **Ru(Me_2SO)(N2pyo)** (N4py=*N, N-bis*(pyridylmethyl)-*N*-(bis-2-pyridyl-methyl)amine, N2pyo=*N, N-bis*(pyridylmethyl)-aminomalonate) are made from *cis*-$RuCl_2(dmso)_4$ and the pentadentate ligands. As $[Ru(N4py)]^+$ or Ru(N2pyo)(Me_2SO)/MCPBA or Cl_2pyNO/CH_2Cl_2 they oxidised adamantane to adamant-1-ol [850].

$RuCl_2$(biox)$_2$ (biox=4,4′,5,5′-tetrahydro-2,2′-bioxazole; (**a**) in Fig. 1.38) is made as a red material by reaction of $RuCl_2(CH_3CN)_4$ and the ligand. Infrared, ^{1}H and ^{13}C NMR spectra were measured [851, 852].

Several simple alkenes were epoxidised by $RuCl_2(biox)_2$/O_2/Me_2CHCHO/aq. Na(HCO_3)/CH_2Cl_2, and it effected the β-stereoselective and regioselective epoxidation of cholesteryl acetate, pivalate, benzoate and caproate and other Δ^5-unsaturated steroids (Table 3.1) [852]. The selectivity may arise from steric hindrance of the β-face by axial methyl groups at C-10 and C-11: the Ru=(O) moiety (presupposing that the active intermediate is a Ru(IV) oxo complex) approaching the alkene in a perpendicular fashion as required for such a reaction ((**b**) in Fig. 1.38) [851, 852]. The system $RuCl_2(biox)_2$/aq. Na(IO_4)/CH_2Cl_2/reflux oxidised the carbinols $ArCH(OH)CF_3$ to ketones $ArCOCF_3$ [853].

[RuCl(tpa)]$_2$$(ClO_4)_2$ (tpa=tris(pyridylmethyl)amine or 5-Me_3tpa=tris(5-methyl-2-pyridyl)-amine) is made from $RuCl_3$ and the ligands with NEt_3. The X-ray crystal structure of the second complex as the $(PF_6)^-$ salt showed that the cation has bridging chloro ligands [854]. Cyclohexene and norbornene were epoxidised in low yields by $[RuCl(tpa)]_2^{2+}$/O_2/CH_3CN. In the oxidation of alkanes by $[RuCl(tpa)]_2^{2+}$/TBHP or CHP/CH_3CN/40°C cyclohexane gave cyclohexanol, cyclohexanone and 1-chlorocyclohexane, while adamantane gave adamant-1-ol, adamant-2-ol and adamantanone. Spin-trapping ESR experiments using 2,6-di-*tert*-butyl-4-methylphenol stopped the oxidations, suggesting involvement of free radical reactions [854, 855].

[Ru(H_2O)(bpy)(app)]Cl_2 (H_2app=*N*-(hydroxyphenyl)pyridine-2-carboxaldimine) is made by reaction of $RuCl_3$ with 2-aminophenol and 2-pyridine carboxaldehyde under reflux followed by addition of (bpy). Infrared and electronic spectra were measured, and the room-temperature magnetic moment is 1.98 B.M. The system $[Ru(H_2O)(bpy)(app)]^{2+}$/TBHP/(BTBAC)/$CH_2Cl_2$ (BTBAC=benzyltributylammonium chloride) oxidised benzyl alcohol to benzaldehde and alkenes to mixtures (e. g. *cis*- and *trans*-stilbene to benzaldehyde and *cis*- and *trans*-stilbene oxides). Alkanes gave mixtures

too: cyclohexane gave cyclohexanol and cyclohexanone, toluene yielded benzyl alcohol and benzaldehyde, and THF gave γ-butyrolactone. A Ru(V) oxo intermediate may be involved [856].

$RuCl_2$(pydim) (pydim=2,6-bis[1-(R-phenylimino)ethyl]pyridine; R=4-Me, 4-MeO, 4-^{t}Bu, 2,4-Me_2, 2,6-Me_2, 3,5-Me_2) are made from $[RuCl_2(p\text{-cymene})]_2$ and the tridentate ligand in refluxing ethanol. Acetonitrile gave $RuCl_2$(pydim)(CH_3CN), the X-ray crystal structure of which with R= 4-MeO showed distorted octahedral coordination with *trans*-chloro ligands. The ^{1}H and ^{13}C NMR spectra of all seven complexes were measured. The system $RuCl_2$(pydim)/PhIO/DCE/70°C epoxidised cyclohexene [857].

$RuCl_2(H_2O)_2$(dmnapy), $RuCl_2(H_2O)_2$(dcnapy) and **$RuCl_2(H_2O)_2$(danapy)**(dmnapy=2,7-dimethoxy-1,8-naphthyridine, dcnapy=2,7-dichloro-1,8-naphthyridine, danapy=2,7-di(phenyl-azo)-1,8-naphthyridine. For the structure of the analogous $[Ru_2(OH)Cl(napy)_2(H_2O)_4](ClO_4)_4$ see Fig. 1.35. The systems $RuCl_2(H_2O)_2$(dmnapy), $RuCl_2(H_2O)_2$(dcnapy) or $RuCl_2(H_2O)_2$(danapy)/aq. Na(BrO_3) oxidised cyclohexanol to cyclohexanone and *n*-butanol to a mixture; as (complex)/O_2/Me_2CHCHO/40°C it slowly epoxidised *trans*-stilbene [794].

$[Ru(H_2O)_2(azpy)_2]^{2+}$(azpy=2(phenylazo)pyridine). The reagent $[Ru(H_2O)_2(azpy)_2]^{2+}$/Na($BrO_3$)/aq. 0.2M phosphate buffer/60°C oxidised carbohydrates; thus 1-decyl-β-D-maltoside at the C_6-primary hydroxy function gave a carboxylic group, and the decyl chain was split from the maltose unit [858, 859].

1.9.2 Ru(II) Complexes with Porphyrin, Phthalocyanine and Macrocyclic Donors

Oxidations with Ru porphyrin complexes, both catalytic and stoicheiometric, have been reviewed [42, 45, 46], as has the use of optically active Ru porphyrin complexes in asymmetric catalysis [44, 63].

Ru(CO)(TMP) and **Ru(CO)(TPP)** are made from the porphyrins and $Ru_3(CO)_{12}$ [578]. The X-ray crystal structure of *trans*-Ru(CO)(TMP).H_2O (made from *trans*-$Ru(O)_2$(TMP), Fig. 1.25, in water-DCE with oct-1-ene) was determined (Ru-C 1.805(12) Å, Ru-O 2.291(8) Å) [591]. Under photolysis Ru(CO)(TMP) with CH_3CN yields *trans*-$Ru(CH_3CN)_2$(TMP) [582]. The system Ru(CO)(TMP)/(Cl_2pyNO)/C_6H_6 catalysed the epoxidation of styrene [595], and cholesteryl acetate was converted to its 5β,6β epoxide by Ru(CO)(TMP)/MCPBA)/C_6H_6 (or by *trans*-$Ru(O)_2$(TMP)/O_2/C_6H_6) [599–601]. The reagent Ru(CO)(TMP)/(Cl_2pyNO)/HCl or HBr-C_6H_6/40°C oxidised aromatic compounds to quinones, e.g. *m*-dimethoxybenzene gave 2-methoxy-*p*-benzoquinone (Table 3.5) [860]. As Ru(CO)(TPP) and Ru(CO)(TMP)/(Cl_2pyNO)/HBr-C_6H_6/40°C they catalysed the oxidation of 5β-steroids to the corresponding 5β-hydroxy derivatives (Table 4.1) [861]. The system Ru(CO)(TPP)/(Cl_2pyNO)/HBr/C_6H_6 epoxidised fullerene (C_{60}) to 1,2-epoxy[60]fullerene with 1,2:3,4 di-epoxy and 1,2:3,4:9,10 + 1,2:3,4:11,12 tri-epoxy species [862].

***Trans*-Ru(MeCN)$_2$(TMP)** is made by photolysis of Ru(CO)(TMP) in CH_3CN [582] or from *trans*-Ru(O)$_2$(TMP) with CH_3CN [863]; its X-ray crystal structure shows the *trans* configuration; ^{1}H NMR and electronic spectra were measured. With O_2 it gives *trans*-Ru(O_2)(TMP) [581], and on vacuum pyrolysis the highly reactive Ru(TMP) is formed [582].

Ru(CO)(TDCPP) reacts with styrene oxide (stO) in CH_2Cl_2 giving Ru(CO)(stO) (TDCPP), the X-ray crystal structure of which was determined. The epoxide is coordinated via its oxygen atom to the Ru (Ru-O 2.220(3) Å) with the coordinated epoxide ring tilted at 49° to the porphyrin ring. Such a species could be a model for intermediates formed during alkene epoxidations catalysed by Ru porphyrinate complexes [864].

Ru(R^{1}R^{2}S)$_2$(OEP) and **Ru(R^{1}R^{2}SO)$_2$(OEP)** (R^1=Me, Et, *n*-decyl, R^2=Me, Et) are made from [Ru(OEP)]$_2$ and the sulfides; ^{1}H NMR, cyclic voltammetry, electronic and IR spectra were measured, the latter suggesting that the sulfoxide complexes are S-bonded to the Ru [865, 866]. The X-ray crystal structure of Ru{(*n*-decyl)$_2$S}(OEP)$_2$ shows the sulfide ligands to be *trans* (Ru-S 2.37(1), Ru-N 2.04(1) Å) and this is the case also for Ru(Et$_2$S)$_2$(OEP) (Ru-S 2.37(1), Ru-N 2.05(1) Å) [866]. With O_2, Ru(R^{1}R^{2}S)$_2$(OEP) and benzoic acid in benzene, toluene or CH_2Cl_2 yield complexes of the corresponding sulfoxide complexes Ru(R^{1}R^{2}SO)$_2$(OEP), and an X-ray crystal structure of Ru(Et$_2$SO)$_2$(OEP) shows the ligands to be *trans* and S-bonded (Ru-S 2.32(1), Ru-N 2.06(3) Å). Mechanisms were proposed for the oxidation of Ru(R^{1}R^{2}S)$_2$(OEP) by O_2 to Ru(R^{1}R^{2}SO)$_2$(OEP) involving an inner-sphere one-electron transfer to Ru(III) and superoxide, the latter disproportionating to give H_2O_2 which then oxidises the free sulfide displaced from coordination by a benzoate ligand [867]. One related system, [Ru{(*n*-decyl)$_2$S}(OEP))]$_2$/O_2/C_6H_6/AcOH, oxidised *n*-decyl sulfide to the sulfoxide [866].

***Trans*-Ru(CO)(porch)** (porch=porphyrinate based on four chiral threitol units attached to the octahydroxy derivatised form of tetraphenylporphyrinate, the product of etherification of 5,10,15,20-*tetrakis*(2,6-dihydroxyphenyl)porphyrin with (*S,S*)-(−)-1,4-di-*O*-tosyl-2,3-*O*-iso-propylidene-L-threitol). Reaction of $Ru_3(CO)_{12}$ and (porch) gives Ru(porch)(CO) which was then oxidised to *trans*-Ru(O)$_2$(porch) [868] and its X-ray crystal structure determined [869]. As *trans*-Ru(CO)(porch)/PhIO or (Cl_2pyNO)/C_6H_6 it epoxidised styrene with e.e. of up to 58% [868, 869].

Ru(CO)(X$_4$-CPP) (X$_4$-CPP=(*tetrakis*(5,10,15,20-bromophenyl)porphyrinate with X=Br, NO_2) is made from $RuCl_3$ with (X$_4$-CPP) and CO. The system Ru(CO)(X$_4$-CPP)/PhIO/CH_2Cl_2 oxidised cyclohexane to cyclohexanol, the catalytic efficiency depending on their storage time, particularly under O_2 [870].

Ru(CO)(den-por) (den-por=dendritic porphyrins). These are made by condensation of Ru(CO)L (L=5,10,15,20-*tetrakis*(4′-hydroxyphenyl)porphyrin or 5,10,15,20-tetrakis(3′,5′-dihydroxy-phenyl)porphyrin), themselves made from $Ru_3(CO)_{12}$ and (L), with poly-(benzylether) dendrons; ^{1}H, ^{13}C NMR, electronic and IR spectra of the products were measured. Epoxidation of cyclic alkenes, *cis*- and *trans*-stilbene, styrene and its 3-methyl, methoxy, chloro and bromo derivatives, dimethylchromene and of cholesteryl esters in high yields and turnovers was effected by Ru(CO)(den-por)/(Cl_2pyNO)/CH_2Cl_2 [871].

$RuH_2(CO)(PPh_3)_3$ The system $RuH_2(CO)(PPh_3)_3$/(Xantphos)/crotonitrile/water-CH_3OH-toluene/110°C/24h (Xantphos=9,9-di-methyl-4,6-bis(dipehenylphopsphino) xanthene) oxidised primary alcohols RCH_2OH to methyl esters RC(O)OMe and octanal to its methyl ester [872, 873]. The system $RuH_2(CO)(PPh_3)_3$/(Xantphos)/crotonitrile/pyrollidine/toluene/110°C effected the coupling of alcohols R^1CH_2OH and $R^2CO(O)CH_2CO(O)H$ by tandem hydrogen transfer and condensation giving the alkenes $R^1CH{=}CHCO(O)R^2$ [874].

Ru(CO)(TFPPCl$_8$) ($TFPPCl_8$=octachloro-*tetrakis*(pentafluorophenyl)-porphyrinate) is made by reaction of the ligand with $Ru_3(CO)_{12}$. Epoxidation of cyclo-octene and cyclohexene by Ru(CO)($TFPPCl_8$)/O_2/CH_2Cl_2 was enhanced under low-intensity tungsten light, though selectivities were poor. The oxidations are probably photo-initiated rather than photocatalytic and may proceed through a radical mechanism, perhaps involving a Ru(III) intermediate [875]. The system Ru(CO)($TFPPCl_8$)/O_2/CH_3CHO/EtOAc oxidised alkanes (cyclohexane, *n*-hexane, cyclohexane and ethylbenzene) to alcohols and ketones [876].

Ru(CO)(TPFPP) (TPFPP=5,10,15,20-tetrapentafluorophenylporphyrinate) is made from the ligand and $Ru_3(CO)_{12}$. The system Ru(CO)(TPFPP)/(Cl_2pyNO)/CH_2Cl_2/65°C catalysed the hydroxylation of adamantane and of *cis*-and *trans*-decalin, with high selectivity and complete stereoretention, and epoxidised 1-octene. Intermediacy of a TPFPP-Ru(III) and an oxo-Ru(V) species was proposed [877].

Ru(CO)(porph^{chir}) (porph^{chir}=chiral poprphyrin from reaction of pyrrole with 1,2,3,4,5,6,7,8-octahydro-1:4,5:8-dimethanothracene-9-carboxaldehyde) is made from (porph^{chir}) and $Ru_3(CO)_{12}$. As Ru(CO)(porph^{chir})/(Cl_2pyNO)/C_6H_6 it catalysed the asymmetric epoxidation of alkenes with e.e. values up to 88% at room temperatures (better yields were obtained in sealed tubes up to 125°C) [878].

Ru(Pc) (PcS=4,4′,4″,4‴-tetrasulfophthalocyaninate dianion) is made from $RuCl_3$, urea and sodium 4-sulfophthalate. Oxidative dehalogenation of halobenzenes, nitrobenzene, benzoic acid and chlorophenols to CO_2 was effected by Ru(Pc)/aq. Oxone®/CH_2Cl_2 or aq. cetyltriethyltriammonium cation; $[Ru(H_2O)_2(dmso)_4]^{2+}$ or *cis*-$RuCl_2(dmso)_2$ were also used. Under some circumstances 90% of the aromatic rings were converted to CO_2 [879]. As Ru(Pc)/aq. Oxone® it oxidised cyclohexanone to adipic acid with small amounts of ε-caprolactone; Fe(Pc) and Co(Pc) were essentially as effective as catalysts. Cyclohexane also gave adipic acid with succinic acid as a minor product; cyclohexanol was oxidised to cyclohexanone. In all cases the catalyst was degraded, presumably ultimately to RuO_4 although this seems not to have been identified. The catalysts $[Ru(H_2O)\{PW_{11}(O)_{39}\}]^{5-}$ and *cis*-$RuCl_2(dmso)_4$ were less effective than Ru(Pc) [880].

1.9.3 Ru(II) complexes with -P, -As and -Sb Donors

Oxidations with the phosphorus-containing polyoxometalate $[Ru(H_2O)\{PW_{11}(O)_{39}\}]^{5-}$ are considered above (1.9.1).

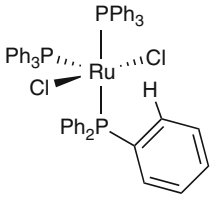

Fig. 1.39 Simplified structure of $RuCl_2(PPh_3)_3$ based on [883], the phenyl ring partly blocking the vacant sixth coordination site is shown

$RuCl_2(PPh_3)_3$ After $[RuO_4]^{n-}$ (n = 0–2), RuO_2 and $RuCl_3$ this is probably the most frequently used Ru oxidation catalyst, particularly for alcohol oxidations. Whereas the catalytic action of $RuCl_3$ or RuO_2 in most cases studied probably derives from their initial oxidation to $[RuO_4]^{n-}$, it is often not clear how $RuCl_2(PPh_3)_3$ operates as a catalyst. There are reviews on its oxidation chemistry [56, 58]. Its CAS number is **15529-49-4**.

It is made by reaction of $RuCl_3$ with PPh_3 in methanol, and forms shiny black crystals [881, 882]. The X-ray crystal structure shows the molecule to have a distorted square-based pyramidal structure, a phosphorus atom forming the axial bond (Ru-P 2.230(8) Å) while the basal plane has two *trans* chloro ligands (Ru-Cl 2.387(7) and 2.388(7) Å) and two *trans* phosphine ligands (Ru-P 2.374(4) and 2.412(6) Å). It can be regarded as octahedral, with the sixth position blocked by a phenyl ring (Fig. 1.39) [883]. The catalytic efficacy of the complex may well depend on the availability of this "vacant" coordination site.

1.9.3.1 Alcohols

There are reviews on earlier work of oxidations of alcohols and cyanohydrins by $RuCl_2(PPh_3)_3$ and by $RuH_2(PPh_3)_4$ [56, 58]. The first report of its use as a catalyst dates to 1981, when it was shown that $RuCl_2(PPh_3)_3$/PhIO/CH_2Cl_2 converted primary alcohols to aldehydes and secondary alcohols to ketones; $RuCl_3$, $RuCl_2(PPh_3)_2(CO)_2$, Cp_2Ru and $Ru_3(CO)_{12}$ are of comparable efficacies [884].

As $RuCl_2(PPh_3)_3$/TBHP/acetone it oxidised primary alcohols to aldehydes and acids, secondary alcohols to ketones and catechols to quinones (Tables 2.1, 2.2 and 2.4) [885]. Similarly $RuCl_2(PPh_3)_3$/NMO/acetone oxidised alcohols (Tables 2.1 and 2.2), and was used for a large-scale (15 g) oxidation of *d*-carveol to *d*-carvone [647]. Oxidation by $RuCl_2(PPh_3)_3$/TBHP/C_6H_6 of α-hydroxy esters $R^1CH(OH)R^2$ gave the ketones $R^1C(O)R^2$, and cyanohydrins RCH(OH)(CN) were oxidised to acylnitriles RCO(CN), reactions also catalysed by $RuCl_3$ and $RuH_2(PPh_3)_4$. An Ru^{II}-OO^{t}Bu intermediate may be involved [718]. The system $RuCl_2(PPh_3)_3$/TBHP/C_6H_6 oxidised cyanohydrins with R^1=Ph, *p*-MeC_6H_4, *p*-ClC_6H_4, *o*-$MeOC_6H_4$; $RuCl_3$ and $RuH_2(PPh_3)_4$ can also be used [695, 719]. Oxidation of *trans*-cinnamaldehyde cyanohydrin, PhCH=CHCH(OH)(CN) to *trans*-cinnamoylcyanide, PhCH=CH(CO)CN, was effected by $RuCl_2(PPh_3)_3$/TBHP/C_6H_6 [886], while pantoyl lactone was oxidised to ketopantoyl lactone by $RuCl_2(PPh_3)_3$/O_2/DCE [887].

The system $RuCl_2(PPh_3)_3$/TEMPO/O_2(10 atm air)/C_6H_5Cl (TEMPO=2,2′,6,6′-tetramethyl-piperidine-*N*-oxyl radical, Fig. 1.40) oxidised primary alcohols to aldehydes and secondary alcohols to ketones. Hammett correlation studies and primary

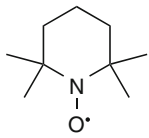

Fig. 1.40 TEMPO, an accelerator of aerobic oxidations catalysed by $RuCl_2(PPh_3)_3$

kinetic isotope effect data for benzyl alcohol oxidation suggested intermediacy of $RuH_2(PPh_3)_3$ as the active catalyst rather than oxo-Ru intermediates. It was suggested that TEMPO acts as a mediator for hydrogen-transfer, either being regenerated by O_2 under aerobic conditions or converted to TEMPH (in which N-O· is replaced by N-H) anaerobically [888–890]. Reaction of primary alcohols with $RuCl_2(PPh_3)_3$/4-BzTEMPO/O_2/toluene/70°C (4-BzTEMPO=4-benzoyloxy-2,2′,6,6′-tetramethyl-piperidine-1-oxy) gave the corresponding TEMPO-substituted α-oxygenated alkanal [891].

Aerobic oxidation of primary alcohols to aldehydes and secondary alcohols to ketones was accomplished in ionic liquids (bmim, 1-butyl-3-methyl-imidazolium cation) as $RuCl_2(PPh_3)_3$/$(bmim)^+$/80°C: $RuCl_3$ or $[RuCl_2(p\text{-cymene})]_2$ were also used [892]. Allylic alcohols $R^1CH{=}CHCH(OH)R^2$ were slowly oxidised to the ketones $R^1CH{=}CHC(O)R^2$ by $RuCl_2(PPh_3)_3/O_2$/DCE with retention of stereochemistry [893]. The system $RuCl_2(PPh_3)_3/K_2(CO_3)$/acetone/56°C dehydrogenated secondary alcohols to ketones; in some cases acetophenone replaced acetone (*cis*-$RuCl_2(dmso)_4$ with PPh_3 was also used, though less effectively) [894]. A similar reaction was noted with $RuCl_2(PPh_3)_3$/paraformaldehyde/toluene/110°C [895].

Long-chain alcohols such as octanol, dodecanol, 1-hexadecanol and 2-hexyl-1-decanol were oxidised to the corresponding aldehydes and carboxylic acids by $RuCl_2(PPh_3)_3$/NMO/CH_2Cl_2 or DCE/70°C; (NMO+aq. H_2O_2 was also used but gave lower yields than did NMO alone; the latter is probably re-cycled by the H_2O_2) [896]. As $RuCl_2(PPh_3)_3/Me_3SiOOSiMe_3/CH_2Cl_2$ primary alcohols were oxidised to aldehydes and secondary alcohols to ketones; for mixtures of allylic primary with secondary alcohols (e.g. benzyl alcohol with 4-dodecanol) the former were oxidised much faster [897]. The reagent was immobilized by microencapsulation on an epoxide-containing polymer, and the encapsulated $RuCl_2(PPh_3)_3$/NMO/toluene, CH_3CN or acetone system oxidised primary alcohols to aldehydes and secondary alcohols to ketones [898].

Diols were converted to diones by $RuCl_2(PPh_3)_3$/benzalacetone/THF/195°C in a process involving H-transfer to an olefinic H-acceptor $Ph(CH)_2COMe$ (Table 2.4) [899].

1.9.3.2 Alkenes, Alkanes

The reagent $RuCl_2(PPh_3)_2/O_2/Me_2CHCHO$/DCE epoxidised (R)-(+)-limonene and other alkenes [697] and cyclohexene was oxidised to a mixture of products including the epoxide by $RuCl_2(PPh_3)_3/O_2/C_6H_6$/60°C [696]. The system $RuCl_2(PPh_3)_3$/PhIO/CH_2Cl_2 oxidatively cleaved alkynes to diketones (Table 3.6); $RuCl_3$, *trans*-$RuCl_2(CO)_2(PPh_3)_2$, Cp_2Ru and $Ru_3(CO)_{12}$ were also effective catalysts for these reactions [376]. Conversion of alkanes $R^1R^2R^3CH$ to alcohols $R^1R^2R^3C(OH)$ and, with R^3=H, to ketones $R^1R^2C{=}O$ was accomplished with $RuCl_2(PPh_3)_3$/TBHP or

CH_3CO_3H/C_6H_6 (and also with $RuH_2(PPh_3)_4$) (Table 4.1). A Ru(IV) oxo intermediate via a Ru(II) peroxo species may be involved [900, 901]. Aerobic oxidation of cyclo-octane and adamantane by $RuCl_2(PPh_3)_3/O_2$/heptanal/CH_2Cl_2 has been described; $RuCl_3$ or Fe powder can be used in place of $RuCl_2(PPh_3)_3$ [753]. Alkylated arenes were oxidised at the methylene group by $RuCl_2(PPh_3)_3$/TBHP/C_6H_6: thus ethylbenzene gave acetophenone, and diphenylmethane and fluorene were converted to the corresponding ketones. The fact that 9-methylflourene gave 9-(*tert*-butoxy)-9-methylfluorene and that indane gave a mixture of 1-methoxyindane and 1-indanone suggested intermediacy of carbocationic species [900]. Cyclic alkanes were oxidised by $RuCl_2(PPh_3)_3$/TBHP or CH_3CO_3H/C_6H_6, and also with $RuH_2(PPh_3)_4$ (Table 4.1) [900, 901].

1.9.3.3 Amines, Amides, Sulfides; Miscellaneous Oxidations

Oxidation of secondary and tertiary amines, amides and β-lactams catalysed by $RuCl_2(PPh_3)_3$ has been reviewed [74]. Oxidation of $R^1R^2CHNHR^3$ to the imines $R^1R^2C{=}NR^3$ was effected with $RuCl_2(PPh_3)_3/TBHP/C_6H_6$ ($RuCl_3$, $RuH_2(PPh_3)_4$ and $Ru_3(CO)_{12}$ were also effective catalysts for the reaction) [902]; similarly oxidation of $R^1CH_2NHR^2$ to $R^1CH{=}NR^2$ was catalysed by $RuCl_2(PPh_3)_3$/PhIO/PMS/CH_2Cl_2 [903]. Dibenzylamine was oxidised to *N*-benzylidenebenzylamine by $RuCl_2(PPh_3)_3/O_2$/toluene/80°C or $RuCl_2(PPh_3)_3$/PhIO/CH_2Cl_2; *cis*-$RuCl_2(dmso)_4$ was also used (Table 5.1) [904]. Tertiary amines were oxidised: thus N-methylamines $R^1R^2NCH_3$ with $RuCl_2(PPh_3)_3/TBHP/C_6H_6$ gave the corresponding α-(*tert*-butyldioxy)alkylamines $R^1R^2NCH_2OO^tBu$ [905, 906], and tertiary *N*-methyl-*N*-alkylanilines $R^1R^2HCNR^3R^4$ were oxidised by $RuCl_2(PPh_3)_3/TBHP/C_6H_6$ to *N*-(*tert*-butyldioxymethyl anilines) $R^1R^2(^tBuOO)CNR^3R^4$ [905]**.** A P-450 type of mechanism was suggested in which a Ru(IV) oxo intermediate effected the oxidation [906]. The α-substitution of N-methoxycarbonylamines $R^1R^2C(H)NR^3(COOMe)$ to the butyldioxygenated products $R^1R^2(^tBuOO)CNR^3(COOMe)$ was catalysed by $RuCl_2(PPh_3)_3$/TBHP/C_6H_6 [907]. The amides $R^1R^2HCNR^3COR^4$ were converted to ^{t}butyldioxyamides $R^1R^2H(^tBuOO)CNR^3COR^4$ by $RuCl_2(PPh_3)_3/TBHP/C_6H_6$. It is likely that a P-450 type of mechanism is involved with an oxo-Ru(V) intermediate [766].

The complexes $RuCl_2(PPh_3)_3$, $RuBr_2(PPh_3)_3$ and $RuCl_2(SbPh_3)_3/O_2$/EtOH/100°C oxidised $^nBu_2S$ to the sulfoxide and a little sulfone [769]. The reagent was immobilized by microencapsulation on an epoxide-containing polymer, and this encapsulated system $RuCl_2(PPh_3)_2$/NMO/PMS/acetone oxidised sulfides to sulfoxides or sulfones (e. g. 2-thiophene-methanol); it also oxidised alcohols to aldehydes and ketones [898]. Reaction of α-substituted nitriles $R^1R^2(CN)$ with $RuCl_2(PPh_3)_3/TBHP/C_6H_6$ gave 2-(t*ert*-butyldioxy)-alkanenitriles $^tBuOOR^1R^2(CN)$. A cytochrome-P450 type of mechanism may operate, in which the catalyst reacts with TBHP to give an oxo-Ru(IV) complex which abstracts a hydrogen atom from the nitrile to give a radical Ru(III) radical intermediate. Electron transfer follows with subsequent nucleophilic attach of TBHP giving $^tBuOOR_1R_2(CN)$ and the $RuCl_2(PPh_3)_3$ catalyst. With R^2=H, facile elimination of ^{t}BuOH occurs giving the acyl cyanide [752].

$RuCl_2(PPh_3)_4$ is made by reaction of $RuCl_3$ in CH_3OH with PPh_3, giving dark brown crystals [881]. With $RuCl_2(PPh_3)_4$/TBHP/CH_2Cl_2 ^{t}BuO(CO)NHOH was oxidised to the corresponding nitroso dienophile ^{t}BuO(CO)N=O and then trapped by cyclohexa-1,3-diene to give the hetero Diels-Alder adduct [908, 909]. It is likely that an oxo-Ru(IV) intermediate stabilised by PPh_3 is involved [908].

$[RuCl_2(PPh_3)_2]_n$ is a black material made from $RuCl_2(PPh_3)_3$ with dimethyl fumarate at 90°C. As $[RuCl_2(PPh_3)_2]_n/O_2/C_6H_6$/60°C it oxidised cyclohexene to several products including the epoxide. The reaction is catalysed by a number of other Ru species including $RuCl_3$, $Ru(acac)_3$, $RuCl_2(PPh_3)_3$, $RuBr_2(PPh_3)_3$ and by *cis*- and *trans*-$RuCl_2(CO)_2(PPh_3)_2$ [696].

$RuCl(OC(O)CH_3)(PPh_3)_3$ is made from silver acetate and $RuCl_2(PPh_3)_3$. It oxidised primary alcohols to aldehydes at room temperatures, using a triple catalytic system of $RuCl(OCOCH_3)(PPh_3)_3$/Co(salophen)$(PPh_3)/O_2$/hydroquinone/CH_2Cl_2 (H_2salophen=N,N′-bis-(salicylidene)-*o*- phenylenediamine) [910].

$RuBr_2(PPh_3)_3$ is made from $RuBr_3$ and PPh_3 in methanol and is dark brown [882]. As $RuBr_2(PPh_3)_3/O_2/C_6H_6$/60°C it oxidised cyclohexene to a mixture including the epoxide; $Ru(acac)_3$, *cis*- and *trans*-$RuCl_2(CO)_2(PPh_3)_2$, $RuCl_2(PPh_3)_3$ and $RuCl_2(SbPh_3)_3$ also catalysed the reaction [696]. As with $RuCl_2(PPh_3)_3$, $RuBr_2(PPh_3)_3/O_2$/EtOH/100°C oxidised Bu^n_2S to Bu^n_2SO and a little $Bu^n_2SO_2$ [769].

$RuH_2(PPh_3)_4$ There is a review on earlier work of oxidations of alcohols and cyanohydrins by $RuH_2(PPh_3)_4$ and $RuCl_2(PPh_3)_3$ [56, 58]. The system $RuH_2(PPh_3)_4$/paraformaldehyde/toluene/110°C converted primary alcohols to aldehydes and secondary alcohols to ketones without competing double bond cleavage [895]. Oxidation of secondary amines $R^1R^2CHNHR^3$ to imines $R^1R^2C{=}NR^3$ was accomplished with $RuH_2(PPh_3)_4$/TBHP/C_6H_6; $RuCl_3$, $RuCl_2(PPh_3)_3$ and $Ru_3(CO)_{12}$ were also effective catalysts [902].

$Ru(O_2)(NO)(NCS)(PPh_3)_2$ As $Ru(O_2)(NO)(NCS)(PPh_3)_2/O_2$/xylene/80°C this oxidised PPh_3 to PPh_3O. The mechanism may involve the coordinated NO^+ ligand, which can function in effect as a one-electron donor (NO^-) when the Ru-N-O unit is bent and, as here, a three-electron donor when linear [911].

$Ru(PPh_3)_2(tr)_2$ (tr=tropolone, benzoylacetone, 3-hydroxy-2-pyridinone, maltol, dibenzoyl-methane, 1,2-dimethyl-3-hydroxy-4-pyridinone) are made from $RuH_2(PPh_3)_4$ with the ligand. The IR, electronic spectra and cyclic voltammograms of these diamagnetic complexes were measured. As $Ru(PPh_3)_2(tr)_2$/NMO/CH_2Cl_2 they oxidised *p*-methoxybenzyl alcohol to the aldehyde [912].

$RuBr_2(PPh_3)_2(RCHO)_2$ (R=C_4H_3O, C_6H_5) [913], *o*-HOC_6H_4, *p*-$MeOC_6H_4$) [914]). These five co-ordinate complexes are made from $RuCl_3$, LiBr and furfural, benzaldehyde, salicylaldehyde or anisaldehyde with PPh_3; electronic and ^{1}H NMR spectra were measured. The system $RuBr_2(PPh_3)_2(RCHO)_2/O_2/^n$BuOH oxidised PPh_3 to PPh_3O [913, 914].

Ru(PPh$_3$)(OEP) and **Ru(PPh$_3$)$_2$(OEP)** The former is made by reduction of Ru(OEP)(PPh_3)Br with Zn/Hg in benzene and the latter by addition of PPh_3; ^{1}H NMR and electronic spectra were measured. Both complexes undergo a remarkable demetallation reaction with O_2:

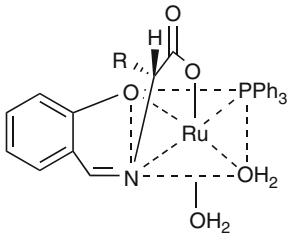

Fig. 1.41 Likely structure of $Ru(PPh_3)(H_2O)_2(SB^{chir})$, the first Ru-based chiral epoxidation catalyst [917]

$$Ru\left(PPh_3\right)_2\left(OEP\right)+1.5O_2+H_2O \rightarrow RuO_2+2PPh_3O+H_2\left(OEP\right) \qquad (1.8)$$

probably via a μ-oxo dimer $[Ru(OH)(OEP)]_2(\mu\text{-}O)$. As complex/$O_2$/toluene/50°C) they oxidised PPh_3 to Ph_3PO. An oxidation atom transfer cycle may be involved, with intermediacy of a dioxygen complex $Ru^{II}(O_2)(OEP)$. For $Ru(PPh_3)_2(OEP)$ an initial outer-sphere mechanism was suggested, generating superoxide and then $HO_2^{\cdot}$ which disproportionates to O_2 and H_2O_2, the latter oxidizing PPh_3 to PPh_3O [915].

$RuCl_2(PhCH_2NH_2)_2(PPh_3)_2$ is a yellow complex made from benzylamine and $RuCl_2(PPh_3)_3$, and as $RuCl_2(PhCH_2NH_2)_2(PPh_3)_2/O_2$/toluene/80°C it oxidised benzylamine to benzonitrile [916].

$Ru(PPh_3)(H_2O)_2(SB^{chir})$ constitutes a series of complexes, made from $RuCl_2(PPh_3)_2$ and a chiral Schiff base SB^{chir} obtained from salicylaldehyde and the L-forms of alanine, valine, serine, arginine, cysteine and aspartic acid. They were characterised by IR, circular dichroism, ^1H and $^{13}C[^1H]$ NMR spectroscopies and by cyclic voltammetry. The supposed structure of one is shown in Fig. 1.41 [917].

The system $Ru(PPh_3)(H_2O)_2(SB^{chir})$/PhIO/$CH_2Cl_2$/4°C asymmetrically epoxidised styrene [917]. Related complexes made from L-histidine with salicylaldehyde, 5-chloro and 5-methoxysalicylaldehyde as $Ru(PPh_3)(H_2O)_2(SB^{chir})$/(PhIO/$CH_2Cl_2$ epoxidised non-functionalised styrenes at unspecified 'low temperatures' in the dark. Possible mechanisms were discussed [918].

$Ru(tSB)(PPh_3)(H_2O)$ and **$Ru(ctSB)(PPh_3)(H_2O)$** (tSB=terdentate chiral Schiff base derived from L-tyrosine and L-phenylaniline with salicylaldehyde and also with 3-*tert*-butyl, 3,5-di-*tert*-butyl, 3,5-dichloro and 3,5-dinitrosalicylaldehyde) is made from $RuCl_2(PPh_3)_3$ and (tSB) [919]. Similar complexes $Ru(ctSB)(H_2O)(PPh_3)$ (ctSB=chiral Schiff base ligand derived from L-leucine and L-histidine with salicylaldehyde, and with 3-*tert*-butyl, 3,5-di*tert*-butyl, 3,5-dichloro and 3,5-dinitrosalicylaldehyde) are made from $RuCl_2(PPh_3)_3$ and (ctSB); IR, electronic, ^1H, $^{31}P\{^1H\}$ NMR and circular dichroism spectra were measured [920]. Asymmetric epoxidation of styrene and 4-chloro, 4-nitro and 4-methylstyrenes effected by $Ru(PPh_3)(tSB)(H_2O)$/PhIO/C_6H_5F/0°C gave good selectivities and e.e. values, particularly with the L-tyrosine derivative [919]; similarly, $Ru(ctSB)(H_2O)(PPh_3)$/PhIO/C_6H_5F/0°C asymmetrically epoxidised 1,2-dihydronaph-thalene. It was suggested that $(tSB)Ru^{IV}(O)$ or $(ctSB)Ru^{IV}(O)$ species were involved [920].

$Ru(salSB)_2(PPh_3)_2$ (salSBH=Schiff base from aniline or *p*-anilines with salicylaldehyde and its 2,3-dihydroxy and 3,5-dibromo forms) are made from the Schiff base and $RuCl_2(PPh_3)_3$. Infrared and electronic spectra were measured as were the cyclic voltammetric properties of the compounds. The system $Ru(salSB)_2(PPh_3)_2$/NMO/PMS/CH_2Cl_2 oxidised primary alcohols to aldehydes and secondary alcohols to ketones [921].

$RuX_2(EPh_3)(SB)$ (X=Cl, Br; E=P, As; SB=tridentate Schiff base from *o*-aminophenol or *o*-thioaminophenol with ethylacetoacetate or ethylbenzoylacetate) are made from $RuX_3(EPh_3)_3$ and (SB); IR and ^1H, ^{13}C NMR were recorded. The systems $RuX_2(EPh_3)(SB)/O_2/CH_2Cl_2$ oxidised primary and secondary alcohols to aldehydes or ketones respectively [922].

$Ru(PPh_3)_2(tetSB)$, $Ru(PPh_3)_2(H_2O)(triSBdSB)$, $Ru(PPh_3)_2(bidSB)_2$ (tetSB=tetra-, triSB tri-dentate, bidSB=bidentate Schiff ligands made from condensation of salicylaldehyde with 1,2-diamonobenzene, 3,4-diaminotoluene, 1,2-diaminocyclohexane, 2-aminophenol) are made from the Schiff base and $RuCl_2(PPh_3)_3$; electronic spectra were recorded. The systems (complex)/NMO/PMS/CH_2Cl_2 oxidised primary alcohols to aldehydes and secondary alcohols to ketones [923].

$Ru(PPh_3)_2(Me_2CO)(\mu\text{-}Cl_3)RhCl(\eta^4\text{-}C_4Ph_4CO)$ This heterobimetallic complex is made from $Ru(PPh_3)_2(Me_2CO))(\mu\text{-}Cl_3Ru(PPh_3)_2Cl)$ with $[(\eta^4\text{-}C_4Ph_4CO)RhCl]_2$ in CH_2Cl_2. The IR, ^1H and ^{13}C NMR spectra were measured and the single-crystal X-ray structure determined. As $Ru(PPh_3)_2(Me_2CO)(\mu\text{-}Cl_3)RhCl(\eta^4\text{-}C_4Ph_4CO)/K_2(CO_3)$/acetone-$C_6H_6$ it catalysed the Oppenauer-type oxidation of primary and of secondary alcohols (e.g. 1-phenylethanol to acetophenone), the acetone functioning as the co-oxidant [924].

RuHCl(CO)(A-^{i}Pr-PNP) This acridine-based 'pincer' complex (A-^{i}Pr-PNP=4, 5-bis-(diisopropylphosphinomethyyl)acridine) is made from the ligand and RuHClCO)$(PPh_3)_3$. Using the alcohol as solvent it catalytically dehydrogenated $R(CH_2)_2OH$ (ethanol, 1-pentanol, 1-hexanol, benzyl alcohol) to acetals $RCH_2C(O(CH_2)_2R)_2$ and, in 0.01M aq. KOH, converted such alcohols to esters $RCH_2(CO)CH_2R$ [925].

***Cis*-$RuCl_2(CO)_2(PPh_3)_2$** is white, made from CO, $RuCl_3$ and PPh_3 in ethanol [882], or from $RuCl_2(PPh_3)_3$ in THF with CO [696]. The reagent *cis*-$RuCl_2(CO)_2(PPh_3)_2$/O_2/C_6H_6/60°C oxidised cyclohexene to a mixture of products including the epoxide; $Ru(acac)_3$, $RuCl_2(PPh_3)_3$, $RuBr_2(PPh_3)_3$, $RuCl_2(SbPh_3)_3$ also catalysed the reaction [696]. The reagent *cis*-$RuCl_2(CO)_2(PPh_3)_2$/PhIO/CH_2Cl_2 oxidatively cleaved alkynes to diketones; $RuCl_3$, $RuCl_2(PPh_3)_3$ and $Ru_3(CO)_{12}$ also catalysed these reactions (Table 3.6) [376].

***Trans*-$RuCl_2(CO)_2(PPh_3)_2$** is a canary-yellow species made from $RuCl_2(PPh_3)_3$ in acetone with CO. As *trans*-$RuCl_2(CO)_2(PPh_3)_2/O_2/C_6H_6$/60°C it oxidised cyclohexene to a mixture of products including the epoxide [696].

$[Ru(ClO_4)(dppm)](ClO_4)$, $[Ru(ClO_4)(dppe)](ClO_4)$ and **$[Ru(ClO_4)(dpae)](ClO_4)$** (dppm=bis-(diphenylphosphino)methane, dppe=1,2-bis(diphenylphosphino)ethane, dpae=1,2-bis-(diphenyl-arsino)ethane) are made from $RuCl_3$, $Li(ClO_4)$ and the ligand. As complex/TBHP or aq. H_2O_2/CH_2Cl_2/50°C they oxidised alkenes to a mixture of products. Linear and long-chain alkenes were not efficiently oxidised,

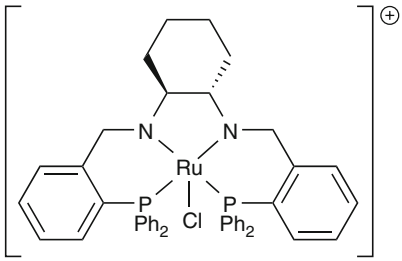

Fig. 1.42 Structure of a $[RuCl(PNNP)]^+$ alkene epoxidation catalyst [929]

but cyclo-octene and *trans*-stilbene gave the epoxides; with H_2O_2, radical-initiation probably occurs [926]. The system complex/CHP or NMO/$CHCl_3$/50°C (CHP=cumene hydroperoxide) epoxidised cyclohexene; 1-heptene and 1-octene) in low yield: CHP is a more effective oxidant than NMO, and the active catalyst is likely to be an oxo-Ru(IV) species [927].

$[RuCl(PNNP)](PF_6)$ and **$[RuCl(H_2O)(PNNP)](PF_6)$** (PNNP=tetradentate chiral ligands, e.g. *N,N′*-[bis(*o*-diphenylphosphino)-benzylidene]-(1*S*,2*S*)-di-iminocyclohexane (Fig. 1.42) [928, 929] and *N,N′*-[bis(*o*-diphenylphosphino)-benzylidene]-2,2*̂*-di-imino-1, 1*̂*-(S)-binaphthylene) [928]. These complexes were made from the ligands and $RuCl_2(PPh_3)_3$ in CH_2Cl_2; ^{31}P NMR spectra were measured [929].

As complex/aq. H_2O_2/CH_2Cl_2 they epoxidised unfunctionalised alkenes $RCH=CH_2$ to a mixture of the epoxide and the aldehyde RCHO with e.e. values from 4% to 41%. Thus (*Z*)-2-methylstyrene gave the *cis*-epoxide with only traces of the *trans*-isomer [928, 929]. The reagent $[RuCl(PNNP)]^+$/aq. H_2O_2/CH_2Cl_2 epoxidised *cis*-stilbene, *Z*-2-methylstyrene and 1,2-dihydro-napthalene [844].

$[RuCl(OEt_2)(S,S\text{-}PNNP)](PF_6)$ (*S,S*-PNNP=*N,N'*-[bis(*o*-diphenylphosphino)-benzylidene]-(1*S*,-2*S*)-di-iminocyclohexane) is made from $[RuCl(PNNP)](PF_6)$ with $(Et_3O)PF_6$ in CH_2Cl_2. The system $[RuCl)(OEt_2)(S,S\text{-}PNNP)]/H_2O_2/CH_2Cl_2$ enantioselectively hydroxylated β-ketoesters [930].

***Trans*-$RuCl_2(dppp)_2$** (dppp=(1,2-diphenylphosphino)propane, sometimes abbreviated as (dpp) in the literature) is made from $K_2[Ru(H_2O)Cl_5]$ and (dppp) in refluxing EtOH. Oxidation of a wide range of ethers to esters or lactones was effected by *trans*-$RuCl_2(dppp)_2$ or $[RuCl(dppp)_2]^+$/aq. Li(ClO)/CH_2Cl_2 (Table 5.2) [931].

$[RuCl(dppp)_2](PF_6)$ and **$[RuCl(ppy)_2](ClO_4)$** (ppy=1-(diphenylphosphino)-2-(2-pyridyl)ethane) are made by refluxing *trans*-$RuCl_2(dppp)_2$ or $RuCl_2(ppy)_2$ in ethanol with NaX (X=$(PF_6)^-$, $(ClO_4)^-$) [932].

The system $[RuCl(dppp)_2]^+$/aq. Oxone®/CH_2Cl_2 oxidised primary and secondary alcohols to aldehydes and ketones ($[Ru(H_2O)\{PW_{11}(O)_{39}\}]^{5-}$, $RuCl_3$ and *cis*-$RuCl_2(dmso)_4$ also catalysed the reaction) [933], while *trans*-$RuCl_2(dppp)_2$ and $[RuCl(ppy)_2]^+$/aq. Li(ClO)/CH_2Cl_2, like *cis*-$RuCl_2(phen)_2$, oxidised octan-2-ol to octan-2-one [934]. As $[RuCl(dppp)_2]^+$ or $[RuCl(ppy)_2]^+$/PhIO/CH_2Cl_2 they epoxidised norbornene, styrene, stilbene, hex-1-ene and *trans*-hex-2-ene; a number of by-products (alcohols, aldehydes and ketones) were also formed. Kinetic measurements and experiments using $H_2{}^{18}O$ suggested the intermediacy of $[Ru^{IV}(O)Cl(dppp)_2]^-$ [932, 935].

These reactions obey the Michaelis-Menten kinetic law, calculated kinetic parameters following a free-energy correlation with the one-electron oxidation potential of the alkenes, suggesting that a charge-transfer mechanism is of predominant importance [936]. The behaviour of these complexes parallels that of some natural enzymes and of some synthetic manganese porphyrin complexes [845]. The system $[RuCl(dppp)_2]^+$/PhIO or aq. $K(HSO_5)$/(BDTAC)/CH_2Cl_2 oxidised adamantane, cyclo-octane and cyclohexane to alcohols and ketones: the same results were obtained with $[RuCl_2(dppe]^+$ or $[RuCl_2(dppp)]^+$ as catalysts [816]. The reagents *trans*-$RuCl_2(dppp)_2$ and $[RuCl(ppy)_2]^+$/aq. Li(ClO)/CH_2Cl_2 converted adamantane to adamantan-1-ol and adamantanone, tetrahydropyran to δ-valerolactone and octan-2-ol to octan-2-one [934].

The systems *trans*-$RuCl_2(dppp)_2$ and $[RuCl(ppy)_2]^+$/aq. Li(ClO)/CH_2Cl_2, like *cis*-$RuCl_2(phen)_2$, oxidised octan-2-ol to octan-2-one, dipropylether to propylpropionate and tetrahydropyran to δ-valerolactone; Ru oxo intermediates are probably involved [834]. Oxidation of a wide range of ethers to esters or lactones was effected by *trans*-$RuCl_2(dpp)_2$ or $[RuCl(dpp)_2]^+$/aq. Li(ClO)/CH_2Cl_2 [931]; $[RuCl(dppp)_2]^+$, *cis*-$RuCl_2(dmso)_4$ or TPAP/aq. Na(ClO)/CH_2Cl_2 were also used (Table 5.2) [423, 424] and the intermediacy of RuO_4 was suggested [424]**.** Kinetic studies on *trans*-$RuCl_2(dpp)_2$/aq. Li(ClO)/CH_2Cl_2 for oxidations of normal and deuteriated THF to γ-butyrolactone suggested that oxo-Ru(IV) intermediates are likely to be involved rather than RuO_4. A mechanism involving these was tentatively proposed in which both α and β carbon atoms are involved in hydrogen atom transfer [931].

$RuCl_2(SbPh_3)_3$ is made from $RuCl_3$ in MeOH with $SbPh_3$, giving deep red crystals of the complex [882]. As $RuCl_2(SbPh_3)_3/O_2/C_6H_6$/60°C it oxidised cyclohexene to a mixture of products including the epoxide [696]. The reagent $RuX_2(SbPh_3)_3/O_2$/EtOH/100°C (X=Cl, Br) converted Bu^n_2S to the sulfoxide and a little sulfone [769].

1.9.4 Ru(II) Complexes with -S and -O Donors

For the sulfur-containing polyoxometalate $[Ru^{II}\{PW_{11}(O)_{39}\}(dmso)]^{5-}$ *cf.* 1.9.1.

***Cis*-$RuCl_2(dmso)_4$** is made from $RuCl_3$ and DMSO as yellow crystals [937], from $RuCl_3$, H_2 and DMSO [938] or from *mer*-$RuCl_3((dmso)_3Cl_3$ and (dppe) with DMSO, this last method giving the orange orthorhombic polymorph [939]. X-ray crystal structures on the monoclinic and orthorhombic polymorphs (*cf.* the brief review in ref. [939]) show essentially the same structures (Fig. 1.43). The orthorhombic form has *cis* chloro ligands, with one O- and three S-bonded (dmso)

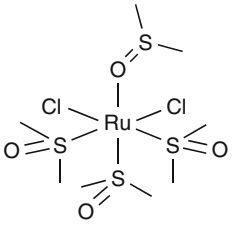

Fig. 1.43 Structure of orthorhombic *cis*-$RuCl_2(dmso)_4$ [939]

ligands. The Ru-S distance of the ligand *trans* to the O-bonded ligand (Ru-O 2.140(2), Ru–S 2.2480(9); Ru-Cl 2.42(2) Å) is longer than the other two Ru-S distances (2.273(8) Å) [939]. A *trans* isomer is made by recrystallising the *cis* form from DMSO in a photoreactor; the X-ray structure shows that all the four (dmso) ligands are S-bonded (Ru–S 2.352(2) Å); Ru-Cl 2.417(9)) [940].

The IR spectra of the normal and deuteriated form have been reported [937]. It is evident that the *cis* form is the thermodynamically stable one [940] and it is this which is likely to be the initial species in catalytic reactions.

Its properties as an oxidation catalyst have been briefly reviewed [941]. The system *cis*-$RuCl_2(dmso)_4$/aq. Oxone®/CH_2Cl_2 oxidised primary alcohols to aldehydes and secondary alcohols to ketones ($[Ru(H_2O)\{PW_{11}(O)_{39}\}]^{5-}$, $RuCl_3$ and $[RuCl(dppp)_2]^+$ also functioned as catalysts) [933]. In DMF *cis*-$RuCl_2(dmso)_4$ appears to form *cis*-$RuCl_2(dmso)_3$(DMF), probably by dissociation of the one O-bonded (dmso) ligand, and kinetics of its catalytic oxidation by *cis*-$RuCl_2(dmso)_3$(DMF)/NMO/DMF/30–50°C of benzhydrol, 1-phenyl-ethanol and α-methyl-2-naphthalenemethaanol to ketones were measured; the intermediacy of $Ru^{IV}(O)Cl_2(dmso)_2$(NM) (NM=N-methylmorpholine) was suggested [942].

The system *cis*-$RuCl_2(dmso)_4$/TBHP/CH_2Cl_2/0°C epoxidised cyclic alkenes with good selectivities (Table 3.1). Addition of (bpy) or the chiral ligand (pymox)=4*S*,5*S*)-(+)-4-hydroxymethyl)-5-phenyl-2-(2-pyridinyl)-4,5-dihydro[2,1-*d*]oxazole improved yields and selectivities. Low epoxide selectivities were found for terminal alkenes, but these were higher for secondary and tertiary alkenes. Possible mechanisms for the reaction involving oxoruthenates(VI) or -(IV) were discussed [943]. Oxidative dehalogenation of halobenzenes, nitrobenzene, benzoic acid and chlorophenols to CO_2 by *cis*-$RuCl_2(dmso)_4$/aq. Oxone®/CH_2Cl_2 or water-cetyltriethyltriammonium cation was reported; $[Ru(H_2O)_2(dmso)_4]^{2+}$ and Ru(Pc) were also used. Under various circumstances some 90% of the aromatic rings were converted to CO_2 [879]. The system *cis*-$RuCl_2(dmso)_4$/aq. Oxone®/CH_2Cl_2 catalysed the oxidative fission of the ring in alkylbenzenes [746]. The reagent *cis*-$RuCl_2(dmso)_4$/aq. Li(ClO)/CH_2Cl_2 oxidised alkanes (e. g. adamantane to adamantan-1-ol and adamantanone, hexane to 2- and 3-hexanones, heptane to 2-, 3- and 4-heptanones). Kinetic studies were made, and it was suggested that a mono-oxo Ru(IV) or a dioxo Ru(VI) intermediate was involved [834, 934].

Cis-$RuCl_2(dmso)_4$/aq. Li(ClO)/CH_2Cl_2 oxidised primary ethers to esters [834, 931] or *cis*-$RuCl_2(dmso)_4$/aq. Na(ClO)/CH_2Cl_2 (Table 5.2) [423, 424]**.** A similar mixture oxidised dipropylether to propylpropionate, terahydropyran to δ-valerolactone and octan-2-ol to octan-2-one [834]. The system *cis*-$RuCl_2(dmso)_4$/NMO/DMF oxidised sulfides to sulfoxides, probably via $RuCl_2(dmso)_3(SR_2)$; oxidation rates dropped in the order benzyl>butyl>phenyl>methylphenyl, and kinetics of the reaction were measured [944]; *cis*-$RuCl_2(dmso)_4/O_2$ (7 atmos)/110°C/CH_3OH oxidised sulfides to sulfoxides [945]. It seems likely that the adamantane hydroxylation catalysed by $[WZnRu_2(OH)(H_2O)_2\{ZnW_9(O)_{34})_2\}]^{11-}/O_2$/(MTCAC)/water-DCE/80°C [701, 705] may have been caused by some contamination of the catalytic species with *cis*-$RuCl_2(dmso)_4$ together with Ru-free $[WZn_3(H_2O)_2\{ZnW_9(O)_{34})_2\}]^{12-}$ [702] (*cf.* 1.7.1)**.**

***cis*-[Ru(H_2O)$_2$(dmso)$_4$]$^{2+}$** is made from *cis*-$RuCl_2(dmso)_4$ and $Ag(BF_4)$ in aq. EtOH. The system *cis*-[$Ru(H_2O)_2(dmso)_4]^{2+}$/aq. Na(ClO) or TBHP/CH_2Cl_2 oxidised alkanes such as adamantane, cyclo-octane, -heptane and -hexane to the corresponding alcohols and ketones as did [$Ru(H_2O)\{PW_{11}(O)_{39}\}]^{5-}$. A free-radical mechanism may be involved for the TBHP oxidations, but those with $(ClO)^-$ probably involve oxoruthenate(VI) or oxoruthenate(IV) intermediates [823]. The oxidative destruction of α-chlorinated alkenes by *cis*-$[Ru(H_2O)_2(dmso)_4]^{2+}$/aq. Oxone®/$Me(CH_2)_{15}N(HSO_4)Me_3$ to carboxylic acids and ultimately to CO_2 and HCl was reported [946].

Cis and ***trans*-RuBr$_2$(dmso)$_4$** The yellow *trans*-isomer is made by reaction of $RuBr_3.nH_2O$ in DMSO with H_2 [938]; recrystallisation from hot DMSO gives the thermodynamically more stable *cis*-complex [940]. The X-ray crystal structure of *cis*-$RuBr_2(dmso)_4$ is similar to that of *cis*-$RuCl_2(dmso)_4$, with *cis* Ru-Br at 2.561(1) Å) with three S-bonded and one O-bonded (dmso) ligands. The Ru-S bond of the ligand is *trans* to the O-bonded ligand (Ru–O 2.253(2), Ru–S 2.289(2) Å) [940].

The system *trans*-$RuBr_2(dmso)_4$/NMO/DMF/30–50°C oxidised benzhydrol; kinetics of the reaction were studied. A first fast step was dissociation of (dmso) to give *trans*-$RuBr_2(dmso)_3$(DMF) and the intermediacy of $Ru^{IV}(O)Br_2(dmso)_2$(NM) (NM=N-methylmorpholine) in subsequent reactions was suggested. The kinetics differed from those of similar reactions using *cis*-$RuCl_2(dmso)_4$ [942]. The reagent *cis*-$RuBr_2(dmso)_4$/aq. Oxone®/CH_2Cl_2 oxidised aromatic rings in aromatic halides and PCBs [879].

[RuCl(dmso)(bpy)$_2$]Cl and **[RuCl(SOMePh)(bpy)$_2$]Cl**, called respectively *rac*-Ru-1 and Δ-Ru-2 by the authors, are made by microwave irradiation of *cis*-$RuCl_2(bpy)_2$ with the the sulfoxide ligands. *Trans*-stilbene, styrene and R-styrene (R=*p*-MeO, α and β-methyl) were epoxidised by $[RuCl(dmso)(bpy)_2]^+$/aq. $Ph(IOAc)_2/CH_2Cl_2$/40°C, while with $[RuCl(SOMePh)(bpy)_2]^+$/ TBHP/water-CH_2Cl_2 *trans*-stilbene, *trans*-β-methylstyrene gave the (*R,R*) epoxides [947].

Ru(dmso)(don)(babp) (babp=dianion of 6,6′-bis(benzoylamino)-2,2′-bipyridyl; don=dmso, imidazole, pyridine, substituted pyridines), made from *cis*-$RuCl_2(dmso)_4$ and the tetradentate square-planar ligand H_2(babp) with (don); ^1H NMR spectra were recorded, and a single crystal X-ray study made on Ru(dmso)(Mepy)(babp). The latter showed that the S-bonded (dmso) and the 4-methylpyridine ligands occupy *trans* positions of the octahedron. The system Ru(dmso)(don)(babp)/PhIO/DCE/40°C epoxidised *cis*-stilbene, *trans*-stilbene and cyclohexene; aldehyde by-products as well as the epoxides were formed. It was suggested that Ru(IV) oxo radicals were involved with (don)=pyridine or substituted pyridines, while Ru(V) oxo intermediates may be implicated with (don)=imidazole [948]. A number of related species Ru(dmso)(don')(babp) with (don')=dmso or heterocycles (e.g. py and substituted py) were similarly prepared and characterised; X-ray crystal structures of the species with don'=dmso, 4-*tert*-pyridine and 4-*N,N*-dimethylaminopyridine) were reported. The reagents Ru(dmso)(don')(babp)/PhIO/DCE/40°C system epoxidised cyclo-octene, *cis*- and *trans*-stilbene and oxidised thioanisole to the sulfoxide and sulfone [949].

$RuCl_2(dmso)_2(pcbo)$ (pcbo=*N*-phenylcarbamoyl derivative, with H, Me, OMe, Cl or NO_2 as a *p*-substituent) is made from *cis*-$RuCl_2(dmso)_4$ and the ligand. As $RuCl_2(dmso)_2(pcbo)$/PhIO/water- CH_3CN it epoxidised norbornene and *cis*-cyclo-octene [950].

[RuCl(dmso)(tpa)](PF_6) and **RuCl(dmso)(BPG)** (tpa=tris(2-pyridylmethyl) amine, BPG=*N,N*-bis(2-pyridylmethyl)glycinate); no preparation was given. The X-ray crystal structure of the (tpa) complex showed sulfur co-ordination from (dmso). As [RuCl(dmso)(tpa)](PF_6) and RuCl(dmso)(BPG)/MCPBA/$CHCl_3$ they catalysed hydroxylation of adamantane [951].

1.9.5 Ru(II) Complexes with -C Donors

Some carbonyl-containing Ru(II) complexes with porphyrin ligands and phosphine ligands have already been mentioned (1.9.2 and 1.9.3 respectively).

[$RuCl_2$(*p*-cymene)]$_2$ The system [$RuCl_2$(*p*-cymene)]$_2$/O_2/$Cs_2(CO_3)$/toluene/100°C oxidised benzylic and allylic alcohols to aldehydes (or secondary alcohols to ketones) without competing double-bond cleavage [952]. As [$RuCl_2$(*p*-cymene)]$_2$/MnO_2/2,6-di-*tert*-butylbenzoquinone/THF/65°C it oxidised non-activated secondary alcohols to ketones; a Ru-alkoxy derivative may be formed which undergoes β-elimination to the ketone and a Ru dihydrido complex. The latter reacts with the quinone to give hydroquinone which is re-oxidised by the MnO_2 and regenerates the Ru catalyst. The complexes $RuCl_2(C_6H_6)(PPh_3)$ and $RuCl_2(PPh_3)_3$ also catalysed the reaction but [$RuCl_2$(*p*-cymene)]$_2$ was by far the most effective [953]. The reagent [$RuCl_2$(*p*-cymene)]$_2$/O_2/$Cs_2(CO_3)$/C_6H_6 oxidised α-hydroxycarbonyl compounds $R^1CH(OH)COR^2$ to diketones R^1COCOR^2: thus benzoin gave benzil [954]. Aerobic oxidation of primary and secondary alcohols was accomplished in ionic liquids as $RuCl_3$ or $RuCl_2(PPh_3)_3$/O_2/$(bmim)^+$/80°C [892].

The system [$RuCl_2$(*p*-cymene)]$_2$/aq. H_2O_2/CH_3CN oxidised silanes $R^1R^2R^3SiH$ to silanols $R^1R^2R^3Si(OH)$ (R^1=H, Ph, PhCH=CH, $CH_3(CH_2)_{17}$, PhCC, ^{n}BuCC, $Cl(CH_2)_3$ or C_6H_9CC, R^2=R^3=Me; R^1=Ph, R^2=R^3=Et, Ph or ^{t}Bu; R^1=R^2=R^3=Et, Ph, ^{t}Bu). A few of these oxidations were effected by [$RuCl_2$(*p*-cymene)]$_2$/O_2/water/80°C. Other catalysts for the reaction include $RuH_2(PPh_3)_4$ and [RuCl(benzene)]$_2$ [955]. Electrochemically Ph_2MeSiH was oxidised to $Ph_2MeSi(OH)$ by [$RuCl_2$(*p*-cymene)]$_2$/water-CH_3CN/Pt disc electrodes [956]. Chelating arenes ArH and cycloalkanes RH were oxidatively cross-coupled to ArR by [$RuCl_2$(*p*-cymene)]$_2$/TBHP/135°C (the reactants were the solvent): thus 2-phenylpyridine and cyclo-octane were cross-coupled. Kinetics and deuterium-isotope effects were measured; no Ru-alkyl intermediates were detected. Other complexes ($Ru(acac)_3$, [$RuCl_2$(COD)]$_2$ and $RuH_2(CO)(PPh_3)_3$) catalysed the reaction [957].

Synthesis of secondary amides via the oxidative coupling (dehydrogenation) of primary alcohols $R^1CH_2(OH)$ and primary amines $R^2(CH_2)NH_2$ to the amides

$R^1C(O)NHCH_2R^2$ was accomplished with $[RuCl_2(p\text{-cymene})]_2$/(dppb)/$Cs_2(CO_3)$/3-methyl-2-butanone/^{t}BuOH/120°C/24h (dppb=bis-(diphenylphosphino)butane). The process is likely to involve oxidation of the alcohol to the aldehyde and formation of an intermediate hemi-aminal, which is oxidised to the amide with elimination of water and return of hydrogen [958].

RuCl(TAZO)(*p*-cymene) ($TAZO^-$=2-methyl-5-oxo-7-phenyl-3-thioxo-3,4,5,6-tetrahydro-2*H*-1,2,4-triazepine; $TAZS^{2-}$=2-methyl-7-phenyl-3, 5-dithioxo-3, 4, 5, 6-tetrahydro-2H-1, 2, 4-triaze-pine). These were made from $[RuCl_2(p\text{-cymene})]_2$ and (TAZO). As RuCl(TAZO)(*p*-cymene)/O_2/Me_2CHCHO/CH_2Cl_2 they epoxidised natural terpenic alkenes (Table 3.1) [959].

Ru(Cp)Cl(PR_3)$_2$ The system Ru(Cp)Cl(*p*-$MeOC_6H_4)_3P]_2$/*N*-hydroxysuccinimide/$Na(HCO_3)$/(*p*-$MeOC_6H_4)_3P$)]/DMF oxidatively cyclised homopropargylic alcohols (1) to δ-lactones (2) and dihydropyrans (3) (Fig. 2.20) [960, 961].

$[RuCl_2(C_6H_6)]_2$ was used for deracemisation of alcohols, by oxidation of secondary alcohols to the ketone with $[RuCl_2(C_6H_6)]_2$/(*R*)-BINAP/(*R,R′*)-DPEN/cyclohexanone/THF/K(^{t}BuO)/60°C. The oxidation may occur by transfer hydrogenation, followed by reduction with H_2 back to the alcohol [962].

$RuCl_2$(COD)(*S,S*)-$R^1_2C(C{=}NCHR^2CR^1_2O)_2$ (COD=cyclo-octa-1,5-diene; R^1=H, R^2=CH_2Ph or ^{i}Pr, R^1=Me, R^2=^{i}Pr) are made from $RuCl_2(COD)(CH_3CN)_2$ with the *bis*hydro-oxazole ligands. The X-ray crystal structure of the benzyl complex showed the chloro ligands to be *trans* (Cl-Ru-Cl angle 160.1(1)°; Ru-Cl 2.45(5), Ru-N 2.16(4), Ru-C 2.20(5) Å). The system $RuCl_2(COD)$(*S,S*)-$R_2{}^1C(C{=}NCHR^2CR_2{}^1O)_2$/$O_2$/aq. $Na(IO_4)$ or TBHP/^{i}PrCHO/DCE epoxidised styrene and *cis*- and *trans*-stilbenes. Mechanistic studies in the presence and the absence of 4-*tert*-butylcatechol as a radical trap suggested that the complexes act as promoters for the formation of Pr^iCO_3H, and that this is responsible for the epoxidation, either directly or via oxo-Ru intermediates [963].

$[RuCl_2(CO)_3]_2$ The oxidative dehydrogenation of α-hydroxy esters RCH(OH)COOR′ and cyanohydrins RCH(OH)(CN) to the corresponding α-keto esters and α-keto nitriles was effected by $[RuCl_2(CO)_3]_2$/TBHP/C_6H_6, and the reaction was also catalysed by $RuBr_3$, $Ru(acac)_3$, $RuCl_2(PPh_3)_3$ and $Ru_3(CO)_{12}$ [695].

$[Ru(CO)_2\{Ph_4(\eta^5\text{-}C_4CO)\}]_2$ The coupled catalytic system of $[Ru(CO)_2\{Ph_4(\eta^5\text{-}C_4CO)\}]_2$ cobalt-salen type complex/O_2/toluene/110°C oxidised secondary amines to aldimines and ketimines [964].

RuCl(chalc)(CO)(EPh_3) and **RuCl(chalc)(CO)(py)** (chalc=2′-hydroxychalconate, made from substituted benzaldehydes and 2-hydroxy-5-methylacetophenone; EPh_3=PPh_3, $AsPh_3$ or (py); these ligands were reacted with $RuHCl(CO)(EPh_3)_3$ or $RuHCl(CO)(PPh_3)_2$(py). Using RuCl(chalc)(CO)(EPh_3) or RuCl(chalc)(CO)(py)/-NMO/PMS/CH_2Cl_2 primary alcohols were oxidised to aldehydes and secondary alcohols to ketones [965, 966].

1.10 Ru(0) Complexes

The only oxidation state not represented in this survey between Ru(VIII) and Ru(0) is Ru(I): the latter and Ru(-I) are the rarest oxidation states of ruthenium, represented mainly by nitrosyl complexes. There are many Ru(0) complexes, mostly containing the carbonyl ligand, but few have been used for oxidation catalysis.

$Ru_3(CO)_{12}$ Rather surprisingly in view of its expense, this has in some cases been used as an oxidant. As $Ru_3(CO)_{12}$/NMO/acetone it oxidised primary alcohols to aldehydes and secondary alcohols to ketones, being as effective in this respect as $RuCl_2(PPh_3)_3$ and more so than $RuCl_3$ [647]. Secondary amines $R^1R^2CHNHR^3$ were oxidised to imines $R^1R^2C{=}NR^3$ by $Ru_3(CO)_{12}$/TBHP/C_6H_6; $RuCl_3$, $RuCl_2(PPh_3)_3$, $RuH_2(PPh_3)_4$ are also effective catalysts for this [902].

$Ru(CO)_3(PPh_3)_2$ As $Ru(CO)_3(PPh_3)_2/O_2/C_6H_6/60°C$ this catalysed the oxidation of cyclohexene to a mixture of products including the epoxide. The reaction was also catalysed by $Ru(acac)_3$, $RuCl_2(PPh_3)_3$, $RuBr_2(PPh_3)_3$, $RuCl_2(SbPh_3)_3$ and by *cis*- and *trans*-$RuCl_2(CO)_2(PPh_3)_2$ [696].

1.11 Appendix: Brief Resumé of Preparations of Ru Oxidants and Oxidation Reactions

In this short section brief experimental details are given for the *in situ* preparations of RuO_4, $[RuO_4]^-$ and $[RuO_4]^{2-}$, the isolation of solid TPAP and of *trans*-$Ru(O)_2(bpy)\{IO_3(OH)_3\}1.5H_2O$. There are also brief notes on specific oxidation procedures using these oxidants with which the author has had some experience. There are several good, practically explicit references in the literature to procedures with Ru oxidants, e.g. that by Haines [51, 202], Courtney [60] and by Lee and van der Engh [203].

All preparations, particularly those involving RuO_4, should be carried out in a fume cupboard. It must be remembered that there is always a potential hazard involved in the handling of high oxidation state ruthenium compounds and of many of their co-oxidants.

1.11.1 Preparations of RuO_4 In Situ for Oxidations

1.11.1.1 The Classic Sharpless Procedure for Oxidations with RuO_4

Although this method is quite old it has stood the test of time, and is the basis of many modern oxidations with RuO_4. Sharpless used it for oxidations of alcohols, ethers, aromatic rings and for alkene cleavage, so clearly it has a high range of applicability.

A representative experiment involved $RuCl_3$ (0.005 g, 0.022 mmol) added to a solution of $Na(IO_4)$ (0.88 g, 4.1 mmol) in water (3 cm^3), CCl_4 (2 cm^3) and CH_3CN

(2 cm^3) with the substrate (1 mmol of *E*-decene in the example given); the mixture was stirred for 2 h [260]. This author recommends pre-dissolution of the $RuCl_3$ in water (*ca.* 3 cm^3) for some 12 h beforehand, and since $Na(IO_4)$ is not very soluble suggests the use of more water, e.g. 10 cm^3.

1.11.1.2 Cleavage of Alkenes with RuO_4

Cyclohexane is more environmentally acceptable than the more commonly-used CCl_4. A recent cleavage of a mono-fluorinated alkene to a ketone was thus effected. The alkene (70 mg, 0.28 mmol) was dissolved in a mixture of acetonitrile (0.5 cm^3) and cyclohexane (0.5 cm^3) and treated with $RuCl_3.nH_2O$ (0.05 g, 0.2 mmol) and $Na(IO_4)$ (0.24 g, 10 mmol) in water (1 cm^3). The mixture was stirred for 1.5 h, the product extracted with diethylether and dried over $MgSO_4$ [330]. Other examples, using $RuCl_3$/aq. $IO(OH)_5/C_6H_{12}$-CH_3CN have been given [216].

1.11.2 Preparations and Use of $[RuO_4]^-$

1.11.2.1 Preparation of TPAP

The reagent is available commercially from a number of suppliers (this is not the case, of course, for RuO_4), but the solid reagent may be simply and cheaply prepared in the laboratory. A pre-made aqueous solution of $RuCl_3$ (0.13 g, 0.5 mmol) in water (5 cm^3) is added to a solution of $Na(BrO_3)$ (6.0 g, 50 mmol) and anhydrous $Na_2(CO_3)$ (1.58 g, 15 mmol) in water (20 cm^3). These solutions are stirred together at room temperature until the typical green colour of $[RuO_4]^-$ appears. An aqueous solution of $(^nPr_4N)OH$ (0.1 g, 0.5 mmol) is then added with stirring; the deep green precipitate extracted into alcohol-free CH_2Cl_2 (50 cm^3), the solution dried over anhydrous $Na_2(CO_3)$, concentrated *in vacuo* and recrystallised from high-grade ethanol-free CCl_4. This gives a yield of some 200 mg (*ca.* 0.5 mmol), sufficient for several catalytic oxidations. The preparation may be scaled up if required [213].

The salt is said to be prone to explosion at temperatures above 60°C although the author has not experienced this. It should not occur since TPAP is normally used at room temperatures, but it should be stored in a refrigerated desiccator.

1.11.2.2 Oxidations with TPAP

The recently published total synthesis of rapamycin involves several steps in which TPAP was used under a variety of conditions [173].

Primary alcohol to aldehyde. The alcohol (2 g, 7.9 mmol) was added to NMO (1.4 g, 11.0 mmol.) with oven-dried 4 Å powdered molecular sieves (PMS) in 1:1 CH_2Cl_2:CH_3CN (40 cm^3) and stirrecd for an hour before addition of TPAP (0.28 g,

0.79 mmol) and the green solution stirred for an hour before Celite filtration, in vacuo concentration and purification [173].

Secondary alcohol to ketone. As a step in the synthesis of avermectin B1a the alcohol (0.024 g, 0.04 mmol) in CH_2Cl_2 with TPAP (0.015 g, 0.004 mmol) and PMS (0.25 g) was mixed with NMO (0.005 g, 0.045 mmol) in CH_2Cl_2 (1 cm^3) and stirred for 1 h under argon, filtered through a Florisil pad and extracted wioth EtOAc [95].

Diol to lactone. To the diol (0.09 g, 0.31 mmol) in CH_2Cl_2 (2.4 cm^3) was added NMO (0.1 g, 0.92 mmol) and 4 Å PMS (0.11 g) and the mixture stirred for 10 min.; solid TPAP (0.01 g, 31.0 μmol) was added in portions, and after 1 h the reaction mixture was purified by flash chromatography [173].

1.11.2.3 Production of $[RuO_4]^-$ in Aqueous Base: the $[RuO_4]^-$ – $(BrO_3)^-$ Reagent

This can be used for oxidations in aqueous base of primary alcohols, aldehydes, activated alkyl halides, *cis*-diols and nitroalkanes to carboxylic acids, and of secondary alcohols and secondary halides to ketones.

A solution of $RuCl_3$ (0.003 g, 0.011 mmol) in water (1 cm^3), prepared some 12 h in advance, is added with stirring to a solution of $Na(BrO_3)$ (1.2 g, 8 mmol) and anhydrous $Na_2(CO_3)$ (0.8 g, 7.5 mmol) in water (10 cm^3). This gives a yellow-green solution of $[RuO_4]^-$ buffered to about pH 11; the electronic spectrum should have bands at 378 and 310 nm [213].

1.11.3 Preparations and Use of $[RuO_4]^{2-}$

This may be used for oxidations in aqueous base of primary alcohols, aldehydes, activated alkyl halides, *cis*-diols and nitroalakanes to carboxylic acids, and of secondary alcohols and secondary halides to ketones.

To a solution of $RuCl_3$ (0.008 g, 0.03 mmol) in water (3 cm^3), prepared some 12 h in advance, is added an aqueous solution of $K_2(S_2O_8)$ (0.7 g, 2.6 mmol) or the more soluble $Na_2(S_2O_8)$ in M KOH or NaOH (50 cm^3) with stirring. This gives a deep orange-red solution of $[RuO_4]^{2-}$ at pH 14; the electronic spectrum should have bands at 466 and 386 nm [213].

1.11.3.1 Oxidation of Amines with Aqueous $[RuO_4]^{2-}$

A useful example is the oxidative dehydrogenation of primary amines to nitriles. The amine (2 mmol) is added dropwise or in small portions to a vigorously stirred solutuion of $[RuO_4]^{2-}$ prepared as above (100 cm^3); the reaction is complete when the dark orange colour of $[RuO_4]^{2-}$ reappears. The solution is extracted with diethylether (3x25 cm^3), dried over $MgSO_4$ and the ether removed [549].

1.11.4 Preparation of trans-$Ru(O)_2(bpy)\{IO_3(OH)_3\}$ $1.5H_2O$ [568]

To a saturated aqueous solution of $Na(IO_4)$ (1.89 g, 9 mmol) is added $RuO_2.nH_2O$ (0.5 g, 4 mmol) suspended in water (5 cm^3). The resulting orange solution containing RuO_4 is added to (bpy) (0.31 g, 2 cm^3) in 1:1 acetone-water (20 cm^3) and stirred for 5 min. The orange product is filtered off.

1.11.4.1 Epoxidation of Alkenes with trans-$Ru(O)_2(bpy)\{IO_3(OH)_3\}1.5H_2O$

The complex (0.012 g, 0.02 mmol) is stirred in water (20 cm^3) at 2°C for 15 min and the alkene (2 mmol) in CH_2Cl_2 (30 cm^3) with $Na(IO_4)$ (3.0 g, 14 mmol) added, and the mixture stirred for 15 h at 2°C. By addition of aqueous M NaOH solution the pH is adjusted to 12 and the mixture extracted with CH_2Cl_2 (4 × 20 cm^3), the extracts combined and dried over anhydrous $MgSO_4$ and the sovent removed [568].

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Chapter 2
Oxidation of Alcohols, Carbohydrates and Diols

Abstract This is one of the most important classes of oxidation effected by Ru complexes, particularly by RuO_4, $[RuO_4]^-$, $[RuO_4]^{2-}$ and $RuCl_2(PPh_3)_3$, though in fact most Ru oxidants effect these transformations. The chapter covers oxidation of primary alcohols to aldehydes (section 2.1), and to carboxylic acids (2.2), and of secondary alcohols to ketones (2.3). Oxidation of primary and secondary alcohol functionalities in carbohydrates (sugars) is dealt with in section 2.4, then oxidation of diols and polyols to lactones and acids (2.5). Finally there is a short section on miscellaneous alcohol oxidations in section 2.6.

In this chapter the first of the two most important categories of oxidations catalysed by Ru complexes (the other being alkene and alkyne oxidations in Chapter 3) are considered. The approach in this and subsequent chapters differs from that of Chapter 1, concentrating here on the substrate rather than on the oxidant. The text is divided into the categories of alcohols and their oxidations. There are summaries in section 2.3.6 of systems of limited applicability which are mentioned only in Chapter 1, and in section 2.3.7 of large-scale (>1 g) oxidations.

The first oxidations of alcohols by stoicheiometric RuO_4/H_2O were reported in 1958, of primary alcohols to aldehydes or carboxylic acids and secondary alcohols to ketones [1]. The first Ru-catalysed oxidation of an alcohol was reported in 1965 when Parikh and Jones used RuO_2/aq. $Na(IO_4)/CCl_4$[1] (Table 2.3) [2] to oxidise secondary alcohol groups in carbohydrates.

Oxidation of alcohols is the most frequently reviewed topic for Ru-catalysed oxidations [3–20]. Mechanisms of alcohol oxidation by Ru complexes have been reviewed [21].

[1]As indicated in 1.2.2 these abbreviations take the form: Ru starting material/co-oxidant/solvent; temperatures are only indicated if not ambient. For brevity, RuO_2 and $RuCl_3$ denote the *hydrates* $RuO_2.nH_2O$ and $RuCl_3.nH_2O$.

W.P. Griffith, *Ruthenium Oxidation Complexes*, Catalysis by Metal Complexes 34,
DOI 10.1007/978-1-4020-9378-4_2, © Springer Science+Business Media B.V. 2011

2.1 Primary Alcohols to Aldehydes (Table 2.1)

$$RCH_2OH + [O] \rightarrow RCHO + H_2O \quad (2.1)$$

This is an overall two-electron oxidation.

Table 2.1 Oxidation of primary alcohols to aldehydes and carboxylic acids

Reactant	Product	Method [Ref.]
For benzyl and cinnamyl alcohols and for geraniol *cf.* 2.1.1 above; for oxidations of aldehydes see 4.1 and Table 4.1		
Allyl alcohol	Acrylic acid	A [40]
Mandelic acid	Benzoic acid	A [40]
n-Butanol	*n*-Butanal	B [16, 31]
2-Chlorobenzyl alcohol	2-Chlorobenzaldehde	B [14, 16, 31]
Chrysanthemyl alcohol	Chrysanthemaldehyde	B [14, 16, 31]; C [29]
Citronellol	Citronellal	B [16, 31]; C [29], D [41]
Cyclohex-3-enylmethanol	Cyclohexene-3-carboxylic acid	A [40]
Cyclohexylmethanol	Cyclohexanecarboxylic acid	E [33]
1-Decanol	Decanal	D [41]
1-Dodecanol	1-Dodecanal	D [41]
3,4-Dimethoxybenzyl alcohol	3,4-Dimethoxybenzaldehyde	B [14, 31], F [69]
3,4-Dimethoxybenzyl alcohol	3,4-Dimethoxybenzoic acid	A [121], G [121]
2-Hydroxymethyl-3-phytyl-1,4-napthoquinone 2,3-epoxide	2-Formyl-3-phytyl-1,4-napthoquinone 2,3-epoxide	B [48]
1-Heptanol	Heptanal	H [34]
3-Hydroxybenzyl alcohol	3-Hydroxybenzaldehyde	D [41]
E-Crotyl alcohol	β-Methacrylic acid	A [40]
4-Methoxybenzyl alcohol	4-Methoxybenzoic acid	A [40]
3-Methyl-2-buten-1-ol	3-Methyl-2-buten-1-al	J [36]
4-Methoxybenzyl alcohol	4-Methoxybezyaldehyde	B [14, 31]; C [29]
4-Nitrobenzyl alcohol	4-Nitrobenzoic acid	A [40, 121], G [121], K [122]
n-Nonanol	Nonanoic acid	A [40]
1-Octanol	1-Octanal	J [36, 37]
1-Octanol	Octanoic acid + octyl octanoate	E [33]
1-Octanol	Octanoic acid	L [25], M [39]
2-Phenyl-1-propanol	2-Phenyl-1-propanal	H [34]
Piperonyl alcohol	Piperonaldehyde	B [14, 16, 31]; C [29]
Piperonyl alcohol	Piperonylic acid	A [121], G [121]
o-Methylbenzyl alcohol	*o*-Toluic acid	A [121], G [121]
Undec-10-en-1-ol	Undec-10-en-1-al	B [16, 31]

A: $RuCl_3/K_2(S_2O_8)$/aq. M KOH [40, 121]; B: TPAP/NMO/PMS/CH_2Cl_2 [14] (Fig. 2.2) [16, 48], or TPAP/NMO/CH_2Cl_2 [31]; C: $[Ru(O)_2Cl_3]^-$/NMO/PMS/CH_2Cl_2 [29]; D: $RuCl_2(PPh_3)_3$/NMO/acetone [41]; E: RuO_2/aq. NaCl @ pH 7/CCl_4/Pt electrodes [33]; F: (PSP)/CH_3CN/THF/70°C [69]; G: $RuCl_3/Na(BrO_3)$/aq. M $Na_2(CO_3)$ [121]; H: RuO_2/aq. $Na(IO_4)/CCl_4$ [34]; J: $RuCl_2(PPh_3)_3$/TEMPO/O_2/C_6H_5Cl/100°C (Fig. 1.41) [36, 37]; K: $RuCl_3/K_2(S_2O_8)$/aq. M KOH [122]; L: $RuCl_3$/TCCA/($^nBu_4N$)Br/aq. $K_2(CO_3)/CH_3CN$ [25]; M: $RuCl_3/CH_3O_3H$ or MCPBA/EtOAc [39].

2.1.1 Model Substrates

Two of the commonest models are benzyl and cinnamyl alcohols – the former because it is easily oxidised beyond benzaldehde to benzoic acid and the latter because its double bond is often attacked, so that oxidation to cinnamaldehyde would show that the oxidant is mild enough to avoid competing double-bond attack. Geraniol is also included as a model substrate as it is in the same category as cinnamyl alcohol. Since there are so many examples of studies on their oxidations a limited selection only is given.

Benzyl alcohol, *$PhCH_2OH$, to PhCHO*. TPAP/NMO/[bmim](BF_4) [22, 23]; $RuCl_3$/aq. NaCl-CCl_4/Pt anode [24]; $RuCl_3$/TCCA/($^nBu_4N$)Br/aq. $K_2(CO_3)$/CH_3CN (Fig. 2.14) [25]; $RuCl_3$ or RuO_2/($^nBu_4N$)Cl/aq. H_2O_2/CH_2Cl_2/60°C [26]; PSP/O_2/toluene/75°C [27]; TPAP/O_2/PMS/CH_2Cl_2 [28]; TPAP/NMO/PMS/CH_2Cl_2 [14, 16]; $[Ru(O)_2Cl_3]^-$/NMO/PMS/CH_2Cl_2 [29]; $[RuO_4]^{2-}$/aq. $K_2(S_2O_8)$/Adogen®/CH_2Cl_2 [30]; TPAP/NMO/PMS/CH_2Cl_2 [31]; $RuCl_3$/aq. Na(BrO_3)/($^nBu_4N$)Br/CH_2Cl_2 [32]; RuO_2/aq. NaCl-Na(H_2PO_4) @ pH 4/Pt electrodes [33]; RuO_2/aq. Na(IO_4)/CCl_4 (Table 2.1) [34].

Cinnamyl alcohol, *$PhCH{=}CHCH_2OH$ to $PhCH{=}CHCHO$* $RuCl_3$/TCCA/($^nBu_4N$)Br/aq. $K_2(CO_3)$/CH_3CN (Fig. 2.14) [25]; TPAPORM/O_2/toluene/75°C [35]; TPAP/NMO/[bmim](BF_4) [22, 36]; $RuCl_2(PPh_3)_3$/TEMPO/air (10 bar)/C_6H_5Cl/100°C (Fig. 1.40, Table 2.1; *cf.* mech. Ch. 1) [36–38]; PSP/O_2/toluene/75°C [27]; TPAP/O_2/PMS/CH_2Cl_2 [28]; TPAP/NMO/PMS/CH_2Cl_2 [14, 16]; $[Ru(O)_2Cl_3]^-$/NMO/PMS/CH_2Cl_2 [29]; $[RuO_4]^{2-}$/aq. $K_2(S_2O_8)$/Adogen®/CH_2Cl_2 [30]; TPAP or TBAP/NMO/CH_2Cl_2 [31].

Geraniol to citral $[Ru(O)_2Cl_3]^-$/NMO/PMS/CH_2Cl_2 [29]; $RuCl_3$/aq. Na(BrO_3)/($^nBu_4N$)Br/CH_2Cl_2 [32]; $RuCl_2(PPh_3)_3$/TBHP/acetone [39]; stoich. *trans*-$Ba[Ru(OH)_2(O)_3/CH_2Cl_2]$ (Table 2.1) [40]; $RuCl_2(PPh_3)_3$/NMO/acetone [41].

2.1.2 Specific Examples

2.1.2.1 Primary Alcohols to Aldehydes

Typical examples are listed in Table 2.1. A few oxidations are effected by RuO_4 but in general it is too powerful an oxidant for this purpose. The system $RuCl_3$/aq. NaCl–CCl_4/Pt anode oxidised benzyl alcohol to benzaldehyde and benzoic acid and *p*-anisaldehyde to *p*-anisic acid [24], and a wide range of primary alcohols and aldehydes were converted to carboxylic acids, secondary alcohols to ketones, 1,*n*-diols to lactones and keto acids from RuO_2/aq. NaCl @ pH 4/Na(H_2PO_4)/Pt electrodes (Tables 2.1–2.4). The system $[RuO_4]^{2-}$/aq. $K_2(S_2O_8)$/Adogen®/CH_2Cl_2 oxidised benzylic alcohols to aldehydes [30].
The oxidation catalyst TPAP (($^nPr_4N$)$[RuO_4]$) (*cf.* 1.3.4) is extremely useful as an oxidant of primary alcohols to aldehydes and secondary alcohols to ketones without

competing double-bond cleavage (Tables 2.1 and 2.2); its uses as an oxidation catalyst have been reviewed [14, 16, 42–45]. It seems to be more effective at oxidising primary than secondary alcohols: in competition experiments a 1:1 mixture of $Me(CH_2)_7OH$ with $Me(CH_2)_3CH(OH)(CH_2)_2Me$ gave 85% of $Me(CH_2)_6CHO$ and 15% of $Me(CH_2)_3CO(CH_2)_2Me$ using TPAP/NMO/PMS/CH_2Cl_2 [46]. In a substrate containing both primary and secondary alcohol functions the system preferentially oxidised the primary group to the unstable hydroxyaldehyde in the presence of a secondary alcohol (Fig. 2.1) [47].

Epoxy alcohols were oxidised by TPAP/NMO/PMS/CH_2Cl_2 without affecting the epoxy group; Fig. 2.2 also illustrates the tolerance of the system to alkenes (Tables 2.1 and 2.2) [16].

There are other examples of the tolerance of TPAP/NMO/PMS/CH_2Cl_2 to epoxy linkages, e.g. [48] (Table 2.1) with examples of epoxy-group tolerance for secondary alcohol oxidations (2.3.2) [49–51]; and by TPAP/NMO/PMS/CH_2Cl_2–CH_3CN [52]; (Fig. 2.7) [53]. In one such example TPAP/NMO/PMS/CH_2Cl_2 succeeded when a wide variety of other reagents failed, e.g. the Swern reagent, Collins' reagent, DMSO, (pyH)[CrO_3Cl] (Fig. 2.8). [54]. The reagent does not affect μ-peroxo linkages [55] (Fig. 2.4), and is tolerant to such sensitive functional groups as well as to double bonds, polyenes, halides, enones, tetrahydropyranyl, cyclopropanes, acetyls, peroxides, catechols, and most protecting groups [14].

The system TPAP/NMO/PMS/CH_2Cl_2 oxidised many primary alcohols to aldehydes, e.g. as steps in the synthesis of natural products (*cf.* 2.1.3), and also for monosilylated alcohols [56], epoxyiodoalcohols [57], allylic alcohols [47, 58],

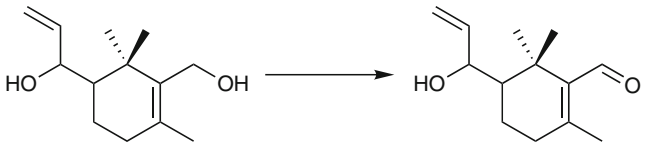

Fig. 2.1 Preferential oxidation by TPAP/NMO of a primary alcohol over a secondary alcohol group [47]

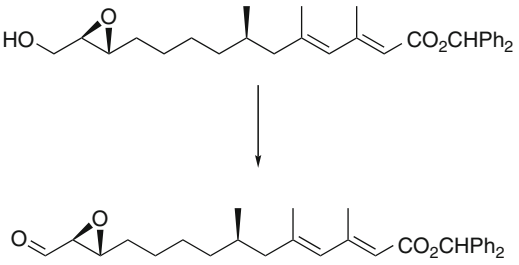

Fig. 2.2 Oxidation of a primary long-chain alcohol by TPAP with retention of its epoxy linkage [16]

aminosugars [59, 60]; substituted 2,3,4,-(5),6-hydroxypyridines [61], lanost-7-en-ols [62]; chiral α-cyclopropylketones [63]. The system TPAP/NMO/PMS/CH_3CN is increasingly used [16, 64, 65], as is TPAP/NMO/PMS/CH_2Cl_2-CH_3CN [52, 66].

Various forms of supported TPAP, though not really homogeneous catalysts, have been used to oxidise primary alcohols to aldehydes (*cf.* 2.1.3 and 1.1.5 for natural products). The reagent stoich. PSP/CH_2Cl_2 effected a number of these [67, 68], as stoich. PSP/CH_3CN-THF (Table 2.1) [69], and catalytically as PSP/O_2/toluene/75°C [27] or Si-TPAP/O_2/toluene/80°C [70]. Oxidations of both primary alcohols to aldehydes and of secondary alcohols to ketones were effected by PSP/NMO or Me_3NO/CH_2Cl_2 [71]; TPAPSIL/PMS/H_2O_2/ether [72]; Si-TPAP/O_2/toluene/75°C [35], and the polymer supported co-oxidant *N*-oxide PNAO (=poly-*N*-methylmorpholine--*N*-oxide) as TPAP/PNAO/CH_2Cl_2 [73]. Two bimetallic systems, TPAP/Cu_2Cl_2/PMS/O_2/2-aminopyridine/CH_2Cl_2 [74], and TPAP/CuCl(phen)/O_2/1,2-bis(ethoxycarbonyl)-hydrazine/toluene/75°C [75] oxidised primary and secondary alcohols. A mobile microreactor using TPAP/NMO/CH_3CN or TPAPAl_2O_3/O_2/mesitylene/75°C oxidised benzyl alcohol to benzaldehyde [76].

For natural product syntheses involving alcohols to acids *cf.* 2.1.3 below; for large-scale oxidations *cf.* 2.3.7. For other examples of primary alcohol to aldehyde oxidations cited in Ch. 1 *cf.* 2.3.6.

2.1.3 Natural Product/Pharmaceutical Syntheses Involving Primary Alcohol Oxidations

The systems TPAP/NMO/PMS/CH_2Cl_2 or TPAP/NMO/PMS/CH_2Cl_2–CH_3CN have been used for parts of the syntheses of such species. Thus TPAP/NMO/PMS/CH_2Cl_2 was used for two such steps in the synthesis of the phytohormone abscisic acid [77]; synthesis of the antitumour styryllactone (+)-altholactone involved a lactol to lactone step [78]; one step in the synthesis of the macrolide altohyrtin A [79]; the cytotoxic benzolactone enamide apicularen A [80]; the anti-parasitic avermectin-B1a (Fig. 2.6) – this also involved oxidation of a secondary alcohol [81, 82]; the AChE inhibitor (+)-arisugacin A and B (secondary alcohol to ketone step also) [83]; the eunicellin astrogorgin [84]; the antibiotic (−)-borrelidin (two such steps involved) [85]; the neurotoxin brevetoxin B [86, 87]; the toxic metabolite (−)-epicylindrospermine [88]; the anti-growth factor 2-epibotcinolide (lactone to ketolactone TPAP oxidation also involved) [89], the antifungal gambieric acids A and C (there is also a secondary alcohol to ketone TPAP-catalysed step) [90]; the ether toxin gambierol (two such steps; also a secondary alcohol to ketone) [91]; the cytotoxic gymnocin-A (also three secondary to ketone steps) [92]; the acetogenin 10-hydroxyasimicin [93] and the xenicane diterpene 4-hydroxydictyolactone [94]. A step in the synthesis of the antitumour agent irisquinone involved the oxidation by TPAP/NMO/PMS/CH_2Cl_2 of 10-[3′-methoxy-2′-(methoxymethoxy)phenyl]-decan-1-ol to the aldehyde (Fig. 2.3) [95].

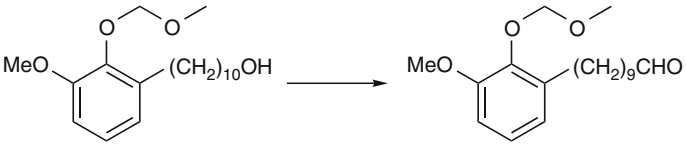

Fig. 2.3 Formation of an aldehyde intermediate with TPAP in the synthesis of irisquinone [95]

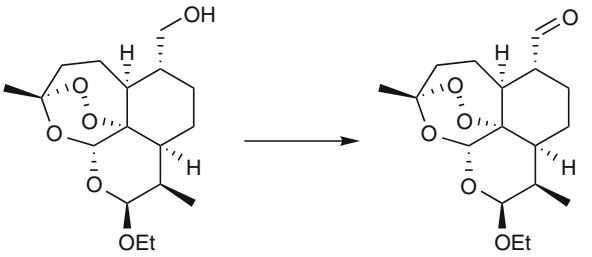

Fig. 2.4 Oxidation by TPAP/NMO of an *endo*peroxidic alcohol, 14-hydroxyarteether [55]

The reagent TPAP/NMO/PMS/CH_2Cl_2 was also used in a step in the synthesis of the colony-stimulating factor leustroducsin B (TPAP) [96]; for the antiparasitic spiroketal macrolide (+)-milbemycin α_1 [97]; the antiparasitic insecticide (+)-milbemycin-β_1 (secondary alcohol to a ketone step also) [98]; the sesquiterpenes nortrilobolide, thapsivillosin F and trilobolide (a second step involving the reagent was a lactol-to-lactone transformation) [64]; the marine alkaloid norzoanthamine (secondary alcohol to ketone step also) [99]; the eunicellin ophirin B [84]; the biologically active diterpene phomactin A [100]; the macrolide prelactone B (primary alcohol to lactone) [101]; the spiroketal ionophore antibiotic routiennocin [102, 103]; the macrolides salicylihalamides A and B [104]; the anti-tumour microtubulin stablising agents sarcodictyins A and B [105]; the polypropionate siphonarienolone [106]; the antibiotic (+)-tetronomycin [107], and the aglycon of the antitumour antibiotic tetronolide [108]. During synthesis of the protein phosphatase inhibitor okadaic acid three oxidations with TPAP/NMO/PMS/CH_2Cl_2 were used, two of a primary alcohol to aldehydes and one of a diol to a lactone [109]; the reagent was used in the synthesis of a fragment of the antibiotic sorangicin A [110].

For a synthesis of the anti-cancer drug taxol® TPAP/NMO was used in three steps, two for oxidation of primary alcohols to aldehydes (by TPAP/NMO/PMS/CH_2Cl_2) and one for a secondary alcohol to ketone (by TPAP/NMO/PMS/CH_2Cl_2-CH_3CN) [66], *cf.* also [111]; and for the SERCA inhibitor thapsigargin (two primary alcohol and one secondary alcohol oxidation steps) [112]. This system was also used during synthesis of the cholesterol biosynthesis inhibitor 1233A [52], the antibiotic and anti-parasitic ionophore tetronasin [113, 114] and for the cytotoxic sponge alkaloids motopuramines A and B [115].

In oxidations by TPAP/NMO/PMS/CH_2Cl_2 for the anti-malarial 14-[2H]-arteether (Fig. 2.4) the μ-peroxo linkage is retained [55].

Some syntheses involved TPAP supported on a polymer, including stoich. PSP/THF [69] and PSP/CH_2Cl_2 [116] which were used for part of a synthesis of the analgesic (±)-epibatidine [117] and the alkaloid (±)-oxomaritidine [69]; stoich. PSP/CH_2Cl_2 for the alkaloid (±)-epimaritidine [116] and, as PSP/O_2/toluene/110°C, for the cytotoxic antitumour epothilone C [118].

For natural product syntheses involving alcohols to acids *cf.* 2.2 below; for large-scale oxidations *cf.* 2.3.7; for oxidation of aldehydes to carboxylic acids *cf.* alkanes, 4.1.1.

2.2 Primary Alcohols to Carboxylic Acids (Table 2.1)

$$RCH_2OH+2[O] \rightarrow RCOOH + H_2O \qquad (2.2)$$

This is a four-electron oxidation.

2.2.1 Model Substrates

As before, benzyl and cinnamyl alcohols are taken as exemplars.

Benzyl alcohol, *$PhCH_2OH$, to PhCOOH*. $RuCl_3$/aq. H_2O_2/AcOH/80°C [119]; $RuCl_3$/TCCA/($^nBu_4N$)Br/aq. $K_2(CO_3)$/CH_3CN (Fig. 2.14) [25]; $RuCl_3$/$[Fe(CN_6]^{3-}$/aq. M NaOH [120]; $RuCl_3$/$Na(BrO_3)$/aq. M $Na_2(CO_3)$ [121]; $RuCl_3$/$K_2(S_2O_8)$/aq. M KOH [40, 121]; RuO_2/aq. NaCl @ pH 7/Pt electrodes [33]; $RuCl_2(PPh_3)_3$/TBHP/acetone [39] and $RuCl_3$/$K_2(S_2O_8)$/aq. M KOH [122].

Cinnamyl alcohol, *$PhCH{=}CHCH_2OH$ to $PhCH{=}CHCOOH$*. $RuCl_3$/$[Fe(CN_6]^{3-}$/aq. M NaOH [120]; $RuCl_3$/$Na(BrO_3)$/aq. M $Na_2(CO_3)$; $RuCl_3$/$K_2(S_2O_8)$/aq. M KOH [121] and $RuCl_3$/$K_2(S_2O_8)$/aq. M KOH [40, 122].

Unlike the situation for oxidation of primary alcohols to aldehydes and secondary alcohols to ketones, TPAP rarely catalyses reactions in this category. However $[RuO_4]^{2-}$ in the admittedly constrained medium of aqueous base is effective, e.g. $RuCl_3$/$K_2(S_2O_8)$/aq. M KOH (generating $[RuO_4]^{2-}$) and also $RuCl_3$/$Na(BrO_3)$/aq. M $Na_2(CO_3)$ (generating $[RuO_4]^{-}$) (Table 2.1) [121]; $RuCl_3$/$K_2(S_2O_8)$/aq. M NaOH [40] and $RuCl_3$/$K_2(S_2O_8)$/aq. M KOH [122]. The 2,3-epoxy alcohols $R^1R^1C(O)CHCH_2OH$ were oxidised by $RuCl_3$/aq. $IO(OH)_5$/CCl_4–CH_3CN to the 2,3-epoxy acids $R^1R^1C(O)CHCOOH$ (R^1=H, R^2=$^nC_7H_{13}$, ^{t}BuPh$_2$SiOCH$_2$, *o*-C_6H_{11}) [123]; $PhCH_2CH(O)CHCH_2OH$ was oxidised to $PhCH_2CH(O)CHCOOH$ by $RuCl_3$/aq. $Na(IO_4)$/CCl_4-CH_3CN [124].

A few syntheses of natural products or pharmaceuticals involving the conversion of primary alcohols to carboxylic acids have been reported. The system $RuCl_3$/aq. $NaIO_4/CCl_4$–CH_3CN was used as part of the total synthesis of the polycyclopropane antiobiotic FR-900848 [125]. Stoicheiometric $[RuO_4]^{2-}$/aq. 0.01 M KOH was used for a step in the synthesis of the growth factor gibberellic acid [126]; the pathogenetic agent mycocerosic acid was prepared *via* a primary alcohol to carboxylic acid step by $RuCl_3$/aq. $Na(IO_4)/CCl_4$–CH_3CN [127] and a similar procedure used for part of the total synthesis of the alkaloid (+)-laccarin [128]. Oxidation of a 2,3-epoxy alcohol to the corresponding acid was effected by $RuCl_3$/aq. $Na(IO_4)/CCl_4$–CH_3CN during the synthesis of the naturally occurring toxin verrucarin A [129]. The reagent TPAP/NMO/PMS/CH_2Cl_2 was used to make the immunosuppressive agent antascomicin B [130], and a step in the synthesis of the microbial metabolite (+)-SCH 351448 involved oxidation of a primary alcohol to an acid also used the reagent [131].

For other examples of alcohol to carboxylic acid oxidations in Ch. 1 *cf.* 2.3.6.

2.3 Secondary Alcohols to Ketones or Lactones

$$R_2CHOH+[O] \rightarrow R_2CO + H_2O \qquad (2.3)$$

2.3.1 Model Substrates

Cyclohexanol, α-tetralol and 2-propanol are often used as models for secondary alcohols.

Cyclohexanol *to cyclohexanone*. $RuCl_3$/aq. H_2O_2/AcOH/80°C [119]; TPAP/NMO/[bmim](BF_4) [22]; $RuCl_3/[Fe(CN_6]^{3-}$/aq. M NaOH [120]; $[RuO_2Cl_3]^-$/NMO/PMS/CH_2Cl_2 (Table 2.2) [29]; $RuCl_2(PPh_3)_2$(acac)/NMO/CH_2Cl_2 [132]; $RuCl_3/Na(BrO_3)$/aq. $Na_2(HPO_4)$/Aliquat®/$CHCl_3$ (Table 2.2) [133]; $RuCl_2(PPh_3)_3$/TBHP/acetone [39]; $RuCl_3/K_2(S_2O_8)$/aq. M KOH [122] and $RuCl_3$/aq. $Na(IO_4)/CCl_4$ (Table 2.2) [34].

α-Tetralol *to α-tetralone* $[RuO_2Cl_3]^-$/NMO/PMS/CH_2Cl_2 [29]; $RuCl_3/[Fe(CN_6]^{3-}$/aq. M NaOH [120]; $RuCl_3/Na(BrO_3)$/aq. M $Na_2(CO_3)$ [121]; $RuCl_3/K_2(S_2O_8)$/aq. M KOH [121]; $RuCl_3/K_2(S_2O_8)$/aq. M KOH [122].

2-Propanol *to acetone*: $RuCl_3/[Fe(CN_6]^{3-}$/aq. M NaOH [120]; stoich. *trans*-$Ru(O)_2$(TMP)/C_6H_6 [134]; $[RuCl(dppp)_2]^+$/aq. Oxone®/CH_2Cl_2 [135]; *cis*-$[Ru(H_2O)_2(Cl_2bpy)_2]^{2+}/CF_3COOH$/Pt electrodes [136]; $RuCl_3$/aq. $Na(BrO_3)/Na_2(HPO_4)$/Aliquat®/$CHCl_3$ [133] and *trans*-$[Ru(O)_2(dpt)]^{2+}/CH_3CN$/UV > 330 nm [137].

Table 2.2 Oxidation of secondary alcohols to ketones

Reactant	Product	Method [Ref.]
For 2-propanol, cyclohexanol, α-tetralol and 2-propanol see 2.2.1 above.		
1-Phenylethanol	Acetophenone	A [39]
5α-Androstan-17β-ol-3-one	5α-Androstan-3,17-dione	B [14, 16, 31]
Benzoin	Benzil	C [25]
Benzhydrol (diphenylmethanol)	Benzophenone	C [25], D [120], E [30] F, G [121]
Diphenylcarbinol	Benzophenone	H [33]
Endo-Norborneol	Bicyclo[2.2.1]heptan-2-one	B [14, 31]
Butan-2-ol	Butanone	D[120]
Borneol	Camphor	B [31]
d-Carveol	*d*-Carveone	J [32], K [41]
Cholesterol	Cholest-4-ene-3,6-dione	L [158]
Cyclobutanol	Cyclobutanone	B [14, 16, 31]
Cyclododecanol	Cyclododecanone	A [39] H [33], J [32]
Cycloheptanol	Cycloheptanone	F, G [121]
Cyclo-octanol	Cyclo-octanone	H [33], M [133]
Cyclopentanol	Cyclopentanone	C [25], M [133], N [29]
Decan-2-ol	Decan-2-one	D [120]
1,1-Dichloro-2-octanol	1,1-Dichloro-2-octanone	H [33]
11-Dodecen-2-ol	11-Dodecen-2-one	J [32]
Ethyl 3-hydroxycyclobutane carboxylate	Ethyl 3-ketocyclobutane caarboxylate	P [34]
Pantolactone	Ketopantoyl lactone	C [25]
Lanost-8-en-3β-ol	Lanost-8-en-3β-one	B [14, 16, 31]
l-Menthol	*l*-Menthone	B [14, 16]; D [120], J [32]
Methyl mandelate	Methylphenylglyoxalate	Q [40]
2-Nitro-3-nonanol	2-Nitro-3-nonanone	H [33]
Norborneol	Norcamphor	B [14, 16, 31]; J [32]
2-Octanol	2-Octanone	A [39], C [25], H [33]

(continued)

Table 2.2 (continued)

Reactant	Product	Method [Ref.]
1-Phenyl-1-propanol	Phenylethylketone	H [33]
Propan-2-ol	Propan-2-one	D [120]
2-Tetradecanol	2-Tetradecanone	H [33]
2,5,5-Trimethylcyclohexanol	2,5,5-Trimethylcyclohexanone	H [33]
(2*E*,4*E*,6*R*,10*S*)-4,6,10-trimethyl-2,4-dodecadien-7-ol	(2*E*,4*E*,6R,10*S*)-4,6,10-tri-methyl-2,4-dodecadien-7-one	B[190]
(2*E*,4*E*,6R,7*R*,10*R*)-4,6,10-trimethyl-2,4-dodecadien-7-ol	(2*E*,4*E*,6R,10*R*)-4,6,10-trimethyl-2,4-dodecadien-7-one(6*R*,10*R*)	B [190]

A: $RuCl_2(PPh_3)_3$/TBHP/acetone [39]; B: TPAP/NMO/PMS/CH_2Cl_2 [14, 16, 31, 190], C: $RuCl_3$/TCCA/($^nBu_4N$)Br/aq. $K_2(CO_3)$/CH_3CN (Fig. 2.14) [25]; D: $RuCl_3$/$[Fe(CN_6]^{3-}$/aq. M NaOH [120]; E: $[RuO_4]^{2-}$/aq. $K_2(S_2O_8)$/Adogen®/CH_2Cl_2 [30]; F: $RuCl_3$/$Na(BrO_3)$/aq. M $Na_2(CO_3$ [121]; G: $RuCl_3$/$K_2(S_2O_8)$/M aq. KOH [121]; H: RuO_2/aq. NaCl–$Na(H_2PO_4)$ @ pH 4/Pt electrodes [33]; J: $RuCl_3$/aq. $Na(BrO_3)$/($^nBu_4N$)Br/CH_2Cl_2 [32]; K: $RuCl_2(PPh_3)_3$/NMO/acetone [41]; L: TPAP/NMO/PMS/CH_2Cl_2 [158]; M: $RuCl_3$/$Na(BrO_3)$/aq. $Na_2(HPO_4)$/Aliquat®/$CHCl_3$ [133]; N: $[Ru(O)_2Cl_3]^-$/NMO/PMS/CH_2Cl_2 [29]; P: $RuCl_3$/aq. $Na(IO_4)$/CCl_4 [34]; Q: $RuCl_3$/$K_2(S_2O_8)$/aq. M KOH [40].

2.3.2 Specific Examples

Some typical examples of secondary alcohol to ketone oxidations are listed in Table 2.2. Early work was carried out by Corey et al. on the oxidation by stoich. RuO_4/Freon-11 (CF_3Cl) of norborneol to norcamphor [138], and stoich. RuO_4/CCl_4 was used for oxidation of steroidal alcohols to ketones (e.g. β-cholestanol to cholestanone, 5α-pregnane-3β,20β-diol to 5α-pregnane-3,20-dione, cholestane-3β,6β-diol 3-acetate to cholestane-3β-ol-6-one, 5α-androstane-3α-ol-17-one and 5β-androstane-3-ol-17-one to the 3,17-diones) [20, 139]. A chiral (Ru(NO)(salen^{chir}) complex was used as Ru(NO)Cl(salen^{chir})/O_2/UV/C_6H_5Cl to oxidise racemic secondary alcohols RCH(OH)MeOH to the ketones (R=$PhCH_2$, PhCC, (*E*)-PhCH=CH, 4-ClC_6H_4, 4-BrC_6H_4) in the presence of 1,3-bis(*p*-bromophenyl)propane-1,3-dione; e.e. values of 55–99% were achieved [140]. Apart from TPAP, effective systems for oxidation of secondary alcohols to ketones include $RuCl_3$/[$Fe(CN_6]^{3-}$/aq. M NaOH [120]; $RuCl_3/K_2(S_2O_8)$/aq. M KOH (generating $[RuO_4]^{2-}$) and $RuCl_3$/$Na(BrO_3)$/aq. M $Na_2(CO_3)$ (generating $[RuO_4]^-$) [121], and $RuCl_3/K_2(S_2O_8)$/aq. M KOH (Table 2.2) [40, 122]. Oxidation of octan-2-ol to octan-2-one by RuO_2/aq. $Na(BrO_3)/CCl_4$ was studied with respect to mixing speeds and sonication. The latter is an effective technique for increasing yields of products [141, 142]. Oxidation of desethermuscarine with $RuCl_3$/aq. Na(ClO) gave the (±)-desethermuscarone trimethylammonium epimer cations (Fig. 2.5) [143].

The oxidation catalyst TPAP (($^nPr_4N$)[RuO_4]) was used as TPAP/NMO/PMS/CH_2Cl_2 for a number of oxidations of secondary alcohols to ketones (Table 2.2). Many reactions involving TPAP/NMO/PMS/CH_2Cl_2 effected the secondary alcohol-to-ketone reaction, e.g. as steps in the synthesis of natural products (*cf.* 2.3.3) and including pyranones [144], sialyl alcohols [145], glucals [146], pyrrolidinones [147], bicyclic ketones [148], acetals [149], synthesis of a vinyl oxirane [49], 3-alkylcyclopentenones [150] and hydroxycyclopentene [151]. Examples of lactol-to-lactone oxidations effected by TPAP/NMO/PMS/CH_2Cl_2 include a step for thapsigargin syntheses [152, 153], and TPAP/NMO/PMS/CH_3CN [64] for a tetrol to lactone oxidation [152]. The supported reagent Si-TPAP/O_2/toluene or supercritical CO_2/75°C oxidised secondary alcohols to ketones [154]; for oxidations using supported TPAP for secondary and primary alcohols *cf.* 2.1.2.

Some oxidations used the system TPAP/NMO/PMS/CH_3CN (*cf.* 2.4.2.2, Fig. 2.17) [155], *cf.* mech. Ch. 1 [156], or TPAP/NMO/CH_2Cl_2-CH_3CN/PMS [66]. In one instance TBAP/NMO/PMS/CH_2Cl_2 (rather than TPAP) was used for an oxidation in which a triple bond was affected by an oxidation involving 2-propargyloxy-cyclopentanone with a –CH_2CCH substituent [157].

The aerobic system TPAP/O_2/PMS/CH_2Cl_2 was used to oxidise primary and secondary alcohols [28]. Oxidation of secondary alcohol functions in 3β-hydroxy-Δ-cholestenes,

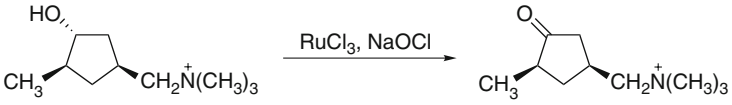

Fig. 2.5 Oxidation of (±)-desethermuscarine by RuO_4 [143]

-pregnenes and -androstenes to the corresponding Δ^4-3,6-diones was accomplished with TPAP/NMO/PMS/CH_2Cl_2 using ultrasonic techniques (simply a conventional laboratory sonochemical cleaning bath) [158]. Homopropargylic alcohols were oxidised to allenic ketones by TPAP/NMO/PMS/CH_2Cl_2 during a total synthesis of the tumour-inhibitory tobacco constituents α- and β-2,7,11-cembratriene-4,6-diol [159], and there are other examples of the TPAP-catalysed oxidations of allylic alcohols to enones using this system [160–162]. The reagent $[RuCl_2(p\text{-cymene})]_2/O_2/Cs_2(CO_3)/C_6H_6$ oxidised hydroxycarbonyl compounds $R^1CH(OH)COR^2$ (R^1=R^2=Ph, pMeC$_6$H$_4$, p-ClC$_6$H$_4$, pMeOC$_6$H$_4$; R^1=Ph, R^2= pMeOC$_6$H$_4$; R^1=Ph, R^2=C$_6$H$_{10;}$ R^1=C$_6$H$_{10}$, R^2=Ph; R^1=Ph, R^2=OEt; R^1= p-BrC$_6$H$_4$, R^2=OEt) to diketones $R^1(CO)(CO)R^2$: thus benzoin gave benzil [163]. Primary alcohols were oxidised to aldehydes and secondary alcohols to ketones by $RuCl_3/O_2$/water/90°C; the (*R*)-phenylethanol enantiomer was racemised [164]. The system $[RuO_2Cl_3]^-$/NMO/PMS/CH_2Cl_2 oxidised primary alcohols to aldehydes and secondary alcohols to ketones without competing double-bond cleavage (Tables 2.1 and 2.2) [29], *cf.* mech. Fig. 1.19 [165].

For other examples of secondary alcohol to ketone oxidations in Chapter 1 *cf.* 2.3.6.

2.3.3 Natural Product/Pharmaceutical Syntheses Involving Secondary Alcohol Oxidations

Most Ru-catalysed oxidations of secondary alcohol to ketone steps involve TPAP; one that does not is a stage in the industrial preparation of the inhibitor thrombin, which used $RuCl_3$/aq. Na(BrO_3)/CH_3CN [166].

Several syntheses of natural products and pharmaceuticals involving the conversion of secondary alcohols to ketones using TPAP/NMO/PMS/CH_2Cl_2 or TPAP/NMO/PMS/CH_2Cl_2 have been reported. A key early example using TPAP/NMO/PMS/CH_2Cl_2 for conversion of a secondary alcohol to a ketone intermediate was for the anti-parasitic avermectin-B1a (Fig. 2.6; *cf.* 1.11) [81, 167].

Other procedures using TPAP/NMO/PMS/CH_2Cl_2 include steps in the synthesis of (+)-altholactone (lactol to lactone) [78]; antheliolide A [168]; the AChE inhibitor (+)-arisugacin A and B (primary alcohol to aldehyde step also) [83]; the marine macrolide amphidinolide T1 [169]; the alkaloid (+)-batzelladine D (*cf.* mech.

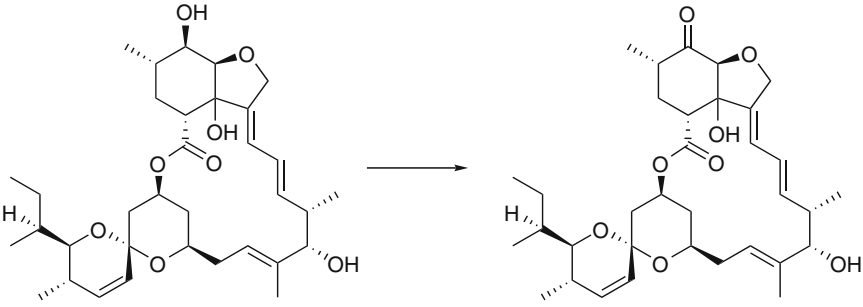

Fig. 2.6 Oxidation by TPAP/NMO of (4S)-3,4-dihydroavermectin B1a aglycone to the (4S)-5-dehydroxy-3,4-dihydro-5-oxo aglycone [81]

Fig. 1.13) [170]; the vinca alkaloid (+)-catharanthine [171]; 2-epibotcinolide (primary alcohol to aldehyde TPAP oxidation also involved) [89]; the spirobicyclic sesquiterpene (±)-erythrodiene (nitro to ketone oxidation also involved; *cf.* 5.6.4) [172]; a secondary alcohol to an enone as a step in the synthesis of the biologically active sequiterpene (−)-diversifolin [51]; the cytotoxic fasicularin [173]; the limonoid fraxinellone [174]; the plasmodial pigment fuligorubin A [160]; the antifungal gambieric acids A and C (also a primary alcohol to aldehyde step) [90]; the ether toxin gambierol (two primary alcohol to aldehyde steps) [91]; the cytotoxic gymnocin-A (also a primary to aldehyde step) [92]; the alkaloid (±)-lapidilectine B [175]; the antiparasitic and insecticide (+)-milbemycin-β_1, (involving both oxidation of a primary alcohol group to an aldehyde and, in a later step, of a secondary alcohol to a ketone) [98]; the acetogenin muricatetrocin C [176] and the sesquiterpenes nortrilobolide, thapsivillosin F and trilobolide [64]; the glutamate receptor neodysiherbaine [177]; the marine alkaloid norzoanthamine (primary alcohol to aldehyde step also) [99]; the anticarcinogenic agent ovalicin [178]; the cytotoxic agent phorboxazole (hemi-acetal to lactone) [179]; the antibacterial agent pseudomonic acid C [180]; the antifungal agent rapamycin (*cf.* 1.11) [181, 182]; the antigen daphane diterpene (+)-resiniferatoxin [183]; the antitumour macrolide (+)-rhizoxin D [184]; the heliobactericidal (+)-spirolaxine methyl ether [185]; the SERCA thapsigargin inhibitors [112, 152, 153]; the antitumour agent tonatzitlolone [186] and the therapeutic hypercholesterolemia agent zaragozic acid A [187]. For synthesis of a fragment of the protein phosphatase inhibitor calyculin A the TPAP/NMO/PMS/CH_2Cl_2 reagent was involved [188]. It was used to oxidise the antimalarial drug arteether [189] and to synthesize a sex attractant pheromone related to matsuone [190].

The reagent TPAP/NMO/PMS/CH_3CN was used in the synthesis of the synthase inhibitor (−)-CP-263,114 [191]. During synthesis of the antifeedant and growth-disruption agent azadirachtin it was used for a lactol to lactone conversion [192–196], and for a step in synthesis of the agonist dysiherbaine [197]. The non-proteinogenic amino acid anticapsin was made using TPAP/NMO/PMS/CH_3CN (Fig. 2.7) [53, 198], yet another example of TPAP tolerating an epoxy linkage.

Other examples in which epoxy linkages are not broken include oxidations with TPAP/NMO/PMS/CH_2Cl_2 for synthesis of the bio-engineered antibiotic *dl*-indolizomycin using [50] and for the limonoid calodendrolide (Fig. 2.8). In the latter example TPAP/NMO/PMS/CH_2Cl_2 succeeded when a wide variety of other reagents failed, e.g. the Swern reagent, Collins' reagent, DMSO and (pyH)[CrO_3Cl] [54].

For the total synthesis of the anti-cancer drug taxol® (paclitaxel) the system was used in three steps, two of primary alcohols to aldehydes (with TPAP/NMO/PMS/CH_2Cl_2 and one of a secondary alcohol to ketones by TPAP/NMO/PMS/CH_2Cl_2–CH_3CN

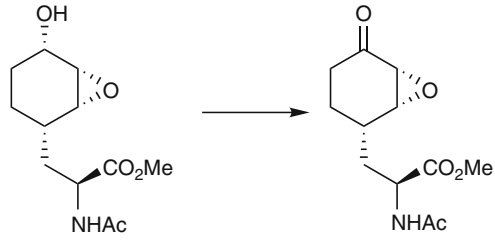

Fig. 2.7 Oxidation of an alcoholic *trans*-epoxide by TPAP/NMO in the synthesis of anticapsin [53]

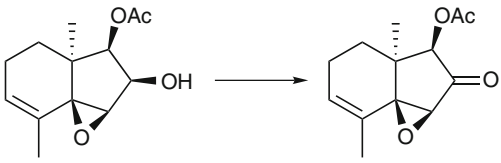

Fig. 2.8 Oxidation of a secondary alcohol during synthesis of calodendrolide [54]

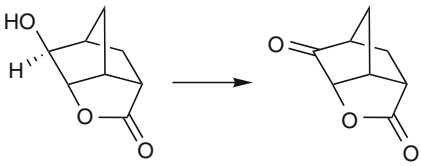

Fig. 2.9 Oxidation by RuO_4 of a hydroxylactone to a ketolactone [201]

[66]. An example of a secondary alcohol to lactone step oxidised by this reagent occurred during the total synthesis of the anti-cancer agent (+)-goniodiol [199, 200].

2.3.4 Hydroxylactones, α-Hydroxy Esters and Cyanohydrins

Use of RuO_2/aq. $Na(IO_4)/CCl_4$ to oxidise the secondary alcohol function in hydroxylactones gave ketolactones, while lactones gave ketocarboxylates [201–203]. The former reaction is exemplified by 5-*exo*-*endo*-dihydroxybicyclo[2.2.1] heptane-2-*endo*carboxylic acid-γ-lactone giving the 5-keto-6-*endo* product (Fig. 2.9). A number of other hydroxylactones were similarly oxidised, as were γ- or δ-hydroxycarboxylates to ketocarboxylates [201].

Oxidation of α-hydroxy esters $R^1CH(OH)R^2$ to the ketones R^1COR^2 was effected with $RuCl_2(PPh_3)_3$/TBHP/C_6H_6 (R^1=Ph, R^2=Me, Ph, COOMe; R^1=*trans*-MeCH=CH, *trans*-PhCH=CH, R^2=Me, Ph, COOMe); the reaction is also catalysed by $RuCl_3$ and $RuH_2(PPh_3)_4$ (*cf.* mech. Ch. 1) [204]. The same reagent $RuCl_2(PPh_3)_3$/TBHP/C_6H_6 oxidised RCH(OH)COOEt to RCOCOOEt (R=Ph, Me, 2-furyl, (*E*)-PhCH=CH) [205]. Cyanohydrins RCH(OH)(CN) were converted by the same reagent to ketonitriles RCO(CN) (R=Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 3,4-$(MeO)_2C_6H_4$, 4-$PhCO_2C_6H_4$, 1-naphthyl, *trans*-C_3H_7CH=CH) [204], and for R^1=Ph, 2-thienyl, (*E*)-PhCH=CH [205]. Similarly $RuCl_2(PPh_3)_3$/TBHP/C_6H_6 oxidised cyanohydrins (R^1=Ph, *p*-MeC_6H_4, *p*-ClC_6H_4, *o*-$MeOC_6H_4$) [206]. Oxidation of *trans*-cinnamaldehyde cyanohydrin, PhCH=CHCH(OH)(CN) to *trans*-cinnamoylcyanide PhCH=CH-(CO)CN was effected by $RuCl_2(PPh_3)_3$/TBHP/C_6H_6 [207]. The system $RuCl_2$(biox)/aq. $Na(IO_4)/CH_2Cl_2$/reflux catalysed oxidation of the trifluoromethyl carbinols $ArCH(OH)CF_3$ to trifluoromethyl ketones $ArCOCF_3$ (e.g. in $R(CH_2)_3CH(OH)CF_3$ where R= Ph, *p*-$MeOC_6H_4$, *p*-ClC_6H_4) (Fig. 1.38) [208].

2.3.5 Deracemisation of Secondary Alcohols

The deracemisation of R^1R^2CHOH (R^1=Ph, R^2=Et, ^{n}Pr ^{n}Bu; R^1=2-naphthyl, *m*-MeC_6H_4, *p*-$MeOC_6H_4$, *m*-ClC_6H_4, *p*-$Me_2NC_6H_4$, R^2=C_5H_{11}; R^1= *p*-$MeOC_6H_4$, R^2=Me) was

accomplished *via* oxidation to R^1R^2CO with $[RuCl_2(benzene)]_2$/(*R*)-BINAP/(*R,R'*)-DPEN/cyclohexanone/THF/K(^{t}BuO)/60°C (*cf.* mech. Ch. 1). Values for e.e. of 57–92% were achieved [209]. The system chiral Ru(NO)Cl(salen)/Cl_2pyNO or TMPNO or O_2/C_6H_6/UV (incandescent or halogen lamp; TMPNO=tetramethylpyridine-*N,N'*-oxide) converted racemic secondary alcohols to ketones (phenylethyl alcohol, 4-phenyl-3-buten-2-ol, 4-pnenyl-3-butyn-2-ol, 1-phenylpropan-2-ol). Only one enantiomer of racemic 4-phenyl-3-butyn-2-ol was oxidised [210].

2.3.6 Alcohols, Carbohydrates and Diols Not Covered Here but included in Chapter 1

Primary alcohols: $RuCl_2(PPh_3)_2$(am)/aq. H_2O_2 [211]; divinylbenzene supported 1-vinyl-3-butylimidazolium chloride TPAP/O_2/supercritical CO_2 [212]; Ru(OH)(PPh_3)(salen)/O_2/CH_2Cl_2 or $CHCl_3$ [213]; RuHCl(CO)(A-^{i}Pr-PNP)/alcohol [214]; TPAPSIL/O_2/supercritical CO_2 [215]; *cis*-$[Ru(H_2O)_2(dmp)_2]^{2+}$/aq. H_2O_2/CH_3CN/55°C [216]; $[Ru(H_2O)(bpy)(app)]^{2+}$/TBHP/(BTBAC)/$CH_2Cl_2$ [217]; $RuX(EPh_3)(sCB)_2$/NMO/EtOH-CH_2Cl_2 [218]; $[RuCl_2(p\text{-cymene})]_2$/$O_2$/$Cs_2(CO_3)$/toluene/100°C [219]; *cis*-$[Ru(H_2O)(py)(bpy)_2]^{2+}$ or *cis*-$[Ru(H_2O)(^t\text{Bupy})(bpy)_2]^{2+}$/aq. Na(ClO)/(BDTAC)/$CH_2Cl_2$ *cf.* mech. Ch. 1) [220]; stoich. $[Ru(O)_2(H_2O)(tpy)]^{2+}$ or *trans*-$[Ru(O)_2(CH_3CN)(tpy)]^{2+}$/water or CH_3CN, *cf.* mech. Ch. 1 [221]; stoich. $[Ru(O)(R_2dppi)(tpy)]^{2+}$/water, *cf.* mech. Ch. 1 [222]; $[Ru\{PW_{11}(O)_{39}\}]^{3-}$/aq. K($ClO_3$)/50°C [223, 224]; $[Ru(C_7F_{15}COCH_2COC_7F_{15})_3]^-$/perfluorinated decalin-toluene/O_2/65°C [225, 226]; stoich. Ru(O)(PHAB) or $[Ru(O)(PHAB)]^-$/CH_2Cl_2 [227]; $RuCl_2(PPh_3)_3$/4-BzTEMPO/O_2/toluene/70°C [228]; $[Ru(O)(N_4O)]^{2+}$/CH_3CN/Nafion-coated electrode, *cf.* mech. Ch. 1 [229]; $RuCl(OCOCH_3)(PPh_3)_3$/Co(salophen)(PPh_3)/O_2/hydroquinone/CH_2Cl_2 [230]; *trans*-$Ru(O)_2$(TMP)/lutidineNO/C_6H_6 [231]; *trans*-$[Ru(O_2)(14\text{-TMC})]^{2+}$/$O_2$/$CH_3CN$/50°C, and *trans*-$[Ru(O)_2(TMEA)]^{2+}$/$O_2$/$CH_3CN$/28°C *cf.* mech. Ch. 1 [232]; *trans*-$[Ru(O)(X)(14\text{-TMC})]^{2+}$/$CH_3CN$/Pt-C electrodes, *cf.* mech. Ch. 1 [233]; $[Ru_3(O)(OCOEt)_6](H_2O)_3]^+$/$O_2$(1.3 atm.)/water/65°C, *cf.* mech. Ch. 1 [234]; $RuCl_2(PPh_3)_3$/O_2/DCE [235].

Secondary alcohols: As $RuCl_3$/$Na(BrO_3)$/$Hg(OAc)_2$/aq. NaOH (cyclopentane, galactose; *cf.* mech. Ch. 1) [236]; and TPAP with silica-supported ionic liquids [237]; $RuCl_2(PPh_3)_3$/1-dodecene/aq. KOH/dioxane/100°C [238]; $[Ru(NH_3)(sq)(tpy)]^{n+}$ (n=1, 2)/water-CH_2Cl_2/Pt electrodes [239]; $RuCl_3(CH_3CN)_3$/aq. Li(ClO_4)/Pt electrodes [240]; $RuCl_3$/aq. $Na_2(CO_3).1½H_2O_2$/Adogen®/83°C [241]; *cis*-$RuCl_2$(DMF)$(dmso)_3$ or *trans*-$RuBr_2(dmso)_4$/NMO/DMF/30–50°C, *cf.* mech. Ch. 1 [242]; *cis*-$[Ru(O)_2Cl_2(OAc)]^-$/NMO/CH_2Cl_2/30°C and by TPAP/NMO/CH_3CN/30°C, *cf.* mech. Ch. 1 [156]; $[Ru(H_2O)_2(azpy)_2]^{2+}$/$Na(BrO_3)$/aq. 0.2 M phosphate/60°C [243, 244]; $[RuCl_2(p\text{-cymene})]_2$/$MnO_2$/2,6-di-*tert*-butylbenzoquinone/THF/65°C, *cf.* mech. Ch. 1 [245]; $RuCl_3$-$Co(OAc)_2$/O_2/CH_3CHO, *cf.* mech. Ch. 1 [246]; stoich. *cis*-$[Ru(O)_2(tetMe_6)]^{2+}$/CH_3CN *cf.* mech. Ch. 1 [247]; stoich. TPAP/CH_2Cl_2, *cf.* mech. Ch. 1 [248]; $RuBr_2(AsPh_3)_2$(HPhb)/NMO/PMS/CH_2Cl_2 [249]; $RuCl_2(PPh_3)_3$/$K_2(CO_3)$/acetone/56°C [250]; $Ru(tr)_2(PPh_3)_3$/NMO/CH_2Cl_2 [251]; *trans*-$Ru(O)_2$(TMP)/Cl_2pyNO/C_6H_6/24h [252]; $RuCl_2(AsPh_3)_2$(lq)/NMO/PMS/CH_2Cl_2 [253]. For the

following systems mechanisms were also studied (*cf.* Ch. 1): stoich. $[RuO_4]^-$ and $[RuO_4]^{2-}$/aq. base [254]; $[Ru(H_2O)(EDTA)]^-/O_2$/aq. ascorbate/ dioxane/30°C [255]; *cis*-$RuCl_2(phen)_2$/aq. Li(ClO)/CH_2Cl_2 [256]; $[Ru(H_2O)(EDTA)]^-$/aq. H_2O_2/ dioxane [257]; stoich. RuO_4/CCl_4 [258, 259]; stoich. $[RuO_4]^{2-}$/aq. base [258, 260]; $[Ru(H_2O)(bpy)(tpy)]^{2+}$/water @ pH 6.8/Pt electrodes [261]; $[RuCl_6]^{3-}$ or $RuCl_3$]/aq. $[Fe(CN)_6]^{4-}$ @ pH 11.9 [262]; stoich. *trans*-$[Ru(O)(bpy)(try)]^{2+}/CH_3CN$ [263].

Primary and secondary alcohols: $RuX_2(EPh_3)(SB)/O_2/CH_2Cl_2$ [264]; $RuX_2(EPh_3)(tSB)/O_2/CH_2Cl_2$ [265]; $Ru(H)(PPh_3)(salen)/O_2/CDCl_3$ (diols to lactols or *n*-hydroxyaldehydes) [213]; RuCl(chalc)(CO)(EPh_3) or RuCl(chalc)(CO)(py)/NMO/PMS/CH_2Cl_2 [266, 267]; $RuCl_2(PPh_3)_2$(am)/aq. H_2O_2 [211]; $[NRuNMe_2(\mu_2\text{-}O)_2Pd((-)\text{-sparteine})]^-$/PMS/$O_2/C_6H_5Cl$/100°C [268]; TPAP/poly(*N*-isoprpoylacrylamide)/O_2/toluene/80°C [269]; $Ru_2(OAc)_3(\mu\text{-}CO_3)/O_2$/water-toluene/80°C, *cf.* mech. Ch. 1 [270]; epoxide-encapsulated $RuCl_2(PPh_3)_3$/NMO/toluene or acetone [271]; $Ru(PPh_3)_2(Me_2CO)(\mu\text{-}Cl_3)RhCl(\eta^4\text{-}C_4Ph_4CO)$/aq. $K_2(CO_3)$/acetone-C_6H_6 [272]; $RuCl_3$ or $RuCl_2(PPh_3)_3$/$(bmim)^+$/80°C [273]; $[Ru(acac)_2(bpy)]^+$ or $RuCl_2$(bac)(bpy)/TBHP/C_6H_6 [274]; $Ru(PPh_3)_2$(tetSB) $Ru(PPh_3)_2(H_2O)$(triSB) or $Ru(PPh_3)_2$(bidSB)$_2$/NMO/CH_2Cl_2 [275]; $[Ru(CF_3COO)_2(H_2O)(tmtacn)]^+$/TBHP/DCE, *cf.* mech. Ch. 1 [276]; stoich. *trans*-$[Ru(O_2)(14\text{-}TMC)]^{2+}/CH_3CN$, *cf.* mech. Ch. 1 [277]; *trans*-$[Ru(H_2O)_2(bpy)_2]^{2+}$ and $[Ru(H_2O)(py)(bpy)_2]^{2+}$)/cyclic voltammetry/water [278]; $[RuCl_2(bpy)_2]^+$ or [Ru(acac)$(bpy)_2]^+$/TBHP/CH_2Cl_2 [279]; $RuCl_2(H_2O)_2$(dmnapy), $RuCl_2(H_2O)_2$(dcnapy) or $RuCl_2(H_2O)_2$(danapy)/aq. Na(BrO_3) [280]; $[RuCl_2(picphen)]^+$/NMO or Tl$(OAc)_3$/water/30°C, *cf.* mech. Ch. 1 [281]; stoich. $[Ru(H_2O)(bpy)(tpy)]^{2+}$/water @ pH 7 (carbohydrates, nucleotides) *cf.* mech. Ch. 1 [282]; *trans*-$Ru(O)_2(bpy)\{TeO_2(OH)_4\}$/aq. Na($IO_4$)/$CH_2Cl_2$/2°C [283]; $RuCl_2(PPh_3)_3$/paraformaldehyde/toluene/110°C [284]; $Ru(salHB)_2(PPh_3)_2$/NMO/PMS/CH_2Cl_2 [285]; *cis*-$[Ru(O)_2Cl_2(OCOR)]$/NMO/CH_2Cl_2 [286, 287]; stoich. *trans*-$[Ru(O)_2(dpt)]^{2+}$/water or CH_3CN, *cf.* mech. Ch. 1 [288]; stoich. $[Ru(O)(PPh_3)(bpy)_2]^{2+}$/water or CH_2Cl_2 [289–291]; $Ru_2(O)_6(py)_4$/NMO/PMS/CH_2Cl_2 [292, 293]; *trans*-$[Ru(O)_2\{(IO_5(OH)\}_2]^{6-}/K(IO_4)$/aq. KOH or aq. Aliquat® [294, 295]; $[Ru(O)_2Cl_2(OCOCH_3)]^-$/NMO/PMS/CH_3CN [296]; stoich. *trans*-$[Ru(O)_2(dmbpy)_2]^{2+}/CH_3CN$, *cf.* mech. Ch. 1 [297]; $RuCl_2(AsPh_3)_2$(lq)/NMO/PMS/CH_2Cl_2 [298]; $RuCl_3$/NMO/DMF, *cf.* mech. Ch. 1 [299]; *trans*-$[Ru(O)_2(py)_4]^{2+}$/NMO or $(^nBu_4N)IO_4/CH_2Cl_2$ [293]; $[Ru(H_2O)(EDTA)]^-$/aq. H_2O_2/ascorbate/dioxane, *cf.* mech. Ch. 1 [300]; $RuCl_3$/aq. H_2O_2/(DDAB)/CH_2Cl_2/80°C [301]; stoich. [Ru(O)(py)$(bpy)_2]^{2+}$/water or CH_3CN, *cf.* mech. Ch. 1 [302]; $RuCl_3$(Hmpi)/O_2/2,6-lutidine or Na(OEt)/water/25–90°C [303]; $RuCl_2(PPh_3)_3/O_2$/DCE [304]; $RuCl_2(PPh_3)_3$/$Me_3SiOOSiMe_3/CH_2Cl_2$ [305]; $RuCl_2(PPh_3)_3$/PhIO/CH_2Cl_2 [306]; $[Ru(O)(bpy)(tpy)]^{2+}$ or $[Ru(H_2O)(bpy)(tpy)]^{2+}$/water @ pH 7–9/Pt electrodes [307].

2.3.7 *Large-Scale Oxidations of Alcohols, Carbohydrates and Diols*

Some syntheses (using ≥1 g of substrate) are explicitly described in the literature; selected oxidations of carbohydrates are included in the first column of Table 2.3.

Substrates include: benzyl (2 g) and cinnamyl (2.7 g) alcohols to acids; cyclopentanol (1 g), benzhydrol (3.9 g), benzoin (4 g), pantolactone (2.6 g) to ketones ($RuCl_3$/TCCA/($^nBu_4N$)Br/aq. $K_2(CO_3)$/CH_3CN) (Fig. 2.14) [25]; [[2-[2-hydroxypropyl) amino]-1,2-dioxoethyl]amino]acetic acid ethyl ester (6.21 kg) to [(1,2-dioxo-2-oxopropyl)amino]ethyl)amino] acetic acid ethyl ester, part of the industrial-scale synthesis of thrombin inhibitor ($RuCl_3$/aq. Na(BrO_3)/CH_3CN) [166]; (+)-dihydrocholesterol (8 g) to cholest-3-one (RuO_2/aq. K(IO_4)/(BTEAC)/$CHCl_3$) [308]; 4-methoxybenzyl alcohol (27 g) and piperonyl (10 g) alcohols to aldehydes (TPAP/NMO/PMS/CH_2Cl_2) [31]; 4-*tert*butylcyclo-hexanol (18 g) to the ketone ([Ru_3(μ-O)(H_2O)$_3$(OAc)$_6$]$^+$/aq. NaCl @ pH 7/CCl_4/Pt electrodes) [33]; benzyl alcohol (54 g) and 4-nitrobenzaldehyde (53 g) to the acid ($RuCl_3$/$K_2(S_2O_8)$/aq. M KOH) [122]; *d*-carveol (15 g) to *d*-carveone ($RuCl_2(PPh_3)_3$/NMO/acetone) [41]; 1,2-cyclododecanediol (10 g) to the dione ($RuCl_2(PPh_3)_3$/benzalacetone/THF/195°C) [309]; 5-*exo*,6-*endo*-dihydroxy-bicyclo[2.2.1]-heptane-2-*endo*-carboxylic acid lactone (5 g) ($RuCl_3$/aq. Na(IO_4)/CCl_4) [203]; ethyl 3-hydroxy-cyclobutane-carboxylate (7 g) to ketone ($RuCl_3$/aq. Na(IO_4/CCl_4) (Tables 2.1 and 2.2) [34]; cyclohexanol (1.5 g) (stoich. RuO_4/H_2O) [1].

2.4 Carbohydrates

Although these encompass primary and secondary alcohols they are considered here in a separate section since so much work has been done in the area, using RuO_4 as the oxidant. In most cases it was used for oxidation of secondary alcohol groups in carbohydrates to ketones, but its first application, albeit stoicheiometrically as RuO_4/CCl_4, was for the conversion of a secondary alcohol unit in 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose to the D-*ribo*-hexofuranos-3-ulose (Fig. 2.13) [310]. There are early but illuminating reviews on carbohydrate oxidations by RuO_4 [18, 311].

Either stoicheiometric or catalytically generated RuO_4 is an excellent reagent for oxidation of isolated secondary alcohol functions in furanoses and pyranoses to the corresponding ketoses – with furanoses, lactone formation can occur. A number of functional groups are unaffected by the reagent, e.g. glycosidic linkages and benzyl, benzoate, benzylidene, isopropylidene, toluene-*p*-sulfonyl, acetamido and trityl groups. Favoured solvents are CCl_4 or $CHCl_3$ while CH_2Cl_2 and acetone are sometimes less satisfactory (Table 2.3) [311–313]. A stoicheiometric RuO_4/CCl_4 reagent is superior to CrO_3/py or $Pb(OAc)_4$ for carbohydrate oxidations [313].

A number of these oxidations involved stoich. RuO_4 usually in CCl_4 (Table 2.3) e.g. [20, 310–320]; (Fig. 2.15) [321–325]. Others, more usefully, were catalytic, e.g. RuO_2/Na(IO_4)/aq. Na(HCO_3)/CCl_4 or -$CHCl_3$ [2, 326], RuO_2/aq. Na(IO_4)/CCl_4 [327]; $RuCl_3$/TCCA/aq. ($^nBu_4N$)Br/CH_3CN (Fig. 2.14) [25]; TPAP/Na(ClO)/Me^{t}BuO/water @ pH 9.5 (Table 2.3, Fig. 2.18) [328]; RuO_2/K(IO_4)/aq. $K_2(CO_3)$($PhCH_2Et_3N$)Cl)/$CHCl_3$ [308]; RuO_2/CCl_4/water @ pH 4/Pt anode (Tables 2.1 through 2.4) [33]; RuO_2/K(IO_4)/aq. $K_2(CO_3)$/$CHCl_3$ Fig. 2.13) [329–331] or EtOAc [332]; RuO_2/aq. Na(ClO)/$CHCl_3$ [333]; RuO_2/aq. Na(IO_4)/Na(HCO_3)/CCl_4 [327] (Table 2.3).

2.4.1 Primary Alcohol Groups in Carbohydrates to Carboxylic Acids

A typical list of secondary carbohydrate oxidations is given in Table 2.3 but we start with primary alcohol oxidations in furanoses. Work on nucleosides and nucleotides is included in this section.

2.4.1.1 Primary Alcohol Groups in Furanoses

Oxidation of the 5′-hydroxy group of 2′,3′-*O*-isopropylideneadenosine to the corresponding 5′-carboxylic acid was effected by $RuCl_3$/aq. $Na(IO_4)/CCl_4$–CH_3CN (Fig. 2.10) [334].

Purine and pyrimidine nucleosides of AZT (Zidovudine, 3′-azido-3′-deoxythymidine) with $[RuO_4]^{2-}$ (from $RuCl_3/K_2S_2O_8$/aq. M KOH) gave 1-((3-azido-2,3-dideoxy-β-D-*erythro*-pentafuranosyl-5-uronic acid)-thymine (Fig. 2.11) [335].

Primary alcohol groups in several protected ribo-, fructo- and glucofuranoses including 2,3,4-tri-O-benzoyl-D-glucose, 1,2-isopropylidene-D-xylo-furanose, 2,3:4,5-di-O-isopropylid-ene-D-fructopyranose, methyl 2,3-O-isopropylidene-β-D-ribofuranoside, 1,2-O-isopropylidene-3,5-O-benzylidene-D-glucofuranose and

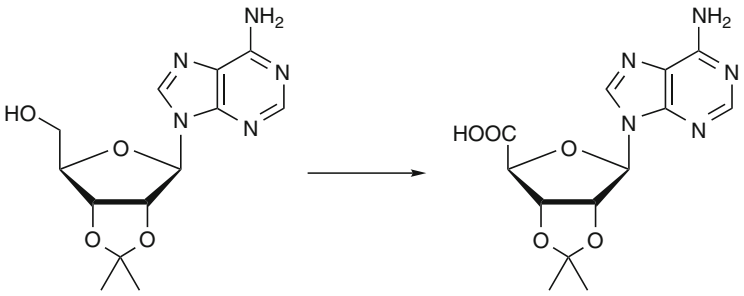

Fig. 2.10 Oxidation by RuO_4 of isopropylideneadenosine to the corresponding acid [334]

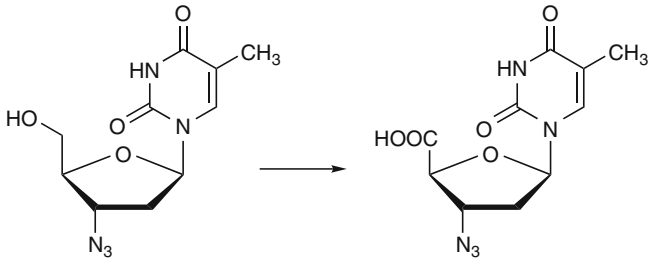

Fig. 2.11 Oxidation by $[RuO_4]^{2-}$ of AZT at the 5′ hydroxyl group [335]

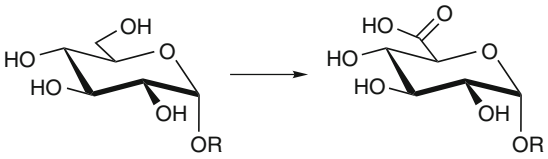

Fig. 2.12 Oxidation of the alkyl glucopyranosides MGP (R = Me) and OGP (R = octyl) by RuO_4, $[RuO_4]^-$ and $[RuO_4]^{2-}$ to glucoronic acids [337]

1,2-O-isopropylidene-5,6-O-benzylidene-D-glucofuran-ose were oxidised by $[RuO_4]^{2-}$/aq. $Na(IO_4)$ and the products esterified to the corresponding uronic acids [336].

2.4.1.2 Primary Alcohol Groups in Pyranoses

Methyl α-D-glucopyranoside (MGP) and octyl α-D-glucopyranoside (OGP) were oxidised to the corresponding α-D-glucuronic acids (Fig. 2.12) by RuO_4, $[RuO_4]^-$and $[RuO_4]^{2-}$, generated from $RuCl_3$/aq. $Na(BrO_3)$ at different pH. Of these RuO_4 was a more effective oxidant than $[RuO_4]^-$, while for $[RuO_4]^{2-}$ the oxidation was stoicheiometric. The primary alcohol group was preferentially oxidised to the secondary alcohol functions, ascribed to the greater steric accessibility of the former; *cf.* mech. Ch. 1 [337].

Oxidations of primary alcohol groups in glycopyranosides by TPAP/NMO/PMS/CH_2Cl_2 were used *en route* to the antiviral agents castanospermine and 1-epicastanospermine [338].

2.4.2 Secondary Alcohol Groups in Carbohydrates to Ketones

Examples of such oxidations are listed in Table 2.3 with furanoses listed first in a roughly alphabetical arrangement mainly by substituent groups of products. Some large-scale oxidations (≥ 1 g) are listed in the first column. The effective oxidant in most cases is RuO_4, with a few by $[RuO_4]^-$ or $[RuO_4]^{2-}$. For oxidations by RuO_4 the overall stoicheiometry of the reaction was shown [312] to be

$$2R^1R^2CHOH + RuO_4 \rightarrow 2R^1R^2CO + RuO_2 + 2H_2O \qquad (2.4)$$

In pyranoses RuO_4-based reagents oxidise equatorial or axial groups with equal ease [312, 317].

Table 2.3 Oxidation of secondary alcohol functions in carbohydrates

Reactant	Product	Method [Ref.]
1,2-*O*-isoPropylidene-L-threose	D-*glycero*-1,2-*O*-isoPropylidene-tetros-3-ulose	A [2]
5-*O*-Benzoyl-1,2-*O*-isopropylidene -α-D-xylofuranose (18 g)	5-*O*-Benzoyl-1,2-*O*-isopropylidene-α-D-*erythro* -pentofuranos-3-ulose	S [316, 322]
3-*O*-Benzyl-1,2-*O*-isopropylidene-6-*O*-(triphenylmethyl) α-D-galactofuranose (3.5 g)	3-*O*-Benzyl-1,2-*O*-isopropylidene-6-*O*-(triphenylmethyl)-β-L-*arabino*-hexofuranos-5-ulose	B [308]
3-*O*-Benzyl-1,2-*O*-isopropylidene-6-*O*-(triphenylmethyl)-α-D-glucofuranose (5.5 g)	3-*O*-Benzyl-1,2-*O*-isopropylidene-6-*O*-(triphenylmethyl) -α-D-*xylo*-hexofuranos-5-ulose	B [308]
3-*O*-Benzyl-1,2-*O*-isopropylidene-6-*O*-(triphenylmethyl) α-D-allofuranose (1 g)	3-*O*-Benzyl-1,2-*O*-isopropylidene-6-*O*-(triphenylmethyl) -α-D-*ribo*-hexofuranos-5-ulose	B [308]
4-*C*-Cyclopropyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranose (2.8 g)	4-*C*-Cyclopropyl-1,2-*O*-isopropylidene-α-D-*erythro* -tetrofuranos-3-ulose	S [314]
Dihydro-3-hydroxy-4,4-dimethyl-2(3*H*)-furanone (2.6 g)	Dihydro-4,4-dimethyl-2,3-furandione	C [25]
Methyl-2-*O*-benzoyl-5-*O*-trityl-α-D-xylofuranoside (18 g)	Methyl-2-*O*-benzoyl-5-O-trityl-α-D-*erythro* pentofuranosid-3-ulose	S [315]
Methyl-2,5-di-*O*-benzoyl-α-D-xylofuranoside (25 g)	Methyl-2,5-di-*O*-benzoyl-β-D-*erythro*-pentofuranoside-3-ulose	S [315]
Methyl-2,5-di-*O*-benzoyl-β-D-xylofuranoside (25 g)	Methyl-2,5-di-*O*-benzoyl-α-D-*erythro*-pentofuranoside-3-ulose	S [315]
Methyl-3,5-di-*O*-benzoyl-α-D-xylofuranoside (3 g)	Methyl-3,5-di-*O*-benzoyl-α-D-*threo*-pentofuranosid-2-ulose	S [315]
Methyl-3,5-di-*O*-benzoyl-β-D-xylofuranoside (3 g)	Methyl-3,5-di-*O*-benzoyl-β-D-*threo*-pentofuranosid-2-ulose	S [315]
1,2:5,6-di-*O*-isoPropylidene-α-D-glucofuranose (125 g [308])	1,2:5,6-di-*O*-isoPropylidene-α-D-*ribo*-hexofuranos-3-ulose (Fig. 2.13)	B [308], D [327, 330]; E [310, 329]; S [313]
2,3:5,6-di-*O*-isoPropylidene-α-D-mannofuranose (2.6 g)	2,3:5,6-di-*O*-isoPropylidene-α-D-mannono-γ-lactone (Fig. 2.14)	C [25]

2,3:4,6-di-*O*-isoPropylidene-α-L-sorbofuranose	2,3:4,6-di*O*-isoPropylidene-2-ketogulonic acid	F [33]
5-*O*-benzoyl-1,2-*O*-isoPropylidene-α-D-xylofuranose	1,2-*O*-isoPropylidene-6-*O*-benzoyl-3-oxa-α-D-*erythro*-4-hexulopyranose	S [325]
1,6-Anhydro-3,4-*O*-isopropylidene-β-D-galactopyranose (1 g)	1,6-Anhydro-3,4-*O*-isopropylidene-β-D-*lyxo*-hexapyranos-2-ulose (Fig. 2.15)	S [321]
1,3:2,5-di-*O*-Methylene-L-rhamnitol	6-Deoxy-1,3:2,5-di-*O*-methylene-L-*glycero*-D-*erythro*-4-hexulose	A [2]
1,3:4,6-di-*O*-Benzylidene-D-mannitol (2 g)	1,3:4,6-di-*O*-Benzylidene-D-*threo*-2,5-hexodiulose	E [332]
Methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucoside (1.5 g)	Methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranosid-3-ulose	S [317]
1,6-Anhydro-2,3-*O*-isopropylidene-β-D-mannopyranose (4 g [320])	1,6-Anhydro-2,3-*O*-isopropylidene-β-D-*lyxo*-hexopyranos-4-ulose (Fig. 2.16)	E [20], S [311, 320, 324]
6-*O*-Benzoyl-1,2-4,5-di-*O*-isopropylidene-dulcitol	6-*O*-Benzoyl-1,2:4,5-di-*O*-isopropylidene-*threo*-*glycero*-3-hexulose	A [2]
Benzyl 6-deoxy-2,3-*O*-isopropylidene-α-L-mannopyranoside (7 g)	Benzyl 6-deoxy-2,3-*O*-isopropylidene-α-L-*lyxo*-hexopyranosid-4-ulose	S [319]
Methyl 2,3-di-*O*-benzoyl-β-L-*p*-arabinopyranoside	Methyl 2,3-di-*O*-benzoyl-β-L-*threo*-pentopyranosid-4-ulose	E [330]
Methyl 2,3-*O*-isopropylidene-α-L-rhamnoside	Methyl 6-deoxy-2,3-*O*-isopropylidene-α-L-*glycero*-D-*erythro*-hexos-4-uloside	A [2]
Methyl 2,3-di-*O*-methyl-6-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside	Methyl 2,3-di-*O*-methyl-6-*O*-*p*-tolylsulfonyl-α-D-*xylo*-hexopyranosid-4-ulose	E [330]
Methyl 2,3,6-trideoxy-α-D-*erythro*-hexapyranoside (5 g)	Methyl 2,3,6-trideoxy-α-D-*glycero*-hexopyranosid-4-ulose	S [318]
Methyl-2,3,6-tri-*O*-benzoyl-α-D-glucopyranoside (6 g)	Methyl-2,3,6-tri-*O*-benzoyl-α-D-*xylo*-hexopyranosid-4-ulose	S [317]
Methyl-3,4-isopropylidene-β-L-arabinoside	Methyl-3,4-isopropylidene-β-L-*erythro*-pentulopyranoside	S [310, 313]
Methyl-3,4-isopropylidene-β-D-arabinoside	Methyl-3,4-isopropylidene-β-D-*erythro*-pentos-2-ulopyranose	A [2]

(continued)

Table 2.3 (continued)

Reactant	Product	Method [Ref.]
Methyl -3,4,6-tri-*O*-benzoyl-α-D-glucopyranoside (1 g)	Methyl 3,4,6-tri-*O*-benzoyl-α-D-*arabino*-hexopyranosidulose	S [313]
Methyl-3,6-di-*O*-benzoyl-2-deoxy-α-D-*arabino*-hexopyranoside (5 g)	Methyl-3,6-di-*O*=-benzoyl-2-deoxy-α-D-*threo*-hexosid-4-ulose	S [317]
Methyl 4,6-*O*-benzylidene-2-*O*-toluene-*p*-sulfonyl-α-D-glucopyranoside (2 g [317])	Methyl 4,6-*O*-benzylidene-2-*O*-toluene-*p*-sulfonyl-α-D-*ribo*-hexopyranosid-3-ulose	E [330], S [317]
Methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*arabino*-hexopyranoside	Methyl 4,6-*O*-benzylidene-2-deoxy-α-L-*erythro*-hexopyran-3-uloside	S [323]
Methyl 6-deoxy-3,4-*O*-isopropylidene-α-L-fucoside	Methyl 6-deoxy-3,4-*O*-isopropylidene-α-L-hexopyranusidulose	S [313]
Methyl-4,6-*O*-benzylidene-2-deoxy-α-D-*lyxo*-hexopyranoside (16 g [313])	Methyl-4,6-*O*-benzylidene-2-deoxy-α-D-*threo*-hexopyranosid -3-ulose	E [330, 331], S [311, 313]
Methyl 6-deoxy- 2,3-*O*-isopropylidene-α-D-gulopyranoside (10g)	Methyl 6-deoxy-2,3-*O*-isopropylidene-α-D-*ribo*-hexopyranosid-4-ulose	G [333]
Phenyl 3,6-di-*O*-benzoyl-2-deoxy-α-D-*lyxo*-hexopyranoside (2 g)	Phenyl 3,6-di-*O*-benzoyl-2-deoxy-α-D-*threo*-hexosid-4-ulose	S [317]
1,2-5,6-di-*O*-isoPropylidene-D-glucofuranose	1,2:5,6-di-*O*-isoPropylidene-α-D-*erythro*D-*glycero*-hexos-3-ribofuranose	A [2]
1,2:4,5-di-*O*-isoPropylidene-β-D-fructopyranose (26 g [340])	1,2:4,5-di-*O*-isoPropylidene-β-D-*erythro*-2,3-hexodiulo-2, 6-pyranose (Fig. 2.18)	E [340], H [328]
2,4-di-*O*-Benzyl-3-*O*-ʳbutyldiphenylsilyl-L-αβ-L-fucopyranose	2,4-di-*O*-benzyl-3-*O*-ʳbutyldiphenylsilyl-L-fuco-1,5-lactone	J [155]

A: RuO_2/aq. $Na(IO_4)/CCl_4$ [2]; B: $RuO_2/K(IO_4)$/aq. $K_2(CO_3)/(PhCH_2Et_3N)Cl.H_2O)/CHCl_3$ [308]; C: $RuCl_3$/TCCA/aq. ($^nBu_4N$)Br/CH_3CN [25]; D: RuO_2/$Na(IO_4)$/aq. $Na(HCO_3)/CCl_4$ [327]; E: $RuO_2/K(IO_4)$/aq. $K_2(CO_3)/CHCl_3$ [20, 329–331, 340], or EtOAc [332]; F: RuO_2/CCl_4/water @ pH 4/Pt anode [33]; G: RuO_2/aq. $Na(ClO)/CHCl_3$ [333]; H: TPAP/aq. Na(ClO) @ pH 9.5/MeʳBuO [328]; J: TPAP/NMO/PMS/CH_3CN [155]; S: stoich. RuO_4/CCl_4 [20, 310, 311, 313–325].

2.4.2.1 Secondary Alcohol Groups in Furanoses

One of the first of these, effected by stoich. RuO_4/CCl_4, was the conversion of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose to 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexofuranos-3-ulose [310, 329], used in the synthesis of D-allose [329] (Fig. 2.13); a number of other furanose and pyranose oxidations (Table 2.3) were similarly carried out [310]. This was subsequently one of the most frequently studied oxidations by RuO_4 catalytically (Table 2.3) by $RuO_2/K(IO_4)$/aq. $K_2(CO_3)$/(BTEAC)/$CHCl_3$ [308]; RuO_2/aq. $K(IO_4)/K_2(CO_3)/CHCl_3$ [329]; or RuO_2/aq. $Na(HCO_3)/CHCl_3$ [327, 330].

Oxidation by stoich. RuO_4/CCl_4 of five xylofuranosides gave the corresponding 2- and 3-uloses (Table 2.3) [315], and that of 5-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose by the reagent to the -α-D-*erythro*-pentafuranos-3-ulose formed part of a synthesis of branched-chain 3′-C-methyladenosine [316, 322]. Likewise the cyclopropyl-substituted 4-*C*-cyclo-propyl-1,2-*O*-isopropyl-idene-D-xylo-tetrafuranose was converted to the 3-ulose [314].

The reagent RuO_2/aq. $Na(IO_4)/CCl_4$ (the first catalytic system for Ru-based carbohydrate oxidations) oxidised 1,2-*O*-isopropylidene-L-threose to D-*glycero*-1,2-*O*-isopropylidene-tetros-3-ulose, and a number of pyranoses were similarly oxidised [2]. Other furanoses were made with $RuCl_3$/TCCA/(^{n}Bu$_4$N)Br (Table 2.3; Fig. 2.14) [25]

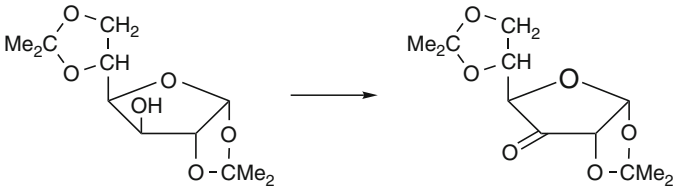

Fig. 2.13 One of the first oxidations by RuO_4 of a secondary alcohol group in a carbohydrate [310, 329]

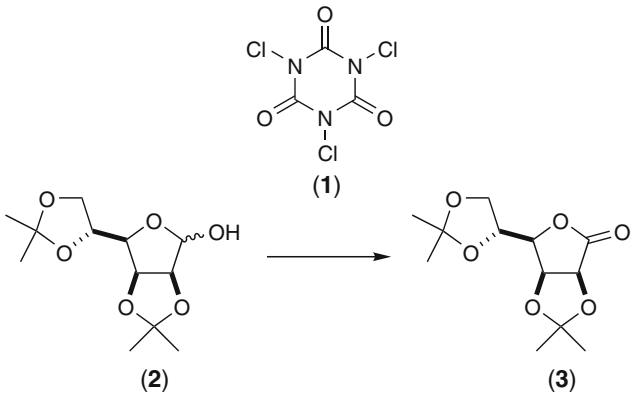

Fig. 2.14 Oxidation by $RuCl_3$/TCCA (**1**) of a mannofuranose (**2**) to a lactone (**3**) [25]

or RuO_2/aq. $Na(IO_4)$/(BTEAC)/CH_3CN [308]; 9-(3′,5′-*O*-isopropylidene-2′-keto-(β-D-xylofuranosyl)adenine was made by oxidation of the -β-D-xylofuranosyl)adenine precursor by RuO_4/$Na(IO_4)$/aq. $Na(HCO_3)$/CCl_4 as part of a synthesis of nucleoside antibiotics containing deoxyamino sugars [326]. With $RuCl_3$/TCCA/($^nBu_4N$)Br/aq. $K_2(CO_3)$/CH_3CN (TCCA=trichloroisocyanuric acid (1)), 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose (2) was oxidised to its γ-lactone (3) (Fig. 2.14) [25].

For oxidation of 2′,3′,5′-tri-*O*-acetyl- or -benzoyl derivatives of N^6,N^6-dimethyladenosines to the corresponding monoamido derivatives *cf.* Fig. 5.4, 5.1.3.4 [339].

2.4.2.2 Secondary Alcohol Groups in Pyranoses

In general RuO_4 – normally likely to be the active species in most Ru-assisted carbohydrate oxidations – is an excellent oxidant for alkylidene and arylidene derivatives [311, 317].

Formation of 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-hexo-furanos-3-ulose (Fig. 2.13, 2.4.2.1; Table 2.3) was one of the first carbohydrate oxidations effected by stoich. RuO_4/CCl_4 [310, 311]. The reagent was also used for oxidation of 1,6-anhydro-3,4-*O*-isopropylidene-β-D-galactopyranose to the -β-D-*lyxo*-hexopyranos-2--ulose, part of a route leading to 1,6-anhydro-β-D-talopyranose (Fig. 2.15) [321].

Stoicheiometric RuO_4/CCl_4 was also used to oxidise several furanoses, partially acylated glycosides and 1,4:3,6-dianhydrohexitols [317]; pyranosides to pyranosiduloses [313]; methyl 2,3,6-tri-*O*-benzoyl-α-D-glucopyranoside and its C-4 epimer to the α-D-*xylo*-hexapyranosid-4-ulose (Table 2.3) [317], and methyl 2,3,6-trideoxy-α-D-*erythro*-hexapyranoside to the -α-D-*glycero*-hexa-pyranosid-4-ulose, an intermediate in the synthesis of forosamine [318]. It was also used to oxidise benzyl 6-deoxy-2,3-*O*-isopropylidene-α-L-mannopyranoside to the α-L-*lyxo*-hexapyranosid-4-ulose [319] and for oxidation of 'isolated' secondary alcohol functions, e.g. in the conversion of 1,6-anhydro-2,3-*O*-isopropylidene-β-D-mannopyranose to the-β-D-*lyxo*-hexa-pyranos-4-ulose mannopyranose (Fig. 2.16, Table 2.3 [20, 320, 324]).

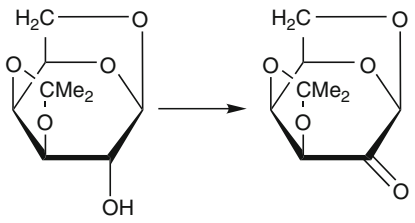

Fig. 2.15 Oxidation by RuO_4 of a 3,4-isopropylidene acetal to a ketone [321]

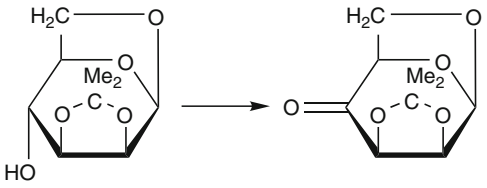

Fig. 2.16 Oxidation of an 'isolated' secondary alcohol group in a carbohydrate by RuO_4 [324]

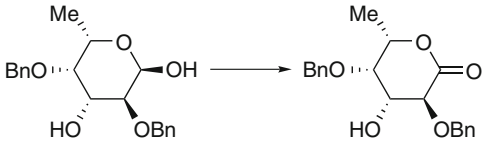

Fig. 2.17 Preparation of aldono-5-lactones from pyranoses using TPAP/NMO [155]

The reagent RuO_2/aq. $Na(IO_4)/CCl_4$ oxidised a number of pyranoses and was the first catalytic Ru-based system for carbohydrates (Table 2.3) [2]. Although use of $Na(IO_4)$ as co-oxidant with RuO_2 or $RuCl_3$ is a common procedure for generating RuO_4 in these reactions, it was noted that the use of the sparingly soluble $K(IO_4)$ in place of $Na(IO_4)$ as co-oxidant reduced over-oxidation [332]; see also [330, 340, 341]. Conversion of pyranoses to lactones has been accomplished; e.g. 2,4-di-*O*-benzyl-3-*O*-^{t}butyldiphenylsilyl-α,β-L-fucopyranose was oxidised by TPAP/NMO/PMS/CH_3CN to 2,4-di-*O*-benzyl-3-*O*-^{t}butyldiphenylsilyl-L-fuco-1,5-lactone (Fig. 2.17) [155].

2.4.3 Syntheses of Carbohydrate Natural Products/ Pharmaceuticals

Oxidation of methyl-4,6-*O*-benzylidene-2-deoxy-α-D-*lyxo*-hexopyranoside to the -hexo-pyranosid-3-ulose was effected by RuO_2/aq. $K(IO_4)/K_2(CO_3)/CHCl_3$, part of a synthesis of D-arcanose [331]. The same reagent oxidised 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose to the α-D-*ribo*-hexofuranos-3-ulose (Fig. 2.13, 2.4.2.1), used in a synthesis of D-allose [329]. Oxidations of primary alcohol groups in glycopyranosides by TPAP/NMO/PMS/CH_2Cl_2 was used *en route* to the antiviral agents castanospermine and 1-epicastanospermine [338]. Methyl 4,6-*O*-benzylidene-2-deoxy-α-L-*arabino*-hexopyranoside was converted by RuO_2/aq. $Na(IO_4)/CHCl_3$ to the α-L-erythro-hexopyran-3-uloside [323]; this and the α-D form were oxidised by stoich. RuO_4/CCl_4 [312] and used during the synthesis of L-cladinose and mycarose [323, 342].

A step in the synthesis of the imino glycal enzyme inhibitor (+)-fagomine was effected by TPAP/NMO/PMS/CH_2Cl_2 [343], and the biologically active amino sugars furanodictines A and B were made from D-glucuronolactone involving an intermediate secondary alcohol to ketone step with TPAP/NMO/PMS/CH_2Cl_2 [344]. The antibiotic carbasugars gabosine I and gabosine G were made from δ-D-gluconolactone, using TPAP/NMO/PMS/$K_2(CO_3)/CH_3CN$ to oxidise a secondary alcohol to ketone intermediate [345], while the antiviral nucleoside (−)-neplanocin A was made *via* an intermediate oxidation with TPAP/NMO/PMS/CH_2Cl_2 from D-glucose [346].

A step in the synthesis of D-psicose involved oxidation of 1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranose to the β-D-*erythro*-2,3-hexodiulo-2,6-pyranose by $RuO_2/K(IO_4)$/aq. $K_2(CO_3)/CHCl_3$ [340] or TPAP/aq. Na(ClO)/Me^{t}BuO pH 9.5 (Fig. 2.18) [328]. The 2,6-pyranose is a valuable material for asymmetric catalytic epoxidation of alkenes [328].

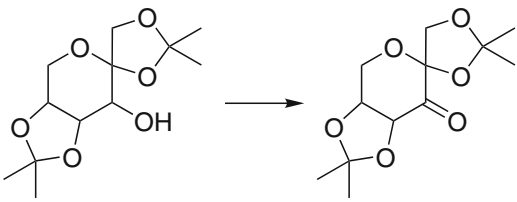

Fig. 2.18 Oxidation of di-*O*-isopropylidene-β-D-fructopyranose by aqueous TPAP with ClO^- [328]

2.4.4 Miscellaneous Carbohydrate Oxidations

For the *cis*-dihydroxylation of protected 1*L*-1,2:3,4-di-*O*-isopropylidenecyclohex-5-ene-1,2,3,4-tetrol (22g) to the diol 1*D*-1,2:3,4-di-*O*-isopropylidene-*allo*-inositol by $RuCl_3$/aq. $Na(IO_4)$/EtOAc-CH_3CN/0°C *cf.* 3.1.2.1 and Fig. 3.3 [347]. Oxygen insertion by stoich. RuO_4/CCl_4 occurred in addition to the secondary alcohol oxidation of the five-membered ring 5-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose, giving the six-membered ring 1,2-*O*-isopropylidene-6-*O*-benzoyl-3-oxa-α-D-*erythro*-4-hexulopyranose-α-D-xylofuranose [325].

Oxidation of kraft pulp cellulose by aq. $RuCl_3$ or RuO_2/aq. Na(ClO) or aq. 0.02 M H_2SO_5 gave oxycellulose containing carbonyl and carboxylate groups; RuO_4 itself is also effective and is likely to be the principal catalyst [348]. The system $RuCl_3$/$Na(BrO_3)$/aq. $Na_2(CO_3)$ @ pH 9.8 oxidised various forms of cellulose [349].

For *large-scale oxidations* of carbohydrates (≥ 1g) *cf.* the first column of Table 2.3. For synthesis of carbohydrates by alkene cyclisation *cf.* 3.1.3.3.

2.5 Diols

2.5.1 Specific Examples

Typical examples of diol oxidations are listed in Table 2.4. Oxidation of $R^1CH(OH)CH(OH)R^2$ to 1,2-diketones $R^1(CO)(CO)R^2$ was effected by $RuCl_3$/aq. bromamine-T @ pH 8.4/acetone (R^1=R^2=Cl, Ph, *p*-MeC_6H_4, *p*-$MeOC_6H_4$, *p*-$NO_2C_6H_4$, *o*-$NCl_2C_6H_3$, Me_2N, $Me(CH_2)_{12}$, $Me(CH_2)_{14}$) [350], and diols to ketones by $[RuO_4]^{2-}$aq. $K_2(S_2O_8)$/Adogen®/CH_2Cl_2 [30]. The systems $RuCl_3/K_2(S_2O_8)$/aq. M KOH [40, 121] and $RuCl_3$/$Na(BrO_3)$/aq. M $Na_2(CO_3)$ [121] converted diols to acids (Table 2.4). In an unusual reaction observed during attempts to synthesise taxol using TPAP/NMO/PMS/CH_2Cl_2 the diol (2-[5,5-[ethylenedioxy)-2,6,6-trimethyl-1-cyclohexenyl]-1,2-ethane-diol) gave 5,5-[ethylenedioxy)-2,6,6-trimethyl-1-cyclohexencarboxaldehyde diol [111]. Several diols were converted to diones by $RuCl_2(PPh_3)_3$/benzalacetone/THF/195°C (mech. *cf.* Ch. 1; Table 2.4), although the need to use a sealed tube at high temperatures is inconvenient [309]; TPAP/NMO/PMS/CH_2Cl_2 was used for diol to dione conversion (Table 2.4) in sensitive steroidal alcohols [351].

Table 2.4 Oxidation of 1,n-diols to ketones or acids

Reactant	Product	Method [Ref.]
Androst-4-ene-3ξ,17β-diol	Androst-4-ene-3,17β-dione	A [351]
cis-Cyclohexane-1,2-diol	Adipic acid	B [33], C, D [121]
trans-Cyclohexane-1,2-diol	Adipic acid	B [33], C, D [121]
1,2-Diphenyl-1,2-dihydroxyethane	Benzil	E [309]
Hydrobenzoin	Benzoic acid	C, D [121]
2,3-Butanediol	2,3-Butanedione	E [309]
4-*tert*-Butylcatechol	4-*tert*-Butyl-1,2-benzoquinone	F [39]
3,4-di-*tert*-Butylcatechol	3,4-di-*tert*-Butyl-1,2-benzoquinone	F [39]
1,2-Cyclododecanediol	1,2-Cyclododecandione	E [309]
Cyclohexane-1,2-diol	Cyclohexane-1,2-dione	E [309]
Cyclohexane-1,4-diol	Cyclohexane-1,4-dione	B [33]
Bicyclo-[1, 2, 2]-heptane-2,3-diol	Cyclopentane-1,3-dicarboxylic acid	B [33]
Decane-1,4-diol	Decan-4-olide	B [33]
Decane-1,5-diol	Decan-5-olide	B [33]
9,10-Dihydroxystearic acid	9,10-Diketostearic acid	E [309]
1-Phenyl-1,3-propanediol	3-Hydroxy-1-phenyl-1-propanone	G [30]
1,3-Dihydroxy-5-phenyl-4-pentene	5-Hydroxy-1-phenyl-1-penten-3-one	G [30]
2,3-Norbornanediol	2,3-Norbornanedione	E [309]
Dodecane-1,7-diol	7-Oxododecanoic acid	B [33]
Undecane-1,10-diol	10-Oxododecanoic acid	B [33]
Hexadecane-1,15-diol	15-Oxohexadecanoic acid	B [33]
Tridecane-1,12-diol	12-Oxotridecanoic acid	B [33]
Undecane-1,6-diol	6-Oxoundecanoic acid	B [33]
Pregn-4-ene-3,20-diol	Progesterone	A [351]
Cyclo-octane-1,2-diol	Suberic acid	C, D [121]
1,4 Butanediol	Succinic acid	H [40]

A: TPAP/NMO/PMS/CH_2Cl_2 [351]; B: RuO_2/aq. NaCl @ pH 7/Pt electrodes [33]; C: $RuCl_3$/$Na(BrO_3)$/aq. M $Na_2(CO_3)$ [121]; D: $RuCl_3/K_2(S_2O_8)$/aq. M KOH [121]; E: $RuCl_2(PPh_3)_3$/benzal-acetone/THF/195°C [309]; F: $RuCl_2(PPh_3)_3$/TBHP/acetone [39]; G: $[RuO_4]^{2-}$/aq. $K_2(S_2O_8)$/Adogen®/CH_2Cl_2 [30]; H: $RuCl_3/Na_2(S_2O_8)$/aq. M NaOH [40].

Diols were converted to lactols by TPAP/NMO/PMS/CH_3CN [352] or TPAP/NMO/PMS/CH_2Cl_2–CH_3CN [353]; oxidation of a keto hemi-ketal by TPAP/NMO/PMS/CH_2Cl_2 in an avermectin synthesis yielded a lactol, *via* an intermediate retro-aldol [354]. The 1,4-diols in Fig. 2.19 (R=C_3H_7, C_7H_{15}, Ph) produced lactones with TPAP/NMO/PMS/CH_2Cl_2 as did the 1,5-diol $HO(CH_2)_4C(OH)C_5H_9$ [46].

2.5.2 Natural Product/Pharmaceutical Syntheses Involving Diols

A diol was converted to a lactone by oxidation with stoich. RuO_4/CCl_4 as part of the total synthesis of the quassinoid (±)-amarolide [355]; stoich. $(PPh_4)[Ru(O)_2Cl_3]$/

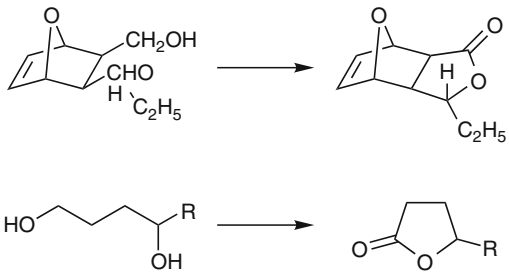

Fig. 2.19 Oxidation by TPAP/NMO of 1,4- and 1,5-diols to lactones [46]

CH_2Cl_2 converted drimanediol to the natural drimane sesquiterpene product *iso*-drimeninol [356]; TPAP/NMO/PMS/CH_2Cl_2–CH_3CN oxidised a diol to a γ-lactone as a step in the synthesis of the tricyclic sesquiterpene (−)-ceratopicanol for an oxidation step [357], and TPAP/NMO/PMS/CH_2Cl_2 was used for synthesis of the marine anti-tumour agent eleutherobin [352]. The reagent TPAP/NMO/PMS/CH_3CN effected a diol to lactone step in the synthesis of the antitumour agent *ent*-clavilactone B [358] and the antileukemic agents (−)-eriolangin and (−)-eriolanin [359]. During synthesis of the protein phosphatase inhibitor okadaic acid three oxidations with TPAP/NMO/PMS/CH_2Cl_2 were used, two of primary alcohol to aldehydes and one of a diol to a lactone [109], and in the synthesis of the immuno-adjuvant QS-21A_{api} a diol-to-lactone step is involved [360], as in the case of the lypophilic macrolide rapamycin (*cf.* 1.11) [181]. In the synthesis of *cis*-solamin the reagent oxidised a triol to a lactone aldehyde (an RuO_4-catalysed cyclisation of a 1,3-diene is also involved, *cf.* 3.2.2.2) [361], and TPAP/NMO/PMS/DCE was used for diol to lactone steps in the synthesis of the marine eicosanoid agardhilactone [362].

2.5.3 Desymmetrisation of Meso-Diols

A chiral complex was used in Ru(NO)Cl(salen^{chir})/O_2/UV/$CHCl_3$ for oxidative desymmetrisation of *meso*-diols to optically active lactols and lactones, e.g. of *cis*-1,2-bis(hydroxylmethyl)-cyclohexane to (1*R*, 6*S*, 7*RS*)-7-hydroxy-8-oxabicyclo[4.3.0] nonane, *cf.* mech. Ch. 1 [363].

For C–C bond cleavage of diols *cf.* 4.2; for oxidations of diols and polyols not covered here but included in Chapter 1 *cf.* 2.3.6; for oxidation of $R^1CH(OH)CH(OH)R^2$ to diol cyclic sulfates $R^1C(O\text{-}SO_2O)CR^2$ see 5.4.4.

2.6 Miscellaneous Oxidations of Alcohols

Oxidative cyclisation of *bis*-homopropargylic alcohols (a) to δ-lactones (b) and dihydropyrans (c) was effected by Ru(Cp)Cl(*p*-$MeOC_6H_4)_3P)_2$/*N*-hydroxy-succinimide/aq. Na(HCO_3)/(*p*-$MeOC_6H_4)_3P$)]/DMF (R^1=Me, R^2=$PhCH_2O$,

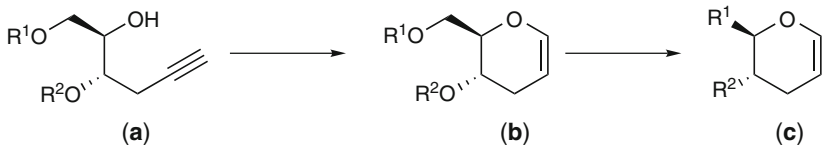

Fig. 2.20 Oxidative cyclisation of *bis*-monopropoargylic alcohols (**a**) to δ-lactones (**b**) or dihydropyrans (**c**) using $Ru(Cp)Cl(R_3P)_2$ catalysts [364, 365]

p-$MeOC_6H_4CH_2$; $R^1={}^nC_7H_{15}$, R^2=H; $PhCH_2O$, *p*-$MeOC_6H_4CH_2$; $R^1=R^2=PhCH_2O$, R^2=MeO, $PhCH_2OCH_2$; $R^1={}^nC_{10}H_{21}CH(OH)$, R^2=H) (Fig. 2.20). Choice of different R groups in the phosphine was used to tune the nature of the reaction products [364, 365].

Sequential TPAP-Wittig oxidation of primary alcohols R^1CH_2OH to aldehydes with TPAP/NMO/PMS/CH_2Cl_2 followed by olefination with $(Ph_3P(CH_2)R^2)Cl/{}^n$BuLi/THF gave $R^1CH{=}CHR^2$ (R^1=benzyl alcohol, dodecanol, phenylpentanol, biphenyl methanol; R^2=H, Me, Cl, Br, COOEt) [366]. Isomerisation of allylic alcohols by TPAP/2-undecanol/C_6H_5F following their oxidation by TPAP/O_2/C_6H_5F was noted (e.g. of 1-phenylprop-2-enol to propiophenone and of geranial to citral, *cf.* mech. Ch. 1) [367]. Oxidation of primary alcohols RCH_2OH to methyl esters RCOOMe was effected by $RuH_2(CO)(PPh_3)_3$/(Xantphos)/MeCH=CHCN/water-CH_3OH-toluene/reflux/24h oxidised primary alcohols RCH_2OH to methyl esters RC(O)OMe (R=Ph, Bn, ${}^nC_7H_{13,}$ ${}^nC_{15}H_{31}$ *(E)*-CH=CHPh,4-(X)$C_6H_4CH_2$; X=OH, Me, NO_2) and octanal to its methyl ester [368, 369]. During reactions studies on oxetanosyl-C-nucleosides, a hydroxy ester was oxidised by TPAP/NMO/PMS/CH_2Cl_2 to give a β-lactone [370]. The dehydrogenative coupling of primary alcohols to indoylamides was effected by TPAP/NMO/PMS/CH_3CN, e.g. of 3-phenyl-1-propanol with pratosine and hippadine [371].

The system $RuH_2(CO)(PPh_3)_3$/(Xantphos)/crotonitrile/pyrollidine/toluene/110°C effected the oxidative dehydrogenation coupling of alcohols R^1CH_2OH and $R^2CO(O)CH_2CO(O)H$ giving the alkenes $R^1CH{=}CHCO(O)R^2$ (R^1=Ph, R^2=Me, Et.CH_2Ph, ^{t}Bu; R^1=*p*-XC_6H_4 (X-DF, Cl, Br, MeO, BnO, CF_3), R^2=Et) [372].

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Chapter 3
Oxidation of Alkenes, Arenes and Alkynes

Abstract This chapter covers one of the most important areas of Ru-catalysed oxidative chemistry. First, alkene oxidations are covered in which the double bond is not cleaved (3.1): epoxidation, cis-dihydroxylation, ketohydroxylation and miscellaneous non-cleavage reactions follow. The second section (3.2) concerns reactions in which C=C bond cleavage does occur (oxidation of alkenes to aldehydes, ketones or carboxylic acids), followed by a short survey of other alkene cleavage oxidations. Section 3.3 covers arene oxidations, and finally, in section 3.4, the corresponding topics for alkyne oxidations are considered, most being cleavage reactions.

Ruthenium complexes catalyse the two main oxidative reactions for alkenes: those in which oxygen atoms or hydroxyl groups span the erstwhile double bond without C=C rupture (e.g. epoxidation, *cis*-dihydroxylation, ketohydroxylation), and cleavage reactions in which the C=C bond is broken. Although RuO_4 has recently been shown to be effective for *cis*-dihydroxylation and ketohdroxylation, epoxidations are in general effected by Ru complexes of lower oxidation states, while RuO_4 excels at cleavage reactions.

Oxidations of alkenes and alkynes have been reviewed, including mechanistic information in some cases. They include treatment of epoxidations [1–9], ketohydroxylations [7–9] and alkene cleavage [4, 6, 10–14]. Oxidations of alkynes have been reviewed in [4, 12, 14, 15].

3.1 Oxidation of Alkenes Involving No C=C Bond Cleavage

In the ensuing discussion we consider first of all those oxidations which do not involve cleavage of the C=C bond (epoxidation, Section 3.1, *cis*-dihydroxylation 3.1.2 and ketohydroxylation 3.1.3, other non-cleavage oxidations 3.1.3.4). Cleavage reactions follow in 3.2 with formation of aldehydes or ketones (3.2.1) and acids (3.2.2).

W.P. Griffith, *Ruthenium Oxidation Complexes,* Catalysis by Metal Complexes 34,
DOI 10.1007/978-1-4020-9378-4_3, © Springer Science+Business Media B.V. 2011

3.1.1 Epoxidation of Cyclic and Linear Alkenes

$$R^1CH=CHR^2+2[O]\rightarrow R^1(CO)CR^2+H_2O \quad (3.1)$$

Epoxidation reactions are important because epoxides are useful intermediates – ring opening allows subsequent reactions at one or both of the carbon atoms, and this is particularly attractive if asymmetric epoxidations can be accomplished (3.1.1.3). This is an increasingly important area for Ru-catalysed oxidations, and a review [2] emphasises in particular mechanistic aspects of such processes. There are also earlier brief reviews of the topic [4, 7, 18], in particular by porphyrin-based systems [17–22].

Few epoxidations have been accomplished with RuO_4 since the reagent is a prime alkene cleavage agent (but see Fig. 3.1 below). Because of the intrinsic interest in, and need for, epoxidations many Ru complexes have been studied for the purpose, but generally only those which are effective (i.e. give good yields and selectivities), are catalytic and do not require forcing conditions are included. Some of those omitted here are mentioned in Ch. 1 and listed in 3.1.1.4 below.

The first Ru-catalysed epoxidation was reported in 1983 by James et al. using $RuBr(PPh_3)$(OEP)/PhIO/CH_2Cl_2[1] with styrene, norbornene and *cis*-stilbene in low yields; *cf.* mech. Ch. 1 [23]. Later work showed that *trans*-$Ru(O)_2$(TMP)/O_2/C_6H_6 catalysed aerobic alkene epoxidation of cyclo-octene, *cis*- and *trans*-β-methylstyrenes and norbornene (Fig. 1.26) [24].

3.1.1.1 Model Substrates

Much exploratory work has been done on model substrates. Epoxidations of cyclo-octene and styrene give relatively clean products, and several studies have also been carried out on styrene, norbornene and 1-octene.

Cyclo-octene Systems epoxidising this include Ru(dmso)(don')(babp)/PhIO/DCE/40°C [25]; $RuCl_2$(Hcbx)(cbx)/O_2/*iso*butyraldehyde/DCE (Fig. 1.36; Table 3.1) [26]; $RuCl_3$/(pyben)/O_2/$Me_2CHCHO+C_8F_{17}Br+C_6H_5Cl$/40°C [27]; $RuCl_2(dmso)_2$(pcbo)/PhIO/water-CH_3CN [28]; $[Ru(CF_3COO)_2(H_2O)$(tmtacn)$]^+$/TBHP/DCE–CH_2Cl_2/SiO_2 [29]; Ru(CO)$(TFPPCl_8)$/O_2/CH_2Cl_2, *cf.* mech. Ch. 1) [30]; $[Ru(CF_3COO)_2(H_2O)$(tmtacn)$]^+$/TBHP/CH_2Cl_2, *cf.* mech. Ch. 1; Table 3.1) [31]; $[Ru(C_7F_{15}COCH_2COC_7F_{15})_3]^-$/perfluorodecalin-toluene/O_2/65°C) [32]; $RuCl_2(biox)_2$/O_2/*iso*butyraldehyde/aq. Na(HCO_3)/CH_2Cl_2 (Table 3.1; Fig. 1.38) [33]; *cis*-$RuCl_2(dmso)_4$/TBHP/CH_2Cl_2/0°C, Table 3.1; *cf.* mech. Ch. 1 [34]; *trans*-$Ru(O)_2$(bpy)$\{IO_3(OH)_3\}$/aq. Na(IO_4)/CH_2Cl_2/2°C [35], (Fig. 1.23) [36]; $[RuCl_2(H_2O)_4]^+$/O_2/-

[1] As indicated in 1.2.2 these abbreviations take the form Ru: starting material/co-oxidant/solvent; temperatures are only indicated if not ambient. For brevity, RuO_2 and $RuCl_3$ denote the *hydrates* RuO_2, nH_2O and $RuCl_3.nH_2O$.

Table 3.1 Epoxidation of alkenes

Reactant	Product	Method [Ref.]
For cyclo-octene and -hexene, styrene, stilbenes, norbornene and 1-octene, *cf.* 3.1.1.1		
2- and 3-Carene	2- and 3-Carene oxides	A [79]
Carvone	Carvone oxide	B [61]
p-Chlorostyrene	*p*-Chlorostyrene oxide	B [61]
Cyclododecene	Cyclododecene oxide	C [35]
Cycloheptene	Cycloheptene oxide	D [46]
Cyclopentene	Cyclopentene oxide	C [35], E [26]
Dec-1-ene	Dec-1-ene oxide	C [35]
trans-5-Decene	*trans*-5-Decene oxide	F [51]
2,3-Dimethylbut-1-ene	2,3-Dimethylbut-1-ene oxide	C [35]
2,3-Dimethylbut-2-ene	2,3-Dimethylbut-2-ene oxide	C [35]
Dodec-1-ene	Dodec-1-ene oxide	C [35]
3-Epicholesteryl acetate	5,6β-Epoxy-5β-cholestan-3α-yl acetate	G [74]
Cholest-4-en-7α-yl acetate	4β,5-Epoxy-5β-cholestan-7α-yl acetate	G [74]
Cholest-4-en-7β-yl acetate	4β,5-Epoxy-5β-cholestan-7β-yl acetate	G [74]
Geraniol	Epoxygeraniol	A [79]
Indene	Epoxyindene	H [34]
Pinene	Epoxypinene	A [79]
3-Fluorostyrene	3-Fluorostyrene oxide	F [51]
cis-2-Heptene	*cis*-2-Heptene oxide	H [34]
Limonene	Limonene oxide	A [79]
(+)-Limonene	*cis* & *trans*-Limonene oxide	J [31]
Methylcyclohexene	1-Methylcyclohexene oxide	E [26], F [51]
α-Methylstyrene	α-Methylstyrene oxide	H [34]
cis-β-Methylstyrene	*cis*-β-Methylstyrene oxide	J [31]
trans-β-Methylstyrene	*trans*-β-Methylstyrene oxide	H [34], J [31]
Oct-1-ene	Oct-1-ene oxide	C [35]
1-Phenylcyclohexene	1-Phenylcyclohexane oxide	E [26]
2,4,4-Trimethylpent-1-ene	2,4,4-Trimethylpent-1-ene oxide	C [35]
Undec-1-ene	Undec-1-ene oxide	K [26]

A: RuCl(TAZO)(*p*-cymene)/O_2/Me_2CHCHO/CH_2Cl_2 [79]; B: *trans*-$Ru(O)_2$(TMP)/(Cl_2pyNO)/C_6H_6 [61]; C: *trans*-$Ru(O)_2$(bpy){$IO_3(OH)_3$}/aq. $Na(IO_4)$/CH_2Cl_2/2°C [35]; D: $RuCl_3$/PhIO/CH_3CN [46]; E: $RuCl_2$(Hcbx)(cbx)/O_2/*iso*butyraldehyde/DCE (Fig. 1.36) [26]; F: $RuCl_3$/pydic/aq. H_2O_2/^{t}AmOH [51]; G: *trans*-$Ru(O)_2$(TMP)/O_2/C_6H_6 [74]; H: *cis*-$RuCl_2(dmso)_4$/TBHP/CH_2Cl_2 [34]; J: $[Ru(CF_3COO)_2(H_2O)(tmtacn)]^+$/TBHP/$CH_2Cl_2$ [31]; K: $RuCl_2$(biox)/O_2/Me_2CHCHO/aq. $Na(HCO_3)$/CH_2Cl_2 (Fig. 1.38) [26].

water-dioxane, *cf.* mech. Ch. 1 [37–39]; $[RuCl(EDTA\text{-}H)]^-$/O_2/water-dioxane/37–62°C, *cf.* mech. Ch. 1 [40]; $RuCl_3$/aq. $Na(IO_4)$/(bpy)/CH_2Cl_2/0–5°C [41].

Cyclohexene Ru(dmso)(don')(babp)/PhIO/DCE/40°C [25]; $[Ru(H_2O)(bpy)(cpsd)]^+$/TBHP/($PhCH_2${$N(CH_2)_3Me$}$_3$)Cl/CH_2Cl_2 [42]; $RuCl_2$(Hcbx)(cbx)/O_2/*iso*butyraldehyde/DCE (Fig. 1.36) [26]; RuCl(bpy)(amp)/TBHP/aq. ($PhCH_2N$($^tBu_3N$)Cl/CH_2Cl_2 [43]; $Ru(CO)(TFPPCl_8)$/O_2/CH_2Cl_2, *cf.* mech. Ch. 1 [30]; $[Ru(CF_3COO)_2(H_2O)(tmtacn)]^+$/TBHP/$CH_2Cl_2$, *cf.* mech. Ch. 1) [31]; *trans*-$Ru(O)_2$(bpy){$IO_3(OH)_3$}/aq. $Na(IO_4)$/CH_2Cl_2/2°C (Fig. 1.23) [36];

$RuCl_2(H\text{-}dmg)_2$/PhIO/water [44]; $[Ru(O)Cl_2(H_2O)_3]^+$/water-dioxane/Pt anode, *cf.* mech. Ch. 1; stoich. $Ru(O)(PDTA)]^-$ or Ru(O)(HEDTA)/water-dioxane, *cf.* mech. Ch. 1 [45]; $[RuCl_2(H_2O)_4]^+/O_2$/water-dioxane, *cf.* mech. Ch. 1 [37–39]; $RuCl_3$/PhIO/CH_3CN, (Table 3.1 *cf.* mech. Ch. 1) [46]; stoich. $[Ru(O)_2Cl_3]^-/CH_3CN$ [47]; $RuCl_3$/O_2/aq. EtOH/30°C, *cf.* mech. Ch. 1 [48]; $[Ru(O)(PPh_3)(bpy)_2]^{2+}/O_2/CH_2Cl_2$, *cf.* mech. Ch. 1 [49]; $RuCl_3$/aq. $Na(IO_4)$/(bpy)/CH_2Cl_2/0–5°C [41]; $RuBr(PPh_3)$(OEP)/PhIO/CH_2Cl_2 [50].

Styrene $RuCl_3$/pydic/H_2O_2/^{t}AmOH [51]; $[RuCl(dmso)(bpy)_2]^+$/aq. $Ph(IOAc)_2$/CH_2Cl_2/40°C [52]; RuCl(bpy)(amp)/TBHP/aq. (BTBAC)/CH_2Cl_2 [43]; Ru(pydic)(tpy)/$PhI(OAc)_2/CH_2Cl_2$ [53, 54]; $[Ru_2(OH)Cl(H_2O)_4(napy)_2]^{4-}/O_2$/aq. Me_2CHCHO/DCE/40°C (Fig. 1.35) [55, 56]; *cis*-$RuCl_2(dmso)_4$/TBHP/CH_2Cl_2/0°C, *cf.* mech. Ch. 1 [34]; $[Ru(CF_3COO)_2(H_2O)(tmtacn)]^+$/TBHP/$CH_2Cl_2$, *cf.* mech. Ch. 1) [31]; $RuCl_3$/pydic/aq. H_2O_2/AmOH [51]; $RuCl_2(biox)/O_2$/*iso*-butyraldehyde/aq. $Na(HCO_3)$/CH_2Cl_2 (Fig. 1.38) [33]; *trans*-$Ru(O)_2(TMP)/(Cl_2pyNO)/C_6H_6$ [57]; $RuCl_2(COD)$ (*S*,*S*)-$R_2{}^1C(C{=}NCHR^2CR_2{}^1O)_2/O_2$/aq. $Na(IO_4)$ or TBHP/^{i}PrCHO/DCE [58]; $RuCl_2(pap)_2$/aq. $Na(IO_4)/CH_2Cl_2$ [59]; *trans*-$Ru(O)_2(bpy)\{IO_3(OH)_3\}_2$/aq. $Na(IO_4)$/CH_2Cl_2/2°C [35] (Fig. 1.23) [36]; $[Ru(H_2O)(EDTA)]^-/O_2$/water-dioxane, *cf.* mech. Ch. 1 [60]; *trans*-$Ru(O)_2(TMP)/(pyNO)/C_6H_6$ [61]; $RuBr(PPh_3)$(OEP)/PhIO/CH_2Cl_2, *cf.* mech. Ch. 1) [23]; $RuCl_3$/aq. $Na(IO_4)$/(bpy)/CH_2Cl_2/0–5°C [41].

Norbornene $RuCl_3$/pydic/H_2O_2/^{t}AmOH [51]; $RuCl_2(dmso)_2$(pcbo)/PhIO/water-CH_3CN [28]; $[Ru(C_7F_{15}COCH_2COC_7F_{15})_3]^-$/perfluorodecalin-toluene/O_2/65°C [32]; stoich. *trans*-$[Ru(O)_2(TMP)]^+$ or *trans*-$[RuO_2(OEP)]^+/CH_2Cl_2$/−45°C [62]; $[Ru(CF_3COO)_2(H_2O)(tmtacn)]^+$/TBHP/$CH_2Cl_2$, *cf.* mech. Ch. 1) [31]; *trans*-$Ru(O)_2(bpy)\{IO_3(OH)_3\}$/aq. $Na(IO_4)/CH_2Cl_2$/2°C [35] (Fig. 1.23) [36]; *trans*-$Ru(O)_2(TMP)/O_2/C_6H_6$, *cf.* mech. Ch. 1 [21] (Fig. 1.26) [24]; $RuCl_3$/aq. $Na(IO_4)$/(bpy)/CH_2Cl_2/0–5°C [41]; $RuBr(PPh_3)$(OEP)/PhIO/CH_2Cl_2, *cf.* mech. Ch. 1) [23]; stoich. $Ru(O)_2(OAc)(py)_2/CH_3CN$ [63] (Fig. 1.22).

1-Octene *Cis*-$RuCl_2(dmso)_4$/TBHP/CH_2Cl_2/0°C, *cf.* mech. Ch. 1 [34]; Ru(CO)(TPFPP)/Cl_2pyNO/CH_2Cl_2/65°C [64]; *trans*-$Ru(O)_2(bpy)\{IO_3(OH)_3\}$/aq. $Na(IO_4)$/CH_2Cl_2/2°C [35]; *trans*-$Ru(O)_2(TMP)/O_2$(1 atm.)/aq. CH_2Cl_2, *cf.* mech. Ch. 1) [65]; $[Ru\{SiW_{11}(H_2O)(O)_{39}\}]^{5-}$/TBHP or aq. $Na(IO_4)$, aq. $(HSO_5)^-$ or PhIO/65°C [66, 67].

3.1.1.2 Specific Examples of Epoxidation of Mono, Di- and Polyalkenes

Some remarkably simple Ru species will catalyse epoxidations. Balavoine et al. showed in 1984 that several linear and cyclic alkenes were epoxidised by $RuCl_3$/aq. $Na(IO_4)$/(bpy)/CH_2Cl_2/0–5°C/15 h [41]; 5-methyl- or 3,4,7,8-tetra-methylphenanthroline [68] can replace (bpy). The active species with (bpy) may be the 'double oxidant' *trans*-$Ru(O)_2(bpy)\{IO_3(OH)_3\}$ in which both the metal centre and the periodato ligand are oxidants (Tables 3.1 and 1.11) [35] (Fig. 1.23) [36]. Competition between epoxidation and cleavage of *trans*-stilbene with bidentate ligands containing two different nitrogen heterocycles (pyridine, oxazoline, oxazolidine and thiophene), either linked or separated by a spacer together with $RuCl_3$/aq. $Na(IO_4)/CH_2Cl_2$/2°C was studied, *cf.* mech. Ch. 1 [69].

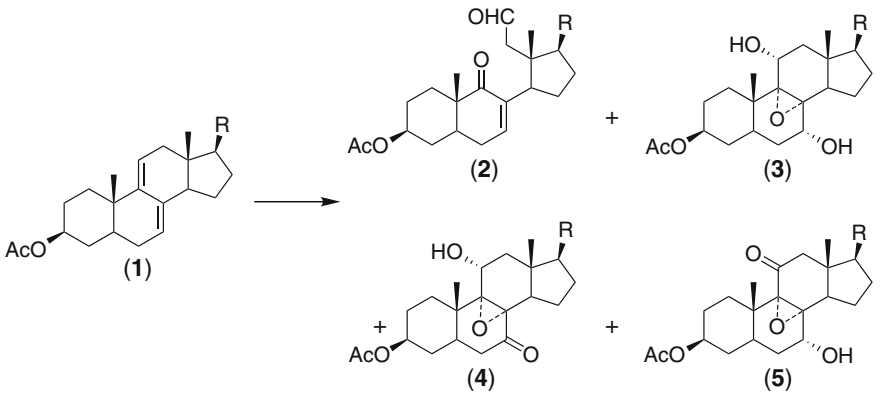


Fig. 3.1 Epoxidation of $\Delta^{7,9(11)}$ conjugated sterol dienes by RuO_4 [77]

A simple system, $RuCl_3$/pydic/H_2O_2/^{t}AmOH (pydic=pyridine-2,6-dicarboxylic acid) epoxidised cyclic and linear alkenes in good yields (Table 3.1) [51]. The β-stereoselective and regioselective oxidation of the Δ^5-unsaturated steroids cholesteryl acetate, pivalate, benzoate and caproate, and of stigmasteryl acetate was effected by $RuCl_2$(biox)/O_2/*iso*butyraldehyde/aq. Na(HCO_3)/CH_2Cl_2 to the corresponding 5β, 6β-epoxides, e.g. cholesteryl pivalate gave 3β-(pivaloyloxy)-5β,6β-epoxy-5β-cholestane with 3β-(pivaloyloxy)-5α,6α-epoxy-5α-cholestane (*cf.* mech. Ch. 1; (b) in Fig. 1.38) [33, 70]; likewise *trans*-Ru(O)$_2$(TMP)/O_2/C_6H_6 or *trans*-Ru(O)$_2$(TMP)/MCPBA/C_6H_6 epoxidised cholest-5-ene derivatives, cholesteryl acetate giving almost pure 5β,6β epoxide (*cf.* mech. Ch. 1) [71–73].

A review covers *cis*-dihydroxylation of polyoxygenated steroids [6]. The system *trans*-Ru(O)$_2$(TMP)/O_2/C_6H_6 (Table 3.1) catalysed the β-stereospecific epoxidation of the acetic esters of cholesterol, 3-epicholesterol, isocholesterol and its 7β-epimer (thus 3-epicholesteryl acetate gave 5β,6β-epoxy-5β-cholestan-3α-yl acetate; 3β-acetoxy-6-methylpregn-5-en-20-one gave 3β-acetoxy-5β,6β-epoxy-6α-methyl-pregnan-20-one; cholestan-4-en-7α-yl acetate gave 4β,5-epoxy-5β-cholestan-7α-yl acetate and 7α-acetoxycholest-4-en-3-one; cholest-4-en-7β-yl acetate gave 4β,5-epoxy-5β-cholestan-7β-yl acetate and 7β-acetoxycholest-4-en-3-one). Possible reasons for these stereospecificities were discussed (*cf.* mech. Ch. 1; Table 3.1) [74]. Similar studies were made on cholesteryl phenyl-acetate, butyrate, crotonate, hydrocinnamate, oleate and elaidate with Ru(CO)(TMP)/MCPBA/C_6H_6 (*cf.* mech. Ch. 1) [71]. Epoxidation of (*Z*)-17-ethylideneandrostane to (17*R*,20*S*)- and (17*R*,20*R*)-17,20-epoxy-5α-pregnanes was effected by *trans*-Ru(O)$_2$(TMP)/MCPBA/C_6H_6 [75].

At low temperatures RuO_4, as RuO_2/aq. Na(IO_4)/acetone/−70°C epoxidised some $\Delta^{7,9(11)}$ conjugated sterols. Thus 5α-cholesta-7,9(11)-dien-3β-yl acetate (1), when so treated, gave 3β-acetoxy-9-oxo-9,11-seco-5α-cholest-7-en-11-al (2) together with three 8α,9α epoxysterols (3–5) (Fig. 3.1) [76, 77].

In geranyl, neryl and linalyl acetates the 6,7-double bonds were epoxidised selectively by *trans*-Ru(O)$_2$(TMP)/2,6-lutidine *N*-oxide/C_6H_6 and also by

trans-$Ru(O)_2(TMP)/O_2/C_6H_6$, there being minor epoxidation only at the 2,3 position and little formation of di-epoxides. Oxidation of *trans,cis,trans*-1,5,9-cyclododecatriene by *trans*-$Ru(O)_2(TMP)$/2,6-lutidine *N*-oxide/C_6H_6 gave mainly the *cis* epoxide, *cf.* mech. Ch. 1 [78]. The system RuCl(TAZO)(*p*-cymene)/O_2/*iso*butyraldehyde/CH_2Cl_2 catalysed the epoxidation by a current of O_2 of a range of natural terpenes (Table 3.1) including pinene, 2- and 3-carene, limonene, geraniol and valencene [79]. Studies were made of the oxidation of cholest-5-ene-3-one to the 6α and 6β alcohols and the enedione by *trans*-$Ru(O)_2(TMP)/O_2/C_6H_6$ (Table 3.2) [80].

3.1.1.3 Asymmetric Epoxidations

There has recently been much work in this area using Ru-based catalysts, particularly with porphyrin-based catalysts, following the work by Sharpless et al. on asymmetric epoxidation of allylic alcohols by a titanium-based tartrate system. There are reviews on asymmetric epoxidations catalysed by chiral Ru porphyrins [5, 18].

As is the case with non-chiral epoxidations model systems are much used, and styrene (and substituted styrenes), stilbenes and 1,2-dihydronaphthalene are the preferred models.

Styrene Ru(pybox)(pydic) or Ru(R_2-pyboxazine)(pydic)/aq. H_2O_2/^{t}AmOH (*cf.* mech. Ch. 1) [81]; *trans*-$Ru(O)_2$(chir-TPP)/(Cl_2pyNO)/C_6H_6 [82]; [RuCl(SOMePh)$(bpy)_2]^+$/TBHP/water-CH_2Cl_2 [52]; $[RuCl(PNNP)]^+$ or $[RuCl(H_2O)(PNNP)]^+$/aq. H_2O_2/CH_2Cl_2 [83]; $Ru(PPh_3)(H_2O)$(tSB)/PhIO/C_6H_3F/0°C, *cf.* mech. Ch. 1 [84]; Ru(NO)Cl(salen^{chir})/(Cl_2pyNO)/CH_2Cl_2/4°C [85]; *trans*-$Ru(O)_2$(por*)/PhIO/CH_2Cl_2, *cf.* mech. Ch. 1 [86–88]; $RuCl(H_2O)(csb)_2/O_2/Me_2CHCHO/CH_2Cl_2$/4°C *cf.* mech. Ch. 1 [89]; *trans*-Ru(CO)(porch)/PhIO or (Cl_2pyNO)/C_6H_6 [90, 91]; Ru(CO)(porph^{chir})/(Cl_2pyNO)/C_6H_6 [92]; $RuCl(H_2O)(csb')_2$/PhIO/CH_3CN, *cf.* mech. Ch. 1 [93]; $Ru(PPh_3)(H_2O)_2(SB^{chir})$/(PhIO/$CH_2Cl_2$ [94] (Fig. 1.41) [95]; stoich. $[Ru(O)(bpy)(thm)]^{2+}/CH_3CN$ [96].

***Trans*-stilbene** Ru(pybox)(pydic) or Ru(R_2-pyboxazine)(pydic)/aq. H_2O_2/^{t}AmOH, *cf.* mech. Ch. 1 [81]; Ru(pydic)(R_2-pybox)/TBHP/^{t}BuOH (Fig. 1.37) [97], [98]; $[RuCl(SOMePh)(bpy)_2]^+$/TBHP/water-CH_2Cl_2 [52]; $RuCl_3$/(oxal)/$Na(IO_4)$/aq. phosphate @ pH 8/4°C, [99]; Ru(pydic)(R_2-pybox)/$PhI(OAc)_2$/toluene [53, 54]; Ru(CO)(porph^{chir})/(Cl_2pyNO)/C_6H_6 [92]; $RuCl_3$/(pyoxal)/aq. $Na(IO_4)/CH_2Cl_2$/0°C [100].

1,2-dihydronaphthalene Ru(NO)(salen^{chir})/TMPZNO/dioxane/UV, *cf.* mech. Ch. 1 [101]; *trans*-$Ru(O)_2$(chir-TPP)/(Cl_2pyNO)/C_6H_6 [82]; $[RuCl(H_2O)(PNNP)]^+$ or $[RuCl(PNNP)]^+$/aq. H_2O_2/CH_2Cl_2 [83]; Ru(CO)(porph^{chir})/(Cl_2pyNO)/C_6H_6 [92]; *trans*-$Ru(O)_2$(por*)/PhIO/CH_2Cl_2, *cf.* mech. Ch. 1 [86–88].

The earliest work, by Kureshy et al. used complexes of chiral Schiff bases, e.g. $Ru(PPh_3)(H_2O)_2(SB^{chir})$ (Fig. 1.41); $Ru(PPh_3)(H_2O)_2(SB^{chir})$/PhIO/$CH_2Cl_2$/4°C catalysed the asymmetric epoxidation of styrene in the dark under an inert atmosphere. Yields of epoxide were however relatively low [95], but later systems of this

type were refined, *cf.* mech. Ch. 1 [89, 93, 94]. Thus asymmetric epoxidation of styrene and 4-chloro, 4-nitro and 4-methylstyrenes was catalysed by $Ru(PPh_3)(H_2O)$(tSB)/PhIO/C_6H_5F/0°C and gave good selectivities and e.e. values particularly in the case of the bases derived from L-tyrosine, *cf.* mech. Ch. 1 [84]; similarly, $Ru(H_2O)(PPh_3)$(ctSB)/(PhIO/C_6H_5F/0°C asymmetrically epoxidised 1,2-dihydronaphthalene; *cf.* mech. Ch. 1 [102].

The following account concentrates on more recently developed systems, some of which are listed in the model system sections above. The chiral system $Ru(NO)Cl(salen^{chir})$/TMPZNO/dioxane/UV (TMPZNO=tetramethyl-pyrazine-*N,N'* dioxide) catalysed the epoxidation of conjugated alkenes under photo-irradiation by a halogen or incandescent lamp. Good yields were obtained of epoxides with high e.e. values (80–97%) and the reactions are highly stereospecific, *cis*- and *trans*- alkenes giving *cis*- and *trans*- epoxides. Thus 6-acetamido-2,2-dimethyl-7-nitrochromene gave (*3S,*4S)-6 acetamido-3,4-epoxy-2,2-dimethyl-7-nitrochromene, while 4-methyl-1-phenylpenten-1-yne gave 3,4-epoxy-4-methyl-1-phenylpent-1-yne (*cf.* mech. Ch. 1) [101]. Similar asymmetric epoxidation of conjugated alkenes can be effected in sunlight or in incandescent light using $Ru(NO)Cl(salen^{chir})$/(Cl_2pyNO)/CH_2Cl_2/4°C; e.e. values of up to 98% were obtained in some cases [85]. The system $[RuCl(PNNP)]^+$ or $[RuCl(H_2O)(PNNP)]^+$/aq. H_2O_2/CH_2Cl_2 (PNNP=tetradentate P,P,N,N donors, (Fig. 1.42)) asymmetrically epoxididised styrenes; thus (*Z*)-2-methylstyrene gave the *cis*-epoxide with only traces of the *trans*-isomer [83]. The reagent epoxidised stilbene, *Z*-2-methylstyrene and 1,2-dihydronapthalene: the latter was converted quantitatively to (-)-(1*S*,2*R*)-epoxide with an e.e. of 41% [104]. In the case of styrene the use of PhIO rather than aq. H_2O_2 gave a very high yield of (*S*)-styrene oxide. Products other than the epoxide resulted when TBHP or ($^nBu_4N$)(HSO_5) were used as co-oxidants while, remarkably, Na(ClO) provided no oxidation at all [103].

The complexes Ru(pydic)(tpy), Ru(pydic)(pybox-R_2) (pydic=pyridine-2,6-dicarboxylate, pybox-R_2=chiral bis(oxazolinyl)pyridines with R=Pr^i, Ph (Fig. 1.37) [105] epoxidised *trans*-stilbene (as complex/PhIO, $PhI(OAc)_2$, TBHP or O_2/CH_2Cl_2). Asymmetric oxidations of *trans*-stilbene were similarly achieved in toluene, benzene and CH_2Cl_2 with e.e. values from 40–80% (*cf.* mech. Ch. 1) [53, 54, 81, 97]. Asymmetric epoxidations of *trans*-stilbene, styrene, *trans*-β-methylstyrene and 1-hexene were catalysed by $[RuCl(SOMePh)(bpy)_2]^+$/TBHP or $Ph(IOAc)_2$/CH_2Cl_2/40°C; e.e. values of 33–94% were obtained of the *(R, R)* forms of the epoxides of *trans*-stilbene, *trans*-β-methylstyrene [52]. The system Ru(CO)(TPP)/(Cl_2pyNO)/HBr/C_6H_6 epoxidised fullerene (C_{60}) to 1,2-epoxy[60]fullerene with 1,2:3,4 di-epoxy and 1,2:3,4:9,10 + 1,2:3,4:11,12 tri-epoxy species [106].

3.1.1.4 Other Alkene Epoxidation Systems Not Covered Here but Included in Chapter 1

The following systems are not covered in this chapter because they lack general applicability; most are epoxidising systems but some others that do not involve

C=C bond cleavage are covered – the length of this section does though give some idea of how much work has been done on Ru-catalysed epoxidations. They include: Ru(CO)(den-por)/(Cl_2pyNO)/CH_2Cl_2 (cyclic alkenes) [107]; *trans*-Ru(O)$_2$(TMP)/N_2O (10 atm.)/C_6H_5F (linear & cyclic alkenes) [108]; $RuCl_2$(pydim)/PhIO/DCE/70°C (cyclohexene) [109]; stoich. $[Ru(O)(biqn)(tmtacn)]^{2+}$ and $[Ru(O)(diopy)(tmtacn)]^{2+}$/$CH_3CN$ (stilbene) [110]; $[Ru(O)_2(CF_3COO)(tmtacn)]^+$/PhIO or TBHP/$CH_2Cl_2$ (cyclic alkenes) [111]; $[Ru\{PW_{11}O_{39}\}]^{3-}$/TBHP/$CH_3CN$/60°C (stilbene) [112]; *trans*-Ru(O)$_2$(TMP)/lutidine-*N*-oxide/C_6H (styrene) [113]; stoich. *trans*-Ru(O)$_2$(OEP)/CH_2Cl_2 (norbornene, styrene, stilbene) [114]; *trans*-$[Ru(O)_2(dpt)]^{2+}$/CH_3CN/UV >330 nm (norbornene, cyclohexene, *trans*-stilbene) [115]; stoich. *trans*-[Ru(O)$_2$(14-TMC)]/CH_3CN/50°C [116]; stoich. *trans*-$[Ru(O)_2(ddd)]^{2+}$/CH_3CN (cyclic alkenes) [117]; $[Ru(O)(bpy)(tpy)]^{2+}$/water @ pH 7–9/Pt anode (cyclohexene) [118]; Ru(acac)$_3$ or $RuCl_2(PPh_3)_3/O_2/C_6H_6$/60°C (cyclohexene) [119].

For the following systems *cf.* Ch. 1 for mechanistic information: stoich. *cis*-$[Ru(O)(py)(bpy)_2]^{2+}$/CH_3CN (cyclohexene, cyclohexen-1-ol, indene) [120]; Ru(dmso)(don')(babp)/PhIO/DCE/40°C (cyclohexene, stilbene) [121]; [Ru(O)(pic)(tpy)]$^+$/CH_3CN (cyclic alkenes) [122]; $[Ru(H_2O)(bpy)(app)]^{2+}$/TBHP/$CH_2Cl_2$/(BTBAC) (stilbenes) [123]; *trans*-Ru(O)$_2$(TMP)/PhIO or Cl_2pyNO/C_6H_6 (substituted styrenes) [124]; $[RuCl(dppp)_2]^+$ and $[RuCl(ppy)_2]^+$/PhIO (linear and cyclic alkenes) [125–128]; $[Ru(ClO_4)(LL)]^+$ (LL=dppm, dppe, dpae)/TBHP/CHP/aq. H_2O_2/CH_2Cl_2/50°C (cyclic alkenes) [129, 130]; stoich. *trans*-[Ru(O)(Cl_2bpy)(tpy)]$^{2+}$ and [Ru(O)(tpy)(tmeda)]$^{2+}$/CH_3CN (cyclic alkenes) [131]; stoich. [Ru(O)(py)(bpy)]$^{2+}$/CH_3CN) [132]; stoich. *cis*-[Ru(O)$_2$(tet-Me_6)]$^{2+}$/CH_3CN (cyclic alkenes) [133]; stoich. $[Ru(O)(bpy)(tmtacn)]^{2+}$/$CH_3CN$ (cyclic, linear alkenes) [134]; *cis*-$[Ru(H_2O)_2(dmp)_2]^{2+}/O_2$(3 atm.)/$CH_3CN$/65–75°C (norbornene) [135–137]; RuCl(bpy)(DPA) and RuCl(phen)(DPA)/PhIO or TBHP/water-dioxane (styrene, norbornene) [138]; Ru(O)$_2$(TDCPP)/O_2/C_6H_6 or Ru(O)$_2$(TMP)/O_2/C_6H_6 (norbornene) [139]; $[Ru(H_2O)(bpy)(bpp)]^{2+}$/aq. Na(ClO/(BDTAC)/$CH_2Cl_2$ (styrene, cyclo-octene, -hexene) [140]; $RuCl_3$/EDTA/O_2/aq. ascorbic acid (cyclohexene) [141]; *cis*-$RuCl_2(bpy)_2$ or *cis*-$RuCl_2phen_2$/aq. H_2O_2/^{t}BuOH (oleic acid) [142]; Ru(hedta) or Ru{$(CH_3)_2$edda}/TBHP/water-CH_2Cl_2 (stilbenes) [143]; $RuCl_3$/EDTA/ascorbate/O_2/water @ pH 2.5/30°C [144–146]; $[Ru(H_2O)(EDTA)]^-/O_2$/water [147]; Ru(NO)(EDTA)/O_2 or PhIO/water-EtOH (cyclohexene, 1-hexene) [148]; *trans*-RuO_2(R-TPP)/CH_2Cl_2 (cyclic alkenes) [149]; $[Ru(H_2O)(EDTA)]^-$/aq. (HSO_5^-) (cyclo-octene, cyclohexene) [150]; $[RuCl(dpp)_2]^+$ or $[RuCl(ppy)_2]^+$/PhIO/CH_2Cl_2 (linear and cyclic alkenes) [127, 128]; $[Ru_3(\mu\text{-}O)(pfb))_6(Et_2O)_3]^+/O_2$(1.3 atm.)/$CH_3CN$/65°C (cyclohexene and norbornene) [151]; $[Ru(O)(bpy)(tpy)]^{2+}$ or *cis*-$[Ru(O)(py)(bpy)_2]^{2+}$/aq. Na(ClO)/(BDTAC)/CH_2Cl_2 and stoich. $[Ru(O)(py)(bpy)_2]^{2+}$/CH_3CN (stilbenes, styrene) [152].

For asymmetric epoxidation of *trans*-β-methylstyrene, *trans*-Ru(O)$_2$(hpp)/(Cl_2pyNO) or O_2 (9 atm.)/C_6H_6 [153, 154]. For epoxide ring-opening of functionalised norbornanes *cf.* 4.1.4, Fig. 4.5.

3.1.2 Cis-Dihydroxylation of Alkenes

$$R^1CH=CHR^2+[O]+H_2O \rightarrow R^1CH(OH)CH(OH)R^2 \qquad (3.2)$$

The development of RuO_4 as a *cis*-dihydroxylation catalyst is a relatively new and potentially important area. Until recently OsO_4 has been the reagent of choice for this, but use of the cheaper RuO_4 may well become competitive, though stringent reaction conditions need to be used because RuO_4 is so much more powerful an oxidant than OsO_4. Reactions are much faster than for OsO_4, but so-called "flash dihydroxylations" in which low temperatures are used have been developed, and are the subject of much current research. There are several reviews including mechanistic aspects [7–9] and one on the synthesis of polyoxygenated steroids [6]. The scope and limitations of the procedure have been discussed [155, 156].

3.1.2.1 Specific Systems for cis-Dihydroxylations

The first observation that RuO_4 is usable for the reaction was made by Sharpless et al. in 1976 in a footnote to a paper on osmylation of alkenes. It was found that *E*- and *Z*-cyclododecene with stoich. RuO_4/EtOAc at −78°C gave the *threo* and *erythro* diols, but the procedure was not deemed viable owing to the low yields obtained and the necessity for working at low temperatures [157].

However, later procedures gave acceptable yields when a wide range of alkenes was *cis*-dihydroxylated with RuO_4 from $RuCl_3$/aq. $Na(IO_4)$/EtOAc–CH_3CN/0°C (Table 3.2) [158]. A useful and practically explicit paper discusses the scope and limitations of the procedure using this reagent (Table 3.2) [159]. More such oxidations were performed by stoich. RuO_4/aq. acetone/−70°C. The 1,2-diols were formed in a *syn*-stereospecific manner; thus (-)-citronellyl acetate gave a 1:1 mixture of diastereoisomeric 1,2-diols, *trans*-oct-2-ene gave the corresponding 1,2-diol; *trans*-tetradec-7-ene gave (*7R,8R*)+(*7S,8S*)-tetradecane-7,8-diol and (+)-*p*-menth-1-ene gave the 1,2-diol [160]. In such cases the intermediacy of Ru(VI) diesters was postulated [159, 160], and such species isolated (Fig. 1.31) [161, 162]. The effect of solvents on the efficacy of the $RuCl_3$/aq. $Na(IO_4)$/EtOAc–CH_3CN/0°C system for *cis*-dihydroxylation was assessed, and acetone rather than ethyl acetate shown to be a useful solvent. Thus conversion of cholesteryl acetate to the ketol or the diol was found to be much more effective if acetone replaced EtOAc [163]. Brönsted acids, e.g. $CeCl_3.7H_2O$ or $H[Ce(IO_6]$ accelerate the reaction (e.g. as $RuCl_3$/aq. $Na(IO_4)$/$CeCl_3.7H_2O$/EtOAc–CH_3CN/0°C, Table 3.2) [164]. This system with $CeCl_3.7H_2O$ *cis*-dihydroxylated glycals stereoselectively (Fig. 3.2; R=AcO, Bz, Bn); thus tri-*O*-acetyl-D-glucal gave 3,4,6-tri-*O*-acetyl-D-glucose-1,2-diol. Exclusive formation of *cis*-diols was observed depending on the stereochemistry of substituents present in the substrates [165].

The system $RuCl_3$/aq. $Na(IO_4)$/$CeCl_3.7H_2O$/EtOAc–CH_3CN/0°C was used to *cis*-dihydroxylate 3-benzyloxy-2,2-difluoro-cyclo-oct-4*Z*-en-1-one to 3*R**-benzyloxy-2,2-difluoro-9-oxa-1*S**,5*R**-bicyclo[3.3.1]nona-1*S**,4*S**-diol and the

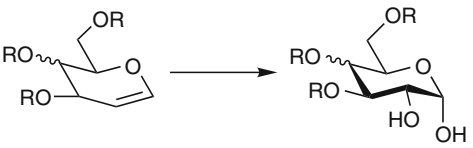
Table 3.2 *Cis*-dihydroxylation and ketohydroxylation of alkenes

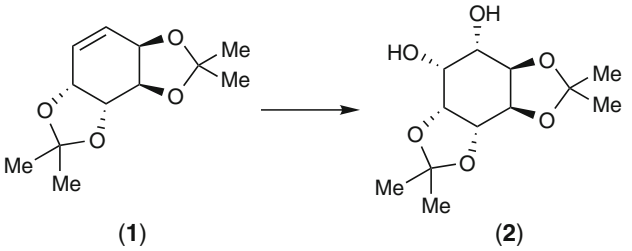
Reactant	Product	Method [Ref.]
Acetic acid 2-hydroxy-3-oxo-3-phenylpropyl ester	Acetic acid 2-hydroxy-3-oxo-3-cyclohexylpropylester + Acetic acid 3-cyclohexyl-3-hydroxy-2-oxo-propyl ester	A [176]
3-Acetoxy-1-cyclohexene	(2*R**,3*S**)-3-Acetoxy-2-hydroxycyclohexanone	B [179]
17β-Acetoxy-estr-5(10)-ene-3-one	17β-Acetoxy-10-hyrdoxyestr-4-ene-3-one	C [80]
trans-Cyclohexenyl diacetate	(1*R**,3*R**,4*)- & (1*R**,3*S**,4*)-4-Acetoxy-3-3-hydroxy-2-oxocyclochexyl acetate	A [181]
4-Acetyl-1-Methylcyclohexene	(1,2,4)-4-Acetyl-1-methylcyclohexane-1,2-diol	D [159]
3-(Azidopropenyl)benzene	3-Azido-2-hydroxy-1-phenylpropan-1-one +3-Azido-2-hydroxy-1-phenylpropan-2-one	A [176]
Allyl azide	(2*R**,3*S**)-3-Azido-2-hydroxycyclohexanone	B [179]
Cis- or *trans*-stilbene	Benzoin	A [9]
1-Benzyloxycyclohexane	(1/2,3)-Benzyloxy-2,3-dihydroxycyclohexane	D [159]
Cyclohexene	Cyclohexane-1,2-diol	D [159], E [164], F [158]
Cyclo-octene	*cis*-Cyclo-octane-1,2-diol	D [159], F [158]
1,2-Decene	(±)-1,2-Decanediol	D [159], F [158]
Coumarin	(3*S**,4*S**)-3,4-Dihydroxy chroman-2-one	E [164], G [155]
3-Cyanocyclohexene	3,4-Dihydroxy-cyclohexanecarbonitrile	G [155]
2-Cyclohexen-1-one	(±)-*cis*-2,3-Dihydroxycyclohexanone	D [159]
Allyl acetate	(1*S**,2*S**,3*S**)-2,3-Dihydroxy cyclohexyl acetate	G [155]
Stilbene	(±)-*threo*-Hydrobenzoin	A [177], D [159]
Styrene	2-Hydroxyacetophenone	A [177]
1,3-Diphenylallyl methylether	(2*R**, 3*S**) & (1*S**, 3*S**)-2-Hydroxy-3-methoxy-1,3-diphenylpropan-1-one	A [181]
1-Methylcyclohexene	2-Hydroxy-2-methylcyclohexanone	B [179], E [164]
2-(3-Phenylallyl)*iso*indole-1,3-dione	2-(2-Hydroxy-3-oxo-3-phenylpropyl) +2--(3-hydroxy-3-oxo-3-phenylpropyl)-*iso*indole-1,3-diones	A [176]
(1*S*)-(-)-α-Pinene	(1*S*,2*S*,5*S*)-2-Hydroxy-2,6,6-trimethylbicyclo [3.3.1]-heptan-3-one	A [176]
Indene	(1*S**,2*S**)-Indane-1,2-diol	G [155]

1-Methyl cyclohexene	(1*S**,2*R**)-Methylcyclohexane-1,2-diol	G [155]
1-Methyl cyclopentene	(1*S**,2*R**)-Methylcyclopentane-1,2-diol	G [155]
4-Nonene	(±)-*threo*-4,5-Nonanediol	D [159]
3β,21-Diacetoxy-5α-pregn-17-ene	20-Oxo-5α-pregnane-3β,17α,21-triol-3,21-acetate	B [179]
3-(Phenoxypropenyl)benzene	3-Phenyloxy-2-hydroxy-1-phenylpropan-1-one +1-Hydroxy-3-phenoxy-1-phenylpropan-2-one	A [176]
2,3-Dimethyl-2-butene	Pinacol	D [159]
2-Carene	1*S*-(1α,2α,3α,4α]-3,7,7-Trimethylbicyclo-[4.1.0]-heptane-2,3-diol	D [159]

A: $RuCl_3$/Oxone®/aq. $Na(HCO_3)$/EtOAc–CH_3CN [9, 176, 177, 181] (Fig. 1.6); B: $RuCl_3$/aq. CH_3CO_3H/CH_3CN–CH_2Cl_2 [179]; C: *trans*-$Ru(O)_2(TMP)/O_2/C_6H_6$ [80]; D: $RuCl_3$/$Na(IO_4)$/aq. $Na(HCO_3)$/EtOAc–CH_3CN/5°C [159]; E: $RuCl_3$/aq. $Na(IO_4)/CeCl_3.7H_2O$/EtOAc–CH_3CN/0°C [164]; F: $RuCl_3$/aq. $Na(IO_4)$/EtOAc–CH_3CN/0°C [158]; G: $RuCl_3$/aq. $Na(IO_4)/H_2SO_4$/EtOAc–CH_3CN/0°C [155]

Fig. 3.2 Stereoselective *cis*-dihydroxylation of glycals by RuO_4 [165]





(**1**) (**2**)

Fig. 3.3 A *cis*-dihydroxylation by RuO_4 yielding 1*D*-1,2:5,6-di-O-isopropylidene-allo-inositol [168]

corresponding -1*R**,5*S**-bicyclo-[3.3.1]nona-1*R**,4*R** diol as part of a total synthesis of pentopyranose derivatives [166]. Reaction with $RuCl_3$/$Na(IO_4)$/aq. M H_2SO_4/EtOAc–CH_3CN/0°C effected the *cis*-dihydroxylation of several alkenes (Table 3.2) [9, 156], including mono- and 1,2-disubstituted alkenes $R^1CH{=}CHR^2$ with $R^1{=}R^2{=}$Ph or COOEt; $R^1{=}$Ph, $R^2{=}$H, COOMe; CN, CH_2Ph, CH_2Cl, CH_2SO_2Ph, CH_2N_3, CH_2NHAc, CH_2OBn, CH_2OAc, $CONEt_2$ (Table 3.2) [155]. *Cis*-dihydroxylation of C_{60} and C_{70} by stoich. RuO_4/CCl_4-1,2,4-trichlorobenzene gave the fullerene diols 1,2-$C_{60}(OH)_2$, 1,2-$C_{70}(OH)_2$ and 5,6-$C_{70}(OH)_2$ [167].

A *cis*-dihydroxylation involved in the synthesis of *allo*-inositol was the conversion of 1*L*-1,2,3,4-di-*O*-*iso*propylidenecyclohex-5-ene-1,2/3,4-tetrol (1) to 1*D*-1,2:5,6-di-*O*-*iso*propyli-dene-*allo*-inositol (2) by $RuCl_3$/aq. $Na(IO_4)$/CH_3CN or EtOAc–CH_3CN (Fig. 3.3) [168]. Directions were given for both small- and a large-scale oxidations.

Two *cis*-dihydroxylation reactions of alkenes formed steps in the synthesis of the antiviral drug (-)-oseltamvir ('tamiflu') were carried out with RuO_2/aq. $Na(IO_4)$/EtOAc–CH_3CN/4°C [169]. Terminal alkene groups in nucleosides were oxidised to alcohols by $RuCl_3$/aq. $Na(IO_4)$/EtOAc–CH_3CN/0°C; thus 3,5-di-O-benzyl-1,2-di-O-isopropylidene-3-C-vinyl-α-D-ribofuranose (1) gave the diol (2) which, on cleavage with $Na(IO_4)$ and reduction with $NaBH_4$ yielded 3,5-di-O-benzyl-1,2-di-O-isopropylidene-3-C-hydroxy-methyl-α-D-ribofuranose (3) (Fig. 3.4) [170].

Formation of the steroidal phytohormone (22*S*, 23*S*)-28-homobrassinolide was achieved *via cis*-dihydroxylation of the 2,22-dien-6-one to (2α,3α,22*S*,23*S*)-2,3,22,23-tetrahydroxy-5α-stigmastan-6-one (Fig. 3.5) with $RuCl_3$/aq. $Na(IO_4)$/acetone-CH_3CN-EtOAc/6°C [171].

Cis-dihydroxylation without reduction of the alkene linkage occured during oxidation by $RuCl_3$/aq. CH_3CO_3H/CH_2Cl_2–CH_3CN of cyclic unsaturated carbonyl and carboxylic acids to the corresponding α-oxo-ene diols (aci-reductones). This is

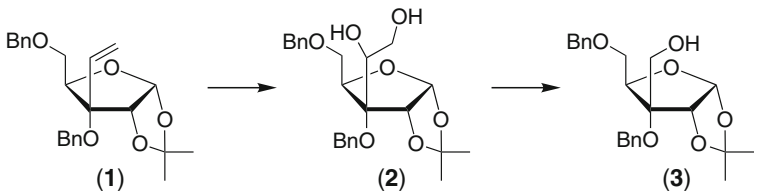


Fig. 3.4 *Cis*-dihydroxylation by RuO_4 of a nucleoside alkene (**a**) to a diol (**b**) followed by cleavage and reduction to (**c**) [170]

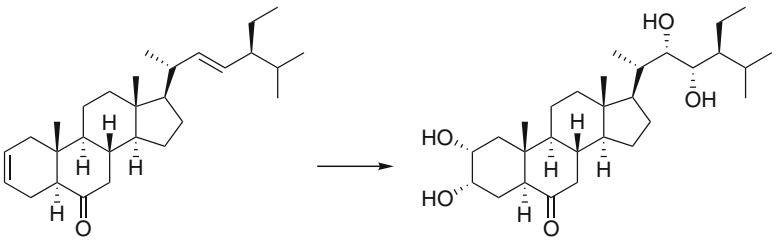
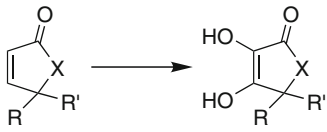


Fig. 3.5 *Cis*-dihydroxylation by RuO_4 in synthesis of (22*S*, 23*S*)-28-homobrassinolide [171]

Fig. 3.6 Oxidation of cyclic α,β unsaturated carbonyl compounds with $RuCl_3$ and peracetic acid [172]



illustrated in Fig. 3.6 for the oxidation of 4-alkyl substituted cyclohex-2-en-1-ones to the lipophilic cyclic aci-reductones (X=CH_2, $(CH_2)_2$ with R=R'=H; X=$(CH_2)_2$, R=H, R'=$MeCH(CH_2)_3CHMe_2$, ^{i}Pr, cyclohexyl; X=*N*-^{n}Bu, R =(=O)) [172].

Asymmetric *cis*-dihydroxylations of α,β-unsaturated carbonyl compounds have been achieved using $RuCl_3$/aq. $Na(IO_4)/CH_3CN$-EtOAc, using N-enoyl sultams as chiral auxiliaries [173].

For oxidative cyclisation of 1,5-dienes to *trans*-2,6-bis(hydroxyl-methyl)-tetrahydropyranyldiols *cf.* (Fig. 3.12) [174]; for large-scale *cis*-dihydroxylation reactions *cf.* 3.2.2.4; for mechanisms of *cis*-dihydroxylations dealt with in Ch. 1 *cf.* 3.2.2.3; for *cis*-diydroxylation of C_{60} and C_{70} *cf.* 5.6.7.

3.1.3 Ketohydroxylations

$$R^1CH=CHR^2+2[O]\rightarrow R^1CH(OH)COR^2 \tag{3.3}$$

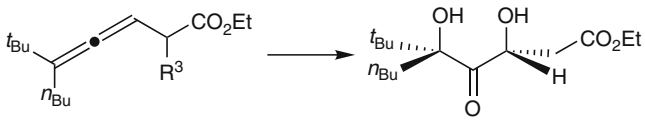


Fig. 3.7 Flash ketohydroxylation of a β-allenic ester by RuO_4 [16]

Alkenes were oxidised by $RuCl_3$/Oxone®/aq. $Na(HCO_3)/CH_3CN$-EtOAc/0°C to unsymmetrical α-hydroxyketones; for such a process the term 'ketohydroxylation' has been coined [175–177] and the subject reviewed [6–9].

3.1.3.1 Specific Examples of Ketohydroxylations

An early ketohydroxylation was that of β-allenic esters $R^1R^2C{=}C{=}CHCHR^3COOEt$ to α,α'-dihydroxyketones $R^1R^2C(OH)COC(OH)CHR^3COOEt$, ($R^1$=Me, Ph, ^{t}Bu; R^2=Me, ^{n}Bu, ^{t}Bu; R^3=H or OEt), effected by 'flash oxidation' with $RuCl_3$/aq. $Na(IO_4)/CH_3CN$-EtOAc/0°C (Fig. 3.7) [16].

With $RuCl_3$/Oxone®/aq. $Na(HCO_3)$/EtOAc–CH_3CN *trans*-stilbene gave benzoin with no hydrobenzoin and a trace only of benzoic acid; many such oxidations were carried out to give a wide range of symmetric and asymmetric α-hydroxyketones (Table 3.2, *cf.* mech. Fig. 1.6) [9]. Ketohydroxylation of alkenes was effected with $RuCl_3$/aq. Oxone®/$Na(HCO_3)$/ CH_3CN-EtOAc (Table 3.2): *trans*-stilbene was converted to the ketol and a variety of other alkenes underwent similar reactions. Other co-oxidants such as TBHP, aq. H_2O_2 and aq. Na(ClO) also worked but less effectively [177]. The scope and limitations of the procedure as well as mechanisms have been discussed; *cf.* also Table 3.2 [176].

Reaction of (-)-α-pinene (1) with stoich. RuO_4/CCl_4 gave a ketoaldehyde (2), probably via a Ru(VI) diester (4). If the reaction is performed using RuO_4 in acetone rather than CCl_4, the α-ketol (3) is the main product. It is likely that a Ru(VI) diester (4) is involved; such a species was isolated and both ^{1}H and ^{13}C NMR data suggest the structure shown in (Fig. 3.8). An X-ray crystal structure determination was carried out on the osmium analogue of (4) [178].

Alkenes reacted with $RuCl_3$/aq. CH_3CO_3H/CH_3CN–CH_2Cl_2 giving α-ketols; thus *cis*-5-(methoxycarbonyl)-2-cyclohexenyl acetate (1) gave (2*R**,3*S**,5*R**)-3-acetoxy-2-hydroxy-5-(methoxycarbonyl)-1-cyclohexanone (2) (Fig. 3.9, Table 3.2). Cortisone acetate was isolated in this way from epiandrosterone after a number of steps [179].

Another example is the ketohydroxidation of the allyl acetate (1) by $RuCl_3$/aq. CH_3CO_3H/CH_3CN–CH_2Cl_2 to (2), a precursor of 4-demethoxyadriamycinone, used in cancer therapy (Fig. 3.10) [180].

3.1.3.2 Asymmetric Ketohydroxylations

Chiral allenes with two different substituents at C-5 gave good diastereoselectivities when oxidised by $RuCl_3$/aq. $Na(IO_4)/CH_3CN$-EtOAc/0°C (Fig. 3.7) [16]. Several

Fig. 3.8 Oxidation of (-)-α-pinene by RuO_4 [178]

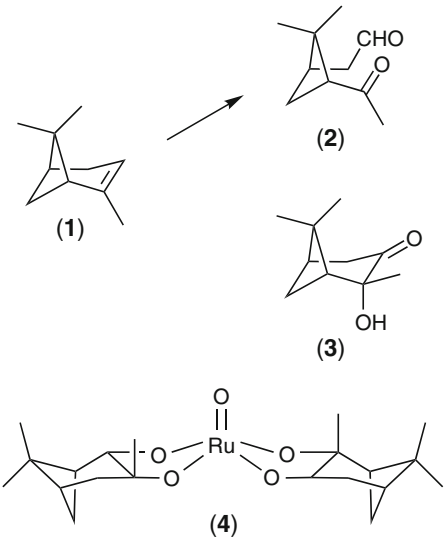
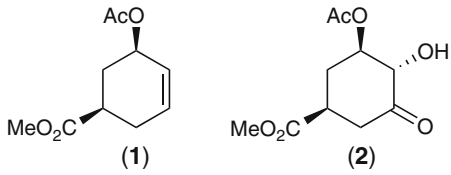


Fig. 3.9 Oxidation of an alkene to an α-ketol with $RuCl_3$-peracetic acid [179].



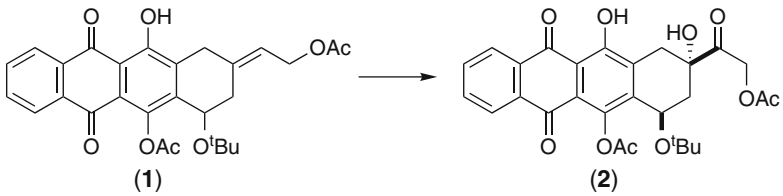


Fig. 3.10 A ketohydroxylation using $RuCl_3$ and CH_3CO_3H [180]

chiral alkenes were oxidised with $RuCl_3$/Oxone®/aq. Na(HCO_3)/CH_3CN-EtOAc (Table 3.2) to give symmetric and unsymmetric α-hydroxyketones, e.g. 1,3-diphenylallenyl acetate yielded the acyloins 3-hydroxy-2-oxo-1,3-diphenylpropyl acetate; (1*S**,2*R**)- and (1*S**,2*R**)-2-hydroxy-3-oxo-1,3-diphenyl-propyl acetate; 1,3-diphenylallyenl methylether gave a mixture of the regio- and diastereomeric acyloins, viz. *syn* and *anti* products (2*R**,3*S**) and (2*S**,3*S**)-2-hydroxy-methoxy-1,3-diphenylpropan-1-ones; with (1*S**,3*S**) and (1*R**,3*S**)-1-hydroxy-methoxy-1,3-diphenylpropan-2-ones; (1*R**, 4*R**)-4-acetoxy-3-hydroxy-2-oxocyclo-2-enyl acetate yielded (1*R**,3*R**,4*R**)- and (1*R**,3*S**,4*R**)-4-acetoxy-3-hydroxy-2-oxocyclohexyl acetates, *cf.* mech. Ch. 1; Table 3.2 [181].

3.1.3.3 Oxidative Cyclisation of Alkenes

Oxidative cyclisation of geraniol- and nerol-type 1,5-dienes to *cis*-2,5-*bis*-(hydroxymethyl)-tetrahydrofuranyldiols was effected with RuO_2/aq. $Na(IO_4)$/CH_3CN-EtOAc/0°C thus neryl acetate (1) gave a *cis*-2,5-bis(hydroxymethyl)tetrahydrofuran diol (2) (Fig. 3.11) [182]. These unexpected results were compared with those obtained by Sharpless who used $RuCl_3$/aq. $Na(IO_4)$/CH_2Cl_2–CH_3CN with geranyl- and neryl-acetates (Tables 3.3 and 3.4) [183].

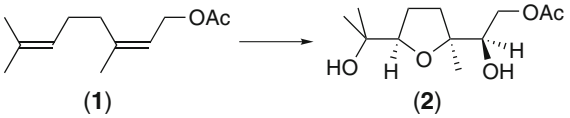


Fig. 3.11 Oxidation by RuO_4 of neryl acetate to a *cis*-THF diol [182]

Table 3.3 Oxidative cleavage of alkenes to aldehydes or ketones

Reactant	Product	Method [Ref.]
Limonene	4-Acetyl-1-methylcyclohexene	A [199]
trans-Stilbene	Benzaldehyde	B [191]
Styrene	Benzaldehyde	A [199]
β-Methylstyrene	Benzaldehyde	A [199]
1-Dehydrotestosterone benzoate	17β-Benzoyloxy-10α-des-A-androstan-5-one	C [203]
Allyl chloride	2-Chloroethanal	A [199]
Vinylcyclohexane	Cyclohexanecarboxaldehyde	A [199]
4-Vinylcyclohexene	Cyclohexene-4-carboxaldehyde	A [199]
Norbornene	Cyclopentanedialdehyde	B [191]
Androsta-1,4-diene-3,11,17-trione	Des-A-androst-9(10)-ene-5,11,17-trione	C [203]
3,4,6-Tri-*O*-acetyl-D-glucal	Formylesteraldehyde	B [191]
1-Octene	*n*-Heptanal	A [199]
2-Methyl-1-heptene	2-Heptanone	A [199]
2,3-Dimethyl-2-octene	2-Heptanone	D [183, 205]
1-Heptene	*n*-Hexanal	A [199]
E-2-Octene	*n*-Hexanal	A [199]
1-Dehydrotestosterone acetate	17β-Hydroxy-10α-des-A-androstan-5-one	C [203]
(+)-Longifolene	Longicamphenilone	D [204, 205]
Methylacrylate	Methylglyoxylate	A [199]
7-Methyl-1,6-octadiene	6-Methyl-5-heptanal	A [199]
Methylmethacrylate	Methylpyruvate	A [199]
1-Hexene	*n*-Pentanal	A [199]
1,4-Hexadiene	3-Pentenal	A [199]

A: *cis*-$[Ru(H_2O)_2(dmp)_2]^{2+}$/aq. H_2O_2/CH_3CN/55°C [199]; B: $RuCl_3$/Oxone®/aq. $Na(HCO_3)$/CH_3CN [191]; C: RuO_2/aq. $Na(IO_4)$/acetone [203]; D: $RuCl_3$/aq. $Na(IO_4)$/CCl_4–CH_3CN [183, 204, 205]

Table 3.4 Oxidation of arenes: phenyl, furyl and other aromatic rings

Reactant	Product	Method [Ref.]
Tetralin	Adipic acid	A [258]
1-Phenyl-1-(acetoxy)pentane	2-(Acetoxy)hexanoic acid	B [251]
Estradiol methylether acetate, or 4-Bromo or 4-Chloroestradiol diacetate	3-(1β-Acetoxy-8β-methyl-5β-carboxy-*trans*-perhydroindanyl-4α) propionic acid	C [250]
1-Phenyl-3-heptanol acetate	4-(Acetoxy)octanoic acid	B [251]
4-Pentabiphenyl	Benzoic + Caproic acids	A [258]
5-Phenyl-3-benzoyloxy)pentane	4-(Benzoyloxy)hexanoic acid	B [251]
1-Phenylpropane	Butyric acid	A [258]
Phenylcyclohexane	Cyclohexanecarboxylic acid	D [183], E [241], F [243]
1-Phenylcyclohexanol	Cyclohexanone	F [243]
1-Phenylcyclopentanol	Cyclopentanone	F [243]
Estradiol diacetate	3,17β-Diacetoxy-9α-hydroxy-6-oxoestra- 1,3,5(10)triene	C [248]
3,17β-Diacetoxy-9α-1-methylestra-1,3,5(10)-triene	3,17β-Diacetoxy-9α-hydroxy-1-methyl--6-estra-1,3,5(10)-triene	C [248]
3-Phenylcyclobutanecarboxylic acid	*cis*-Dimethyl-cyclobutane-1,3-dicarboxylate	E [241]
Indane	Glutaric acid	A [258]
Dibenzyl	Hydrocinnamic + succinic acids	A [258]
m-Dimethoxybenzene	2-Methoxy-*p*-benzoquinone	G [254]
2-Phenylbutane	2-Methylbutyric acid + 2-Phenyl-2-butanol	A [258]
5-Phenyl-3-pentanone	4-Oxohexanoic acid	B [251]
Estrone acetate	3-(1-Oxo-8β-methyl-5β-carboxy-*trans*-perhydroidnayl-4α)propionic acid	C [248]
Estrone, or 1,17β-Dihydroxy-4-methylestra-1,3,5(10)triene	3-(1-Oxo-8β-methyl-5β-carboxy-*trans*-perhydroindanyl-4α)propionic acid	C [248]
Diphenylmethane	Phenylacetic acid + Benzophenone	A [258]
p-tert-Butylphenol	Pivalic acid	E [241], F [243]
1-Phenyltridecane	Tetradecanoic acid + tetradecanophenone	A [258]
2,3,5,6-Tetramethylphenol	Tetramethybenzoquinone	H [262]
Diphenylcholene	3α,7α,12α-Triacetoxy-24-nor-5β-cholan-23-al &3α,7α,12α-Triacetoxy-24-nor-5β-cholan-23-oic acid	S [238]
2,3,6-Trimethylphenol	Trimethyl-*p*-benzoquinone	H [262]

A: $RuCl_3$/aq. $Na(IO_4)/CCl_4–CH_3CN$ [258]; B: $RuCl_3$/aq. $IO(OH)_5/CCl_4–CH_3CN$ [251]; C: RuO_2/aq. $Na(IO_4)$/acetone [248, 250], D: $RuCl_3$/aq. $Na(IO_4)/CCl_4–CH_3CN$ [183]; E: $RuCl_3$ or RuO_2/aq. $Na(IO_4)/CCl_4$/60°C [241]; F: $RuCl_3$/aq. Na(ClO) [243]; G: Ru(CO)(TMP)/$(Cl_2pyNO)/C_6H_6$/aq. HBr or HCl/40°C [254]; H: $RuCl_3$/aq. H_2O_2/AcOH [262]; S: stoich. RuO_4/CCl_4 [238]

Oxidation of 1,5-dienes to *cis*-tetrahydrofurandiols was accomplished with RuO_2/aq. $Na(IO_4)$/acetone-EtOAc; thus 2,5-dimethyl-1,5-hexadiene gave tetrahydrofurandiol, geranyl acetate yielded *cis*-tetrahydrofurandiol, and *trans, trans*-2,6-dimethyl-2,6-octadiene-1,8-diol diacetate (1) gave tetrahydrofuran ketol diacetate (2) (Fig. 3.12; *cf.* mech. Ch. 1) [174].

Oxidative cyclisation of 1,6-dienes to *trans*-2,6-bis(hydroxyl-methyl)-tetrahydropyranyl-diols was effected by $RuCl_3$/aq. $Na(IO_4)/CH_3CN$-EtOAc/0°C; 1,6-heptadiene (1) and 7-methyl-1,6-octadiene (2) were so oxidised (Fig. 3.13; *cf.* mech. Ch. 1) [184]. .

The isoprenoid polyenes farnesyl acetate, geranyl acetate and squalene underwent oxidative polycyclisation to bis-, tris- and penta-tetrahydrofurans with RuO_2/aq. $Na(IO_4)/CH_3CN$-EtOAc [185]-[188]. This oxidative polycyclisation of squalene with RuO_4 was shown to lead to the *cis-threo-cis-threo-trans-threo-trans-threo-trans* penta-tetrahydrofuranyl diol product, this configuration being determined by 2D-NMR (Fig. 3.14) [185]-[188]; *cf.* mech. Fig. 1.8 [185].

Selective synthesis of natural and non-natural carbohydrates was accomplished via a possible oxidative fragmentation pathway (a) for cyclisation of alkenes (1) at pH 4–6, or a dehydrogenation dihydroxylation cyclisation (b) at pH >7 or <4) (Fig. 3.15). An oxidative C=C cleavage followed by cyclisation (path (a)) was obtained from (1) with $RuCl_3$/aq. $Na(IO_4)$/ acetone-CH_3CN followed by acylation to give (2); path (b), of dehydrogenation-dihydroxylation-cyclisation, was effected by $RuCl_3$/aq. $Na(BrO_3)$ @ pH 10/acetone-CH_3CN/50°C followed by treatment with $CeCl_3$ and $Na(IO_4)$ to give lactols (3). A number of new and known highly-substituted carbohydrates were made in this way (*cf.* mech. Ch. 1) [189].

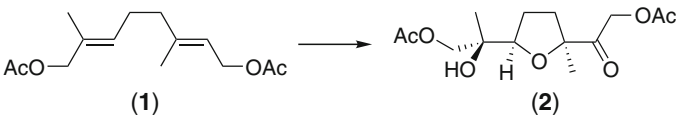


Fig. 3.12 Oxidation by RuO_4 of 2,6-dimethyl-2,6-octadiene-1,8-diol diacetate (**1**) to tetrahydrofuran ketol diacetate (**2**) [174]

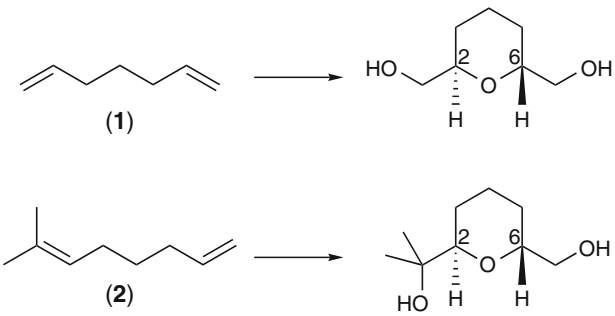


Fig. 3.13 Oxidative cyclisation by RuO_4 of 1,6-heptadiene (**1**) and 7-methyl-1,6-octadiene (**2**) [184]

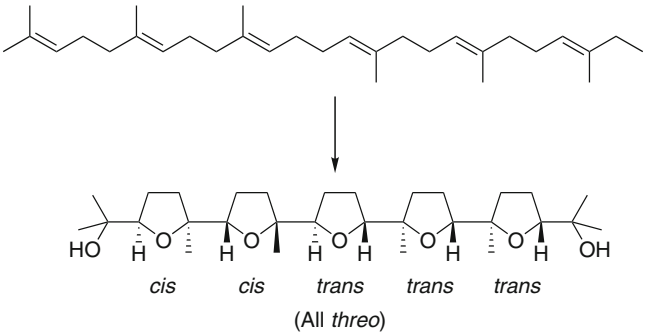
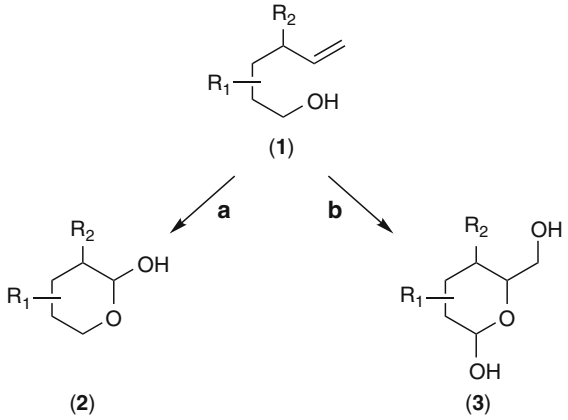


Fig. 3.14 Oxidative polycyclisation of squalene catalysed by RuO_4 [185]

Fig. 3.15 RuO_4-catalysed oxidative cyclisations for synthesis of carbohydrates [189]



3.1.3.4 Other Alkene Oxidations Not Involving Cleavage of the C=C Bond

$$RCH=CH_2+[O]\rightarrow RCH_2CHOH \tag{3.4}$$

$$R^1CH=CHR^2+3[O]\rightarrow R^1COCOR^2+H_2O \tag{3.5}$$

In early work *cis*-9-octadecane gave 9.10-diketo-octadecane with RuO_2/aq. Na(ClO)/($^nBu_4N$)Br/CH_2Cl_2 (Table 3.6) [190].

Cyclo-octene was oxidised by $RuCl_3$/aq. $Na(IO_4)$/DCE to 8-oxo-octanal [191]. Oxidation of Δ^2, $\Delta^{2,4}$ and $\Delta^{4,6}$ steroids using stoich. RuO_4/aq. acetone gave *cis*-diols, dicarbonyls or carboxylic acids. Thus oxidation of 5α-cholest-2-en-3-ol 3-acetate gave the 5α-cholestane-2,3-dione and -2,3-seco-5α-cholestane-2.3-dicarboxylic acid [192], while 2,3-dichlorodecene was oxidised by RuO_2/aq. $Na(IO_4)$/CH_2Cl_2–CH_3CN to decane-2,3-dione [193]. The system $RuCl_2$(TMP) or $RuCl_2$(TDCPP)/(Cl_2pyNO)/$CDCl_3$ oxidised alkenes RCH_2=CH to the aldehydes RCH_2CHO;

1,3-dienes gave the unsaturated aldehyde – thus 1-phenyl-1,3-butadiene gave the β,γ-unsaturated aldehyde 4-phenylbut-3-enal (styrylacetaldehyde) [194].

3.2 Oxidative Cleavage of Alkenes

$$R^1CH=CHR^2+2[O]\rightarrow R^1CHO+R^2CHO \tag{3.6}$$

$$R^1R^2C=CH_2+2[O]\rightarrow R^1R^2CO+HCHO \tag{3.7}$$

$$R^1CH=CHR^2+4[O]\rightarrow R^1COOH+R^2COOH \tag{3.8}$$

Cleavage of alkenes and alkynes and the consequent degradation of large molecules and introduction of oxygen functionalities into molecules is one of the most important applications for RuO_4. The topic has been reviewed [4, 10–15].

The earliest paper in this field used RuO_4 from RuO_2/aq. $Na(IO_4)$/AcOH for cleavage of 4-cholesten-3-one and hexahydroindene to the corresponding carboxylic acids (Fig. 1.5) [195]; minimal experimental data were given. An early example (1959) for RuO_2/aq. $Na(IO_4)$/acetone involved oxidation of 3α-acetoxy-24,24-diphenylchol-23-ene to 3α-acetoxynorcholanic acid [196].

3.2.1 Alkene Cleavage to Aldehydes or Ketones

$$R^1CH=CHR^2+2[O]\rightarrow R^1CHO+R^2CHO \tag{3.9}$$

$$R^1R^2C=CH_2+2[O]\rightarrow R^1R^2CO+HCHO \tag{3.10}$$

These are relatively rare reactions for RuO_4 – as with primary alcohols, further oxidation to carboxylic acids normally occurs. Examples are given in Table 3.3. Generally, under neutral conditions, aldehydes are formed but under acidic or alkaline conditions carboxylic acids are the main oxidation products.

3.2.1.1 Specific Examples of Alkene Cleavage to Aldehydes and Ketones

Early examples of aldehyde or ketone oxidation by stoich. RuO_4/H_2O are of 1-octene to heptaldehyde, of cyclohexene to adipaldehyde [197] and of 3-alkylidenegris-2-ens to grisen-3-ones [198]. Similarly methyl 3-isopropylidene-5,6,2′-trimethyl-4′-oxogris-2′-en-3′-carboxylate gave methyl 5,6,2′-trimethyl-3,4′-dioxogris-2′-en-3′-carboxylate, and ethyl-3-ethylidene-4,6,2′-trimethyl-3,4′-oxocyclopent-2′-ene-1′-spiro-2-benzofuran-3′-carboxylate produced ethyl 4,6,2′-trimethyl-3,4′-dioxocyclopent-2′-ene-1′-spiro-2-benzo-furan-3′-carboxylate [198].

The system $RuCl_3$/Oxone®/aq. $Na(HCO_3)/CH_3CN$ converted aryl alkenes to the corresponding aldehydes, e.g. symmetrical stilbenes, trisubstituted aryl alkenes and styrene gave good clean yields of the corresponding aldehydes, while norbornene gave a dialdehyde. This procedure did not give clean yields for aliphatic alkenes; for these $RuCl_3$/aq. $Na(IO_4)/CH_2Cl_2$ or CH_3CN was preferable. Thus cyclo-octene gave 8-oxo-octanal and 3,4,6-tri-*O*-acetyl-d-glucal gave formylesteraldehyde (see also Tables 3.3 and 3.6) [191]. The system *cis*-$[Ru(H_2O)_2(dmp)_2]^{2+}$/aq. H_2O_2/CH_3CN/55°C cleaved several alkenes and dienes to aldehydes or occasionally ketones (Table 3.3) [199].

As part of a preparation of marine odourants, oxidation by $RuCl_3$/aq. $Na(IO_4)/CCl_4$ of the $=CH_2$ moiety in the marine floral-aldehyde 1-methyl-7-methylene-2,3,7,8-tetrahydro-1*H*,6*H*-5,9-dioxacyclohepta[*f*]indene gave 1-methyl-2,3-dihydro-1*H*-5,9-dioxa-cyclohepta[*f*]-inden-7-one (Fig. 3.16) [200].

During the enantioselective total synthesis of the tricyclic sesquiterpene (-)-ceratopicanol two Ru-catalysed oxidations are involved: cleavage of an isopropylidene side-chain in a bicyclic enone to a diquinane dione with $RuCl_3$/aq. $Na(IO_4)/CCl_4$–CH_3CN and oxidation of a diol to a γ-lactone by TPAP/NMO/PMS/CH_2Cl_2–CH_3CN (*cf.* 2.5.2) [201]. Oxidative cleavage of enolic alkenes to the corresponding ketones was effected by RuO_2/aq. $Na(IO_4)/CCl_4$, e.g. the oxidation of α-D-glucal triacetate to the keto acid and of dihydropyran to the dialdehyde and diacid [202]. Oxidative cleavage of conjugated and cross-conjugated steroidal alkenes to ketones can be effected with RuO_2/aq. $Na(IO_4)$/acetone (Table 3.3) [203].

Degradation of (*R*)-α-terpinyl acetate (1) to the keto aldehyde (2) was effected by $RuCl_3$/aq. $Na(IO_4)$/DCE (Fig. 3.17) [191].

A mono-fluorinated alkene has recently been oxidised to the corresponding ketone by $RuCl_3$/aq. $Na(IO_4)/C_6H_{12}$–CH_3CN. Hydrolysis of the CF_2 unit to C=O did not occur; in contrast neutral aq. $KMnO_4$ gave no ketone but there was extensive hydrolysis, *cf.* 1.11

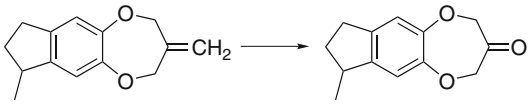
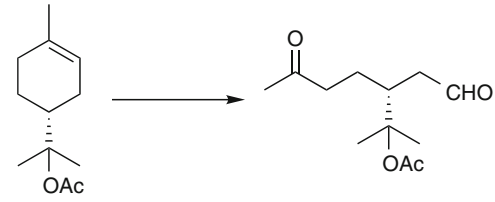


Fig. 3.16 Oxidation by RuO_4 of an indene derivative to a dioxacyclohepta(*f*)indenone [200]



(**1**) (**2**)

Fig. 3.17 Oxidation of (*R*)-α-terpinyl acetate by RuO_4 [191]

Table 3.5 Oxidation of polycyclic arenes

Reactant	Product (major product listed first)	Method [Ref.]
Anthracene	Anthraquinone	A [269]
4-Biphenyltrifluoroacetate	Benzoic + 4-Hydroxybenzoic acids	B [213]
2-Chloronaphthalene	Chlorophthalic + Pthalic acids	C [265]
5-Methoxy-1-naphthol	Diethylmethoxyphthalate	D [266]
(-)-3-*tert*-3-(1′,2′,3′,4′-Tetrahydro -5′-naphthyl) propionic acid	(+)Dimethyl-*tert*-butylsuccinate	E [268]
1,4-Dimethylnaphthalene	3,6-Dimethylphthalic + Pthalic acids	C [265]
Quinoline	Dimethylpyridine-2,3-carboxylate	D [264]
Quinoline-8-ol	Dimethylpyridine-2,3-carboxylate	D [264]
9,10-Dihydrophenanthrene	Diphenic + 3-(2-Carboxyyphenyl) propionic acids	F [258]
Phenanthrene	Diphenic + Pthalic acids	B [208], F [258]
1-Fluoronaphthalene	Fluorophthalic + Phthalic acids	C [265]
5-Methoxy-1-naphthol	3-Methoxyphthalic acid	D [264]
2-Methoxynaphthalene	4-Methoxyphthalic + Phthalic acids	C [265]
1-Methylnaphthalene	3-Methylphthalic + Phthalic acids	C [265]
2-Methylnaphthalene	4-Methylphthalic + Phthalic acids	C [265]
Naphthalene	1,4-Naphthoquinone	G [254]
1-Nitronaphthalene	3-Nitrophthalic + Phthalic acids	C [265]
Phenanthrene	9,10-Phenanthrenequinone	S [239]
Phenanthrene	9,10-Phenanthrenequinone + Diphenic acid	A [269]
Methyl-1-naphthyl ether	Phthalic acid	D [266]
2,3-Dimethylnaphthalene	Phthalic acid	C [265]
Isoquinoline	Phthalic acid	D [264]
1-Methoxynaphthalene	Phthalic acid	C [265]
2,3-Dimethylnaphthalene	Phthalic acid	C [265]
2-Methylnaphthalene	Phthalic acid	H [251]
1-Naphthol (α-Naphthol)	Phthalic acid	C [265], D [264, 266]
2-Naphthol (β-Naphthol)	Phthalic acid	C [265], D [264, 266]
3-Hydroxy-2-naphthoic acid	Phthalic acid	C [265]
Naphthalene	Phthalic acid	C [265]
1-Naphthoic acid	1,2,3-Tricarboxybenzene + Phthalic acid	C [265]
2-Naphthoic acid	1,2,4-Tricarboxybenzene + Phthalic acid	C [265]
2-Naphthaldehyde	1,2,4-Tricarboxybenzene + Phthalic acid	C [265]
Tert-Butylnaphthalene	Valeric + Phthalic acids	F [258]

A: $RuCl_3$/aq. H_2O_2/CH_2Cl_2/80°C [269]; B: $RuCl_3$/aq. $Na(IO_4)$/EtOAc–CH_3CN [208, 213]; C: RuO_2/aq. Na(ClO)/CCl_4 [265]; D: RuO_2/aq. $Na(IO_4)$ or Na(ClO)/acetone or CCl_4 [264, 266]; E: RuO_2/aq. $Na(IO_4)$/acetone [268]; F: $RuCl_3$/aq. $Na(IO_4)$/CCl_4–CH_3CN [258]; G: Ru(CO)(TMP)/(Cl_2pyNO)/C_6H_6/aq. HBr or HCl/40°C [254]; H: $RuCl_3$/aq. $IO(OH)_5$)/CCl_4–CH_3CN [251]; S: stoich RuO_4/CCl_4 [239]

Table 3.6 Oxidative cleavage of alkenes to acids and alkynes to ketones or acids

Reactant	Product	Method [Ref.]
4-Methoxyflavylium chloride	2-Acetoxybenzoic + 4-Methoxybenzoic acids	A [216]
7-Hydroxy-4′-methoxyflavylium chloride	2-Acetoxybenzoic + 4-Methoxybenzoic acids	A [216]
Cyclohexene	Adipic acid	B [268], C [207], D [19]
Petroselenic acid	Adipic + Lauric acids	B [208]
Oleic acid	Azelaic + Pelargonic acids	B [208]
Palmitoleic acid	Azelaic + Heptanoic acids	B [208]
β-Bromostyrene	Benzoic acid	E [193]
α-Chlorostyrene	Benzoic acid	E [193]
Diphenylacetylene	Benzoic acid	C [207], D [19]
Phenylacetylene	Benzoic acid	C [207], D [19], F [284]
Phenylmethylacetylene	Benzoic acid	G [233]
Styrene	Benzoic acid	C [207], D [19], E [193]
5.7-Dihydroxyflavone	Benzoic acid + 1,3,5-Triacetoxybenzol	A [216]
3′,4′,7-Trihydroxyflavone	Benzoic acid + 1,3,5-Triacetoxybenzol	A [216]
Erucic acid	Brassylic + Pelargonic acids	B [208]
1-Pentyne	*n*-Butyric acid	H [289]
4-Octyne	*n*-Butyric acid	G [233], H [289], J [235]
Norbornene	*cis*-1,3-Cyclopentanedicarboxylic acid	K [232]
Cyclododecene	1,10-Decanoic acid	D [19]
5-Decyne	Decane-5,6-dione + Pentanoic acid	F [284]
3′,4′,7-Trihydroxymethyl-flavylium chloride	2,4-Diacetoxy + 3,4-Diacetoxybenzoic acids	A [216]
2,3′,4,4′-Tetrahydroxychalcone	2,4-Diacetoxy + 3,4-Diacetoxybenzoic acids	A [216]
2,4-Diacetoxy-4′-methoxychalcone	2,4-Diacetoxybenzoic + 4-Methoxybenzoic acids	A [216]
7-Hydroxycoumarin	2,4-Dihydroxybenzoic acid	B [213]
Isophorone	3,3-Dimethyl-5-oxohexanoic acid	L [237]
Cyclopentene	Glutaric acid	C [207], D [19]
2-Nonyne	Heptanoic acid	G [233]
1-Octene	Heptanoic acid	D [19]
1-Octyne	Heptanoic acid	H [289]
1-Heptyne	Hexanoic acid	D [19]
(+)-Pulegone	(+)-3-Methyladipic acid	L [237]
1,5-Dimethyl-2-(1-methylidene)-cyclohexan-1-ol	(+)-4-Methyl-6-oxoheptanoic acid	L [237]
1-Pentadecene	Myristic acid	M [190]
1,2-Dibromodecene-1	Nonanoic acid	E [193]
1-Decyne	Nonanoic acid	D [19]
1-Decene	1-Nonanoic acid	C [207], D [19]
Norbornylene	Norcamphoric acid	B [208]
4-Octyne	4,5-Octanedione + Butyric acid	J [235]
2,3-Chlorodecene-2	Octanoic acid	E [193]

(continued)

Table 3.6 (continued)

Reactant	Product	Method [Ref.]
1-Methylcyclohexene	5-Oxohexanoic acid	B [208]
9,10-Octadecene	Pelargonic acid	M [190]
1-Decene	Pelargonic acid	B [208]
trans-5-Decene	Pentanoic acid	D [19]
1-Hexene	Pentanoic acid	D [19]
1-Hexene	Pentanoic acid	N [251]
1-Hexyne	Pentanoic acid	D [19], J [235]
E-5-Decene	Pentanoic acid	L [183, 205]
Perfluoropropene	Perfluoroacetic acid	P [211]
(diPerfluorohexyl)ethylene	Perfluoroheptanoic acid	P [211]
(Perfluoro-octyl)ethylene	Perfluorononanoic acid	P [211]
Cycloheptene	Pimelic acud	C [207], D [19]
trans-Verbenol	(+)-*cis*-Pinononic acid	L [237]
(+)-*trans*-Pinocarveol	(-)-*cis*-Pinic acid	L [237]
Tert-Butylacetylene	Pivalic acid	J [235]
10-Undecylenic acid	Sebacic acid	B [208]
Cis-Cyclo-octene	Suberic acid	B [208], C [207], D [19]
(*E*)-5-Decene	Suberic acid	B [208]
Di-*n*-hexylacetylene	Tetradecane-7,8-dione + Heptanoic acid	G [233]
1-Dodecene	Undecanoic acid	C [207]
(*E*)-5-Decene	Valeric acid	B [208]
Isoeugenyl trifluoroacetate	Vanilli	B [213]

A: RuO_2/aq. $Na(IO_4)$/AcOH [216]; B: $RuCl_3$/aq. $Na(IO_4)$/EtOAc–CH_3CN [208, 213]; C: $RuCl_3$/aq. $IO(OH)_5/C_6H_{12}$–CH_3CN [207]; D: $RuCl_3$/aq. $IO(OH)_5/CCl_4$–CH_3CN [19]; E: RuO_2/aq. $Na(IO_4)$/CH_2Cl_2–CH_3CN [193]; F: RuO_2/aq. NaCl @ pH 4/0°C/Pt electrodes [284]; G: RuO_2/Oxone®/aq. $Na(HCO_3)$/EtOAc–CH_3CN [233]; H: $RuCl_2(PPh_3)_3$/PhIO/water-CH_2Cl_2 [289]; J: RuO_2/aq. Na(ClO)/CCl_4/0°C [235]; K: $RuCl_3$/aq. $Na(IO_4)/CHCl_3$ [232]; L: $RuCl_3$/aq. $Na(IO_4)/CCl_4$–CH_3CN [205, 237]; M: RuO_2/aq. Na(ClO)/(^{n}Bu_4N)Br/CH_2Cl_2 [190]; N: $RuCl_3$/aq. $IO(OH)_5/CCl_4$–CH_3CN [251]; P: RuO_2/aq. $IO(OH)_5$, Na(ClO) or CH_3COOOH/Freon 113 [211]

3.2.1.2 Natural Product/Pharmaceutical Syntheses Involving Alkene Cleavage to Ketones

The sesquiterpene (+)-longifolene was oxidised by $RuCl_3$/aq. $Na(IO_4)/CCl_4$ to longicamphelinone (Table 3.3) [204, 205].

For *large-scale alkene cleavage reactions cf.* 3.2.2.4

3.2.2 Alkene Cleavage to Carboxylic Acids

$$R^1CH=CHR^2+4[O]\rightarrow R^1COOH+R^2COOH \tag{3.11}$$

This is one of the commonest reactions of RuO_4 and perhaps its current major application. Examples of such reactions are given in Table 3.4. As mentioned

above, cleavage of cholest-4-en-3-one (1) to the acid using RuO_2/$Pb(OAc)_4$/aq. AcOH (Fig. 1.5) was the first example of catalysed alkene cleavage (indeed of the use of any Ru oxidising catalyst) [195].

3.2.2.1 Specific Examples of Alkene Cleavage to Acids

An early example is cleavage of an alkene linkage with RuO_4 (Fig. 3.18) in the conversion of a diketo diphenyl ethylene to a nor-diketo acid by RuO_4/aq. $Na(IO_4)$/acetone; concomitant destruction of the phenyl rings also occurs [206].

Sharpless et al. in a classic observation showed that, for oxidation of alkenes such as one- and 5-decenes and citronellyl acetate to acids, addition of CH_3CN to the solvent viz. $RuCl_3$/aq. $Na(IO_4)$/CCl_4–CH_3CN greatly increased reaction rates; the cleavage of (*E*)-decene to pentanoic acid was closely studied (Table 3.3) [183]. Alkenes are cleaved to carboxylic acids by RuO_4 generated from $RuCl_3$/aq. $IO(OH)_5$/CH_3CN-cyclohexane – a number of organic solvents were tested for these reactions (CCl_4, acetone, EtOAc and cyclohexane) and cyclohexane was found to be the best and environmentally most acceptable (Table 3.6) [207]. The systems $RuCl_3$/aq. $IO(OH)_5$/CCl_4–CH_3CN, and $RuCl_3$/aq. $Na(IO_4)$/EtOAc–CH_3CN are also effective [19, 208, 213] (Table 3.6).

Oxidation of diethyl 2-allyl-2-hydroxypentanedioate by $RuCl_3$/aq. $Na(IO_4)$/CH_3CN-EtOAc gave triethyl homocitrate and the corresponding lactone [209]. Oxidation of cyclopentene to glutaric acid by $RuCl_3$/aq. Na(ClO)/CCl_4 or CH_2Cl_2 showed that addition of CH_3CN and also NaOH greatly improved yields [210]. Perfluoro alkenes were cleaved by RuO_2/$IO(OH)_5$, Na(ClO) or CH_3COOOH/water-Freon 113 to carboxylic acids; CO_2 was also formed or, in the case of perfluoropropene, pefluoroacetic acid and COF_2 (Table 3.6) [211].

Several alkenes $R^1CX{=}CYR^2$ were oxidised to R^1COOH and/or R^2COOH by RuO_2/aq. $Na(IO_4)$/CH_2Cl_2–CH_3CN or RuO_2/aq. Na(ClO): R^1=H, R^2=Ph, X=Y=H or X=Br, Y=H or X=Y=Cl or Br; R^1=Y=H, X=Cl, R^2=Ph; R^1=R^2=Ph, X=Y=Cl; R^1=Br, R^2=Ph, X=Y=H; R^1=^{n}C_7H_{15}, R^2= Me, X=Y=Cl or Br; R^1=^{n}C_8H_{17}, R^2= H, X=Y=Cl or Br; R^1=^{n}Bu, R^2= ^{i}Pr, X=Br, Y = H; R^1=^{n}Bu, R^2=H, X=Br, Y=H (Table 3.6) [193]. Cleavage of 3-*N*-substituted 5-allenyl-2,5-dichloro-4,4-dimethoxycyclopent-2-en-1-ones by $RuCl_3$/aq.$Na(IO_4)$/CCl_4–CH_3CN gave 3-*N*-substituted 5-(1*Z*-carboxy-methylene)-2-chloro-4,4-dimethoxycyclopent-2-en-1-ones. Thus (±)-5-allenyl-2,5-dichloro-4,4-dimethoxy-3-(*N*-methyl)piperazino)-cyclopenten-4-en-1-one gave 5-(1*Z*-carboxy-methylene)-2-chloro-4, 4-dimethoxy-3-(*N*-methylpiperazino)cyclopent-

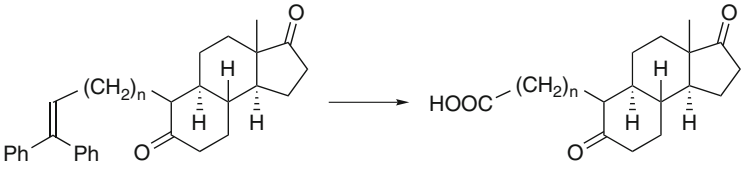


Fig. 3.18 Oxidation of an alkene by RuO_4 with concomitant cleavage of phenyl rings [206]

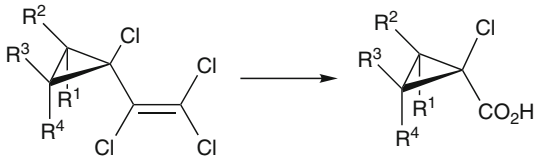


Fig. 3.19 Oxidation of 1-chloro-1-trichloroethenylcyclopropanes by RuO_4 to the corresponding acids [214]

2-en-1-one, while (±)-5-allenyl-2, 5-dichloro-3-diethylamino-4,4-dimethoxy-cyclopenten-4-en-1-one yielded 5-(1*Z*-carboxymethylene)-2-chloro-3-diethylamino-4, 4-dimethoxycyclopent-2-en-1-one [212].

The trifluoroactate group can protect aromatic rings against oxidation by RuO_4 generated from RuO_2/aq. $Na(IO_4)/CCl_4$. Thus isoeugenyl trifluoroacetate gave vanillin and vanillic acid (Table 3.6) [213]. Oxidation of various substituted 1-chloro-1-trichloro-ethenylcyclopropanes to the corresponding 1-chlorocyclopropanecarboxylic acids (R^1=Me, Et, ^{t}Bu, $–(CH_2)_2–$, CH_2Cl, $SiMe_3$, CH_2SiMe_3 with $R^2=R^3=R^4$; also with $R^1=R^2=R^3=R^4$=Me) was achieved with $RuCl_3$/aq. $Na(IO_4)/CCl_4–CH_3CN$ (Fig. 3.19) [214].

Oxidation of Δ^2, $\Delta^{2,4}$ and $\Delta^{4,6}$ steroids using stoich. RuO_4/aq. acetone yielded *cis*-diols, dicarbonyls or carboxylic acids: thus 5α-cholest-2-en-3-ol 3-acetate gave 2,3-seco-5α-cholestane-2,3- dicarboxylic acid [192]. Conversion of steroidal alkenes to acids was effected in early work with RuO_2/aq. $Na(IO_4)$/acetone; thus testosterone acetate gave 17β-hydroxy-3,5-seco-4-nor-5-oxandrostan-3-oic acid; 3,11,17-trioxoandostra-1,4-diene was oxidised to 1,5-seco-2,3,4-trisnor-5,11,17-trioxandrostane; 1-dehydrotestosterone acetate to 7β-hydroxy-1,5-seco-2,3,4-trisnor-5-oxoandrostan-1-oic acid; 17β-acetoxy-3-oxo-5α-androst-1-ene to 17β-hydroxy-1,3-seco-2-nor-androstane-1,3-dioic acid; 1-dehydroprogesterone to 5,20-dioxo-1,5-seco-2,3,4-trisnorpregnan-1-oic acid, and tigogenin acetate gave 3β-acetoxy-16,22-dioxo-5α-cholestan-26-oic acid [203] (Table 3.3). Oxidation by RuO_2/aq. $Na(IO_4)$/acetone of 5-ethyl-5-(1-methyl-4-pentenyl)-barbituric acid produced 5-ethyl-5-(1-methyl-3-carboxypropyl)-barbituric acid, an important metabolite of pentobarbital [215]. Cleavage of a double bond in anthocyanidins, flavones, chalcones and coumarins to the corresponding carboxylic acids was done with RuO_2/aq. $Na(IO_4)/CH_3COOH$ (Table 3.6) [216].

Oxidative destruction of α-chlorinated alkenes by *cis*-$[Ru(H_2O)_2(dmso)_4]^{2+}$/aq. Oxone®/$Me(CH_2)_{15}N(HSO_4)Me_3$ gave carboxylic acids and ultimately CO_2 and HCl for perchoroethylene, trichloroethylene, *cis*-1,2-dichloroethylene, 1,1-dichloropropene, 2-chloro- and 2-bromo-obut-2-enes [217].

3.2.2.2 Natural Product/Pharmaceutical Syntheses Involving Alkene Cleavage to Acids

The fragrance (-)-Ambrox® (a commercial substitute for ambergris from the blue sperm whale) was made by oxidation of (-)-sclareol (1) with $RuCl_3$/aq. $Na(IO_4)/CCl_4–CH_3CN$/40°C: a mixture of (+)-sclareolide (2) with the (-)-acetoxy acid

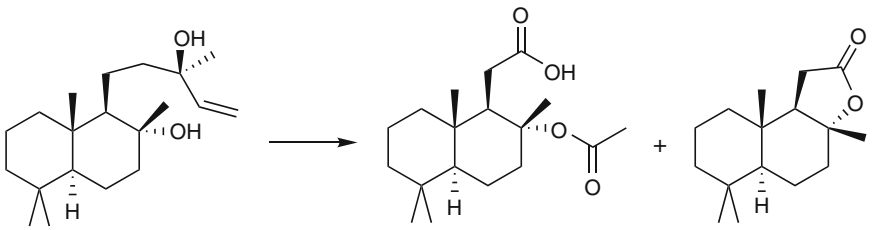


Fig. 3.20 Oxidation of (-)-sclareol (**1**) to (+)-sclareolide (**2**) and the (-)-acetoxy acid (**3**) with RuO_4 or $[RuO_4]^-$ [218]

(3) by loss of four carbon atoms from cleavage of the alkene side-chain was produced, and these were converted to (-)-Ambrox®. Oxidation of (1) with $[RuO_4]^-$, generated from $RuCl_3$/Ca(ClO)$_2$/aq. (^{n}Bu$_4$N)Br/CCl_4–CH_3CN in the same solvent system gave (2) free from (3) (Fig. 3.20) [218].

As part of the total synthesis of the triterpene (+)-α-onocerin, one of the first total syntheses in which RuO_4 played a key role, a diphenylethyleneacetoxyketone was oxidised to the corresponding acetoxyketoacid by RuO_2/aq. Na(IO_4)/acetone. Aromatic ring oxidation was also involved (*cf.* 3.3.1 below) [219]. An oxidative cyclisation of a 1,5-diene to a diol by $RuCl_3$/Na(IO_4)/wet SiO_2/THF formed part of the synthesis of the antitumour agent *cis*-solamin [220].

3.2.2.3 Alkene and Alkyne Cleavage Systems Not Covered Here but Included in Chapter 1

For *alkenes* these include: $RuCl_3$/aq. Na(IO_4)/Aliquat® (oleic acid, *cf.* mech. Ch. 1) [221]; stoich. *cis*-[Ru(O)$_2$(CF_3COO)(tmtacn)]$^+$/CF_3COOH–CH_3CN (disubstituted silylalkyne cleavage, *cf.* Fig. 1.30 and mech. Ch. 1), [222]; [Ru{$PW_{11}O_{39}$}(dmso)]$^{5-}$/aq. Na(IO_4) (cyclo-octene to suberic acid) [223]; stoich.RuO_4/CCl_4–CH_3CN (styrenes to benzoic acids, Fig. 1.7; *cf.* mech. Ch. 1) [224, 225]; $RuCl_3$/MoO_3/(DDAB)/aq. H_2O_2/^{t}BuOH/80°C (linear and cyclic alkenes to acids) [226]; stoich. $[RuO_4]^-$/aq. NaOH and stoich. $[RuO_4]^{2-}$/aq. NaOH (cinnamate; Fig. 1.16, *cf.* mech. Ch. 1) [227, 228]; stoich. RuO_4/CCl_4 (oleic acid, methyl oleate) [229]; RuO_2/aq. Na(ClO)/–CH_2Cl_2 (sodium undecylenate to sebacic acid) [230]; stoich. RuO_4/CCl_4 (cinnamic, substituted cinnamic acids to benzoic and oxalic acids, *cf.* mech. Ch. 1) [225]; stoich. $[RuO_4]^-$/aq. NaOH (crotonates, fumarates, cinnamates; *cf.* mech. Ch. 1) [231].

For *alkynes*: *cis*-[Ru(O)$_2$(CF_3COO)(tmtacn)]$^+$/PhIO or TBHP/CH_2Cl_2 (diphenylacetylene to benzil) [111].

3.2.2.4 Large Scale Oxidations of Alkenes and Alkynes

Cis-*dihydroxylation* of protected 1*L*-1,2:3,4-di-*O*-isopropylidenecyclohex-5-ene-1,2,3,4-tetrol (22 g) gave the diol 1*D*-1,2:3,4-di-*O*-isopropylidene-*allo*-inositol; (Fig. 3.3), $RuCl_3$/aq. Na(IO_4)/CH_3CN/0°C) [168].

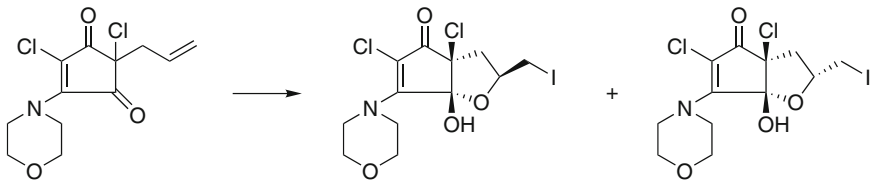


Fig. 3.21 Formation of iodohydrins by RuO_4 – IO_4^- oxidation showing iodine incorporation from the periodate co-oxidant [236]

Alkene cleavage: styrene (2.8 g) to benzoic acid ($RuCl_3$/aq. $IO(OH)_5$/CCl_4–CH_3CN) [19]; norbornene (9.4 g) to *cis* -1,3-cyclopentanedicarboxylic acid (RuO_2 or $RuCl_3$/aq. $Na(IO_4)$/$CHCl_3$) [232].

Alkyne cleavage: di-*n*-hexylacetylene (4 g) to heptanoic acid (RuO_2/Oxone®/aq. $Na(HCO_3)$/CH_3CN–EtOAc) [233]; alkyne (~4 g) to α-diketone + acid mixtures (RuO_2/aq. $Na(IO_4)$ or Na(ClO)/CCl_4) [234] based on [235].

3.2.2.5 Cleavage of Alkenes Involving Other Reactions

An unusual incorporation of iodine derived from the $Na(IO_4)$ used in $RuCl_3$/aq. $Na(IO_4)$/CCl_4–CH_3CN was noted in the oxidation of the terminal alkene 2-allyl-2,5-dichloro-4-morpholino-cyclopent-4-ene-1,3-dione giving the iodohydrin 5β,7-dichloro-1-β-hydroxy-3β-iodomethyl-8-morpholino-2-oxabicyclo[3.3.0]-oct-7-en-6-one and its 3α-epimer. The iodine apparently derives from the formation of I_2 or I^- from the IO_3^- to which IO_4^- is reduced after the $RuCl_3$/IO_4^- reaction (Fig. 3.21) [236].

Oxidative cleavage of monocyclic and bicyclic allylic alcohols to keto acids and di-acids respectively is effected by $RuCl_3$/aq. $Na(IO_4)$/CCl_4–CH_3CN; thus *trans*-verbenol gave (+)-*cis*-pinononic acid and (+)-*trans*-pinocarveol yielded (-)-*cis*-pinic acid (Table 3.6) [237]. The double bond in diphenylcholene was cleaved by RuO_2/aq. $Na(IO_4)$/CCl_4 to aldehyde and acid (Table 3.4) and the adjoining phenyl rings destroyed [238].

For *oxidative destruction of alkenes*, e.g. oxidation of an alkene by RuO_4 with concomitant cleavage of phenyl rings *cf.* above, 3.2.2.1, Fig. 3.18 [206].

3.3 Oxidation of Arenes

Included in this section are oxidations of benzene and phenyl rings, and in general the oxidation of aromatic and polycyclic aromatic compounds. The main catalyst for this type of reaction is RuO_4. The earliest example was the use of stoich. RuO_4/CCl_4 for phenanthrene oxidation [239], while the first catalytic reagent was RuO_2/aq. $Na(IO_4)$/acetone for oxidation of pyrene [240]. Another early example was the conversion of diketo compounds to the *nor*-diketo acids, with concomitant destruction of the two phenyl rings by RuO_2/aq. $Na(IO_4)$/acetone (Fig. 3.18, 3.2.2.1) [206].

Other early oxidation of phenyl rings by $RuCl_3$ or RuO_2/aq. $Na(IO_4)/CCl_4/60°C$ were noted (Table 3.4) – *cf.* also large-scale preparations, 3.3.5 below [241].

Oxidations of alkylaromatic, phenol and hydroquinone substrates by macrocyclic complexes containg the *trans*-$Ru^{VI}(O)_2$ unit have been reviewed, with emphasis on mechanistic aspects [242].

3.3.1 Aromatic Rings to Carboxylic Acids or to CO_2

Oxidative cleavage of an alkene linkage and destruction of the phenyl rings in the conversion of a diketo diphenyl ethylene to a nor-diketo acid by RuO_4/aq. $Na(IO_4)$/acetone has already been mentioned (Fig. 3.18, 3.2.2.1) [206]; another example (Table 3.4, 3.2.2.5) is the total oxidation of phenyl rings in diphenylcholene by RuO_2/aq. $Na(IO_4)/CCl_4$ [238]. The reagent $RuCl_3$/aq. Na(ClO) oxidised alkylaromatic compounds, e.g. 1-phenylcyclohexanol to cyclohexanone to acetophenone (Table 3.4) [243]. The reagent $[RuCl_2(bpy)_2]^+$/TBHP/CH_2Cl_2 oxidised 3, 5-di(*tert*-butyl)catechol to the *o*-benzoquinone [244] as does $RuBr_2(AsPh_3)_2$(HPhb) or $RuBr_2(AsPh_3)_2$(Hdhb)/NMO/CH_2Cl_2 [245]. Chemoselective oxidation of aromatic groups (Ar=Ph, *p*-$MeOC_6H_4$) attached to tetrahydropyran rings yielded carboxylic acids with $RuCl_3$/aq. $IO(OH)_5/CCl_4$–CH_3CN. Thus oxidation of 4-chloro-2-ethyl-6-phenyl-tetrahydropyran gave 4-chloro-6-ethyl-tetrahydropyran-2-carboxylic acid (Fig. 3.22). Use of $RuCl_3$/aq. $Na(IO_4)/CCl_4$–CH_3CN gave some of the diketone 3-chloro-1-(4-methoxyphenyl)-heptane-1,5-dione [246].

The system $RuCl_3$/aq. Oxone®/CH_2Cl_2 effected the oxidative fission of the ring in alkylbenzenes (ethylbenzene, benzaldehyde, benzoic acid, benzonitrile, benzyl chloride and bromide), giving CO_2 and water. Other catalysts including *cis*-$RuCl_2(dmso)_4$, $RuCl_2(PPh_3)_3$ and $[Ru^{II}(H_2O)\{PW_{11}O_{39}\}]^{5-}$ effected the reactions [247]. Several aromatic steroids were selectively degraded by RuO_2/aq. $Na(IO_4)$/acetone (Table 3.4) [248]. Oxidative dehalogenation of phenol, 2,6-dichlorophenol, 2,4,6-trichlorophenol; and pentachlorophenol to CO_2 and HCl by $[Ru(H_2O)_2(dmso)_4]^{2+}$, Ru(Pc)/aq. Oxone®/$CH_2Cl_2$ or cetyltriethyltriammonium cation was reported [249]. With RuO_2/aq. $Na(IO_4)$/acetone there was some aromatic ring cleavage of aromatic steroids to acids (Tables 3.4 and 4.1) [250].

Oxidation of a number of substrates in which phenyl groups were converted to carboxylic acids was described (Tables 3.4 and 3.5) using $RuCl_3$/aq. $IO(OH)_5/CCl_4$–CH_3CN; such oxidations were an intermediate in synthesis of the

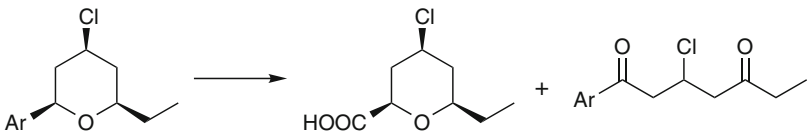


Fig. 3.22 Oxidation of a phenyl group by RuO_4 in the presence of a tetrahydropyran ring [246]

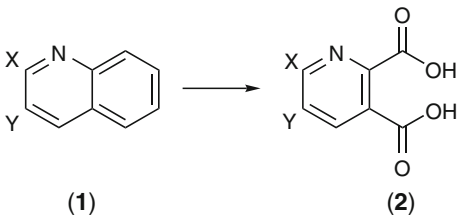


Fig. 3.23 Oxidation of halogenated quinolines to halogenopyridine-2,3-dicarboxylic acids [260]

pheromone *R*-γ-caprolactone [251] and, using $RuCl_3$/aq. $Na(IO_4)/CCl_4$–CH_3CN, oxidation of a phenyl group to the acid to synthesise flurbiprofen [252]. As part of the total synthesis of the triterpene (+)-α-onocerin, one of the first total syntheses in which RuO_4 played a key role, a diphenylethyleneacetoxyketone was oxidised to the corresponding acetoxyketoacid by RuO_2/aq. $Na(IO_4)$/acetone, involving the scission of a double bond (3.2.2.2) but also oxidation of two aromatic rings [219]. The electrocatalytic system $RuCl_3(CH_3CN)_3$/aq. $Li(ClO_4)$/Pt electrodes converted teralin to tetralone [253]. The reagent Ru(CO)(TMP)/$(Cl_2pyNO)/C_6H_6$/HBr or HCl/40°C oxidised aromatic compounds to quinones, e.g. *m*-dimethoxybenzene gave 2-methoxy-*p*-benzoquinone (Tables 3.4 and 3.5, *cf.* mech. Ch. 1). For 1,3,5-trimethoxybenzene; a turnover number of 33,000 was claimed [254].

Amongst PCBs (polychlorinated biphenyls) 4-chlorophenol, pentachlorophenyl and 2,4,6-trichlorophenol were oxidised to mixtures of products by $RuCl_3$/Na(ClO)/aq. 0.1 M NaOH or $RuCl_3/K_2(S_2O_8)$/aq. 0.1 M NaOH/60°C; under these conditions $Na(IO_4)$ was relatively ineffectual [255]. The use of $RuCl_3$/aq. $Na(ClO)/CCl_4$/50–70°C for pentachlorobiphenyl, resulted in complete oxidation to RuO_2, CO_2 and HCl [256]. Oxidation by stoich. RuO_4/CCl_4 of 2,7-dichlorobenzo-*p*-dioxin and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin occurred overnight by the reagent [257]. A number of substrates containing aromatic rings were oxidised by $RuCl_3$/aq. $Na(IO_4)/CCl_4$–CH_3CN [258] (part of a study on hydrocarbon oxidation in coals (Tables 3.4 and 3.5; *cf.* 5.6.3). The system $[Ru(H_2O)(bpy)(amp)]^+$/TBHP/(BTBAC)/C_6H_6 oxidised benzene to phenol and phenol to benzoquinones (*cf.* mech. Ch. 1) [259]. Aromatic rings in quinolines (1) were oxidised to diacids (2) by RuO_2/aq. $Na(ClO/CCl_4$ (X=F, Cl, Br, I, Y=H; X=H, Y=F, Cl, Br; Fig. 3.23). Thus 2-chloroquinoline gave 6-chloro-pyridine-2,3-dicarboxylic acid [260].

The system $[Ru(CF_3COO)_2(H_2O)(tmtacn)]^+$/TBHP/$CH_2Cl_2$ oxidised a variety of anisoles to protected *p*-benzoquinones (with R^n=H unless otherwise indicated: R^1=R^2=OMe, R^5=MeO, R^6=O^{t}Bu; R^1=OMe, R^5=MeO, R^6=O^{t}Bu; R^1=OMe, R^2=Me, R^5=MeO, R^6=O^{t}Bu; R^1=OMe, R^4=Me, R^5=MeO, R^6=O^{t}Bu; R^1=OMe, R^3=R^4=Me, R^5=MeO, R^6=O^{t}Bu; R^1=R^3=R^4=OMe, R^5+R^6=O; R^1=OMe, R^2=NHAc, R^5+R^6=O; R^1=OMe, R^4=NHAc, R^5+R^6=O, R^2=NHAc, R^4=NHAc; R^1=OMe, R2=Br, R^5=MeO, $R^{5\prime}$=O^{t}Bu, Fig. 3.24) [261].

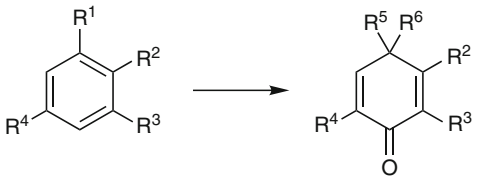


Fig. 3.24 Oxidation of anisoles to *p*-benzoquinones monoketals catalysed by $[Ru(CF_3COO)_2(H_2O)(tmtacn)]^+$ [261]

3.3.2 Phenols

Biomimetic Ru-catalysed oxidations of phenols have been reviewed [175].

Phenols were oxidised by $RuCl_3$ or $RuCl_2(PPh_3)_3$/TBHP/EtOAc–C_6H_6 to 2-substituted protected *p*-quinones; e.g. *p*-cresol gave 4-*tert*-(butyldioxy)-4-methyl-2,5-cyclohexadienone; other *p*-R-phenols gave the *p*-quinones (R=Me, ^{i}Pr, Ph, CH_2Ph CH_2COOMe, $(CH_2)_2COMe$) [263]. Methylphenols were oxidised to the corresponding *p*-benzoquinones by $[Ru_3(\mu\text{-}O)(OAc)_6(H_2O)_3]^+$) or $RuCl_3$/aq. H_2O_2/AcOH (Table 3.4) [262].

3.3.3 Polycyclic Arenes

Djerassi and Engle showed that stoich. RuO_4/CCl_4 oxidised phenanthrene to 9,10-phenanthrenequinone (Table 3.5) [239]. The first catalytic reaction involving RuO_4 was that of pyrene with RuO_2/aq. $Na(IO_4)$/acetone, giving a mixture of pyrene-4,5-quinone, pyrene-1,6-quinone, the lactol of 4-formylphenanthrene-5-carboxylic acid (OsO_4/H_2O_2/acetone was more specific, giving pyrene-4,5-quinone) [240].

Polycyclic substrates were oxidised by $RuCl_3$/aq. $Na(IO_4)/CCl_4$–CH_3CN as part of a study on hydrocarbon oxidation in coals (Table 3.5 and 5.6.3) [258]. A number of substituted naphthalenes were oxidised by RuO_2/aq. Na(ClO)/CCl_4, mainly to phthalic acids (Tables 3.4 and 3.5). When the substituent is electron-donating the yield of phthalic acid was increased, when electron-withdrawing a mixture of products was produced and the overall reaction time increased [264, 265]. The system $RuCl_3$/aq. Na(ClO) oxidised naphthols to phthalic acid or phthalates (Table 3.5) [266]. Oxidation of the polycyclic quinone (1*SR*)-*tert*-butyl(1-(benzyloxycarbonyl)-4,9-dioxo-1,3,4,9-tetrahydronaphtho-[2,3-c]furan-1-yl)acetate (2.6 g) to benzyl(1*SR*,3a*SR*,9a*RS*)-1-((*tert*-butyloxycarbonyl)methyl)-3a,9a-dihydroxy-4,9-dioxo-1,3,3a,4,-9,9a-hexahydronaphtho-[2,3c]-furan-1-carboxylate formed a key part of the synthesis of the the antimicrobial lactonamycin with $RuCl_3$/aq. $Na(IO_4)$/CH_3CN–EtOAc/0°C [267]. Oxidation of (-)-3-*tert*-3-(1′,2′,3′,4′-tetra-hydro-5′-naphthyl) propionic acid to (+)dimethyl-*tert*-butylsuccinate was effected by RuO_2/aq. $Na(IO_4)$/acetone, as part of a determination of the absolute configuration of

dimethyl-*tert*-butylsuccinate (Table 3.5) [268]. The system $RuCl_3/H_2O_2$/AcOH/80°C oxidised anthracene and phenanthrene to the quinones (Table 3.5) [269]. Several arenes were oxidised by $RuCl_3.nH_2O$/aq. $Na(IO_4)/CH_2Cl_2$–CH_3CN assisted by ultrasound: thus naphthalene gave phthalaldehyde, pyrene gave pyrene-4,5-dione and chrysene gave chrysene-5,6-dione and 2-(2-formylphenyl)-1-napthaldehyde; *cf.* mech. Ch. 1 [270]. The reagent $RuCl_3$/aq. $Na(IO_4)/CH_2Cl_2$–CH_3CN oxidised pyrene and 2,7-R_2pyrene (R=^{t}Bu, ^{n}Hx) to the corresponding pyrene-4,5-diones, while at 30°C the 4,5,9,10-pyrene tetra-ones were formed [271].

3.3.4 Oxidative Coupling of Arenes and Napththols

A variety of 2-naphthols were oxidatively coupled by $RuCl_3/O_2$/[bmim](PF_6) to give binaphthols in the ionic liquid [bmim](PF_6) (bmim=1-butyl-3-methylimidazolium); chlorobenzene, toluene or CCl_4 were also used as solvents but yields were better in the ionic liquid. Examples included formation of 1,1′-binaphthyl-2,2′-diol, 6,6′-dibromo-1,1′-binaphthyl-2,2′-diol, 7,7′-dimethoxy-1,1′-binaphthyl-2,2′-diol, 3,3′-bismethoxycarbonyl-1,1′-binaphthyl-2,2′-diol, 2,2′-di-hydroxy-5,5′-dichloro-4,4′,6,6′-tetramethylbiphenyl and 2,2′-dihydroxy-3,3′,5,5′-tetramethylbiphenyl [272]. Phenanthrene gave a mixture of 1,1′-biphenyl-2,2′-dicarbaldehyde and phenanthrene-9,10-dione with $RuCl_3$/aq. $Na(IO_4)$/aq. H_2SO_4/EtOAc–CH_3CN/0°C [9]. Phenanthrene was *cis*-dihydroxylated to *cis*-9,10-dihydro-9,10-phenanthrenediol by $RuCl_3$/aq. $Na(IO_4)/Na(HCO_3)$/EtOAc–CH_3CN/5°C [159]; some other reactions are shown in Table 3.5. The chelating arenes ArH and cycloalkanes RH were oxidatively cross-coupled to ArR by $[RuCl_2(p\text{-cymene})]_2$/TBHP/135°C (the solvent constituted the reactants): thus 2-phenylpyridine and cyclo-octane were cross-coupled. Other complexes ($Ru(acac)_3$, $[RuCl_2(COD)]_2$ and $RuH_2(CO)(PPh_3)_3$ catalysed the reaction [273].

3.3.5 Large-Scale Oxidations of Arenes

These include oxidation of 1-phenyl-3-heptanol acetate (12 g) to 4-(acetyloxy) octanoic acid ($RuCl_3$/aq. $IO(OH)_5/CCl_4$–CH_3CN) [251]; phenylcyclohexane (4 g) to cyclohexanecarboxylic acid ($RuCl_3$/aq. $Na(IO_4/CCl_4)$; *p-tert*-butylphenol (3 g) to pivalic acid, phenylcyclohexane (4g) to cyclohexanecarboxylic acid ($RuCl_3$ or RuO_2/aq. $Na(IO_4)/CCl_4$/60°C) [241].

3.3.6 Aromatic Substrates Not Covered Here but Included in Chapter 1

These include stoich. $[Ru(O)(pic)(tpy)]^+$/water (phenol to *p*-quinone) [274]; *trans*-$[Ru(O)_2(14\text{-TMC})]^{2+}/CH_3CN$ (hydroquinone to p-benzoquinone, *cf.* mech. Ch. 1)

[134, 275]; *trans*-Ba[$Ru(OH)_2(O)_3$]/CF_3COOH/(bpy)/CH_2Cl_2 (benzene to 1,4-benzoquinone) [276]; stoich. $[Ru(O)(py)(bpy)_2]^{2+}$/water (normal and substituted hydroquinones, *cf.* mech. Ch. 1) [277], $RuCl_3$/$(NH_4)_2[Cr_2O_7]$/aq. $HClO_4$/CH_3CN (2-methylnaphthalene to 2-methyl-1,4-naphthoquinone, *cf.* mech. Ch. 1) [278]; stoich. *trans*-$Ru(O)_2(OAc)_2(py)_2$/CH_3CN (2,6-di-*tert*-butylphenol) [63]; stoich. $[Ru(O)(py)(bpy)_2]^{2+}$/CH_3CN (phenols, alkylated phenols, *cf.* mech. Ch. 1) [279, 280]; $[Ru(H_2O)(bpy)(tpy)]^{2+}$/water @ pH 6.8/Pt electrodes (4-methylbenzoate to terephthalic acid, toluene to benzoate; *cf.* mech. Ch. 1) [281]; (2,6-dichlorophenoxide and arylfurans, *cf.* mech. Ch. 1) [282]; stoich. RuO_4/CCl_4 (normal and substituted naphthalenes; *cf.* mech. Ch. 1) [283].

3.4 Oxidation of Alkynes

As with alkene cleavage the main reagent for alkyne oxidations is RuO_4. Oxidative cleavage of alkynes by a variety of reagents has been reviewed [4, 6, 12, 14, 15]. The first oxidation of alkynes was noted by Pappo and Becker in 1956: they showed that 1,2-*bis*(1-acetoxycyclohexyl)ethyne (2) (Fig. 1.5) gave the diketone. Minimal experimental details were given [195].

3.4.1 Oxidation of Alkynes Involving No C=C Bond Cleavage

As with alkenes we consider first those oxidations which do not cleave the acetylenic bond giving α-diketones, or oxidation of alkynyl amines and ethers to α-keto amides and esters, and then consider oxidative alkyne cleavage to acids.

3.4.1.1 Alkynes to α-Diketones

$$R^1CCR^2 + 2[O] \rightarrow R^1(CO)(CO)R^2 \qquad (3.12)$$

In an early example oxidation of R^1CCR^2 by RuO_2/aq. Na(ClO)/CCl_4/0°C gave the α-diketones (R^1=R^2=Ph, Bu and Pr) together with some of the cleavage acids (Table 3.6) [235]. Alkynes were oxidised to 1,2-diketones by $RuCl_3$/$Na(IO_4)$/aq. $Na(HCO_3)$/$Mg(SO_4)$/CH_3CN–CCl_4 (R^1=Ph, R^2=Ph, *p*-$CH_3OC_6H_4$, *p*-ClC_6H_4, *p*-$NO_2C_6H_4$, *p*-$CH_3OCOC_6H_4$; R^1=2,4-$BnOC_6H_3$, R^2= *p*-$CH_3OC_6H_4$, *p*-CH_3OC-OC_6H_4). Thus 1-benzyloxy-2-[2-(2,2-diethoxy-ethoxy)-4-methoxy-phenylethynyl]-4,5-dimethoxybenzene gave 1-(2-benzyloxy-4,5-dimethoxy-phenyl-2-[(2,2-diethoxy-ethoxy)-4-methoxyphenyl]-ethane-1,2-dione [284]. Alkynes were also oxidised electrolytically to α-diketones by RuO_4 (electrogenerated from RuO_2/saturated aq. NaCl @ pH 4/0°C/Pt electrodes). Thus R^1CCR^2 gave R^1COCOR^2 for R^1=R^2=MeCH(OAc), $^nC_4H_9$, $^nC_6H_{13}$; R^1=Ph, R^2=Et, $^nC_4H_9$, $^nC_6H_{13}$; R^1=$^nC_4H_9$, $^nC_6H_{13}$, $^nC_{10}H_{21}$ with R^2=CH_2OAc. Use of such a pH and low temperature avoids

over-oxidation to the dicarboxylic acid (Table 3.6) [285]. The reagent stoich. *cis*-$[Ru(O)_2(CF_3COO)(tmtacn)]^+/CF_3COOH–CH_3CN$ oxidised R^1CCR^2 to the diketones (R^1=R^2=Me, Ph, C_3H_7; R^1=Ph, R^2=H, Me, $SiMe_3$, Fig. 1.30), *cf.* mech. Ch. 1) [222], while *cis*-$[Ru(O)_2(CF_3COO)(tmtacn)]^+$/PhIO/water-$CH_2Cl_2$ oxidised diphenylacetylene to benzil [111]. Oxidation of ynamides gave α-ketoimides with RuO_2/aq. $Na(IO_4)/CH_2Cl_2–CH_3CN$ [287].

As a part of research on the immunosuppresant rapamycin it was found that acetylenic amides derived from diethylamine and proline gave the corresponding amide-diones with RuO_2/aq. $Na(IO_4)/CCl_4–CH_3CN$ [287].

3.4.1.2 Alkynyl Amines and Ethers to α-Keto Amides and Esters

$$R^1CCNR^2R^3 + 2[O] \rightarrow R^1(CO)(CO)NR^2R^3 \quad (3.13)$$

$$R^1CCR^2 + 2[O] \rightarrow R^1(CO)(CO)R^2 \quad (3.14)$$

The amine oxidations were effected by $RuCl_2(PPh_3)_3$/PhIO/acetone (RuO_4, $RuCl_3$, $RuCl_2(CO)_2(PPh_3)_2$ and $Ru_3(CO)_{12}$ were also effective catalysts but little detail was given) for R^1 =Me, R^2=R^3=Et; R^1=^{i}Pr, R^2=R^3=Me; R^1=Ph, R^2=R^3=Me, Et. Thus dimethyl(phenyl-ethynyl)amine gave *N,N*-dimethyl-2-*oxo*-benzylamide in good yield. The same reagent effected alkynyl ether oxidations (R^1=H, Me or Ph, R^2=R^3= Et; R^1=^{i}Pr, ^{n}C_6H_{13}, R^2=R^3=Me; R^1=^{n}C_4H_9, R^2=R^3=^{i}C_3H_7) [288].

3.4.2 Oxidative Cleavage of Alkynes to Carboxylic Acids

$$R^1CCR^2 + 3[O] + H_2O \rightarrow R^1COOH + R^2COOH \quad (3.15)$$

This is a common reaction, particularly with RuO_4 (Table 3.6). The reagent RuO_2/aq. $Na(ClO)/CCl_4$ oxidised alkynes R^1CCR^2 to mixtures of the corresponding α-diketones or carboxylic acids (R^1=R^2=Ph, Bu, Pr; R^1=H, R^2=Ph, ^{t}Bu; for ^{n}BuC-C^{n}Bu $Na(IO_4)$ can replace Na(ClO) in the recipe) [235]. Alkynes were oxidised to carboxylic acids by $RuCl_3$/aq. $IO(OH)_5/C_6H_{12}–CH_3CN$ [207] and also by $RuCl_3$/aq. $IO(OH)_5/CCl_4–CH_3CN$ [19]; another ubiquitous reagent for such oxidations is RuO_2/Oxone®/aq. $Na(HCO_3)$/EtOAc–CH_3CN (Table 3.6; Fig. 1.9; *cf.* mech. Ch. 1) [233]. An electrocatalytic system was devised in which alkynes were oxidised to acids by RuO_4 generated from RuO_2/aq. NaCl @ pH 4/0°C/Pt electrodes. Thus R^1CCR^2 gave acids (R^1=H, R^2=Ph, C_6H_{13}, C_8H_{17}) in good yield. For the following α-diketones were the main products but acids were also formed as by-products: R^1=R^2=MeCH(OAc), ^{n}C_4H_9, ^{n}C_6H_{13}; R^1=Ph, R^2=Et, ^{n}C_4H_9, ^{n}C_6H_{13}; R^1=^{n}C_4H_9, ^{n}C_6H_{13}, ^{n}$C_{10}H_{21}$ with R^2=CH_2OAc. Use of such a pH and low temperature avoids over-oxidation to the dicarboxylic acid [284]. With $RuCl_2(PPh_3)_3$/PhIO/CH_2Cl_2

terminal alkynes (phenylacetylene, 1-octyne, 1-pentyne) were cleaved to carboxylic acids (Table 3.6) while disubstituted alkynes gave α-diketones (from diphenylacetylene, 1-phenyl-1-heptyne, 1-phenyl-1-propyne and 2-pentyne). Other catalysts for this were $RuCl_2(PPh_3)_3$, $Ru(CO)_2Cl_2(PPh_3)_2$ and $Ru_3(CO)_{12}$ [289].

For other alkyne oxidation systems mentioned in Chapter 1 but not considered here *cf.* 3.2.2.3 and for large-scale alkyne oxidations *cf.* 3.2.2.4.

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Chapter 4
Oxidation of Alkanes

Abstract This chapter covers oxidation of C–H and C–C bonds in alkanes. Section 4.1 concerns oxidation of C–H bonds: aldehydes and other CH species (4.1.1), methylene ($–CH_2$ groups) (4.1.2) and methyl ($–CH_3$) groups (4.1.3). This is followed by the oxidation of cyclic alkanes (4.1.4) and large-scale alkane oxidations (4.1.5). Alkane oxidations not considered here but covered in Chapter 1 are listed in Section 4.1.6. The final section (4.2) concerns oxidative cleavage of C–C bonds.

4.1 Oxidation of C–H Bonds in Alkanes

Whereas Ru catalysts are of considerable use in organic chemistry, in particular for the oxidation of alcohols and alkenes, they have not as yet found great practical application for alkane oxidation, although much work is being carried out in the area. In general RuO_4 is best able to effect C–H bond activation, though some other Ru-containing reagents will also do this.

There are several reviews on alkane oxidation by Ru complexes (principally by RuO_4) including [1–6]. Most of the oxidations catalysed are of C–H bonds; C–C cleavage is considered in 4.2. We begin with what in principle is the simplest oxidation, that of the C–H bond in aldehydes and related substrates.

As has been pointed out in Chapter 5, oxidation of some primary and secondary amines, and of amides, may equally well be regarded as alkane oxidations (*cf.* 4.1.2, 4.1.3 and 5.1.3.1).

4.1.1 Aldehydes and Other $R^1R^2R^3CH$ Substrates

The commonest examples occur with aldehydes:

$$RCHO + [O] \rightarrow RCOOH \tag{4.1}$$

W.P. Griffith, *Ruthenium Oxidation Complexes*, Catalysis by Metal Complexes 34,
DOI 10.1007/978-1-4020-9378-4_4, © Springer Science+Business Media B.V. 2011

Some examples are given in Table 4.1. The system $RuCl_3$/aq. H_2O_2/AcOH/80°C[1] oxidised benzaldehydes (4-chloro-, 4-methoxy-, 2-hydroxy-, 4-hydroxy 3-methoxy- and cinnamaldehyde) to the corresponding carboxylic acids [7], as did $RuCl_3/K_2(S_2O_8)$/aq. M KOH (Table 4.1) [8, 9] and $RuCl_3/Na_2(BrO_3)$/aq. M $Na_2(CO_3)$ [8]. Electrocatalytic oxidations by $RuCl_3$/aq. NaCl–CCl_4/Pt anode [10] and by RuO_2/aq. NaCl @ pH 7/CCl_4/Pt electrodes [11] were also effective. Octanal was converted to its methyl ester by $RuH_2(CO)(PPh_3)_3$/(Xantphos)/MeCH=CHCN/water-CH_3OH-toluene/reflux/24 h. [12], and the α-hydroxyester MeCH(OH)COOEt was oxidised to the keto-ester Me(CO)COOEt by $Ru(acac)_3$/TBHP/C_6H_6, a reaction also catalysed by $RuCl_3$, $RuBr_3$, $RuCl_2(PPh_3)_3$ and $Ru_3(CO)_{12}$ [13].

Enantioselective hydroxylation of 2-benzyl β-ketoesters was catalysed by [RuCl(OEt$_2$)(PNNP)]/aq. H_2O_2/CH_2Cl_2: thus ethyl 2-benzyl-3-oxo-butanoate gave ethyl 2-hydroxy-2-benzyl-3-oxo-butanoate. Better results were obtained with cumyl hydroperoxide as co-oxidant [14]. The reagent Ru(CO)(TPP) or Ru(CO)(TMP)/(Cl_2pyNO)/aq. HBr/C_6H_6/40°C oxidised 5β-steroids to the corresponding 5β-hydroxy derivatives with retention of configuration [15].

For oxidations of adamantane and cyclohexane *cf.* 4.1.4; for acetoxylation of β-lactams *cf.* 5.2.2 (Fig. 5.8); for oxidation of silanes $R^1R^2R^3SiH$ to silanols $R^1R^2R^3Si(OH)$ *cf.* 5.6.1.

4.1.2 Methylene Groups to Ketones

$$\mathbf{R^1R^2CH_2 + 2[O] \rightarrow R^1R^2C=O + H_2O} \tag{4.2}$$

One of the first RuO_4-catalysed oxidations of a methylene to a ketone group (Fig. 4.1) was effected by $RuCl_3$/aq. $Na(IO_4)/CCl_4$–CH_3CN, e.g. with R=Me$(CH_2)_9$ and R′=H or Me; thus 6-*tert*-butylspiro[2.5]octane gave the corresponding ketone [16].

Oxidation of diphenylmethane to benzophenone and other substrates was accomplished with $RuCl_2(PPh_3)_3$/TBHP/C_6H_6 (Table 4.1, *cf.* mech. Ch. 1) [17]; other alkanes were oxidised by $RuCl_2(PPh_3)_3$/TBHP or CH_3CO_3H/C_6H_6 (and also by $RuH_2(PPh_3)_4$), *cf.* mech. Ch. 1) [18], while diphenylmethane and fluorene were oxidised by $[Ru(acac)_2(bpy)]^+$ or $RuCl_2$(bac)(bpy)/TBHP/C_6H_6 (Table 4.1) [19]. Benzylic nitriles RCH_2CN were converted to acyl cyanides RCOCN (R=4-MeOC_6H_4, 3,4-$Me_2OC_6H_3$) by $RuCl_3$/TBHP/C_6H_6 [20]. The system *trans*-

[1]As indicated in 1.2.2 these abbreviations take the form: Ru starting material/co-oxidant/solvent; temperatures are only indicated if not ambient. For brevity, RuO_2 and $RuCl_3$ denote the *hydrates* $RuO_2.nH_2O$ and $RuCl_3.nH_2O$.

Table 4.1 Oxidation of alkanes

Reactant	Product	Method [Ref.]
For adamantane and cyclohexane see 4.1.4		
$R^1R^2R^3CH$		
p-Anisaldehyde	*p*-Anisic acid	A [10]
Benzaldehyde	Benzoic acid	A [10], B [8], [9]; C [8]; D [11]
Cinnamaldehyde	Cinnamic acid	B [8]
Heptanal	Heptanoic acid	D [11]
2-Hydroxybenzaldehyde	Hydroxybenzoic acid	B [9]
4-Methoxybenzaldehyde	4-Methoxybenzoic acid	B [8], [9]; C [8]
4-Nitrobenzaldehyde	4-Nitrobenzoic acid	B [9]
Cumene	2-Phenylpropane-2-ol + Acetophenone	E [17], F [24]
$R^1R^2CH_2$		
Ethylbenzene	Acetophenone	E [17], [18]; F [24], G [23]
Diphenylmethane	Benzophenone	E [17], [18]; H [19]
Tetrahydrofuran	γ-Butyrolactone	S [60]
1,3-Diphenylpropane	1,3-Diphenylpropanone	E [17]
Fluorene	Fluoren-9-one	H [19]
p-Cymene	2-*p*-Tolylpropanol + 4-*iso*Propylbenzoic acid	F [24]
RCH_3		
p-Methoxytoluene	Anisaldehyde	F [24]
Toluene	Benzaldehyde	E [17], [18]; F [24]
Toluene	Benzoic acid	G [23]
4-Chloro-*o*-xylene	4-Chloro-2-methylbenzoic acid	J [22]
p-Methoxytoluene	*p*-Methoxybenzoic acid	G [23]
4-Nitro-*o*-xylene	2-Methyl-5-nitrobenzoic acid	J [22]
o-Xylene	*o*-Toluic acid + phthalic acid	G [23]
m-Xylene	*m*-Toluic acid + *iso*phthalic acid	G [23]
p-Xylene	*p*-Toluic acid + terephthalicacid	G [23]
Cyclic alkanes		
Estrone acetate	3-Acetoxy-9α-hydroxy-1,3,5(10) estratriene-6,17-dione	K [67]
Adamantane	2-Adamantyl trifluoroacetate + Adamanatan-1-ol	L [65]
Epicedrane	8α-Cedranol (Fig. 4.4)	M [69]
Cycloheptane	Cycloheptanone + glutaric acid	N [25]
Cyclohexane	Cyclohexyl trifluoroacetate	E [17]
Cyclo-octane	Cyclo-octyl trifluoroacetate + cylcohexanone	L [65]
Cyclopentane	Cyclopentanone + pimelic acid	N [25]
trans-Decahydronaphthalene	*trans*-9-Decahydronaphthol + decalones	N [25]
Estradiol-17α diacetate	3,17α-Diacetoxy-9α-hydroxy-1,3,5(10) estratriene-6-one	K [67]
Cedrol	2α,8β-Dihydroxycedrane	M [69]

(continued)

Table 4.1 (continued)

Reactant	Product	Method [Ref.]
5α-Cholestan-3-one	(20*S*)-Dihydroxycholestan-3-one	P [15]
Estradiol-17β dipropionate	3,17β-Dipropionyloxy-9α-hydroxy-1,3,5(10)-estratriene-6-one	K [67]
Hexane	Hexyl trifluoroacetates + hexanones	L [65]
Cedryl acetate	2α-Hydroxy-8β-acetoxycedrane	M [69]
Neo*iso*cedranol acetate	2α-Hydroxy-8α-H-9α-acetoxycedrane	M [69]
Neo*iso*cedranol carbonate	2α-Hydroxy-8α-H-9α-[(methoxycarbonyl) oxy]-cedrane	M [69]
endo-Tetrahydrodicyclo pentadiene	4-Hydroxy-*endo*-tetrahydrodicyclopentadiene	Q [47], [48]
Indane	Indan-1-one	E [17]
Norbornane	2-Norbornanone	Q [47], [48]
Norbornane	*exo*-2-Norbornyl trifluoroacetate	L [65]
Neo*iso*cedranol oxide	5β,9β-Oxy-8α-hydroxycedrane + ketolactone	M [69]
Estriol triacetate	3,16α,17α-Triacetoxy-9α-hydroxy-1,3,5(10) estratriene-6-one	K [67]

A: $RuCl_3$/aq. NaCl/CCl_4/Pt anode [10]; **B:** $RuCl_3/K_2(S_2O_8)$/aq. M KOH [8], [9]; **C:** $RuCl_3$/$Na(BrO_3)$/aq. M $Na_2(CO_3)$ [8]; **D:** RuO_2/CCl_4/aq. NaCl @ pH 7/Pt electrodes [11]; **E:** $RuCl_2(PPh_3)_2$/TBHP/C_6H_6 [17], [18]; **F:** $RuCl_3$/aq. H_2O_2/(DDAB)/80°C [24]; **G:** $[Ru(OH)(bpy)(tpy)]^{2+}$/^{t}BuOH/water @ pH 6.8/Pt electrodes/50°C [23]; **H:** $[Ru(acac)_2(bpy)]^+$ or $RuCl_2$(bac)(bpy)/TBHP/C_6H_6 [19]; **J:** $RuCl_3$/aq. Na(ClO) @ pH 9/(^{n}Bu$_4$N)HSO_4 [22]; **K:** RuO_2/aq. $Na(IO_4)$/acetone [67]; **L:** $RuCl_3/CH_3CO_3H/CF_3COOH$-$CH_2Cl_2$ [65]; **M:** $RuCl_3$/aq. $Na(IO_4)/CH_3CN$-CCl_4 [69]; **N:** RuO_2/aq. Na(ClO) or aq. $Na(IO_4)$ [25]; **P:** Ru(CO)(TPP) or Ru(CO)(TMP)/(Cl_2pyNO)/aq. HBr-C_6H_6/40°C [15]; **Q:** RuO_2/aq. $Na(IO_4)/CCl_4$-CH_3CN [47], [48]; **S:** stoich. *trans*-$[Ru(O)_2(ddd)]^{2+}/CH_3CN$ [60]

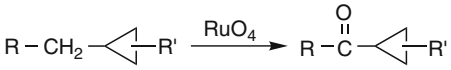


Fig. 4.1 Oxidation by RuO_4 of alkanes containing cyclopropane rings [16]

$[Ru(H_2O)_2(bpy)_2]^{2+}$/TBHP/water-C_6H_6 oxidised pentane, hexane, heptane and octane to the corresponding alcohols and ketones; *trans*-$Ru(O)_2(bpy)\{IO_3(OH)_3\}$/aq. $Na(IO_4)/CH_2Cl_2$/80°C (Fig. 1.23) also did this but less effectively [21].

For oxidation of $–CH_2$ groups adjacent to amine centres *cf.* 5.1.1, 5.1.2.1, 5.1.3.1 and Figs. 5.5, 5.6, 5.7, 5.9, and 5.10; e.g. oxidations of *N*-acylated cyclic α-amino

acid esters to the corresponding lactams *cf.* Fig. 5.6, 5.2.1 and of perhydro-azepines and -azocines to N-acyllactams *cf.* Fig. 5.11, 5.2.4.

4.1.3 Methyl Groups to Aldehydes or Carboxylic Acids

$$\text{e.g. } R^1R^2R^3CCH_3 + 2[O] \rightarrow R^1R^2R^3CCHO + H_2O \quad (4.3)$$

$$R^1R^2R^3CCH_3 + 3[O] \rightarrow R^1R^2R^3COOH + H_2O \quad (4.4)$$

Oxidation of CH_3 side-chains in aromatic compounds, e. g. of substituted xylenes to toluic acids, was carried out with $RuCl_3$/Na(ClO)/aq. (^{n}Bu$_4$N)HSO$_4$ @ pH 9; thus 4-chloro-*o*-xylene in 1,2-dichloroethane gave 4-chloro-2-methyl benzoic acid [22]. Toluene or xylenes were oxidised to the corresponding acids by several reagents (Table 4.1), e.g. using [Ru(OH)(bpy)(tpy)]$^{2+}$/aq. ^{t}BuOH @ pH 6.8/Pt electrodes/50°C) [23], and methyl groups of alkylaromatic compounds by $RuCl_3$/aq. H_2O_2/(DDAB)/80°C to aldehydes, ketones or alcohols (Table 4.1) [24].

For oxidations of amines involving oxidation of CH, CH_2 or CH_3 groups adjacent to tertiary amine centres *cf.* 5.1.1, 5.1.2.1 and 5.1.3.1; e.g. for conversion of tertiary amines $RNMe_2$ to the corresponding α-aminonitriles RNCH(CN)Me (Fig. 5.3, 5.1.3.4) and of proline methyl esters to pyrrolidin-5-ones (5.2.3, Fig. 5.9).

4.1.4 Cyclic Alkanes

One of the first RuO_4-catalysed alkane oxidations was of cyclic alkanes by RuO_2/aq. Na(ClO) or Na(IO_4) (Table 4.1) [25]. Some of the oxidations with Ru-based catalysts were evaluated using adamantane as a model substrate: the common oxidation products are shown in Fig. 4.2.

Reported oxidations of model substrates include:

Adamantane [Ru(N4py)]$^+$ or Ru(Me$_2$SO)/(N2pyo)/MCPBA or Cl$_2$pyNO/CH_2Cl_2 [26]; [RuCl(tpa)]$_2^{2+}$/TBHP or CHP/CH_3CN/40°C, *cf.* mech. Ch. 1 [27, 28]; [Ru{$PW_{11}O_{39}$}(dmso)]$^{5-}$/aq. Oxone®/^{n}Bu(HSO$_4$)/DCE/50°C [29]; [RuCl(dmso)(tpa)](PF_6) and RuCl(dmso)(BPG)/MCPBA/$CHCl_3$ [30]; stoich. RuO_4/water/CH_3CN-CCl_4 or water-acetone, *cf.* mech. Ch. 1, Fig. 1.10 [31–33]; [$RuCl_2$(tpa)]$^+$/(MCPBA)/CH_3CN [34]; *trans*-[$RuCl_2$(dppp)$_2$]$^+$, *trans*-[$RuCl_2$(dppe)$_2$]$^+$ or [RuCl(dppp)$_2$]$^+$/PhIO/(BDTAC)/CH_2Cl_2 [35]; stoich. *trans*-Ba[Ru(OH)$_2$(O)$_3$]/CF_3COOH/(bpy)/CH_2Cl_2 [36] or *trans*-Ba[Ru(OH)$_2$(O)$_3$]/^{n}Bu$_4$N(IO_4)/AcOH-CH_2Cl_2 [37]; $RuCl_3$-Co(OAc)$_2$.4H_2O/O_2/CH_3CHO [38]; $RuCl_3$/O_2/heptanal/CH_2Cl_2 [39]; *cis*-[Ru(H_2O)$_2$(dmso)$_4$]$^{2+}$/aq. Na(ClO) or TBHP/CH_2Cl_2 and [Ru(H_2O){$PW_{11}(O)_{39}$}]$^{5-}$/aq. Na(ClO) or TBHP/CH_2Cl_2, *cf.* mech. Ch. 1 [40]; [$RuCl_2$(saloph)]$^-$/O_2/water-dioxane, *cf.* mech. Chapter 1

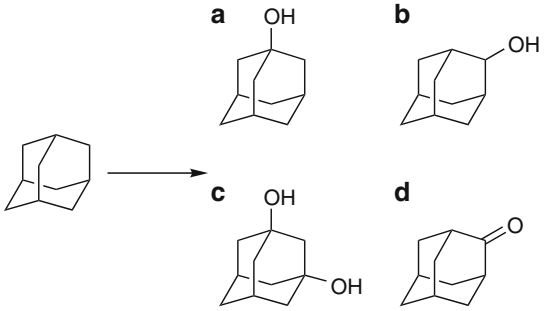


Fig. 4.2 Oxidation of adamantane to (**a**) adamant-1-ol; (**b**) adamant-2-ol; (**c**) adamant-1,3-diol; (**d**) adamant-2-one

[41]; *trans*-$Ru(O)_2(TMP)/(Cl_2pyNO)/C_6H_6$/24 h [42]; *trans*-$RuCl_2(dppp)_2$ or $[RuCl(ppy)_2]^+$/aq. Li(ClO)/CH_2Cl_2, *cf.* mech. Ch. 1 [43]; stoich. $[Ru(O)(N_4O)]^{2+}$/CH_3CN [44]; $[Ru(H_2O)(EDTA)]^-/O_2$/water @ pH 1.75/dioxane/35°C, *cf.* mech. Ch. 1 [45], [46]; RuO_2/aq. Na(IO_4)/CCl_4-CH_3CN, Table 4.1, *cf.* mech. Ch. 1 [47]; $RuCl_3$/aq. Na(IO_4)/CCl_4-CH_3CN/40°C, Table 4.1, *cf.* mech. Ch. 1 [48].

Cyclohexane. This was used as a substrate with *trans*-$[Ru(O)_2(14\text{-}TMC)]^{2+}/O_2$/-$CH_3CN$/50°C/17h. (*cf.* mech. Ch. 1) [49]; $Ru(CO)(X_4\text{-}CPP)$/PhIO/CH_2Cl_2 [50]; $[Ru(H_2O)(bpy)(cpsd)]^+$ or $Ru(H_2O)(pic)(bpy)(cpsd)$/TBHP/$(PhCH_2\{N(CH_2)_3Me\}_3)Cl$/$CH_2Cl_2$ [51]; Ru(Pc) or $[Ru(H_2O)\{PW_{11}(O)_{39}\}]^{5-}$/aq. Oxone® (to adipic acid) [52]; $[RuCl(tpa)]_2$/TBHP or CHP/CH_3CN/40°C, *cf.* mech. Ch. 1 [27], [28]; $[Ru_3(O)(OCOR)_6](py)_3$ or $Ru_2(OAc)_2(py)_4$/Zn/O_2/(py)/AcOH [53]; $RuCl_2(PPh_3)_3$/TBHP/C_6H_6, *cf.* mech. Ch. 1, Table 4.1 [17], [18]; α-$(^nHx_4N)_5[Ru\{Si(H_2O)W_{11}(O)_{39}\}]^{5-}$/TBHP/$C_6H_6$ [54]; $Ru(O)_2(TMP)/(Cl_2pyNO)/C_6H_6$ [55]; stoich. *trans*-$Ba[Ru(OH)_2(O)_3]/CF_3COOH$/(bpy)/$CH_2Cl_2$ [36] or *trans*- $Ba[Ru(OH)_2(O)_3]/^nBu_4N(IO_4)$/AcOH-$CH_2Cl_2$ [37]; *trans*-$[RuCl_2(dppe)_2]^+$, $[RuCl(dppp)_2]^+$ or *trans*-$[RuCl_2(dppp)]^+$/PhIO or $K(HSO_5)$/(BDTAC)/CH_2Cl_2 [35]; $RuCl_3$-$Co(OAc)_2.4H_2O/O_2/CH_3CHO$ [38]; $[RuCl_2(saloph)]^-$/O_2/water-dioxane, *cf.* mech. Ch. 1 [41]; *trans*-$Ru(O)_2(TMP)/(Cl_2pyNO)/C_6H_6$/24h.[42]; *trans*-$RuCl_2(dppp)_2$ or $[RuCl(ppy)_2]^+$/aq. Li(ClO)/CH_2Cl_2, *cf.* mech. Ch. 1 [43]; stoich. Ru(O)(PDTA)]$^-$ or Ru(O)(HEDTA)/water-dioxane, *cf.* mech. Ch. 1 [56]; $[RuCl_2(H_2O)_4]^+$/O_2/water-dioxane [57–59]; *cis*-$[Ru(H_2O)_2(dmso)_4]^{2+}$/aq. Na(ClO) or TBHP/$CH_2Cl_2$ or $[Ru(H_2O)\{PW_{11}(O)_{39}\}]^{5-}$/aq. Na(ClO) or TBHP/$CH_2Cl_2$, *cf.* mech. Ch. 1 [40]. stoich. *trans*-$[Ru(O)_2(ddd)]^{2+}/CH_3CN$, *cf.* mech. Ch. 1 [60]; *cis*-$[Ru(H_2O)_2(Cl_2bpy)_2]^{2+}$/TBHP/acetone [61]; RuBr(PPh_3)(OEP)/PhIO/CH_2Cl_2 [62]; RuO_2/aq. Na(ClO) or Na(IO_4) (Table 4.1) [25].

It was shown in 1994 that $RuCl_3/CH_3CO_3H/CF_3COOH$-$CH_2Cl_2$ oxidised a number of alkanes to ketones and alcohols [63]. Although subsequent work suggested that such oxidations could be effected in the absence of $RuCl_3$, e.g. simply by CF_3COOH/H_2O_2 [64], this was later disputed [65], and it was shown that oxidation of alkanes by $RuCl_3/CH_3CO_3H/CF_3COOH$-$CH_2Cl_2$ gave trifluoroacetates and ketones; *cf.* mech. Ch. 1 [65]. Grundmann's ketone, a derivative of vitamin D_3, when oxidised with $RuCl_3$/aq. Na(IO_4)/CCl_4-CH_3CN gave a 25-hydroxy ketone [66]. Oxidation of

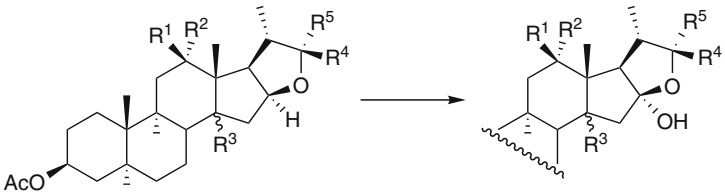
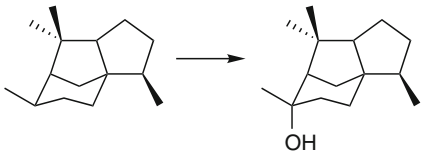


Fig. 4.3 Mild C–H oxyfunctionalisation of cyclic steroidal ethers by RuO_4 [68]

Fig. 4.4 Oxidation by RuO_4 of epicedrane [69]



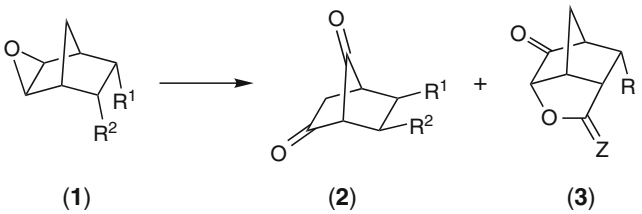
CH_2 groups in aromatic steroids gave ketones with RuO_2/aq. $Na(IO_4)$/acetone with some aromatic ring cleavage to acids [67]. Oxidation of several cyclic alkanes by RuO_2/aq. $Na(IO_4)/CCl_4$-CH_3CN was accomplished [47], [48] and also by $RuCl_2(PPh_3)_3$/TBHP or CH_3CO_3H/C_6H_6 (Table 4.1) [17], [18].

The mild C-H oxyfunctionalisation of cyclic steroidal ethers was effected with RuO_4 generated from $RuCl_3$/aq. $Na(IO_4)$/EtOAc-CH_3CN (Fig. 4.3) ($R^1R^2=H_2$, β-OBz, =O, α/β-OH, R^3=α-H, -OBz; R^4R^5=side chain or spiroketal). A large-scale preparation of 14,16-dihydroxyhecogenin acetate from C12,14-dihydroxyhecogenin acetate using $RuCl_3$/aq. $Na(BrO_3)$/EtOAc-CH_3CN was reported [68].

Oxidation of cedranes and their derivatives by $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN (anhydrous $RuCl_3$ does not work) was studied; thus epicedrane was hydroxylated regioselectively with retention of configuration to 8α-cedranol (Fig. 4.4), and other oxyfunctionalisations of non-activated C-H bonds in cedranes were similarly accomplished (Table 4.1, *cf.* mech. Ch. 1) [69].

The system $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN/60°C oxidised bridged polycyclic alkanes, e.g. neo*iso*cedranol oxide to the alcohol and ketolactone, *cf.* mech. Ch. 1 [70]; perhydroboraphenalene was oxidised to the corresponding triketone by RuO_2/aq. $Na(IO_4)$/Na(OAc)/acetone [71]. Epoxide ring-opening of functionalised norbornanes was achieved with $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN/60°C. Thus for R^1=R^2=H or R^1=CH_2OAc, R^2=H oxidation of (**1**) gave the diketo compounds (**2**); for R^1=R^2=CH_2OAc the ketoether (Z=H_2) and ketolactone (Z=O) were formed, while with R^1=R^2=$CH_2OSiMe_2{}^tBu$ only the ketoether (**3**, Z=H_2) resulted (Fig. 4.5) [72].

Oxidation of 2,3-epoxynorbornane to diol, ketohydroxy, and diketone derivatives was studied with $RuCl_3$/aq. oxidant/CCl_4-CH_3CN (co-oxidant=$(IO_4)^-$, H_2O_2, Oxone®, $(ClO)^-$, $(S_2O_8)^{2-}$; $(BrO_2)^-$ was ineffectual) [73]. The system $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN oxidised substituted epoxides containing bicyclic [2.2.1] heptane skeletons, e.g. *exo*-2,3-epoxynorbornanes to the corresponding diketo compounds [74]. Stoicheiometric RuO_4/CCl_4 converted 20,21-dihydroxy-11β,



(1) (2) (3)

Fig. 4.5 Oxidation by RuO_4 of epoxynorbornanes to diketones or ketolactones [72]

18-epoxy-5α-pregnan-3-one to 3-oxo-11β-,20,21-trihydroxy-5α-pregnan-18-oic acid, an intermediate product in the total synthesis of the hormone *d*-aldosterone [75], [76]**.** Oxidation of a substituted pyrrolidine to a pyroglutamate; part of the total synthesis of the antibiotic biphenomycin B, was carried out with RuO_2/aq. $Na(IO_4)$/EtOAc [77].

Cycloalkanes $R^1R^2R^3H$ and chelating arenes ArH were oxidatively cross-coupled to Ar $R^1R^2R^3$ by $[RuCl_2(p\text{-cymene})]_2$/TBHP/135°C (the reactants were the solvent): thus 2-phenylpyridine and cyclo-octane were cross-coupled; *cf.* mech. Ch. 1. Other complexes $(Ru(acac)_3$, $[RuCl_2(COD)]_2$ and $RuH_2(CO)(PPh_3)_3)$ also catalysed the reaction [78].

4.1.5 Large-Scale Oxidations of Alkanes

These include 14,16-dihydroxyhecogenin acetate from C12,14-dihydroxyhecogenin acetate (100 g) ($RuCl_3$/aq. $Na(BrO_3)$/EtOAc-CH_3CN) [68]; 1,4-bis(2-phenylethyl) piperazine (2.5 g) to the 2,3-piperazine dione (RuO_2/aq. $Na(IO_4)$/EtOAc) [79] and *endo*-tetrahydrodicyclopentadiene (15 g) to 4-hydroxy-*endo*-tetrahydrodicyclop entadiene (RuO_2/aq. $Na(IO_4)$/CCl_4-CH_3CN); *cf.* mech. Ch. 1 [47].

4.1.6 Alkane Oxidations Not Covered Here but Included in Chapter 1

These include: $[Ru(H_2O)(bpy)(cpsd)]^+$ or $Ru(H_2O)(pic)(bpy)(cppc)$/TBHP/-$(PhCH_2\{N(CH_2)_3Me\}_3)Cl/CH_2Cl_2$ (cyclohexane and toluene) [51]; $[Ru(H_2O)(bpy)(app)]^{2+}$/TBHP/PhN(*t*Bu)Cl/$CH_2Cl_2$ (cyclohexane, toluene, *cf.* mech. Ch. 1) [80]; $RuCl_3(CH_3CN)_3$/aq. $Li(ClO_4)$/Pt electrodes (tetralin) [81]; $Ru_2(OAc)_2(py)_4$/Zn/O_2/(py)/AcOH (cyclohexane) [53]; $[RuCl_2(bpy)_2]^+$ or $[Ru(bpy)_2(acac)]^+$/TBHP/CH_2Cl_2 (ethylbenzene, fluorene) [82]; $[Ru(C_7F_{15}COCH_2COC_7F_{15})_3]^-$/perfluorodecalin-toluene/O_2/65°C (aldehydes) [83]; Ru(CO)(TPFPP)/(Cl_2pyNO)/CH_2Cl_2/65°C (adamantane, cyclohexane, *cis*-and *trans*-decalin, *cf.* mech. Ch. 1)

[84]; stoich. *cis*-[$Ru(O)_2$(tet-Me_6)]$^{2+}$/CH_3CN (toluene, ethylbenzene, cumene, adamantane, 2,3-dimethylbutane, *cf.* mech. Ch. 1) [85], [86]. $RuCl_3$/aq. $Na(IO_4)$/CCl_4-CH_3CN (*cis* and *trans*-pinane fragmentation, *cf.* mech. Ch. 1) [87]; *cis*-[$Ru(H_2O)_2(dmp)_2$]$^{2+}$/aq. H_2O_2/ CH_3CN/75°C (adamantane, cyclohexane, *cf.* mech. Ch. 1) [88]; *cis*-[$Ru(O)_2(CF_3COO)$(tmtacn)]$^+$/PhIO or TBHP/water-CH_2Cl_2 (cyclohexane) [89]; RuCl(bpy)(DPA) and RuCl(phen)(DPA)/PhIO or TBHP/aq. dioxane (cyclohexane) [90]; $RuCl_3$/EDTA/O_2/aq. ascorbate (cyclohexane, *cf.* mech. Ch. 1) [91]; [$Ru(H_2O)$(EDTA)]$^-$/O_2/water (cyclohexane, toluene, *n*-hexane, *cf.* mech. Ch. 1) [92]; stoich. [$Ru(O)(N_4O)$]$^{2+}$/THF-CH_3CN (cumene, ethylbenzene etc., *cf.* mech. Ch. 1) [93], [94]; stoich. [Ru(O)(EDTA)]$^-$ and [Ru(O)(PDTA)]$^-$/ water-dioxane, *cf.* mech. Ch. 1 [95]; stoich. *trans*-[$Ru(O)_2$(dmbpy)$_2$]$^{2+}$/CH_3CN (2,3-dimethylbutane, adamantane, cyclohexane, *cf.* mech. Ch. 1) [96]; Ru(CO)(TFPPCl_8)/O_2/CH_3CHO/EtOAc oxidised alkanes (cyclohexane, *n*-hexane, cyclohexane and ethylbenzene) to alcohols and ketones [97]; stoich. *trans*-$Ru(O)_2$(R-TPP)/CH_2Cl_2 (cyclic alkanes, *cf.* mech. Ch. 1) [98]; *cis*-[Ru(dmphen)$_2$$(S)_2$]$^{2+}$/ aq. H_2O_2/75°C with S=CH_3CN or H_2O (methane, ethane) [99]; stoich. [Ru(O)(EDTA)]$^-$/ water-dioxane (cyclohexane, toluene *cf.* mech. Ch. 1) [100]; [Ru_3(μ-O)(pfb))$_6$$(Et_2O)_3$]$^+$/$O_2$ (1.3 atm.)/CH_3CN/65°C (cyclohexane, methylcyclohexane) [101]; [$Ru(H_2O)$(EDTA)]$^-$/aq. H_2O_2/dioxane (cyclohexane, *cf.* mech. Ch. 1) [102]**;** R_5[Ru{$SiW_{11}(H_2O)O_{39}$}]/aq. Oxone®/60°C (adamantane, cyclohexane) [103]; [$Ru(H_2O)$(EDTA)]$^-$/O_2/aq. cetyltrimethylammonium bromide/dioxane (cyclohexane, *cf.* mech. Ch. 1) [104]; stoich. [Ru(O)(py)(bpy)$_2$]$^{2+}$/CH_3CN (cyclohexene to 2-cyclohexenol, *cf.* mech. Ch. 1) [105]; stoich. *trans*-Ru(O)14-TMC)]/CH_3CN/50°C (cyclohexane, toluene; Fig. 1.29) [106]; [$Ru(H_2O)$(bpy)(tpy)]$^{2+}$/water @ pH 6.8/Pt electrodes (C-H bonds adjacent to aromatic groups) [107]; $RuCl_3$/aq. $Na(IO_4)$/CCl_4-CH_3CN (several alkanes) [108]; stoich. *trans*-[Ru(O)(bpy)(tpy)]$^{2+}$/CH_3CN (toluene, cumene, *cf.* mech. Ch. 1) [109]; $RuCl_3$/MnO_4^-/aq. NaOH (D-panthenol) [110].

For oxidation of Si-H bonds in organosilanes *cf.* 5.6.1.

4.2 Oxidation of C–C Bonds in Alkanes

There are fewer examples of this for such Ru-catalysed oxidations than for C-H activation, cleavage of the C-C bond in diols being the main example [111]. Optically pure D- and L-glyceric acids were made by cleavage of vicinal diols or of α-hydroxy acids by $RuCl_3$/aq. Na(ClO) @ pH 8, e.g. 1,2:5,6-di-*O*-isopropylidene-D-mannitol to 2,3-*O*-isopropylidene-D-glyceric acid (Fig. 4.6) [112].

Other examples include the oxidation of PhCMeCH(OH)CH_2OH to PhCMeCOOH and of 1,2-dihydroxycyclohexane to adipic acid by $RuCl_3$/aq. $Na(IO_4)$/CH_3CN-CCl_4 [113], and by $RuCl_3$/aq. Na(ClO/0°C [114].

For an example of C-C bond cleavage with β-hydroxyethers to keto-lactones *cf.* 5.3.3, Fig. 5.13) [115].

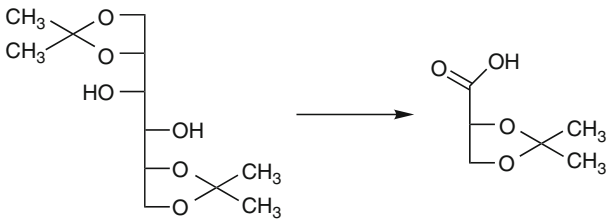


Fig. 4.6 Cleavage of the central C–C bond in a mannitol [112]

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Chapter 5
Oxidations of Amines, Amides, Ethers, Sulfides, Phosphines, Arsines, Stibines and Miscellaneous Substrates

Abstract This chapter principally concerns oxidations of organic substrates containing N, O, S, P, As and Sb. Oxidations of amines are covered first, including primary amines to nitriles or amides; secondary amines to imines or other products; tertiary amines to N-oxides or other products (Section 5.1) and the oxidation of amides (5.2). Oxidation of ethers to esters or lactones follows (5.3), then of sulfides to sulfoxides or sulfones (5.4) and of phosphines, arsine and stibines to their oxides (5.5). A final section (5.6) concerns such miscellaneous oxidations not covered by other sections in the book.

5.1 Oxidation of Amines

The subject of Ru-catalysed amine oxidations has been reviewed [1–7]. The first catalytic oxidation (1978) used $RuCl_3/O_2$/water-toluene/100°C[1] to oxidise primary and secondary amines to nitriles and imines respectively [8].

Some oxidations of primary and secondary amines (and of amides) may be considered as amine or as alkane oxidations (in this latter instance as of CH, CH_2 or CH_3 groups): for convenience they are dealt with here as amine oxidations, but cross-references with Chapter 4 are given where appropriate; *cf.* 4.1.2, 4.1.3 and 5.1.3.1.

5.1.1 Primary Amines RCH_2NH_2 to Nitriles, Amides or Ketones

$$RCH_2NH_2 + 2[O] \rightarrow RCN + 2H_2O \tag{5.1}$$

[1]As indicated in 1.2.2 these abbreviations take the form: Ru starting material/co-oxidant/solvent; temperatures are only indicated if not ambient. For brevity, RuO_2 and $RuCl_3$ denote the *hydrates* $RuO_2.nH_2O$ and $RuCl_3.nH_2O$.

W.P. Griffith, *Ruthenium Oxidation Complexes*, Catalysis by Metal Complexes 34,
DOI 10.1007/978-1-4020-9378-4_5, © Springer Science+Business Media B.V. 2011

Conversion of primary amines to nitriles is sometimes called oxidative dehydrogenation. In 1972 it was shown that $[RuO_4]^{2-}$/aq. M KOH oxidised benzylamine to benzonitrile stoicheiometrically [9] while the catalytic reagent $RuCl_3/O_2$/water-toluene/100°C converted primary amines (benzylamine, *n*-butylamine) to nitriles, and 2-aminoalkanes to imines [8]. Later work showed that $RuCl_3/K_2(S_2O_8)$/aq. M KOH oxidised benzylamine to benzonitrile (Table 5.1, *cf.* mech. Ch. 1) [10–12]; $RuCl_2(PhCH_2NH_2)_2(PPh_3)_2/O_2$/toluene/80°C can also be used [13].

Table 5.1 Oxidation of amines and amides

Reactant	Product	Method [Ref.]
Primary, RNH_2		
Benzylamine	Benzonitrile	A [10], B [15]
Ethylphenylglycine	Benzonitrile	C [16]
o- or *m*-Bromobenzylamine	*o*- or *m*-Bromobenzonitrile	A [10]
n-Butylamine	Butyronitrile	B [15]
o-, *m*-,or *p*-Chlorobenzylamine	*o*-, *m*-,or *p*-Chlorobenzonitrile	A [10]
n-Hexylamine	Hexanenitrile	A [10]
o- or *p*-Methoxylbenzylamine	*o*- or *p*-Methoxybenzonitrile	A [10]
o-, *m*-,or *p*-Methylbenzylamine	*o*-, *m*-,or *p*-Methylbenzonitrile	A [10]
n-Octylamine	Octanenitrile	A [10]
Secondary, R^1R^2NH		
Dibenzylamine	*N*-Benzylidenebenzylamine+Benzylamine	D [21]
Indoline	Indole	E [19]
1,2,3,4-Tetrahydroisoquinoline	3,4-Dihydroisoquinoline+*iso*Quinoline	F [18]
1,2,3,4-Tetrahydroquinoline	3,4-Dihydroquinoline (Fig. 5.1)	E [19]
Tertiary and hetero-aromatics, $R^1R^2R^3N$:		
(*R,S*)-(−)-*N*-Benzyl-3-ethylpiperidine	(*R,S*)-(−)-*N*-Benzyl-3-ethylpiperidine-2, 6-dione	G [36]
(*S*)-(−)-*N*-Benzyl-3-ethylpiperidine	(*S*)-(−)-*N*-Benzyl-3-ethylpiperidine-2, 6-dione	G [37]
(*R*)-(+)-*N*-Benzyl-3-methylpiperidine	(*R*)-(+)-*N*-Benzyl-3-methylpiperidine-2, 6-dione	G [36]
(*S*)-(−)-*N*-Benzyl-3-phenylpiperidine	(*S*)-(−)-*N*-Benzyl-3-phenylpiperidine-2, 6-dione	G [36]
N,N-Dibenzylhydroxylamine	*Z*-*N*-Benzyl-α-phenylnitrone	H [29], J [28]
N,N-Diethylaniline	*N,N*-Diethylaniline-*N*-oxide	K [26]
(*R*)-(−)-1,3-Diethylpiperidine	(*R*)-(+)-1,3-Diethylpiperidine-2,6-dione	G [37]
N-Benzylpiperidine	*N*-Benzylpiperidine-2,6-dione	G [36]
N-Benzylpyrrolidine	*N*-Benzylpyrrolidone-2,5-dione	G [36]
2-Cyanopyridine	2-Cyanopyridine-*N*-oxide	K [26]
3-Cyanopyridine	3-Cyanopyridine-*N*-oxide	K[26]

(continued)

Table 5.1 (continued)

Reactant	Product	Method [Ref.]
4-Cyanopyridine	4-Cyanopyridine-*N*-oxide	K[26]
N,N-Diethylhydroxylamine	*Z*-α-Methyl-*N*-ethylnitrone	H [29]
N-Methylmorpholine	*N*-Methylmorpholine-*N*-oxide	K [26]
1-Hydroxy-2-methylpiperidine	2-Methyl-3,4,5,6-tetrahydropyridine-*N*-oxide	H [29]
1-Hydroxy-2-methylpyrrolidine	2-Methylpyrroline-*N*-oxide	H [29]
N-Hydroxypyrrolidine	Pyrroline-*N*-oxide	H [29], J [28]
2-Picoline	2-Picoline-*N*-oxide	K [26], L [27]
3-Picoline	3-Picoline-*N*-oxide	K [26], L [27]
4-Picoline	4-Picoline-*N*-oxide	K [26], L [27]
Quinoline	Quinoline-*N*-oxide	K [26]
Isoquinoline	*iso*Quinoline-*N*-oxide	L [27]
1-Hydroxypiperidine	3,4,5,6-Tetrahydropyridine-*N*-oxide	H [29]
Triethylamine	Triethylamine -*N*-oxide	K [26], L [27]
Amides		
(R)+)-N-Acetyl-2-phenylpyrrolidine	*(R)+)-N*-Acetyl-5-phenyl-2-pyrrolidinone	G [62]
N-Acetyl-2-methylpiperidine	*N*-Acetyl-5-methyl-2-piperidone	G [62]
N,N'-Diacetylpiperazine	*N,N'*-Diacetyl-2,3-diketopiperazine	G [68]
N,N'-Dibenzylpiperazine	*N,N'*-Dibenzyl-2,3-diketopiperazine	G [68]

A: $RuCl_3/K_2(S_2O_8)$/aq. M KOH [10]; B: *trans*-$Ru(O)_2(TMP)/O_2/C_6H_6$/50°C [15]; C: $RuCl_2(PPh_3)_3$/PhIO/PMS/CH_2Cl_2 [16]; D: $RuCl_3$/PhIO/CH_2Cl_2 [21]; E: TPAP/NMO/PMS/CH_3CN [19]; F: $Ru_2(OAc)_4Cl/O_2$/toluene/50°C [18]; G: RuO_2/aq. $Na(IO_4)/CCl_4$ [36, 37, 62, 68]; H: TPAP/NMO/PMS/CH_3CN [29]; J: TPAP/O_2/TFE or CH_2Cl_2/PMS [28]; K: $RuCl_3/O_2$/DCE [26]; L: $RuCl_3$/aq. bromamine-T/CH_3CN/80°C [27].

Trans-$Ru(O)_2$(TMP) or *trans*-$Ru(O)_2$(TDCPP)/O_2/C_6H_6/50°C/24h oxidised primary and secondary amines (e.g. benzylamine to benzonitrile, dibenzylamine to $PhCH{=}NCH_2Ph$, benzonitrile and benzaldehyde; *cf.* mech. Ch. 1) [14, 15]. The reagent $RuCl_3/O_2$/water-toluene/100°C converted 2-aminohexane to 2-(methyl-(pentyl)imino)hexane and hexan-2-one [8]. Oxidation of amines $R^1CH_2NH_2$ to imines $R^1CH{=}NR^2$ (R^1=Ph, R^2=Ph, CH_2Ph) was effected by $RuCl_2(PPh_3)_3$/PhIO/PMS/CH_2Cl_2, while benzylamine was oxidised to benzaldehyde and benzhydrylamine to diphenylketone [16]. With $RuX_2(R_2\text{-pybox})(C_2H_4)$/PhI$(OAc)_2$/MgO/$CH_2Cl_2$ sulfamate esters gave cyclic imines, thus effecting enantioselective C-H amination [17].

5.1.2 Secondary Amines, R^1R^2NH

Some examples of oxidations of these are listed in Table 5.1.

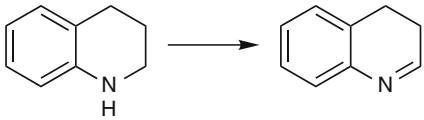


Fig. 5.1 Oxidation of 1,2,3,4-tetrahydroquinoline to 3,4-dihydroquinoline by TPAP/NMO [19]

5.1.2.1 Secondary Amines to Imines

$$R^1R^2CHNHR^3 + [O] \rightarrow R^1R^2C = NR^3 + H_2O \tag{5.2}$$

The system $Ru_2(OAc)_4Cl/O_2$/toluene/50°C oxidised $R^1CH_2NHR^2$ to imines $R^1CH{=}NR^2$, converted 1,2,3,4-tetrahydroisoquinoline to the 3,4-dihydroisoquinoline with isoquinoline, and 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline to 6,7-dimethoxy-3,4-dihydro-iso-quinoline (*cf.* mech. Ch. 1) [18]. Such oxidations were also catalysed by TPAP/NMO/PMS/CH_3CN, e.g. the conversion of indoline to indole (in which indoline undergoes a double-bond shift and aromatisation), and the oxidation of 1,2,3,4-tetrahydroquinoline to 3,4-dihydroquinoline (Fig. 5.1, Table 5.1) [19].

Similar oxidations of $R^1R^2CH_2NHR^3$ were effected with $RuCl_2(PPh_3)_3$/TBHP/C_6H_6 (R^1=Ph and R^2=H with R^3=Ph, CH_2Ph; R^1=Ph and R^2=CN with R^3=Ph; and R^1=PhCH=CH, R^2=H, R^3=Ph, *p*-ClC_6H_4 and *p*-$MeOC_6H_4$). Other catalysts ($RuCl_3$; $RuH_2(PPh_3)_4$ and $Ru_3(CO)_{12}$) were also effective [20]. Dibenzylamine gave *N*-benzylidenebenzylamine $PhCH{=}NCH_2Ph$ with some benzylamine using $RuCl_2(PPh_3)_3$ or $RuCl_2(dmso)_4/O_2$/toluene/80°C, but the same reaction occured at room temperature with $RuCl_3$/PhIO/CH_2Cl_2 [21]. Oxidation of $R^1CH_2NHR^2$ to $R^1CH{=}NR^2$ (R^1=Ph, R^2=Ph, CH_2Ph) was effected by $RuCl_2(PPh_3)_3$/PhIO/PMS/CH_2Cl_2 [16]. The biomimetic coupled system $[Ph_4(\eta^5\text{-}C_4CO)Ru(CO_3)_2]$/cobalt-salen type complex/O_2/toluene/110°C converted secondary amines to aldimines and ketimines; products formed include *N*-(2,4,6-trimethylphenyl)-(1-phenylethylidene)amine, *N*-(2-methylphenyl)-(1-phenylethylidene)-amine, *N*-(4-methoxy-phenyl)-(1-phenylethylidene)amine and *N*-(4-methoxy-phenyl)-(4-cyanophenyl)-ethylidene)amine [22].

Cyclic secondary amines with pyrrolo[2,1-*c*][1, 4]-benzodiazepine rings were oxidised with TPAP/NMO/PMS/CH_3CN to the corresponding imines. Thus (11aS)-1,2,3,10,11,11a-hexahydro-5H-pyrrolo[2,1-*c*][1, 4]-benzodiazepine-5-one gave (11aS)-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-*c*][1, 4]benzo-diazepine-5-one [23].

5.1.2.2 L-α,ω-Diamino Acids to L-ω-Carbamoyl-α-Diamino Acids

$$R^1NHCH_2(CH_2)_nR^1NHCHCOOR^2 + 2[O] \rightarrow R^1NHCO(CH_2)_nR^1NHCHCOOR^2 + H_2O \tag{5.3}$$

These reactions were effected by RuO_2/aq. $Na(IO_4)$/EtOAc when the reactants bore urethane-type protecting groups (n = 1, R^1=Boc, R^2=Me, NBzI; n = 2,

R^1=Boc, R^2=Me, ^{t}Bu, NBzI; R^1=Troc, R^2=Me, NBzI; n = 3, R^1=Boc, R^2=Me, ^{t}Bu, NBzI; R^1=Boc, R^2=Me, ^{t}Bu, NBzI; R^1=Troc, R^2=Me, ^{t}Bu, NBzI; Boc=*tert*-butoxycarbonyl, Troc=trichloroethoxycarbonyl, NBzI=p-$NO_2C_6H_4$). Thus L-ornithine was converted to L-glutamine and L-lysine to L-2-aminoadipic acid 6-amide [24, 25].

5.1.3 Tertiary Amines $R^1R^2R^3N$

$$R^1R^2R^3N + [O] \rightarrow R^1R^2R^3NO \tag{5.4}$$

Included here and in Table 5.1 are oxidations of hetero-aromatic systems such as pyridines and picolines (5.1.3.3, Table 5.1).

5.1.3.1 Tertiary Amines to Amine Oxides and Hydroxylamines to Nitrones

Oxidation of R_3N to R_3NO was catalysed by $RuCl_3/O_2$/DCE; $RuCl_2(PPh_3)_3$, $RuCl_2(PPh_3)_4$ and $RuH_2(CO)(PPh_3)_3$ also catalysed the reactions [26]. Reaction of a variety of tertiary amines with $RuCl_3$/bromamine-T/water @ pH 8.4/CH_3CN/80°C gave the *N*-oxides in good yields; triethylamine, 4-picoline and *N,N*-dimethylphenylamine reacted in this way (Table 5.1) [27].

The system TPAP/O_2/TFE or CH_2Cl_2/PMS (TFE=trifluoroethanol) oxidised *N,N*-disubstituted hydroxylamines $R^1CH_2N(OH)R^2$ to the corresponding nitrones $R^1CH{=}N^+(R^2)O^-$; thus *N,N*-dibenzylhydroxylamine gave the nitrone (Table 5.1) [28]; TPAP/NMO/PMS/CH_3CN also effected such reactions (Table 5.1) [29, 30]. In a competitive reaction with a primary alcohol (1-undecanol), hydroxylamine was preferentially oxidised to the corresponding nitrone, giving a >50:1 reaction rate of amine to alcohol [29]. With $RuCl_2(PPh_3)_4$/TBHP/CH_2Cl_2, ^{t}BuOCONHOH was oxidised to the corresponding nitroso dienophile ^{t}BuOCON=O which was then trapped by cyclohexa-1,3-diene to give the hetero Diels-Alder adduct (*cf.* mech. Ch. 1) [31]. Thus *tert*-butyl-*N*-hydroxycarbamate and cyclohexa-1,3-diene gave by this procedure *tert*-butyl-2-oxa-3-bicyclo[2, 2, 2]oct-5-ene-3-carboxylate, a potentially useful chiral synthon for the preparation of piperidine alkaloids and aza-sugars, and several similar reactions were carried out. Either $RuCl_3$ or $RuO_2/PPh_3O/CH_2Cl_2$ can also be used to catalyse the reaction (*cf.* mech. Ch. 1) [32]. Oxidation of *N*-Boc-piperidines by RuO_2/aq. $Na(IO_4)$/EtOAc formed a step in the synthesis of the nutritional supplement L-carnitine (*cf.* 1.2.7.6).

Oxidation of dihydroxyimidazolidine derivatives to nitronyl nitroxide radicals (Fig. 5.2) was accomplished by TPAP/NMO/PMS/CH_2Cl_2 (R=p-$MeOCC_6H_4$, 3,4-$(MeO)_2C_6H_3$, $O_2NC_6H_4$, p-H_2O_3P, p-$C_2H_5C_6H_4$–, p-$MeSCH_2C_6H_4$–, $Me(CH_2(CH_2)_{13})$ [30].

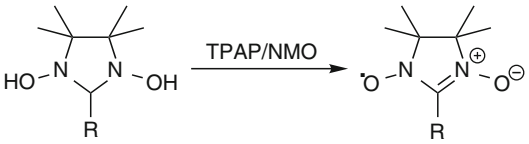


Fig. 5.2 Oxidation by TPAP of dihydroxyimidazolidines to nitronyl nitroxide radicals [30]

5.1.3.2 The α-Methoxylation and Tert-Butoxylation of Tertiary Amines

Oxidation of $R^1R^2NCH_3$ to α-methoxymethylamines $R^1R^2NCH_2OCH_3$ was effected by $RuCl_3$/aq. H_2O_2/CH_3OH; $RuCl_2(PPh_3)_3$ is a slightly less effective catalyst. Thus, MePhNMe gave $MePhNCH_2OCH_3$; (CH_3CH_2)PhNMe yielded $(CH_3CH_2)PhNCH_2OCH_3$, and similarly reactions were carried out with R^1=Me, R^2=*p*-MeC_6H_4–, *p*-$MeOC_6H_4$– or *m*-ClC_6H_4 (*cf.* mech. Ch. 1) [33]. Oxidation of tertiary N-methylamines $R^1R^2NCH_3$ by $RuCl_2(PPh_3)_3$/TBHP/C_6H_6 yielded the corresponding α-(*tert*-butyldioxy)alkylamines $R^1R^2NCH_2OO^tBu$, providing also a strategy for the generation of iminium ion intermediates *cf.* mech. Ch. 1) [34, 35]. Similar reactions were performed with R^1=Me, R^2=*p*-$CH_3C_6H_4$ or *p*-BrC_6H_4; for R^1=Ph, R^2=$(CH_2)_2CH{=}CH_2$; R^1=*p*-ClC_6H_4, R^2=$(CH_2)_2COOCH_3$ [35].

5.1.3.3 Hetero-Aromatic Substrates and Heterocyclic Substrates

A number of oxidations of pyridines and picolines have been effected, e.g. by $RuCl_3$ or $K_2[Ru(H_2O)Cl_5]/O_2$/DCE [26]. Optically active *N*-ethyl and *N*-benzylpiperidines oxidised by RuO_2/aq. $Na(IO_4)/CCl_4$ gave the 2,6-diones (Table 5.1); selective oxidation of endocyclic methylene groups adjacent to the nitrogen atom was explained in terms of different conformational freedom of *endo* and *exo* –CH_2– groups [36, 37]. *N*-protected secondary amines were oxidised by electrogenerated RuO_4 from RuO_2/aq. NaCl-acetone/Pt electrodes. A number of piperidines and proline esters were prepared in this way: thus *N*-ethoxycarbonyl-2-methylpiperidine gave *N*-ethoxycarbonyl-6-methyl-2-piperidone, and *N*-ethoxycarbonyl-2-methoxypiperidine gave the piperidone [38].

5.1.3.4 Other Oxidations of Tertiary Amines

Cyanation of tertiary amines $RNMe_2$ to the corresponding α-aminonitriles RNCH(CN)Me was catalysed by $RuCl_3$/Na(CN)/CH_3OH–AcOH/60°C (R=Ph, *m*-MeC_6H_4, *p*-MeC_6H_4, *p*-BrC_6H_4 or *p*-$PhOC_6H_4$). Thus *N,N*-dimethylaniline gave *N*-methyl-*N*-phenylaminoacetonitrile in 93% yield after 2 h (Fig. 5.3; *cf.* mech. Ch. 1) [39].

Several oxidations of amines involved oxidation of methyl groups adjacent to tertiary amines to carbonyl groups. Oxidation by RuO_2/aq. $Na(IO_4)/CCl_4$ of 2′,3′,5′-tri-O-acetyl- or -benzoyl derivatives of N^6,N^6-dimethyladenosine, N^6,N^6-

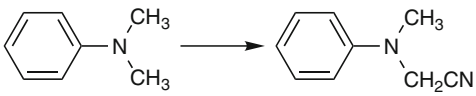


Fig. 5.3 Oxidative cyanation of *N,N*-dimethylaniline with $RuCl_3$ [39]

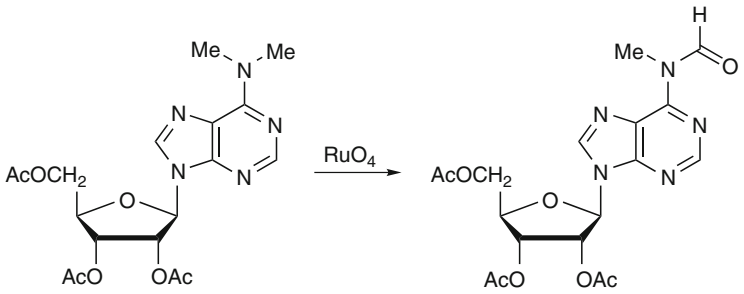


Fig. 5.4 Oxidation by RuO_4 of adenosine derivatives [40]

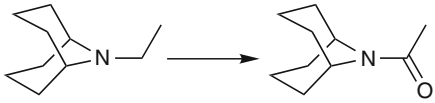


Fig. 5.5 Oxidation of a tertiary polycyclic amine by RuO_4 [41]

diethyladenosine, N^6,N^6-dibenzyladenosine, 6-(*N*-pyrrolidino)-nebularine and 6-(N-piperidino)-nebularine gave the corresponding monoamido derivatives Thus N^6, N^6-dimethyl-2′,3′, 4′-tri-O-acetyladenosine yielded the N^6-formyl- N^6-methyl derivative (Fig. 5.4) [40].

Methylene groups adjacent to the N atom in tertiary polycyclic amines were oxidised by RuO_2/aq. $Na(IO_4)$/CCl_4, depending on reaction conditions. Thus *N*-benzyl-9-azabicyclo-[1, 3, 3]-nonane yielded *N*-benzoyl-9-azabicyclo-[1, 3, 3]-nonane (Fig. 5.5); and *N*-benzyl-1,3-dioxo-iso-quinoline gave the *N*-benzoyl compound, while *N*-benzyl-5,6-dihydro-11H-dibenz[b,e]azepine, which has *exi* and *endo*cyclic benzyl groups, were oxidised to the *N*-benzyl-6-oxo derivative [41].

For oxidation of alkynylamines $R^1CCNR^2R^3$ to α-keto amides $R^1(CO)CO)NR^2R^3$ by $RuCl_2(PPh_3)_3$/PhIO/CH_2Cl_2 *cf.* 3.4.1.2. A number of oxidations of $–CH_2–$ groups adjacent to the N centre in tertiary amines are covered in Chapter 4, e.g. 4.1.2.

5.1.4 Large-Scale Oxidation of Amines

Ethyl 1-cyclohexanecarbonyl-2-azetidinecarboxylate (2.7 g) was oxidised to ethyl 1-cyclohexane-carbonyl-4-oxo-2-azetidinecarboxylate (RuO_2/aq. $Na(IO_4)$/CCl_4) [42].

5.1.5 *Amine Oxidations Not Covered Here but Included in Chapter 1*

These include: $RuCl_3$/N-bromophthalimide/$Hg(OAc)_2$/aq. AcOH (β-alanine), *cf.* mech. Ch. 1 [43]; $RuCl_3$/$[Ag^{III}\{IO(OH)_5\}_2]^{5-}$/water (gabapentin, *cf.* mech. Ch. 1) [44]; $RuCl_3$/bromamine-T/aq. HCl (isatins to anthranilic acids; *cf.* mech. Ch. 1) [45]; $RuCl_3$/chloramine-T/aq. $HClO_4$ (sulfanilic acid) [46]; $[Ru(acac)_2(bpy)]^+$ or $RuCl_2$(bac)(bpy)/TBHP/C_6H_6 (primary amines) [47]; stoich. $[Ru(O)(EDTA)]^-$/water (diethylamine, triethylamine, *cf.* mech. Ch. 1) [48]; $[Ru(H_2O)(EDTA)]^-/O_2$/water/25–45°C (diethylamine, triethylamine, *cf.* mech. Ch. 1) [49]; $RuCl_3$/aq. H_2O_2/(DDAB)/DCE/90°C (aniline) [50]; $[Ru(H_2O)(PPh_3)(bpy)_2]^{2+}/O_2$/α,α,α-trifluorotoluene (*N, N*-dimethylaniline to *N*-methylaniline, *cf.* mech. Ch. 1) [51].

5.2 Oxidation of Amides

The first oxidation by a Ru complex of an amide was carried out by Berkowitz and Rylander in 1958, using stoich. RuO_4/CCl_4 to convert γ-butyrolactam to succinimide [52].

For oxidation of primary amines to alkylamides, *tert*-butoxycarbonyl (Boc) protecting groups were used to give the amide RCH_2NH-Boc, which was then oxidised by RuO_2/aq. $Na(IO_4)$/EtOAc to the corresponding *N*-Boc amides RCONH-Boc. The Boc was then removed hydrolytically giving $RCONH_2$ (R=Me, Et, Pr, Ph, $PhCH_2$, $C_{17}H_{35}$, $NH_2CH_2CH_2$, $ClCH_2$, $ClCH_2CH_2$, 4-Me-C_6H_4, 4-MeO_6H_4, 4-$MeOOH_4$, 4-NO_2-C_6H_4, 4-ClC_6H_4, 4-BrC_6H_4) [53]. Ynamides where R^1 is an electron-withdrawing group to α-keto-imides by RuO_2/aq. $Na(IO_4)/CH_2Cl_2$-CH_3CN (R^1=tosyl, R^2=Bn, R^3=Ph; R^1R^2=2-pyridone, R^3=Ph) [54]. Synthesis of secondary amides via oxidative coupling of primary alcohols $R^1CH_2(OH)$ and primary amines $R^2(CH_2)NH_2$ to the amides $R^1C(O)NHCH_2R^2$ was accomplished with $[RuCl_2(p\text{-cymene})]_2$/(dppb)/$Cs_2(CO_3)$/3-methyl-2-butanone/^{t}BuOH/120°C/24h (dppb=bis-(diphenylphosphino)butane) (R^1=$Ph(CH_2)_2$, $Ph(CH_2)_3$, $Ph(CH_2)_7$, *p*-MeO-$C_6H_4CH_2$, $MeOCH_2$, Ph_2CH, R^2=Ph, $PhCH_2$, *p*-$MeOC_6H_4$, *p*-$ClOC_6H_4$). The bidentate (4*S*,5*S*-(+)-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane was more effective than (dppb), but the latter is cheaper; *cf.* mech.Ch. 1 [55].

5.2.1 *Cyclic α-Amino Acid Esters*

The reagent RuO_2/aq. $Na(IO_4)/CCl_4$ or EtOAc-CH_3CN oxidised *N*-acylated cyclic α-amino acid esters to the corresponding lactams (Fig. 5.6) with no appreciable racemisation (for n = 1 and 2, R^1=OMe, R^2=Et; R^1=OEt, R^2=Me; R^1=OC_6H_{11},

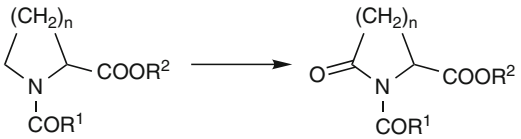


Fig. 5.6 Oxidation of cyclic α-amino acid esters with RuO_4 [42]

R^2=Et; for n = 2, R^1=OEt, R^2=Me; for n = 3, R^1=OMe, R^2=Et; R^1=OEt, R^2= Et; R^1=OC_6H_{11}, R^2=Et; R^1=OEt, R^2=Et); oxidation of *N*-acylated (±)-2-azetidincarboxylic acid esters was very sluggish [42].

Oxidation of L-proline esters to L-pyroglutamic acids was accomplished with RuO_2/aq. $Na(IO_4)$/EtOAc with *N*-protection, using *tert*-butoxycarbonyl (Boc), trichloroethoxycarbonyl (Troc), benzyloxycarbonyl and *p*-nitrobenzyloxycarbonyl, Boc being the most effective. Thus methyl L-1-benzyloxycarbonylprolinate gave methyl L-1-benzyloxycarbonylpyroglutamate and methyl L-1-trichloroethoxycarbonylprolinate gave the pyroglutamate [56, 57]. The reaction constituted part of the first chemical conversion of L-proline to L-glutamic acid [57].

5.2.2 *N-Alkyllactams; β-Lactams to Acyloxy-β-Lactams*

Oxidation of *N*-alkyllactams by RuO_2/aq. $Na(IO_4)$/EtOAc was regioselective, depending on the size of the lactam ring (Fig. 5.7) [58]. Four- and eight-membered *N*-methyl and *N*-ethyllactams were oxidised at the exocyclic α-carbon atom adjacent to the N atom yielding *N*-acyllactams and *NH*-lactams, while five- and six-membered lactams gave the cyclic imides having undergone endocyclic oxidation. Seven-membered rings gave mixtures of products arising from exo- and endocyclic oxidations. Thus, for R=H and n = 1 (1) was formed, n = 2 or 3 gave (3); n = 4 yielded a mixture of (1), (2) and (3); for n = 5, both (1) and (2) were produced. With R=Me and n = 1 (2) was formed; n = 2 or 3 (3) was formed; n = 4 yielded a mixture of (2) and (3); n = 5 (1) and (2) [58].

Acetyloxylation of β-lactams by $RuCl_3/O_2/CH_3OH–CH_3CHO–EtOAc/40°C$ gave the corresponding 4-acyloxy-β-lactams (Fig. 5.8). Thus (1′*R*,3*S*)-3-[1′-[*tert*-butyl-di-methylsilyl)-oxy]ethyl]-azetidin-one gave (1′*R*,3*R*,4*R*)-4-acetoxy-3-[1′-[*tert*-butyl-dimethylsilyl)oxy]ethyl]-azetidin-2-one, a key intermediate for synthesis of carbapenem antibiotics, and similar oxidations were effected with susbtrates containing 4-methoxyacetoxy, 4-phenylacetoxy, 4-cyanoacetoxy and 4-dichloroacetoxy groups replacing 4-acetoxy, *cf.* mech. Ch. 1. Other such oxidations were effected with R^1=R^2=R^3=H, R=Ac or CHO; R^1=R^2=H, R^3=CH_3, R=Ac [59, 60].

5.2.3 *Substituted Pyrrolidines*

Proline methyl esters with *N*-Boc-4-acetoxy or 4-O-TBDMS groups were converted by $RuCl_3$/aq. $Na(IO_4)$/EtOAc or $CCl_4–CH_3CN$ to the corresponding pyrrolidin-5-ones

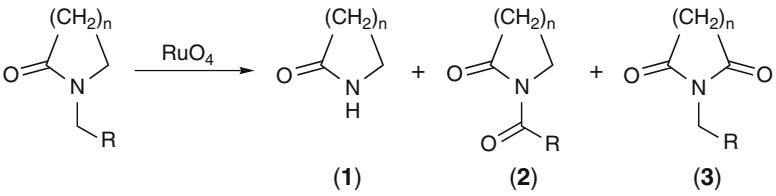


Fig. 5.7 Oxidations of *N*-alkyl lactams by RuO_4 [58]

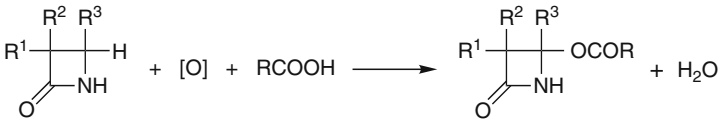


Fig. 5.8 Acetoxylation of β-lactams by O_2 + RCOOH catalysed by $RuCl_3$ [59]

(TBDMS=*tert*-butyl-dimethylsilyl); X=OAc, OTBDMS; Fig. 5.9); other *N*-(Boc-aminoethyl)-4-(*R/S*) substituted proline esters were similarly oxidised (X=H, OCOMe, OSO_2Me) [61].

Regiospecific oxidations of two substituted -*N*-acetyl pyrrolidines and -piperidines to the corresponding diones or ketones were similarly effected (Table 5.1) [36, 62]. Methylene groups adjacent to tertiary amines in N,C-protected short glycine-containing peptides were selectively oxidised at the C^{α} position of glycine by $RuCl_3/CH_3CO_3H$/AcOH-EtOAc. Thus, AcGlyAlaOEt gave Ac-NHCOCO-Ala-OEt, and AcGlyGlyOEt the corresponding α-ketoamide (cf. mech. Ch. 1) [63]. Oxidation of a pyrrolidone to a γ-lactam, viz. of (2S,4R)-2-azidomethyl-1-(tert-butoxycarbonyl)-3-(tertbutyldimethylsilyoxy)-pyrrolidine to the corresponding pyrrolid-2-one, was effected with RuO_2/aq. $Na(IO_4)$/EtOAc (Fig. 5.10) [64].

Oxidation of the anorexigen drug *trans*-phendimetrazine by $RuCl_3$/aq. $Na(IO_4)$/CCl_4 gave 4-formyl-3-methyl-2-phenyl-morpholine together with some *trans*-4,5-dimethyl-6-phenyl-3-morpholinone [65]. In the conversion of N-acylalkyamines to the corresponding imides by RuO_2/aq. $Na(IO_4)$/EtOAc the alkyl group adjacent to the amine group was oxidised, while *N*-acylpropylamines $CH_3CH_2CH_2NH(COR)$ gave the corresponding imides $CH_3CH_2CONH(COR)$ (R=Me, $Me(CH_2)_2$, $Me(CH_2)_{10}$, Me_2CH, Me_3C, Cl_3C, Ph, C_6H_{11}). Oxidations of $RCH_2NHCO(CH_2)_2Me$ to $RCONHCO(CH_2)_2Me$ were effected for R=Me_2CH, $ClCH_2$, and of $PhCH_2NHCOMe$ to PhCONHCOMe, but did not work for the electron-withdrawing groups R=$EtOOCCH_2$, NC and EtOOC [66]. The system $RuO_2/Na(IO_4)$/aq. H_2SO_4/EtOAc-CH_3CN converted 1,4-bis(2-phenylethyl)piperazine to the dicarbonyl 1,4-bis(2-phenylethyl)-2,3-piperazine dione [67], while diacetyl and dibenzylpiperazines with RuO_2/aq. $Na(IO_4)/CCl_4$ gave diketo compounds (Table 5.1) [68].

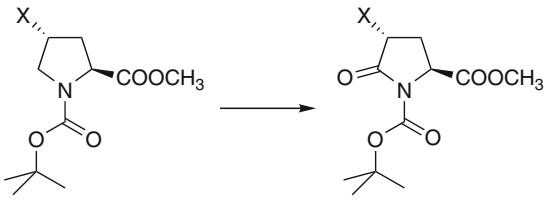


Fig. 5.9 Oxidation by RuO_4 of *N*-alkylpyrrolidines to pyrrolidin-5-ones (X=OAc or OTBDMS) [61]

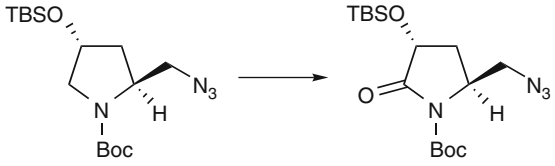
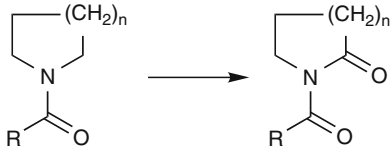


Fig. 5.10 Oxidation of a pyrrolidone to a γ-lactam [64]

Fig. 5.11 Oxidation of *N*-acylamines to *N*-lactams by RuO_4 [73]



5.2.4 Miscellaneous Amides

The α-substitution of N-methoxycarbonylamines $R^1R^2C(H)NR^3(COOMe)$ to the butyl-dioxygenated products $R^1R^2(^t BuOO)CNR^3(COOMe)$ was catalysed by $RuCl_2(PPh_3)_3$/TBHP/C_6H_6: e.g. 2-methoxycarbonyl-1,2,3,4-tetrahydro-isoquinoline gave 1-(^{t}butyldioxy)-2-methoxy-carbonyl-1,2,3,4-tetrahydro-isoquinoline [69]. Oxidation of 3,4-dihydroisoquinolin-1(*2H*)-ones by RuO_2/aq. $Na(IO_4)$/EtOAc gave the corresponding isoquinolin-1,3,4(*2H*)-triones [70]. With RuO_2/aq. $Na(IO_4)$/$CHCl_3$ acylated amines gave lactams and/or imides: 1,2-di-tertbutylaziridine gave *N*-tert-butryl-2,2-dimethylpropionamide [71]. The dehydrogenative coupling of primary alcohols to indoylamides was effected by TPAP/NMO/PMS/CH_3CN, e.g. of 3-phenyl-1-propanol with pratosine and hippadine [72]. Oxidations of 1-formyl, 1-acetyl and 1-benzoyl-perhydro-azepines and -azocines to the corresponding N-acyllactams were effected by RuO_2/aq. $Na(IO_4)$/CCl_4 (Fig. 5.11, Table 5.1) where n = 3, 4, R=C_6H_5 or C_6H_5CO [73].

A step in the synthesis of the antiviral drug (-)-oseltamivir (Tamiflu) was the conversion of an amide to an imide with RuO_2/aq. $Na(IO_4)/CH_2Cl_2$ [74].

5.3 Oxidation of Ethers, R^1R^2O

The reagent most commonly used for oxidation of ethers is RuO_4. The subject is well summarized in an early review by Gore [75]. Primary methyl ethers RCH_2OCH_3 are oxidised to esters $RCOOCH_3$, and secondary methyl ethers $R^1R^2C(H)OCH_3$ to ketones R^1COR^2, while with benzyl ethers $PhCH_2OR$ the esters PhCOOR are formed. For cyclic ethers, the carbon atoms adjacent to the O atom are oxidised, and if there are two secondary carbon atoms the main products are lactones, sometimes with partial hydrolysis to carboxylic acids [75]. There is a short review on oxidation of ethers by RuO_4, principally on the mechanisms involved [76].

5.3.1 Ethers to Esters

$$R^1CH_2OR^2 + [O] \rightarrow R^1COOR^2 + H_2O \tag{5.5}$$

The first oxidation of an ether by RuO_4, was reported in 1958 when it was shown that *n*-butylether with stoich. RuO_4/CCl_4/10°C gave *n*-butyl-*n*-butyrate [52]. A later general study using stoich. RuO_4/CCl_4 or catalytic RuO_2/aq. $Na(IO_4)/CCl_4$ showed that ethers were efficiently oxidised to esters or lactones by both procedures [77]. Oxidation by RuO_2/aq. $Na(IO_4)/CCl_4$–CH_3CN of benzyl ethers of primary, secondary and tertiary alcohols to the corresponding esters was effected [78]. Use of TPAP, *cis*-$RuCl_2(dmso)_4$, *trans*-$RuCl_2(dppp)$ or RuO_2/Na(ClO) or aq. Li(ClO) @ pH 9.5/CH_2Cl_2 gave esters or lactones (Table 5.2) [79, 80]. Sharpless et al. showed that addition of a little CH_3CN to the solvent for $RuCl_3$/aq. $Na(IO_4)/CCl_4$ substantially improved yields in ether oxidations [81].

The systems *trans*-$RuCl_2(dppp)_2$ or $[RuCl(dppp)_2]^+$/aq. $Li(ClO)/CH_2Cl_2$ oxidised a range of primary ethers to esters (Table 5.2), while *iso*propyl ether gave acetone and secondary ethers bearing β-CH_2 groups produced β-keto esters (*cf.* mech. Ch. 1) [82]. Benzyl-alkyl, dialkyl, cyclic and acyclic ethers were converted to esters or lactones by $RuCl_3$/aq. Na(ClO) or $Ca(ClO)_2/CH_2Cl_2$. Amongst such oxidations of R^1R^2O were $^nBu_2O$ to $^nBuOCO^nPr$ and ^nPrCOOH, $PhCH_2O^nBu$ to $PhCOO^nBu$, $PhCH_2OPh$ to PhCOOH, *p*-$MeOC_6H_4CH_2OMe$ to $MeOC_6H_4COOMe$ and $MeOC_6H_4COOH$, PhCHMeOMe to PhCOMe, PhCOOH and AcOH (*cf.* mech. Ch. 1) [83].

Table 5.2 Oxidation of ethers to esters or lactones and sulfides to sulfoxides or sulfones

Reactant	Product	Method [Ref.]
Ethers to esters or ketones		
Di-(^{i}Propyl)ether	Acetone	A [82]
Benzylmethylether	Benzyl acetate	B [79], C [81]
^{t}Butylethylether	^{t}Butylacetate	B [79, 80]
Di-(^{n}Butyl)ether	Butyl butyrate	B [79, 80], D [83]
2,5-Dimethylfuran	2,5-Dimethylfuran-3-one	A [82]
Methyl^{n}butylether	Methyl butyrate	A [82]
^{n}Methyldecylether	Methyl nonanoate	C [81]
Dibenzylether	Phenylacetic acid phenyl ester	B [79, 80]
Di-(^{n}Propyl)ether	Propylpropionate	A [82], B [79, 80], E [95]
Ethers to lactones		
2,3-Dihydrofuran	γ-Butyrolactone	A [82]
Tetrahydrofuran	γ-Butyrolactone	A [82], D [83], F [77]
2,5-Dimethylfuran	2,5-Dimethylfuran-3-one	A [82]
2,5-Dimethyltetrahydrofuran	2,5-Dimethyldihydrofuran-3-one	A [82]
Methyl ^{n}butylether	Methylbutyrate	A [82]
2-Methyltetrahydrofuran	2-Methyldihydrofuran-3-one + δ-Valerolactone	A [82], F [77]
Tetrahydropyran	δ-Valerolactone	A [82], B [79, 80]
Sulfides to sulfoxides		
Allylmethyl sulfide	Allylmethylsulfoxide	G [112]
n-Butyl sulfide	*n*-Butyl sulfoxide & sulfone	H [131, 141]
Diphenylsulfide	Diphenyl sulfoxide	H [131, 141], S [99]
Diphenyl sulfide	Diphenyl sulfoxide	J [107], S [99]
Phenylmethyl sulfide	Phenylmethyl sulfone	G [112]
Thioanisole	Phenylmethyl sulfone	G [112]
Tetrahydrothiophene	Sulfolane	G [112]
Triphenylmethyl(phenyl) sulfide	Triphenylcarbinol	S [99]
Sulfides to sulfones		
2-Acetyloxy-1-phenylthiohexane	2-Acetyloxy-1-benzenesulfonylhexane	J [107]
2-Phenylthioacetic acid	2-Benzenesulfonylacetic acid	J [107]
2-Phenylthiopropionic acid	2-Benzenesulfonylpropionic acid	J [107]
Benzylmethyl sulfide	Benzylmethyl sulfone	G [112], H [131, 141]
Dibenzyl sulfide	Dibenzyl sulfone	G [112]
Diphenylsulfide	Dipenylsulfone	G [112], J [107]
Ethyl 2-phenylthioacetate	Ethyl 2-benzenesulfonylacetate	J [107]
Ethyl 2-phenylthiopropionate	Ethyl 2-benzenesulfonylpropionate	J [107]
Ethyl-2-ethylthioacetate	Ethyl-2-ethylsulfonylacetate	J [107]
Ethyl 2-*tert*-butylthioacetate	Ethyl 2-*tert*-butylsulfonylacetate	J [107]
2-Ethylthioacetic acid	2-Ethylsulfonylacetic acid	J [107]
Methylbenzyl sulfide	Methylbenzyl sulfone	H [131, 141], S [99]
Methyl-*p*-tolyl sulfide	Methyl-*p*-tolyl sulfone	S [99]

A: *Cis*-$RuCl_2(dmso)_4$, *trans*-$RuCl_2(dppp)_2$, or $[RuCl(dppp)_2]^+$/aq. $Li(ClO)/CH_2Cl_2$ [82]; B: *cis*-$RuCl_2(dmso)_4$ or TPAP/aq. Li(ClO) or RuO_2/aq. $Na(ClO)/CH_2Cl_2$ [79, 80]; C: $RuCl_3$/aq. $Na(IO_4)/CCl_4$-CH_3CN [81]; D: $RuCl_3$/aq. Na(ClO) or $Ca(ClO)_2/CH_2Cl_2$ [83]; E: *cis*-$RuCl_2(phen)_2$/aq. $Li(ClO)/CH_2Cl_2$ [95]; F: RuO_2/aq. $Na(IO_4)/CCl_4$ or stoich. RuO_4/CCl_4 [77]; G: TPAP/NMO/PMS/CH_3CN/40°C [112]; H: *cis*-$(PPh_4)[Ru(O)_2Cl_2(OAc)]$/NMO/PMS/$CH_3CN$ [131, 141]; J: $RuCl_3$/aq. $IO(OH)_5/CCl_4$-CH_3CN [107]; S: stoich. RuO_4/CCl_4 [99]

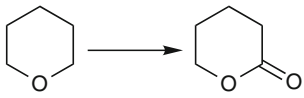


Fig. 5.12 Oxidation by RuO_4 of tetrahydropyran to δ-valerolactone

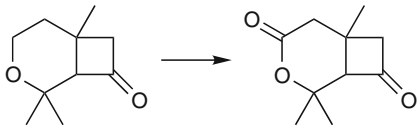


Fig. 5.13 Oxidation by RuO_4 of an alkane-ester intermediate in the synthesis of ±-lineatin [85]

5.3.2 Ethers to Lactones

Commonly used 'models' for cyclic ether oxidations are tetrahydropyran (e.g. Fig. 5.12) and THF – some oxidations of both are given in Table 5.2. For the oxidation of THF to γ-butyrolactone – a common test reaction for ether oxidations - a curious circumstance is that for oxidation with stoich. RuO_4/CCl_4 the lactone was the main product [52, 77], but when effected catalytically with RuO_2/aq. $Na(IO_4)/CCl_4$ [77], or $RuCl_3$/aq. $Na(ClO)/CH_2Cl_2$ (*cf.* mech. Ch. 1) [83] some succinic acid was also formed. Other oxidations of THF by RuO_4 have been reported, e.g. using *trans*-$RuCl_2(dppp)_2$/aq. $Li(ClO)/CH_2Cl_2$ (*cf.* mech. Ch. 1) [82], *cis*-$RuCl_2(dmso)_4$/aq. $Na(ClO)/CH_2Cl_2$ (Table 5.2) [79] and TPAP/aq. $Na(ClO)/CH_2Cl_2$ (Table 5.2) [80]. Oxidation of 3α,5α-cyclocholestan-6β-yl ethers (Me, Et, ^{i}Pr) with RuO_2/aq. $Na(IO_4)$/acetone-CCl_4 gave the corresponding formate or acetate esters; thus 3α,5α-cholestan-6β-yl ^{i}propylether gave 3α,5α-cholestan-6-one (*cf.* mech. Ch. 1) [84]. Oxidation by the same reagent of 2,2,6-trimethyl-3-oxabicyclo-[4.2.0]octan-8-one gave 2,2,6-trimethyl-3-oxabi-cyclo[4.2.0]octane-4,8-dione, an intermediate for the synthesis of the pheromone (±)-lineatin (Fig. 5.13) [85].

For the mild C–H oxyfunctionalisation of cyclic steroidal ethers by $RuCl_3$/aq. $Na(IO_4)$/EtOAc-MeCN *cf.* Fig. 4.3, 4.1.4 [86].

5.3.3 Other Ether Oxidations

Oxidative cleavage of β-hydroxyethers to keto-lactones was accomplished by $RuCl_3$/aq. $Na(IO_4)/CCl_4$–CH_3CN; thus hexahydro-benzofuran-3α-diol gave the corresponding nine-membered ketolactones (R^1=Me, ^{t}Bu, R^2=H, Me; Fig. 5.14) [87].

Oxidation of alkynyl ethers to α-keto esters R^1CCOR^2 to $R^1CO(COOR^2)$ was effected by $RuCl_2(PPh_3)_3/PhIO/CH_2Cl_2$ ($RuCl_3$, $RuCl_2(CO)_2(PPh_3)_2$ and $Ru_3(CO)_{12}$ also catalysed these oxidations but little detail was given) for R^1=H, Me or Ph, R^2=Et; $R^1=^i$Pr, $^n C_6H_{13}$, R^2=Me; $R^1=^n C_4H_9$, $R^2=^i C_3H_7$ [88]. The furan ring in 3-alkyl-4(2-furyl)-4-oxobutanenitriles was converted by $RuCl_3$/aq. $K(IO_4)/CH_2Cl_2$–CH_3CN to the corresponding 2-alkyl-3-cyanopropanoate esters $MeO(CO)C(H)RCH_2CN$ with removal of the carbon skeleton of the furan ring. Thus 3-butyl-4-(2-furyl)-4-

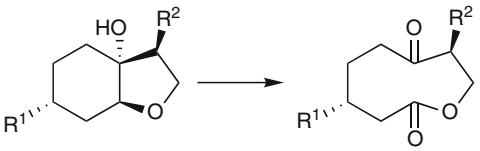


Fig. 5.14 Oxidative cleavage of β-hydroxyethers by RuO_4 to keto-lactones [87]

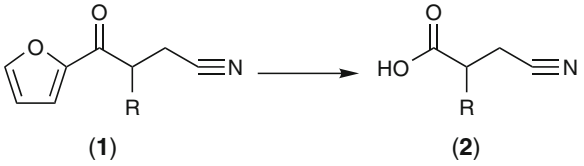


Fig. 5.15 Oxidation of a furan ring by RuO_4 [89]

oxobutanenitrile gave methyl-2-butyl-3-cyanopropanoate, and 3-phenylsulfonyl-4-(2-furyl)-4-oxobutanenitrile gave the cyanopropanoate (R=Me, Et, ^{n}Bu, ^{s}Bu, 2-C_5H_{11}, 1-C_6H_{13}, C_6H_{11}, BnO, Me_3SiCH_2) (Fig. 5.15) [89].

5.3.4 Ether Oxidations Not Covered Here but Included in Chapter 1

These include: $[Ru(H_2O)(bpy)(app)]^{2+}$/TBHP/(BTBAC)/$CH_2Cl_2$ (THF, *cf.* mech. Ch. 1) [90]; stoich. RuO_4/water-CCl_4–CH_3CN (benzylmethylethers to benzoates; *cf.* mech. Fig. 1.11) [76, 91]; *trans*-$[Ru(O)_2(dmbpy)_2]^{2+}$/CH_3CN (THF, *cf.* mech. Ch. 1) [92]; stoich. *trans*-$Ru(O)_2(OCOEt)_2(py)_2$/CH_3CN (THF; Fig. 1.22) [93]; stoich. $[Ru(O)(N_4O)]^{2+}$/CH_3CN (THF) [94]; *trans*-$RuCl_2(dppp)_2$ or *cis*-$RuCl_2(phen)_2$/aq. Li(ClO)/CH_2Cl_2 (dipropylether, tetrahydropyran, Table 5.2, *cf.* mech. Ch. 1) [95]; stoich. RuO_4/aq. $HClO_4$ (THF to γ-butyrolactone; *cf.* mech. Ch. 1) [96].

5.4 Oxidation of Sulfides (thioethers), R^1R^2S

$$R^1R^2S + [O] \rightarrow R^1R^2SO; R^1R^2S + 2[O] \rightarrow R^1R^2SO_2 \tag{5.6}$$

Oxidations of sulfides catalysed by Ru porphyrin complexes have been reviewed [4, 97, 98]. In their pioneering work of 1953 Djerassi and Engle showed that stoich. RuO_4/CCl_4 oxidised several sulfides to sulfones (Table 5.2) [99].

5.4.1 Sulfides to Sulfoxides

$$R_2S + [O] \rightarrow R_2SO \tag{5.7}$$

A selection of such reactions using mild conditions is summarized in Table 5.2 below. Other methods involve the inconvenient use of O_2 under pressure and/or the use of high temperatures and are not listed therein. For example, methyl-*p*-tolylsulfide was oxidised to the sulfoxide by *mer*-$RuCl_3$((dmso)$_2$(MePhSMe) and by *mer*-$RuCl_3$(dmso)(MePhSMe)$_2$/O_2 (7 atm.)/MeOH/80°C [100], and also by the hetero-scorpionate complex *fac*-[Ru(H_2O)(dpzp)(tppm)]$^+$/O_2/*o*-$C_6H_4Cl_2$ (*cf.* mech. Ch. 1) [101]. The system *cis*-$RuCl_2$(dmso)$_4$/O_2 (7 atm.)/110°C/MeOH converted sulfides to sulfoxides (dimethyl, dibutyl, decylmethyl and methylbenzyl sulfides) [102]. Diethyl sulfide and ^{n}Bu$_2$S were oxidised to Bu$_2^n$SO and some Bu$_2^n$SO$_2$ by $RuCl_2(PPh_3)_3$ or $RuBr_2(PPh_3)$/O_2/EtOH/100°C [103]; *trans*-Ru(O)$_2$(TMP)/O_2/benzene/65°C oxidised Et_2S to Et_2SO, and to $EtSO_2$ at 100°C (*cf.* mech. Ch. 1) [104]. There is a brief allusion to oxidation of sulfides to sulfoxides and sulfones by *trans*-Ru(O)$_2$(TMP)/2,6-disubstituted aromatic N-oxides/C_6H_6 [105]; *trans*-Ru(O)$_2$(TMP)/lutidine-*N*-oxide/C_6H_6/80°C oxidised PhMeS and benzyl sulfide to the sulfoxides and a small quantity of sulfones [106].

5.4.2 Sulfides to Sulfones

$$R_2S + 2[O] \rightarrow R_2SO_2 \tag{5.8}$$

An effective reagent for this is $RuCl_3$/aq. $IO(OH)_5$/CCl_4–CH_3CN, used for oxidation of the lactone (2*R*,3*R*,4*R*)-2-methyl-2-phenylthio-3-methoxycarbonyl-methyl-4-(2′-*tert*-butyl-diphenylsilyloxy)ethyl-γ-butyrolactone to the sulfonyl analogue (Fig. 5.16); other oxidations are listed in Table 5.2 [107].

The electrocatalytic system [Ru{$PW_{11}(H_2O)O_{39}$}]$^{4-}$/DMSO/graphite anode oxidised DMSO to Me_2SO_2 [108]. Microencapsulated $RuCl_2(PPh_3)_3$ on an epoxide-containing polymer/NMO or iodosylacetate/acetone converted sulfides to sulfoxides or sulfones (e.g. 2-thiophenemethanol) [109], similarly [Ru($C_7F_{15}COCH_2COC_7F_{15})_3$]$^-$/perfluoro decalin-toluene/O_2/65°C) [110, 111]. An effective chemoselective oxidation catalyst for conversion of sulfides to sulfones without competing double-bond cleavage is TPAP/NMO/PMS/CH_3CN/40°C (Table 5.2) [112].

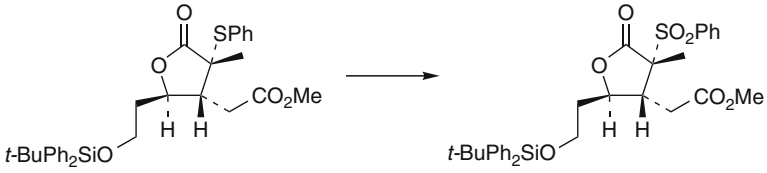


Fig. 5.16 Oxidation of a complex sulfide to a sulfone by RuO_4 [107]

5.4.3 Sulfoxides to Sulfones

Electrocatalytic formation of Me_2SO_2 from DMSO was effected using *cis*-[Ru(O)(py)$(bpy)_2]^{2+}$/Pt electrode/water-DMSO; *cf.* mech. Ch. 1 [113]. Oxidation of thianthrene-5-oxide by RuO_2/aq. $Na(IO_4)/CCl_4$/0°C gave a mixture of the sulfone and thianthrene-5,5-dioxide with minor amounts of the disulfoxide and also thianthrene-5,5,10-trioxide; comparisons were made between the behaviour of RuO_4, CrO_2Cl_2 and $[MnO_4]^-$ for these reactions (*cf.* mech. Ch. 1) [114].

5.4.4 Sulfides to Sulfates; Cyclic Sulfites to Sulfates

Oxidations of a number of thiophenes and a wide variety of alkyl- and aryl-substituted thiophenes by $RuCl_3$/aq. Na(ClO) have been compared with similar oxidations effected stoicheiometrically by $[MnO_4]^-$, the aim being the destruction of these compounds for environmental reasons. Some were 'totally' oxidised to sulfate, but in many cases end-products were not identified, though 2-ethylthiophene gave 2-acetylthiophene and 2-*n*-butylthiophene gave 2-butyroylthiophene [115].

A cyclic ring sulfite (with an –O–SO–O– ring in a carbocyclic nucleoside) was oxidised by $RuCl_3$/aq. $Na(IO_4)/CCl_4$–CH_3CN/0°C as a synthon for the convergent synthesis of carbocyclic nucleosides (Fig. 5.17) [116].

Oxidation of cyclic sulfite diesters to the corresponding cyclic sulfate diesters (Fig. 5.18) e.g. 2-oxo-1,3,2-dioxathiolanes (1) to 2,2-dioxo-1,3,2-dioxathiolanes (2) and 2-oxo-1,3,2-dioxa-thianes (3) to 2,2-dioxo-1,3,2-dioxathianes (4) was carried out with RuO_2/aq. $Na(IO_4)/CHCl_3$: for (1)→(2): $R^1{=}R^2{=}R^3{=}R^4{=}H$; R^1=Ph, $R^2{=}R^3{=}R^4{=}H$; $R^1{=}R^2{=}R^4{=}H$, R^3=Ph; $R^1{=}R^4$=Ph, $R^2{=}R^3{=}H$; $R^1{=}R^4{=}H$, $R^2{=}R^3$=Ph; and for (3)→(4): $R^1{=}R^2{=}R^3{=}R^4{=}H$; $R^1{=}R^2{=}R^3{=}H$, R^4=Me; R^1=Me, $R^2{=}R^3{=}R^4{=}H$; $R^1{=}R^3{=}H$, $R^2{=}R^4$=Me. Retention of configuration at the sulfur atom was demonstrated by the use of lanthanide shift reagents [117].

Oxidation of diols $R^1CH(OH)CH(OH)R^2$ to diol cyclic sulfates $R^1C(O–SO_2O)CR^2$ was effected by $SOCl_2/CCl_4$/60°C followed by $RuCl_3$/aq. $Na(IO_4)/CH_3CN$ ($R^1{=}R^2$=COO^iPr, COOMe, COOEt, $^nC_4H_9$; $R^1{=}{}^nC_8H_{17}$, $^cC_6H_{11}$ with R^2=H; $R^1{=}{}^nC_{15}H_{31}$, R^2=COOMe; $R^1{=}{}^cC_6H_{11}$, R^2=COOEt; R^1=H, $R^2{=}COO^cC_6H_{11}$, $CONHCH_2Ph$) [118].

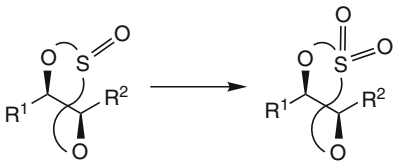


Fig. 5.17 Oxidation by RuO_4 of cyclic sulfites to sulfates [116]

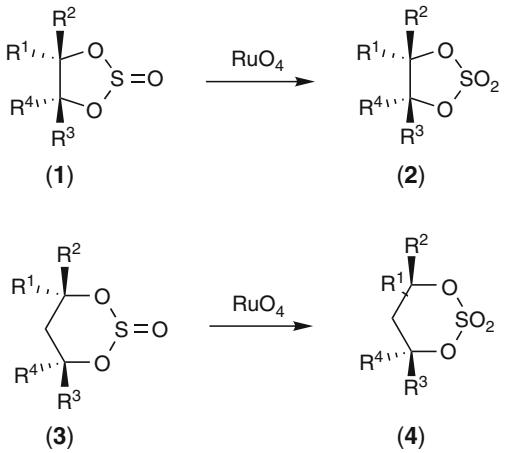


Fig. 5.18 Cyclic sulphites oxidised to cyclic sulfate diesters by RuO_4 [117]

5.4.5 Sulfilimines to Sulfoximes; N-Sulfonylsulfilimines to N-Sulfonylsulfoximines

$$R^1R^2S=NR^3+[O]\rightarrow R^1R^2S(O)=NR^3 \tag{5.9}$$

$$R^1R^2S=NS(O)_2R^3+[O]\rightarrow R^1R^2S(O)=NS(O)_2R \tag{5.10}$$

Oxidation of sulfilimines by RuO_2/aq. $Na(IO_4)/CH_2Cl_2$ was demonstrated using a number of S,S-dimethyl-N-sulfonyl- and N-acylsulfilimines [119]. A wide variety of N-sulfonylsulfilimines were oxidised to the corresponding sulfoximines by RuO_2/aq. CH_3CO_3H/CH_2Cl_2 (R^1=Me, R^2=Me, Et, ^{n}Pr, or Ph, R^3=*p*-MeC_6H_4; R^1=R^2=Me, R^3=Me, Ph, *p*-ClC_6H_5; R^1= Et, ^{i}Pr, or Ph, R^2=Et, ^{i}Pr, or Ph, R^3= *p*-MeC_6H_4; R^1=R^2= -$(CH_2)_n$-, R^3=*p*-MeC_6H_4 (n=3, 4)) [120].

5.4.6 Asymmetric Epoxidations of Sulfides

Little work has been done in this area with Ru catalysts. *Cis*-Λ-$[Ru(O)(py)(bpy)_2]^{2+}$/water-CH_3CN was used for the stoicheiometric oxidation of methyl-*p*-tolyl sulfide to (R)-methyl-*p*-tolyl sulfoxide with an e.e. of *ca* 15% [121].

5.4.7 Large-Scale Oxidations of Sulfides and Sulfites

$RuCl_3$/aq. $Na(IO_4)/CH_3CN–CCl_4$/0°C (*D*-mannitol-1,2:5,6-diacetonide-2,3-cyclic sulfite (6 g) to the sulfate) [116], and stoich. RuO_4/CCl_4 (*ca.* 5 g; methyl-*p*-tolyl, methylbenzyl and triphenyl-methyl phenyl and diphenyl sulfides to the sulfones) [99, 122].

5.4.8 *Sulfide Oxidations Not Covered Here but Included in Chapter 1*

These include: Ru(dmso)(don)(babp)/PhIO/DCE/40°C (thioanisole) [123]; stoich. RuO_4/CH_3CN (*cf.* mech. Fig. 1.12) [124]; $[Ru(H_2O)(EDTA)]^-$/pyridine-*N*-oxide/water (Me_2S to Me_2SO) [125]; stoich. $[RuO_4]^-$/DMF/0.5 M NaOH (R^1R^2S to R^1R^2SO; R^1=Me, Ph, $R^2=CH_2COO$) (Fig. 1.14; *cf.* mech.) [126]; *cis*-$[Ru(O)_2(CF_3COO)(tmtacn)]^+$/PhIO or TBHP/$CH_2Cl_2$ (dimethyl sulfide) [127]; stoich. $[Ru(O)(PR_3)(bpy)_2]^{2+}/CH_3CN$ (sulfides to sulfoxides and sulfones; *cf.* mech. Ch. 1) [128]; stoich. *trans*-$[Ru(O)_2(OEP)]^+/CH_2Cl_2$ (Ph_2S) [129]; $[Ru(H_2O)(EDTA)]^-/O_2$/water-dioxane (Me_2S to Me_2SO) [130]; $[Ru(O)_2Cl_2(OCOCH_3)]^-$/NMO/PMS/CH_3CN [131]; *trans*-$Ru(O)_2(TMP)/O_2/C_6H_6$ (Et_2S, $^nBu_2S$, decyl methylsulfide to sulfoxides; *cf.* mech. Ch. 1) [98]; (Fig. 1.27) [132]; *cis*-$RuCl_2(dmso)_4$/NMO/DMF (R_2S to R_2SO, R=Bz, Bu, Ph, MeC_6H_4) *cf.* mech. Ch. 1 [133]; $[Ru(n\text{-decyl})_2S(OEP)]_2/O_2$/benzene/AcOH (*n*-decyl sulfide to the sulfoxide) [134]; *trans*-$[Ru(O)_2(dpt)]^{2+}/CH_3CN/\lambda > 330$ nm (dibenzyl sulfide to the sulfoxides) [135].

5.5 Oxidation of Phosphines, Arsines and Stibines

$$R_3X + [O] \rightarrow R_3XO \quad (X = P, As \text{ or } Sb) \tag{5.11}$$

This topic has been reviewed, mainly for porphyrin complexes [4, 97, 136], with most examples concerning the oxidation of PPh_3 to PPh_3O; mechanistic aspects were also covered.

The first Ru-catalysed oxidation of phosphines (PPh_3 to PPh_3O) was reported in 1970, using $Ru(O_2)(NO)(NCS)(PPh_3)_2/O_2$/xylene/80°C; *cf.* mech. Ch. 1 [137]. Other catalytic systems for PPh_3 to PPh_3O include: $RuBr_2(PPh_3)_2(RCHO)_2/O_2/^nBuOH$) (R=$C_4H_3O$, C_6H_5) [138], *o*-HOC_6H_4, *p*-$MeOC_6H_4$) [139]; Ru(O)(PHAB) or $[Ru(O)(PHAB)]^-/O_2/CH_2Cl_2$ [140]; $[Ru(O)_2Cl_2(OAc)]^-$/NMO/PMS/CH_3CN (sulfides to sulfoxides) [131]; *cis*-$(PPh_4)[Ru(O)_2Cl_2(OAc)]$/NMO/PMS/$CH_3CN$ [131, 141]; $[Ru(H_2O)(EDTA)]^-$/aq. Na(ClO) (*cf.* mech. Ch. 1) [142]; $Ru(PPh_3)(OEP)$ and $Ru(PPh_3)_2(OEP)/O_2$/benzene/50°C; *cf.* mech. Ch. 1 [136].

A number of systems stoicheiometrically oxidised these substrates to their oxides: *trans*-$Ru(O)_2(TMP)/O_2/C_6H_6$ for $((p\text{-}RC_6H_4)_3P$ (R=H, F, Cl, Me, CF_3, OMe) and for $AsPh_3$, $SbPh_3$; *cf.* mech. Ch. 1) [143]; *trans*-$[Ru(O)_2(H_2O)(tpy)]^{2+}/CH_3CN$ (PPh_3 and diphosphines $Ph_2P(CH_2)_nPPh_2$ (n=1 (dppm) and n=2 (dppe)); *cf.* mech. Ch. 1) [144]; $[Ru(H_2O)(EDTA)]^-/O_2$/water (PPh_3; *cf.* mech. Ch. 1) [145]; *trans*-$Ru(O)_2(OC(O)Et)_2(py)_2/CH_3CN$ (PPh_3; Fig. 1.22) [93]; $[Ru(O)_2Cl_3]^-/CH_3CN$ (Fig. 1.19) (PPh_3 and $PhMe_2P$) [146]; *trans*-$Ru(O)_2(TMP)/C_6H_6$ (PPh_3; *cf.* mech. Ch. 1) [147]; $[Ru(O)(bpy)_2(PEt_3)]^{2+}$/water [148]; stoich. *trans*-[Ru(O)

$Cl(py)_4]^+/CH_3CN$ (PPh_3) [149]; stoich. $Ru(O)(OEP^{+\cdot})Br/CH_2Cl_2$ (Ph_3P) [150]; *cis*-$[Ru^{18}(O)(py)(bpy)_2]^{2+}/CH_3CN$ (PPh_3; *cf.* mech. Ch. 1) [151].

5.5.1 Asymmetric Oxidations of Phosphines to Phosphine Oxides

Trans-$Ru(O)_2$(pfp)/CH_2Cl_2 containing optically active picket-fence α,β,α,β and α,α,β,β porphyrins stoicheiometrically oxidised racemic phosphines to the corresponding oxides. Thus $PhMePCH_2Ph$ gave the (−)-(*S*) oxide with complete retention of configuration and 41% e.g. (*cf.* mech. Ch. 1) [152, 153].

5.6 Oxidations of Miscellaneous Substrates

5.6.1 Si–H Bonds in Organosilanes

$$R^1R^2R^3SiH + [O] \rightarrow R^1R^2R^3Si(OH) \tag{5.12}$$

The system $[RuCl_2(p\text{-cymene})]_2/H_2O_2/CH_3CN$ oxidised silanes $R^1R^2R^3SiH$ to silanols $R^1R^2R^3Si(OH)$ (R^1=H, Ph, PhCH=CH, $CH_3(CH_2)_{17}$, PhCC, ^{n}BuCC, $Cl(CH_2)_3$ or C_6H_9CC; R^2=R^3=Me; R^1=Ph, R^2=R^3=Et, Ph or ^{t}Bu; R^1=R^2=R^3=Et, Ph, ^{t}Bu). Some of these oxidations were also effected by $[RuCl_2(p\text{-cymene})]_2/O_2$/water/80°C, and other catalysts for the reaction include $[RuCl(benzene)]_2$ and $RuH_2(PPh_3)_4$ [154]. The system $[RuCl_2(p\text{-cymene})]_2$/water-$CH_3CN$/Pt electrodes oxidised Ph_2MeSiH to $Ph_2MeSi(OH)$ [155].

5.6.2 Nitriles

Oxidation of α-substituted nitriles $R^1R^2CH(CN)$ with $RuCl_2(PPh_3)_3$/TBHP/C_6H_6 yielded the 2-(*tert*-butyldioxy)-alkanenitriles ^{t}BuOOCR^1R^2(CN) (R^1=Ph, R^2=Me, Ph, $CH_2COOEMe$, CH_2COOEt, $OSiMe_3$; R^1=4-ClC_6H_4, R^2=Me; R^1=$Me(CH_2)_2CO$, R^2=Me) [156].

5.6.3 Hydrocarbons in Coals

Hydrocarbons in coals have been oxidised by RuO_4. A Pocahontas coal of empirical formula $C_{100}H_{62.9}N_{1.15}S_{0.17}O_{3.26}$ was treated with $RuCl_3$/aq. $Na(IO_4)/CCl_4$–CH_3CN to give acetic, butanedioic, pentanedioic, hexanedioic, heptanedioic and other acids

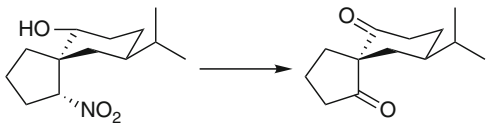


Fig. 5.19 Oxidation by TPAP of a nitro and secondary alcohol groups [163]

[157]. Low-rank coals were oxidised with $RuCl_3$/aq. $Na(IO_4)/CCl_4$, and both aliphatic and aromatic acids were detected [158, 159]. The system $RuCl_3$/aq. $Na(IO_4)/CCl_4$–CH_3CN was used for oxidation of Illinois No. 6 coal (see also arenes, 3.3.1, 3.3.3, Tables 3.4 and 3.5) [160].

5.6.4 Nitro and Halide Compounds

Primary nitro compounds RNO_2 were oxidised to RCOOH (e.g. nitro-ethane, -propane, -butane, -pentane and -hexane to acetic, propionic, butyric, pentanoic and hexanoic acids) by $[RuO_4]^-$ from $RuCl_3/Na(BrO_3)^-$/aq. M $Na_2(CO_3)$ or by $[RuO_4]^{2-}$ from $RuCl_3/K_2(S_2O_8)$/aq. M KOH [161]. Secondary nitro compounds were oxidised to ketones by TPAP/NMO/PMS/$K_2(CO_3)/CH_2Cl_2$. Thus $PhC(OMe)CH(NO_2)$ Me gave $PhC(OMe)COMe$, and $Ph(CH_2)_2(C(OCH_2Ph)CH(NO_2)$ Me gave $Ph(CH_2)_2(C(OCH_2Ph)$ COMe [162]. As part of the total synthesis of the naturally-occurring sesquiterpene (±)-erythrodiene a nitro-alcohol intermediate was converted to the diketone (both nitro and secondary alcohol groups having been oxidised, *cf.* Fig. 5.19, by TPAP/NMO/PMS/CH_2Cl_2 [163].

Corey et al. used $[RuO_4]^{2-}$ (as $RuCl_3/S_2O_8^{2-}$/aq. base @ pH 14) to accomplish a form of the Nef reaction, oxidising a carbon-bearing nitro group to a carbonyl function as part of a total synthesis of the plant hormone antheridiogen (A_{An}, 2) [164]. The systems $RuCl_3/Na(BrO_3)^-$/aq. M $Na_2(CO_3)$ and $RuCl_3/K_2(S_2O_8)$/aq. M KOH. oxidised activated primary alkyl halides RX (X=Cl, Br, I) to carboxylic acids RCOOH (C_6H_5Cl, C_6H_5Br, *p*-$MeOC_6H_4Cl$, $C_6H_5CH_2Cl$, 2,6-$Cl_2C_6H_4$, $C_6H_5CH_2Br$, BuI) and secondary alkyl halides to ketones, e.g. 1-bromophenylethane to acetophenone and 1-bromo-1,1-diphenylethane to benzophenone. The use of a phase-transfer agent (Aliquat®) gave reduced yields and turnovers for these reactions [161] It was reported that $[Ru(O)_2Cl_2(OAc)]^-$/NMO/PMS/CH_3CN oxidised activated primary halides to the aldehydes [131], but subsequently it was found that NMO/CH_3CN/PMS effected this reaction in the absence of a Ru catalyst [165].

5.6.5 Azidolactones; Depyrimidination of DNA

Carbohydrate azidolactones were converted to bicyclic amines (from an N_3R moiety to H_2N–R) by TPAP/NMO/PMS/CH_3CN as part of a synthesis of 1-*epi*hyantocidin from D-ribose [166]. Thymidine-specific depyrimidination of DNA by this and

other Ru(IV) oxo complexes, e.g. electrocatalytically by $[Ru(O)(bpy)_2(tpy)]^{2+}$/formate buffer, was studied and related to their Ru(IV)/Ru(II) redox potentials [167].

5.6.6 Acids; Diones

Formate and formic acid were oxidised to CO_2 by stoich. *cis*-$[Ru(O)(py)(bpy)_2]^{2+}$/water (*cf.* mech. Ch. 1) [168]. Cyclohexane-1,2-dione gave glutaric and adipic acids with $RuCl_3$/aq. $Na(ClO)/CH_2Cl_2$ [169].

5.6.7 Fullerenes

Cis-dihydroxylation of C_{60} and C_{70} by RuO_4/CCl_4-1,2,4-trichlorobenzene followed by acid hydrolysis gave the fullerene diols 1,2-$C_{60}(OH)_2$, 1,2-$C_{70}(OH)_2$ and 5,6-$C_{70}(OH)_2$ [170], while Ru(CO)(TPP)/(Cl_2pyNO)/HBr/C_6H_6 epoxidised fullerene (C_{60}) to 1,2-epoxy[60]fullerene with 1,2:3,4 di-epoxy and 1,2:3,4:9,10 + 1,2:3,4:11,12 tri-epoxy species [171].

For oxidation of aldehydes see 4.1.

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W.P. Griffith, *Ruthenium Oxidation Complexes*, Catalysis by Metal Complexes 34,
DOI 10.1007/978-1-4020-9378-4, © Springer Science+Business Media B.V. 2011

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