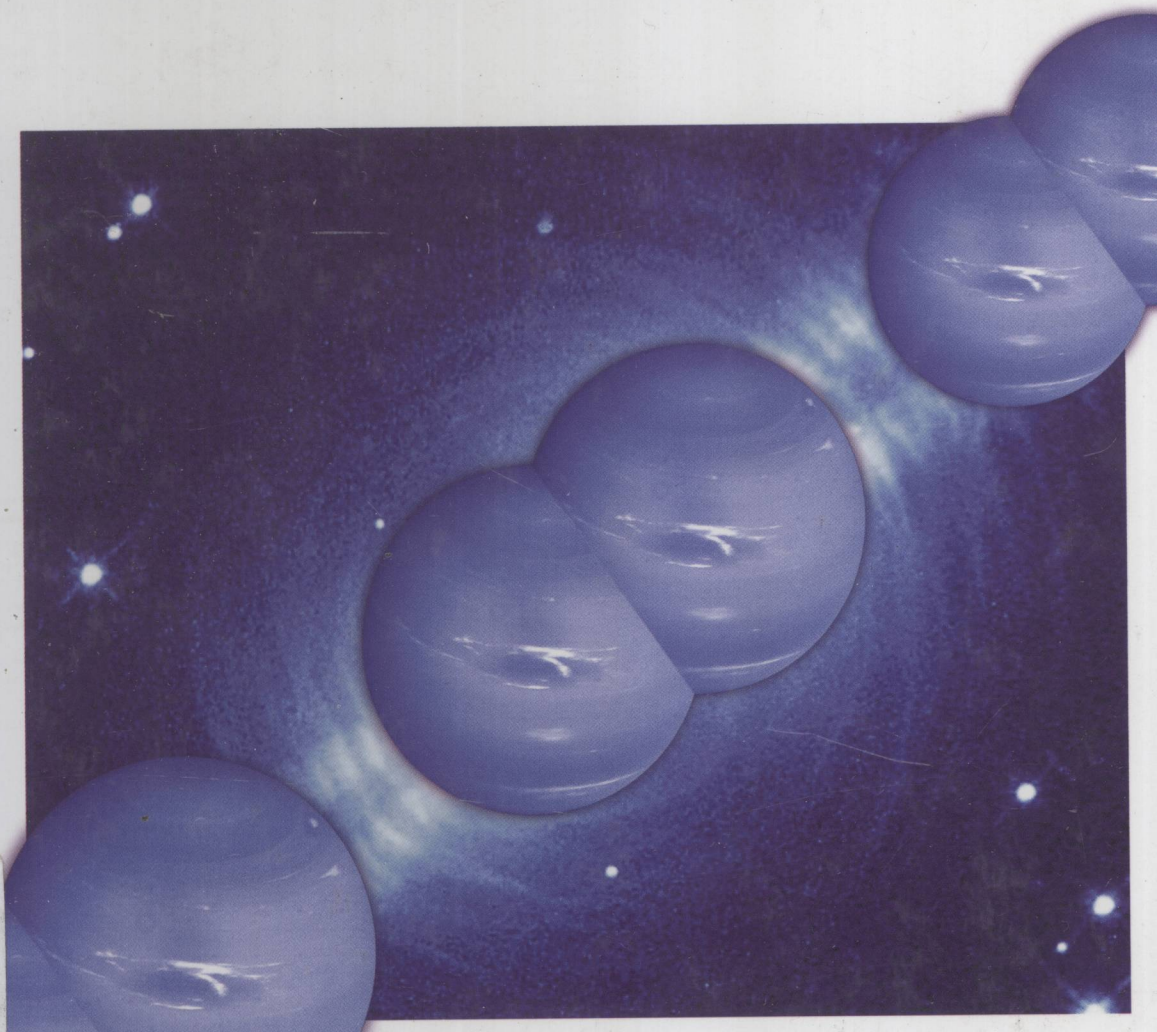


Edited by  
J.-E. Bäckvall

 WILEY-VCH

# Modern Oxidation Methods



0621.25  
M 689

# Modern Oxidation Methods

*Edited by*  
*Jan-Erling Bäckvall*



E200601293

WILEY-VCH Verlag GmbH & Co. KGaA

**Editor:**

**Professor Dr. Jan-Erling Bäckvall**

Department of Organic Chemistry  
Arrhenius Laboratory  
Stockholm University  
SE 106 91 Stockholm  
Sweden

■ This book was carefully produced. Nevertheless, authors, editor and publisher do not warrant the information contained therein to be free of errors. Readers are advised to keep in mind that statements, data, illustrations, procedural details or other items may inadvertently be inaccurate.

**Library of Congress Card No.: applied for**

**British Library Cataloguing-in-Publication**

**Data:** A catalogue record for this book is available from the British Library.

**Bibliographic information published by**

**Die Deutsche Bibliothek**

Die Deutsche Bibliothek lists this publication in the Deutsche Nationalbibliografie; detailed bibliographic data is available in the Internet at <<http://dnb.ddb.de>>.

© 2004 Wiley-VCH Verlag GmbH & Co.  
KGaA, Weinheim,

All rights reserved (including those of translation into other languages). No part of this book may be reproduced in any form – nor transmitted or translated into a machine language without written permission from the publishers. Registered names, trademarks, etc. used in this book, even when not specifically marked as such, are not to be considered unprotected by law.

Printed in the Federal Republic of Germany  
Printed on acid-free paper

**Composition** ProSatz Unger, Weinheim

**Printing** Strauss GmbH, Mörlenbach

**Bookbinding** Litges & Dopf Buchbinderei  
GmbH, Heppenheim

**ISBN** 3-527-30642-0

## **Modern Oxidation Methods**

*Edited by*  
*Jan-Erling Bäckvall*

*Further Reading from Wiley-VCH*

R. Mahrwald (Ed.)

**Modern Aldol Reactions, 2 Vols.**

2004

ISBN 3-527-30714-1

A. de Meijere, F. Diederich (Eds.)

**Metal-Catalyzed Cross-Coupling Reactions, 2 Vols., 2<sup>nd</sup> Ed.**

2004

ISBN 3-527-30518-1

B. Cornils, W. A. Herrmann (Eds.)

**Aqueous-Phase Organometallic Catalysis, 2<sup>nd</sup> Ed.  
Concepts and Applications**

2004

ISBN 3-527-30712-5

M. Beller, C. Bolm (Eds.)

**Transition Metals for Organic Synthesis, 2 Vols., 2<sup>nd</sup> Ed.  
Building Blocks and Fine Chemicals**

2004

ISBN 3-527-30613-7

## Preface

Oxidation reactions play an important role in organic chemistry and there is an increasing demand for selective and mild oxidation methods in modern organic synthesis. During the last two decades there has been a spectacular development in the field and a large number of novel and useful oxidation reactions have been discovered. Significant progress has been achieved within the area of catalytic oxidations, which has led to a range of selective and mild processes. These reactions may be based on organocatalysis, metal catalysis or biocatalysis. In this regard enantioselective catalytic oxidation reactions are of particular interest.

Due to the rich development of oxidation reactions in recent years there was a need for a book covering the area. The purpose of this book on “Modern Oxidation Methods” is to fill this need and provide the chemistry community with an overview of some recent developments in the field. In particular some general and synthetically useful oxidation methods that are frequently used by organic chemists are covered. These methods include catalytic as well as non-catalytic oxidation reactions in the science frontier of the field. Today there is an emphasis on the use of environmentally friendly oxidants (“green” oxidants) that lead to a minimum amount of waste. Examples of such oxidants are molecular oxygen and hydrogen peroxide. Many of the oxidation methods discussed and reviewed in this book are based on the use of “green” oxidants.

In this multi-authored book selected authors in the field of oxidation provide the reader with an up to date of a number of important fields of modern oxidation methodology. Chapter 1 summarizes recent advances on the use of “green oxidants” such as  $\text{H}_2\text{O}_2$  and  $\text{O}_2$  in the osmium-catalyzed dihydroxylation of olefins. Immobilization of osmium is also discussed and with these recent achievements industrial applications seem to be near. Another important transformation of olefins is epoxidation. In Chapter 2 transition metal-catalyzed epoxidations are reviewed and in Chapter 3 recent advances in organocatalytic ketone-catalyzed epoxidations are covered. Catalytic oxidations of alcohols with the use of environmentally benign oxidants have developed tremendously during the last decade and in Chapter 4 this area is reviewed. Aerobic oxidations catalyzed by *N*-hydroxyphthalimides (NHPI) are reviewed in Chapter 5. In particular oxidation of hydrocarbons via C–H activation are treated but also oxidations of alkenes and alcohols are covered.

In Chapter 6 ruthenium-catalyzed oxidation of various substrates are reviewed including alkenes, alcohols, amines, amides,  $\beta$ -lactams, phenols, and hydrocarbons. Many of these oxidations involve oxidations by “green oxidants” such as molecular oxygen and alkyl hydroperoxides. Chapter 7 deals with heteroatom oxidation and selective oxidations of sulfides (thioethers) to sulfoxides and tertiary amines to amine oxides are discussed. The chapter covers stoichiometric and catalytic reactions including biocatalytic reactions. Oxidations catalyzed by polyoxymetalates have increased in use during the last decade and this area is covered in Chapter 8. Oxidations with various monooxygen donors, peroxides (including hydrogen peroxide) and molecular oxygen are reviewed. Also, recent attempts to heterogenize homogeneous polyoxymetalate catalysts are discussed. Chapter 9 comprises an extensive review on oxidation of ketones with some focus on recent advances in Baeyer-Villiger oxidations. Catalytic as well as stoichiometric reactions are covered. Finally, in Chapter 10 manganese-catalyzed hydrogen peroxide oxidations are reviewed. The chapter includes epoxidation, dihydroxylation of olefins, oxidation of alcohols and sulfoxidation.

I hope that this book will be of value to chemists involved in oxidation reactions in both academic and industrial research and that it will stimulate further development in this important field.

Stockholm, July 2004

*Jan-E. Bäckvall*

## List of Contributors

Hans Adolfsson  
Department of Organic Chemistry  
Arrhenius Laboratory  
Stockholm University  
106 91 Stockholm  
Sweden

Isabel W. C. E. Arends  
Delft University of Technology  
Biocatalysis and Organic Chemistry  
Julianalaan 136  
2628 BL Delft  
The Netherlands

Jan-E. Bäckvall  
Department of Organic Chemistry  
Arrhenius Laboratory  
Stockholm University  
106 91 Stockholm  
Sweden

Matthias Beller  
Institut für Organische Katalyse-  
forschung an der Universität Rostock e. V.  
(IfOK)  
Buchbinderstrasse 5–6  
18055 Rostock  
Germany

Johannes W. de Boer  
Laboratory of Organic Chemistry  
Stratingh Institute  
University of Groningen  
Nijenborgh 4  
9747 AG Groningen  
The Netherlands

Carsten Bolm  
Institute of Organic Chemistry  
RWTH Aachen  
Professor-Pirlet-Str. 1  
52056 Aachen  
Germany

Jelle Brinksma  
Laboratory of Organic Chemistry  
Stratingh Institute  
University of Groningen  
Nijenborgh 4  
9747 AG Groningen  
The Netherlands

Christian Döbler  
Institut für Organische Katalyse-  
forschung an der Universität Rostock e. V.  
(IfOK)  
Buchbinderstrasse 5–6  
18055 Rostock  
Germany



Ben L. Feringa  
Laboratory of Organic Chemistry  
Stratingh Institute  
University of Groningen  
Nijenborgh 4  
9747 AG Groningen  
The Netherlands

Jean-Cédric Frison  
Institute of Organic Chemistry  
RWTH Aachen  
Professor-Pirlet-Str. 1  
52056 Aachen  
Germany

Ronald Hage  
Unilever R&D  
Po Box 114  
3130 AC Vlaardingen  
The Netherlands

Yasutaka Ishii  
Department of Applied Chemistry  
Faculty of Engineering  
Kansai University  
Suita  
Osaka 564-8680  
Japan

Naruyoshi Komiya  
Department of Chemistry  
Graduate School of Engineering Science  
Osaka University  
1-3, Machikaneyama  
Toyonaka  
Osaka 560-8531  
Japan

Jacques Le Pailh  
Institute of Organic Chemistry  
RWTH Aachen  
Professor-Pirlet-Str. 1  
52056 Aachen  
Germany

Shun-Ichi Murahashi  
Department of Applied Chemistry  
Okayama University of Science  
1-1 Ridai-cho  
Okayama  
Okayama 700-0005  
Japan

Ronny Neumann  
Department of Organic Chemistry  
Weizmann Institute of Science  
Rehovot  
76100 Israel

Satoshi Sakaguchi  
Department of Applied Chemistry  
Faculty of Engineering  
Kansai University  
Suita  
Osaka 564-8680  
Japan

Roger A. Sheldon  
Delft University of Technology  
Biocatalysis and Organic Chemistry  
Julianalaan 136  
2628 BL Delft  
The Netherlands

Yian Shi  
Department of Chemistry  
Colorado State University  
Fort Collins  
Colorado 80523  
USA

Uta Sundermeier  
Institut für Organische Katalyse-  
forschung an der Universität Rostock e. V.  
(IfOK)  
Buchbinderstrasse 5–6  
18055 Rostock  
Germany

## Contents

Preface V

List of Contributors XIII

### 1 Recent Developments in the Osmium-catalyzed Dihydroxylation of Olefins 1

UTA SUNDERMEIER, CHRISTIAN DÖBLER, and MATTHIAS BELLER

- 1.1 Introduction 1
- 1.2 Environmentally Friendly Terminal Oxidants 2
  - 1.2.1 Hydrogen Peroxide 2
  - 1.2.2 Hypochlorite 5
  - 1.2.3 Oxygen or Air 7
- 1.3 Supported Osmium Catalyst 12
- 1.4 Ionic Liquids 16
- References 17

### 2 Transition Metal-catalyzed Epoxidation of Alkenes 21

HANS ADOLFSSON

- 2.1 Introduction 21
- 2.2 Choice of Oxidant for Selective Epoxidation 22
- 2.3 Epoxidations of Alkenes Catalyzed by Early Transition Metals 23
- 2.4 Molybdenum and Tungsten-catalyzed Epoxidations 23
  - 2.4.1 Homogeneous Catalysts – Hydrogen Peroxide as the Terminal Oxidant 24
  - 2.4.2 Heterogeneous Catalysts 27
- 2.5 Manganese-catalyzed Epoxidations 28
- 2.6 Rhenium-catalyzed Epoxidations 32
  - 2.6.1 MTO as an Epoxidation Catalyst – Original Findings 35
  - 2.6.2 The Influence of Heterocyclic Additives 35
  - 2.6.3 The Role of the Additive 38
  - 2.6.4 Other Oxidants 39
  - 2.6.5 Solvents/Media 41
  - 2.6.6 Solid Support 42
  - 2.6.7 Asymmetric Epoxidations Using MTO 43

2.7	Iron-catalyzed Epoxidations	44
2.8	Concluding Remarks	46
	References	47
<b>3</b>	<b>Organocatalytic Oxidation. Ketone-catalyzed Asymmetric Epoxidation of Olefins</b>	<b>51</b>
	YIAN SHI	
3.1	Introduction	51
3.2	Early Ketones	52
3.3	C <sub>2</sub> Symmetric Binaphthyl-based and Related Ketones	53
3.4	Ammonium Ketones	58
3.5	Bicyclo[3.2.1]octan-3-ones	59
3.6	Carbohydrate Based and Related Ketones	60
3.7	Carbocyclic Ketones	72
3.8	Ketones with an Attached Chiral Moiety	75
3.9	Conclusion	76
	Acknowledgments	78
	References	78
<b>4</b>	<b>Modern Oxidation of Alcohols Using Environmentally Benign Oxidants</b>	<b>83</b>
	I. W. C. E. ARENDS and R. A. SHELDON	
4.1	Introduction	83
4.2	Oxoammonium-based Oxidation of Alcohols – TEMPO as Catalyst	83
4.3	Metal-mediated Oxidation of Alcohols – Mechanism	87
4.4	Ruthenium-catalyzed Oxidations with O <sub>2</sub>	88
4.5	Palladium-catalyzed Oxidations with O <sub>2</sub>	100
4.6	Copper-catalyzed Oxidations with O <sub>2</sub>	105
4.7	Other Metals as Catalysts for Oxidation with O <sub>2</sub>	109
4.8	Catalytic Oxidation of Alcohols with Hydrogen Peroxide	111
4.9	Concluding Remarks	113
	References	114
<b>5</b>	<b>Aerobic Oxidations and Related Reactions Catalyzed by <i>N</i>-Hydroxyphthalimide</b>	<b>119</b>
	YASUTAKA ISHII and SATOSHI SAKAGUCHI	
5.1	Introduction	119
5.2	NHPI-catalyzed Aerobic Oxidation	120
5.2.1	Alkane Oxidations with Dioxygen	120
5.2.2	Oxidation of Alkylarenes	125
5.2.2.1	Oxidation of Alkylbenzenes	125
5.2.2.2	Synthesis of Terephthalic Acid	127
5.2.2.3	Oxidation of Methylpyridines and Methylquinolines	129
5.2.2.4	Oxidation of Hydroaromatic and Benzylic Compounds	131
5.2.3	Preparation of Acetylenic Ketones by Direct Oxidation of Alkynes	132
5.2.4	Oxidation of Alcohols	133

5.2.5	Epoxidation of Alkenes Using Dioxygen as Terminal Oxidant	136
5.2.6	Baeyer-Villiger Oxidation of KA-Oil	137
5.2.7	Preparation of $\epsilon$ -Caprolactam Precursor from KA-Oil	138
5.3	Functionalization of Alkanes Catalyzed by NHPI	139
5.3.1	Carboxylation of Alkanes with CO and O <sub>2</sub>	139
5.3.2	First Catalytic Nitration of Alkanes Using NO <sub>2</sub>	140
5.3.3	Sulfoxidation of Alkanes Catalyzed by Vanadium	142
5.3.4	Reaction of NO with Organic Compounds	144
5.3.5	Ritter-type Reaction with Cerium Ammonium Nitrate (CAN)	145
5.4	Carbon–Carbon Bond Forming Reaction <i>via</i> Generation of Carbon Radicals Assisted by NHPI	147
5.4.1	Oxyalkylation of Alkenes with Alkanes and Dioxygen	147
5.4.2	Synthesis of $\alpha$ -Hydroxy- $\gamma$ -lactones by Addition of $\alpha$ -Hydroxy Carbon Radicals to Unsaturated Esters	148
5.4.3	Hydroxyacylation of Alkenes Using 1,3-Dioxolanes and Dioxygen	149
5.4.4	Hydroacylation of Alkenes Using NHPI as a Polarity-reversal Catalyst	150
5.5	Conclusions	152
	References	153

## 6 Ruthenium-catalyzed Oxidation of Alkenes, Alcohols, Amines, Amides, $\beta$ -Lactams, Phenols, and Hydrocarbons 165

SHUN-ICHI MURAHASHI and NARUYOSHI KOMIYA

6.1	Introduction	165
6.2	RuO <sub>4</sub> -promoted Oxidation	165
6.3	Oxidation with Low-valent Ruthenium Catalysts and Oxidants	169
6.3.1	Oxidation of Alkenes	169
6.3.2	Oxidation of Alcohols	172
6.3.3	Oxidation of Amines	175
6.3.4	Oxidation of Amides and $\beta$ -Lactams	179
6.3.5	Oxidation of Phenols	181
6.3.6	Oxidation of Hydrocarbons	183
	References	186

## 7 Selective Oxidation of Amines and Sulfides 193

JAN-E. BÄCKVALL

7.1	Introduction	193
7.2	Oxidation of Sulfides to Sulfoxides	193
7.2.1	Stoichiometric Reactions	194
7.2.1.1	Peracids	194
7.2.1.2	Dioxiranes	194
7.2.1.3	Oxone and Derivatives	195
7.2.1.4	H <sub>2</sub> O <sub>2</sub> in “Fluorous Phase”	195
7.2.2	Chemocatalytic Reactions	196
7.2.2.1	H <sub>2</sub> O <sub>2</sub> as Terminal Oxidant	196
7.2.2.2	Molecular Oxygen as Terminal Oxidant	205

7.2.2.3	Alkyl Hydroperoxides as Terminal Oxidant	207
7.2.2.4	Other Oxidants in Catalytic Reactions	209
7.2.3	Biocatalytic Reactions	209
7.2.3.1	Haloperoxidases	209
7.2.3.2	Ketone Monooxygenases	210
7.3	Oxidation of Tertiary Amines to <i>N</i> -Oxides	211
7.3.1	Stoichiometric Reactions	212
7.3.2	Chemocatalytic Oxidations	213
7.3.3	Biocatalytic Oxidation	216
7.3.4	Applications of Amine <i>N</i> -oxidation in Coupled Catalytic Processes	216
7.4	Concluding Remarks	218
	References	218

## 8 Liquid Phase Oxidation Reactions Catalyzed by Polyoxometalates 223

RONNY NEUMANN

8.1	Introduction	223
8.2	Polyoxometalates (POMs)	224
8.3	Oxidation with Mono-oxygen Donors	226
8.4	Oxidation with Peroxygen Compounds	231
8.5	Oxidation with Molecular Oxygen	238
8.6	Heterogenization of Homogeneous Reaction Systems	245
8.7	Conclusion	247
	References	248

## 9 Oxidation of Carbonyl Compounds 253

JACQUES LE PAIH, JEAN-CÉDRIC FRISON and CARSTEN BOLM

9.1	Introduction	253
9.2	Oxidations of Aldehydes	253
9.2.1	Conversions of Aldehydes to Carboxylic Acid Derivatives by Direct Oxidations	253
9.2.1.1	Metal-free Oxidants	254
9.2.1.2	Metal-based Oxidants	255
9.2.1.3	Halogen-based Oxidants	257
9.2.1.4	Sulfur- and Selenium-based Oxidants	258
9.2.1.5	Nitrogen-based Oxidants	259
9.2.1.6	Miscellaneous	259
9.2.2	Conversions of Aldehydes into Carboxylic Acid Derivatives by Aldehyde Specific Reactions	259
9.2.2.1	Dismutations and Dehydrogenations	259
9.2.2.2	Oxidative Aldehyde Rearrangements	261
9.2.3	Conversions of Aldehyde Derivatives into Carboxylic Acid Derivatives	263
9.2.3.1	Acetals	263
9.2.3.2	Nitrogen Derivatives	263
9.2.3.3	Miscellaneous Substrates	264
9.2.4	Oxidative Decarboxylations of Aldehydes	265

9.3	Oxidations of Ketones	265
9.3.1	Ketone Cleavage Reactions	265
9.3.1.1	Simple Acyclic Ketones	265
9.3.1.2	Simple Cyclic Ketones	266
9.3.1.3	Functionalized Ketones	267
9.3.2	Oxidative Rearrangements of Ketones	267
9.3.2.1	Baeyer-Villiger Reactions	267
9.3.2.2	Ketone Amidations	272
9.3.2.3	Miscellaneous Rearrangements	275
9.3.3	Willgerodt Reactions	276
9.4	Conclusions	277
	References	277
<b>10</b>	<b>Manganese-based Oxidation with Hydrogen Peroxide</b>	<b>295</b>
	JELLE BRINKSMA, JOHANNES W. DE BOER, RONALD HAGE, and BEN L. FERGINGA	295
10.1	Introduction	295
10.2	Biomimetic Manganese Oxidation Catalysis	296
10.3	Bleaching Catalysis	298
10.4	Catalytic Epoxidation	298
10.4.1	Manganese Porphyrin Catalysts	299
10.4.2	Manganese–salen Catalysts	302
10.4.3	Mn-1,4,7-triazacyclononane Catalysts	305
10.4.4	Miscellaneous Catalysts	311
10.5	cis-Dihydroxylation	314
10.6	Alcohol Oxidation to Aldehydes	317
10.7	Sulfide to Sulfoxide Oxidation	318
10.8	Conclusions	321
	References	321
	<b>Subject Index</b>	<b>327</b>

## 1

## Recent Developments in the Osmium-catalyzed Dihydroxylation of Olefins

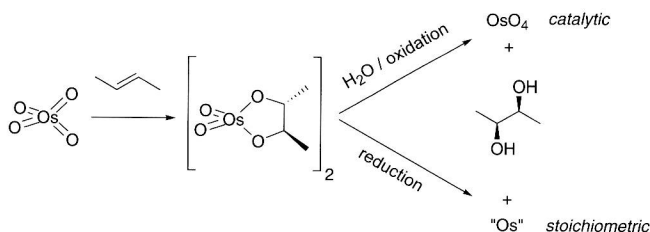
UTA SUNDERMEIER, CHRISTIAN DÖBLER, and MATTHIAS BELLER

### 1.1

#### Introduction

The oxidative functionalization of olefins is of major importance for both organic synthesis and the industrial production of bulk and fine chemicals [1]. Among the different oxidation products of olefins, 1,2-diols are used in a wide variety of applications. Ethylene- and propylene-glycol are produced on a multi-million ton scale per annum, due to their importance as polyester monomers and anti-freeze agents [2]. A number of 1,2-diols such as 2,3-dimethyl-2,3-butanediol, 1,2-octanediol, 1,2-hexanediol, 1,2-pentanediol, 1,2- and 2,3-butanediol are of interest in the fine chemical industry. In addition, chiral 1,2-diols are employed as intermediates for pharmaceuticals and agrochemicals. At present 1,2-diols are manufactured industrially by a two step sequence consisting of epoxidation of an olefin with a hydroperoxide or a peracid followed by hydrolysis of the resulting epoxide [3]. Compared with this process the dihydroxylation of C=C double bonds constitutes a more atom-efficient and shorter route to 1,2-diols. In general the dihydroxylation of olefins is catalyzed by osmium, ruthenium or manganese oxo species. The osmium-catalyzed variant is the most reliable and efficient method for the synthesis of *cis*-1,2-diols [4]. Using osmium in catalytic amounts together with a secondary oxidant in stoichiometric amounts various olefins, including mono-, di-, and trisubstituted unfunctionalized, as well as many functionalized olefins, can be converted into the corresponding diols. OsO<sub>4</sub> as an electrophilic reagent reacts only slowly with electron-deficient olefins, and therefore higher amounts of catalyst and ligand are necessary in these cases. Recent studies have revealed that these substrates react much more efficiently when the pH of the reaction medium is maintained on the acidic side [5]. Here, citric acid appears to be superior for maintaining the pH in the desired range. On the other hand, in another study it was found that providing a constant pH value of 12.0 leads to improved reaction rates for internal olefins [6].

Since its discovery by Sharpless and coworkers, catalytic asymmetric dihydroxylation (AD) has significantly enhanced the utility of osmium-catalyzed dihydroxylation (Scheme 1.1) [7]. Numerous applications in organic synthesis have appeared in recent years [8].



**Scheme 1.1** Osmylation of olefins

While the problem of enantioselectivity has largely been solved through extensive synthesis and screening of cinchona alkaloid ligands by the Sharpless group, some features of this general method remain problematic for larger scale applications. Firstly, the use of the expensive osmium catalyst must be minimized and an efficient recycling of the metal should be developed. Secondly, the applied reoxidants for  $\text{Os}^{\text{VI}}$  species are expensive and lead to overstoichiometric amounts of waste.

In the past several reoxidation processes for osmium(VI) glycolates or other osmium(VI) species have been developed. Historically, chlorates [9] and hydrogen peroxide [10] were first applied as stoichiometric oxidants, however in both cases the dihydroxylation often proceeds with low chemoselectivity. Other reoxidants for osmium(VI) are *tert*-butyl hydroperoxide in the presence of  $\text{Et}_4\text{NOH}$  [11] and a range of *N*-oxides, such as *N*-methylmorpholine *N*-oxide (NMO) [12] (the Upjohn process) and trimethylamine *N*-oxide.  $\text{K}_3[\text{Fe}(\text{CN})_6]$  gave a substantial improvement in the enantioselectivities in asymmetric dihydroxylations when it was introduced as a reoxidant for osmium(VI) species in 1990 [13]. However, even as early on as 1975 it was already being described as an oxidant for Os-catalyzed oxidation reactions [14]. Today the “AD-mix”, containing the catalyst precursor  $\text{K}_2[\text{OsO}_2(\text{OH})_4]$ , the co-oxidant  $\text{K}_3[\text{Fe}(\text{CN})_6]$ , the base  $\text{K}_2\text{CO}_3$ , and the chiral ligand, is commercially available and the dihydroxylation reaction is easy to carry out. However, the production of overstoichiometric amounts of waste remains as a significant disadvantage of the reaction protocol.

This chapter will summarize the recent developments in the area of osmium-catalyzed dihydroxylations, which bring this transformation closer to a “green reaction”. Hence, special emphasis is given to the use of new reoxidants and recycling of the osmium catalyst.

## 1.2

### Environmentally Friendly Terminal Oxidants

#### 1.2.1

##### Hydrogen Peroxide

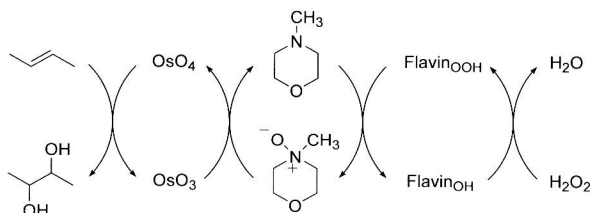
Ever since the Upjohn procedure was published in 1976 the *N*-methylmorpholine *N*-oxide-based procedure has become one of the standard methods for osmium-catalyzed dihydroxylations. However, in the asymmetric dihydroxylation NMO has not



been fully appreciated since it was difficult to obtain high *ee* with this oxidant. Some years ago it was demonstrated that NMO could be employed as the oxidant in the AD reaction to give high *ee* in aqueous *tert*-BuOH with slow addition of the olefin [15].

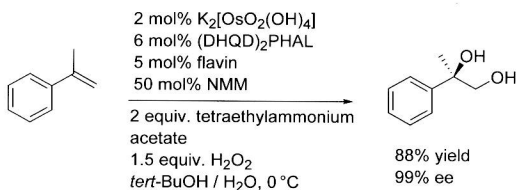
In spite of the fact that hydrogen peroxide was one of the first stoichiometric oxidants to be introduced for the osmium-catalyzed dihydroxylation it was not actually used until recently. When using hydrogen peroxide as the reoxidant for transition metal catalysts, very often there is the big disadvantage that a large excess of  $\text{H}_2\text{O}_2$  is required, implying that the unproductive peroxide decomposition is the major process.

Recently Bäckvall and coworkers were able to improve the  $\text{H}_2\text{O}_2$  reoxidation process significantly by using *N*-methylmorpholine together with flavin as co-catalysts in the presence of hydrogen peroxide [16]. Thus a renaissance of both NMO and  $\text{H}_2\text{O}_2$  was induced. The mechanism of the triple catalytic  $\text{H}_2\text{O}_2$  oxidation is shown in Scheme 1.2.



**Scheme 1.2** Osmium-catalyzed dihydroxylation of olefins using  $\text{H}_2\text{O}_2$  as the terminal oxidant

The flavin hydroperoxide generated from flavin and  $\text{H}_2\text{O}_2$  recycles the *N*-methylmorpholine (NMM) to *N*-methylmorpholine *N*-oxide (NMO), which in turn reoxidizes the  $\text{Os}^{\text{VI}}$  to  $\text{Os}^{\text{VIII}}$ . While the use of hydrogen peroxide as the oxidant without the electron-transfer mediators (NMM, flavin) is inefficient and nonselective, various olefins were oxidized to diols in good to excellent yields employing this mild triple catalytic system (Scheme 1.3).



**Scheme 1.3** Osmium-catalyzed dihydroxylation of  $\alpha$ -methylstyrene using  $\text{H}_2\text{O}_2$

By using a chiral Sharpless ligand high enantioselectivities were obtained. Here, an increase in the addition time for olefin and  $\text{H}_2\text{O}_2$  can have a positive effect on the enantioselectivity.