## Contents

Preface XI List of Contributors XIII

## 1 Recent Developments in Metal-catalyzed Dihydroxylation of Alkenes 1 Man Kin Tse, Kristin Schröder, and Matthias Beller

- 1.1 Introduction 1
- 1.2 Environmentally Friendly Terminal Oxidants 3
- 1.2.1 Hydrogen Peroxide 3
- 1.2.2 Hypochlorite 5
- 1.2.3 Chlorite 8
- 1.2.4 Oxygen or Air 9
- 1.3 Supported Osmium Catalyst 16
- 1.3.1 Nitrogen-group Donating Support 16
- 1.3.2 Microencapsulated OsO<sub>4</sub> 17
- 1.3.3 Supports Bearing Alkenes 19
- 1.3.4 Immobilization by Ionic Interaction 21
- 1.4 Ionic Liquid 22
- 1.5 Ruthenium Catalysts 23
- 1.6 Iron Catalysts 26
- 1.7 Conclusions 32 References 32
- 2 Transition Metal-Catalyzed Epoxidation of Alkenes 37
  - Hans Adolfsson
- 2.1 Introduction 37
- 2.2 Choice of Oxidant for Selective Epoxidation 38
- 2.3 Epoxidations of Alkenes Catalyzed by Early Transition Metals 39
- 2.4 Molybdenum and Tungsten-Catalyzed Epoxidations 42
- 2.4.1 Homogeneous Catalysts Hydrogen Peroxide as the Terminal Oxidant 42
- 2.4.2 Heterogeneous Catalysts 46
- 2.5 Manganese-Catalyzed Epoxidations 47

Modern Oxidation Methods. Edited by Jan-Erling Bäckvall Copyright © 2010 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim ISBN: 978-3-527-32320-3 ۷



- Contents
  - 2.6 Rhenium-Catalyzed Epoxidations 52
  - 2.6.1 MTO as Epoxidation Catalyst - Original Findings 54
  - 2.6.2 The Influence of Heterocyclic Additives 55
  - 2.6.3 The Role of the Additive 58
  - 2.6.4 Other Oxidants 59
  - 2.6.5 Solvents/Media 61
  - 2.6.6 Solid Support 63
  - 2.6.7 Asymmetric Epoxidations Using MTO 64
  - 2.7 Iron-Catalyzed Epoxidations 64
  - 2.7.1 Iron-Catalyzed Asymmetric Epoxidations 72
  - 2.8 Ruthenium-Catalyzed Epoxidations 74
  - 2.9 Epoxidations Using Late Transition Metals 76
  - 2.10 Concluding Remarks 79
    - References 80
  - 3 Organocatalytic Oxidation. Ketone-Catalyzed Asymmetric Epoxidation of Alkenes and Synthetic Applications 85
    - Yian Shi
  - Introduction 85 3.1
  - 3.2 Catalyst Development 86
  - Synthetic Applications 3.3 98
  - Conclusion 109 3.4
    - References 109

4 Catalytic Oxidations with Hydrogen Peroxide in Fluorinated Alcohol Solvents 117

- Albrecht Berkessel
- 4.1 Introduction 117
- 4.2 Properties of Fluorinated Alcohols 118
- 4.2.1 A Detailed Look at the Hydrogen Bond Donor Features of HFIP 120
- 4.3 Epoxidation of Alkenes in Fluorinated Alcohol Solvents 123
- 4.3.1 Alkene Epoxidation with Hydrogen Peroxide - in the Absence of Further Catalysts 123
- 4.3.1.1 On the Mechanism of Epoxidation Catalysis by Fluorinated Alcohols 123
- Alkene Epoxidation with Hydrogen Peroxide in the Presence 4.3.2 of Further Catalysts 129
- 4.3.2.1 Arsines and Arsine Oxides as Catalysts 129
- 4.3.2.2 Arsonic Acids as Catalysts 130
- 4.3.2.3 Diselenides/Seleninic Acids as Catalysts 132
- 4.3.2.4 Rhenium Compounds as Catalysts 133
- 4.3.2.5 Fluoroketones as Catalysts 135
- Sulfoxidation of Thioethers in Fluorinated Alcohol Solvents 4.4 136
- 4.5 Baever-Villiger Oxidation of Ketones in Fluorinated Alcohol Solvents 136

Contents VII

4.5.1	Acid-Catalyzed Baeyer-Villiger Oxidation of Ketones in Fluorinated Alcohol Solvents – Mechanism 139
4.5.2	Baeyer-Villiger Oxidation of Ketones in Fluorinated Alcohol Solvents – Catalysis by Arsonic and Seleninic Acids 141
4.6	Epilog 142
	References 143
5	Modern Oxidation of Alcohols using Environmentally
	Benign Oxidants 147
	Isabel W.C.E. Arends and Roger A. Sheldon
5.1	Introduction 147
5.2	Oxoammonium based Oxidation of Alcohols – TEMPO as Catalyst 147
5.3	Metal-Mediated Oxidation of Alcohols – Mechanism 151
5.4	Ruthenium-Catalyzed Oxidations with $O_2$ 153
5.5	Palladium-Catalyzed Oxidations with O <sub>2</sub> 163
5.5.1	Gold Nanoparticles as Catalysts 169
5.6	Copper-Catalyzed Oxidations with $O_2$ 170
5.7	Other Metals as Catalysts for Oxidation with $O_2$ 174
5.8	Catalytic Oxidation of Alcohols with Hydrogen Peroxide 176
5.8.1	Biocatalytic Oxidation of Alcohols 179
5.9	Concluding Remarks 180
	References 180
6	Aerobic Oxidations and Related Reactions Catalyzed by
	N-Hydroxyphthalimide 187
	Yasutaka Ishii, Satoshi Sakaguchi, and Yasushi Obora
6.1	Introduction 187
6.2	NHPI-Catalyzed Aerobic Oxidation 188
6.2.1	Alkane Oxidations with Dioxygen 188
6.2.2	Oxidation of Alkylarenes 193
6.2.2.1	Synthesis of Terephthalic Acid 196
6.2.2.2	Oxidation of Methylpyridines and Methylquinolines 199
6.2.2.3	Oxidation of Hydroaromatic and Benzylic Compounds 201
6.2.3	Preparation of Acetylenic Ketones by Direct Oxidation of Alkynes 203
6.2.4	
6.2.5	Oxidation of Alcohols 205
	Epoxidation of Alkenes using Dioxygen as Terminal Oxidant 208
6.2.6	Epoxidation of Alkenes using Dioxygen as Terminal Oxidant 208 Baeyer-Villiger Oxidation of KA Oil 209
6.2.6 6.2.7	Epoxidation of Alkenes using Dioxygen as Terminal Oxidant 208 Baeyer-Villiger Oxidation of KA Oil 209 Preparation of ɛ-Caprolactam Precursor from KA Oil 210
6.2.7 6.3	Epoxidation of Alkenes using Dioxygen as Terminal Oxidant 208 Baeyer-Villiger Oxidation of KA Oil 209 Preparation of ε-Caprolactam Precursor from KA Oil 210 Functionalization of Alkanes Catalyzed by NHPI 211
6.2.7 6.3 6.3.1	Epoxidation of Alkenes using Dioxygen as Terminal Oxidant 208 Baeyer-Villiger Oxidation of KA Oil 209 Preparation of $\varepsilon$ -Caprolactam Precursor from KA Oil 210 Functionalization of Alkanes Catalyzed by NHPI 211 Carboxylation of Alkanes with CO and O <sub>2</sub> 211
6.2.7 6.3 6.3.1 6.3.2	Epoxidation of Alkenes using Dioxygen as Terminal Oxidant 208 Baeyer-Villiger Oxidation of KA Oil 209 Preparation of $\varepsilon$ -Caprolactam Precursor from KA Oil 210 Functionalization of Alkanes Catalyzed by NHPI 211 Carboxylation of Alkanes with CO and O <sub>2</sub> 211 First Catalytic Nitration of Alkanes using NO <sub>2</sub> 212
6.2.7 6.3 6.3.1	Epoxidation of Alkenes using Dioxygen as Terminal Oxidant 208 Baeyer-Villiger Oxidation of KA Oil 209 Preparation of $\varepsilon$ -Caprolactam Precursor from KA Oil 210 Functionalization of Alkanes Catalyzed by NHPI 211 Carboxylation of Alkanes with CO and O <sub>2</sub> 211 First Catalytic Nitration of Alkanes using NO <sub>2</sub> 212 Sulfoxidation of Alkanes Catalyzed by Vanadium 214
6.2.7 6.3 6.3.1 6.3.2	Epoxidation of Alkenes using Dioxygen as Terminal Oxidant 208 Baeyer-Villiger Oxidation of KA Oil 209 Preparation of $\epsilon$ -Caprolactam Precursor from KA Oil 210 Functionalization of Alkanes Catalyzed by NHPI 211 Carboxylation of Alkanes with CO and O <sub>2</sub> 211 First Catalytic Nitration of Alkanes using NO <sub>2</sub> 212 Sulfoxidation of Alkanes Catalyzed by Vanadium 214 Reaction of NO with Organic Compounds 217
6.2.7 6.3 6.3.1 6.3.2 6.3.3	Epoxidation of Alkenes using Dioxygen as Terminal Oxidant 208 Baeyer-Villiger Oxidation of KA Oil 209 Preparation of $\varepsilon$ -Caprolactam Precursor from KA Oil 210 Functionalization of Alkanes Catalyzed by NHPI 211 Carboxylation of Alkanes with CO and O <sub>2</sub> 211 First Catalytic Nitration of Alkanes using NO <sub>2</sub> 212 Sulfoxidation of Alkanes Catalyzed by Vanadium 214

6.3.6 Ritter-type Reaction with Cerium Ammonium Nitrate (CAN) 220

VIII	Contents
------	----------

6.4	Carbon-Carbon Bond-Forming Reaction via Catalytic Carbon
	Radicals Generation Assisted by NHPI 222
6.4.1	Oxyalkylation of Alkenes with Alkanes and Dioxygen 222
6.4.2	Synthesis of $\alpha$ -Hydroxy- $\gamma$ -lactones by Addition of $\alpha$ -Hydroxy
	Carbon Radicals to Unsaturated Esters 223
6.4.3	Hydroxyacylation of Alkenes using 1,3-Dioxolanes and Dioxygen 224
6.4.4	Hydroacylation of Alkenes Using NHPI as a Polarity Reversal
	Catalyst 226
6.4.5	Chiral NHPI Derivatives as Enantioselective Catalysts: Kinetic
	Resolution of Oxazolidines 228
6.5	Conclusions 229
	References 230
7	Ruthenium-Catalyzed Oxidation for Organic Synthesis 241
,	Shun-Ichi Murahashi and Naruyoshi Komiya
7.1	Introduction 241
7.2	RuO <sub>4</sub> -Promoted Oxidation $241$
7.3	Oxidation with Low-Valent Ruthenium Catalysts and Oxidants 245
7.3.1	Oxidation of Alkenes 245
7.3.2	Oxidation of Alcohols 249
7.3.3	Oxidation of Amines 255
7.3.4	Oxidation of Amides and $\beta$ -Lactams 260
7.3.5	Oxidation of Phenols 262
7.3.6	Oxidation of Hydrocarbons 265
	References 268
8	Selective Oxidation of Amines and Sulfides 277
	Selective Oxidation of Amines and Sulfides 277 Jan-E. Bäckvall
8.1	Selective Oxidation of Amines and Sulfides 277 Jan-E. Bäckvall Introduction 277
8.1 8.2	<b>Selective Oxidation of Amines and Sulfides</b> 277 Jan-E. Bäckvall Introduction 277 Oxidation of Sulfides to Sulfoxides 277
8.1 8.2 8.2.1	Selective Oxidation of Amines and Sulfides277Jan-E. BäckvallIntroduction277Oxidation of Sulfides to Sulfoxides277Stoichiometric Reactions278
8.1 8.2 8.2.1 8.2.1.1	Selective Oxidation of Amines and Sulfides 277 Jan-E. Bäckvall Introduction 277 Oxidation of Sulfides to Sulfoxides 277 Stoichiometric Reactions 278 Peracids 278
8.1 8.2 8.2.1 8.2.1.1 8.2.1.2	Selective Oxidation of Amines and Sulfides 277 Jan-E. Bäckvall Introduction 277 Oxidation of Sulfides to Sulfoxides 277 Stoichiometric Reactions 278 Peracids 278 Dioxiranes 278
8.1 8.2 8.2.1 8.2.1.1 8.2.1.2 8.2.1.3	Selective Oxidation of Amines and Sulfides 277 Jan-E. Bäckvall Introduction 277 Oxidation of Sulfides to Sulfoxides 277 Stoichiometric Reactions 278 Peracids 278 Dioxiranes 278 Oxone and Derivatives 279
8.1 8.2 8.2.1 8.2.1.1 8.2.1.2 8.2.1.3 8.2.1.4	Selective Oxidation of Amines and Sulfides 277 Jan-E. Bäckvall Introduction 277 Oxidation of Sulfides to Sulfoxides 277 Stoichiometric Reactions 278 Peracids 278 Dioxiranes 278 Oxone and Derivatives 279 $H_2O_2$ in "Fluorous Phase" and Related Reactions 279
8.1 8.2 8.2.1 8.2.1.1 8.2.1.2 8.2.1.3 8.2.1.4 8.2.2	Selective Oxidation of Amines and Sulfides 277 Jan-E. Bäckvall Introduction 277 Oxidation of Sulfides to Sulfoxides 277 Stoichiometric Reactions 278 Peracids 278 Dioxiranes 278 Oxone and Derivatives 279 $H_2O_2$ in "Fluorous Phase" and Related Reactions 279 Chemocatalytic Reactions 280
8.1 8.2 8.2.1 8.2.1.1 8.2.1.2 8.2.1.3 8.2.1.4 8.2.2 8.2.2.1	Selective Oxidation of Amines and Sulfides 277 Jan-E. Bäckvall Introduction 277 Oxidation of Sulfides to Sulfoxides 277 Stoichiometric Reactions 278 Peracids 278 Dioxiranes 278 Oxone and Derivatives 279 $H_2O_2$ in "Fluorous Phase" and Related Reactions 279 Chemocatalytic Reactions 280 $H_2O_2$ as Terminal Oxidant 280
8.1 8.2 8.2.1 8.2.1.1 8.2.1.2 8.2.1.3 8.2.1.4 8.2.2 8.2.2.1 8.2.2.1 8.2.2.2	Selective Oxidation of Amines and Sulfides 277 Jan-E. Bäckvall Introduction 277 Oxidation of Sulfides to Sulfoxides 277 Stoichiometric Reactions 278 Peracids 278 Dioxiranes 278 Oxone and Derivatives 279 $H_2O_2$ in "Fluorous Phase" and Related Reactions 279 Chemocatalytic Reactions 280 $H_2O_2$ as Terminal Oxidant 280 Molecular Oxygen as Terminal Oxidant 293
8.1 8.2 8.2.1 8.2.1.1 8.2.1.2 8.2.1.3 8.2.1.4 8.2.2 8.2.2.1 8.2.2.2 8.2.2.2 8.2.2.3	Selective Oxidation of Amines and Sulfides 277 Jan-E. Bäckvall Introduction 277 Oxidation of Sulfides to Sulfoxides 277 Stoichiometric Reactions 278 Peracids 278 Dioxiranes 278 Oxone and Derivatives 279 $H_2O_2$ in "Fluorous Phase" and Related Reactions 279 Chemocatalytic Reactions 280 $H_2O_2$ as Terminal Oxidant 280 Molecular Oxygen as Terminal Oxidant 293 Alkyl Hydroperoxides as Terminal Oxidant 295
8.1 8.2 8.2.1 8.2.1.1 8.2.1.2 8.2.1.3 8.2.1.4 8.2.2 8.2.2.1 8.2.2.2 8.2.2.2 8.2.2.3 8.2.2.4	Selective Oxidation of Amines and Sulfides 277 Jan-E. Bäckvall Introduction 277 Oxidation of Sulfides to Sulfoxides 277 Stoichiometric Reactions 278 Peracids 278 Dioxiranes 278 Oxone and Derivatives 279 $H_2O_2$ in "Fluorous Phase" and Related Reactions 279 Chemocatalytic Reactions 280 $H_2O_2$ as Terminal Oxidant 280 Molecular Oxygen as Terminal Oxidant 293 Alkyl Hydroperoxides as Terminal Oxidant 295 Other Oxidants in Catalytic Reactions 297
8.1 8.2 8.2.1 8.2.1.1 8.2.1.2 8.2.1.3 8.2.1.4 8.2.2 8.2.2.1 8.2.2.2 8.2.2.3 8.2.2.4 8.2.3	Selective Oxidation of Amines and Sulfides 277 Jan-E. Bäckvall Introduction 277 Oxidation of Sulfides to Sulfoxides 277 Stoichiometric Reactions 278 Peracids 278 Dioxiranes 278 Oxone and Derivatives 279 $H_2O_2$ in "Fluorous Phase" and Related Reactions 279 Chemocatalytic Reactions 280 $H_2O_2$ as Terminal Oxidant 280 Molecular Oxygen as Terminal Oxidant 293 Alkyl Hydroperoxides as Terminal Oxidant 295 Other Oxidants in Catalytic Reactions 297 Biocatalytic Reactions 297
8.1 8.2 8.2.1 8.2.1.1 8.2.1.2 8.2.1.3 8.2.1.4 8.2.2 8.2.2.1 8.2.2.2 8.2.2.1 8.2.2.2 8.2.2.3 8.2.2.4 8.2.3.1	Selective Oxidation of Amines and Sulfides 277 Jan-E. Bäckvall Introduction 277 Oxidation of Sulfides to Sulfoxides 277 Stoichiometric Reactions 278 Peracids 278 Dioxiranes 278 Oxone and Derivatives 279 $H_2O_2$ in "Fluorous Phase" and Related Reactions 279 Chemocatalytic Reactions 280 $H_2O_2$ as Terminal Oxidant 280 Molecular Oxygen as Terminal Oxidant 293 Alkyl Hydroperoxides as Terminal Oxidant 295 Other Oxidants in Catalytic Reactions 297 Biocatalytic Reactions 297 Peroxidases 298
8.1 8.2 8.2.1 8.2.1.1 8.2.1.2 8.2.1.3 8.2.1.4 8.2.2 8.2.2.1 8.2.2.2 8.2.2.3 8.2.2.4 8.2.3.1 8.2.3.1 8.2.3.2	Selective Oxidation of Amines and Sulfides 277 Jan-E. Bäckvall Introduction 277 Oxidation of Sulfides to Sulfoxides 277 Stoichiometric Reactions 278 Peracids 278 Dioxiranes 278 Oxone and Derivatives 279 $H_2O_2$ in "Fluorous Phase" and Related Reactions 279 Chemocatalytic Reactions 280 $H_2O_2$ as Terminal Oxidant 280 Molecular Oxygen as Terminal Oxidant 293 Alkyl Hydroperoxides as Terminal Oxidant 293 Alkyl Hydroperoxides as Terminal Oxidant 297 Biocatalytic Reactions 297 Peroxidases 298 Ketone Monooxygenases 299
8.1 8.2 8.2.1 8.2.1.1 8.2.1.2 8.2.1.3 8.2.1.4 8.2.2 8.2.2.1 8.2.2.2 8.2.2.3 8.2.2.4 8.2.3.1 8.2.3.2 8.3	Selective Oxidation of Amines and Sulfides 277 Jan-E. Bäckvall Introduction 277 Oxidation of Sulfides to Sulfoxides 277 Stoichiometric Reactions 278 Peracids 278 Dioxiranes 278 Oxone and Derivatives 279 $H_2O_2$ in "Fluorous Phase" and Related Reactions 279 Chemocatalytic Reactions 280 $H_2O_2$ as Terminal Oxidant 280 Molecular Oxygen as Terminal Oxidant 293 Alkyl Hydroperoxides as Terminal Oxidant 293 Other Oxidants in Catalytic Reactions 297 Biocatalytic Reactions 297 Peroxidases 298 Ketone Monooxygenases 299 Oxidation of Tertiary Amines to N-Oxides 300
8.1 8.2 8.2.1 8.2.1.1 8.2.1.2 8.2.1.3 8.2.1.4 8.2.2 8.2.2.1 8.2.2.2 8.2.2.3 8.2.2.4 8.2.3.1 8.2.3.1 8.2.3.2	Selective Oxidation of Amines and Sulfides 277 Jan-E. Bäckvall Introduction 277 Oxidation of Sulfides to Sulfoxides 277 Stoichiometric Reactions 278 Peracids 278 Dioxiranes 278 Oxone and Derivatives 279 $H_2O_2$ in "Fluorous Phase" and Related Reactions 279 Chemocatalytic Reactions 280 $H_2O_2$ as Terminal Oxidant 280 Molecular Oxygen as Terminal Oxidant 293 Alkyl Hydroperoxides as Terminal Oxidant 293 Alkyl Hydroperoxides as Terminal Oxidant 297 Biocatalytic Reactions 297 Peroxidases 298 Ketone Monooxygenases 299

8.3.3 Biocatalytic Oxidation 306 8.3.4 Applications of Amine N-Oxidation in Coupled Catalytic Processes 306 8.4 Concluding Remarks 308 References 309 9 Liquid Phase Oxidation Reactions Catalyzed by Polyoxometalates 315 Ronny Neumann 9.1 Introduction 315 9.2 Polyoxometalates (POMs) 316 9.3 Oxidation with Mono-Oxygen Donors 317 9.4 Oxidation with Peroxygen Compounds 323 9.5 Oxidation with Molecular Oxygen 331 9.6 Heterogenization of Homogeneous Reactions - Solid-Liquid, Liquid-Liquid, and Alternative Reaction Systems 341 9.6.1 Solid-Liquid Reactions 341 9.6.2 Liquid-Liquid Reactions and Reactions in 'Alternative' Media 343 9.7 Conclusion 346 References 346 10 Oxidation of Carbonyl Compounds 353 Eric V. Johnston and Jan-E. Bäckvall 10.1 Introduction 353 10.2 Oxidation of Aldehydes to Carboxylic Acids 353 10.2.1 Metal-Free Oxidation of Aldehydes to Carboxylic Acids 354 10.2.2 Metal-Catalyzed Oxidation of Aldehydes to Carboxylic Acids 355 10.3 Oxidation of Ketones 356 10.3.1 Baeyer-Villiger Reactions 356 10.3.2 Catalytic Asymmetric Baeyer-Villiger Reactions 356 10.3.2.1 Chemocatalytic Versions 357 Biocatalytic Versions 358 10.3.2.2 References 365 11 Manganese-Catalyzed Oxidation with Hydrogen Peroxide 371 Wesley R. Browne, Johannes W. de Boer, Dirk Pijper, Jelle Brinksma, Ronald Hage, and Ben L. Feringa 11.1 Introduction 371 Bio-inspired Manganese Oxidation Catalysts 372 11.2 11.3 Manganese-Catalyzed Bleaching 375 Epoxidation and cis-Dihydroxylation of Alkenes 375 11.4 11.4.1 Manganese Salts 376 11.4.2 Porphyrin-Based Catalysis 378 11.4.3 Salen-Based Systems 381 Tri- and Tetra-azacycloalkane Derivatives 385 11.4.4 Tetra-azacycloalkane Derivatives 386 11.4.4.1 11.4.4.2 Triazacyclononane Derivatives 387

X Contents

11.4.4.3	Manganese Complexes for Alkene Oxidation Based
	on Pyridyl Ligands 403
11.5	Manganese Catalysts for the Oxidation of Alkanes, Alcohols, and Aldehydes 406
11.5.1	Oxidation of Alkanes 406
11.5.2	Oxidation of Alcohols and Aldehydes 407
11.5.3	Sulfides, Sulfoxides, and Sulfones 408
11.6	Conclusions 411
	References 412
12	Biooxidation with Cytochrome P450 Monooxygenases 421
	Marco Girhard and Vlada B. Urlacher
12.1	Introduction 421
12.2	Properties of Cytochrome P450 Monooxygenases 422
12.2.1	Structure 422
12.2.2	Enzymology 423
12.2.3	Reactions Catalyzed by P450s 425
12.2.4	P450s as Industrial Biocatalysts 429
12.2.4.1	Advantages 429
12.2.4.2	Challenges in the Development of Technical P450 Applications 429
12.2.4.3	General Aspects of Industrial Application and Engineering of P450s 430
12.3	Application and Engineering of P450s for the Pharmaceutical
	Industry 430
12.3.1	Microbial Oxidations with P450s for Synthesis
	of Pharmaceuticals 431
12.3.2	Application of Mammalian P450s for Drug Development 434
12.3.2.1	Enhancement of Recombinant Expression in E. coli 435
12.3.2.2	Enhancement of Activity and Selectivity and Engineering of
	Novel Activities 436
12.3.2.3	Construction of Artificial Self-Sufficient Fusion Proteins 436
12.4	Application of P450s for Synthesis of Fine Chemicals 437
12.5	Engineering of P450s for Biocatalysis 438
12.5.1	Cofactor Substitution and Regeneration 438
12.5.1.1	Cofactor Substitution In Vitro 438
12.5.1.2	Cofactor Regeneration In Vitro 439
12.5.1.3	Cofactor Regeneration in Whole-Cells 439
12.5.2	Construction of Artificial Fusion Proteins 440
12.5.3	Engineering of New Substrate Specificities 440
12.5.3.1	P450 <sub>cam</sub> from Pseudomonas putida 440
12.5.3.2	P450 <sub>BM3</sub> from Bacillus megaterium 442
12.6	Future Trends 443
	References 444

Index 451