

Contents

Preface

xi

Part 1 Novel reaction conditions for biotransformation

1

CHAPTER 1

Biotransformation in ionic liquid

3

Toshiyuki Itoh

1. Introduction	3
2. Ionic Liquids as a Reaction Medium for Biotransformation	3
3. Lipase-Catalyzed Reaction in an Ionic Liquid Solvent System	7
4. Activation of Lipase by an Ionic Liquid	10
5. Various Biotransformations in an Ionic Liquid Solvent System	15
6. Concluding Remarks	18
References	18

CHAPTER 2

Temperature control of the enantioselectivity in the lipase-catalyzed resolutions

21

Takashi Sakai

1. Introduction	21
2. Finding of the "Low-Temperature Method" in the Lipase-Catalyzed Kinetic Resolution	22
3. Theory of Temperature Effect on the Enantioselectivity	23
4. General Applicability of the "Low-Temperature Method" Examined	28
4.1. Application to solketal and other primary and secondary alcohols	28
4.2. Resolution of ($\pm$)-2-hydroxy-2-(pentafluorophenyl)acetonitrile	30
4.3. Immobilization of lipase on porous ceramic support (<i>Toyonite</i>) for acceleration	31
4.4. Structural optimization of organic bridges on <i>Toyonite</i>	32
4.5. Practical resolution of azirine 1 by the "low-temperature method" combined with <i>Toyonite</i> -immobilized lipase and optimized acylating agent	33
4.6. Resolution of ($2R^*$, $3S^*$)- and ($2R^*$, $3R^*$)-3-methyl-3-phenyl-2-aziridinemethanols	34
4.7. Resolution of 5-(hydroxymethyl)-3-phenyl-2-isoxazoline	36
4.8. Application of temperature control to asymmetric protonation	37
4.9. Lipase-catalyzed resolutions at high temperatures up to 120°C	37
5. Low-Temperature Reactions in Literatures	37
6. Lipase-Catalyzed Resolution of Primary Alcohols: Promising Candidates for the "Low-Temperature Method"	40
7. Conclusion	45
References	45

CHAPTER 3**Future directions in photosynthetic organisms-catalyzed reactions 51***Kaoru Nakamura*

1. Introduction	51
2. Reduction Reaction	51
3. Oxidation and Hydroxylation	55
4. Removal of Organic and Inorganic Substances in Wastewater	56
5. Conclusion	57
References	57

CHAPTER 4**Catalysis by enzyme-metal combinations 59***Mahn-Joo Kim, Jaiwook Park, Yangsoo Ahn, Palakodety R. Krishna*

1. Introduction	59
2. Dynamic Kinetic Resolutions by Enzyme-Metal Combinations	60
2.1. DKR of secondary alcohols	60
3. Asymmetric Transformations by Enzyme-Metal Combinations	73
3.1. Asymmetric transformation of ketone	73
3.2. Asymmetric transformation of enol ester	75
3.3. Asymmetric transformation of ketoxime	76
4. Conclusion	78
Acknowledgements	78
References	79

Part 2 Uncomon kind of biocatalytic reaction 81**CHAPTER 5****Biological Kolbe-Schmitt carboxylation 83****Possible use of enzymes for the direct carboxylation of organic substrates***Toyokazu Yoshida, Toru Nagasawa*

1. Introduction	83
2. Enzymes Catalyzing the Carboxylation of Phenolic Compounds	84
2.1. 4-Hydroxybenzoate decarboxylase (EC 4.1.1.61)	85
2.2. 3,4-Dihydroxybenzoate decarboxylase (EC 4.1.1.63)	87
2.3. Phenolphosphate carboxylase (EC 4.1.1.-) in <i>Thauera aromatica</i>	88
2.4. 2,6-Dihydroxybenzoate decarboxylase	91
2.5. 2,3-Dihydroxybenzoate decarboxylase	95
3. Enzymes Catalyzing the Direct Carboxylation of Heterocyclic Compounds	95
3.1. Pyrrole-2-carboxylate decarboxylase	96
3.2. Indole-3-carboxylate decarboxylase	99
4. Structure Analysis of Decarboxylases Catalyzing CO ₂ Fixation	101
4.1. Class I decarboxylases	102
4.2. Class II decarboxylases	103
4.3. Phenylphosphate carboxylase	103
5. Conclusion	103
References	104

CHAPTER 6**Discovery, redesign and applications of Baeyer–Villiger monooxygenases 107***Daniel E. Torres Pazmiño, Marco W. Fraaije*

1. Introduction	107
2. Biocatalytic Properties of Recombinant Available BVMOs	110
2.1. Discovery of novel BVMOs	112
2.2. Exploring sequenced (meta)genomes for novel BVMOs	114
2.3. Screening the metagenome for novel BVMOs	118
2.4. Redesign of BVMOs	119
3. Conclusions: Future Directions	122
References	125

CHAPTER 7**Enzymes in aldoxime–nitrile pathway: versatile tools in biocatalysis 129***Yasuhisa Asano*

1. Introduction	129
2. Screening for New Microbial Enzymes by Enrichment and Acclimation Culture Techniques	129
3. Development of Nitrile-Degrading Enzymes	131
4. Screening for Heat-Stable NHase	131
5. Screening for NHase with PCR	132
6. Nitrile Synthesis Using a New Enzyme, Aldoxime Dehydratase	133
6.1. Aldoxime-converting enzymes	133
6.2. Isolation of microorganisms having aldoxime dehydratase activity	134
6.3. Purification, characterization and primary structure determination of aldoxime dehydratase	134
6.4. Synthesis of nitriles from aldoxime with aldoxime dehydratase	135
6.5. Distribution of aldoxime dehydratase	136
6.6. Molecular screening for “aldoxime–nitrile pathway”	136
7. Conclusions	137
Acknowledgments	137
References	137

CHAPTER 8**Addition of hydrocyanic acid to carbonyl compounds 141***Franz Effenberger, Anja Bohrer, Siegfried Förster*

1. Introduction	141
2. Optimized Reaction Conditions for the HNL-Catalyzed Formation of Chiral Cyanohydrins	143
3. Synthetic Potential of Chiral Cyanohydrins in Stereoselective Synthesis	145
3.1. Chiral 2-hydroxy carboxylic acids	145
3.2. Optically active 1,2-amino alcohols	147
3.3. Stereoselective substitution of the hydroxyl group in chiral cyanohydrins	148
3.4. Stereoselective synthesis of substituted cyclohexanone cyanohydrins	149

4. Crystal Structures of Hydroxynitrile Lyases and Mechanism of Cyanogenesis	149
4.1. Crystal structures of HNLs	151
4.2. Reaction mechanism of cyanogenesis	151
4.3. Changing substrate specificity and stereoselectivity applying Trp128 mutants of wt-MeHNL	152
5. Conclusions	153
References	154

Part 3 Novel compounds synthesized by biotransformations 157

CHAPTER 9 Chiral heteroatom-containing compounds 159

Piotr Kielbasiński, Marian Mikołajczyk

1. Introduction	159
2. Organosulfur Compounds	160
2.1. C-chiral hydroxy sulfides and derivatives	160
2.2. C-chiral hydroxyalkyl sulfones	163
2.3. C-chiral alkyl sulfates	165
2.4. Other C-chiral organosulfur compounds	166
2.5. S-chiral sulfinylcarboxylates	166
2.6. S-chiral hydroxy sulfoxides	168
2.7. S-chiral sulfinamides	169
2.8. S-chiral sulfoximines	171
3. Organophosphorus Compounds	172
3.1. C-chiral hydroxy phosphorus derivatives	172
3.2. C-chiral amino phosphorus compounds	180
3.3. P-chiral phosphoro-acetates	183
3.4. P-chiral hydroxy phosphoryl compounds	186
3.5. P-chiral hydroxy phosphorus P-boranes	191
3.6. Stereocontrolled transformations of organophosphorus acid esters	192
4. Organosilanes	196
5. Organogermanes	197
6. Future Perspectives	197
References	199

CHAPTER 10 Enzymatic polymerization 205

Hiroshi Uyama

1. Introduction	205
2. Enzymatic Synthesis of Polyesters	206
2.1. Ring-opening polymerization to polyesters	207
2.2. Polycondensation of dicarboxylic acid derivatives and glycols to polyesters	212
2.3. Enzymatic synthesis of functional polyesters	219
3. Enzymatic Synthesis of Phenolic Polymers	228
3.1. Enzymatic oxidative polymerization of phenols	228
3.2. Enzymatic synthesis of functional phenolic polymers	233

3.3. Artificial urushi	238
3.4. Enzymatic synthesis and biological properties of flavonoid polymers	240
4. Concluding Remarks	244
References	245

CHAPTER 11

Synthesis of naturally occurring β -D-glucopyranosides based on enzymatic β -glucosidation using β -glucosidase from almond 253

Hiroyuki Akita

1. Introduction	253
2. Synthesis of β -D-Glucopyranoside Under Kinetically Controlled Condition	255
2.1. Synthesis of naturally occurring β -D-glucopyranoside	259
3. Synthesis of β -D-Glucopyranoside Under Equilibrium-Controlled Condition	262
3.1. Immobilization of β -D-glucosidase using prepolymer	263
3.2. Enzymatic transglucosidation	263
3.3. Synthesis of naturally occurring benzyl β -D-glucopyranoside	267
3.4. Synthesis of phenethyl β -D-glycopyranoside	270
3.5. Synthesis of (3Z)-hexenyl β -D-glycopyranoside	272
3.6. Synthesis of geranyl β -D-glycopyranoside	275
3.7. Synthesis of Sacranosides A (89) and B (90)	277
3.8. Synthesis of naturally occurring <i>n</i> -octyl β -D-glucopyranosides	278
3.9. Synthesis of naturally occurring hexyl β -D-glucopyranosides	280
3.10. Synthesis of naturally occurring phenylpropenoid β -D-glucopyranoside	282
4. Future Aspect	287
5. Conclusion	289
References	289

Part 4 Use of molecular biology technique to find novel biocatalyst 291

CHAPTER 12

Future directions in alcohol dehydrogenase-catalyzed reactions 293

Jon D. Stewart

1. Introduction	293
2. Future Progress in the Discovery Phase of Dehydrogenases	295
2.1. Accurately predicting dehydrogenase structures	295
2.2. Predicting dehydrogenase substrate acceptance and stereoselectivities.	296
2.3. Rapid screening of novel dehydrogenases	296
2.4. Dehydrogenases for large substrates	299
2.5. Dehydrogenase modules within larger assemblies as monofunctional catalysts	299
2.6. Dehydrogenase catalysis of other 1,2-carbonyl additions	300
3. Future Progress in Dehydrogenase Process Development	300
3.1. Improving the kinetic properties of dehydrogenases	301
3.2. Reductions of highly hydrophobic substrates	301
3.3. Cofactorless dehydrogenases?	302
4. Conclusions	302
Acknowledgments	303
References	303

CHAPTER 13**Enzymatic decarboxylation of synthetic compounds****305***Kenji Miyamoto, Hiromichi Ohta*

1. Introduction	305
2. Arylmalonate Decarboxylase	309
2.1. Discovery of arylmalonate decarboxylase and its substrate specificity	310
2.2. Purification of the enzyme and cloning of the gene	311
2.3. Reaction mechanism	312
2.4. Inversion of enantioselectivity based on the reaction mechanism and homology	317
2.5. Addition of racemase activity	319
3. Transketolase-Catalyzed Reaction	321
3.1. Substrate specificity and stereochemical source of TKase-catalyzed reaction	322
3.2. Application of TKase-catalyzed reaction in organic syntheses	322
3.3. Tertiary structure and mutagenesis studies	329
4. Future Trends of this Area	331
4.1. Application of decarboxylation reaction to dialkylmalonates	331
4.2. Decarboxylation of various carboxylic acids	332
4.3. Oxidative decarboxylation of β -hydroxycarboxylic acids	333
4.4. Carboxylation	336
4.5. Development of biotransformation via enolate	337
4.6. Utilization of database and informatics	339
5. Conclusion	339
References	340

Index**345**