

Contents

Preface XI

List of Contributors XIII

1	Asymmetric Transformations by Coupled Enzyme and Metal Catalysis: Dynamic Kinetic Resolution	1
	<i>Mahn-joo Kim, Jaiwook Park, and Yoon Kyung Choi</i>	
1.1	Introduction	1
1.2	Some Fundamentals for DKR	2
1.2.1	Enzymes for Kinetic Resolution	2
1.2.2	Metal Catalysts for Racemization	3
1.2.3	Enzyme–Metal Combination for DKR	5
1.2.4	(<i>R</i>)- and (<i>S</i>)-Selective DKR	5
1.3	Examples of DKR	6
1.3.1	First DKR of Secondary Alcohols	6
1.3.2	DKR of Secondary Alcohols with Racemization Catalyst 1	6
1.3.3	DKR of Secondary Alcohols with Racemization Catalyst 2	8
1.3.4	DKR of Secondary Alcohols with Racemization Catalyst 3	9
1.3.5	DKR of Secondary Alcohols with Racemization Catalyst 4	10
1.3.6	DKR of Secondary Alcohols with Racemization Catalyst 5	10
1.3.7	DKR of Secondary Alcohols with Racemization Catalyst 6	11
1.3.8	DKR of Secondary Alcohols with Racemization Catalyst 7	12
1.3.9	DKR of Secondary Alcohols with Air-Stable Racemization Catalysts	13
1.3.10	DKR of Secondary Alcohols with Racemization Catalyst 10	14
1.3.11	DKR of Secondary Alcohols with Aluminum Catalysts	14
1.3.12	DKR of Secondary Alcohols with Vanadium Catalysts	15
1.4	Conclusions	16
	References	17

2	Chemoenzymatic Routes to Enantiomerically Pure Amino Acids and Amines	21
	<i>Nicholas J. Turner</i>	
2.1	Introduction	21
2.2	Amino Acids	23
2.3	Amines	33
	References	38
3	Oxidizing Enzymes in Multi-Step Biotransformation Processes	41
	<i>Stephanie G. Burton and Marilize le Roes-Hill</i>	
3.1	Oxidizing Enzymes in Biocatalysis	41
3.2	Classes of Oxidizing Enzymes	41
3.3	Mechanisms of Biological Oxidation and Implications for Multi-Enzyme Biocatalysis	44
3.4	Multi-Step Biotransformation Processes Involving Oxidation	45
3.5	Design and Development of New Multi-Enzyme Oxidizing Processes	
3.5.1	Coupling Redox Enzymes	48
3.5.2	Cofactor Recycle in Multi-Step Oxidizing Biocatalytic Systems	51
3.6	Examples of Multi-Enzyme Biotransformation Processes Involving Oxidizing Enzymes	52
3.6.1	Coupling of Oxidases with Non-Redox Enzymes	53
3.6.2	Biocatalytic Systems Involving Coupled Oxidizing Enzymes	53
3.7	Multi-Enzyme Systems in Whole-Cell Biotransformations and Expression of Redox Systems in Recombinant Hosts	55
3.8	Other Applications of Multi-Enzyme Oxidizing Systems	56
3.9	Conclusions	58
	References	58
4	Dihydroxyacetone Phosphate-Dependent Aldolases in the Core of Multi-Step Processes	61
	<i>Laura Iturrate and Eduardo García-Junceda</i>	
4.1	Introduction	61
4.2	DHAP-Dependent Aldolases	63
4.2.1	Problem of DHAP Dependence	63
4.2.2	DHAP-Dependent Aldolases in the Core of Aza Sugar Synthesis	68
4.2.3	Combined Use of Aldolases and Isomerases for the Synthesis of Natural and Unnatural Sugars	71
4.2.4	DHAP-Dependent Aldolases in the Synthesis of Natural Products	73
4.3	Fructose-6-Phosphate Aldolase: An Alternative to DHAP-Dependent Aldolases?	76
4.4	Conclusions	78
	References	79

5	Multi-Enzyme Systems for the Synthesis of Glycoconjugates	83
	<i>Birgit Sauerzapfe and Lothar Elling</i>	
5.1	Introduction	83
5.2	<i>In Vitro</i> and <i>In Vivo</i> Multi-Enzyme Systems	85
5.3	Combinatorial Biocatalysis	86
5.3.1	Synthesis and <i>In Situ</i> Regeneration of Nucleotide Sugars	88
5.3.2	Synthesis of Oligosaccharides, Glycopeptides and Glycolipids	
	Oligosaccharides	94
5.4	Combinatorial Biosynthesis	97
5.4.1	Synthesis of Oligosaccharides with Metabolically Engineered Cells	98
5.5	Conclusions	102
	References	102
6	Enzyme-Catalyzed Cascade Reactions	109
	<i>Roger A. Sheldon</i>	
6.1	Introduction	109
6.2	Enzyme Immobilization	110
6.3	Reaction Types: General Considerations	111
6.4	Chiral Alcohols	112
6.5	Chiral Amines	114
6.6	Chiral Carboxylic Acid Derivatives	121
6.7	C–C Bond Formation: Aldolases	127
6.8	Oxidations with O ₂ and H ₂ O ₂	130
6.9	Conclusions and Prospects	131
	References	132
7	Multi-modular Synthases as Tools of the Synthetic Chemist	137
	<i>Michael D. Burkart and Junhua Tao</i>	
7.1	Introduction	137
7.2	Excised Domains for Chemical Transformations	139
7.2.1	Function of Individual Domains and Domain Autonomy	139
7.2.2	Heterocyclization and Aromatization	139
7.2.3	Macrocyclization	144
7.2.4	Halogenation	147
7.2.5	Glycosylation	150
7.2.6	Methyltransferases	151
7.2.7	Oxidation	153
7.3	Conclusions	155
	References	156

- 8 Modifying the Glycosylation Pattern in Actinomycetes by Combinatorial Biosynthesis 159**
José A. Salas and Carmen Méndez
- 8.1 Bioactive Natural Products in Actinomycetes 159
- 8.2 Deoxy Sugar Biosynthesis and Gene Clusters 161
- 8.3 Characterization of Sugar Biosynthesis Enzymes 161
- 8.4 Strategies for the Generation of Novel Glycosylated Derivatives 165
- 8.4.1 Gene Inactivation 165
- 8.4.2 Gene Expression 166
- 8.4.3 Combining Gene Inactivation and Gene Expression 166
- 8.4.4 Endowing a Host with the Capability of Synthesizing Different Sugars 166
- 8.5 Generation of Glycosylated Derivatives of Bioactive Compounds 166
- 8.5.1 Macrolides 167
- 8.5.2 Aureolic Acid Group 175
- 8.5.3 Angucyclines 181
- 8.5.4 Anthracyclines 186
- 8.5.5 Indolocarbazoles 191
- 8.5.6 Aminocoumarins 193
- References 194
- 9 Microbial Production of DNA Building Blocks 199**
Jun Ogawa, Nobuyuki Horinouchi, and Sakayu Shimizu
- 9.1 Introduction 199
- 9.2 Screening of Acetaldehyde-Tolerant Deoxyriboaldolase and Its Application for DR5P Synthesis 200
- 9.3 Construction of Deoxyriboaldolase-Overexpressing *E. coli* and Metabolic Analysis of the *E. coli* Transformants for DR5P Production from Glucose and Acetaldehyde 201
- 9.4 Efficient Production of DR5P from Glucose and Acetaldehyde by Coupling of the Alcoholic Fermentation System of Baker's Yeast and Deoxyriboaldolase-Expressing *E. coli* 203
- 9.5 Biochemical Retrosynthesis of 2'-Deoxyribonucleosides from Glucose Acetaldehyde and a Nucleobase: Three-Step Multi-Enzyme-Catalyzed Synthesis 204
- 9.6 One-Pot Multi-Step Enzymatic Synthesis of 2'-Deoxyribonucleoside from Glucose, Acetaldehyde and a Nucleobase 206
- 9.7 Improvement of the One-Pot Multi-Step Enzymatic Process for Practical Production of 2'-Deoxyribonucleoside from Glucose, Acetaldehyde and a Nucleobase 207
- 9.8 Conclusions 208
- References 210

10	Combination of Biocatalysis and Chemical Catalysis for the Preparation of Pharmaceuticals Through Multi-Step Syntheses	213
	<i>Vicente Gotor-Fernández, Rosario Brieva, and Vicente Gotor</i>	
10.1	Introduction: Biocatalysis and Chemical Catalysis	213
10.2	Pharmaceuticals with Hydrolases	214
10.2.1	Enzymatic Hydrolysis	214
10.2.2	Enzymatic Transesterification	219
10.2.3	Enzymatic Aminolysis	222
10.3	Pharmaceuticals with Oxidoreductases	226
10.4	Pharmaceuticals with Lyases	227
10.5	Conclusions	230
	References	231
	Index	235