

Handbook of Green Chemistry

Edited by Paul T. Anastas

 WILEY-VCH

Green Catalysis

Volume 3: Biocatalysis

Volume Editor:
Robert H. Crabtree



Contents

About the Editors XI

List of Contributors XIII

1	Catalysis with Cytochrome P450 Monooxygenases	1
	<i>Vlada B. Urlacher</i>	
1.1	Properties of Cytochrome P450 Monooxygenases	1
1.1.1	General Aspects	1
1.1.2	Chemistry of Substrate Oxidation by P450 Monooxygenases	2
1.1.3	Redox Partners of P450 Monooxygenases	4
1.1.4	Major Reactions Catalyzed by P450 Monooxygenases	5
1.2	Biotechnological Applications of P450 Monooxygenases	7
1.2.1	Human P450s in Drug Development	7
1.2.2	Microbial Oxidation for Synthesis of Pharmaceutical Intermediates	8
1.2.3	Plant P450s and Transgenic Plants	10
1.3	Optimization of P450 Monooxygenase-Based Catalytic Systems	12
1.3.1	Replacement or Regeneration of the Cofactor NAD(P)H	12
1.3.2	Engineering of New Substrate Specificities of P450s	14
1.3.2.1	Engineering of Bacterial P450s	14
1.3.2.2	Engineering of Mammalian P450s	16
1.3.3	Stability of P450s	17
1.3.3.1	Thermostability of P450s	17
1.3.3.2	Process Stability of P450s	17
1.4	Outlook	18
	References	19
2	Biocatalytic Hydrolysis of Nitriles	27
	<i>Dean Brady</i>	
2.1	The Problem with Nitrile Hydrolysis	27
2.2	Biocatalysis as a Green Solution	28
2.3	Nitrile Biocatalysts	29

2.3.1	Nitrilase	29
2.3.2	Nitrile Hydratase	30
2.3.3	Amidase	32
2.4	Synthetic Utility	32
2.4.1	Chemoselectivity	32
2.4.2	Regioselectivity	33
2.4.3	Enantioselectivity	33
2.5	Commercial Examples	35
2.5.1	Chemical Synthesis	35
2.5.1.1	Acrylamide	35
2.5.1.2	Nicotinamide and Nicotinic Acid	35
2.5.1.3	Atorvastatin	36
2.5.1.4	5-Cyanovaleramide	37
2.5.1.5	Mandelic Acid	37
2.5.1.6	Pyrazinecarboxylic Acid	38
2.5.1.7	(<i>E</i>)-2-Methyl-2-Butenoic Acid	38
2.5.1.8	1,5-Dimethyl-2-Piperidone, a Lactam	38
2.5.1.9	3-Hydroxyvaleric Acid	39
2.5.2	Surface Modification of Polymers	40
2.5.3	Bioremediation	41
2.6	Challenges	41
2.6.1	Biocatalyst Stability	41
2.6.2	Availability	43
2.7	Conclusion	44
	References	45

3 Biocatalytic Processes Using Ionic Liquids and Supercritical Carbon Dioxide 51

Pedro Lozano, Teresa De Diego, and José L. Iborra

3.1	Introduction	51
3.2	Biocatalytic Processes in Ionic Liquids	52
3.2.1	Solvent Properties of ILs for Biocatalysis	52
3.2.2	Enzymes in ILs	54
3.3	Biocatalytic Processes in Supercritical Carbon Dioxide	59
3.3.1	Basic Properties of scCO ₂	59
3.3.2	Enzymes in scCO ₂	61
3.4	Biocatalysis in IL–scCO ₂ Biphasic Systems	63
3.4.1	Phase Behavior of IL–scCO ₂ Systems	64
3.4.2	Biocatalytic Processes in IL–scCO ₂ Biphasic Systems	66
3.5	Future Trends	69
	References	70

4 Thiamine-Based Enzymes for Biotransformations 75

Martina Pohl, Dörte Gocke, and Michael Müller

4.1	Introduction	75
-----	--------------	----

4.1.1	Thiamine Diphosphate	76
4.1.2	Enzyme Structures	79
4.1.3	Reaction Mechanism	79
4.1.3.1	Lyase and Carboligase Activity Occur at the Same Active Site	79
4.2	Carboligation: Chemo- and Stereoselectivity	81
4.2.1	Carboligations with Two Different Aldehydes	81
4.2.1.1	Chemoselectivity	81
4.2.1.2	Stereoselectivity	83
4.3	Selected Enzymes	84
4.3.1	2-Keto Acid Decarboxylases	84
4.3.1.1	Pyruvate Decarboxylases	84
4.3.1.2	Branched-Chain Keto Acid Decarboxylases	90
4.3.1.3	Benzoylformate Decarboxylases	90
4.3.1.4	Phenylpyruvate Decarboxylases/Indole-3-pyruvate Decarboxylases	91
4.3.2	Benzaldehyde Lyases	92
4.3.3	Acetohydroxy Acid Synthases	94
4.4	Enzymes for Special Products	94
4.4.1	Mixed Carboligation of Benzaldehyde and Acetaldehyde	94
4.4.2	Mixed Carboligation of Larger Aliphatic and Substituted Aromatic Aldehydes	97
4.4.3	Self-Ligation of Aromatic Aldehydes	97
4.4.4	Self-Ligation of Aliphatic Aldehydes	97
4.4.5	Carboligation of Unstable Aldehydes	98
4.4.5.1	LlKdcA Catalyzes the Mixed Carboligation of CH-Acidic Aldehydes and Acetaldehyde	98
4.4.6	Accessing (<i>S</i>)-2-Hydroxy Ketones	98
4.5	Investigation of Structure–Function Relationships	100
4.5.1	Deducing General Principles for Chemo- and Enantioselectivity	100
4.5.2	Substrate Channel	103
4.5.3	Proton Relay System	103
4.5.4	Donor Binding Site	103
4.5.5	Acceptor Binding Site	104
4.5.5.1	The <i>S</i> -Pocket Approach	105
4.5.5.2	<i>S</i> -Pockets are Widespread Among ThDP-dependent Enzymes but Not Always Accessible	105
4.5.5.3	Carboligation of Two Similar Aldehydes	107
	References	108

5 **Baeyer–Villiger Monooxygenases in Organic Synthesis** 115

Anett Kirschner and Uwe T. Bornscheuer

5.1	Introduction	115
5.2	General Aspects of the Baeyer–Villiger Oxidation	116
5.2.1	Mechanistic Aspects	116

5.2.2	Chemical Versus Enzymatic Baeyer–Villiger Oxidation	116
5.3	Biochemistry of Baeyer–Villiger Monooxygenases	119
5.3.1	Catalytic Mechanism	119
5.3.2	Structural Features	120
5.4	Application of Baeyer–Villiger Monooxygenases in Organic Chemistry	121
5.4.1	Isolated Enzymes Versus Whole Cells	121
5.4.2	Baeyer–Villiger Monooxygenases Relevant for Synthetic Applications	124
5.4.3	Representative Synthetic Applications	126
5.4.3.1	Kinetic Resolutions of Racemic Ketones	126
5.4.3.2	Desymmetrization of Prochiral Ketones	130
5.4.3.3	Regiodivergent Transformations	135
5.4.3.4	Large-Scale Application	138
5.4.3.5	Heteroatom Oxidation	138
5.5	Protein Engineering	140
5.6	Conclusions and Perspectives	143
	References	143
6	Bioreduction by Microorganisms	151
	<i>Leandro Helgueira Andrade and Kaoru Nakamura</i>	
6.1	Introduction	151
6.2	Enzymes and Coenzymes	152
6.2.1	Classification	152
6.2.2	Hydrogen Source	153
6.2.2.1	Alcohols as a Hydrogen Source for Reduction	153
6.2.2.2	Sugars as a Hydrogen Source for Reduction	153
6.2.2.3	Formate as a Hydrogen Source for Reduction	154
6.2.2.4	Molecular Hydrogen as a Hydrogen Source for Reduction	154
6.2.2.5	Light Energy as a Hydrogen Source for Reduction	155
6.2.2.6	Electric Power as a Hydrogen Source for Reduction	155
6.3	Methodologies	156
6.3.1	Search for the Ideal Biocatalysts	156
6.3.1.1	Biocatalysts from Screening Techniques	157
6.3.1.2	Biocatalysts from Recombinant Microorganisms	158
6.3.2	Reaction Systems for Bioreduction	159
6.3.2.1	Bioreduction Using Whole-Cell Biocatalysts in an Aqueous Solvent	160
6.3.2.2	Bioreduction Using Whole-Cell Biocatalysts in a Conventional Organic Solvent and an Aqueous–Organic Solvent	161
6.3.2.3	Bioreduction Using Whole-Cell Biocatalysts in Supercritical Carbon Dioxide, Ionic Liquids and Fluorous Solvents	164
6.3.2.4	Bioreduction Using Isolated Enzymes	165
6.4	Conclusion	167
	References	167

7	Biotransformations and the Pharma Industry	171
	<i>Hans-Peter Meyer, Oreste Ghisalba, and James E. Leresche</i>	
7.1	Introduction	171
7.2	Small-Molecule Pharmaceuticals	172
7.3	The Concept of Green Chemistry	174
7.4	The Organic Chemistry Toolbox	176
7.4.1	Small-Molecule Synthesis	177
7.4.2	Peptide Synthesis	177
7.4.3	What Should Chemists Consider?	189
7.5	The Enzyme Toolbox (a Selective Analysis)	190
7.5.1	EC 1 Oxidoreductases	191
7.5.1.1	EC 1.2.1 Dehydrogenases	192
7.5.1.2	EC 1.14.14 P450 Monooxygenases	194
7.5.1.3	EC 1.14.13 Baeyer–Villiger Monooxygenases	195
7.5.1.4	EC 1.4.3 Oxidases	196
7.5.2	EC 2 Transferases	196
7.5.2.1	EC 2.3 Acyltransferases	196
7.5.2.2	EC 2.4 Glycosyltransferases	196
7.5.2.3	EC 2.6 Transfer of N-Containing Groups	197
7.5.2.4	EC 2.7 Phosphotransferases	197
7.5.3	EC 3 Hydrolases	198
7.5.3.1	EC 3.1.1.1 Esterases and EC 3.1.1.3 Lipases	199
7.5.3.2	EC 3.2 Glycosidases	200
7.5.3.3	EC 3.3 Reaction with Ether Bonds	201
7.5.3.4	EC 3.4 Peptidases	201
7.5.3.5	EC 3.5 Reactions with C–N Bonds Except Peptide Bonds	201
7.5.3.6	EC 3.7 Reactions with C–C Bonds	202
7.5.3.7	EC 3.8 Reactions with Halogen Bonds	202
7.5.4	EC 4 Lyases	202
7.5.4.1	EC 4.2.1 Nitrile Hydratases	202
7.5.4.2	EC 4.3.1.5 Phenylalanine Ammonia Lyase (PAL)	202
7.5.4.3	EC 4.1.2 Aldolases	203
7.5.4.4	EC 4.1.2 Hydroxynitrile Lyases (Oxynitrilases)	205
7.5.4.5	EC 4.1.1 Decarboxylases	206
7.5.5	EC 5 Isomerases	206
7.5.6	EC 6 Ligases	207
7.6	Outlook and Conclusions	207
	References	209
8	Hydrogenases and Alternative Energy Strategies	213
	<i>Olaf Rüdiger, António L. De Lacey, Victor M. Fernández, and Richard Cammack</i>	
8.1	Introduction: The Future Hydrogen Economy	213
8.1.1	Biological Hydrogen Energy Metabolism	215
8.2	Chemistry of Hydrogenase Catalytic Sites	216

8.2.1	NiFe	217
8.2.2	NiFeSe	219
8.2.3	FeFe	219
8.2.4	Fe (non-Fe-S) Hydrogenase (Hmd)	220
8.2.5	Biosynthesis of the Active Sites	221
8.3	Experimental Approaches	221
8.3.1	EPR and Related Methods	222
8.3.2	FTIR Spectroscopy	222
8.3.3	Protein Film Voltammetry (PFV)	223
8.4	Catalytic Mechanisms of Hydrogenases	224
8.5	Progress So Far with Biological Hydrogen Production Systems	225
8.5.1	Fermentation	225
8.5.2	Oxygenic Photosynthesis	226
8.5.3	Anaerobic Photosynthesis	227
8.5.4	Emulsion: Hydrogenase Model Compounds	228
8.5.5	Hydrogenases on Electrodes	230
8.5.5.1	Sensitivity and Resistance of Hydrogenases to O ₂ , CO and Other Inhibitory Gases	233
8.6	Conclusion and Future Directions	235
	References	236

9 PAH Bioremediation by Microbial Communities and Enzymatic Activities 243

Vincenza Andreoni and Liliana Gianfreda

9.1	Introduction	243
9.2	<i>Fate of PAHs in the Environment</i>	244
9.3	Population of PAH-Polluted Environments	246
9.4	Microbial Degradation of PAHs	248
9.5	Dioxygenases as Key Enzymes in the Aerobic Degradation of PAHs and Markers of Bacterial Degradation	251
9.6	PAH Transformation by Extracellular Fungal Enzymes	254
9.7	<i>In Situ</i> Strategies to Remediate Polluted Soils	257
9.7.1	Intrinsic or Natural Attenuation	257
9.7.2	Biostimulation and Bioaugmentation	258
9.7.3	Phytoremediation	261
9.7.4	Feasibility of Bioremediation Technologies	264
	References	265