

Index

A

- 7-ACA · 189
- Acetic acid assay · 79
- Acetylcholine esterase · *see AChE*
- AChE · 175
 - from Electric eel · 175
 - from *Torpedo californica* · 175
 - physiological role · 175
 - resolution of *meso*-diesters · 176
- Acrylamide
 - enzymatic synthesis of · 233
- Activity
 - AChE · 176
 - effect of solvent · 27
 - lipase · 77
 - protease · 191
 - staining · *see zymogram*
 - water activity · 30
- Acyl donors · 74
- Acyl migration · 107
- Acylase · 209
- Adrenaline test · 81
- Adsorption · *see immobilization*
- Agrobacterium radiobacter*
 - epoxide hydrolase · 220
- Alcaligenes faecalis*
 - nitrile hydrolyzing activity · 239
- Alcaligenes* sp. lipase
 - resolution of secondary alcohols · 103
- Alcohols
 - in non-sugars · 155
 - in sugars
 - primary · 142
 - secondary · 150
 - resolution of
 - axially-disymmetric · 117
 - phosphorus stereocenter · 120
 - primary · 106
 - quaternary · 113
 - remote stereocenters · 118
 - secondary · 84
 - spiro · 117
 - sulfur stereocenter · 120
 - tertiary · 113
 - with amidase · 195
 - with esterase · 172, 176, 183
 - with lipase · 84, 106
 - with protease · 195
- Aldol addition · 56
- Aliphatic hydroxyls
 - acylation/deacylation of diols · 156
- Amano AH · *see PCL*
- Amano D · *see ROL*
- Amano N · *see ROL*
- Amano P · *see PCL*
- Amano PS · *see PCL*
- Amberlite · 40
- Amidase
 - active site model · 206
 - availability · 185
 - commercial reactions · 209
 - enantioselective reactions · 195
 - hydrolysis of nitriles · 227
 - occurrence · 185
 - resolution of
 - amino acids · 206
 - carboxylic acids · 200
 - structure · 193
 - substrate binding nomenclature · 186
 - synthesis of amides · 187
- Amides, synthesis of
 - with amidase · 187
 - with protease · 187
- Amines
 - protection/deprotection
 - with lipase · 159
 - resolution of
 - with amidase · 195
 - with lipase · 121
 - with protease · 195
- Amino acid acylase
 - availability · 185
 - general features · 191
 - resolution of amides · 199
- Amino acids, resolution of · 200
- 7-Aminocephalosporanic acid · *see 7-ACA*
- 6-Aminopenicillanic acid · *see 6-APA*
- Anhydrides
 - as acyl donors · 76
 - resolution of · 132
- ANL
 - availability · 64
 - classification · 65
 - in dynamic kinetic resolution · 11

- in polymerization · 164
- in protection/deprotection · 159
- resolution of
 - amino acids · 158
 - carboxylic acids · 128
 - primary alcohols · 112
 - secondary hydroxyls in sugars · 150
- 6-APA · 191
- Arthrobacter globiformis* esterase · 183
- Aspartame · 188
- Assays
 - AChE · 176
 - acylase · 49
 - amidase · 49
 - epoxide hydrolase · 49
 - esterase · 49, 77
 - fluorimetric · 49, 78
 - for directed evolution · 47
 - lipase · 49, 77
 - nitrile hydratase · 231
 - protease · 191
 - spectrophotometric · 78
- Asymmetric synthesis · *see also lipase, esterase, epoxide hydrolase, nitrilase, amidase, protease*
 - principle · 23
- Availability
 - amidases · 185
 - esterase · 68, 167
 - lipase · 62
 - proteases · 185
- Azide
 - ring-opening with epoxide hydrolase · 220

B

- Bacillus coagulans* esterase · 183
- Bacillus subtilis* esterase · *see also Carboxylesterase NP*
 - directed evolution of · 51
- BChE · 175
- β -Blockers · 105
- BMIM · *see ionic liquids*
- Burkholderia cepacia*
 - lipase · *see PCL*
- 1-butyl-3-methylimidazolium tetrafluoroborate · 32
- Butyrylcholine esterase · *see BChE*

C

- CAL-A
 - availability · 64
 - classification · 65
- CAL-B
 - availability · 64
 - classification · 65
 - properties · 67
 - protection/deprotection of carboxyl groups · 161
 - resolution of
 - amides · 122
 - amines · 121
 - anhydrides · 132
 - carboxylic acids
 - α -stereocenter · 124
 - β -stereocenter · 128, 129
 - ferrocenes · 120
 - primary alcohols · 112
 - secondary alcohols · 89, 91, 93
 - thiols · 123
 - substrate binding site · 73
 - synthesis of
 - alkyl glycosides · 146
 - bioesters · 146
 - nucleosides · 147
 - peroxycarboxylic acids · 165
- Candida antarctica* lipase · *see CAL-A, CAL-B*
- Candida cylindrea* lipase · *see CRL*
- Candida rugosa* lipase · *see CRL*
- Carbohydrates
 - alkyl glycosides · 144
 - primary hydroxyls · 142
 - secondary hydroxyls · 150
 - synthesis of surfactants/detergents · 143, 145
- Carboxylesterase NP · 181
 - resolution of
 - carboxylic acids · 182
 - naproxen · 181
- Carboxylic acids
 - resolution of
 - with amidase · 200, 207
 - with esterase · 171, 174, 176, 183
 - with lipase · 124
 - with protease · 200, 207
- Catalytic promiscuity · 54
- CE
 - availability · 64
 - classification · 65
 - resolution of
 - phosphorus stereocenters · 120

secondary alcohols · 85, 176
sulfur stereocenters · 120
thiols · 123
cEH · *see soluble epoxide hydrolase*
Celite · 39
Cephalosporin · 189
Cephalosporinase
 directed evolution · 48
Chemoselective reactions · 141
Chicken liver esterase · *see CLE*
Cholesterol esterase · *see CE*
Chromobacterium viscosum lipase · *see CVL*
Chrysanthemic acid, resolution of · 183
Chymotrypsin
 active site structure · 204
 availability · 185
 general features · 190
 resolution of
 alcohols · 198
 amino acids · 203
 carboxylic acids · 203, 207
 structure · 193, 204
Citronellol · 36
CLE · 176
CLEA's · 42
CLEC · 41
CLL
 availability · 64
 classification · 65
Cobalt NHases · 231
Corynebacterium
 epoxide hydrolase · 220
CRL
 availability · 63, 64
 classification · 65
 effect of vinyl acetate · 75
 PEG-modified · 42
 polymerization · 163
 primary hydroxyls in sugars · 142
 properties · 66
 protection/deprotection of
 carboxyl groups · 161
 reaction with phenolic hydroxyls · 155
 resolution of
 amino acids · 158
 carboxylic acids
 α -stereocenter · 125
 β -stereocenter · 128
 ferrocenes · 120
 phosphorus stereocenters · 120
 primary alcohols · 112
 secondary alcohols · 91
 proposed binding site · 86
 silanes · 121

sulfur stereocenters · 120
secondary hydroxyls in sugars · 150
substrate binding site · 73
 in supercritical carbon dioxide · 36
 synthesis of alkyl glycosides · 146
Cross-linked enzyme aggregates · *see CLEA's*
Cross-linked enzyme crystals · *see CLEC*
CVL
 availability · 63, 64
 classification · 65
 in reverse micelles · 35
 resolution of silanes · 121
 secondary hydroxyls in sugars · 152
Cytosolic epoxide hydrolase · *see soluble epoxide hydrolase*

D

D-4-hydroxyphenylglycine · 10
Diisopropyl fluorophosphatases · 248
Diketene · 76
Diltiazem · 138
Directed evolution · 45
 assay systems · 47
 esterase · 51
 examples · 50
 focused · 52
 hydantoinase · 51
 library creation · 45
 lipase · 50
 organophosphorous hydrolase · 246
 principle · 45
 protease · 52
 screening · 49
 selection · 47
 DKR · *see dynamic kinetic resolution*
DNA-shuffling · 46
Double enantioselection · 131
D-phenylglycine · 10
Dynamic kinetic resolution · 9
 by addition/elimination · 14
 by deprotonation/protonation · 12
 by nucleophilic substitution · 17
 by oxidation/reduction · 17
 of acylloins · 12
 of carboxylic acids · 12
 of cyanohydrins · 15
 resolution of hydantoin · 10
 with palladium catalysts · 16

E

E · *see enantiomeric ratio*
Enantioconvergence · 217, 222, 224
Enantiomeric ratio
 definition · 5
Enantioselective reactions
 asymmetric synthesis · 24
 carboxylic acids · 171
 diols · 172, 176, 244
 epoxides · 219
 principle · 23
 commercial · 138
 dynamic kinetic resolution · 9
 in situ recycling · 6
 of triglycerides · 113
 quantitative analysis · 5
 recycling · 6
 resolution of
 amines · 195
 carboxylic acids · 172, 174, 182, 183,
 200, 210
 epoxides · 219, 221, 223, 225
 nitriles · 237
 primary alcohols · 106, 183
 quaternary stereocenters · 113, 116
 secondary alcohols · 84, 173, 176, 183,
 195
 electronic effects · 85
 tertiary alcohols · 113
 sequential kinetic resolution · 6, 7
Enantioselectivity
 definition · 5
 influence of solvent · 28
 influence of temperature · 28
Enol esters · 75
Entrapment · *see immobilization*
Epoxide, resolution of · 215, 219, 221, 223,
 225
Epoxide hydrolase · 215
 active site residues · 216
 Aspergillus niger · 223
 Beauveria sulfurescens · 224
 degradation of aromatics · 215
 Diploida gossipina · 225
 enantioselectivity · 217
 mammalian · 218
 microsomal · 216
 resolution with · 219
 soluble · 216
 mechanism · 216
 microbial
 bacterial · 220
 fungal · 223

 yeast · 225
 Nocardia sp. · 222
 regioselectivity · 217
 resolution of
 epoxides · 221
 Rhodococcus sp. · 221
 Rhodotorula sp. · 225
epPCR · 46
Error-prone polymerase chain reaction
 · *see epPCR*
Esterase · 166
 assay · 77
 catalytic promiscuity · 54
 directed evolution · 48, 51
 distinction from lipase/protease · 83
 mammalian · 166
 microbial · 177
 structure · 68
 transesterification / principle · 25
 zymogram · 82

F

FACS · 49
Ferric NHases · 228
Ferrocenes, resolution of · 120
Flap · *see lid*
Fluorimetric assays · 78
Focused directed evolution · 52

G

GCL
 availability · 64
 classification · 65
 effect of vinyl acetate · 75
 resolution of amino acids · 158
Gene-shuffling · *see DNA-shuffling*
Geotrichum candidum lipase · *see GCL*
Glycidol · 138
Glycosidase · 241
 asymmetrization of *meso*-diols · 244
 resolution of racemic alcohols · 244
Glycosynthases · 243

H

Haloalcohol dehalogenase · 245
Head group exchange · 212
High-throughput screening · *see HTS*
HLE · 176

HLL

- availability · 64
 - classification · 65
 - Horse liver esterase · *see HLE*
 - HTS · 78
 - Humicola lanuginosa* lipase · *see HLL*
 - Hydantoinase
 - application · 205
 - commercial reactions · 209
 - directed evolution · 51
 - α/β -Hydrolase fold · 68
 - Hydrolases · *see lipase, esterase, protease, nitrilase, nitrile hydratase, epoxide hydrolase*
 - classification · 65
 - Hydrolysis, principle · 25
-

I

- Ibuprofen, resolution of
 - in reverse micelles · 35
 - in supercritical carbon dioxide · 37
 - with CAL-B · 124
 - Immobilization · 39
 - adsorption and entrapment · 39
 - CLEA's · 42
 - CLEC's · 41
 - covalent · 40
 - protein-coated micro-crystals · 40
 - sol gel-entrapment · 40
 - In situ* racemization · *see dynamic kinetic resolution*
 - In situ* recycling · 239
 - in vitro compartmentalization · *see IVC*
 - Inducers · 227
 - Inositols · 104
 - Interfacial activation · 70, 84
 - Ionic liquids · 32
 - Isopropenyl acetate · 74
 - IVC · 48
-

K

- Kinetic control
 - in peptide synthesis · 187
- Kinetic resolution
 - principle · 5
 - recycling · 6
 - sequential · 6

L

- Lactones · 133
 - macrolactonization · 136
 - resolution of
 - with esterase · 173, 176
 - with lipase · 133
 - rule · 135
- Lid · 70
- Lipase
 - acyl donors · 74
 - assay · 77
 - asymmetric synthesis · 23
 - availability · 61, 64
 - catalytic promiscuity · 55
 - chemoselective reactions · 141
 - classification · 65
 - commercial reactions · 138
 - directed evolution · 50
 - distinction from esterase/protease · 83
 - hydrolysis, principle · 25
 - in lipid modification · 163
 - in oligomerization · 163
 - in polymerization · 163
 - in reverse micelles · 34
 - mechanism · 69
 - primary hydroxyls in sugars · 142
 - protection/deprotection of amines · 159
 - carboxyl groups · 160
 - regioselective reactions · 141
 - regioselectivity, solvent effects · 26
 - resolution of alcohols
 - axially-disymmetric · 117
 - non-carbon stereocenters · 119
 - primary · 106
 - remote stereocenter · 118
 - secondary · 84
 - spiro · 117
 - tertiary · 113
 - amines · 121
 - anhydrides · 132
 - carboxylic acids · 124
 - quaternary stereocenter · 130
 - remote stereocenter · 130
 - sulfur stereocenter · 130
 - α -stereocenter · 124
 - β -stereocenter · 128
 - lactones · 133
 - organometallics · 119
 - peroxides · 123
 - thiols · 123
 - triglycerides · 113

secondary hydroxyls in sugars · 150
 soluble in organic solvents · 42
 structure · 71
 substrate binding site · 72
 supercritical carbon dioxide · 36
 synthesis of
 alkyl glycosides · 144, 149
 diltiazem · 138
 peroxy-carboxylic acids · 165
 pharmaceutical precursors · 140
 surfactants/detergents · 143, 145
 transesterification / principle · 25
 zymogram · 83
 Lipid modification · 163
 logP · 27

M

Mammalian epoxide hydrolase · 218
 resolution with · 219
 Mammalian esterase · 176, *see also* PLE,
 AChE
 Mandelic acid · 239
 Mass spectroscopy assay · 82
 mEH's · *see* *microsomal epoxide hydrolase*
 Metagenome approach · 43
 Metal carbonyl complexes resolution of ·
 120
 Mevalonolactone · 222
 Michael addition · 15, 56
 Microbial epoxide hydrolase
 bacterial · 220
 fungal · 223
 yeast · 223
 Microbial esterase · 177
 other esterases · 183
 Microsomal epoxide hydrolase · 216
 Mitsunobu inversion · 22
 Molecular evolution · *see* *directed evolution*
 Mutator strain · 46

N

Naproxen, synthesis of
 with Carboxylesterase NP · 125, 181
 with nitrilase · 237
 NHase · *see* *nitrile hydratase*
 Nitrilase · 227
 from metagenome · 43, 239
 mechanism · 227
 properties · 228
 Nitrile hydratase · 227

enantioselectivity · 237
 mild conditions · 233
 properties · 228, 232
 regioselectivity · 236
 Nitriles
 enzymatic hydrolysis · 227
 enantioselectivity · 237
 induction of enzymes · 227
 mild conditions · 233
 regioselectivity · 236
Nocardia sp. epoxide hydrolase · 222
 Non-steroidal anti-inflammatory drugs · *see*
also *ibuprofen*, *naproxen*
 synthesis of
 with carboxylesterase NP · 181
 with nitrile hydrolyzing enzymes · 237
 NSAID · *see* *non-steroidal anti-*
inflammatory drugs

O

Occurrence
 amidase · 185
 epoxide hydrolase · 214
 esterase · 68, 167
 lipase · 62
 nitrilase · 227
 nitrile hydratase · 227
 phospholipase · 211
 protease · 185
 Oligomerization · 163
 Organometallics, resolution of · 119
 Organophosphorus compounds · 246
 Organophosphorus hydrolase · 246
 Oxime esters · 74
 Oxyanion · 69

P

Pantolactone · 183
 Papain, availability · 185
 Paroxonases · 246
 PcamL
 availability · 64
 classification · 65
 PCL
 availability · 64
 classification · 65
 dynamic kinetic resolution · 11
 polymerization · 163
 properties · 67
 reaction with

- phenolic hydroxyls · 155
- resolution of
 - amines · 121
 - amino acids · 158
 - anhydrides · 132
 - carboxylic acids
 - α -stereocenter · 127
 - β -stereocenter · 128
 - ferrocenes · 120
 - peroxides · 123
 - primary alcohols · 107, 108
 - rule · 106
 - secondary alcohols · 95
 - rule · 85
 - thiols · 123
 - secondary hydroxyls in sugars · 151
 - structure · 71
 - substrate binding site · 72
 - supercritical carbon dioxide · 36
- PCL-AH · *see also PCL*
 - availability · 64
- PEG
 - for lipase modification · 42
- Penicillin amidase
 - availability · 185
 - resolution of
 - alcohols · 198
 - amines · 198
 - carboxylic acids · 209
 - structure · 193
- Penicillin G acylase
 - general features · 191
 - in cephalosporin synthesis · 189
- Penicillium camembertii* lipase · *see PcamL*
- Penicillium roquefortii* lipase · *see ProqL*
- Peroxides
 - resolution with lipase · 123
- Peroxy-carboxylic acids · 165
- PFL · *see also PCL*
 - availability · 64
- PfragiL
 - availability · 64
- PGA · *see penicillin G acylase*
- Phage display · 49
- Phenolic hydroxyls · 155
- Phospholipase · 211. *see also PLA₁, PLA₂, PLC, PLD*
 - regioselectivity · 211
- Phospholipase A₁ · *see PLA₁*
- Phospholipase A₂ · *see PLA₂*
- Phospholipase C · *see PLC*
- Phospholipase D · *see PLD*
- Phospholipids · 211
- Phosphotriesterases · 246
- pH-stat assay · 78
- Pig liver esterase *see PLE*
- Pipecolic acid · 233
- PLA₁ · 211
- PLA₂ · 211
- PLC · 212
- PLD · 212
- PLE · 166
 - active site model · 169
 - biochemical properties · 166
 - preparation · 167
 - resolution of
 - alcohols/lactones · 173
 - carboxylic acids · 174
 - α -stereocenter · 171
 - β -stereocenter · 172
 - miscellaneous substrates · 174
 - primary or secondary *meso*-diols · 172
 - substrate model · 170
 - substrate spectra · 169
- Polyethylene glycol · *see PEG*
- Polymerization · 163
- Porcine pancreatic lipase · *see PPL*
- PPL
 - availability · 64
 - classification · 65
 - in dynamic kinetic resolution · 11
 - in polymerization · 163
 - primary hydroxyls
 - in diols · 156
 - in sugars · 142
 - properties · 66
 - protection/deprotection of carboxyl groups · 162
 - reaction with phenolic hydroxyls · 155
 - resolution of carboxylic acids
 - α -stereocenter · 127
 - β -stereocenter · 128, 129
 - lactones · 133
 - peroxides · 123
 - primary alcohols · 110, 111
 - secondary alcohols · 93
 - rule · 85
 - thiols · 123
 - secondary hydroxyls in sugars · 150
 - sugar deprotection · 141
- Prolidase · 248
- Propranolol · 105
- ProqL · 64
- Protease
 - activity assay · 191
 - availability · 185
 - commercial reactions · 209
 - distinction from lipase/esterase · 83
 - enantioselective reactions · 195
 - occurrence · 185

resolution of
 alcohols · 195
 amides · 195
 amines · 195
 carboxylic acids · 200
 structure · 193
 substrate binding nomenclature · 186
 synthesis of amides · 187
Proteinase K
 availability · 185
 structure · 193
Pseudomonas aeruginosa
 esterase · 183
 lipase · 121
Pseudomonas cepacia lipase · *see PCL*
Pseudomonas fluorescens
 esterase · 183
 lipase · *see PCL*
Pseudomonas fragi lipase · *see PfragiL*
Pseudomonas glumae lipase · *see CVL*
Pseudomonas lipase · *see also PCL, P. aeruginosa* lipase
 dynamic kinetic resolution · 11
 resolution of
 primary alcohols · 107
 rule · 106
 secondary alcohols · 95
Pseudomonas marginata esterase · 183
Pseudomonas putida esterase · 183
Pseudomonas sp. KWI-56 lipase · *see also PCL*
 directed evolution of · 52

Q

Quaternary stereocenters
 resolution with lipase · 113, 116
 Quick E · 79

R

Rabbit liver esterase · *see RLE*
 Racemase · 13
 lactate · 14
 mandelate · 14, 22
 Random mutagenesis · 44
 Recycling in kinetic resolution · 6
 Regioselective reactions · 141
 Regioselectivity, solvent effects · 26
 Resolution of
 alcohols
 with amidase · 195

with esterase · 172, 176, 183
 with lipase
 survey · 84, 106
 with protease · 195
 amino acids · 199
 anhydrides · 132
 carboxylic acids
 with amidase · 200
 with esterase · 171, 176, 183
 with lipase · 124
 with protease · 200
 epoxides · 219
 lactones
 with esterase · 176
 with lipase · 133
 nitriles · 237
 Resorufin · 80
 Retaining glycosidase · 241
 Reverse micelles · 34
Rhizopus delemar lipase · *see ROL*
Rhizopus javanicus lipase · *see RJL, ROL*
Rhizopus niveus lipase · *see ROL*
Rhodococcus rhodochrous
 in synthesis of
 acrylamide · 233
 nicotinamide · 233
 others · 234
 SP409
 epoxide hydrolase activity · 220
 nitrile hydrolysis · 235
Rhodococcus sp. NCIMB11216
 epoxide hydrolase · 220
 nitrile hydrolyzing enzymes · 227
Rhodococcus butanica · *see R. rhodochrous*
 RJL · 64
 RLE · 176
 RML
 availability · 64
 classification · 65
 in dynamic kinetic resolution · 11
 polymerization · 163
 properties · 67
 resolution of
 ferrocenes · 120
 primary alcohols · 112
 secondary alcohols · 102
 substrate binding site · 73
 supercritical carbon dioxide · 36
 synthesis of
 alkyl glycosides · 146
ROL
 availability · 64
 classification · 65
 protection/deprotection of
 carboxyl groups · 160

resolution of
primary alcohols · 112

S

SAM-II lipase · *see PCL*
SCCO₂ · *see supercritical carbon dioxide*
Screening · 49
sEH · *see soluble epoxide hydrolase*
Selection · 47
Selenosubtilisin · 58
Sequence-based discovery · 43
Sequential kinetic resolution · 6
Shvo's catalyst · 18
Sol gel entrapment · *see immobilization*
Soluble epoxide hydrolase · 216
Solvent
 effect on enantioselectivity · 28
 effect on regioselectivity · 26
 selection criteria · 27
Spectrophotometric assays · 78, 191
Structures
 AChE · 175
 amidases · 193
 esterase · 68
 lipase · 68
 proteases · 193
Subtilisin
 availability · 185
 chemical modification · 52
 directed evolution · 52
 general features · 189
 in peptide synthesis · 189
 occurrence · 185
 resolution of
 alcohols · 195
 amines · 195
 carboxylic acids · 201, 202, 207
 site-directed mutagenesis · 52
 structure · 193
Sugars
 alkyl glycosides · 144
 primary hydroxyls · 142
 secondary hydroxyls · 150
 synthesis of
 surfactants/detergents · 143
Supercritical carbon dioxide · 36
Synthesis activity assay · 82

T

Tertiary alcohols

 resolution with lipase · 113

TG · *see triglyceride*

Thermitase

 availability · 185

 in deprotection of carboxyl groups · 160

 structure · 193

Thermodynamic control

 in peptide synthesis · 187

Thermolysin

 availability · 185

 general features · 190

 in aspartame synthesis · 188

 structure · 193

Thioglycoligase · 243

Thioglycosynthase · 244

Thiols, resolution with lipase · 123

Transesterifications, principles · 25

Transglycosylation · 242

Transphosphatidylation · 212

Triglycerides · 163

 stereochemical numbering · 113

U

Umbelliferone · 49, 80

V

Vinyl acetate · 74, 75

W

Water activity · 30

Water content · 30

Wheat germ lipase · 147

X

XAD-8 · *see Amberlite*

Z

Zymogram · 8