

Contents

Foreward XI

Preface XIII

List of Contributors XV

Symbols and Abbreviations XIX

- 1 Important Natural Products 1**
Hirokazu Arimoto and Daisuke Uemura
- 1.1 Introduction 1
1.2 Alkylation of Tertiary Carbon Centers 2
1.3 Cycloaddition to Alkenes 5
1.3.1 Diels–Alder Reaction 5
1.3.2 Other Types of Cycloaddition 9
1.4 Rearrangement Reactions 10
1.5 Carbometallation Reactions 14
1.5.1 Addition of a Carbon Nucleophile to a β,β -Disubstituted α,β -Unsaturated Enone 14
1.5.2 Asymmetric and Diastereomeric Addition of a Carbon Nucleophile to Unactivated Alkenes Catalyzed by Palladium 14
1.6 C–H Functionalization Reactions 17
1.7 Asymmetric Modification of Enantiotopic/Diastereotopic Substituents of Quaternary Carbon Centers 20
1.8 Summary 21
- 2 Important Pharmaceuticals and Intermediates 25**
Johannes G. de Vries
- 2.1 The Chirality of Drugs and Agrochemicals 25
2.2 Steroids 27
2.3 Pharmaceuticals and Agrochemicals Based on α -Dialkylated Amino Acids 32

VI Contents

- 2.4 Azole Antimycotics 36
- 2.5 Alkaloids 37
- 2.6 HIV Inhibitors 39
- 2.7 β -Lactam Antibiotics 43
- 2.8 The Tetracyclines 46
- 2.9 Summary and Outlook 46

- 3 Aldol Reactions 51**
Bernd Schetter and Rainer Mahrwald
- 3.1 Introduction 51
- 3.2 Metal Enolates 52
 - 3.2.1 Lithium Enolates 54
 - 3.2.2 Titanium and Zirconium Enolates 54
 - 3.2.3 Boron Enolates 58
- 3.3 Catalytic Aldol Additions 61
 - 3.3.1 Fluoride-ion-mediated Aldol Addition 61
 - 3.3.2 Lewis-acid-mediated Mukaiyama-type Aldol Reactions 63
 - 3.3.3 Direct Aldol Additions 65
 - 3.3.4 Organocatalysis 72
 - 3.3.5 Enzyme and Antibody Catalysis 76
- 3.4 Conclusions 79
- 3.5 Note Added in Proof 79

- 4 Michael Reactions and Conjugate Additions 83**
Angelika Baro and Jens Christoffers
- 4.1 Introduction 83
- 4.2 Chiral Brønsted Bases 84
 - 4.2.1 Cinchona Alkaloids 84
 - 4.2.2 Polymer-bound Alkaloids 85
 - 4.2.3 Organocatalysis 86
 - 4.2.4 Miscellaneous Examples 88
- 4.3 Chiral Metal Complexes 90
 - 4.3.1 Cobalt and Copper Catalysis 90
 - 4.3.2 Rhodium Catalysis 92
 - 4.3.3 Heterobimetallic Catalysis 93
 - 4.3.4 Miscellaneous Examples 96
- 4.4 Chiral Auxiliaries 98
 - 4.4.1 α -Phenethylamine 98
 - 4.4.2 L-Valine Ester 105
 - 4.4.3 L-Valine Diethylamide 107
 - 4.4.4 Miscellaneous Examples 111

5	Rearrangement Reactions	117
	<i>Annett Pollex and Martin Hiersemann</i>	
5.1	Introduction	117
5.2	Applications	120
5.2.1	The Claisen Rearrangement	120
5.2.2	The Overman Rearrangement	128
5.2.3	The Cope Rearrangement	129
5.2.4	The Wittig Rearrangement	131
5.2.5	Semipinacol Rearrangements	134
5.2.6	Miscellaneous	137
5.3	Summary	139
6	Cycloaddition Reactions	143
	<i>Giovanni Desimoni and Givseppe Faita</i>	
6.1	Introduction	143
6.2	[2+1] Cycloaddition Reactions	144
6.3	[2+2] Cycloaddition Reactions	149
6.4	1,3-Dipolar Cycloaddition Reactions	150
6.4.1	Nitrone Cycloadditions	152
6.4.2	Other 1,3-Dipolar Cycloadditions	153
6.5	Diels–Alder Reactions	154
6.6	Hetero-Diels–Alder Reactions	164
6.6.1	The Carbonyl Group as Dienophile	166
6.6.2	α,β -Unsaturated Carbonyl Derivatives as Heterodienes	170
6.6.3	Imine Derivatives as Heterodienophiles	170
6.7	Consecutive Cycloaddition Reactions	173
7	Asymmetric Cross-coupling and Mizoroki–Heck Reactions	185
	<i>Louis Barriault and Effiette L. O. Sauer</i>	
7.1	The Asymmetric Heck Reaction	185
7.1.1	Introduction	185
7.1.2	Mizoroki–Heck Reaction Mechanism	185
7.1.3	Asymmetric Formation of Quaternary Carbon Centers	187
7.2	Metal-catalyzed Cross-coupling Reactions	195
7.2.1	Palladium-catalyzed α -Arylation	195
7.2.2	Palladium-catalyzed α -Vinylolation	197
7.2.3	Intramolecular Palladium-catalyzed α -Arylation of Amides	197
7.2.4	Palladium-catalyzed Rearrangements	199
7.2.5	Desymmetrizing Suzuki Couplings of <i>meso</i> -Substrates	200
7.3	Summary	204

VIII Contents

- 8 Alkylation of Ketones and Imines 207**
Diego J. Ramón and Miguel Yus
- 8.1 Introduction 207
- 8.2 Diastereoselective Additions 208
- 8.2.1 Chiral Nucleophiles 208
- 8.2.2 Chiral Electrophiles 209
- 8.3 Enantioselective Additions by Modulated Processes 219
- 8.3.1 Alkylation Processes 219
- 8.3.2 Allylation Processes 222
- 8.3.3 Alkynylation Processes 223
- 8.4 Enantioselective Additions by Promoted Processes 226
- 8.4.1 Alkylation Processes 227
- 8.4.2 Allylation Processes 231
- 8.4.3 Arylation Processes 233
- 8.4.4 Alkenylation Processes 234
- 8.4.5 Alkynylation Processes 235
- 8.4.6 Miscellaneous Processes 235
- 9 Asymmetric Allylic Alkylation 243**
Manfred Braun
- 9.1 Introduction 243
- 9.2 Electrophilic Allylic Alkylation 244
- 9.2.1 Direct Allylation of Enolates 244
- 9.2.2 Palladium-catalyzed Allylation 250
- 9.2.3 γ -Attack on Electrophilic Allylic Substrates 254
- 9.3 Nucleophilic Allylic Alkylation 256
- 9.3.1 Allylation of Trisubstituted Electrophilic Carbon Centers 256
- 9.3.2 γ -Addition of Allylic Nucleophiles to Aldehydes 258
- 9.4 Miscellaneous Methods 260
- 9.5 Outlook 262
- 10 Phase-Transfer Catalysis 265**
Takashi Ooi and Keiji Maruoka
- 10.1 Introduction 265
- 10.2 Carbon–Carbon Bond Formation Through PTC 266
- 10.2.1 Alkylation 266
- 10.2.2 Michael Addition Reaction 275
- 10.2.3 The Darzens Reaction 277
- 10.2.4 Cyclopropanation 279
- 10.3 Carbon–Heteroatom Bond Formation Through PTC 279

10.3.1	α -Hydroxylation	279
10.3.2	Epoxidation	280
10.3.3	α -Fluorination	282
10.4	Conclusion	283
11	Radical Reactions	
	<i>Kalyani Patil and Mukund P. Sibi</i>	287
11.1	Introduction	287
11.2	Radical Cyclization	288
11.3	Atom- and Group-transfer Cyclizations	295
11.3.1	Diastereoselective Atom- and Group-transfer Cyclizations	296
11.3.2	Enantioselective Atom-transfer Cyclizations	297
11.4	Intermolecular Radical Allylations	299
11.4.1	Diastereoselective Allylation	299
11.4.2	Enantioselective Allylation	300
11.5	Other Metallic Reagents	302
11.5.1	Cobalt-catalyzed Tandem Radical Cyclization/Cross-coupling	302
11.5.2	Samarium Diiodide-mediated Radical Reactions	304
11.5.3	Manganese(III)-based Oxidative Radical Cyclizations	306
11.5.4	Titanocene-mediated Radical Cyclizations	307
11.6	Radical Reactions in the Solid State	309
11.7	Conclusion	311
11.8	Experimental	311
12	Enzymatic Methods	315
	<i>Uwe T. Bornscheuer, Erik Henke, and Jürgen Pleiss</i>	
12.1	Introduction	315
12.2	Strategies for the Kinetic Resolution of Sterically Demanding Substrates	316
12.2.1	Kinetic Resolution of Chiral Substrates	316
12.2.2	Directed Evolution	317
12.2.3	Screening of Biocatalysts	318
12.2.4	Systematic Analysis of Sequence and Structure	318
12.2.5	Molecular Modeling and Protein Engineering	323
12.2.6	Use of Remote or Alternative Cleavage Sites	323
12.2.7	Reaction Engineering	324
12.3	Conclusion	326
Index		329