

Contents

Preface XV

List of Contributors XIX

1	BINAP	1
	<i>Takeshi Ohkuma and Nobuhito Kurono</i>	
1.1	Introduction: Structural Consideration	1
1.2	Hydrogenation of Olefins	3
1.3	Hydrogenation of Ketones	6
1.3.1	Functionalized Ketones	6
1.3.2	Simple Ketones	9
1.4	Isomerization of Allylamines and Allylalcohols	13
1.5	Hydroboration, Hydrosilylation, Hydroacylation, and Hydroamination	14
1.6	Allylic Alkylation	18
1.7	Heck Reaction	18
1.7.1	Intramolecular Reaction	18
1.7.2	Intermolecular Reaction	19
1.8	Aldol and Mannich-Type Reactions	21
1.8.1	Aldol Reaction	21
1.8.2	Mannich-Type Reaction	23
1.9	Nucleophilic Additions to Carbonyl and Imino Compounds	24
1.9.1	Allylation	24
1.9.2	Alkenylation and Arylation	25
1.9.3	Dienylation	26
1.9.4	Cyanation	27
1.10	α -Substitution Reactions of Carbonyl Compounds	28
1.10.1	Fluorination and Amination	28
1.10.2	Arylation and Orthoester Alkylation	29
1.11	Michael-Type Reactions	30

1.11.1	Michael Reaction	30
1.11.2	Aza-Michael Reaction	32
1.12	Conjugate Additions Using Organoboron and Grignard Reagents	32
1.13	Diels–Alder Reaction	35
1.14	Ene Reaction	38
1.15	Cyclization	38
1.15.1	Intramolecular Reactions of Enynes	38
1.15.2	[3 + 2] and [5 + 2] Cycloaddition Reactions	39
1.15.3	[2 + 2 + 2] Cycloaddition Reactions	42
1.15.4	Pauson–Khand Type Reactions	43
1.16	Ring-Opening Reactions	45
1.17	Concluding Remarks	45
2	Bisphosphacycles — From DuPhos and BPE to a Diverse Set of Broadly Applied Ligands	55
	<i>Weicheng Zhang and Xumu Zhang</i>	
2.1	Introduction	55
2.2	Development of Bisphosphacycle Ligands	55
2.2.1	Structural Features of DuPhos and BPE	55
2.2.2	Strategies of Ligand Design	58
2.3	Applications of Bisphosphacycle Ligands	65
2.3.1	Asymmetric Hydrogenation	65
2.3.2	Asymmetric Hydroformylation	75
2.3.3	Asymmetric Hydrosilylation	77
2.3.4	Asymmetric Hydroacylation	77
2.3.5	Asymmetric Cycloisomerization, Cycloaddition, and Cyclization	78
2.3.6	Asymmetric Phosphination	81
2.3.7	Asymmetric Nucleophilic Addition to Ketones and Ketimines	82
2.3.8	Asymmetric Conjugate Addition	85
2.3.9	Miscellaneous Reactions	85
2.4	Concluding Remarks	87
3	Josiphos Ligands: From Discovery to Technical Applications	93
	<i>Hans-Ulrich Blaser, Benoît Pugin, Felix Spindler, Esteban Mejía, and Antonio Togni</i>	
3.1	Introduction and Background	93
3.2	Discovery and Development of the Josiphos Ligand Family	94
3.3	Why Are Josiphos Ligands So Effective?	97

3.3.1	General Considerations	97
3.3.2	Structural Aspects of Transition Metal Complexes Containing Josiphos and Josiphos-Like Ligands	99
3.4	Catalytic Profile of the Josiphos Ligand Family	104
3.4.1	Enantioselective Reductions of C = C, C = O and C = N Bonds	104
3.4.1.1	Enantioselective Hydrogenation of C = C Bonds	104
3.4.1.2	Copper-Catalyzed Reduction of Activated C = C bonds with PMHS (Conjugate Reduction)	110
3.4.1.3	Enantioselective Hydrogenation of C = O Bonds	111
3.4.1.4	Enantioselective Hydrogenation of C = N Bonds	114
3.4.2	Enantioselective Hydrofunctionalizations	118
3.4.2.1	Hydroboration	118
3.4.2.2	Hydroamination and Hydrophosphonation	119
3.4.2.3	Hydrocarboxylation	120
3.4.3	Enantioselective C–C Bond Forming Reactions	120
3.4.3.1	Allylic Alkylation	120
3.4.3.2	Michael Addition	121
3.4.3.3	Heck Reaction	122
3.4.3.4	Miscellaneous C–C Reactions	123
3.4.4	Miscellaneous Enantioselective Reactions	125
3.4.4.1	Isomerization of Allylamines	125
3.4.4.2	Ring-Opening of Oxabicycles	125
3.4.4.3	Allylic Substitution	126
3.4.5	Application in Non-Enantioselective Reactions	127
3.5	Concluding Remarks	127
4	Chiral Spiro Ligands	137
	<i>Shou-Fei Zhu and Qi-Lin Zhou</i>	
4.1	Introduction	137
4.2	Preparation of Chiral Spiro Ligands	139
4.3	Asymmetric Hydrogenation	144
4.3.1	Hydrogenation of Functionalized Olefins	144
4.3.1.1	Hydrogenation of Enamides	144
4.3.1.2	Hydrogenation of Enamines	146
4.3.1.3	Hydrogenation of α,β -Unsaturated Acids	146
4.3.2	Hydrogenation of Ketones and Aldehydes	151
4.3.2.1	Hydrogenation of Simple Ketones	151
4.3.2.2	Hydrogenation of Racemic 2-Substituted Ketones via DKR	151
4.3.2.3	DKR Hydrogenation of Racemic 2-Substituted Aldehydes	153
4.3.3	Hydrogenation of Imines	154
4.3.4	Hydrogenation of 2-Substituted Quinolines	154
4.4	Asymmetric Carbon–Carbon Bond Forming Reaction	155

4.4.1	Rhodium-Catalyzed Arylation of Carbonyl Compounds and Imines	155
4.4.2	Palladium-Catalyzed Umpolung Allylation of Aldehydes	158
4.4.3	Copper-Catalyzed Conjugate Addition Reaction	158
4.4.4	Copper-Catalyzed Ring-Opening Reaction with Grignard Reagents	158
4.4.5	Nickel-Catalyzed Three-Component Coupling Reaction	159
4.4.6	Nickel-Catalyzed Hydrovinylation Reaction	161
4.4.7	Rhodium-Catalyzed Hydrosilylation/Cyclization Reaction	161
4.4.8	Palladium-Catalyzed Asymmetric Oxidative Cyclization	162
4.4.9	Gold-Catalyzed Ring Expanding Cycloisomerization	163
4.5	Asymmetric Carbon–Heteroatom Bond Forming Reaction	163
4.5.1	Palladium-Catalyzed Hydrosilylation	163
4.5.2	Palladium-Catalyzed Wacker-Type Oxidative Cyclization Reaction	163
4.5.3	Copper-Catalyzed Carbene Insertion into X–H Bonds	164
4.5.4	Allene-Based Allylic Cyclization Reactions	166
4.6	Conclusion	167
5	Chiral Bisoxazoline Ligands	171
	<i>Levi M. Stanley and Mukund P. Sibi</i>	
5.1	Introduction	171
5.2	Enantioselective Carbon–Carbon Bond Formation	176
5.2.1	Addition of Carbon Nucleophiles to C = O and C = N Bonds	176
5.2.1.1	Aldol Reactions	176
5.2.1.2	Mannich-Type Reactions	177
5.2.1.3	Nitroaldol (Henry) Reactions	179
5.2.1.4	Nitro-Mannich (Aza-Henry) Reactions	181
5.2.1.5	Addition of Activated Carbon Nucleophiles to Carbonyl Electrophiles	182
5.2.1.6	Addition of Activated Carbon Nucleophiles to Imines	183
5.2.1.7	Ene Reactions	184
5.2.1.8	Friedel–Crafts Reactions of Aromatic Compounds with C = O and C = N Bonds	184
5.2.2	1,4-Addition of Carbon Nucleophiles to α,β -Unsaturated Acceptors	186
5.2.3	Reactions of Radicals Alpha to Carbonyls	190
5.2.4	Cyclization Reactions	191
5.2.5	Rearrangement Reactions	191
5.3	Enantioselective Carbon–Heteroatom Bond Formation	193
5.3.1	1,4-Addition of Heteroatom Nucleophiles to α,β -Unsaturated Acceptors	193
5.3.1.1	1,4-Addition of Nitrogen Nucleophiles	193

5.3.1.2	1,4-Addition of Sulfur and Oxygen Nucleophiles	195
5.3.1.3	1,4-Addition of Boron Nucleophiles	195
5.3.2	Allylic Functionalization Reactions	196
5.3.3	α -Heteroatom Functionalization of Carbonyl Compounds	196
5.3.3.1	Amination	196
5.3.3.2	Oxygenation	197
5.3.3.3	Halogenation	197
5.3.4	X-H Insertion Reactions (X = O, N, S)	198
5.3.5	Cyclization Reactions	199
5.3.5.1	Carbonylative Cyclization	199
5.3.5.2	Wacker-Type Cyclizations	199
5.3.5.3	Hydroamination	201
5.3.6	Kinetic Resolution and Desymmetrization Reactions	201
5.3.6.1	Kinetic Resolution	201
5.3.6.2	Desymmetrization	201
5.4	Enantioselective Cycloaddition Reactions	202
5.4.1	Carbo-Diels–Alder Cycloadditions	202
5.4.2	Hetero-Diels–Alder Cycloadditions	204
5.4.3	Cyclopropanations	205
5.4.4	Aziridination	208
5.4.5	1,3-Dipolar Cycloadditions	209
5.4.6	Additional Cycloaddition Reactions	211
5.5	Conclusions	212

6 PHOX Ligands 221

Cory C. Bausch and Andreas Pfaltz

6.1	Introduction	221
6.2	Synthesis of PHOX Ligands	222
6.3	Nucleophilic Allylic Substitution	224
6.3.1	Palladium-Catalyzed Allylic Substitution	224
6.3.2	Tungsten- and Iridium-Catalyzed Allylic Substitution	229
6.3.3	Allylic Substitution in Total Synthesis	230
6.4	Decarboxylative Tsuji Allylations	231
6.4.1	Method Development	231
6.4.2	Application to Fluorinated Derivatives	234
6.4.3	Applications in Total Synthesis	235
6.5	Heck Reaction	237
6.5.1	Intermolecular Heck Reaction	237
6.5.2	Intramolecular Heck Reaction	238
6.6	Hydrogenation	240
6.6.1	Hydrogenation of Imines	240
6.6.2	Hydrogenation of Trisubstituted Olefins	240
6.6.3	Hydrogenation of Tetrasubstituted Olefins	243
6.6.4	Hydrogenation of Vinyl Phosphonates	243

6.6.5	Hydrogenation of α,β -Unsaturated Ketones	244
6.6.6	Hydrogenation of Ketones	244
6.6.7	Transfer Hydrogenation of Ketones	246
6.7	Cycloadditions	246
6.7.1	[3 + 2] Cycloadditions	246
6.7.2	Diels–Alder Reactions	247
6.8	Miscellaneous Reactions	248
6.8.1	Hydrosilylations	248
6.8.2	Pauson–Khand Reaction	248
6.8.3	Decarboxylative Protonation	249
6.8.4	Sigmatropic Rearrangements	250
6.8.5	Desymmetrization Reactions	251
6.8.6	Asymmetric Arylations	253
6.9	Conclusion	253
7	Chiral Salen Complexes	257
	<i>Wen-Zhen Zhang and Xiao-Bing Lu</i>	
7.1	Introduction	257
7.2	Synthesis of Chiral Salen Complexes	257
7.3	Structural Properties of Chiral Salen Complexes	259
7.4	Asymmetric Reactions Catalyzed by Chiral Salen Complexes	262
7.4.1	Asymmetric Epoxidation	262
7.4.2	Asymmetric Ring-Opening of Epoxides	266
7.4.2.1	Desymmetrization of Meso-Epoxides	266
7.4.2.2	Kinetic Resolution of Racemic Epoxides	269
7.4.2.3	Enantioselective Addition of Carbon Dioxide to Propylene Oxide	271
7.4.2.4	Asymmetric Alternating Copolymerization of Racemic Epoxides and Carbon Dioxide	272
7.4.2.5	Enantioselective Homopolymerization of Epoxides	273
7.4.3	Asymmetric Cyclopropanation	274
7.4.4	Asymmetric Conjugate Addition Reaction	277
7.4.5	Asymmetric Diels–Alder Reaction	281
7.4.6	Asymmetric Cyanohydrin Synthesis	284
7.4.7	Miscellaneous Reactions	287
7.5	Conclusion and Outlook	289
8	BINOL	295
	<i>Masakatsu Shibasaki and Shigeki Matsunaga</i>	
8.1	Introduction	295
8.2	Applications in Reduction and Oxidation	296
8.3	Metal/BINOL Chiral Lewis Acid Catalysts in Asymmetric C–C Bond Forming Reactions	300

8.3.1	Group IV Metal/BINOL Lewis Acid Catalysts	300
8.3.2	Group XIII Metal/BINOL Lewis Acid Catalysts	304
8.3.3	Rare Earth Metal/BINOL Lewis Acid Catalysts	307
8.4	Acid/Base Bifunctional Metal/BINOL Catalysts	308
8.4.1	Rare Earth Metal/Alkali Metal/BINOL Catalysts	308
8.4.2	Group XIII Metal/Alkali Metal/BINOL Catalysts	312
8.4.3	Other Metal/BINOL Complexes as Acid/Base Bifunctional Catalysts	316
8.4.4	Lewis Acid/Lewis Base Bifunctional Aluminium-Catalyst	321
8.5	BINOL in Organocatalysis	324
8.6	Summary	329

9 TADDOLate Ligands 333

Hélène Pellissier

9.1	Introduction	333
9.2	Nucleophilic Additions to C=O Double Bonds	334
9.2.1	Organozinc Additions to Aldehydes	334
9.2.2	Allylations	335
9.2.3	Aldol-Type Reactions	336
9.2.4	Miscellaneous Reactions	338
9.3	Nucleophilic Conjugate Additions to Electron-Deficient C=C Double Bonds	339
9.4	Nucleophilic Substitutions	342
9.4.1	Allylic Substitutions	342
9.4.2	α -Halogenations of Carbonyl Compounds	344
9.4.3	Miscellaneous Substitutions	345
9.5	Cycloaddition Reactions	345
9.5.1	Diels–Alder reactions	346
9.5.2	Hetero-Diels–Alder Reactions	347
9.5.3	Miscellaneous Cycloadditions	348
9.6	Oxidation and Reduction Reactions	349
9.7	Miscellaneous Reactions	351
9.8	Conclusions	354

10 Cinchona Alkaloids 361

Hongming Li, Yonggang Chen and Deng Li

10.1	Introduction	361
10.2	Metal Catalysis	363
10.3	Phase-Transfer Catalysis	367
10.3.1	Asymmetric Alkylations	367
10.3.2	Asymmetric Conjugate Additions	368
10.3.3	Asymmetric Aldol Reactions	368
10.3.4	Examples of Recent Applications	369
10.4	Nucleophilic Catalysis	370

10.4.1	Asymmetric Reactions with Ketenes	370
10.4.2	Asymmetric Morita–Baylis–Hillman Reactions	373
10.4.3	Asymmetric Cyanation of Simple Ketones	374
10.4.4	Recent Applications of Nucleophilic Catalysis by Cinchona Alkaloids	375
10.4.4.1	Asymmetric Conjugate Additions	375
10.4.4.2	Asymmetric Electrophilic Halogenations of Olefins	376
10.5	Base Catalysis	377
10.5.1	Asymmetric Alcoholysis of Cyclic Anhydrides	377
10.5.2	Conjugate Additions	380
10.5.3	Asymmetric Mannich and Aldol Reactions	381
10.6	Cooperative and Multifunctional Catalysis	382
10.6.1	Acid–Base Cooperative Catalysis	382
10.6.1.1	Asymmetric Conjugate Additions	382
10.6.1.2	Asymmetric 1,2-Additions to Carbonyls	386
10.6.1.3	Asymmetric 1,2-Additions to Imines	390
10.6.1.4	Asymmetric Friedel–Crafts Reactions	391
10.6.1.5	Asymmetric Diels–Alder Reactions	393
10.6.1.6	Asymmetric Fragmentation	394
10.6.2	Base–Iminium Cooperative Catalysis	396
10.6.2.1	Asymmetric Conjugate Additions	396
10.6.2.2	Asymmetric Friedel–Crafts Additions	398
10.6.2.3	Asymmetric Diels–Alder Reactions	399
10.6.2.4	Semipinacol-Type 1,2-Carbon Migration	399
10.6.3	Multifunctional Cooperative Catalysis	400
10.6.3.1	Tandem Conjugate Addition–Protonation Reactions	400
10.6.3.2	Catalytic Asymmetric Peroxidations	400
10.7	Conclusion	404
11	Proline Derivatives	409
	<i>Shilei Zhang and Wei Wang</i>	
11.1	Introduction	409
11.2	Proline as Organocatalyst	410
11.2.1	Aldol Reactions	410
11.2.1.1	Intermolecular Aldol Reactions	410
11.2.1.2	Intramolecular Aldol Reactions	412
11.2.1.3	Synthesis of Carbohydrates by Proline-Catalyzed Aldol Reactions	413
11.2.2	Mannich Reactions Catalyzed by Proline	414
11.2.3	Michael Addition Reactions Catalyzed by Proline	415
11.2.4	Morita–Baylis–Hillman (MBH) Reactions Catalyzed by Proline	416
11.2.5	α -Amination, α -Aminoxylation, and α -Alkylation of Carbonyl Compounds Catalyzed by Proline	417

11.2.6	Cascade/One-Pot Reactions Catalyzed by Proline	418
11.3	Proline Analogs as Organocatalysts	419
11.3.1	4-Hydroxyproline as Organocatalyst	419
11.3.2	Other Proline Analogs as Organocatalysts	421
11.4	5-Pyrrolidin-2-yltetrazole as Organocatalyst	422
11.5	Pyrrolidine-Based Sulfonamides as Organocatalysts	424
11.6	Pyrrolidine-Based Amides as Organocatalysts	425
11.7	Pyrrolidine Diamine Catalysts	427
11.8	Diarylprolinols or Diarylprolinol Ether Catalysts	429
11.8.1	Aldol Reactions, Mannich Reactions, and Other α -Functionalizations of Aldehydes Catalyzed by Diarylprolinols or Diarylprolinol Silyl Ethers	429
11.8.2	Michael Addition Reactions Catalyzed by Diarylprolinols or Diarylprolinol Silyl Ethers.	430
11.8.2.1	Michael Additions through an Enamine Pathway	430
11.8.2.2	Michael Additions through an Iminium Mechanism	430
11.8.3	Cycloaddition Reactions Catalyzed by Diarylprolinols or Diarylprolinol Silyl Ethers	433
11.8.4	Cascade Reactions Catalyzed by Diarylprolinol Silyl Ethers	435
11.8.4.1	Three-Membered Rings Formed by a [1 + 2] Strategy	435
11.8.4.2	Five-Membered Rings Formed by a [3 + 2] Strategy	436
11.8.4.3	Six-Membered Rings Formed by a [4 + 2] Strategy	437
11.8.4.4	Six-Membered Rings Formed by a [3 + 3] Strategy	437
11.8.4.5	Six-Membered Rings Formed by a [2 + 2 + 2] Strategy	438
11.8.4.6	Other Cascade Reactions	439
11.9	Concluding Remarks	439

Index	447
--------------	-----

