

Water in Organic Synthesis

Preface	V
Volume Editor's Preface	VII
Abstracts	IX
Table of Contents	XXIX
1	Introduction
	S. Kobayashi
	1
2	Structure and Properties of Water
	S. Otto and J. B. F. N. Engberts
	17
3	Aqueous Media: Reactions of C–C Multiple Bonds
	53
3.1	Asymmetric Oxidation Reactions: Sulfoxidation, Epoxidation, Dihydroxylation, and Aminohydroxylation
	T. Katsuki
	53
3.2	Hydrogenation of Alkenes, Alkynes, Arenes, and Hetarenes
	F. Joó
	95
3.3	Hydroformylation and Related Reactions
	L. T. Mika and I. T. Horváth
	121
3.4	Conjugate Addition Reactions
	N. Mase
	155
3.5	Cyclopropanation Reactions
	G. Simonneaux, P. Le Maux, and S. Chevance
	211
3.6	Metathesis Reactions
	C. Torborg, C. Samojlowicz, and K. Grela
	225
4	Aqueous Media: Reactions of Carbonyl and Imino Groups
	257
4.1	Reduction of Carbonyl and Imino Groups
	X. Wu and J. Xiao
	257
4.2	Alkylation, Allylation, and Benzylation of Carbonyl and Imino Groups
	L. Zhao and C.-J. Li
	301
4.3	Arylation, Vinylation, and Alkynylation of Carbonyl and Imino Groups
	L. Zhao and C.-J. Li
	333

4.4	Aldol Reaction M. Woyciechowska, O. El-Sepelgy, and J. Mlynarski	353
4.5	Mannich Reaction and Baylis–Hillman Reaction M. Benohoud and Y. Hayashi	385
5	Aqueous Media: Cyclization, Rearrangement, Substitution, Cross Coupling, Oxidation, and Other Reactions	433
5.1	Cycloaddition and Cyclization Reactions G. Molteni	433
5.2	Pericyclic Rearrangements: Sigmatropic, Electrocyclic, and Ene Reactions F. Fringuelli and O. Piermatti	481
5.3	Allylic and Aromatic Substitution Reactions Y. Uozumi	511
5.4	Cross-Coupling and Heck Reactions D. A. Alonso and C. Nájera	535
5.5	Ring Opening of Epoxides and Aziridines C. Ogawa and S. Kobayashi	579
5.6	Asymmetric α-Functionalization of Carbonyl Compounds and Alkylation of Enolates S. Shirakawa and K. Maruoka	601
5.7	Oxidation of Alcohols, Allylic and Benzylic Oxidation, Oxidation of Sulfides R. A. Sheldon	617
5.8	Free-Radical Reactions H. Yorimitsu and K. Oshima	645
5.9	Polymerization M. Ouchi and M. Sawamoto	679
6	Special Techniques with Water	697
6.1	Organic Synthesis “On Water” A. Chanda and V. V. Fokin	697
6.2	Sub- and Supercritical Water A. Kruse and E. Dinjus	749
6.3	β-Cyclodextrin Chemistry in Water F. Hapiot and E. Monflier	773
7	Industrial Application	807

7.1	Hydroformylation	E. Wiebus, K. Schmid, and B. Cornils	807
7.2	Industrial Applications Other than Hydroformylation	Y. Mori and S. Kobayashi	831
8	Perspective: The New World of Organic Chemistry Using Water as Solvent	S. Kobayashi	855
 Keyword Index		869	
Author Index		917	
Abbreviations		955	

Table of Contents

1	Introduction	
	S. Kobayashi	
<hr/>		
1	Introduction	1
1.1	Water-Compatible Lewis Acids	1
1.2	Lewis Acid–Surfactant Combined Catalysts for Organic Reactions in Water	5
<hr/>		
2	Structure and Properties of Water	
	S. Otto and J. B. F. N. Engberts	
<hr/>		
2	Structure and Properties of Water	17
2.1	The Single Water Molecule	18
2.2	Liquid Water	20
2.3	Water as a Reaction Medium for Organic Synthesis	24
2.4	Thermodynamics of Hydration	25
2.5	Solvent Properties of Water	26
2.5.1	The Size of the Water Molecule	26
2.5.2	Polarizability	27
2.5.3	Solvent Polarity Indicators	28
2.5.4	Solvatochromic Solvent Parameters	29
2.5.5	The Solvatochromic Comparison Method: Linear Solvation Energy Relationships	30
2.5.6	Cohesive Energy Density	32
2.5.7	Internal Pressure	32
2.5.8	The Ionic Product of Water: Proton and Hydroxide Ion Mobilities	32
2.5.9	Water at High and Low Temperatures and Pressures	33
2.5.10	Water and Deuterium Oxide	34
2.6	Aqueous Electrolyte Solutions	35
2.6.1	Ionic Hydration: Hydration Numbers	35
2.6.2	Dynamics of Ion Hydration	37
2.7	Hydrophobic Effects	38
2.7.1	Hydrophobic Hydration	39
2.7.2	Hydrophobic Interactions	41
2.8	Organic Reactivity in Water	42
2.8.1	Catalysis in Water	42
2.8.2	Micellar Catalysis	43

2.8.3	Hydrophobic Effects on Reactivity: Initial-State versus Transition-State Effects	44
2.8.4	Effects of Additives on Reactivity in Water	46
2.8.4.1	Salt Effects	46
2.8.4.2	Cosolvent Effects	46
2.8.5	Reactions on Water	47
2.8.6	Reactions in Supercritical Water	47
2.8.7	Water as a Green Solvent	48
2.9	Epilogue	48

3 Aqueous Media: Reactions of C–C Multiple Bonds

3.1	Asymmetric Oxidation Reactions: Sulfoxidation, Epoxidation, Dihydroxylation, and Aminohydroxylation	
	T. Katsuki	
3.1	Asymmetric Oxidation Reactions: Sulfoxidation, Epoxidation, Dihydroxylation, and Aminohydroxylation	53
3.1.1	Catalyst Tuning by Water	54
3.1.1.1	Enantioselective Oxidation of Sulfides Using a Water-Modified Titanium/Tartrate Catalyst	54
3.1.1.2	Asymmetric Aerobic Epoxidation Using a Water-Bound Ruthenium–Salen Complex as Catalyst	54
3.1.2	Enantioselective Oxidation of Sulfides under Aqueous Conditions	55
3.1.2.1	Enantioselective Oxidation of Sulfides Using Chiral Metal–Schiff Base Catalysts	55
3.1.2.1.1	Vanadium-Catalyzed Oxidation	55
3.1.2.1.2	Iron-Catalyzed Oxidation	56
3.1.2.2	Enantioselective Oxidation of Sulfides Using Metallosalen and Related Complexes as Catalysts	57
3.1.2.2.1	Manganese–Salen-Catalyzed Oxidation	57
3.1.2.2.2	Titanium–Salen-Catalyzed Oxidation	57
3.1.2.2.3	Aluminum–Salalen-Catalyzed Oxidation	58
3.1.2.3	Asymmetric Oxidation of Sulfides in Water	59
3.1.2.3.1	Platinum-Catalyzed Asymmetric Oxidation of Sulfides	59
3.1.2.3.2	Iron–Salan-Catalyzed Oxidation	60
3.1.3	Enantioselective Epoxidation	61
3.1.3.1	Asymmetric Epoxidation of Allylic Alcohols	62
3.1.3.1.1	Asymmetric Epoxidation of Allylic Alcohols under Aqueous Conditions	62
3.1.3.1.2	Asymmetric Epoxidation of Allylic Alcohols Using Aqueous Hydrogen Peroxide	63

3.1.3.2	Asymmetric Epoxidation of Unfunctionalized Alkenes	64
3.1.3.2.1	Metalloporphyrin-Catalyzed Enantioselective Epoxidation	64
3.1.3.2.2	Enantioselective Epoxidation Using Metal–Salen/Salalen/Salan Complexes as Catalyst	65
3.1.3.2.2.1	Bioinspired Enantioselective Epoxidation Using Manganese–Salalen or Manganese–Salen Complexes as Catalyst	66
3.1.3.2.2.2	Enantioselective Epoxidation Using Titanium–Salalen or Titanium–Salan Complexes as Catalyst	67
3.1.3.2.3	Iron-Catalyzed Enantioselective Epoxidation	71
3.1.3.2.4	Ruthenium-Catalyzed Enantioselective Epoxidation	71
3.1.3.2.5	Platinum-Catalyzed Enantioselective Epoxidation	72
3.1.3.3	Enantioselective Epoxidation Using Organic Compounds as Catalysts	74
3.1.3.3.1	Chiral Ketone Catalyzed Enantioselective Epoxidation	74
3.1.3.3.2	Enantioselective Epoxidation of Electron-Deficient Alkenes Using Organocatalysts	76
3.1.3.3.2.1	Polyamino Acid Catalyzed Asymmetric Epoxidation	76
3.1.3.3.2.2	Phase-Transfer Catalyst Mediated Epoxidation	77
3.1.3.3.2.3	Amine-Catalyzed Asymmetric Epoxidation	79
3.1.4	Enantioselective Dihydroxylation	81
3.1.4.1	Osmium-Catalyzed Enantioselective Dihydroxylation	81
3.1.4.2	Iron-Catalyzed Enantioselective Dihydroxylation	88
3.1.5	Enantioselective Aminohydroxylation	88
3.1.6	Conclusions	91
3.2	Hydrogenation of Alkenes, Alkynes, Arenes, and Hetarenes	
	F. Joó	
3.2	Hydrogenation of Alkenes, Alkynes, Arenes, and Hetarenes	95
3.2.1	Catalysts and General Techniques for Hydrogenations in Water	95
3.2.2	Hydrogenation of Alkenes	96
3.2.2.1	Alkanes by Hydrogenation of Alkenes with Water-Soluble Analogues of Wilkinson’s Catalyst	97
3.2.2.1.1	Using Preprepared Rhodium(I)-Sulfonated Triphenylphosphine Catalysts	97
3.2.2.1.2	Using In Situ Prepared Rhodium(I)-Sulfonated Triphenylphosphine Catalysts	97
3.2.2.1.3	Using In Situ Prepared Rhodium(I) Catalysts in Microemulsions	99
3.2.2.2	Alkanes by Hydrogenation of Alkenes with Rhodium(I)-Based Catalysts Attached to Proteins	100
3.2.2.3	Alkanes by Hydrogenation of Alkenes with Ruthenium(II) Catalysts	100

3.2.2.4	Alkanes by Hydrogenation of Alkenes with Polymer-Stabilized Colloidal Metal Catalysts	101
3.2.2.4.1	Using an In Situ Prepared Palladium–Poly(vinylpyrrolidone) Catalyst	101
3.2.2.4.2	Using a Preprepared Palladium–Poly(vinylpyrrolidone) Catalyst	102
3.2.2.5	Isotope Labeling by Hydrogenation in Water	103
3.2.3	Asymmetric Hydrogenation of Alkenes	104
3.2.3.1	Chiral Alkanes by Hydrogenation of Prochiral Alkenes Catalyzed by Rhodium(I) Complexes	105
3.2.3.2	Chiral Alkanes by Hydrogenation of Prochiral Alkenes Catalyzed by Ruthenium(II) Complexes	107
3.2.3.2.1	In Homogeneous Aqueous Solution with a Ruthenium(II)–Tetrasulfonated 2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl Catalyst	107
3.2.3.2.2	Alcanoic Acids by Hydrogenation of Alkenoic Acids with a Water-Soluble Chiral Ruthenium(II)–Bisphosphine Catalyst	108
3.2.4	Hydrogenation of Dienes	108
3.2.4.1	Alkenes by Selective Hydrogenation of Dienes with Potassium Pentacyanohydridocobaltate(III)	108
3.2.4.2	Alkenoic Acids by Selective Hydrogenation of Hexa-2,4-dienoic Acid with a Ruthenium(II)–Sulfonated Phosphine Catalyst	109
3.2.5	Hydrogenation of Polymers	110
3.2.5.1	Modified Elastomers by Hydrogenation of Polymers	110
3.2.6	Hydrogenation of Alkynes	112
3.2.6.1	Alkenes by Selective Hydrogenation of Alkynes	112
3.2.6.1.1	Hydrogenation of Pent-2-yne with Polymer-Stabilized Metal Colloids	112
3.2.6.1.2	Hydrogenation of Diphenylacetylene with a Ruthenium(II)–Sulfonated Triphenylphosphine Catalyst	113
3.2.7	Hydrogenation of Arenes and Hetarenes	114
3.2.7.1	Hydrogenation of Benzene Derivatives with a Homogeneous Ruthenium-Based Catalyst	114
3.2.7.2	Hydrogenation of Aromatics with Stabilized Metal Nanoparticles	115
3.2.7.2.1	Arene Hydrogenation Catalyzed by Aqueous Solutions of Rhodium(III) Chloride Trihydrate and Aliquat 336	115
3.2.7.2.2	Arene Hydrogenation Catalyzed by Aqueous Solutions of Rhodium(III) Chloride and <i>N</i> -Alkyl- <i>N</i> -(2-hydroxyethyl)- <i>N,N</i> -dimethylammonium Surfactants	115
3.2.7.2.3	Hydrogenation of Arenes with Poly(<i>N</i> -vinylpyrrolidone)-Stabilized Ruthenium Nanoparticles	116
3.2.7.2.4	4-Propylcyclohexanols by Stereoselective Hydrogenation of 4-Propylphenols (Lignin Degradation Model Compounds)	117
3.2.7.2.5	Hydrogenation of Hetarenes with Water-Soluble Ruthenium(II) Complexes	118

3.3	Hydroformylation and Related Reactions	
	L. T. Mika and I. T. Horváth	
<hr/>		
3.3	Hydroformylation and Related Reactions	121
3.3.1	Background to Hydroformylation and Related Reactions	123
3.3.2	Ligands for Hydroformylation in Aqueous Media	123
3.3.3	Hydroformylation in Aqueous Media	127
3.3.3.1	Hydroformylation of Higher Alkenes	131
3.3.3.2	Hydroformylation of Functionalized Alkenes	139
3.3.3.3	Asymmetric Hydroformylation Reactions	140
3.3.3.4	Laboratory Techniques	142
3.3.3.4.1	Biphasic Hydroformylation under Batch Conditions	142
3.3.3.4.2	Biphasic Hydroformylation under Continuous Conditions	143
3.3.4	Supported Aqueous-Phase Hydroformylation	144
3.3.5	Hydrocarboxylation in Aqueous Media	147
<hr/>		
3.4	Conjugate Addition Reactions	
	N. Mase	
<hr/>		
3.4	Conjugate Addition Reactions	155
3.4.1	C—H Bond Formation	155
3.4.1.1	Metal-Complex-Mediated Conjugate Reduction	155
3.4.1.2	Metal-Free Catalytic Conjugate Reduction of Enals	156
3.4.2	C—C Bond Formation	158
3.4.2.1	Addition of Alkyl Groups in C—C Bond Formation	158
3.4.2.1.1	Radical-Mediated Addition of Alkyl Groups	158
3.4.2.1.2	Metal-Complex-Mediated Addition of Alkyl Groups	159
3.4.2.1.3	Metal-Free Catalytic Addition of Alkyl Groups	160
3.4.2.2	Addition of Alkenyl and Aryl Groups in C—C Bond Formation	163
3.4.2.2.1	Catalyst-Free Addition of Aryl Groups	163
3.4.2.2.2	Metal-Complex-Catalyzed Addition of Alkenyl and Aryl Groups	164
3.4.2.2.2.1	Addition of Alkenyl and Aryl Groups to Carbonyl Compounds	164
3.4.2.2.2.2	Asymmetric Addition of Aryl Groups to Carbonyl Compounds	166
3.4.2.2.2.3	Addition of Indoles to Electron-Deficient Alkenes	167
3.4.2.2.3	Metal-Free Catalytic Addition of Aryl Groups	169
3.4.2.2.3.1	Brønsted Acid Catalyzed Addition of Indoles to Electron-Deficient Alkenes	169
3.4.2.2.3.2	Asymmetric Addition of Pyrroles and Indoles to Enals via Iminium Catalysis	170
3.4.2.3	Addition of Alkynyl Groups in C—C Bond Formation	171

3.4.2.3.1	Metal-Complex-Catalyzed Addition of Alkynyl Groups	171
3.4.2.4	Addition of Carbonyl Compounds in C—C Bond Formation	174
3.4.2.4.1	Catalyst-Free Addition of Carbonyl Compounds	174
3.4.2.4.2	Metal-Complex-Catalyzed Addition of Carbonyl Compounds to Enones	174
3.4.2.4.3	Metal-Free Catalytic Addition of Carbonyl Compounds	176
3.4.2.4.3.1	Addition of Carbonyl Compounds to Enals or Enones via Iminium Catalysis	176
3.4.2.4.3.2	Addition of Carbonyl Compounds to α,β -Unsaturated Esters via Enamine Catalysis	179
3.4.2.4.3.3	Addition of Carbonyl Compounds to Nitroalkenes via Enamine Catalysis	180
3.4.2.4.3.4	Addition of Carbonyl Compounds Using Other Metal-Free Catalysts	186
3.4.3	C—N Bond Formation	188
3.4.3.1	Catalyst-Free Addition in C—N Bond Formation	188
3.4.3.1.1	Addition of Amines to Enones	188
3.4.3.1.2	Addition of Amines to α,β -Unsaturated Carboxylic Acid Derivatives	189
3.4.3.1.3	Addition of Amines to Acrylonitrile	191
3.4.3.1.4	Addition of Amines to Nitro, Phosphonate, and Sulfonate Derivatives	193
3.4.3.2	Metal-Complex-Catalyzed Addition in C—N Bond Formation	195
3.4.3.3	Metal-Free Catalytic Addition in C—N Bond Formation	196
3.4.4	C—O Bond Formation	198
3.4.4.1	Metal-Free Catalytic Addition in C—O Bond Formation	198
3.4.4.1.1	Phosphine-Catalyzed Hydration	198
3.4.4.1.2	Asymmetric Addition of Alcohols to Enals via Iminium Catalysis	198
3.4.5	C—S and C—Se Bond Formation	199
3.4.5.1	Catalyst-Free Addition in C—S Bond Formation	199
3.4.5.1.1	Addition of Thiols to Enones and Quinones	199
3.4.5.1.2	Addition of Thiols to α,β -Unsaturated Carboxylic Acid Derivatives	201
3.4.5.1.3	Addition of Thiols to Acrylonitrile	204
3.4.5.1.4	Addition of Thiols to Nitroalkenes	205
3.4.5.2	Catalytic Addition in C—S Bond Formation	206
3.4.5.3	C—Se Bond Formation: Reaction of Zinc Selenolates	207
3.5	Cyclopropanation Reactions	
	G. Simonneaux, P. Le Maux, and S. Chevance	
<hr/>		
3.5	Cyclopropanation Reactions	211
3.5.1	Transition-Metal-Catalyzed Reaction of Diazo Compounds	211
3.5.1.1	Reaction Using Water-Soluble Catalysts	212
3.5.1.1.1	Using pybox–Ruthenium Catalysts	212

3.5.1.1.2	Using Metalloporphyrin Catalysts	213
3.5.1.2	Using Diazo Esters in Biphasic Media	216
3.5.1.3	In Situ Generation of the Diazo Reagent	218
3.5.2	Triphenylarsine-Catalyzed Cyclopropanation	221
3.5.3	Radical Reaction from Halogenated Compounds and Zinc Powder	222
3.6	Metathesis Reactions	
	C. Torborg, C. Samojlowicz, and K. Grela	
<hr/>		
3.6	Metathesis Reactions	225
3.6.1	Aqueous Alkene Metathesis Using Poorly Defined Catalytic Systems	227
3.6.1.1	Polymerization of 7-Oxabicyclo[2.2.1]hept-2-ene Derivatives	227
3.6.1.2	Polymerization of 7-Oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate Derivatives	227
3.6.2	Aqueous Alkene Metathesis Using Water-Insoluble Well-Defined Catalysts	229
3.6.2.1	Applications in Homogeneous Aqueous Solutions	229
3.6.2.1.1	Ring-Closing Metathesis Using Ruthenium-Based Defined Catalysts in Homogeneous Water/Organic Solvent Mixtures	229
3.6.2.1.2	Cross Metathesis Using Ruthenium-Based Defined Catalysts in Homogeneous Water/Organic Solvent Mixtures	230
3.6.2.2	Applications in Water-Containing Heterogeneous Mixtures	231
3.6.2.2.1	Metathesis in the Presence of Water without a Cosolvent, Additives, or Surfactants	231
3.6.2.3	Metathesis in Aqueous Emulsions	232
3.6.2.3.1	Ring-Opening Metathesis Polymerization in Aqueous Emulsions	232
3.6.2.3.1.1	Ring-Opening Polymerization Using Dodecytrimethylammonium Bromide as a Surfactant	232
3.6.2.3.1.1.1	Polymerization of Bicyclo[2.2.1]hept-2-enes and 7-Oxa Derivatives	232
3.6.2.3.1.1.2	Polymerization of Bicyclo[2.2.1]hept-5-ene-2-carboxamides and 7-Oxa Derivatives	233
3.6.2.3.1.1.3	Polymerization of Vancomycin-Based Oligomers	234
3.6.2.3.1.2	Polymerization Using Sodium Dodecyl Sulfate as a Surfactant	235
3.6.2.3.1.2.1	Polymerization of Bicyclo[2.2.1]hept-2-ene	235
3.6.2.3.1.2.2	Polymerization of Cyclooctadiene and Cyclooctene	235
3.6.2.3.1.3	Polymerizations Using Acacia Gum as a Surfactant	235
3.6.2.3.2	Ring-Closing Metathesis and Cross Metathesis in Aqueous Emulsions	236
3.6.2.3.2.1	Ring-Closing Metathesis and Cross Metathesis in Aqueous Emulsions Using Surfactants	236

3.6.2.3.2.1.1	Ring-Closing Metathesis of Diethyl 2,2-Diallylmalonate Using Sodium Dodecyl Sulfate	236
3.6.2.3.2.1.2	Homo-Cross Metathesis of Vancomycin Derivatives Using Dodecyltrimethylammonium Bromide	236
3.6.2.3.2.1.3	Cross Metathesis Using Polyoxyethyl α -Tocopheryl Sebacate	237
3.6.2.3.2.1.4	Ring-Closing Metathesis Using Polyoxyethyl α -Tocopherol Sebacate	238
3.6.2.3.2.1.5	Ring-Closing Metathesis and Cross Metathesis in the Presence of Calix[n]arenes	239
3.6.2.3.2.2	Ring-Closing Metathesis and Cross Metathesis in Aqueous Emulsions Using Other Methods	239
3.6.2.3.2.2.1	Non-Water-Soluble Catalysts Embedded in Poly(dimethylsiloxane)	239
3.6.2.3.2.2.2	Ring-Closing Metathesis and Cross Metathesis Using Dendrimers	240
3.6.2.4	Applications of Water-Insoluble Catalysts for Protein Modification	242
3.6.2.4.1	Cross Metathesis with SBL-156Sac	242
3.6.2.4.2	Intramolecular Alkene Metathesis in O-Crotylserine Containing cpVenus-2TAG	243
3.6.3	Tagged Metathesis Catalysts	243
3.6.3.1	Catalysts Tagged to Hydrophilic Polymers	243
3.6.3.2	Small-Molecule Polar Catalysts	247
3.6.3.3	Applications in Heterogeneous Aqueous Media	252

4**Aqueous Media: Reactions of Carbonyl and Imino Groups**

4.1**Reduction of Carbonyl and Imino Groups**

X. Wu and J. Xiao

4.1	Reduction of Carbonyl and Imino Groups	257
4.1.1	Reduction of Carbonyl Groups	257
4.1.1.1	Hydrogenation of Carbonyl Groups	257
4.1.1.1.1	Nonsymmetric Hydrogenation of Aldehydes and Ketones	257
4.1.1.1.2	Hydrogenation of Carbon Dioxide	262
4.1.1.1.3	Asymmetric Hydrogenation of Ketones	264
4.1.1.2	Transfer Hydrogenation of Carbonyl Groups	265
4.1.1.2.1	Nonsymmetric Transfer Hydrogenation	268
4.1.1.2.2	Asymmetric Transfer Hydrogenation	272
4.1.1.2.2.1	Of Ketones with Molecular Catalysts	272
4.1.1.2.2.2	Of Ketones with Immobilized Catalysts	276
4.1.1.2.2.3	Of Ketones by Biomimetic Reduction	279
4.1.1.2.2.4	Of Functionalized Ketones	282

4.1.2	Reduction of Imino Groups	286
4.1.2.1	Hydrogenation of Imino Groups	286
4.1.2.1.1	Nonsymmetric Hydrogenation	286
4.1.2.1.2	Asymmetric Hydrogenation	288
4.1.2.2	Transfer Hydrogenation of Imino Groups	290
4.1.2.2.1	With Water-Soluble Catalysts	290
4.1.2.2.2	With Water-Insoluble Catalysts	291
4.2	Alkylation, Allylation, and Benzylation of Carbonyl and Imino Groups	
	L. Zhao and C.-J. Li	
4.2	Alkylation, Allylation, and Benzylation of Carbonyl and Imino Groups	301
4.2.1	Metal-Mediated Alkylation of Carbonyl and Imino Groups	301
4.2.1.1	Alkylation of Carbonyl Groups	301
4.2.1.1.1	Metal-Mediated Alkylation Reactions with Alkyl Halides	301
4.2.1.1.2	Metal-Mediated Reformatsky-Type Reactions	303
4.2.1.2	Alkylation of Imino Groups	304
4.2.2	Metal-Mediated Allylation of Carbonyl and Imino Groups	306
4.2.2.1	Allylation of Carbonyl Groups	307
4.2.2.1.1	Mediated by Zinc	307
4.2.2.1.2	Mediated by Tin	308
4.2.2.1.3	Mediated by Indium	311
4.2.2.1.4	Mediated by Other Metals	319
4.2.2.1.5	Regio- and Stereoselectivity	320
4.2.2.1.6	Asymmetric Allylation	325
4.2.2.2	Allylation of Imino Groups	325
4.2.3	Metal-Mediated Benzylation of Carbonyl and Imino Groups	327
4.3	Arylation, Vinylation, and Alkynylation of Carbonyl and Imino Groups	
	L. Zhao and C.-J. Li	
4.3	Arylation, Vinylation, and Alkynylation of Carbonyl and Imino Groups	333
4.3.1	Arylation and Vinylation of Carbonyl and Imino Groups	333
4.3.1.1	Arylation and Vinylation of Aldehydes	333
4.3.1.2	Arylation and Vinylation of Imino Groups	336
4.3.1.2.1	Asymmetric Arylation of Imino Groups	337
4.3.2	Alkynylation of Carbonyl and Imino Groups	338
4.3.2.1	Alkynylation of Carbonyl Compounds	339

4.3.2.1.1	Alkynylation of Aldehydes	339
4.3.2.1.2	Alkynylation of Acid Chlorides	343
4.3.2.1.3	Alkynylation of Ketones	344
4.3.2.2	Alkynylation of Imino Groups	345
4.3.2.2.1	Alkynylation of Imines	345
4.3.2.2.2	Alkynylation of Iminium Ions	347
4.3.2.2.3	Alkynylation of Acylimines or Acyliminium Ions	349
 4.4	Aldol Reaction	
	M. Woyciechowska, O. El-Sepelgy, and J. Mlynarski	
<hr/> 4.4	Aldol Reaction	353
4.4.1	Indirect Catalytic Aldol Addition Reactions	353
4.4.1.1	Mukaiyama-Type Aldol Reactions	354
4.4.1.1.1	Application of Bis(4,5-dihydrooxazole) Ligands	355
4.4.1.1.2	Application of Crown Ether Type Ligands	356
4.4.1.1.3	Europium-Catalyzed Mukaiyama Aldol Reactions	358
4.4.1.1.4	Application of a Trost-Type Semicrown Ligand	359
4.4.1.1.5	Application of Iron(II) and Zinc(II) Complexes	360
4.4.1.1.6	Hydroxymethylation of Silyl Enol Ethers	361
4.4.2	Direct Catalytic Aldol Reactions	363
4.4.2.1	Enamine-Based Direct Aldol Reactions	364
4.4.2.1.1	Synthesis of 2-[Aryl(hydroxy)methyl]cycloalkanones	365
4.4.2.1.2	Synthesis of 4-Aryl-4-hydroxybutan-2-ones	369
4.4.2.1.3	Synthesis of <i>syn</i> - α -Methyl- β -hydroxy Ketones	370
4.4.2.1.4	Synthesis of Alcohols Containing a Quaternary Carbon Atom	370
4.4.2.1.5	Synthesis of 1,4-Dihydroxylated Ketones	372
4.4.2.1.6	Synthesis of <i>syn</i> -3,4-Dihydroxylated Ketones	373
4.4.2.1.7	Synthesis of 1,3,4-Trihydroxylated Ketones	374
4.4.2.1.8	Synthesis of 1,3-Dihydroxylated Compounds	377
4.4.2.1.9	Synthesis of Erythrose and Threose Derivatives	378
4.4.2.2	Direct Aldol Reactions Assisted by Chiral Metal Complexes	380
4.4.2.2.1	Synthesis of Hydroxymethyl Ketones	381

4.5	Mannich Reaction and Baylis–Hillman Reaction	
	M. Benhoud and Y. Hayashi	
<hr/>		
4.5	Mannich Reaction and Baylis–Hillman Reaction	385
4.5.1	Mannich Reaction	385
4.5.1.1	Reaction Catalyzed by Organometals	386
4.5.1.1.1	Lewis Acids	386
4.5.1.1.1.1	Reaction Using a Preformed Imine or a Preformed Enolate	386
4.5.1.1.1.2	One-Pot Three-Component Reaction	389
4.5.1.1.1.3	Stereoselective Methods	391
4.5.1.1.2	Lewis Bases	395
4.5.1.2	Reaction Catalyzed by Brønsted Acids or Bases	396
4.5.1.2.1	Brønsted Acids	396
4.5.1.2.2	Brønsted Bases	400
4.5.1.2.3	Enantioselective Methods	400
4.5.1.3	Chiral Amine Catalysis via an Enamine Intermediate	403
4.5.1.3.1	<i>syn</i> -Selective Mannich Reaction	405
4.5.1.3.2	<i>anti</i> -Selective Mannich Reaction	413
4.5.1.3.3	Application in Total Synthesis	416
4.5.1.4	Autocatalysis	418
4.5.1.5	Biocatalyzed Mannich Reaction	419
4.5.2	Baylis–Hillman Reaction	420
4.5.2.1	Stereoselective Baylis–Hillman Reaction	426
4.5.2.2	Biocatalyzed Baylis–Hillman Reaction	430
<hr/>		
5	Aqueous Media: Cyclization, Rearrangement, Substitution, Cross Coupling, Oxidation, and Other Reactions	
<hr/>		
5.1	Cycloaddition and Cyclization Reactions	
	G. Molteni	
<hr/>		
5.1	Cycloaddition and Cyclization Reactions	433
5.1.1	Cycloadditions	434
5.1.1.1	Diels–Alder Cycloadditions	434
5.1.1.1.1	Hetero-Diels–Alder Cycloadditions	442
5.1.1.1.2	Lewis Acid Catalyzed Diels–Alder Cycloadditions	448
5.1.1.2	1,3-Dipolar Cycloadditions	454
5.1.1.2.1	Nitrile Imine Cycloadditions	455

5.1.1.2.2	Nitrile Oxide Cycloadditions	457
5.1.1.2.3	Diazo Compound Cycloadditions	462
5.1.1.2.4	Azide Cycloadditions	463
5.1.1.2.5	Azomethine Ylide Cycloadditions	467
5.1.1.2.6	Nitrone Cycloadditions	468
5.1.2	Cyclization Reactions	470
5.1.2.1	Barbier-Type Cyclizations	470
5.1.2.2	Epoxide-Opening Cascade Cyclizations	473
5.1.2.3	Radical Cyclizations	474
 5.2	Pericyclic Rearrangements: Sigmatropic, Electrocyclic, and Ene Reactions	
	F. Fringuelli and O. Piermatti	
<hr/> 5.2	Pericyclic Rearrangements: Sigmatropic, Electrocyclic, and Ene Reactions	481
5.2.1	Sigmatropic Rearrangement	481
5.2.1.1	Claisen Rearrangement	481
5.2.1.1.1	First Examples in Water	482
5.2.1.1.2	Rearrangement of Allyl Vinyl Ethers	483
5.2.1.1.3	Rearrangement of Allyl Aryl Ethers	485
5.2.1.1.4	Claisen Rearrangement Coupled with Other Reactions	487
5.2.1.1.5	Aza-Claisen Rearrangements	490
5.2.1.2	Cope Rearrangement	493
5.2.1.2.1	Rearrangement of Compounds Containing a Hydrophilic Group	494
5.2.1.2.2	Catalyzed Rearrangement	494
5.2.1.2.3	Aza-Cope Rearrangement	495
5.2.1.3	[1,5] Rearrangement	495
5.2.1.4	[2,3] Rearrangement	496
5.2.1.4.1	Rearrangement of Allyl Sulfoxides	496
5.2.1.4.2	Rearrangement of Sulfonium and Ammonium Ylides	497
5.2.2	Electrocyclic Rearrangement	500
5.2.2.1	4π -Electrocyclic Rearrangement	500
5.2.2.2	6π -Electrocyclic Rearrangement	501
5.2.3	Ene Reaction	502
5.2.3.1	Photoinduced Reaction	503
5.2.3.2	Aza-Ene Reaction	504
5.2.3.3	Ene-Like Reaction	505
5.2.3.4	Catalyzed Reactions	506

5.3	Allylic and Aromatic Substitution Reactions	
	Y. Uozumi	
<hr/>		
5.3	Allylic and Aromatic Substitution Reactions	511
5.3.1	Allylic Substitution	511
5.3.1.1	Palladium-Catalyzed Substitution	511
5.3.1.1.1	Using Water-Soluble Ligands	511
5.3.1.1.1.1	Substitution of Allylic Esters	512
5.3.1.1.1.1.1	Intermolecular Allylic Substitution	512
5.3.1.1.1.1.2	Intramolecular Allylic Substitution	513
5.3.1.1.1.2	Substitution of Allylic Alcohols	514
5.3.1.1.2	Using Amphiphilic Polymeric Ligands	515
5.3.1.1.3	Using Additives	517
5.3.1.1.4	Miscellaneous Metal-Catalyzed Systems	519
5.3.1.2	Metal-Mediated Substitution	521
5.3.1.3	Allylic Substitution with Calixarene Catalysts	521
5.3.1.4	Asymmetric Allylic Substitution	522
5.3.1.4.1	Substitution of Acyclic Allylic Systems	522
5.3.1.4.2	Substitution of Cyclic Allylic Systems	523
5.3.2	Aromatic Substitution	525
5.3.2.1	Electrophilic Aromatic Substitution	525
5.3.2.1.1	Electrophilic Substitution of Indoles	525
5.3.2.1.1.1	Synthesis of Bis(indolyl)methanes	525
5.3.2.1.1.2	Synthesis of 3-Substituted Indoles	527
5.3.2.1.1.2.1	Nucleophilic Addition of Indoles	527
5.3.2.1.1.2.2	Michael Addition of Indoles	527
5.3.2.1.2	Electrophilic Substitution of Benzenes	528
5.3.2.1.2.1	Indium-Catalyzed Aromatic Substitution	528
5.3.2.1.2.2	Sulfonic Acid Catalyzed Aromatic Substitution	529
5.3.2.2	Nucleophilic Aromatic Substitution	530
5.3.2.2.1	Intermolecular C—N and C—S Bond-Forming Substitution	530
5.3.2.2.2	Intramolecular C—N and C—S Bond-Forming Substitution	531

5.4	Cross-Coupling and Heck Reactions	
	D. A. Alonso and C. Nájera	
<hr/>		
5.4	Cross-Coupling and Heck Reactions	535
5.4.1	Palladium-Catalyzed Coupling Reactions	535
5.4.1.1	C–C Bond-Forming Reactions	536
5.4.1.1.1	Mizoroki–Heck Reaction	536
5.4.1.1.1.1	Aqueous Ligand-Free Palladium-Catalyzed Heck Coupling	537
5.4.1.1.1.2	Aqueous Heck Coupling Catalyzed by Palladium–Nitrogen Complexes	538
5.4.1.1.1.3	Aqueous Palladium-Catalyzed Heck Coupling Employing Hydrophobic Phosphine Ligands	539
5.4.1.1.1.4	Aqueous Palladium-Catalyzed Heck Couplings Employing Hydrophilic Phosphine Ligands	541
5.4.1.1.1.5	Aqueous Palladacycle-Catalyzed Heck Coupling	541
5.4.1.1.1.6	Aqueous Heck Couplings Catalyzed by Supported Palladium Complexes	542
5.4.1.1.2	Suzuki–Miyaura Coupling	545
5.4.1.1.2.1	Aqueous Ligand-Free Palladium-Catalyzed Suzuki–Miyaura Coupling	545
5.4.1.1.2.2	Aqueous Suzuki–Miyaura Coupling Catalyzed by Palladium–Nitrogen Complexes	546
5.4.1.1.2.3	Aqueous Palladium-Catalyzed Suzuki–Miyaura Coupling Employing Hydrophobic Phosphine or N-Heterocyclic Carbene Ligands	547
5.4.1.1.2.4	Palladium-Catalyzed Suzuki–Miyaura Coupling Employing Hydrophilic Ligands	549
5.4.1.1.2.5	Aqueous Palladacycle-Catalyzed Suzuki–Miyaura Coupling	550
5.4.1.1.2.6	Aqueous Suzuki–Miyaura Couplings Catalyzed by Supported Palladium Complexes	552
5.4.1.1.3	Sonogashira Coupling	555
5.4.1.1.3.1	Aqueous Ligand-Free Palladium-Catalyzed Sonogashira Coupling	555
5.4.1.1.3.2	Aqueous Sonogashira Coupling Catalyzed by Palladium–Nitrogen Complexes	556
5.4.1.1.3.3	Aqueous Sonogashira Coupling Employing Hydrophobic Phosphine Ligands	556
5.4.1.1.3.4	Aqueous Sonogashira Coupling Catalyzed by Supported Palladium Complexes	557
5.4.1.1.4	Hiyama Coupling	559
5.4.1.1.4.1	Aqueous Ligand-Free Palladium-Catalyzed Hiyama Coupling	559
5.4.1.1.4.2	Aqueous Hiyama Coupling Catalyzed by Palladium–Nitrogen Complexes	559
5.4.1.1.4.3	Aqueous Hiyama Coupling Catalyzed by Palladium–Phosphine Complexes	560
5.4.1.1.4.4	Aqueous Oxime Palladacycle Catalyzed Hiyama Coupling	561
5.4.1.1.5	Kosugi–Migita–Stille Coupling	563
5.4.1.1.6	Ullmann-Type Coupling	563
5.4.1.1.7	Negishi Coupling	564
5.4.1.1.8	C–H Activation	565

5.4.1.1.9	Cyanation Reactions	566
5.4.1.2	Carbon—Heteroatom Bond-Forming Reactions	567
5.4.1.2.1	Buchwald—Hartwig Amination	567
5.4.2	Copper-Catalyzed Cross-Coupling Reactions	569
5.4.2.1	C—C Bond-Forming Reactions	569
5.4.2.1.1	Sonogashira—Hagihara Reaction	569
5.4.2.1.2	Cyanation Reactions	570
5.4.2.2	Carbon—Heteroatom Bond-Forming Reactions	570
5.4.2.2.1	Aqueous Copper-Catalyzed C—N Bond-Forming Reactions	570
5.4.2.2.2	Aqueous Copper-Catalyzed C—S Bond-Forming Reactions	572
5.4.2.2.3	Aqueous Copper-Catalyzed C—O Bond-Forming Reactions	572

5.5 Ring Opening of Epoxides and Aziridines

C. Ogawa and S. Kobayashi

5.5	Ring Opening of Epoxides and Aziridines	579
5.5.1	Ring-Opening Reactions of Epoxides	579
5.5.1.1	Epoxide Ring Opening with Oxygen Nucleophiles	579
5.5.1.1.1	Noncatalyzed Epoxide Ring Opening	579
5.5.1.1.2	Small Organic Molecule Catalyzed Epoxide Ring Opening	580
5.5.1.1.3	Metal-Catalyzed Epoxide Ring Opening	581
5.5.1.1.3.1	Using Zirconium(IV) Tetrakis(dodecyl sulfate)	581
5.5.1.1.3.2	Using Cobalt—Salen Complexes	581
5.5.1.1.3.3	Using Scandium—Chiral Bipyridine Complexes	582
5.5.1.2	Epoxide Ring Opening with Nitrogen Nucleophiles	583
5.5.1.2.1	Epoxide Ring Opening with Amines	583
5.5.1.2.1.1	Noncatalyzed Epoxide Ring Opening with Amines in Water	583
5.5.1.2.1.2	Small Organic Molecule Catalyzed Aminolysis	585
5.5.1.2.1.3	Metal-Catalyzed Aminolysis	586
5.5.1.2.1.4	Aminolysis Catalyzed by Chiral Lewis Acids	587
5.5.1.2.2	Epoxide Ring Opening with Azide	589
5.5.1.2.2.1	Metal-Catalyzed Azidolysis	589
5.5.1.2.2.1.1	Using Zirconium(IV) Tetrakis(dodecyl sulfate)	589
5.5.1.2.2.1.2	Using Copper(II) Nitrate	590
5.5.1.2.3	Epoxide Ring Opening with Other Nitrogen-Containing Nucleophiles	590
5.5.1.3	Epoxide Ring Opening with Thiols	591
5.5.1.3.1	Noncatalyzed Epoxide Ring Opening with Thiols	591
5.5.1.3.2	Metal-Catalyzed Epoxide Ring Opening with Thiols	592

5.5.1.3.2.1	Using Indium(III) Chloride	592
5.5.1.3.2.2	Using Scandium(III) Tris(dodecyl sulfate)	593
5.5.1.4	Epoxide Ring Opening with Carbon Nucleophiles	594
5.5.2	Ring-Opening Reactions of Aziridines	594
5.5.2.1	Aziridine Ring Opening with Oxygen Nucleophiles	594
5.5.2.1.1	Noncatalyzed Aziridine Ring Opening with Oxygen Nucleophiles	594
5.5.2.1.2	Aziridine Ring Opening with Oxygen Nucleophiles Promoted by Tributylphosphine and Silica Gel	595
5.5.2.2	Aziridine Ring Opening with Nitrogen Nucleophiles	596
5.5.2.2.1	Noncatalyzed Aziridine Ring Opening with Nitrogen Nucleophiles	596
5.5.2.2.2	Small Organic Molecule Catalyzed Aziridine Ring Opening with Nitrogen Nucleophiles	596
5.5.2.3	Aziridine Ring Opening with Sulfur Nucleophiles	597

5.6 Asymmetric α -Functionalization of Carbonyl Compounds and Alkylation of Enolates

S. Shirakawa and K. Maruoka

5.6	Asymmetric α-Functionalization of Carbonyl Compounds and Alkylation of Enolates	601
5.6.1	Asymmetric Alkylation	601
5.6.1.1	Asymmetric Benzylation of Glycine Derivatives for the Synthesis of Phenylalanine Derivatives	601
5.6.1.1.1	Asymmetric Alkylation of Glycine Derivatives for the Synthesis of α -Alkyl- α -amino Acids	604
5.6.1.2	Asymmetric α -Alkylation of Ketones	604
5.6.1.3	Asymmetric Alkylation of β -Keto Esters	605
5.6.1.4	Asymmetric Alkylation of Diaryloxazolidine-2,4-diones	606
5.6.1.5	Asymmetric α -Alkylation of Aldehydes with Alcohols	607
5.6.2	Asymmetric Alkenylation and Alkynylation	607
5.6.2.1	Asymmetric Alkenylation of β -Keto Esters	607
5.6.2.1.1	Asymmetric Alkynylation of β -Keto Esters	609
5.6.3	Asymmetric Oxidation	609
5.6.3.1	Asymmetric α -Hydroxylation of Ketones	609
5.6.3.2	Asymmetric α -Oxyamination of Aldehydes	610
5.6.4	Asymmetric Amination	611
5.6.4.1	Asymmetric Amination of β -Keto Esters	611
5.6.5	Asymmetric Fluorination	612
5.6.5.1	Asymmetric Fluorination of β -Keto Esters	612

5.7	Oxidation of Alcohols, Allylic and Benzylic Oxidation, Oxidation of Sulfides	
	R. A. Sheldon	
<hr/>		
5.7	Oxidation of Alcohols, Allylic and Benzylic Oxidation, Oxidation of Sulfides	617
5.7.1	Water-Soluble Ligands	618
5.7.2	Biomimetic Metalloporphyrins and Metallophthalocyanines	619
5.7.3	Enzymatic Oxidations: Oxidoreductases	620
5.7.4	Alcohol Oxidations in Aqueous Media	620
5.7.4.1	Tungsten(VI) Catalysts	621
5.7.4.2	Palladium–Diamine Complexes as Catalysts	623
5.7.4.3	Noble Metal Nanoparticles as Quasi-homogeneous Catalysts	627
5.7.4.4	Ruthenium and Manganese Catalysts	628
5.7.4.5	Organocatalysts: Hypervalent Iodine Compounds and Stable N-Oxyl Radicals	628
5.7.4.6	Enzymatic Oxidation of Alcohols	631
5.7.5	Benzylic and Allylic Oxidations in Water	632
5.7.5.1	Benzylic Oxidations	632
5.7.5.2	Allylic Oxidations	633
5.7.6	Sulfoxidations in Water	634
5.7.6.1	Tungsten- and Vanadium-Catalyzed Oxidations with Hydrogen Peroxide	634
5.7.6.2	Enantioselective Sulfoxidation with Enzymes	636
5.7.6.3	Flavins as Organocatalysts for Sulfoxidation	638
5.7.7	Concluding Remarks	639
<hr/>		
5.8	Free-Radical Reactions	
	H. Yorimitsu and K. Oshima	
<hr/>		
5.8	Free-Radical Reactions	645
5.8.1	Reductive Processes	646
5.8.1.1	Reductions with Metal Hydrides	646
5.8.1.2	Reduction with Phosphinic Acid and Its Derivatives	652
5.8.1.3	Reductions with Trialkylboranes	662
5.8.1.3.1	With Trialkylborane–Water Complexes	662
5.8.1.3.2	Triethylborane-Mediated Radical Addition to a C=N Bond	665
5.8.1.4	Reduction with Inorganic Reducing Agents	666
5.8.2	Atom Transfer Processes	669
5.8.3	Fragmentation Processes	674

5.9	Polymerization	
	M. Ouchi and M. Sawamoto	
<hr/>		
5.9	Polymerization	679
5.9.1	Living Radical Polymerization	680
5.9.1.1	Nitroxide-Mediated Polymerization	681
5.9.1.2	Metal-Catalyzed Living Radical Polymerization or Atom-Transfer Radical Polymerization	681
5.9.1.3	Reversible Addition–Fragmentation Chain-Transfer Polymerization	682
5.9.2	Living Radical Suspension Polymerization	682
5.9.2.1	Iron-Catalyzed Living Radical Polymerization	682
5.9.2.2	Copper-Catalyzed Living Radical Polymerization	683
5.9.3	Living Radical Mini-emulsion Polymerization	684
5.9.3.1	Mini-emulsion with Reverse Atom-Transfer Radical Polymerization	685
5.9.3.2	Mini-emulsion with AGET Atom-Transfer Radical Polymerization	686
5.9.3.3	Mini-emulsion with Nitroxide-Mediated Polymerization	687
5.9.4	Living Radical Emulsion Polymerization	689
5.9.4.1	Emulsion with Nitroxide-Mediated Polymerization	689
5.9.4.2	Emulsion with Reversible Addition–Fragmentation Chain-Transfer Polymerization	691
5.9.5	Homogeneous Aqueous Living Radical Polymerization	692
5.9.5.1	Homogeneous Aqueous Atom-Transfer Radical Polymerization	693
5.9.5.2	Homogeneous Aqueous Reversible Addition–Fragmentation Chain-Transfer Polymerization	694
<hr/>		
6	Special Techniques with Water	
<hr/>		
6.1	Organic Synthesis “On Water”	
	A. Chanda and V. V. Fokin	
<hr/>		
6.1	Organic Synthesis “On Water”	697
6.1.1	On-Water Reactions	699
6.1.1.1	Diels–Alder Reactions	699
6.1.1.2	Dipolar Cycloadditions	702
6.1.1.3	Cycloadditions of Azodicarboxylates	708
6.1.1.4	Claisen Rearrangement	710
6.1.1.5	Passerini and Ugi Reactions	712
6.1.1.6	Nucleophilic Opening of Three-Membered Rings	715

6.1.1.7	Nucleophilic Substitution Reactions	720
6.1.1.8	Transformations Catalyzed by Transition Metals	722
6.1.1.9	Metal-Free Carbon–Carbon Bond-Forming Processes	731
6.1.1.10	Bromination Reactions	734
6.1.1.11	Oxidations and Reductions	737
6.1.2	Theoretical Studies	741
6.1.3	Concluding Remarks	744
6.2	Sub- and Supercritical Water	
	A. Kruse and E. Dinjus	
6.2	Sub- and Supercritical Water	749
6.2.1	Properties of Water	750
6.2.1.1	Macroscopic Properties	750
6.2.1.2	Microscopic Properties	751
6.2.1.3	Special Aspects of Heterogeneous Catalysis	752
6.2.2	Synthesis Reactions	753
6.2.2.1	Hydrolysis/Water Addition Reactions	753
6.2.2.2	Condensation/Water Elimination Reactions	755
6.2.2.3	Addition Reactions	757
6.2.2.3.1	Hydroformylation	757
6.2.2.3.2	Diels–Alder Reaction	757
6.2.2.3.3	Other Addition and Coupling Reactions	758
6.2.2.4	Rearrangements	760
6.2.2.5	Oxidations	762
6.2.2.6	Reductions	763
6.2.2.6.1	Using Formic Acid/Formates	763
6.2.2.6.2	Using Hydrogen and a Noble Metal Catalyst	763
6.2.2.6.3	Using Zinc	764
6.2.3	Summary	764
6.2.4	Outlook	765
6.2.5	Conclusion	765

6.3	β-Cyclodextrin Chemistry in Water	
	F. Hapiot and E. Monflier	
<hr/>		
6.3	β-Cyclodextrin Chemistry in Water	773
6.3.1	Cyclodextrins as Mass-Transfer Additives or Organocatalysts for Organic Synthesis in Water	774
6.3.1.1	Glycoside Hydrolysis Using Modified α- and β-Cyclodextrin Dicyanohydrins in Water	774
6.3.1.2	Oxidation of Benzylic Alcohols	776
6.3.1.3	Deprotection of Aromatic Acetals under Neutral Conditions Using β-Cyclodextrin in Water	777
6.3.1.4	Cyclodextrin-Promoted Synthesis of 3,4,5-Trisubstituted Furan-2(5H)-ones	778
6.3.1.5	β-Cyclodextrin-Catalyzed Strecker Synthesis of α-Aminonitriles in Water	779
6.3.1.6	Synthesis of 3-Hydroxy-3-(1 <i>H</i> -indol-3-yl)-1,3-dihydro-2 <i>H</i> -indol-2-ones under Neutral Conditions in Water	780
6.3.1.7	Synthesis of Pyrrole-Substituted 1,3-Dihydro-2 <i>H</i> -indol-2-ones	781
6.3.1.8	Friedel-Crafts Alkylation of Indoles	782
6.3.1.9	Supramolecular Synthesis of Selenazoles Using Selenourea in Water	783
6.3.1.10	Cyclodextrin-Promoted Nucleophilic Opening of Oxiranes	784
6.3.1.11	Cyclodextrin-Promoted Michael Reactions of Thiols to Conjugated Alkenes	785
6.3.1.12	Cyclodextrin-Promoted Mild Oxidation of Alcohols with 1-Hydroxy-1,2-benziodoxol-3(1 <i>H</i>)-one 1-Oxide	786
6.3.1.13	Synthesis of Thiiranes from Oxiranes in the Presence of β-Cyclodextrin in Water	788
6.3.2	Cyclodextrins as Organocatalyst Solubilizers	789
6.3.2.1	For Organocatalysts with an Adamantyl Subunit	789
6.3.2.2	For Organocatalysts with a 4- <i>tert</i> -Butylphenyl Subunit	791
6.3.3	Cyclodextrins as Mass-Transfer Additives in Aqueous Organometallic Catalysis	792
6.3.4	Cyclodextrins as Ligands for Metal-Catalyzed Reactions	797
6.3.5	Cyclodextrins as Stabilizers of Water-Soluble Noble Metal Nanoparticles	797
6.3.6	Cyclodextrins as Dispersing Agents of Catalytically Active Solids	800
6.3.6.1	Cyclodextrins as Dispersing Agents of Supported Metals	800
6.3.6.2	Cyclodextrins as Dispersing Agents of Metallic Powder	802

7 Industrial Application

7.1	Hydroformylation	
	E. Wiebus, K. Schmid, and B. Cornils	
<hr/>		
7.1	Hydroformylation	807
7.1.2	Immobilized Oxo Catalysts	809
7.1.3	Biphasic Catalyst System	810
7.1.4	Ruhrchemie/Rhône-Poulenc Process	812
7.1.4.1	Reaction	812
7.1.4.2	Recycle and Recovery of the Aqueous Catalyst	816
7.1.4.2.1	Recycle	816
7.1.4.2.2	Recovery	819
7.1.4.3	Economics of the Process	822
7.1.4.4	Environmental Aspects	823
7.1.5	Conclusions	825
<hr/>		
7.2	Industrial Applications Other than Hydroformylation	
	Y. Mori and S. Kobayashi	
<hr/>		
7.2	Industrial Applications Other than Hydroformylation	831
7.2.1	Classical Reactions	832
7.2.1.1	Hydrolysis	832
7.2.1.2	Hydration	833
7.2.1.3	Homogeneous Mixed-Solvent Systems	833
7.2.1.4	Heterogeneous Mixed-Solvent Systems	834
7.2.2	Metal-Catalyzed Reactions	835
7.2.2.1	Palladium-Catalyzed Coupling Reactions	835
7.2.2.2	Palladium-Catalyzed Telomerization of Butadiene	837
7.2.2.3	Lewis Acid Catalysis	837
7.2.3	Enzymatic Reactions	837
7.2.3.1	Synthesis of Tamiflu	837
7.2.3.2	Synthesis of Statins (Lipitor and Crestor)	838
7.2.3.3	Synthesis of LY300164	840
7.2.3.4	Synthesis of Pregabalin	840
7.2.3.5	Synthesis of 6-Aminopenicillanic Acid	841
7.2.3.6	Synthesis of Rhinovirus Protease Inhibitor Intermediates	842

7.2.3.7	Synthesis of a GABA Inhibitor	842
7.2.3.8	Synthesis of an HIV Protease Inhibitor	842
7.2.3.9	Synthesis of Pelitrexol	843
7.2.4	Other Reactions	844
7.2.5	Conclusions and Perspectives	849
 8	 Perspective: The New World of Organic Chemistry Using Water as Solvent	
	S. Kobayashi	
 8	 Perspective: The New World of Organic Chemistry Using Water as Solvent	855
8.1	Palladium-Catalyzed Allylic Amination Using Aqueous Ammonia	855
8.2	Aldehyde Allylation with Allylboronates in Aqueous Media	858
8.3	Catalytic Use of Indium(0) for C—C Bond Transformations in Water	861
8.4	Conclusions and Outlook	865
 Keyword Index	869
 Author Index	917
 Abbreviations	955