
C-1 Building Blocks in Organic Synthesis 2

Alkenations, Cross Couplings, Insertions, Substitutions, and Halomethylations

	Preface	V
	Volume Editor's Preface	VII
	Abstracts	XI
	Table of Contents	XXIII
2.1	C-1 Alkenation	1
2.1.1	Modern Variants of Wittig, Peterson, and Tebbe Protocols C. Müller, M. Cokoja, and F. E. Kühn	1
2.2	C–C Cross Coupling	31
2.2.1	Cross-Coupling Methods for Methylation G. A. Molander and D. Ryu	31
2.2.2	Carbonylation of Aryl and Vinyl Halides H. Neumann and J. Schranck	67
2.2.3	Cyanation of Aryl Halides A. Ouali and M. Taillefer	95
2.2.4	Oxidative Coupling of Nitromethane R. Ballini and M. Petrini	127
2.3	Insertion into C–H Bonds	145
2.3.1	Carbene Insertion into C–H Bonds with C-1 M. C. Nicasio and T. R. Belderrain	145
2.4	Insertion into C–O and C–N Bonds	161
2.4.1	Carbon Monoxide Insertion into Epoxides and Oxetanes H. Ibrahim	161
2.4.2	Carbon Monoxide Insertion into Aziridines H. Ibrahim	193

2.5	Substitution Reactions	207
2.5.1	Hydroformylation of Epoxides K. Takahashi and K. Nozaki	207
2.5.2	Cyanation of Epoxides C. te Grotenhuis, L. Schoonen, and F. P. J. T. Rutjes	219
2.5.3	Cyanation of Aziridines L. Schoonen, C. te Grotenhuis, and F. P. J. T. Rutjes	245
2.5.4	Carboxylation of Organometallic Reagents J. Takaya and N. Iwasawa	263
2.5.5	Reaction of Formaldehyde with Organometallic Reagents M. Kaposi, J. Witt, M. Cokoja, and F. E. Kühn	289
2.5.6	Mannich-Type Reactions P. Merino	311
2.5.7	Formylation and the Vilsmeier Reagent N. Zhang and D. Dong	333
2.5.8	Metathesis Adding a C-1 Unit C. Bruneau and C. Fischmeister	349
2.6	Halomethylation	367
2.6.1	Trifluoromethylation A. Lishchynskyi, P. Novák, and V. V. Grushin	367
2.6.2	Difluoro- and Fluoromethylation J. Hu and C. Ni	409
2.6.3	Kharasch Reaction (Atom-Transfer Radical Addition Reactions) J. M. Muñoz-Molina and T. R. Belderrain	459
	Keyword Index	475
	Author Index	501
	Abbreviations	519

Table of Contents

2.1	C-1 Alkenation	
<hr/>		
2.1.1	Modern Variants of Wittig, Peterson, and Tebbe Protocols C. Müller, M. Cokoja, and F. E. Kühn	
<hr/>		
2.1.1	Modern Variants of Wittig, Peterson, and Tebbe Protocols	1
2.1.1.1	Wittig Methylenation	1
2.1.1.1.1	Wittig Methylenation under Nonbasic Conditions	2
2.1.1.1.2	Catalytic Wittig Methylenation	5
2.1.1.2	Peterson Methylenation	7
2.1.1.2.1	Using (Trimethylsilyl)methylolithium	7
2.1.1.2.2	Cerium-Modified Peterson Methylenation	10
2.1.1.2.3	Peterson Methylenation with Other Metal Reagents	13
2.1.1.3	Tebbe Reagent and Variants	13
2.1.1.3.1	Tebbe Reagent	14
2.1.1.3.2	Petasis Reagent	18
2.1.1.3.3	Halomethane-Zinc-Titanium(IV) or -Zirconium(IV) Reagents	21
2.2	C-C Cross Coupling	
<hr/>		
2.2.1	Cross-Coupling Methods for Methylation G. A. Molander and D. Ryu	
<hr/>		
2.2.1	Cross-Coupling Methods for Methylation	31
2.2.1.1	Boron Reagents	31
2.2.1.1.1	2,4,6-Trimethylboroxin	31
2.2.1.1.1.1	Aryl and Hetaryl Electrophiles	31
2.2.1.1.1.2	Alkenyl Electrophiles	34
2.2.1.1.1.3	Methylation by C-H Activation	35
2.2.1.1.2	Methylboronic Acid	39
2.2.1.1.2.1	Aryl, Hetaryl, and Alkenyl Electrophiles	39
2.2.1.1.2.2	Enol 4-Toluenesulfonate Electrophiles	41
2.2.1.1.2.3	Methylation by C-H Activation	41
2.2.1.1.3	Potassium Methyltrifluoroborate	43
2.2.1.1.3.1	Aryl and Hetaryl Electrophiles	43

2.2.1.1.3.2	Alkenyl Electrophiles	44
2.2.1.2	Zinc Reagents	45
2.2.1.2.1	Aryl and Hetaryl Electrophiles	45
2.2.1.2.2	Alkenyl Electrophiles	48
2.2.1.2.3	Methylation of Other Systems	50
2.2.1.3	Tin Reagents	51
2.2.1.3.1	Aryl and Hetaryl Electrophiles	52
2.2.1.3.2	Methylation by C—H Activation	55
2.2.1.4	Magnesium Reagents	56
2.2.1.4.1	Aryl and Hetaryl Electrophiles	56
2.2.1.4.2	Alkenyl Electrophiles	58
2.2.1.4.3	Methylation of Other Systems	59
2.2.1.5	Aluminum Reagents	61
2.2.1.6	Silicon Reagents	63
2.2.2	Carbonylation of Aryl and Vinyl Halides H. Neumann and J. Schranck	
2.2.2	Carbonylation of Aryl and Vinyl Halides	67
2.2.2.1	Carbonylation of Aryl and Vinyl Halides to Carboxylic Acid Derivatives with O- and N-Nucleophiles	67
2.2.2.1.1	Alkoxy- and Hydroxycarbonylation	68
2.2.2.1.2	Aminocarbonylation with Primary and Secondary Amines	74
2.2.2.1.3	Amino- and Azidocarbonylation with Ammonia and Azides	75
2.2.2.2	Reductive Carbonylation	77
2.2.2.3	Carbonylation with Formates	78
2.2.2.4	Double Carbonylation	79
2.2.2.4.1	Synthesis of α -Keto Acids	80
2.2.2.4.2	Synthesis of α -Keto Amides	80
2.2.2.5	Carbonylative C—C Cross-Coupling Reactions	81
2.2.2.5.1	Carbonylative Mizoroki–Heck Reactions	82
2.2.2.5.2	Carbonylative Sonogashira Reactions	85
2.2.2.5.3	Carbonylative Suzuki–Miyaura Reactions	88

2.2.3	Cyanation of Aryl Halides A. Ouali and M. Taillefer	
<hr/>		
2.2.3	Cyanation of Aryl Halides	95
2.2.3.1	Nickel-Based Catalysts	97
2.2.3.2	Palladium-Based Catalysts	99
2.2.3.2.1	Use of Alkali Metal Cyanides as Cyanating Agents	99
2.2.3.2.2	Use of Zinc(II) Cyanide as Cyanating Agent	103
2.2.3.2.3	Use of Potassium Hexacyanoferrate(II) as Cyanating Agent	108
2.2.3.2.4	Use of Cyanohydrins as Cyanating Agents	114
2.2.3.2.5	Use of Trimethylsilyl Cyanide as Cyanating Agent	115
2.2.3.2.6	Conclusion Concerning Cyanation Methods Involving Palladium Catalysts ...	116
2.2.3.3	Copper-Based Catalysts	117
2.2.3.3.1	Use of Alkali Metal Cyanides as Cyanating Agents	117
2.2.3.3.2	Use of Potassium Hexacyanoferrate(II) as Cyanating Agent	119
2.2.3.3.3	Use of Cyanohydrins as Cyanating Agents	121
2.2.3.3.4	Conclusion Concerning Cyanation Methods Involving Copper Catalysts	123
2.2.3.4	Conclusions	123
2.2.4	Oxidative Coupling of Nitromethane R. Ballini and M. Petrini	
<hr/>		
2.2.4	Oxidative Coupling of Nitromethane	127
2.2.4.1	Catalyzed Cross-Dehydrogenative Coupling	127
2.2.4.1.1	Copper-Catalyzed Reactions	127
2.2.4.1.2	Vanadium-Catalyzed Reactions	129
2.2.4.1.3	Reactions Catalyzed by Other Metals	130
2.2.4.1.4	Metal-Free Coupling Reactions	133
2.2.4.1.5	Photoinduced Coupling Reactions	139
2.2.4.2	Nitromethyl Radical Addition to Alkenes	142
2.2.4.3	Methyl Radical Addition to Styrenes	143

2.3	Insertion into C–H Bonds	
<hr/>		
2.3.1	Carbene Insertion into C–H Bonds with C-1	
	M. C. Nicasio and T. R. Belderrain	
<hr/>		
2.3.1	Carbene Insertion into C–H Bonds with C-1	145
2.3.1.1	Generation of Alkylidene Carbenes Using Diazo(trimethylsilyl)methane	145
2.3.1.2	Generation of Alkylidene Carbenes Using (Diazoalkyl)phosphonates	157
2.4	Insertion into C–O and C–N Bonds	
<hr/>		
2.4.1	Carbon Monoxide Insertion into Epoxides and Oxetanes	
	H. Ibrahim	
<hr/>		
2.4.1	Carbon Monoxide Insertion into Epoxides and Oxetanes	161
2.4.1.1	Carbonylation of Epoxides	164
2.4.1.1.1	Ring-Expansion Carbonylation of Epoxides	164
2.4.1.1.1.1	β-Lactones by Ring-Expansion Carbonylation of Epoxides	164
2.4.1.1.1.1.1	Using Systems Based on Tetracarbonylcobaltate(–I) Salts	166
2.4.1.1.1.1.1.1	Bis(triphenylphosphoranylidene)ammonium Tetracarbonylcobaltate(–I)/ Boron Trifluoride–Diethyl Ether Complex as Catalytic System	166
2.4.1.1.1.1.2	Cationic Metal Complex Tetracarbonylcobaltate(–I) Salts as Catalysts (Coates' Catalysts)	167
2.4.1.1.1.2	Using Octacarbonyldicobalt(0)-Based Systems	171
2.4.1.1.1.2.1	Trimethylaluminum/Octacarbonyldicobalt(0) as Catalytic System	171
2.4.1.1.1.2.2	Chloro(5,10,15,20-tetraphenylporphyrinato)chromium(III)/ Octacarbonyldicobalt(0) as Catalytic System	172
2.4.1.1.1.3	Ring-Expansion Carbonylation of Epoxides at Low Carbon Monoxide Pressure	173
2.4.1.1.1.4	Asymmetric Ring-Expansion Carbonylation of Epoxides	176
2.4.1.1.1.4.1	Carbonylative Kinetic Resolution of Epoxides	176
2.4.1.1.1.4.2	Asymmetric Ring-Expansion Carbonylation of <i>meso</i> -Epoxides	177
2.4.1.1.2	Succinic Anhydrides by Double Carbonylation of Epoxides	178
2.4.1.1.3	1,3-Oxazinane-2,4-diones by Carbonylation of Epoxides	180
2.4.1.1.4	3-Hydroxy δ-Lactones by Carbonylation of Homoglycidols	181
2.4.1.2	Ring-Opening Carbonylation of Epoxides	182
2.4.1.2.1	Alkoxy-carbonylation of Epoxides	182
2.4.1.2.1.1	Methoxycarbonylation of Epoxides Catalyzed by the Octacarbonyldicobalt(0)/3-Hydroxypyridine System	182

2.4.1.1.2.1.2	Methoxycarbonylation of Epoxides at 1 Atmosphere of Carbon Monoxide	183
2.4.1.1.2.1.3	Alkoxy carbonylation of Epoxides Catalyzed by the Gold/Cobalt(II,III) Oxide System	184
2.4.1.1.2.1.4	Alkoxy carbonylation of Epoxides Catalyzed by Other Cobalt-Based Systems	185
2.4.1.1.2.2	Aminocarbonylation of Epoxides	186
2.4.1.1.2.2.1	Silylaminocarbonylation of Epoxides at 1 Atmosphere of Carbon Monoxide	186
2.4.1.1.2.2.2	Enantiopure β -Hydroxy Morpholine Amides by Aminocarbonylation	187
2.4.1.2	Carbonylation of Oxetanes	188
2.4.1.2.1	γ -Lactones by Ring-Expansion Carbonylation of Oxetanes	188
2.4.1.2.2	Ring-Opening Carbonylation of Oxetanes	189

2.4.2 Carbon Monoxide Insertion into Aziridines

H. Ibrahim

2.4.2	Carbon Monoxide Insertion into Aziridines	193
2.4.2.1	β -Lactams by Ring-Expansion Carbonylation of Aziridines	195
2.4.2.1.1	Using Cobalt-Based Systems	195
2.4.2.1.1.1	Octacarbonyldicobalt(0) as Catalyst	195
2.4.2.1.1.2	Tetracarbonylcobaltate(-I) Salts as Catalysts	198
2.4.2.1.1.2.1	Bis(triphenylphosphoranylidene)ammonium Tetracarbonylcobaltate(-I)/ Tris(pentafluorophenyl)borane as Catalytic System	198
2.4.2.1.1.2.2	Cationic Metal Complex Tetracarbonylcobaltate(-I) Salts as Catalysts	198
2.4.2.1.2	Using Rhodium(I)-Based Catalysts	200
2.4.2.1.3	Using Palladium(0)-Based Catalysts	201
2.4.2.2	α -Methylene β -Lactams by Palladium(0)-Catalyzed Carbonylation of Methyleneaziridines	203
2.4.2.3	Azetidine-2,4-diones by Rhodium(I)-Catalyzed Carbonylation of α -Lactams	204
2.4.2.4	1,3-Diazetid-2-ones by Palladium(0)-Catalyzed Carbonylation of Diaziridines	205

2.5 Substitution Reactions

2.5.1 Hydroformylation of Epoxides

K. Takahashi and K. Nozaki

2.5.1	Hydroformylation of Epoxides	207
2.5.1.1	Reaction Mechanism of Epoxide Hydroformylation	207
2.5.1.2	Cobalt-Catalyzed Hydroformylation of Epoxides	208
2.5.1.2.1	Nonmodified Catalyst Systems	208

2.5.1.2.2	Modified Catalyst Systems	209
2.5.1.2.2.1	Phosphine-Modified Systems	209
2.5.1.2.2.2	Salt-Modified Systems	210
2.5.1.2.2.3	Ruthenium-Modified Systems	211
2.5.1.2.2.4	Phosphine/Phosphine Oxide Modified Systems	212
2.5.1.2.3	In Situ Protection of Hydroformylation Products	213
2.5.1.3	Silylformylation of Epoxides	214
2.5.2	Cyanation of Epoxides C. te Grotenhuis, L. Schoonen, and F. P. J. T. Rutjes	
2.5.2	Cyanation of Epoxides	219
2.5.2.1	Nucleophilic Attack	221
2.5.2.2	Lewis Acid Activation	227
2.5.2.2.1	Stoichiometric Activation with Diethylaluminum Cyanide (Nagata's Reagent)	227
2.5.2.2.2	Catalytic Activation with Titanium(IV) Isopropoxide	231
2.5.2.2.3	Catalytic Activation with Other Metal-Based Catalysts	232
2.5.2.2.4	Asymmetric Epoxide Opening	237
2.5.2.2.4.1	Desymmetrization	237
2.5.2.2.4.2	Kinetic Resolution	241
2.5.3	Cyanation of Aziridines L. Schoonen, C. te Grotenhuis, and F. P. J. T. Rutjes	
2.5.3	Cyanation of Aziridines	245
2.5.3.1	Cyanation of Nonactivated Aziridines	246
2.5.3.2	Cyanation of Activated Aziridines	249
2.5.3.2.1	Reactions without Additives	249
2.5.3.2.2	Lewis Acid Catalyzed Reactions	252
2.5.3.2.3	Lewis Base Catalyzed Reactions	254
2.5.3.2.4	Metal-Catalyzed Reactions	257
2.5.3.2.5	Tetrabutylammonium Fluoride Mediated Reactions	261
2.5.4	Carboxylation of Organometallic Reagents J. Takaya and N. Iwasawa	
2.5.4	Carboxylation of Organometallic Reagents	263
2.5.4.1	Carboxylation of Organometallic Compounds	263
2.5.4.1.1	Transition-Metal-Catalyzed Carboxylation of Organotin Compounds	264

2.5.4.1.2	Transition-Metal-Catalyzed Carboxylation of Organoboron Compounds	265
2.5.4.1.3	Transition-Metal-Catalyzed Carboxylation of Organozinc Compounds	270
2.5.4.1.4	Carboxylation of Organometallic Compounds without Use of a Transition-Metal Catalyst	271
2.5.4.2	Carboxylation of Organic Compounds via C—X Bond Activation (X = H, Halogen)	275
2.5.4.2.1	Carboxylation of Terminal Alkynes	275
2.5.4.2.2	Carboxylation of Aromatic Compounds	277
2.5.4.2.3	Carboxylation of Indole at the 3-Position	282
2.5.4.2.4	Transition-Metal-Catalyzed Carboxylation of Aryl and Alkenyl Halides	283
2.5.5	Reaction of Formaldehyde with Organometallic Reagents M. Kaposi, J. Witt, M. Cokoja, and F. E. Kühn	
2.5.5	Reaction of Formaldehyde with Organometallic Reagents	289
2.5.5.1	Hydroxymethylation	289
2.5.5.1.1	Aldol Reactions	289
2.5.5.1.2	Grignard Reactions	292
2.5.5.1.3	Reactions with Lithiated Compounds	293
2.5.5.2	Acid-Catalyzed Reactions of Formaldehyde with Alkenes	295
2.5.5.2.1	Prins Reaction	295
2.5.5.2.2	Carbonyl-Ene Reactions	296
2.5.5.2.3	Stabilization of Monomeric Formaldehyde	298
2.5.5.3	Hydroformylation	301
2.5.5.4	Hydrohydroxymethylation	302
2.5.5.5	Reactivity of Organometallic Complexes with Formaldehyde	303
2.5.5.5.1	Addition of Formaldehyde to Metal Centers; η^2 -Formaldehyde Complexes	304
2.5.5.5.2	Carbonyl Complexes Obtained from Formaldehyde	306
2.5.6	Mannich-Type Reactions P. Merino	
2.5.6	Mannich-Type Reactions	311
2.5.6.1	Addition to Iminium Ions	311
2.5.6.1.1	Addition of Aldehydes and Ketones	311
2.5.6.1.2	Addition of Esters and Lactams	313
2.5.6.1.3	Addition of Active Methylene Compounds	316
2.5.6.1.4	Addition of Silyl and Boron Enolates	317
2.5.6.1.5	Addition of Unsaturated Carbonyl Compounds	319

2.5.6.1.6	Addition of α -Bromo Carbonyl Compounds and Amides	321
2.5.6.1.7	Addition of Imidoyl Chlorides	323
2.5.6.2	Addition to Imines	324
2.5.6.3	Addition to Nitrones and Oximes	325
2.5.6.4	Addition to Hydrazones	328
2.5.7	Formylation and the Vilsmeier Reagent N. Zhang and D. Dong	
2.5.7	Formylation and the Vilsmeier Reagent	333
2.5.7.1	Formylation with Magnesium Methoxide and Paraformaldehyde	333
2.5.7.2	Formylation with Hexamethylenetetramine and Acid	335
2.5.7.3	Formylation with Carbon Monoxide	335
2.5.7.4	Formylation with <i>N</i> -Methylaniline and a Transition-Metal Catalyst	336
2.5.7.5	Vilsmeier Reactions	337
2.5.7.5.1	Reaction of Arenes with Halomethyleniminium Salts	338
2.5.7.5.2	Reactions of Hetarenes with Halomethyleniminium Salts	339
2.5.7.5.3	Reactions of Carbonyl Compounds with Halomethyleniminium Salts	341
2.5.7.5.4	Reactions of Alkenes with Halomethyleniminium Salts	342
2.5.7.5.5	Reactions of Carboxylic Acids with Halomethyleniminium Salts	343
2.5.7.5.6	Vilsmeier Reagents in Cyclization Reactions	343
2.5.8	Metathesis Adding a C-1 Unit C. Bruneau and C. Fischmeister	
2.5.8	Metathesis Adding a C-1 Unit	349
2.5.8.1	Catalysts for Ethenolysis	349
2.5.8.2	Mechanism of Ethenolysis	351
2.5.8.3	Scope and Limitations of Ethenolysis	352
2.5.8.4	Applications of Ethenolysis in Fine Chemistry	352
2.5.8.4.1	Formation of Dienes via Ring Opening	352
2.5.8.4.2	Formation of Terminal Alkenes from Functionalized Alkenes	356
2.5.8.5	Applications of Ethenolysis of Industrial Relevance	358
2.5.8.5.1	Cleavage of Nonfunctionalized Polyalkenes	358
2.5.8.5.2	Cleavage of Nonfunctionalized Monoalkenes	359
2.5.8.5.3	Cleavage of Functionalized Monoalkenes	360
2.5.8.6	Conclusions	363

2.6	Halomethylation	
2.6.1	Trifluoromethylation	
	A. Lishchynskiy, P. Novák, and V. V. Grushin	
2.6.1	Trifluoromethylation	367
2.6.1.1	Trifluoromethyl Sources	368
2.6.1.2	sp ³ -C—CF ₃ Bond Formation	369
2.6.1.2.1	α-Trifluoromethylation of Carbonyl Compounds	369
2.6.1.2.1.1	Copper-Promoted Nucleophilic Trifluoromethylation of α-Diazo Esters	369
2.6.1.2.1.2	Copper-Mediated Nucleophilic Trifluoromethylation of α-Halo Ketones	370
2.6.1.2.1.3	Ruthenium-Catalyzed Radical Trifluoromethylation of <i>N</i> -Acyloxazolidinones	371
2.6.1.2.1.4	Copper-Catalyzed Enantioselective Electrophilic Trifluoromethylation of β-Keto Esters	372
2.6.1.2.1.5	Enantioselective Electrophilic Trifluoromethylation of Aldehydes	374
2.6.1.2.2	Trifluoromethylation of Alkenes and Alkynes	375
2.6.1.2.2.1	Palladium-Catalyzed Nucleophilic Trifluoromethylation of Alkenes	376
2.6.1.2.2.2	Silver-Mediated Nucleophilic Trifluoromethylation of Alkynes	377
2.6.1.2.2.3	Copper-Catalyzed Intramolecular Tandem Electrophilic Trifluoromethylation of Alkenes	378
2.6.1.2.2.4	Copper-Catalyzed Intermolecular Tandem Electrophilic Trifluoromethylation of Alkenes	379
2.6.1.2.3	Trifluoromethylation at Allylic and Propargylic Positions	380
2.6.1.2.3.1	Copper-Catalyzed Nucleophilic Allylic Trifluoromethylation of Terminal Alkenes	381
2.6.1.2.3.2	Copper-Catalyzed Nucleophilic Trifluoromethylation of Terminal Allylic Halides	382
2.6.1.2.3.3	Copper-Catalyzed Electrophilic Trifluoromethylation of Allylsilanes	383
2.6.1.2.3.4	Copper-Catalyzed Electrophilic Allylic Trifluoromethylation of Terminal Alkenes	384
2.6.1.2.4	Trifluoromethylation of Alkyl Halides	385
2.6.1.3	sp ² -C—CF ₃ Bond Formation	385
2.6.1.3.1	Aromatic Trifluoromethylation	385
2.6.1.3.1.1	Copper-Promoted Trifluoromethylation of Aryl Halides	385
2.6.1.3.1.2	Copper-Catalyzed Trifluoromethylation of Aryl Halides	387
2.6.1.3.1.3	Oxidative Trifluoromethylation of Arylboronic Acids and Arylboronate Esters	388
2.6.1.3.1.4	Palladium-Catalyzed Trifluoromethylation of Aryl Halides	389
2.6.1.3.1.5	Trifluoromethylation of Aromatic C—H Bonds	390

2.6.1.3.2	Vinyl Trifluoromethylation	393
2.6.1.3.2.1	Copper-Mediated Trifluoromethylation of Vinyl Halides	393
2.6.1.3.2.2	Palladium-Catalyzed Trifluoromethylation of Vinyl Sulfonates	395
2.6.1.3.2.3	Copper-Promoted Trifluoromethylation of Vinylboronic Acids	397
2.6.1.3.2.4	Iron-Catalyzed Trifluoromethylation of Potassium Vinyltrifluoroborates	398
2.6.1.3.2.5	Copper-Catalyzed Decarboxylative Trifluoromethylation of Alk-2-enoic Acids	399
2.6.1.3.2.6	Copper-Catalyzed Trifluoromethylation of Enamides	400
2.6.1.4	sp-C—CF ₃ Bond Formation	401
2.6.1.4.1	Copper-Mediated Nucleophilic Trifluoromethylation of Alkynes with Ruppert's Reagent	402
2.6.1.4.2	Copper-Catalyzed Electrophilic Trifluoromethylation of Alkynes with Umemoto's Reagent	403
2.6.1.4.3	Copper-Catalyzed Electrophilic Trifluoromethylation of Alkynes with Togni's Reagent	404
2.6.2	Difluoro- and Fluoromethylation J. Hu and C. Ni	
2.6.2	Difluoro- and Fluoromethylation	409
2.6.2.1	Difluoromethylation	409
2.6.2.1.1	Nucleophilic Difluoromethylation	410
2.6.2.1.1.1	Using (Difluoromethyl)trimethylsilane	410
2.6.2.1.1.2	Using Difluoromethyl Phenyl Sulfone	411
2.6.2.1.1.3	Using [Difluoro(phenylsulfonyl)methyl]trimethylsilane	415
2.6.2.1.1.4	Using [Difluoro(phenylsulfanyl)methyl]trimethylsilane	417
2.6.2.1.1.5	Using (Difluoromethyl)phosphonates and Their Derivatives	418
2.6.2.1.1.6	Using S-(Difluoromethyl)sulfoximides	421
2.6.2.1.1.7	Using Trimethyl(trifluoromethyl)silane	422
2.6.2.1.1.8	Using Difluoromethylenation Reagents	423
2.6.2.1.2	Electrophilic Difluoromethylation	424
2.6.2.1.2.1	Using Chloro(difluoro)methane and Bromo(difluoro)methane	425
2.6.2.1.2.2	Using Trifluoromethane	426
2.6.2.1.2.3	Using Trifluoro(iodo)methane	427
2.6.2.1.2.4	Using S-(Difluoromethyl)sulfoximides and Tributyl(difluoromethyl)ammonium Salts	427
2.6.2.1.2.5	Using S-[Bromo(difluoro)methyl]sulfonium Salts	428
2.6.2.1.2.6	Using Difluoro(phenylsulfonyl)methyl Hypercovalent Iodine Compounds	429
2.6.2.1.3	Free-Radical Difluoromethylation	431

2.6.2.1.3.1	Using Difluoro(iodo)methane	431
2.6.2.1.3.2	Using Zinc(II) Difluoromethanesulfinate	431
2.6.2.1.3.3	Using Dibromo(difluoro)methane	432
2.6.2.1.3.4	Using Difluoro(iodo)methyl Phenyl Sulfone	435
2.6.2.1.4	Difluoromethylation with Transition-Metal Complexes	435
2.6.2.1.4.1	Using (Difluoromethyl)trimethylsilane and Tributyl(difluoromethyl)stannane ..	436
2.6.2.1.4.2	Using Ethyl 2,2-Difluoro-2-(trimethylsilyl)acetate	438
2.6.2.1.4.3	Using [Difluoro(phenylsulfonyl)methyl]trimethylsilane	439
2.6.2.2	Fluoromethylation	439
2.6.2.2.1	Nucleophilic Fluoromethylation	440
2.6.2.2.1.1	Using Fluoromethyl Phenyl Sulfone	440
2.6.2.2.1.2	Using <i>S</i> -(Fluoromethyl)sulfoximides	442
2.6.2.2.1.3	Using Fluorobis(phenylsulfonyl)methane	442
2.6.2.2.2	Electrophilic Fluoromethylation	450
2.6.2.2.2.1	Using Chloro(fluoro)methane and Bromo(fluoro)methane	451
2.6.2.2.2.2	Using <i>S</i> -(Fluoromethyl)sulfonium Salts	451
2.6.2.2.3	Free-Radical Fluoromethylation	451
2.6.2.2.3.1	Using Zinc(II) Fluoromethanesulfinate	451
2.6.2.2.3.2	Using Fluoro(iodo)bis(phenylsulfonyl)methane	452
2.6.2.2.4	Fluoromethylation with Transition-Metal Complexes	452
2.6.2.2.4.1	Using Fluoro(iodo)methane	452
2.6.2.2.4.2	Using Fluoro(iodo)methyl 2-Pyridyl Sulfone	453
2.6.3	Kharasch Reaction (Atom-Transfer Radical Addition Reactions) J. M. Muñoz-Molina and T. R. Belderrain	
2.6.3	Kharasch Reaction (Atom-Transfer Radical Addition Reactions)	459
2.6.3.1	Copper Complexes as Catalysts	461
2.6.3.2	Ruthenium Complexes as Catalysts	466
	Keyword Index	475
	Author Index	501
	Abbreviations	519