

## Contents

### Preface *xiii*

<b>1</b>	<b>Alkane Functionalization by Metal-Catalyzed Carbene Insertion from Diazo Reagents</b>	<b>1</b>
	<i>María Álvarez, Ana Caballero, and Pedro J. Pérez</i>	
1.1	Introduction	1
1.2	Chemo- and Regioselectivity	3
1.2.1	Definitions	3
1.2.2	Catalysts	5
1.2.3	Chemoselectivity	6
1.2.4	Regioselectivity	8
1.3	Enantioselectivity	9
1.4	Methane and Gaseous Alkanes as Substrates	14
1.5	Alkane Nucleophilicity Scale	18
1.6	Conclusions and Outlook	22
	Acknowledgments	22
	References	22
 <b>2</b>	 <b>Catalytic Radical Approach for Selective Carbene Transfers via Cobalt(II)-Based Metalloradical Catalysis</b>	 <b>25</b>
	<i>Xiaoxu Wang and X. Peter Zhang</i>	
2.1	Introduction	25
2.2	Intermolecular Radical Cyclopropanation of Alkenes	26
2.2.1	Cyclopropanation with Acceptor-Substituted Diazo Compounds	27
2.2.2	Cyclopropanation with Acceptor/Acceptor-Substituted Diazo Compounds	32
2.2.3	Cyclopropanation with Donor-Substituted Diazo Compounds	37
2.3	Intramolecular Radical Cyclopropanation of Alkenes	39
2.4	Intermolecular Radical Cyclopropanation of Alkynes	43
2.5	Intramolecular Radical Alkylation of C(sp <sup>3</sup> )-H Bonds	44
2.5.1	Intramolecular C-H Alkylation with Acceptor/Acceptor-Substituted Diazo Compounds	45

- 2.5.2 Intramolecular C–H Alkylation with Donor-Substituted Diazo Compounds 46
- 2.6 Other Catalytic Radical Processes for Carbene Transfers 54
- 2.7 Summary and Outlook 59
- Acknowledgment 60
- References 60

### 3 Catalytic Enantioselective Carbene Insertions into Heteroatom–Hydrogen Bonds 67

*Ming-Yao Huang, Shou-Fei Zhu, and Qi-Lin Zhou*

- 3.1 Introduction 67
- 3.2 N–H Bond Insertion Reactions 67
  - 3.2.1 Chiral Metal Catalysts 68
    - 3.2.1.1 Chiral Cu Catalysts 68
    - 3.2.1.2 Chiral Pd Catalysts 70
    - 3.2.1.3 Other Chiral Metal Catalysts 70
    - 3.2.1.4 Enzymes 72
    - 3.2.1.5 Chiral Proton-Transfer Shuttle Catalysts 72
    - 3.2.1.6 Chiral Phosphoric Acids as CPTS Catalysts 72
    - 3.2.1.7 Chiral Amino Thioureas as CPTS Catalysts 73
  - 3.3 O–H Bond Insertion Reactions 74
    - 3.3.1 Chiral Metal Catalysts 74
      - 3.3.1.1 Chiral Cu Catalysts 74
      - 3.3.1.2 Chiral Fe Catalysts 76
      - 3.3.1.3 Chiral Pd Catalysts 77
      - 3.3.1.4 Chiral Au Catalysts 78
      - 3.3.1.5 Chiral Bases as CPTS Catalysts 78
      - 3.3.1.6 Chiral Phosphoric Acids as CPTS Catalysts 79
    - 3.4 S–H Bond Insertion Reactions 80
      - 3.4.1 Chiral Metal Catalysts 80
      - 3.4.2 CPTS Catalysts 81
      - 3.4.3 Enzymes 81
    - 3.5 F–H Bond Insertion Reactions 82
    - 3.6 Si–H Bond Insertion Reactions 83
      - 3.6.1 Chiral Rh Catalysts 83
      - 3.6.2 Chiral Cu Catalysts 85
      - 3.6.3 Other Chiral Metal Catalysts 86
      - 3.6.4 Enzymes 87
    - 3.7 B–H Bond Insertion Reactions 88
      - 3.7.1 Chiral Cu Catalysts 88
      - 3.7.2 Chiral Rhodium Catalysts 89
      - 3.7.3 Enzymes 89
    - 3.8 Summary and Outlook 90
    - References 91

<b>4</b>	<b>Engineering Enzymes for New-to-Nature Carbene Chemistry</b>	<b>95</b>
	<i>Soumitra V. Athavale, Kai Chen, and Frances H. Arnold</i>	
4.1	Introduction: Biology Inspires Chemistry Inspires Biology	95
4.2	P411-Catalyzed Cyclopropanation	99
4.3	The Workflow of Directed Evolution	101
4.4	Expanding Cyclopropanation with Diverse Hemeprotein Carbene Transferases	102
4.5	C–H Functionalization with Carbene Transferases	109
4.6	Biocatalytic Carbene X–H Insertion	113
4.7	Carbene Transfer Reactions with Artificial Metalloproteins	118
4.8	Structural Studies of Carbene Intermediates in Heme Proteins	125
4.9	Summary	128
	Acknowledgments	129
	References	129
<b>5</b>	<b>Metal Carbene Cycloaddition Reactions</b>	<b>139</b>
	<i>Kostiantyn O. Marichev, Haifeng Zheng, and Michael P. Doyle</i>	
5.1	Introduction	139
5.2	[3+1]-Cycloaddition	142
5.3	[3+2]-Cycloaddition	145
5.3.1	[3+2]-Cycloaddition with Imines and Indoles	145
5.3.2	[3+2]-Cycloaddition with Polarized Alkenes	149
5.3.3	[3+2]-Cycloaddition with Nitrones	150
5.3.4	Divergent Behavior of Catalysts	151
5.4	[3+3]-Cycloaddition of Enoldiazo Compounds	152
5.4.1	[3+3]-Cycloaddition with Nitrones	152
5.4.2	[3+3]-Cycloaddition with Pyridinium Ylides and Hydrazones	155
5.4.3	Diastereoselective [3+3]-Cycloaddition with Achiral Catalysts	157
5.4.4	[3+3]-Cycloaddition with Diaziridines	158
5.4.5	[3+3]-Cycloaddition with Donor–Acceptor Cyclopropanes and Oxiranes	159
5.5	[3+4]-Cycloaddition	160
5.6	[3+5]-Cycloaddition	161
5.7	Summary	162
	References	163
<b>6</b>	<b>Metal-Catalyzed Decarbenations by Retro-Cyclopropanation</b>	<b>169</b>
	<i>Mauro Mato and Antonio M. Echavarren</i>	
6.1	Introduction	169
6.2	Reactivity and Generation of Metal Carbenes	169
6.2.1	Decomposition of Diazo Compounds	170
6.2.2	Alternative Methods for the Generation of Metal Carbenes	170

6.2.3	Decarbenation Reactions: General Process and Definition	170
6.3	Retro-Cyclopropanation Reactions: A Historical Walkthrough	171
6.3.1	Early Observations	171
6.3.2	Decarbenation Reactions from Gas Phase to Solution	173
6.3.3	The Discovery of the Gold(I)-Catalyzed Retro-Buchner Reaction	173
6.4	Metal-Catalyzed Aromative-Decarbenation Reactions: A Mechanistic Analysis	175
6.4.1	Basic Mechanistic Picture	175
6.4.2	Alternative Generation of the Same Carbenes from Carbenoids	175
6.4.3	Theoretical Studies on the Mechanism of the Retro-Buchner Reaction	177
6.4.4	Second-Generation Cycloheptatrienes: Low Temperature and Other Metals	179
6.4.5	Mechanism of the Rh(II)-Catalyzed Aromative Decarbenation	181
6.5	Synthetic Methodologies and Applications	181
6.5.1	Cyclopropanation Reactions	181
6.5.1.1	Aryl Cyclopropanations	183
6.5.1.2	Alkenyl Cyclopropanations	184
6.5.1.3	Reactions with Furans	185
6.5.2	Higher Formal Cycloadditions	186
6.5.2.1	(4+1) Cycloadditions	187
6.5.2.2	(3+2) Cycloadditions	187
6.5.2.3	(4+3) Cycloadditions	189
6.5.3	Intramolecular Friedel–Crafts Reactivity	190
6.5.4	Insertion Reactions	190
6.5.4.1	C–H Insertion	190
6.5.4.2	Si–H Insertion	192
6.5.5	Oxidation Reactions	192
6.5.6	Alternative Precursors	193
6.5.7	Decarbenations Based on the Release of Alkenes	193
6.6	General Outlook and Concluding Remarks	195
	References	196
<b>7</b>	<b>Gold-Catalyzed Oxidation of Alkynes by <i>N</i>-Oxides or Sulfoxides</b>	<b>199</b>
	<i>Kaylaa Gutman, Tianyou Li, and Liming Zhang</i>	
7.1	Introduction: Gold-Activated Alkynes Attacked by Nucleophilic Oxidants	199
7.2	Sulfoxides as Nucleophilic Oxidants	201
7.3	<i>N</i> -Oxides as Nucleophilic Oxidants	202
7.3.1	Reactions of Carbene/Carbenoid Intermediates with Oxygen-Based Nucleophiles	205
7.3.2	Reactions of Carbene/Carbenoid Intermediates with Nitrogen-Based Nucleophiles	212

7.3.3	Reactions of Carbene/Carbenoid Intermediates with Other Heteronucleophiles	214
7.3.4	Friedel–Crafts Reactions of Carbene/Carbenoid Intermediates with Arenes	215
7.3.5	Reactions of Carbene/Carbenoid Intermediates with Alkenes	218
7.3.6	Reactions of Carbene/Carbenoid Intermediates with C—C Triple Bonds	224
7.3.7	1,2-C—C and 1,2-C—H Insertions of Carbene/Carbenoid Intermediates	226
7.3.8	Remote C(sp <sup>3</sup> )—H Functionalizations by Carbene/Carbenoid Intermediates	231
7.4	Conclusion	238
	References	238
<b>8</b>	<b>Transition-Metal-Catalyzed Carbene Transformations for Polymer Syntheses</b>	<b>243</b>
	<i>Eiji Ihara and Hiroaki Shimomoto</i>	
8.1	Introduction	243
8.2	Transition-Metal-Catalyzed C1 Polymerization of Diazoacetates	243
8.2.1	PdCl <sub>2</sub> -Initiated Polymerization	244
8.2.2	(NHC)Pd(nq)/Borate-Initiated Polymerization	245
8.2.3	$\pi$ -AllylPdCl-Based System-Initiated Polymerization	246
8.2.4	(nq) <sub>2</sub> Pd/Borate- and (cod)PdCl(Cl-nq)/Borate-Initiated Polymerization	251
8.2.5	Preparation of Polymers with Densely Packed Functional Groups Around Polymer Main Chain	254
8.2.5.1	Hydroxy Group-Containing Polymers	254
8.2.5.2	Oligo(oxyethylene)-Containing Polymers	256
8.2.5.3	Pyrene-Containing Polymers	257
8.2.5.4	Fluoroalkyl and Fluoroaryl Group-Containing Polymers	258
8.3	Polycondensation of Bis(diazocarbonyl) Compounds	259
8.3.1	Three-Component Polycondensation of Bis(diazocarbonyl) Compound, Diol, and THF	259
8.3.2	Three-Component Polycondensation of Bis(diazocarbonyl) Compound, Dicarboxylic Acid, and THF	262
8.3.3	Three-Component Polycondensation of Bis(diazocarbonyl) Compound, Enol-form of 1,3-Diketone, and THF	263
8.3.4	Two-Component Polycondensation of Bis(diazocarbonyl) Compound with Aromatic Diamine	264
8.3.5	Single-Component Polycondensation of Bis(diazocarbonyl) Compound to Afford Unsaturated Polyesters	264
8.3.6	Single-Component Polycondensation of Bis(diazocarbonyl) Compound to Afford Poly(arylene vinylene)s (PAV)	265

8.4	Concluding Remarks	266
	References	266
<b>9</b>	<b>Metal-Catalyzed Quinoid Carbene (QC) Transfer Reactions</b>	<b>269</b>
	<i>Hai-Xu Wang, Vanessa K.-Y. Lo, and Chi-Ming Che</i>	
9.1	Introduction	269
9.2	Metal–Quinoid Carbene (QC) Complexes and Stoichiometric Reactivity	269
9.3	Metal-Catalyzed QC Transfer Reactions	273
9.3.1	Cyclopropanation Reactions	273
9.3.2	C(sp <sup>2</sup> )–H Insertion Reactions	275
9.3.3	C(sp <sup>3</sup> )–H Insertion Reactions	284
9.3.4	Nucleophilic Addition and Miscellaneous Reactions	286
9.4	Conclusion	293
	Acknowledgment	295
	References	295
<b>10</b>	<b>Asymmetric Rearrangement and Insertion Reactions with Metal–Carbenoids Promoted by Chiral <i>N,N'</i>-Dioxide or Guanidine-Based Catalysts</b>	<b>299</b>
	<i>Xiaobin Lin, Xiaohua Liu, and Xiaoming Feng</i>	
10.1	Introduction	299
10.2	The Introduction of Chiral <i>N,N'</i> -Dioxide/Metal Complexes and Guanidine Catalysts	299
10.3	Chiral <i>N,N'</i> -Dioxide/Metal Complexes-Catalyzed Rearrangement Reactions	302
10.4	Chiral Guanidine-Based Catalyst-Mediated Asymmetric Carbene Insertion Reactions	315
10.5	Conclusion and Outlook	323
	References	323
<b>11</b>	<b>Multi-Component Reaction via <i>gem</i>-Difunctionalization of Metal Carbene</b>	<b>325</b>
	<i>Mengchu Zhang, Xinfang Xu, and Wenhao Hu</i>	
11.1	Introduction	325
11.2	Mannich-Type Interception	327
11.2.1	Interception of Ammonium Ylide	327
11.2.2	Interception of Oxonium Ylide	328
11.2.3	Interception of Zwitterionic Intermediate	339
11.3	Aldol-Type Interception	340
11.3.1	Interception of Ammonium Ylide	340
11.3.2	Interception of Oxonium Ylide	342

11.3.3	Interception of Zwitterionic Intermediate	343
11.4	Michael-Type Interception	345
11.4.1	Interception of Ammonium Ylide	345
11.4.2	Interception of Oxonium Ylide	346
11.4.3	Interception of Zwitterionic Intermediate	348
11.5	Miscellaneous Transformations	349
11.5.1	Interception Other Types of Active Intermediates	349
11.5.2	Interception of Active Intermediates with Other Electrophiles	353
11.5.3	Applications in Cascade Reactions	355
11.6	Synthetic Applications	358
11.6.1	Synthesis and Modification of Natural Products	358
11.6.2	Synthesis of Bioactive Molecules	362
11.7	Conclusion	364
	References	365
<b>12</b>	<b>Transition-Metal-Catalyzed Cross-Coupling with Carbene Precursors</b>	<b>371</b>
	<i>Kang Wang and Jianbo Wang</i>	
12.1	Introduction	371
12.2	Palladium-Catalyzed Carbene Cross-Coupling Reactions	372
12.2.1	Diazo Compounds as Carbene Precursors	372
12.2.1.1	Reactions with Electrophiles	372
12.2.1.2	Reactions with Nucleophiles	373
12.2.1.3	Palladium-Catalyzed Cascade Cross-Coupling Reactions	374
12.2.2	<i>N</i> -Tosylhydrazones as Carbene Precursors	377
12.2.2.1	Reactions with Electrophiles	377
12.2.2.2	Reactions with Nucleophiles	379
12.2.2.3	Palladium-Catalyzed Cascade Cross-Coupling Reactions	380
12.2.3	Non-Diazo Compounds as Carbene Precursors	382
12.3	Copper-Catalyzed Carbene Cross-Coupling Reactions	385
12.3.1	Reactions with Terminal Alkynes	385
12.3.1.1	Multi-substituted Allenes as the Coupling Products	385
12.3.1.2	Internal Alkynes as the Coupling Products	386
12.3.2	Reactions with Other Coupling Partners	387
12.4	Rhodium-Catalyzed Carbene Cross-Coupling Reactions	388
12.4.1	Generating Organorhodium Species Through Transmetalation	388
12.4.2	Generating Organorhodium Species Through C—C Bond Cleavage	389
12.5	Transition-Metal-Catalyzed C—H Bond Functionalizations with Carbene Precursors	391
12.5.1	Non-Directing-Group-Assisted C—H Functionalizations	391
12.5.2	Directing-Group-Assisted C—H Bond Functionalizations	393
12.5.2.1	Generating Acyclic Products Through C—H Bond Activation	393
12.5.2.2	Generating Cyclic Products Through C—H Bond Activation	394

12.6	Conclusion Remarks	396
	Acknowledgment	397
	References	397

<b>Index</b>	<b>401</b>
--------------	------------