Contents

Preface xv

1	Pridged Lastams as Model Systems for Amidis Distortion 1					
Bridged Lactams as Model Systems for Amidic Distortion <i>Tyler J. Fulton, Yun E. Du, and Brian M. Stoltz</i>						
1.1	Introduction and Scope 1					
1.2	General Properties of Bridged Lactams 3					
1.2.1	Parameters of Amide Bond Distortion 3					
1.2.2	Bond Lengths, Bond Angles, and Spectroscopic Properties of Bridge					
	Lactams 5					
1.2.3	N- vs. O-protonation and Methylation and Structural Effects of					
	N-coordination 7					
1.2.4	Twisted Amide Basicity and pK_a Measurements 14					
1.3	Reactivity of Bridged Lactams 15					
1.3.1	Reactivity of the Lactam Nitrogen 15					
1.3.1.1	Hydrolysis of the N–C(O) Bond 15					
1.3.1.2	Cleavage of the σ C–N Bond 17					
1.3.2	Reactivity of the Carbonyl Group 18					
1.3.2.1	Heteroatom Nucleophiles 18					
1.3.2.2	Organometallics 19					
1.3.2.3	Reduction of the Carbonyl 20					
1.3.2.4	Olefination and Epoxidation Reactions 20					
1.3.2.5	Enolate and Conjugate Addition Chemistry 21					
1.3.3	Polymerization Reactions 22					
1.3.4	Miscellaneous Reactions 23					
1.3.4.1	Ring Opening via Olefin Metathesis 23					
1.4	Conclusions and Outlook 24					
	References 24					

:	

2	Modification of Amidic Resonance Through Heteroatom				
	Substitution at Nitrogen: Anomeric Amides 29				
2.1	Stephen A. Glover and Adam A. Rosser				
2.1	Introduction 29				
2.2	Properties of Anomeric Amides 32				
2.2.1	Structural Properties 32				
2.2.2	Natural Bond Order Analysis 33				
2.2.3	Theoretical Determination of Amide Bond Resonance 35 Sources of Anomeric Amides 37				
2.2.5	Experimental Evidence for Reduced Resonance in Anomeric				
2.2.3	Amides 38				
2.2.6	Spectroscopic Properties of Anomeric Amides 43				
2.2.7	Theoretical Structures and Amidicities of Model Anomeric Amides 46				
2.3	Reactivity of Anomeric Amides 50				
2.3.1	The Anomeric Effect 50				
2.3.2	Reactivity at the Anomeric Amide Nitrogen 53				
2.3.2.1	S_N 2 Reactions 53				
2.3.2.2	Elimination Reactions (S_N 1-Type Processes) 56				
2.3.3					
2.3.3.1					
2.3.3.2	HERON Reactions of <i>N</i> -Alkoxy- <i>N</i> -Aminoamides 58 Other HERON Reactions 60				
2.3.3.3	The Role of the n_y - σ^*_{NX} Anomeric Effect and Resonance in HERON				
2.3.3.3	Reactions 63				
2.4	Concluding Remarks 66				
	References 68				
3	Amide Bond Activation by Twisting and Nitrogen				
	Pyramidalization 79				
	Yuko Otani and Tomohiko Ohwada				
3.1	Introduction 79				
3.2	Nonplanar Amides that Are Sufficiently Stable for Chemical				
	Modification 80				
3.2.1	Nonplanar Amides 80				
3.2.2	Thioamides 83				
3.2.3	Chemical Stability of Nitrogen Pyramidal Amides 83				
3.3	Application to Amino Acids: Artificial Helices Composed of Bicyclic				
	Amino Acids 85				
3.3.1	Conformational Preference of Bicyclic β-Amino Acids 85				
3.3.2	Bridgehead-Substituted Bicyclic Amino Acids 88				
3.3.3	Application to Artificial Helices and Strand Mimics 90				
3.3.3.1	Heterooligomers 90				
3.4	Applications of Helical Peptides as Inhibitors of p53-MDM2/MDMX				
	Interaction 92				

3.5	Nonplanar Lactam Amide Spinning 93				
3.5.1	Lactam Amide Rotation 94				
3.6	Conclusion and Prospects 95				
	References 96				
4	Transition-Metal-Free Reactions of Amides by Tetrahedral Intermediates 101				
	Marco Blangetti, Karen de la Vega-Hernández, Margherita Miele, and Vittorio Pace				
4.1	Introduction 101				
4.2	Synthesis of Carbonyls from Amides 102				
4.2.1	Addition to Canonical Amides 102				
4.2.2	Variation of the Amide Structure 107				
4.2.3	Isolation of Tetrahedral Intermediates 115				
4.3	Recent Uses of Amides and <i>N</i> -Alkoxyamides for the Synthesis of Amines 119				
4.4	Electrophilic Amide Linkage Activation 128				
4.4.1	General Concept 128				
4.4.2	Synthesis of Carbonyl-Like Compounds 129				
4.4.3	Synthesis of Amine-Like Compounds 137				
4.4.4	Activation of Amides with Different Electrophilic Agents 144				
4.5	Synthesis of Heterocycles 145				
4.6	Conclusions and Outlook 150				
	References 150				
5	Electrophilic Amide Bond Functionalization 157 Carlos R. Gonçalves and Daniel Kaiser				
5.1	Introduction: Electrophilic Activation 157				
5.2	Introduction: Electrophilic Activation of Amides 158				
5.3	Early Endeavors in Electrophilic Amide Activation 159				
5.3.1	History of the Activation of Secondary Amides 159				
5.3.2	History of the Activation of Tertiary Amides 160				
5.4	Amide Bond Functionalization of Activated Tertiary Amides 164				
5.4.1	[2+2]-Cycloadditions 164				
5.4.2	Stereoselective Cycloadditions 167				
5.4.3	Nucleophile Addition 168				
5.4.3.1	Carbon Nucleophiles 168				
5.4.3.2	Hydridic Reduction 170				
5.4.3.3	Heteroatom Nucleophiles 171				
5.5	Amide Bond Functionalization of Activated Secondary Amides 175				
5.5.1	Synthesis and Functionalization of Heterocycles 176				
5.5.2	Ketone Synthesis 179				
5.6	Conclusions 180				
	References 181				

6	Transamidation of Carboxamides and Amide Derivatives:				
	Mechanistic Insights, Concepts, and Reactions 187 Paola Acosta-Guzmán, John Corredor-Barinas, and Diego Gamba-Sánchez				
6.1	Paola Acosta-Guzmán, John Corredor-Barinas, and Diego Gamba-Sánchez Introduction 187				
6.2	Historical Background 188				
6.3	Direct Transamidation of Carboxamides 190				
6.3.1	Mechanistic Insights 190				
6.3.2	Transition Metal Catalysis 193				
6.3.3	Organocatalysis 195				
6.3.4	Other Catalytic and Promoted Processes 198				
6.3.4.1	Bases 198				
6.3.4.1	Boron Derivatives 199				
6.3.4.3	Heterogeneous Catalysis 200				
6.3.4.4	Other Promoters 201				
6.3.5	Catalyst and Promoter-Free Processes 203				
6.4	Transamidation by the Previous Functionalization of the Amide				
0.4	Bond 204				
6.4.1	Transamidation of Activated Substrates Using Metallic Catalysts 205				
6.4.2					
0.1.2	Auxiliary 207				
6.4.3	Transamidation of Activated Substrates Using Other Promoters 208				
6.4.4					
0.1.1	Catalysts 209				
6.5	Transamidation with Atypical Substrates 211				
6.5.1	Reductive Transamidation 211				
6.5.2	Oxidative Transamidation 212				
6.5.3	Using Carbonyl and Thiocarbonyl Heterocycles as Activators 213				
6.5.4	From Amidines 214				
6.6	Conclusions and Perspectives 215				
	References 216				
-	A CLB LEGGE CONTROL OF THE CONTROL O				
7	Amide Bond Esterification and Hydrolysis 221				
	Kazushi Mashima, Takahiro Hirai, and Haruki Nagae				
7.1	Stoichiometric Reactions 221				
7.2	Catalytic Reactions 228				
7.3	N-β-Hydroxyethyl Amides 232				
7.4	Chelating Auxiliary at the Nitrogen Atom of Amides 234				
7.5	Activated Amides 235				
	References 237				

8	Activation of Amide C-N Bonds by Nickel Catalysis 243			
	Liana Hie and Tejas K. Shah			
8.1	Introduction 243			
8.2	Esterification of Amides 243			
8.3	Hydrolysis of Amides 248			
8.4	Transamidation 249			
8.5	Suzuki–Miyaura Coupling of Amides 255			
8.6	Negishi Coupling of Amides 258			
8.7	Mizoroki–Heck Coupling of Amides 261			
8.8	Reduction and Reductive Coupling of Amides 265			
	References 269			
9	Pd-NHC Catalysis in Cross-Coupling of Amides 273			
	Faez S. Alotaibi, Michael R. Chhoun, and Gregory R. Cook			
9.1	Introduction 273			
9.2	Pd(II)–NHC-Catalyzed Cross-Coupling Reactions of Amides 274			
9.3				
	Amides 275			
9.4 Pd(η ³ -1-t-Bu-Indenyl)(IPr)Cl-Catalyzed Suzuki–Miyaura Cros				
	of Amides 279			
9.5	Pd-PEPPSSI Precatalyst in the Suzuki-Miyaura Cross-Coupling of			
	Amides 281			
9.6	Various Pd-NHC Precatalysts Suitable for Cross-Coupling of			
	Amides 286			
9.7	9.7 Conclusion 288			
	References 288			
10	Cross-Coupling of Amides Through Decarbonylation 293			
	Hong Lu and Hao Wei			
10.1	Introduction 293			
10.2	Decarbonylation of Cyclic Amide Derivatives 294			
10.2.1	Phthalimides 295			
10.2.2	Saccharins and Other Cyclic Amide Derivatives 297			
10.3	Decarbonylation of Acyclic Amide Derivatives 298			
10.3.1	N-Acyl-Glutarimides 298			
10.3.2	N-Acylsaccharin Amides 302			
10.3.3	Other Acyclic Amides 302			
10.4	Conclusion 305			
	References 305			

11	Transition Metal-Catalyzed Radical Reactions of Amides 307 <i>Taline Kerackian, Didier Bouyssi, Nuno Monteiro, and</i>			
	Abderrahmane Amgoune			
11.1	Introduction 307			
11.2	Reactions Involving Amides as Precursors to Organometallic			
	Compounds 308			
11.2.1	Radical Reactions of Amides via Metal-Catalyzed C–N Bond Activation 308			
11.2.1.1	Reductive Cross-Electrophile Cross-Coupling Reactions 309			
11.2.1.2	Photoredox Cross-Coupling Reactions 312			
11.2.2	Chelation-Assisted Radical Reactions of Amides 316			
11.2.2.1	Amide-Directed C–H Bond Functionalization 316			
11.2.2.2	Amide-Directed Functionalization of Unactivated Alkenes 318			
11.3	Reactions Involving Amides as Precursors to Nitrogen- or Carbon-Centered Radicals 323			
11.3.1	Reactions of Amides via Amidyl Radicals 323			
11.3.1.1	Vicinal Difunctionalization of Pendant Olefins 324			
11.3.1.2	Distant C-H Bond Functionalization 325			
11.3.2	Reactions of Amides via α-Aminoalkyl Radicals 328			
11.3.2.1	•			
	to Alkenes 328			
11.3.2.2	C–H Bond Functionalization via Cross-coupling 329			
11.3.3	Reactions of Amides via Carbamoyl Radicals 331			
11.4	Conclusion 333			
	References 334			
12	Weinreb Amide as a Multifaceted Directing Group in C-H			
	Activation 339			
	Jayabrata Das and Debabrata Maiti			
12.1	Introduction 339			
12.2	Weinreb Amide-Directed C(sp ²)–H Activation 340			
12.2.1	Ru-Catalyzed Reactions 340			
12.2.2	Co-Catalyzed Reactions 344			
12.2.3	Pd-Catalyzed Reactions 346			
12.2.4	Rh-Catalyzed Reactions 352			
12.2.5	Ir-Catalyzed Reactions 354			
12.3	Weinreb Amide-Directed C(sp ³)–H Activation 359			
12.4	Conclusions and Outlook 362			
	References 362			

13	Computational Studies of Amide C-N Bond Activation 365 Xin Hong, Pei-Pei Xie, Zhi-Xin Qin, and Shuo-Qing Zhang			
13.1	Introduction 365			
13.2	General Mechanisms of Amide C–N Bond Cleavage and Derivatization 367			
13.3	Computational Studies on the Mechanism and Selectivity of Lewis Acid-Mediated Nucleophilic Substitution of Amides 368			
13.3.1	Computational Studies on the Mechanism and Selectivity of LiHMDS-Mediated Transamidation 369			
13.3.2	Computational Studies on the Mechanism and Reactivity of Zn-Catalyzed Esterification of Amides 373			
13.3.3	Computational Studies on the Mechanism of Ammonium Salt-Mediated Hydrazinolysis of Amides 375			
13.3.4	Computational Studies on the Mechanism of Organocatalytic Asymmetric Alcoholysis of <i>N</i> -Sulfonyl Amide 378			
13.4	Computational Studies on the Mechanism and Selectivity of Transition Metal-Catalyzed Cross-coupling of Amides 380			
13.4.1	Computational Study on the Mechanism and Reactivity of Ni-Catalyzed Esterification of Amides 381			
13.4.2	Computational Study on the Mechanism of Ni-Catalyzed Suzuki–Miyaura Coupling of Amides 387			
13.4.3	Computational Study on the Mechanism and Selectivity of Ni-Catalyzed C–N Bond Activation of Twisted Amides 388			
13.4.4	Computational Study on the Structure–Activity Relationship of Ni-Catalyzed C–N Bond Activation of Amides 391			
13.4.5	Computational Study on the Mechanism of Pd-Catalyzed Suzuki–Miyaura Coupling of Amides 395			
13.4.6	Computational Study on the Mechanism of Pd-Catalyzed Transamidation of Amides 398			
13.5	Outlook 398 References 399			
14	Esters as Viable Acyl Cross-Coupling Electrophiles 403 Omid Daneshfar and Stephen G. Newman			
14.1	Introduction 403			
14.2	Early Work in the Cross-coupling of Carboxylic Acid Derivatives 404			
14.3	Decarbonylative Coupling of Aryl Esters 408			
14.3.1	Mizoroki–Heck-Type Coupling 408			
14.3.2	C–H Biaryl Coupling 409			

-		
	14.3.3	Suzuki–Miyaura Coupling 412
	14.3.4	Silylation and Borylation 417
	14.3.5	Other C-C/C-H Bond Forming Reactions 419
	14.3.5.1	Sonogashira-Type Couplings 419
	14.3.5.2	Reduction 421
	14.3.5.3	Negishi-Type Coupling 421
	14.3.5.4	Cyanation 422
	14.3.5.5	Methylation 422
	14.3.6	Other C-Heteroatom Bond Forming Reactions 424
	14.3.6.1	Etherification 424
	14.3.6.2	Amination 424
	14.3.6.3	Thioetherification 427
	14.3.6.4	Carbon–Phosphorus Bond Formation 428
	14.4	Carbonyl Retentive Coupling of Phenyl Esters 429
	14.4.1	Suzuki–Miyaura Coupling 429
	14.4.2	Amidation 433
	14.4.3	Cross-Electrophile Coupling 434
	14.4.4	Ester Transfer and Ester Dance 435
	14.4.5	Deoxygenative Organophosphorus Coupling 437
	14.4.6	Alkyne Insertion 438
	14.5	Carbonyl Retentive Coupling of Alkyl Esters 439
	14.5.1	Amidation 439
	14.5.2	Mizoroki-Heck-Type Domino Reactions 441
	14.5.3	Suzuki–Miyaura Coupling 443
	14.6	Decarbonylative Couplings of Alkyl Esters 444
	14.6.1	Directing Group Assistance 444
	14.6.2	Methylation 445
	14.6.3	Organostannane Formation 445
	14.7	Conclusion and Outlook 446
		References 447
	15	Cross-Coupling of Aromatic Esters by Decarbonylation 453
		Kei Muto and Junichiro Yamaguchi
	15.1	Introduction 453
	15.2	Overview of Decarbonylative Coupling 453
	15.3	Decarbonylative Mizoroki–Heck Reaction 457
	15.4	Decarbonylative Alkyne Insertions 459
	15.5	Suzuki–Miyaura Coupling 460
	15.6	Negishi Coupling 463
	15.7	Sonogashira Coupling 464
	15.8	α-Arylation 465
	15.9	Cyanation 465
	15.10	C-H Arylation 466
	15.11	C–N Bond Formations 470
	15 12	C_P Rond Formation 471

15.13	Etherincation 4/3	
15.14	Thioetherification 473	
15.15	Hydrogenation 473	
15.16	Borylation, Silylation, and Stannylation	475
15.17	Miscellaneous 478	
15.18	Summary 483	
	References 483	

Index 487