

Contents

<i>Preface to Fourth Edition</i>	xii
<i>Introduction to the Fourth Edition</i>	xiii
<i>Definitions and Abbreviations</i>	xvi
1. Structures and Spectroscopic Properties of Aromatic Heterocycles	1
1.1 Carbocyclic Aromatic Systems	1
1.2 Structure of Six-membered Heteroaromatic Systems	3
1.3 Structure of Five-membered Heteroaromatic Systems	5
1.4 Structures of Bicyclic Heteroaromatic Compounds	7
1.5 Tautomerism in Heterocyclic Systems	7
1.6 Mesoionic Systems	8
1.7 Some Spectroscopic Properties of Some Heteroaromatic Systems	8
References	14
2. Reactivity of Aromatic Heterocycles	16
2.1 Electrophilic Addition at Nitrogen	16
2.2 Electrophilic Substitution at Carbon	17
2.3 Nucleophilic Substitution at Carbon	20
2.4 Radical Substitution at Carbon	23
2.5 Deprotonation of <i>N</i> -hydrogen	26
2.6 Organometallic Derivatives	26
2.7 Palladium-catalysed Reactions	40
2.8 Oxidation and Reduction of Heterocyclic Rings	46
2.9 Bioprocesses in Heterocyclic Chemistry	46
References	47

3. Synthesis of Aromatic Heterocycles	53
3.1 Reaction Types Most Frequently Used in Heterocyclic Ring Synthesis	53
3.2 Typical Reactant Combinations	54
3.3 Summary	56
3.4 Electrocyclic Processes in Heterocyclic Ring Synthesis	57
3.5 Nitrenes in Heterocyclic Ring Synthesis	58
3.6 <i>ortho</i> -Quinodimethanes in Heterocyclic Compound Synthesis	59
References	61
4. Typical Reactivity of Pyridines, Quinolines and Isoquinolines	63
5. Pyridines: Reactions and Synthesis	71
5.1 Reactions with Electrophilic Reagents	72
5.2 Reactions with Oxidising Agents	77
5.3 Reactions with Nucleophilic Reagents	78
5.4 Reactions with Bases	80
5.5 Reactions of C-metallated Pyridines	81
5.6 Reactions with Radical Reagents; Reactions of Pyridyl Radicals	84
5.7 Reactions with Reducing Agents	86
5.8 Electrocyclic Reactions (Ground State)	86
5.9 Photochemical Reactions	87
5.10 Oxy- and Aminopyridines	88
5.11 Alkylpyridines	93
5.12 Pyridine Aldehydes, Ketones, Carboxylic Acids and Esters	94
5.13 Quaternary Pyridinium Salts	95
5.14 Pyridine <i>N</i> -oxides	100
5.15 Synthesis of Pyridines	103
Exercises for Chapter 5	110
References	112
6. Quinolines and Isoquinolines: Reactions and Synthesis	121
6.1 Reactions with Electrophilic Reagents	122
6.2 Reactions with Oxidising Agents	123
6.3 Reactions with Nucleophilic Reagents	123

6.4	Reactions with Bases	126
6.5	Reactions of C-metallated Quinolines and Isoquinolines	126
6.6	Reactions with Radical Reagents	127
6.7	Reactions with Reducing Agents	127
6.8	Electrocyclic Reactions (Ground State)	128
6.9	Photochemical Reactions	128
6.10	Oxyquinolines and -isoquinolines	128
6.11	Aminoquinolines and -isoquinolines	130
6.12	Alkylquinolines and -isoquinolines	130
6.13	Quinoline and Isoquinoline Carboxylic Acids and Esters	130
6.14	Quaternary Quinolinium and Isoquinolinium Salts	131
6.15	Quinoline and Isoquinoline <i>N</i> -oxides	132
6.16	Synthesis of Quinolines and Isoquinolines	133
	Exercises for Chapter 6	142
	References	143
7.	Typical Reactivity of Pyrylium and Benzopyrylium Ions, Pyrones and Benzopyrones	148
8.	Pyryliums, 2- and 4-pyrones: Reactions and Synthesis	151
8.1	Reactions of Pyrylium Cations	151
8.2	2-pyrones and 4-pyrones (2 <i>H</i> -pyran-2-ones and 4 <i>H</i> -pyran-4-ones; α -pyrones and γ -pyrones)	156
8.3	Synthesis of Pyryliums	160
8.4	Synthesis of 2-pyrones	162
8.5	Synthesis of 4-pyrones	164
	Exercises for Chapter 8	165
	References	166
9.	Benzopyryliums, Benzopyrones: Reactions and Synthesis	170
9.1	Reactions of Benzopyryliums	170
9.2	Benzopyrones (Chromones, Coumarins, and Isocoumarins)	173
9.3	Synthesis of Benzopyryliums, Chromones, Coumarins and Isocoumarins	179
	Exercises for Chapter 9	186
	References	186

10. Typical Reactivity of the Diazines: Pyridazine, Pyrimidine and Pyrazine	190
11. The Diazines: Pyridazine, Pyrimidine, and Pyrazine: Reactions and Synthesis	194
11.1 Reactions with Electrophilic Reagents	196
11.2 Reactions with Oxidising Agents	198
11.3 Reactions with Nucleophilic Reagents	198
11.4 Reactions with Bases	201
11.5 Reactions of C-metallated Diazines	202
11.6 Reactions with Reducing Agents	204
11.7 Reactions with Radical Reagents	204
11.8 Electrocyclic Reactions	204
11.9 Diazine <i>N</i> -oxides	205
11.10 Oxydiazines	206
11.11 Aminodiazines	214
11.12 Alkyldiazines	215
11.13 Quaternary Azinium Salts	215
11.14 Synthesis of Diazines	216
11.15 Pteridines	224
Exercises for Chapter 11	225
References	226
12. Typical Reactivity of Pyrroles, Thiophenes, and Furans	233
13. Pyrroles: Reactions and Synthesis	237
13.1 Reactions with Electrophilic Reagents	238
13.2 Reactions with Oxidising Agents	246
13.3 Reactions with Nucleophilic Reagents	246
13.4 Reactions with Bases	246
13.5 Reactions of <i>N</i> -metallated Pyrroles	247
13.6 Reactions of C-metallated Pyrroles	248
13.7 Reactions with Radical Reagents	249
13.8 Reactions with Reducing Agents	250
13.9 Electrocyclic Reactions (Ground State)	250

13.10 Reactions with Carbenes and Carbenoids	252
13.11 Photochemical Reactions	252
13.12 Pyrrol-C-X Compounds	252
13.13 Pyrrole Aldehydes and Ketones	253
13.14 Pyrrole Carboxylic Acids	253
13.15 Pyrrole Carboxylic Acid Esters	254
13.16 Halopyrroles	254
13.17 Oxy- and Aminopyrroles	254
13.18 Synthesis of Pyrroles	255
Exercises for Chapter 13	265
References	266
14. Thiophenes: Reactions and Synthesis	273
14.1 Reactions with Electrophilic Reagents	273
14.2 Reactions with Oxidising Agents	278
14.3 Reactions with Nucleophilic Reagents	279
14.4 Reactions with Bases	279
14.5 Reactions of C-metallated Thiophenes	280
14.6 Reactions with Radical Reagents	282
14.7 Reactions with Reducing Agents	283
14.8 Electrocyclic Reactions (Ground State)	283
14.9 Photochemical Reactions	284
14.10 Thiophene-C-X Compounds: Thenyl Derivatives	284
14.11 Thiophene Aldehydes and Ketones, and Carboxylic Acids and Esters	285
14.12 Oxy- and Aminothiophenes	285
14.13 Synthesis of Thiophenes	286
Exercises for Chapter 14	290
References	291
15. Furans: Reactions and Synthesis	296
15.1 Reactions with Electrophilic Reagents	296
15.2 Reactions with Oxidising Agents	300
15.3 Reactions with Nucleophilic Reagents	300
15.4 Reactions with Bases	301
15.5 Reactions of C-metallated Furans	302

15.6	Reactions with Radical Reagents	303
15.7	Reactions with Reducing Agents	303
15.9	Electrocyclic Reactions (Ground State)	303
15.10	Photochemical Reactions	305
15.11	Furyl-C-X compounds; Side-chain Properties	305
15.12	Furan Carboxylic Acids and Esters	306
15.13	Oxy- and Aminofurans	306
15.14	Synthesis of Furans	308
	Exercises for Chapter 15	313
	References	314
16.	Typical Reactivity of Indoles, Benzo[<i>b</i>]thiophenes, Benzo[<i>b</i>]furans, Isoindoles, Benzo[<i>c</i>]thiophenes and Isobenzofurans	319
17.	Indoles: Reactions and Synthesis	324
17.1	Reactions with Electrophilic Reagents	325
17.2	Reactions with Oxidising Agents	336
17.3	Reactions with Nucleophilic Reagents (See Also Section 17.14.4)	337
17.4	Reactions with Bases	337
17.5	Reactions of <i>N</i> -metallated Indoles	338
17.6	Reactions of <i>C</i> -metallated Indoles	339
17.7	Reactions with Radicals	341
17.8	Reactions with Reducing Agents	342
17.9	Reactions with Carbenes	342
17.10	Electrocyclic and Photochemical Reactions	343
17.11	Alkylindoles	345
17.12	Reactions of Indolyl-C-X Compounds	345
17.13	Indole Carboxylic Acids	346
17.14	Oxyindoles	347
17.15	Aminoindoles	350
17.16	Azaindoles	351
17.17	Synthesis of Indoles	353
	Exercises for Chapter 17	370
	References	371

18. Benzo[<i>b</i>]thiophenes and Benzo[<i>b</i>]furans: Reactions and Synthesis	380
18.1 Reactions with Electrophilic Reagents	380
18.2 Reactions with Nucleophilic Reagents	382
18.3 Reactions with Bases; Reactions of C-metallated Benzo[<i>b</i>]thiophenes and Benzo[<i>b</i>]furans	382
18.4 Reactions with Oxidising and Reducing Agents	383
18.5 Electrocyclic Reactions	384
18.6 Oxy- and Amino-benzothiophenes and -benzofurans	384
18.7 Synthesis of Benzo[<i>b</i>]thiophenes and Benzo[<i>b</i>]furans	384
Exercises for Chapter 18	389
References	389
19. Isoindoles, Benzo[<i>c</i>]thiophenes and Isobenzofurans: Reactions and Synthesis	392
19.1 Reactions with Electrophilic Reagents	392
19.2 Electrocyclic Reactions	393
19.3 Phthalocyanines	393
19.4 Synthesis of Isoindoles, Benzo[<i>c</i>]thiophenes, and Isobenzofurans	394
Exercises for Chapter 19	397
References	397
20. Typical Reactivity of 1,3- and 1,2-azoles	399
21. 1,3-azoles: Imidazoles, Thiazoles, and Oxazoles: Reactions and Synthesis	402
21.1 Reactions with Electrophilic Reagents	403
21.2 Reactions with Oxidising Agents	408
21.3 Reactions with Nucleophilic Reagents	408
21.4 Reactions with Bases	409
21.5 Reactions of <i>N</i> -metallated Imidazoles	409
21.6 Reactions of C-metallated 1,3-azoles	410
21.7 Reactions with Radical Reagents	412
21.8 Reactions with Reducing Agents	412
21.9 Electrocyclic Reactions	412
21.10 Alkyl-1,3-azoles	414

21.11 Quaternary 1,3-azolium Salts	414
21.12 Oxy- and Amino-1,3-azoles	416
21.13 1,3-azole <i>N</i> -oxides	418
21.14 Synthesis of 1,3-azoles	418
Exercises for Chapter 21	424
References	425
22. 1,2-Azoles: Pyrazoles, Isothiazoles, Isoxazoles: Reactions and Synthesis	431
22.1 Reactions with Electrophilic Reagents	432
22.2 Reactions with Oxidising Agents	434
22.3 Reactions with Nucleophilic Reagents	434
22.4 Reactions with Bases	434
22.5 Reactions of <i>N</i> -metallated Pyrazoles	435
22.6 Reactions of <i>C</i> -metallated 1,2-azoles	435
22.7 Reactions with Radicals	436
22.8 Reactions with Reducing Agents	436
22.9 Electrocyclic Reactions	437
22.10 Alkyl-1,2-azoles	438
22.11 Quaternary 1,2-azolium Salts	438
22.12 Oxy- and Amino-1,2-azoles	439
22.13 Synthesis of 1,2-azoles	440
Exercises for Chapter 22	444
References	445
23. Benzanellated Azoles: Reactions and Synthesis	449
23.1 Reactions with Electrophilic Reagents	449
23.2 Reactions with Nucleophilic Reagents	450
23.3 Reactions with Bases	451
23.4 Reactions of <i>C</i> -metallated Derivatives	451
23.5 Reactions with Reducing Agents	452
23.6 Electrocyclic Reactions	452
23.7 Quaternary Salts	453
23.8 Oxy- and Amino-1,3-azoles	453

23.9	Synthesis	454
	References	458
24.	Purines: Reactions and Synthesis	461
24.1	Nucleic Acids, Nucleosides, and Nucleotides	463
24.2	Reactions with Electrophilic Reagents	464
24.3	Reactions with Radical Reagents	469
24.4	Reactions with Oxidising Agents	469
24.5	Reactions with Reducing Agents	469
24.6	Reactions with Nucleophilic Reagents	470
24.7	Reactions with Bases	472
24.8	Reactions of <i>N</i> -metallated Purines	473
24.9	Reactions of <i>C</i> -metallated Purines	473
24.10	Oxy- and Aminopurines	475
24.11	Alkylpurines	479
24.12	Purine Carboxylic Acids	479
24.13	Synthesis of Purines	479
	Exercises for Chapter 24	485
	References	485
25.	Heterocycles Containing a Ring-junction Nitrogen	489
25.1	Indolizines	489
25.2	Aza-indolizines	492
25.3	Quinoliziniums and Related Systems	498
25.4	Pyrrolizines and Related Systems	499
25.5	Cyclazines	499
	Exercises for chapter 25	500
	References	501
26.	Heterocycles Containing More Than Two Hetero Atoms	504
26.1	Five-membered Rings	504
26.2	Six-membered Rings	516
26.3	Benzotriazoles	520
	Exercises for Chapter 26	522
	References	522

27. Saturated and Partially Unsaturated Heterocyclic Compounds: Reactions and Synthesis	526
27.1 Five- and Six-membered Rings	527
27.2 Three-membered Rings	530
27.3 Four-membered Rings	534
27.4 Metallation	535
27.5 Ring Synthesis	536
References	540
28. Heterocycles at Work	543
28.1 Solid Phase Reactions	543
28.2 Heterocycles in the Pharmaceutical Industry: Large Scale Heterocyclic Synthesis	545
28.3 Electronic Applications	546
References	549
Appendix: Answers to Exercises	551
Chapter 5	551
Chapter 6	552
Chapter 8	552
Chapter 9	553
Chapter 11	553
Chapter 13	553
Chapter 14	554
Chapter 15	554
Chapter 17	554
Chapter 18	555
Chapter 19	555
Chapter 21	556
Chapter 22	556
Chapter 24	556
Chapter 25	557
Chapter 26	557
Index	559