Contents

Pr	Preface			xi
1	Bonding			1
	1.1		ic structure	1
			The chemical bond	1
			The periodic table	1
			Valence electrons	3
		1.1.4	Lewis structures	
		1.1.5	Conventions for drawing structures	5
			Atomic orbital theory	6
			Molecular orbital theory	7
	1.2		ent bonding	10
		1.2.1	•	11
		1.2.2	Bonding in compounds containing heteroatoms	12
		1.2.3	Bonding in common functional groups	12
			Electronic effects	14
		1.2.5	Steric effects	18
			Stereoelectronic effects	18
		1.2.7	Double bond equivalents	20
2	Stru	ıcture		21
	2.1	Confi	guration	21
			Geometrical isomerism	22
		2.1.2	Optical isomerism	23
		2.1.3		25
		2.1.4	Molecules with one stereogenic centre	27
		2.1.5	Molecules with more than one stereogenic centre	27
		2.1.6		
			optically active	28
		2.1.7	1 1 11 A A A A A A A A A A A A A A A A	
			molecular asymmetry	29
		2.1.8	Asymmetric heteroatoms	30
	2.2		ormation	31
		2.2.1	Representation of conformers	31
		2.2.2	Open-chain compounds	31
		2.2.3	Ring compounds	33
	2.3	Sumn	nary of stereochemical relationships	39
	2.4	Natur	ally occurring chiral compounds	39
	2.5	Asym	metric synthesis	4

vi Contents

		2.5.1 Enantioselective synthesis	41
		2.5.2 Diastereoselective synthesis	41
		2.5.3 Methods for the determination of enantiomeric purity	43
3	Re	eactivity	
	3.1	·	47
		3.1.1 Gibbs free energy	47
		3.1.2 Enthalpy	47
		3.1.3 Entropy	48 50
		3.1.4 Chemical equilibrium	52
	3.2	· · · · · · ·	54
		3.2.1 Rates of reaction	54
		3.2.2 Reactions with competing steps	57
	3.3	3.2.3 Overcoming activation energy barriers Reaction mechanism	58
	3.3	3.3.1 What is reactivity?	60
		3.3.2 Lewis acids and bases: 'philicity'	60
		3.3.3 Polarisability effects: Hard–Soft Acid–Base theory	60
		3.3.4 Curly ('curved') arrows	61
	3.4		63
		3.4.1 Polar mechanisms	66
		3.4.2 Radical mechanisms	66 67
		3.4.3 Pericyclic mechanisms	67
	a =	3.4.4 Ligand coupling reaction mechanisms	67
	3.5	Principle of microscopic reversibility	68
	3.6	/	69
	3.7 3.8	Granic chemistry	71
	3.0	Redox reactions in organic chemistry	72
4	Inte	ermediates	77
	4.1	Carbocations	77 77
		4.1.1 Structure	77 77
		4.1.2 Factors stabilising carbocations	77
		4.1.3 Generation of carbocations	81
	4.2	4.1.4 Rearrangements of carbocations Carbanions	82
	4.2		82
			82
		surbumons derived from simple alkanes	84
	4.3	4.2.3 Factors stabilising carbanions Carbanions with covalent character	85
		4.3.1 Grignard reagents (RMgX)	88
		4.3.2 Organolithium reagents (RLi)	88
		4.3.3 Organocadmium reagents	89
	4.4	Radicals	89
		4.4.1 Structure	90 90
		4.4.2 Factors stabilising radicals	90 90
		4.4.3 Generation of radicals	92

Contents	
----------	--

vii

	4.5	Carbenes	94
	1.0	4.5.1 Stability and structure	94
		4.5.2 Generation of carbenes	95
	4.6	Benzynes	96
		4.6.1 Stability and structure	96
		4.6.2 Generation of benzynes	97
	4.7	Ketenes	98 98
		4.7.1 Stability and structure	98 98
		4.7.2 Generation of ketenes	90
5	Acid	lity and Basicity	99
5	5.1	Lowry-Brønsted Acid-Base theory	99
	5.2	Organic acidity	100
	3.2	5.2.1 Organic acids	100
	5.3		111
	5.5	5.3.1 Organic bases	112
		a and of the time	117
6		leophilic Substitution	117
	6.1	The S _N 1 reaction 6.1.1 Factors affecting the S _N 1 reaction	118
			123
	6.2	- 1 ' the C 2 reaction	124
		6.2.1 Factors enhancing the SN2 reaction Synthetic applications of nucleophilic substitution reactions	128
	6.3	6.3.1 Protecting-group chemistry	128
		6.3.2 Stereocontrolled alkylation reactions	131
		O.S.D. Ottakes	139
7	Ado	lition Reactions	139
	7.1	Electrophilic addition reactions	139
		7.1.1 Addition of halogens	141
		7.1.2 Addition of hydrogen halides	143
		7.1.2 Addition of hydrogen halides to conjugated dienes 7.1.3 Addition of hydrogen halides to conjugated dienes	143
		7.1.4 Addition of diborane (hydroboration)	147
		7.1.5 Addition of hydrogen	148
		7.1.6 Addition of oxygen	153
		7.1.7 Addition of carbon	153
	7.2	Nucleophilic addition reactions	154
		7.2.1 Irreversible nucleophilic addition	159
		7.2.1 Inteversible nucleophilic conjugate addition	160
		7.2.3 Reversible nucleophilic addition	165
	7.3		165
	7.4		166
	7.5	Synthetic applications	
8	Eli	mination Reactions	1 69 169
,	8.1		169
		8.1.1 E ₁ reactions	169
		8.1.2 E ₁ CB reactions	107

viii Contents

		0.1.2 7	
		8.1.3 E ₂ reactions	170
		8.1.4 Eliminations leading to isomeric products	173
		8.1.5 Competition between substitution and elimination	175
	8.2	6.1.6 The leaving group	176
	8.3	Oxidation processes	178
	8.4	α-Eliminations leading to carbenes and nitrenes	181
	8.5	Eliminations of phosphorus	182
	8.6	Eliminations of sulfur and selenium	182
	0.0	Eliminations in protecting-group chemistry	184
!	9 Aron	natic Substitution	
	9.1	Aromaticity	189
		9.1.1 Benzene	189
		9.1.2 Heteroaromatics	189
	9.2	Reactions	189
		9.2.1 Acidity and basicity	191
		9.2.2 Electrophilic aromatic substitution	191
		9.2.3 Orientation effects in electrophilic aromatic substitution	191
		(S _E Ar)	
		9.2.4 o-Lithiation	202
		9.2.5 Nucleophilic aromatic substitution	205
		9.2.6 Arene chromium tricarbonyl complexes	206
			211
10	Seque	ntial Addition and Elimination Reactions	212
	10.1	Addition-elimination reactions	213
		10.1.1 Addition of hydride	213
		10.1.2 Addition of heteroatom nucleophiles	220
		Addition of carbon nucleophiles	221
		10.1.4 Addition of phosphorus nucleophiles	222
	10.2	haddlon-elimination reactions in conjugated contains	225
		reactions in beterografic and	230
		reaction reactions in ring-closing metal.	230
	10.5	Addition-elimination reactions in deprotections	231
11			234
11		Reactions	237
		Generation	237
		deactions	237
		1.2.1 Termination	237
		1.2.2 Propagation	238
		1.2.3 Substitution	239
		1.2.4 Addition reactions	239 242
		1.2.5 Fragmentation	242 249
		1.2.6 Rearrangement	249
	11.5	Inthetic utility	255
			433

Contents	IX
----------	----

12	Ligar	nd Coupling Reactions	263
	12.1	Palladium-mediated couplings	263
		12.1.1 Palladium-mediated coupling processes	264
		12.1.2 Heck coupling	271
		12.1.3 Allylic coupling processes	273
	12.2	19 11 11 11 11 11 11	275
		12.2.1 Copper	276
		12.2.2 Magnesium	277
		12.2.3 Lead	279
13	Pericyclic Reactions		283
	13.1 Molecular orbitals and the FMO approach		283
	13.2	Pericyclic reactions	284
		13.2.1 Electrocyclic reactions	285
		13.2.2 Cycloaddition reactions	287
		13.2.3 Sigmatropic reactions	293
	13.3	Synthetic applications of pericyclic reactions	296
Ina	lex		303