

CONTENTS

PREFACE

xxvii

INTRODUCTION

xxxii

CHAPTER 1

CHEMICAL BONDING

6

1.1	Atoms, Electrons, and Orbitals	6
1.2	Ionic Bonds	9
1.3	Covalent Bonds	11
1.4	Multiple Bonding in Lewis Structures	13
1.5	Polar Covalent Bonds and Electronegativity	13
1.6	Formal Charge	15
1.7	Writing Structural Formulas of Organic Molecules	18
1.8	Constitutional Isomers	21
1.9	Resonance	22
1.10	The Shapes of Some Simple Molecules	26
	<i>Molecular Models</i>	27
1.11	Molecular Dipole Moments	29
1.12	Molecular Orbitals of the Hydrogen Molecule	30
1.13	sp^3 Hybridization and Bonding in Methane	32
1.14	sp^3 Hybridization and Bonding in Ethane	34
1.15	sp^2 Hybridization and Bonding in Ethylene	35
1.16	sp Hybridization and Bonding in Acetylene	37
1.17	Which Theory of Chemical Bonding Is Best?	39
1.18	Summary	40
	<i>Problems</i>	42
	<i>Molecular Modeling Exercises</i>	46

CHAPTER 2

ALKANES

48

2.1	Classes of Hydrocarbons	48
2.2	Functional Groups in Hydrocarbons	49

2.3	Functionally Substituted Derivatives of Alkanes	50
2.4	Carbonyl-Containing Functional Groups	51
2.5	Introduction to Alkanes: Methane	51
2.6	Ethane and Propane	52
2.7	Isomeric Alkanes: The Butanes	53
2.8	Higher <i>n</i> -Alkanes	54
2.9	The C ₅ H ₁₂ Isomers	54
2.10	Systematic IUPAC Nomenclature of Unbranched Alkanes	56
	<i>A Brief History of Systematic Organic Nomenclature</i>	58
2.11	Applying the IUPAC Rules: The Names of the C ₆ H ₁₄ Isomers	58
2.12	Alkyl Groups	60
2.13	IUPAC Names of Highly Branched Alkanes	62
2.14	Cycloalkane Nomenclature	64
2.15	Sources of Alkanes and Cycloalkanes	65
2.16	Physical Properties of Alkanes and Cycloalkanes	66
2.17	Chemical Properties. Combustion of Alkanes	69
	<i>Thermochemistry</i>	72
2.18	Oxidation-Reduction in Organic Chemistry	73
2.19	Summary	75
	<i>Problems</i>	79
	<i>Molecular Modeling Exercises</i>	82

CHAPTER 3

CONFORMATIONS OF ALKANES AND CYCLOALKANES 84

3.1	Conformational Analysis of Ethane	85
3.2	Internal Rotation in Ethane	85
3.3	Conformational Analysis of Butane	89
	<i>Molecular Mechanics Applied to Alkanes and Cycloalkanes</i>	91
3.4	Conformations of Higher Alkanes	92
3.5	The Shapes of Cycloalkanes: Planar or Nonplanar?	93
3.6	Conformations of Cyclohexane	94
3.7	Axial and Equatorial Bonds in Cyclohexane	96
3.8	Conformational Inversion (Ring Flipping) in Cyclohexane	99
3.9	Conformational Analysis of Monosubstituted Cyclohexanes	100
	<i>Enthalpy, Free Energy, and Equilibrium Constant</i>	102
3.10	Small Rings: Cyclopropane and Cyclobutane	103
3.11	Cyclopentane	104
3.12	Medium and Large Rings	105
3.13	Disubstituted Cycloalkanes. Stereoisomers	105
3.14	Conformational Analysis of Disubstituted Cyclohexanes	107
3.15	Polycyclic Ring Systems	111
3.16	Heterocyclic Compounds	113
3.17	Summary	114
	<i>Problems</i>	116
	<i>Molecular Modeling Exercises</i>	121

CHAPTER 4

ALCOHOLS AND ALKYL HALIDES 122

4.1	IUPAC Nomenclature of Alkyl Halides	123
4.2	IUPAC Nomenclature of Alcohols	123

4.3	Classes of Alcohols and Alkyl Halides	124
4.4	Bonding in Alcohols and Alkyl Halides	125
4.5	Physical Properties of Alcohols and Alkyl Halides. Intermolecular Forces in Polar Molecules	126
4.6	Acids and Bases: General Principles	129
4.7	Acid-Base Reactions: A Mechanism for Proton Transfer	132
4.8	Acidity of Alcohols. Alkoxide Ions	134
4.9	Preparation of Alkyl Halides from Alcohols and Hydrogen Halides	135
4.10	Mechanism of the Reaction of Alcohols with Hydrogen Halides	137
4.11	Structure, Bonding, and Stability of Carbocations	138
4.12	Potential Energy Diagrams for Multistep Reactions. The S_N1 Mechanism	141
4.13	Effect of Alcohol Structure on Reaction Rate	143
4.14	Reaction of Primary Alcohols with Hydrogen Halides. The S_N2 Mechanism	144
4.15	Other Methods for Converting Alcohols to Alkyl Halides	145
4.16	Halogenation of Alkanes	146
4.17	Chlorination of Methane	147
4.18	Structure and Stability of Free Radicals	148
4.19	Mechanism of Methane Chlorination <i>From Bond Energies to Heats of Reaction</i>	152 154
4.20	Halogenation of Higher Alkanes. Regioselectivity	155
4.21	Summary	158
	<i>Problems</i>	162
	<i>Molecular Modeling Exercises</i>	166

CHAPTER 5

STRUCTURE AND PREPARATION OF ALKENES. ELIMINATION REACTIONS

167

5.1	Alkene Nomenclature <i>Ethylene</i>	167 170
5.2	Structure and Bonding in Alkenes	170
5.3	Isomerism in Alkenes	172
5.4	Naming Stereoisomeric Alkenes by the <i>E-Z</i> Notational System	173
5.5	Physical Properties of Alkenes	177
5.6	Relative Stabilities of Alkenes	178
5.7	Sources of Strain in Cycloalkenes	181
5.8	Preparation of Alkenes: Elimination Reactions	183
5.9	Dehydration of Alcohols	184
5.10	Regioselectivity in Alcohol Dehydration: The Zaitsev Rule	185
5.11	Stereoselectivity in Alcohol Dehydration	187
5.12	The Mechanism of Acid-Catalyzed Dehydration of Alcohols	187
5.13	Rearrangements in Alcohol Dehydration	189
5.14	Dehydrohalogenation of Alkyl Halides	193
5.15	Mechanism of the Dehydrohalogenation of Alkyl Halides: The $E2$ Mechanism	195
5.16	Anti Elimination in $E2$ Reactions: Stereoelectronic Effects	197
5.17	A Different Mechanism for Alkyl Halide Elimination: The $E1$ Mechanism	199

5.18	Summary	201
	<i>Problems</i>	204
	<i>Molecular Modeling Exercises</i>	210

CHAPTER 6

REACTIONS OF ALKENES: ADDITION REACTIONS 211

6.1	Hydrogenation of Alkenes	211
6.2	Heats of Hydrogenation	213
6.3	Stereochemistry of Alkene Hydrogenation	215
6.4	Electrophilic Addition of Hydrogen Halides to Alkenes	217
6.5	Regioselectivity of Hydrogen Halide Addition: Markovnikov's Rule	218
6.6	Mechanistic Basis for Markovnikov's Rule	219
6.7	Carbocation Rearrangements in Hydrogen Halide Addition to Alkenes	222
6.8	Free-Radical Addition of Hydrogen Bromide to Alkenes	223
6.9	Addition of Sulfuric Acid to Alkenes	226
6.10	Acid-Catalyzed Hydration of Alkenes	228
6.11	Hydroboration-Oxidation of Alkenes	231
6.12	Stereochemistry of Hydroboration-Oxidation	233
6.13	Mechanism of Hydroboration-Oxidation	234
6.14	Addition of Halogens to Alkenes	237
6.15	Stereochemistry of Halogen Addition	237
6.16	Mechanism of Halogen Addition to Alkenes. Halonium Ions	238
6.17	Conversion of Alkenes to Vicinal Halohydrins	241
6.18	Epoxidation of Alkenes	243
6.19	Ozonolysis of Alkenes	245
6.20	Analysis of Alkenes: Molecular Formula as a Clue to Structure	247
6.21	Reactions of Alkenes with Alkenes. Polymerization <i>Ethylene and Propene: The Most Important Industrial Organic Chemicals</i>	249
6.22	Introduction to Organic Chemical Synthesis	254
6.23	Summary	256
	<i>Problems</i>	259
	<i>Molecular Modeling Exercises</i>	264

CHAPTER 7

STEREOCHEMISTRY 265

7.1	Molecular Chirality. Enantiomers	265
7.2	The Stereogenic Center	267
7.3	Symmetry in Achiral Structures	269
7.4	Properties of Chiral Molecules: Optical Activity	271
7.5	Absolute and Relative Configuration	273
7.6	The Cahn-Ingold-Prelog <i>R-S</i> Notational System	274
7.7	Fischer Projection Formulas	278
7.8	Physical Properties of Enantiomers	279

<i>Chiral Drugs</i>	280
7.9 Reactions That Create a Stereogenic Center	281
7.10 Chiral Molecules with Two Stereogenic Centers	284
7.11 Achiral Molecules with Two Stereogenic Centers	287
<i>Chirality of Disubstituted Cyclohexanes</i>	288
7.12 Molecules with Multiple Stereogenic Centers	289
7.13 Reactions That Produce Diastereomers	291
7.14 Resolution of Enantiomers	294
7.15 Stereoregular Polymers	296
7.16 Stereogenic Centers Other Than Carbon	298
7.17 Summary	298
<i>Problems</i>	301
<i>Molecular Modeling Exercises</i>	308

CHAPTER 8**NUCLEOPHILIC SUBSTITUTION 309**

8.1 Functional Group Transformation by Nucleophilic Substitution	310
8.2 Substitution of One Halogen by Another	312
8.3 Relative Reactivity of Halide Leaving Groups	313
8.4 The Bimolecular (S_N2) Mechanism of Nucleophilic Substitution	314
8.5 Stereochemistry of S_N2 Reactions	315
8.6 How S_N2 Reactions Occur	317
8.7 Steric Effects in S_N2 Reactions	318
8.8 Nucleophiles and Nucleophilicity	320
8.9 The Unimolecular (S_N1) Mechanism of Nucleophilic Substitution	323
8.10 Carbocation Stability and the Rate of Substitution by the S_N1 Mechanism	324
8.11 Stereochemistry of S_N1 Reactions	326
8.12 Carbocation Rearrangements in S_N1 Reactions	327
8.13 Effect of Solvent on the Rate of Nucleophilic Substitution	329
8.14 Substitution and Elimination as Competing Reactions	332
8.15 Sulfonate Esters as Substrates in Nucleophilic Substitution	334
8.16 A Retrospective Look: Reactions of Alcohols with Hydrogen Halides	338
8.17 Summary	339
<i>Problems</i>	342
<i>Molecular Modeling Exercises</i>	347

CHAPTER 9**ALKYNES 349**

9.1 Sources of Alkynes	349
9.2 Nomenclature	350
9.3 Structure and Bonding in Alkynes. sp Hybridization	351
9.4 Cycloalkynes	353
<i>Natural and "Designed" Eneidyne Antibiotics</i>	354
9.5 Physical Properties of Alkynes	354
9.6 Acidity of Acetylene and Terminal Alkynes	355

9.7	Preparation of Alkynes by Alkylation of Acetylene and Terminal Alkynes	357
9.8	Preparation of Alkynes by Elimination Reactions	359
9.9	Reactions of Alkynes	361
9.10	Hydrogenation of Alkynes	362
9.11	Metal-Ammonia Reduction of Alkynes	364
9.12	Addition of Hydrogen Halides to Alkynes	365
9.13	Hydration of Alkynes	367
9.14	Addition of Halogens to Alkynes	369
9.15	Ozonolysis of Alkynes	370
9.16	Summary	371
	<i>Problems</i>	372
	<i>Molecular Modeling Exercises</i>	377

CHAPTER 10

CONJUGATION IN ALKADIENES AND ALLYLIC SYSTEMS 378

10.1	The Allyl Group	378
10.2	Allylic Carbocations	379
10.3	Allylic Free Radicals	382
10.4	Allylic Halogenation	383
10.5	Classes of Dienes	385
10.6	Relative Stabilities of Alkadienes	387
10.7	Electron Delocalization in Conjugated Dienes	388
10.8	Bonding in Allenes	390
10.9	Preparation of Dienes	392
10.10	Addition of Hydrogen Halides to Conjugated Dienes	393
10.11	Halogen Addition to Dienes	396
	<i>Diene Polymers</i>	396
10.12	The Diels-Alder Reaction	397
10.13	Stereoselectivity of Diels-Alder Reactions	400
10.14	Electrocyclic Reactions of Polyenes	402
10.15	The π Molecular Orbitals of Alkenes and Conjugated Polyenes	404
10.16	A π Molecular Orbital Analysis of the Diels-Alder Reaction	407
10.17	A π Molecular Orbital Analysis of Electrocyclic Reactions	408
10.18	Summary	409
	<i>Problems</i>	412
	<i>Molecular Modeling Exercises</i>	418

CHAPTER 11

ARENES AND AROMATICITY 419

11.1	Benzene	420
11.2	Benzene Reactivity	420
11.3	Kekulé's Formulation of the Benzene Structure	421
	<i>Benzene, Dreams, and Creative Thinking</i>	422
11.4	Structural Features of Benzene	423
11.5	A Resonance Description of Bonding in Benzene	423
11.6	The Stability of Benzene	424

11.7	An Orbital Hybridization Model of Bonding in Benzene	426
11.8	The π Molecular Orbitals of Benzene	426
11.9	Substituted Derivatives of Benzene and Their Nomenclature	427
11.10	Polycyclic Aromatic Hydrocarbons	430
	<i>Carbon Clusters and Fullerenes</i>	431
11.11	Physical Properties of Arenes	433
11.12	Reactions of Arenes: A Preview	433
11.13	The Birch Reduction	434
11.14	Free-Radical Halogenation of Alkylbenzenes	436
11.15	Oxidation of Alkylbenzenes	438
11.16	Nucleophilic Substitution in Benzylic Halides	440
11.17	Preparation of Alkenylbenzenes	442
11.18	Addition Reactions of Alkenylbenzenes	442
11.19	Polymerization of Styrene	444
11.20	Cyclobutadiene and Cyclooctatetraene	445
11.21	Hückel's Rule. Annulenes	447
11.22	Aromatic Ions	450
11.23	Heterocyclic Aromatic Compounds	453
11.24	Heterocyclic Aromatic Compounds and Hückel's Rule	455
11.25	Summary	456
	<i>Problems</i>	459
	<i>Molecular Modeling Exercises</i>	464

CHAPTER 12

REACTIONS OF ARENES.

ELECTROPHILIC AROMATIC SUBSTITUTION

466

12.1	Representative Electrophilic Aromatic Substitution Reactions of Benzene	467
12.2	Mechanistic Principles of Electrophilic Aromatic Substitution	468
12.3	Nitration of Benzene	470
12.4	Sulfonation of Benzene	471
12.5	Halogenation of Benzene	472
12.6	Friedel-Crafts Alkylation of Benzene	474
12.7	Friedel-Crafts Acylation of Benzene	477
12.8	Synthesis of Alkylbenzenes by Acylation-Reduction	479
12.9	Rate and Orientation in Electrophilic Aromatic Substitution	480
12.10	Rate and Orientation in the Nitration of Toluene	482
12.11	Rate and Orientation in the Nitration of (Trifluoromethyl)Benzene	484
12.12	Substituent Effects in Electrophilic Aromatic Substitution: Activating Substituents	487
12.13	Substituent Effects in Electrophilic Aromatic Substitution: Deactivating Substituents	491
12.14	Substituent Effects in Electrophilic Aromatic Substitution: Halogen Substituents	493
12.15	Multiple Substituent Effects	495
12.16	Regioselective Synthesis of Disubstituted Aromatic Compounds	497

12.17	Substitution in Naphthalene	499
12.18	Substitution in Heterocyclic Aromatic Compounds	500
12.19	Summary	501
	<i>Problems</i>	505
	<i>Molecular Modeling Exercises</i>	511

CHAPTER 13 SPECTROSCOPY

512

13.1	Principles of Molecular Spectroscopy: Electromagnetic Radiation	512
13.2	Principles of Molecular Spectroscopy: Quantized Energy States	514
13.3	Proton Magnetic Resonance (^1H NMR) Spectroscopy	515
13.4	Nuclear Shielding and Chemical Shift	517
13.5	How Chemical Shift Is Measured	518
13.6	Chemical Shift and Molecular Structure	519
13.7	Interpreting Proton NMR Spectra	521
13.8	Spin-Spin Splitting in NMR Spectroscopy	525
13.9	Patterns of Spin-Spin Splitting: The Ethyl Group	528
13.10	Patterns of Spin-Spin Splitting: The Isopropyl Group	530
13.11	Patterns of Spin-Spin Splitting: Pairs of Doublets	530
13.12	Geminal Coupling	532
13.13	Complex Splitting Patterns	532
13.14	Proton NMR Spectra of Alcohols	534
13.15	NMR and Conformations	535
13.16	Carbon-13 Nuclear Magnetic Resonance: The Sensitivity Problem	536
13.17	Carbon-13 Nuclear Magnetic Resonance: Interpretation of Spectra	537
	<i>Magnetic Resonance Imaging</i>	541
13.18	Infrared Spectroscopy	542
13.19	Ultraviolet-Visible (UV-VIS) Spectroscopy	547
13.20	Mass Spectrometry	549
	<i>Gas Chromatography, GC/MS, and MS/MS</i>	554
13.21	Summary	555
	<i>Problems</i>	557
	<i>Molecular Modeling Exercises</i>	565

CHAPTER 14 ORGANOMETALLIC COMPOUNDS

566

14.1	Carbon-Metal Bonds in Organometallic Compounds	566
14.2	Organometallic Nomenclature	567
14.3	Preparation of Organolithium Compounds	568
14.4	Preparation of Organomagnesium Compounds: Grignard Reagents	569
14.5	Organolithium and Organomagnesium Compounds as Brønsted Bases	571
14.6	Synthesis of Alcohols Using Grignard Reagents	573

14.7	Synthesis of Alcohols Using Organolithium Reagents	575
14.8	Synthesis of Acetylenic Alcohols	576
14.9	Retrosynthetic Analysis	577
14.10	Preparation of Tertiary Alcohols from Esters and Grignard Reagents	580
14.11	Alkane Synthesis Using Organocopper Reagents	582
14.12	An Organozinc Reagent for Cyclopropane Synthesis	584
14.13	Carbenes and Carbenoids	585
14.14	Organic Derivatives of Mercury. Oxymercuration-Demercuration of Alkenes	587
14.15	Transition Metal Organometallic Compounds	591
	<i>An Organometallic Compound That Occurs Naturally:</i>	
	<i>Coenzyme B₁₂</i>	593
14.16	Summary	594
	<i>Problems</i>	597
	<i>Molecular Modeling Exercises</i>	601

CHAPTER 15**ALCOHOLS, DIOLS, AND THIOLS 603**

15.1	Sources of Alcohols	603
15.2	Preparation of Alcohols by Reduction of Aldehydes and Ketones	605
15.3	Preparation of Alcohols by Reduction of Carboxylic Acids and Esters	611
15.4	Preparation of Alcohols from Epoxides	612
15.5	Preparation of Diols	613
15.6	Reactions of Alcohols: A Review and a Preview	615
15.7	Conversion of Alcohols to Ethers	617
15.8	Esterification	619
15.9	Esters of Inorganic Acids	621
15.10	Oxidation of Alcohols	622
	<i>Economic and Environmental Factors in Organic Synthesis</i>	624
15.11	Biological Oxidation of Alcohols	626
15.12	Oxidative Cleavage of Vicinal Diols	628
15.13	Preparation of Thiols	629
15.14	Properties of Thiols	630
15.15	Spectroscopic Analysis of Alcohols	632
15.16	Mass Spectrometry of Alcohols	633
15.17	Summary	633
	<i>Problems</i>	637
	<i>Molecular Modeling Exercises</i>	644

CHAPTER 16**ETHERS, EPOXIDES, AND SULFIDES 645**

16.1	Nomenclature of Ethers, Epoxides, and Sulfides	645
16.2	Structure and Bonding in Ethers and Epoxides	647
16.3	Physical Properties of Ethers	648
16.4	Crown Ethers	649

	<i>Polyether Antibiotics</i>	651
16.5	Preparation of Ethers	652
16.6	The Williamson Ether Synthesis	652
16.7	Reactions of Ethers: A Review and a Preview	654
16.8	Acid-Catalyzed Cleavage of Ethers	654
16.9	Preparation of Epoxides: A Review and a Preview	657
16.10	Conversion of Vicinal Halohydrins to Epoxides	657
16.11	Reactions of Epoxides: A Review and a Preview	659
16.12	Nucleophilic Ring-Opening Reactions of Epoxides	660
16.13	Acid-Catalyzed Ring-Opening Reactions of Epoxides	662
16.14	Epoxides in Biological Processes	665
16.15	Preparation of Sulfides	666
16.16	Oxidation of Sulfides: Sulfoxides and Sulfones	666
16.17	Alkylation of Sulfides: Sulfonium Salts	667
16.18	Spectroscopic Analysis of Ethers	669
16.19	Mass Spectrometry of Ethers	670
16.20	Summary	670
	<i>Problems</i>	674
	<i>Molecular Modeling Exercises</i>	679

CHAPTER 17

ALDEHYDES AND KETONES.

NUCLEOPHILIC ADDITION TO THE CARBONYL GROUP 680

17.1	Nomenclature	680
17.2	Structure and Bonding: The Carbonyl Group	683
17.3	Physical Properties	684
17.4	Sources of Aldehydes and Ketones	685
17.5	Reactions That Lead to Aldehydes and Ketones: Review and Applications	686
17.6	Reactions of Aldehydes and Ketones: A Review and a Preview	688
17.7	Principles of Nucleophilic Addition to Carbonyl Groups: Hydration of Aldehydes and Ketones	690
17.8	Cyanohydrin Formation	694
17.9	Acetal Formation	696
17.10	Acetals as Protecting Groups	698
17.11	Reaction with Primary Amines. Nucleophilic Addition-Elimination	700
	<i>Imines in Biological Chemistry</i>	703
17.12	Reaction with Secondary Amines: Enamines	703
17.13	The Wittig Reaction	704
17.14	Planning an Alkene Synthesis via the Wittig Reaction	706
17.15	Stereoselective Addition to Carbonyl Groups	708
17.16	Oxidation of Aldehydes	709
17.17	Baeyer-Villiger Oxidation of Ketones	710
17.18	Spectroscopic Analysis of Aldehydes and Ketones	712
17.19	Mass Spectrometry of Aldehydes and Ketones	714
17.20	Summary	714
	<i>Problems</i>	718
	<i>Molecular Modeling Exercises</i>	725

CHAPTER 18**ENOLS AND ENOLATES****727**

18.1	The α Carbon Atom and Its Hydrogens	728
18.2	α Halogenation of Aldehydes and Ketones	729
18.3	Mechanism of α Halogenation of Aldehydes and Ketones	730
18.4	Enolization and Enol Content	731
18.5	Stabilized Enols	733
18.6	Base-Catalyzed Enolization. Enolate Anions	735
18.7	The Haloform Reaction	737
	<i>The Haloform Reaction and the Biosynthesis of Trihalomethanes</i>	739
18.8	Some Chemical and Stereochemical Consequences of Enolization	740
18.9	The Aldol Condensation: Aldehydes	741
18.10	The Aldol Condensation: Ketones	745
18.11	Mixed Aldol Condensations	746
18.12	The Aldol Condensation in Synthetic Organic Chemistry	747
18.13	Effects of Conjugation in α , β -Unsaturated Aldehydes and Ketones	748
18.14	Conjugate Nucleophilic Addition to α , β -Unsaturated Carbonyl Compounds	749
18.15	Additions of Carbanions to α , β -Unsaturated Ketones: The Michael Reaction	751
18.16	Conjugate Addition of Organocopper Reagents to α , β -Unsaturated Carbonyl Compounds	752
18.17	Alkylation of Enolate Anions	753
18.18	Summary	754
	<i>Problems</i>	758
	<i>Molecular Modeling Exercises</i>	764

CHAPTER 19**CARBOXYLIC ACIDS****766**

19.1	Carboxylic Acid Nomenclature	767
19.2	Structure and Bonding	768
19.3	Physical Properties	769
19.4	Acidity of Carboxylic Acids	770
	<i>Quantitative Relationships Involving Carboxylic Acids</i>	772
19.5	Salts of Carboxylic Acids	773
19.6	Substituents and Acid Strength	775
19.7	Ionization of Substituted Benzoic Acids	778
19.8	Dicarboxylic Acids	779
19.9	Carbonic Acid	779
19.10	Sources of Carboxylic Acids	780
19.11	Synthesis of Carboxylic Acids by the Carboxylation of Grignard Reagents	782
19.12	Synthesis of Carboxylic Acids by the Preparation and Hydrolysis of Nitriles	783
19.13	Reactions of Carboxylic Acids: A Review and a Preview	784
19.14	Mechanism of Acid-Catalyzed Esterification	784

19.15	Intramolecular Ester Formation: Lactones	788
19.16	α Halogenation of Carboxylic Acids. The Hell-Volhard-Zelinsky Reaction	790
19.17	Decarboxylation of Malonic Acid and Related Compounds	792
19.18	Spectroscopic Analysis of Carboxylic Acids	794
19.19	Summary	796
	<i>Problems</i>	798
	<i>Molecular Modeling Exercises</i>	803

CHAPTER 20

CARBOXYLIC ACID DERIVATIVES.

NUCLEOPHILIC ACYL SUBSTITUTION

805

20.1	Nomenclature of Carboxylic Acid Derivatives	806
20.2	Structure of Carboxylic Acid Derivatives	808
20.3	Nucleophilic Acyl Substitution in Acyl Chlorides	811
20.4	Preparation of Carboxylic Acid Anhydrides	814
20.5	Reactions of Carboxylic Acid Anhydrides	815
20.6	Sources of Esters	819
20.7	Physical Properties of Esters	820
20.8	Reactions of Esters: A Review and a Preview	822
20.9	Acid-Catalyzed Ester Hydrolysis	822
20.10	Base-Promoted Ester Hydrolysis: Saponification	826
20.11	Reaction of Esters with Ammonia and Amines	831
20.12	Thioesters	832
20.13	Preparation of Amides	833
20.14	Lactams	835
20.15	Imides	836
20.16	Hydrolysis of Amides	837
	<i>Condensation Polymers. Polyamides and Polyesters</i>	840
20.17	The Hofmann Rearrangement of <i>N</i> -Bromo Amides	843
20.18	Preparation of Nitriles	847
20.19	Hydrolysis of Nitriles	847
20.20	Addition of Grignard Reagents to Nitriles	849
20.21	Spectroscopic Analysis of Carboxylic Acid Derivatives	850
20.22	Mass Spectrometry of Carboxylic Acid Derivatives	852
20.23	Summary	852
	<i>Problems</i>	855
	<i>Molecular Modeling Exercises</i>	862

CHAPTER 21

ESTER ENOLATES

864

21.1	Base-Promoted Ester Condensation: The Claisen Condensation	865
21.2	Intramolecular Claisen Condensation: The Dieckmann Reaction	868
21.3	Mixed Claisen Condensations	869
21.4	Acylation of Ketones with Esters	870
21.5	Ketone Synthesis via β -Keto Esters	871
21.6	The Acetoacetic Ester Synthesis	872

21.7	The Malonic Ester Synthesis	875
21.8	Barbiturates	879
21.9	Michael Additions of Stabilized Anions	880
21.10	α Deprotonation of Carbonyl Compounds by Lithium Dialkylamides	881
21.11	Summary	884
	<i>Problems</i>	887
	<i>Molecular Modeling Exercises</i>	892

CHAPTER 22**AMINES 893**

22.1	Amine Nomenclature	894
22.2	Structure and Bonding	896
22.3	Physical Properties	898
22.4	Measures of Amine Basicity	899
22.5	Basicity of Amines	900
	<i>Amines as Natural Products</i>	906
22.6	Tetraalkylammonium Salts as Phase-Transfer Catalysts	908
22.7	Reactions That Lead to Amines: A Review and a Preview	910
22.8	Preparation of Amines by Alkylation of Ammonia	910
22.9	The Gabriel Synthesis of Primary Alkylamines	913
22.10	Preparation of Amines by Reduction	915
22.11	Reductive Amination	917
22.12	Reactions of Amines: A Review and a Preview	919
22.13	Reaction of Amines with Alkyl Halides	921
22.14	The Hofmann Elimination	922
22.15	Electrophilic Aromatic Substitution in Arylamines	924
22.16	Nitrosation of Alkylamines	927
22.17	Nitrosation of Arylamines	929
22.18	Synthetic Transformations of Aryl Diazonium Salts	931
22.19	Azo Coupling	934
	<i>From Dyes to Sulfa Drugs</i>	935
22.20	Spectroscopic Analysis of Amines	936
22.21	Mass Spectrometry of Amines	939
22.22	Summary	939
	<i>Problems</i>	940
	<i>Molecular Modeling Exercises</i>	954

CHAPTER 23**ARYL HALIDES 955**

23.1	Bonding in Aryl Halides	955
23.2	Sources of Aryl Halides	956
23.3	Physical Properties of Aryl Halides	956
23.4	Reactions of Aryl Halides: A Review and a Preview	958
23.5	Nucleophilic Substitution in Nitro-Substituted Aryl Halides	960
23.6	The Addition-Elimination Mechanism of Nucleophilic Aromatic Substitution	961

23.7	Related Nucleophilic Aromatic Substitution Reactions	964
23.8	The Elimination-Addition Mechanism of Nucleophilic Aromatic Substitution. Benzyne	965
23.9	Diels-Alder Reactions of Benzyne	969
23.10	Summary	970
	<i>Problems</i>	971
	<i>Molecular Modeling Exercises</i>	976

CHAPTER 24**PHENOLS****977**

24.1	Nomenclature	977
24.2	Structure and Bonding	978
24.3	Physical Properties	979
24.4	Acidity of Phenols	980
24.5	Substituent Effects on the Acidity of Phenols	982
24.6	Sources of Phenols	984
24.7	Naturally Occurring Phenols	986
24.8	Reactions of Phenols. Electrophilic Aromatic Substitution	987
24.9	Acylation of Phenols	989
24.10	Carboxylation of Phenols. Aspirin and the Kolbe-Schmitt Reaction	991
24.11	Preparation of Aryl Ethers	993
	<i>Agent Orange and Dioxin</i>	994
24.12	Cleavage of Aryl Ethers by Hydrogen Halides	995
24.13	Claisen Rearrangement of Allyl Aryl Ethers	996
24.14	Oxidation of Phenols: Quinones	997
24.15	Spectroscopic Analysis of Phenols	999
24.16	Summary	999
	<i>Problems</i>	1002
	<i>Molecular Modeling Exercises</i>	1010

CHAPTER 25**CARBOHYDRATES****1011**

25.1	Classification of Carbohydrates	1011
25.2	Fischer Projections and the D-L Notational System	1012
25.3	The Aldotetroses	1013
25.4	Aldopentoses and Aldohexoses	1015
25.5	A Mnemonic for Carbohydrate Configurations	1017
25.6	Cyclic Forms of Carbohydrates: Furanose Forms	1017
25.7	Cyclic Forms of Carbohydrates: Pyranose Forms	1021
25.8	Mutarotation	1024
25.9	Ketoses	1025
25.10	Deoxy Sugars	1026
25.11	Amino Sugars	1027
25.12	Branched-Chain Carbohydrates	1028
25.13	Glycosides	1028
25.14	Disaccharides	1031

25.15	Polysaccharides	1034
25.16	Cell-Surface Glycoproteins	1035
25.17	Carbohydrate Structure Determination	1037
25.18	Reduction of Carbohydrates	1037
25.19	Oxidation of Carbohydrates	1038
25.20	Cyanohydrin Formation and Carbohydrate Chain Extension	1041
25.21	Epimerization, Isomerization, and Retro-Aldol Cleavage	
	Reactions of Carbohydrates	1042
25.22	Acylation and Alkylation of Hydroxyl Groups in Carbohydrates	1044
25.23	Periodic Acid Oxidation of Carbohydrates	1046
25.24	Summary	1047
	<i>Problems</i>	1051
	<i>Molecular Modeling Exercises</i>	1055

CHAPTER 26**ACETATE-DERIVED NATURAL PRODUCTS****1056**

26.1	Acetyl Coenzyme A	1057
26.2	Fatty Acids	1058
26.3	Fatty Acid Biosynthesis	1060
26.4	Phospholipids	1063
26.5	Waxes	1065
26.6	Prostaglandins	1065
26.7	Terpenes. The Isoprene Rule	1067
26.8	Isopentenyl Pyrophosphate: The Biological Isoprene Unit	1070
26.9	Carbon-Carbon Bond Formation in Terpene Biosynthesis	1071
26.10	The Pathway from Acetate to Isopentenyl Pyrophosphate	1074
26.11	Steroids. Cholesterol	1076
26.12	Vitamin D	1079
26.13	Bile Acids	1080
26.14	Corticosteroids	1081
26.15	Sex Hormones	1081
	<i>Anabolic Steroids</i>	1082
26.16	Carotenoids	1083
26.17	Summary	1084
	<i>Problems</i>	1085
	<i>Molecular Modeling Exercises</i>	1090

CHAPTER 27**AMINO ACIDS, PEPTIDES, AND PROTEINS. NUCLEIC ACIDS****1092**

27.1	Classification of Amino Acids	1093
27.2	Stereochemistry of Amino Acids	1096
27.3	Acid-Base Behavior of Amino Acids	1097
	<i>Electrophoresis</i>	1100
27.4	Synthesis of Amino Acids	1101
27.5	Reactions of Amino Acids	1103
27.6	Some Biochemical Reactions Involving Amino Acids	1104
27.7	Peptides	1106

27.8	Peptide Structure Determination: Amino Acid Analysis	1109
27.9	Peptide Structure Determination: Sequence Analysis	1110
27.10	End Group Analysis: The N Terminus	1111
27.11	End Group Analysis: The C Terminus	1115
27.12	Selective Hydrolysis of Peptides	1115
27.13	The Strategy of Peptide Synthesis	1117
27.14	Amino Group Protection	1119
27.15	Carboxyl Group Protection	1122
27.16	Peptide Bond Formation	1122
27.17	Solid-Phase Peptide Synthesis. The Merrifield Method	1125
27.18	Secondary Structures of Peptides and Proteins	1127
27.19	Tertiary Structures of Peptides and Proteins	1130
27.20	Coenzymes	1131
27.21	Protein Quaternary Structure. Hemoglobin	1133
27.22	Pyrimidines and Purines	1133
27.23	Nucleosides	1135
27.24	Nucleotides	1136
27.25	Nucleic Acids	1137
27.26	Structure and Replication of DNA. The Double Helix	1138
27.27	DNA-Directed Protein Biosynthesis	1141
	<i>AIDS</i>	1143
27.28	DNA Sequencing	1143
27.29	Summary	1146
	<i>Problems</i>	1148
	<i>Molecular Modeling Exercises</i>	1151
APPENDIX 1		
PHYSICAL PROPERTIES		A-0
APPENDIX 2		
ANSWERS TO IN-TEXT PROBLEMS		A-8
GLOSSARY		A-65
INDEX		I-1