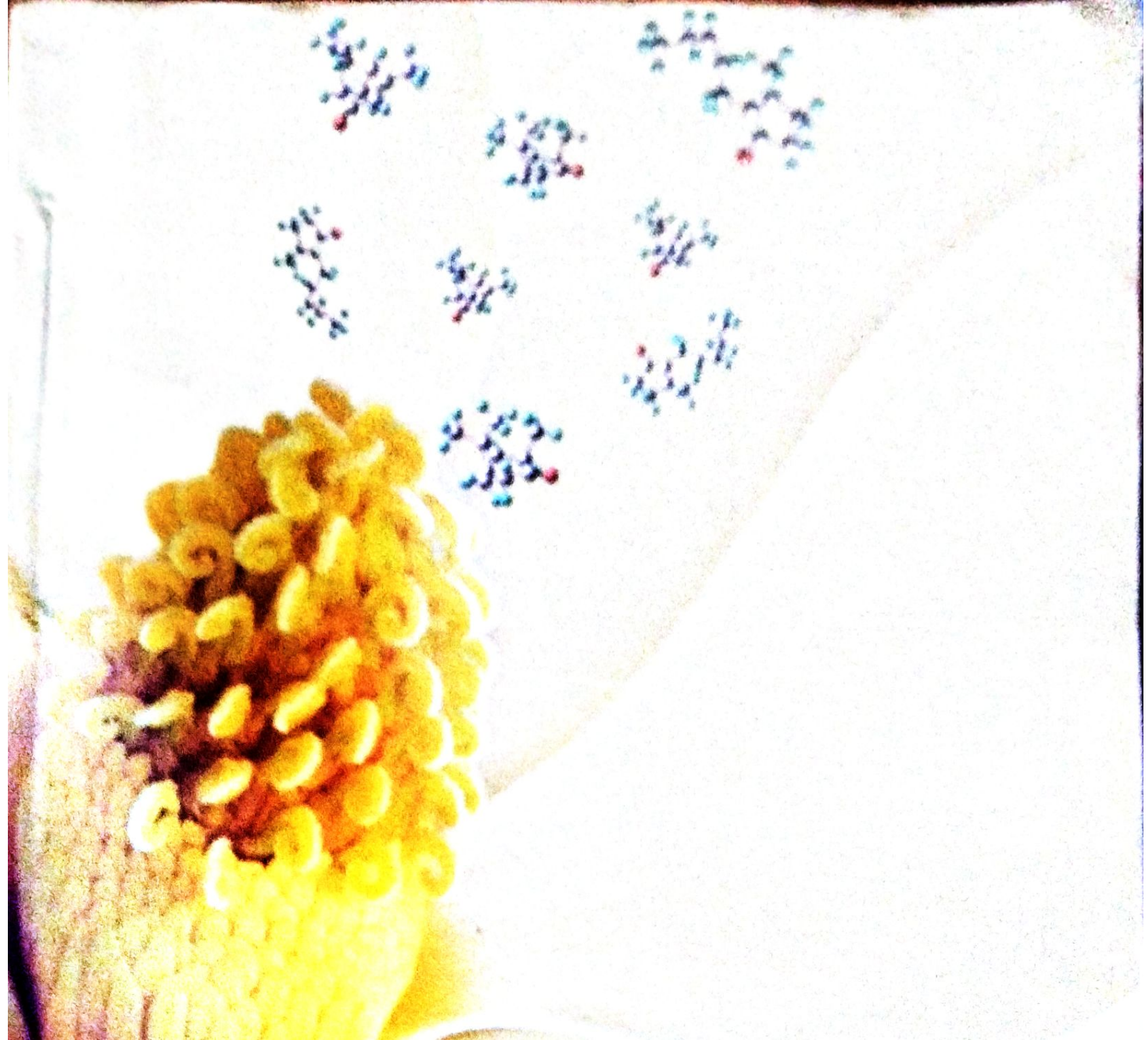




- 1 **The Basics** Bonding and Molecular Structure 1
- 2 **Families of Carbon Compounds** Functional Groups, Intermolecular Forces, and Infrared (IR) Spectroscopy 53
- 3 **An Introduction to Organic Reactions and Their Mechanisms** Acids and Bases 98
- 4 **Nomenclature and Conformations of Alkanes and Cycloalkanes** 137
- 5 **Stereochemistry** Chiral Molecules 186
- 6 **Ionic Reactions** Nucleophilic Substitution and Elimination Reactions of Alkyl Halides 230
- 7 **Alkenes and Alkynes I** Properties and Synthesis, Elimination Reactions of Alkyl Halides 285
- 8 **Alkenes and Alkynes II** Addition Reactions 331
- 9 **Nuclear Magnetic Resonance and Mass Spectrometry** Tools for Structure Determination 385
- 10 **Radical Reactions** 459
- 11 **Alcohols and Ethers** Synthesis and Reactions 502
- 12 **Alcohols From Carbonyl Compounds** Oxidation-Reduction and Organometallic Compounds 548
- 13 **Conjugated Unsaturated Systems** 585
- 14 **Aromatic Compounds** 632
- 15 **Reactions of Aromatic Compounds** 676
- 16 **Aldehydes and Ketones** Nucleophilic Addition to the Carbonyl Group 729
- 17 **Carboxylic Acids and Their Derivatives** Nucleophilic Addition-Elimination at the Acyl Carbon 779
- 18 **Reactions at the α Carbon of Carbonyl Compounds** Enols and Enolates 831
- 19 **Condensation and Conjugate Addition Reactions of Carbonyl Compounds** More Chemistry of Enolates 869
- 20 **Amines** 911
- 21 **Phenols and Aryl Halides** Nucleophilic Aromatic Substitution 964
- Special Topic G Carbon-Carbon Bond-Forming and Other Reactions of Transition Metal Organometallic Compounds G-1**
- 22 **Carbohydrates** 1000
- 23 **Lipids** 1050
- 24 **Amino Acids and Proteins** 1084
- 25 **Nucleic Acids and Protein Synthesis** 1131
- Answers to Selected Problems A-1**
- Glossary GL-1**
- Photo Credits C-1**
- Index I-1**

1 The Basics Bonding and Molecular Structure 1

- 1.1 We Are Stardust 2
- 1.2 Atomic Structure 2
- 1.3 The Structural Theory of Organic Chemistry 5
- 1.4 Chemical Bonds: The Octet Rule 7
- 1.5 How to Write Lewis Structures 9
- 1.6 Exceptions to the Octet Rule 11
- 1.7 Formal Charges and How to Calculate Them 13
- 1.8 Resonance Theory 15
- 1.9 Quantum Mechanics and Atomic Structure 20
- 1.10 Atomic Orbitals and Electron Configuration 21
- 1.11 Molecular Orbitals 23
- 1.12 The Structure of Methane and Ethane: sp^3 Hybridization 25
- THE CHEMISTRY OF ... Calculated Molecular Models: Electron Density Surfaces 29
- 1.13 The Structure of Ethene (Ethylene): sp^2 Hybridization 30
- 1.14 The Structure of Ethyne (Acetylene): sp Hybridization 34
- 1.15 A Summary of Important Concepts that Come from Quantum Mechanics 36
- 1.16 Molecular Geometry: The Valence Shell Electron Pair Repulsion Model 38
- 1.17 How to Interpret and Write Structural Formulas 41
- 1.18 Applications of Basic Principles 46

2 Families of Carbon Compounds Functional Groups, Intermolecular Forces, and Infrared (IR) Spectroscopy 53

- 2.1 Hydrocarbons: Representative Alkanes, Alkenes, Alkynes, and Aromatic Compounds 54
- 2.2 Polar Covalent Bonds 57

● THE CHEMISTRY OF ... Calculated Molecular Models: Maps of Electrostatic Potential 59

- 2.3 Polar and Nonpolar Molecules 60
- 2.4 Functional Groups 62
- 2.5 Alkyl Halides or Haloalkanes 64
- 2.6 Alcohols 65
- 2.7 Ethers 67

● THE CHEMISTRY OF ... Ethers as General Anesthetics 67

- 2.8 Amines 68
- 2.9 Aldehydes and Ketones 69
- 2.10 Carboxylic Acids, Esters, and Amides 70
- 2.11 Nitriles 72

- 2.12 Summary of Important Families of Organic Compounds 72
- 2.13 Physical Properties and Molecular Structure 73

● THE CHEMISTRY OF ... Fluorocarbons and Teflon 78

- 2.14 Summary of Attractive Electric Forces 82

● THE CHEMISTRY OF ... Organic Templates Engineered to Mimic Bone Growth 82

- 2.15 Infrared Spectroscopy: An Instrumental Method for Detecting Functional Groups 83
- 2.16 Interpreting IR Spectra 87
- 2.17 Applications of ...

3 An Introduction to Organic Reactions and Their Mechanisms Acids and Bases 98

- 3.1 Reactions and Their Mechanisms 99
- 3.2 Acid-Base Reactions 101
- 3.3 Lewis Acids and Bases 102
- 3.4 Heterolysis of Bonds to Carbon: Carbocations and Carbanions 104
- **THE CHEMISTRY OF ... HOMOs and LUMOs in Reactions** 105
- 3.5 How to Use Curved Arrows in Illustrating Reactions 106
- 3.6 The Strength of Brønsted-Lowry Acids and Bases: K_a and pK_a 109
- 3.7 How to Predict the Outcome of Acid-Base Reactions 113
- 3.8 Relationships between Structure and Acidity 115
- 3.9 Energy Changes 119
- 3.10 The Relationship between the Equilibrium Constant and the Standard Free-Energy Change, ΔG° 120
- 3.11 The Acidity of Carboxylic Acids 121
- 3.12 The Effect of the Solvent on Acidity 125
- 3.13 Organic Compounds as Bases 126
- 3.14 A Mechanism for an Organic Reaction 127
- 3.15 Acids and Bases in Nonaqueous Solutions 128
- 3.16 Acid-Base Reactions and the Synthesis of Deuterium- and Tritium-Labeled Compounds 130
- 3.17 Applications of Basic Principles 131

4 Nomenclature and Conformations of Alkanes and Cycloalkanes 137

- 4.1 Introduction to Alkanes and Cycloalkanes 138
- **THE CHEMISTRY OF ... Petroleum Refining** 139
- 4.2 Shapes of Alkanes 140
- 4.3 IUPAC Nomenclature of Alkanes, Alkyl Halides, and Alcohols 142
- 4.4 How to Name Cycloalkanes 149
- 4.5 Nomenclature of Alkenes and Cycloalkenes 151
- 4.6 Nomenclature of Alkynes 154
- 4.7 Physical Properties of Alkanes and Cycloalkanes 154
- **THE CHEMISTRY OF ... Pheromones: Communication by Means of Chemicals** 156
- 4.8 Sigma Bonds and Bond Rotation 157
- 4.9 Conformational Analysis of Butane 160
- **THE CHEMISTRY OF ... Muscle Action** 162
- 4.10 The Relative Stabilities of Cycloalkanes: Ring Strain 162
- 4.11 Conformations of Cyclohexane: The Chair and the Boat 163
- **THE CHEMISTRY OF ... Nanoscale Motors and Molecular Switches** 166
- 4.12 Substituted Cyclohexanes: Axial and Equatorial Hydrogen Groups 167
- 4.13 Disubstituted Cycloalkanes: Cis-Trans Isomerism 171
- 4.14 Bicyclic and Polycyclic Alkanes 175
- **THE CHEMISTRY OF ... Elemental Carbon** 176
- 4.15 Chemical Reactions of Alkanes 177
- 4.16 Synthesis of Alkanes and Cycloalkanes 177
- 4.17 How to Gain Structural Information from Molecular Formulas and the Index of Hydrogen Deficiency 178
- 4.19 Applications of Basic Principles 181

PLUS See **SPECIAL TOPIC A: ^{13}C NMR Spectroscopy – A Practical Introduction in WileyPLUS**

5.1	Chirality and Stereochemistry	186
5.2	Isomerism: Constitutional Isomers and Stereoisomers	188
5.3	Enantiomers and Chiral Molecules	190
5.4	A Single Chirality Center Causes a Molecule to Be Chiral	191
5.5	THE CHEMISTRY OF ... Life's Molecular Handedness	193
5.6	More about the Biological Importance of Chirality	194
5.7	How to Test for Chirality: Planes of Symmetry	195
5.8	Naming Enantiomers: The R,S-System	196
5.9	Properties of Enantiomers: Optical Activity	201
5.10	The Origin of Optical Activity	205
5.11	The Synthesis of Chiral Molecules	207
5.12	Chiral Drugs	209
5.13	THE CHEMISTRY OF ... Selective Binding of Drug Enantiomers to Left- and Right-Handed Coiled DNA	211
5.14	Molecules with More than One Chirality Center	211
5.15	Fischer Projection Formulas	215
5.16	Stereoisomerism of Cyclic Compounds	217
5.17	Relating Configurations through Reactions in Which No Bonds to the Chirality Center Are Broken	219
5.18	Separation of Enantiomers: Resolution	223
5.19	Compounds with Chirality Centers Other than Carbon	224
5.20	Chiral Molecules that Do Not Possess a Chirality Center	224
6	Ionic Reactions Nucleophilic Substitution and Elimination Reactions of Alkyl Halides	230

6.1	Organic Halides	231
6.2	Nucleophilic Substitution Reactions	233
6.3	Nucleophiles	234
6.4	Leaving Groups	237
6.5	Kinetics of a Nucleophilic Substitution Reaction: An S_N2 Reaction	237
6.6	A Mechanism for the S_N2 Reaction	238
6.7	Transition State Theory: Free-Energy Diagrams	240
6.8	The Stereochemistry of S_N2 Reactions	243
6.9	The Reaction of tert-Butyl Chloride with Hydroxide Ion: An S_N1 Reaction	246
6.10	A Mechanism for the S_N1 Reaction	247
6.11	Carbocations	248
6.12	The Stereochemistry of S_N1 Reactions	251
6.13	Factors Affecting the Rates of S_N1 and S_N2 Reactions	254
6.14	Organic Synthesis: Functional Group Transformations Using S_N2 Reactions	264
6.15	THE CHEMISTRY OF ... Biological Methylation: A Biological Nucleophilic Substitution Reaction	266
6.16	Elimination Reactions of Alkyl Halides	268
6.17	The E2 Reaction	269
6.18	The E1 Reaction	271
6.19	How to Determine whether Substitution or Elimination Is Favored	273
6.20	Overall Summary	276

7 Alkenes and Alkynes | Properties and Synthesis. Elimination Reactions of Alkyl Halides 285

7.1	Introduction	286
7.2	The (E)-(Z) System for Designating Alkene Diastereomers	286
7.3	Relative Stabilities of Alkenes	288

- 7.4 Cycloalkenes 290
- 7.5 Synthesis of Alkenes via Elimination Reactions 291
- 7.6 Dehydrohalogenation of Alkyl Halides 291
- 7.7 Acid-Catalyzed Dehydration of Alcohols 297
- 7.8 Carbocation Stability and the Occurrence of Molecular Rearrangements 303
- 7.9 The Acidity of Terminal Alkynes 307
- 7.10 Synthesis of Alkynes by Elimination Reactions 308
- 7.11 Replacement of the Acetylenic Hydrogen Atom of Terminal Alkynes 310
- 7.12 Alkylation of Alkynide Anions: Some General Principles of Structure and Reactivity Illustrated 312
- 7.13 Hydrogenation of Alkenes 313
- **THE CHEMISTRY OF ... Hydrogenation in the Food Industry 313**
- 7.14 Hydrogenation: The Function of the Catalyst 314
- 7.15 Hydrogenation of Alkynes 315
- 7.16 An Introduction to Organic Synthesis 317
- **THE CHEMISTRY OF ... From the Inorganic to the Organic 321**

8 Alkenes and Alkynes II Addition Reactions 331

- 8.1 Addition Reactions of Alkenes 332
- 8.2 Electrophilic Addition of Hydrogen Halides to Alkenes: Mechanism and Markovnikov's Rule 334
- 8.3 Stereochemistry of the Ionic Addition to an Alkene 339
- 8.4 Addition of Sulfuric Acid to Alkenes 340
- 8.5 Addition of Water to Alkenes: Acid-Catalyzed Hydration 340
- 8.6 Alcohols from Alkenes through Oxymercuration–Demercuration: Markovnikov Addition 344
- 8.7 Alcohols from Alkenes through Hydroboration–Oxidation: Anti-Markovnikov Syn Hydration 347
- 8.8 Hydroboration: Synthesis of Alkylboranes 347
- 8.9 Oxidation and Hydrolysis of Alkylboranes 350
- 8.10 Summary of Alkene Hydration Methods 353
- 8.11 Protonolysis of Alkylboranes 353
- 8.12 Electrophilic Addition of Bromine and Chlorine to Alkenes 354
- **THE CHEMISTRY OF ... The Sea: A Treasury of Biologically Active Natural Products 357**
- 8.13 Stereospecific Reactions 358
- 8.14 Halohydrin Formation 359
- 8.15 Divalent Carbon Compounds: Carbenes 361
- 8.16 Oxidations of Alkenes: Syn 1,2-Dihydroxylation 363
- **THE CHEMISTRY OF ... Catalytic Asymmetric Dihydroxylation 365**
- 8.17 Oxidative Cleavage of Alkenes 365
- 8.18 Electrophilic Addition of Bromine and Chlorine to Alkynes 368
- 8.19 Addition of Hydrogen Halides to Alkynes 369
- 8.20 Oxidative Cleavage of Alkynes 370
- 8.21 How to Plan a Synthesis: Some Approaches and Examples 370

9 Nuclear Magnetic Resonance and Mass Spectrometry Tools for Structure Determination 385

- 9.1 Introduction 386
- 9.2 Nuclear Magnetic Resonance (NMR) Spectroscopy 386
- 9.3 How to Interpret Proton NMR Spectra 392
- 9.4 Nuclear Spin: The Origin of the Signal 395
- 9.5 Detecting the Signal: Fourier Transform NMR Spectrometers 397
- 9.6 Shielding and Deshielding of Protons 399

Contents

- 9.7 The Chemical Shift 409
- 9.8 Chemical Shift Equivalent and Nonequivalent Protons 409
- 9.9 Signal Splitting: Spin-Spin Coupling 409
- 9.10 Proton NMR Spectra and Rate Processes 415
- 9.11 Carbon-13 NMR Spectroscopy 417
- 9.12 Two-Dimensional (2D) NMR Techniques 422
- THE CHEMISTRY OF ... Magnetic Resonance Imaging in Medicine 425
- 9.13 An Introduction to Mass Spectrometry 426
- 9.14 Formation of Ions: Electron Impact Ionization 427
- 9.15 Depicting the Molecular Ion 427
- 9.16 Fragmentation 428
- 9.17 How to Determine Molecular Formulas and Molecular Weights Using Mass Spectrometry 435
- 9.18 Mass Spectrometer Instrument Designs 440
- 9.19 GC/MS Analysis 442
- 9.20 Mass Spectrometry of Biomolecules 443

10 Radical Reactions 459

- 10.1 Introduction: How Radicals Form and How They React 460
- 10.2 Homolytic Bond Dissociation Energies (DH°) 461
- 10.3 Reactions of Alkanes with Halogens 465
- 10.4 Chlorination of Methane: Mechanism of Reaction 467
- 10.5 Chlorination of Methane: Energy Changes 470
- 10.6 Halogenation of Higher Alkanes 477
- 10.7 The Geometry of Alkyl Radicals 480
- 10.8 Reactions that Generate Tetrahedral Chirality Centers 481
- 10.9 Radical Addition to Alkenes: The Anti-Markovnikov Addition of Hydrogen Bromide 484
- 10.10 Radical Polymerization of Alkenes: Chain-Growth Polymers 486
- 10.11 Other Important Radical Reactions 490
- THE CHEMISTRY OF ... Calicheamicin γ_1^1 : A Radical Device for Slicing the Backbone of DNA 492
- THE CHEMISTRY OF ... Antioxidants 494
- THE CHEMISTRY OF ... Ozone Depletion and Chlorofluorocarbons (CFCs) 495

PLUS See SPECIAL TOPIC B: Chain-Growth Polymers in WileyPLUS

11 Alcohols and Ethers Synthesis and Reactions 502

- 11.1 Structure and Nomenclature 503
- 11.2 Physical Properties of Alcohols and Ethers 505
- 11.3 Important Alcohols and Ethers 507
- THE CHEMISTRY OF ... Ethanol as a Biofuel 508
- 11.4 Synthesis of Alcohols from Alkenes 509
- 11.5 Reactions of Alcohols 511
- 11.6 Alcohols as Acids 513
- 11.7 Conversion of Alcohols into Alkyl Halides 514
- 11.8 Alkyl Halides from the Reaction of Alcohols with Hydrogen Halides 514
- 11.9 Alkyl Halides from the Reaction of Alcohols with PBr_3 or SOCl_2 517
- 11.10 Tosylates, Mesylates, and Triflates: Leaving Group Derivatives of Alcohols 518
- THE CHEMISTRY OF ... Alkyl Phosphates 521
- 11.11 Synthesis of Ethers 522
- 11.12 Reactions of Ethers 527
- 11.13 Epoxides 528
- THE CHEMISTRY OF ... The Sharpless Asymmetric Epoxidation 529

- 11.14 Reactions of Epoxides 531
- **THE CHEMISTRY OF ... Epoxides, Carcinogens, and Biological Oxidation** 533
- 11.15 And 1,2-Dihydroxylation of Alkenes via Epoxides 535
- **THE CHEMISTRY OF ... Environmentally Friendly Alkene Oxidation Methods** 537
- 11.16 Crown Ethers 537
- **THE CHEMISTRY OF ... Transport Antibiotics and Crown Ethers** 539
- 11.17 Summary of Reactions of Alkenes, Alcohols, and Ethers 540

12 Alcohols From Carbonyl Compounds Oxidation-Reduction and Organometallic Compounds 548

- 12.1 Structure of the Carbonyl Group 549
- 12.2 Oxidation-Reduction Reactions in Organic Chemistry 550
- 12.3 Alcohols by Reduction of Carbonyl Compounds 552
- **THE CHEMISTRY OF ... Alcohol Dehydrogenase - A Biochemical Hydride Reagent** 554
- **THE CHEMISTRY OF ... Stereoselective Reductions of Carbonyl Groups** 555
- 12.4 Oxidation of Alcohols 557
- 12.5 Organometallic Compounds 561
- 12.6 Preparation of Organolithium and Organomagnesium Compounds 562
- 12.7 Reactions of Organolithium and Organomagnesium Compounds 563
- 12.8 Alcohols from Grignard Reagents 566
- 12.9 Protecting Groups 575

PLUS See the **First Review Problem Set** in WileyPLUS

13 Conjugated Unsaturated Systems 585

- 13.1 Introduction 586
- 13.2 Allylic Substitution and the Allyl Radical 586
- **THE CHEMISTRY OF ... Allylic Bromination** 590
- 13.3 The Stability of the Allyl Radical 590
- 13.4 The Allyl Cation 594
- 13.5 Resonance Theory Revisited 595
- 13.6 Alkadienes and Polyunsaturated Hydrocarbons 599
- 13.7 1,3-Butadiene: Electron Delocalization 600
- 13.8 The Stability of Conjugated Dienes 602
- 13.9 Ultraviolet-Visible Spectroscopy 604
- **THE CHEMISTRY OF ... The Photochemistry of Vision** 609
- 13.10 Electrophilic Attack on Conjugated Dienes: 1,4 Addition 612
- 13.11 The Diels-Alder Reaction: A 1,4-Cycloaddition Reaction of Dienes 616
- **THE CHEMISTRY OF ... Molecules with the Nobel Prize in Their Synthetic Lineage** 620

14 Aromatic Compounds 632

- 14.1 The Discovery of Benzene 633
- 14.2 Nomenclature of Benzene Derivatives 634
- 14.3 Reactions of Benzene 637
- 14.4 The Kekulé Structure for Benzene 638
- 14.5 The Thermodynamic Stability of Benzene 639
- 14.6 Modern Theories of the Structure of Benzene 640
- 14.7 Hückel's Rule: The $4n + 2\pi$ Electron Rule 643
- 14.8 Other Aromatic Compounds 651
- **THE CHEMISTRY OF ... Nanotubes** 655
- 14.9 Heterocyclic Aromatic Compounds 655
- 14.10 Aromatic Compounds in Biochemistry 657
- 14.11 Spectroscopy of Aromatic Compounds 660

THE CHEMISTRY OF ... Sunscreens (Catching the Sun's Rays and What Happens to Them) 664

15 Reactions of Aromatic Compounds 676

- 15.1 Electrophilic Aromatic Substitution Reactions 677
- 15.2 A General Mechanism for Electrophilic Aromatic Substitution 678
- 15.3 Halogenation of Benzene 680
- 15.4 Nitration of Benzene 681
- 15.5 Sulfonation of Benzene 682
- 15.6 Friedel-Crafts Alkylation 684
- 15.7 Friedel-Crafts Acylation 685
- 15.8 Limitations of Friedel-Crafts Acylations: The Clemmensen Reduction 690
- 15.9 Synthetic Applications of Friedel-Crafts Acylations: The Clemmensen Reduction 690
- 15.10 Substituents Can Affect Both the Reactivity of the Ring and the Orientation of the Incoming Group 691
- 15.11 How Substituents Affect Electrophilic Aromatic Substitution: A Closer Look 697
- 15.12 Reactions of the Side Chain of Alkylbenzenes 706
- THE CHEMISTRY OF ... Iodine Incorporation in Thyroxine Biosynthesis 707
- THE CHEMISTRY OF ... Industrial Styrene Synthesis 709
- 15.13 Alkenylbenzenes 712
- 15.14 Synthetic Applications 714
- 15.15 Allylic and Benzylic Halides in Nucleophilic Substitution Reactions 717
- 15.16 Reduction of Aromatic Compounds 719

16 Aldehydes and Ketones Nucleophilic Addition to the Carbonyl Group 729

- 16.1 Introduction 730
- 16.2 Nomenclature of Aldehydes and Ketones 730
- 16.3 Physical Properties 732
- THE CHEMISTRY OF ... Aldehydes and Ketones in Perfumes 733
- 16.4 Synthesis of Aldehydes 733
- 16.5 Synthesis of Ketones 738
- 16.6 Nucleophilic Addition to the Carbon-Oxygen Double Bond 741
- 16.7 The Addition of Alcohols: Hemiacetals and Acetals 744
- 16.8 The Addition of Primary and Secondary Amines 751
- THE CHEMISTRY OF ... A Very Versatile Vitamin, Pyridoxine (Vitamin B₆) 753
- 16.9 The Addition of Hydrogen Cyanide: Cyanohydrins 755
- 16.10 The Addition of Ylides: The Wittig Reaction 757
- 16.11 Oxidation of Aldehydes 761
- 16.12 Chemical Analyses for Aldehydes and Ketones 761
- 16.13 Spectroscopic Properties of Aldehydes and Ketones 762
- 16.14 Summary of Aldehyde and Ketone Addition Reactions 765

17 Carboxylic Acids and Their Derivatives Nucleophilic Addition-Elimination at the Acyl Carbon 779

- 17.1 Introduction 780
- 17.2 Nomenclature and Physical Properties 780
- 17.3 Preparation of Carboxylic Acids 789
- 17.4 Acyl Substitution: Nucleophilic Addition-Elimination at the Acyl Carbon 792
- 17.5 Acyl Chlorides 794
- 17.6 Carboxylic Acid Anhydrides 796
- 17.7 Esters 797
- 17.8 Amides 804

- **THE CHEMISTRY OF ... Penicillins** 811
- 17.9 Derivatives of Carbonic Acid 812
- 17.10 Decarboxylation of Carboxylic Acids 814
- 17.11 Chemical Tests for Acyl Compounds 816
- 17.12 Polyesters and Polyamides: Step-Growth Polymers 817
- 17.13 Summary of the Reactions of Carboxylic Acids and Their Derivatives 818

18 Reactions at the α Carbon of Carbonyl Compounds Enols and Enolates 831

- 18.1 The Acidity of the α Hydrogens of Carbonyl Compounds: Enolate Anions 832
- 18.2 Keto and Enol Tautomers 833
- 18.3 Reactions via Enols and Enolates 834
- **THE CHEMISTRY OF ... Chloroform in Drinking Water** 839
- 18.4 Lithium Enolates 841
- 18.5 Enolates of β -Dicarbonyl Compounds 844
- 18.6 Synthesis of Methyl Ketones: The Acetoacetic Ester Synthesis 845
- 18.7 Synthesis of Substituted Acetic Acids: The Malonic Ester Synthesis 850
- 18.8 Further Reactions of Active Hydrogen Compounds 853
- 18.9 Synthesis of Enamines: Stork Enamine Reactions 854
- 18.10 Summary of Enolate Chemistry 857

PLUS See **SPECIAL TOPIC C: Step-Growth Polymers** in WileyPLUS

19 Condensation and Conjugate Addition Reactions of Carbonyl Compounds More Chemistry of Enolates 869

- 19.1 Introduction 870
- 19.2 The Claisen Condensation: The Synthesis of β -Keto Esters 870
- 19.3 β -Dicarbonyl Compounds by Acylation of Ketone Enolates 875
- 19.4 Aldol Reactions: Addition of Enolates and Enols to Aldehydes and Ketones 876
- **THE CHEMISTRY OF ... A Retro-Aldol Reaction in Glycolysis—Dividing Assets to Double the ATP Yield** 878
- 19.5 Crossed Aldol Condensations 882
- 19.6 Cyclizations via Aldol Condensations 888
- 19.7 Additions to α,β -Unsaturated Aldehydes and Ketones 889
- **THE CHEMISTRY OF ... Calicheamicin γ_1 Activation for Cleavage of DNA** 894
- 19.8 The Mannich Reaction 894
- **THE CHEMISTRY OF ... A Suicide Enzyme Substrate** 895
- 19.9 Summary of Important Reactions 897

PLUS See **SPECIAL TOPIC D: Thiols, Sulfur Ylides, and Disulfides** in WileyPLUS

PLUS See **SPECIAL TOPIC E: Thiol Esters and Lipid Biosynthesis** in WileyPLUS

20 Amines 911

- 20.1 Nomenclature 912
- 20.2 Physical Properties and Structure of Amines 913
- 20.3 Basicity of Amines: Amine Salts 915
- **THE CHEMISTRY OF ... Biologically Important Amines** 922
- 20.4 Preparation of Amines 924
- 20.5 Reactions of Amines 933
- 20.6 Reactions of Amines with Nitrous Acid 935
- **THE CHEMISTRY OF ... N-Nitrosoamines** 936
- 20.7 Replacement Reactions of Arenediazonium Salts 937
- 20.8 Coupling Reactions of Arenediazonium Salts 941

Contents

- 20.9 Reactions of Amines with Sulfonyl Chlorides 943
● **THE CHEMISTRY OF ... Chemotherapy and Sulfonamides** 944
20.10 Synthesis of Sulfonamides 947
20.11 Analysis of Amines 947
20.12 Eliminations Involving Ammonium Compounds 949
20.13 Summary of Preparations and Reactions of Amines 950
PLUS See **SPECIAL TOPIC F: Alkaloids in WileyPLUS**

21. Phenols and Aryl Halides Nucleophilic Aromatic Substitution 964

- 21.1 Structure and Nomenclature of Phenols 965
21.2 Naturally Occurring Phenols 966
21.3 Physical Properties of Phenols 966
21.4 Synthesis of Phenols 967
21.5 Reactions of Phenols as Acids 969
21.6 Other Reactions of the O—H Group of Phenols 972
21.7 Cleavage of Alkyl Aryl Ethers 973
21.8 Reactions of the Benzene Ring of Phenols 973
● **THE CHEMISTRY OF ... Polyketide Anticancer Antibiotic Biosynthesis** 975
21.9 The Claisen Rearrangement 977
21.10 Quinones 978
● **THE CHEMISTRY OF ... The Bombardier Beetle's Noxious Spray** 979
21.11 Aryl Halides and Nucleophilic Aromatic Substitution 980
● **THE CHEMISTRY OF ... Bacterial Dehalogenation of a PCB Derivative** 983
21.12 Spectroscopic Analysis of Phenols and Aryl Halides 988
● **THE CHEMISTRY OF ... Aryl Halides: Their Uses and Environmental Concerns** 989
PLUS See the **Second Review Problem Set in WileyPLUS**
SPECIAL TOPIC G: Carbon-Carbon Bond-Forming and Other Reactions of Transition Metal Organometallic Compounds G-1

- PLUS See **SPECIAL TOPIC H: Electrocyclic and Cycloaddition Reactions in WileyPLUS**

22. Carbohydrates 1000

- 22.1 Introduction 1001
22.2 Monosaccharides 1004
22.3 Mutarotation 1009
22.4 Glycoside Formation 1010
22.5 Other Reactions of Monosaccharides 1013
22.6 Oxidation Reactions of Monosaccharides 1016
22.7 Reduction of Monosaccharides: Alditols 1022
22.8 Reactions of Monosaccharides with Phenylhydrazine: Osazones 1022
22.9 Synthesis and Degradation of Monosaccharides 1023
22.10 The D Family of Aldoses 1025
22.11 Fischer's Proof of the Configuration of D-(+)-Glucose 1027
22.12 Disaccharides 1029
● **THE CHEMISTRY OF ... Artificial Sweeteners (How Sweet It Is)** 1032
22.13 Polysaccharides 1033
22.14 Other Biologically Important Sugars 1037
22.15 Sugars That Contain Nitrogen 1038
22.16 Glycolipids and Glycoproteins of the Cell Surface: Cell Recognition and the Immune System 1040
22.17 Carbohydrate Antibiotics 1042
22.18 Summary of Reactions of Carbohydrates 1042

23 Lipids 1050

23.1 Introduction 1051

23.2 Fatty Acids and Triacylglycerols 1052

● **THE CHEMISTRY OF ... Olestra and Other Fat Substitutes 1055**● **THE CHEMISTRY OF ... Self-Assembled Monolayers—Lipids in Materials Science and Bioengineering 1060**

23.3 Terpenes and Terpenoids 1061

23.4 Steroids 1064

23.5 Prostaglandins 1072

23.6 Phospholipids and Cell Membranes 1074

● **THE CHEMISTRY OF ... STEALTH[®] Liposomes for Drug Delivery 1077**

23.7 Waxes 1078

24 Amino Acids and Proteins 1084

24.1 Introduction 1085

24.2 Amino Acids 1086

24.3 Synthesis of α -Amino Acids 1092

24.4 Polypeptides and Proteins 1094

24.5 Primary Structure of Polypeptides and Proteins 1097

24.6 Examples of Polypeptide and Protein Primary Structure 1101

● **THE CHEMISTRY OF ... Sickle-Cell Anemia 1103**

24.7 Polypeptide and Protein Synthesis 1104

24.8 Secondary, Tertiary, and Quaternary Structure of Proteins 1110

24.9 Introduction to Enzymes 1115

24.10 Lysozyme: Mode of Action of an Enzyme 1116

● **THE CHEMISTRY OF ... Carbonic Anhydrase: Shuttling the Protons 1119**

24.11 Serine Proteases 1120

24.12 Hemoglobin: A Conjugated Protein 1122

● **THE CHEMISTRY OF ... Some Catalytic Antibodies 1123**

24.13 Purification and Analysis of Polypeptides and Proteins 1125

24.14 Proteomics 1126

25 Nucleic Acids and Protein Synthesis 1131

25.1 Introduction 1132

25.2 Nucleotides and Nucleosides 1133

25.3 Laboratory Synthesis of Nucleosides and Nucleotides 1137

25.4 Deoxyribonucleic Acid: DNA 1139

25.5 RNA and Protein Synthesis 1146

25.6 Determining the Base Sequence of DNA: The Chain-Terminating (Dideoxynucleotide) Method 1155

25.7 Laboratory Synthesis of Oligonucleotides 1157

25.8 The Polymerase Chain Reaction 1158

25.9 Sequencing of the Human Genome: An Instruction Book for the Molecules of Life 1162

Answers to Selected Problems A-1**Glossary GL-1****Photo Credits C-1****Index I-1**

Chapter 3

Reaction of Water with Hydrogen Chloride: The Use of
Curved Arrows 187

Reaction of *tert*-Butyl Alcohol with Concentrated Aqueous
HCl 127

Chapter 4

Mechanism for the S_N2 Reaction 239

The Stereochemistry of an S_N2 Reaction 245

Mechanism for the S_N1 Reaction 248

The Stereochemistry of an S_N1 Reaction 252

Mechanism for the E2 Reaction 270

Mechanism for the E1 Reaction 272

Chapter 7

E2 Elimination Where There Are Two Axial β
Hydrogens 294

E2 Elimination Where the Only Axial β Hydrogen Is from a
Less Stable Conformer 296

Acid-Catalyzed Dehydration of Secondary or Tertiary
Alcohols: An E1 Reaction 301

Dehydration of a Primary Alcohol: An E2 Reaction 302

Formation of a Rearranged Alkene during Dehydration of a
Primary Alcohol 306

Dehydrohalogenation of *vic*-Dibromides to Form
Alkenes 309

The Dissolving Metal Reduction of an Alkyne 316

Chapter 8

Addition of a Hydrogen Halide to an Alkene 335

Addition of HBr to 2-Methylpropene 337

Ionic Addition to an Alkene 339

Acid-Catalyzed Hydration of an Alkene 341

Oxymercuration 345

Hydroboration 349

Oxidation of Trialkylboranes 351

Addition of Bromine to an Alkene 356

Addition of Bromine to *cis*- and *trans*-2-Butene 359

Halohydrin Formation from an Alkene 360

Ozonolysis of an Alkene 368

Chapter 10

Hydrogen Atom Abstraction 461

Radical Addition to a π Bond 461

Radical Chlorination of Methane 468

Radical Halogenation of Ethane 477

The Stereochemistry of Chlorination at C2 of
Pentane 481

The Stereochemistry of Chlorination at C3 of
(*S*)-2-Chloropentane 482

Anti-Markovnikov Addition 485

Radical Polymerization of Ethene 487

Chapter 11

Conversion of an Alcohol into a Mesylate (an *alkyl*
Methanesulfonate) 520

Intermolecular Dehydration of Alcohols to Form an
Ether 522

The Williamson Ether Synthesis 523

Ether Cleavage by Strong Acids 527

Alkene Epoxidation 529

Acid-Catalyzed Ring Opening of an Epoxide 531

Base-Catalyzed Ring Opening of an Epoxide 531

Chapter 12

Reduction of Aldehydes and Ketones by Hydride
Transfer 554

Chromate Oxidations: Formation of the Chromate
Ester 559

The Grignard Reaction 566

Chapter 15

Electrophilic Aromatic Bromination 680

Nitration of Benzene 682

Sulfonation of Benzene 683

Friedel-Crafts Alkylation 684

Friedel-Crafts Acylation 687

Benzylic Halogenation 710

Birch Reduction 720

Chapter 16

Reduction of an Acyl Chloride to an Aldehyde 736

Reduction of an Ester to an Aldehyde 737

Reduction of a Nitrile to an Aldehyde 737

Addition of a Strong Nucleophile to an Aldehyde or
Ketone 742

Acid-Catalyzed Nucleophilic Addition to an Aldehyde or
Ketone 742

Hemiacetal Formation 744

Acid-Catalyzed Hemiacetal Formation 745

Base-Catalyzed Hemiacetal Formation 746

Hydrate Formation 746

Acid-Catalyzed Acetal Formation 748

Imine Formation 751

Enamine Formation 754

Cyanohydrin Formation 755

The Wittig Reaction 758

Chapter 17

Acyl Substitution by Nucleophilic Addition-
Elimination 792

Synthesis of Acyl Chlorides Using Thionyl Chloride 795

Acid-Catalyzed Esterification 798

Base-Promoted Hydrolysis of an Ester 801

DCC-Promoted Amide Synthesis 807

Acid Hydrolysis of an Amide	808
Base Hydrolysis of an Amide	808
Acid Hydrolysis of a Nitrile	810
Base Hydrolysis of a Nitrile	810
Chapter 18	
Base-Catalyzed Enolization	835
Acid-Catalyzed Enolization	835
Base-Promoted Halogenation of Aldehydes and Ketones	837
Acid-Catalyzed Halogenation of Aldehydes and Ketones	837
The Haloforn Reaction	839
The Malonic Ester Synthesis of Substituted Acetic Acids	850
Chapter 19	
The Claisen Condensation	871
The Dieckmann Condensation	873
The Aldol Addition	877
Dehydration of the Aldol Addition Product	879
The Acid-Catalyzed Aldol Reaction	880
A Directed Aldol Synthesis Using a Lithium Enolate	886
The Aldol Cyclization	889

The Conjugate Addition of HCN	891
The Conjugate Addition of an Amine	893
The Michael Addition	897
The Mannich Reaction	899
Chapter 20	
Alkylation of NH_3	926
Reductive Amination	928
The Hofmann Rearrangement	931
Diazotization	936
Chapter 21	
The Kolbe Reaction	975
The $\text{S}_{\text{N}}\text{Ar}$ Mechanism	982
The Benzyne Elimination-Addition Mechanism	985
Chapter 22	
Formation of a Glycoside	1011
Hydrolysis of a Glycoside	1012
Phenyllosazone Formation	1023
Chapter 24	
Formation of an α -Aminonitrile during the Strecker Synthesis	1093



THE CHEMISTRY OF . . . BOXES

Chapter 1	
Calculated Molecular Models: Electron Density Surfaces	29
Chapter 2	
Calculated Molecular Models: Maps of Electrostatic Potential	59
Ethers as General Anesthetics	67
Fluorocarbons and Teflon	78
Organic Templates Engineered to Mimic Bone Growth	82
Chapter 3	
HOMOs and LUMOs in Reactions	105
Chapter 4	
Petroleum Refining	139
Pheromones: Communication by Means of Chemicals	156
Muscle Action	162
Nanoscale Motors and Molecular Switches	166
Elemental Carbon	176
Chapter 5	
Life's Molecular Handedness	193
Selective Binding of Drug Enantiomers to Left- and Right-Handed Coiled DNA	211
Chapter 6	
Biological Methylation: A Biological Nucleophilic Substitution Reaction	266
Chapter 7	
Hydrogenation in the Food Industry	313
From the Inorganic to the Organic	321
Chapter 8	
The Sea: A Treasury of Biologically Active Natural Products	357
Catalytic Asymmetric Dihydroxylation	365
Chapter 9	
Magnetic Resonance Imaging in Medicine	425
Chapter 10	
Calicheamicin γ_1^1 : A Radical Device for Slicing the Backbone of DNA	492
Antioxidants	494
Ozone Depletion and Chlorofluorocarbons (CFCs)	495
Chapter 11	
Ethanol as a Biofuel	508
Alkyl Phosphates	521

The Sharpless Asymmetric Epoxidation Epoxides, Carcinogens, and Biological Oxidation 530	Chapter 18 Chloroform in Drinking Water 839
Environmentally Friendly Alkene Oxidation Methods 537	Chapter 19 A Retro-Aldol Reaction in Glycolysis—Dividing Assets to Double the ATP Yield 878
Transport Antibiotics and Crown Ethers 539	Calicheamicin γ_1 Activation for Cleavage of DNA 894
Chapter 12 Alcohol Dehydrogenase—A Biochemical Hydride Reagent 554	A Suicide Enzyme Substrate 895
Stereoselective Reductions of Carbonyl Groups 555	Chapter 20 Biologically Important Amines 922
Chapter 13 Allylic Bromination 590	N-Nitrosamines 936
The Photochemistry of Vision 609	Chemotherapy and Sulfa Drugs 944
Molecules with the Nobel Prize in Their Synthetic Lineage 620	Chapter 21 Polyketide Anticancer Antibiotic Biosynthesis 975
Chapter 14 Nanotubes 655	The Bombardier Beetle's Noxious Spray 979
Sunscreens (Catching the Sun's Rays and What Happens to Them) 664	Bacterial Dehalogenation of a PCB Derivative 983
Chapter 15 Iodine Incorporation in Thyroxine Biosynthesis 707	Aryl Halides: Their Uses and Environmental Concerns 988
Industrial Styrene Synthesis 709	Chapter 22 Artificial Sweeteners (How Sweet It Is) 1032
Chapter 16 Aldehydes and Ketones in Perfumes 733	Chapter 23 Olestra and Other Fat Substitutes 1055
A Very Versatile Vitamin, Pyridoxine (Vitamin B ₆) 753	Self-Assembled Monolayers—Lipids in Materials Science and Bioengineering 1060
Chapter 17 Penicillins 811	STEALTH® Liposomes for Drug Delivery 1077
	Chapter 24 Sickle-Cell Anemia 1103
	Carbonic Anhydrase: Shuttling the Protons 1119
	Some Catalytic Antibodies 1123