

# Abbreviated Contents

---

## PART I: Molecular Structure and Thermodynamics

- CHAPTER 1. Introduction to Structure and Models of Bonding 3  
2. Strain and Stability 65  
3. Solutions and Non-Covalent Binding Forces 145  
4. Molecular Recognition and Supramolecular Chemistry 207  
5. Acid–Base Chemistry 259  
6. Stereochemistry 297
- 

## PART II: Reactivity, Kinetics, and Mechanisms

- CHAPTER 7. Energy Surfaces and Kinetic Analyses 355  
8. Experiments Related to Thermodynamics and Kinetics 421  
9. Catalysis 489  
10. Organic Reaction Mechanisms, Part 1:  
Reactions Involving Additions and / or Eliminations 537  
11. Organic Reaction Mechanisms, Part 2:  
Substitutions at Aliphatic Centers and Thermal  
Isomerizations/Rearrangements 627  
12. Organotransition Metal Reaction Mechanisms and Catalysis 705  
13. Organic Polymer and Materials Chemistry 753
- 

## PART III: Electronic Structure: Theory and Applications

- CHAPTER 14. Advanced Concepts in Electronic Structure Theory 807  
15. Thermal Pericyclic Reactions 877  
16. Photochemistry 935  
17. Electronic Organic Materials 1001
- 

- APPENDIX 1. Conversion Factors and Other Useful Data 1047  
2. Electrostatic Potential Surfaces for Representative Organic Molecules 1049  
3. Group Orbitals of Common Functional Groups:  
Representative Examples Using Simple Molecules 1051  
4. The Organic Structures of Biology 1057  
5. Pushing Electrons 1061  
6. Reaction Mechanism Nomenclature 1075

List of Highlights	xix
Preface	xxiii
Acknowledgments	xxv
A Note to the Instructor	xxvii

---

## PART I MOLECULAR STRUCTURE AND THERMODYNAMICS

---

### CHAPTER 1: Introduction to Structure and Models of Bonding 3

#### Intent and Purpose 3

#### 1.1 A Review of Basic Bonding Concepts 4

1.1.1 Quantum Numbers and Atomic Orbitals	4
1.1.2 Electron Configurations and Electronic Diagrams	5
1.1.3 Lewis Structures	6
1.1.4 Formal Charge	6
1.1.5 VSEPR	7
1.1.6 Hybridization	8
1.1.7 A Hybrid Valence Bond/Molecular Orbital Model of Bonding	10
<i>Creating Localized <math>\sigma</math> and <math>\pi</math> Bonds</i>	11
1.1.8 Polar Covalent Bonding	12
<i>Electronegativity</i>	12
<i>Electrostatic Potential Surfaces</i>	14
<i>Inductive Effects</i>	15
<i>Group Electronegativities</i>	16
<i>Hybridization Effects</i>	17
1.1.9 Bond Dipoles, Molecular Dipoles, and Quadrupoles	17
<i>Bond Dipoles</i>	17
<i>Molecular Dipole Moments</i>	18
<i>Molecular Quadrupole Moments</i>	19
1.1.10 Resonance	20
1.1.11 Bond Lengths	22
1.1.12 Polarizability	24
1.1.13 Summary of Concepts Used for the Simplest Model of Bonding in Organic Structures	26

#### 1.2 A More Modern Theory of Organic Bonding 26

1.2.1 Molecular Orbital Theory	27
1.2.2 A Method for QMOT	28
1.2.3 Methyl in Detail	29
<i>Planar Methyl</i>	29
<i>The Walsh Diagram: Pyramidal Methyl</i>	31
<i>"Group Orbitals" for Pyramidal Methyl</i>	32
<i>Putting the Electrons In—The <math>MH_3</math> System</i>	33
1.2.4 The $CH_2$ Group in Detail	33
<i>The Walsh Diagram and Group Orbitals</i>	33
<i>Putting the Electrons In—The <math>MH_2</math> System</i>	33

#### 1.3 Orbital Mixing—Building Larger Molecules 35

1.3.1 Using Group Orbitals to Make Ethane	36
---	----

1.3.2 Using Group Orbitals to Make Ethylene	38
1.3.3 The Effects of Heteroatoms—Formaldehyde	40
1.3.4 Making More Complex Alkanes	43
1.3.5 Three More Examples of Building Larger Molecules from Group Orbitals	43

*Propene*

*Methyl Chloride*

*Butadiene*

1.3.6 Group Orbitals of Representative $\pi$ Systems: Benzene, Benzyl, and Allyl	46
--	----

1.3.7 Understanding Common Functional Groups as Perturbations of Allyl	49
--	----

1.3.8 The Three Center–Two Electron Bond	50
--	----

1.3.9 Summary of the Concepts Involved in Our Second Model of Bonding	51
---	----

#### 1.4 Bonding and Structures of Reactive Intermediates 52

1.4.1 Carbocations	52
--------------------	----

*Carbenium Ions*

*Interplay with Carbonium Ions*

*Carbonium Ions*

1.4.2 Carbanions	56
------------------	----

1.4.3 Radicals	57
----------------	----

1.4.4 Carbenes	58
----------------	----

#### 1.5 A Very Quick Look at Organometallic and Inorganic Bonding 59

#### Summary and Outlook 61

#### EXERCISES 62

#### FURTHER READING 64

---

#### CHAPTER 2: Strain and Stability 65

#### Intent and Purpose 65

#### 2.1 Thermochemistry of Stable Molecules 66

2.1.1 The Concepts of Internal Strain and Relative Stability	66
--	----

2.1.2 Types of Energy	68
-----------------------	----

*Gibbs Free Energy*

*Enthalpy*

*Entropy*

2.1.3 Bond Dissociation Energies	70
----------------------------------	----

*Using BDEs to Predict Exothermicity and Endothermicity*

2.1.4 An Introduction to Potential Functions and Surfaces—Bond Stretches	73
--	----

*Infrared Spectroscopy*

2.1.5 Heats of Formation and Combustion	77
---	----

2.1.6 The Group Increment Method	79
----------------------------------	----

2.1.7 Strain Energy	82
---------------------	----

<b>2.2 Thermochemistry of Reactive Intermediates</b>	82	<i>Electrostatic Interactions</i>	131
2.2.1 Stability vs. Persistence	82	<i>Hydrogen Bonding</i>	131
2.2.2 Radicals	83	<i>The Parameterization</i>	132
<i>BDEs as a Measure of Stability</i>	83	<i>Heat of Formation and Strain Energy</i>	132
<i>Radical Persistence</i>	84	<b>2.6.2 General Comments on the Molecular Mechanics Method</b>	133
<i>Group Increments for Radicals</i>	86	<b>2.6.3 Molecular Mechanics on Biomolecules and Unnatural Polymers—“Modeling”</b>	135
2.2.3 Carbocations	87	<b>2.6.4 Molecular Mechanics Studies of Reactions</b>	136
<i>Hydride Ion Affinities as a Measure of Stability</i>	87		
<i>Lifetimes of Carbocations</i>	90		
2.2.4 Carbanions	91		
2.2.5 Summary	91		
<b>2.3 Relationships Between Structure and Energetics—Basic Conformational Analysis</b>	92	<b>Summary and Outlook</b>	137
2.3.1 Acyclic Systems—Torsional Potential Surfaces	92	<b>EXERCISES</b>	138
<i>Ethane</i>	92	<b>FURTHER READING</b>	143
<i>Butane—The Gauche Interaction</i>	95		
<i>Barrier Height</i>	97		
<i>Barrier Foldedness</i>	97		
<i>Tetraalkylethylenes</i>	98		
<i>The g+g– Pentane Interaction</i>	99		
<i>Allylic (<math>\text{A}^{1,3}</math>) Strain</i>	100		
2.3.2 Basic Cyclic Systems	100		
<i>Cyclopropane</i>	100		
<i>Cyclobutane</i>	100		
<i>Cyclopentane</i>	101		
<i>Cyclohexane</i>	102		
<i>Larger Rings—Transannular Effects</i>	107		
<i>Group Increment Corrections for Ring Systems</i>	109		
<i>Ring Torsional Modes</i>	109		
<i>Bicyclic Ring Systems</i>	110		
<i>Cycloalkenes and Bredt's Rule</i>	110		
<i>Summary of Conformational Analysis and Its Connection to Strain</i>	112		
<b>2.4 Electronic Effects</b>	112		
2.4.1 Interactions Involving $\pi$ Systems	112		
<i>Substitution on Alkenes</i>	112		
<i>Conformations of Substituted Alkenes</i>	113		
<i>Conjugation</i>	115		
<i>Aromaticity</i>	116		
<i>Antiaromaticity, An Unusual Destabilizing Effect</i>	117		
<i>NMR Chemical Shifts</i>	118		
<i>Polycyclic Aromatic Hydrocarbons</i>	119		
<i>Large Annulenes</i>	119		
2.4.2 Effects of Multiple Heteroatoms	120		
<i>Bond Length Effects</i>	120		
<i>Orbital Effects</i>	120		
<b>2.5 Highly-Strained Molecules</b>	124		
2.5.1 Long Bonds and Large Angles	124		
2.5.2 Small Rings	125		
2.5.3 Very Large Rotation Barriers	127		
<b>2.6 Molecular Mechanics</b>	128		
2.6.1 The Molecular Mechanics Model	129		
<i>Bond Stretching</i>	129		
<i>Angle Bending</i>	130		
<i>Torsion</i>	130		
<i>Nonbonded Interactions</i>	130		
<i>Cross Terms</i>	131		
<b>CHAPTER 3: Solutions and Non-Covalent Binding Forces</b>	145		
<b>Intent and Purpose</b>	145		
<b>3.1 Solvent and Solution Properties</b>	145		
3.1.1 Nature Abhors a Vacuum	146		
3.1.2 Solvent Scales	146		
<i>Dielectric Constant</i>	147		
<i>Other Solvent Scales</i>	148		
<i>Heat of Vaporization</i>	150		
<i>Surface Tension and Wetting</i>	150		
<i>Water</i>	151		
3.1.3 Solubility	153		
<i>General Overview</i>	153		
<i>Shape</i>	154		
<i>Using the “Like-Dissolves-Like” Paradigm</i>	154		
3.1.4 Solute Mobility	155		
<i>Diffusion</i>	155		
<i>Fick's Law of Diffusion</i>	156		
<i>Correlation Times</i>	156		
3.1.5 The Thermodynamics of Solutions	157		
<i>Chemical Potential</i>	158		
<i>The Thermodynamics of Reactions</i>	160		
<i>Calculating <math>\Delta H^\circ</math> and <math>\Delta S^\circ</math></i>	162		
<b>3.2 Binding Forces</b>	162		
3.2.1 Ion Pairing Interactions	163		
<i>Salt Bridges</i>	164		
3.2.2 Electrostatic Interactions Involving Dipoles	165		
<i>Ion–Dipole Interactions</i>	165		
<i>A Simple Model of Ionic Solvation—The Born Equation</i>	166		
<i>Dipole–Dipole Interactions</i>	168		
3.2.3 Hydrogen Bonding	168		
<i>Geometries</i>	169		
<i>Strengths of Normal Hydrogen Bonds</i>	171		
<i>i. Solvation Effects</i>	171		
<i>ii. Electronegativity Effects</i>	172		
<i>iii. Resonance Assisted Hydrogen Bonds</i>	173		
<i>iv. Polarization Enhanced Hydrogen Bonds</i>	174		
<i>v. Secondary Interactions in Hydrogen Bonding Systems</i>	175		

<i>vi. Cooperativity in Hydrogen Bonds</i>	175	<i>Molecular Recognition via Hydrogen Bonding in Water</i>	232
<i>Vibrational Properties of Hydrogen Bonds</i>	176	<b>4.2.4 Molecular Recognition with a Large Hydrophobic Component</b>	234
<i>Short–Strong Hydrogen Bonds</i>	177	<i>Cyclodextrins</i>	234
<b>3.2.4 <math>\pi</math> Effects</b>	180	<i>Cyclophanes</i>	234
<i>Cation–<math>\pi</math> Interactions</i>	181	<i>A Summary of the Hydrophobic Component of Molecular Recognition in Water</i>	238
<i>Polar–<math>\pi</math> Interactions</i>	183		
<i>Aromatic–Aromatic Interactions (<math>\pi</math> Stacking)</i>	184	<b>4.2.5 Molecular Recognition with a Large <math>\pi</math> Component</b>	239
<i>The Arene–Perfluoroarene Interaction</i>	184	<i>Cation–<math>\pi</math> Interactions</i>	239
<i><math>\pi</math> Donor–Acceptor Interactions</i>	186	<i>Polar–<math>\pi</math> and Related Effects</i>	241
<b>3.2.5 Induced-Dipole Interactions</b>	186		
<i>Ion–Induced-Dipole Interactions</i>	187	<b>4.2.6 Summary</b>	241
<i>Dipole–Induced-Dipole Interactions</i>	187		
<i>Induced-Dipole–Induced-Dipole Interactions</i>	188		
<i>Summarizing Monopole, Dipole, and Induced-Dipole Binding Forces</i>	188		
<b>3.2.6 The Hydrophobic Effect</b>	189		
<i>Aggregation of Organics</i>	189		
<i>The Origin of the Hydrophobic Effect</i>	192		
<b>3.3 Computational Modeling of Solvation</b>	194		
<b>3.3.1 Continuum Solvation Models</b>	196		
<b>3.3.2 Explicit Solvation Models</b>	197		
<b>3.3.3 Monte Carlo (MC) Methods</b>	198		
<b>3.3.4 Molecular Dynamics (MD)</b>	199		
<b>3.3.5 Statistical Perturbation Theory / Free Energy Perturbation</b>	200		
<b>Summary and Outlook</b>	201	<b>4.3 Supramolecular Chemistry</b>	243
<b>EXERCISES</b>	202	<b>4.3.1 Supramolecular Assembly of Complex Architectures</b>	244
<b>FURTHER READING</b>	204	<i>Self-Assembly via Coordination Compounds</i>	244
		<i>Self-Assembly via Hydrogen Bonding</i>	245
		<b>4.3.2 Novel Supramolecular Architectures—Catenanes, Rotaxanes, and Knots</b>	246
		<i>Nanotechnology</i>	248
		<b>4.3.3 Container Compounds—Molecules within Molecules</b>	249
		<b>Summary and Outlook</b>	252
		<b>EXERCISES</b>	253
		<b>FURTHER READING</b>	256

---

## CHAPTER 4: Molecular Recognition and Supramolecular Chemistry 207

### Intent and Purpose 207

#### 4.1 Thermodynamic Analyses of Binding Phenomena 207

##### 4.1.1 General Thermodynamics of Binding 208

*The Relevance of the Standard State* 210

*The Influence of a Change in Heat Capacity* 212

*Cooperativity* 213

*Enthalpy–Entropy Compensation* 216

##### 4.1.2 The Binding Isotherm 216

##### 4.1.3 Experimental Methods 219

*UV/Vis or Fluorescence Methods* 220

*NMR Methods* 220

*Isothermal Calorimetry* 221

#### 4.2 Molecular Recognition 222

##### 4.2.1 Complementarity and Preorganization 224

*Crowns, Cryptands, and Spherands—Molecular Recognition with a Large Ion–Dipole Component* 224

*Tweezers and Clefts* 228

##### 4.2.2 Molecular Recognition with a Large Ion Pairing Component 228

##### 4.2.3 Molecular Recognition with a Large Hydrogen Bonding Component 230

*Representative Structures* 230

---

## CHAPTER 5: Acid–Base Chemistry 259

### Intent and Purpose 259

#### 5.1 Brønsted Acid–Base Chemistry 259

##### 5.2 Aqueous Solutions 261

###### 5.2.1 $pK_a$ 261

###### 5.2.2 pH 262

###### 5.2.3 The Leveling Effect 264

###### 5.2.4 Activity vs. Concentration 266

###### 5.2.5 Acidity Functions: Acidity Scales for Highly Concentrated Acidic Solutions 266

###### 5.2.6 Super Acids 270

#### 5.3 Nonaqueous Systems 271

##### 5.3.1 $pK_a$ Shifts at Enzyme Active Sites 273

##### 5.3.2 Solution Phase vs. Gas Phase 273

#### 5.4 Predicting Acid Strength in Solution 276

##### 5.4.1 Methods Used to Measure Weak Acid Strength 276

##### 5.4.2 Two Guiding Principles for Predicting Relative Acidities 277

###### 5.4.3 Electronegativity and Induction 278

###### 5.4.4 Resonance 278

###### 5.4.5 Bond Strengths 283

###### 5.4.6 Electrostatic Effects 283

###### 5.4.7 Hybridization 283

5.4.8 Aromaticity 284	6.6.3 Nonplanar Graphs 326
5.4.9 Solvation 284	6.6.4 Achievements in Topological and Supramolecular Stereochemistry 327
5.4.10 Cationic Organic Structures 285	<b>6.7 Stereochemical Issues in Polymer Chemistry 331</b>
<b>5.5 Acids and Bases of Biological Interest 285</b>	<b>6.8 Stereochemical Issues in Chemical Biology 333</b>
<b>5.6 Lewis Acids/Bases and Electrophiles/ Nucleophiles 288</b>	6.8.1 The Linkages of Proteins, Nucleic Acids, and Polysaccharides 333
5.6.1 The Concept of Hard and Soft Acids and Bases, General Lessons for Lewis Acid–Base Interactions, and Relative Nucleophilicity and Electrophilicity 289	Proteins 333
<b>Summary and Outlook 292</b>	Nucleic Acids 334
<b>EXERCISES 292</b>	Polysaccharides 334
<b>FURTHER READING 294</b>	6.8.2 Helicity 336
<hr/>	Synthetic Helical Polymers 337
<b>CHAPTER 6: Stereochemistry 297</b>	6.8.3 The Origin of Chirality in Nature 339
<b>Intent and Purpose 297</b>	<b>6.9 Stereochemical Terminology 340</b>
<b>6.1 Stereogenicity and Stereoisomerism 297</b>	<b>Summary and Outlook 344</b>
6.1.1 Basic Concepts and Terminology 298	<b>EXERCISES 344</b>
<i>Classic Terminology</i> 299	<b>FURTHER READING 350</b>
<i>More Modern Terminology</i> 301	<hr/>
6.1.2 Stereochemical Descriptors 303	<b>PART II</b>
<i>R,S System</i> 304	<b>REACTIVITY, KINETICS, AND MECHANISMS</b>
<i>E,Z System</i> 304	<b>CHAPTER 7: Energy Surfaces and Kinetic Analyses 355</b>
<i>D and L</i> 304	<b>Intent and Purpose 355</b>
<i>Erythro and Threo</i> 305	<b>7.1 Energy Surfaces and Related Concepts 356</b>
<i>Helical Descriptors—M and P</i> 305	7.1.1 Energy Surfaces 357
<i>Ent and Epi</i> 306	7.1.2 Reaction Coordinate Diagrams 359
<i>Using Descriptors to Compare Structures</i> 306	7.1.3 What is the Nature of the Activated Complex/Transition State? 362
6.1.3 Distinguishing Enantiomers 306	7.1.4 Rates and Rate Constants 363
<i>Optical Activity and Chirality</i> 309	7.1.5 Reaction Order and Rate Laws 364
<i>Why is Plane Polarized Light Rotated by a Chiral Medium?</i> 309	<b>7.2 Transition State Theory (TST) and Related Topics 365</b>
<i>Circular Dichroism</i> 310	7.2.1 The Mathematics of Transition State Theory 365
<i>X-Ray Crystallography</i> 310	7.2.2 Relationship to the Arrhenius Rate Law 367
<b>6.2 Symmetry and Stereochemistry 311</b>	7.2.3 Boltzmann Distributions and Temperature Dependence 368
6.2.1 Basic Symmetry Operations 311	7.2.4 Revisiting “What is the Nature of the Activated Complex?” and Why Does TST Work? 369
6.2.2 Chirality and Symmetry 311	7.2.5 Experimental Determinations of Activation Parameters and Arrhenius Parameters 370
6.2.3 Symmetry Arguments 313	7.2.6 Examples of Activation Parameters and Their Interpretations 372
6.2.4 Focusing on Carbon 314	7.2.7 Is TST Completely Correct? The Dynamic Behavior of Organic Reactive Intermediates 372
<b>6.3 Topicity Relationships 315</b>	<b>7.3 Postulates and Principles Related to Kinetic Analysis 374</b>
6.3.1 Homotopic, Enantiotopic, and Diastereotopic 315	7.3.1 The Hammond Postulate 374
6.3.2 Topicity Descriptors— <i>Pro-R/Pro-S and Re/Si</i> 316	7.3.2 The Reactivity vs. Selectivity Principle 377
6.3.3 Chirotopicity 317	
<b>6.4 Reaction Stereochemistry: Stereoselectivity and Stereospecificity 317</b>	
6.4.1 Simple Guidelines for Reaction Stereochemistry 317	
6.4.2 Stereospecific and Stereoselective Reactions 319	
<b>6.5 Symmetry and Time Scale 322</b>	
<b>6.6 Topological and Supramolecular Stereochemistry 324</b>	
6.6.1 Loops and Knots 325	
6.6.2 Topological Chirality 326	

7.3.3 The Curtin–Hammett Principle	378
7.3.4 Microscopic Reversibility	379
7.3.5 Kinetic vs. Thermodynamic Control	380
<b>7.4 Kinetic Experiments</b>	<b>382</b>
7.4.1 How Kinetic Experiments are Performed	382
7.4.2 Kinetic Analyses for Simple Mechanisms	384
<i>First Order Kinetics</i>	385
<i>Second Order Kinetics</i>	386
<i>Pseudo-First Order Kinetics</i>	387
<i>Equilibrium Kinetics</i>	388
<i>Initial-Rate Kinetics</i>	389
<i>Tabulating a Series of Common Kinetic Scenarios</i>	389
<b>7.5 Complex Reactions—Deciphering Mechanisms</b>	<b>390</b>
7.5.1 Steady State Kinetics	390
7.5.2 Using the SSA to Predict Changes in Kinetic Order	395
7.5.3 Saturation Kinetics	396
7.5.4 Prior Rapid Equilibria	397
<b>7.6 Methods for Following Kinetics</b>	<b>397</b>
7.6.1 Reactions with Half-Lives Greater than a Few Seconds	398
7.6.2 Fast Kinetics Techniques	398
<i>Flow Techniques</i>	399
<i>Flash Photolysis</i>	399
<i>Pulse Radiolysis</i>	401
7.6.3 Relaxation Methods	401
7.6.4 Summary of Kinetic Analyses	402
<b>7.7 Calculating Rate Constants</b>	<b>403</b>
7.7.1 Marcus Theory	403
7.7.2 Marcus Theory Applied to Electron Transfer	405
<b>7.8 Considering Multiple Reaction Coordinates</b>	<b>407</b>
7.8.1 Variation in Transition State Structures Across a Series of Related Reactions—An Example Using Substitution Reactions	407
7.8.2 More O’Ferrall–Jencks Plots	409
7.8.3 Changes in Vibrational State Along the Reaction Coordinate—Relating the Third Coordinate to Entropy	412
<b>Summary and Outlook</b>	<b>413</b>
<b>EXERCISES</b>	<b>413</b>
<b>FURTHER READING</b>	<b>417</b>

<b>CHAPTER 8: Experiments Related to Thermodynamics and Kinetics</b>	<b>421</b>
<b>Intent and Purpose</b>	<b>421</b>
<b>8.1 Isotope Effects</b>	<b>421</b>
8.1.1 The Experiment	422
8.1.2 The Origin of Primary Kinetic Isotope Effects	422
<i>Reaction Coordinate Diagrams and Isotope Effects</i>	424

Primary Kinetic Isotope Effects for Linear Transition States as a Function of Exothermicity and Endothermicity	425
Isotope Effects for Linear vs. Non-Linear Transition States	428
8.1.3 The Origin of Secondary Kinetic Isotope Effects	428
<i>Hybridization Changes</i>	429
<i>Steric Isotope Effects</i>	430
8.1.4 Equilibrium Isotope Effects	432
<i>Isotopic Perturbation of Equilibrium—Applications to Carbocations</i>	432
8.1.5 Tunneling	435
8.1.6 Solvent Isotope Effects	437
<i>Fractionation Factors</i>	437
<i>Proton Inventories</i>	438
8.1.7 Heavy Atom Isotope Effects	441
8.1.8 Summary	441
<b>8.2 Substituent Effects</b>	<b>441</b>
8.2.1 The Origin of Substituent Effects	443
<i>Field Effects</i>	443
<i>Inductive Effects</i>	443
<i>Resonance Effects</i>	444
<i>Polarizability Effects</i>	444
<i>Steric Effects</i>	445
<i>Solvation Effects</i>	445
<b>8.3 Hammett Plots—The Most Common LFER. A General Method for Examining Changes in Charges During a Reaction</b>	<b>445</b>
8.3.1 Sigma ( $\sigma$ )	445
8.3.2 Rho ( $\rho$ )	447
8.3.3 The Power of Hammett Plots for Deciphering Mechanisms	448
8.3.4 Deviations from Linearity	449
8.3.5 Separating Resonance from Induction	451
<b>8.4 Other Linear Free Energy Relationships</b>	<b>454</b>
8.4.1 Steric and Polar Effects—Taft Parameters	454
8.4.2 Solvent Effects—Grunwald–Winstein Plots	455
8.4.3 Schleyer Adaptation	457
8.4.4 Nucleophilicity and Nucleofugality	458
<i>Basicity/Acidity</i>	459
<i>Solvation</i>	460
<i>Polarizability, Basicity, and Solvation Interplay</i>	460
<i>Shape</i>	461
8.4.5 Swain–Scott Parameters—Nucleophilicity Parameters	461
8.4.6 Edwards and Ritchie Correlations	463
<b>8.5 Acid–Base Related Effects—Brønsted Relationships</b>	<b>464</b>
8.5.1 $\beta_{\text{Nuc}}$	464
8.5.2 $\beta_{\text{LG}}$	464
8.5.3 Acid–Base Catalysis	466
<b>8.6 Why do Linear Free Energy Relationships Work?</b>	<b>466</b>
8.6.1 General Mathematics of LFERs	467
8.6.2 Conditions to Create an LFER	468
8.6.3 The Isokinetic or Isoequilibrium Temperature	469

<p>8.6.4 Why does Enthalpy–Entropy Compensation Occur? 469  <i>Steric Effects</i> 470  <i>Solvation</i> 470</p> <p><b>8.7 Summary of Linear Free Energy Relationships</b> 470</p> <p><b>8.8 Miscellaneous Experiments for Studying Mechanisms</b> 471</p> <p>8.8.1 Product Identification 472</p> <p>8.8.2 Changing the Reactant Structure to Divert or Trap a Proposed Intermediate 473</p> <p>8.8.3 Trapping and Competition Experiments 474</p> <p>8.8.4 Checking for a Common Intermediate 475</p> <p>8.8.5 Cross-Over Experiments 476</p> <p>8.8.6 Stereochemical Analysis 476</p> <p>8.8.7 Isotope Scrambling 477</p> <p>8.8.8 Techniques to Study Radicals: Clocks and Traps 478</p> <p>8.8.9 Direct Isolation and Characterization of an Intermediate 480</p> <p>8.8.10 Transient Spectroscopy 480</p> <p>8.8.11 Stable Media 481</p> <p><b>Summary and Outlook</b> 482</p> <p><b>EXERCISES</b> 482</p> <p><b>FURTHER READING</b> 487</p>	<p>9.3.4 Concerted or Sequential General-Acid–General-Base Catalysis 515</p> <p><b>9.3.5 The Brønsted Catalysis Law and Its Ramifications</b> 516  <i>A Linear Free Energy Relationship</i> 516  <i>The Meaning of <math>\alpha</math> and <math>\beta</math></i> 517  <math>\alpha + \beta = 1</math> 518  <i>Deviations from Linearity</i> 519</p> <p><b>9.3.6 Predicting General-Acid or General-Base Catalysis</b> 520  <i>The Libido Rule</i> 520  <i>Potential Energy Surfaces Dictate General or Specific Catalysis</i> 521</p> <p><b>9.3.7 The Dynamics of Proton Transfers</b> 522  <i>Marcus Analysis</i> 522</p> <p><b>9.4 Enzymatic Catalysis</b> 523</p> <p>9.4.1 Michaelis–Menten Kinetics 523</p> <p>9.4.2 The Meaning of <math>K_M</math>, <math>k_{cat}</math>, and <math>k_{cat}/K_M</math> 524</p> <p>9.4.3 Enzyme Active Sites 525</p> <p>9.4.4 <math>[S]</math> vs. <math>K_M</math>—Reaction Coordinate Diagrams 527</p> <p>9.4.5 Supramolecular Interactions 529</p> <p><b>Summary and Outlook</b> 530</p> <p><b>EXERCISES</b> 531</p> <p><b>FURTHER READING</b> 535</p>
<hr/> <p><b>CHAPTER 9: Catalysis</b> 489</p> <p><b>Intent and Purpose</b> 489</p> <p><b>9.1 General Principles of Catalysis</b> 490</p> <p>9.1.1 Binding the Transition State Better than the Ground State 491</p> <p>9.1.2 A Thermodynamic Cycle Analysis 493</p> <p>9.1.3 A Spatial Temporal Approach 494</p> <p><b>9.2 Forms of Catalysis</b> 495</p> <p>9.2.1 “Binding” is Akin to Solvation 495</p> <p>9.2.2 Proximity as a Binding Phenomenon 495</p> <p>9.2.3 Electrophilic Catalysis 499  <i>Electrostatic Interactions</i> 499  <i>Metal Ion Catalysis</i> 500</p> <p>9.2.4 Acid–Base Catalysis 502</p> <p>9.2.5 Nucleophilic Catalysis 502</p> <p>9.2.6 Covalent Catalysis 504</p> <p>9.2.7 Strain and Distortion 505</p> <p>9.2.8 Phase Transfer Catalysis 507</p> <p><b>9.3 Brønsted Acid–Base Catalysis</b> 507</p> <p>9.3.1 Specific Catalysis 507  <i>The Mathematics of Specific Catalysis</i> 507  <i>Kinetic Plots</i> 510</p> <p>9.3.2 General Catalysis 510  <i>The Mathematics of General Catalysis</i> 511  <i>Kinetic Plots</i> 512</p> <p>9.3.3 A Kinetic Equivalency 514</p> <p><b>CHAPTER 10: Organic Reaction Mechanisms, Part 1: Reactions Involving Additions and/or Eliminations</b> 537</p> <p><b>Intent and Purpose</b> 537</p> <p><b>10.1 Predicting Organic Reactivity</b> 538</p> <p>10.1.1 A Useful Paradigm for Polar Reactions 539  <i>Nucleophiles and Electrophiles</i> 539  <i>Lewis Acids and Lewis Bases</i> 540  <i>Donor–Acceptor Orbital Interactions</i> 540</p> <p>10.1.2 Predicting Radical Reactivity 541</p> <p>10.1.3 In Preparation for the Following Sections 541</p> <p style="text-align: center;">—ADDITION REACTIONS— 542</p> <p><b>10.2 Hydration of Carbonyl Structures</b> 542</p> <p>10.2.1 Acid–Base Catalysis 543</p> <p>10.2.2 The Thermodynamics of the Formation of Geminal Diols and Hemiacetals 544</p> <p><b>10.3 Electrophilic Addition of Water to Alkenes and Alkynes: Hydration</b> 545</p> <p>10.3.1 Electron Pushing 546</p> <p>10.3.2 Acid-Catalyzed Aqueous Hydration 546</p> <p>10.3.3 Regiochemistry 546</p> <p>10.3.4 Alkyne Hydration 547</p> <p><b>10.4 Electrophilic Addition of Hydrogen Halides to Alkenes and Alkynes</b> 548</p> <p>10.4.1 Electron Pushing 548</p>	

10.4.2 Experimental Observations Related to Regiochemistry and Stereochemistry 548	10.12.2 Stereochemical and Isotope Labeling Evidence 577
10.4.3 Addition to Alkynes 551	10.12.3 Catalysis of the Hydrolysis of Acetals 578
<b>10.5 Electrophilic Addition of Halogens to Alkenes 551</b>	10.12.4 Stereoelectronic Effects 579
10.5.1 Electron Pushing 551	10.12.5 CrO <sub>3</sub> Oxidation—The Jones Reagent 580 <i>Electron Pushing</i> 580 <i>A Few Experimental Observations</i> 581
10.5.2 Stereochemistry 552	
10.5.3 Other Evidence Supporting a σ Complex 552	
10.5.4 Mechanistic Variants 553	
10.5.5 Addition to Alkynes 554	
<b>10.6 Hydroboration 554</b>	<b>10.13 Elimination Reactions for Aliphatic Systems—Formation of Alkenes 581</b>
10.6.1 Electron Pushing 555	10.13.1 Electron Pushing and Definitions 581
10.6.2 Experimental Observations 555	10.13.2 Some Experimental Observations for E2 and E1 Reactions 582
<b>10.7 Epoxidation 555</b>	10.13.3 Contrasting Elimination and Substitution 583
10.7.1 Electron Pushing 556	10.13.4 Another Possibility—E1cB 584
10.7.2 Experimental Observations 556	10.13.5 Kinetics and Experimental Observations for E1cB 584
<b>10.8 Nucleophilic Additions to Carbonyl Compounds 556</b>	10.13.6 Contrasting E2, E1, and E1cB 586
10.8.1 Electron Pushing for a Few Nucleophilic Additions 557	10.13.7 Regiochemistry of Eliminations 588
10.8.2 Experimental Observations for Cyanohydrin Formation 559	10.13.8 Stereochemistry of Eliminations—Orbital Considerations 590
10.8.3 Experimental Observations for Grignard Reactions 560	10.13.9 Dehydration 592 <i>Electron Pushing</i> 592 <i>Other Mechanistic Possibilities</i> 594
10.8.4 Experimental Observations in LAH Reductions 561	10.13.10 Thermal Eliminations 594
10.8.5 Orbital Considerations 561 <i>The Bürgi–Dunitz Angle</i> 561 <i>Orbital Mixing</i> 562	<b>10.14 Eliminations from Radical Intermediates 596</b> —COMBINING ADDITION AND ELIMINATION REACTIONS (SUBSTITUTIONS AT <i>sp</i> <sup>2</sup> CENTERS)— 596
10.8.6 Conformational Effects in Additions to Carbonyl Compounds 562	<b>10.15 The Addition of Nitrogen Nucleophiles to Carbonyl Structures, Followed by Elimination 597</b>
10.8.7 Stereochemistry of Nucleophilic Additions 563	10.15.1 Electron Pushing 598
<b>10.9 Nucleophilic Additions to Olefins 567</b>	10.15.2 Acid–Base Catalysis 598
10.9.1 Electron Pushing 567	
10.9.2 Experimental Observations 567	<b>10.16 The Addition of Carbon Nucleophiles, Followed by Elimination—The Wittig Reaction 599</b>
10.9.3 Regiochemistry of Addition 567	10.16.1 Electron Pushing 600
10.9.4 Baldwin’s Rules 568	
<b>10.10 Radical Additions to Unsaturated Systems 569</b>	<b>10.17 Acyl Transfers 600</b>
10.10.1 Electron Pushing for Radical Additions 569	10.17.1 General Electron-Pushing Schemes 600
10.10.2 Radical Initiators 570	10.17.2 Isotope Scrambling 601
10.10.3 Chain Transfer vs. Polymerization 571	10.17.3 Predicting the Site of Cleavage for Acyl Transfers from Esters 602
10.10.4 Termination 571	10.17.4 Catalysis 602
10.10.5 Regiochemistry of Radical Additions 572	
<b>10.11 Carbene Additions and Insertions 572</b>	<b>10.18 Electrophilic Aromatic Substitution 607</b>
10.11.1 Electron Pushing for Carbene Reactions 574	10.18.1 Electron Pushing for Electrophilic Aromatic Substitutions 607
10.11.2 Carbene Generation 574	10.18.2 Kinetics and Isotope Effects 608
10.11.3 Experimental Observations for Carbene Reactions 575	10.18.3 Intermediate Complexes 608
—ELIMINATIONS— 576	10.18.4 Regiochemistry and Relative Rates of Aromatic Substitution 609
<b>10.12 Eliminations to Form Carbonyls or “Carbonyl-Like” Intermediates 577</b>	<b>10.19 Nucleophilic Aromatic Substitution 611</b>
10.12.1 Electron Pushing 577	10.19.1 Electron Pushing for Nucleophilic Aromatic Substitution 611
	10.19.2 Experimental Observations 611

<b>10.20 Reactions Involving Benzyne</b>	612
10.20.1 Electron Pushing for Benzyne Reactions	612
10.20.2 Experimental Observations	613
10.20.3 Substituent Effects	613
<b>10.21 The S<sub>RN</sub>1 Reaction on Aromatic Rings</b>	615
10.21.1 Electron Pushing	615
10.21.2 A Few Experimental Observations	615
<b>10.22 Radical Aromatic Substitutions</b>	615
10.22.1 Electron Pushing	615
10.22.2 Isotope Effects	616
10.22.3 Regiochemistry	616
<b>Summary and Outlook</b>	617
<b>EXERCISES</b>	617
<b>FURTHER READING</b>	624

**CHAPTER 11: Organic Reaction Mechanisms,  
Part 2: Substitutions at Aliphatic  
Centers and Thermal Isomerizations/  
Rearrangements** 627

<b>Intent and Purpose</b>	627
<b>—SUBSTITUTION <math>\alpha</math> TO A CARBONYL CENTER: ENOL AND ENOLATE CHEMISTRY—</b> 627	
<b>11.1 Tautomerization</b>	628
11.1.1 Electron Pushing for Keto–Enol Tautomerizations	628
11.1.2 The Thermodynamics of Enol Formation	628
11.1.3 Catalysis of Enolizations	629
11.1.4 Kinetic vs. Thermodynamic Control in Enolate and Enol Formation	629
<b>11.2 <math>\alpha</math>-Halogenation</b>	631
11.2.1 Electron Pushing	631
11.2.2 A Few Experimental Observations	631
<b>11.3 <math>\alpha</math>-Alkylation</b>	632
11.3.1 Electron Pushing	632
11.3.2 Stereochemistry: Conformational Effects	633
<b>11.4 The Aldol Reaction</b>	634
11.4.1 Electron Pushing	634
11.4.2 Conformational Effects on the Aldol Reaction	634
<b>—SUBSTITUTIONS ON ALIPHATIC CENTERS—</b> 637	
<b>11.5 Nucleophilic Aliphatic Substitution Reactions</b>	637
11.5.1 S <sub>N</sub> 2 and S <sub>N</sub> 1 Electron-Pushing Examples	637
11.5.2 Kinetics	638
11.5.3 Competition Experiments and Product Analyses	639
11.5.4 Stereochemistry	640
11.5.5 Orbital Considerations	643
11.5.6 Solvent Effects	643
11.5.7 Isotope Effect Data	646
11.5.8 An Overall Picture of S <sub>N</sub> 2 and S <sub>N</sub> 1 Reactions	646
<b>11.5.9 Structure–Function Correlations with the Nucleophile</b>	648
<b>11.5.10 Structure–Function Correlations with the Leaving Group</b>	651
<b>11.5.11 Structure–Function Correlations with the R Group</b>	651
<i>Effect of the R Group Structure on S<sub>N</sub>2 Reactions</i>	651
<i>Effect of the R Group Structure on S<sub>N</sub>1 Reactions</i>	653
<b>11.5.12 Carbocation Rearrangements</b>	656
<b>11.5.13 Anchimeric Assistance in S<sub>N</sub>1 Reactions</b>	659
<b>11.5.14 S<sub>N</sub>1 Reactions Involving Non-Classical Carbocations</b>	661
<i>Norbornyl Cation</i>	662
<i>Cyclopropyl Carbonyl Carbocation</i>	664
<b>11.5.15 Summary of Carbocation Stabilization in Various Reactions</b>	667
<b>11.5.16 The Interplay Between Substitution and Elimination</b>	667
<b>11.6 Substitution, Radical, Nucleophilic</b>	668
11.6.1 The SET Reaction—Electron Pushing	668
11.6.2 The Nature of the Intermediate in an SET Mechanism	669
11.6.3 Radical Rearrangements as Evidence	669
11.6.4 Structure–Function Correlations with the Leaving Group	670
11.6.5 The S <sub>RN</sub> 1 Reaction—Electron Pushing	670
<b>11.7 Radical Aliphatic Substitutions</b>	671
11.7.1 Electron Pushing	671
11.7.2 Heats of Reaction	671
11.7.3 Regiochemistry of Free Radical Halogenation	671
11.7.4 Autoxidation: Addition of O <sub>2</sub> into C–H Bonds	673
<i>Electron Pushing for Autoxidation</i>	673
<b>—ISOMERIZATIONS AND REARRANGEMENTS—</b> 674	
<b>11.8 Migrations to Electrophilic Carbons</b>	674
11.8.1 Electron Pushing for the Pinacol Rearrangement	675
11.8.2 Electron Pushing in the Benzilic Acid Rearrangement	675
11.8.3 Migratory Aptitudes in the Pinacol Rearrangement	675
11.8.4 Stereoelectronic and Stereochemical Considerations in the Pinacol Rearrangement	676
11.8.5 A Few Experimental Observations for the Benzilic Acid Rearrangement	678
<b>11.9 Migrations to Electrophilic Heteroatoms</b>	678
11.9.1 Electron Pushing in the Beckmann Rearrangement	678
11.9.2 Electron Pushing for the Hofmann Rearrangement	679
11.9.3 Electron Pushing for the Schmidt Rearrangement	680
11.9.4 Electron Pushing for the Baeyer–Villiger Oxidation	680
11.9.5 A Few Experimental Observations for the Beckmann Rearrangement	680

11.9.6 A Few Experimental Observations for the Schmidt Rearrangement	681
11.9.7 A Few Experimental Observations for the Baeyer–Villiger Oxidation	681
<b>11.10 The Favorskii Rearrangement and Other Carbanion Rearrangements</b>	682
11.10.1 Electron Pushing	682
11.10.2 Other Carbanion Rearrangements	683
<b>11.11 Rearrangements Involving Radicals</b>	683
11.11.1 Hydrogen Shifts	683
11.11.2 Aryl and Vinyl Shifts	684
11.11.3 Ring-Opening Reactions	685
<b>11.12 Rearrangements and Isomerizations Involving Biradicals</b>	685
11.12.1 Electron Pushing Involving Biradicals	686
11.12.2 Tetramethylene	687
11.12.3 Trimethylene	689
11.12.4 Trimethylenemethane	693
<b>Summary and Outlook</b>	695
<b>EXERCISES</b>	695
<b>FURTHER READING</b>	703

## CHAPTER 12: Organotransition Metal Reaction Mechanisms and Catalysis 705

<b>Intent and Purpose</b>	705
<b>12.1 The Basics of Organometallic Complexes</b>	705
12.1.1 Electron Counting and Oxidation State	706
<i>Electron Counting</i>	706
<i>Oxidation State</i>	708
<i>d</i> <i>Electron Count</i>	708
<i>Ambiguities</i>	708
12.1.2 The 18-Electron Rule	710
12.1.3 Standard Geometries	710
12.1.4 Terminology	711
12.1.5 Electron Pushing with Organometallic Structures	711
12.1.6 <i>d</i> Orbital Splitting Patterns	712
12.1.7 Stabilizing Reactive Ligands	713

<b>12.2 Common Organometallic Reactions</b>	714
12.2.1 Ligand Exchange Reactions	714
<i>Reaction Types</i>	714
<i>Kinetics</i>	716
<i>Structure–Function Relationships with the Metal</i>	716
<i>Structure–Function Relationships with the Ligand</i>	716
<i>Substitutions of Other Ligands</i>	717
12.2.2 Oxidative Addition	717
<i>Stereochemistry of the Metal Complex</i>	718
<i>Kinetics</i>	718
<i>Stereochemistry of the R Group</i>	719
<i>Structure–Function Relationship for the R Group</i>	720

<b>Structure–Function Relationships for the Ligands</b>	720
<b>Oxidative Addition at <i>sp</i><sup>2</sup> Centers</b>	721
<b>Summary of the Mechanisms for Oxidative Addition</b>	721
<b>12.2.3 Reductive Elimination</b>	724
<i>Structure–Function Relationship for the R Group and the Ligands</i>	724
<i>Stereochemistry at the Metal Center</i>	725
<i>Other Mechanisms</i>	725
<i>Summary of the Mechanisms for Reductive Elimination</i>	726
<b>12.2.4 <math>\alpha</math>- and <math>\beta</math>-Eliminations</b>	727
<i>General Trends for <math>\alpha</math>- and <math>\beta</math>-Eliminations</i>	727
<i>Kinetics</i>	728
<i>Stereochemistry of <math>\beta</math>-Hydride Elimination</i>	729
<b>12.2.5 Migratory Insertions</b>	729
<i>Kinetics</i>	730
<i>Studies to Decipher the Mechanism of Migratory Insertion Involving CO</i>	730
<i>Other Stereochemical Considerations</i>	732
<b>12.2.6 Electrophilic Addition to Ligands</b>	733
<i>Reaction Types</i>	733
<i>Common Mechanisms Deduced from Stereochemical Analyses</i>	734
<b>12.2.7 Nucleophilic Addition to Ligands</b>	734
<i>Reaction Types</i>	735
<i>Stereochemical and Regiochemical Analyses</i>	735
<b>12.3 Combining the Individual Reactions into Overall Transformations and Cycles</b>	737
12.3.1 The Nature of Organometallic Catalysis—Change in Mechanism	738
12.3.2 The Monsanto Acetic Acid Synthesis	738
12.3.3 Hydroformylation	739
12.3.4 The Water-Gas Shift Reaction	740
12.3.5 Olefin Oxidation—The Wacker Process	741
12.3.6 Palladium Coupling Reactions	742
12.3.7 Allylic Alkylation	743
12.3.8 Olefin Metathesis	744
<b>Summary and Outlook</b>	747
<b>EXERCISES</b>	748
<b>FURTHER READING</b>	750

---

## CHAPTER 13: Organic Polymer and Materials Chemistry 753

### Intent and Purpose 753

<b>13.1 Structural Issues in Materials Chemistry</b>	754
13.1.1 Molecular Weight Analysis of Polymers	754
<i>Number Average and Weight Average Molecular Weights—<math>M_n</math> and <math>M_w</math></i>	754
13.1.2 Thermal Transitions—Thermoplastics and Elastomers	757
13.1.3 Basic Polymer Topologies	759

13.1.4	Polymer–Polymer Phase Behavior	760
13.1.5	Polymer Processing	762
13.1.6	Novel Topologies—Dendrimers and Hyperbranched Polymers	763
	Dendrimers	763
	Hyperbranched Polymers	768
13.1.7	Liquid Crystals	769
13.1.8	Fullerenes and Carbon Nanotubes	775
<b>13.2</b>	<b>Common Polymerization Mechanisms</b>	779
13.2.1	General Issues	779
13.2.2	Polymerization Kinetics	782
	Step-Growth Kinetics	782
	Free-Radical Chain Polymerization	783
	Living Polymerizations	785
	Thermodynamics of Polymerizations	787
13.2.3	Condensation Polymerization	788
13.2.4	Radical Polymerization	791
13.2.5	Anionic Polymerization	793
13.2.6	Cationic Polymerization	794
13.2.7	Ziegler–Natta and Related Polymerizations	794
	Single-Site Catalysts	796
13.2.8	Ring-Opening Polymerization	797
13.2.9	Group Transfer Polymerization (GTP)	799
	<b>Summary and Outlook</b>	800
	<b>EXERCISES</b>	801
	<b>FURTHER READING</b>	803

### PART III

## ELECTRONIC STRUCTURE: THEORY AND APPLICATIONS

### CHAPTER 14: Advanced Concepts in Electronic Structure Theory 807

#### Intent and Purpose 807

#### 14.1 Introductory Quantum Mechanics 808

- 14.1.1 The Nature of Wavefunctions 808
- 14.1.2 The Schrödinger Equation 809
- 14.1.3 The Hamiltonian 809
- 14.1.4 The Nature of the  $\nabla^2$  Operator 811
- 14.1.5 Why do Bonds Form? 812

#### 14.2 Calculational Methods—Solving the Schrödinger Equation for Complex Systems 815

- 14.2.1 *Ab Initio* Molecular Orbital Theory 815
  - Born–Oppenheimer Approximation 815
  - The Orbital Approximation 815
  - Spin 816
  - The Pauli Principle and Determinantal Wavefunctions 816
  - The Hartree–Fock Equation and the Variational Theorem 818

	SCF Theory	821
	Linear Combination of Atomic Orbitals—Molecular Orbitals (LCAO–MO)	821
	Common Basis Sets—Modeling Atomic Orbitals	822
	Extension Beyond HF—Correlation Energy	824
	Solvation	825
	General Considerations	825
	Summary	826
14.2.2	Secular Determinants—A Bridge Between <i>Ab Initio</i> , Semi-Empirical/Approximate, and Perturbational Molecular Orbital Theory Methods	828
	The “Two-Orbital Mixing Problem”	829
	Writing the Secular Equations and Determinant for Any Molecule	832
14.2.3	Semi-Empirical and Approximate Methods	833
	Neglect of Differential Overlap (NDO) Methods	833
	i. CNDO, INDO, PNDO (C=Complete, I=Intermediate, P=Partial)	834
	ii. The Semi-Empirical Methods: MNDO, AM1, and PM3	834
	Extended Hückel Theory (EHT)	834
	Hückel Molecular Orbital Theory (HMOT)	835
14.2.4	Some General Comments on Computational Quantum Mechanics	835
14.2.5	An Alternative: Density Functional Theory (DFT)	836

#### 14.3 A Brief Overview of the Implementation and Results of HMOT 837

- 14.3.1 Implementing Hückel Theory 838
- 14.3.2 HMOT of Cyclic  $\pi$  Systems 840
- 14.3.3 HMOT of Linear  $\pi$  Systems 841
- 14.3.4 Alternate Hydrocarbons 842

#### 14.4 Perturbation Theory—Orbital Mixing Rules 844

- 14.4.1 Mixing of Degenerate Orbitals—First-Order Perturbations 845
- 14.4.2 Mixing of Non-Degenerate Orbitals—Second-Order Perturbations 845

#### 14.5 Some Topics in Organic Chemistry for Which Molecular Orbital Theory Lends Important Insights 846

- 14.5.1 Arenes: Aromaticity and Antiaromaticity 846
- 14.5.2 Cyclopropane and Cyclopropylcarbinyl—Walsh Orbitals 848
  - The Cyclic Three-Orbital Mixing Problem 849
  - The MOs of Cyclopropane 850
- 14.5.3 Planar Methane 853
- 14.5.4 Through-Bond Coupling 854
- 14.5.5 Unique Bonding Capabilities of Carbocations—Non-Classical Ions and Hypervalent Carbon 855
  - Transition State Structure Calculations 856
  - Application of These Methods to Carbocations 857
  - NMR Effects in Carbocations 857
  - The Norbornyl Cation 858
- 14.5.6 Spin Preferences 859
  - Two Weakly Interacting Electrons:  $H_2$  vs. Atomic C 859

<b>14.6 Organometallic Complexes</b>	862
14.6.1 Group Orbitals for Metals	863
14.6.2 The Isolobal Analogy	866
14.6.3 Using the Group Orbitals to Construct Organometallic Complexes	867
<b>Summary and Outlook</b>	868
<b>EXERCISES</b>	868
<b>FURTHER READING</b>	875

---

## CHAPTER 15: Thermal Pericyclic Reactions 877

### Intent and Purpose 877

#### 15.1 Background 878

#### 15.2 A Detailed Analysis of Two Simple Cycloadditions 878

##### 15.2.1 Orbital Symmetry Diagrams 879

[2+2] 879

[4+2] 881

##### 15.2.2 State Correlation Diagrams 883

[2+2] 883

[4+2] 886

##### 15.2.3 Frontier Molecular Orbital (FMO) Theory 888

*Contrasting the [2+2] and [4+2]* 888

##### 15.2.4 Aromatic Transition State Theory/Topology 889

##### 15.2.5 The Generalized Orbital Symmetry Rule 890

##### 15.2.6 Some Comments on "Forbidden" and "Allowed" Reactions 892

##### 15.2.7 Photochemical Pericyclic Reactions 892

##### 15.2.8 Summary of the Various Methods 893

#### 15.3 Cycloadditions 893

##### 15.3.1 An Allowed Geometry for [2+2] Cycloadditions 894

##### 15.3.2 Summarizing Cycloadditions 895

##### 15.3.3 General Experimental Observations 895

##### 15.3.4 Stereochemistry and Regiochemistry of the Diels–Alder Reaction 896

*An Orbital Approach to Predicting*

*Regiochemistry* 896

*The Endo Effect* 899

##### 15.3.5 Experimental Observations for [2+2] Cycloadditions 901

##### 15.3.6 Experimental Observations for 1,3-Dipolar Cycloadditions 901

##### 15.3.7 Retrocycloadditions 902

#### 15.4 Electrocyclic Reactions 903

##### 15.4.1 Terminology 903

##### 15.4.2 Theoretical Analyses 904

##### 15.4.3 Experimental Observations: Stereochemistry 906

##### 15.4.4 Torquoselectivity 908

#### 15.5 Sigmatropic Rearrangements 910

##### 15.5.1 Theory 911

##### 15.5.2 Experimental Observations: A Focus on Stereochemistry 913

##### 15.5.3 The Mechanism of the Cope Rearrangement 916

##### 15.5.4 The Claisen Rearrangement 921

*Uses in Synthesis* 921

*Mechanistic Studies* 923

##### 15.5.5 The Ene Reaction 924

#### 15.6 Cheletropic Reactions 924

##### 15.6.1 Theoretical Analyses 926

##### 15.6.2 Carbene Additions 927

#### 15.7 In Summary—Applying the Rules 928

### Summary and Outlook 928

### EXERCISES 929

### FURTHER READING 933

---

## CHAPTER 16: Photochemistry 935

### Intent and Purpose 935

#### 16.1 Photophysical Processes—

##### The Jablonski Diagram 936

##### 16.1.1 Electromagnetic Radiation 936

*Multiple Energy Surfaces Exist* 937

##### 16.1.2 Absorption 939

##### 16.1.3 Radiationless Vibrational Relaxation 944

##### 16.1.4 Fluorescence 945

##### 16.1.5 Internal Conversion (IC) 949

##### 16.1.6 Intersystem Crossing (ISC) 950

##### 16.1.7 Phosphorescence 951

##### 16.1.8 Quantum Yield 952

##### 16.1.9 Summary of Photophysical Processes 952

#### 16.2 Bimolecular Photophysical Processes 953

##### 16.2.1 General Considerations 953

##### 16.2.2 Quenching, Excimers, and Exciplexes 953

*Quenching* 954

*Excimers and Exciplexes* 954

*Photoinduced Electron Transfer* 955

##### 16.2.3 Energy Transfer I. The Dexter Mechanism—Sensitization 956

##### 16.2.4 Energy Transfer II. The Förster Mechanism 958

##### 16.2.5 FRET 960

##### 16.2.6 Energy Pooling 962

##### 16.2.7 An Overview of Bimolecular Photophysical Processes 962

#### 16.3 Photochemical Reactions 962

##### 16.3.1 Theoretical Considerations—Funnels 962

*Diabatic Photoreactions* 963

*Other Mechanisms* 964

##### 16.3.2 Acid–Base Chemistry 965

16.3.3 Olefin Isomerization	965
16.3.4 Reversal of Pericyclic Selection Rules	968
16.3.5 Photocycloaddition Reactions	970
<i>Making Highly Strained Ring Systems</i>	973
<i>Breaking Aromaticity</i>	974
16.3.6 The Di- $\pi$ -Methane Rearrangement	974
16.3.7 Carbonyls Part I: The Norrish I Reaction	976
16.3.8 Carbonyls Part II: Photoreduction and the Norrish II Reaction	978
16.3.9 Nitrobenzyl Photochemistry: "Caged" Compounds	980
16.3.10 Elimination of N <sub>2</sub> : Azo Compounds, Diazo Compounds, Diazirines, and Azides	981
<i>Azoalkanes (1,2-Diazenes)</i>	981
<i>Diazo Compounds and Diazirines</i>	982
<i>Azides</i>	983

#### 16.4 Chemiluminescence 985

16.4.1 Potential Energy Surface for a Chemiluminescent Reaction	985
16.4.2 Typical Chemiluminescent Reactions	986
16.4.3 Dioxetane Thermolysis	987

#### 16.5 Singlet Oxygen 989

#### Summary and Outlook 993

EXERCISES 993

FURTHER READING 999

---

### CHAPTER 17: Electronic Organic Materials 1001

#### Intent and Purpose 1001

#### 17.1 Theory 1001

17.1.1 Infinite $\pi$ Systems—An Introduction to Band Structures	1002
17.1.2 The Peierls Distortion	1009
17.1.3 Doping	1011

#### 17.2 Conducting Polymers 1016

17.2.1 Conductivity	1016
17.2.2 Polyacetylene	1017
17.2.3 Polyarenes and Polyarenevinylanes	1018
17.2.4 Polyaniline	1021

#### 17.3 Organic Magnetic Materials 1022

17.3.1 Magnetism	1023
17.3.2 The Molecular Approach to Organic Magnetic Materials	1024
17.3.3 The Polymer Approach to Organic Magnetic Materials—Very High-Spin Organic Molecules	1027

#### 17.4 Superconductivity 1030

17.4.1 Organic Metals/Synthetic Metals	1032
--	------

#### 17.5 Non-Linear Optics (NLO) 1033

#### 17.6 Photoresists 1036

17.6.1 Photolithography	1036
17.6.2 Negative Photoresists	1037
17.6.3 Positive Photoresists	1038

#### Summary and Outlook 1041

EXERCISES 1042

FURTHER READING 1044

---

#### APPENDIX 1: Conversion Factors and Other Useful Data 1047

#### APPENDIX 2: Electrostatic Potential Surfaces for Representative Organic Molecules 1049

#### APPENDIX 3: Group Orbitals of Common Functional Groups: Representative Examples Using Simple Molecules 1051

#### APPENDIX 4: The Organic Structures of Biology 1057

#### APPENDIX 5: Pushing Electrons 1061

A5.1 The Rudiments of Pushing Electrons	1061
A5.2 Electron Sources and Sinks for Two-Electron Flow	1062
A5.3 How to Denote Resonance	1064
A5.4 Common Electron-Pushing Errors	1065
Backwards Arrow Pushing	1065
Not Enough Arrows	1065
Losing Track of the Octet Rule	1066
Losing Track of Hydrogens and Lone Pairs	1066
Not Using the Proper Source	1067
Mixed Media Mistakes	1067
Too Many Arrows—Short Cuts	1067

A5.5 Complex Reactions—Drawing a Chemically Reasonable Mechanism	1068
---	------

A5.6 Two Case Studies of Predicting Reaction Mechanisms	1069
--	------

A5.7 Pushing Electrons for Radical Reactions	1071
Practice Problems for Pushing Electrons	1073

#### APPENDIX 6: Reaction Mechanism Nomenclature 1075

#### Index 1079

## CHAPTER 1

- How Realistic are Formal Charges? 7  
NMR Coupling Constants 10  
Scaling Electrostatic Surface Potentials 15  
1-Fluorobutane 16  
Particle in a Box 21  
Resonance in the Peptide Amide Bond? 23  
A Brief Look at Symmetry and Symmetry Operations 29  
 $\text{CH}_5^+$ —Not Really a Well-Defined Structure 55  
Pyramidal Inversion:  $\text{NH}_3$  vs.  $\text{PH}_3$  57  
Stable Carbenes 59

## CHAPTER 2

- Entropy Changes During Cyclization Reactions 71  
A Consequence of High Bond Strength:  
    The Hydroxyl Radical in Biology 73  
The Half-Life for Homolysis of Ethane  
    at Room Temperature 73  
The Probability of Finding Atoms at Particular  
    Separations 75  
How do We Know That  $n = 0$  is Most Relevant  
    for Bond Stretches at  $T = 298\text{ K}$ ? 76  
Potential Surfaces for Bond Bending Motions 78  
How Big is 3 kcal/mol? 93  
Shouldn't Torsional Motions be Quantized? 94  
The Geometry of Radicals 96  
Differing Magnitudes of Energy Values in  
    Thermodynamics and Kinetics 100  
"Sugar Pucker" in Nucleic Acids 102  
Alternative Measurements of Steric Size 104  
The Use of  $A$  Values in a Conformational Analysis  
    Study for the Determination of Intramolecular  
    Hydrogen Bond Strength 105  
The NMR Time Scale 106  
Ring Fusion—Steroids 108  
A Conformational Effect on the Material Properties  
    of Poly(3-Alkylthiophenes) 116  
Cyclopropenyl Cation 117  
Cyclopropenyl Anion 118  
Porphyrins 119  
Protein Disulfide Linkages 123  
From Strained Molecules to Molecular Rods 126  
Cubane Explosives? 126  
Molecular Gears 128

## CHAPTER 3

- The Use of Solvent Scales to Direct Diels–Alder  
    Reactions 149  
The Use of Wetting and the Capillary Action  
    Force to Drive the Self-Assembly of  
    Macroscopic Objects 151  
The Solvent Packing Coefficient and  
    the 55% Solution 152  
Solvation Can Affect Equilibria 155  
A van't Hoff Analysis of the Formation of a  
    Stable Carbene 163

- The Strength of a Buried Salt Bridge 165  
The Angular Dependence of Dipole–Dipole Interactions—  
    The "Magic Angle" 168  
An Unusual Hydrogen Bond Acceptor 169  
Evidence for Weak Directionality Considerations 170  
Intramolecular Hydrogen Bonds are Best  
    for Nine-Membered Rings 170  
Solvent Scales and Hydrogen Bonds 172  
The Extent of Resonance can be Correlated with  
    Hydrogen Bond Length 174  
Cooperative Hydrogen Bonding in Saccharides 175  
How Much is a Hydrogen Bond in an  $\alpha$ -Helix Worth? 176  
Proton Sponges 179  
The Relevance of Low-Barrier Hydrogen Bonds  
    to Enzymatic Catalysis 179  
 $\beta$ -Peptide Foldamers 180  
A Cation– $\pi$  Interaction at the Nicotine Receptor 183  
The Polar Nature of Benzene Affects Acidities  
    in a Predictable Manner 184  
Use of the Arene–Perfluorarene Interaction in the  
    Design of Solid State Structures 185  
Donor–Acceptor Driven Folding 187  
The Hydrophobic Effect and Protein Folding 194  
More Foldamers: Folding Driven by  
    Solvophobic Effects 195  
Calculating Drug Binding Energies by SPT 201

## CHAPTER 4

- The Units of Binding Constants 209  
Cooperativity in Drug Receptor Interactions 215  
The Hill Equation and Cooperativity in  
    Protein–Ligand Interactions 219  
The Benesi–Hildebrand Plot 221  
How are Heat Changes Related to Enthalpy? 223  
Using the Helical Structure of Peptides and the  
    Complexation Power of Crowns to Create  
    an Artificial Transmembrane Channel 226  
Preorganization and the Salt Bridge 229  
A Clear Case of Entropy Driven Electrostatic  
    Complexation 229  
Salt Bridges Evaluated by Non-Biological Systems 230  
Does Hydrogen Bonding *Really* Play a Role in  
    DNA Strand Recognition? 233  
Calixarenes—Important Building Blocks for Molecular  
    Recognition and Supramolecular Chemistry 238  
Aromatics at Biological Binding Sites 239  
Combining the Cation– $\pi$  Effect and Crown Ethers 240  
A Thermodynamic Cycle to Determine the Strength  
    of a Polar– $\pi$  Interaction 242  
Molecular Mechanics/Modeling and Molecular  
    Recognition 243  
Biotin/Avidin: A Molecular Recognition/  
    Self-Assembly Tool from Nature 249  
Taming Cyclobutadiene—A Remarkable Use of  
    Supramolecular Chemistry 251

**CHAPTER 5**

- Using a pH Indicator to Sense Species Other Than the Hydronium Ion 264  
 Realistic Titrations in Water 265  
 An Extremely Acidic Medium is Formed During Photo-Initiated Cationic Polymerization in Photolithography 269  
 Super Acids Used to Activate Hydrocarbons 270  
 The Intrinsic Acidity Increase of a Carbon Acid by Coordination of  $\text{BF}_3$  276  
 Direct Observation of Cytosine Protonation During Triple Helix Formation 287  
 A Shift of the Acidity of an N–H Bond in Water Due to the Proximity of an Ammonium or Metal Cation 288  
 The Notion of Superelectrophiles Produced by Super Acids 289

**CHAPTER 6**

- Stereoisomerism and Connectivity 300  
 Total Synthesis of an Antibiotic with a Staggering Number of Stereocenters 303  
 The Descriptors for the Amino Acids Can Lead to Confusion 307  
 Chiral Shift Reagents 308  
 $\text{C}_2$  Ligands in Asymmetric Synthesis 313  
 Enzymatic Reactions, Molecular Imprints, and Enantiotopic Discrimination 320  
 Biological Knots—DNA and Proteins 325  
 Polypropylene Structure and the Mass of the Universe 331  
 Controlling Polymer Tacticity—The Metallocenes 332  
 CD Used to Distinguish  $\alpha$ -Helices from  $\beta$ -Sheets 335  
 Creating Chiral Phosphates for Use as Mechanistic Probes 335  
 A Molecular Helix Created from Highly Twisted Building Blocks 338

**CHAPTER 7**

- Single-Molecule Kinetics 360  
 Using the Arrhenius Equation to Determine Differences in Activation Parameters for Two Competing Pathways 370  
 Curvature in an Eyring Plot is Used as Evidence for an Enzyme Conformational Change in the Catalysis of the Cleavage of the Co–C Bond of Vitamin  $\text{B}_{12}$  371  
 Where TST May be Insufficient 374  
 The Transition States for  $\text{S}_{\text{N}}1$  Reactions 377  
 Comparing Reactivity to Selectivity in Free Radical Halogenation 378  
 Using the Curtin–Hammett Principle to Predict the Stereochemistry of an Addition Reaction 379  
 Applying the Principle of Microscopic Reversibility to Phosphate Ester Chemistry 380  
 Kinetic vs. Thermodynamic Enolates 382  
 Molecularity vs. Mechanism. Cyclization Reactions and Effective Molarity 384  
 First Order Kinetics: Delineating Between a Unimolecular and a Bimolecular Reaction of Cyclopentyne and Dienes 386  
 The Observation of Second Order Kinetics to Support a Multistep Displacement Mechanism for a Vitamin Analog 387

**Pseudo-First Order Kinetics: Revisiting the Cyclopentyne Example**

- 388  
 Zero Order Kinetics 393  
 An Organometallic Example of Using the SSA to Delineate Mechanisms 395  
 Saturation Kinetics That We Take for Granted— $\text{S}_{\text{N}}1$  Reactions 397  
 Prior Equilibrium in an  $\text{S}_{\text{N}}1$  Reaction 398  
 Femtochemistry: Direct Characterization of Transition States, Part I 400  
 “Seeing” Transition States, Part II: The Role of Computation 401  
 The Use of Pulse Radiolysis to Measure the  $\text{p}K_{\text{a}}$  of Protonated Ketol Anions 402  
 Discovery of the Marcus Inverted Region 406  
 Using a More O’Ferrall–Jencks Plot in Catalysis 410

**CHAPTER 8**

- The Use of Primary Kinetic Isotope Effects to Probe the Mechanism of Aliphatic Hydroxylation by Iron(III) Porphyrins 425  
 An Example of Changes in the Isotope Effect with Varying Reaction Free Energies 428  
 The Use of an Inverse Isotope Effect to Delineate an Enzyme Mechanism 431  
 An Ingenious Method for Measuring Very Small Isotope Effects 432  
 An Example of Tunneling in a Common Synthetic Organic Reaction 436  
 Using Fractionation Factors to Characterize Very Strong Hydrogen Bonds 439  
 The Use of a Proton Inventory to Explore the Mechanism of Ribonuclease Catalysis 440  
 A Substituent Effect Study to Decipher the Reason for the High Stability of Collagen 444  
 Using a Hammett Plot to Explore the Behavior of a Catalytic Antibody 450  
 An Example of a Change in Mechanism in a Solvolysis Reaction Studied Using  $\sigma^+$  452  
 A Swain–Lupton Correlation for Tungsten-Bipyridine-Catalyzed Allylic Alkylation 453  
 Using Taft Parameters to Understand the Structures of Cobaloximes; Vitamin  $\text{B}_{12}$  Mimics 455  
 The Use of the Schleyer Method to Determine the Extent of Nucleophilic Assistance in the Solvolysis of Arylvinyl Tosylates 459  
 The Use of Swain–Scott Parameters to Determine the Mechanism of Some Acetal Substitution Reactions 462  
 ATP Hydrolysis—How  $\beta_{\text{LG}}$  and  $\beta_{\text{Nuc}}$  Values Have Given Insight into Transition State Structures 465  
 How Can Some Groups be Both Good Nucleophiles and Good Leaving Groups? 466  
 An Example of an Unexpected Product 472  
 Designing a Method to Divert the Intermediate 473  
 Trapping a Phosphorane Legitimizes Its Existence 474  
 Checking for a Common Intermediate in Rhodium-Catalyzed Allylic Alkylations 475  
 Pyranoside Hydrolysis by Lysozyme 476  
 Using Isotopic Scrambling to Distinguish Exocyclic vs. Endocyclic Cleavage Pathways for a Pyranoside 478

- Determination of 1,4-Biradical Lifetimes Using a Radical Clock 480  
 The Identification of Intermediates from a Catalytic Cycle Needs to be Interpreted with Care 481

**CHAPTER 9**

- The Application of Figure 9.4 to Enzymes 494  
 High Proximity Leads to the Isolation of a Tetrahedral Intermediate 498  
 The Notion of "Near Attack Conformations" 499  
 Toward an Artificial Acetylcholinesterase 501  
 Metal and Hydrogen Bonding Promoted Hydrolysis of 2',3'-cAMP 502  
 Nucleophilic Catalysis of Electrophilic Reactions 503  
 Organocatalysis 505  
 Lysozyme 506  
 A Model for General-Acid-General-Base Catalysis 514  
 Anomalous Brønsted Values 519  
 Artificial Enzymes: Cyclodextrins Lead the Way 530

**CHAPTER 10**

- Cyclic Forms of Saccharides and Concerted Proton Transfers 545  
 Squalene to Lanosterol 550  
 Mechanisms of Asymmetric Epoxidation Reactions 558  
 Nature's Hydride Reducing Agent 566  
 The Captodative Effect 573  
 Stereoelectronics in an Acyl Transfer Model 579  
 The Swern Oxidation 580  
 Gas Phase Eliminations 588  
 Using the Curtin–Hammett Principle 593  
 Aconitase—An Enzyme that Catalyzes Dehydration and Rehydration 595  
 Enzymatic Acyl Transfers I: The Catalytic Triad 604  
 Enzymatic Acyl Transfers II: Zn(II) Catalysis 605  
 Enzyme Mimics for Acyl Transfers 606  
 Peptide Synthesis—Optimizing Acyl Transfer 606

**CHAPTER 11**

- Enolate Aggregation 631  
 Control of Stereochemistry in Enolate Reactions 636  
 Gas Phase S<sub>N</sub>2 Reactions—A Stark Difference in Mechanism from Solution 641  
 A Potential Kinetic Quandary 642  
 Contact Ion Pairs vs. Solvent-Separated Ion Pairs 647  
 An Enzymatic S<sub>N</sub>2 Reaction: Haloalkane Dehydrogenase 649  
 The Meaning of  $\beta_{LG}$  Values 651  
 Carbocation Rearrangements in Rings 658  
 Anchimeric Assistance in War 660  
 Further Examples of Hypervalent Carbon 666  
 Brominations Using N-Bromosuccinimide 673  
 An Enzymatic Analog to the Benzilic Acid Rearrangement: Acetohydroxy-Acid Isomeroeductase 677  
 Femtochemistry and Singlet Biradicals 693

**CHAPTER 12**

- Bonding Models 709  
 Electrophilic Aliphatic Substitutions (S<sub>E</sub>2 and S<sub>E</sub>1) 715  
 C–H Activation, Part I 722

- C–H Activation, Part II 723  
 The Sandmeyer Reaction 726  
 Olefin Slippage During Nucleophilic Addition to Alkenes 737  
 Pd(0) Coupling Reactions in Organic Synthesis 742  
 Stereocontrol at Every Step in Asymmetric Allylic Alkylations 745  
 Cyclic Rings Possessing Over 100,000 Carbons! 747

**CHAPTER 13**

- Monodisperse Materials Prepared Biosynthetically 756  
 An Analysis of Dispersity and Molecular Weight 757  
 A Melting Analysis 759  
 Protein Folding Modeled by a Two-State Polymer Phase Transition 762  
 Dendrimers, Fractals, Neurons, and Trees 769  
 Lyotropic Liquid Crystals: From Soap Scum to Biological Membranes 774  
 Organic Surfaces: Self-Assembling Monolayers and Langmuir–Blodgett Films 778  
 Free-Radical Living Polymerizations 787  
 Lycra/Spandex 790  
 Radical Copolymerization—Not as Random as You Might Think 792  
 PMMA—One Polymer with a Remarkable Range of Uses 793  
 Living Polymers for Better Running Shoes 795  
 Using <sup>13</sup>C NMR Spectroscopy to Evaluate Polymer Stereochemistry 797

**CHAPTER 14**

- The Hydrogen Atom 811  
 Methane—Molecular Orbitals or Discrete Single Bonds with sp<sup>3</sup> Hybrids? 827  
 Koopmans' Theorem—A Connection Between *Ab Initio* Calculations and Experiment 828  
 A Matrix Approach to Setting Up the LCAO Method 832  
 Through-Bond Coupling and Spin Preferences 861  
 Cyclobutadiene at the Two-Electron Level of Theory 862

**CHAPTER 15**

- Symmetry Does Matter 887  
 Allowed Organometallic [2+2] Cycloadditions 895  
 Semi-Empirical vs. *Ab Initio* Treatments of Pericyclic Transition States 900  
 Electrocyclization in Cancer Therapeutics 910  
 Fluxional Molecules 913  
 A Remarkable Substituent Effect: The Oxy-Cope Rearrangement 921  
 A Biological Claisen Rearrangement—The Chorismate Mutase Reaction 922  
 Hydrophobic Effects in Pericyclic Reactions 923  
 Pericyclic Reactions of Radical Cations 925

**CHAPTER 16**

- Excited State Wavefunctions 937  
 Physical Properties of Excited States 944  
 The Sensitivity of Fluorescence—Good News and Bad News 946  
 GFP, Part I: Nature's Fluorophore 947

- Isosbestic Points—Hallmarks of One-to-One Stoichiometric Conversions 949  
The “Free Rotor” or “Loose Bolt” Effect on Quantum Yields 953  
Single-Molecule FRET 961  
*Trans*-Cyclohexene? 967  
Retinal and Rhodopsin—The Photochemistry of Vision 968  
Photochromism 969  
UV Damage of DNA—A [2+2] Photoreaction 971  
Using Photochemistry to Generate Reactive Intermediates: Strategies Fast and Slow 983

- Photoaffinity Labeling—A Powerful Tool for Chemical Biology 984  
Light Sticks 987  
GFP, Part II: Aequorin 989  
Photodynamic Therapy 991

## CHAPTER 17

- Solitons in Polyacetylene 1015  
Scanning Probe Microscopy 1040  
Soft Lithography 1041