## Contents

**Preface**  IX

**Glossary and Abbreviations**  XI

### 1  Organic Synthesis: General Remarks  1

1.1  Introduction  1

1.2  Synthesis Design  2

1.2.1  Convergent vs Linear Syntheses  2

1.2.2  Retrosynthetic Analysis  3

1.3  Hard and Soft Acids and Bases  9

1.4  The Curtin–Hammett Principle  13

### 2  Stereoelectronic Effects and Reactivity  17

2.1  Hyperconjugation with $\sigma$ Bonds  17

2.2  Hyperconjugation with Lone Electron Pairs  19

2.2.1  Effects on Conformation  19

2.2.2  The Anomeric Effect  20

2.2.3  Effects on Spectra and Structure  21

2.3  Hyperconjugation and Reactivity  23

2.3.1  Basicity and Nucleophilicity  23

2.3.2  Rates of Oxidation  25

2.3.3  Rates of Deprotonation  26

2.3.4  Other Reactions  27

2.4  Conclusion  30

### 3  The Stability of Organic Compounds  35

3.1  Introduction  35

3.2  Strained Bonds  35

3.3  Incompatible Functional Groups  41

3.4  Conjugation and Hyperconjugation of Incompatible Functional Groups  42

3.5  Stability Toward Oxygen  45

3.5.1  Hydrogen Abstraction  45


3.5.2 Oxidation by SET 48
3.5.3 Addition of Oxygen to C–C Double Bonds 51
3.6 Detonations 52

4 Aliphatic Nucleophilic Substitutions: Problematic Electrophiles 59
4.1 Mechanisms of Nucleophilic Substitution 59
4.2 Structure of the Leaving Group 62
4.2.1 Good and Poor Leaving Groups 62
4.2.2 Nucleophilic Substitution of Fluoride 66
4.2.3 Nucleophilic Substitution of Sulfonates 70
4.3 Structure of the Electrophile 72
4.3.1 Steric Effects 72
4.3.2 Conjugation 75
4.3.3 Electrophiles with $\alpha$-Heteroatoms 79
4.3.4 Electrophiles with $\beta$-Heteroatoms 84
4.3.5 Electrophiles with $\alpha$-Electron-withdrawing Groups 86
4.3.6 Neighboring-group Participation 90
4.3.7 Allylic and Propargylic Electrophiles 93
4.3.8 Epoxides 97

5 The Alkylation of Carbanions 143
5.1 Introduction 143
5.2 The Kinetics of Deprotonations 144
5.3 Regioselectivity of Deprotonations and Alkylations 146
5.3.1 Introduction 146
5.3.2 Kinetic/Thermodynamic Enolate Formation 148
5.3.3 Allylic and Propargylic Carbanions 150
5.3.4 Succinic Acid Derivatives and Amide-derived Carbanions 155
5.3.5 Bridgehead Carbanions 157
5.3.6 Dianions 158
5.3.7 $\alpha$-Heteroatom Carbanions 161
5.3.8 Vinylic Carbanions 171
5.3.9 Acyl, Imidoyl, and Related Carbanions 173
5.3.10 Aromatic Carbanions 175
5.3.11 Aromatic vs Benzylic Deprotonation 180
5.4 The Stability of Carbanions 182
5.4.1 Introduction 182
5.4.2 $\alpha$-Elimination 183
5.4.3 $\beta$-Elimination 184
5.4.4 Cyclization 190
5.4.5 Rearrangement 193
5.4.6 Oxidation 195
5.4.7 Other Factors which Influence the Stability of Carbanions 196
5.4.8 Configurational Stability of Carbanions 197
<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.4</td>
<td>Ring Size</td>
<td>319</td>
</tr>
<tr>
<td>9.4.1</td>
<td>Formation of Cyclopropanes</td>
<td>321</td>
</tr>
<tr>
<td>9.4.2</td>
<td>Formation of Cyclobutanes</td>
<td>325</td>
</tr>
<tr>
<td>9.5</td>
<td>Heterocycles</td>
<td>327</td>
</tr>
<tr>
<td>10</td>
<td>Monofunctionalization of Symmetric Difunctional Substrates</td>
<td>333</td>
</tr>
<tr>
<td>10.1</td>
<td>Introduction</td>
<td>333</td>
</tr>
<tr>
<td>10.2</td>
<td>Monofunctionalization of Dicarboxylic Acids</td>
<td>334</td>
</tr>
<tr>
<td>10.3</td>
<td>Monofunctionalization of Diols</td>
<td>336</td>
</tr>
<tr>
<td>10.4</td>
<td>Monofunctionalization of Diamines</td>
<td>342</td>
</tr>
<tr>
<td>10.5</td>
<td>Monoalkylation of C,H-Acidic Compounds</td>
<td>346</td>
</tr>
<tr>
<td>10.6</td>
<td>Monoderivatization of Dihalides</td>
<td>348</td>
</tr>
</tbody>
</table>

**Index**  
355