To Rose
## CONTENTS

**Preface** xiii

**Preface to the First Edition** xv

1 **Functional Groups and Chemical Bonding** 1

- Functional Groups / 1
- Orbitals / 5
- Bonding Schemes / 7
- Antibonding Orbitals / 13
- Resonance / 18
- Conjugated \( \pi \) Systems / 21
- Aromaticity / 23
- Bibliography / 26
- Problems / 27

2 **Oxidation States of Organic Compounds** 32

- Oxidation Levels / 32
- Oxidation States in Alkanes / 34
- Oxidation States in Alkenes / 34
- Oxidation States in Common Functional Groups / 35
- Oxidation Level Changes During Reactions / 35
- Bibliography / 41
- Problems / 41

3 **Acidity and Basicity** 47

- Bronsted and Lewis Acids and Bases / 47
- Acid Strength / 49
- Acid–Base Equilibria / 53
4 Curved-Arrow Notation

Electron Movement / 69
Heterolytic Bond Cleavages / 70
Heterolytic Bond Formation / 71
Homolytic Bond Making and Bond Breaking / 73
Resonance Structures / 75
Depiction of Mechanism / 76
Bibliography / 82
Problems / 82

5 Mechanisms of Organic Reactions

Activation Energy / 87
Activated Complex / 88
Reaction Energetics / 89
Structure of the Activated Complex / 91
Hammond Postulate / 96
Reaction Kinetics / 99
Determining Activation Energies / 104
Isotope Effects / 105
Electronic Effects / 110
Hammett Equation / 111
Bibliography / 118
Problems / 118

6 Stereochemical and Conformational Isomerism

Stereochemical Structures / 125
Chirality / 128
Configuration of Chiral Centers / 129
Multiple Stereocenters / 132
Optical Activity / 137
Absolute Configuration / 138
Physical Properties of Enantiomers / 139
Resolution of Enantiomers / 140
Stereoselective Reactions / 144
Formation of Enantiomers / 144  
Formation of Diastereomers / 146  
Stereochemistry to Deduce Mechanism / 152  
Conformational Analysis / 157  
Conformational Energies / 164  
$A$ Values / 166  
Strain in Ring Systems / 167  
Stereoelectronic Effects / 172  
Bibliography / 176  
Problems / 176  

7 Functional Group Synthesis 183  
Functional Group Manipulation / 183  
Carboxylic Acids / 185  
Esters / 188  
Amides / 190  
Acid Chlorides / 191  
Aldehydes / 192  
Ketones / 194  
Imines and Imine Derivatives / 197  
Alcohols / 198  
Amines / 201  
Alkenes / 203  
Alkanes / 207  
Bibliography / 208  
Problems / 209  

8 Carbon–Carbon Bond Formation between Carbon Nucleophiles and Carbon Electrophiles 216  
Synthetic Strategy / 217  
Nucleophilic Carbon / 218  
Electrophilic Carbon / 220  
Reactivity Matching / 223  
Generation of Nucleophilic Carbon Reagents / 224  
Generation of Electrophilic Carbon Reagents / 227  
Matching Nucleophiles with Electrophiles / 227  
Enolates / 228  
Enolate Regioisomers / 234  
Diastereoselection in Aldol Reactions / 236  
Organometallic Compounds / 239  
Neutral Carbon Nucleophiles / 239  
C=C Formation / 242  
Cyclopropanation Reactions / 244
9 Carbon–Carbon Bond Formation by Free-Radical Reactions 272

Free-Radical Reactions / 272
Free-Radical Polymerization / 277
Nonpolymerization Reactions / 278
Free-Radical Initiation / 280
Free-Radical Cyclization / 283
Bibliography / 288
Problems / 288

10 Planning Organic Syntheses 292

Retrosynthetic Analysis / 292
Carbon Skeleton Synthesis / 296
Umpolung Synthons / 302
Acetylide Nucleophiles / 305
Ring Construction / 306
Robinson Annulation / 310
Diels–Alder Reaction / 312
HOMO–LUMO Interactions / 313
Stereoelectronic Factors / 316
1,3-Dipolar Cycloadditions / 319
Bibliography / 323
Problems / 324

11 Structure Determination of Organic Compounds 332

Structure Determination / 332
Chromatographic Purification / 333
Instrumental Methods / 335
Nuclear Magnetic Resonance / 336
Chemical Shift / 338
Spin–Spin Coupling / 344
Descriptions of Spin Systems / 350
In keeping with a mechanistic emphasis, the book was reorganized. The chapter on mechanism is now Chapter 5 instead of Chapter 10. Thus the first six chapters focus on the mechanistic and structural underpinnings of organic chemistry. Synthetic aspects of organic chemistry are then discussed from a mechanistic and structural point of view. Several new sections have been added and others expanded. An expanded discussion of resonance and aromaticity is found in Chapter 1. A section on organopalladium chemistry and olefin metathesis has been added to Chapter 8 as they relate to current methods of carbon–carbon bond formation. Chapter 9 on free-radical reactions for carbon–carbon bond formation has been revised. The discussion of Diels–Alder chemistry has been moved to Chapter 10 and expanded. A number of new problems have been added which serve to further illustrate the principles developed in each chapter. Finally, thanks to input from many people who have read this text and taught from it, the discussion has been further honed and errors corrected.

What has evolved is a greater initial emphasis of the mechanistic and structural approach to organic chemistry. The application of these principles in a discussion of modern synthetic methodology (functional group manipulation, carbon–carbon bond formation, retrosynthetic analysis) provides a new organizational framework for understanding many of the most common and most important synthetic reactions.

What has not changed is the premise that this text is meant to provide the tools students need to master the material in advanced courses or compete successfully in the workplace.

ROBERT V. HOFFMAN
PREFACE TO THE FIRST EDITION

This text was inspired by two observations. The first is that many entering graduate students took organic chemistry as sophomores but since that time have had little exposure to organic chemistry in a formal sense. Because of this time lapse in their organic preparation, they often have difficulty performing well when placed directly into mainstream graduate level organic courses. What is much more effective is to first place them in a course which will bring them back up to speed in basic organic chemistry and at the same time introduce many of the advanced topics which are crucial to understanding current advances in the field. A course well suited for this purpose is a one-semester, advanced organic course at the senior undergraduate/beginning graduate level. Most departments, including ours, have such a course in place. Textbook selection for this course is problematic, however. If one of the standard advanced texts is used, only a small part is actually covered and students are not prepared to master the complexities, whereas if an undergraduate text is used, it often fails to push the students to the next level. Consequently, there is a real need for a one-semester text which gives a review of basic principles in addition to an exposure to the ideas which are currently of great importance in organic chemistry. This text was written to fill this need.

A second observation instrumental in shaping the approach of this text was made during group discussions of the organic faculty and students. One common exercise is to present practice cumulative exam problems to the group and discuss ways in which they might be solved. It is very common for the students to analyze the question in terms of reactions and transformations and try to arrive at a solution based on the question as written. On the other hand, it is very common for the faculty to ask very simple questions first—for example, “What is the oxidation change?” “What is the $pK_a$ of the acid and what is the base?” and “What stereochemical changes occur?” It is clear that more experienced organic chemists begin from a very basic point of view and progress to a more complex solution, whereas novice organic chemists tend to jump in at a much more difficult level. It thus appears very important to initially emphasize the basic principles on which organic chemistry depends and then progress to more specialized topics, all the while emphasizing their relationship to the basic principles. This text utilizes this organizational approach.
The result is a textbook designed for a one-semester advanced organic chemistry course. First and foremost it is a textbook and not a reference text. There is plenty of material to fill a semester, but it is not comprehensive in its coverage. Topics were chosen to provide a basic and well-rounded discussion of ideas important in modern organic chemistry and to provide students with the necessary tools to succeed in more specialized advanced courses. It is a book to be taught from; thus instructors should take the opportunity to include special or favorite topics at appropriate points. References to alternative textbook and literature reviews of the subjects are included so that students can go to the library and get a different explanation. This is important for encouraging students to do library work as a means to independently gain insight and understanding. Finally, there are abundant problems included at the end of each chapter so that students can practice applying what they are learning. Working problems is the single most effective way to learn and organize the large amount of information that is encountered in organic chemistry, so there are a large number of practice problems available at all levels of difficulty.

The goal of this text is to provide senior undergraduate students the organic background required to move on successfully in their careers. For beginning graduate students lacking this background, it provides a succinct yet rigorous preparation for advanced organic courses.

R.V.H.