

GLOBAL
EDITION



Organic Chemistry

EIGHTH EDITION

Paula Yurkanis Bruice



ALWAYS LEARNING

PEARSON

To the Student

Welcome to the fascinating world of organic chemistry. You are about to embark on an exciting journey. This book has been written with students like you in mind—those who are encountering the subject for the first time. The book's central goal is to make this journey through organic chemistry both stimulating and enjoyable by helping you understand central principles and asking you to apply them as you progress through the pages. You will be reminded about these principles at frequent intervals in references back to sections you have already mastered.

You should start by familiarizing yourself with the book. At the back of the book is information you may want to refer to often during the course. The list of Some Important Things to Remember and the Reaction Summary at each chapter's end provide helpful checklists of the concepts you should understand after studying the chapter. The Glossary at the end of the book can also be a useful study aid, as can the Appendices, which consolidate useful categories of information. The molecular models and electrostatic potential maps that you will find throughout the book are provided to give you an appreciation of what molecules look like in three dimensions and to show how charge is distributed within a molecule. Think of the margin notes as the author's opportunity to inject personal reminders of ideas and facts that are important to remember. Be sure to read them.

Work all the problems *within* each chapter. These are drill problems that you will find at the end of each section that allow you to check whether you have mastered the skills and concepts the particular section is teaching before you go on to the next section. Some of these problems are solved for you in the text. Short answers to some of the others—those marked with a diamond—are provided at the end of the book. Do not overlook the “Problem-Solving Strategies” that are also sprinkled throughout the text; they provide practical suggestions on the best way to approach important types of problems.

In addition to the *within-chapter* problems, work as many *end-of-chapter* problems as you can. The more problems you work, the more comfortable you will be with the subject matter and the better prepared you will be for the material in subsequent chapters. Do not let any problem frustrate you. Be sure to visit www.MasteringChemistry.com, where you can explore study tools including Exercise Sets, an Interactive Molecular Gallery, and Biographical Sketches of historically important chemists, and where you can access content on many important topics.

The most important advice to remember (and follow) in studying organic chemistry is DO NOT FALL BEHIND! The individual steps to learning organic chemistry are quite simple; each by itself is relatively easy to master. But they are numerous, and the subject can quickly become overwhelming if you do not keep up.

The key to succeeding in this course is paying attention to unifying principles. Before many of the theories and mechanisms were figured out, organic chemistry was a discipline that could be mastered only through memorization. Fortunately, that is no longer true. You will find many unifying principles that allow you to use what you have learned in one situation to predict what will happen in other situations. So, as you read the book and study your notes, always make sure that you understand *why* each chemical event or behavior happens. For example, when the reasons behind reactivity are understood, most reactions can be predicted. Approaching the course with the misconception that to succeed you must memorize hundreds of unrelated reactions could be your downfall. There is simply too much material to memorize. Understanding and reasoning, not memorization, provide the necessary foundation on which to lay subsequent learning. Nevertheless, from time to time some memorization will be required: some fundamental rules will have to be memorized, and you will need to learn the common names of a number of organic compounds. But that should not be a problem; after all, your friends have common names that you have been able to learn and remember.

Students who study organic chemistry to gain entrance into medical school sometimes wonder why medical schools pay so much attention to this topic. The importance of organic chemistry is not in the subject matter alone, however. Mastering organic chemistry requires a thorough understanding of certain fundamental principles and the ability to use those fundamentals to analyze, classify, and predict. The study of medicine makes similar demands: a physician uses an understanding of certain fundamental principles to analyze, classify, and diagnose.

Good luck in your study. I hope you will enjoy studying organic chemistry and learn to appreciate the logic of this fascinating discipline. If you have any comments about the book or any suggestions for improving it, I would love to hear from you. Remember, positive comments are the most fun, but negative comments are the most useful.

Paula Yurkanis Bruice

Organic Chemistry, Global Edition

Table of Contents

Cover

Title Page

Copyright Page

Preface

ACKNOWLEDGMENTS

About the Author

Contents

PART ONE: An Introduction to the Study of Organic Chemistry

1 Remembering General Chemistry: Electronic Structure and Bonding

CHEMICAL CONNECTION: Natural versus Synthetic Organic Compounds

1.1 The Structure of an Atom

1.2 How the Electrons in an Atom are Distributed

1.3 Covalent Bonds

1.4 How the Structure of a Compound is Represented

PROBLEM-SOLVING STRATEGY

1.5 Atomic Orbitals

1.6 An Introduction to Molecular Orbital Theory

1.7 How Single Bonds are Formed in Organic Compounds

1.8 How a Double Bond is Formed: The Bonds in Ethene

CHEMICAL CONNECTION: Diamond, Graphite, Graphene, and Fullerenes: Substances that Contain Only Carbon Atoms

1.9 How a Triple Bond is Formed: The Bonds in Ethyne

1.10 The Bonds in the Methyl Cation, the Methyl Radical, and the Methyl Anion

1.11 The Bonds in Ammonia and in the Ammonium Ion

1.12 The Bonds in Water

CHEMICAL CONNECTION: WaterA Unique Compound

1.13 The Bond in a Hydrogen Halide

1.14 Hybridization and Molecular Geometry

PROBLEM-SOLVING STRATEGY

1.15 Summary: Hybridization, Bond Lengths, Bond Strengths, and Bond Angles

PROBLEM-SOLVING STRATEGY

1.16 Dipole Moments of Molecules

Table of Contents

ESSENTIAL CONCEPTS

PROBLEMS

2 Acids and Bases: Central to Understanding Organic Chemistry

2.1 An Introduction to Acids and Bases

2.2 pK_{a} and pH

PROBLEM-SOLVING STRATEGY

CHEMICAL CONNECTION: Acid Rain

2.3 Organic Acids and Bases

BIOLOGICAL CONNECTION: Poisonous Amines

PROBLEM-SOLVING STRATEGY

2.4 How to Predict the Outcome of an Acid-Base Reaction

2.5 How to Determine the Position of Equilibrium

2.6 How the Structure of an Acid Affects its pK_{a} Value

2.7 How Substituents Affect the Strength of an Acid

PROBLEM-SOLVING STRATEGY

2.8 An Introduction to Delocalized Electrons

PROBLEM-SOLVING STRATEGY

MEDICAL CONNECTION: Fosamax Prevents Bones from Being Nibbled Away

2.9 A Summary of the Factors that Determine Acid Strength

2.10 How pH Affects the Structure of an Organic Compound

PROBLEM-SOLVING STRATEGY

CHEMICAL CONNECTION: Derivation of the Henderson-Hasselbalch Equation

MEDICAL CONNECTION: Aspirin Must Be in its Basic Form to be Physiologically Active

2.11 Buffer Solutions

MEDICAL CONNECTION: Blood: A Buffered Solution

2.12 Lewis Acids and Bases

ESSENTIAL CONCEPTS

PROBLEMS

TUTORIAL Acids and Bases

3 An Introduction to Organic Compounds: Nomenclature, Physical Properties, and Structure

3.1 Alkyl Groups

3.2 The Nomenclature of Alkanes

INDUSTRIAL CONNECTION: How is the Octane Number of Gasoline Determined?

3.3 The Nomenclature of Cycloalkanes

PROBLEM-SOLVING STRATEGY

3.4 The Nomenclature of Alkyl Halides

3.5 The Nomenclature of Ethers

3.6 The Nomenclature of Alcohols

Table of Contents

3.7 The Nomenclature of Amines

CHEMICAL CONNECTION: Bad-Smelling Compounds

3.8 The Structures of Alkyl Halides, Alcohols, Ethers, and Amines

3.9 Noncovalent Interactions

PROBLEM-SOLVING STRATEGY

MEDICAL CONNECTION: Drugs Bind to Their Receptors

3.10 The Solubility of Organic Compounds

BIOLOGICAL CONNECTION: Cell Membranes

3.11 Rotation Occurs about CarbonCarbon Single Bonds

3.12 Some Cycloalkanes Have Angle Strain

CHEMICAL CONNECTION: Von Baeyer, Barbituric Acid, and Blue Jeans

PROBLEM-SOLVING STRATEGY

3.13 Conformers of Cyclohexane

3.14 Conformers of Monosubstituted Cyclohexanes

CHEMICAL CONNECTION: Starch and CelluloseAxial and Equatorial

3.15 Conformers of Disubstituted Cyclohexanes

PROBLEM-SOLVING STRATEGY

PROBLEM-SOLVING STRATEGY

3.16 Fused Cyclohexane Rings

MEDICAL CONNECTION: Cholesterol and Heart Disease

MEDICAL CONNECTION: How High Cholesterol is Treated Clinically

ESSENTIAL CONCEPTS

PROBLEMS

PART TWO: Electrophilic Addition Reactions, Stereochemistry, and Electron Delocalization

TUTORIAL Using Molecular Models

4 Isomers: The Arrangement of Atoms in Space

4.1 CisTrans Isomers Result from Restricted Rotation

CHEMICAL CONNECTION: Cis-Trans Interconversion in Vision

4.2 Using the E,Z System to Distinguish Isomers

PROBLEM-SOLVING STRATEGY

4.3 A Chiral Object Has a Nonsuperimposable Mirror Image

4.4 An Asymmetric Center is a Cause of Chirality in a Molecule

4.5 Isomers with One Asymmetric Center

4.6 Asymmetric Centers and Stereocenters

4.7 How to Draw Enantiomers

4.8 Naming Enantiomers by the R,S System

PROBLEM-SOLVING STRATEGY

Table of Contents

PROBLEM-SOLVING STRATEGY

4.9 Chiral Compounds Are Optically Active

4.10 How Specific Rotation Is Measured

4.11 Enantiomeric Excess

4.12 Compounds with More than One Asymmetric Center

4.13 Stereoisomers of Cyclic Compounds

PROBLEM-SOLVING STRATEGY

4.14 Meso Compounds Have Asymmetric Centers but Are Optically Inactive

PROBLEM-SOLVING STRATEGY

4.15 How to Name Isomers with More than One Asymmetric Center

PROBLEM-SOLVING STRATEGY

4.16 Nitrogen and Phosphorus Atoms Can Be Asymmetric Centers

4.17 Receptors

MEDICAL CONNECTION: The Enantiomers of Thalidomide

4.18 How Enantiomers Can Be Separated

PHARMACEUTICAL CONNECTION: Chiral Drugs

ESSENTIAL CONCEPTS

PROBLEMS

TUTORIAL Interconverting Structural Representations

5 Alkenes: Structure, Nomenclature, and an Introduction to Reactivity Thermodynamics and Kinetics

ENVIRONMENTAL CONNECTION: Pheromones

5.1 Molecular Formulas and the Degree of Unsaturation

5.2 The Nomenclature of Alkenes

5.3 The Structure of Alkenes

PROBLEM-SOLVING STRATEGY

5.4 How An Organic Compound Reacts Depends on Its Functional Group

5.5 How Alkenes React Curved Arrows Show the Flow of Electrons

GENERAL CONNECTION: A Few Words About Curved Arrows

5.6 Thermodynamics: How Much Product is Formed?

5.7 Increasing the Amount of Product Formed in a Reaction

5.8 Calculating ΔH° Values

5.9 Using ΔH° Values to Determine the Relative Stabilities of Alkenes

PROBLEM-SOLVING STRATEGY

NUTRITIONAL CONNECTION: Trans Fats

5.10 Kinetics: How Fast is the Product Formed?

5.11 The Rate of a Chemical Reaction

CHEMICAL CONNECTION: The Difference between 5.11 The Rate of a Chemical Reaction ΔG° and E_a

Table of Contents

5.12 A Reaction Coordinate Diagram Describes the Energy Changes That Take Place During a Reaction

5.13 Catalysis

5.14 Catalysis by Enzymes

ESSENTIAL CONCEPTS

PROBLEMS

CHEMICAL CONNECTION: Calculating Kinetic Parameters

TUTORIAL Drawing Curved Arrows

6 The Reactions of Alkenes The Stereochemistry of Addition Reactions

6.1 The Addition of a Hydrogen Halide to an Alkene

6.2 Carbocation Stability Depends on the Number of Alkyl Groups Attached to the Positively Charged Carbon

6.3 What Does the Structure of the Transition State Look Like?

6.4 Electrophilic Addition Reactions Are Regioselective

PROBLEM-SOLVING STRATEGY

6.5 The Addition of Water to an Alkene

6.6 The Addition of an Alcohol to an Alkene

6.7 A Carbocation Will Rearrange if It Can Form a More Stable Carbocation

6.8 The Addition of Borane to an Alkene: HydroborationOxidation

CHEMICAL CONNECTION: Borane and Diborane

6.9 The Addition of a Halogen to an Alkene

PROBLEM-SOLVING STRATEGY

6.10 The Addition of a Peroxyacid to an Alkene

6.11 The Addition of Ozone to an Alkene: Ozonolysis

PROBLEM-SOLVING STRATEGY

6.12 Regioselective, Stereoselective, And Stereospecific Reactions

6.13 The Stereochemistry of Electrophilic Addition Reactions

CHEMICAL CONNECTION: Cyclic Alkenes

PROBLEM-SOLVING STRATEGY

6.14 The Stereochemistry of Enzyme-Catalyzed Reactions

6.15 Enantiomers Can Be Distinguished by Biological Molecules

CHEMICAL CONNECTION: Chiral Catalysts

6.16 Reactions and Synthesis

ENVIRONMENTAL CONNECTION: Which are More Harmful: Natural Pesticides or Synthetic Pesticides?

ESSENTIAL CONCEPTS

SUMMARY OF REACTIONS

PROBLEMS

7 The Reactions of Alkynes An Introduction to Multistep Synthesis

MEDICAL CONNECTION: Synthetic Alkynes Are Used to Treat Parkinson's Disease

Table of Contents

PHARMACEUTICAL CONNECTION: Why Are Drugs so Expensive?

7.1 The Nomenclature of Alkynes

MEDICAL CONNECTION: Synthetic Alkynes Are Used for Birth Control

7.2 How to Name a Compound That Has More than One Functional Group

7.3 The Structure of Alkynes

BIOLOGICAL CONNECTION: How a Banana Slug Knows What to Eat

7.4 The Physical Properties of Unsaturated Hydrocarbons

7.5 The Reactivity of Alkynes

7.6 The Addition of Hydrogen Halides and the Addition of Halogens to an Alkyne

7.7 The Addition of Water to an Alkyne

7.8 The Addition of Borane to an Alkyne: HydroborationOxidation

7.9 The Addition of Hydrogen to an Alkyne

7.10 A Hydrogen Bonded to an sp Carbon Is "Acidic"

CHEMICAL CONNECTION: Sodium Amide and Sodium in Ammonia

PROBLEM-SOLVING STRATEGY

7.11 Synthesis Using Acetylide Ions

7.12 DESIGNING A SYNTHESIS I: An Introduction to Multistep Synthesis

ENVIRONMENTAL CONNECTION: Green Chemistry: Aiming for Sustainability

ESSENTIAL CONCEPTS

SUMMARY OF REACTIONS

PROBLEMS

8 Delocalized Electrons: Their Effect on Stability, pK_{a} , and the Products of a Reaction Aromaticity and Electronic Effects: An Introduction to the Reactions of Benzene

8.1 Delocalized Electrons Explain Benzene's Structure

HISTORICAL CONNECTION: Kekule's Dream

8.2 The Bonding in Benzene

8.3 Resonance Contributors and the Resonance Hybrid

8.4 How to Draw Resonance Contributors

BIOLOGICAL CONNECTION: Electron Delocalization Affects the Three-Dimensional Shape of Proteins

8.5 The Predicted Stabilities of Resonance Contributors

PROBLEM-SOLVING STRATEGY

8.6 Delocalization Energy is the Additional Stability Delocalized Electrons Give to a Compound

8.7 Delocalized Electrons Increase Stability

INDUSTRIAL CONNECTION: Organic Compounds That Conduct Electricity

8.8 A Molecular Orbital Description of Stability

8.9 Delocalized Electrons Affect pK_{a} Values

PROBLEM-SOLVING STRATEGY

8.10 Electronic Effects

Table of Contents

8.11 Delocalized Electrons Can Affect the Product of a Reaction

8.12 Reactions of Dienes

8.13 Thermodynamic Versus Kinetic Control

8.14 The DielsAlder Reaction is a 1,4-Addition Reaction

8.15 Retrosynthetic Analysis of the DielsAlder Reaction

8.16 Benzene is an Aromatic Compound

8.17 The Two Criteria for Aromaticity

8.18 Applying the Criteria for Aromaticity

CHEMICAL CONNECTION: Buckyballs

PROBLEM-SOLVING STRATEGY

8.19 A Molecular Orbital Description of Aromaticity

8.20 Aromatic Heterocyclic Compounds

8.21 How Benzene Reacts

8.22 Organizing What We Know About the Reactions of Organic Compounds (Group I)

ESSENTIAL CONCEPTS

SUMMARY OF REACTIONS

PROBLEMS

TUTORIAL Drawing Resonance Contributors

PART THREE: Substitution and Elimination Reactions

9 Substitution and Elimination Reactions of Alkyl Halides

ENVIRONMENTAL CONNECTION: The Birth of the Environmental Movement

9.1 The S_N2 Reaction

9.2 Factors That Affect S_N2 Reactions

CHEMICAL CONNECTION: Why Are Living Organisms Composed of Carbon Instead of Silicon?

9.3 The S_N1 Reaction

9.4 Factors That Affect S_N1 Reactions

9.5 Competition Between S_N2 and S_N1 Reactions

PROBLEM-SOLVING STRATEGY

BIOLOGICAL CONNECTION: Naturally Occurring Alkyl Halides That Defend Against Predators

9.6 Elimination Reactions of Alkyl Halides

9.7 The E2 Reaction

9.8 The E1 Reaction

PROBLEM-SOLVING STRATEGY

9.9 Competition Between E2 and E1 Reactions

9.10 E2 and E1 Reactions are Stereoselective

PROBLEM-SOLVING STRATEGY

9.11 Elimination from Substituted Cyclohexanes

9.12 Predicting the Products of the Reaction of an Alkyl Halide with a Nucleophile/Base

Table of Contents

9.13 Benzylic Halides, Allylic Halides, Vinylic Halides, and Aryl Halides

PROBLEM-SOLVING STRATEGY

PROBLEM-SOLVING STRATEGY

9.14 Solvent Effects

CHEMICAL CONNECTION: Solvation Effects

ENVIRONMENTAL CONNECTION: Environmental Adaptation

9.15 Substitution and Elimination Reactions in Synthesis

9.16 Intermolecular Versus Intramolecular Reactions

PROBLEM-SOLVING STRATEGY

9.17 DESIGNING A SYNTHESIS II: Approaching the Problem

ESSENTIAL CONCEPTS

SUMMARY OF REACTIONS

PROBLEMS

10 Reactions of Alcohols, Ethers, Epoxides, Amines, and Sulfur-Containing Compounds

10.1 Nucleophilic Substitution Reactions of Alcohols: Forming Alkyl Halides

CHEMICAL CONNECTION: The Lucas Test

GENERAL CONNECTION: Grain Alcohol and Wood Alcohol

10.2 Other Methods Used to Convert Alcohols into Alkyl Halides

10.3 Converting an Alcohol Into a Sulfonate Ester

10.4 Elimination Reactions of Alcohols: Dehydration

PROBLEM-SOLVING STRATEGY

BIOLOGICAL CONNECTION: Biological Dehydrations

10.5 Oxidation of Alcohols

GENERAL CONNECTION: Blood Alcohol Concentration

MEDICAL CONNECTION: Treating Alcoholism with Antabuse

MEDICAL CONNECTION: Methanol Poisoning

10.6 Nucleophilic Substitution Reactions of Ethers

MEDICAL CONNECTION: Anesthetics

10.7 Nucleophilic Substitution Reactions of Epoxides

CHEMICAL CONNECTION: Crown Ethers Another Example of Molecular Recognition

CHEMICAL CONNECTION: Crown Ethers Can be Used to Catalyze S_N2 Reactions

10.8 Arene Oxides

ENVIRONMENTAL CONNECTION: Benzo[a]pyrene and Cancer

ENVIRONMENTAL CONNECTION: Chimney Sweeps and Cancer

10.9 Amines Do Not Undergo Substitution or Elimination Reactions

BIOLOGICAL CONNECTION: Alkaloids

PHARMACEUTICAL CONNECTION: Lead Compounds for the Development of Drugs

10.10 Quaternary Ammonium Hydroxides Undergo Elimination Reactions

10.11 Thiols, Sulfides, and Sulfonium Ions

HISTORICAL CONNECTION: Mustard Gas A Chemical Warfare Agent

Table of Contents

MEDICAL CONNECTION: Alkylating Agents as Cancer Drugs

10.12 Methylating Agents Used by Chemists versus Those Used by Cells

CHEMICAL CONNECTION: Eradicating Termites

MEDICAL CONNECTION: S-Adenosylmethionine: A Natural Antidepressant

10.13 Organizing What We Know About the Reactions of Organic Compounds (Group II)

ESSENTIAL CONCEPTS

SUMMARY OF REACTIONS

PROBLEMS

11 Organometallic Compounds

11.1 Organolithium and Organomagnesium Compounds

11.2 Transmetallation

11.3 Organocuprates

11.4 Palladium-Catalyzed Coupling Reactions

PROBLEM-SOLVING STRATEGY

11.5 Alkene Metathesis

HISTORICAL CONNECTION: Grubbs, Schrock, Suzuki, and Heck Receive the Nobel Prize

HISTORICAL CONNECTION: The Nobel Prize

ESSENTIAL CONCEPTS

SUMMARY OF REACTIONS

PROBLEMS

12 Radicals

12.1 Alkanes are Unreactive Compounds

GENERAL CONNECTION: Natural Gas and Petroleum

GENERAL CONNECTION: Fossil Fuels: A Problematic Energy Source

12.2 The Chlorination and Bromination of Alkanes

HISTORICAL CONNECTION: Why Radicals No Longer Have to Be Called Free Radicals

12.3 Radical Stability Depends on the Number of Alkyl Groups Attached to the Carbon with the Unpaired Electron

12.4 The Distribution of Products Depends on Probability and Reactivity

12.5 The ReactivitySelectivity Principle

PROBLEM-SOLVING STRATEGY

12.6 Formation of Explosive Peroxides

12.7 The Addition of Radicals to an Alkene

12.8 The Stereochemistry of Radical Substitution and Radical Addition Reactions

12.9 Radical Substitution of Allylic and Benzylic Hydrogens

CHEMICAL CONNECTION: Cyclopropane

12.10 DESIGNING A SYNTHESIS III: More Practice with Multistep Synthesis

12.11 Radical Reactions in Biological Systems

NUTRITIONAL CONNECTION: Decaffeinated Coffee and the Cancer Scare

Table of Contents

NUTRITIONAL CONNECTION: Food Preservatives

NUTRITIONAL CONNECTION: Is Chocolate a Health Food?

12.12 Radicals and Stratospheric Ozone

MEDICAL CONNECTION: Artificial Blood

ESSENTIAL CONCEPTS

SUMMARY OF REACTIONS

PROBLEMS

TUTORIAL Drawing Curved Arrows in Radical Systems

PART FOUR: Identification of Organic Compounds

13 Mass Spectrometry; Infrared Spectroscopy; UV/Vis Spectroscopy

13.1 Mass Spectrometry

13.2 The Mass Spectrum Fragmentation

13.3 Using The m/z Value of the Molecular Ion to Calculate the Molecular Formula

PROBLEM-SOLVING STRATEGY

13.4 Isotopes in Mass Spectrometry

13.5 High-Resolution Mass Spectrometry Can Reveal Molecular Formulas

13.6 The Fragmentation Patterns of Functional Groups

13.7 Other Ionization Methods

13.8 Gas ChromatographyMass Spectrometry

GENERAL CONNECTION: Mass Spectrometry in Forensics

13.9 Spectroscopy and the Electromagnetic Spectrum

13.10 Infrared Spectroscopy

13.11 Characteristic Infrared Absorption Bands

13.12 The Intensity of Absorption Bands

13.13 The Position of Absorption Bands

GENERAL CONNECTION: The Originator of Hooke's Law

13.14 The Position and Shape of an Absorption Band is Affected by Electron Delocalization and Hydrogen Bonding

PROBLEM-SOLVING STRATEGY

13.15 C-H Absorption Bands

13.16 The Absence of Absorption Bands

13.17 Some Vibrations are Infrared Inactive

13.18 How to Interpret an Infrared Spectrum

13.19 Ultraviolet and Visible Spectroscopy

GENERAL CONNECTION: Ultraviolet Light and Sunscreens

13.20 The BeerLambert Law

13.21 The Effect of Conjugation on ϵ_{max}

13.22 The Visible Spectrum and Color

Table of Contents

CHEMICAL CONNECTION: What Makes Blueberries Blue and Strawberries Red?

13.23 Some Uses of UV/Vis Spectroscopy

ESSENTIAL CONCEPTS

PROBLEMS

14 NMR Spectroscopy

14.1 An Introduction to NMR Spectroscopy

HISTORICAL CONNECTION: Nikola Tesla (1856-1943)

14.2 Fourier Transform NMR

14.3 Shielding Causes Different Nuclei to Show Signals at Different Frequencies

14.4 The Number of Signals in an ^1H NMR Spectrum

PROBLEM-SOLVING STRATEGY

14.5 The Chemical Shift Tells How Far the Signal Is from the Reference Signal

14.6 The Relative Positions of ^1H NMR Signals

14.7 The Characteristic Values of Chemical Shifts

14.8 Diamagnetic Anisotropy

14.9 The Integration of NMR Signals Reveals the Relative Number of Protons Causing Each Signal

14.10 The Splitting of Signals Is Described by the $N + 1$ Rule

14.11 What Causes Splitting?

14.12 More Examples of ^1H NMR Spectra

14.13 Coupling Constants Identify Coupled Protons

PROBLEM-SOLVING STRATEGY

14.14 Splitting Diagrams Explain the Multiplicity of a Signal

14.15 Enantiotopic and Diastereotopic Hydrogens

14.16 The Time Dependence of NMR Spectroscopy

14.17 Protons Bonded to Oxygen and Nitrogen

14.18 The Use of Deuterium in ^1H NMR Spectroscopy

14.19 The Resolution of ^1H NMR Spectra

14.20 ^{13}C NMR Spectroscopy

PROBLEM-SOLVING STRATEGY

14.21 DEPT ^{13}C NMR Spectra

14.22 Two-Dimensional NMR Spectroscopy

14.23 NMR Used in Medicine is Called Magnetic Resonance Imaging

14.24 X-Ray Crystallography

GENERAL CONNECTION: Structural Databases

ESSENTIAL CONCEPTS

PROBLEMS

PART FIVE: Carbonyl Compounds

15 Reactions of Carboxylic Acids and Carboxylic Acid Derivatives

Table of Contents

15.1 The Nomenclature of Carboxylic Acids and Carboxylic Acid Derivatives

MEDICAL CONNECTION: Nature's Sleeping Pill

15.2 The Structures of Carboxylic Acids and Carboxylic Acid Derivatives

15.3 The Physical Properties of Carbonyl Compounds

15.4 How Carboxylic Acids and Carboxylic Acid Derivatives React

PROBLEM-SOLVING STRATEGY

15.5 The Relative Reactivities of Carboxylic Acids and Carboxylic Acid Derivatives

15.6 Reactions of Acyl Chlorides

15.7 Reactions of Esters

15.8 Acid-Catalyzed Ester Hydrolysis and Transesterification

15.9 Hydroxide-Ion-Promoted Ester Hydrolysis

PHARMACEUTICAL CONNECTION: Aspirin, NSAIDs, and COX-2 Inhibitors

15.10 Reactions of Carboxylic Acids

PROBLEM-SOLVING STRATEGY

15.11 Reactions of Amides

BIOLOGICAL CONNECTION: Dalmatians: Do Not Fool with Mother Nature

15.12 Acid-Catalyzed Amide Hydrolysis and Alcoholysis

HISTORICAL CONNECTION: The Discovery of Penicillin

MEDICAL CONNECTION: Penicillin and Drug Resistance

PHARMACEUTICAL CONNECTION: Penicillins in Clinical Use

BIOLOGICAL CONNECTION: A Semisynthetic Penicillin

15.13 Hydroxide-Ion-Promoted Hydrolysis of Amides

INDUSTRIAL CONNECTION: Synthetic Polymers

MEDICAL CONNECTION: Dissolving Sutures

15.14 Hydrolysis of an Imide: a Way to Synthesize a Primary Amine

15.15 Nitriles

15.16 Acid Anhydrides

GENERAL CONNECTION: What Drug-Enforcement Dogs Are Really Detecting

15.17 Dicarboxylic Acids

15.18 How Chemists Activate Carboxylic Acids

15.19 How Cells Activate Carboxylic Acids

CHEMICAL CONNECTION: Nerve Impulses, Paralysis, and Insecticides

ESSENTIAL CONCEPTS

SUMMARY OF REACTIONS

PROBLEMS

16 Reactions of Aldehydes and Ketones More Reactions of Carboxylic Acid Derivatives

16.1 The Nomenclature of Aldehydes and Ketones

GENERAL CONNECTION: Butanedione: An Unpleasant Compound

16.2 The Relative Reactivities of Carbonyl Compounds

Table of Contents

16.3 How Aldehydes and Ketones React

16.4 Reactions of Carbonyl Compounds with Carbon Nucleophiles

CHEMICAL CONNECTION: Enzyme-Catalyzed Carbonyl Additions

PROBLEM-SOLVING STRATEGY

16.5 Reactions of Carbonyl Compounds with Hydride Ion

16.6 More About Reduction Reactions

16.7 Chemoselective Reactions

16.8 Reactions of Aldehydes and Ketones with Nitrogen Nucleophiles

PHARMACEUTICAL CONNECTION: Serendipity in Drug Development

16.9 Reactions of Aldehydes and Ketones with Oxygen Nucleophiles

BIOLOGICAL CONNECTION: Preserving Biological Specimens

CHEMICAL CONNECTION: Carbohydrates

PROBLEM-SOLVING STRATEGY

16.10 Protecting Groups

16.11 Reactions of Aldehydes and Ketones with Sulfur Nucleophiles

16.12 Reactions of Aldehydes and Ketones with a Peroxyacid

16.13 The Wittig Reaction Forms an Alkene

CHEMICAL CONNECTION: β -Carotene

16.14 DESIGNING A SYNTHESIS IV: Disconnections, Synthons, and Synthetic Equivalents

CHEMICAL CONNECTION: Synthesizing Organic Compounds

PHARMACEUTICAL CONNECTION: Semisynthetic Drugs

16.15 Nucleophilic Addition to α,β -Unsaturated Aldehydes and Ketones

16.16 Nucleophilic Addition to α,β -Unsaturated Carboxylic Acid Derivatives

CHEMICAL CONNECTION: Enzyme-Catalyzed Cis-Trans Interconversion

16.17 Conjugate Addition Reactions in Biological Systems

MEDICAL CONNECTION: Cancer Chemotherapy

ESSENTIAL CONCEPTS

SUMMARY OF REACTIONS

PROBLEMS

17 Reactions at the α -Carbon

17.1 The Acidity of an α -Hydrogen

PROBLEM-SOLVING STRATEGY

17.2 KetoEnol Tautomers

17.3 KetoEnol Interconversion

17.4 Halogenation of the α -Carbon of Aldehydes and Ketones

17.5 Halogenation of the α -Carbon of Carboxylic Acids

17.6 Forming an Enolate Ion

17.7 Alkylating the α -Carbon

PROBLEM-SOLVING STRATEGY

Table of Contents

INDUSTRIAL CONNECTION: The Synthesis of Aspirin

17.8 Alkylating and Acylating the α -Carbon Via an Enamine Intermediate

17.9 Alkylating the α -Carbon

17.10 An Aldol Addition Forms a β -Hydroxyaldehyde or a β -Hydroxyketone

17.11 The Dehydration of Aldol Addition Products Forms α,β -Unsaturated Aldehydes and Ketones

17.12 A Crossed Aldol Addition

MEDICAL CONNECTION: Breast Cancer and Aromatase Inhibitors

17.13 A Claisen Condensation Forms a β -Keto Ester

17.14 Other Crossed Condensations

17.15 Intramolecular Condensations and Intramolecular Aldol Additions

17.16 The Robinson Annulation

PROBLEM-SOLVING STRATEGY

17.17 CO_2 Can be Removed from a Carboxylic Acid that has a Carbonyl Group at the 3-Position

17.18 The Malonic Ester Synthesis: A Way to Synthesize a Carboxylic Acid

17.19 The Acetoacetic Ester Synthesis: A Way to Synthesize a Methyl Ketone

17.20 DESIGNING A SYNTHESIS V: Making New CarbonCarbon Bonds

17.21 Reactions at the α -Carbon in Living Systems

17.22 Organizing What We Know About the Reactions of Organic Compounds (Group III)

ESSENTIAL CONCEPTS

SUMMARY OF REACTIONS

PROBLEMS

TUTORIAL Synthesis and Retrosynthetic Analysis

PART SIX: Aromatic Compounds

18 Reactions of Benzene and Substituted Benzenes

GENERAL CONNECTION: Measuring Toxicity

18.1 The Nomenclature of Monosubstituted Benzenes

GENERAL CONNECTION: The Toxicity of Benzene

18.2 The General Mechanism for Electrophilic Aromatic Substitution Reactions

18.3 Halogenation of Benzene

MEDICAL CONNECTION: Thyroxine

18.4 Nitration of Benzene

18.5 Sulfonation of Benzene

18.6 FriedelCrafts Acylation of Benzene

18.7 FriedelCrafts Alkylation of Benzene

CHEMICAL CONNECTION: Incipient Primary Carbocations

BIOLOGICAL CONNECTION: A Biological Friedel-Crafts Alkylation

18.8 Alkylation of Benzene by AcylationReduction

Table of Contents

- 18.9 Using Coupling Reactions to Alkylate Benzene
- 18.10 How Some Substituents on a Benzene Ring Can Be Chemically Changed
- 18.11 The Nomenclature of Disubstituted and Polysubstituted Benzenes
- 18.12 The Effect of Substituents on Reactivity
- 18.13 The Effect of Substituents on Orientation
- 18.14 The OrthoPara Ratio
- 18.15 Additional Considerations Regarding Substituent Effects
- 18.16 DESIGNING A SYNTHESIS VI: The Synthesis of Monosubstituted and Disubstituted Benzenes
- 18.17 The Synthesis of Trisubstituted Benzenes
- 18.18 Synthesizing Substituted Benzenes Using Arenediazonium Salts
- 18.19 Azobenzenes
 - HISTORICAL CONNECTION: Discovery of the First Antibiotic
 - PHARMACEUTICAL CONNECTION: Drug Safety
- 18.20 The Mechanism for the Formation of a Diazonium Ion
 - MEDICAL CONNECTION: A New Cancer-Fighting Drug
 - NUTRITIONAL CONNECTION: Nitrosamines and Cancer
- 18.21 Nucleophilic Aromatic Substitution
- 18.22 DESIGNING A SYNTHESIS VII: The Synthesis of Cyclic Compounds
 - ESSENTIAL CONCEPTS
 - SUMMARY OF REACTIONS
 - PROBLEMS

19 More About Amines Reactions of Heterocyclic Compounds

- 19.1 More About Nomenclature
- 19.2 More About the AcidBase Properties of Amines
 - MEDICAL CONNECTION: Atropine
- 19.3 Amines React as Bases and as Nucleophiles
- 19.4 Synthesis of Amines
- 19.5 Aromatic Five-Membered-Ring Heterocycles
 - PROBLEM-SOLVING STRATEGY
- 19.6 Aromatic Six-Membered-Ring Heterocycles
- 19.7 Some Heterocyclic Amines Have Important Roles in Nature
 - PHARMACEUTICAL CONNECTION: Searching for Drugs: An Antihistamine, a Nonsedating Antihistamine, and a Drug for Ulcers
 - MEDICAL CONNECTION: Porphyrin, Bilirubin, and Jaundice
- 19.8 Organizing What We Know About the Reactions of Organic Compounds (Group IV)
 - ESSENTIAL CONCEPTS
 - SUMMARY OF REACTIONS
 - PROBLEMS

PART SEVEN: Bioorganic Compounds

Table of Contents

20 The Organic Chemistry of Carbohydrates

20.1 Classifying Carbohydrates

20.2 The D and L Notation

20.3 The Configurations of Aldoses

20.4 The Configurations of Ketoses

20.5 The Reactions of Monosaccharides in Basic Solutions

20.6 Oxidation/Reduction Reactions of Monosaccharides

20.7 Lengthening the Chain: The KilianiFischer Synthesis

20.8 Shortening the Chain: The Wohl Degradation

MEDICAL CONNECTION: Measuring the Blood Glucose Levels in Diabetes

20.9 The Stereochemistry of Glucose: The Fischer Proof

GENERAL CONNECTION: Glucose/Dextrose

20.10 Monosaccharides Form Cyclic Hemiacetals

20.11 Glucose is the Most Stable Aldohexose

20.12 Formation of Glycosides

20.13 The Anomeric Effect

20.14 Reducing and Nonreducing Sugars

20.15 Disaccharides

NUTRITIONAL CONNECTION: Lactose Intolerance

MEDICAL CONNECTION: Galactosemia

BIOLOGICAL CONNECTION: A Toxic Disaccharid

20.16 Polysaccharides

MEDICAL CONNECTION: Why the Dentist is Right

BIOLOGICAL CONNECTION: Controlling Fleas

20.17 Some Naturally Occurring Compounds Derived from Carbohydrates

MEDICAL CONNECTION: Resistance to Antibiotics

MEDICAL CONNECTION: HeparinA Natural Anticoagulant

HISTORICAL CONNECTION: Vitamin C

20.18 Carbohydrates on Cell Surfaces

20.19 Artificial Sweeteners

NUTRITIONAL CONNECTION: Acceptable Daily Intake

ESSENTIAL CONCEPTS

SUMMARY OF REACTIONS

PROBLEMS

21 Amino Acids, Peptides, and Proteins

21.1 The Nomenclature of Amino Acids

NUTRITIONAL CONNECTION: Proteins and Nutrition

21.2 The Configuration of Amino Acids

MEDICAL CONNECTION: Amino Acids and Disease

Table of Contents

PHARMACEUTICAL CONNECTION: A Peptide Antibiotic

21.3 AcidBase Properties of Amino Acids

21.4 The Isoelectric Point

21.5 Separating Amino Acids

GENERAL CONNECTION: Water Softeners: Examples of Cation-Exchange Chromatography

21.6 Synthesis of Amino Acids

21.7 Resolution of Racemic Mixtures of Amino Acids

21.8 Peptide Bonds and Disulfide Bonds

MEDICAL CONNECTION: Diabetes

CHEMICAL CONNECTION: Hair: Straight or Curly?

21.9 Some Interesting Peptides

21.10 The Strategy of Peptide Bond Synthesis: N-Protection and C-Activation

21.11 Automated Peptide Synthesis

21.12 An Introduction to Protein Structure

BIOLOGICAL CONNECTION: Primary Structure and Taxonomic Relationship

21.13 How to Determine the Primary Structure of a Polypeptide or a Protein

PROBLEM-SOLVING STRATEGY

21.14 Secondary Structure

CHEMICAL CONNECTION: Right-Handed and Left-Handed Helices

CHEMICAL CONNECTION: α -Peptides: An Attempt to Improve on Nature

21.15 Tertiary Structure

MEDICAL CONNECTION: Diseases Caused by a Misfolded Protein

21.16 Quaternary Structure

21.17 Protein Denaturation

ESSENTIAL CONCEPTS

PROBLEMS

22 Catalysis in Organic Reactions and in Enzymatic Reactions

22.1 Catalysis in Organic Reactions

22.2 Acid Catalysis

22.3 Base Catalysis

22.4 Nucleophilic Catalysis

22.5 Metal-Ion Catalysis

22.6 Intramolecular Reactions

22.7 Intramolecular Catalysis

22.8 Catalysis in Biological Reactions

22.9 An Enzyme-Catalyzed Reaction That Is Reminiscent of Acid-Catalyzed Amide Hydrolysis

22.10 Another Enzyme-Catalyzed Reaction That Is Reminiscent of Acid-Catalyzed Amide Hydrolysis

22.11 An Enzyme-Catalyzed Reaction That Involves Two Sequential S_N2 Reactions

Table of Contents

MEDICAL CONNECTION: How Tamiflu Works

22.12 An Enzyme-Catalyzed Reaction That Is Reminiscent of the Base-Catalyzed Eneiol Rearrangement

22.13 An Enzyme Catalyzed-Reaction That Is Reminiscent of a Retro-Aldol Addition

ESSENTIAL CONCEPTS

PROBLEMS

23 The Organic Chemistry of the Coenzymes, Compounds Derived from Vitamins

HISTORICAL CONNECTION: Vitamin B[Sub(1)]

23.1 Niacin: The Vitamin Needed for Many Redox Reactions

HISTORICAL CONNECTION: Niacin Deficiency

23.2 Riboflavin: Another Vitamin Used in Redox Reactions

23.3 Vitamin B[Sub(1)] : The Vitamin Needed for Acyl Group Transfer

GENERAL CONNECTION: Curing a Hangover with Vitamin B[Sub(1)]

23.4 Biotin: The Vitamin Needed for Carboxylation of an α -Carbon

23.5 Vitamin B[Sub(6)] : The Vitamin Needed for Amino Acid Transformations

MEDICAL CONNECTION: Assessing the Damage After a Heart Attack

23.6 Vitamin B[Sub(12)] : The Vitamin Needed for Certain Isomerizations

23.7 Folic Acid: The Vitamin Needed for One-Carbon Transfer

HISTORICAL CONNECTION: The First Antibiotics

MEDICAL CONNECTION: Cancer Drugs and Side Effects

BIOLOGICAL CONNECTION: Competitive Inhibitors

23.8 Vitamin K: The Vitamin Needed for Carboxylation of Glutamate

MEDICAL CONNECTION: Anticoagulants

NUTRITIONAL CONNECTION: Too Much Broccoli

ESSENTIAL CONCEPTS

PROBLEMS

24 The Organic Chemistry of the Metabolic Pathways

NUTRITIONAL CONNECTION: Differences in Metabolism

24.1 ATP is Used for Phosphoryl Transfer Reactions

CHEMICAL CONNECTION: Why Did Nature Choose Phosphates?

24.2 Why ATP is Kinetically Stable in a Cell

24.3 The "High-Energy" Character of Phosphoanhydride Bonds

24.4 The Four Stages of Catabolism

24.5 The Catabolism of Fats: Stages 1 and 2

24.6 The Catabolism of Carbohydrates: Stages 1 and 2

PROBLEM-SOLVING STRATEGY

NUTRITIONAL CONNECTION: Fats Versus Carbohydrates as a Source of Energy

24.7 The Fate of Pyruvate

24.8 The Catabolism of Proteins: Stages 1 and 2

Table of Contents

MEDICAL CONNECTION: Phenylketonuria (PKU): An Inborn Error of Metabolism

MEDICAL CONNECTION: Alcaptonuria

24.9 The Citric Acid Cycle: Stage 3

24.10 Oxidative Phosphorylation: Stage 4

NUTRITIONAL CONNECTION: Basal Metabolic Rate

24.11 Anabolism

24.12 Gluconeogenesis

24.13 Regulating Metabolic Pathways

24.14 Amino Acid Biosynthesis

ESSENTIAL CONCEPTS

PROBLEMS

25 The Organic Chemistry of Lipids

25.1 Fatty Acids Are Long-Chain Carboxylic Acids

NUTRITIONAL CONNECTION: Omega Fatty Acids

25.2 Waxes Are High-Molecular-Weight Esters

25.3 Fats and Oils Are Triglycerides

NUTRITIONAL CONNECTION: Olestra: Nonfat with Flavor

BIOLOGICAL CONNECTION: Whales and Echolocation

25.4 Soaps and Micelles

25.5 Phospholipids Are Components of Cell Membranes

BIOLOGICAL CONNECTION: Snake Venom

MEDICAL CONNECTION: Multiple Sclerosis and the Myelin Sheath

25.6 Prostaglandins Regulate Physiological Responses

25.7 Terpenes Contain Carbon Atoms in Multiples of Five

25.8 How Terpenes Are Biosynthesized

MEDICAL CONNECTION: How Statins Lower Cholesterol Levels

PROBLEM-SOLVING STRATEGY

CHEMICAL CONNECTION: Protein Prenylation

25.9 How Nature Synthesizes Cholesterol

25.10 Steroids

MEDICAL CONNECTION: One DrugTwo Effects

25.11 Synthetic Steroids

ESSENTIAL CONCEPTS

PROBLEMS

26 The Chemistry of the Nucleic Acids

26.1 Nucleosides and Nucleotides

HISTORICAL CONNECTION: The Structure of DNA: Watson, Crick, Franklin, and Wilkins

BIOLOGICAL CONNECTION: Cyclic AMP

26.2 Nucleic Acids Are Composed of Nucleotide Subunits

Table of Contents

26.3 The Secondary Structure of DNA

26.4 Why DNA Does Not Have A 2'-OH Group

26.5 The Biosynthesis of DNA Is Called Replication

26.6 DNA and Heredity

PHARMACEUTICAL CONNECTION: Natural Products That Modify DNA

26.7 The Biosynthesis of RNA Is Called Transcription

BIOLOGICAL CONNECTION: There Are More Than Four Bases in DNA

26.8 The RNAs Used for Protein Biosynthesis

26.9 The Biosynthesis of Proteins Is Called Translation

MEDICAL CONNECTION: Sickle Cell Anemia

MEDICAL CONNECTION: Antibiotics That Act by Inhibiting Translation

26.10 Why DNA Contains Thymine Instead of Uracil

MEDICAL CONNECTION: Antibiotics Act by a Common Mechanism

26.11 Antiviral Drugs

HISTORICAL CONNECTION: Influenza Pandemics

26.12 How the Base Sequence of DNA Is Determined

26.13 Genetic Engineering

ENVIRONMENTAL CONNECTION: Resisting Herbicides

PHARMACEUTICAL CONNECTION: Using Genetic Engineering to Treat the Ebola Virus

ESSENTIAL CONCEPTS

PROBLEMS

PART EIGHT: Special Topics in Organic Chemistry

27 Synthetic Polymers

27.1 There Are Two Major Classes of Synthetic Polymers

27.2 An Introduction To Chain-Growth Polymers

27.3 Radical Polymerization

INDUSTRIAL CONNECTION: Teflon: An Accidental Discovery

ENVIRONMENTAL CONNECTION: Recycling Symbols

27.4 Cationic Polymerization

27.5 Anionic Polymerization

27.6 Ring-Opening Polymerizations

27.7 Stereochemistry of Polymerization Ziegler-Natta Catalysts

27.8 Polymerization of Dienes

27.9 Copolymers

PHARMACEUTICAL CONNECTION: Nanocontainers

27.10 An Introduction to Step-Growth Polymers

27.11 Classes of Step-Growth Polymers

MEDICAL CONNECTION: Health Concerns: Bisphenol A and Phthalates

Table of Contents

INDUSTRIAL CONNECTION: Designing a Polymer

27.12 Physical Properties of Polymers

NUTRITIONAL CONNECTION: Melamine Poisoning

27.13 Recycling Polymers

27.14 Biodegradable Polymers

ESSENTIAL CONCEPTS

PROBLEMS

28 Pericyclic Reactions

28.1 There Are Three Kinds of Pericyclic Reactions

28.2 Molecular Orbitals and Orbital Symmetry

28.3 Electrocyclic Reactions

28.4 Cycloaddition Reactions

28.5 Sigmatropic Rearrangements

28.6 Pericyclic Reactions in Biological Systems

CHEMICAL CONNECTION: Bioluminescence

NUTRITIONAL CONNECTION: The Sunshine Vitamin

NUTRITIONAL CONNECTION: Animals, Birds, Fish And Vitamin D

28.7 Summary of the Selection Rules for Pericyclic Reactions

ESSENTIAL CONCEPTS

PROBLEMS

Appendices

I: PK[Sub(A)] VALUES

II: KINETICS

III: SUMMARY OF METHODS USED TO SYNTHESIZE A PARTICULAR FUNCTIONAL GROUP

IV: SUMMARY OF METHODS EMPLOYED TO FORM CARBON-CARBON BONDS

V: SPECTROSCOPY TABLES

VI: PHYSICAL PROPERTIES OF ORGANIC COMPOUNDS

ANSWERS TO SELECTED PROBLEMS

GLOSSARY

A

B

C

D

E

F

G

Table of Contents

H
I
K
L
M
N
O
P
Q
R
S
T
U
V
W
X
Z

CREDITS
INDEX