

Overview of Contents

| | |
|---|------|
| Foreword | v |
| Preface | vi |
| A Note to Students | viii |
| Abbreviations | x |
| Prologue: The History and Scope of Organic Chemistry | xxvi |
| Chapter 1 Atoms, Molecules, and Chemical Bonding—a Review | 1 |
| Chapter 2 Molecular Structure and Shapes of Organic Molecules | 22 |
| Chapter 3 Organic Compounds: their Functional Groups, Intermolecular Interactions, and Physical Properties | 42 |
| Chapter 4 Conformation and Strain in Molecules | 71 |
| Chapter 5 Conjugation, π -Electron Delocalization, and Aromaticity | 89 |
| Chapter 6 Acids and Bases | 110 |
| Chapter 7 Organic Reactions and the Concept of Mechanism | 138 |
| Chapter 8 Nucleophilic Addition to the Carbonyl Group in Aldehydes and Ketones | 165 |
| Chapter 9 Nucleophilic Substitution Reactions of Carboxylic Acid Derivatives | 188 |
| Chapter 10 Reactions of Carbonyl Compounds with Hydride Donors and Organometallic Reagents | 208 |
| Chapter 11 Stereochemistry and Molecular Chirality | 225 |
| Chapter 12 Nucleophilic Substitution Reactions of Haloalkanes and Related Compounds | 250 |
| Chapter 13 Elimination Reactions of Haloalkanes and Related Compounds | 273 |
| Chapter 14 Reactions of Alcohols, Ethers, Thiols, Sulfides, and Amines | 289 |
| Chapter 15 Addition Reactions of Alkenes and Alkynes | 314 |
| Chapter 16 Electrophilic Aromatic Substitution | 341 |
| Chapter 17 Enolate Ions, their Equivalents, and Reactions | 373 |
| Chapter 18 Reactions of Nucleophiles with Alkenes and Aromatic Compounds | 402 |
| Chapter 19 Polycyclic and Heterocyclic Aromatic Compounds | 423 |
| Chapter 20 Reactions involving Radicals | 444 |

| | | |
|----------------------|---|-----|
| Chapter 21 | Pericyclic Reactions: Cycloadditions, Electrocyclic Reactions, and Sigmatropic Rearrangements | 469 |
| Chapter 22 | Rearrangement Reactions involving Polar Molecules and Ions | 490 |
| Chapter 23 | Organic Synthesis | 506 |
| Chapter 24 | Chemistry of Biomolecules | 528 |
| Chapter 25 | Structural Determination of Organic Compounds | 561 |
| Appendices | | 602 |
| Additional Resources | | 617 |
| Index | | 619 |

Contents in Detail

| | |
|--|------|
| Foreword | v |
| Preface | vi |
| A Note to Students | viii |
| Abbreviations | x |
| Prologue: The History and Scope of Organic Chemistry | xxvi |

Chapter 1 Atoms, Molecules, and Chemical Bonding—a Review

| | |
|--|----|
| 1.1 The Electronic Structure of Atoms | 1 |
| 1.1.1 Atomic structure | 1 |
| 1.1.2 Electrons and atomic orbitals | 2 |
| Panel 1.1 Radiocarbon dating | 3 |
| 1.1.3 Electronic configuration of an atom | 4 |
| 1.1.4 Lewis representation of atoms | 6 |
| 1.2 Chemical Bonding | 6 |
| 1.2.1 Formation of ions | 6 |
| 1.2.2 Ionic and covalent bonds | 8 |
| 1.2.3 Polar covalent bonds and dipoles | 10 |
| Panel 1.2 Masses and sizes of atoms | 12 |
| 1.3 Lewis Structures of Molecules and Ions | 12 |
| 1.3.1 How to draw Lewis structures | 12 |
| 1.3.2 Further examples of drawing Lewis structures | 15 |
| 1.4 Introduction to Resonance | 18 |
| Summary | 20 |
| Problems | 20 |

Chapter 2 Molecular Structure and Shapes of Organic Molecules

| | |
|---|----|
| 2.1 Shapes of Molecules and the VSEPR Model | 22 |
| 2.1.1 Tetrahedral shapes | 22 |
| 2.1.2 Trigonal planar shapes | 24 |
| 2.1.3 Linear shapes | 24 |
| 2.2 Orbital Description of Covalent Bonding | 25 |
| 2.2.1 Atomic orbitals and their shapes | 25 |
| 2.2.2 Overlap of atomic orbitals to give molecular orbitals | 27 |
| 2.3 Hybridization of Atomic Orbitals | 28 |
| 2.3.1 Three types of hybrid orbitals | 28 |
| Panel 2.1 The work of Linus Pauling | 28 |
| 2.3.2 Energies of hybrid orbitals | 29 |
| 2.4 Bonding in Methane | 30 |
| 2.5 Bonding in Ethene | 31 |
| 2.5.1 Trigonal planar carbons | 31 |
| 2.5.2 The pi (π) orbitals | 31 |
| 2.6 Bonding in Ethyne | 33 |
| 2.7 Hybridization of Carbon and Bond Lengths | 35 |
| 2.8 Drawing Organic Structures | 35 |
| 2.9 Isomerism | 37 |

| | | |
|----------|---|----|
| 2.9.1 | Constitutional isomers | 37 |
| 2.9.2 | <i>cis-trans</i> isomerism | 37 |
| 2.9.3 | <i>E,Z</i> nomenclature for <i>cis-trans</i> isomers of alkenes | 38 |
| Summary | | 40 |
| Problems | | 40 |

Chapter 3 Organic Compounds: their Functional Groups, Intermolecular Interactions, and Physical Properties

| | | |
|-----------|--|----|
| 3.1 | Functional Groups | 42 |
| 3.2 | Hydrocarbons | 43 |
| 3.2.1 | Alkanes and cycloalkanes | 43 |
| Panel 3.1 | Organic resources: coal, oil, and natural gas | 46 |
| 3.2.2 | Alkenes and alkynes | 49 |
| Panel 3.2 | Ethene as an industrial raw material | 49 |
| 3.2.3 | Arenes | 50 |
| 3.3 | Alcohols, Ethers, and their Sulfur Analogues | 50 |
| 3.3.1 | Alcohols | 51 |
| 3.3.2 | Ethers | 52 |
| 3.3.3 | Thiols | 52 |
| 3.4 | Haloalkanes | 52 |
| 3.5 | Nitrogen Compounds | 53 |
| 3.5.1 | Amines | 53 |
| 3.5.2 | Nitro compounds | 54 |
| 3.6 | Aldehydes and Ketones | 54 |
| 3.7 | Carboxylic Acids and their Derivatives | 55 |
| 3.8 | Elements of Organic Nomenclature | 56 |
| 3.8.1 | IUPAC nomenclature | 56 |
| 3.8.2 | Naming a non-aromatic hydrocarbon | 57 |
| 3.8.3 | Naming a compound with one or more functional groups | 58 |
| 3.8.4 | Naming aromatic compounds | 60 |
| 3.9 | Intermolecular Interactions and Physical Properties of Organic Compounds | 61 |
| 3.9.1 | van der Waals forces | 61 |
| 3.9.2 | Hydrogen bonds | 62 |
| 3.9.3 | States of matter and phase changes | 63 |
| 3.9.4 | Boiling points of organic compounds | 63 |
| 3.9.5 | Solubility | 65 |
| Panel 3.3 | Chromatography | 66 |
| Summary | | 68 |
| Problems | | 69 |

Chapter 4 Conformation and Strain in Molecules

| | | |
|-----------|--|----|
| 4.1 | Molecular Vibrations and Internal Rotation | 71 |
| 4.1.1 | Bond stretching and bending vibrations | 71 |
| 4.1.2 | Internal rotation | 72 |
| 4.2 | Conformations of Alkanes | 72 |
| 4.2.1 | Ethane and torsional strain | 72 |
| 4.2.2 | Butane and steric strain | 76 |
| 4.3 | Cycloalkanes | 77 |
| 4.3.1 | Cyclopropane and angle strain | 77 |
| 4.3.2 | Cyclobutane and cyclopentane | 78 |
| 4.3.3 | Cyclohexane: chair conformations | 79 |
| Panel 4.1 | Heterocyclic chair compounds: tetrodotoxin | 82 |

| | | |
|---|--|------------|
| 4.3.4 | Cyclohexane: ring inversion of chair conformations | 82 |
| 4.4 | Disubstituted Cycloalkanes: <i>cis</i> – <i>trans</i> Isomerism | 84 |
| 4.5 | Strain in Cycloalkanes: Heat of Combustion | 85 |
| Panel 4.2 | Bicycloalkanes | 86 |
| Summary | | 87 |
| Problems | | 87 |
| Chapter 5 Conjugation, π-Electron Delocalization, and Aromaticity | | 89 |
| 5.1 | Extended π Bonds and the Concept of Conjugation | 90 |
| 5.2 | Bonding in Butadiene | 90 |
| 5.3 | Allylic Systems | 92 |
| 5.3.1 | Molecular orbitals of allylic systems | 92 |
| 5.3.2 | Resonance description of allylic systems | 93 |
| 5.3.3 | Allyl anion analogues | 94 |
| 5.4 | Resonance Revisited | 95 |
| 5.4.1 | The nature of resonance | 95 |
| 5.4.2 | Resonance forms and their relative contributions | 95 |
| 5.5 | Benzene | 98 |
| 5.5.1 | Structure of benzene | 98 |
| 5.5.2 | Molecular orbitals of benzene | 98 |
| 5.5.3 | Stabilization energy of benzene | 99 |
| Panel 5.1 | The structure of benzene and Kekulé's dreams | 100 |
| 5.6 | Aromaticity in General | 100 |
| 5.6.1 | Hückel's rule | 100 |
| 5.6.2 | Annulenes | 104 |
| 5.7 | Photoexcited Organic Molecules | 104 |
| 5.7.1 | Interactions of organic molecules with electromagnetic radiation | 104 |
| 5.7.2 | Properties of photoexcited states | 105 |
| Panel 5.2 | The perception of colours | 106 |
| 5.7.3 | Photochemical reactions | 106 |
| Panel 5.3 | The chemistry of vision | 107 |
| Summary | | 108 |
| Problems | | 108 |
| Chapter 6 Acids and Bases | | 110 |
| 6.1 | Definitions of Acids and Bases | 111 |
| 6.1.1 | Brønsted acids and bases | 111 |
| 6.1.2 | Lewis acids and bases | 112 |
| 6.2 | Equilibrium in Brønsted Acid–Base Reactions | 113 |
| 6.2.1 | Acid dissociation constants and pK_a | 114 |
| Panel 6.1 | pK_a values for water and the oxonium ion | 115 |
| 6.2.2 | Equilibrium in acid–base reactions | 115 |
| 6.2.3 | Acidity of aqueous solutions and ratios of conjugate acid–base pairs | 117 |
| 6.2.4 | Buffer solutions | 118 |
| Panel 6.2 | pH indicators and colours of flowers | 119 |
| 6.3 | Factors which affect the Strength of an Acid | 120 |
| 6.3.1 | The element bearing the acidic hydrogen | 120 |
| 6.3.2 | Charge delocalization in anions | 121 |
| 6.3.3 | Substituent effects | 122 |
| 6.4 | Carbon Acids and Carbanions | 124 |
| 6.4.1 | Hydrocarbons | 124 |
| 6.4.2 | Effects of electron-withdrawing groups on C–H acidity | 127 |

| | | |
|------------------|---|-----|
| 6.5 | Basicity of Organic Compounds | 129 |
| 6.5.1 | Definition of base strengths | 129 |
| 6.5.2 | Nitrogen bases | 129 |
| 6.5.3 | Weakly basic organic compounds | 130 |
| 6.6 | Polyfunctional Acids and Bases | 131 |
| 6.7 | Solvent Effects on Acid–Base Reactions | 133 |
| 6.7.1 | The levelling effect of water | 133 |
| Panel 6.3 | Extraction of morphine from opium | 134 |
| 6.7.2 | Acid–base reactions in non-aqueous solvents | 135 |
| Summary | | 136 |
| Problems | | 136 |

Chapter 7 Organic Reactions and the Concept of Mechanism 138

| | | |
|------------------|---|-----|
| 7.1 | Classes of Organic Chemical Reactions | 138 |
| 7.2 | Elementary Steps in a Chemical Reaction | 140 |
| 7.2.1 | Homolysis | 140 |
| 7.2.2 | Heterolysis | 141 |
| 7.2.3 | Concerted bond formation and cleavage in an elementary reaction | 143 |
| 7.2.4 | The transition structure in a concerted elementary reaction | 144 |
| 7.2.5 | Site of nucleophilic attack at a cationic electrophile | 145 |
| 7.2.6 | Sigma and pi bonds as nucleophilic centres | 146 |
| 7.3 | A Molecular Orbital Description of Polar Elementary Reactions | 147 |
| 7.3.1 | Orbital interactions in bimolecular elementary reactions | 147 |
| 7.3.2 | HOMO–LUMO interactions | 148 |
| 7.3.3 | Orbital overlap and orientation | 149 |
| 7.4 | Reaction Energetics, Reaction Profiles, and Equilibria | 150 |
| 7.4.1 | Energy change for a one-step reaction of a single molecule | 150 |
| 7.4.2 | From reaction of a single molecule to reaction on a molar scale | 150 |
| Panel 7.1 | Reaction profiles for unimolecular bond-cleavage elementary reactions | 151 |
| 7.4.3 | Gibbs energy reaction profiles | 152 |
| 7.4.4 | Profiles of multistep reactions | 153 |
| 7.4.5 | Equilibrium constant | 155 |
| 7.5 | Characterization of Organic Reactions and Investigation of their Mechanisms | 156 |
| 7.5.1 | Product studies and mechanistic proposals | 156 |
| Panel 7.2 | The Hammond postulate | 157 |
| 7.5.2 | Detection of intermediates in stepwise mechanisms | 158 |
| 7.5.3 | The rate law as an indicator of mechanism | 159 |
| 7.5.4 | Effect of substrate structure and reaction conditions on rate constants | 160 |
| Summary | | 161 |
| Problems | | 162 |

Chapter 8 Nucleophilic Addition to the Carbonyl Group in Aldehydes and Ketones 165

| | | |
|------------------|--|-----|
| 8.1 | Polarity of the Carbonyl Bond | 166 |
| Panel 8.1 | Common carbonyl compounds: methanal, ethanal, and propanone | 168 |
| 8.2 | Formation of Cyanohydrins | 169 |
| 8.3 | Addition of Water to Aldehydes and Ketones | 171 |
| 8.3.1 | Hydration equilibrium | 171 |
| 8.3.2 | The mechanism of hydration of carbonyl compounds and catalysis | 173 |
| 8.3.3 | Reversibility of hydration and oxygen isotope exchange | 175 |
| 8.4 | Addition of Alcohols to Aldehydes and Ketones | 176 |
| 8.4.1 | Formation of hemiacetals | 176 |
| 8.4.2 | Formation of acetals | 177 |

| | | |
|-------------------|---|------------|
| 8.4.3 | Addition of thiols | 180 |
| 8.5 | Addition of Bisulfite to Aldehydes and Ketones | 180 |
| 8.6 | Imines and Enamines | 181 |
| 8.6.1 | Reactions of primary amines with aldehydes and ketones | 181 |
| 8.6.2 | Reactions of secondary amines with aldehydes and ketones | 183 |
| 8.7 | The Wittig Reaction | 183 |
| Panel 8.2 | Imines in biochemical reactions | 184 |
| Summary | | 185 |
| Problems | | 186 |
| Chapter 9 | Nucleophilic Substitution Reactions of Carboxylic Acid Derivatives | 188 |
| 9.1 | Reactions of Carboxylic Acid Derivatives | 189 |
| Panel 9.1 | Common names of carboxylic acids | 189 |
| 9.2 | Hydrolysis of Esters | 190 |
| 9.2.1 | Hydration of the carbonyl group | 190 |
| 9.2.2 | Reaction under alkaline conditions | 190 |
| 9.2.3 | Acid-catalysed hydrolysis | 192 |
| 9.2.4 | Evidence for a tetrahedral intermediate | 193 |
| 9.3 | Other Reactions of Esters | 195 |
| 9.3.1 | Ester exchange reactions | 195 |
| 9.3.2 | Reactions of esters with amines | 195 |
| 9.4 | Generalized Nucleophilic Addition-Elimination Reactions | 196 |
| 9.4.1 | Reaction mechanism | 196 |
| 9.4.2 | Relative reactivities of carboxylic acid derivatives | 197 |
| 9.4.3 | Comparison of reactions of nucleophiles with carboxylic acid derivatives and with aldehydes and ketones | 198 |
| 9.5 | Interconversion of Carboxylic Acid Derivatives | 199 |
| 9.5.1 | Acyl chlorides | 199 |
| 9.5.2 | Acid anhydrides | 200 |
| 9.5.3 | Amides | 201 |
| 9.5.4 | Carboxylic acids | 201 |
| Panel 9.2 | Lactones and lactams | 202 |
| 9.5.5 | Summary of relative reactivities | 203 |
| 9.6 | Polycondensation | 203 |
| Panel 9.3 | Recycling of PET | 204 |
| Summary | | 205 |
| Problems | | 206 |
| Chapter 10 | Reactions of Carbonyl Compounds with Hydride Donors and Organometallic Reagents | 208 |
| 10.1 | Hydride Reduction of Carbonyl Groups | 208 |
| 10.1.1 | Reduction of aldehydes and ketones | 208 |
| Panel 10.1 | Bonding in BH_4^- | 209 |
| 10.1.2 | Reduction of carboxylic acid derivatives | 210 |
| 10.2 | Indirect Reduction of Aldehydes and Ketones | 211 |
| 10.2.1 | Reductive amination | 212 |
| 10.2.2 | Reduction of the C=O of aldehydes and ketones to give CH_2 | 212 |
| 10.3 | Hydride Transfer from Carbon | 213 |
| Panel 10.2 | The Meerwein-Ponndorf-Verley-Oppenauer reaction | 214 |
| Panel 10.3 | Nature's hydride donor: NADH | 215 |
| 10.4 | Reactions with Organometallic Reagents: C–C Bond Formation | 215 |
| 10.4.1 | Organometallic compounds | 215 |

| | |
|---|-----|
| 10.4.2 The Grignard reaction | 217 |
| 10.4.3 Side reactions with Grignard reagents | 219 |
| 10.5 Planning Organic Syntheses: Synthesis of Alcohols | 220 |
| 10.5.1 An introduction to organic synthesis | 220 |
| 10.5.2 Examples of alcohol synthesis | 220 |
| 10.5.3 Protection of carbonyl groups and deprotection | 221 |
| Summary | 223 |
| Problems | 223 |

Chapter 11 Stereochemistry and Molecular Chirality 225

| | |
|--|-----|
| 11.1 Chirality | 225 |
| 11.1.1 Chiral molecules | 226 |
| 11.1.2 The basis of chirality in molecules | 227 |
| Panel 11.1 Right- and left-handed helices | 228 |
| Panel 11.2 Summary of isomeric hierarchy | 230 |
| 11.2 <i>R,S</i> nomenclature for Chirality Centres | 231 |
| 11.3 The Fischer Convention for representing the Configuration of Chirality Centres | 232 |
| 11.4 Compounds with two Chirality Centres | 233 |
| 11.4.1 Enantiomers and diastereoisomers | 233 |
| 11.4.2 Meso compounds | 235 |
| 11.5 Properties of Stereoisomers | 237 |
| 11.5.1 Properties in achiral environments | 237 |
| 11.5.2 Optical activity | 237 |
| Panel 11.3 Configurations of sugars and amino acids | 238 |
| 11.5.3 Resolution of enantiomers | 240 |
| Panel 11.4 Pasteur's resolution of a salt of (\pm) -tartaric acid | 242 |
| 11.6 Chirality of Conformationally Mobile Molecules | 243 |
| 11.7 Enantiomers with a Chirality Axis | 244 |
| 11.8 Reactions which give Enantiomeric Products | 245 |
| Summary | 247 |
| Problems | 247 |

Chapter 12 Nucleophilic Substitution Reactions of Haloalkanes and Related Compounds 250

| | |
|--|-----|
| 12.1 Reactivity of Haloalkanes with Nucleophiles | 251 |
| 12.2 The S_N2 Mechanism | 252 |
| Panel 12.1 Biological alkylation | 252 |
| 12.2.1 Steric hindrance in S_N2 reactions | 253 |
| 12.2.2 Stereochemistry of the S_N2 mechanism | 254 |
| 12.2.3 Stereoelectronic description of the S_N2 mechanism | 255 |
| 12.2.4 Nucleophiles and nucleofuges | 255 |
| 12.3 Solvent Effects | 257 |
| 12.3.1 Polarity of the transition structure | 257 |
| 12.3.2 Classes of solvents | 259 |
| 12.4 The S_N1 Mechanism | 260 |
| Panel 12.2 Phase-transfer catalysis | 260 |
| 12.4.1 Carbenium ion intermediates | 261 |
| 12.4.2 Stereochemistry of the S_N1 mechanism | 262 |
| 12.4.3 Stability of carbenium ions | 263 |
| Panel 12.3 The S_N1 mechanism in biological substitution reactions | 265 |
| 12.5 Intramolecular Nucleophilic Displacement: Neighbouring Group Participation | 266 |
| 12.6 Competition between S_N1 and S_N2 Mechanisms | 268 |

| | |
|--|------------|
| Summary | 270 |
| Problems | 270 |
| Chapter 13 Elimination Reactions of Haloalkanes and Related Compounds | 273 |
| 13.1 The E1 Elimination Mechanism | 273 |
| 13.2 The E2 Elimination Mechanism | 275 |
| 13.2.1 Stereoelectronic description of the E2 mechanism | 276 |
| 13.3 The E1cB Elimination Mechanism and Graded Transition Structures in the E2 Mechanism | 277 |
| 13.4 Reaction Maps | 278 |
| 13.5 Regioselectivity in Elimination | 280 |
| 13.5.1 Regioselectivity in E1 eliminations | 280 |
| 13.5.2 Regioselectivity in E2 eliminations | 281 |
| Panel 13.1 Hofmann and Zaitsev regioselectivity, and Bredt's rule | 283 |
| 13.6 Competition between Elimination and Substitution | 284 |
| Panel 13.2 Polyhalogenated compounds and the environment | 284 |
| Summary | 286 |
| Problems | 287 |
| Supplementary Problems | 288 |
| Chapter 14 Reactions of Alcohols, Ethers, Thiols, Sulfides, and Amines | 289 |
| 14.1 Acid-Catalysed Reactions of Alcohols and Ethers | 290 |
| 14.1.1 Leaving ability of hydroxide and alkoxide | 290 |
| 14.1.2 Reactions with hydrogen halides | 291 |
| 14.1.3 Dehydration of alcohols | 292 |
| 14.2 Rearrangements involving Carbenium Ions | 293 |
| Panel 14.1 Industrial productions of alcohols | 294 |
| 14.3 Conversion of OH into a Better Nucleofuge | 296 |
| 14.3.1 Sulfonate esters | 296 |
| 14.3.2 Sulfur and phosphorus reagents | 296 |
| Panel 14.2 The Mitsunobu reaction | 298 |
| 14.4 Oxidation of Alcohols | 298 |
| Panel 14.3 Breath test for alcohol | 299 |
| Panel 14.4 Swern oxidation | 300 |
| 14.5 Ring Opening of Epoxides | 300 |
| 14.5.1 Acid-catalysed ring opening | 300 |
| 14.5.2 Base-catalysed ring opening | 301 |
| Panel 14.5 Crown ethers and cryptands | 302 |
| Panel 14.6 Fluorodeoxyglucose in cancer diagnosis: rapid synthesis by an S_N2 reaction using a cryptand | 302 |
| 14.6 Thiols and Other Sulfur Compounds | 304 |
| 14.6.1 Thiols and their derivatives | 304 |
| 14.6.2 Biological thiols: their functions and derivatives | 305 |
| 14.6.3 Dual electronic effects of alkylthio groups | 307 |
| 14.6.4 Compounds of S(IV) and S(VI) | 308 |
| 14.7 Reactions of Amines | 308 |
| 14.7.1 Amines as nucleophiles and nucleofuges | 308 |
| 14.7.2 Reactions of alkylamines with nitrous acid | 309 |
| 14.7.3 Alkanediazonium ions | 310 |
| Summary | 311 |
| Problems | 311 |
| Supplementary Problems | 313 |

Chapter 15 Addition Reactions of Alkenes and Alkynes

| | | |
|------------------------|---|-----|
| 15.1 | Electrophilic Addition to Alkenes | 315 |
| Panel 15.1 | Ethene as a plant hormone | 316 |
| 15.2 | Addition of Hydrogen Halides: Hydrohalogenation | 316 |
| 15.2.1 | Reaction mechanism | 316 |
| 15.2.2 | Regioselectivity in addition to unsymmetrical alkenes | 317 |
| 15.2.3 | Stereochemistry of addition | 319 |
| 15.2.4 | Electrophilic addition to alkynes | 319 |
| Panel 15.2 | Cyclic enediyne antitumour antibiotics | 320 |
| 15.3 | Addition of Water | 321 |
| 15.3.1 | Acid-catalysed hydration | 321 |
| 15.3.2 | Oxymercuration–demercuration | 322 |
| 15.3.3 | Hydroboration–oxidation | 323 |
| 15.3.4 | Hydration of alkynes | 324 |
| 15.4 | Addition of Halogens | 325 |
| 15.5 | Epoxidation | 327 |
| 15.6 | Addition of Carbenes | 327 |
| 15.7 | Addition of Carbenium Ions to Alkenes and Cationic Polymerization | 329 |
| 15.8 | Electrophilic Additions to Butadiene | 330 |
| 15.8.1 | 1,2-Addition and 1,4-addition | 330 |
| 15.8.2 | Kinetic and thermodynamic control | 331 |
| 15.9 | Diels–Alder Reactions | 332 |
| 15.9.1 | Stereospecificity in Diels–Alder reactions | 333 |
| 15.10 | Addition of Hydrogen | 334 |
| Panel 15.3 | Relative stabilities and heats of hydrogenation of alkenes | 335 |
| Panel 15.4 | Oxidation and reduction in organic chemistry | 336 |
| Summary | | 338 |
| Problems | | 338 |
| Supplementary Problems | | 339 |

Chapter 16 Electrophilic Aromatic Substitution

| | | |
|------------|---|-----|
| 16.1 | Structures of Substituted Benzenes | 342 |
| 16.2 | Electrophilic Aromatic Substitution by an Addition–Elimination Mechanism | 342 |
| 16.3 | Main Classes of Electrophilic Aromatic Substitution | 345 |
| 16.3.1 | Halogenation | 345 |
| 16.3.2 | Nitration | 346 |
| 16.3.3 | Sulfonylation | 346 |
| 16.3.4 | Friedel–Crafts alkylation | 347 |
| 16.3.5 | Friedel–Crafts acylation | 348 |
| 16.4 | Reactivity of Substituted Benzenes and Regioselectivity | 349 |
| 16.4.1 | Activating and deactivating substituents in electrophilic aromatic substitution | 349 |
| 16.4.2 | Effects of substituents on the stability of the benzenium ion | 350 |
| 16.4.3 | Classification of substituents | 352 |
| 16.4.4 | Reactions of disubstituted benzenes | 354 |
| 16.5 | Reactivity of Phenol | 355 |
| Panel 16.1 | Biological electrophilic aromatic substitution: thyroxine biosynthesis | 356 |
| 16.6 | Reactivity of Aniline | 359 |
| 16.6.1 | Electrophilic substitution | 359 |
| Panel 16.2 | Quinones | 360 |
| Panel 16.3 | Naturally occurring phenols | 360 |
| 16.6.2 | Diazotization | 362 |
| 16.7 | Synthesis of Substituted Benzenes | 364 |
| 16.7.1 | Limitations to Friedel–Crafts alkylation | 364 |

| | |
|---|-----|
| 16.7.2 Indirect introduction of a primary alkyl group | 365 |
| 16.7.3 Oxidation of alkyl side-chains | 365 |
| 16.7.4 Transformations of haloarenes via Grignard reagents | 366 |
| 16.7.5 Control of reactivity and regioselectivity in syntheses of substituted benzenes | 366 |
| Panel 16.4 2-Arylethylamines which have psychological effects | 368 |
| Summary | 369 |
| Problems | 369 |
| Supplementary Problems | 371 |
| Chapter 17 Enolate Ions, their Equivalents, and Reactions | 373 |
| 17.1 Keto-Enol Tautomerism | 373 |
| 17.1.1 Allylic anions and enolate ions | 373 |
| 17.1.2 Equilibria involving enols | 374 |
| 17.2 Mechanisms of Enolization | 376 |
| 17.2.1 Acid-catalysed enolization | 376 |
| 17.2.2 Base-catalysed enolization | 376 |
| 17.3 Reactions via Reversible Enolization | 377 |
| 17.3.1 Deuterium isotope exchange | 377 |
| 17.3.2 Racemization | 378 |
| 17.3.3 Isomerization | 379 |
| 17.4 α -Halogenation | 380 |
| 17.4.1 Acid-catalysed halogenation | 380 |
| 17.4.2 Base-induced halogenation and the haloform reaction | 381 |
| 17.5 The Aldol Reaction | 382 |
| 17.5.1 Base-catalysed dimerization of simple aldehydes and ketones | 382 |
| Panel 17.1 Borodin: a composer and a chemist | 383 |
| Panel 17.2 A biological aldol reaction | 384 |
| 17.5.2 Dehydration of aldols | 385 |
| 17.5.3 Intramolecular aldol condensations | 386 |
| 17.5.4 Crossed aldol reactions | 386 |
| 17.6 Claisen Condensation | 388 |
| 17.6.1 Mechanism of the Claisen condensation | 389 |
| Panel 17.3 A biological Claisen condensation | 389 |
| 17.6.2 Intramolecular Claisen condensation | 391 |
| 17.6.3 Crossed Claisen condensations | 391 |
| 17.7 Enolate Ions of 1,3-Dicarbonyl Compounds | 392 |
| 17.8 Alkylation of Enolate Ions | 393 |
| 17.8.1 Alkylation of 1,3-dicarbonyl compounds | 393 |
| 17.8.2 Synthesis of ketones and carboxylic acid via enolates of 1,3-dicarbonyl compounds | 394 |
| 17.9 Lithium Enolates | 395 |
| 17.9.1 Kinetic and thermodynamic enolates of ketones | 396 |
| 17.10 Enolate Equivalents | 397 |
| 17.10.1 Enamines | 397 |
| 17.10.2 Enol silyl ethers | 397 |
| Summary | 398 |
| Problems | 399 |
| Supplementary Problems | 401 |
| Chapter 18 Reactions of Nucleophiles with Alkenes and Aromatic Compounds | 402 |
| 18.1 Nucleophilic Addition to α , β -Unsaturated Carbonyl Compounds | 403 |
| 18.1.1 Conjugate addition and carbonyl addition | 404 |

| | |
|---|-----|
| 18.1.2 Kinetic and thermodynamic control of carbonyl and conjugate additions | 406 |
| 18.1.3 Addition of organometallic reagents and metal hydrides to α, β -unsaturated carbonyl compounds | 406 |
| 18.2 Nucleophilic Addition to Other Electrophilic Alkenes | 408 |
| 18.3 Anionic Polymerization | 409 |
| Panel 18.1 Cyanoacrylate esters in instant glues, for the detection of fingerprints, and in medicine | 410 |
| 18.4 Conjugate Addition of Enolate Ions to α, β -Unsaturated Carbonyl Compounds | 410 |
| 18.4.1 The Michael reaction | 410 |
| 18.4.2 The Robinson annulation | 411 |
| 18.5 Substitution by a Conjugate Addition-Elimination Mechanism | 412 |
| 18.6 Nucleophilic Aromatic Substitution by the Addition-Elimination Mechanism | 412 |
| 18.7 Nucleophilic Aromatic Substitution by the Elimination-Addition Mechanism | 414 |
| 18.8 Reactions of Arenediazonium Salts | 416 |
| Panel 18.2 Benzyne intermediates | 417 |
| Summary | 418 |
| Problems | 419 |
| Supplementary Problems | 421 |
| Chapter 19 Polycyclic and Heterocyclic Aromatic Compounds | 423 |
| 19.1 Polycyclic Aromatic Compounds | 424 |
| 19.1.1 Structures of polycyclic aromatic hydrocarbons | 424 |
| Panel 19.1 Graphene, nanotubes, and fullerenes | 425 |
| 19.1.2 Reactions of polycyclic aromatic hydrocarbons | 426 |
| Panel 19.2 Carcinogenicity of polycyclic aromatic compounds: epoxide intermediates and detoxification | 428 |
| 19.2 Structures of Aromatic Heterocyclic Compounds | 429 |
| 19.3 Acid-Base Properties of Heteroaromatic Compounds containing Nitrogen Atoms | 430 |
| 19.3.1 Basicity of nitrogen-containing heteroaromatic compounds | 430 |
| 19.3.2 Acidity of pyrrole and imidazole | 432 |
| 19.4 Reactions of Heteroaromatic Compounds | 432 |
| 19.4.1 Reactions of pyrrole, furan, and thiophene | 432 |
| Panel 19.3 Alkaloids: amines in nature | 433 |
| 19.4.2 Reactions of pyridine and its derivatives | 435 |
| 19.5 Synthesis of Aromatic Heterocyclic Compounds | 439 |
| Summary | 441 |
| Problems | 441 |
| Supplementary Problems | 442 |
| Chapter 20 Reactions involving Radicals | 444 |
| 20.1 Homolysis | 445 |
| 20.2 Structure and Stability of Radicals | 446 |
| Panel 20.1 The first radical observed by Gomberg | 446 |
| 20.3 Halogenation of Alkyl Groups | 447 |
| 20.3.1 Chlorination of methane | 447 |
| 20.3.2 Selectivity in the halogenation of alkanes | 448 |
| 20.3.3 Halogenation at allylic and benzylic positions | 450 |
| 20.4 Dehalogenation and Related Reductions | 452 |
| 20.5 Radical Addition Reactions | 453 |
| 20.5.1 Radical addition of HBr to alkenes | 453 |
| 20.5.2 Radical additions to alkenes involving Bu_3SnH | 455 |

| | |
|---|-----|
| 20.6 Intramolecular Reactions of Radicals | 455 |
| 20.6.1 Cyclization of alkenyl radicals | 455 |
| 20.6.2 1,5-Hydrogen transfer | 456 |
| 20.6.3 Fragmentation of radicals | 458 |
| 20.7 Radical Polymerization of Alkenes | 459 |
| 20.8 Autoxidation | 460 |
| 20.9 Formation of Radical Ions by Single Electron Transfer and their Reactions | 461 |
| 20.9.1 Dissolving metal reduction | 462 |
| 20.9.2 One-electron reduction of carbonyl compounds and radical coupling | 463 |
| 20.9.3 The radical mechanism of nucleophilic substitution | 464 |
| 20.9.4 Electrode reactions | 465 |
| Panel 20.2 Chlorofluorocarbons and the ozone layer | 465 |
| Summary | 466 |
| Problems | 466 |
| Supplementary Problems | 468 |

Chapter 21 Pericyclic Reactions: Cycloadditions, Electrocyclic Reactions, and Sigmatropic Rearrangements 469

| | |
|--|-----|
| 21.1 Three Main Types of Pericyclic Reactions | 470 |
| 21.2 Cycloadditions | 470 |
| 21.2.1 Diels–Alder reactions | 471 |
| 21.2.2 1,3-Dipolar cycloaddition | 475 |
| 21.2.3 Ozonolysis of alkenes | 476 |
| 21.2.4 Reaction of osmium tetroxide with alkenes | 477 |
| 21.2.5 Other cycloadditions and related reactions | 478 |
| 21.3 Electrocyclic Reactions | 481 |
| 21.4 Sigmatropic Rearrangements of Nonpolar Molecules | 482 |
| 21.4.1 [3,3] Sigmatropic rearrangements | 483 |
| 21.4.2 [1,5] Sigmatropic rearrangements | 484 |
| Panel 21.1 Biological pericyclic reactions in vitamin D formation | 486 |
| Summary | 486 |
| Problems | 487 |
| Supplementary Problems | 488 |

Chapter 22 Rearrangement Reactions involving Polar Molecules and Ions 490

| | |
|---|-----|
| 22.1 1,2-Shifts in Carbenium Ions | 490 |
| 22.2 Concerted 1,2-Shifts bypassing the Formation of Unstable Carbenium Ions | 493 |
| 22.3 Catalysed Rearrangement of Carbonyl Compounds involving 1,2-Shifts | 494 |
| 22.4 Concerted 1,2-Shifts from Carbon to Oxygen and Nitrogen | 495 |
| 22.4.1 The Baeyer–Villiger oxidation | 495 |
| 22.4.2 The Beckmann rearrangement | 496 |
| 22.5 Rearrangements involving Carbenes and Nitrenes or their Precursors | 497 |
| 22.5.1 Carbenes | 497 |
| 22.5.2 Nitrenes | 497 |
| 22.6 Rearrangements involving Neighbouring Group Participation | 498 |
| 22.6.1 Participation by groups with lone pairs | 498 |
| 22.6.2 Participation by aryl groups | 500 |
| 22.6.3 Participation by carbon–carbon double bonds | 500 |
| 22.6.4 Participation by carbon–carbon σ bonds | 501 |
| Summary | 503 |
| Problems | 503 |
| Supplementary Problems | 505 |

Chapter 23 Organic Synthesis

| | |
|--|-----|
| 23.1 Reactions used in Organic Synthesis | 506 |
| 23.2 Planning Organic Syntheses: Retrosynthetic Analysis | 507 |
| Panel 23.1 Recent C–C bond-forming reactions using catalytic organometallic complexes | 507 |
| 23.2.1 Disconnections: synthons and the corresponding reagents | 508 |
| 23.2.2 Exploiting functional group interconversions: synthesis of a representative secondary alcohol | 510 |
| 23.2.3 Disconnections at heteroatoms | 512 |
| 23.2.4 Multiple functionalities which lead to standard disconnections | 513 |
| 23.3 Chemoselectivity and Functional Group Protection | 516 |
| 23.3.1 Selectivity in chemical reactions | 516 |
| 23.3.2 Protection and deprotection | 517 |
| 23.4 Efficiency in Organic Synthesis | 519 |
| 23.5 Stereoselectivity and Asymmetric Synthesis | 521 |
| 23.6 An Example of a Multistep Synthesis | 523 |
| Summary | 524 |
| Problems | 525 |

Chapter 24 Chemistry of Biomolecules

| | |
|---|-----|
| 24.1 Carbohydrates | 528 |
| 24.1.1 Monosaccharides | 529 |
| 24.1.2 Glycosides | 530 |
| Panel 24.1 The anomeric effect | 531 |
| 24.1.3 Reduction and oxidation of monosaccharides | 531 |
| 24.1.4 Disaccharides and polysaccharides | 533 |
| 24.2 Nucleic Acids | 534 |
| 24.2.1 Nucleosides and nucleotides | 535 |
| 24.2.2 DNA and RNA | 537 |
| 24.2.3 Base pairing in nucleic acids | 537 |
| 24.3 Amino Acids, Peptides, and Proteins | 539 |
| 24.3.1 α -Amino acids | 539 |
| 24.3.2 Structures of peptides | 542 |
| 24.3.3 Synthesis of peptides | 543 |
| 24.3.4 Determination of peptide and protein sequences | 546 |
| 24.3.5 Structures of proteins | 547 |
| 24.4 Lipids | 550 |
| 24.4.1 Fats and oils | 550 |
| Panel 24.2 Micelles and detergents | 551 |
| 24.4.2 Phospholipids | 551 |
| 24.4.3 Terpenes | 553 |
| Panel 24.3 Origin of the isoprene unit for terpene biosynthesis | 554 |
| 24.4.4 Steroids | 554 |
| Panel 24.4 Biosynthesis of cholesterol from squalene | 555 |
| 24.4.5 Eicosanoids | 557 |
| Summary | 557 |
| Problems | 558 |

Chapter 25 Structural Determination of Organic Compounds

| | |
|---|-----|
| 25.1 Electromagnetic Radiation and Spectroscopy | 561 |
| 25.1.1 The electromagnetic spectrum and types of spectroscopy | 561 |
| 25.1.2 Interactions of electromagnetic radiation with molecules | 562 |
| 25.2 Ultraviolet and Visible Spectroscopy | 563 |

| | |
|--|-----|
| 25.3 Infrared Spectroscopy | 564 |
| 25.3.1 Introduction to IR spectroscopy | 564 |
| 25.3.2 Examples of IR spectra | 566 |
| 25.4 Nuclear Magnetic Resonance Spectroscopy: Proton NMR Spectra | 571 |
| 25.4.1 Physical basis of NMR | 571 |
| 25.4.2 Proton chemical shifts | 572 |
| 25.4.3 Integration: proton counting | 575 |
| Panel 25.1 Aromaticity and ring currents | 575 |
| 25.4.4 Spin–spin splitting | 576 |
| 25.4.5 Interpretation of ^1H NMR spectra | 580 |
| Panel 25.2 Topicity | 582 |
| 25.4.6 Disappearance of spin–spin coupling | 584 |
| 25.4.7 The nuclear Overhauser effect | 585 |
| 25.5 Carbon-13 NMR Spectra | 586 |
| 25.5.1 Introduction to ^{13}C NMR spectra | 586 |
| 25.5.2 Interpretation of ^{13}C NMR spectra | 587 |
| 25.6 Mass Spectrometry | 589 |
| 25.6.1 The mass spectrometric method | 589 |
| 25.6.2 The mass spectrum and fragment ions | 590 |
| 25.6.3 High-resolution mass spectrometry: determination of molecular formulas | 598 |
| 25.6.4 Advanced types of mass spectrometry | 599 |
| Summary | 599 |
| Problems | 599 |

Appendices

| | |
|--|-----|
| Appendix 1 pK_a Values of Representative Compounds | 602 |
| Appendix 2 Principal Reactions of Functional Groups | 605 |
| Appendix 3 Syntheses of Classes of Compounds | 608 |
| Appendix 4 Reactions for the Formation of Carbon–Carbon Bonds | 615 |

Additional Resources

| | |
|--|-----|
| Symbols and Recommended Values of Some Physical Constants / Unit Conversions | 617 |
| Symbols of SI Prefixes for Multiplicities and Fractions | 618 |
| Fundamental Classes of Reactions and Guidelines for Writing Curly Arrows | 618 |
| Index | 619 |