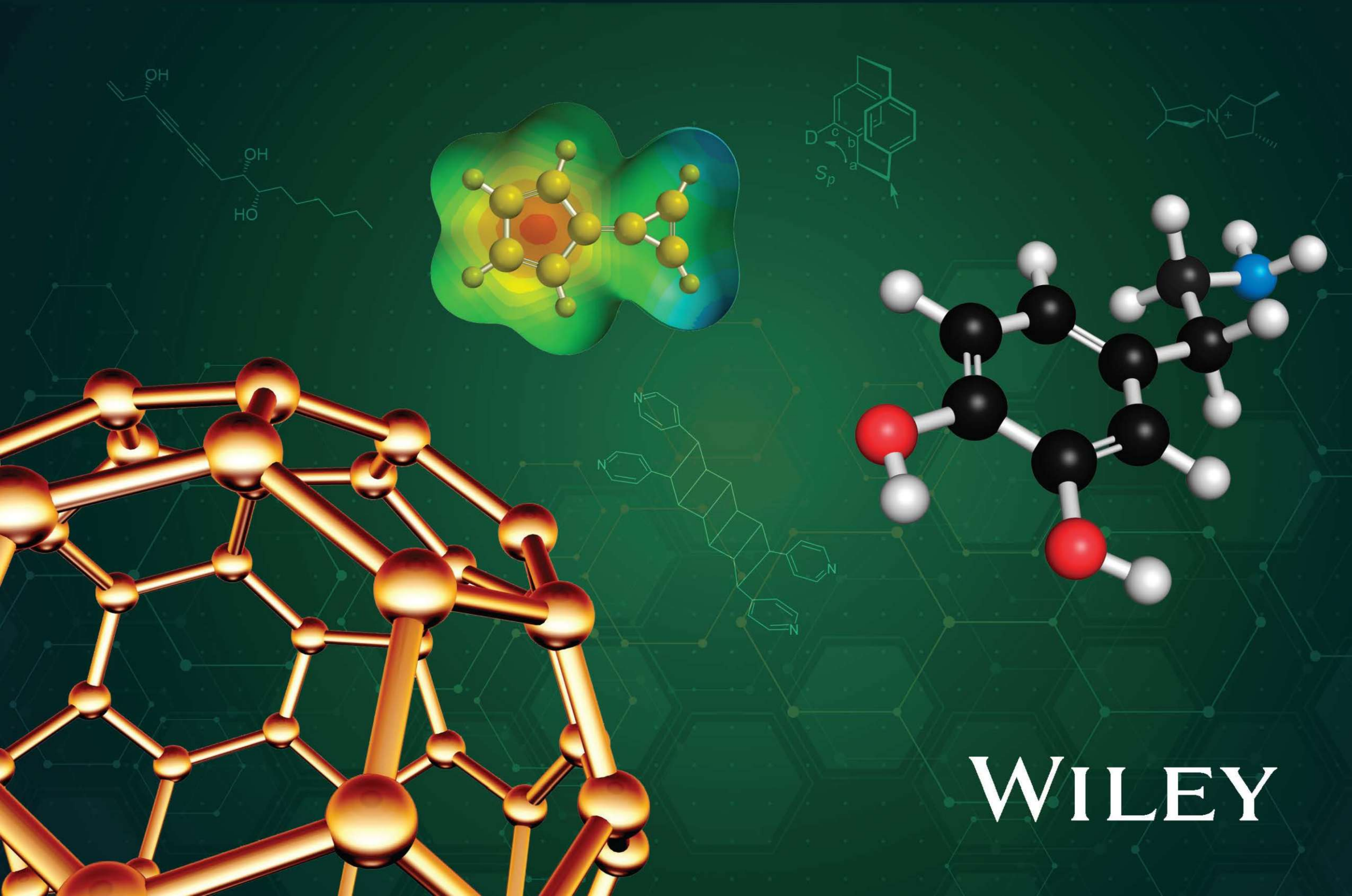
THIRD EDITION

PERSPECTIVES ON STRUCTURE AND MECHANISM IN ORGANIC CHEMISTRY

FELIX A. CARROLL



OH
OH
HO
D
c
b
a
S_p
N+
N
N
N
N

WILEY

PERSPECTIVES ON STRUCTURE AND MECHANISM IN ORGANIC CHEMISTRY

PERSPECTIVES ON STRUCTURE AND MECHANISM IN ORGANIC CHEMISTRY

Third Edition

Felix A. Carroll
Emeritus Professor
Davidson College, North Carolina, United States

WILEY

Copyright © 2023 by John Wiley & Sons, Inc. All rights reserved.

Published by John Wiley & Sons, Inc., Hoboken, New Jersey.
Published simultaneously in Canada.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, scanning, or otherwise, except as permitted under Section 107 or 108 of the 1976 United States Copyright Act, without either the prior written permission of the Publisher, or authorization through payment of the appropriate per-copy fee to the Copyright Clearance Center, Inc., 222 Rosewood Drive, Danvers, MA 01923, (978) 750-8400, fax (978) 750-4470, or on the web at www.copyright.com. Requests to the Publisher for permission should be addressed to the Permissions Department, John Wiley & Sons, Inc., 111 River Street, Hoboken, NJ 07030, (201) 748-6011, fax (201) 748-6008, or online at http://www.wiley.com/go/permission.

Trademarks: Wiley and the Wiley logo are trademarks or registered trademarks of John Wiley & Sons, Inc. and/or its affiliates in the United States and other countries and may not be used without written permission. All other trademarks are the property of their respective owners. John Wiley & Sons, Inc. is not associated with any product or vendor mentioned in this book.

Limit of Liability/Disclaimer of Warranty: While the publisher and author have used their best efforts in preparing this book, they make no representations or warranties with respect to the accuracy or completeness of the contents of this book and specifically disclaim any implied warranties of merchantability or fitness for a particular purpose. No warranty may be created or extended by sales representatives or written sales materials. The advice and strategies contained herein may not be suitable for your situation. You should consult with a professional where appropriate. Further, readers should be aware that websites listed in this work may have changed or disappeared between when this work was written and when it is read. Neither the publisher nor authors shall be liable for any loss of profit or any other commercial damages, including but not limited to special, incidental, consequential, or other damages.

For general information on our other products and services or for technical support, please contact our Customer Care Department within the United States at (800) 762-2974, outside the United States at (317) 572-3993 or fax (317) 572-4002.

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic formats. For more information about Wiley products, visit our web site at www.wiley.com.

Library of Congress Cataloging-in-Publication Data applied for

ISBN: 9781119808619; epub:9781119808633; ePDF: 9781119808640

Cover Image: © berCheck/Shutterstock; MOLEKUUL/SCIENCE PHOTO LIBRARY; ALFRED PASIEKA/SCIENCE PHOTO LIBRARY; Calicene image created by and courtesy of Felix A. Carroll
Cover Design: Wiley

Set in 10/12pt Palatino by Straive, Pondicherry, India

Contents

Preface *xi*

Chapter 1 | ***Fundamental Models of Organic Chemistry*** ***1***

1.1 Atoms and Molecules 1
Basic Concepts 1
Molecular Dimensions 5
1.2 Heats of Formation and Reaction 8
Experimental Determination of Heats of Formation 8
Bond Increment Calculation of Heats of Formation 10
Group Increment Calculation of Heats of Formation 11
Heats of Formation and the Concept of Protobranching 13
Homolytic and Heterolytic Bond Dissociation Energies 15
1.3 Bonding Models 18
Electronegativity and Bond Polarity 20
Complementary Theoretical Models of Bonding 23
Pictorial Representations of Bonding Concepts 27
sp^3 Hybridization 28
Are There sp^3 Hybrid Orbitals in Methane? 30
Hybridization and Molecular Geometry 34
Variable Hybridization 35
1.4 Complementary Models for the Double Bond 41
The σ,π Description of Ethene 41
The Bent Bond Description of Ethene 42
Predictions of Physical Properties with the Two Models 42
1.5 The Role of Complementary Models in Organic Chemistry 46
Problems 47

Chapter 2 | ***Introduction to Computational Chemistry*** ***53***

2.1 Hückel Molecular Orbital Theory 53
Correlation of Physical Properties with Results of HMO Calculations 63
Other Parameters Generated Through HMO Theory 67
Properties of Odd Alternant Hydrocarbons 69
The Frost Circle 74
2.2 Aromaticity 75
Benzene 77
Other Aromatic Systems 81
Polycyclic Conjugated Systems 85
Larger Annulenes 90
Dewar Resonance Energy and Absolute Hardness 93

2.3 Contemporary Computational Methods 95
Extended Hückel Theory 95
Semiempirical Methods 96
Ab Initio Theory 97
2.4 Localized Molecular Orbitals 100
Perturbational Molecular Orbital Theory 104
Atoms in Molecules 108
2.5 Density Functional Theory 112
2.6 Another Look at Valence Bond Theory 114
Resonance Structures and Resonance Energies 114
Interpreting Computational Results 117
Problems 119

Chapter 3 | *Stereochemistry* *127*

3.1 Representations of Three-Dimensional Structures 127
3.2 Stereoisomerism 130
Isomerism 130
Symmetric, Asymmetric, Dissymmetric, and Nondissymmetric Molecules 133
Fischer Projections 146
Additional Stereochemical Designations 149
3.3 Physical Manifestations of Chirality 159
Optical Activity 159
Configuration and Optical Activity 161
Other Physical Properties of Stereoisomers 166
3.4 Stereotopicity 167
Stereochemical Relationships of Substituents 167
Chirotopicity and Stereogenicity 171
Problems 172

Chapter 4 | *Molecular Geometry and Steric Energy* *183*

4.1 Designation of Molecular Conformation 183
4.2 Conformational Analysis 187
Torsional Strain 187
van der Waals Strain 191
Angle Strain and Baeyer Strain Theory 193
Application of Conformational Analysis to Cycloalkanes 194
Conformational Analysis of Substituted Cyclohexanes 198
4.3 Molecular Mechanics 204
4.4 Anomeric Effect 221
4.5 Strain and Molecular Stability 225
Problems 237

Chapter 5 | *Reactive Intermediates* *243*

5.1 Reaction Coordinate Diagrams 243
5.2 Radicals 244
Early Evidence for the Existence of Radicals 244
Detection and Characterization of Radicals 246
Structure and Bonding of Radicals 251
Thermochemical Data for Radicals 253

Generation of Radicals 255
Radical Chain Reactions 256
5.3 Carbenes 263
Structure and Geometry of Carbenes 263
Generation of Carbenes 267
Reactions of Carbenes 268
5.4 Carbocations 272
Carbonium Ions and Carbenium Ions 272
Structure and Geometry of Carbocations 274
The 2-Norbornyl Cation 281
Carbocation Rearrangements 283
Radical Cations 285
5.5 Carbanions 290
Generation of Carbanions 294
Stability of Carbanions 296
Reactions of Carbanions 296
5.6 Choosing Models of Reactive Intermediates 298
Problems 299

Chapter 6 | *Determining Reaction Mechanisms* *305*

6.1 Reaction Mechanisms 305
6.2 Methods to Determine Reaction Mechanisms 306
Identification of Reaction Products 306
Determination of Intermediates 306
Crossover Experiments 311
Isotopic Labeling 313
Stereochemical Studies 314
Solvent Effects 315
Computational Studies 317
6.3 Applications of Kinetics in Studying Reaction Mechanisms 319
6.4 Arrhenius Theory and Transition State Theory 326
6.5 Reaction Barriers and Potential Energy Surfaces 337
6.6 Kinetic Isotope Effects 348
Primary Kinetic Isotope Effects 349
Secondary Kinetic Isotope Effects 354
Tunneling and Isotope Effects 359
Solvent Isotope Effects 362
6.7 Substituent Effects 363
6.8 Linear Free Energy Relationships 368
Problems 383

Chapter 7 | *Acid and Base Catalysis of Organic Reactions* *393*

7.1 Acidity and Basicity of Organic Compounds 393
Acid–Base Measurements in Solution 393
Acid–Base Reactions in the Gas Phase 402
Comparison of Gas Phase and Solution Acidities 408
Acidity Functions 410
7.2 Acid and Base Catalysis of Chemical Reactions 413
Specific Acid Catalysis 413
General Acid Catalysis 414
Brønsted Catalysis Law 417

7.3 Acid and Base Catalysis of Reactions of Carbonyl Compounds and Carboxylic Acid Derivatives 418
Addition to the Carbonyl Group 418
Enolization of Carbonyl Compounds 422
Hydrolysis of Acetals 426
Acid-Catalyzed Hydrolysis of Esters 428
Alkaline Hydrolysis of Esters 431
Hydrolysis of Amides 437
Problems 441

Chapter 8 | *Substitution Reactions* *449*

8.1 Introduction 449
8.2 Nucleophilic Aliphatic Substitution 450
8.3 The S_N1 Reaction 453
Kinetics 453
Structural Effects in S_N1 Reactions 454
Solvent Polarity and Nucleophilicity 455
Solvated Ions and Ion Pairs 459
Anchimeric Assistance in S_N1 Reactions 464
Nonclassical Carbocations in S_N1 Reactions 469
8.4 The S_N2 Reaction 471
Stereochemistry 471
Solvent Effects 473
Substrate Effects 477
8.5 Quantitative Measures of Nucleophilicity 480
Brønsted Correlations 481
Hard–Soft Acid–Base Theory and Nucleophilicity 482
Edwards Equations 483
Swain-Scott Equation 484
Mayr Equations 485
The α-Effect 488
Leaving Group Effects in S_N2 Reactions 489
Aliphatic Substitution and Single Electron Transfer 490
8.6 Electrophilic Aromatic Substitution 495
The S_EAr Reaction 495
Quantitative Measurement of S_EAr Rate Constants: Partial Rate Factors 498
Lewis Structures as Models of Reactivity in S_EAr Reactions 500
8.7 Nucleophilic Aromatic and Vinylic Substitution 504
Nucleophilic Aromatic Substitution 504
Nucleophilic Vinylic Substitution 509
8.8 Substitution Involving Benzyne Intermediates 511
8.9 Radical-Nucleophilic Substitution 518
8.10 The Impermanence of Mechanistic Labels 521
Problems 521

Chapter 9 | *Elimination Reactions* *529*

9.1 Introduction 529
9.2 Dehydrohalogenation and Related 1,2-Elimination Reactions 534
Potential Energy Surfaces for 1,2-Elimination 534
Competition Between Substitution and Elimination 540
Stereochemistry of 1,2-Elimination Reactions 541

Elimination Reactions to Produce Alkynes 547
Regiochemistry of 1,2-Elimination Reactions 548
9.3 Other 1,2-Elimination Reactions 558
Dehalogenation of Vicinal Dihalides 558
Dehydration of Alcohols 561
Deamination of Amines 568
Pyrolytic Eliminations 572
Problems 578

Chapter 10 | *Addition Reactions* *587*

10.1 Introduction 587
10.2 Addition of Halogens to Alkenes 588
Electrophilic Addition of Bromine to Alkenes 588
Role of Charge-Transfer Complexes in Bromine Addition Reactions 592
Kinetics of Bromine Addition Reactions 593
Solvent Effects in Bromine Additions 596
Reversibility of Bromine Addition 598
Intermediates in the Addition of Bromine to Alkyl-Substituted Alkenes 599
Intermediates in the Addition of Bromine to Aryl-Substituted Alkenes 604
Summary of Bromine Addition 608
Addition of Other Halogens to Alkenes 609
10.3 Other Addition Reactions 618
Addition of Hydrogen Halides to Alkenes 618
Hydration of Alkenes 625
Oxymercuration 628
Hydroboration 632
Epoxidation 637
Electrophilic Addition to Alkynes and Cumulenes 639
Nucleophilic Addition to Alkenes and Alkynes 647
Nucleophilic Addition to Carbonyl Compounds 651
Problems 656

Chapter 11 | *Pericyclic Reactions* *661*

11.1 Introduction 661
11.2 Electrocyclic Transformations 665
Definitions and Selection Rules 665
MO Correlation Diagrams 670
State Correlation Diagrams 675
11.3 Sigmatropic Reactions 678
Selection Rules for Sigmatropic Reactions 679
Other Examples of Sigmatropic Reactions 687
11.4 Cycloaddition Reactions 691
Introduction 691
Ethene Dimerization 692
The Diels–Alder Reaction 694
Selection Rules for Cycloaddition Reactions 698
11.5 Other Pericyclic Reactions 705
Cheletropic Reactions 705
Double Group Transfer Reactions 707
Ene Reactions 709

11.6 A General Selection Rule for Pericyclic Reactions 711
11.7 Alternative Conceptual Models for Pericyclic Reactions 713
  Frontier Molecular Orbital Theory 713
  Hückel and Möbius Aromaticity of Transition Structures 719
  Synchronous and Nonsynchronous Pericyclic Reactions 725
  Potential Energy Surfaces and Ambimodal Reactions 729
11.8 Reaction Dynamics and Potential Energy Surfaces 729
  Problems 735

Chapter 12 | *Organic Photochemistry* *745*

12.1 Energy and Electronic States 745
12.2 Photophysical Processes 747
  Designation of Spectroscopic Transitions 748
  Selection Rules for Radiative Transitions 754
  Fluorescence and Phosphorescence 756
  Energy Transfer and Electron Transfer 759
12.3 Photochemical Kinetics 763
  Actinometry and Quantum Yield Determinations 763
  Rate Constants for Unimolecular Processes 764
  Transient Detection and Monitoring 765
  Bimolecular Decay of Excited States: Stern–Volmer Kinetics 768
12.4 Physical Properties of Excited States 770
  Acidity and Basicity in Excited States 770
  Bond Angles and Dipole Moments of Excited-State Molecules 774
12.5 Representative Photochemical Reactions 777
  Photochemical Reactions of Alkenes and Dienes 778
  Photochemical Reactions of Carbonyl Compounds 790
  Photochemical Reactions of α,ß-Unsaturated Carbonyl Compounds 798
  Photochemical Reactions of Aromatic Compounds 800
  Photosubstitution Reactions 802
  σ Bond Photodissociation Reactions 803
  Singlet Oxygen and Organic Photochemistry 808
12.6 Applications of Organic Photochemistry 811
  Problems 822

References for Selected Problems 831

Index 837

Preface

This is the third edition of an advanced textbook about the structures of organic compounds and the mechanisms of their reactions. The word *Perspectives* in the title suggests an approach to understanding physical organic chemistry in terms of complementary conceptual and mathematical models. All of the chapters in this edition have been updated, and new topics have been added. In addition, chapters are now arranged for better concept flow. For example, discussing theoretical chemistry in Chapter 2 provides background information for additional topics in the chapters on stereochemistry and molecular geometry. The discussion of elimination reactions now follows the chapter on substitutions, and the discussion of addition reactions now precedes the chapter on pericyclic reactions.

It is essential for an advanced textbook to provide complete references. Citations ranging in date from 1851 to 2022 direct readers to further discussion of the topics and acknowledge the researchers whose work produced the information. A teaching text must also provide problems of varying difficulty. The 438 problems in this edition encourage readers to actively engage the chemical literature and to develop and defend their own ideas. Some problems involve straightforward applications of material in the text, while other problems can best be answered by consulting primary and secondary sources for background information before attempting a solution. Still other problems are open ended and are designed to stimulate independent thinking and discussion.

As discussed in the Preface to the second edition, my thinking about physical organic chemistry was influenced by George Hammond and the works of Jakob Bronowski. Hammond's name is well known to organic chemists, but Bronowski is less familiar. In the film *Knowledge or Certainty*, Bronowski showed different portraits of the same human face and observed that "We are aware that these pictures do not so much fix the face as explore it… and that each line that is added strengthens the picture but never makes it final."[1] In many ways, a textbook is a portrait of a particular field of study.

---

[1] The quotation is from Bronowski, J. *The Ascent of Man*; Little, Brown and Company: Boston, **1973**, p. 353.

I hope the lines added to the third edition of this book will help readers develop an even deeper and more complete understanding of physical organic chemistry.

FELIX A. CARROLL
Professor Emeritus
Davidson College

CHAPTER 1

Fundamental Models of Organic Chemistry

1.1 ATOMS AND MOLECULES

Basic Concepts

Organic chemists think of atoms and molecules as basic units of matter. We work with mental pictures of atoms and molecules, and we rotate, twist, disconnect, and reassemble physical models in our hands.[1,2] Where do these mental images and physical models come from? It is useful to begin thinking about the fundamental models of organic chemistry by asking a simple question: What do we know about atoms and molecules, and how do we know it? As Kuhn pointed out,

> Though many scientists talk easily and well about the particular individual hypotheses that underlie a concrete piece of current research, they are little better than laymen at characterizing the established bases of their field, its legitimate problems and methods.[3]

Much of what we know in organic chemistry consists of what we were taught. Underlying that teaching are observations that someone has made and someone has interpreted. The most fundamental observations are those that can be made directly with human senses. We note the physical state of a substance—solid, liquid, or gas. We see its color or lack of color. We observe whether it dissolves in a given solvent and whether it evaporates if exposed to the atmosphere. We might get some sense of its density by seeing it float or sink when added to an immiscible liquid. These are qualitative observations, but they provide an important foundation for further experimentation.

It is only a modest extension of direct observation to the use of some simple experimental apparatus for quantitative measurements. A heat source and a thermometer allow determination of melting and boiling ranges. Other

---

[1] For a detailed discussion of physical models in chemistry, see Walton, A. *Molecular and Crystal Structure Models*; Ellis Horwood: Chichester, England, 1978.

[2] For applications of physical models to infer molecular properties, see Teets, D. E.; Andrews, D. H. *J. Chem. Phys.* **1935**, *3*, 175.

[3] Kuhn, T. S. *The Structure of Scientific Revolutions*, 2nd ed.; The University of Chicago Press: Chicago, 1970; p. 47.

Perspectives on Structure and Mechanism in Organic Chemistry, Third Edition. Felix A. Carroll.
© 2023 John Wiley & Sons, Inc. Published 2023 by John Wiley & Sons, Inc.

equipment allows measurement of indices of refraction, densities, surface tensions, viscosities, and heats of reaction. Classical elemental analysis indicates the elements present in a sample and their mass ratios. In all of these experiments, the experimenter uses some equipment but *still makes the actual experimental observations by eyes*. These simple techniques can provide essential data, nonetheless. For example, finding that 159.8 grams of bromine will always be decolorized by 82.15 grams of cyclohexene leads to the law of definite proportions. In turn, that suggests a model of matter in which submicroscopic particles combine with each other in characteristic patterns, just as the macroscopic samples do. It is then only a matter of definition to call the submicroscopic particles: atoms or molecules. It is essential, however, to remember that laboratory experiments are conducted with *materials*. The chemist may talk about the addition of bromine to cyclohexene in terms of individual molecules, but that can only be inferred from experimental data collected with macroscopic samples of the reactants.

Electronic instrumentation opened the door to a variety of investigations that expand the range of observations beyond those of the human senses. These instruments extend our eyes from seeing only a limited portion of the electromagnetic spectrum to detecting practically the entire spectrum, from X-rays to radio waves, and they let us "see" light in other ways (e.g. in polarimetry). They allow us to use entirely new tools, such as electron or neutron beams, magnetic fields, and electrical potential or current. They extend the range of conditions for studying matter from near atmospheric pressure to high vacuum or high pressure. They effectively expand and compress the time scale of the observations, allowing study of events that require eons or that occur in zeptoseconds.[4,5,6]

The unifying characteristic of modern instrumentation is that we no longer observe the chemical or physical change directly. Instead, it is detected only indirectly, such as through changes in pixels on a computer display. With such instruments, it is essential to recognize the difficulty in freeing the observations from constraints imposed by expectations. *To a layperson*, a UV-vis spectrum may not seem very different from an upside-down infrared spectrum, and a capillary gas chromatogram of a complex mixture may appear to resemble a mass spectrum. But the chemist sees these images not as lines on a paper or a computer display but as vibrating or rotating molecules, as electrons moving from one place to another, as substances separated from a mixture, or as fragments produced in a mass spectrometer. Thus, implicit assumptions about the origins of experimental data both make the observations interpretable and influence the interpretation of the data.[7]

With that caveat, what do we know about molecules and how do we know it? The first assumption is that all substances are composed of

---

[4] A picosecond (ps) is 10^{-12} s. A femtosecond (fs) is 10^{-15} s. An attosecond (as) is 10^{-18} s. A zeptosecond (zs) is 10^{-21} s. For a table of metric prefixes for values ranging from 10^{30} to 10^{-30}, see Adam, A. *Science*, **2019**, *363*, 681. Rosker, M. J.; Dantus, M.; Zewail, A. H. *Science* **1988**, *241*, 1200 reported that the photodissociation of ICN to I and CN occurs in ca. 100 femtoseconds. See also Dantus, M.; Zewail, A. *Chem. Rev.* **2004**, *104*, 1717; Nisoli, M.; Decleva, P.; Calegari, F.; et al. *Chem. Rev.* **2017**, *117*, 10760.

[5] Baker, S.; Robinson, J. S.; Haworth, C. A.; et al. *Science* **2006**, *312*, 424; Osborne, I.; Yeston, J. *Science* **2007**, *317*, 765; Drescher, L.; Galbraith, M. C. E.; Reitsma, G. et al. *J. Chem. Phys.* **2016**, *145*, 011101.

[6] Grundmann, S.; Trabert, D.; Fehre, K. et al. *Science* **2020**, *370*, 6514 found the time for a photoionized electron to transverse a molecule to be 247 zs.

[7] "Innocent, unbiased observation is a myth." P. Medawar, quoted in *Science* **1985**, *227*, 1188.

atoms—indivisible particles that are the smallest units of that particular kind of matter that still retain all its properties.[8] As noted, it is convenient to correlate observations that substances combine only in certain proportions with the notion that these submicroscopic entities called atoms combine with each other only in certain ways.

Much fundamental information about molecules has been obtained from spectroscopy.[9] For example, a 4000 V electron beam has a wavelength of 0.06 Å, so it is diffracted by objects larger than that size.[10] Interaction of the electron beam with gaseous molecules produces characteristic circular patterns that can be interpreted in terms of molecular dimensions.[11] We can determine internuclear distance through infrared spectroscopy of diatomic molecules and can use X-ray or neutron scattering to calculate distances of atoms in crystals.

"Pictures" of atoms and molecules may be obtained through atomic force microscopy (AFM) and scanning tunneling microscopy (STM).[12,13] For example, investigators reported images of pentacene that displayed individual atoms,[14] polycyclic aromatic hydrocarbons that allowed determination of bond order,[15] products of single-molecule chemical reactions,[16] molecule-gears,[17] and a video of a single fullerene molecular shuttling in a vibrating carbon nanotube.[18] Investigators also reported visualizing atomic orbitals,[19] imaging the lateral profiles of individual sp^3 hybrid orbitals, and determining the electronegativity of individual surface atoms.[20,21] AFM was used to characterize the strength of intermolecular hydrogen bonds.[22] Some investigators reported imaging single organic molecules in motion with transmission electron microscopy,[23] and others reported studying electron transfer to single polymer molecules with single-molecule spectroelectrochemistry.[24]

---

[8] This idea can be traced to ancient Greek philosophers. Cf. Asimov, I. *A Short History of Chemistry*; Anchor Books: Garden City, NY, 1965; pp. 8–14.

[9] For a review of structure determination methods, see Gillespie, R. J.; Hargittai, I. *The VSEPR Model of Molecular Geometry*; Allyn and Bacon: Boston, 1991; pp. 25–39.

[10] Moore, W. J. *Physical Chemistry*, 3rd ed.; Prentice-Hall: Englewood Cliffs, NJ, 1962; p. 575 ff.

[11] For discussions of structure determination with gas phase electron diffraction, see Karle, J. in Maksić, Z. B.; Eckert-Maksić, M., Eds. *Molecules in Natural Science and Medicine*; Ellis Horwood: Chichester, England, 1991; pp. 17–27; Hedberg, K. *ibid*.; pp. 29–42.

[12] Hou, J. G.; Wang, K. *Pure Appl. Chem.* **2006**, *78*, 905.

[13] See Ottensmeyer, F. P.; Schmidt, E. E.; Olbrecht, A. J. *Science* **1973**, *179*, 175 and references therein; Robinson, A. L. *Science* **1985**, *230*, 304; *Chem. Eng. News* **1986** (Sept. 1), 4; Hansma, P. K.; Elings, V. B.; Marti, O.; et al. *Science* **1988**, *242*, 209; Parkinson, B. A. *J. Am. Chem. Soc.* **1990**, *112*, 1030; Frommer, J. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1298.

[14] Gross, L.; Mohn, F.; Moll, N.; et al. *Science* **2009**, *325*, 1110.

[15] Gross, L.; Mohn, F.; Moll, N.; et al. *Science* **2012**, *337*, 1326.

[16] de Oteyza, D. G.; Gorman, P.; Chen, Y.-C.; et al. *Science* **2013**, *340*, 1434. Albrecht, F.; Fatayer, S.; Pozo, I. et al. *Science* **2022**, *377*, 298 reported switching among three different structures with voltage applied by an STM tip.

[17] Soe, W.-H.; Srivastava, S.; Joachim, C. *J. Phys. Chem. Lett.* **2019**, *10*, 6462.

[18] Shimizu, T.; Lungerich, D.; Stuckner, J.; et al. *Bull. Chem. Soc. Jpn.* **2020**, *93*, 1079.

[19] Pardini, L.; Löffler, S.; Biddau, G.; et al. *Phys. Rev. Lett.* **2016**, *117*, 036801.

[20] Chen, J. C. *Nanotechnology* **2006**, *17*, S195.

[21] Onoda, J.; Ondráček, M.; Jelinek, P.; et al. *Nature Commun.* **2016**, *8*, 15155.

[22] Zhang, J.; Chen, P.; Yuan, B.; et al. *Science* **2013**, *342*, 611; Monig, H.; Amirjalayer, S.; Timmer, A.; et al. *Nature Nanotech.* **2018**, *13*, 371.

[23] Koshino, M.; Tanaka, T.; Solin, N.; et al. *Science* **2007**, *316*, 853.

[24] Palacios, R. E.; Fan, F.-R. F.; Bard, A. J.; et al. *J. Am. Chem. Soc.* **2006**, *128*, 9028.

Even though "seeing is believing," it is important to remember that these experiments do not really show molecules—just computer graphics. Some examples illustrate this point: STM features that had been associated with DNA molecules were later assigned to the surface used to support the DNA.[25] An STM image of benzene molecules was reinterpreted as possibly showing groups of acetylene molecules instead.[26] AFM images suggesting the visualization of intermolecular hydrogen bonds were questioned when it was shown that similar images could be observed when such hydrogen bonding should not be possible.[27,28]

Organic chemists also reach conclusions about molecular structure on the basis of logic. For example, the fact that one and only one substance has been found to have the molecular formula CH_3Cl is consistent with a structure in which three hydrogen atoms and one chlorine atom are attached to a carbon atom in a tetrahedral arrangement. If methane were a trigonal pyramid, then two different compounds with the formula CH_3Cl might be possible—one with chlorine at the apex of the pyramid and another with chlorine in the base of the pyramid. The existence of only one isomer of CH_3Cl does not require a tetrahedral arrangement; however, since there could also be only one isomer if the four substituents to the carbon atom were arranged in a square pyramid with a carbon atom at the apex or in a square planar structure with a carbon atom at the center. Since no one has identified more than one CH_2Cl_2 molecule, the latter two geometries seem unlikely. Therefore, the parent compound, methane, may be tetrahedral as well. This view is reinforced by the existence of two different structures (enantiomers) with the formula CHClBrF. Similarly, we infer the flat, aromatic structure for benzene by noting that there are three and only three isomers of dibromobenzene.[29]

Organic chemists do not think of molecules only in terms of atoms, however. We often envision molecules as collections of nuclei and electrons and consider the electrons to be constrained to certain regions of space (orbitals) around the nuclei. Thus, we interpret UV-vis absorption and emission spectroscopy in terms of movement of electrons from one orbital to another. These concepts resulted from the development of quantum mechanics. The Bohr model of the atom, the Heisenberg uncertainty principle, and the Schrödinger equation laid the foundation for current ways of thinking about chemistry. Although there may be some truth in the statement that

> The why? and how? as related to chemical bonding were in principle answered in 1927; the details have been worked out since that time.[30]

there are still uncharted frontiers of those details to explore in organic chemistry.

---

[25] Clemmer, C. R.; Beebe, T. P, Jr. *Science* **1991**, *251*, 640.

[26] Moler, J. L.; McCoy, J. R. *Chem. Eng. News* **1988** (Oct. 24), 2.

[27] Hämäläinen, S. I.; van der Heijden, N.; van der Lit, J.; et al. *Phys. Rev. Lett.* **2014**, *113*, 186102; Guo, C.-S.; Xin, X.; Van Hove, M. A.; et al. *J. Phys. Chem. C* **2015**, *119*, 14195.

[28] Reports that orbitals can be imaged were challenged because molecular orbitals "are not unique and are not observable." Pham, B. Q.; Gordon, M. S. *J. Phys. Chem. A* **2017**, *121*, 4851. See also Autschbach, J. *J. Chem. Educ.* **2012**, *89*, 1032.

[29] These examples were discussed in an analysis of "topological thinking" in organic chemistry by Turro, N. J. *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 882.

[30] Ballhausen, C. J. *J. Chem. Educ.* **1979**, *56*, 357.

Molecular Dimensions

Data from spectroscopy or from X-ray, electron, or neutron diffraction measurements allow us to determine the distance between atomic centers as well as to measure the angles between sets of atoms in covalently bonded molecules.[31] The most detailed information comes from microwave spectroscopy, although that technique is more useful for lower molecular weight than higher molecular weight molecules because the sample must be in the gas phase.[32] Diffraction methods locate a center of electron density instead of a nucleus, but center of electron density is close to the nucleus for atoms that have electrons below the valence shell. For hydrogen, however, the electron density is shifted toward the atom to which it is bonded, and bonds to hydrogen are determined by diffraction methods to be shorter than bond lengths determined with spectroscopy.[33] With solid samples, the possible effect of crystal-packing forces must also be considered. Therefore, the various techniques give slightly different measures of molecular dimensions.

Table 1.1 shows data for the interatomic distances and angles of the methyl halides.[34,35] These distances and angles only provide geometric information about the location of nuclei (or local centers of electron density) as points in space. Chemists infer that those points are connected by chemical bonds, so the distance $r_{\text{C–H}}$ is the length of a C–H bond and the angle $\angle_{\text{H–C–H}}$ is the angle between two C–H bonds on the same carbon atom.

We may also define atomic dimensions, including the ionic radius (r_{i}), the covalent radius (r_{c}), and the van der Waals radius (r_{vdW}) of an atom.[36] The ionic radius is the apparent size of the electron cloud around an ion as deduced from the packing of ions into a crystal lattice.[37] As might be expected, this value varies with the charge on the ion. The ionic radius for a C^{4+} ion is

TABLE 1.1 Bond Lengths and Bond Angles for Methyl Halides

Molecule	$r_{\text{C–H}}$ (Å)	$r_{\text{C–X}}$ (Å)	$\angle_{\text{H–C–H}}$	$\angle_{\text{H–C–X}}$
CH_3F	1.105	1.385	109°54′	109°2′
CH_3Cl	1.096	1.781	110°52′	108°0′
CH_3Br	1.10	1.939	111°38′	107°14′
CH_3I	1.096	2.139	111°50′	106°58′

Source: Adapted from reference 34.

---

[31] A tabulation of common bond length values was provided by Allen, F. H.; Kennard, O.; Watson, D. G.; et al. *J. Chem. Soc. Perkin Trans. 2* **1987**, S1.

[32] Wilson, E. B. *Chem. Soc. Rev.* **1972**, *1*, 293 and references therein; see also Harmony, M. D. *Acc. Chem. Res.* **1992**, *25*, 321.

[33] Clark, T. *A Handbook of Computational Chemistry*; John Wiley & Sons: New York, 1985; chapter 2.

[34] (a) Tabulations of bond length and bond angle measurements for specific molecules are available in *Tables of Interatomic Distances and Configuration in Molecules and Ions*; compiled by Bowen, H. J. M.; Donohue, J.; Jenkin, D. G.; et al. Special Publication No. 11, Chemical Society (London): Burlington House, W1, London, 1958. (b) See also the 1965 Supplement.

[35] See Johnson, R. D., III, Ed. *NIST Computational Chemistry Comparison and Benchmark Database*. NIST Standard Reference Database Number 101, Release 21, August 2020, http://cccbdb.nist.gov/.

[36] Pauling, L. *Nature of the Chemical Bond*, 3rd ed.; Cornell University Press: Ithaca, NY, 1960.

[37] For an extensive discussion of ionic radii, see Marcus, Y. *Ion Properties*; Marcel Dekker: New York, 1997.

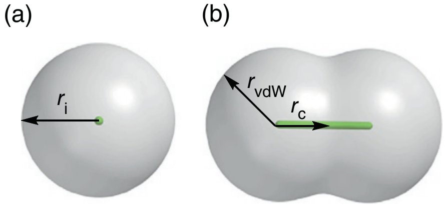


FIGURE 1.1
Radii values for chlorine.

0.15 Å, while that for a C^{4-} ion is 2.60 Å.[36] The van der Waals radius is the effective size of the electron cloud around a covalently bonded atom as perceived by another atom to which it is not bonded, and it also is determined from interatomic distances found in crystals. Note that the van der Waals radius is not the distance at which the repulsive interactions of the electrons on the two atoms outweigh the attractive forces between them, as is often assumed. Rather, it is a crystal packing measurement that gives a smaller value.[38,39] The term van der Waals *radius* implies a spherical electron density distribution, but calculations indicate that many electron density distributions are spheroidal.[40,41,42] The covalent radius of an atom indicates the size of an atom when it is part of a covalent bond, and this distance is much less than the van der Waals radius.[43] Figure 1.1 illustrates these radii for chlorine. The computer-drawn plots of electron density surfaces represent Figure 1.1(a) r_i for chloride ion; Figure 1.1(b) r_c and r_{vdW} for chlorine in Cl_2.[44]

Table 1.2 lists ionic and covalent radii values for several atoms.[45] Note that the covalent radius for an atom depends on its bonding pattern. A carbon atom with four single bonds has a covalent radius of 0.76 Å. The value is 0.73 Å for a carbon atom with one double bond, while the covalent radius for a triple-bonded carbon atom is 0.69 Å. We can also assign an r_{vdW} to a group of atoms. The value for a CH_3 or CH_2 group is 2.0 Å, while the van der Waals thickness of half the electron cloud in an aromatic ring is 1.85 Å.[36] Knowledge of van der Waals radii is important in calculations of molecular structure and reactivity, particularly with regard to proteins.[46]

Atomic radii may be used to calculate the volume and the surface area of an atom. Such calculations were described by Bondi, and a selected set of atomic volume and surface areas is given in Table 1.3. The **principle of additivity** then allows calculation of the volumes and surface areas of molecules.[47] For example, the molecular volume of propane is estimated by counting $2 \times 13.67\ \text{cm}^3/\text{mol}$ for the two methyl groups plus $10.23\ \text{cm}^3/\text{mol}$ for the methylene group, giving a total volume of $37.57\ \text{cm}^3/\text{mol}$. Similarly, we

---

[38] Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441.

[39] The difference is that distances between atoms in a crystal are determined by all of the forces acting on the molecules containing those atoms, not just the forces between those two atoms alone.

[40] Badenhoop, J. K.; Weinhold, F. *J. Chem. Phys.* **1997**, *107*, 5422.

[41] Eramian, H.; Tian, Y.-H.; Fox, Z.; et al. *J. Phys. Chem. A* **2013**, *117*, 14184.

[42] Grumman, A. S.; Carroll, F. A. *J. Chem. Educ.* **2019**, *96*, 1157.

[43] Cordero, B.; Gómez, V.; Platero-Prats, A. E.; et al. *Dalton Trans.* **2008**, 2832.

[44] The images were produced with *Spartan '20*.

[45] Many sets of van der Waals radii are available in the literature. The data shown are values reported by Chauvin, R. *J. Phys. Chem.* **1992**, *96*, 9194. These values correlate well with—but are sometimes slightly different from—values given by Pauling (reference 36), Bondi (reference 38), and O'Keefe, M.; Brese, N. E. *J. Am. Chem. Soc.* **1991**, *113*, 3226. A set of van der Waals radii of atoms found in proteins was reported by Li, A.-J.; Nussinov, R. *Proteins* **1998**, *32*, 111.

[46] For example, see Proserpio, D. M.; Hoffmann, R.; Levine, R. D. *J. Am. Chem. Soc.* **1991**, *113*, 3217.

[47] Additivity means predicting a quantity by summing the contributions of its component parts.

TABLE 1.2 Comparison of van der Waals, Ionic, and Covalent Radii for Selected Atoms (Å)

		Ionic Radius (r_i)		Covalent Radii (r_c)		
Atom	van der Waals Radius (r_{vdW})[45]	Ion	r_i	Single Bonded[43]	Double Bonded	Triple Bonded
H	1.11 Å	H^-	2.08 Å	0.31 Å		
C	1.68	C^{4-}	2.60	0.76	0.73[43]	0.69[43]
N	1.53	N^{3-}	1.71	0.71		
O	1.50	O^{2-}	1.40	0.66		
F	1.51	F^-	1.36	0.57		
Cl	1.84	Cl^-	1.81	1.02	0.89	
Br	1.96	Br^-	1.95	1.20	1.04	
I	2.13	I^-	2.16	1.39	1.23	
P	1.85	P^{3-}	2.12	1.07	1.00	0.93
S	1.82	S^{2-}	1.64	1.05	0.94	0.87
Si	2.04	Si^{4-}	2.71	1.11	1.07	1.00

Source: Reference 36 except as noted/Cornell University Press.

TABLE 1.3 Group Contributions to van der Waals Atomic Volume (V_{vdW}) and Surface Area (A_{vdW})

Group	V_{vdw} (cm^3/mol)	A_{vdw} ($cm^2/mol \times 10^9$)
Alkane, C bonded to four other carbon atoms	3.33	0
Alkane, CH bonded to three other carbon atoms	6.78	0.57
Alkane, CH_2 bonded to two other carbon atoms	10.23	1.35
Alkane, CH_3 bonded to one other carbon atom	13.67	2.12
CH_4	17.12	2.90
F, bonded to a 1° carbon atom	5.72	1.10
F, bonded to a 2° or 3° carbon atom	6.20	1.18
Cl, bonded to a 1° carbon atom	11.62	1.80
Cl, bonded to a 2° or 3° carbon atom	12.24	1.82
Br, bonded to a 1° carbon atom	14.40	2.08
Br, bonded to a 2° or 3° carbon atom	14.60	2.09
I, bonded to a 1° carbon atom	19.18	2.48
I, bonded to a 2° or 3° carbon atom	20.35	2.54

Source: Adapted with permission from reference 38. © 1964 American Chemical Society.

calculate that the volume of the atoms in hexane is $2 \times 13.67\ cm^3/mol$ for the two methyl groups plus $4 \times 10.23\ cm^3/mol$ for the four methylene groups, making a total volume of $68.26\ cm^3/mol$. The volume of one mole of liquid hexane at 20° is 130.5 mL, which means that much of the volume occupied by liquid hexane corresponds to space that is outside the boundaries of the carbon and hydrogen atoms as defined above.[48]

Values for atomic and molecular volume are increasingly available from theoretical calculations. The calculated values vary somewhat, depending on

---

[48] Wong, M. W.; Wiberg, K. B.; Frisch, M. J. *J. Comp. Chem.* **1995**, *16*, 385 calculated that the volume of a mole of hexane molecules corresponds to about 71% of the volume of a mole of liquid hexane.

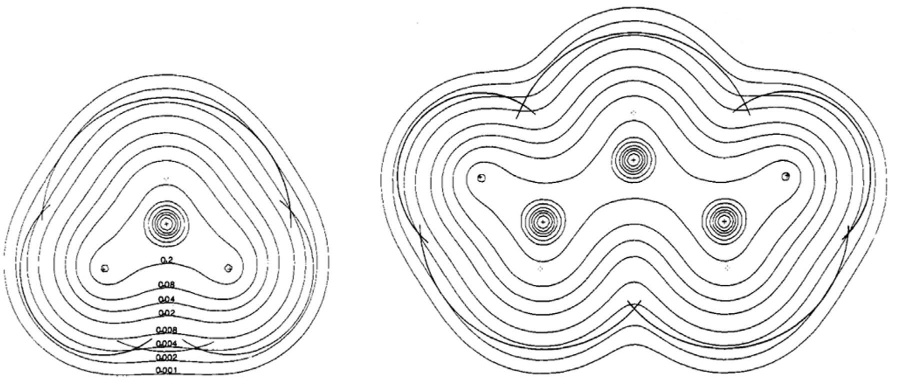


FIGURE 1.2

Contour maps and van der Waals radii arcs for methane (left) and propane (right). (Reprinted with permission from reference 49. © 1987 American Chemical Society.)

the definition of the surface of the atom or molecule. Usually the boundary of an atom is defined as a certain minimum value of electron density in units of au, where 1.00 au = 6.748 e/Å^3. Bader and co-workers determined that the 0.001 au volumes of methane and ethane are 25.53 and 39.54 cm^3/mol, respectively, while the corresponding 0.002 au volumes are 19.58 and 31.10 cm^3/mol.[49] Thus, it appears that the 0.002 au values are closer to, but still somewhat larger than, those calculated empirically using the values in Table 1.3. The relationships between atomic volumes and van der Waals radii are illustrated for cross sections through methane and propane in Figure 1.2. The contour lines represent the electron density contours and the intersecting arcs represent the van der Waals radii of the atoms.

1.2 HEATS OF FORMATION AND REACTION

Experimental Determination of Heats of Formation

Thermochemical measurements provide valuable insights into organic reactions. The **heat of formation** (ΔH_f°) of a compound is defined as the difference in enthalpy between the compound and the starting elements in their standard states.[50] For a hydrocarbon with molecular formula (C_mH_n), ΔH_f° is the heat of reaction for the reaction

$$mC_{(\text{graphite})} + (n/2)H_{2(\text{gas})} \rightarrow C_mH_n \tag{1.1}$$

The heat of formation of an organic compound can be found indirectly by determining the heat of reaction of the compound to form other substances for which the heats of formation are known. The heat of combustion ($\Delta H^\circ_{\text{combustion}}$) of a substance is often used for this purpose. Consider the combustion of a compound with the formula C_mH_n. The balanced chemical equation is

---

[49] Bader, R. F. W.; Carroll, M. T.; Cheeseman, J. R.; et al. *J. Am. Chem. Soc.* **1987**, *109*, 7968. See the discussion of the theory of atoms in molecules in Chapter 2.

[50] Mortimer, C. T. *Reaction Heats and Bond Strengths*; Pergamon Press: New York, 1962; Clark, T.; McKervey, M. A. in Stoddart, J. F., Ed. *Comprehensive Organic Chemistry*, Vol. 1; Pergamon Press: Oxford, England, 1979; p. 66 ff. For a discussion of the experimental techniques involved in calorimetry experiments, see (a) Wiberg, K. in Liebman, J. F.; Greenberg, A., Eds. *Molecular Structure and Energetics*, Vol. 2; VCH Publishers: New York, 1987; p. 151; (b) Sturtevant, J. M. in Weissberger, A.; Rossiter, B. W., Eds. *Physical Methods of Chemistry*, Vol. I, Part V; Wiley-Interscience: New York, 1971; p. 347. For a discussion of experimental and theoretical methods, see Rogers, D. W.; Zavitsas, A. A.; Matsunaga, N. *WIREs Comput. Mol. Sci.* **2013**, *3*, 21.

$$C_mH_n + (m + n/4)O_2 \rightarrow mCO_2 + (n/2)H_2O \tag{1.2}$$

We know the heats of formation of CO_2 and H_2O:

For the reaction $$C_{(\text{graphite})} + O_{2\,(\text{gas})} \rightarrow CO_{2\,(\text{gas})} \tag{1.3}$$

$$\Delta H^\circ_r = \Delta H^\circ_f(CO_2) \tag{1.4}$$

And for the reaction $$H_{2\,(\text{gas})} + \frac{1}{2}O_{2\,(\text{gas})} \rightarrow H_2O_{(\text{liquid})} \tag{1.5}$$

$$\Delta H^\circ_r = \Delta H^\circ_f(H_2O) \tag{1.6}$$

Combining the above equations leads to

$$\Delta H^\circ_f(C_mH_n) = m\Delta H^\circ_f(CO_2) + (n/2)\Delta H^\circ_f(H_2O) - \Delta H^\circ_{(\text{combustion})}(C_mH_n) \tag{1.7}$$

As an example, the heat of combustion of 1,3-cyclohexanedione was found to be −735.9 kcal/mol.[51,52] Taking −94.05 kcal/mol and −68.32 kcal/mol as the standard heats of formation of CO_2 and H_2O, respectively, gives a standard heat of formation for crystalline 1,3-cyclohexanedione of $6(-94.05) + 4(-68.32) - (-735.9) = -101.68$ kcal/mol. It is sometimes necessary to correct heats of reaction for the heats associated with phase changes in the reactants or products. To convert from a condensed phase to the gas phase (e.g. for comparison with values calculated theoretically), the relevant terms are the heat of vaporization (ΔH°_v) of a liquid or heat of sublimation (ΔH°_s) of a solid.[53,54,55] Correcting for the standard heat of sublimation of 1,3-cyclohexanedione, +21.46 kcal/mol, gives its standard heat of formation in the gas phase as −80.22 kcal/mol.

The relative enthalpies of two compounds can be determined more accurately by measuring ΔH values of a reaction in which the two different reactants combine with identical reagents to give the same product(s). Figure 1.3 illustrates how the difference in enthalpy of reactants A and B can be calculated in this manner. If the reaction of A and C to give D has a ΔH_r

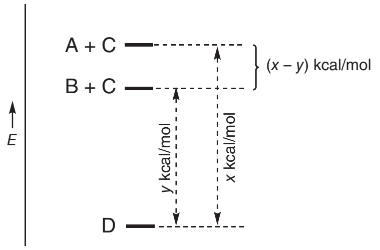


FIGURE 1.3
Calculation of the enthalpy difference of isomers.

---

[51] Pilcher, G.; Parchment, O. G.; Hillier, I. H.; et al. *J. Phys. Chem.* **1993**, *97*, 243.

[52] The reported value (converted from kJ/mol) was −735.9 ± 0.2 kcal/mol. Experimental uncertainties will not be carried through this discussion because the emphasis is on the calculation procedure and not the precision of the experimental method.

[53] Determination of heats of sublimation was discussed by Chickos, J. S. in Liebman, J. F.; Greenberg, A., Eds. *Molecular Structure and Energetics*, Vol. 2; VCH Publishers: New York, 1987; p. 67.

[54] The enthalpy associated with transformation of a solid to a liquid is the **heat of fusion**. For a discussion, see Chickos, J. S.; Braton, C. M.; Hesse, D. G.; et al. *J. Org. Chem.* **1991**, *56*, 927.

[55] Data for heat capacity can be used to correct ΔH values measured at one temperature to another temperature. See Orchin, M.; Kaplan, F.; Macomber, R. S.; et al. *The Vocabulary of Organic Chemistry*; Wiley-Interscience: New York, 1980; pp. 255–256.

of $-x$ kcal/mol, and if the reaction of B and C to give D has a ΔH_r of $-y$ kcal/mol, then the difference in energy between A and B must be $(x - y)$ kcal/mol. For example, ΔH_r values for the reaction of trifluoroacetic acid with 2-methyl-1-butene and with 2-methyl-2-butene were −10.93 and −9.11 kcal/mol, respectively.[56] Therefore, the 2-alkene is judged to be 1.82 kcal/mol lower in energy than the 1-alkene. Heats of hydrogenation are also used to determine the difference in heats of formation of alkenes even though heats of combustion may be measured much more *precisely* than heats of hydrogenation. Heats of hydrogenation are smaller in magnitude than are heats of combustion, so small enthalpy differences between isomers may be determined more *accurately* by hydrogenation.[57]

Bond Increment Calculation of Heats of Formation

Table 1.4 shows experimental ΔH_f° values for some linear alkanes.[58] There is a general trend in the data, with each homolog higher than ethane having a ΔH_f° value about 5 kcal/mol more negative than the previous alkane. This observation suggests that it should be possible to use the principle of additivity to predict the heat of formation of an organic compound by summing the contribution each component makes to ΔH_f°.[59] Benson published extensive tables of **bond increment contributions** to heats of formation and other thermodynamic properties.[59,60,61,62,63,64] A portion of one such table is reproduced as Table 1.5.

The heats of formation of some linear alkanes calculated by the bond increment method are shown in Table 1.4. Consider the calculation of ΔH_f° values for methane and ethane. Methane has four C—H bonds, each contributing −3.83 kcal/mol, so the ΔH_f° value is −15.32 kcal/mol. For ethane, the ΔH_f° value is 6×-3.83 for the six C—H bonds plus 1×2.73 for the one C–C bond, and the total is −20.25 kcal/mol. As the chain is extended, each additional CH_2 group contributes $2 \times (-3.83) + 1 \times (2.73) = -4.93$ kcal/mol to the ΔH_f° value.

There is a problem with the ΔH_f° values obtained from the bond increment data in Table 1.5. The five isomers of hexane listed in Table 1.6 all have five C—C bonds and fourteen C—H bonds. The bond increment values in Table 1.5 thus predict each of them to have the same heat of formation (−39.97 kcal/mol). As shown in Table 1.6, however, the experimental heats of formation become more negative as the branching increases. The structure with a quaternary carbon atom is more stable than an isomeric structure with two tertiary carbon atoms, and it is more stable than structures with only one

---

[56] Wiberg, K. B.; Hao, S. *J. Org. Chem.* **1991**, *56*, 5108.

[57] Davis, H. E.; Allinger, N. L.; Rogers, D. W. *J. Org. Chem.* **1985**, *50*, 3601.

[58] Experimental data for ΔH_f° at 298 K are from tabulations in Stull, D. R.; Westrum, E. F., Jr.; Sinke, G. C. *The Thermodynamics of Organic Compounds*; John Wiley & Sons: New York, 1969; pp. 243–245.

[59] Benson, S. W. *Thermochemical Kinetics*, 2nd ed.; Wiley-Interscience: New York, 1976; p. 24.

[60] Benson, S. W.; Buss, J. H. *J. Chem. Phys.* **1959**, *29*, 546.

[61] Benson, S. W.; Cruickshank, F. R.; Golden, D. M.; et al. *Chem. Rev.* **1969**, *69*, 279.

[62] For a discussion of the development of bond increment and group increment calculations, see Schleyer, P. v. R.; Williams, J. E.; Blanchard, K. R. *J. Am. Chem. Soc.* **1970**, *92*, 2377.

[63] Calculation of group increments to heats of formation of linear hydrocarbons was reported by Pitzer, K. S. *J. Chem. Phys.* **1940**, *8*, 711 and to nonlinear hydrocarbons by Franklin, J. L. *Ind. Eng. Chem.* **1949**, *41*, 1070.

[64] Cohen, N.; Benson, S. W. *Chem. Rev.* **1993**, *93*, 2419.

TABLE 1.4 Experimental and Calculated Heats of Formation of Linear Alkanes at 298 K

Compound	ΔH_f° (kcal/mol) obs.	ΔH_f° (kcal/mol) calc.[a]
Methane	−17.89	−15.32
Ethane	−20.24	−20.25
Propane	−24.82	−25.18
Butane	−30.15	−30.11

[a] Calculations are based on bond increment values in Table 1.5.

TABLE 1.5 Bond Increment Contributions to ΔH_f°

Bond	ΔH_f° (kcal/mol)	Bond	ΔH_f° (kcal/mol)
C–H	−3.83	N–H	−2.6
C–D	−4.73	S–H	−0.8
C–C	2.73	S–S	−6.0
C–F	−52.5	C–S	6.7
C–Cl	−7.4	C_d–C	6.7
C–Br	2.2	C_d–H	3.2
C–I	14.1	C_d–F	−39.0
C–O	−12.0	C_d–Cl	−5.0
O–H	−27.0	C_d–Br	9.7
O–D	−27.9	C_d–I	21.7
O–O	21.5	C_d–C_d	7.5

Source: Reference 59/John Wiley & Sons.

TABLE 1.6 Heats of Formation (kcal/mol) of Isomeric C_6H_{14} Structures

Compound	ΔH_f°, obs.[a]	ΔH_f°, calc.[b]	ΔH_f°, corr.[c]
Hexane	−39.96	−39.96	−39.96
2-Methylpentane	−41.66	−42.04	−41.24
3-Methylpentane	−41.02	−42.04	−41.24
2,2-Dimethylbutane	−44.35	−44.77	−43.16
2,3-Dimethylbutane	−42.49	−44.12	−42.52

[a] Experimental data for ΔH_f° at 298 K are from reference 58/John Wiley & Sons.

[b] Calculated from group increments in Table 1.7 without correcting for gauche interactions.

[c] Data from the previous column corrected for gauche interactions. See Table 1.7 and Figure 1.4.

tertiary carbon atom. This leads to the conclusion that the heat of formation of a compound depends not only on the number of carbon–carbon bonds but also on the pattern of carbon–carbon bonding.

Group Increment Calculation of Heats of Formation

An alternative to the bond increment method is the **group increment** approach, which allows calculation of enthalpy differences that result from different arrangements of bonds within molecules.[65] That means considering

---

[65] Holmes, J. L.; Aubry, C. *J. Phys. Chem. A* **2011**, *115*, 10576 reported updated group additivity values.

TABLE 1.7 Group Increment Contributions to Heats of Formation

Group	$\Delta H^{\circ}_{f\,298}$ (kcal/mol)	Group	$\Delta H^{\circ}_{f\,298}$ (kcal/mol)
$C{-}(H)_3(C)$	−10.08	$C_d{-}(C_B)(C)$	8.64
$C{-}(H)_2(C)_2$	−4.95	$C{-}(C_B)(C)(H)_2$	−4.86
$C{-}(H)(C)_3$	−1.90	$C{-}(C_B)(C)_2(H)$	−0.98
$C{-}(C)_4$	0.50	$C_t{-}(H)$	26.93
$C_d{-}(H)_2$	6.26	$C_t{-}(C)$	27.55
$C_d{-}(H)(C)$	8.59	$C_t{-}(C_d)$	29.20
$C_d{-}(C)_2$	10.34	$C_B{-}(H)$	3.30
$C_d{-}(C_d)(H)$	6.78	$C_B{-}(C)$	5.51
$C_d{-}(C_d)(C)$	8.88	$C_B{-}(C_d)$	5.68
$[C_d{-}(C_B)(H)]$	6.78		

Source: Adapted from reference 61.

not only the bonds holding atoms together but also the groups that result from these bonds. Table 1.7 lists the group increment values for a series of organic functional groups.[61] These data lead to a close approximation of the heats of formation of the isomeric hexanes. Consider 2-methylpentane. Three methyl groups [$C{-}(H)_3(C)$ in the table] contribute −10.08 kcal/mol each to the heat of formation; two methylene units [$C{-}C(H)_2(C)_2$] contribute −4.95 kcal/mol each; and one methine unit [$C{-}(H)(C)_3$] contributes −1.90 kcal/mol. Thus, the estimated heat of formation is

$$\Delta H^{\circ}_{f} = 3 \times (-10.08) + 2 \times (-4.95) + 1 \times (-1.90) = -42.04\ \text{kcal/mol} \quad (1.8)$$

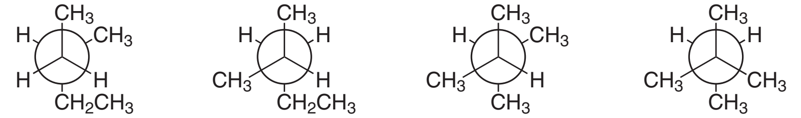
The experimental value is −41.66 kcal/mol.[58]

The heats of formation calculated in this way assign the same contribution to each group without regard to its position in the molecule and without regard to strain. In branched acyclic alkanes, the major form of strain is van der Waals repulsion due to *unavoidable* butane gauche interactions, which may be assigned 0.8 kcal/mol each.[66] Figure 1.4 shows a Newman projection and gives the minimum number of gauche interactions for each hexane. Correcting the initial ΔH°_{f} of 2-methylpentane for one such interaction gives −41.24 kcal/mol, which is closer to the experimental value. Angle strain corrections must be applied for ring compounds. For example, cyclopropane, cyclobutane, and cyclopentane rings add 27.6, 26.2, and 6.3 kcal/mol, respectively, to a heat of formation calculated from the data in Table 1.7.[61,67]

---

[66] Deviations from staggered dihedral angles may also contribute somewhat to steric energy. Energies of different conformations will be discussed in Chapter 4.

[67] These examples only hint at the analysis of heats of formation of organic compounds that is possible. Benson and co-workers summarized the methods and data for calculations for the major functional groups in organic chemistry.[59,61] In addition, the data allow calculation of heat capacities and entropies of these compounds in the same manner in which heats of formation are determined. Heats of formation are valuable reference points in discussing the stabilities of various isomers or products of reactions, whether they are calculated by bond increments or group increments or are derived as part of a theoretical calculation.



3-methylpentane
1 gauche interaction

2-methylpentane
1 gauche interaction

2,3-dimethylbutane
2 gauche interactions

2,2-dimethylbutane
2 gauche interactions

FIGURE 1.4
Gauche interactions in branched hexane isomers.

Heats of Formation and the Concept of Protobranching

The origin of the increased stability of branched alkanes relative to nonbranched isomers has been the subject of some debate. Benson and Luria proposed that alkanes have polarized $C^{\delta-}$—$H^{\delta+}$ bonds and that the sum of the electrostatic interactions of a branched compound is lower in energy than the sum of electrostatic interactions in a linear structure.[68] Laidig calculated that branched hydrocarbons have overall smaller distances between atoms than do linear isomers and that the resulting increase in nucleus–electron attraction in a branched compound outweighs the increase in nuclear–nuclear and electron–electron repulsion.[69] Schreiner attributed the stabilization of branched alkanes to attractive interactions involving alkyl groups bonded to the same carbon atom.[70]

Gronert proposed a different explanation based on the observation that van der Waals interactions between nonbonded groups that are closer than the sum of their van der Waals radii, such as C1 and C4 in the gauche conformation of butane, are known to be repulsive.[71] Since C1 and C3 in neopentane are even closer to each other than are C1 and C4 in gauche butane, he suggested that their interaction should be repulsive as well. Moreover, the interactions between two hydrogen atoms bonded to the same carbon as well as those between hydrogen and carbon atoms bonded to the same carbon were also suggested to be repulsive. The effect of branching (e.g. conversion of butane to isobutane) is to reduce the number of H–C–C interactions while increasing the number of H–C–H and C–C–C interactions. Gronert proposed that the steric energy of an H–C–C interaction is less than the average of those for the H–C–H and C–C–C interactions, so the effect of the branching is to decrease overall intramolecular repulsion and produce a more stable isomer. Using equations 1.9 and 1.10, along with the interaction values (E) for C–H and C–C bonding and specific values for repulsive 1,3 interactions shown in Table 1.8, Gronert was able to reproduce the observed gas phase ΔH_f° values of a series of alkanes quite well. For example, the ΔH_f° of *n*-pentane in kcal/mol is calculated as shown in equation 1.11.

$$\Delta H_f = n_{C-C}E_{C-C} + n_{C-H}E_{C-H} + n_{C-C-C}E_{C-C-C} + n_{C-C-H}E_{C-C-H} + n_{H-C-H}E_{H-C-H} + f(C,H) \qquad (1.9)$$

---

[68] Benson, S. W.; Luria, M. *J. Am. Chem. Soc.* **1975**, *97*, 704.

[69] Laidig, K. E. *J. Phys. Chem.* **1991**, *95*, 7709.

[70] Schreiner, P. R. *Angew. Chem. Int. Ed.* **2007**, *46*, 4217.

[71] Gronert, S. *J. Org. Chem.* **2006**, *71*, 1209; 9560. The literature values in Table 1.8 are from this source. The values of the E parameters at the bottom of the table are shown to two decimal places, while those in the sources cited here were reported to one decimal place.

TABLE 1.8 Calculated Gas Phase ΔH_f° of Alkanes Assuming Repulsive Geminal Interactions[a]

Compound	$n_{C–C}$	$n_{C–H}$	$n_{H–C–H}$	$n_{H–C–C}$	$n_{C–C–C}$	n_C	n_H	ΔH_f (calc.)	ΔH_f (lit.)
Methane	0	4	6	0	0	1	4	−17.2	−17.9
Ethane	1	6	6	6	0	2	6	−20.4	−20.0
Propane	2	8	7	10	1	3	8	−25.3	−25.0
Butane	3	10	8	14	2	4	10	−30.2	−30.4
2-Methylpropane	3	10	9	12	3	4	10	−31.9	−32.1
n-Pentane	4	12	9	18	3	5	12	−35.1	−35.1
2-Methylbutane	4	12	10	16	4	5	12	−36.8	−36.7
2,2-Dimethylpropane	4	12	12	12	6	5	12	−40.3	−40.1
Hexane	5	14	10	22	4	6	14	−40.0	−40.0
Cyclohexane	6	12	6	24	6	6	12	−29.4	−29.4
	$E_{C–C}$	$E_{C–H}$	$E_{H–C–H}$	$E_{H–C–C}$	$E_{C–C–C}$	E_C	E_H		
	−146.00	−124.20	6.64	9.29	10.20	60.70	52.10		

[a] Energies are in kcal/mol.

Source: Adapted with permission from reference 71. © 2006 American Chemical Society.

where *f*(C, H) is given by equation 1.10.

$$f(\mathrm{C,H}) = (170.6 + E_{\mathrm{C}})n_{\mathrm{C}} + 52.1n_{\mathrm{H}} \tag{1.10}$$

$$\begin{aligned}\Delta H_{\mathrm{f}} &= 4(-146) + 12(-124.2) + 9(6.64) + 18(9.29) + 3(10.2)\\ &\quad + 5(231.3) + 12(52.1) = -35.1\,\mathrm{kcal/mol}\end{aligned} \tag{1.11}$$

Gronert's explanation for the stability of branched alkanes was supported by some investigators but questioned by others.[72,73] Wodrich and Schleyer pointed out that comparable results could be obtained by assuming that the interactions of geminal methyl groups are stabilizing, an interaction which was termed protobranching (equation 1.12).[74,75,76] Here $n_{\mathrm{CH_2}}$ is the number of methylene units conceptually added to methane to form the alkane, $n_{\text{primary branches}}$ is the number of C–CH$_2$–C units, $n_{\text{tertiary branches}}$ is the number of 3° carbon units, and $n_{\text{quaternary branches}}$ is the number of 4° carbons in the structure. Some results obtained with this approach are shown in Table 1.9, and a calculation of ΔH_f° for *n*-pentane is shown in equation 1.13.

$$\begin{aligned}\Delta H_{\mathrm{f}} = &-17.89 - 2.15n_{\mathrm{CH_2}} - 2.83n_{\text{primary branches}} - 7.74n_{\text{tertiary branches}}\\ &- 13.49n_{\text{quartenary branches}}\end{aligned} \tag{1.12}$$

$$\begin{aligned}\Delta H_{\mathrm{f}} = &-17.89 + 4(-2.15) + 3(-2.83) + 0(-7.74)\\ &+ 0(-13.49) = -34.98\,\mathrm{kcal/mol}\end{aligned} \tag{1.13}$$

---

[72] Mitoraj, M.; Zhu, H.; Michalak, A.; et al. *J. Org. Chem.* **2006**, *71*, 9208.

[73] Bartell, L. S. *J. Phys. Chem. A* **2012**, *116*, 10460 argued that the Gronert explanation makes the incorrect assumption that C–H interactions are more repulsive than the average of C–C and C–H interactions.

[74] Wodrich, M. D.; Schleyer, P. v. R. *Org. Lett.* **2006**, *8*, 2135.

[75] Wodrich, M. D.; Wannere, C. S.; Mo, Y.; et al. *Chem. Eur. J.* **2007**, *13*, 7731.

[76] Schleyer, P. v. R.; McKee W. C. *J. Phys. Chem. A* **2010**, *114*, 3737.

TABLE 1.9 Calculation of Gas Phase ΔH_f° Values of Alkanes Assuming Geminal Methyl Interactions Are Stabilizing[a]

Alkane	n_{CH2}	n primary branches	n tertiary branches	n quaternary branches	ΔH_f° (calc.)	ΔH_f° (lit)
Methane	0	0	0	0	−17.89	−17.89
Ethane	1	0	0	0	−20.04	−20.04
Propane	2	1	0	0	−25.02	−25.02
Butane	3	2	0	0	−30.00	−30.04
Isobutane	3	0	1	0	−32.08	−32.07
Pentane	4	3	0	0	−34.98	−35.08
Isopentane	4	1	1	0	−37.06	−36.73
Neopentane	4	0	0	1	−39.98	−40.14
Hexane	5	4	0	0	−39.96	−39.96

[a] Energies are in kcal/mol.

Source: Adapted from reference 74.

The two explanations produced a spirited discussion for several years.[77] It is sufficient here to note that sometimes opposite models can be used to predict the same experimental values. Even when only one model seems applicable, therefore, it is important to remember that a good correlation does not establish a cause-and-effect relationship.

Homolytic and Heterolytic Bond Dissociation Energies

Heats of reaction are important values for processes that involve reactive intermediates. For example, the **standard homolytic bond dissociation enthalpy** of compound A–B, denoted ΔH° (A–B) or ΔH_{298} (A–B), is the heat of reaction (ΔH_r°) at 298 K for the gas phase dissociation reaction in equation 1.14.

$$\mathrm{A-B}_{(g)} \rightarrow \mathrm{A}\bullet_{(g)} + \mathrm{B}\bullet_{(g)} \tag{1.14}$$

ΔH°(A–B) values can be calculated from the relationship[78,79]

$$\Delta H^{\circ}(\mathrm{A-B}) = \Delta H^{\circ}_{r\,(\text{equation1.14})} = \Delta H_f^{\circ}(\mathrm{A}\bullet) + \Delta H_f^{\circ}(\mathrm{B}\bullet) - \Delta H_f^{\circ}(\mathrm{A-B}) \tag{1.15}$$

Here $\Delta H_f^{\circ}(\mathrm{A}\bullet)$ is the heat of formation of radical A•, and $\Delta H_f^{\circ}(\mathrm{B}\bullet)$ is the heat of formation of radical B•. Table 1.10 gives a list of standard bond dissociation enthalpies for bonds involving hydrogen atoms, and Table 1.11 gives a list of

---

[77] Gronert, S. *Chem. Eur. J.* **2009**, *15*, 5372; Kemnitz, C. R.; Mackey, J. L.; Loewen, M. J.; et al. *Chem. Eur. J.* **2010**, *16*, 6942; reference 73; Kemnitz, C. R. *Chem. Eur. J.* **2013**, *19*, 11093; McKee, W. C.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **2013**, *135*, 13008; Silva, A. F.; Duarte, L. J.; Popelier, P. L. A. *Struct. Chem.* **2020**, *31*, 507; Joyce, J. P.; Shores, M. P.; Rappè, A. K. *Phys. Chem. Chem. Phys.* **2020**, *22*, 16998.

[78] Benson, S. W. *J. Chem. Educ.* **1965**, *42*, 502.

[79] A standard bond dissociation energy is different from an **average** bond dissociation energy. The latter is just the value obtained by calculating the heat of atomization of a compound (the enthalpy change on converting the molecule to individual atoms) divided by the number of bonds from one atom to another in the molecule. For more details on this distinction, see reference 78.

TABLE 1.10 ΔH° Values (kcal/mol) for Bonds to Hydrogen

Compound	ΔH° (kcal/mol)	Compound	ΔH° (kcal/mol)
H–H	104.2	H–F	136.3
H–CN	126.3	H–Cl	103.2
$H–NH_2$	107.6	H–Br	87.5
HO–H	118.8	H–I	71.3
$H–CH_2OH$	96.1	HS–H	91.2
$CH_3O–H$	104.6	$H–ONO_2$	101.7
$CH_3S–H$	87.4	$CH_3CH_2O–H$	104.7
$H–CH_2SH$	94	$(CH_3)_2CHO–H$	105.7
HOO–H	87.8	$(CH_3)_3CO–H$	106.3
$CH_3OO–H$	88	$C_6H_5O–H$	90
H–CHO	88.1	$CH_3CH_2OO–H$	85
$CH_3C(O)–H$	89.4	$(CH_3)_3COO–H$	84
HCOO–H	112	$CH_3COO–H$	112
H–COOH	>96	$C_6H_5COO–H$	111

Source: Adapted with permission from reference 80. © 2003 American Chemical Society.

TABLE 1.11 ΔH° Values (kcal/mol) for Selected Bonds to Alkyl Groups

Subst.\R	CH_3	CH_3CH_2	$(CH_3)_2CH$	$(CH_3)_3C$	$CH_2{=}CH$	$CH_2{=}CHCH_2$	C_6H_5	$C_6H_5CH_2$	CH_3O	HC(O)	CH_3CH(O)
H	104.9	101.1	98.6	96.5	110.7	88.8	112.9	89.7	104.6	88.1	89.4
F	115	—	110.6	—	123.3	—	127.2	98.7	—	—	122.2
Cl	83.7	84.8	85.2	84.9	91.2	—	97.1	74	—	—	84.7
Br	72.1	72.4	73.9	72.6	80.8	59	84	63	—	—	71.7
I	57.6	56.9	57	55.6	—	45.6	67	51	—	—	53.8
HO	92.1	94.0	95.5	95.8	—	80.1	112.4	82.6	—	109.5	109.9
CH_3O	83.2	85	85.8	84	—	—	101	—	38	99.6	100
NH_2	85.2	84.8	86.0	85.7	—	—	104.2	71.7	—	—	99.1
CN	122.4	121.6	120.9	117.8	133	108.7	134	—	—	—	—
NO_2	61.0	61.6	62.9	62.8	—	—	72.5	50.5	42	—	—
CH_3	90.1	89.0	88.6	87.5	101.4	76.5	103.5	77.6	*	84.8	84.5
CH_3CH_2	*	87.9	87.1	85.6	100.0	75.4	102.2	76.7	*	83.3	83.5
$(CH_3)_2CH$	*	*	85.6	82.7	99.2	75.2	101.0	76.4	*	83.1	81.9
$(CH_3)_3C$	*	*	*	78.6	97.8	73.2	98.3	—	*	—	79.4
$CH_2{=}CH$	*	*	*	*	116	87.3	116	—	—	—	41
CH_2CHCH_2	*	*	*	*	*	62.7	—	—	—	—	—
$HC\equiv C$	126.5	125.1	124.5	122.3	—	—	—	—	—	—	—
$HC\equiv CCH_2$	78	77	—	—	—	—	—	—	—	—	—
C_6H_5	*	*	*	*	*	—	118	*	*	99.3	98.8
$C_6H_5CH_2$	*	*	*	—	—	—	97	65.2	—	—	71.4

Note: * Indicates a redundant entry. — Indicates not available.

Source: Adapted with permission from reference 80. © 2003 American Chemical Society.