Organic and Biological Chemistry

SECOND EDITION JOHN R. HOLUM

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Preface

At many institutions, students preparing for careers in any of the many professional health care fields enroll first in a one-term or a two-term course in general chemistry. Then they move into a separate course that includes selected topics of organic and biological chemistry. This book is intended for such a course. A basic knowledge of atomic and molecular structure, chemical equations, states of matter, solutions, and acid-base theory is assumed. Because acid-base theory is particularly important, and because students emerging from just a one-term experience with general chemistry often have not yet studied the Brønsted theory, a detailed Appendix on this vital topic is included, complete with worked examples, practice exercises, and review exercises. Parts could be taken up just prior to the study of carboxylic acids, and the material on buffers could fit well into the study of the chemistry of respiration or anytime prior to a study of the acid-base balance of body fluids.

This book is the last 20 chapters of another textbook, *Fundamentals of General, Organic, and Biological Chemistry*, 3rd edition (which we can call *Fundamentals*). *Fundamentals* is for students at the freshman or sophomore college level preparing for careers in professional health care fields and who need a one-year survey of chemistry that includes the whole sweep of general, organic, and biological chemistry. Very typically, the chapters on organic and biological chemistry — the chapters in the present book — are studied in the second semester of such a course.

The theme of this book is the molecular basis of life. We believe that no other text so consciously remains faithful to a consistent theme, and we know from years of experience that students respond with gratitude to the careful effort to make the chemistry they study as relevant as possible to their professional needs. Our students are overwhelmingly career-oriented, and we capitalize on this rather than fight it. For example, we know that it motivates students to high efforts, as they patiently work their way through a survey of organic functional groups — topics that initially seem to be so remote from their careers — to be gently reminded that life does have a molecular basis and we can't talk about it until we know some of the physical and chemical things to expect of its molecules.

During the study of organic chemistry, frequent mention is made of the kinds of biological chemicals that have the particular functional group currently being studied, because students appreciate the reminders that the theme of the course dominates all of the study of organic chemistry.

To students, the whole concept of functional groups takes some getting used to. Just learning how to learn the properties of such groups requires patience and practice. Therefore, to leap from simple molecules such as alcohols or aldehydes to complex polyfunctional systems such as carbohydrates and then back again to another simple group should never be attempted. All but the top students find this Tilt-A-Whirl approach dizzying or worse, and want not just to get off the ride, but to leave the park — forever. Thus we believe that the most sound pedagogical approach is to introduce the functional groups, one after the other, as they occur among the *simplest*, monofunctional compounds. Large, complex structures such as glucose or hemoglobin or DNA can be sources of terror rather than wonder when they are introduced too early.

Of course, there remains the question of which functional groups to study. There is no possibility, even in a full-fledged, one-year course in organic chemistry to "cover" this vast field. What is taught in the one-year course is something of a consensus of what today's organic chemists think should be included and, quite rightly, the needs of future organic chemists have the highest priority. A short course that includes organic and biological chemistry must also be geared to high priority needs. And what our students need is not a whistle-stop tour of every topic in the two-term organic sequence. "Today Is Tuesday So We Must Be in Grignard Country," isn't amusing when students later realize that this famous topic has utterly no relevance to the biological chemistry they study.

One of our two major priorities has been on those functional groups that most often occur among the biochemicals to be studied later. Thus, alkyl halides are barely mentioned because this system occurs nowhere among the biochemicals of later study. Not even a mention is made of the reactions of Grignard, Friedel-Crafts, Wittig, Williamson, or many others. Very little is done with aromatic chemistry, because the details of aromatic electrophilic substitution reactions will not be exploited later. (What it means to be *aromatic,* and some of the characteristic reactions of the benzene ring are studied, of course, because this ring does occur among some amino acids and proteins.)

In the study of functional groups, the emphasis is on their chemical properties rather than on strategies for making them. Thus our second major priority in organic chemistry concerns three types of reactants — water, oxidizing agents and reducing agents — the types of reactants that abound in cells.

We look briefly at a few mechanisms so that students can see that reactions are rational, that they don't just happen by the operation of "lassos." However, the elaborate dictionary of mechanistic terminology, which students who go on in chemistry must learn, is here kept to the barest of levels. Thus you can see that the chapters on organic chemistry are wholly devoted to preparing the students for the biochemistry and molecular biology that follows — no more, no less.

Chapters 9 – 19 focus everything that has gone before onto a study of the principal organic substances found in cells — carbohydrates, lipids, proteins, and nucleic acids — and their chief functions as chemicals when they are in cells. Among these chapters are found most of the changes from the preceding edition. Some changes in the biochemistry chapters make the level of the treatment more realistic for the freshman level. They reflect our own experiences in the classroom. Thus, in Chapter 16 ("Biochemical Energetics") we have found that the treatment flows much better when we do not try to relate phosphate group transfer potential to the concept of free energy.

Among the topics new to this edition is a study of the chemiosmotic theory (Chapter 16), which is now widely accepted as the process used in oxidative phosphorylation. Recent developments in the area of lipoprotein complexes and the transport of cholesterol in the blood prompted a new opening section to Chapter 18 ("Metabolism of Lipids"). Recombinant DNA (Chapter 12) is studied. While this material is new, it is not difficult, and future health professionals ought to have a background in this area.

There are innumerable small changes in the text. The preparation of this edition involved a total rewriting of the entire book, sentence by sentence, in an effort to improve its clarity and readability for students. Of course, not every sentence was changed, but every sentence was scrutinized to see if a worthwhile change were warranted. There was no cutting and pasting and handing the rough draft to a typist. The author retyped the entire manuscript himself.

The design of this edition is quite unlike that of the previous edition. There are **margin comments** some of which are reminders. Some restate a point. Some are small, illustrative tables to which the neighboring paragraph refers. Some are structures that need not be memorized.

There are **Special Topics** on matters of current interest, and a list is provided following the table of contents. One is on physiologically active amines, another on interferon, and another goes into the probable connection between the regulation of fatty acid catabolism in brown adipose tissue and our ability to eat without gaining excessive weight.

Our overall goal has been to make this text the most modern, up-to-date, and readable introduction to organic and biological chemistry that is available anywhere. We are well aware that perfection is an ever-receding horizon, but we owe our students our finest efforts. We have gone to much greater pains than ever before to produce a zero-mechanical-defect product. Extra professional help in proofreading and in checking the answers to Review Exercises and Review Problems has been engaged. As always, the author stands responsible for any errors that remain and wants very much to learn of any at your earliest convenience.

A comprehensive package of instructional materials, described in detail on page xi, is available to help the students. The accompanying laboratory manual has been revised and updated with special attention given to improving the clarity of the experimental directions.

Two packages of computer-aided instructional disks have been prepared to accompany this study.

Four-color, overhead transparencies can be obtained. (These are the actual transparencies, not masters that would be used to make them.)

A Teachers' Manual includes the answers to all of the Practice Exercises and Review Exercises.

OTHER DESIGN FEATURES THAT AID STUDENTS

Chemistry is one of the disciplines in which important scientific terms can be sharply defined. We have tried to do so at the first occasion of using each term or as soon thereafter as possible—at or near the place where the **key term** is highlighted by a boldface color treatment. Then our aim has been to use these terms as carefully and consistently as possible. As an aide in reviewing, these terms are listed at the ends of the chapters. Then, at the end of the book, there is a **glossary** where each of the key terms is defined.

Each chapter has a **Summary** that uses the key terms in a narrative survey. Each main section of each chapter also begins with a **summary statement** that announces what is coming and that serves during test review periods to highlight the major topics.

A new design feature is the use of labels to identify sets of **Review Exercises** that are about a common topic. Within many chapters are several **Practice Exercises,** and most of these immediately follow a **worked example** that provides a step-by-step description of how to solve a certain kind of problem. The **answers** to all Practice Exercises are found at the back of the book.

Continuing a long tradition, we have tried to make the **index** the most thorough, most cross-referenced index in any text of this type.

JOHN R. HOLUM

Augsburg College

Acknowledgments

Over the many years of writing instructional materials, my family — Mary, my wife, and our daughters, Liz, Ann, and Kathryn — have been Gibralters of support. They, rather than my teaching or writing, are my career and so such teaching and writing is seen by us as one of the ways by which our family has tried to be of help to others. I am pleased to say "thank you" to them for being such nice people.

Here, at Augsburg College, I have enjoyed many years and years of support from Dr. Earl Alton, Chemistry Department Chair, and Dr. Charles S. Anderson, President. My freedom to write stems in no small measure from the freedom that these caring people have accorded me.

Nice people abound at John Wiley & Sons, too. They do good work. I think of the special support of my Chemistry Editor, Dennis Sawicki, and of that of Executive Editor, Clifford Mills.

Chief Illustrator John Balbalis has been skillful, artistic, and faithful in handling art work for many years.

Picture Editor Stella Kupferberg solves problems and makes this facet of production worry-free.

The Designer, Kevin Murphy stands in the long Wiley tradition of artistry and imagination.

Copy Editor Pam Landau has been superb in smoothing out stylistic and grammatical problems.

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All in all, it's an impressive team, and I count myself to be fortunate indeed for having become associated with John Wiley & Sons in the first place.

Part of the process of preparing a manuscript involves the professional critiques of teachers. I am pleased to acknowledge and to thank the following professors and scientists for their work: Hugh Akers, Associate Professor, Lamar University; Charles E. Bell, Jr., Professor of Chemical Sciences, Old Dominion University; Lois Dalla-Riva, Professor of Chemistry, Golden West College; Dr. Estelle Gearon, Professor of Chemistry, Montgomery College; Dr. Arlin Gyberg, Augsburg College; Dr. Robert G. Martinek, Manager, Chicago Laboratory, Illinois Department of Health; Sandra Olmstead, Professor, Augsburg College; Dr. James R. Paulson, Chemistry Department, University of Wisconsin-Oshkosh; Salvatore Profeta, Jr., Adjunct Professor of Chemistry, Louisiana State University; and Dr. Neal Thorpe, Augsburg College

J.R.H.

Supplementary Materials for Students and Teachers

The complete package of supplements that are available to help students study and teachers to plan the course and operate the associated laboratory work includes the following.

Laboratory Manual for Fundamentals of General, Organic, and Biological Chemistry, 3rd edition. This has been prepared by Professor Sandra Olmsted. An instructor's manual is a section in the general Teachers' Manual described below. Although this lab manual was prepared for *Fundamentals*, its experiments in organic and biological chemistry fit ideally to the topics of the present book.

Study Guide for Fundamentals of General, Organic, and Biological Chemistry, 3rd edition. The Study Guide for the larger book, *Fundamentals*, serves as the study guide to the present book. The only precaution is to remember that chapter 1 in the present book goes with chapter 11 in the Study Guide, and so on. Thus each chapter number in this book is 10 less than in the Study Guide. The Study Guide contains chapter objectives, chapter glossaries, additional worked examples and exercises, sample examinations for each chapter, and the answers to all Review Exercises. Students have found the many drill exercises on the chemistry of functional groups particularly valuable.

Teachers' Manual for Fundamentals of General, Organic, and Biological Chemistry, 3rd edition. This softcover supplement is available to teachers, and it contains all of the usual services for *both the text and the laboratory manual.* Those who adopt this book may also request from John Wiley & Sons a set of questions that can be used to prepare examinations. (The address is given in the next paragraph.)

Transparency Masters. Instructors who adopt this book can receive from John Wiley & Sons, without charge, a set of slides (actual slides, not slide masters), many in color, of several figures and tables in this book. Write to Chemistry Editor, John Wiley & Sons, Inc., 605 Third Ave., New York, NY 10158

Computer-Aided Instructional Packages. Two sets of instructional software are available as supplements, one for the use of students when they are reviewing and the other for their use as pre-lab studies. Professor Richard Cornelius of Wichita State University wrote the lecture-oriented software, and Sandra and Richard Olmsted (Augsburg College) prepared the lab-oriented materials. The latter package has several units that work exceptionally well in classrooms equipped with electronic blackboards. The animated sequences that explain difficult concepts such as mutarotation and DNA-directed polypeptide synthesis are outstanding teaching devices. For further information write to: Chemistry Editor, John Wiley & Sons, Inc., 605 Third Ave., New York, NY, 10158, or to Professor Sandra Olmsted, Angsburg College, Minneapolis, MN 55454.

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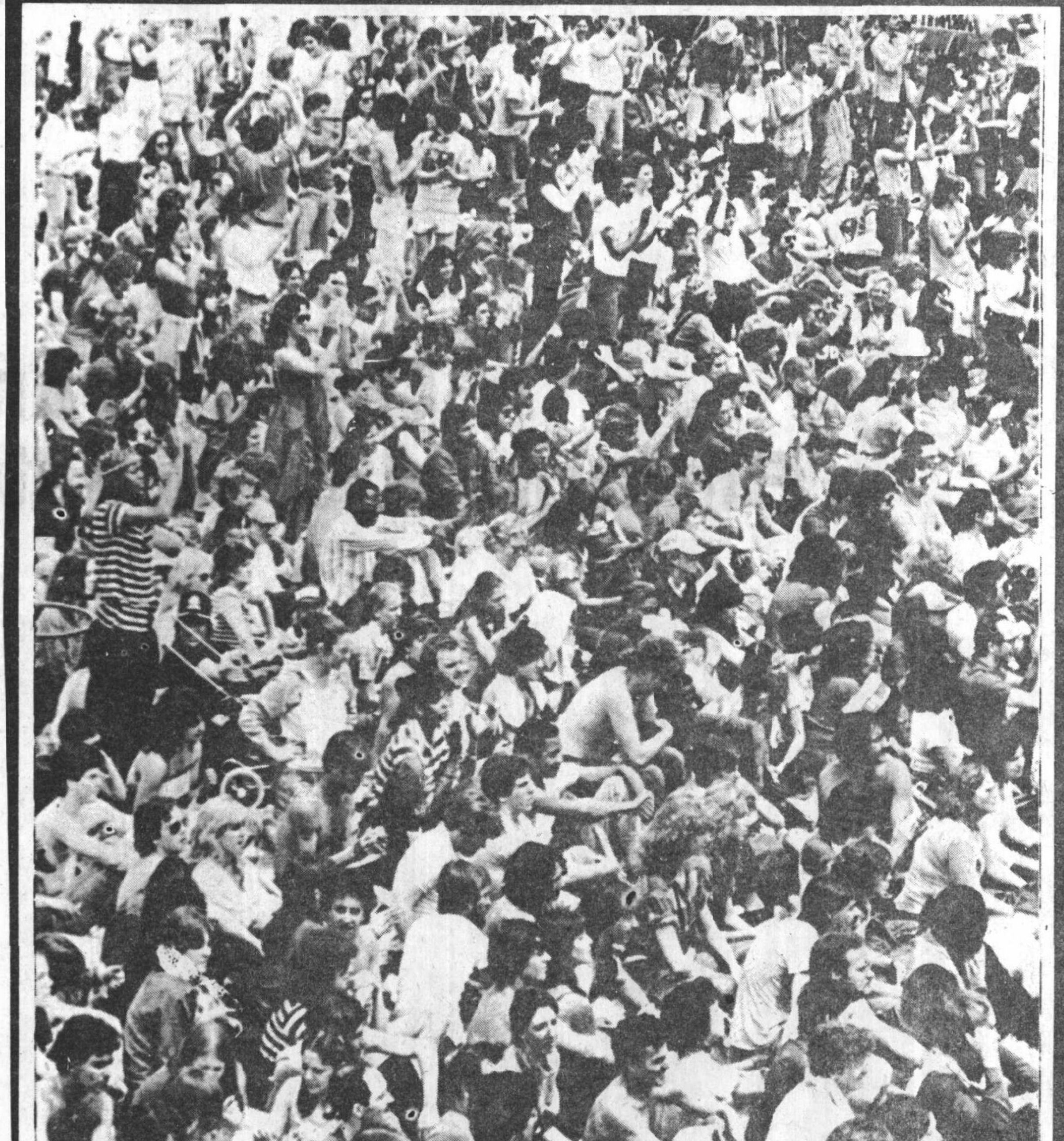
Organic and Biological Chemistry

Chapter 1

Introduction to Organic Chemistry



The marvel of it is that the atoms making up these people ultimately came from such simple things as water, carbon dioxide, air, and a few salts. A study of how this can be has a new beginning in this chapter as we introduce organic compounds.

1.1 ORGANIC AND INORGANIC COMPOUNDS

Because most compounds of carbon — organic compounds — are molecular, not ionic, they have relatively low boiling points, melting points, and solubilities in water.

A mineral is a solid with a *definite* formula that can be obtained from the earth's crust.

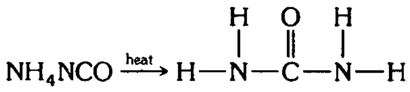
Vita- is from a Latin root meaning "life."

Organic compounds are compounds of carbon, and there are more of these compounds than of all the other elements combined, except hydrogen. The name itself, implying *organism,* arose when scientists believed that organic compounds could be made only by and within living organisms. Prior to 1828 no one had succeeded in making an organic compound in the laboratory either directly from the elements or from minerals in the earth's crust. In fact, scientists who tried to overcome this difficulty eventually concluded that a law of nature made the task impossible in principle. After all, what we cannot do is just as significant in science as what we can. For example, we cannot create or destroy energy, and this natural limitation is labeled a scientific law. Similarly, the inability to synthesize an organic compound in the laboratory led to a theory known as the **vital force theory,** which declared that a catalyst-like agent — a vital force — is essential to this synthesis. And only living things, according to the theory, possessed the vital force. Organic compounds, therefore, were those that only living things could make, and **inorganic compounds** were all the rest, those not requiring the vital force for their preparation.

Wöhler's Experiment. In 1828, Friedrich Wöhler (1800 – 1882) succeeded in making urea, a white solid that can be obtained from urine and that everyone regarded as an organic compound. His synthesis was the wholly unexpected result of an attempt to prepare the inorganic compound, ammonium cyanate, NH_4NCO. He prepared an aqueous solution that contained the ammonium ion, NH_4^+, and the cyanate ion, NCO^-, and evaporated it to dryness in full expectation that these oppositely charged ions would be forced to aggregate as a crystalline solid.

Urea is the chief nitrogen waste from the body. It is also manufactured from ammonia and used as a commercial fertilizer.

Wöhler obtained a white powder, but it had none of the expected properties of the salt or of any compound of ammonia. Instead of throwing the solid away, Wöhler analyzed it and found that it was urea. Evidently, the heat that was added to the system to remove the water caused the following reaction:



$$NH_4NCO \xrightarrow{heat} H{-}\overset{\displaystyle H}{\overset{|}{N}}{-}\overset{\displaystyle O}{\overset{\|}{C}}{-}\overset{\displaystyle H}{\overset{|}{N}}{-}H$$

Ammonium cyanate

Urea

Other syntheses of organic compounds from minerals quickly followed Wöhler's discovery, and the vital force theory was soon dead. Roughly 6 million organic compounds are known, and all of them have been made or could in principle be made from substances of mineral origins.

Some Differences Between Organic and Inorganic Compounds. Relatively few inorganic compounds contain carbon. Those that do are mostly the carbonates, bicarbonates, and cyanides of metal ions, but there are a few other types that need not concern us. As we have said, carbon is always present in organic compounds where its atoms, covalently bound together, form the structural "skeletons" of organic molecules. Atoms of several other nonmetal elements can be appended to these skeletons, also by covalent bonds. Such nonmetals include hydrogen, oxygen, nitrogen, sulfur, and the halogens.

Besides differences in composition, there are variations in bond types, which help to explain important differences in some properties. Covalent bonds are far more prevalent among organic compounds than among inorganic compounds, but ionic bonds are present more frequently among inorganic compounds. In other words, most organic compounds are molecular and most inorganic compounds are ionic. Because forces of attraction between polar molecules are generally much less than between oppositely charged ions, most organic compounds melt at temperatures well below those at which ionic compounds melt. A great number of organic compounds are liquids, not solids, at room temperature, but all ionic compounds are solids and melt generally well above 400 °C. Most organic compounds also have normal boiling points below 400 °C, but most inorganic compounds have very high boiling points. The exceptions are the inorganic compounds that are not ionic, such as a large number of gases (e.g., hydrogen halides, carbon dioxide, and the oxides of sulfur) and some inorganic liquids (e.g., water).

Typically, ionic compounds melt and boil well above 350 °C.

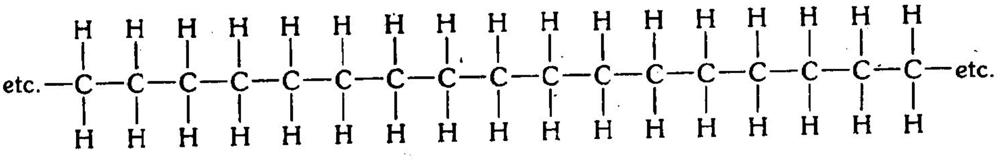
Relatively few organic compounds dissolve in water, but many inorganic compounds are water-soluble. Organic molecules often are not polar enough to be hydrated by water. However, the organic compounds that do dissolve in water are particularly important at the molecular level of life, because water is the central solvent in living things.

1.2 STRUCTURAL FEATURES OF ORGANIC MOLECULES

Organic molecules have flexible chains or rings of carbon atoms, and they almost always have a functional group.

The uniqueness of carbon among the elements is that its atoms can bond to each other successively many times and still form equally strong bonds to atoms of other nonmetals. A typical molecule in the familiar plastic, polyethylene, has hundreds of carbon atoms covalently joined in succession, and each carbon binds enough hydrogen atoms to fill out its full complement of four bonds.

Only a short segment of a typical molecule of polyethylene is shown here.



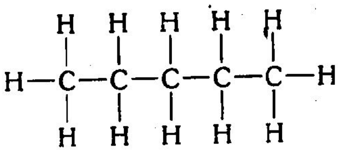
$$\text{etc.}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\text{etc.}$$

Polyethylene

Recall that each line in a structural formula stands for one shared pair of electrons. Each carbon, therefore, has four lines, meaning four shared pairs of electrons for a total of eight outside-level electrons. In all organic compounds, carbon *always* has four bonds from it, *never* five and *never* three bonds.

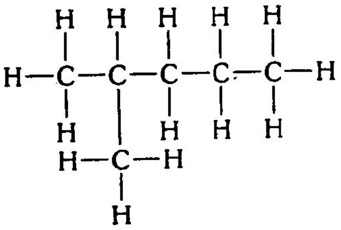
Straight Chains and Branched Chains. A succession of carbon atoms that are bonded covalently together, as shown in the segment of the polyethylene molecule, is called a **straight chain.** Pentane, a constituent of gasoline, consists of molecules with straight chains that are just five carbons long. It is important to realize that "straight" has a very limited, technical meaning when used in this context. It means the absence of carbon branches. "Straight chain" means that one carbon follows another and no additional carbons are joined to this system at intermediate points.

A molecule of 2-methylpentane illustrates a **branched chain**, which means it has one (or more) carbon atoms joined to carbons that are *between* the ends of some parent chain.

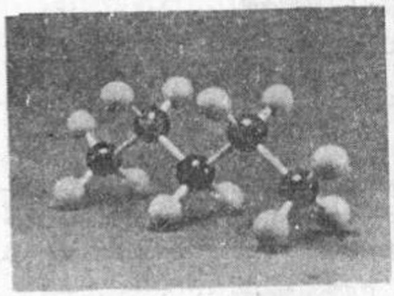


$$\text{H}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}-\text{H}$$

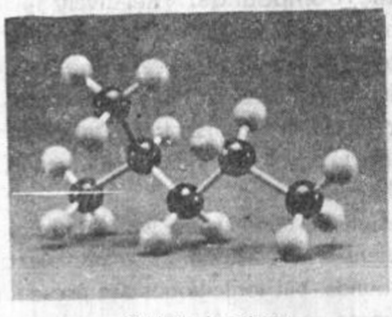
Pentane
(straight chain)



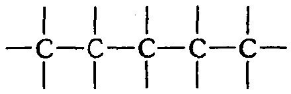
2-Methylpentane
(branched chain)



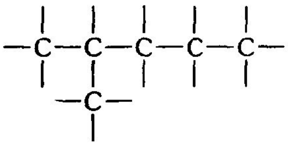
Pentane.



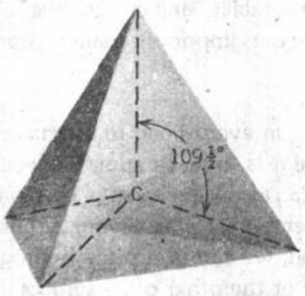
2-Methylpentane.



Pentane skeleton



2-Methylpentane skeleton



Tetrahedral carbon

When you compare the photographs of the ball-and-stick models of the molecules of pentane and 2-methylpentane with their structural formulas, be sure to notice that the written (or printed) structures disregard the correct bond angles at carbon. A carbon that has four single bonds has a tetrahedral geometry with bond angles of 109.5°. The ball-and-stick models faithfully show the correct angles at each carbon, but the printed symbols do not. The point here is that it is perfectly all right to let bond angles be "understood" unless there is some important reason to the contrary. And this isn't the only point we have to understand when we use printed structural formulas. We'll learn about another one next.

Free Rotation at Single Bonds. Pieces of either straight chain or branched chain molecules that are connected by *single* bonds have a property called **free rotation.** This means that such pieces can be set into rotation with respect to each other around the single bonds as the result of collisions with other molecules. In an actual sample of pentane, for example, not all of the molecules are in the fully extended form shown in Figure 1.1. Pentane molecules are kinked and twisted into an almost infinite number of contorted forms, called **conformations.** Models of just a few of those of pentane are shown in Figure 1.1.

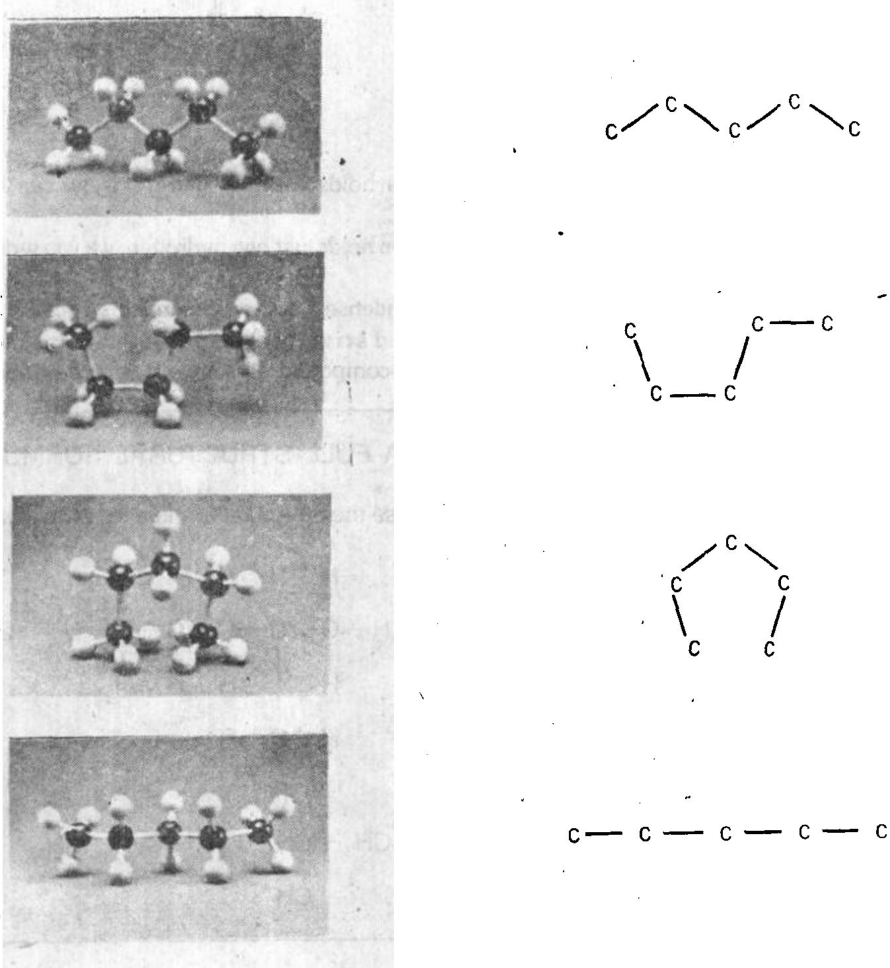


FIGURE 1.1
Free rotation at single bonds. Photographs of models of four of the innumerable conformations of the pentane molecule are shown here followed by drawings of just their carbon skeletons. When we write the structure of pentane as $CH_3CH_2CH_2CH_2CH_3$, it stands for any of these because some of each (and many others) exist in a sample of pentane.