



# CHEMISTRY

*Second Edition*

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### **ORGANIC CHEMISTRY**

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# ORGANIC CHEMISTRY

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## *Preface*

In the five years that have elapsed since the appearance of the first edition of our book, substantial changes have occurred in the teaching of organic chemistry. The new textbooks, as well as the new editions of the older books, have moved in the direction of integrating fact and theory. Some have abandoned the essentially taxonomic organization based on classes of compounds, which had dominated elementary courses since the turn of the century. More and more, classes of reactions are being used as an integral part of the organization. These changes reflect the advances that have been made both in pedagogy and in our understanding of reaction mechanisms and the relationships between structure and reactivity.

Two major considerations prompted our decision to revise "Organic Chemistry." First, our experience and that of our critics pointed to the need for refinement of sections of the book. Second, many of the new and exciting results of the past five years warrant inclusion in the first course in organic chemistry.

The new edition retains the same overall organization, since we are more convinced than ever of the fundamental soundness of our approach. The first seven chapters deal with structure, nomenclature, occurrence, and uses of the main classes of compounds. A few simple reactions are introduced here to illustrate the interconversion of functional groups and to show the principles involved in degradative structure determination. The development is both more thorough and simpler than it was in the first edition, where it was compressed into four chapters. Chapter 8 treats the chemical bond in terms of both resonance and molecular-orbital methods. In Chapter 9 stereochemistry is discussed, the main themes being bond angles and distances, free and restricted rotation about bonds, symmetry properties of molecules, and configurations of ring compounds. Chapter 10 presents the relationships between physical properties and structures of organic compounds. Chapter 11 introduces the subject of correlation of structure with chemical reactivity. Acid-base reactions are used as a vehicle to illustrate resonance, inductive, and steric effects. Chapter 12 explains our scheme for classification of organic reactions and introduces reaction mechanisms. Chapters 11 and 12 provide a transition between the static and dynamic aspects of the science.

In Chapters 13 through 24 reactions are discussed class by class. Preparative methods are stressed, and synthetic sequences are frequently

presented as units. The chapter order has been changed from that of the first edition, and a new chapter on organic synthesis has been added.

The last nine chapters are concerned with timely and useful special topics. Included are a chapter on heterocyclic compounds, three chapters on natural products (grouped according to biogenetic relationships), a chapter on natural and synthetic polymers, and chapters on petroleum, spectra, nomenclature, and chemical literature.

In a sense, we have attempted to examine organic chemistry from three different points of view. The first group of chapters treats relationships based on structure; the second group emphasizes the relationship among organic reactions; and the third group illustrates associations based upon the origin, use, and chemical technology of organic compounds. Thus students are given a thorough introduction to the descriptive part of the subject before they are exposed to a comprehensive treatment of reactions, and they have a good grasp of fundamental concepts of both structure and reactivity before they encounter the subject of complex molecules and their reactions. In this scheme, the important facts and concepts are repeatedly reviewed in varying contexts.

We believe that certain further advantages are associated with this organization. Chemical reactions and their applications to synthesis are introduced only after the structures of both reactant and product are familiar to the student. The early introduction of stereochemistry and theories of chemical reactivity allows these concepts to be used throughout the discussions of reactions. The organization of reactions into classes allows consideration of mechanism, scope, limitations, and side reactions to be applied to whole groups of transformations. Many subjects, such as physical properties, acid-base theory, structure elucidation, spectra, nomenclature, and bibliography, which are ordinarily scattered are given integrated treatment. The relationship between laboratory and lecture is strengthened by introduction in the first seven chapters of enough structural concepts and reactions to provide a background for laboratory work for at least a term. The discussions of physical properties and acid-base reactions early in the course serve as useful adjuncts to laboratory work.

Much new material has been added and some deleted. For example, subjects such as cycloaddition, hydroboration, and organic photochemistry have been introduced or expanded, and the discussion of the chemistry of dyestuffs has been omitted to make room for new material.

Perhaps the single biggest change from the first edition is that discussions are much less compressed, definitions have been made more explicit, and examples are more abundant. We hope this edition is more digestible for both elementary and advanced students and more agreeable for teachers.

A new production feature, the use of a second color, has been introduced in the second edition. When the possibility was first suggested we were unenthusiastic. However, reflection and experimentation with formulas convinced us that color provided a powerful teaching aid. At first we attempted to use color in a rigid code in which the fate of certain atoms or groups of



atoms was traced through one or more transformations. However, more experience convinced us that such a rigid convention would eliminate many opportunities to create emphasis and contrast within formulas. Consequently we arrived at the simplest of rules: The green characters in formulas mean that the writer wishes to draw the attention of the reader to a particular feature of the formula.

Some of the uses to which color has been put are as follows: gray is used to depict *p* orbitals; green, *s* orbitals; and blends of the two, the various *sp* hybrid orbitals. The functional group that is about to undergo change in a reaction is usually green. In three-dimensional formulas, groups above the plane of the page are frequently in green. Isoprene units, or other structural parts to be delineated in large molecules (e.g., protective groups), are frequently green. The bonds made and broken in molecular rearrangements are traced with color. Acidic or basic groups, chromophores, or other structural features that impart particular physical properties are sometimes indicated in color.

This book provides more material than can be included in short courses. However, in every chapter except for the first seven, sections of material may be omitted without loss of continuity. We have found that this flexibility allows the teacher to stress whichever of the three general sections he chooses. A course designed for both chemistry and nonchemistry majors could emphasize the material in the first and third sections, whereas a course designed only for chemistry majors might stress the second group of chapters.

Our greatest ambition in writing this book has been to bring students in their first course closer to the frontiers of organic chemistry. We hope that our organization eliminates the waste usually involved in reorientation of students' thinking when they pass from an elementary course either to an advanced course or to research. If this book serves these purposes, we have succeeded.

We wish to thank the many users of the first edition who provided us with suggestions, comments, criticisms, and corrections. This help from the outside was invaluable when we prepared the second edition. Professors D. M. Lemal and K. L. Nelson provided detailed criticisms of the entire manuscript, leading to many improvements. Professor J. H. Richards made certain suggestions that were incorporated into the three chapters on natural products. Dr. Alan Wingrove read proof on the entire book and improved the problem sections.

Donald J. Cram  
George S. Hammond



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## Introduction

### Nature of Organic Chemistry

Originally the term *organic chemistry* referred to the chemistry of materials derived from living things. Until about the middle of the nineteenth century it was generally believed that such "organic" compounds contained a mysterious *vital force*. However, repeated demonstration that compounds identical in all respects with those obtained from plants and animals could be prepared from mineral materials showed that the origin of a compound is not a reliable means for classification. Since most of the compounds called "organic" contained the element carbon, "organic chemistry" was limited to compounds of carbon, with a few substances, such as metal carbonates, carbides, and cyanides, being arbitrarily excluded. In recent years organic chemistry has been more precisely defined as the *chemistry of compounds of carbon and hydrogen and their derivatives*. Two considerations led to the emphasis on the role of hydrogen along with that of carbon. First, most carbon compounds contain hydrogen; second, a certain amount of hydrogen seemed necessary in order to make large stable molecules containing many carbon atoms. However, recently fluorine has also been found in combination with carbon in large stable compounds. At present organic chemistry is perhaps best defined as the *chemistry of carbon-containing compounds*. Inclusion or exclusion of compounds such as carbonates is best left to individual chemists.

The striking feature of organic chemistry is the vast number of organic compounds known and the fact that the potential number is virtually limitless. Over one million different organic compounds have now been characterized, and every year thousands of new substances are added to the list, either by discovery in nature or by preparation in the laboratory. Commonly a research chemist prepares *over a thousand new compounds* during his lifetime. The rate of increase in the numbers of known compounds provides an interesting record of the explosive development of organic chemistry: in 1880, the number was approximately 12,000; in 1910, about 150,000; in 1940, about 500,000.

Organic compounds show remarkable variation in physical and chemical properties. A constituent of natural gas called methane, which has a boiling point of  $-162^{\circ}$ ,<sup>†</sup> is found at one extreme; plastics and rubber are found at the other. These substances are composed of giant molecules and exhibit a wide range in the physical properties characteristic of solid and glassy materials, such as rigidity, tensile strength, and elasticity. Extremes in chemical reactivity are illustrated, on the one hand, by a simple substance of formula  $C_4H_4$ , which explodes if warmed to room temperature, and, on the other hand, by phthalocyanine pigments, which can be heated to red heat without decomposition, and Teflon, a plastic material that can be brought into contact with elemental fluorine without corrosion.

Organic chemicals are put to many varied uses. They are worn as clothes, eaten as foods, and used as both fuels and cosmetic aids. They include "wonder" drugs, vitamins, and hormones as well as deadly poisons. A large number of organic chemicals are used in agriculture as fertilizers, soil conditioners, and insecticides. The best-known explosives are compounds of carbon.

Organic compounds constitute most of the material associated with living organisms. The principal source of carbon in living things is carbon dioxide, which is converted to simple chemicals by green plants by means of photosynthesis. These simple chemicals are converted to a multitude of natural products by the metabolic processes of plants and animals.

The chief sources of organic materials are coal, petroleum, wood, and agricultural products. These are the fundamental raw materials upon which the organic chemical industry is built. They also constitute a huge reservoir for the storage of solar energy. This energy can be released by combustion of organic compounds, with the liberation of heat. The fundamental energy cycle can be illustrated by means of two highly simplified equations.



## History

Although organic reactions have been deliberately carried out since the discovery of fire, the science of organic chemistry did not evolve until the nineteenth century. Its development from that point can be divided roughly into three overlapping periods.

The first period began with the general advance of chemistry as a science, an advance that gathered momentum at the beginning of the nineteenth century. In this period, chemical transformations were shown to be reproducible and to proceed independently of supernatural influences. Quantitative procedures for monitoring the course of chemical reactions were developed.

During the first half of the nineteenth century, progress in organic chem-

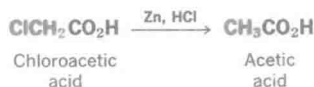
<sup>†</sup> All temperatures in this book are given in degrees centigrade.

istry was marked by the conversion of compounds considered to be inorganic into compounds identical to those derived from living organisms. Such experiments led to abandonment of the "vitalistic theory," which maintained that some of the seemingly unique properties of organic compounds were due to their containing a mysterious "vital force" derived from living things. The disappearance of the vitalistic theory has an interesting and somewhat obscure history. In 1828 Wöhler observed the transformation of ammonium cyanate to urea, a substance which had been isolated from many animal sources.



In retrospect it seems that this experiment should have demonstrated unequivocally the continuity between organic and inorganic chemicals. At the time this conclusion was not as obvious as it is now. For example, it was pointed out that Wöhler's ammonium cyanate had been obtained by the calcination of bones and might, therefore, contain vital force. Wöhler himself reported his work in circumspect language, and modern chemical historians disagree as to whether or not he intended his report to establish a fundamental principle.

By 1850 the vitalistic theory was entirely dead. Some authorities attribute the crucial experiments to Kolbe, who produced acetic acid by the reaction of zinc with chloroacetic acid.



Throughout this book parts of many formulas will be displayed in color. The color always indicates that the authors wish to draw attention to some special part of the formula. The above equation illustrates the most common use of color—to trace the "functional" part of a molecule from a reactant to a product.

Probably the theory of vitalism, like many other scientific theories, disappeared slowly under the weight of accumulated evidence rather than as a consequence of any single brilliant and illuminating experiment. Similar slow change is characteristic of most chemical theories including, no doubt, those which are found most useful today by organic chemists.

Two other developments of the first period set the stage for revolutionary advances. First, the increase in the number of known organic compounds gave chemists some notion of the vastness of the field and the need for systematizing the description of compounds. Second, reliable methods for the estimation of molecular weights were developed. Coupled with methods of elementary analysis that had been available for a number of years, molecular-weight measurements made *molecular formulas* possible (page 6).

The second period in the history of organic chemistry started in 1858,

with the birth of *structural theory*. The development of a detailed picture, by purely inductive reasoning, of both the atomic organization and the shapes of molecules stands as a major accomplishment of the human intellect. One of the most fruitful concepts in the history of science was advanced almost simultaneously by Kekulé in Germany and by Couper in Scotland in 1859. They suggested that the atoms in molecules are bound together by bonds and that a given atom is characterized by having the same number of bonds in most stable compounds. The key feature of organic compounds, the existence of strong carbon-carbon bonds, was recognized and used to predict the existence of large molecules, containing networks of carbon atoms. Now that chemists have used, developed, and verified for a century the idea that organic molecules have definite structural features, with carbon atoms as the main building blocks and chemical bonds as the mortar, it seems so "right" that it is difficult to appreciate the genius of the original suggestion. A third dimension was added to the concept of molecular architecture in 1874 by van't Hoff and LeBel, who suggested that the four bonds in most carbon compounds are directed toward the corners of a tetrahedron. This period extended roughly to the end of World War I and was devoted primarily to exploitation and refinement of the structural theory. Many reactions were discovered and used in the design of procedures for synthesizing new compounds. Reagents were found that degraded complex natural products to simple known compounds, and thus the structures of more complicated compounds were elucidated. Whole groups of naturally occurring compounds, for example, the carbohydrates, became known through investigations such as those of Emil Fischer and his students.

Three significant developments have occurred during the third and present era of organic chemistry. The first advance was the application of electronic theories of valence to organic compounds, which permits the structural theory to apply to a number of compounds whose detailed structure could not be described with the classical theories. Chemists in the classic era of structural chemistry had thought almost exclusively in terms of "ball-and-stick" models for organic compounds. Lewis, and later Pauling, replaced the sticks with electron pairs, and a more fluid concept of the chemical bond was generated.

The second development of the present period has been a dramatic increase in the understanding of organic reactions. In a sense, the development of large numbers of reactions during the second era resembled the proliferation of numbers of compounds during the first era. In the 1920s many workers, such as Ingold and Robinson in England, Meerwein in Germany, and Conant and Lucas in the United States, turned their attention to the detailed study of the mechanisms of organic reactions. General theories were evolved that have already had a dramatic effect on the classic problems of the science. The concepts of reaction mechanisms have provided indispensable guidance in synthesizing natural products whose structures are so complex that their syntheses were considered 30 years ago to be out of reach. The most brilliant exponent of synthetic sequences programmed in theoretical terms has been R. B. Woodward, who in 1960 announced the synthesis of chlorophyll. At the

same time theory has also aided in the preparation of many new small molecules that have unusual and interesting structures.

The third big advance is the development of instruments for separating, analyzing, and identifying organic compounds. Optical and nuclear-magnetic-resonance spectroscopy can give in minutes information about the structures of unknown compounds that previously was obtained only by weeks or even years of chemical study. Total determination of structure is made by analysis of the X-ray diffraction patterns of organic crystals, but this method is still sufficiently involved and tedious to allow a great deal of room for structural study by combined chemical and less definitive physical methods.

In addition to these exciting developments, the past few decades have been characterized by the prodigious expansion of the organic-chemical industry. Before World War I a vigorous chemical industry existed, especially in Germany. However, its scope was limited to relatively few fields, notably dyestuffs and explosives and a few preliminary successes with medicines. Since the 1920s, the industry has thrust into many new fields on a massive scale. Plastics, elastomers, fibers, and films are now produced in enormous volumes for myriad purposes. The pharmaceutical industry introduces new drugs so rapidly that it is difficult for the practicing physician to distinguish the new from the obsolete. For 30 years we have been in an organic chemical age. While we may now be *thinking* in terms of an atomic age, many years will pass before the impact on our daily lives of organic chemistry is rivaled by that of atomic physics. The cultural movement of the twentieth century is largely in the hands of scientists, and the organic chemist plays a prominent role.

Organic chemistry of the future will undoubtedly draw inspiration for new theoretical advances from the related fields of physical chemistry and physics. Textbook writers in the year 2000 may be able to point to developments in quantitative analysis of reaction mechanisms from some new theoretical basis, an advance that would parallel the refinement of structural theory between 1910 and 1960. Many organic chemists are now turning toward biochemistry. The last natural products to have resisted synthetic work are the natural macromolecules: proteins, polysaccharides, and nucleic acids. Syntheses of these compounds are now difficult to envision, just as syntheses of some of the larger alkaloids could not be imagined in 1930. An understanding of the mechanisms of enzyme-catalyzed reactions will undoubtedly lead to the use of simpler "model catalysts" in many organic reactions, and knowledge of the mechanisms of organic reactions will contribute heavily to the field of molecular biology. The chemistry of compounds containing carbon in combination with elements such as the metals will undoubtedly be investigated on a grand scale.

### Characterization of Organic Compounds

One of the goals of organic chemistry is to achieve complete descriptions of individual organic compounds. General procedures have evolved which can be applied to most organic compounds and which provide a step-by-step



approach to the final goal, the detailed structural formula. This section of the book is devoted to a description of those steps which permit a compound to be thoroughly enough characterized so that it may be distinguished from all other compounds.

**Molecular Homogeneity.** Every organic compound possesses a distinct set of physical and chemical properties that differentiate it from every other compound. The physical properties most commonly used to characterize a compound are melting point, boiling point, adsorption behavior, and interactions (absorption, refraction, diffraction, and rotation) with light and other radiation. Common techniques for separating organic compounds from one another are differential extraction, crystallization, distillation, and adsorption. A compound is usually considered pure if its physical (and sometimes chemical) properties do not change when it is subjected to procedures based on the above techniques.

**Quantitative Elemental Analysis and Molecular Formulas.** In quantitative combustion analysis, a weighed portion of a compound is burned in oxygen over hot copper oxide at about 700°. Carbon dioxide and water are produced in essentially 100% yields and are individually captured and weighed in absorption tubes. This is accomplished by first passing the combustion gases through a tube containing a neutral desiccant, such as magnesium perchlorate (Anhydron), which absorbs the water vapor and converts it to water of hydration; then by leading them through a tube containing finely divided sodium hydroxide (Ascarite), which absorbs and converts the carbon dioxide to sodium carbonate.

The weight per cent of carbon and hydrogen in the unknown compound can be calculated by the stoichiometric principles of general chemistry. Should the sum of these percentages equal approximately 100%, no other elements are present in the molecule. If the sum is less than 100% and qualitative tests reveal the absence of elements such as nitrogen, sulfur, and halogens, then oxygen is probably present. Frequently the oxygen content is assumed to be the difference between the sum of the percentages of carbon and hydrogen and 100%. A better procedure involves the direct determination of oxygen content by decomposing the substance in an atmosphere of oxygen-free nitrogen. The products are passed over carbon at 900° or above, and the oxygen is quantitatively converted to carbon monoxide. This gas is passed into iodine pentoxide, and the liberated iodine is titrated with thiosulfate.

The following example illustrates the method of calculating the per cent composition of an unknown compound (I) known to contain only carbon, hydrogen, and oxygen.

Wt. of I	Wt. of CO <sub>2</sub>	Wt. of H <sub>2</sub> O
4.337 mg	10.35 mg	3.42 mg
$10.35 \text{ mg (CO}_2\text{)} \cdot \frac{12.01 \text{ (formula wt. C)}}{44.01 \text{ (formula wt. CO}_2\text{)}} = 2.824 \text{ mg C}$		
$3.42 \text{ mg (H}_2\text{O)} \cdot \frac{2.018 \text{ (formula wt. H}_2\text{)}}{18.02 \text{ (formula wt. H}_2\text{O)}} = 0.383 \text{ mg H}$		

$$\% \text{ C in I} = \frac{\text{mg C}}{\text{mg sample}} \cdot 100\% = \frac{2.824}{4.337} \cdot 100\% = 65.11\% \text{ C}$$

$$\% \text{ H in I} = \frac{\text{mg H}}{\text{mg sample}} \cdot 100\% = \frac{0.383}{4.337} \cdot 100\% = 8.83\% \text{ H}$$

$$100.00\% - 65.11\% - 8.83\% = 26.06\% \text{ O}$$

The *empirical formula* of I can now be determined.

$$\frac{65.11 (\% \text{ C})}{12.01 (\text{at. wt. C})} = 5.421 \quad \frac{8.83 (\% \text{ H})}{1.008 (\text{at. wt. H})} = 8.76 \quad \frac{26.06 (\% \text{ O})}{16.00 (\text{at. wt. O})} = 1.628$$

Compound I contains carbon, hydrogen, and oxygen atoms in the same ratios as the subscripts of the formula



The lowest of the numbers (that of oxygen in this case) is divided into each of the three numbers appearing as subscripts in the formula, and a new formula results in which oxygen has the value of unity.



The subscript numbers are now converted to the smallest possible set of whole numbers by multiplying each of them by the smallest integer that will accomplish this objective. In this calculation, the integer is 3. When the best integral multiplier cannot be found by inspection, a series of trial multiplications are carried out and the results compared.



The small deviations from whole numbers of the resulting subscripts represent the experimental error, and the empirical formula is written as follows:



The *molecular formula*, which denotes the actual number of atoms of each element in the molecule, can now be indicated in a general way,  $n$  being some integer. To find the value of  $n$ , the approximate molecular weight of I must be determined.



A number of physical methods can be employed to determine molecular weight. The *vapor-density method* makes use of the appearance of the molecular-weight term in the ideal gas law [Eq. (1)]. It can be applied only to gases and low-boiling liquids.

$$(1) \quad \text{Mol. wt.} = \frac{gRT}{PV}$$

$g$  = grams  
 $R$  = 0.08205 (liter)(atm)/(deg)(mole)  
 $T$  = absolute temperature  
 $P$  = pressure, atm  
 $V$  = volume, liters