ORGANIC CHEMISTRY

FIESER AND FIESER

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BY

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and

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1944

D. C. HEATH AND COMPANY

Boston

Printed in the United States of America

4K7

Offices

BOSTON NEW YORK CHICAGO ATLANTA

SAN FRANCISCO DALLAS LONDON

PREFACE

The main theme of this book, like that of its many predecessors, is the development of the fundamental chemistry of the hydrocarbons, alcohols, acids, and other classes of organic compounds. Aromatic compounds are introduced at an early stage and illustrative examples from this field are used throughout, but the theory of the nature and substitution reactions of aromatic substances is reserved for specific discussion at a later point, after adequate groundwork has been laid. This is in keeping with a general plan to increase the tempo as the book progresses and to present material of a more and more advanced nature as the reader gains in experience and background. Thus the empirical correlation of phenomena prevalent in the early chapters gradually gives place to interpretations in terms of modern theory. The treatment of aromatic chemistry is somewhat more extensive than the relative importance of this branch of the subject alone would justify, but this apparent emphasis is in part merely because expansion at this stage of the book is practicable. Furthermore, aliphatic chemistry is usually reviewed and expanded in a second course so occupied with an abundance of special topics as to leave little room for aromatics. The chemistry of the quinones has been allotted more space than usual because of the growing importance of these substances. While endeavoring to make the presentation readable, we have included an extensive body of factual data in the form of tables and citations under formulas. The physical constants have been taken largely from Beilstein or the original literature, with some selection, and use has been made of the special compilations of Egloff and others. Type reactions are illustrated for the most part with actual examples of a practical nature; many of these are taken from "Organic Syntheses," and they are documented whenever possible with data concerning the conditions of the reaction and the yield. Specific references have been omitted, regretfully, in the interest of brevity, but a key to the literature on the more prominent discoveries is provided by the citation of names and dates.

The most novel feature of the book is the inclusion of a number of chapters for optional reading dealing with significant applications of organic chemistry to technology and to the biological and medical sciences. These essay chapters, which we hope are extensive enough to provide a practical orientation in the fields concerned, are interspersed throughout the book at such points as the subject matter can be fully understood. A selection can be made, according to the special interests of the reader, and the chapters can be omitted without detriment to the development of the main theme. The rather extensive excursions into the two fields of applied science have so lengthened the book that an abridged edition has been prepared which covers most of the subjects presented in the large volume in a briefer form. Thus for use in college courses the choice of editions might be left open to the student.

Work on this book was started in April, 1942, with the idea that, with help from my wife, Mary, I might make some contribution to the training of chemists in a period when I was obliged to give up normal teaching activities to conduct various projects for the Office of Scientific Research and Development. The book was to follow the scheme of my past lectures in Chemistry 2, and my wife was to supply material from the literature by day and I to use it by night. The supply soon exceeded any possible utilization on my part, and eventually Mary took up authorship in her own right. She, indeed, is responsible for the special feature of the book, for she wrote nearly all of the essay chapters, and certain others, namely, Chapters 5, 13–20, 34–36, 38–40. She also prepared the index, handled the many technical matters concerned, and helped me collect material for the much easier assignment of writing on familiar topics, which I was obliged to do in large part in trains, planes, hotels, and army camps in the course of more than one hundred trips.

We are very grateful to the following gentlemen for reviewing parts of the book and giving us the benefit of their experience and advice: D. F. Brown, W. P. Campbell, H. E. Carter, H. J. Creech, Bradley Dewey, J. W. Foster, R. H. Gerke, E. A. Hauser, C. S. Hudson, M. H. Ittner, C. D. Lowry, Jr., J. B. Mair, H. K. Nason, C. R. Noller, L. B. Parsons, Erwin Schwenk, A. M. Seligman, D. E. Strain, N. B. Talbot, Bert Taylor, K. V. Thimann, T. R. Wood. We are indebted also to Dr. Ernst Berliner and Dr. Hans Heymann for reading the entire manuscript and to Dr. R. B. Woodward for advice on many points of theory.

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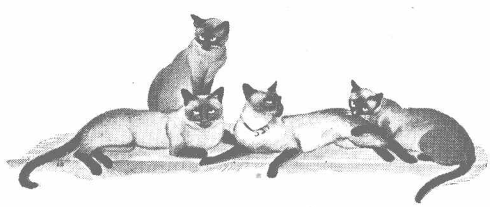

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CHAPTER 1

THE NATURE OF ORGANIC COMPOUNDS

The designation "organic," which means pertaining to plant or animal organisms, was introduced into early chemical terminology as a convenient means of classifying a number of chemical substances recognized as associated with one another by virtue of their common derivation from organic sources. A few of these substances of plant or animal origin had been known in reasonably homogeneous form since earliest antiquity. Prehistoric peoples were familiar with sugar, with the fermentation of the sweet principle of grape sugar and the production of wine, and with the souring of wine under the agency of *Acetobacter* to produce vinegar, a dilute solution of acetic acid (L. *acetum*, vinegar). The process of rectifying alcoholic beverages by distillation, as a means of increasing the proportion of alcohol, was discovered as early as A.D. 900, and a crude mode of distillation had previously been applied to the production of oil of turpentine from pine resin. Vegetable oils and animal fats, and the process of making soap from these substances, have been known for centuries past. Methods of applying the beautiful vegetable dye indigo and of dyeing with madder root (alizarin) were developed by ancient Romans and Egyptians, and for many centuries these natural pigments provided the chief means of dyeing fabrics. Tyrian purple was a prized dye extracted by the Phoenicians from a rare species of mollusk.

The Middle Ages afforded but few additions to the list of chemical compounds of organic origin. During the 16th and 17th centuries, some advances resulted from application of the method of pyrolysis, or heat treatment, to certain plant products. The dry distillation of wood was found to afford a crude substance called pyroligneous acid (1661), which is now known to contain methyl alcohol, acetone, and acetic acid. Succinic acid was obtained by the destructive distillation of amber, and benzoic acid was isolated as a product of the pyrolysis of gum benzoin (1608). Toward the end of the 18th century, a start was made on the more significant problem of examining plant and animal products in the native state, that is, as obtained by solvent extraction and without the alterations now known to be attendant upon the brutal process of destructive distillation. In the years 1769–1785 the gifted Swedish chemist Scheele conducted a brilliant series of investigations that constituted a forerunner of fully modern studies of the chemistry of biological products. He isolated tar-

taric acid as the sour principle of the grape, citric acid from the lemon, malic acid from apples, gallic acid from nut galls, lactic acid from sour milk, uric acid from urine, and oxalic acid from wood sorrel, where it occurs as the acid potassium salt. Scheele further prepared oxalic acid by the oxidation of sugar with nitric acid, and he discovered glycerol and characterized it as the sweet principle common to animal fats and vegetable oils. Other early chemists of the period isolated urea from human urine (Rouelle, 1773), hippuric acid from horse urine (Liebig, 1829), cholesterol from gall stones (Poulletier-de-Lasalle), morphine from opium (Sertürner, 1805), and the alkaloidal drugs quinine, strychnine, brucine, and cinchonine (Pelletier and Caventou, 1820).

Nothing was known of the chemical nature of these substances derived from living organisms until the time of Lavoisier's classical investigations of the process of combustion (1772–1777). Lavoisier established the fact that air is composed of oxygen, discovered by Scheele and by Priestley in 1772–1774, and a second inert gas that he termed "azote" (nitrogen), and he was the first to recognize that combustion consists in an interaction of the burning substance with oxygen of the air. In carefully conducted experiments with weighed amounts of materials, he proved that sulfur, phosphorus, and carbon combine with oxygen on burning to yield products that, in the presence of moisture, appear in the form of sulfuric, phosphoric, and carbonic acid. Metals were found to afford bases on oxidation. Turning to the as yet unexplored "organic" substances, Lavoisier devised a method for burning them in a small lamp floating on mercury in a bell jar containing air or oxygen. Every one of the compounds examined was found to yield carbon dioxide and water, and hence must contain the elements carbon and hydrogen. Lavoisier determined the amount of carbon dioxide present in the mixture of the two products of combustion by absorption in potassium hydroxide solution, and by this first and rather crude technique of quantitative analysis he was able to make at least an approximate estimation of the amounts of carbon and hydrogen present in the substances investigated.

By application and elaboration of Lavoisier's scheme of combustion analysis, certain of the compounds of organic origin were shown to be composed of carbon and hydrogen alone (hydrocarbons). In a considerable number of other substances, the combined carbon and hydrogen content was much too low to account for the whole, and yet the sole products of combustion were carbon dioxide and water. This indicated that the compounds in question must be composed of carbon, hydrogen, and oxygen (e.g., sugar, alcohol, acetic acid). A certain few of the organic compounds known at the time were found to yield nitrogen in addition to carbon dioxide and water, when burned in an atmosphere of oxygen, and this element was thereby recognized as a further constituent (e.g., urea, hippuric acid, morphine). As more and more examples of the rapidly expanding list of plant and animal products were investigated, the surprising conclusion became inescapable that the great majority of these natural products of widely diversified properties and types are made up of combinations of the same small group of elements consisting of carbon, hydrogen, oxygen, and nitrogen. Different combinations of the first three of these elements give rise to solid, liquid, and gaseous substances, to materials that are sour and to those that are sweet, to blue and to red dyes, and to substances essential to the human diet, as well as to plant products poisonous to the animal organism. In sharp contrast to this situation was the status of the results of parallel investigations of substances of mineral or "inorganic" origin. Discoveries in this field were made in abundance in the early part of the 19th century, particularly under the leadership of a succession of able Swedish and Finnish chemists and mineralogists working with supplies of rare ores found in Sweden. Here diversification in elemental composition proved to be the rule, and the investigator who succeeded in achieving the first chemical analysis of a mineral was often rewarded with the discovery of a new element. By 1807 some thirty-six elements were known, and by 1830 the list had mounted to fifty-three.

The fact that substances associated with living organisms were all found to be derived from but a selected few of the large number of known elements was only one of the seemingly mysterious attributes of these compounds, the study of which was first referred to as organic chemistry by Berzelius in 1807. In contrast to most mineral substances, the organic compounds are as a rule easily combustible, and often are destroyed or damaged by even moderate application of heat. They tend to be more or less delicate and sensitive in nature, and in this respect certain of them even resemble actual plant and animal tissues. Since all the first-known members of the group had been isolated as products of the life process, it is understandable that for a time the belief was current that organic compounds in general could arise only through the operation of a vital force inherent in the living cell. Although inorganic compounds had been prepared artificially in the laboratory, the production of organic substances was regarded as a specific function of living organisms. Berzelius, a leading figure of the period, held the view that the chemical synthesis of such substances was beyond the realm of possibility, and apparently no experiments were made in the direct attempt to achieve such a synthesis.

The doctrine of an essential vital force indeed remained unchallenged until Wöhler was led, through a chance observation reported in 1828, to the discovery that organic compounds can arise without the agency of any organism. In experimenting with ammonium cyanate, a substance of purely mineral or inorganic character, this early German chemist discovered to his surprise that the evaporation of an aqueous solution of the salt resulted in the production of urea, a representative compound of the organic type excreted in human urine. The result was so contrary to the

$$\underset{\text{Ammonium cyanate}}{NH_4OCN} \longrightarrow \underset{\text{Urea}}{CO(NH_2)_2}$$

thought of the time that Wöhler repeated the experiment many times before publication of his results. When fully satisfied with the experimental evidence, Wöhler saw that it constituted a refutation of the postulated "vital force," and in a letter to Berzelius he stated, "I must tell you that I can prepare urea without requiring a kidney or an animal, either man or dog."[1]

Although Berzelius, Gerhardt, and other contemporary chemists would not at first concede the evidence of this initial experiment, the discovery in subsequent years of a number of other instances of the artificial production of organic components eventually led to the abandonment of the idea of a vital force. The preparation of organic compounds presents no special mystery but is merely a matter of knowledge and experimental skill.

The designation "organic" lost some of the original connotation with the recognition that compounds of the group can be synthesized from starting materials not associated with living organisms, but the term has persisted as a convenient and reasonably descriptive means of classifying a group of chemical compounds having a number of characteristics in common. Most, but not all, of these compounds contain hydrogen, a large number contain oxygen as well, many contain nitrogen as a constituent, and some further members of the series contain halogen, sulfur, phosphorus, and other elements. They all contain carbon, and since this is the one essential element, organic chemistry may be defined as the chemistry of the carbon compounds.

Distinguishing Characteristics of Organic Compounds. — Although carbon compounds are so varied and extensive that broad generalizations concerning their properties are almost inevitably subject to some exceptions, several rather general characteristics differentiate organic from inorganic compounds. Organic compounds, with very few exceptions (e.g., CCl_4), are combustible, and this constitutes the basis of the chief methods avail-

[1] In 1824 Wöhler identified oxalic acid as a product of the action of water on cyanogen, $(CN)_2 + 4H_2O \longrightarrow (CO_2H)_2 + 2NH_3$, but he did not appreciate that this constituted the conversion of an inorganic into an organic compound, possibly because oxalic acid occurs in plants in the partly "mineral" form of the potassium salt. Wöhler isolated a substance later identified as urea as a minor component of this reaction mixture, and in subsequent experimentation found that ammonium cyanate is produced as one product of the reaction and is the immediate precursor of urea.