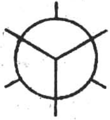
ADVANCED ORGANIC CHEMISTRY

WHELAND

Third Edition



Advanced Organic Chemistry

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Third Edition

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Preface

The teacher of an advanced course in organic chemistry has so broad a field from which to choose that he is forced drastically and arbitrarily to limit the material that he attempts to cover. This book, which has developed from the lecture notes that I prepared over a period of several years for such a course, is largely restricted to those aspects of the science that seem to me to be inadequately treated in the other textbooks and reference books that are now available. More particularly, the structural theory in its broadest sense is here described in considerable detail; on the other hand, such further topics as descriptive organic chemistry in general, the narrower and more highly specialized chemistries of carbohydrates, alkaloids, steroids, or the like, the finer details of physical organic chemistry, and so on are ordinarily introduced only briefly in order to illustrate or to explain fundamental principles. A course based solely on this book would therefore be incomplete. At the University of Chicago, for example, one-half to two-thirds of the second year of organic chemistry is devoted to the material that, although omitted here, can be obtained from the many excellent textbooks and reference books referred to above. In this way, a well rounded one-year course results.

In bringing the preceding edition of this book more nearly up to date, I have found it necessary to make several important changes. Thus, although the over-all approach is essentially the same as before, I have briefly introduced several such additional topics as electronic and nuclear magnetic resonance, conformational analysis, inclusion and charge-transfer compounds, and the Hammett rho–sigma relations. I have also extended the discussion of reaction mechanisms, and I have on several occasions indicated the value of kinetic data. For example, the S_N1, S_N2, S_Ni, and certain other types of displacement reactions are now discussed; the distinguishing characteristics of general acid or base catalysis, of specific hydrogen-ion or hydroxide-ion catalysis, and so on are mentioned; and the distinction between $[H^+]$ and h_0 is shown to be sometimes capable of leading to useful information regarding the natures of activated complexes. I have continued to emphasize the resonance theory since I am convinced that it gives the most easily understandable description of the states of molecules with intermediate structures, but I have also treated the molecular-orbital theory at least superficially. In order to provide space for the several additions without unreasonably increasing the size of the book, I have eliminated some of the less important material.

It is a pleasure to acknowledge that Figures 10.2 and 10.3 are reproduced by permission of Professors L. Ruzicka and V. Prelog, respectively; that, in Chapters 2 and 6 through 10, many passages (which are too numerous to list) are reprinted by permission of the *Encyclopaedia Britannica* from my articles Isomerism and Stereochemistry; that Professor F. H. Westheimer has revised part of Chapter 11, to supplement his original memorandum upon which this chapter was based in the second edition; that the translation of the "S. C. H. Windler" letter in Section 15.7 is adapted, with permission, from an earlier translation by Dr. H. B. Friedman; that Professors R. A. Clement, K. D. Kopple, C. A. Hutchison Jr., Dr. G. V. D. Tiers, and Professor W. H. Urry have read part or all of the manuscript and have given me the benefit of their valuable criticism and advice; and that Dr. W. J. le Noble has checked most of the journal references in the manuscript.

Since I realize that it is impossible for this book to be entirely free either from misprints or from more serious errors, I will appreciate corrections and criticisms from its readers.

G. W. WHELAND

Chicago, Illinois
March, 1960

Contents

chapter 1

Some Fundamental Concepts

1.1 Introduction

This first chapter is devoted to a critical examination of some of the fundamental concepts that will be employed throughout the book. The purpose of this examination is not so much to reveal the "true" or "correct" interpretations of these concepts, whatever they may be, as to call attention to the complexity of even the most familiar ideas of chemistry which "everyone understands" but which practically no one takes the trouble to define precisely and unambiguously. It will be found that the attempt to define these ideas encounters great difficulties—difficulties that are in no way lightened by the fact that, in many instances, chemists have never reached general agreement as to what the desired precise meanings are. No claim therefore is made that the definitions formulated in this chapter, and on numerous further occasions in subsequent chapters, are the best and most logical ones that can be devised, or even that they represent the views of all organic chemists. The maximum claim that can be made for them is that they provide a convenient compromise between the desire, on the one hand, to achieve precision and self-consistency, and, on the other hand, to adhere as closely as possible to common usage, to the extent that a common usage can be said to exist. In those instances, of which there are several, in which the definitions either leave room for ambiguity or depart considerably from common usage, or both, an attempt will be made to give the reader proper warning.

1.2 Organic Chemistry

The historical reasons that led to the adoption of the word "organic" as a description of the branch of chemistry with which this book is concerned are well known. Moreover, the fact that those historical reasons soon lost their validity as the doctrine of "vital force" fell into disrepute is also well known. (See the following paragraphs in fine print.) Nevertheless, the division of chemistry into "organic" and "inorganic" has continued to be useful, and so has been retained. At the present time, the distinction between organic and inorganic compounds is based not upon their origin in living or nonliving matter, respectively, but rather upon their elementary composition. The most common statement of the distinction is now that a substance is organic if it contains carbon and is inorganic if it does not. Although this statement is probably as nearly satisfactory as any that can be simply formulated, it is still not completely adequate. On the one hand, it classifies elementary carbon, carbon dioxide, and the metal carbonates, for example, as organic, although these substances have been found to be most conveniently grouped with the inorganic substances. On the other hand, it classifies molecular hydrogen, water, and ammonia, for example, as inorganic, although an organic chemist might wish to claim them as the simplest paraffin, the simplest alcohol, and the simplest amine, respectively, just as he claims formaldehyde as the simplest aldehyde.

The abandonment of the doctrine of "vital force" presents an interesting problem for historical research.[1] In 1828, Wöhler reported[2] that, without the assistance of any living organism, ammonium cyanate can be converted into urea. This discovery was at once recognized as extremely significant, but its effect on the subsequent development of organic chemical theory is still the subject of much discussion. According to one familiar account,[3] all (or, at any rate, many) of the competent scientists of the day immediately recognized that Wöhler's synthesis demonstrated the nonexistence of any fundamental distinction between organic and inorganic compounds and accordingly discarded (or, at any rate, began to question) the concept of vital force. Although this account has been accepted by many eminent chemists,[3,4] the literature of the

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[1] The author wishes to thank Professors E. Campaigne and T. Kuhn for helpful correspondence regarding this problem.

[2] F. Wöhler, *Ann. Physik* [2] **12**, 253 (1828); *Ann. chim.* [2] **37**, 330 (1828).

[3] This account is often said to stem from a statement made by A. W. Hofmann, *Ber.* **15**, 3127, 3152 (1882), in the obituary that he wrote for Wöhler, but it had then already been current for some time. See, for example, H. E. Armstrong, *Introduction to the Study of Organic Chemistry*, Longmans, Green & Co., London, 1874, pages 1*f*; the author is indebted to Mr. E. R. DuFresne, who called this reference to his attention.

[4] For documented discussions of the evidence favoring the view that Wöhler's preparation of urea from ammonium cyanate played an important role in the overthrow of vitalism, see, for example, W. H. Warren, *J. Chem. Educ.* **5**, 1539 (1928); E. Campaigne, *ibid.* **32**, 403 (1955).

period in which the subject was presumably being most actively discussed provides little direct support for it. Wöhler himself, apparently, did not claim that he has disproved vitalism. In his original paper,[2] he did state that the reaction which he had discovered was "remarkable" since it involved the preparation of an organic compound from an inorganic one; and, in a letter to Berzelius,[4] he did consider the possibility that the organic origin of the ammonium cyanate which he had used was an essential factor in his production of urea. Although it may therefore appear that he recognized a relation between his discovery and the doctrine of vitalism, alternative interpretations both of his published papers and of his correspondence are possible and have, in fact, been advanced by several authors.[5] In any event, it is probably significant that, if Wöhler (or, for that matter, any other chemist writing in the 10 to 15 years after 1828) made any clear and unambiguous statements regarding the necessity of discarding vitalism, none of these statements have been cited in the recent articles[4,5] in which the events leading to the abandonment of that theory are critically examined.

Wöhler's contemporaries also discussed the formation of urea from ammonium cyanate at considerable length, and they clearly considered this reaction unexpected and of great theoretical importance. Not until somewhat later,[3] however, was there any explicit suggestion that the reaction was important *because of its relation to vitalism.* Instead, some more recent authors have concluded that much of the initial emphasis was upon the discovery of a strange and interesting example of *isomerism.*[6]

The belief that Wöhler's synthesis of urea was a dominant factor in the overthrow of vitalism has been more explicitly disputed by a number of organic chemists.[5–8] This lack of general agreement is, however, hardly surprising since, as was noted by Wöhler himself,[4] the inorganic character of the original ammonium cyanate was not beyond question, and since also the preparation of the more definitely organic oxalic acid by hydrolysis of cyanogen had been reported still earlier.[9] Furthermore, many chemists felt[8] that urea was too simple a compound to be fully organic, and that it was therefore at most only intermediate between the organic and inorganic extremes; for this reason, its formation from inorganic reagents was not considered inconsistent with the belief in vital forces. Gerhardt, in particular, was clearly of this opinion in 1842,[10] when he stated that, although the chemist can prepare compounds like urea and carbon dioxide, which are merely decomposition products formed from organic materials by ordinary chemical means, he would need a "supernatural

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[5] See, for example, D. McKie, *Nature* **153,** 608 (1944); L. Hartman, *J. Chem. Educ.* **34,** 141 (1957).

[6] This view, which has been stated, for example, by J. B. Cohen, *Organic Chemistry for Advanced Students,* E. Arnold & Co., London, 3rd ed., 1920, vol. I, page 9, has been contested by other authors. See, for example, the references listed in footnote 4.

[7] P. Karrer, *Organic Chemistry* (translated by A. J. Mee, and revised and enlarged by H. V. Simon and N. G. Bisset), Elsevier Publishing Co., New York, 1950, page 2.

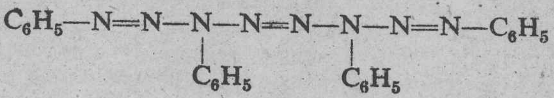
[8] C. Schorlemmer, *The Rise and Development of Organic Chemistry,* rev. ed., edited by A. Smithells, Macmillan & Co., London and New York, 1894, page 22.

[9] F. Wöhler, *Kongl. Vetens. Akad. Hand.* **1824,** 328; *Pog. Ann.* 3, 177 (1825). Cf. the paper by W. H. Warren, quoted in footnote 4.

[10] For references to the original literature and for quotations of the pertinent statements, see D. McKie, footnote 5.

power" to synthesize such more complex and truly organic substances as uric acid and sugar. In any event, for a number of years after 1828, many of the leading chemists of the day continued to speak of vital force as a valid concept. Not until the middle of the nineteenth century, or perhaps even later, was there general recognition of the fact that this doctrine had become untenable, not solely because of Wöhler's discovery but also as a consequence of the slow accumulation of still further knowledge.[5] As late as the 1840's, for example, Berzelius,[7,10] as well as Gerhardt,[7,10] was still of the opinion that life forces are required for the preparation of organic compounds, and there is little or no contemporary evidence to show that this view had ceased to be widely held.

Although the usual definition of organic chemistry is unambiguous, it does not (as was seen above) always agree with the way in which the term is used in practice, and it sometimes draws a sharp distinction where relatively little chemically important difference exists. A further peculiarity of this definition is that it assigns to carbon a unique role, which is not shared by any of the remaining elements. There is, for example, no separate branch of chemistry that deals exclusively with the compounds of boron, or of zirconium, or of the like. Why then is carbon so honored? A common explanation is that carbon forms a much greater number of compounds than any other element, so that the number of organic compounds reported in the chemical literature is several times as large as the number of all the inorganic compounds combined. This explanation is often supplemented by the statement that the existence of such a tremendous number of carbon compounds is due to the unique ability of carbon atoms to form long chains. Although carbon chains of more than one hundred atoms have been prepared, and have been found stable, the longest nitrogen chain that is known at present is composed of only eight atoms, and any compound containing such a chain, as, for example, 1,3,6,8-tetraphenyloctazatriene I,[11] is very unstable.



$$C_6H_5-N=N-\underset{C_6H_5}{\underset{|}{N}}-N=N-\underset{C_6H_5}{\underset{|}{N}}-N=N-C_6H_5$$

I

Throughout this book, structural formulas are designated, as above, by Roman numerals. The numeration starts again with I in each section.

A consideration of the question whether carbon does indeed possess the unique properties attributed to it will be both interesting and instructive. In the first place, it is probably not true that there are more known compounds of carbon than of any other element. Although there are undoubtedly more organic than inorganic compounds, nearly all the

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[11] A. Wohl and H. Schiff, *Ber.* 33, 2741 (1900).

organic substances contain hydrogen as well as carbon (the formula index of *Beilsteins Handbuch der organischen Chemie* lists only about 500 compounds not containing hydrogen), and a great many of the inorganic compounds contain hydrogen too. It appears likely, therefore, that the compounds of hydrogen outnumber those of carbon. Indeed, from a sampling of the formula indexes of *Chemical Abstracts* for the ten-year period 1942 through 1951, Wiswesser has estimated[12] that, although 96 per cent of the known compounds contain hydrogen, only 95 per cent contain carbon, and the remaining elements are much less common.

A different way of viewing the situation is suggested by Table 1.1, in which are listed the numbers of known binary compounds R_mQ_n, where R represents O, Cl, F, or H; and Q represents an element of the first short period. The figure given for the hydrides of carbon is indefinite, but it correctly reflects the enormous number of such compounds that have been described. The remaining figures, however, are more precise and should be fairly accurate. From the first row of the table, carbon is seen to be by no means unusual in its ability to form oxides; in fact, there are fewer known oxides of carbon than there are of nitrogen. From the second row, carbon is seen to be somewhat, but not extraordinarily, superior to any of the other first-period elements in its ability to form chlorides. Here, however, it should be noted that several of the chlorides included in this list were poorly characterized by their discoverers and may not actually exist, and also that the relatively large number of reported carbon chlorides can be considered a consequence of the enormous number of hydrocarbons from which they can conveniently be made. From the third row of the table, the ability of carbon to form fluorides appears not to be tremendously greater than its ability to form chlorides. There is, however, an important difference that exists between the two types of halide but is not brought out in the table; although the number of known carbon chlorides has increased slowly since, say, 1850, only a few of the carbon fluorides were known until after about 1940.[13] It can, therefore, be expected that the fluorides will soon outnumber the chlorides by a much greater margin than they do now. (See also below.) Finally, from the last row of the table, carbon is seen to be little short of phenomenal in its

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[12] W. J. Wiswesser, *A Line-Formula Chemical Notation*, Thomas Y. Crowell Co., New York, 1954, page 125.

[13] For a discussion of the organic fluorine compounds, see the papers which were presented at the symposium on fluorine chemistry held at the Chicago meeting of the American Chemical Society in September 1946, and which are published in *Ind. Eng. Chem.* 39, 236–434 (1947). Cf. also F. Smith, *Ann. Repts. Progr. Chem.* (*Chem. Soc. London*) 44, 86 (1947); J. H. Simons, *Fluorine Chemistry*, Academic Press, New York, vol. I, 1950; vol. II, 1954.

ability to form hydrides (i.e., hydrocarbons). Consequently, even if it is admitted that many additional carbon fluorides will be prepared within the next few years, the hydrides must for a long time, and probably must always, remain by far the most numerous class of compounds containing only carbon and some other single element. Clearly, therefore, although carbon does indeed possess an exceptional ability to form a large number of compounds, it shows this property to the full extent only in combination with hydrogen. Which is then the unique element: carbon or hydrogen?

Table 1.1

NUMBER OF KNOWN BINARY COMPOUNDS R_mQ_n

Q R	Li	Be	B	C	N	O	F
O	2[a]	1[b]	3[c]	5[d]	9[e]	3[f]	3[g]
Cl	1[h]	1[i]	4[j]	~40[k]	2[l]	7[m]	3[n]
F	1[o]	1[p]	1[q]	~80[r]	3[s]	2[g]	1[t]
H	1[u]	1[v]	6[w]	several thousand[x]	5[y]	2[z]	1[aa]

[a] Li_2O and Li_2O_2. For the incompletely characterized Li_2O_3 and Li_2O_4 (LiO_2 ?), see M. Tzentnershver and M. Blumenthal, *Bull. intern. acad. polon. sci., Classe sci. math. nat.* **1933A,** 499 [*C.A.* **28,** 4284 (1934)].

[b] BeO.

[c] B_2O_3 and two different substances, BO. Cf. T. Wartik and E. F. Apple, *J. Am. Chem. Soc.* **77,** 6400 (1955).

[d] CO, CO_2, carbon suboxide $O{=}C{=}C{=}C{=}O$, pentacarbon dioxide $O{=}C{=}C{=}C{=}C{=}C{=}O$ [A. Klemenc and G. Wagner, *Ber.* **70,** 1880 (1937)], and mellitic anhydride $C_{12}O_9$ (i.e., the anhydride of benzene hexacarboxylic acid).

[e] N_2O, NO, N_2O_2, $(N_3O_4)_x$, N_2O_3, NO_2, N_2O_4, N_2O_5, and NO_3.

[f] O_2, O_3, and O_4. In regard to the last of these substances, see G. N. Lewis, *J. Am. Chem. Soc.* **46,** 2027 (1924).

[g] OF_2, O_2F_2, and O_3F_2. In regard to the last of these substances, see A. D. Kirshenbaum and A. V. Grosse, *J. Am. Chem. Soc.* **81,** 1277 (1959).

[h] LiCl.

[i] $BeCl_2$.

[j] BCl_3, B_2Cl_4, B_4Cl_4, and B_8Cl_8. For the last of these compounds, see R. A. Jacobson and W. N. Lipscomb, *J. Am. Chem. Soc.* **80,** 5571 (1958). Cf. also G. Urry, T. Wartik, R. E. Moore, and H. I. Schlesinger, *ibid.* **76,** 5293 (1954).

[k] Too numerous to list. Cf. the formula indexes in *Beilsteins Handbuch der organischen Chemie* and in the abstract journals.

[l] NCl_3 and ClN_3.

[m] Cl_2O, ClO, ClO_2, ClO_3, Cl_2O_6, Cl_2O_7, and $(ClO_4)_x$. The last of these substances is possibly the dimer Cl_2O_8.

[n] ClF, ClF_3, and Cl_2F_6.

[o] LiF.

[p] BeF_2.

[q] BF_3 and B_2F_4. For the latter compound, see A. Finch and H. I. Schlesinger, *J. Am. Chem. Soc.* **80,** 3573 (1958).

[r] Too numerous to list. Cf. A. V. Grosse and G. H. Cady, *Ind. Eng. Chem.* **39,** 367 (1947) and the formula indexes in the abstract journals.

[s] NF_3, FN_3, and N_2F_2. For the last two substances, see J. F. Haller, Doctoral Dissertation, Cornell University, 1942, quoted by S. H. Bauer, *J. Am. Chem. Soc.* **69,** 3104 (1947).

[t] F_2.

[u] LiH.

[v] BeH_2.

[w] B_2H_6, B_4H_{10}, B_5H_9, B_5H_{11}, B_6H_{10}, and $B_{10}H_{14}$.

[x] Too numerous to list. Cf. the formula indexes in the abstract journals.

[y] NH_3, $H_2N{-}NH_2$, HN_3, $NH_4{}^+N_3{}^-$, and $H_3N{-}NH_3{}^+N_3{}^-$.

[z] H_2O and H_2O_2.

[aa] Hydrogen fluoride is here considered to be one compound; however, it probably consists, in the gaseous state, of a mixture of HF, $(HF)_2$, $(HF)_3$, and so on. Cf. G. Briegleb, *Z. physik. Chem.* **B51,** 9 (1941); R. A. Oriani and C. P. Smyth, *J. Am. Chem. Soc.* **70,** 125 (1948).

The above considerations may seem arbitrary since there can be no assurance that the relative numbers of now-known binary compounds have any theoretical significance. Indeed, these relative numbers could conceivably be so drastically altered within, say, the next hundred years that hydrogen would become no more important than any one of a dozen or more other elements. Although such a criticism may be valid, it is, however, not relevant to the discussion; the question here being considered is the significance and appropriateness, *at the present time,* of the distinction between inorganic and organic compounds. There can, in fact, be no doubt that now, just as throughout the history of the science, organic chemistry assigns to hydrogen a role that rivals, if indeed it does not equal, that of carbon itself. It may also be questioned whether the distinction that is now made between inorganic and organic chemistry might not need to be drastically revised, or even discarded, if at some future time hydrogen should lose its present predominant importance.

Even the ability of carbon atoms to join together into long chains seems to be dependent on the presence of hydrogen atoms (or of fluorine atoms, see below). For example, if a paraffin hydrocarbon C_nH_{2n+2} is treated with an excess of chlorine, the completely chlorinated product C_nCl_{2n+2} is not obtained if n is greater than 3. Under such circumstances, either the chlorination is incomplete, so that more or less hydrogen remains in the molecule, or else the molecule breaks up into (often unsaturated) fragments containing no more than about four carbon atoms per molecule.[14] Hexachloroethane and hexachloro-1,3-butadiene are, in fact, often the final products of exhaustive chlorination of many higher aliphatic

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[14] For a review of these reactions and for references to earlier work in the field, see A. Roedig, *Ann.* **574,** 122 (1951).