2 Introduction. Characteristics of organic compounds

1-1 What is organic chemistry?

With the rapid growth of the science of chemistry in the past half-century has come its separation into a number of special areas: physical chemistry, analytical chemistry, biological chemistry, organic chemistry, and others. These areas are not mutually exclusive, for each permeates the others; yet each is characterized by the emphasis that is placed upon it, by some special approach in the techniques utilized, or by the kinds of compounds that are dealt with. Organic chemistry deals with the chemical compounds of carbon, and principally with compounds in which carbon is combined with hydrogen, oxygen, nitrogen, sulfur, and the halogens. It is a special area of chemistry because of the enormous number of carbon compounds—over a million are known, and the number is increasing at the rate of about five percent per year. More than ninety percent of these are synthetic substances, the remainder having been isolated from living organisms (animals, plants, fungi, microorganisms) and their fossil remains (coal, petroleum).

The *naturally occurring* organic compounds are of concern to the biochemist as well as to the organic chemist, and indeed it is in dealing with such substances that biochemistry and organic chemistry come together and lose their individual identity. The naturally occurring compounds include the proteins, fats, carbohydrates, vitamins, and hormones that compose living cells; many of the drugs used to control disease and relieve suffering; the perfumes and colors of the plant world; and thousands of other substances that participate in the metabolic activities of living things.

The synthetic organic compounds are derived largely from natural sources of carbon—coal and petroleum—but are the products of man's voluntary ingenuity rather than of the involuntary activities of living organisms. There is no limit to the number of organic compounds that can be made, and indeed the known synthetic compounds include many naturally occurring compounds that have been prepared synthetically as final confirmation of their structures. The only kinds of compounds that have so far resisted the attack of the synthetic organic chemist are the complex carbohydrates, the nucleic acids, and the complex combinations of these that make up the essential stuff of the living cell. Although the complete synthesis of only a few substances identical in structure and function with these natural materials has been accomplished, further achievement will surely come in time. It is to the new generations of scientists who will pursue these goals that this book is addressed, in the hope that it will help to impart that basic understanding of the scientific principles of organic chemistry that must underlie future progress in both chemistry and biology.

1-2 The development of organic chemistry

The scientific revolution of the sixteenth and seventeenth centuries was characterized by the birth of a spirit of inquiry and skepticism that marked a new phase of the successful with reactive halides. Methyl, allyl, benzyl, and α -alkoxyl halides react most readily:



 α,β -Unsaturated carbonyl compounds also act as alkylating agents in a reaction equivalent to the Michael condensation (Chapter 25):



The advantage of alkylating by way of the enamine is that poly-alkylation seldom occurs and the mono-alkylated ketone is generated in good yield.

The scope of enamine chemistry is too wide to be dealt with fully in this text. One example of the use of a bicyclic enamine to produce a unique polycyclic system will show the versatility of the reaction. The ring system that is formed is found in alkaloids that occur naturally in the seeds of *Erythrina* (coral tree):



The formyl hydrogen atom is indeed "activated," but only after the initial combination with cyanide, which acts as an "operator" that enters and leaves the reaction sequence but does not appear in the overall expression.

22-20 Biological synthesis of acetoin

A product sometimes formed in the biological degradation (metabolism) of carbohydrates is acetoin, $CH_3COCHOHCH_3$. It can be seen that this compound could be formed from acetaldehyde just as benzoin is formed from benzaldehyde. That the dimerization of acetaldehyde in a biological system is catalyzed by cyanide ion itself is, however, scarcely to be believed, because of the highly cytotoxic properties of cyanide and its absence from normal biological systems.

Biological systems do contain, as a prosthetic group, a compound that can perform the same catalytic function as cyanide in the benzoin condensation. This is *thiamin pyrophosphate*. Its role as a biological catalyst will be described in Section 22-24.

22-21 Enzymes as biological catalysts

The transformations of organic molecules in biological systems proceed by rational mechanisms that can be interpreted and understood in the same terms as those used for describing organic reactions of all kinds. The enzyme catalyzes the reaction, it does not cause it. It brings about an enormous increase in the rate of the reaction, and often directs its stereochemical course. When a reacting molecule (the *substrate*) is so constituted that two or more pathways, leading to different products, can be envisaged, the enzymatic reaction often directs it to only one of the several products that might be regarded as possible on purely structural or energetic grounds.

What peculiarities do enzymes possess that enable them to act with such efficiency and precision?

1. Enzymes are proteins. Many (but not all) of them contain as part of their structure low-molecular-weight compounds called co-enzymes or *prosthetic groups*. As polypeptides consisting of long sequences of L-amino acids, enzymes are asymmetric molecules. The asymmetry is due not only to the chirality of the amino acids but also to the fact that the long peptide chains are coiled, with parts of the chains connected by bridging elements. Consequently, in the enzyme or upon the enzyme surface, portions of the amino acid components are uniquely oriented to provide a region upon which a substrate molecule can fit in only one (preferred) attitude.

- Write the structure of the predominant product that would be formed by the base-catalyzed aldol condensation of each of the following pairs: (a) acetone, acetone; (b) acetone, acetaldehyde; (c) cyclohexanone, acetaldehyde; (d) isobutyraldehyde, formaldehyde; (e) propionaldehyde, 2,4-pentanedione; (f) nitromethane, acetaldehyde.
- 8. The aldol condensation of vinylacetaldehyde, CH₂=CHCH₂CHO, with acetaldehyde in the presence of alkali as a catalyst yields the product CH₃CH=CH-CH=CHCHO. Explain this result and formulate the sequence of steps that leads to it.
- 9. The reaction of 3,3-dimethyl-2,4-pentanedione with alcoholic sodium ethoxide gives ethyl acetate and methyl isotropyl ketone. Formulate this reaction, recalling the principles of nucleophilic attack upon carbonyl groups, and point out the relationship of the cleavage of the diketone to the "reversal" of the aldol condensation.
- 10. A useful method for demonstrating the presence of the grouping -CH₂-C=O in an organic compound consists in treating the compound with benzaldehyde, C₆H₅CHO, and a trace of alkali (such as sodium ethoxide). The aldol condensation at the active methylene group gives rise to a "benzal" derivative, of the partial structure -C=CHC₈H₅. Show the formation of the benzal -C=O

derivatives of the following: (a) acetone, (b) cyclopentanone, (c) diethylketone, (d) pinacolone.

- How could a chemical test distinguish between (a) acetone and diethyl ketone,
 (b) methyl isopropyl ketone and isobutyraldehyde, (c) diisopropyl ketone and
 di-n-propyl ketone, (d) di-n-butyl ether and 2-butanone, and (e) 2-pentanone
 and 3-pentanone?
- 12. Explain why acetylacetone CH₃COCH₂COCH₃ is a stronger acid than acetonylacetone, CH₃COCH₂CH₂COCH₃. Write the structures of the monoanions formed by the reactions of these two ketones with a base such as sodium ethoxide.
- 13. What product would you predict to be formed by the intramolecular aldol condensation of 2,8-nonanedione?
- 14. Using acetone as the starting material, devise practical syntheses for the following. Show steps and reagents.

(a)
$$(CH_3)_2CHCH_2COOH$$
 (b) $CH_3CHOHCH_2CH_2OH$
(c) H_3C $O-CH_2$
 H_3C $O-CH_2$

15. A compound (A), C_6H_8O , gave cyclohexanone upon catalytic reduction. It had no high-intensity ultraviolet absorption above 200 m μ , but had a weak