

S.E. ZURABYAN

FUNDAMENTALS OF BIOORGANIC CHEMISTRY

TEXTBOOK FOR MEDICAL STUDENTS

С.Э. ЗУРАБЯН

ОСНОВЫ БИООРГАНИЧЕСКОЙ ХИМИИ

УЧЕБНИК

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Chapter 1

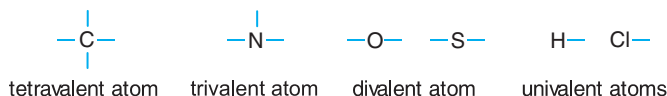
CHEMICAL STRUCTURE AND BONDING

Probably many students have already acquired some knowledge in a beginner's chemistry course. Nevertheless, it would be expedient to recall in this opening chapter some information on general chemistry and the structural theory of organic chemistry that will be helpful in studying the entire course.

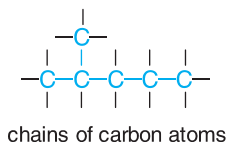
1.1. THE STRUCTURAL THEORY OF ORGANIC COMPOUNDS

In the mid-nineteenth century (1858–1860), F.A. Kekulé (in Germany) and A.S. Couper (in Scotland) independently formulated the basis of one of the most fundamental theories in modern organic chemistry, the structural theory. It comprises two main ideas.

- Atoms in organic compounds form a definite number of bonds. A measure of bonding ability of atoms is known today as *valence*. Thus, a carbon atom forms four bonds when it is linked to other atoms and is tetravalent. Nitrogen forms usually three bonds and is trivalent, oxygen forms two bonds and is divalent, hydrogen and halogens are univalent.



- Carbon atoms can bond to each other to form extended chains of atoms linked together.



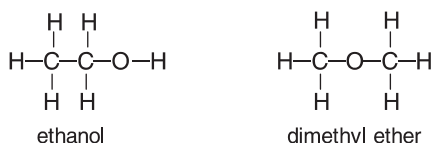
At that time, in 1861, the Russian chemist A. Butlerov made an outstanding contribution to organic chemistry when he developed new ideas in this field. The main of them stated:

 The chemical nature of a complex particle is determined by the nature of its elementary constituent parts, their number and chemical structure.

Butlerov stated that all the atoms in a molecule interact with one another, and a mutual influence is the strongest between directly linked atoms. It was Butlerov who introduced the term *chemical structure* into chemistry.

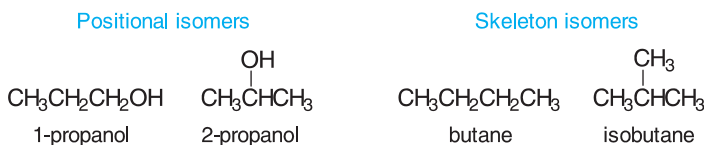
Butlerov's theory of chemical structure gave a rational explanation of isomerism.

There are many compounds that have the same molecular formula, but they differ in physical and chemical properties due to their different molecular structure. Such compounds are called *isomers* (from the Greek *isos* – equal, and *meros* – part). One of the simplest examples of isomeric compounds is a pair of *ethanol* and *dimethyl ether* with the molecular formula C_2H_6O . The former is a liquid, the latter is a gas at room temperature (their boiling points are 78 and $-25\text{ }^{\circ}\text{C}$, respectively). Ethanol reacts with sodium, dimethyl ether does not. It is quite enough to look at the structural formulas for these compounds to reveal their difference.



This is an example of constitutional isomerism when isomers differ from each other in their functional groups. Isomers can also differ in the position of the same functional group at the same carbon skeleton (positional isomers are, for example, isomeric alcohols 1-propanol and 2-propanol shown below). But the main reason for constitutional isomerism consists in the great variety of carbon skeletons. Thus, hydrocarbons C_4H_{10} represent the simplest example of skeleton isomerism.

The term *structural isomerism* is often used but it has a broader sense than constitutional isomerism. Really, structural isomers differ in *all* details of their structure including spatial arrangement of atoms (Chapter 10).



The structural theory originated by Kekulé, Couper, and Butlerov was extended into three dimensions by the Dutch physico-chemist J.H. van't Hoff¹ and J.A. Le Bel (from France). In 1874, they independently proposed that four atoms to which carbon is bonded do not lie in one plane, but sit at the corners of a tetrahedron, with carbon in the centre (Fig. 1.1).

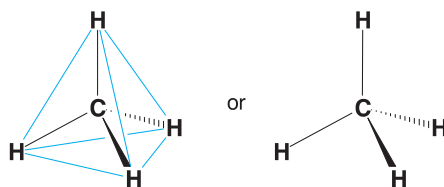


Figure 1.1. The tetrahedral structure of methane.

To show the three-dimensional arrangement of groups around the central carbon the following conventions are generally used: normal lines represent bonds in the plane of the paper, heavy wedged line represents a bond coming towards the viewer, and a dashed line represents a bond moving away from the viewer.

¹ Jacobus Hendricus van't Hoff (1852–1911), the first Nobel Prize winner in Chemistry (1901). His famous paper on stereochemistry, *The Position of Atoms in Space*, was published when he was 22 years old.

After the discovery of the electron (in 1897), the atomic theory penetrated into organic chemistry very intensively. Developments of quantum mechanics were also applied to organic chemistry, thus forming by the 1930's the basis of the modern understanding of the subject. These concepts are considered in greater detail in the following sections.

1.2. THE STRUCTURE OF ATOMS

An atom consists of a positively charged nucleus surrounded by negatively charged electrons. The nucleus, in its turn, consists of protons, carriers of the total positive charge, and neutral particles called neutrons (except the light isotope of hydrogen). Both particles are equal in mass, whereas the mass of the electron is about 1/1840 of the mass of the proton.

The number of protons determines the charge of the nucleus and identifies the atom as belonging to an individual element. In a neutral atom the positive charge of the nucleus is balanced by the negative charge of the electrons. The atomic number of an element is the number of protons (or electrons), and the mass number is the total of protons and neutrons.

Electrons are of the most interest to chemistry because their number and arrangement accounts for constitution and chemical properties of molecules. Above all, we will consider electron arrangement in carbon and hydrogen and then elements frequent in organic molecules, such as oxygen, nitrogen, sulfur, and halogens.

1.2.1. Atomic Orbitals

Electrons are located in certain regions of space called orbitals.

 The orbital is a region of space where the probability of finding an electron is large, about 95% of its time.

In other words, this is the region within which the electron density is the greatest. According to the *Pauli exclusion principle*, each orbital can contain a maximum of two electrons but they must be of opposite spin.

An electron spins about its axis and spin orientation is usually shown by arrows, either $\uparrow$ or $\downarrow$. Thus, two spin-paired electrons would be designated $\uparrow\downarrow$.

Electrons occupy different shells (energy levels) designated by the numbers 1, 2, 3, and so on. The total number of orbitals in a given shell is n^2 where n is the shell's number. The farther the shell is from the nucleus, the greater the energy of those electrons is (Table 1.1).

Table 1.1. Distribution of electrons in the first three shells

Shell number	Energy increasing	Orbitals' number of each type			Electron capacity of the filled shell
		s	p	d	
1		1	0	0	2
2		1	3	0	8
3		1	3	5	18

Orbitals also differ in their shapes. There are four types of orbitals, specified s , p , d , and f . Only s and p orbitals will be concerned since they are the most important in organic chemistry. Taking into account both the size and the shape of orbitals, we designate them $1s$, $2s$, $2p$, $3s$, and so on. The s orbitals are spherical in shape. The three p orbitals are dumb-bell-shaped and oriented in such a way as to point mutually at right angles (Cartesian coordinates with the axes x , y , and z). They are sometimes called the $2p_x$, $2p_y$, and $2p_z$ orbitals to emphasize their directional character. The shapes of the s and p orbitals are shown in Fig. 1.2.

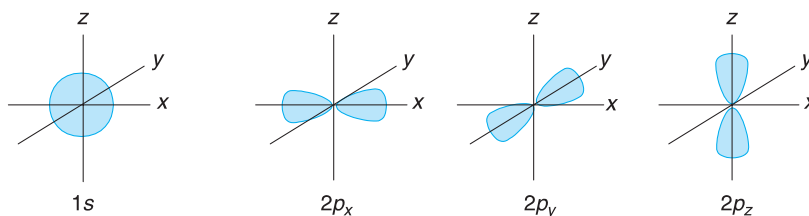


Figure 1.2. The shapes of the s and p atomic orbitals.
The nucleus is at the origin of the three coordinate axes.

The $2s$ and $3s$ orbitals have the same shape as the $1s$ orbital, but they are bigger and higher in energy. Similarly, the $3p$ orbital has the same shape as $2p$ one.

1.2.2. Electronic Configuration

A description of the orbitals that electrons occupy in an atom is called electronic configuration. The most stable state (so called ground-state) of an atom is that in which the electrons are at the lowest energy level, that is, in shells which are closest to the nucleus. To arrive at electronic configuration of any atom we should follow a few simple rules:

- Orbitals of the lowest energy are filled first. This is the *aufbau principle* (from the German *Aufbau* – building up);
- The Pauli exclusion principle mentioned above;
- The orbitals of a given shell are first filled with one electron each, and then with a second. This is known as the *Hund's rule*.

The application of these rules indicates a $1s$ configuration of hydrogen. Electronic configuration of helium, the next element after hydrogen, will consequently be $1s^2$. Six electrons of a ground-state carbon atom are arranged to give a $1s^2 2s^2 2p_x 2p_y$ orbital configuration (a simpler form is usually preferred, without sub-division of p orbitals, but it is less informative). These and other examples are shown in Table 1.2.

In representations of electronic configuration, a superscript is used to indicate the number of electrons at a particular orbital. Remember that numerals in front of the orbital symbols indicate the shell's number.

1.3. THE NATURE OF CHEMICAL BONDING

An understanding of the nature of a chemical bond is one of the major aims of chemistry. W. Kössel (a German physicist) and G.N. Lewis (an American physico-