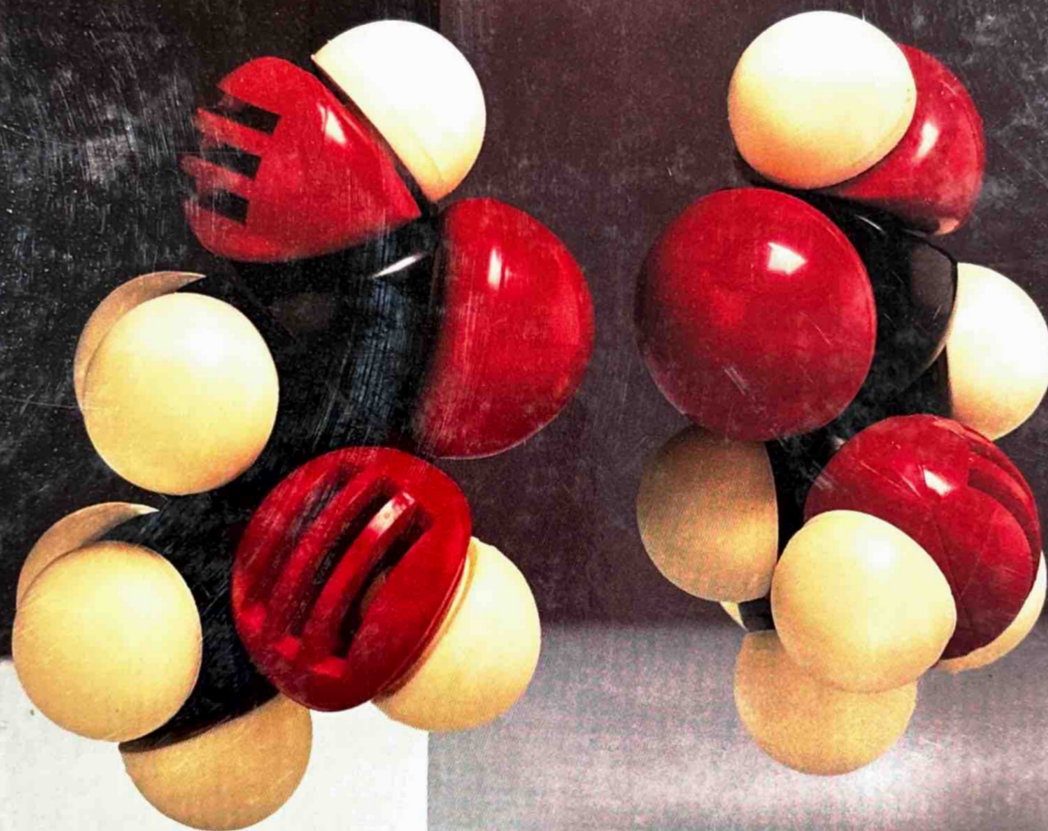


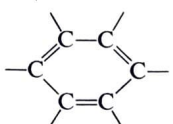
INTRODUCTION TO ORGANIC CHEMISTRY

F O U R T H E D I T I O N

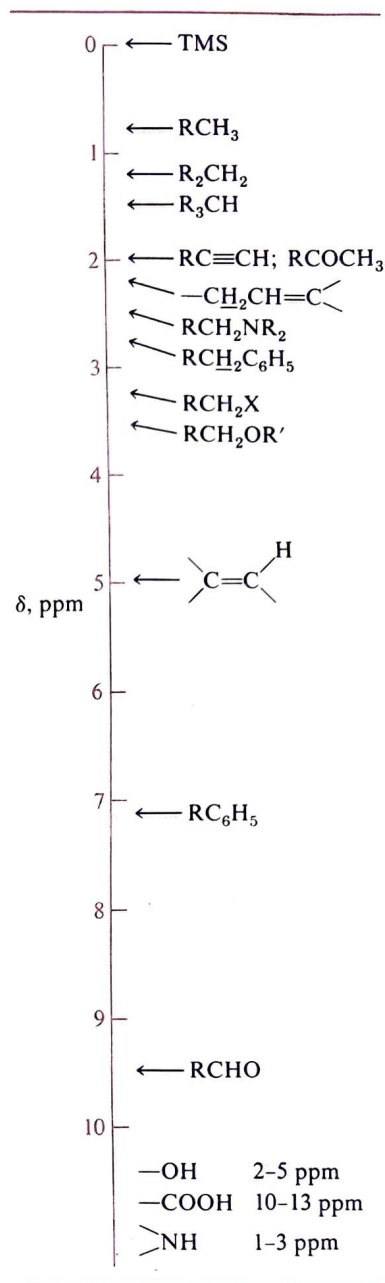


Andrew Streitwieser
Clayton H. Heathcock
Edward M. Kosower

Common Organic Functions

Class	Formula	Functional Group	IUPAC Prefix or Suffix
acyl halide	RCX	$\text{—}\overset{\text{O}}{\parallel}\text{CX}$	-oyl halide
alcohol	ROH	—OH	-ol
aldehyde	RCH=O	$\text{—}\overset{\text{O}}{\parallel}\text{CH}$	-al
alkane	RH	none	-ane
alkene	$\text{R}_2\text{C=CR}_2$	>C=C<	-ene
alkyne	$\text{RC}\equiv\text{CR}$	$\text{—C}\equiv\text{C—}$	-yne
amide	RCNR_2	$\text{—}\overset{\text{O}}{\parallel}\text{CN—}$	-amide
amine	R_3N	—N—	amino-
arene	ArH		
azide	RN_3	$\text{—N}^+=\text{N}=\text{N}^-$	azido-
carboxylic acid	RCOOH	$\text{—}\overset{\text{O}}{\parallel}\text{COH}$	-oic acid
ester	RCOR	$\text{—}\overset{\text{O}}{\parallel}\text{CO—}$	
ether	R_2O	—O—	alkoxy-
halide	RF	—F—	fluoro-
	RCl	—Cl—	chloro-
	RBr	—Br—	bromo-
	RI (RX)	—I (—X)—	iodo- (halo-)
ketone	RC(=O)R	$\text{—}\overset{\text{O}}{\parallel}\text{C—}$	-one
nitrile	$\text{RC}\equiv\text{N}$	$\text{—C}\equiv\text{N}$	-nitrile
nitro compound	RNO_2	—NO_2	nitro-
phenol	ArOH	—OH	
sulfide	R_2S	—S—	alkylthio-
sulfone	$\text{RS(=O)}_2\text{R}$	$\text{—}\overset{\text{O}}{\parallel}\text{S}\overset{\text{O}}{\parallel}\text{—}$	
sulfonic acid	RSO_3H	$\text{—}\overset{\text{O}}{\parallel}\text{SO}_2\text{H}$	-sulfonic acid
sulfoxide	RS(=O)R	$\text{—}\overset{\text{O}}{\parallel}\text{S—}$	
thiol	RSH	—SH	-thiol

Approximate NMR Chemical Shifts



Symbols for Amino Acids

Ala	alanine
Arg	arginine
Asn	asparagine
Asp	aspartic acid
Cys	cysteine
Gln	glutamine
Glu	glutamic acid
Gly	glycine
His	histidine
Ile	isoleucine
Leu	leucine
Lys	lysine
Met	methionine
Phe	phenylalanine
Pro	proline
Ser	serine
Thr	threonine
Trp	tryptophan
Tyr	tyrosine
Val	valine

Greek Alphabet

Lower Case	Capital	Name
α	A	alpha
β	B	beta
γ	Γ	gamma
δ	Δ	delta
ϵ	E	epsilon
ζ	Z	zeta
η	H	eta
θ	Θ	theta
ι	I	iota
κ	K	kappa
λ	Λ	lambda
μ	M	mu
ν	N	nu
ξ	Ξ	xi
$\omicron$	O	omicron
π	Π	pi
ρ	P	rho
σ	Σ	sigma
τ	T	tau
υ	Υ	upsilon
ϕ	Φ	phi
χ	X	chi
ψ	Ψ	psi
ω	Ω	omega

Chemical Abbreviations

Ac	acetyl, $\text{CH}_3\text{C}(=\text{O})-$
Boc	<i>t</i> -butoxycarbonyl, $(\text{CH}_3)_3\text{COC}(=\text{O})-$
<i>n</i> -Bu	<i>n</i> -butyl, $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2-$
<i>t</i> -Bu	<i>t</i> -butyl, $(\text{CH}_3)_3\text{C}-$
Cbz	benzyloxycarbonyl, $\text{C}_6\text{H}_5\text{CH}_2\text{OC}(=\text{O})-$
DCC	dicyclohexylcarbodiimide, $\text{C}_6\text{H}_{11}\text{N}=\text{C}=\text{NC}_6\text{H}_{11}$
DIBAL	diisobutylaluminum hydride, $[(\text{CH}_3)_2\text{CHCH}_2]_2\text{AlH}$
diglyme	bis(2-methoxyethyl) ether, $(\text{CH}_3\text{OCH}_2\text{CH}_2)_2\text{O}$
DMF	dimethylformamide, $(\text{CH}_3)_2\text{NCHO}$
DMSO	dimethyl sulfoxide, $(\text{CH}_3)_2\text{SO}$
DNP	2,4-dinitrophenyl, $2,4-(\text{O}_2\text{N})_2\text{C}_6\text{H}_3-$
Et	ethyl, CH_3CH_2-
glyme	1,2-dimethoxyethane, $\text{CH}_3\text{OCH}_2\text{CH}_2\text{OCH}_3$
HMPT	hexamethylphosphoric triamide, $[(\text{CH}_3)_2\text{N}]_3\text{PO}$
LAH	lithium aluminum hydride, LiAlH_4
LDA	lithium diisopropylamide, $\text{LiN}[\text{CH}(\text{CH}_3)_2]_2$
Me	methyl, CH_3-
PPA	polyphosphoric acid
THF	tetrahydrofuran, $\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$
TMS	tetramethylsilane, $(\text{CH}_3)_4\text{Si}$
Ts	<i>p</i> -toluenesulfonyl, $p\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2-$

Equilibria and Free Energy

$$\text{A} \rightleftharpoons \text{B} \quad K = \frac{[\text{B}]}{[\text{A}]}$$

$$\Delta G^\circ = -RT \ln K$$

<i>K</i>	Percent B	Percent A	ΔG° , kcal mole ⁻¹ (25°)
0.0001	0.01	99.99	+5.46
0.001	0.1	99.9	+4.09
0.01	0.99	99.0	+2.73
0.1	9.1	90.9	+1.36
0.33	25	75	+0.65
1	50	50	0
3	75	25	-0.65
10	90.9	9.1	-1.36
100	99.0	0.99	-2.73
1000	99.9	0.1	-4.09
10000	99.99	0.01	-5.46

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FOURTH EDITION

ANDREW STREITWIESER
UNIVERSITY OF CALIFORNIA, BERKELEY

CLAYTON H. HEATHCOCK
UNIVERSITY OF CALIFORNIA, BERKELEY

EDWARD M. KOSOWER
TEL AVIV UNIVERSITY

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The Theta Molecular Model Set marketed by John Wiley & Sons uses small plastic nuclei like “jacks” and plastic tubing. The Prentice-Hall Framework molecular models are similar, but use metal nuclei. The HGS-Maruzen models use plastic atoms with holes drilled to accommodate bonds. The Darling models also use plastic parts that are fitted together. Models such as these are relatively inexpensive and are indispensable as an aid in visualizing three-dimensional aspects of organic structures and reactions.

Corey-Pauling-Koltun (CPKTM) molecular models are an example of space-filling models. The models are constructed from an acrylic polyester plastic and have sizes proportional to the covalent and atomic radii of the atoms. They are held together by connectors made of a hard rubber-like elastomer. They are fairly expensive and are mainly used by professional chemists for constructing models where a knowledge of molecular shape and intramolecular interactions is important.

A new modeling tool called *molecular graphics* is coming into use, both on personal computers of the IBM and Macintosh types and on more sophisticated workstations like the Silicon Graphics IRIS. Both 2D formulas and 3D models can be generated on the computer screen. The 3D models can be turned, brought together (“docked”), and manipulated in some ways like physical models.

EXERCISE 3.3 Using your molecular model set, construct models of some of the organic molecules previously illustrated in this chapter.

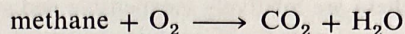
3.4 The Determination of Organic Structures

In previous sections, we have reviewed some basic concepts of electronic structure and bonding and have introduced the subject of organic structures and functional groups. In subsequent chapters, we shall take up the structures and chemical reactions of various classes of organic compounds and examine them in detail. At this point, an additional question must be addressed before we embark upon our systematic study of organic chemistry. How does the chemist know the structure of a compound? The question is an important one, and it is encountered over and over again by researchers in the field. In fact, the rate of development of organic chemistry as a science has been intimately related to our ability to *determine structure*.

Mentally transport yourself back a hundred years—imagine that you are a nineteenth-century scientist and have laboriously purified an organic substance from some source. How do you determine its structure? It is possible to measure various physical properties such as boiling point, melting point, density, and refractive index. A catalog of these properties constitutes the **characterization** of a compound. Just as no two people have identical fingerprints, no two compounds have all physical properties in common. It is relatively easy to assemble a list of physical properties for the compound and to decide that it is different from other previously isolated substances. Your new compound also undergoes various chemical reactions, and from its behavior with various reagents you may be able to decide what kinds of functional groups are present. For example, suppose that your material reacts with sodium to produce hydrogen gas. Since simple alcohols such as methyl alcohol are known to undergo this reaction, you can make the deduction that your new compound contains the functional group OH. But still, from all these data, how do you write a molecular structure for the compound? This problem challenged chemists for over a hundred years.

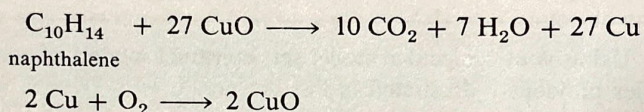
The first major breakthrough came with the development of methods of elemental analysis. The first attempts to determine the elemental compositions of organic compounds were made by Lavoisier in the late eighteenth century in connection with his

pioneering work on the reactions of oxygen. Lavoisier examined the combustion products from various compounds and could deduce which elements were present in the substance burned. For example, combustion of methane gives carbon dioxide and water. Hence, methane must be built up from carbon and hydrogen in some way.



Although Lavoisier attempted to quantitate combustion as a method to determine accurate formulas for organic compounds, the apparatus at his disposal was not sufficiently accurate for him to obtain precise formulas. The next significant advance came in 1831 when Liebig developed the Lavoisier method into a precise quantitative technique. For the first time, it was possible to determine accurate empirical formulas for organic compounds. In connection with methods for the determination of molecular weights, it was then possible to determine molecular formulas.

The method of combustion analysis, as developed by Liebig, is conceptually very simple. A weighed quantity of the sample to be analyzed is burned in the presence of red-hot copper oxide, which is reduced to metallic copper. The sample is swept through the combustion tube with pure oxygen gas, which reoxidizes the copper to copper oxide.



The combustion products are swept through a calcium chloride tube, which absorbs the water formed, and then through a tube containing aqueous potassium hydroxide, which absorbs the carbon dioxide produced. The two tubes are weighed before and after combustion to determine the weights of water and carbon dioxide produced. From the weights of the two products, the weight of sample burned, and the atomic weights of carbon and hydrogen, it is possible to compute an empirical formula for the substance burned.

$$\text{weight of H in sample} = \text{weight of H}_2\text{O} \times \frac{2.016}{18.016}$$

$$\text{weight of C in sample} = \text{weight of CO}_2 \times \frac{12.01}{44.01}$$

$$\% \text{ H in sample} = \frac{\text{weight of H}}{\text{weight of sample}} \times 100$$

$$\% \text{ C in sample} = \frac{\text{weight of C}}{\text{weight of sample}} \times 100$$

If the percentages of carbon and hydrogen do not add up to 100 and no other element has been detected by qualitative tests, the deficiency is taken as the percentage of oxygen.

As an example, consider the analysis of propyl alcohol, $\text{C}_3\text{H}_8\text{O}$. An ideal analysis on a 0.500-g sample would give 0.600 g of H_2O and 1.099 g of CO_2 . The calculations proceed as follows.

$$\text{weight of H in sample} = 0.600 \text{ g} \times \frac{2.016}{18.016} = 0.067 \text{ g}$$

$$\text{weight of C in sample} = 1.099 \text{ g} \times \frac{12.01}{44.01} = 0.300 \text{ g}$$

$$\% \text{ H in sample} = \frac{0.067}{0.500 \text{ g}} \times 100 = 13.4$$

$$\% \text{ C in sample} = \frac{0.300}{0.500} \times 100 = 60.0$$

The percentages of hydrogen and carbon add up to 73.4%, and the remaining 26.6% is taken as the percentage of oxygen in the sample. In actual practice, the analytical values are usually accurate to $\pm 0.3\%$.

EXERCISE 3.4 How much CO_2 and H_2O are produced by the combustion of 3.74 mg of $\text{C}_6\text{H}_{12}\text{O}$?

From the elemental analysis of a compound, one can easily calculate its **empirical formula**, which expresses the ratio of the elements present. In the present case, for example, the analysis tells us that 100 g of propyl alcohol contains 60.0 g of carbon, 13.4 g of hydrogen, and 26.6 g of oxygen. Dividing each of these weights by the appropriate atomic weights gives us the number of moles of each element in 100 g of sample.

$$\frac{60.0}{12.01} = 5.00 \text{ moles of carbon}$$

$$\frac{13.4}{1.008} = 13.29 \text{ moles of hydrogen}$$

$$\frac{26.6}{16} = 1.66 \text{ moles of oxygen}$$

This calculation gives us an empirical formula of $\text{C}_{5.00}\text{H}_{13.29}\text{O}_{1.66}$. However, because the atoms in a molecule must be present in whole numbers, the initially derived formula must be normalized. If we divide each of the factors derived above by the smallest, we have

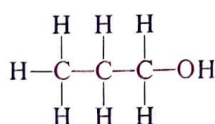
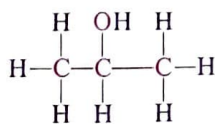
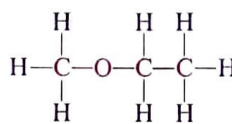
$$\text{C}_{5.00/1.66}\text{H}_{13.29/1.66}\text{O}_{1.66/1.66} = \text{C}_{3.01}\text{H}_{8.01}\text{O}_{1.00}$$

Thus, the empirical formula of propyl alcohol is calculated from its elemental analysis to be $\text{C}_3\text{H}_8\text{O}$. The molecular formula expresses the total number of each atom present and is the same as the empirical formula or some multiple of it. For example, if the molecular formula of propyl alcohol were $\text{C}_6\text{H}_{16}\text{O}_2$, the percentages of carbon, hydrogen, and oxygen would be the same. (Actually, because of the rules of valence, $\text{C}_6\text{H}_{16}\text{O}_2$ is an impossible formula, as a little trial and error will readily reveal.)

EXERCISE 3.5 Combustion of 0.250 g of di-*n*-butyl ether gives 0.677 g of CO_2 and 0.311 g of H_2O . Calculate the empirical formula of di-*n*-butyl ether.

The Lavoisier-Liebig method of analysis provided a tremendous boost to the development of organic chemistry but required relatively large amounts of sample, on the order of 0.25–0.50 g. In 1911 Fritz Pregl introduced a technique of microanalysis that allows combustion analysis to be carried out with only 3–4 mg of sample. Elements such as N, S, Cl, Br, I, and P are determined on a micro scale by other analytical methods that we shall not detail. Highly accurate molecular formulas can now be determined with a few micrograms of substance by the technique of high-resolution mass spectrometry (Chapter 34).

From the molecular formula, the next step is to derive a molecular structure. How are the atoms bonded to one another? For our present example of $\text{C}_3\text{H}_8\text{O}$, which of the following structures corresponds to propyl alcohol?



As indicated previously, some insight may be gained by a consideration of the gross chemical properties of the material. For example, if we know that the compound reacts with sodium to liberate hydrogen, this would indicate the presence of the OH functional group and would eliminate the third possible structure above. In a similar manner, an examination of other chemical properties could lead to the elimination of other candidate structures. For example, we shall see in later chapters that the OH functional group has slightly different chemical properties when it is bonded to a carbon having two hydrogens than when it is bonded to a carbon having only one hydrogen. Thus, a careful consideration of the properties of a substance could eventually lead to a structure consistent with all the data. The modern chemist relies heavily on spectroscopic methods for the determination of structure. As we shall see in subsequent chapters, spectroscopy is the experimental evaluation of the manner in which a substance interacts with electromagnetic radiation. Thus, by examining the various spectra of a material, the chemist is evaluating some physical properties of the substance. In fact, knowledge of these particular physical properties is a very powerful aid to structural analysis. In our study of organic chemistry we shall consider various kinds of spectroscopy: nuclear magnetic resonance (Chapter 13), infrared spectroscopy (Chapter 17), mass spectrometry (Chapter 34), and ultraviolet spectroscopy (Chapter 22).

EXERCISE 3.6 Elemental analysis of an organic compound reveals it to have the empirical formula C_3H_6O . Determination of its molecular weight gives a value of 57 ± 2 . These data, together with the rules of valence, are compatible with eight structures. Write these eight structures. What two structures are possible if the infrared spectrum of the unknown compound reveals the presence of a carbon-oxygen double bond?

3.5 *n*-Alkanes, the Simplest Organic Compounds

The straight-chain alkanes constitute a family of hydrocarbons in which a chain of CH_2 groups is terminated at both ends by a hydrogen. They have the general formula $H(CH_2)_nH$ or C_nH_{2n+2} . Such a family of compounds, which differ from each other by the number of CH_2 groups in the chain, is called a **homologous series**. The individual members of the family are known as **homologs** of one another. Straight-chain alkanes are called **normal alkanes**, or simply ***n*-alkanes**, to distinguish them from the branched alkanes, which we shall study later.

Alkanes are sometimes called **saturated** hydrocarbons. This term means that the carbon skeleton is "saturated" with hydrogen. That is, in addition to its bonds to other carbons, each carbon bonds to enough hydrogens to give a maximum covalence of 4. The general formula for an *n*-alkane is C_nH_{2n+2} because there are two hydrogens bonded to each carbon atom of the chain plus one additional hydrogen bonded to each end of the chain. In saturated hydrocarbons, there are only single bonds. Later, we shall study **unsaturated** hydrocarbons, compounds that contain double and triple carbon-carbon bonds. The normal alkanes are named according to the number of carbon atoms in the chain (Table 3.2).

These names derive from the generic name alkane with the **alk-** stem replaced by a stem characteristic of the number of carbons in the chain. The first four members of this series, methane, ethane, propane, and butane, are names that came into widespread use before any attempts were made to systematize the names of organic compounds. The remaining names derive quite obviously from Greek numbers; compare **pentagon**, **octal**, **decimal**, and so on. The student should memorize the names of the *n*-alkanes up through dodecane and know the logical procedure for developing names for larger compounds.

TABLE 3.2

<i>n</i>	Name	Formula
1	methane	CH ₄
2	ethane	CH ₃ CH ₃
3	propane	CH ₃ CH ₂ CH ₃
4	butane	CH ₃ CH ₂ CH ₂ CH ₃
5	pentane	CH ₃ (CH ₂) ₃ CH ₃
6	hexane	CH ₃ (CH ₂) ₄ CH ₃
7	heptane	CH ₃ (CH ₂) ₅ CH ₃
8	octane	CH ₃ (CH ₂) ₆ CH ₃
9	nonane	CH ₃ (CH ₂) ₇ CH ₃
10	decane	CH ₃ (CH ₂) ₈ CH ₃
11	undecane	CH ₃ (CH ₂) ₉ CH ₃
12	dodecane	CH ₃ (CH ₂) ₁₀ CH ₃
13	tridecane	CH ₃ (CH ₂) ₁₁ CH ₃
14	tetradecane	CH ₃ (CH ₂) ₁₂ CH ₃
15	pentadecane	CH ₃ (CH ₂) ₁₃ CH ₃
20	eicosane	CH ₃ (CH ₂) ₁₈ CH ₃
21	heneicosane	CH ₃ (CH ₂) ₁₉ CH ₃
22	docosane	CH ₃ (CH ₂) ₂₀ CH ₃
30	triacontane	CH ₃ (CH ₂) ₂₈ CH ₃
40	tetracontane	CH ₃ (CH ₂) ₃₈ CH ₃

A “group” is a portion of a molecule in which a collection of atoms is considered together as a unit. For purposes of naming more complicated compounds, it is necessary to have names for such groups. A group name is derived by replacing the *-ane* of the corresponding alkane name by the suffix *-yl*.

<i>Alkane</i>	<i>Group</i>	<i>Sample Molecule</i>
CH ₄ methane	CH ₃ — methyl group	CH ₃ —OH methyl alcohol
CH ₃ CH ₃ ethane	CH ₃ CH ₂ — ethyl group	CH ₃ CH ₂ —Cl ethyl chloride
CH ₃ CH ₂ CH ₃ propane	CH ₃ CH ₂ CH ₂ — propyl group	CH ₃ CH ₂ CH ₂ —Br propyl bromide

EXERCISE 3.7 Write the structures of the pentyl group and of pentyl iodide.

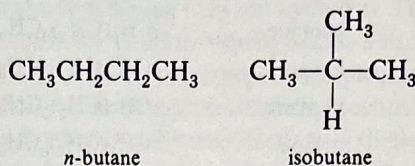


Highlight 3.2

Chains of carbon atoms form families of organic structures. A straight chain of carbons combined with hydrogen forms the alkane family C_nH_{2n+2} or H(CH₂)_nH in which the first member is methane CH₄. The longest alkane in current use is linear polymethylene (usually called polyethylene) with *n* > 1000.

3.6 Systematic Nomenclature

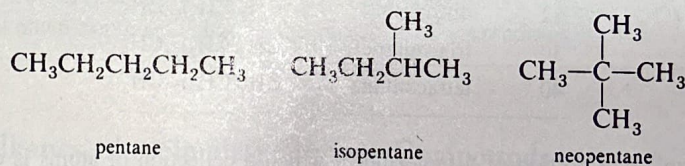
There is only one compound corresponding to each of the formulas CH_4 , C_2H_6 , and C_3H_8 . There are two **isomeric** compounds having the formula C_4H_{10} . **Isomers** are defined as compounds that have identical formulas but differ in the nature or sequence of bonding of their atoms or in the arrangement of their atoms in space. One of the C_4H_{10} isomers is *n*-butane, discussed previously. The other is isobutane.



In general, isomers have different physical and chemical properties. For example, with the two C_4H_{10} compounds, isobutane has the lower melting point and boiling point. The lower boiling point reflects the branched-chain structure of isobutane, which provides less effective contact area for van der Waals attraction (Chapter 5).

Interconversion of the two butane isomers requires breaking bonds. Since carbon-carbon bonds have bond strengths of about $80 \text{ kcal mole}^{-1}$, these isomers are completely stable under normal conditions. Interconversion requires very high temperatures or special catalysts.

There are three C_5H_{12} isomers.



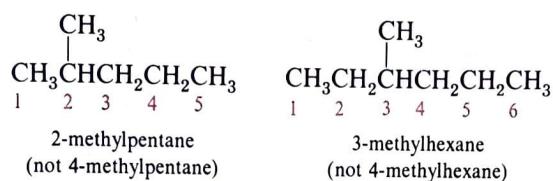
The prefix **iso-** serves to name one of these isomers, the one with the greatest structural similarity to isobutane. The third isomer was named neopentane, the prefix **neo-** being derived from the Greek word for "new." With more carbons the number of possible isomers increases rapidly. As shown in Table 3.3, there are 5 possible hexanes, 9 heptanes, and 75 decanes, and with larger alkanes the number of possible isomers becomes astronomic. It is obviously not possible to coin a set of unique prefixes like **iso-** and **neo-** to name all of the dodecane isomers, or, for that matter, even the heptane isomers. Clearly, it is essential that a method of systematic nomenclature be devised, so that each different compound may be assigned an unambiguous name.

TABLE 3.3 Number of Isomers
of $\text{C}_n\text{H}_{2n+2}$

n	Number of Isomers
4	2
5	3
6	5
7	9
8	18
9	35
10	75
12	355
15	4,347
20	366,319

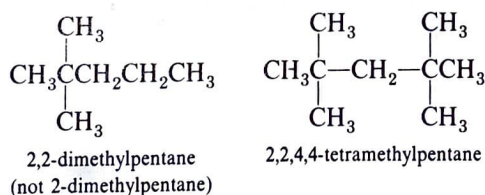
This problem was first addressed by an International Congress of Chemists, held in Geneva in 1892. The forty chemists in attendance at this meeting adopted a set of systematic rules for naming organic compounds. For the most part, the Geneva rules were based on a suggestion originally made by Laurent, whereby hydrocarbons are the base compounds, with other classes of compounds being treated as substitution products. The International Congresses evolved into an organization now known as the International Union of Pure and Applied Chemistry (IUPAC), which maintains several committees whose job it is to see that the rules for systematic nomenclature are continually updated.

The IUPAC system of alkane nomenclature is based on the simple fundamental principle of considering all compounds to be **derivatives of the longest single carbon chain** present in the compound. Appendages to this chain are designated by appropriate prefixes. The chain is then numbered from one end to the other. The end chosen as number 1 is that which gives the *smaller number (a locant) at the first point of difference*.



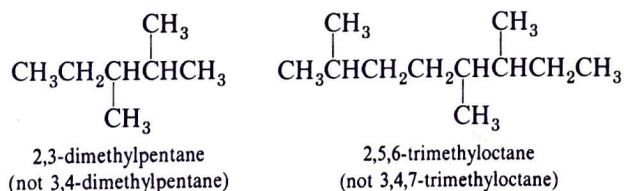
EXERCISE 3.8 Write the structure of 3-ethylhexane. Why is “2-ethylhexane” not an acceptable name under the IUPAC system?

When there are two or more identical appendages, the modifying prefixes di-, tri-, tetra-, penta-, hexa-, and so on are used, but every appendage group still gets its own number.



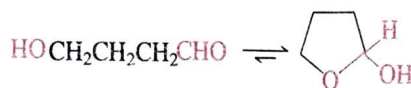
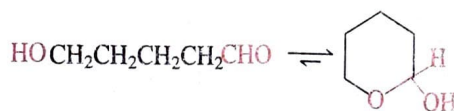
EXERCISE 3.9 (a) Write the structure of 2,3,4-trimethyloctane. (b) Why is 1,4-dimethylbutane an incorrect name?

When two or more appendage locants are employed, the longest chain is numbered from the end that produces the lowest series of locants. When comparing one series of locants with another, that series is lower which contains the *lower number at the first point of difference*.

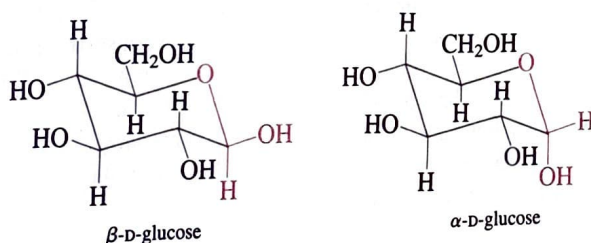


28.3 Cyclic Hemiacetals: Anomerism; Glycosides

In the last chapter (Section 27.4), we learned that 4- and 5-hydroxy aldehydes and ketones exist mainly in the cyclic hemiacetal form.

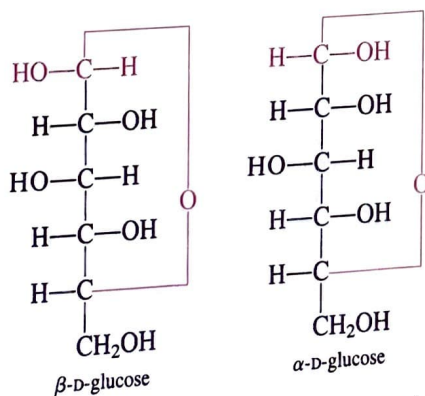


It is not surprising then that the sugars also exist in such a cyclic form. Although either the five- or six-membered hemiacetal structure is possible, almost all of the simple sugars exist in the six-membered ring form (see Table 27.3, page 870). Note that when the hemiacetal is formed, *the former aldehyde carbon becomes a stereocenter*. Thus, there are two cyclic forms of glucose.



The two cyclic isomers of glucose differ only in the configuration at C-1, the hemiacetal carbon (former aldehyde carbon). Such isomers are called **anomers**, and the hemiacetal carbon is called the **anomeric carbon**. The two anomers are commonly differentiated by the Greek letters α and β ; for example, α -D-glucose, β -D-glucose. For the aldohexoses, the β -anomer is the one that has the OH at C-1 and the CH_2OH at C-5 *cis* with respect to each other on the ring.

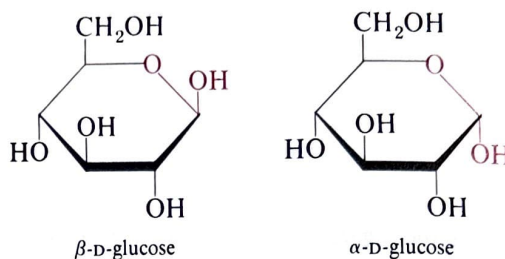
The Fischer projection formulas shown in Table 28.1 are a convenient way in which to represent the open-chain form of sugars. Modified Fischer projections have frequently been used to depict the cyclic hemiacetal form. For example, the two D-glucose anomers can be represented as follows.



Note the convention used to represent stereochemistry at anomeric carbon. The OH at C-1 in the β -anomer is written to the left and that in the α -anomer is written to the right.

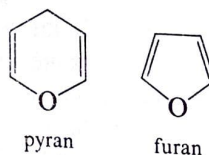
Because these modified projections lead to awkward drawings of bond lengths, which offend the sensibilities of many chemists, Haworth introduced an alternate projection

formula, which is used extensively by sugar chemists. In a **Haworth projection**, the sugar ring is written as a planar hexagon with the oxygen in the upper right vertex. Substituents are indicated by straight lines through each vertex, either above or below the plane. The OH at the anomeric carbon is up in the β -anomer and down in the α -anomer. Hydrogens attached to the ring are omitted.



There is a simple way to convert a Fischer projection to a Haworth projection, or vice versa. The OH groups that project to the left in a Fischer projection project up in a Haworth projection. In this book, we shall use Fischer projections to depict open-chain sugars and the more accurate chair representations to depict cyclic forms.

The six-membered ring form of a sugar is called a **pyranose** from the name of the simplest heterocyclic compound containing such a ring, pyran. Thus, β -D-glucose is a pyranose form, and it may be completely described by the name β -D-glucopyranose. Although the free sugars normally do not exist as the five-membered ring form, numerous derivatives are known that have such a structure. They are called **furanoses** from the name of the parent heterocyclic compound, furan.

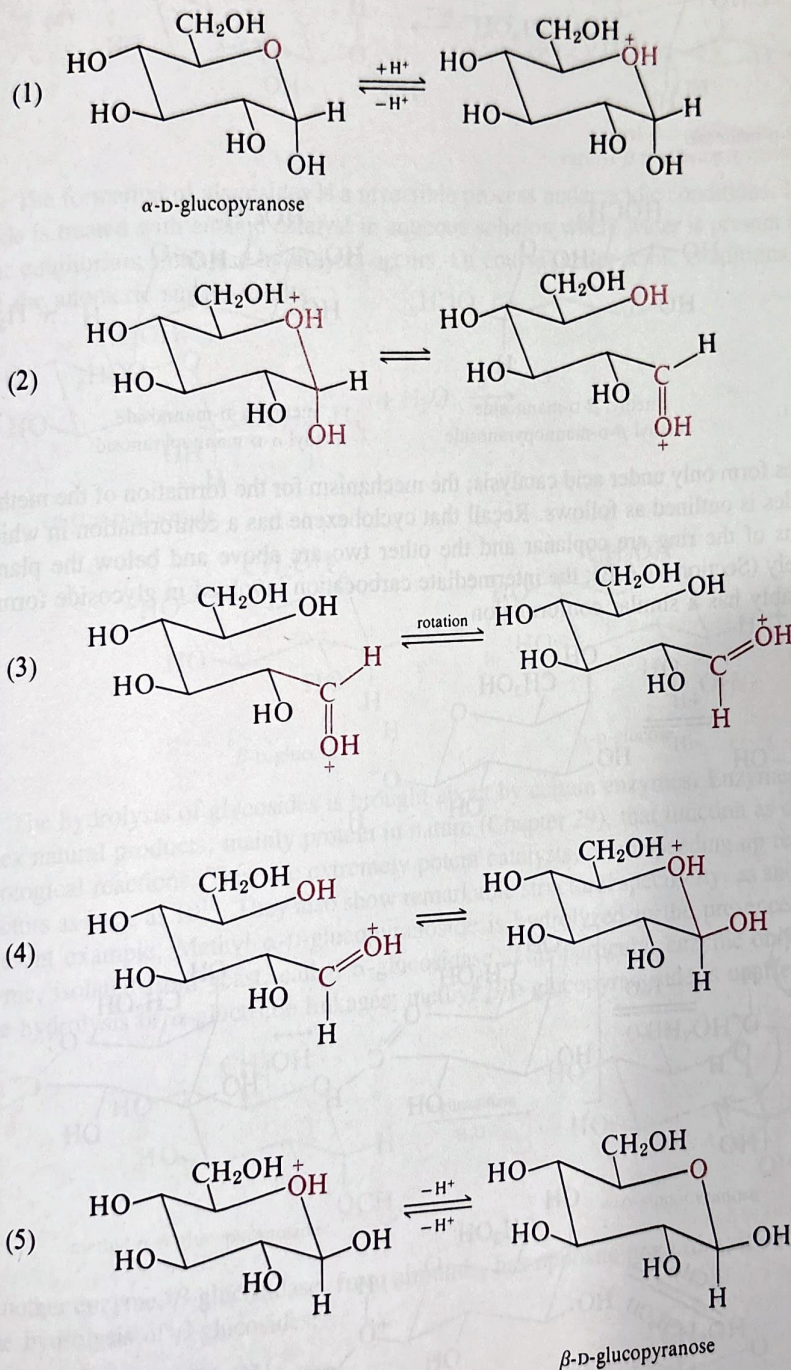


Pure β -D-glucose has an optical rotation $[\alpha]_D = +18.7$; the α -anomer has $[\alpha]_D = +112$. Both anomers have been isolated in pure crystalline states. If either pure anomer is dissolved in water, the optical rotation of the solution gradually changes until it reaches an equilibrium value of $+52.7$. This phenomenon, which was first observed in 1846, results from the interconversion of the two anomers in solution and is called **mutarotation**. At equilibrium, the solution contains 63.6% of the more stable β -anomer and 36.4% of the α -anomer.

The phenomenon of anomerism caused considerable confusion for the early workers in carbohydrate chemistry, who believed the sugars to be acyclic compounds. After their cyclic structures were recognized, there arose the problem of how to name the two anomers for each sugar. In 1909, a system of nomenclature based purely on optical rotation was adopted. In the D series, the more dextrorotatory member of a pair of anomers is defined as the α -D-anomer and the less dextrorotatory member is the β -D-anomer. When reliable methods for determining the configuration at C-1 became available, it turned out that all α -anomers have the same absolute configuration at C-1.

Interconversion of the two anomers is subject to both acid and base catalysis and occurs by the normal mechanism for acetal formation and hydrolysis (Sections 14.6.B and 27.4.B). The open-chain form is probably an intermediate in the process. The mechanism

of acid-catalyzed interchange of the α - and β -anomers of glucose is outlined as follows (all ring hydrogens except the one on the anomeric carbon are omitted for clarity).



When an aldose is dissolved in an alcohol and the solution is treated with a mineral acid catalyst, a cyclic acetal is produced (Section 27.4.B). In carbohydrate chemistry such cyclic acetals are called **glycosides**. A glycoside derived from glucose is a **glucoside**, one derived from mannose is a **mannoside**, and so on. Like the hemiacetals, these cyclic acetals can exist in both α - and β -anomeric forms as shown below for the methyl mannosides.