Chemistry: Basic Principles

7

> *The underlying physical laws necessary for the mathematical theory of a large part of physics and the whole of chemistry are thus completely known, and the difficulty is only that the application of these laws leads to equations much too complicated to be soluble.*
>
> Paul Dirac

7.1 Chemical Elements

In general, chemistry is the study of matter and energy and the interaction between them. More specifically, chemistry is the study of matter, including its composition, properties, structure, the changes which matter undergoes, and the laws governing those changes. Chemical elements are the building blocks of all types of matter in the universe and, at present, 116 elements are known to exist. In nature, however, only 91 elements have been discovered. Some elements are only present in trace amounts while some are man made or artificially produced. From the point of view of chemistry, the smallest unit of an element is the atom, representing the chemical identity of that element. Among the elements that exist in nature, hydrogen is the lightest ($Z = 1$, $A = 1$) atom, while uranium is the heaviest atom ($Z = 92$, $A = 238$).

Chemical reactions take place between atoms of the same element or atoms of different elements to form molecules of compounds. Chemical interactions involve only the electrons in the outer orbits, while protons and neutrons of an atom do not participate in any chemical reactions. The chemical properties of an element are determined only by the number of electrons in an atom, which is equal to the number of protons in the nucleus (Z).

7.1.1 Chemistry and Radioactivity

Radioactivity is a process which primarily involves the decay of the unstable nucleus of an element, but all the chemical reactions of an element involve the outermost orbital electrons. Atoms of different isotopes of an element, both stable and radioactive, will have a similar chemistry, regardless of the radioactive emissions from an unstable nucleus. Similarly, the chemistry of an atom does not, in any way, affect the radioactive decay characteristics of an atom. In nuclear medicine, *tracer principle* is based on the fact that the chemistry and physiological behavior of radioisotopes of an element are identical to the corresponding naturally occurring stable isotopes of that element. Because, the mass of different isotopes of an element is slightly different, there may be some differences in the chemistry among the isotopes of an element. This effect known as *isotope effect* is only significant if the mass difference is substantial, as in the case of hydrogen isotopes, where the mass difference of the three isotopes is 200–300%. In contrast, the isotopes of iodine have only about 3% difference in their mass.

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7.1.2 Periodic Table

The periodic table (Table 3.3) is a listing of the elements in the order of increasing atomic number (*Z*). More specifically, elements with similar chemical properties are aligned vertically in columns (called *groups* or *families*). It must be noted that in the modern periodic table, this order is based only on the atomic number and not the atomic weight. The horizontal series of elements are referred to as periods; the first two periods are short periods and consist of eight groups, while the remaining periods are called long periods, consisting of 18 groups. The position of an element in the periodic table explains the general chemical behavior of an element.

Most of the elements found in nature are metals and are shown in the periodic table as *alkali metals* (Group-1), *alkaline earth metals*, (Group-2), and *transition metals* including lanthanides and actinides (Groups 3–12). Elements in groups 13–16 are regarded as metals or *metalloids*; elements in Group 17 are known as *halogens*; and elements in Group 18 are known as inert or *noble gases*. Some of the important elements and their radioisotopes, useful for PET and SPECT, are listed in Table 7.1.

Table 7.1 Important elements and their useful radioisotopes for PET and SPECT

Element	Atomic number	Stable isotope	Natural abundance (%)	Useful radio-isotopes	Decay mode
Carbon	6	^{12}C	98.9	^{11}C	β^+
		^{13}C	1.10	^{14}C	β^-
Nitrogen	7	^{14}N	99.634	^{13}N	β^+
		^{15}N	0.366		
Oxygen	8	^{16}O	99.762	^{15}O	β^+
		^{17}O	0.038		
		^{18}O	0.200		
Fluorine	9	^{19}F	100	^{18}F	β^+
Copper	29	^{63}Cu	69.17	^{62}Cu	β^+
		^{63}Cu	30.83	^{64}Cu	β^+, β^-, EC
				^{67}Cu	β^-, γ
Gallium	31	^{69}Ga	60.1	^{66}Ga	β^+, EC, γ
		^{69}Ga	39.9	^{67}Ga	EC, γ
				^{68}Ga	β^+, EC, γ
				^{72}Ga	β^-, γ
Bromine	35	^{79}Br	50.69	^{75}Br	β^+, EC
		^{81}Br	40.31	^{77}Br	EC, γ
Rubidium	37	^{85}Rb	72.165	^{82}Rb	β^+
		^{87}Rb	27.845		
Yttrium	39	^{89}Y	100	^{86}Y	β^+, EC, γ
				^{87}Y	EC, γ
Zirconium					
Technetium	43	–	–	^{94}Tc	β^+
				^{99m}Tc	IT, γ
Indium	49	^{113}In	4.3	^{111}In	EC, γ
		^{115}In	95.7		
Iodine	53	^{127}I	100	^{123}I	EC, γ
				^{124}I	β^+, EC, γ
				^{131}I	β^-, γ

7.1.2.1 Electronic Structure of Atom

The atom consists of an extremely dense, small, positively charged nucleus surrounded by a cloud of electrons with small size and mass, each carrying a single negative charge equal but opposite to that of a proton in the nucleus. Because the number of electrons and protons in an atom are the same, the whole atom is electrically neutral. The atomic volume (10^{-8} cm diameter) with the cloud of electrons is significantly larger than the volume of the nucleus (10^{-13} cm diameter). According to Bohr's model of atom, an electron in a hydrogen atom rotates around the nucleus at high speeds in closed circular orbits associated with a characteristic quantum number. The electron, in general, exists in a low energy orbit (*ground state*). Gain or loss of a quantum of energy occurs only when an electron moves from one orbital to another of greater or lesser energy. As a result, an atom can absorb or emit energy in discrete units or quanta.

7.1.2.2 Quantum Model of Atom

At first Bohr's model appeared to be very promising. By the mid 1920s, however, it had become apparent that this model needed refinement. The wave mechanics or quantum mechanics developed by Werner Heisenberg, Louis deBroglie, and Edwin Schrodinger finally provided a wave or quantum mechanical description of an atom. According to this model, the electron bound to the nucleus is similar to a standing or stationary wave. The circumference of a particular orbit corresponds to a whole number of wavelengths. Schrodinger's famous wave equation $(H\psi = E\psi)$

describes an electron in an atom, where ψ, called the wave function, is a function of the coordinates (x, y, and z) of the electron's position, in three dimensional space, and H represents a set of mathematical instructions, called an *operator*. When this equation is analyzed, many solutions are found. Each solution consists of a wave function ψ, that is characterized by a particular value of energy, E. A specific wave function for a given electron is often called an *orbital* (an orbital is not a Bohr's orbit). The wave function corresponding to the lowest energy of hydrogen atom is called 1*s* orbital. The theory of quantum mechanics only provides the probable position of the electrons around the nucleus, but not the electrons motions around the nucleus.

Schrodingr's equation for the hydrogen atom or other multielectron atoms have many solutions with many wave functions or orbitals characterized by a set of quantum numbers (Table 7.2). In order to describe a given electron in atom a set of four quantum numbers are needed. The values and the physical meaning of these quantum numbers can be described as follows:

> The *principal quantum number* (n), which can have integral values (such as 1,2,3,4,…,), is related to the size and energy of the orbital. As n increases, the orbital size and the energy increases. The value of n, or the shell number is represented by K, L, M, N,.., (old terminology)
>
> The *angular momentum quantum number* (l), relates to the ellipticity of the orbital or the angular momentum of an electron in a given orbital. It can have integral values of 0 to $n - 1$, for each value of n and the value of l determines the shape of the orbital (such as s, p, d, f,...). These orbitals are also called subshells
>
> The *magnetic quantum number* (m_e), which can have integral values between l, and $-l$. including 0. The value of m_e, relates to the orientation in space of the angular momentum associated with the orbital
>
> The *electron spin quantum number* (m_s), which has values of +½ and −½. The value of m_s represents the direction of the electron spin

Each electron in an atom has a unique set of quantum numbers. *In a given atom, no two electrons can have the same set of four quantum numbers* (n, l, m_e, m_s). This is called *Pauli Exclusion Principle*, which can also be stated as follows: *An orbital can hold only two electros, and they must have opposite spins*.

The electrons in atoms other than hydrogen and helium also occupy various energy levels or shells. The maximum number of electrons that can occupy a

Table 7.2 The electron configuration in different energy levels and the possible quantum numbers

			Quantum numbers					
Energy level	Principal shell	$2n^2$	n	l	m_e	Symbol	Electrons in each orbital	Explicit symbol
1	*K*	2	1	0	0	1*s*	2	1*s*
2	*L*	8	2	0	0	2*s*	2	
			2	1	0	2*p*	6	2*px*
			2	1	1			2*py*
			2	1	−1			2*pz*
3	*M*	18	3	0	0	3*s*	2	3*s*
			3	1	0	3*p*	6	3*px*
			3	1	1			3*py*
			3	1	−1			3*pz*
			3	2	0	3*d*	10	$3dz^2$
			3	2	1			3*dxz*
			3	2	−1			3*dyz*
			3	2	2			$3dx^2-y^2$
			3	2	−2			3*dxy*
4	*N*	32				4*s*	2	
						4*d*	6	
						4*p*	10	
						4*f*	14	
5	*O*	50				5*s*	2	
						5*p*	6	
						5*d*	10	
						5*f*	14	
						5*g*	18	

given energy level or shell (n) is $2n^2$. For example, if $n = 2$, then the total number of electrons in the 2nd shell (L) is eight. The number of orbitals (l) in 2nd shell is two since l can have values of 0 (called *s*) and 1 (called *p*). These two orbitals in the 2nd shell are called 2*s* and 2*p*. Since the number of electrons in each orbital is $2(2l + 1)$, a 2*s* orbital can hold two electrons while a 2*p* orbital can have six electrons. Further, because m_e can have values between l, and $-l$. including 0, the 2*p* orbital has three orientations in space (2*px*, 2*py*, 2*pz*), and each one of them, in turn, can only hold a maximum of two electrons (since m_s has only two values +½ and ½). The permitted values for quantum numbers for the electrons in the 2nd shell are shown in Table 7.3. The electron configuration in different energy levels and the possible quantum numbers are shown in Table 7.4.

Table 7.3 Permitted values of quantum numbers for the 2nd energy level ($n = 2$)[a]

N	2	2	2	2	2	2	2	2
l	0	0	1	1	1	1	1	1
m_e	0	0	−1	0	+1	−1	0	+1
m_s	−½	+½	−½	−½	−½	+½	+½	+½

[a] The second shell can have eight electrons and each vertical set of quantum numbers represents one electron

Table 7.4 Electron configuration of some of the elements

	K	*L*		*M*			*N*				*O*			
Element	1*s*	2*s*	2*p*	3*s*	3*p*	3*d*	4*s*	4*p*	4d	4^f	5*s*	5*p*	5*d*	5*f*
H	1													
He	2													
Li	2	1												
C	2	2	2											
N	2	2	3											
O	2	2	4											
F	2	2	5											
Ne	2	2	6											
Na	2	2	6	1										
K	2	2	6	2	6		1							
Cu	2	2	6	2	6	10	1							
Ga	2	2	6	2	6		2	1						
Kr	2	2	6	2	6	10	2	6						
Rb	2	2	6	2	6	10	2	6			1			
Y	2	2	6	2	6	10	2	6	1		2			
Tc	2	2	6	2	6	10	2	6	5		2			
In	2	2	6	2	6	10	2	6	10		2	1		
I	2	2	6	2	6	10	2	6	10		2	5		
Xe	2	2	6	2	6	10	2	6	10		2	6		

7.1.2.3 Arrangement of Electrons in Orbitals

Since the chemical properties of an element are determined by the electrons, it is important to understand how these electrons are arranged in the orbitals (Fig. 7.1). According to the *Aufbau principle*, as protons are added one by one to the atomic orbitals to build elements, electrons are added one by one to the nucleus to build up the elements. In the ground state, the lowest-energy orbitals contain the electrons. The high-energy orbitals, however, are filled only after the lower-energy orbitals are filled. The various orbitals arranged in order of increasing energy are:

1*s*, 2*s*, 2*p*, 3*s*, 3*p*, 4*s*, 4*p*, 5*p*, 6*s*, 4*f*, 5*d*, 6*p*, 7*s*, 5*f*, 6*d*.

It is important to note that the 3*d* orbital is not filled until after the 4*s* is filled, the 4*d* until after the 5*s*, the 4*f* until after the 6*s*, and the 5*d* until the 4*f* orbital is filled. The series of elements in which the *d* orbital is being filled are called *transition metals*.

In a group of elements ($Z = 57–70$) known as *lanthanides* (elements that are also transition elements), each of the elements differs from the other element only in the number of electrons in the 4*f* orbital, while the 5*s*, 5*p*, and 6*s* orbital are completely filled. Similarly, in *actinides* ($Z = 89–102$), 5*f* electrons are being filled, while the 6*s*, 6*p*, and 7*s* orbitals are completely filled.

Pauli exclusion principle requires that only two electrons with opposite spin occupy any given subshell. The *Hund's rule* states that the lowest energy configuration for an atom is the one having the maximum number of unpaired electrons in a particular set of degenerate orbitals (orbitals with the same energy level), such as *p*, *d*, and *f*. The electron configuration of several elements, shown in Table 7.5, clearly illustrates the Hund's rule.

Valence Electrons and Stable Octet

The electrons in the outermost principle quantum level of an atom are known as *valence* electrons and the shell is frequently referred to as *valence shell*. These electrons are the most important elements in chemistry, because they are involved in the formation of *chemical bonds*. The inner electrons are known as *core electrons* and generally do not participate in forming chemical bonds. The elements listed in the same group of the

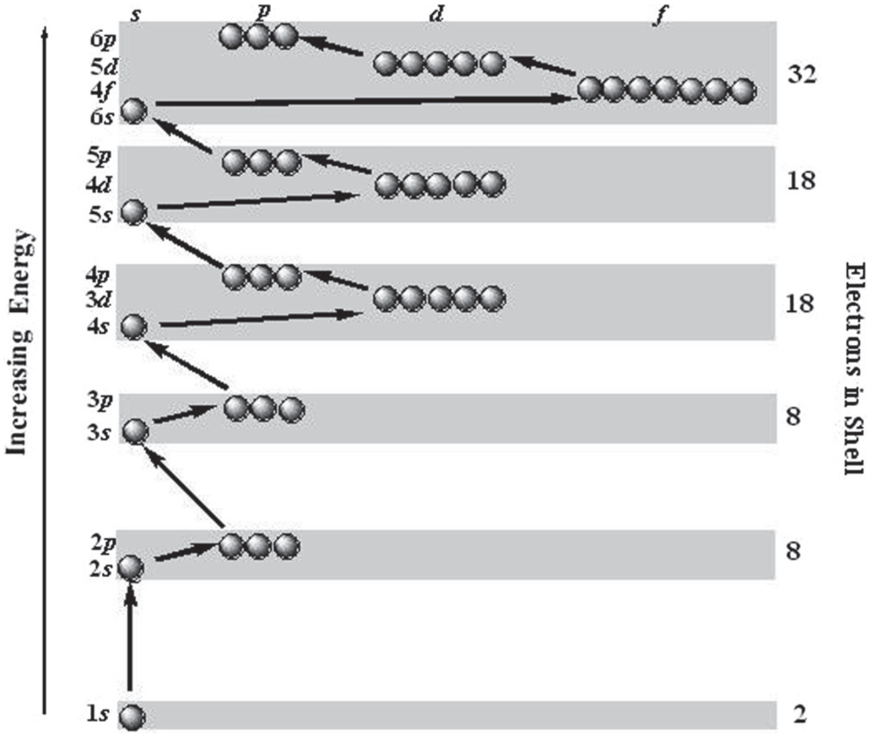


Fig. 7.1 Arrangement of electrons in orbitals. In the ground state, the lowest-energy orbitals contain the electrons. The high-energy orbitals, however, are filled only after the lower-energy orbitals are filled

Table 7.5 Valence electrons of elements in the eight groups of the periodic table

	K	*L*			
Element	1*s*	2*s*	2p*x*	2*py*	2*pz*
H	↑				
He	↑↓				
Li	↑↓	↑			
Be	↑↓	↑↓			
B	↑↓	↑↓	↑		
C	↑↓	↑↓	↑	↑	
N	↑↓	↑↓	↑	↑	↑
O	↑↓	↑↓	↑↓	↑	↑
F	↑↓	↑↓	↑↓	↑↓	↑
Ne	↑↓	↑↓	↑↓	↑↓	↑↓

periodic table (Table 3.3) have the same electron configuration and therefore, have similar chemical behavior.

The elements listed in Group-18 of the periodic table are known as noble or inert gases because they lack chemical reactivity, in general they form very few chemical compounds. The outer electron configuration for the inert gases (except for He) has eight electrons in the *s* and *p* orbitals. Based on this observation, the theory of chemical compound formation postulates that the stable electron configuration for the outer electron shell is eight electrons. More specificall, the *stable octet rule* postulates that compounds are formed between atoms of the same or different elements as a result of the loss, gain or sharing of electrons so that each atom attains a stable octet electron configuration.

The valency of an element is determined by the number of electrons in the outermost shell (Table 7.5) that can participate in a chemical reaction. For example, the valency of hydrogen and fluorine is 1, while the valency for nitrogen is 3 or 5, and 4 for carbon.

7.1.3 Chemical Bonding

John Dalton was probably the first to recognize that chemical compounds are a collection of atoms. Only in twentieth century, however, was it realized that electrons participate in the bonding of one atom to another atom. The forces that hold the atoms together in compounds are called *chemical bonds*. The driving force behind the bond formation of any two atoms is the decreased overall energy state of the individual atoms.

7.1.3.1 Ionic or Electrovalent Bonds

Atoms are electrically neutral. An *ion* is an atom or a group of atoms that has a net positive (cation) or negative (anion) charge. The force of attraction between oppositely charged ions is called *ionic or electrovalent bond*. Ionic compounds are formed when a metal reacts with a nonmetal. Alkali and alkaline earth metals have one or two electrons in the outer shell. In order to reach a stable octet electron configuration, they can easily donate the valence electrons and become positively charged ions. Nonmetals such as halogens need only one electron to reach a stable octet configuration and so are willing to receive or gain an electron, and form a negatively charged ion. The *ionic bond* is formed when an atom that looses electrons easily interacts with an atom that has a high affinity for electrons. *The ion pair has lower energy than the separated ions*. For a mole of Na^+ and Cl^- ions, the energy of interaction is $-504\,kJ\,mole^{-1}$.

NaCl, NaF, NaI, CaO, and $CaCl_2$ are all known as ionic compounds or salts. When these compounds are dissolved in water, the ionic compound dissociates resulting in the regeneration of ions. Ionic compounds, however, are very sturdy materials; they have great thermal stability and high melting points. For example, NaCl crystal has a melting point of about 800°C. Ionic compounds conduct electricity in the solid state as well as in liquid state. Solutions of ionic compounds are known as *electrolytes*.

7.1.3.2 Covalent Bond

When atoms of the same element or different elements share a pair of electrons, a *covalent bond* is formed. The covalent bonding results from the mutual attraction of the two nuclei for the shared electron pair. The total energy of the molecule is less than that of the individual atoms. In the *diatomic* H_2 molecule both hydrogen atoms share a pair of electrons so that the 1*s* orbital has the maximum of two electrons needed for stability. Sometimes it is necessary for two atoms to share more than one pair of electrons to reach stable octet configuration. Based on the number of pairs of electrons shared, covalent bonds may be called a *single bond*, *double bond* or *triple bond*. In the O_2 molecule, the two oxygen atoms share two pairs of electrons while in the N_2 molecule, the two nitrogen atoms share three pairs of electrons. Also, molecules such as H_2O, NH_3, and CH_4 contain covalent bonds. Covalent bonds are most common between carbon atoms in organic compounds. Molecules containing covalent bonds are nonionic and are poor conductors of electricity because the pair of electrons is normally shared equally by each atom participating in the bond formation. When the electron sharing by the two atoms is unequal, *polar covalent bonds* are formed. For example, in the HF molecule, the electron pair is drawn more towards fluorine nucleus. As a result, the H atom has a fractional positive charge (δ^+) and the F atom has a fractional negative charge (δ^-).

Coordinate Covalent Bond

In a covalent bond, the pair of electrons required for sharing is donated equally by the two atoms. In contrast, in a *coordinate covalent bond*, the pair of electrons required for bond formation is provided by an atom to another atom, which can accommodate the pair in octet formation. These bonds are also called *semipolar bonds* because the donor atom has a partial positive charge, while the acceptor atom has a partial negative charge, just like in polar covalent bonds. Some donor atoms, such as N, O and S, have a lone pair of electrons, and these atoms form coordinate covalent bonds with metal ions to form metal complexes that can be cationic, anionic or neutral and which are very stable.

7.1.3.3 Hydrogen Bond

Molecules that contain hydrogen atoms bonded covalently to very *electronegative* atoms, such as F, O, and N, also form another chemical bond called a *hydrogen bond*. The strong electronegative atom has greater attraction for the pair of electrons and, as a result, acquires a partial negative charge (δ^-). Therefore, a hydrogen atom has a partial positive charge (δ^+). Now there is an electrostatic attraction between the partial opposite charges of the hydrogen atom of one molecule and the electronegative atom of another molecule. Such bonds between the partial opposite charges of hydrogen and the electronegative atoms are known as *hydrogen* *bonds*. Although, hydrogen bonds are weak chemical bonds, are important for the solvent properties of water and for the stability of the DNA structure.

7.1.3.4 Electronegativity

Different atoms have different affinities for the electrons that are being shared in a chemical bond. *Electronegativity* is a property, which describes the ability of an atom in a molecule to attract shared electrons. Linus Pauling developed a scale for electronegativity of different elements. In the periodic table of elements, electronegativity generally increases across a period and decreases down a group. For example, the value for Li is only 1.0 compared to a value of 4.0 for F (the most electronegative atom). In a chemical bond, the electronegativity difference between two identical atoms is zero and, therefore, no polarity occurs and covalent bonds are formed. When two atoms with widely differing electronegativities interact, ionic bonds are formed while unequal electron sharing results in polar covalent bonds.

7.1.3.5 Lewis Structures

In 1902, Lewis conceived the octet rule. The Lewis structure of a molecule represents the arrangement of valence electrons among the atoms in a molecule. In a covalent bond formation, the pair of electrons found in the space between atoms are called *bonding pairs* while those pairs of electrons localized on an atom are called *lone pairs*.

In ionic compounds, such as NaCl, the Lewis structure shows all eight electrons on the Cl^- ion while the Na^+ ion has no valence electrons.

$$\mathrm{Na}^+ + \mathrm{Cl}^- \rightarrow [\mathrm{Na}]^+[:\underset{..}{\overset{..}{\mathrm{Cl}}}:]^- \tag{7.1}$$

In molecules with covalent bonds, the Lewis structures show the bonding electron pairs in the place between the two sharing atoms.

$$\mathrm{H{:}H} \quad :\underset{..}{\overset{..}{\mathrm{F}}}::\underset{..}{\overset{..}{\mathrm{F}}}: \tag{7.2}$$

Sometimes more than one valid structure is possible for a given molecule. *Resonance* occurs when more than one Lewis structure can be written for a molecule and the electron structure represents an average of the resonance structures. For example, the nitrate ion is represented by a resonance structure. In reality, however, the electrons are delocalized or move around the entire molecule. Resonance is an exception to the general Lewis representation of electron configuration.

7.1.3.6 Formulas of Compounds

The formula of a compound indicates the numbers of atoms in the compound. An *empirical formula* represents the whole-number ratio of the various types of atoms in a compound. However, sometimes different compounds have the same ratio of moles of atoms of the same element. For example, the compounds acetylene (C_2H_2) and benzene (C_6H_6), each have 1:1 ratios of moles of carbon atoms to moles of hydrogen atoms. For both these compounds, the empirical formula is CH and it will not be able to establish the identity of a given molecule. The *molecular formula*, however, is a formula which gives all the information that the empirical formula does, plus information about the number of atoms present in each molecule. For an unknown compound, the molecular formula can be determined from the empirical formula, if the molar mass is known.

In organic chemistry, a *structural formula* is very important to establish the real identity of a specific molecule or substance. For example, the molecular formula $C_6H_{12}O_6$ may represent several different sugar molecules. The structural formula provides a detailed orientation of different atoms of a molecule in a 3-dimensional space.

7.1.3.7 Stoichiometry

All chemical reactions are dependent on the mass of the reactants. Therefore, it is essential to measure the absolute quantities of materials consumed and produced in chemical reactions. This area of study is called *chemical stoichiometry*.

The modern system of atomic masses, instituted in 1961, is based on ^{12}C as the standard and was assigned a mass of exactly 12 *atomic mass units* (amu). The masses of all other atoms are given relative to this standard. *Mass spec*trometer is used to determine the exact mass of atoms. The atomic mass of every element is shown in the periodic table as atomic weight.

It is important to note that the atomic weight of every element is the average mass of all stable isotopes of an element, present in nature. For example, the atomic weight of carbon is given as 12.01 amu since the natural carbon is a mixture of ^{12}C (98.89%) and ^{13}C (1.11%). Similarly, the atomic weight of copper is 63.55 since the natural copper is a mixture of 69.09% of ^{63}Cu (62.93 amu) and 30.91% of ^{65}Cu (64.93 amu).

The Mole

Mole (mol) is generally defined as the number equal to the number of carbon atoms in exactly 12 g of pure ^{12}C atoms. The number of atoms in one mol of ^{12}C was determined to be 6.022137×10^{23} (also known as *Avogadro's number*). Since the atomic mass of natural carbon is 12.011 amu, 12.011 g of a carbon element will have exactly 6.022137×10^{23} atoms. Thus m the mass of one mole of an element is equal to its atomic mass, expressed in grams.

Molar Mass (Molecular Weight)

A chemical molecule, compound, or substance is also a collection of atoms. For example, a molecule of methane (CH_4) contains 1 atom of carbon and 4 atoms of hydrogen. The mass of one mole of CH_4 contains one mole of carbon (12.011 g) and 4 moles of atomic hydrogen (4 × 1.008 g), or 2 moles of H_2 molecule (2.016 g). Therefore, the *molar mass* of CH_4 gas is 16.043 g. The term *molecular weight* was traditionally used to describe the molar mass of a substance. Thus, one mole of any substance is equal to the molecular weight or molar mass of that substance, expressed in grams. In case of salts and ionic compounds, such as NaCl or K_2CO_3, the term *formula weight* is used instead of the term molar mass or molecular weight.

It is often useful to know a compound's composition in terms of masses of its elements. For example the molar mass of glucose ($C_6H_{12}O_6$) is 181.122 g. In a glucose molecule, the mass percent (or weight percent) of carbon is 39.79%, of oxygen it is 53%, and of hydrogen it is 6.68%.

7.1.3.8 Solutions

Solutions are described in terms of the type of substance or *solute* that is dissolved in a medium known as the *solvent*. Both the solute and solvent may be solid, liquid or gas. The solvent, however, is mostly chosen based on the chemical properties of the solute, compatibility and physiologic conditions.

An *ionic solution* (also known as an *electrolyte*) is one that contains charged or ionic species, surrounded by solvent molecules. For example, in a NaCl solution Na^+ and Cl^- ions are solvated by the water molecules that are dipolar. In *molecular solutions*, such as a glucose solution, the individual glucose molecule with covalent bonds, retains its integrity and does not dissociate.

The amount or mass of a solute in a given solvent determines the strength or concentration of a solution.

Molarity and Normality

The term *molarity* (M) is defined as the number of moles of a substance (solute) per liter of a solvent and is a measure of the number of molecules per unit volume.

$$\text{Molarity(M)} = \text{moles (m)/volume(v)}$$

Different dilutions of a molar solution can also be expressed as millimolar (mM), micromolar (μM), etc. These concentration terms are very important in chemical equations and reactions, since these terms specify the number of atoms or molecules in a given volume. For example, 1 M glucose solution contains 6.022×10^{23} molecules of glucose in one liter, 6.022×10^{20} molecules in ml, and 6.022×10^{17} molecules in 1 μl.

In chemical reactions, it is, sometimes, very important to know the amount of reactive groups rather than the molecule itself. *Normality* (N) indicates the number of reactive groups (*equivalents*), such as proton (H^+), hydroxide (OH^-), or electron units per unit volume. For example, 1 M HCl is also equivalent to 1 N HCl since HCl has only one acidic hydrogen ion (H^+). In contrast, 1 MH_2SO_4 is equivalent to 2 NH_2SO_4 solution since it has two H^+ ions.

Volume Percent

Solutions can be prepared using certain mass, g (w) dissolved in 100 g of a solvent or in 100 ml (v) of a solvent. Generally, solutions are prepared on the w/v basis. For example, the 0.9% NaCl solution (physiological saline) and the 5% dextrose solution are quite common in a clinic. It is important to recognize that in chemistry, solutions prepared on w/v basis are not useful for balancing chemical reactions and must be expressed in terms of molar concentrations. For example, a 0.9% NaCl solution represents a 0.15 molar solution of sodium chloride.

Radioactive Concentration

With radioactive solutions, it is quite common to express the concentration in units of activity/volume, such as mCi/ml or mBq/ml, etc. These radioactive concentration terms are mistakenly applied to SA, which really is an expression of activity per mass of the radionuclide or radiotracer.

7.2 Chemical Reactions

In a chemical reaction one or more substances, called *reactants* or *reagents*, are allowed to react to form one or more other substances, called *products*. A chemical change involves reorganization of the atoms in the reactants to form the product (bonds have been broken and new ones have been formed). This process is represented by a *chemical equation*. For example, methane gas reacts with oxygen to produce carbon dioxide and water.

$$CH_4 + O_2 \rightarrow CO_2 + H_2O \tag{7.3}$$

The law of conservation of mass dictates that in a chemical reaction atoms are neither created nor destroyed. All atoms in the reactants must be accounted for among the products. To show the quantitative relationships, the chemical equation must be balanced. *Coefficients* are, therefore, used before the molecular formula of each compound to represent the number of moles of the reactant or the product. The above equation is not balanced and is not correct. A *balanced chemical equation* of the above reaction is written as follows:

$$CH_4 + 2O_2 \rightarrow CO_2 + 2H_2O \tag{7.4}$$

In the above reaction, 2 moles of oxygen interact with 1 mole of methane to produce 1 mole of carbon dioxide and 2 moles of water. Stoichiometric calculations of chemical reactions are very important for determining the amount of reactants required to form a specific amount of a product.

7.2.1 Types of Chemical Reactions

In order to balance a chemical reaction, it is necessary to know the molecular and structural formulas of reactants and products. Also, one must be able to predict the products from the reactants. Simple chemical reactions are generally classified into five types. In a *Combination reaction*, two or more reactants combine to form one product. In a *decomposition reaction*, the reactant decomposes into its component elements or a simpler compound. Different elements have varying abilities to combine. In reactions involving several reactants, the possible product formation depends on the relative affinities, valency, and electronegativities of elements. *Substitution* (single or double) or *replacement reactions* involve the exchange of different elements based on their relative reactivities. In *combustion reactions*, compounds containing C, H, O, S and N atoms involve burning with the liberation of energy and heat.

There are millions of reactions described in chemistry (both inorganic and organic). Most of these reactions occur among substances dissolved in water. Certain organic compounds are relatively nonpolar and do not dissolve in water. As a result chemical reactions are performed in organic solvents. Both aqueous and nonaqueous chemical reactions can be categorized into three groups: *precipitation reactions*, *acid–base reactions*, and *oxidation–reduction reactions*.

(a) *Precipitation reactions*: When two solutions are mixed, an insoluble substance (a solid) sometimes forms and separates from the solution. Such a reaction is called a precipitation reaction and the solid that is formed is called a precipitate. For example, when a solution of barium chloride and a solution of sodium sulfate are mixed, a white, solid barium sulfate is formed, which can be separated from the sodium chloride solution simply by filtration. When ions combine to form a solid compound, the compound has to be neutral and not soluble in the solvent. The balanced equation can be written as a *molecular equation* or as a complete *ionic equation*.

$$BaCl_2{+}Na_2SO_4 \rightarrow BaSO_4(s){+}2NaCl \qquad (7.5)$$

$$Ba^{2+} + 2Cl^{-} + 2Na^{+} + SO_4^{2-} \rightarrow BaSo_4(s) + 2Na^{+} + 2Cl^{-} \qquad (7.6)$$

(b) *Acid–Base reactions*: Acids (from Latin word *acidus*) were first recognized as a class of substances that taste sour. In contrast, bases or *alkalis*, are characterized by their bitter taste and slippery feel. In the 1880s, Savante Arrhenius proposed that in a solution, an acid is a substance that produces a proton, H^+ ions, while bases produces hydroxide, OH^- ions. Since this concept applies only to aqueous solutions, Bronsted and Lowry, in 1923, defined an acid to be a proton donor, and a base to be a proton acceptor. In the 1920s, Lewis suggested a general definition for acid–base behavior in terms of electron pairs. An *acid is an electron pair acceptor* and a *base is an electron pair donor*.

(c) Acids react with bases (and vice versa) to produce salts. Such a reaction is called a neutralization reaction, resulting in the formation of a salt and water, as shown in the examples below. The hydrolysis of salts in turn can regenerate H^+ ions.

$$HCl + KOH \rightarrow KCl + H_2O \qquad (7.7)$$

$$H_2SO_4 + 2NaOH \rightarrow Na_2SO_4 + H_2O \qquad (7.8)$$

Strong acids, such as HCl, H_2SO_4 and $HClO_4$ (perchloric acid), dissociate completely in aqueous solution, forming hydronium, H_3O^+ ion. In solvents other than water, however, the dissociation can only be partial. For example, hydrogen cyanide molecule may dissociate to form.

$$HCN \leftrightarrow H^{+}{+}CN^{-} \qquad (7.9)$$

$$NH_3 + H^{+} \rightleftharpoons NH_4^{+} \qquad (7.10)$$

Based on the Bronsted–Lowry definition, HCN is an acid since it can donate a proton and CN is a base since it can accept a proton. These two ions are called a *conjugate acid–base pair*. Similarly, ammonia is a base since it can accept a proton. A proton does not generally exist by itself, therefore, the Bronstead–Lowry equations usually show two sets of conjugate acid–base pairs and no protons, as shown in the example below.

$$HCN + NH_3 \rightarrow NH_4^{+}{+}Cl^{-} \qquad (7.11)$$

When HCl reacts with a CN^- ion, HCN is formed because a cyanide ion is a stronger base than a chloride ion and HCl is a stronger acid than HCN.

$$HCl + CN^{-} \rightarrow HCN + Cl^{-} \qquad (7.12)$$

Arhenius acids and bases deal with a H_3O^+ ion and a OH^- ion in aqueous solutions, while Bronstead–Lowry acids and bases deal with only protons or H+ ions in nonaqueous solvents. Lewis acids and bases deal with a pair of electrons in coordinate covalent bonds. A Lewis base can be an electron rich negative ion such as OH^- and HSO_4^-, or a molecule, such as NH_3, where the nitrogen atom has a lone pair of electrons to donate. Lewis acids include positive ions, such as H^+, Ag^+, and Al^{3+}, or a molecule, such as BF_3 and SO_3, with an atom that can accept a pair of electrons. The reaction between NH_3 and BF_3 forming NH_3BF_3 is a good example of an acid–base reaction, as shown below, there are covalent bonds between N and Hydrogen and coordinate covalent bond between N and B atoms.

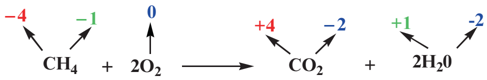
$$NH_3 + BF_3 \rightarrow H_3N{:}\ BF_3 \qquad (7.13)$$

(d) *Oxidation–Reduction reactions*: Chemical reactions in which one or more electrons are transferred are called *oxidatio–reduction reactions* or *redox reactions*. Many important reactions, such as combustion and oxidation of sugars and fats, involve redox reactions. *Oxidation* is the loss of electron(s) from the electron configuration of an atom or ion, while *reduction* is the gain of electron(s) by the electron configuration of an atom or ion. In some of these reactions, the transfer of electrons occurs in a literal sense to form ions, as in the case of NaCl formation, while in the combustion of methane by oxygen transfer occurs in a formal sense by covalent bond breaking and new bond formation. In the oxidation of methane, none of the reactants and products are ionic (as one would expect when electrons are transferred), however, the reaction is still assumed to involve transfer of electrons from carbon to oxygen.

$$2Na(s) + Cl_2(g) \rightarrow 2NaCl(s) \qquad (7.14)$$

$$CH_4 + 2O_2 \rightarrow CO_2(g) + 2H_2O(g) \qquad (7.15)$$

The concept of *oxidation states* or *oxidation numbers* provides a way to keep track of electrons in redox reactions. In the reaction of methane with oxygen, the carbon undergoes a change in oxidation state from –4 in CH_4 to +4 in CO_2. Such a change can be accounted for by a loss of eight electrons. Because each of the oxygen atoms has gained two electrons in CO_2 and H_2O molecules, the oxidation rate of oxygen changes from 0 in O_2 to –2 in CO_2 and H_2O molecules. Based on this example, the oxidation number is defined as the number of valence electrons in the free atom minus the number "controlled" by the atom in the compound. In any molecule with a covalent bond, the nonmetals with the highest attraction for shared electrons are F, O, N and Cl. The relative electronegativity of these atoms is F >>O >N ≈ Cl.



(7.16)

In the above reaction, carbon is *oxidized* as it loses electrons and the oxidation state is increased, while the oxygen is *reduced* because it gains electrons, and the oxidation state is decreased. In addition, because oxygen looses electrons, it is called the *reducing agent*, while methane is called the *oxidizing agent* since it gains electrons. It is important to remember that in a covalent bond electrons are shared between the atoms. However, in redox reactions, the shared electrons are drawn more towards the more electronegative atoms and, therefore, the atom has a net gain of the shared electrons.

7.2.2 Chemical Equilibrium

Many chemical reactions proceed to completion until one of the reactants is completely consumed and the product formation is finished. For example, sodium metal and chlorine gas combine to form NaCl salt, which can decompose only when it is electrolyzed. On the other hand, many other reactions stop far short of completion since such reactions can be *reversible*. The products formed react to give back the original reactants, even as the reactants are forming more products. In fact, the system (the chemical reaction) has reached *chemical equilibrium*, when the concentration of all reactants and products remain constant with time.

When nitrogen and hydrogen gases react with each other at 500°C and high pressure, ammonia is formed. Under the same conditions, ammonia is also decomposed. This situation, where two opposing reactions (forward and backward) occur at the same time and, leads to a state known as chemical equilibrium.

$$3H_2 + N_2 \rightleftharpoons 2NH_3 \tag{7.17}$$

Some reactions proceed slowly, while other reactions can proceed very fast. The *rate of a reaction* is defined as the change in the concentration of any of its reactants or products per unit time. The nature and concentration of reactants, temperature, presence of a catalyst, pressure and the size of solid reactants, all contribute to the changes in the rate of a chemical reaction.

Le Chatelier's principle states that if a stress (such as change in concentration, temperature, pressure, or addition of a catalyst) is applied to the system at equilibrium, then the equilibrium will shift in order to reduce that stress. The reaction may shift to the right (product formation) or to the left (product decomposition). Soon, however, the system will reach a new equilibrium at the new set of conditions. Le Chatelier's principle, however, cannot predict how much an equilibrium will shift under different conditions of stress.

Based on empirical data, Guldberg and Waage, in 1864 proposed the *law of mass action* as a general description of equilibrium condition. For a chemical reaction in general,

$$aA + bB \underset{k_2}{\overset{k_1}{\rightleftharpoons}} cC + dD \tag{7.18}$$

$$K_{eq} = \frac{[C]^c\,[D]^d}{[A]^a\,[B]^b} \tag{7.19}$$

In the above equation, k_1 and k_2 are the forward and backward rate constants, while K_{eq}, is a constant called equilibrium constant. The square brackets indicate the concentration (in moles) of products and reactants at equilibrium and the coefficients represent the number of moles in the balanced chemical equation. The value of K_{eq} for a given reaction system can be calculated from the observed concentrations of reactants and products at equilibrium. For example, in the synthesis of ammonia, described above, under the conditions specified, $K_{eq} = 6.0 \times 10^{-2}\ L^2\ mol^{-2}$. The higher the value of K_{eq}, the more likely the reaction will shift to the right with a net increase in the product concentration or formation. There is only one value for K_{eq} for a particular system, and at a particular temperature, but there are an infinite number of equilibrium positions.

7.2.2.1 Ionic Equilibria

Various salts, acids and bases, and their dissociated ions in solution also exist in equilibrium. The equation for the equilibrium constant is the same for any of the chemical reactions discussed above. Certain salts, such as NaCl and KCl, ionize completely in a solution. For very slightly soluble salts, the equilibrium constant, is called *solubility product constant*, K_{sp}, because most of the salt concentration is relatively constant. For example, for very slightly soluble silver bromide (AgBr) salt,

$$K_{sp} = [Ag^+][Br^-] \tag{7.20}$$

The ionic equilibrium constant may be K_a (*acidity constant*) if it represents the dissociation of an acid or K_b if it represents the dissociation of a base. A strong acid (or base) is a strong electrolyte that dissociates completely into its ions in aqueous solution. A weak acid (or base) is a weak electrolyte that dissociates only partially in aqueous solution. The stronger the acid or base, the higher the K_a or K_b value.

7.2.2.2 Dissociation of Water

Water is said to be amphoteric because it can behave as either an acid or a base. Pure water behaves like a weak electrolyte. As a result of the autoionization of a very small extent of water, H_3O^+ and OH^- exist in water at 25°C. The concentration of each of these ions is 10^{-7}M.

$$H_2O \rightleftharpoons H_2O^+ + OH^- \tag{7.21}$$

$$K_i = \frac{\left[H_3O^+\right]\left[OH^-\right]}{H_2O} = \frac{\left[1\times10^{-7}M\right]\left[1\times10^{-7}M\right]}{55.6M} \tag{7.22}$$

Since the water concentration is relatively unchanged, K_i of water is the ion product of water, $K_w = 1 \times 10^{-14} M^2$. At neutrality, the concentration of H_3O^+ and OH^- ions is the same and is equal to 1×10^{-7}M.

The pH Scale

The acidity of a solution depends on the hydrogen (H^+) ion or hydronium (H_3O^+) ion concentration. Because the hydrogen ion concentration is typically very small, the *pH scale* provides a convenient way to represent the acidity of an aqueous solution.

$$pH = -\log[H^+] \tag{7.23}$$

Thus for a solution in which

$$[H^+] = 1.0 \times 10^{-7} M \tag{7.24}$$

$$pH = -(-7.0) = 7.0 \tag{7.25}$$

The hydrogen ion concentration of an aqueous solution can be as high as 1.0 M and as low as 1×10^{-14}M. Therefore, the pH scale (Fig. 7.2) ranges from 0 to 14.

Buffer Systems

A buffer solution is defined as solution that resists pH changes when acid or base equivalents are added to it. The components of a buffer solution are a weak acid and its anion. Similarly, a buffer solution can be made from a weak base and its salt. The addition of any acid or base to a buffer is neutralized by ions in the buffer keeping the pH relatively unchanged.

Acetate, citrate, and phosphate buffers are some of the most common buffer systems used. The pH of a buffer system can be calculated based on pK_a of the weak acid used (based on the *Henderson–Hasselbach equation*).

$$pH = pK_a + \frac{\left[A^-\right]}{\left[HA\right]} \tag{7.26}$$

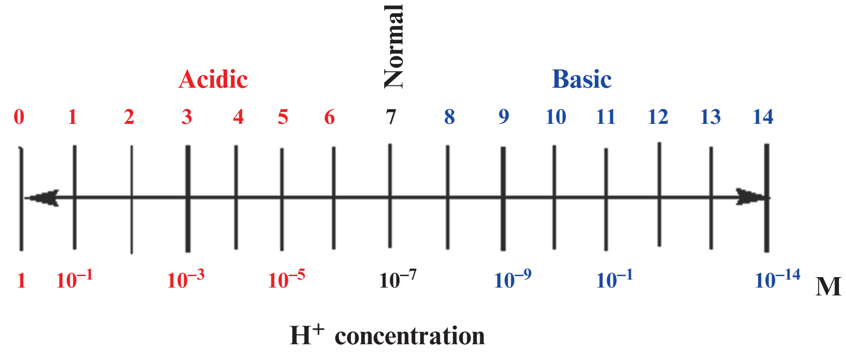
For example, in the preparation of an acetate buffer, the concentrations of the acetic acid and acetate ion is the same and is equal to 0.2 M and K_a of the acetic acid is 1.8×10^{-5}M and the pH of the acetate buffer is 4.8.

$$CH_3COOH \rightleftharpoons CH_3COO^{\blacklozenge} + H^+ \tag{7.27}$$

$$pH = 1.8\times10^{-5}M + \frac{\left[0.2M\right]}{\left[0.2M\right]} = 4.8 \tag{7.28}$$

There are several things that must considered before selecting an appropriate buffer for a specific purpose. First, it is important to make sure that the buffer does not

Fig. 7.2 The pH is a log scale based on 10



chemically interfere with the chemical reaction. Buffer systems are most effective at pH values near the pK_a values. Further, buffers should be used at relative concentrations (>0.1 M) to have a high capacity of buffering. Finally, buffers are very important physilogically. More specifically, because the pH of blood is maintained in a narrow range of 7.3–7.5. Also the enzyme activities within cells and in the plasma are pH dependent.

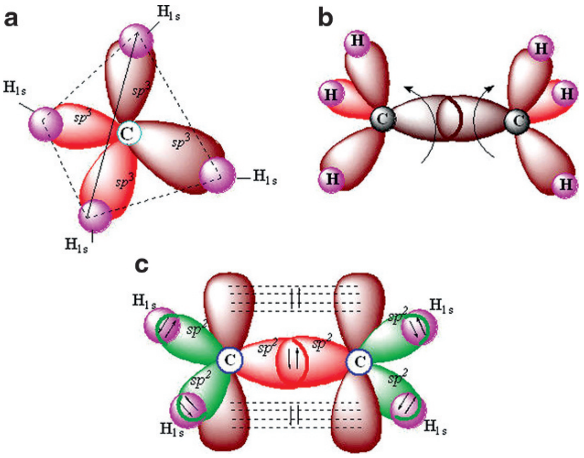


Fig. 7.3 The tetrahedral structure of methane (**a**) can be described in terms of carbon atom using an sp^3 hybrid set of orbitals to bond to the four hydrogen atoms. In case of acetylene, the carbon can be described as sp^2 hybridized (**c**), in which the C–C bond is formed by sharing an electron pair between sp^2 orbitals, while the π bond is formed by sharing a pair of electrons between *p* orbitals. As a result, the free rotation of the two CH_2 group is prevented. However, with ethane (**b**) the free rotation of two CH_3 groups is possible

7.3 Organic Chemistry

Historically, the term organic chemistry has been associated with the study of compounds, obtained from plants and animals. In modern terms, the study of carbon containing compounds and their properties is called organic chemistry. In addition to carbon and hydrogen, the elements most likely to be present in organic compounds are nonmetals, such as oxygen, nitrogen, phosphorous, sulfur, and the halogens.

The element carbon is in group IV (or group 14) of the periodic table. The chemical bonds between atoms of carbon and between carbon and the other elements are essentially covalent. With a valence of 4 and an electronegativity of 2.5, carbon can be expected to form nonpolar covalent bonds with other carbon and hydrogen atoms, and increasingly polar covalent bonds with O, N, and halides. With an atomic number of 6, the orbital electron configuration is $1s^22s^22p^2$. The carbon adopts a set of orbitals for bonding other than its native 2*s* and 2*p* orbitals. This modification of the native atomic orbitals, to form special orbitals for bonding, is called *hybridization* (Fig. 7.3). The four new orbitals, called sp^3, are identical in shape, each having a larger lobe and a smaller lobe. The four orbitals are oriented in space so that the larger lobes form a tetrahedral arrangement, as in the case of a methane (CH_4) molecule with bond angles of 109.5°. In a sp^2 hybridization, a set of three orbitals, arranged at 120-degree angles, can be obtained, as in the case of ethyle (CH_2CH_2) by combining one *s* orbital and 2*p* orbitals. For each bond, the shared electron pair occupies the region between the atoms. This type of covalent bond is called a *sigma (σ) bond*. The parallel *p* orbitals share an electron pair in the space above and below the sigma bond to form a *pi (π) bond*. In a *sp* hybridization, two hybrid orbitals form two sigma bonds, arranged at 180-degrees, oriented in opposite directions, as in the case of the carbon dioxide molecule (CO_2). The p orbitals can also form two pi bonds, perpendicular to each other. A combination of sigma and pi bonds can also facilitate the formation of a triple bond between two carbon atoms, as in the case of acetylene (C_2H_2). It is important to realize that this hybridization of orbitals in a carbon atom determines the shape and the 3-dimensional organization of atoms in organic compounds.

7.3.1 Hydrocarbons

Compounds composed of only carbon and hydrogen are called *hydrocarbons*. Compounds, in which carbon–carbon bonds are all single bonds, are called *saturated hydrocarbons* and, if the carbon–carbon bonds involve multiple bonds, they are called *unsaturated hydrocarbons*. Hydrocarbons can be classified into four fundamental series; *alkanes*, *alkenes*, *alkynes* and *aromatic* hydrocarbons.

The simplest member of saturated hydrocarbons or alkanes, is *methane* (CH_4), followed by *ethane* (CH_3CH_3), and *propane* ($CH_3CH_2CH_3$). Alkanes in which the carbon atoms form long "strings" or chains are called *normal*, *straight-chain*, or *unbranched* hydrocarbons, which can be represented by the general formula, C_nH_{2n+2}. The four carbon butane and the subsequent members of alkanes exhibit *structural isomerism*. For example, butane can exist as a straight chain molecule (*n-butane*) or as a branched chain structure (*isobutane*). Besides forming chains, carbon atoms can also form rings, known as cyclic alkanes (C_nH_{2n}), *such as cyclopropane*, *cyclohexane*, etc.

Alkene series of unsaturated hydrocarbons are also known as *olefins* and have at least one double bond in the carbon chain (C_nH_{2n}) of each molecule. The simplest olefin is a *diene*, called *ethylene* (CH_2CH_2). Because of the restricted rotation of methylene ($-CH_2$) groups around double bonded carbon atoms, alkenes exhibit *cis–trans isomerism*. For example, there are two stereoisomers of 2-butene (Fig. 7.4). Idential substituents on the same side of the double bond are called *cis* and those on the opposite side are called *trans*. In a series of alkanes, if only one saturated carbon separates the double bond, then it is called *conjugated*, however, if more than one saturated carbon separates the double bond, then the alkene is said to be *unconjugated*.

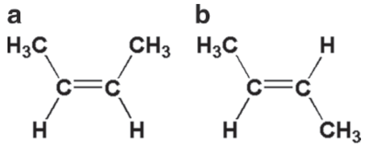


Fig. 7.4 The two stereoisomers of 2-butene: *cis*-2-butene (**a**) and *trans*-2-butene (**b**)

Alkynes are unsaturated hydrocarbons containing at least one triple carbon–carbon bond and have the general formula, C_nH_{2n-2}. The simplest alkyne is *ethyne* (C_2H_2), commonly called *acetylene*.

A special class of cyclic unsaturated hydrocarbons is known as the aromatic hydrocarbons. A six carbon conjugated olefin, cyclohexatriene, an aromatic hydrocarbon, also known as *benzene* (C_6H_6), has a planar ring structure. Benzene exhibits resonance, since all the three double bonds in benzene are equivalent. The delocalization of π electrons is usually indicated by a circle inside the ring. Benzene is the simplest aromatic molecule. More complex aromatic molecules, such as naphthalene, anthracene, phenathrene, and 3,4-benzpyrene, consist of a number of "fused" benzene rings.

7.3.1.1 Reactions of Hydrocarbons

Combustion Reaction

Chemically, alkanes are relatively strong and fairly unreactive. Because of their limited reactivity, saturated hydrocarbons are called *paraffins* (meaning little affinity). At high temperatures, however, they react with oxygen, and these combustion reactions are the basis for their use as fuels.

Substitution Reaction

Alkanes can also undergo substitution reactions primarily where the more electronegative halogen atoms replace hydrogen atoms. For example, chlorine reacts with methane forming *chloromethane*, *dichloromethane*. Substituted methanes containing chlorine and fluorine are known as *freons* which are very unreactive and can be used as coolant fluids. Alkanes can also be converted to alkenes by *dehydrogenation* reactions in which hydrogen atoms are removed.

Benzene being unsaturated is expected to be very reactive but, actually it is quite unreactive. The relative lack of reactivity of aromatic hydrocarbons is attributed to the delocalized double bonds. Because of its great stability, the benzene ring persists in most reactions. Substitution reactions are characteristic of alkanes. However, benzene also undergoes substitution reactions in which the hydrogen atoms are replaced by other atoms and functional groups, such as chlorine atom, nitro group ($-NO_2$), methyl group ($-CH_3$) and even a phenyl ($-C_6H_5$) group. These substitution reactions occur as a result of the attack of an *electrophilic* or electron-seeking ion on the π electrons of the benzene ring.

When the aromatic ring already contains a substituent, its reactivity will be greater or less than that of benzene itself. Electron releasing groups (such as $-OH$, $-OCH_3$, $-NH_2$) can be *activating* the benzene ring while electron withdrawing groups (such as $-F$, $-NO_2$, $-COOH$) can be *deactivating* the benzene ring. For example, both phenylalanine and tyrosine amino acids contain the benzene ring. However, iodination (or radioiodination) of tyrosine is chemically easier since the hydroxyl ($-OH$) group already present on the benzene ring activates the electrophilic attack of iodine (Fig. 7.5). A benzene ring can have more than one substitutent attached to the ring. If two identical substituents are attached to the ring, they are referred to as *ortho* (*o*), *meta* (*m*), or *para* (*p*), depending on their relative position.

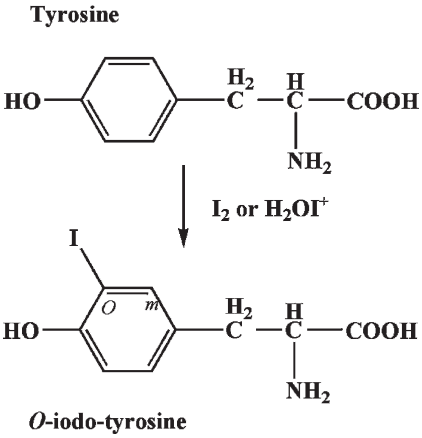


Fig. 7.5 Iodination of tyrosine is chemically easier since the hydroxyl (–OH) group already present on the benzene ring activates the electrophilic attack of iodine

Addition Reactions

Because alkenes and alkynes are unsaturated, their most important reactions are addition reactions. In these reactions, π bonds, which are weaker than the σ bonds, are broken, and new σ bonds are formed with the atoms being added. For example, *hydrogenation reactions* involve addition of hydrogen atoms to carbon atoms with double bonds in the presence of catalysts such as platinum, palladium and nickel, which help break the strong covalent bonds of molecular hydrogen.

$$H_2C = CHCH_3 + H_2 \xrightarrow{\text{catalyst}} CH_3CH_2CH_3 \quad (7.29)$$

Halogenation of olefins involves the addition of halogen atoms to the carbon atoms with double bonds. Unlike the unsaturated hydrocarbons, benzene does not undergo rapid addition reactions.

7.3.1.2 Hydrocarbon Derivatives

The millions of organic compounds, other than hydrocarbons, can all be regarded as derivatives of hydrocarbons, where one or more of the hydrogen atoms on the parent molecule is replaced by another type of atom or groups of atoms, known as *radicals* and *functional groups*. A radical is a hydrocarbon with one hydrogen atom less and is reactive. For example, methyl ($-CH_3$) and ethyl ($-CH_2CH_3$) are often called radicals (Table 7.6) and usually denoted as "R" in formulas. If the radical is derived from an alkane, the radical is called *alkyl radical*; and if it is derived from an aromatic hydrocarbon, it is called *aryl radical* and if it is derived from benzene, it is called *phenyl radical*. Specific groups of atoms responsible for the characteristic properties of the organic compounds are called *functional groups*. The most common functional groups are listed in Table 7.7.

Alcohols are characterized by the presence of the hydroxyl ($-OH$) group. Alcohols are classified as primary, secondary and tertiary, depending on whether one, two, or three radical groups attached to the carbon atom where the hydroxyl group is attached. Some common alcohols are methyl alcohol (methanol), ethyl alcohol (ethanol), glycerol, and phenol. Methanol is highly toxic while ethanol is the alcohol found in many beverages, such as beer, wine and whiskey. The fermentation of glucose by yeast generates ethanol from grains (barley, corn) and grapes. Some of the important polyhydroxyl alcohols are ethylene glycol and glycerol, which are 2 and 3 carbon alcohols. Alcohols are good solvents of organic compounds since the hydroxyl groups of alcohols contain polar C–O and O–H bonds, which help to form hydrogen bonds. As the number of carbon atoms in an alcohol increases, its water solubility decreases. A chemical reaction that removes a water molecule between two alcohol molecules results in the formation of an *ether*. Diethyl ether ($CH_3CH_2OCH_2CH_3$), or simply ether, is used as a solvent and as an anesthetic.

Aldehydes and *ketones* contain the carbonyl (–C=O) group. In an aldehyde, the *carbonyl* group is attached to at least one hydrogen atom while in ketones, the carbonyl group is attached to carbon atoms. Aldehydes have very strong odors. Formaldehyde (HCHO) or for-

Table 7.6 The most common alkyl and phenyl substituents and their names

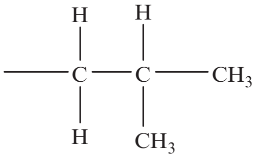
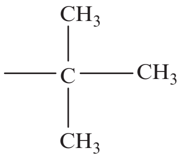
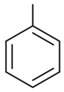
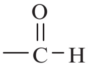
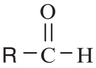
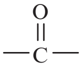
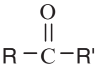
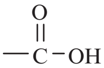
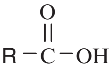
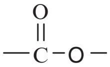
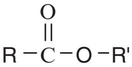
Structure	Name
$-CH_3$	Methyl
$-CH_2CH_3$	Ethyl
$-CH_2CH_2CH_3$	Propyl
$-CH_2CH_2CH_2CH_3$	Butyl
 $CH_3\overset{\vert}{C}HCH_3$	Isopropyl
	Isobutyl
	*tert*-Butyl
	Phenyl

Table 7.7 The common functional groups

Class	Functional group	General formula	Example
Halohydrocarbons	–X (F, Cl, Br, I)	R–X	CH_3I Methyl iodide
Alcohols	–OH	R-OH	CH_3CH_2OH Ethanol
Ethers	–O–	R–O–R’	CH_3OCH_3 Dimethyl ether
Aldehydes	 $-\overset{O}{\overset{\Vert}{C}}-H$	 $R-\overset{O}{\overset{\Vert}{C}}-H$	HCHO Formaldehyde
Ketones	 $-\overset{O}{\overset{\Vert}{C}}-$	 $R-\overset{O}{\overset{\Vert}{C}}-R'$	CH_3COCH_3 Acetone
Carboxylic acids	 $-\overset{O}{\overset{\Vert}{C}}-OH$	 $R-\overset{O}{\overset{\Vert}{C}}-OH$	CH_3COOH Acetic acid
Esters	 $-\overset{O}{\overset{\Vert}{C}}-O-$	 $R-\overset{O}{\overset{\Vert}{C}}-O-R'$	$CH_3COOCH_2CH_3$ Ethyl acetate
Amines	$-NH_2$	$R-NH_2$	CH_3NH_2 Methylamine

malin is generally used in pathology to store tissue specimens. Vanillin is responsible for the pleasant odor in vanilla beans, while butyraldehyde is responsible for the unpleasant odor in rancid butter. The most common ketone is *acetone*, commonly used as a solvent for hydrophobic molecules and as a nail polish remover. Methylethylketone or MEK is a solvent used in the chromatography of ^{99m}Tc pertechnetate. Alcohols and aldehydes or ketones can be interconverted by oxidation and reduction reactions.

Caboxylic acids are characterized by the presence of the carboxyl (–COOH) group and are also known as the organic acids with a general formula of RCOOH. The simplest and most common acid is acetic acid (found in vinegar), while citric acid is found in all citrus fruits. Unlike inorganic acids, organic acids are weak acids in aqueous solution. Reaction with a strong base such as NaOH, converts them into caboxylate anion or sodium salt form, which increases water solubility. Carboxylic acids can be synthesized by oxidizing primary alcohols. For example, ethanol can be oxidized to acetic acid, using potassium permanganate

A carboxylic acid reacts with an alcohol to form an ester and a water molecule

$$CH_3COOH + HOCH_2CH_3 \rightarrow CH_3COOCH_2CH_3 + H_2O \quad (7.30)$$

The reaction of CO_2 gas with organic magnesium halides (*Grignard* reagent) also results in the formation of carboxylic acids (Fig. 7.6). This method is commonly used to prepare ^{11}C labeled organic acids, such as palmitic acid. Carboxylic acids can be converted to very reactive acid chlorides by the reaction of the acids with thionyl chloride ($SOCl_2$). The reaction of acid chloride with an alcohol will result in the formation of an *ester* (Fig. 7.6).

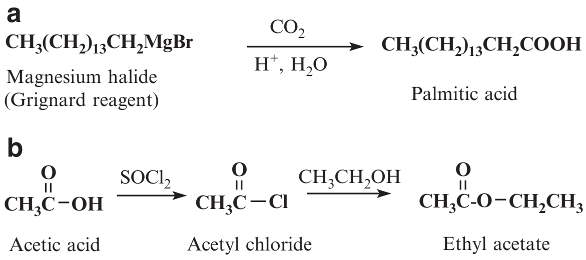


Fig. 7.6 The reaction of CO_2 gas with *Grignard* reagent to form carboxylc acid, which can then be converted to very reactive acid chloride by the reaction of the acid with thionyl chloride ($SOCl_2$). The reaction of acid chloride with an alcohol will result in the formation of an *ester*

Naturally occurring esters are fats and triglycerides and often have a sweet, fruity odor. For example, *n*-amyl acetate smells like bananas and *n*-octyl acetate smells like oranges. One of the very important *esters is acetylsalicylic acid* (aspirin) formed from the reaction of salicylic acid and acetic acid.

Amines can be considered derivatives of ammonia (NH_3), in which one or more hydrogen atoms have been replaced by organic radicals. Amines can be classified as the primary amines (RNH_2), secondary amines (R_2NH), and tertiary amines (R_3N). Many amines have unpleasant "fishlike" odors. *Putrescine* and cadaverin are responsible for the odor associated with decaying animal and human tissues. Also, amines are the bases of organic chemistry. Like ammonia, amines react as *Bronsted* bases by reacting with water and acids to form positively charged ammonium species (RNH_3^+), which are soluble in water. Amines react with acid chlorides to form amides that contain an amide group (–CONH), commonly found in peptides and proteins (Fig. 7.8). Amines also react with aldehydes and ketones to give *Schiff* bases.

7.4 Biochemistry

Biochemistry is the study of the chemistry of living systems. The *essential elements* for human life are known to include 30 elements. However, only six of these elements contribute to 99% of the body mass. The most abundant elements are oxygen 65%, carbon (18%) and hydrogen (10%). Certain transition elements, such as iron, zinc, copper, cobalt, and iodine, are present in *trace amounts*. Life is organized around the functions of the cell, the smallest unit of life, and the building block of all tissues and organs. The main thrust of biochemistry is to understand how cells operate at the molecular level. The *nucleus*, which contains the *chromosomes* and DNA, is separated from the *cytoplasm* (the cell fluid) by a membrane and the cell, in turn, is separated from the extracellular fluid by the cell membrane. A number of subcellular structures carry out various cell functions. For example, *mitochondria* process nutrients and produce the energy, the enzymes in *lysosomes* digest the proteins, and the *ribosomes* synthesize the proteins based on mRNA. The four major categories of natural chemical compounds present in living systems are proteins, carbohydrates, lipids, and nucleic acids.

7.4.1 Proteins

Proteins make up about 15% of our body mass and perform many functions. *Fibrous proteins* provide structural integrity and strength to many tissues, such as muscle and cartilage, while *globular proteins* are the "worker molecules" in various processes, such as transport of oxygen and nutrients. Globular proteins also act as catalysts for thousands of chemical reactions and participate in the body's regulatory systems. Chemically, proteins are a class of natural polymers and the basic building blocks are α-*amino acids*, molecules containing both, a basic amino group and an acid carboxyl group.

7.4.1.1 Amino Acids

Amino acids are the basic structural units of proteins, peptide hormones, and peptide antibiotics. The 20 natural amino acids most commonly found in proteins are grouped as polar and nonpolar classes or as neutral, basic and acidic amino acids. The α-amino acids have the general formula (Fig. 7.7), where "R" represents a variable, organic polar (hydrophilic), or nonpolar (hydrophobic) side chain. They are called α- amino acids because the amino group is attached to the α-carbon, the one next to the carboxyl group. At the pH in biological fluids, the amino acids exist in a dipolar ionic form (known as *zwitterions*), where the proton from a carboxyl group is transferred to the amino group. Most of the amino acids are neutral. The basic amino acids (*lysine, arginine and histidine*) have two amino groups, while the acidic amino acids (*aspartic acid* and *glutamic acid*) have two carboxyl groups. The amino acids, *cysteine* and *methionine* contain organic sulfur atoms. The thiol group (–SH), similar to the hydroxyl group, can be oxidized in cysteine to a disulfide form, *cystine*. Methionine has a thioether linkage and serves as a biosynthetic intermediate in supplying the methyl group methylation reactions, in vivo. The amino acid, tyrosine, is important for radioiodination reactions, while lysine and arginine are useful to attach bifunctional chelating agents for labeling peptides and proteins with radiometals.

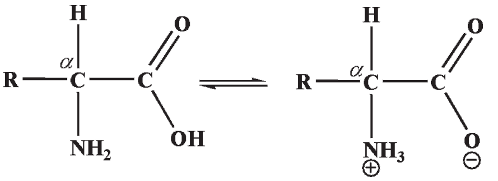


Fig. 7.7 The building blocks of all proteins are the α-amino acids, where R may represent H, CH_3, or a more complex substituent. At the physiological pH, there may be equilibrium between the neutral and charged species

Stereochemistry of Amino Acids

When a carbon atom is attached to four different groups, it is called an *asymmetric* carbon atom. The compounds containing asymmetric carbon atoms, like mirror images, are said to be nonsuperimposable. The mirror image, *optical isomers* are called *enantiomers* (L and D forms). The amino acids in the solution can also rotate the plane-polarized light to the right (designated as *d* for dextrorotatory) or to the left (designated as *l* for levorotatory). Interestingly, L-amino acids are often dextrorotatory, while D-amino acids are levorotatory. The physical properties of L and D amino acids are identical. In biological systems, however, the reactivity of these two forms is quite different. For example, only the L-amino acids are mostly found in proteins. It is also important to recognize that the stereoche-mical requirements for biological activity are essential in the design of radiolabeled amino acids as molecular imaging agents.

Peptide Linkage

A condensation reaction between the amino group of one amino acid with the carboxy group of another amino acid will result in the formation of a dipeptide with reduced polarity. The structure, CONH is called a *peptide linkage* (also called an *amide*). Such peptide bonds (Fig. 7.8) between several amino acids lengthen the polymer chain to produce a polypeptide, and eventually a protein. A naturally occurring tripeptide, glutathione is derived from only three amino acids

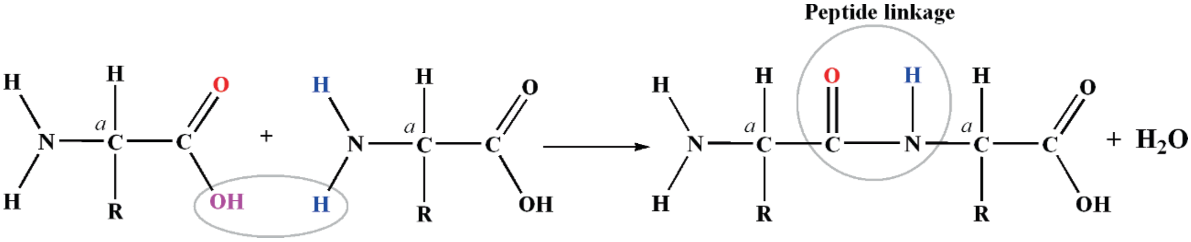


Fig. 7.8 A condensation reaction between two amino acids results in the formation of a peptide bond and one water molecule

(glu–cys–gly), while insulin with a molecular weight of 5,700 is made up of 51 amino acids. Polypeptides with molecular weights of approximately 6,000 or higher are generally called proteins. The sequence and the number of amino acids in a polypeptide, determines the biological function of the molecule. With the 20 natural amino acids, which can be assembled in any order, there is essentially an infinite (10^{18}) variety of possible sequences of protein molecules.

7.4.1.2 Protein Structure and Function

The order, or sequence of amino acids in the protein chain, is called the *primary structure*, which determines the biological property. The arrangement of the chain of the long molecule is called the *secondary structure*, determined to a large extent by the hydrogen bonding within the chain coils, forming a spiral structure called an α-helix, which gives the protein elasticity. Proteins having nostructural functions are *globular*. The overall shape of the protein, long and narrow or globular is called its *tertiary structure*. The amino acid cysteine plays a special role in stabilizing the tertiary structure of proteins because of disulfide linkage. The process of breaking down the three dimensional structure of proteins is called *denaturation*. Proteins have a wide range of specific functions in the body such as structure, movement, transport, catalysis, energy transformation, control, and buffering. Receptor protein molecules on the cell membrane are highly specific and bind to hormones, neurotransmitters, and specific molecules to initiate specific functions within the cell. Nearly all chemical reactions in living systems are catalyzed by enzymes, which are almost always proteins. Expression of genetic information is also under the control of proteins.

7.4.2 Carbohydrates

Carbohydrates or sugars are characterized by structures in which each carbon atom has an oxygen atom attached to it. All the carbon atoms in the molecule, except one, have hydroxyl groups attached to them. The remaining one carbon atom has the oxygen in the form of an aldehyde (sugar is called *aldose*) or ketone (sugar is called *ketose*). For example, glucose is an aldose, while fructose is a ketose. Carbohydrates, such as starch and cellulose, are polymers composed of monomers called *monosaccharides* or *simple sugars*. Specific examples of pentoses (containing five carbon atoms), D-*ribose*, D-*arabinose*, and hexoses (containing six carbon atoms), and D-*glucose* and D-*fructose* (found in honey and fruit) are shown in Fig. 7.9.

7.4.2.1 Stereochemistry of Sugars

The number of optical isomers each sugar may have depends on the number of *chiral* centers or asymmetric carbon atoms. It turns out that there are 2^n possible different stereochemical forms, where n represents the number of chiral centers. For example, glyceraldehyde has one chiral center and two optical isomers; D and L forms (Fig. 7.10). On the other hand, glucose has four chiral centers and 16 optical isomers that differ in their ability to rotate plane-polarized light. The mirror-image forms of a pair of enantiomers will rotate the plane-polarized light in opposite directions to the same extent, but have identical properties. If we invert the stereochemistry of one of the chiral centers, the chemical properties also change. Compounds like glucose and mannose, that differ by the inversion of only one optical center are called *diastereomers*.

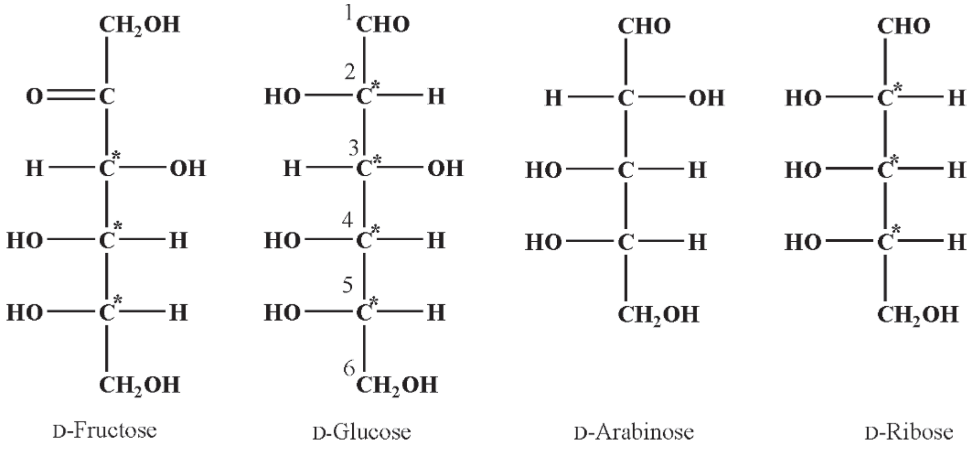


Fig. 7.9 Most important carbohydrates, such as starch and cellulose, are polymers composed of monomers called *monosaccharides*, or simple sugars; *pentoses* (such as arabinose and ribose) contain five carbon atoms, while *hexoses* (such as fructose and glucose) contain six carbon atoms

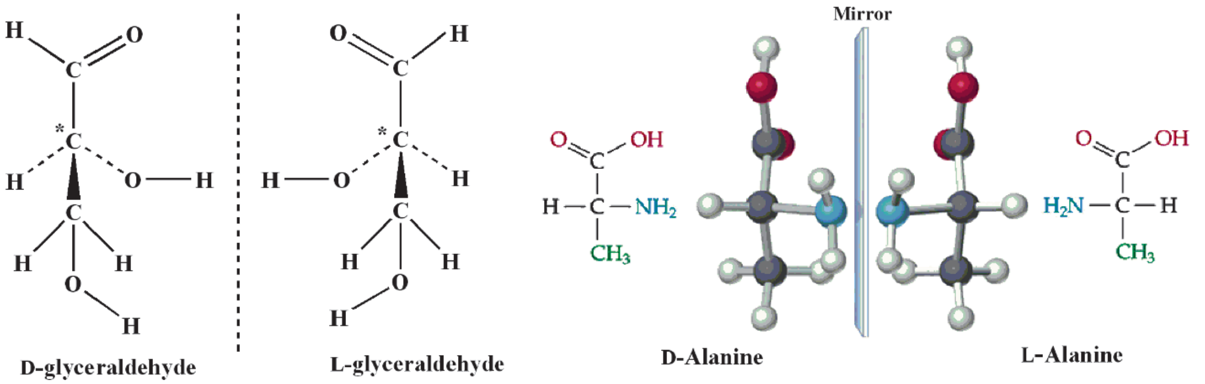


Fig. 7.10 A carbon atom with four different groups (also known as asymmetric carbon) bonded to it in a tetrahedral arrangement gives rise to a pair of *optical isomers* that are *nonsuperimposable*. The D,L forms are based on glyceraldehydes. Similar optical isomers also exist with amino acids

The absolute configuration, designated by D- or L-, depends on the sugar's relationship to glyceraldehydes. In a sugar, if the terminus most remote from the carbonyl group has the D- configuration of glyceraldehyde, then that sugar is also called D- form. For example, the 5-carbon in D-glucose and D-fructose, has the same configuration as the D-glyceraldehyde. However, in terms of optical rotation, glucose D-glucose is dextrorotatory (*d* or (+)), while D-fructose is levorotatory (*l* or (–)).

Simple sugars in solution, usually *cyclize*, or form a ring structure due to the creation of a new bond between the oxygen atom of the terminal hydroxyl group and the carbon of the aldehyde or ketone group. The cyclization of glucose resulting in the formation of a *hemiacetal*, will have two different rings, designated as α and β forms, which differ in the orientation of the hydroxy group and hydrogen atom on 1-carbon, as shown in the Fig. 7.11.

Polysaccharides

More complex carbohydrates are formed by combining simple sugars. For example, sucrose, common

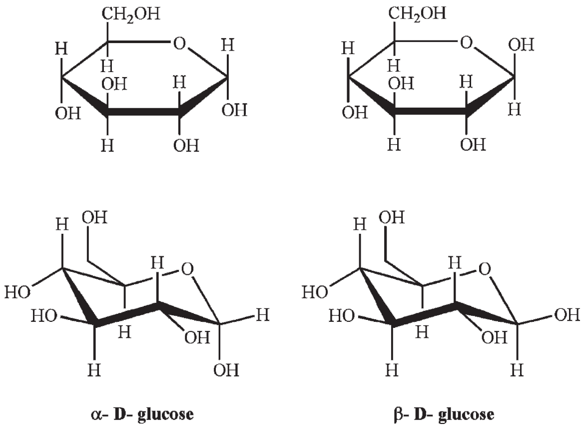


Fig. 7.11 The cyclization of glucose. Two different rings are possible; the two different forms designated as α and β, differ in the orientation of H and OH groups on C-1. The structural arrangement of atoms can be shown in the cyclohexane ring form (*top*) or the chair cyclohexane ring form (*bottom*)

table sugar, is a *disaccharide* formed from glucose and fructose by elimination of water to form a C–O–C bond between the rings, which is called a *glycoside linkage*. Another disachharide is lactose of milk sugar, which is a combination of glucose and galactose. Most of the carbohydrates in nature are polymers of repeating sugar units, called *polysaccharides* such as *starch*, *cellulose*, and *glycogen*. They are polymers of glucose (300–3,000 units) that yield only glucose upon hydrolysis. These polymers differ from each other in the nature of glycoside linkage, the amount of branching, and molecular weight.

Sugar derivatives

Carboxylic acid derivatives of glucose are quite common. If the C-1 aldehyde group is oxidized to a carboxyl group, the acid formed is called *gluconic acid*. On the other hand, if the C-6 hydroxy group is oxidized to a carboxyl group, *glucuronic acid* results. In vivo, the nonpolar drug metabolites are converted to polar metabolites by linking glucuronic acid, via a hydroxyl group. Such metabolites are called *glucuronides*. One of the most popular analogs of glucose, used in nuclear medicine, is glucoheptonic acid, which is a C-7 homologue of glucose.

7.4.3 Lipids

Lipids have widely variable chemical structures but a common nonpolar nature. They are defined as water-insoluble substances. The lipids found in the human body can be divided into four different classes according to their molecular structure: *fats*, *phospholipids*, *waxes*, and *steroids*. Fats and phospholipids are derived from trihydroxy alcohol, *glycerol* and *fatty aci*ds, while waxes are derived from monohydroxy alcohol and fatty acids. Steroids are derived from C_{30} compounds or *triterpenes*.

7.4.3.1 Fats

The most common fats in meats and the milk butterfat are esters made when glycerol reacts with long-chain carboxylic acids or *fatty acids*. Fats that are esters of glycerol are called triglycerides where the fatty acids may be saturated or unsaturated. Naturally occuring fatty acids (Table 7.8) are monocarboxylic acids that are unbranched and contain even number of carbon atoms.

In a process called *saponification*, fats are heated in the presence of an alkali (such as NaOH and KOH) to hydrolyze the ester and produce glycerol and salts of fatty acids (also known as *soaps*). The sparingly soluble salts of fatty acids, when dispersed in water, form *micelles* that are aggregates of fatty acid anions, which have nonpolar tails in the interior, while the polar anionic heads point outward to interact with the water molecules.

7.4.3.2 Phospholipids

Phopholipids are also esters of glycerol. However, unlike fats, phospholipids contain only two fatty acids, while the third ester linkage involves an phosphate group. The simplest form is phosphatidic acid, a major constituent of membranes. This molecule has a central asymmetric atom and can have a L or D configuration. It is the L-phosphatidic acid form which occurs naturally. Further, substitution on the phosphate group by molecules such as choline, ethanolamine and inositol, will produce phospholipids derivatives, which are con-

Table 7.8 Common fatty acids

Fatty acid	Molecular formula	Structural formula
Saturated fatty acids		
Butyric acid	$C_4H_8O_2$	$CH_3(CH_2)_2{-}COOH$
Caproic acid	$C_6H_{12}O_2$	$CH_3(CH_2)_4{-}COOH$
Lauric acid	$C_{12}H_{24}O_2$	$CH_3(CH_2)_{10}{-}COOH$
Palmitic acid	$C_{16}H_{32}O_2$	$CH_3(CH_2)_{14}{-}COOH$
Stearic acid	$C_{18}H_{36}O_2$	$CH_3(CH_2)_{16}{-}COOH$
Arachidic acid	$C_{20}H_{40}O_2$	$CH_3(CH_2)_{18}{-}COOH$
Unsaturated fatty acids		
Oleic acid	$C_{18}H_{34}O_2$	$CH_3(CH_2)_7CH{=}CH(CH_2)_7{-}COOH$
Linoleic acid	$C_{18}H_{32}O_2$	$CH_3(CH_2)_4CH{=}CH{-}CH_2{-}CH{=}CH(CH_2)_7{-}COOH$
Linolenic acid	$C_{18}H_{30}O_2$	$CH_3CH_2CH{=}CH{-}CH_2{-}CH{=}CH{-}CH_2{-}CH{=}CH(CH_2)_7{-}COOH$
Arachidonic acid	$C_{20}H_{30}O_2$	$CH_3(CH_2)_4CH{=}CH{-}CH_2{-}CH{=}CH{-}CH_2{-}CH{=}CH{-}CH_2{-}CH{=}CH(CH_2)_3{-}COOH$

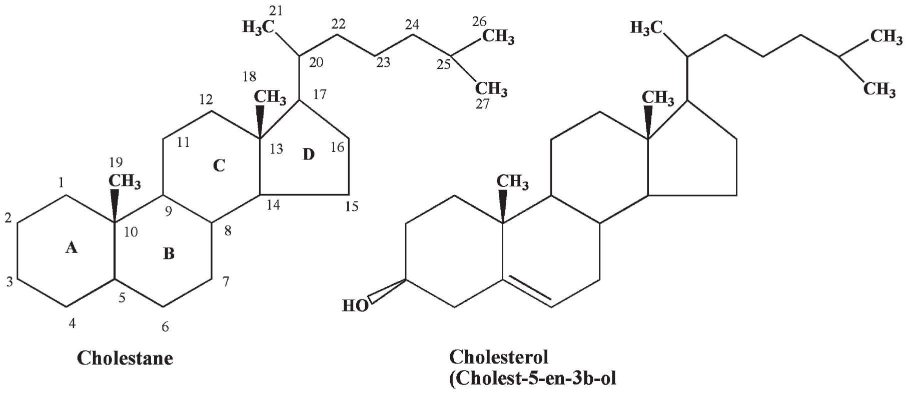


Fig. 7.12 The structure of steroids can be illustrated based on the completely saturated 27 carbon compound, cholestane while cholesterol is an unsaturated steroid alcohol, derived from cholestane

stituents of specialized membranes. One of the important phospholipids is L-*phosphatidylcholine* (*lecithin*).

The phospholipids have two distinct parts: the long nonpolar tail and the polar substituted phosphate head. Because of this dual nature, phospholipids tend to form bilayers in aqueous solution, similar to micelles described above. The bilayers of larger phospholipids can close to form *vesicles*. According to *the fluid mosaic model* of cell membranes, small uncharged molecules (such as H_2O, O_2, CO_2) can diffuse through the membrane, while other molecules pass through special *channels* and *transporters* provided by special proteins embedded in the cell membranes.

7.4.3.3 Steroids

Steroids are a class of lipids that have a characteristic ring structure consisting of four fused rings. Steroids include four major groups; cholesterol, adrenocorticoid hormones (such as cortisol and aldosterone), sex hormones (such as testosterone and estradiol), and bile acids. The simplest completely saturated compound is cholestane, which consists of 27 carbons, 17 of which constitute the ring system (Fig. 7.12), and three substituent groups; two methyl groups attached at C 10 and 13 and 8-carbon alkyl group at C 18 of the ring.

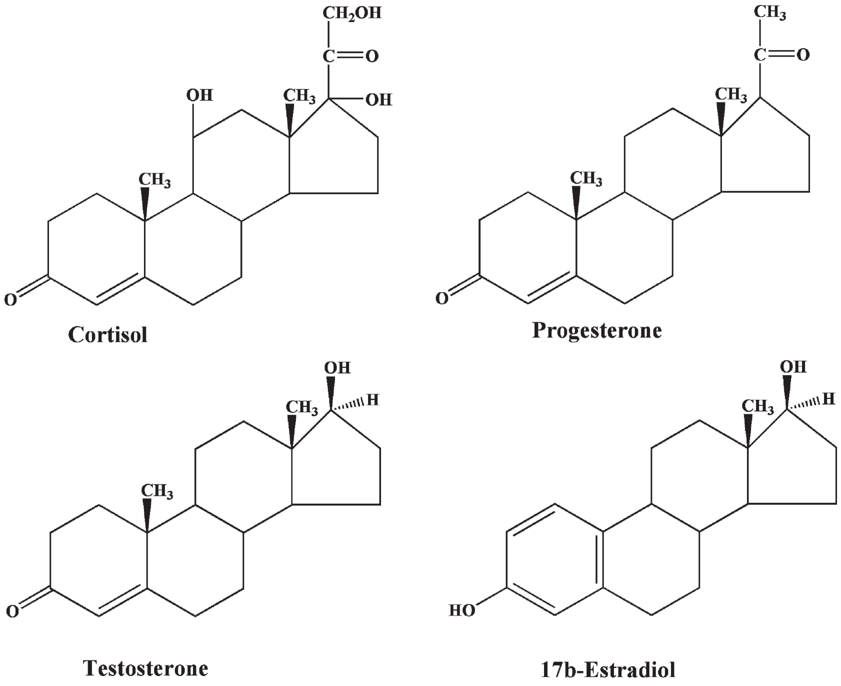
The biosynthesis of cholesterol starts with *lanosterol*, a 30 carbon steroid, first made from the triterpene, *squalene*. The liver synthesizes cholesterol and also disposes of it by transforming it into bile. In plasma, most of the cholesterol is conjugated to fatty acids by an ester linkage to the 3-hydroxyl group. Cholesterol also serves as a *precursor* for the formation of bile acids, steroid hormones and vitamin D. The 21 carbon adrenocorticoid hormones are synthesized in the adrenal gland. *Aldosterone* is involved in the regulation of water and the electrolyte balance in body fluids, while *cortisol* is primarily involved in the regulation of protein and carbohydrate metabolism. The 19 carbon male sex hormone (*androgens*) *testosterone* is synthesized in the testes and adrenal cortex, but subsequently reduced to dihydrotetosterone in the prostate gland. There are two types of female sex hormones; 21 carbon progesterone, is produced by the corpus luteum and placenta, while the 18 carbon estrogens (17β-estradiol and estrone) are produced in the ovaries. Only in estrogens, is the A ring benzene-like or aromatic. Steroids are relatively nonpolar and in plasma they are solubilized by binding to transport proteins. The structures of steroid sex hormones are shown in Fig. 7.13.

7.4.4 Nucleic Acids

The ability of cells to maintain a high degree of order depends on the hereditary or genetic information that is stored in a polymer called *deoxyribonucleic acid* (DNA). Within the nucleus of all mammalian cells a full complement of genetic information is stored and the entire DNA is packaged into 23 pairs of *chromosomes*. A chromosome is formed from a single enormously long DNA molecule that consists of many small subsets called *genes* that represent a specific combination of DNA sequence, designed for a specific cellular function.

The chromosomes can undergo *self-replication* that permits DNA to make copies of itself. More specifically, as the cell divides and transfers the DNA (23 pairs of chromosomes) to daughter cells, which can thus inherit every property and characteristic of the original cell. There are approximately 30,000 genes per human genome, and the genes control every aspect of cellular function, primarily through protein synthesis. The sequence of amino acids in a particular protein or enzyme is encoded in a specific gene. The central dogma of molecular biology is that the overall process of information transfer in the cell involves the *transcription* of DNA into *ribonucleic acids* (RNA) molecules, which are much smaller than DNA and found in the cytoplasm. Subsequently, RNA is responsible for generating specific proteins on ribosomes by a process known as *translation*.

A major characteristic of DNA is its ability to encode an enormous quantity of biological information. Only a few picograms (10^{-12} g) of DNA are sufficient to direct synthesis of as many as 100,000 distinct proteins within a cell. This supreme coding effectiveness of DNA is due to its unique chemical structure.



Cortisol

Progesterone

Testosterone

17b-Estradiol

Fig. 7.13 The most common steroids hormones

7.4.4.1 DNA Structure

DNA was first discovered in 1869 by the chemist Friedrich Miescher who extracted a white substance from the cell nuclei of human pus and called it *nuclein*. Since nuclein is slightly acidic, it is known as nucleic acid. In the 1920s, the biochemist, P.A. Levine identified that there are two sorts of nucleic acids: DNA and RNA. Both DNA and RNA are *polynucleotide molecules* formed by the polymerization of nucleotides. Each nucleotide molecule is composed of three basic elements; a phosphate group, a five-carbon sugar, *deoxyribose* (in DNA) or *ribose* (in RNA), and one of the five types of nitrogen containing organic bases (Fig. 7.14). Three of the bases, *cytosine* (C), *thymine* (T) and *uracil* (U) are called *pyrimidines*, while the other two bases, *adenine* (A) and *guanine* (G) are called *purines*. Of the five bases, thymine is present only in DNA, while uracil is present only in RNA. The base and the sugar combine to form a unit called *nucleoside* by the elimination of one water molecule. The nucleoside in turn reacts with a phosphate group to form a unit called, nucleotide (Fig. 7.15), which is an ester. The nucleotides become connected through condensation reactions that eliminate water to give a polymer, which may contain billions of nucleotides in a single DNA molecule with a molecular weight as high as several billion grams per mole. In contrast, RNA molecules are small with molecular weights of 20,000–40,000.

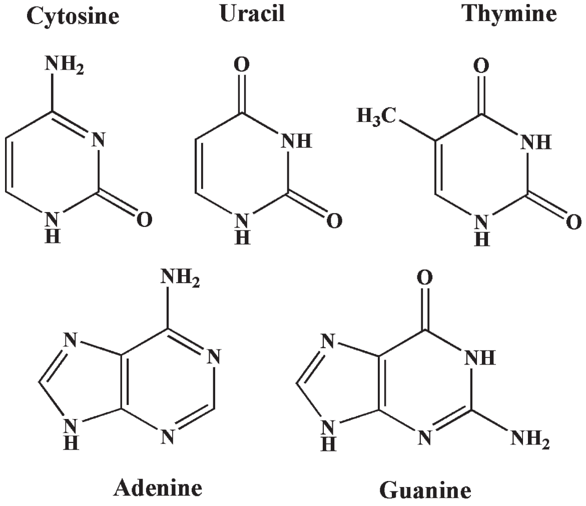
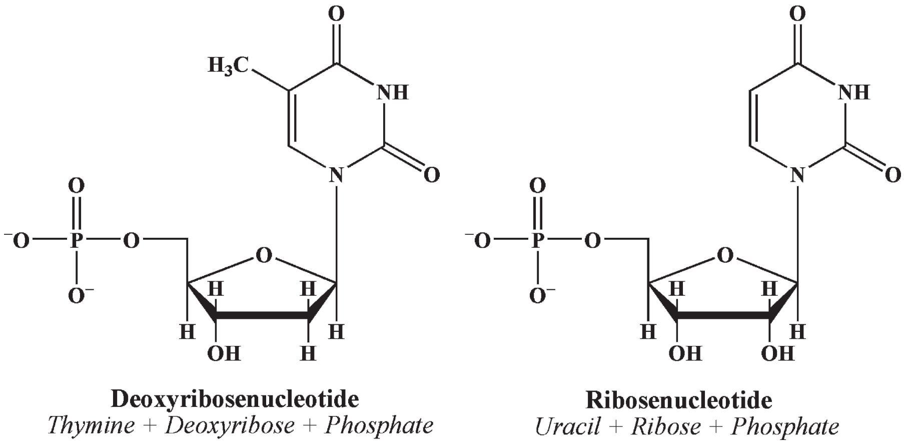


Fig. 7.14 The organic bases found in DNA and RNA. Thymidine is present only in DNA, while uracil is present only in RNA

The presence of 5′-phosphate and the 3′-hydroxyl groups in the deoxyribose molecule allows the DNA to form a long chain of polynucleotides by the joining of nucleotides by phosphodiester bonds (Fig. 7.16). Any linear strand of DNA will always have a free 5′-phosphate group at one end and a free 3′-hydroxyl group at the other end. Therefore, the DNA molecule has an intrinsic directionality (5′ to 3′ direction).

Although some forms of cellular DNA exist as single-stranded structures, the most widespread DNA structure, discovered by Watson and Crick in 1953, represents DNA as a double helix containing two polynucleotide strands that are complementary mirror images of each other. The "backbone" of the DNA molecule is composed of deoxyribose sugars joined by phosphodiester bonds to phosphate group, while the bases are linked in the middle of the molecule by hydrogen bonds. The relationship between bases in the double helix is



Deoxyribosenucleotide
Thymine + Deoxyribose + Phosphate

Ribosenucleotide
Uracil + Ribose + Phosphate

Fig. 7.15 The monomers of *nucleic acids* (DNA and RNA) are called *nucleotides*, which are composed of an organic base, a five-carbon sugar and a phosphoric acid molecule

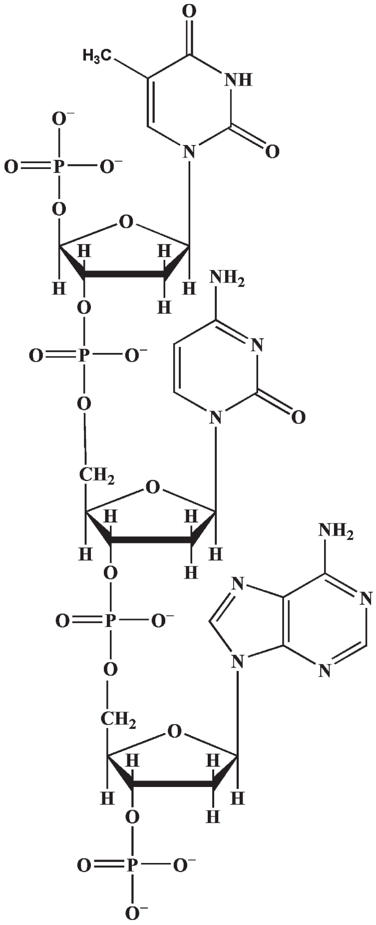


Fig. 7.16 In a DNA molecule, the nucleotides become connected through condensation reactions to form a polymer, which may contain a billion units. DNA molecule, however, is a double-helical structure with complementary bases on the two strands that are connected by the bases, which form hydrogen bonds to each other

described as complementarity since adenine always bonds with thymine, and guanine always bonds with cytosine. As a consequence, the double-stranded DNA contains equal amounts of purines and pyrimidines. An important structural characteristic of the double-stranded DNA is that its strands are antiparallel meaning that the two strands are aligned in opposite directions. During cell division, the two strands of DNA unwind and new complementary strands are generated.

7.4.4.2 Protein Synthesis

A given segment of DNA is called *gene*, which contains the code, the specific sequence of amino acids for a specific protein. The code is specific for each amino acid and consists of a set of three bases called a *codon* (Table 8.6). Gene expression involves the synthesis of a specific protein. This process is initiated by building a special RNA molecule, called *messenger RNA* (mRNA), in the nucleus from an appropriate gene. mRNA migrates into the cytoplasm where the protein is synthesized. Small RNA fragments, called *transfer RNA* (tRNA), containing only 75–80 nucleotides, decode the genetic message from the mRNA, using a complementary triplet of bases called an *anticodon*. mRNA builds the protein with the assistance of a ribosome. The tRNA molecule brings an appropriate amino acid to the mRNA. Soon after the codon and anticodon match, another tRNA, with its specific amino acid, moves to the second codon position. Once the two amino acids join together by peptide linkage, tRNA breaks away from its position. The process is repeated until the synthesis of protein is completed. The number of protein molecules synthesized by each cell, however, depends on the degree of gene expression that is warranted by the cell and the number of RNA molecules within the cytoplasm.

Additional Reading

Zumdahl SS (1998) Chemical principles, 3rd edn. Houghton Mifflin, Boston, MA, USA

Billinghurst MW, Fritzberg AR (1981) Chemistry for nuclear medicine. Year Book Medical, Chicago