Part I
Setting the Stage: Basic Biochemistry Concepts

The 5th Wave   By Rich Tennant

"Look — I'm only going to do this once, but it should help you remember the nonpolar hydrophobic principle and its effect on the surface tension of water."

In this part . . .

*W*e go over some basic aspects of chemistry, organic chemistry, and biochemistry. First we survey the field of biochemistry and its relationship to other disciplines within chemistry and biology. We cover several different types of cells and their parts. Then we look at some features of water chemistry that apply to biochemistry, paying attention to pH and buffers. In the end, you get a brush-up on your organic chemistry, which sets the stage for Part II.

Chapter 1

Biochemistry: What You Need to Know and Why

*I*f you are enrolled in a biochemistry course, you may want to skip this chapter and go right to the chapter(s) where we discuss the material you are having trouble with. But if you are *thinking* about taking a course in biochemistry or just want to explore an area that you know little about, keep reading. This chapter gives you basic information about cell types and the parts of the cell — which are extremely important in biochemistry.

Sometimes it's easy to get lost in the technical stuff and forget about the big picture. This chapter sets the stage for the details.

Why Biochemistry?

We suppose the flippant answer would be "Why not?" or "Because it is required."

That first response is not too bad an answer, actually. Look around. See all the living or once living things around you? The processes that allow them to grow, multiply, age, and die are all biochemical in nature. Sometimes we sit back and marvel at the complexity of life, the myriad of chemical reactions that are taking place right now within our own bodies, how all these biochemical reactions are working together so that we can sit and contemplate them. When John learned about the minor structural difference between starch and cellulose he remembers thinking: "Just that little difference in the one linkage

between those units is basically the difference between a potato and a tree?" It made him want to learn more, to delve into the complexity of the chemistry of living things, to try to understand. We encourage you to step back from the details occasionally and marvel at the complexity and beauty of life.

What Is Biochemistry and Where Does It Take Place?

Biochemistry is the chemistry of living organisms. Biochemists study the chemical reactions that occur at the molecular level of organisms. Normally it is listed as a separate field of chemistry. However, in some schools it is part of biology, and in others it is separate from both chemistry and biology.

Biochemistry really reaches out and combines aspects of all the fields of chemistry. Because carbon is the element of life, *organic chemistry* plays a large part in biochemistry. Many times biochemists study how fast reactions occur — that's *physical chemistry.* Often metals are incorporated into bio-chemical structures (such as iron in hemoglobin) — that's *inorganic chemistry.* Biochemists use sophisticated instrumentation to determine amounts and structures — that's *analytical chemistry.* Biochemistry is similar to *molecular biology;* both study living systems at the molecular level, but biochemists concentrate on the chemical reactions that are occurring.

Biochemists may study individual electron transport within the cell, or they may study the processes involved in digestion. If it's alive, biochemists will study it.

Types of Living Cells

All living organisms contain cells. A *cell* is a prison of sorts. The working apparatus of the cell is imprisoned within the "bars" — known as the *cell membrane*. Just as a prison inmate can still communicate with the outside world, so can the cell contents. The prisoner must be fed, so nutrients must be able to enter every living cell. There is a sanitary system for the elimination of waste. And, just as inmates may work to provide materials for society outside the prison, a cell may produce materials for life outside the cell.

There are two types of cells: prokaryotes and eukaryotes. (Viruses also bear some similarities to cells, but these are limited.) Prokaryotic cells are the simplest type of cells. Many one-celled organisms are prokaryotes.

TIP

The simplest way to distinguish these two types is that a *prokaryotic cell* contains no well-defined nucleus, whereas the opposite is true for a *eukaryotic cell*.

Prokaryotes

Prokaryotes are mostly bacteria. Besides the lack of a nucleus, there are few well-defined structures inside a prokaryotic cell. The prison wall has three components: a cell wall, an outer membrane, and a plasma membrane. This wall allows a controlled passage of material into or out of the cell. The materials necessary for proper functioning of the cell float about inside it, in a soup known as the *cytoplasm*. Figure 1-1 depicts a simplified version of a prokaryotic cell.

Plasma membrane

Cell wall

Ribosomes

DNA
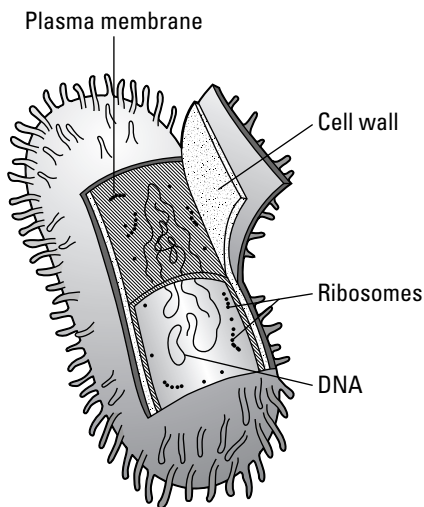
Figure 1-1:
Simplified
prokaryotic
cell.

Eukaryotes

Eukaryotes are animals, plants, fungi, and protists. *You* are a eukaryote. In addition to having a nucleus, eukaryotic cells have a number of membrane-enclosed components known as *organelles*. Eukaryotic organisms may be either unicellular or multicellular. In general, eukaryotic cells contain much more genetic material than prokaryotic cells.

Animal Cells and How They Work

All animal cells (which are, as you now know, eukaryotic cells) have a number of components, most of which are considered to be organelles. The primary components of animal cells are listed in Table 1-1. (These components, and a few others, are also present in plant cells.) Figure 1-2 illustrates a simplified animal cell.

Table 1-1	Parts of an Animal Cell
Cell membrane	Centrioles
Endoplasmic reticulum	Golgi apparatus
Lysosomes	Mitochondria
Nucleus and nucleolus	Ribosomes
Small vacuoles	
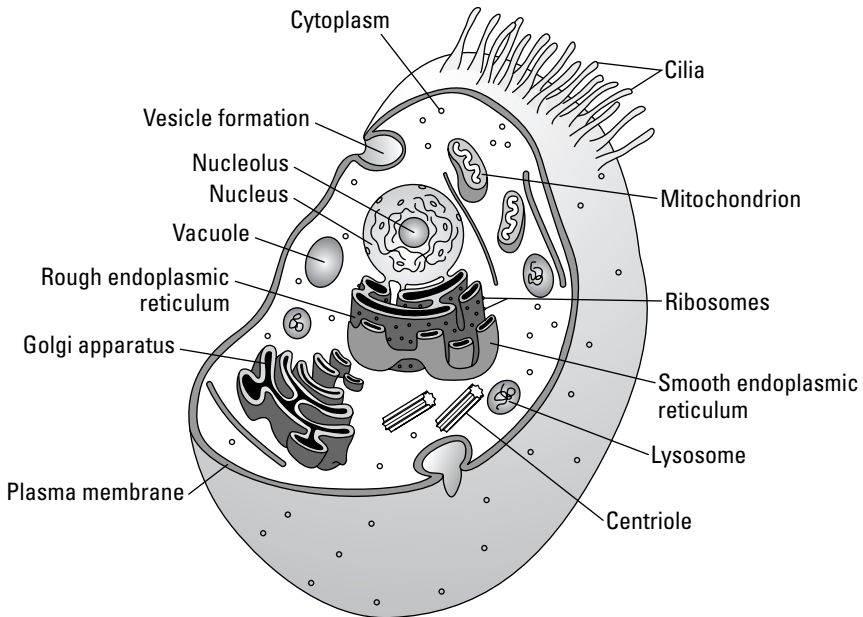
Figure 1-2: Simplified illustration of an animal cell.

The plasma membrane separates the material inside the cell from everything outside the cell. The *plasma* or cytoplasm is the fluid inside the cell. It is important for the health of the cell to prevent this fluid from leaking out. However, necessary materials must be able to enter through the membrane, and other materials, including waste, must be able to exit through the membrane.

REMEMBER

Transport through the membrane may be active or passive. *Active transport* requires that a price be paid for a ticket to enter (or leave) the cell. The cost of the ticket is energy. *Passive transport* does not require a ticket. Passive transport methods include diffusion, osmosis, and filtration.

Centrioles behave as the "train conductors" of the cell. They organize microtubules, which help move the parts of the cell during cell division.

The cell can be thought of as a smoothly running factory. The *endoplasmic reticulum* is the main part of the cell factory. There are two basic regions to this structure, known as the *rough* endoplasmic reticulum and the *smooth* endoplasmic reticulum. The rough endoplasmic reticulum contains ribosomes, and the smooth endoplasmic reticulum contains no ribosomes (more about ribosomes and their function is coming up in this chapter). The rough endoplasmic reticulum, through the ribosomes, is the assembly line of the factory. The smooth endoplasmic reticulum is more like the shipping department, which ships the products of the reactions that occur within the cell, to the Golgi apparatus.

The *Golgi apparatus* serves as the postal system of the cell. It looks a bit like a maze, and within it, materials produced by the cell are packaged in vesicles, small membrane-enclosed sacs. The vesicles are then mailed to other organelles or to the cell membrane for export. The cell membrane contains "customs officers" (called *channels*), who allow secretion of the contents from the cell. Secreted substances are then available for other cells or organs.

Lysosomes are the landfills of the cell. They contain digestive enzymes that break down substances that may harm the cell (Chapter 6 has a lot more about enzymes). The products of this digestion may then safely reenter the cell. Lysosomes also digest "dead" organelles. This slightly disturbing process, called *autodigestion,* is really part of the cell digesting itself.

The *mitochondria* (singular mitochondrion) are the cell's power plants, where the cell produces energy. Mitochondria use food, primarily the carbohydrate *glucose,* to produce energy, which comes mainly in the form of *adenosine triphosphate* (ATP — to which Chapter 13 is dedicated).

Each cell has a *nucleus* and, inside it, a *nucleolus.* These serve as the control center of the cell and are the root from which all future generations originate. A double layer known as the *nuclear membrane* surrounds the nucleus. Usually the nucleus contains a mass of material called *chromatin.* If the cell is entering a stage leading to reproducing itself through cell division, the chromatin separates into *chromosomes.*

In addition to conveying genetic information to future generations, the nucleus produces two important molecules for the interpretation of this information. These molecules are *messenger ribonucleic acid* (mRNA) and *transfer ribonucleic acid* (tRNA). The nucleolus produces a third type of ribonucleic acid known as *ribosomal ribonucleic acid* (rRNA). (Chapter 9 is all about nucleic acids.)

Ribosomes contain protein and ribonucleic acid subunits. It is in the ribosomes where the amino acids are assembled into *proteins.* Many of these proteins are enzymes, which are part of nearly every process occurring in the organism. (Part II of this book is devoted to amino acids, proteins, and enzymes.)

The *small vacuoles,* or simply *vacuoles,* serve a variety of functions, including storage and transport of materials. The stored materials may be for later use or may be waste material no longer needed by the cell.

A Brief Look at Plant Cells

Plant cells contain the same components as animal cells — plus a cell wall, a large vacuole, and, in the case of green plants, chloroplasts. Figure 1-3 illustrates a typical plant cell.
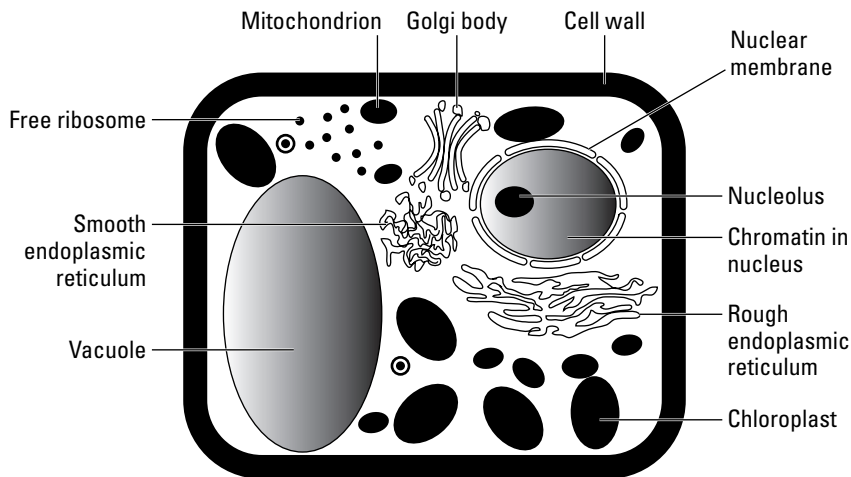
Figure 1-3: Simplified illustration of a plant cell.

The *cell wall* is composed of cellulose. Cellulose, like starch, is a polymer of glucose. The cell wall provides structure and rigidity.

The *large vacuole* serves as a warehouse for large starch molecules. Glucose, which is produced by photosynthesis, is converted to *starch,* a polymer of glucose. At some later time, this starch is available as an energy source. (Chapter 7 talks a lot more about glucose and other carbohydrates.)

Chloroplasts, present in green plants, are specialized chemical factories. These are the sites of photosynthesis, in which *chlorophyll* absorbs sunlight and uses this energy to combine carbon dioxide and water to produce glucose and release oxygen gas.

The green color of many plant leaves is due to the magnesium-containing compound chlorophyll.

Now that you know a little about cells, press on and let's do some biochemistry!

Chapter 2

Dive In: Water Chemistry

● ●

In This Chapter
▶ Understanding the roles and properties of water

▶ Exploring the differences between acids and bases

▶ Examining acid-base equilibria with the Brønsted-Lowry theory

▶ Controlling pH with buffers

● ●

*W*ater is one of the most important substances on earth. We swim, bathe, boat, and fish in it. It carries our waste from our homes and is used in the generation of electrical power. We drink it in a variety of forms: pure water, soft drinks, tea, coffee, margaritas, and so on. Water, in one form or another, moderates the temperature of the earth and of our bodies.

In the area of biochemistry, water is also one of the lead actors. Our bodies are about 70 percent water. Water plays a role in the transport of material to and from cells. And many, many aqueous solutions take part in the biochemical reactions in the body.

In this chapter, we examine the structure and properties of the water molecule. We explain how water behaves as a solvent. We look at the properties of acids and bases and the equilibria that they may undergo. Finally, we discuss the pH scale and buffers, including the infamous Henderson-Hasselbalch equation. Sit back, grab a glass of water, and dive in!

The Fundamentals of H_2O

Water is essential to life; in fact, human beings are essentially big sacks of water. Water accounts for 60–95 percent of our living cells, and 55 percent of the water in the human body is in intracellular fluids. The remaining 45 percent (extracellular) is divided between the following:

  ✔ Plasma (8 percent)

  ✔ Interstitial and lymph (22 percent)

  ✔ Connective tissue, cartilage, and bone (15 percent)

Water also is necessary as a solvent for the multitude of biochemical reactions that occur in the body:

- Water acts as a transport medium across membranes, carrying substances into and out of cells.
- Water helps maintain the temperature of the body.
- Water acts as a solvent (carrying dissolved chemicals) in the digestive and waste excretion systems.

Healthy humans have an intake/loss of about two liters of water per day. The intake is about 45 percent from liquids and 40 percent from food, with the remainder coming from the oxidation of food. The loss is about 50 percent from urine and 5 percent from feces, with the remainder leaving through evaporation from the skin and lungs. A water balance must be maintained within the body. If the loss of water significantly exceeds the intake, the body experiences dehydration. If the water loss is significantly less than the intake, water builds up in the body and causes *edema* (fluid retention in tissues).

# Let's get wet! Physical properties of water

The medium in which biological systems operate is water, and physical properties of water influence the biological systems. Therefore, it is important to review some properties of water that you learned in general chemistry.

Water is a polar molecule

Because it's *polar,* water has a tendency to "wet" substances, like grandma's fine dining-room table or a baby's diaper. It's also a *bent* molecule , not linear (see Figure 2-1). The hydrogen atoms have a partially positive charge ($\delta+$); the oxygen atom has a partially negative charge ($\delta-$). This charge distribution is due to the *electronegativity* difference between hydrogen and oxygen atoms (the attraction that an atom has for a bonding pair of electrons). The water molecule in Figure 2-1 is shown in its bent shape with a bond angle of about 105°.

Normally, such partial charges result in an intermolecular force known as a *dipole-dipole force,* in which the positive end of one molecule attracts the negative end of another molecule. The very high electronegativity of oxygen combined with the fact that a hydrogen atom has only one electron results in a charge difference significantly greater than you'd normally expect. This leads to stronger-than-expected intermolecular forces. These unexpectedly strong intermolecular forces have a special name: *hydrogen bonds.*

Figure 2-1:
Structure of
a water
molecule.

H $\diagup$ O $\diagdown$ H

REMEMBER
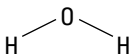
The term *hydrogen bond* doesn't refer to an actual bond to a hydrogen atom, but to the overall *interaction* of a hydrogen atom bonded to either oxygen, nitrogen, or fluorine atoms with an oxygen, nitrogen or fluorine on another molecule (intermolecular) or the same molecule (intramolecular). Hence the term *intermolecular force.* (Note that although hydrogen bonds occur when hydrogen bonds to fluorine, you don't normally find such combinations in biological systems.)

Water has strong intermolecular forces

Hydrogen bonds in oxygen- and nitrogen-containing molecules are very important in biochemistry because they influence reactions between such molecules and the structures of these biological molecules. The interaction between water and other molecules in which there may be an opportunity for hydrogen bonding explains such properties as solubility in water and reactions that occur with water as a solvent.

The term *hydrogen bond* doesn't refer to an actual bond to a hydrogen atom, but to an overall interaction.

REAL WORLD

One environmentally important consequence of hydrogen bonding is that, upon freezing, water molecules are held in a solid form that's less dense than the liquid form. The hydrogen bonds lock the water molecules into a crystalline lattice that contains large holes, which decreases the density of the ice. The less-dense ice — whether in the form of an ice cube or an iceberg — floats on liquid water. In nearly all other cases where a solid interacts with water, the reverse is true: The solid sinks in the liquid. So, why is the buoyancy of ice important? Ask ice fishermen! The layer of ice that forms on the surface of cold bodies of water insulates the liquid from the cold air, protecting the organisms still living under the ice.

Water has a high specific heat

Specific heat is the amount of heat required to change the temperature of a gram of water 1° Celsius. A high specific heat means it isn't easy to change the temperature of water. Water also has a high *heat of vaporization.* Humans can rid their bodies of a great deal of heat when their sweat evaporates from their skin, making sweat a very effective cooling method. We're sure you'll notice this cooling effect during your biochem exams.

REAL WORLD

As a result of water's high specific heat and heat of vaporization, lakes and oceans can absorb and release a large amount of heat without a dramatic change in temperature. This give and take helps moderate the earth's temperature and makes it easier for an organism to control its body temperature. Warm-blooded animals can maintain a constant temperature, and cold-blooded animals — including lawyers and some chemistry teachers — can absorb enough heat during the day to last them through the night.

Water's most important biochemical role: The solvent

The polar nature of water means that it attracts (soaks up) other polar materials. Water is often called *the universal solvent* because it dissolves so many types of substances. Many ionic substances dissolve in water, because the negative ends of the water molecules attracts the *cations* (positively charged ions) from the *ionic* compound (compound resulting from the reaction of a metal with a non-metal) and the positive ends attract the *anions* (negatively charged ions). Covalently bonded (resulting from the reactions between non-metals) polar substances, such as alcohols and sugars, also are soluble in water because of the dipole-dipole (or hydrogen-bonding) interactions. However, covalently bonded nonpolar substances, such as fats and oils are *not* soluble in water.
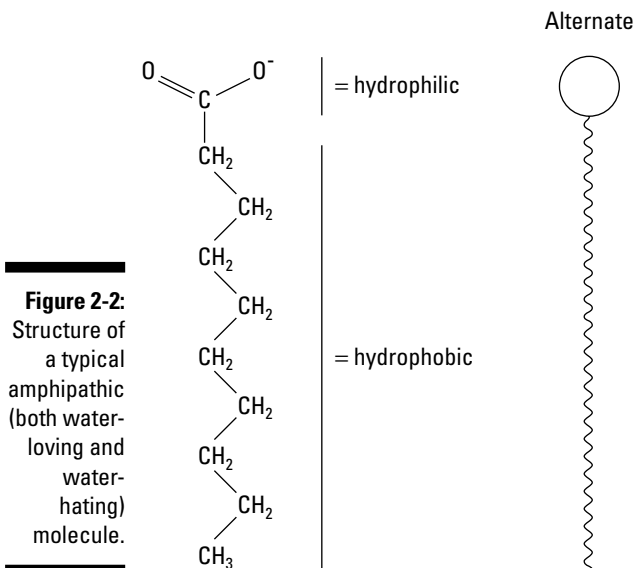
REMEMBER

Polar molecules, because of their ability to interact with water molecules, are classified as *hydrophilic* (water-loving). Nonpolar molecules, which don't appreciably interact with (dissolve in) water, are classified as *hydrophobic* (water-hating). Some molecules are *amphipathic* because they have both hydrophilic and hydrophobic regions.

Figure 2-2 shows the structure of a typical amphipathic molecule. The molecule appears on the left, with its hydrophilic and hydrophobic regions shown. The alternate portion of the figure is a symbolic way of representing the molecule. The round "head" is the hydrophilic portion, and the long "tail" is the hydrophobic portion.

Certain amphipathic molecules, such as soap molecules, can form *micelles,* or very tiny droplets that surround insoluble materials. This characteristic is the basis of the cleaning power of soaps and detergents. The hydrophobic portion of the molecule (a long hydrocarbon chain) dissolves in a nonpolar substance, such as normally insoluble grease and oil, leaving the hydrophilic portion (commonly an ionic end) out in the water. Soap or detergent breaks up the grease or oil and keeps it in solution so it can go down the drain.

A micelle behaves as a large polar molecule (see Figure 2-3). The structure of a micelle is closely related to the structure of cell membranes.

Alternate

= hydrophilic

= hydrophobic

O O^-
C
CH_2
CH_2
CH_2
CH_2
CH_2
CH_2
CH_2
CH_2
CH_3

Figure 2-2:
Structure of
a typical
amphipathic
(both water-
loving and
water-
hating)
molecule.

Figure 2-3:
Structure of
a micelle,
composed
of
amphipathic
molecules,
with their
hydrophilic
"heads"
pointing
"out."

polar
(water)

nonpolar

hydrophilic head

hydrophobic tail
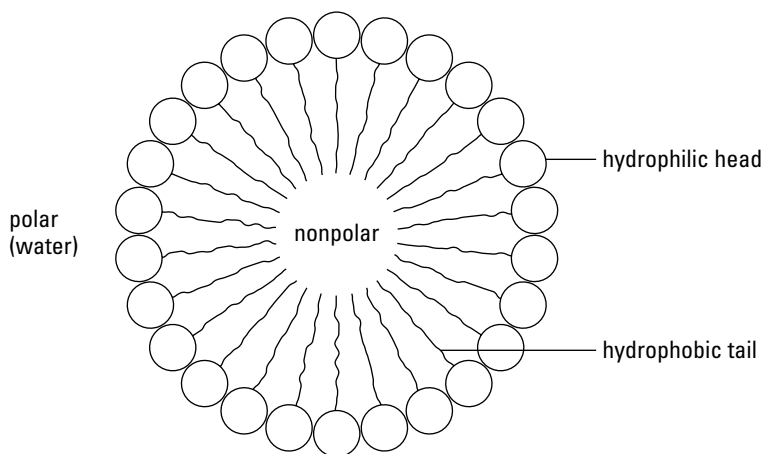
Hydrogen Ion Concentration: Acids and Bases

In aqueous solutions — especially in biological systems — the concentration of hydrogen ions (H^+) is very important. Biological systems often take great pains to make sure that their hydrogen ion concentration — represented as [H^+] or by the measurement of pH (the measure of acidity in a solution) — doesn't change.

Even minor changes in hydrogen ion concentration can have dire consequences to a living organism. For example, in our blood, only a very small range of hydrogen ion allows the body to function properly. Hydrogen ion concentrations higher or lower than this range can cause death.

Because living organisms are so dependent on pH, let's take a few moments to review the concepts of acids, bases, and pH.
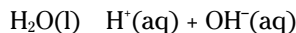
Achieving equilibrium

When the concentrations of hydrogen ion (H^+) and hydroxide ion (OH^-) are the same, the solution is *neutral.* If the hydrogen ion concentration exceeds the hydroxide ion concentration, the solution is *acidic.* If the hydroxide ion concentration is greater, the solution is *basic.* These chemical species are related through a chemical equilibrium.

REAL WORLD

Acidic solutions, such as lemon juice, taste sour. Basic solutions, such as tonic water, taste bitter. (The addition of gin doesn't change the bitter taste!)

The equilibrium of hydrogen ions is present in all aqueous solutions. It may or may not be the major hydrogen ion source (usually it isn't). Water is a contributor to the hydrogen ion concentration because it undergoes *autoionization*, as shown by the following equation:

$$H_2O(l) \quad H^+(aq) + OH^-(aq)$$

You often see $H^+(aq)$ represented as H_3O^+.

The double arrow ( ) indicates that this is an equilibrium; as such, there must be an associated *equilibrium constant* (K). The equilibrium constant in the preceding equation is K_w. The value of K_w is the product of the concentrations of the hydrogen ion and the hydroxide ion:

$$K_w = [H^+] [OH^-] = 1.0 \times 10^{-14} \text{ (at } 25°C)$$

The value of the constant K_w, like all Ks, is only constant if the temperature is constant. In the human body, where T = 37°C, $K_w = 2.4 \times 10^{-14}$.

In pure water, at 25°C, $[H^+] = 1.0 \times 10^{-7}$ M (1.6×10^{-7} M at 37°C). The hydroxide ion concentration is the same as the hydrogen ion concentration, because they are formed in equal amounts during the autoionization reaction.

REMEMBER

M is a concentration term, the molarity. *Molarity* is the number of moles of solute per liter of solution.

Sour and bitter numbers: The pH scale

It isn't always convenient to report hydrogen ion concentrations in an exponential form, such as 1.0×10^{-7}. Thankfully, you have a way of simplifying the representation of the hydrogen ion concentration: the pH. You can calculate the pH for any solution by using the following equation:

$$pH = -\log [H^+]$$

For instance, in the case of a solution with a hydrogen ion concentration of 1.0×10^{-7} M, the pH would be

$$pH = -\log (1.0 \times 10^{-7}) = 7.0$$

Table 2-1 gives similar calculations for my hydrogen ion concentrations.

Table 2-1	The pH Scale and the Associated Hydrogen Ion Concentration	
[H⁺]	*pH*	*Solution Property*
1.0×10^{0} M	0	Acidic
1.0×10^{-1} M	1	Acidic
1.0×10^{-2} M	2	Acidic
1.0×10^{-3} M	3	Acidic
1.0×10^{-4} M	4	Acidic
1.0×10^{-5} M	5	Acidic
1.0×10^{-6} M	6	Acidic
1.0×10^{-7} M	7	**Neutral**
1.0×10^{-8} M	8	Basic
1.0×10^{-9} M	9	Basic
1.0×10^{-10} M	10	Basic
1.0×10^{-11} M	11	Basic
1.0×10^{-12} M	12	Basic
1.0×10^{-13} M	13	Basic
1.0×10^{-14} M	14	Basic

REMEMBER

If a solution has a pH less than 7, it's acidic. Solutions with a pH greater than 7 are basic. Solutions whose pH is 7 are neutral. The pH of pure water is 7. Be careful, though: Not every solution that has a pH of 7 is pure water! For example, if you add table salt to water, the pH will remain at 7, but the resulting solution is certainly not pure water.

The pH scale is an open-ended scale, meaning you can have a pH greater than 14 or less than 0. For example, the pH of a 1.0×10^1 M solution of hydrochloric acid is –1. John loves to ask questions based on this topic to his advanced chemistry students! The 0–14 scale is a convenient part of the pH scale for most real-world solutions — especially ones found in biochemistry. Most biological systems have a pH near 7, although significant deviations may exist (the pH in your stomach is close to 1).

Calculating pOH

You can calculate pOH in a similar manner to the pH calculation. That is, you can use the equation pOH = –log [OH⁻]. You can calculate the hydroxide ion concentration from the hydrogen ion concentration and the K_w (equilibrium constant) relationship:

$$[OH^-] = K_w \div [H^+]$$

TIP

A useful shortcut to get from pH to pOH is the following relationship: pH + pOH = 14.00 for any aqueous solution ($14.00 = pK_w = -\log K_w = -\log 1.0 \times 10^{-14}$).

For example, if a solution has a $[H^+] = 6.2 \times 10^{-6}$, its pH would be

pH = –log [H⁺]

pH = –log [6.2×10^{-6}]

pH = 5.21

The calculation for the pOH of that solution becomes pretty simple: 14.00 – pH = 14.00 – 5.21 = 8.79.

Now, if you have the pH or pOH, getting the corresponding [H⁺] or [OH⁻] becomes a pretty simple task:

$$[H^+] = 10^{-pH} \text{ and } [OH^-] = 10^{-pOH}$$

For example, a solution with a pH of 7.35 has a $[H^+] = 10^{-7.35} = 2.2 \times 10^{-7}$.

Strong and weak: Brønsted-Lowry theory

Since the acidity (pH) of the biological medium is so very important, let's take a look at one of the most accepted theories concerning acids and bases – the Brønsted-Lowry theory. According to this theory, acids are proton (H^+) donors, and bases are proton acceptors.

Strong and weak acids

Acids increase the hydrogen ion concentration of a solution (they lower the pH, in other words). Some acids, known as *strong acids,* are very efficient at changing hydrogen ion concentration; they essentially completely ionize in water. Most acids — particularly biologically important acids — aren't very efficient at generating hydrogen ions; they only partially ionize in water. These acids are known as *weak acids.*

Bases accept (react with) rather than donate hydrogen ions in solutions. Bases decrease the hydrogen ion concentration in solutions because they react with these ions. Strong bases, although they can accept hydrogen ions very well, aren't too important in biological systems. The majority of biologically important bases are weak bases.

REMEMBER

The Brønsted-Lowry theory helps to explain the behavior of acids and bases with respect to equilibrium. A Brønsted-Lowry acid is a hydrogen ion (H^+) donor, and a Brønsted-Lowry base is a hydrogen ion acceptor. Acetic acid, a weak acid found in vinegar, partially ionizes in solution, evidenced by the following equation:

$$CH_3COOH \quad H^+ + CH_3COO^-$$

The double arrow indicates that the acetic acid doesn't completely ionize. (For a strong acid, complete ionization would occur, and a single arrow would be present.) The equilibrium arrow ( ) indicates that all three chemical species are present in the solution: the acetic acid, the acetate ion, and the hydrogen ion, along with the water solvent.

In the Brønsted-Lowry theory, you consider the acetate ion to be a base because it can accept a hydrogen ion to become acetic acid. According to this theory, two substances differing by only one hydrogen ion — such as acetic acid and the acetate ion — are members of a *conjugate acid-base pair*. The species with one additional hydrogen ion is the *conjugate acid* (CA), and the species with one less hydrogen ion is the *conjugate base* (CB).

TIP

You can express the equilibrium from the acetate example, like all equilibria, by using a *mass-action expression* — as long as a balance among the species is present. This expression is also known as a *reaction quotient* and as an *equilibrium constant.* For acetic acid, this expression is as follows:

$$K_a = \frac{[H^+][CH_3COO^-]}{[CH_3COOH]}$$

The *a* subscript means that this expression represents an acid. The square brackets refer to the molar equilibrium concentrations of the species present. You can express the K_a as a pK_a. The calculation of pK_a is similar to the calculation of pH:

$$pK_a = -\log K_a$$

In terms of conjugate acids and bases, every K_a expression appears as

$$K_a = \frac{[H^+][CB]}{[CA]}$$

REMEMBER

No variations are allowed in this equation other than the actual formulas of the conjugate acid and base.

Like an acid, a base has a K_b value (the subscript *b* meaning base). A weak base, like ammonia, is part of the following equilibrium:

$$NH_3 + H_2O \quad OH^- + NH_4^+$$

The equilibrium constant expression for this equilibrium is

$$K_b = \frac{[OH^-][NH_4^+]}{[NH_3]}$$

The generic form of a K_b expression is

$$K_b = \frac{[OH^-][CA]}{[CB]}$$

As with a K_a expression, a K_b expression has no variations other than the actual formulas of the conjugate acid and base.

Every conjugate acid has a K_a, and its corresponding conjugate base has a K_b. The K_a and the K_b of a conjugate acid-base pair are related by the K_w— the ionization constant for water. For a conjugate acid-base pair, $K_a K_b = K_w = 1.0 \times 10^{-14}$. In addition, you can use the following shortcut: $pK_a + pK_b = 14.00$.

The K_b for the acetate ion, the conjugate base of acetic acid, is

$$CH_3COO^- + H_2O \quad OH^- + CH_3COOH$$
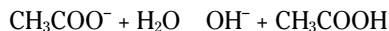
The K_a for the ammonium ion, the conjugate acid of ammonia, is

$$NH_4^+ \quad H^+ + NH_3$$

An acid may be capable of donating more than one hydrogen ion. A biologically important example of this type of acid is phosphoric acid (H_3PO_4), which is a triprotic acid (meaning that it can donate three hydrogen ions). This acid is capable of donating three hydrogen ions, one at a time. The equilibria for this acid are

$$\mathbf{K_{a1}:} \; H_3PO_4 \quad H^+ + H_2PO_4^-$$

$$\mathbf{K_{a2}:} \; H_2PO_4^- \quad H^+ + HPO_4^{2-}$$
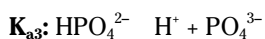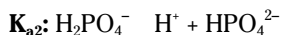
$$\mathbf{K_{a3}:} \; HPO_4^{2-} \quad H^+ + PO_4^{3-}$$

The subscripts are modified to indicate the loss of hydrogen 1, hydrogen 2, or hydrogen 3. The associated K_a expressions are all of the form

$$K_a = \frac{[H^+][CB]}{[CA]}$$

Here's the breakdown for each K_a:

$$K_{a_1} = \frac{[H^+][H_2PO_4^-]}{[H_3PO_4]}$$

$$K_{a_2} = \frac{[H^+][HPO_4^{2-}]}{[H_2PO_4^-]}$$

$$K_{a_3} = \frac{[H^+][PO_4^{3-}]}{[HPO_4^{2-}]}$$

REMEMBER

The value for each successive equilibrium constant often is significantly lower than the preceding value. Table 2-2 runs through some biologically important acids. You can refer to this table when working buffer problems or determining which acid is stronger.

Table 2-2	The K_a Values for Biologically Important Acids		
Acid	K_{a1}	K_{a2}	K_{a3}
Acetic acid (CH_3COOH)	1.7×10^{-5}		
Pyruvic acid ($CH_3COCOOH$)	3.2×10^{-3}		
Lactic acid ($CH_3CHOHCOOH$)	1.4×10^{-4}		
Succinic acid ($HOOCCH_2CH_2COOH$)	6.2×10^{-5}	2.3×10^{-6}	
Carbonic acid (H_2CO_3)	4.5×10^{-7}	5.0×10^{-11}	
Citric acid ($HOOCCH_2C(OH)(COOH)CH_2COOH$)	8.1×10^{-4}	1.8×10^{-5}	3.9×10^{-6}
Phosphoric acid (H_3PO_4)	7.6×10^{-3}	6.2×10^{-8}	2.2×10^{-13}

Acid or base? They just can't decide

Some substances can't make up their minds about what they are; they can act as either an acid or a base. Chemists classify these substances as *amphiprotic* or *amphoteric* substances. For example, the bicarbonate ion (HCO_3^-) can act as either an acid or a base:

$HCO_3^- \quad H^+ + CO_3^{2-}$

$HCO_3^- + H_2O \quad OH^- + H_2CO_3$

Biochemically important molecules may also exhibit amphiprotic behavior. Amino acids contain both a basic amine ($-NH_2$) group and an acidic carboxyl ($-COOH$) group. Therefore, they can act as either acids or bases. For example, glycine (H_2N-CH_2-COOH) may undergo the following reactions:

$H_2N-CH_2-COOH \quad H^+ + H_2N-CH_2-COO^-$

$H_2N-CH_2-COOH + H_2O \quad OH^- + {}^+H_3N-CH_2-COOH$
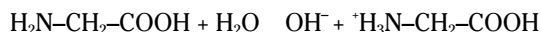
In fact, amino acids may undergo proton transfer from the carboxyl end to the amine end, forming an overall neutral species that has a positive and negative end. Species such as these are called *zwitterions:*

$$H_2N–CH_2–COOH \quad {}^+H_3N–CH_2–COO^-$$

Buffers and pH Control

A solution that contains the conjugate acid-base pair of any weak acid or base is a *buffer solution.* A buffer solution resists changes in pH when either an acid or a base is added. Therefore, buffers control the pH of the solution. Buffer solutions are important in most biological systems. Many biological processes proceed effectively only within a limited pH range. The presence of buffer systems keeps the pH within this limited range.

Identifying common physiological buffers

In the human body, the pH of various body fluids is important. The pH of blood is 7.4, the pH of stomach acid is 1–2, and the pH in the intestinal tract is 8–9. If the pH of blood is more than 0.2 pH units lower than normal, a condition known as *acidosis* results; a corresponding increase in pH is *alkalosis.* Acidosis and alkalosis may lead to serious health problems. There are two general causes of acidosis and of alkalosis:

✔ Respiratory acidosis is the result of many diseases that impair respiration. These diseases include pneumonia, emphysema, and asthma. These diseases lead to inefficient expulsion of carbon dioxide. This leads to an increase in the concentration of the acid H_2CO_3.

✔ Metabolic acidosis is due to a decrease in the concentration of HCO_3^-. This may be the results of certain kidney diseases, uncontrolled diabetes, and cases of vomiting involving nonacid fluids. Poisoning by an acid salt may also lead to metabolic acidosis.

✔ Respiratory alkalosis may be the result of hyperventilation, as there is an excessive removal of carbon dioxide, which leads to a decrease in the H_2CO_3 concentration. Immediate treatment may include breathing into a paper bag, thus increasing the carbon dioxide concentration in the inhaled air and therefore in the blood.

✔ Metabolic alkalosis may result from excessive vomiting of stomach acid.

To resist these pH problems, the blood has a number of buffer systems. These include several proteins in blood plasma and the bicarbonate buffer system.

The *bicarbonate buffer system* is the main extracellular buffer system. This system also provides a means of eliminating carbon dioxide. The dissolution of carbon dioxide in aqueous systems sets up the following equilibria:

$$CO_2 + H_2O \quad H_2CO_3 + H^+ + HCO_3^-$$

The presence of the conjugate acid-base pair (H_2CO_3 and HCO_3^-) means this is a buffer system. The conjugate acid-base ratio is about 20:1 at a pH of 7.4 in the bloodstream. This buffer system is coupled with the following equilibrium (nstrumental in the removal of carbon dioxide in the lungs):

$$CO_2(blood) \quad CO_2(g)$$
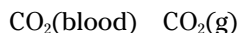
The second ionization of phosphoric acid, K_{a2}, is the primary intracellular buffer system. The pH of this conjugate acid-base pair ($H_2PO_4^-$ and HPO_4^{2-}) is 7.21 for a solution with equal concentrations of these two species.

Calculating a buffer's pH

To determine a buffer's pH, you may use a K_a or K_b calculation, discussed previously, or the Henderson-Hasselbalch equation, which gives a shortcut.

There are two forms of the Henderson-Hasselbalch equation:

$$pH = pK_a + \log \frac{[CB]}{[CA]}$$

and

$$pOH = pK_b + \log \frac{[CA]}{[CB]}$$

The terms in either form are the same as defined earlier. For example, suppose we wanted to calculate the pH of a buffer composed of 0.15 M pyruvic acid and 0.25 M sodium pyruvate. Looking at Table 2-2, you see that the K_a of pyruvic acid is 3.2×10^{-3}.

The pK_a would be 2.50. Therefore:

$$pH = pK_a + \log \frac{[CB]}{[CA]}$$

$$pH = -\log 3.2 \times 10^{-3} + \log \frac{[CH_3COCOO^-]}{[CH_3COCOOH]}$$

$$pH = 2.50 + \log \frac{[.25]}{[.15]}$$

$$pH = 2.50 + \log (1.67)$$

$$pH = 2.50 + 0.22 = 2.72$$

REMEMBER

The greater the values of [CA] and [CB], the greater the buffer capacity of the solution is. The buffer capacity indicates how much acid or base may be added to a buffer before the buffer ceases to function.

Chapter 3

Fun with Carbon: Organic Chemistry

*M*ost biologically important molecules are composed of *organic compounds,* which means compounds of carbon. Therefore, the student of biochemistry must have a general knowledge of organic chemistry, which is the study of carbon compounds, in order to understand the function and reactions of biochemical molecules. In this chapter we review the basics of organic chemistry, including the various functional groups and isomers that are important in the field of biochemistry.

The Role of Carbon in the Study of Life

Long ago, scientists believed that all carbon compounds were the result of biological processes, which meant organic chemistry was synonymous with biochemistry under this Vital Force theory. In the mid-1800s, though, researchers debunked that long-held notion — the synthesis of urea from inorganic materials showed that there were other paths to the production of carbon compounds. Organic chemists now synthesize many important organic chemicals without the use of living organisms; however, biosynthesis is still an important source of many organic compounds.

Why are there so many carbon compounds? The answer lies primarily in two reasons, both tied to carbon's versatility in creating stable bonds:

✓ **Carbon bonds to itself.** Carbon atoms are capable of forming stable bonds to other carbon atoms. The process of one type of atom bonding to identical atoms is *catenation*. Many other elements can catenate, but carbon is the most effective at it. There appears to be no limit to how many carbon atoms can link together. These linkages may be in chains, branched chains, or rings, as shown in Figure 3-1.

✓ **Carbon bonds to other elements.** Carbon is capable of forming stable bonds to a number of other elements. These include the biochemically important elements hydrogen, nitrogen, oxygen, and sulfur. The latter three elements form the foundation of most of the *functional groups* (reactive groups of a molecule) necessary for life. Bonds between carbon and hydrogen are usually unreactive under biochemical conditions; thus, hydrogen often serves as an "inert" substituent.

It's All in the Numbers: Carbon Bonds

REMEMBER

Carbon is capable of forming four bonds. In bonding to itself and other elements, carbon uses a variety of types of *hybridization* — when it bonds to another carbon molecule, for example, these may have four single bonds, a double and two single bonds, two double bonds, or a triple and a single bond. Double bonds to oxygen atoms are particularly important in many biochemicals. Table 3-1 shows the number of bonds carbon may have with some selected non-metals, along with the hybridization of those bonds.

Figure 3-1:
Top: straight chain hydro-carbon, expanded and condensed. Middle: branched chain hydro-carbon. Bottom: ring hydro-carbon.

hexane

hexane

2-methylhexane

cyclohexane
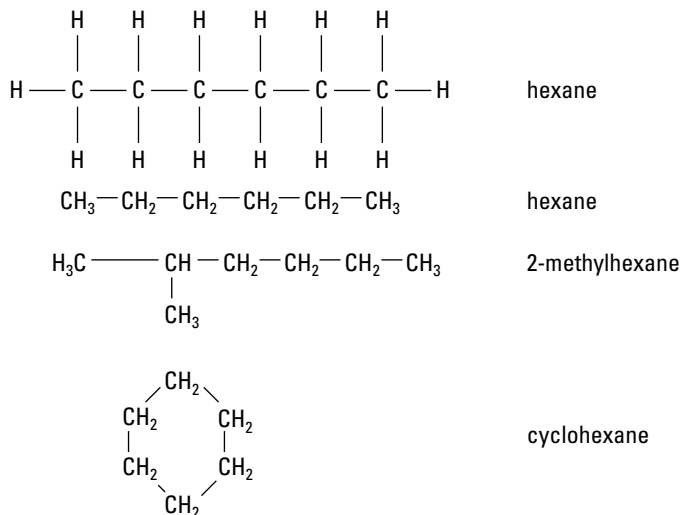
Table 3-1	Possible Bonds of Carbon and Selected Non-metals	
Element	*Number of Possible Bonds with Carbon*	*Some Possible Hybridizations for Second Period Elements*
Carbon (C)	4	4 single (sp^3) 2 single and one double (sp^2) 1 single and one triple (sp) 2 doubles (sp)
Nitrogen (N)	3	3 single (sp^3) 1 single and 1 double (sp^2) 1 triple (sp)
Oxygen (O)	2	2 single (sp^3) 1 double (sp^2)
Sulfur (S)	2	2 single (sp^3) 1 double (sp^2)
Hydrogen (H)	1	1 single
Fluorine (F)	1	1 single
Chlorine (Cl)	1	1 single
Bromine (Br)	1	1 single
Iodine (I)	1	1 single

Sticky Chemistry: Bond Strengths

Covalent bonds are important *intramolecular forces* (forces within the same molecule) in biochemistry. *Intermolecular forces* (forces between chemical species) are also extremely important. Among other things, intermolecular forces are important to hydrophilic (water-loving) and hydrophobic (water-hating) interactions.

Everybody has 'em: Intermolecular forces

All intermolecular forces are *van der Waals forces,* that is they are not true bonds in the sense of sharing or transferring electrons, but are weaker attractive forces. These forces include dipole-dipole forces, hydrogen bonding, and ionic interactions.

Dipole-dipole forces

Dipole-dipole forces exist between polar regions of different molecules. The presence of a dipole means that the molecule has a partially positive ($\delta+$) end and a partially negative ($\delta-$) end. Opposite partial charges will attract each other, whereas like partial charges will repel. In most cases, biological systems utilize a special type of dipole-dipole force known as *hydrogen bonding* (see next section).

Hydrogen bonding

Hydrogen bonding, as the name implies, involves hydrogen. The hydrogen atom must be bonded to either an oxygen atom or a nitrogen atom. (In nonbiological situations, hydrogen bonding also occurs when a hydrogen atom bonds to a fluorine atom.) Hydrogen bonding is significantly stronger than a "normal" dipole-dipole force and is very much stronger than London dispersion forces (very weak and short-lived attractions between molecules that arise due to the nucleus of one atom attracting the electron cloud of another atom). The hydrogen that is bonded to either a nitrogen or oxygen atom is strongly attracted to a different nitrogen or oxygen atom. Hydrogen bonding may be either intramolecular or intermolecular.

Ionic interactions

In biological systems, ionic interactions may serve as intermolecular or intramolecular forces. In some cases, these may involve metal cations, such as Na^+, or anions, such as Cl^-. In many cases, the cation is an ammonium ion from an amino group, such as RNH_3^+; the anion may be from a carboxylic acid, such as $RCOO^-$. Oppositely charged ions attract each other strongly.

Water-related interactions: Both the lovers and the haters

The predominant factor leading to hydrophobic (water-hating) interactions is the presence of portions of a molecule containing only carbon and hydrogen. Hydrocarbon regions are nonpolar and are attracted to other nonpolar regions by London dispersion forces.

REMEMBER

In general, the presence of any atom other than carbon and hydrogen makes a region polar. Oxygen and nitrogen are the most effective elements in biochemistry for making a region of a molecule polar. Sulfur is least effective of the common biologically important elements at imparting polar character. Dipole-dipole, hydrogen bonding, and ionic interactions are all hydrophilic interactions. London dispersion forces are hydrophobic interactions.

The more carbon and hydrogen atoms, without other atoms, the more important the hydrophobic nature of a region becomes in defining the properties of the molecule. Note that a molecule may have both a hydrophilic and a hydrophobic region, and both regions are important to the behavior of the molecule. The formation of a micelle is an example of using molecules with both hydrophilic and hydrophobic regions.

How bond strengths affect physical properties of substances

The physical properties of biological substances depend on the intermolecular forces present. The sequence of strength is: ions > hydrogen bonding > dipole-dipole > London. The strongest types of intermolecular forces involve ions. Next strongest is hydrogen bonding. Polar substances interact through dipole-dipole forces, which are weaker than hydrogen bonds. All biological substances containing oxygen, nitrogen, sulfur, or phosphorus are polar. London forces, the weakest intermolecular forces, are important in nonpolar situations. The hydrocarbon portion of biological molecules is nonpolar.

Melting points, boiling points, and solubility

As the strength of forces decreases, so do the melting points, boiling points, and solubility in water. Besides that, the vapor pressure and the solubility in nonpolar solvents also increases.

Substances that have a high solubility in water are hydrophilic, and substances with a low solubility in water are hydrophobic.

A molecule may have both hydrophilic and hydrophobic regions. The region that represents a greater portion of the molecule will predominate. For this reason, for example, CH_3COOH is more hydrophilic than $CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2COOH$. In addition, $HOCH_2CH_2CH_2CH_2CH_2CH_2OH$ is more hydrophilic than $CH_3CH_2CH_2CH_2CH_2CH_2OH$.

Odors

Many functional groups have distinctive odors. Small carboxylic acids smell like acetic acid (vinegar), while larger ones have unpleasant odors. Most esters, if volatile, have pleasant odors — that is why esters are used extensively in the flavor and perfume industry. Most sulfur-containing compounds have strong unpleasant odors. Small amines have an ammonia odor, whereas larger amines have a fishy odor or worse.

Defining a Molecule's Reactivity: Functional Groups

Most carbon compounds have one or more reactive sites composed of a specific grouping of atoms in their structure. It is at these sites that chemical reactions occur. These specific grouping of atoms that react are called *functional groups.* These functional groups contain atoms other than carbon and hydrogen and/or double or triple bonds and define the reactivity of the organic molecule.

Hydrocarbons

Alkanes are hydrocarbons — compounds containing only carbon and hydrogen, with no traditional functional groups. For this reason, they are not very reactive. *Alkenes* and *alkynes* are also hydrocarbons. They contain a carbon-carbon double and triple bond, respectively. The presence of more than one bond makes them more reactive. *Aromatic hydrocarbons,* normally ring structures with alternating single and double carbon-to-carbon bonds, contain one or more *aromatic systems*, which are much less reactive than other systems containing double bonds. Alkynes are not very common in biological systems. Figure 3-2 shows the structure of these compounds.

Figure 3-2:
Examples
of alkanes,
alkenes,
alkynes, and
aromatic
hydro-
carbons.

CH_3—CH_2—CH_2—CH_2—CH_2—CH_3 alkane

CH_3—CH=CH—CH_2—CH_2—CH_3 alkene

CH_3—C≡C——CH_2—CH_2—CH_3 alkyne

aromatic
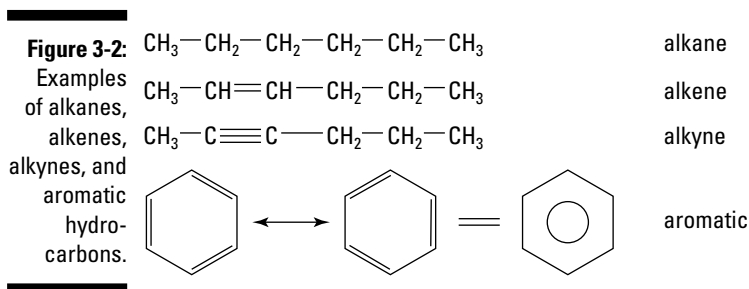
Functional groups with oxygen and sulfur

Many functional groups contain oxygen, including alcohols, ethers, aldehydes, and ketones, which appear in carbohydrates. In carbohydrates, many ether groups are known as *glycoside linkages*. In addition, carboxylic acids and esters are important functional groups that appear as fatty acids and in fats and oils.
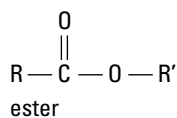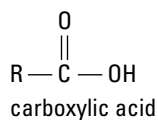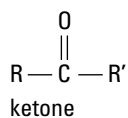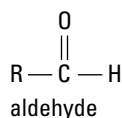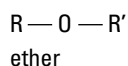
Alcohols and ethers contain only singly bonded oxygen atoms. An alcohol group attached to an aromatic ring is a phenol. Aldehydes and ketones contain only doubly bonded oxygen atoms. Carboxylic acids and esters contain both singly and doubly bonded oxygen atoms. The combination of a carbon atom connected to an oxygen atom by a double bond is a carbonyl group.

Sulfur, the element immediately below oxygen on the periodic table, may replace oxygen in both alcohols and ethers to give *thiols* (mercaptans) and *thioethers.* Many of these sulfur-containing compounds really stink! Sulfur may also form a disulfide where there is a bond between two sulfur atoms. Figure 3-3 illustrates these compounds.

R = any organic (hydrocarbon) group

R' = any organic group, which may or may not = R

R — OH
alcohol

R — O — R'
ether

$$O$$
$$\|$$
R — C — H
aldehyde

$$O$$
$$\|$$
R — C — R'
ketone

$$O$$
$$\|$$
R — C — OH
carboxylic acid

$$O$$
$$\|$$
R — C — O — R'
ester
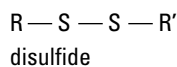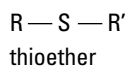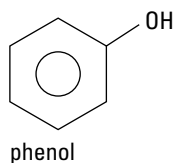
Figure 3-3:
Oxygen-
and sulfur-
containing
functional
groups.

phenol

R — SH
thiol

R — S — R'
thioether

R — S — S — R'
disulfide

Functional groups containing nitrogen

Amines and amides are two important functional groups containing nitrogen. *Amines* are present in amino acids and alkaloids. *Amides* are present in proteins, where they are known as *peptide bonds*.

The difference between an amine and an amide is that amides have a carbonyl group adjacent to the nitrogen atom. Amines are derivatives of ammonia, NH_3, where one or more organic groups replace hydrogen atoms. In a *primary amine,* an organic group replaces one hydrogen atom. In *secondary* and *tertiary amines,* two and three organic groups, respectively, replace two or three hydrogen atoms. Figure 3-4 shows these compounds.
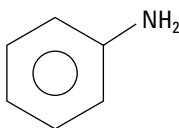
H — N — H
    |
    H
ammonia

R — N — H
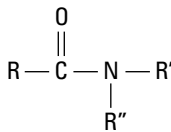 |
    H
primary amine

R — N — H
    |
    R'
secondary amine
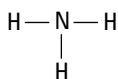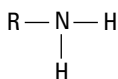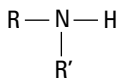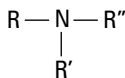
R — N — R''
    |
    R'
tertiary amine

Figure 3-4:
Some nitrogen-containing functional groups.

aniline

     O
     ||
R — C — N — R'
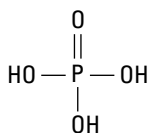 |
        R''
amide

Alkaloids are basic compounds produced by plants. Examples include nicotine, caffeine, and morphine.

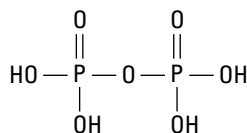## Functional groups containing phosphorus

Phosphorus is also an important element in biological systems and is normally present as part of a phosphate group. Phosphate groups come from phosphoric acid, H_3PO_4. The phosphate groups may be alone, part of a diphosphate, part of a triphosphate, or part of a phosphate ester.
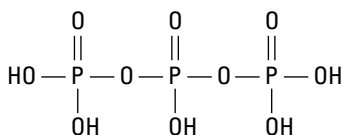
Phosphates appear in teeth and bone and are a part of the energy transport molecules ATP and ADP (see Chapter 12 for more on these). Figure 3-5 illustrates phosphorous-containing functional groups.
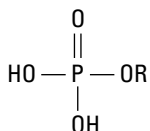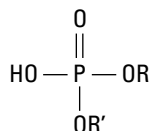
```
        O
        ||
HO — P — OH
        |
        OH
```
phosphoric acid

```
        O         O
        ||        ||
HO — P — O — P — OH
        |         |
        OH        OH
```
diphosphoric acid

```
        O         O         O
        ||        ||        ||
HO — P — O — P — O — P — OH
        |         |         |
        OH        OH        OH
```
triphosphoric acid

```
        O
        ||
HO — P — OR
        |
        OH
```
monophosphate ester

```
        O
        ||
HO — P — OR
        |
        OR′
```
diphosphate ester

Figure 3-5: Phosphate-containing functional groups.
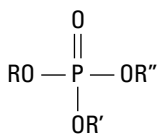
```
        O
        ||
RO — P — OR″
        |
        OR′
```
triphosphate ester

Reactions of functional groups

As you study the different biochemical molecules and their functions within the living organism, you see that the way a certain molecule reacts is primarily determined by the functional groups in the molecule's structure. Take a few minutes and refresh your organic chemistry knowledge about the typical reactions of the various functional groups.

Alcohols

Alcohols are subject to oxidation. Mild oxidation of a primary alcohol (where the –OH is attached to an end carbon) produces an aldehyde, which may undergo further oxidation to a carboxylic acid. Under similar conditions, a secondary alcohol (–OH is attached to a carbon bonded to two other carbons) will yield a ketone, and a tertiary alcohol (–OH attached to a carbon bonded to three other carbons) will not react. This behavior is important in the chemistry of many carbohydrates.
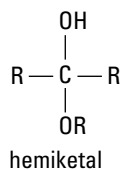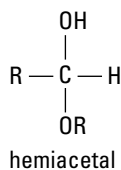
REMEMBER

The presence of the OH leads people mistakenly to assume that alcohols are bases. Nothing could be further from the truth! Alcohols, under biological conditions, are neutral compounds. Phenols, though, are weak acids.
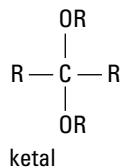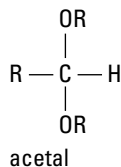
Aldehydes and ketones

Aldehydes easily undergo oxidation to carboxylic acids, but ketones do not undergo mild oxidation. With difficulty, it is possible to reduce aldehydes and ketones back to the appropriate alcohols.

Reducing sugars behave as such due to mild oxidation of the carbonyl groups present. Tollen's test uses silver nitrate, in which a reducing sugar generates a silver mirror on the walls of the container. Both Benedict's and Fehling's tests use copper compounds, and a reducing sugar produces a red precipitate with either of these tests. These simple organic qualitative tests find some use in biochemical tests described later in this book.

The carbonyl group of an aldehyde or ketone may interact with an alcohol to form acetals and hemiacetals. (Modern terminology only uses the terms acetals and hemiacetals — you may sometime see the terms *hemiketal,* which is a type of hemiacetal, and *ketal,* a type of acetal.) See Figure 3-6 for an illustration of these.

$$
\begin{array}{c}
OH \\
| \\
R - C - H \\
| \\
OR
\end{array}
\qquad
\begin{array}{c}
OH \\
| \\
R - C - R \\
| \\
OR
\end{array}
$$

hemiacetal   hemiketal

Figure 3-6:
Acetals,
hemiacetals,
hemiketals,
and ketals.

$$
\begin{array}{c}
OR \\
| \\
R - C - H \\
| \\
OR
\end{array}
\qquad
\begin{array}{c}
OR \\
| \\
R - C - R \\
| \\
OR
\end{array}
$$

acetal   ketal

Carboxylic acids

TIP

Carboxylic acids, along with phosphoric acid, are the most important biological acids. Carboxylic acids react with bases such as the amines to produce salts. The salts contain an ammonium ion from the amine and a carboxylate ion from the acid.

Carboxylic acids combine with alcohols to form esters and can indirectly combine with amines to form amides. Hydrolysis of an ester or an amide breaks the bond and inserts water. An acid, base, or enzyme is needed to
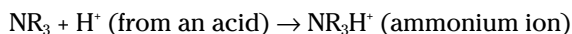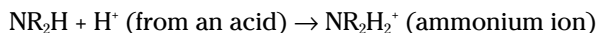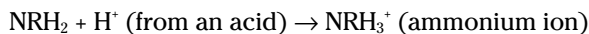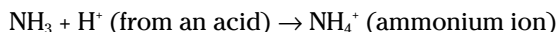
catalyze it. Under acidic conditions, it is possible to isolate the acid and either the alcohol or the ammonium ion from the amine. Under basic conditions, you can isolate the carboxylate ion and either the alcohol or the amine.

Thiols and amines

Under mild oxidation, two thiols join to form a disulfide. Mild reducing conditions, catalyzed by enzymes, reverse this process. Such formation of disulfide linkages is important in the chemistry of many proteins, such as insulin.

TIP

Amines are the most important biological bases. As bases, they can react with acids. The behavior is related to the behavior of ammonia.

$NH_3 + H^+$ (from an acid) $\rightarrow NH_4^+$ (ammonium ion)

$NRH_2 + H^+$ (from an acid) $\rightarrow NRH_3^+$ (ammonium ion)

$NR_2H + H^+$ (from an acid) $\rightarrow NR_2H_2^+$ (ammonium ion)

$NR_3 + H^+$ (from an acid) $\rightarrow NR_3H^+$ (ammonium ion)

REAL WORLD

Many medications have amine groups. In order to make them more readily soluble, it is necessary to convert many of these amines to ammonium ions. For example, the reaction of the medication with hydrochloric acid forms the chloride, which often appears on the label as the hydrochloride.

It is possible to replace all the hydrogen atoms from an ammonium ion, NH_4^+, to produce a quaternary ammonium ion, NR_4^+.

Phosphoric acid

Phosphoric acid, H_3PO_4, may behave like a carboxylic acid and form esters. The esters will have an organic group, R, replacing one, two, or three of the hydrogen atoms. The resultant compounds are monoesters, diesters, and triesters. The hydrogen atoms remaining in the mono- and diesters are acidic.

pH and functional groups

Many of the biological functions of substances are pH dependent. For this reason, it is important to know which functional groups are acidic, basic, or neutral. Neutral functional groups behave the same no matter what the pH is. Table 3-3 lists the functional groups and whether or not they are acidic, neutral, or basic. In addition, we list whether they are of medium weakness, weak, or very weak. The weaker a substance in terms of pH, the less likely it will be affected by its solution pH.

| Table 3-3	Acid-Base Properties of Biologically Important Functional Groups	
Acids:		
	Monophosphate esters and diphosphate esters (medium)	
	Carboxylic acids (weak)	
	Phenols (very weak)	
	Thiols (very weak)	
	Amine salts (very weak)	
Bases:		
	Amines (weak)	
	Carboxylate ions (very weak)	
Neutral:		
	Alcohols	Carboxylic esters
	Ethers	Triphosphate esters
	Thioethers	Disulfides
	Amides	Ketones
	Aldehydes	

Same Content, Different Structure: Isomerism

Isomers are compounds that have the same molecular formula, but different structural formulas. Some organic and biochemical compounds may exist in different isomeric forms. Many times, especially in biological systems, these different isomers have different properties. The two most common types of isomers in biological systems are cis-trans isomers and isomerism due to the presence of a chiral carbon.

Cis-trans isomers

The presence of carbon-carbon double bonds leads to the possibility of having isomers present. Double bonds are rather restrictive and limit molecular movement. Groups on the same side of the double bond tend to remain in that position (cis), whereas groups on opposite sides tend to remain across the bond from each other (trans). See Figure 3-7 for an illustration.

Figure 3-7:
Cis and
trans
isomers.

cis isomer   trans isomer
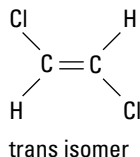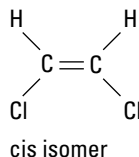
If the two groups attached to either of the carbon atoms of the double bond are the same, cis-trans isomers are not possible. Cis isomers are the normal form of fatty acids, whereas food processing tends to convert some of the cis isomers to the trans isomers.

Cis-trans isomers are also possible in cyclic systems. The cis form has similar groups on the same side of the ring, whereas the trans form has similar groups above and below the ring.

Chiral carbons

Trying to put your gloves on the wrong hands is kind of like another property of biological systems: handedness. There are *left-handed* molecules and *right-handed* molecules.

TIP
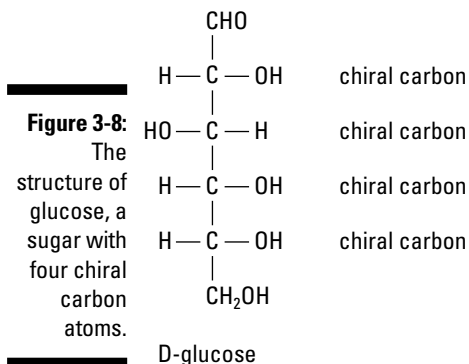
Identifying chiral molecules

The presence of an asymmetric, or *chiral,* carbon atom is sufficient to produce a "handed" molecule.

REMEMBER

A chiral carbon atom has four different groups attached to it. The majority of biological molecules have one or more chiral carbon atoms and, for this reason, they are chiral. Figure 3-8 shows the chiral nature of glucose.

```
              CHO
               |
         H — C — OH          chiral carbon
               |
        HO — C — H           chiral carbon
               |
         H — C — OH          chiral carbon
               |
         H — C — OH          chiral carbon
               |
              CH₂OH

         D-glucose
```

Figure 3-8:
The structure of glucose, a sugar with four chiral carbon atoms.

Determining the chiral form: Enantiomer or sterioisomer?

All substances have a mirror image (okay, except vampires); however, if there is a chiral carbon atom present, the mirror images are nonsuperimposable. Hold out your left and right hands, palms up — they are nonsuperimposable mirror images. These two mirror images are called *enantiomers.* The different chiral forms differ from each other in two aspects:

- ✔ How they affect light

- ✔ How they interact with other chiral substances (usually only one chiral form will be biologically active)
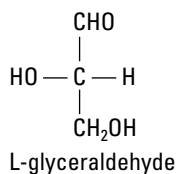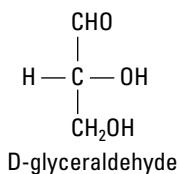
To determine how a particular form affects light, it is necessary to use *plane polarized light,* in which all the light waves vibrate in the same plane. When you use this kind of light, a chiral substance rotates the vibrational plane of the light — one form (the dextrorotatory, *d,* (+) isomer) rotates the plane to the right, while the other (the levorotatory, *l,* (–) isomer) rotates the plane to the left. The *d* and *l* forms are *stereoisomers* and are optically active.

Illustrating the chiral compound: Fisher projection formulas

A chemist named Emil Fischer developed a method of drawing a compound to illustrate which stereoisomer was present. These Fischer projection formulas are very useful in biochemistry. In a projection formula, a chiral carbon is placed in the center of a + pattern. The vertical lines (bonds) are pointing away from the viewer, and the horizontal lines are pointing toward the viewer. Fischer used the D designation if the most important group (the group whose central atom had the largest atomic number) was to the right of the carbon, and the L designation if the most important group (lowest atomic number) was to the left of the carbon. Figure 3-9 shows two Fischer projection formulas.

Figure 3-9:
Fischer
projection
formulas
distinguish
stereo-
isomers.

```
        CHO                    CHO
         |                      |
  H —— C —— OH         HO —— C —— H
         |                      |
        CH₂OH                  CH₂OH
  D-glyceraldehyde       L-glyceraldehyde
```

WARNING!

The *d* and *l* symbols are not necessarily the D and L forms respectively; thus, confusion may occur and lead to incorrect predictions. For this reason, the use of *d* and *l* is diminishing. The use of D and L is gradually being replaced by the R and S system of designating isomers. This system is particularly useful when more than one chiral carbon atom is present. For a description of this system, see *Organic Chemistry For Dummies* by Arthur Winter (Wiley).