Ionic Equilibria

Brönsted–Lowry Theory

According to the Brönsted–Lowry theory, an acid is a substance, charged or uncharged, that is capable of donating a proton, and a base is a substance, charged or uncharged, that is capable of accepting a proton from an acid. The relative strengths of acids and bases are measured by the tendencies of these substances to give up and take on protons. Hydrochloric acid is a strong acid in water because it gives up its proton readily, whereas acetic acid is a weak acid because it gives up its proton only to a small extent. The strength of an acid or a base varies with the solvent. Hydrochloric acid is a weak acid in glacial acetic acid and acetic acid is a strong acid in liquid ammonia. Consequently, the strength of an acid depends not only on its ability to give up a proton but also on the ability of the solvent to accept the proton from the acid. This is called the *basic strength* of the solvent.

In the Brönsted–Lowry classification, acids and bases may be anions such as HSO_4^- and CH_3COO^-, cations such as NH_4^+ and H_3O^+, or neutral molecules such as HCl and NH_3. Water can act as either an acid or a base and thus is amphiprotic. Acid–base reactions occur when an acid reacts with a base to form a new acid and a new base. Because the reactions involve a transfer of a proton, they are known as *protolytic reactions* or *protolysis.*

In the reaction between HCl and water, HCl is the acid and water the base:

$$\begin{array}{cccc} HCl & + H_2O & \rightarrow H_3O^+ & + Cl^- \\ \text{Acid}_1 & \text{Base}_2 & \text{Acid}_2 & \text{Base}_1 \end{array} \qquad (7\text{–}1)$$

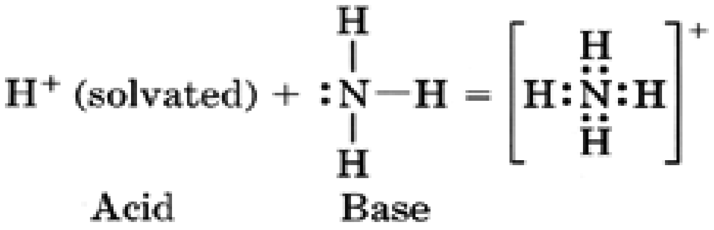
Acid$_1$ and Base$_1$ stand for an *acid–base pair* or *conjugate pair*, as do Acid$_2$ and Base$_2$. Because the bare proton, H^+, is practically nonexistent in aqueous solution, what is normally referred to as the hydrogen ion consists of the hydrated proton, H_3O^+, known as the *hydronium ion*. Higher solvated forms can also exist in solution. In an ethanolic solution, the "hydrogen ion" is the proton attached to a molecule of solvent, represented as $C_2H_5OH_2^+$. In equation (7-1), hydrogen chloride, the acid, has donated a proton to water, the base, to form the corresponding acid, H_3O^+, and the base, Cl^-.

<u>The reaction of HCl with water is one of ionization</u>. Neutralization and hydrolysis are also considered as acid–base reactions or proteolysis following the broad definitions of the Brönsted–Lowry concept.

Lewis Electronic Theory

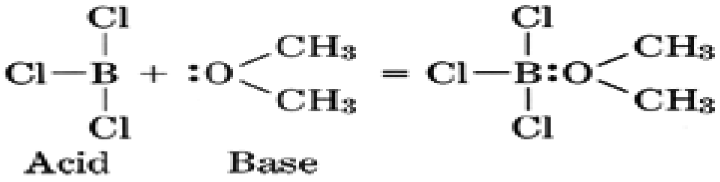
Other theories have been suggested for describing acid–base reactions, the most familiar of which is the *electronic theory* of Lewis.

According to the Lewis theory, an acid is a molecule or an ion that accepts an electron pair to form a covalent bond. A base is a substance that provides the pair of unshared electrons by which the base coordinates with an acid. Certain compounds, such as boron trifluoride and aluminum chloride, although not containing hydrogen and consequently not serving as proton donors, are nevertheless acids in this scheme. Many substances that do not contain hydroxyl ions, including amines, ethers, and carboxylic acid anhydrides, are classified as bases according to the Lewis definition. Two Lewis acid–base reactions are



$$H^{+}\ \text{(solvated)} + :NH_3 = \left[H:\overset{H}{\underset{H}{\ddot{N}}}:H\right]^{+}$$

(7–2)



$$Cl-BCl_2 + :O(CH_3)_2 = Cl-BCl_2:O(CH_3)_2$$

(7–3)

The Lewis system is probably too broad for convenient application to ordinary acid–base reactions, and those processes that are most conveniently expressed in terms of this electronic classification should be referred to simply as a form of electron sharing rather than as acid–base reactions. The Lewis theory is finding increasing use for describing the mechanism of many organic and inorganic reactions. *The Brönsted–Lowry nomenclature is particularly useful for describing ionic equilibria and is used extensively in this chapter*.

Acid–Base Equilibria

The ionization or proteolysis of a weak electrolyte, acetic acid, in water can be written in the Brönsted–Lowry manner as

$$\underset{\text{Acid}_1}{HAc} + \underset{\text{Base}_2}{H_2O} \rightleftharpoons \underset{\text{Acid}_2}{H_3O^+} + \underset{\text{Base}_1}{Ac^-} \qquad (7\text{–}4)$$

The arrows pointing in the forward and reverse directions indicate that the reaction is proceeding to the right and left simultaneously. According to the law of mass action, the velocity or rate of the forward reaction, R_f, is proportional to the concentration of the reactants:

$$R_f = k_1 \times [HAc]^1 \times [H_2O]^1 \qquad (7\text{–}5)$$

The speed of the reaction is usually expressed in terms of the decrease in the concentration of either the reactants per unit time. The terms rate, speed, and velocity have the same meaning here. The reverse reaction

$$R_r = k_2 \times [H_3O^+]^1 \times [Ac^-]^1 \qquad (7\text{–}6)$$

$$\underset{\text{Acid}_1}{HAc} + \underset{\text{Base}_2}{H_2O} \rightleftharpoons \underset{\text{Acid}_2}{H_3O^+} + \underset{\text{Base}_1}{Ac^-} \qquad (7\text{–}4)$$

Because only 1 mole of each constituent appears in the reaction, each term is raised to the first power, and the exponents need not appear in subsequent expressions for the dissociation of acetic acid and similar acids and bases. The symbols k_1 and k_2 are proportionality constants commonly known as *specific reaction rates* for the forward and the reverse reactions, respectively, and the brackets indicate concentrations. A better representation of the facts would be had by replacing concentrations with activities, but for the present discussion, the approximate equations are adequate.

Ionization of Weak Acids

According to the concept of equilibrium, the rate of the forward reaction decreases with time as acetic acid is depleted, whereas the rate of the reverse reaction begins at zero and increases as larger quantities of hydrogen ions and acetate ions are formed. Finally, a balance is attained when the two rates are equal, that is, when

$$R_f = R_r \qquad (7\text{–}7)$$

The *concentrations* of products and reactants are not necessarily equal at equilibrium; the *speeds* of the forward and reverse reactions are what are the same. Because equation (7-7) applies at equilibrium, equations (7-5) and (7-6) may be set equal:

$$k_1 \times [HAc] \times [H_2O] = k_2 \times [H_3O^+] \times [Ac^-] \qquad (7\text{–}8)$$

and solving for the ratio k_1/k_1, one obtains

$$k = \frac{k_1}{k_2} = \frac{[H_3O^+][Ac^-]}{[HAc][H_2O]} \qquad (7\text{–}9)$$

In dilute solutions of acetic acid, water is in sufficient excess to be regarded as constant at about 55.3 moles/liter (1 liter H_2O at 25°C weights 997.07 g, and 997.07/18.02 = 55.3). It is thus combined with k_1/k_2 to yield a new constant K_a, the *ionization constant* or the *dissociation constant* of acetic acid.

$$K_a = 55.3k = \frac{[H_3O^+][Ac^-]}{[HAc]} \qquad (7\text{–}10)$$

Equation (7-10) is the equilibrium expression for the dissociation of acetic acid, and the dissociation constant K_a is an equilibrium constant in which the essentially constant concentration of the solvent is incorporated and the term *basicity constant* is now often used for K_b.

In general, the acidity constant for an uncharged weak acid HB can be expressed by

$$HB + H_2O \rightleftharpoons H_3O^+ + B^- \qquad (7\text{–}11)$$

$$K_a = \frac{[H_3O^+][B^-]}{[HB]} \qquad (7\text{–}12)$$

Equation (7-10) can be presented in a more general form, using the symbol *c* to represent the initial molar concentration of acetic acid and *x* to represent the concentration $[H_3O^+]$. The latter quantity is also equal to $[Ac^-]$ because both ions are formed in equimolar concentration. The concentration of acetic acid remaining at equilibrium [HAc] can be expressed as $c - x$. The reaction [equation (7-4)] is

$$\begin{array}{llll} \mathrm{HAc} + \mathrm{H_2O} \rightleftharpoons & \mathrm{H_3O^+} & + & \mathrm{Ac^-} \\ (c - x) & x & & x \end{array} \qquad (7\text{–}13)$$

and the equilibrium expression (7-10) becomes

$$K_a = \frac{x^2}{c - x} \qquad (7\text{–}14)$$

where *c* is large in comparison with *x*. The term *c* - *x* can be replaced by *c* without appreciable error, giving the equation

$$K_a \cong \frac{x^2}{c} \qquad (7\text{–}15)$$

which can be rearranged as follows for the calculation of the hydrogen ion concentration of weak acids:

$$x^2 = K_a c$$

$$x = [\mathrm{H_3O^+}] = \sqrt{K_a c} \qquad (7\text{–}16)$$

When a salt formed from a strong acid and a weak base, such as ammonium chloride, is dissolved in water, it dissociates completely as follows:

$$NH_4^+Cl^- \xrightarrow{H_2O} NH_4^+ + Cl^- \qquad (7\text{-}17)$$

The Cl^- is the conjugate base of a strong acid, HCl, which is 100% ionized in water. Thus, the Cl^- cannot react any further. In the Brönsted–Lowry system, NH_4^+ is considered to be a cationic acid, which can form its conjugate base, NH_3, by donating a proton to water as follows:

$$NH_4^+ + H_2O \rightleftharpoons H_3O^+ + NH_3 \qquad (7\text{-}18)$$

$$K_a = \frac{[H_3O^+][NH_3]}{[NH_4^+]} \qquad (7\text{-}19)$$

In general, for charged acids BH^+, the reaction is written as

$$BH^+ + H_2O \rightleftharpoons H_3O^+ + B \qquad (7\text{-}20)$$

and the acidity constant is

$$K_a = \frac{[H_3O^+][B]}{[BH^+]} \qquad (7\text{-}21)$$

Ionization of Weak Bases

Nonionized weak bases B, exemplified by NH_3, react with water as follows:

$$B + H_2O \rightleftharpoons OH^- + BH^+ \qquad (7\text{-}22)$$

$$K_b = \frac{[OH^-][BH^+]}{[B]} \qquad (7\text{–}23)$$

which, by a procedure like that used to obtain equation (7-16), leads to

$$[OH^-] = \sqrt{K_b c} \qquad (7\text{–}24)$$

Salts of strong bases and weak acids, such as sodium acetate, dissociate completely in aqueous solution to given ions:

$$Na^+CH_3COO^- \xrightarrow{H_2O} Na^+ + CH_3COO^- \quad (7\text{–}25)$$

The sodium ion cannot react with water, because it would form NaOH, which is a strong electrolyte and would dissociate completely into its ions. The acetate anion is a Brönsted–Lowry weak base, and

$$CH_3COO^- + H_2O \rightleftharpoons OH^- + CH_3COOH$$

$$K_b = \frac{[OH^-][CH_3COOH]}{[CH_3COO^-]} \quad (7\text{–}26)$$

In general, for an anionic base B^-,

$$B^- + H_2O \rightleftharpoons OH^- + HB$$

$$K_b = \frac{[OH^-][HB]}{[B^-]} \qquad (7\text{–}27)$$

The Ionization of Water

In a manner corresponding to the dissociation of weak acids and bases, water ionizes slightly to yield hydrogen and hydroxyl ions. As previously observed, a weak electrolyte requires the presence of water or some other polar solvent for ionization. Accordingly, one molecule of water can be thought of as a weak electrolytic solute that reacts with another molecule of water as the solvent. This *autoprotolytic* reaction is represented as

$$H_2O + H_2O \rightleftharpoons H_3O^+ + OH^- \qquad (7\text{–}28)$$

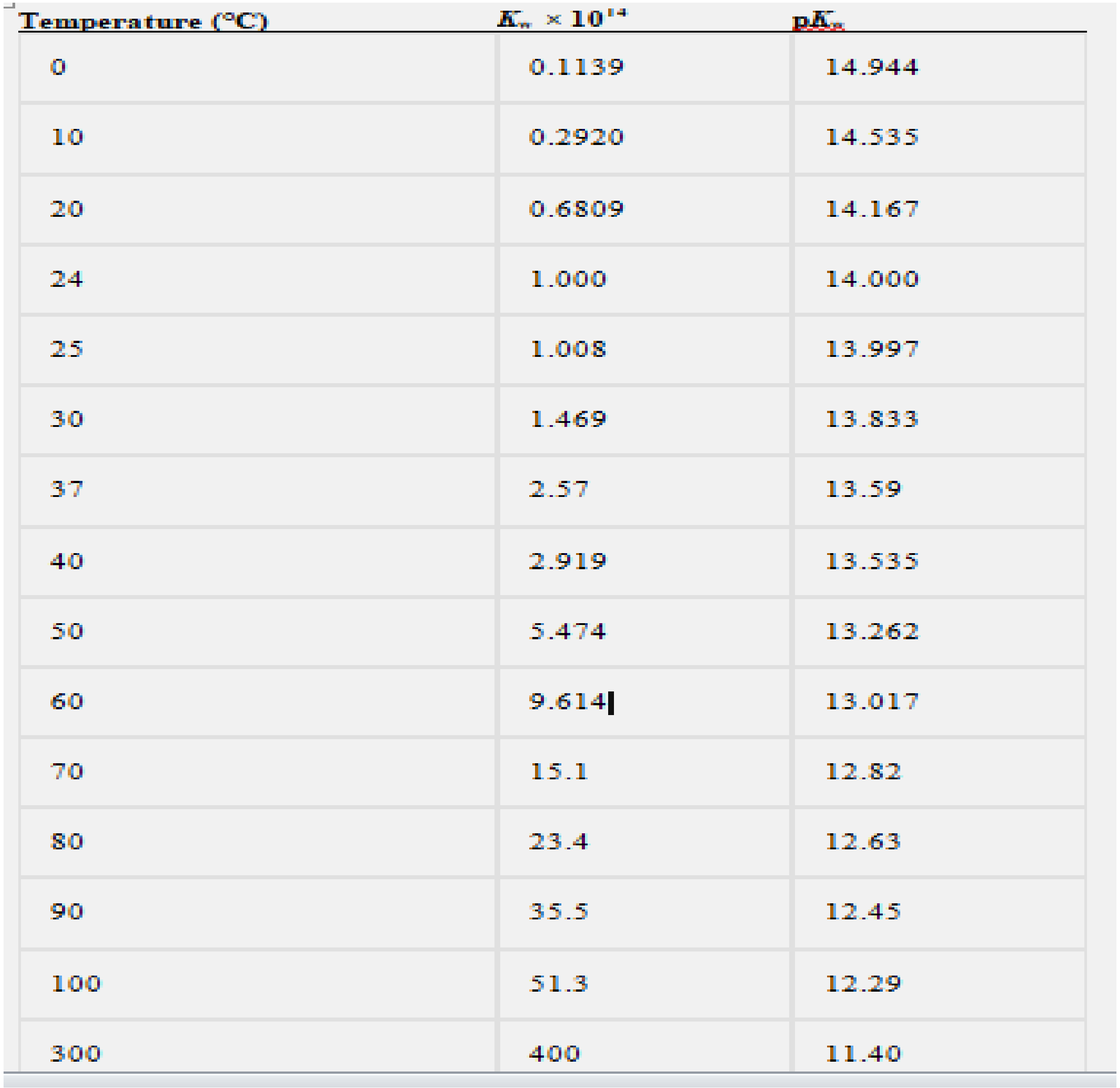
The law of mass action is then applied to give the equilibrium expression

$$\frac{[H_3O^+][OH^-]}{[H_2O]^2} = k \qquad (7\text{–}29)$$

The term for molecular water in the denominator is squared because the reactant is raised to a power equal to the number of molecules appearing in the equation, as required by the law of mass action. Because molecular water exists in great excess relative to the concentrations of hydrogen and hydroxyl ions, [H_2O]2 is considered as a constant and is combined with *k* to give a new constant, K_w, known as the *dissociation constant*, the *autoprotolysis constant*, or the *ion product* of water:

$$K_w = k \times [H_2O]^2 \qquad (7\text{–}30)$$

The value of the ion product is approximately 1×10^{-14} at 25°C; it depends strongly on *temperature*. In any calculations involving the ion product, one must be certain to use the proper value of K_w for the temperature at which the data are obtained.



Temperature (°C)	K_w × 10^{14}	pK_w
0	0.1139	14.944
10	0.2920	14.535
20	0.6809	14.167
24	1.000	14.000
25	1.008	13.997
30	1.469	13.833
37	2.57	13.59
40	2.919	13.535
50	5.474	13.262
60	9.614	13.017
70	15.1	12.82
80	23.4	12.63
90	35.5	12.45
100	51.3	12.29
300	400	11.40

Substituting equation (7-30) into (7-29) gives the common expression for the ionization of water:

$$[H_3O^+] \times [OH^-] = K_w \cong 1 \times 10^{-14} \text{ at } 25°C \quad (7\text{–}31)$$

In *pure* water, the hydrogen and hydroxyl ion concentrations are equal, and each has the value of approximately 1×10^{-7} mole/liter at 25°C.*

$$[H_3O^+] = [OH^-] \cong \sqrt{1 \times 10^{-14}} \cong 1 \times 10^{-7} \quad (7\text{–}32)$$

When an acid is added to pure water, some hydroxyl ions, provided by the ionization of water, must always remain. The increase in hydrogen ions is offset by a decrease in the hydroxyl ions so that K_w remains constant at about 1×10^{-14} at 25°C.

Relationship Between K_a and K_b

A simple relationship exists between the dissociation constant of a weak acid HB and that of its conjugate base B^-, or between BH^+ and B, when the solvent is amphiprotic. This can be obtained by multiplying equation (7-12) by equation (7-27):

$$HB + H_2O \rightleftharpoons H_3O^+ + B^- \quad (7\text{–}11)$$

$$K_a = \frac{[H_3O^+][B^-]}{[HB]} \quad (7\text{–}12)$$

$$B^- + H_2O \rightleftharpoons OH^- + HB$$

$$K_b = \frac{[OH^-][HB]}{[B^-]} \quad (7\text{–}27)$$

$$K_a K_b = \frac{[H_3O^+][B^-]}{[HB]} \cdot \frac{[OH^-][HB]}{[B^-]}$$

$$= [H_3O^+][OH^-] = K_w \qquad (7\text{–}33)$$

$$K_b = \frac{K_w}{K_a} \qquad (7\text{–}34)$$

$$K_a = \frac{K_w}{K_b} \qquad (7\text{–}35)$$

Ionization of Polyprotic Electrolytes

Acids that donate a single proton and bases that accept a single proton are called *monoprotic electrolytes*. A polyprotic (polybasic) acid is one that is capable of donating two or more protons, and a polyprotic base is capable of accepting two or more protons. A diprotic (dibasic) acid, such as carbonic acid, ionizes in two stages, and a triprotic (tribasic) acid, such as phosphoric acid, ionizes in three stages. The equilibria involved in the protolysis or ionization of phosphoric acid, together with the equilibrium expressions, are

$$H_3PO_4 + H_2O = H_3O^+ + H_2PO_4^- \quad (7\text{–}36)$$

$$\frac{[H_3O^+][H_2PO_4^-]}{[H_3PO_4]} = K_1 = 7.5 \times 10^{-3} \quad (7\text{–}37)$$

$$H_2PO_4^- + H_2O = H_3O^+ + HPO_4^{2-}$$

$$\frac{[H_3O^+][HPO_4^{2-}]}{[H_2PO_4^-]} = K_2 = 6.2 \times 10^{-8} \quad (7\text{–}38)$$

$$HPO_4^{2-} + H_2O = H_3O^+ + PO_4^{3-}$$

$$\frac{[H_3O^+][PO_4^{3-}]}{[HPO_4^{2-}]} = K_3 = 2.1 \times 10^{-13} \quad (7\text{–}39)$$

In any polyprotic electrolyte, the primary protolysis is greatest, and succeeding stages become less complete at any given acid concentration.

The negative charges on the ion HPO_4^{2-} make it difficult for water to remove the proton from the phosphate ion, as reflected in the small value of K_3. Thus, phosphoric acid is weak in the third stage of ionization, and a solution of this acid contains practically no PO_4^{3-} ions. Each of the species formed by the ionization of a polyprotic acid can also act as a base. Thus, for the phosphoric acid system,

$$PO_4^{3-} + H_2O \rightleftharpoons HPO_4^{2-} + OH^- \quad (7\text{–}40)$$

$$K_{b1} = \frac{[HPO_4^{2-}][OH^-]}{[PO_4^{3-}]} = 4.8 \times 10^{-2} \quad (7\text{–}41)$$

$$HPO_4^{2-} + H_2O \rightleftharpoons H_2PO_4^- + OH^- \quad (7\text{–}42)$$

$$K_{b2} = \frac{[H_2PO_4^-][OH^-]}{[HPO_4^{2-}]} = 1.6 \times 10^{-7} \quad (7\text{–}43)$$

$$H_2PO_4^- + H_2O \rightleftharpoons H_3PO_4 + OH^- \quad (7\text{–}44)$$

$$K_{b3} = \frac{[H_3PO_4][OH^-]}{[H_2PO_4^-]} = 1.3 \times 10^{-12} \quad (7\text{–}45)$$

Ampholytes

In the preceding section, equations (7-37), (7-38), (7-41), and (7-43) demonstrated that in the phosphoric acid system, the species $H_2PO_4^-$ and HPO_4^{2-} can function either as an acid or a base. A species that can function either as an acid or as a base is called an *ampholyte* and is said to be *amphoteric* in nature. In general, for a polyprotic acid system are amphoteric. Amino acids and proteins are ampholytes of particular interest in pharmacy. If glycine hydrochloride is dissolved in water, it ionizes as follows:

$$^{+}NH_3CH_2COOH + H_2O \rightleftharpoons {}^{+}NH_3CH_2COO^{-} + H_3O^{+} \quad (7\text{–}50)$$

$$^{+}NH_3CH_2COO^{-} + H_2O \rightleftharpoons {}^{+}NH_2CH_2COO^{-} + H_3O^{+} \quad (7\text{–}51)$$

The species $^{+}NH_3CH_2COO^{-}$ is amphoteric in that, in addition to reacting as an acid as shown in equation (7-51), it can react as a base with water as follows:

$$^{+}NH_3CH_2COO^{-} + H_2O \rightleftharpoons {}^{+}NH_3CH_2COOH + OH^{-} \quad (7\text{–}52)$$

The amphoteric species $^{+}NH_3CH_2COO^{-}$ is called a *zwitterion* and differs from the amphoteric species formed from phosphoric acid in that it carries both a positive and a negative charge, and the whole molecule is electrically neutral. The pH at which the zwitterion concentration is a maximum is known as the *isoelectric point*. At the isoelectric point the net movement of the solute molecules in an electric field is negligible.

Sörensen's pH

The hydrogen ion concentration of a solution varies from approximately 1 in a 1 M solution of a strong acid to about 1 × 10^{-14} in a 1 M solution of a strong base, and the calculations often become unwieldy. To alleviate this difficulty, Sörensen suggested a simplified method of expressing hydrogen ion concentration. He established the term *pH*, which was originally written as p_H^+, to represent the hydrogen ion potential, and he defined it as the common logarithm of the reciprocal of the hydrogen ion concentration:

$$pH = \log \frac{1}{[H_3O^+]} \qquad (7\text{-}53)$$

According to the rules of logarithms, this equation can be written as

$$pH = \log 1 - \log[H_3O^+] \qquad (7\text{–}54)$$

$$pH = -\log[H_3O^+] \qquad (7\text{–}55)$$

Equations (7-53) and (7-55) are identical; they are acceptable for approximate calculations involving pH.

The pH of a solution can be considered in terms of a numeric scale having values from 0 to 14, which expresses in a quantitative way the degree of acidity (7 to 0) and alkalinity (7-14). The value 7 at which the hydrogen and hydroxyl ion concentrations are about equal at room temperature is referred to as the *neutral point*, or neutrality. The neutral pH at 0°C is 7.47, and at 100°C it is 6.15 (Table 7-2).

Conversion of Hydrogen Ion Concentration to pH
Conversion of pH to Hydrogen Ion Concentration

A better definition of pH involves the activity rather than the concentration of the ions:

$$\text{pH} = -\log a_{\text{H}^+} \qquad (7\text{–}56)$$

and because the activity of an ion is equal to the activity coefficient multiplied by the molal or molar concentration [equation (7-42)],

$$\begin{aligned}\text{Hydronium ion concentration} \times \text{Activity coefficient} \\ = \text{Hydronium ion activity}\end{aligned}$$

the pH may be computed more accurately from the formula

$$\text{pH} = -\log(\gamma_{\pm} \times c) \qquad (7\text{–}57)$$

pK and pOH

The use of pH to designate the negative logarithm of hydronium ion concentration has proved to be so convenient that expressing numbers less than unity in "p" notation has become a standard procedure. The mathematician would say that "p" is a *mathematical operator* that acts on the quantity $[H^+]$, K_a, K_b, K_w, and so on to convert the value into the negative of its common logarithm. In other words, the term "p" is used to express the negative logarithm of the term following the "p." For example, pOH expresses $-\log[OH^-]$, pK_a is used for $-\log K_a$, and pK_w is $-\log K_w$. Thus, equations (7-31) and (7-33) can be expressed as

$$\mathrm{pH} + \mathrm{pOH} = \mathrm{p}K_w \qquad (7\text{–}58)$$

$$\mathrm{p}K_a + \mathrm{p}K_b = \mathrm{p}K_w \qquad (7\text{–}59)$$

where p*K* is often called the *dissociation exponent*.

The p*K* values of weak acidic and basic drugs are ordinarily determined by ultraviolet spectrophotometry and potentiometric titration. They can also be obtained by solubility analysis and by a partition coefficient method.