

3 Thermodynamics

Chapter Objectives

At the conclusion of this chapter the student should be able to:

1. Understand the theory of thermodynamics and its use for describing energy-related changes in reactions.
2. Understand the first law of thermodynamics and its use.
3. Understand the second law of thermodynamics and its use.
4. Understand the third law of thermodynamics and its use.
5. Define and calculate free energy functions and apply them to pharmaceutically relevant issues.
6. Understand the basic principles of the impact of thermodynamics on pharmaceutically relevant applications.
7. Define the chemical potential and equilibrium processes.

Thermodynamics deals with the quantitative relationships of interconversion of the various forms of *energy*, including mechanical, chemical, electric, and radiant energy. Although thermodynamics was originally developed by physicists and engineers interested in the efficiencies of steam engines, the concepts formulated from it have proven to be extremely useful in the chemical sciences and related disciplines like pharmacy. As illustrated later in this chapter, the property called *energy* is broadly applicable, from determining the fate of simple chemical processes to describing the very complex behavior of biologic cells.

Thermodynamics is based on three “laws” or facts of experience that have never been proven in a direct way, in part due to the ideal conditions for which they were derived. Various conclusions, usually expressed in the form of mathematical equations, however, may be deduced from these three principles, and the results consistently agree with observations. Consequently, the laws of thermodynamics, from which these equations are obtained, are accepted as valid for systems involving large numbers of molecules.

It is useful at this point to distinguish the attributes of the three types of systems that are frequently used to describe thermodynamic properties. Figure 3-1a shows an *open* system in which energy and matter can be exchanged with the surroundings. In contrast, Figure 3-1b and c are examples of *closed* systems, in which there is no exchange of matter with the surroundings, that is, the system's mass is constant. However, energy can be transferred by *work* (Fig. 3-1b) or *heat* (Fig. 3-1c) through the *closed* system's boundaries. The last example (Fig. 3-1d) is a system in which neither matter nor energy can be exchanged with the surroundings; this is called an *isolated* system.

For instance, if two immiscible solvents, water and carbon tetrachloride, are confined in a closed container and iodine is distributed between the two phases, each phase is an open system, yet the total system made up of the two phases is closed because it does not exchange matter with its surroundings.



Key Concept

Basic Definitions of Thermodynamics

Before beginning with details about the origin and concepts involving these three laws, we define the language commonly used in thermodynamics, which has precise scientific meanings. A *system* in thermodynamics is a well-defined part of the universe that one is interested in studying. The system is separated from *surroundings*, the rest of the universe and from which the observations are made, by physical (or virtual) barriers defined as *boundaries*. *Work* (W) and *heat* (Q) also have precise thermodynamic meanings. *Work* is a transfer of energy that can be used to change the height of a weight somewhere in the surroundings, and *heat* is a transfer of energy resulting from a temperature difference between the system and the surroundings. It is important to consider that

both *work* and *heat* appear only at the system's *boundaries* where the *energy* is being transferred.

The First Law of Thermodynamics

The first law is a statement of the conservation of energy. It states that, although energy can be transformed from one kind into another, it cannot be created or destroyed. Put in another way, the total energy of a system and its immediate surroundings remains constant during any operation. This statement follows from the fact that the various forms of energy are equivalent, and when one kind is formed, an equal amount of another kind must disappear. The relativistic picture of the universe expressed by Einstein's equation

$$\text{Energy} = (\text{Mass change}) \times (\text{Velocity of light})^2$$

suggests that matter can be considered as another form of energy, 1 g being equivalent to 9×10^{13} joules. These enormous quantities of energy are involved in nuclear transformations but are not important in ordinary chemical reactions.

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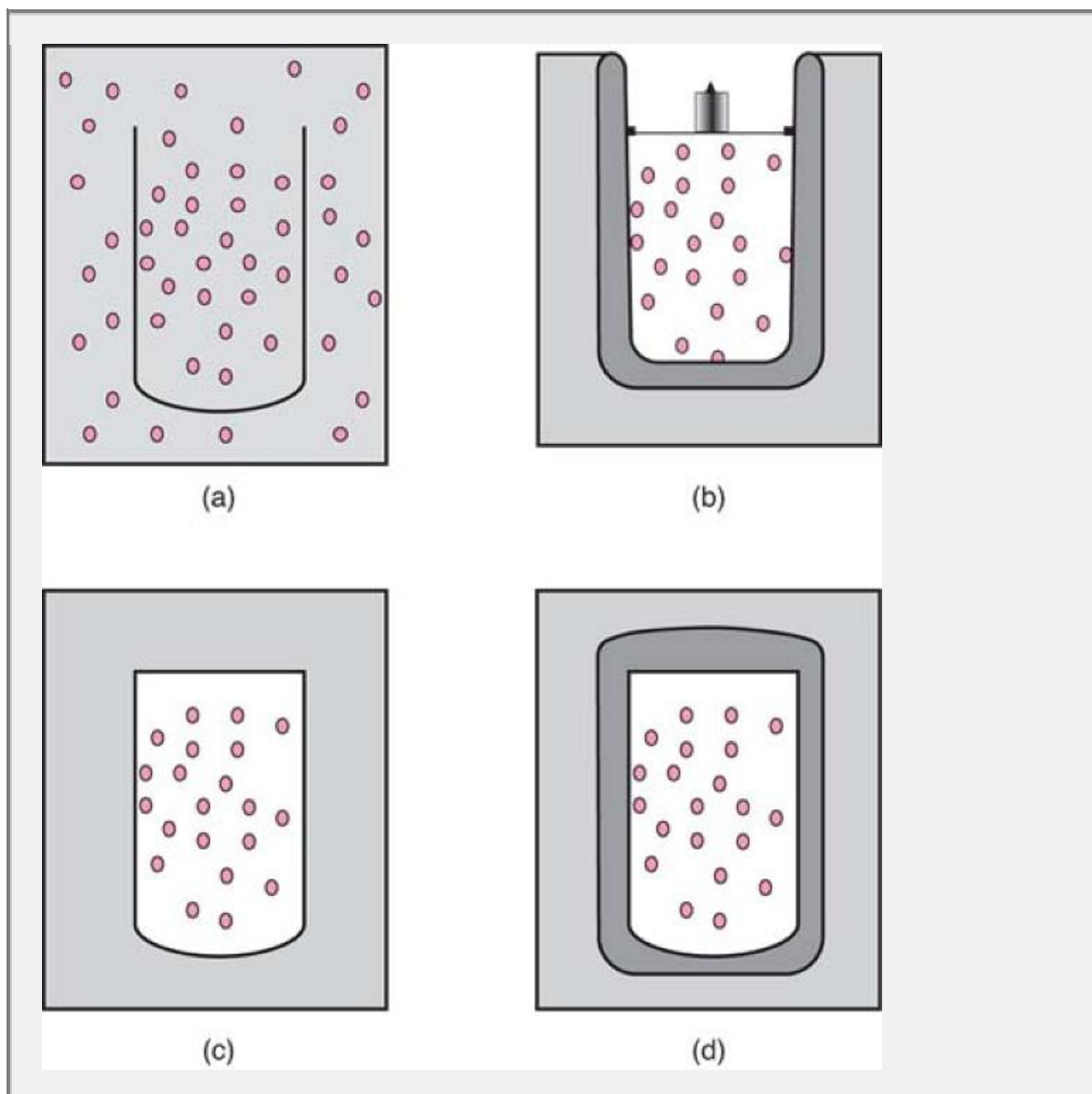


Fig. 3-1. Examples of thermodynamic systems. (a) An open system exchanging mass with its surroundings; (b) a closed system exchanging work with its surroundings; (c) a closed system exchanging heat with its surroundings; (d) an isolated system, in which neither work nor heat can be exchanged through boundaries.

According to the first law, the effects of Q and W in a given system during a transformation from an initial thermodynamic state to a final thermodynamic state are related to an intrinsic property of the system called the *internal energy*, defined as

$$\Delta E = E_2 - E_1 = Q + W \quad (3-1)$$

where E_2 is the internal energy of the system in its final state and E_1 is the internal energy of the system in its initial state, Q is the heat, and W is the work. The change in internal energy ΔE is related to Q and W transferred between the system and its surroundings. Equation (3-1) also expresses the fact that *work* and *heat* are equivalent ways of changing the internal energy of the system.

The internal energy is related to the microscopic motion of the atoms, ions, or molecules of which the system is composed. Knowledge of its absolute value would tell us something about the microscopic motion of the vibrational, rotational, and translational components. In addition, the absolute value would also provide information about the kinetic and potential energies of their electrons and nuclear elements, which in practice is extremely difficult to attain. Therefore, change of internal energy rather than absolute energy value is the concern of thermodynamics.

Example 3-1

Thermodynamic State

Consider the example of transporting a box of equipment from a camp in a valley to one at the top of a mountain. The main concern is with the potential energy rather than the internal energy of a system, but the principle is the same. One can haul the box to the top of the mountain by a block and tackle suspended from an overhanging cliff and produce little heat by this means. One can also drag the box up a path, but more work will be required and considerably more heat will be produced owing to the frictional resistance. The box can be carried to the nearest airport, flown over the appropriate spot, and dropped by parachute. It is readily seen that each of these methods involves a different amount of heat and work. The change in potential energy depends only on the difference in the height of the camp in the valley and the one at the top of the mountain, and it is independent of the path used to transport the box.

By using equation (3-1) (the first law), one can evaluate the change of internal energy by measuring Q and W during the change of state. However, it is useful to relate the change of internal energy to the *measurable properties* of the system: P , V , and T . Any two of these variables must be specified to define the internal energy. For an infinitesimal change in the energy dE , equation (3-1) is written as

$$dE = dq + dw \quad (3-2)$$

where dq is the heat absorbed and dw is the work done during the infinitesimal change of the system. Capital letters Q and W are used for heat and work in equation (3-1) to signify finite changes in these quantities. The symbol d in equation (3-2) signifies infinitesimal changes of properties that depend on the “path,” also called inexact differentials. Hence, dq and dw are not in these circumstances thermodynamic properties.

The infinitesimal change of any state property like dE , also called an exact differential, can be generally written, for instance, as a function of T and V as in the following equation for a closed system (i.e., constant mass):

$$dE = \left(\frac{\partial E}{\partial T} \right)_V dT + \left(\frac{\partial E}{\partial V} \right)_T dV \quad (3-3)$$

The partial derivatives of the energy in equation (3-3) are important properties of the system and show the rate of change in energy with the change in T at constant volume or with the change of V at constant temperature. Therefore, it is useful to find their expression in terms of measurable properties. This can be done by combining equations (3-2) and (3-3) into

$$dq + dw = \left(\frac{\partial E}{\partial T} \right)_V dT + \left(\frac{\partial E}{\partial V} \right)_T dV \quad (3-4)$$

This equation will be used later to describe some properties of E as a function of T and V .

Isothermal and Adiabatic Processes

When the temperature is kept constant during a process, the reaction is said to be conducted *isothermally*. An isothermal reaction may be carried out by placing the system in a large constant-temperature bath so that heat is drawn from or returned to it without affecting the temperature significantly. When heat is neither lost nor gained during a process, the reaction is said to occur *adiabatically*. A reaction carried on inside a sealed Dewar flask or “vacuum bottle” is adiabatic because the system is thermally insulated from its surroundings. In thermodynamic terms, it can be said that an adiabatic process is one in which $dq = 0$, and the first law under adiabatic conditions reduces to



Thermodynamic State

The term *thermodynamic state* means the condition in which the measurable properties of the system have a definite value. The state of 1 g of water at E_1 may be specified by the conditions of, say, 1 atm pressure and 10°C, and the state E_2 by the conditions of 5 atm and 150°C. Hence, the states of most interest to the chemist ordinarily are defined by specifying any two of the three variables, temperature (T), pressure (P), and volume (V); however, additional independent variables sometimes are needed to specify the state of the system. Any equation relating the necessary variables—for example, $V = f(T, P)$ —is an *equation of state*. The ideal gas law and the van der Waals equation described in Chapter 2 are equations of state. Thus, V , P , and T are variables that define a state, so they are called *state variables*. The variables of a thermodynamic state are independent of how the state has been reached.

A feature of the change of internal energy, ΔE , discovered by the first law is that it depends only on the initial and final thermodynamic states, that is, it is a variable of state; it is a thermodynamic property of the system. On the other hand, both Q and W depend on the manner in which the change is conducted. Hence, Q and W are not variables of state or thermodynamic properties; they are said to depend on the “path” of the transformation.

$$dw = dE \quad (3-5)$$

According to equation (3-5), when work is done by the system, the internal energy decreases, and because heat cannot be absorbed in an adiabatic process, the temperature must fall. Here, the work done becomes a thermodynamic property dependent only on the initial and final states of the system.

Work of Expansion Against a Constant Pressure

We first discuss the work term. Because of its importance in thermodynamics, initial focus is on the work produced by varying the volume of a system (i.e., expansion work or compression work) against a *constant* opposing external pressure, P_{ex} . Imagine a vapor confined in a hypothetical cylinder fitted with a weightless, frictionless piston of area A , as shown in Figure 3-2. If a constant external pressure P_{ex} is exerted on the piston, the total force is $P_{\text{ex}} \times A$ because $P = \text{Force}/\text{Area}$. The vapor in the cylinder is now made to expand by increasing the temperature, and the piston moves a distance h . The work done against the opposing pressure in one single stage is

$$W = -P_{\text{ex}} \times A \times h \quad (3-6)$$

Now $A \times h$ is the increase in volume, $\Delta V = V_2 - V_1$, so that, at constant pressure,

$$W = -P_{\text{ex}} \Delta V = -P_{\text{ex}}(V_2 - V_1) \quad (3-7)$$

Reversible Processes

Now let us imagine the hypothetical case of water at its boiling point contained in a cylinder fitted with a weightless and frictionless piston (Fig. 3-3a). The apparatus is immersed in a constant-temperature bath maintained at the same temperature as the water in the cylinder. By definition, the vapor pressure of water at its boiling point is equal to the atmospheric pressure, represented in Figure 3-3 by a set of weights equivalent to the atmospheric pressure of 1 atm; therefore, the temperature is 100°C. The process is an isothermal one, that is, it is carried out at constant temperature. Now, if the external pressure is decreased slightly by removing one of the infinitesimally small weights (Fig. 3-3b), the volume of the system increases and the vapor pressure falls infinitesimally. Water then evaporates to maintain the vapor pressure constant at its original value, and heat is extracted from the bath to keep the temperature constant and bring about the vaporization. During this process, a heat exchange between the system and the temperature bath will occur.

On the other hand, if the external pressure is increased slightly by adding an infinitesimally small weight (Fig. 3-3c), the system is compressed and the vapor pressure also rises infinitesimally. Some of the water condenses to reestablish the equilibrium vapor pressure, and the liberated heat

is absorbed by the constant-temperature bath. If the process could be conducted infinitely slowly so that

no work is expended in supplying kinetic energy to the piston, and if the piston is considered to be frictionless so that no work is done against the force of friction, all the work is used to expand or compress the vapor. Then, because this process is always in a state of virtual thermodynamic equilibrium, being reversed by an infinitesimal change of pressure, it is said to be *reversible*. If the pressure on the system is increased or decreased rapidly or if the temperature of the bath cannot adjust instantaneously to the change in the system, the system is not in the same thermodynamic state at each moment, and the process is irreversible.

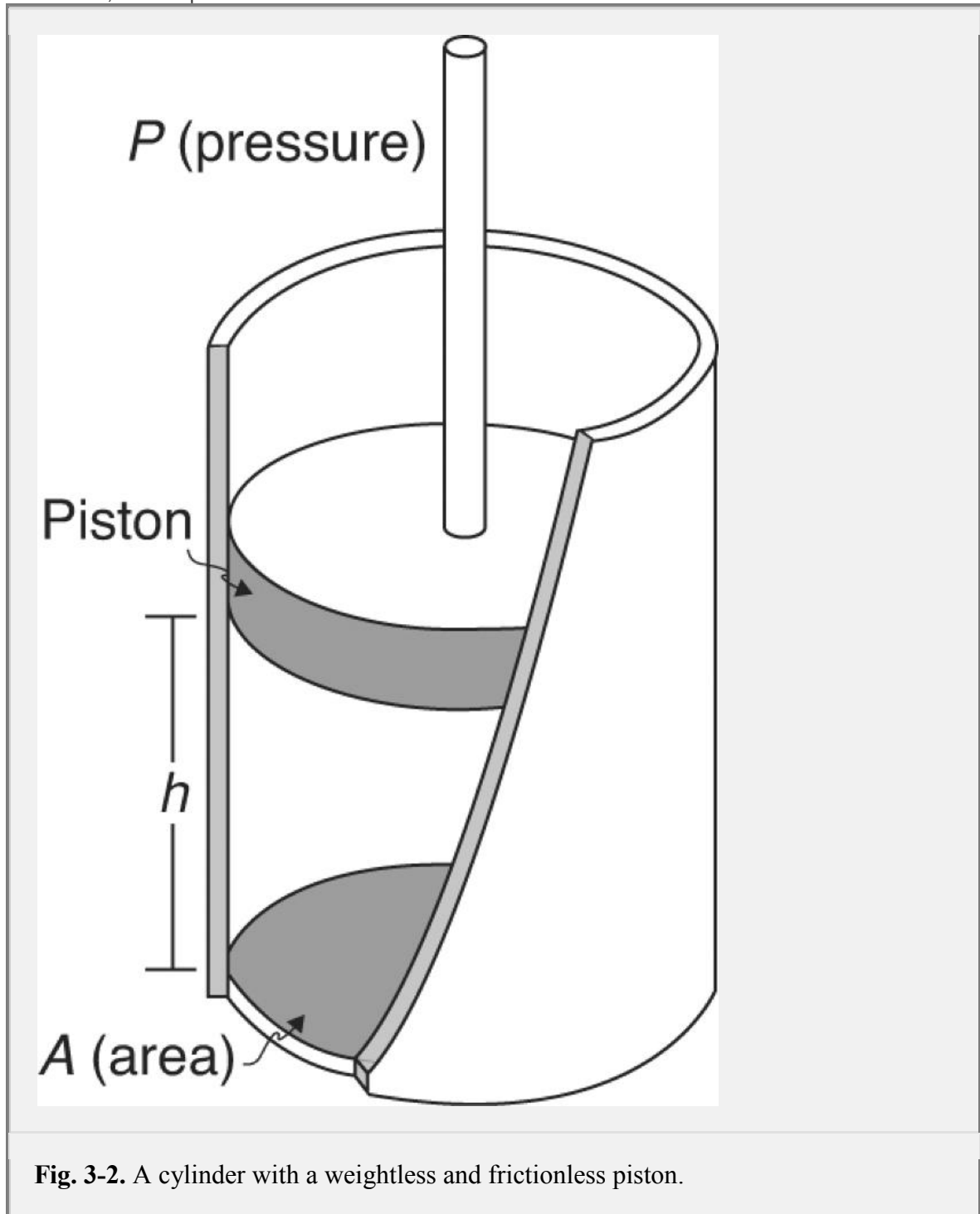


Fig. 3-2. A cylinder with a weightless and frictionless piston.

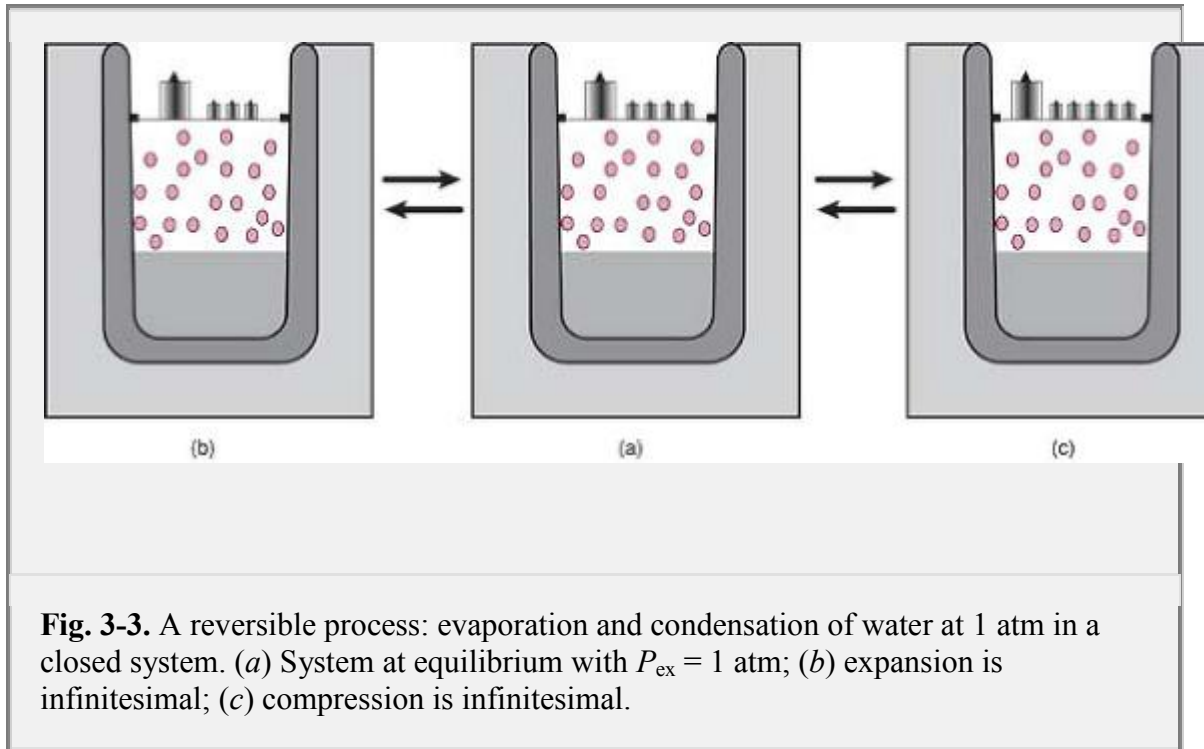


Fig. 3-3. A reversible process: evaporation and condensation of water at 1 atm in a closed system. (a) System at equilibrium with $P_{\text{ex}} = 1 \text{ atm}$; (b) expansion is infinitesimal; (c) compression is infinitesimal.

Although no real system can be made strictly reversible, some are nearly so. One of the best examples of reversibility is that involved in the measurement of the potential of an electrochemical cell using the potentiometric method.

Maximum Work

The work done by a system in an isothermal expansion process is at a maximum when it is done reversibly. This statement can be shown to be true by the following argument. No work is accomplished if an ideal gas expands freely into a vacuum, where $P = 0$, because any work accomplished depends on the external pressure. As the external pressure becomes greater, more work is done by the system, and it rises to a maximum when the external pressure is infinitesimally less than the pressure of the gas, that is, when the process is reversible. Of course, if the external pressure is continually increased, the gas is compressed rather than expanded, and work is done *on* the system rather than *by* the system in an isothermal reversible process.

Then the maximum work done for a system that is expanded in reversible fashion is

$$W = \int_1^2 dw = - \int_{V_1}^{V_2} PdV \quad (3-8)$$

where P_{ex} was replaced by P because the external pressure is only infinitesimally smaller than the pressure of the system. In similar fashion, it can be deduced that the minimum work in a reversible compression of the system will also lead to equation (3-8), because at each stage P_{ex} is only infinitesimally larger than P . The right term in equation (3-8) is depicted in the shaded area in Figure 3-4, which represents the maximum expansion work or the minimum compression work in a reversible process.

Example 3-2

A gas expands by 0.5 liter against a constant pressure of 0.5 atm at 25°C. What is the work in ergs and in joules done by the system?

$$W = P\Delta V$$

$$1 \text{ atm} = 1.013 \times 10^6 \text{ dynes/cm}^2$$

$$\begin{aligned} W &= (0.507 \times 10^6 \text{ dynes/cm}^2) \times 500 \text{ cm}^3 \\ &= 2.53 \times 10^8 \text{ ergs} = 25.3 \text{ joules} \end{aligned}$$

The following example demonstrates the kind of problem that can be solved by an application of the first law of thermodynamics.

The external pressure in equation (3-8) can be replaced by the pressure of an ideal gas, $P = nRT/V$, and by ensuring that the temperature of the gas remains constant during the change of state (isothermal process); then one can take nRT outside the integral, giving the equation

$$W_{\max} = \int dw_{\max} = -nRT \int_{V_1}^{V_2} \frac{dV}{V} \quad (3-9)$$

$$W_{\max} = -nRT \ln \frac{V_2}{V_1} \quad (3-10)$$

Note that in expansion, $V_2 > V_1$, and $\ln(V_2/V_1)$ is a positive quantity; therefore, the work is done by the system, so that its energy decreases (negative sign). When the opposite is true, $V_2 < V_1$, and $\ln(V_2/V_1)$ is negative due to gas compression, work is done by the system, so that its energy increases

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(positive sign). The process itself determines the sign of W and ΔE .

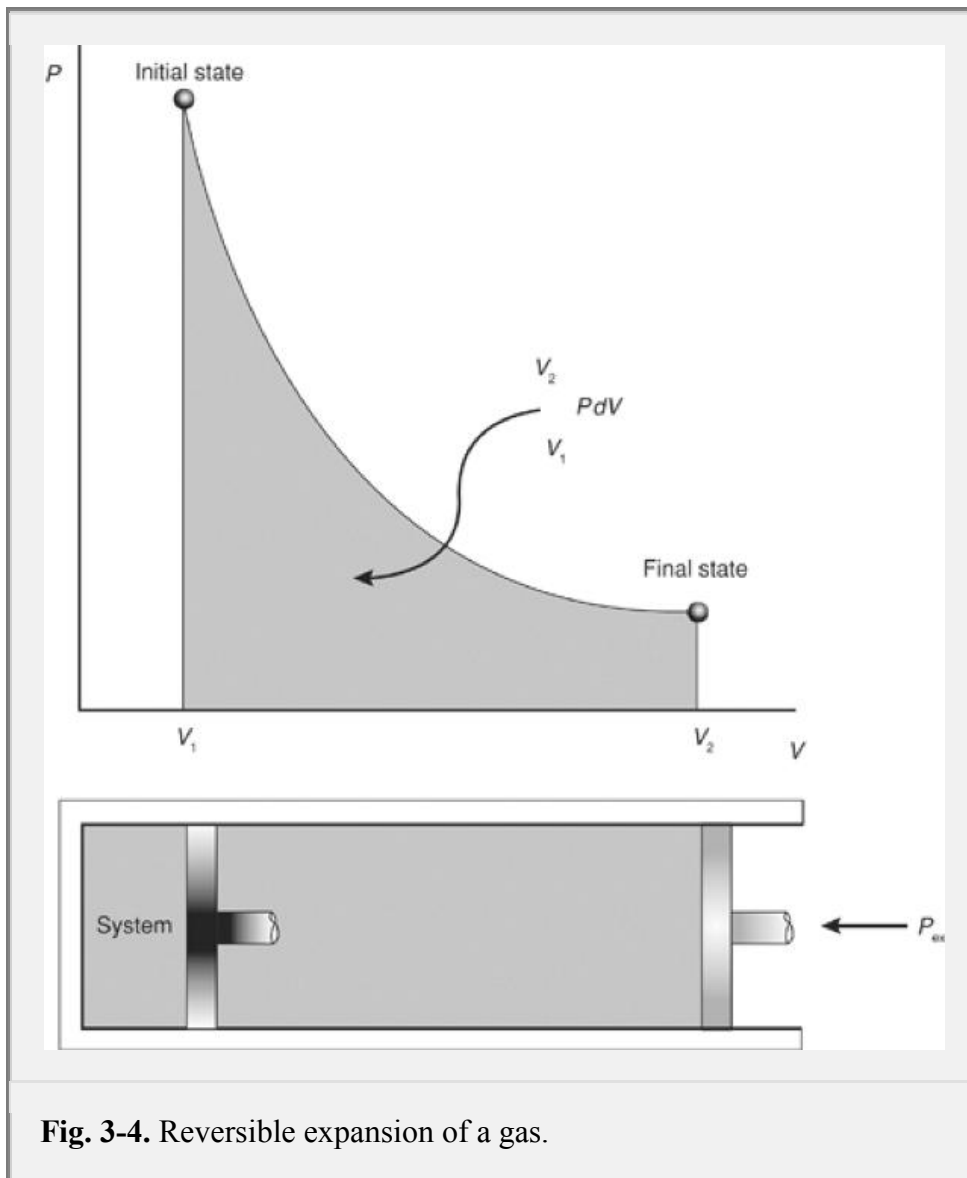


Fig. 3-4. Reversible expansion of a gas.

Equation (3-10) gives the maximum work done in the expansion as well as the heat absorbed, because $Q = \Delta E - W$, and, as will be shown later, ΔE is equal to zero for an ideal gas in an isothermal process. The maximum work in an isothermal reversible expansion may also be expressed in terms of pressure because, from Boyle's law, $V_2/V_1 = P_1/P_2$ at constant temperature. Therefore, equation (3-10) can be written as

$$W_{\max} = -nRT \ln \frac{P_1}{P_2} \quad (3-11)$$

Example 3-3

One mole of water in equilibrium with its vapor is converted into steam at 100°C and 1 atm. The heat absorbed in the process (i.e., the heat of vaporization of water at 100°C) is about 9720 cal/mole. What are the values of the three first-law terms Q , W , and ΔE ?

The amount of heat absorbed is the heat of vaporization, given as 9720 cal/mole. Therefore, $Q = 9720 \text{ cal/mole}$

The work W performed against the constant atmospheric pressure is obtained by using equation (3-10), $W = -nRT \ln(V_2/V_1)$. Now, V_1 is the volume of 1 mole of liquid water at 100°C, or about 0.018 liter. The volume V_2 of 1 mole of steam at 100°C and 1 atm is given by the gas law, assuming that the vapor behaves ideally:

$$V_2 = \frac{RT}{P} = \frac{0.082 \times 373}{1} = 30.6 \text{ liters}$$

It is now possible to obtain the work,

$$W = -(1 \text{ mole})(1.9872 \text{ cal/K mole})(398.15 \text{ K}) \ln (30.6/0.018)$$

$$W = -5883 \text{ cal}$$

The internal energy change ΔE is obtained from the first-law expression,

$$\Delta E = 9720 - 5883 = 3837 \text{ cal}$$

Therefore, of the 9720 cal of heat absorbed by 1 mole of water, 5883 cal is employed in doing the work of expansion, or "PV work," against an external pressure of 1 atm. The remaining 3837 cal increases the internal energy of the system. This quantity of heat supplies potential energy to the vapor molecules, that is, it represents the work done against the noncovalent forces of attraction.

Example 3-4

What is the maximum work done in the isothermal reversible expansion of 1 mole of an ideal gas from 1 to 1.5 liters at 25°C?

The conditions of this problem are similar to those of *Example 3-2*, except that equation (3-10) can now be used to obtain the (maximum) work involved in expanding reversibly this gas by 0.5 liters; thus,

$$W = -(1 \text{ mole})(8.3143 \text{ joules/K mole})(298.15 \text{ K}) \ln (1.5/1.0)$$

$$W = -1005.3 \text{ joules}$$

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When the solution to Example 3-4 (work done in a reversible fashion) is contrasted with the results from Example 3-3 (work done in one stage against a fixed pressure), it becomes apparent that the amount of work required for expansion between separate pathways can dramatically differ.

Changes of State at Constant Volume

If the volume of the system is kept constant during a change of state, $dV = 0$, the first law can be expressed as

$$dE = dQ_v \quad (3-12)$$

where the subscript V indicates that volume is constant. Similarly, under these conditions the combined equation (3-4) is reduced to

$$dq_v = \left(\frac{\partial E}{\partial T} \right)_v dT \quad (3-13)$$

This equation relates the heat transferred during the process at constant volume, dQ_v , with the change in temperature, dT . The ratio between these quantities defines the molar heat capacity at constant volume:

$$\bar{C}_v \equiv \frac{dq_v}{dT} = \left(\frac{\partial E}{\partial T} \right)_v \quad (3-14)$$

Ideal Gases and the First Law

An ideal gas has no internal pressure, and hence no work needs be performed to separate the molecules from their cohesive forces when the gas expands. Therefore, $dW = 0$, and the first law becomes

$$dE = dq \quad (3-15)$$

Thus, the work done by the system in the isothermal expansion of an ideal gas is equal to the heat absorbed by the gas. Because the process is done isothermally, there is no temperature change in the surroundings, $dT = 0$, and $q = 0$. Equation (3-5) is reduced to

$$dE = \left(\frac{\partial E}{\partial V} \right)_T dV = 0 \quad (3-16)$$

In this equation, $dV \neq 0$ because there has been an expansion, so that we can write

$$\left(\frac{\partial E}{\partial V} \right)_T = 0 \quad (3-17)$$

Equation (3-17) suggests that the internal energy of an ideal gas is a function of the *temperature* only, which is one of the conditions needed to define an ideal gas in thermodynamic terms.

Changes of State at Constant Pressure

When the work of expansion is done at *constant pressure*, $W = -P \Delta V = -P(V_2 - V_1)$ by equation (3-7), and under these conditions, the first law can be written as

$$\Delta E = Q_P - P(V_2 - V_1) \quad (3-18)$$

where Q_P is the heat absorbed at constant pressure. Rearranging the equation results in

$$\begin{aligned} Q_P &= E_2 - E_1 + P(V_2 - V_1) \\ &= (E_2 + PV_2) - (E_1 + PV_1) \end{aligned} \quad (3-19)$$

The term $E + PV$ is called the *enthalpy*, H . The increase in enthalpy, ΔH , is equal to the heat absorbed at constant pressure by the system. It is the heat required to increase the internal energy and to perform the work of expansion, as seen by substituting H in equation (3-19),

$$Q_P = H_2 - H_1 = \Delta H \quad (3-20)$$

and writing equation (3-18) as

$$\Delta H = \Delta E + P \Delta V \quad (3-21)$$

For an infinitesimal change, one can write as

$$dq_P = dH \quad (3-22)$$

The heat absorbed in a reaction carried out at atmospheric pressure is independent of the number of steps and the mechanism of the reaction. It depends only on the initial and final conditions. This fact will be used in the section on thermochemistry.

It should also be stressed that $\Delta H = Q_P$ only when nonatmospheric work (i.e., work other than that against the atmosphere) is ruled out. When electric work, work against surfaces, or centrifugal forces are considered, one must write as

$$\Delta H = Q_P - W_{\text{nonatm}} \quad (3-23)$$

The function H is a composite of state properties, and therefore it is also a state property that can be defined as an exact differential. If T and P are chosen as variables, dH can be written as

$$dH = \left(\frac{\partial H}{\partial T} \right)_P dT + \left(\frac{\partial H}{\partial P} \right)_T dP \quad (3-24)$$

When the pressure is held constant, as, for example, when a reaction proceeds in an open container in the laboratory at essentially constant atmospheric pressure, equation (3-24) becomes

$$dH = \left(\frac{\partial H}{\partial T} \right)_P dT \quad (3-25)$$

Because $dq_P = dH$ at constant pressure according to equation (3-22), the molar heat capacity C_P at constant pressure is defined as

$$\bar{C}_P \equiv \frac{dq_P}{dT} = \left(\frac{\partial H}{\partial T} \right)_P \quad (3-26)$$

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and for a change in enthalpy between products and reactants,

$$\Delta H = H_{\text{products}} - H_{\text{reactants}}$$

Table 3-1 Modified First-Law Equations for Processes Occurring Under Various Conditions
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Specified Conditions		Process	Common Me Establishing Condition
(a) Constant heat	$dq = 0$	Adiabatic	Insulated vess Dewar flas
(b) Reversible process at a constant temperature	$dT = 0$	Isothermal	Constant-tem
(c) Ideal gas at a constant temperature	$(\delta E/\delta V)_T = 0$	Isothermal	Constant-tem
(d) Constant volume	$dV = 0$	Isometric (isochoric)	Closed vessel volume, su calorimeter
(e) Constant pressure	$dP = 0$	Isobaric	Reaction occu open contai (atmosph

equation (3-26) may be written as

$$\left[\frac{\partial(\Delta H)}{\partial T} \right]_P = \Delta \bar{C}_P \quad (3-27)$$

where $\Delta C_P = (C_P)_{\text{products}} - (C_P)_{\text{reactants}}$. Equation (3-27) is known as the *Kirchhoff equation*.

Summary

Some of the special restrictions that have been placed on the first law up to this point in the chapter, together with the resultant modifications of the law, are brought together in Table 3-1. A comparison of the entries in Table 3-1 with the material that has gone before will serve as a comprehensive review of the first law.

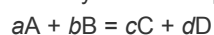
Thermochemistry

Many chemical and physical processes of interest are carried out at atmospheric (essentially constant) pressure. Under this condition, the heat exchanged during the process equals the change in enthalpy according to equation (3-20), $Q_P = \Delta H$. Thus, the change in enthalpy accompanying a chemical reaction remains a function only of temperature as stated in equation (3-27). A negative ΔH and Q_P means that heat is released (exothermic); a positive value of ΔH and Q_P means that heat is absorbed (endothermic). It is also possible that a reaction takes place in a closed container; in such a case the heat exchanged equals the change in internal energy (i.e., $Q_V = \Delta E$).

Thermochemistry deals with the heat changes accompanying isothermal chemical reactions at constant pressure or volume, from which values of ΔH or ΔE can be obtained. These thermodynamic properties are, of course, related by the definition of H , equation (3-21). In solution reactions, the $P \Delta V$ terms are not significant, so that ΔH [congruent] ΔE . This close approximation does not hold, however, for reactions involving gases.

Heat of Formation

For any reaction represented by the chemical equation



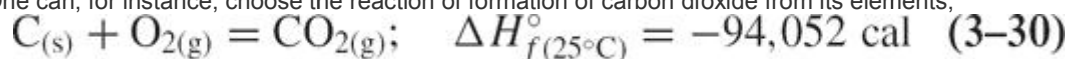
the enthalpy change can be written as

$$\Delta H = \sum \bar{H}_{\text{products}} - \sum \bar{H}_{\text{reactants}} \quad (3-28)$$

$$\Delta H = c\bar{H}_C + d\bar{H}_D - a\bar{H}_A - b\bar{H}_B \quad (3-29)$$

where \bar{H} = enthalpy per mole (called the molar enthalpy) and a , b , c , and d are stoichiometric coefficients. It is known that only the molar enthalpies of compounds, either as reactants or products, contribute to the change of enthalpy of a chemical reaction. Enthalpies are all relative magnitudes, so it is useful to define the heat involved in the formation of chemical compounds.

One can, for instance, choose the reaction of formation of carbon dioxide from its elements,



Here

$$\Delta H_{f(25^\circ\text{C})}^\circ = \bar{H}(\text{CO}_2, \text{g}, 1 \text{ atm}) - \bar{H}(\text{C}, \text{s}, 1 \text{ atm}) - \bar{H}(\text{O}_2, \text{g}, 1 \text{ atm}) \quad (3-31)$$

The subscripts represent the physical states, (s) standing for solid and (g) for gas. Additional symbols, (l) for liquid and (aq) for dilute aqueous solution, will be found in subsequent thermochemical equations.

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Key Concept

Standard Enthalpy

In thermodynamics, the convention of assigning zero enthalpy to all elements in their most stable physical state at 1 atm of pressure and 25°C is known as choosing a standard or reference state:

$$\bar{H}^\circ(\text{compound}) \equiv \Delta \bar{H}_f^\circ$$

If the \bar{H} values for the elements $\text{C}_{(s)}$ and $\text{O}_{2(g)}$ are chosen arbitrarily to be zero, then according to equation (3-31), the molar enthalpy of the compound, $\bar{H}(\text{CO}_2, \text{g}, 1 \text{ atm})$, is equal to the enthalpy of the formation reaction, $\Delta H_{f(25^\circ\text{C})}^\circ$, for the process in equation (3-30) at 1 atm of pressure and 25°C.

The standard heat of formation of gaseous carbon dioxide is $\Delta H^\circ_{f(25^\circ\text{C})} = -94,052$ cal. The negative sign accompanying the value for ΔH signifies that heat is evolved, that is, the reaction is exothermic. The state of matter or allotropic form of the elements also must be specified in defining the standard state. Equation (3-30) states that when 1 mole of solid carbon (graphite) reacts with 1 mole of gaseous oxygen to produce 1 mole of gaseous carbon dioxide at 25°C, 94,052 cal is liberated. This means that the reactants contain 94,052 cal in excess of the product, so that this quantity of heat is evolved during the reaction. If the reaction were reversed and CO₂ were converted to carbon and oxygen, the reaction would be endothermic. It would involve the absorption of 94,052 cal, and ΔH would have a positive value.

The standard heats of formation of thousands of compounds have been determined, and some of these are given in Table 3-2.

Table 3-2 Standard Heats of Formation at 25°C*

Substance	ΔH° (kcal/mole)	Substance	ΔH° (kcal/mole)
H _{2(g)}	0		
H _(g)	52.09	Methane _(g)	-17.889
O _{2(g)}	0	Ethane _(g)	-20.236
O _(g)	59.16	Ethylene _(g)	12.496
I _{2(g)}	14.88	Benzene _(g)	19.820
H ₂ O _(g)	-57.798	Benzene _(l)	11.718
H ₂ O _(l)	-68.317	Acetaldehyde _(g)	-39.76
HCl _(g)	-22.063	Ethyl alcohol _(l)	-66.356
HI _(g)	6.20	Glycine _(g)	-126.33
CO _{2(g)}	-94.052	Acetic acid _(l)	-116.4

*From F. D. Rossini, K. S. Pitzer, W. J. Taylor, et al., *Selected Values of Properties of Hydrocarbons* (Circular of the National Bureau of Standards 461), U.S. Government Printing Office, Washington, D.C., 1947; F. D. Rossini, D. D. Wagman, W. H. Evans, et al., *Selected Values of Chemical Thermodynamic Properties* (Circular of the National Bureau of Standards

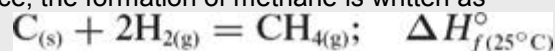
500), U.S. Government Printing Office, Washington, D.C., 1952.

Hess's Law and Heat of Combustion

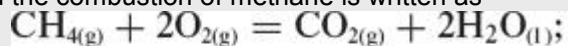
It is not possible to directly measure the heats of formation of every known compound as in equation (3-30). Incomplete or side reactions often complicate such determinations. However, as early as 1840, Hess showed that because ΔH depends only on the initial and final states of a system, thermochemical equations for several steps in a reaction could be added and subtracted to obtain the heat of the overall reaction. The principle is known as *Hess's law of constant heat summation* and is used to obtain heats of reaction that are not easily measured directly.

Example 3-5

It is extremely important to use the heat of combustion, that is, the heat involved in the complete oxidation of 1 mole of a compound at 1 atm pressure, to convert the compound to its products. For instance, the formation of methane is written as

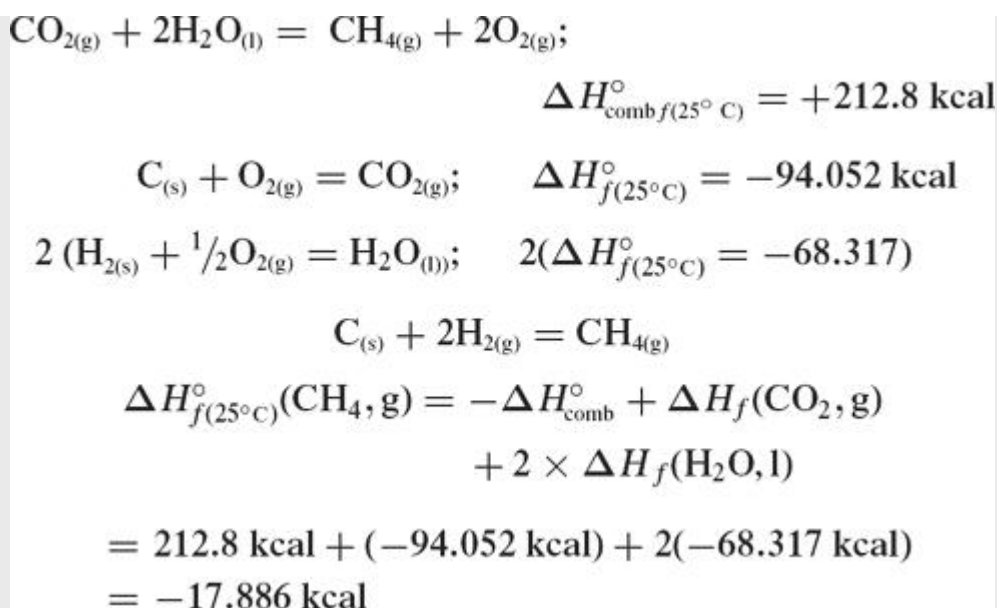


and the combustion of methane is written as



$$\Delta H_{\text{comb}(25^\circ\text{C})}^\circ = -212.8 \text{ kcal}$$

The enthalpies of formation of both $\text{CO}_{2(g)}$ and $\text{H}_2\text{O}_{(l)}$ have been measured with extreme accuracy; therefore, $\Delta H_{f(25^\circ\text{C})}^\circ$ for methane gas can be obtained by subtracting $\Delta H_{f(25^\circ\text{C})}^\circ$ of $\text{CO}_{2(g)}$ and twice that of $\text{H}_2\text{O}_{(l)}$ from the heat of combustion:



The heat of formation of $\text{CH}_{4(g)}$, methane, is reported in Table 3-2 as -17.889.

Heats of Reaction from Bond Energies

In Chapter 2, energies of bonding were discussed in terms of binding forces that hold molecules (*intramolecular bonding*) or states of matter (*noncovalent forces*) together. For example, the energies associated with covalent bonding between atoms range from 50 to 200 kcal/mole. These figures encompass many of the types of bonding that you learned about in general and organic chemistry courses, including double and triple bonds that arise from π -electron orbital overlap, but they are weaker than covalent σ -electron orbital bonds. Electrovalent or ionic bonds occurring between atoms with opposing permanent charges can be much stronger than a covalent bond. In a molecule, the forces enabling a bond

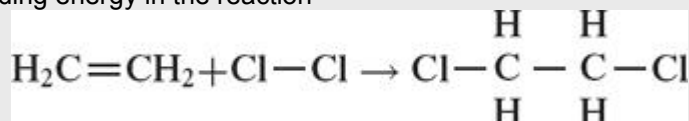
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to form between atoms arise from a combination of attractive and repulsive energies associated with each atom in the molecule. These forces vary in strength because of interplay between attraction and repulsion. Therefore, the net bonding energy that holds a series of atoms together in a molecule is the additive result of all the individual bonding energies.

In a chemical reaction, bonds may be broken and new bonds may be formed to give rise to the product. The net energy associated with the reaction, the heat of reaction, can be estimated from the bond energies that are broken and the bond energies that are formed during the reaction process. Many of the common covalent and other bonding-type energies can be commonly found in books on thermodynamics, like the ones listed in the footnote in the opening of this chapter.

Example 3-6

The covalent bonding energy in the reaction



can be calculated from knowing a $\text{C}=\text{C}$ bond is broken (requiring 130 kcal), a $\text{Cl}-\text{Cl}$ bond is broken (requiring 57 kcal), a $\text{C}-\text{C}$ bond is formed (liberating 80 kcal), and two $\text{C}-\text{Cl}$ bonds are formed (liberating 2×78 or 156 kcal). Thus, the energy ΔH of the reaction is $\Delta H = 130 + 57 - 80 - 156 = -49 \text{ kcal}$

Because 1 cal = 4.184 joules, -49 kcal is expressed in SI units as -2.05×10^5 joules.

The foregoing process is not an idealized situation; strictly speaking, it applies only to reactions in a gas phase. If there is a change from a gas into a condensed phase, then condensation, solidification, or crystallization heats must be involved in the overall

calculations. This approach may find some use in estimating the energy associated with chemical instability.

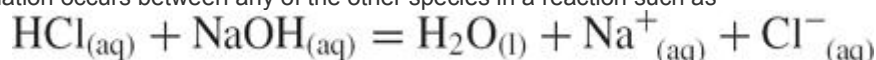
Additional Applications of Thermochemistry

Thermochemical data are important in many chemical calculations. Heat-of-mixing data can be used to determine whether a reaction such as precipitation is occurring during the mixing of two salt solutions. If no reaction takes place when dilute solutions of the salts are mixed, the heat of reaction is zero.

The constancy of the heats of neutralization obtained experimentally when dilute aqueous solutions of various strong acids and strong bases are mixed shows that the reaction involves only



No combination occurs between any of the other species in a reaction such as



because HCl, NaOH, and NaCl are completely ionized in water. In the neutralization of a weak electrolyte by a strong acid or base, however, the reaction involves ionization in addition to neutralization, and the heat of reaction is no longer constant at about -13.6 kcal/mole. Because some heat is absorbed in the ionization of the weak electrolyte, the heat evolved falls below the value for the neutralization of completely ionized species. Thus, knowledge of ΔH of neutralization allows one to differentiate between strong and weak electrolytes.

Another important application of thermochemistry is the determination of the number of calories obtained from various foods. The subject is discussed in biochemistry texts as well as books on food and nutrition.

The Second Law of Thermodynamics

In ordinary experience, most natural phenomena are observed as occurring only in one direction. For instance, heat flows spontaneously only from hotter to colder bodies, whereas two bodies having the same temperature do not evolve into two bodies having different temperatures, even though the first law of thermodynamics does not prohibit such a possibility. Similarly, gases expand naturally from higher to lower pressures, and solute molecules diffuse from a region of higher to one of lower concentration. These spontaneous processes will not proceed in reverse without the intervention of some external force to facilitate their occurrence. Although spontaneous processes are not thermodynamically reversible, they can be carried out in a nearly reversible manner by an outside force. Maximum work is obtained by conducting a spontaneous process reversibly; however, the frictional losses and the necessity of carrying out the process at an infinitely slow rate preclude the possibility of complete reversibility in real processes.

The first law of thermodynamics simply observes that energy must be conserved when it is converted from one form to another. It has nothing to say about the probability that a process will occur. The second law refers to the probability of the occurrence of a process based on the observed tendency of a system to approach a state of energy equilibrium.

The historical development of the thermodynamic property that explains the natural tendency of the processes to occur, now called *entropy*, has its origins in studies of the efficiency of steam engines, from which the following observation was made: "A steam engine can do work only with a fall in temperature and a flow of heat to the lower temperature. No useful work can be obtained from heat at constant temperature." This is one way to state the second law of thermodynamics.

The Efficiency of a Heat Engine

An important consideration is that of the possibility of converting heat into work. Not only is heat isothermally unavailable for work, *it can never be converted completely into work.*

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The spontaneous character of natural processes and the limitations on the conversion of heat into work constitute the second law of thermodynamics. Falling water can be made to do work owing to the

difference in the potential energy at two different levels, and electric work can be done because of the difference in electric potential (emf). A heat engine (such as a steam engine) likewise can do useful work by using two heat reservoirs, a “source” and a “sink,” at two different temperatures. Only part of the heat at the source is converted into work, with the remainder being returned to the sink (which, in practical operations, is often the surroundings) at the lower temperature. The fraction of the heat, Q , at the source converted into work, W , is known as the *efficiency* of the engine:

$$\text{Efficiency} \equiv \frac{W}{Q} \quad (3-33)$$

The efficiency of even a hypothetical heat engine operating without friction cannot be unity because W is always less than Q in a continuous conversion of heat into work according to the second law of thermodynamics.

Imagine a hypothetical steam engine operating reversibly between an upper temperature T_{hot} and a lower temperature T_{cold} . It absorbs heat Q_{hot} from the hot boiler or source, and by means of the working substance, steam, it converts the quantity W into work and returns heat Q_{cold} to the cold reservoir or sink. Carnot, in 1824, proved that the efficiency of such an engine, operating reversibly at every stage and returning to its initial state (cyclic process), could be given by the expression

$$\frac{W}{Q_{\text{hot}}} = \frac{Q_{\text{hot}} - Q_{\text{cold}}}{Q_{\text{hot}}} \quad (3-34)$$

It is known that heat flow in the operation of the engine follows the temperature gradient, so that the heat absorbed and rejected can be related directly to temperatures. Lord Kelvin used the ratios of the two heat quantities Q_{hot} and Q_{cold} of the Carnot cycle to establish the Kelvin temperature scale:

$$\frac{Q_{\text{hot}}}{Q_{\text{cold}}} = \frac{T_{\text{hot}}}{T_{\text{cold}}} \quad (3-35)$$

By combining equations (3-33) through (3-35), we can describe the efficiency by

$$\text{Efficiency} = \frac{Q_{\text{hot}} - Q_{\text{cold}}}{Q_{\text{hot}}} = \frac{T_{\text{hot}} - T_{\text{cold}}}{T_{\text{hot}}} \quad (3-36)$$

It is observed from equation (3-36) that the higher T_{hot} becomes and the lower T_{cold} becomes, the greater is the efficiency of the engine. When T_{cold} reaches absolute zero on the Kelvin scale, the reversible heat engine converts heat completely into work, and its theoretical efficiency becomes unity. This can be seen by setting $T_{\text{cold}} = 0$ in equation (3-36). Because absolute zero is considered unattainable, however, an efficiency of 1 is impossible, and heat can never be completely converted to work. This statement can be written using the notation of limits as follows:

$$\lim_{T_{\text{cold}} \rightarrow 0} \frac{W}{Q} = 1 \quad (3-37)$$

If $T_{\text{hot}} = T_{\text{cold}}$ in equation (3-36), the cycle is isothermal and the efficiency is zero, confirming the earlier statement that heat is isothermally unavailable for conversion into work.

Example 3-7

A steam engine operates between the temperatures of 373 and 298 K. (a) What is the theoretical efficiency of the engine? (b) If the engine is supplied with 1000 cal of heat Q_{hot} , what is the theoretical work in ergs?

(a)

$$\text{Efficiency} = \frac{W}{Q_{\text{hot}}} = \frac{373 - 298}{373} = 0.20, \quad \text{or} \quad 20\%$$

(b)

$$W = 1000 \times 0.20 = 200 \text{ cal}$$

$$200 \text{ cal} \times 4.184 \times 10^7 \text{ ergs/cal} = 8.36 \times 10^9 \text{ ergs}$$

Entropy

In analyzing the properties of reversible cycles, one feature was unveiled; the sum of the quantities Q_{rev}/T_i is zero for the cycle, that is,

$$\frac{Q_{\text{hot}}}{T_{\text{hot}}} + \frac{Q_{\text{cold}}}{T_{\text{cold}}} = 0 \quad (3-38)$$

This behavior is similar to that of other state functions such as ΔE and ΔH ; Carnot recognized that when Q_{rev} , a path-dependent property, is divided by T , a new path-independent property is generated, called *entropy*. It is defined as

$$\Delta S = \frac{Q_{\text{rev}}}{T} \quad (3-39)$$

and for an infinitesimal change,

$$dH = \left(\frac{\partial H}{\partial T} \right)_P dT \quad (3-40)$$

Thus, the term $Q_{\text{hot}}/T_{\text{hot}}$ is known as the *entropy change* of the reversible process at T_{hot} , and $Q_{\text{cold}}/T_{\text{cold}}$ is the *entropy change* of the reversible process at T_{cold} . The entropy change ΔS_{hot} during the absorption of heat from T_{hot} is positive, however, because Q_{hot} is positive. At the lower temperature, Q_{cold} is negative and the entropy change ΔS_{cold} is negative. The total entropy change ΔS_{cycle} in the reversible cyclic process is zero. Let us use the data from Example 3-7 to demonstrate this. It can be seen that only part of the heat Q_{hot} (1000 cal) is converted to work (200 cal) in the engine. The difference in energy (800 cal) is the heat Q_{cold} that is returned to the sink at the lower temperature and is unavailable for work. When the entropy changes at the two temperatures are calculated, they are both found to equal 2.7 cal/deg:

$$\Delta S = \frac{Q_{\text{hot,rev}}}{T_{\text{hot}}} = \frac{1000 \text{ cal}}{373} = 2.7 \text{ cal/deg}$$

$$\Delta S = -\frac{Q_{\text{cold,rev}}}{T_{\text{cold}}} = -\frac{800 \text{ cal}}{298} = -2.7 \text{ cal/deg}$$

Therefore,

$$\Delta S_{\text{cycle}} = \Delta S_{\text{hot}} + \Delta S_{\text{cold}} = 0$$

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It may also be noted that if Q_{hot} is the heat absorbed by an engine at T_{hot} , then $-Q_{\text{hot}}$ must be the heat lost by the surroundings (the hot reservoir) at T_{hot} , and the entropy of the surroundings is

$$\Delta S_{\text{surr}} = -\frac{Q_{\text{hot}}}{T_{\text{hot}}} \quad (3-41)$$

Hence, for any system and its surroundings or *universe*,

$$\Delta S_{\text{univ}} = \Delta S_{\text{sys}} + \Delta S_{\text{surr}} = 0 \quad (3-42)$$

Therefore, there are two cases in which $\Delta S = 0$: (a) a system in a reversible cyclic process and (b) a system and its surroundings undergoing any reversible process.

In an *irreversible process*, the entropy change of the total system or universe (a system and its surroundings) is always positive because ΔS_{surr} is always less than ΔS_{sys} in an irreversible process. In mathematical symbols, we write,

$$\Delta S_{\text{univ}} = \Delta S_{\text{sys}} + \Delta S_{\text{surr}} > 0 \quad (3-43)$$

and this can serve as a criterion of spontaneity of a real process.

Equations (3-42) and (3-43) summarize all of the possibilities for the entropy; for irreversible processes (real transformations) entropy always increases until it reaches its maximum at equilibrium, at which point it remains invariable (i.e., change equals zero).

Two examples of entropy calculations will now be given, first, a reversible process, and second, an irreversible process.

Example 3-8

What is the entropy change accompanying the vaporization of 1 mole of water in equilibrium with its vapor at 25°C? In this reversible isothermal process, the heat of vaporization ΔH_v required to convert the liquid to the vapor state is 10,500 cal/mole.

The process is carried out at a constant pressure, so that $Q_P = \Delta H_v$, and because it is a reversible process, the entropy change can be written as

$$\Delta S = \frac{\Delta H_v}{T} = \frac{10,500}{298} = 35.2 \text{ cal/mole deg}$$

The entropy change involved as the temperature changes is often desired in thermodynamics; this relationship is needed for the next example. The heat absorbed at constant pressure is given by equation (3-26), $dq_P = C_P dT$, and for a reversible process

$$\frac{C_P dT}{T} = \frac{dq_{\text{rev}}}{T} = dS \quad (3-44)$$

Integrating between T_1 and T_2 yields

$$\Delta S = C_P \ln \frac{T_2}{T_1} = 2.303 C_P \log \frac{T_2}{T_1} \quad (3-45)$$

Example 3-9

Compute the entropy change in the (irreversible) transition of 1 mole of liquid water to crystalline water at -10°C, at constant pressure. The entropy is obtained by calculating the entropy changes for several *reversible* steps.

First consider the reversible conversion of supercooled liquid water at -10°C to liquid water at 0°C, then change this to ice at 0°C, and finally cool the ice reversibly to -10°C. The sum of the entropy changes of these steps gives ΔS_{water} . To this, add the entropy change undergone by the surroundings so as to obtain the total entropy change. If the process is spontaneous, the result will be a positive value. If the system is at equilibrium, that is, if liquid water is in equilibrium with ice at -10°C, there is no tendency for the transition to occur, and the total entropy change will be zero. Finally, if the process is not spontaneous, the total entropy change will be negative.

The heat capacity of water is 18 cal/deg and that of ice is 9 cal/deg within this temperature range.

The reversible change of water at -10°C to ice at -10°C is carried out as follows:

$$\text{H}_2\text{O}_{(l,-10^\circ)} \rightarrow \text{H}_2\text{O}_{(l,0^\circ)}; \quad \Delta S = C_P \ln \frac{T_{\text{final}}}{T_{\text{initial}}} = 0.67$$

$$\text{H}_2\text{O}_{(l,0^\circ)} \rightarrow \text{H}_2\text{O}_{(s,0^\circ)}; \quad \Delta S = \frac{q_{\text{rev}}}{T} = \frac{-1437}{273.2} = -5.26$$

$$\text{H}_2\text{O}_{(s,0^\circ)} \rightarrow \text{H}_2\text{O}_{(s,-10^\circ)}; \quad \Delta S = C_P \ln \frac{T_{\text{final}}}{T_{\text{initial}}} = -0.34$$

$$\text{H}_2\text{O}_{(l,-10^\circ)} \rightarrow \text{H}_2\text{O}_{(s,-10^\circ)}; \quad \Delta S_{\text{H}_2\text{O}} = -4.93 \text{ cal/mole deg}$$

The entropy of water decreases during the process because ΔS is negative, but the spontaneity of the process cannot be judged until one also calculates ΔS of the surroundings. For the entropy change of the surroundings, the water needs to be considered to be in equilibrium with a large bath at -10°C , and the heat liberated when the water freezes is absorbed by the bath without a significant temperature increase. Thus, the reversible absorption of heat by the bath is given by

$$\Delta S_{\text{surr}} = -\frac{Q_{\text{rev}}}{T} = \frac{1343}{263.2} = 5.10 \text{ cal/mole, deg}$$

where 1343 cal/mole is the heat of fusion of water at -10°C . Thus,

$$\begin{aligned} \Delta S_{\text{total system}} &= \Delta S_{\text{H}_2\text{O}} + \Delta S_{\text{bath}} \\ &= -4.91 + 5.10 \\ &= 0.17 \text{ cal/mole deg} \end{aligned}$$

The process in Example 3-8 is spontaneous because $\Delta S > 0$. This criterion of spontaneity is not a convenient one, however, because it requires a calculation of the entropy change both in the system and the surroundings. The free energy functions, to be treated in a later section, do not require information concerning the surroundings and are more suitable criteria of spontaneity.

Entropy and Disorder

The second law provides a criterion for deciding whether a process follows the *natural* or *spontaneous* direction. Even though the causes for the preference for a particular direction of change of state or the impossibility for the reverse direction are unknown, the underlying reason is not that the reverse process is impossible, but rather that it is extraordinarily improbable.

Thermodynamic systems described by macroscopic properties such as T , P , or composition can also be described in terms of microscopic quantities such as molecular random motions. The microscopic or molecular interpretation of

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entropy is commonly stated as a measure of disorder owing to molecular motion. As disorder increases, entropy will also increase. The impossibility of converting all thermal energy into work results from the "disorderliness" of the molecules existing in the system. Disorder can be seen as the number of ways the inside of a system can be arranged so that from the outside the system looks the same. A quantitative interpretation of entropy was given long before by Boltzmann; the equation for the entropy of a system in a given thermodynamic state is

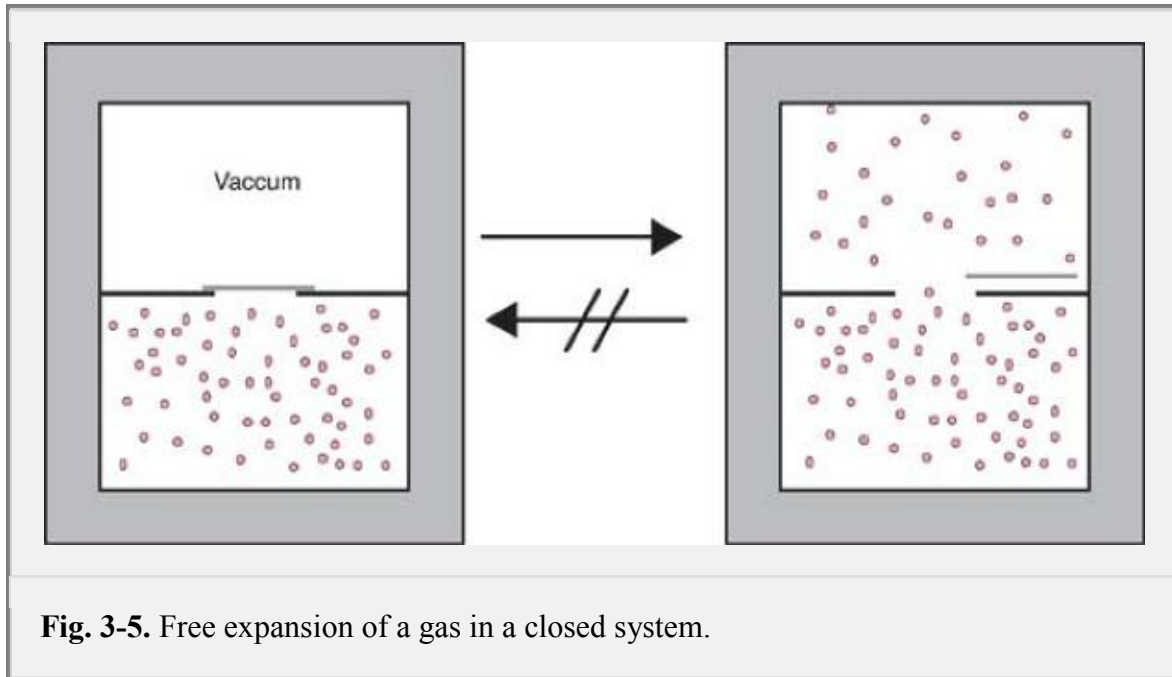


Fig. 3-5. Free expansion of a gas in a closed system.

$$S = k \ln O \quad (3-46)$$

where k is the Boltzmann constant and O is the number of microscopic states or configuration that the system may adopt. Unlike the thermodynamic definition of entropy in equation (3-39) or (3-40), to understand what a configuration means (i.e., O), a structural model of the system is needed.

Let us imagine that the system consists of a gas in a closed container that is allowed to expand freely into a vacuum (Fig. 3-5). The initial state corresponds to V_1 and the final state corresponds to V_2 , which is larger than V_1 : $V_2 = 2V_1$.

If only one gas particle is in the initial state, statistically there are two equal possibilities for a particle to occupy V_2 , whereas only one exists for V_1 . In other words, the probability P for that particle to stay in V_1 is $P = 1/2$ (Fig. 3-6a). Now consider two independent particles; the probability of finding both in V_1 after V_2 is available is $P = (1/2)^2 = 1/4$ (Fig. 3-6b). For three particles there are eight possible configurations, so the probability for all particles to stay in V_1 is only $1/8$. For a system composed of N particles the probability becomes $P = (1/2)^N$. Now, if N is on the order of regular molecular quantities, that is, $\sim 10^{23}$ molecules, the probability of finding all of them in the initial state is extraordinarily small, $P = 1/2^{10^{23}}$.

Thus, in this model system, by changing from the initial state V_1 to a final state V_2 , we significantly increase the number of distribution possibilities of the N particles. Once the system has expanded, it is extremely improbable that they will be found by chance only in V_1 . For this simple system, the probability expressed by the number of configurations after an irreversible process from state 1 to state 2 is generally related to the volumes as

$$P = (O_1/O_2) = (V_1/V_2)^N \quad (3-47)$$

and, therefore, the change of entropy for 1 mole of gas is given by

$$\Delta S = S_2 - S_1 = k \ln(O_2/O_1) = kN_A \ln(V_2/V_1) \quad (3-48)$$

From the standpoint of this simple model, the isothermal expansion of an ideal gas increases the entropy because of

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the enhanced number of configurations in a larger volume compared to a smaller one. The larger the number of configurations, the more disordered a system is considered. Thus, the increase in entropy with increasing number of configurations is nicely described by Boltzmann concept given in equation (3-46).

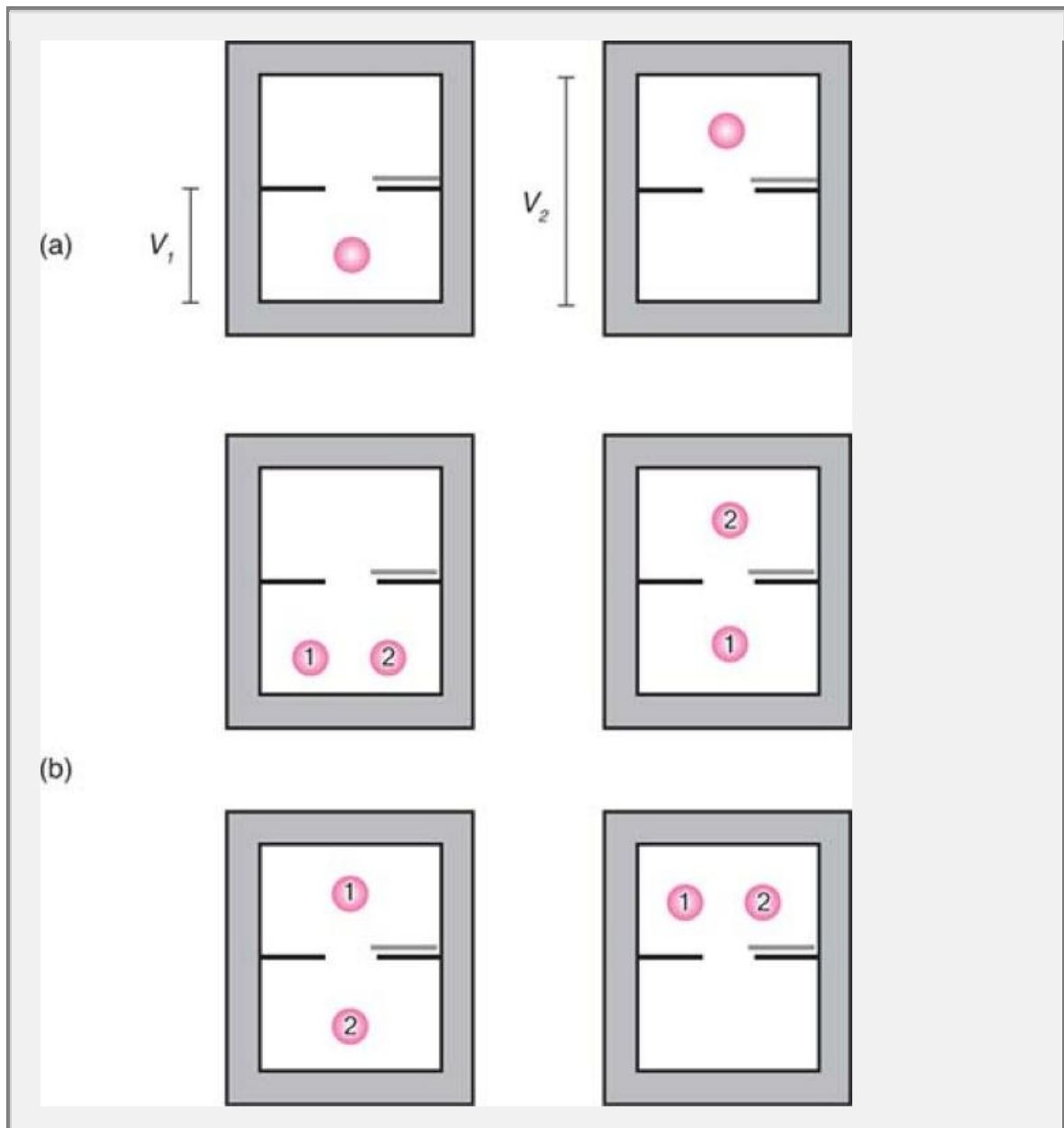


Fig. 3-6. (a) The two possible states of a system of one molecule. (b) The four possible states of a system of two independent molecules.

The Third Law of Thermodynamics

The third law of thermodynamics states that the entropy of a pure crystalline substance is zero at absolute zero because the crystal arrangement must show the greatest orderliness at this temperature. In other words, a pure perfect crystal has only one possible configuration, and according to equation (3-46), its entropy is zero [i.e., $S = k \ln(1) = 0$]. As a consequence of the third law, the temperature of absolute zero (0 K) is not possible to reach even though sophisticated processes that use the orientation of electron spins and nuclear spins can reach very low temperatures of 2×10^{-3} and 10^{-5} K, respectively. The third law makes it possible to calculate the absolute entropies of pure substances from equation (3-44) rearranged as

$$S_T = \sum \frac{dq_{\text{rev},i}}{T_i} + S_0 \quad (3-49)$$

where S_0 is the molar entropy at absolute zero and S_T is the absolute molar entropy at any temperature. The magnitude dq_{rev} can be replaced by the corresponding $C_P dT$ values at constant pressure according to equation (3-26), so that S_T may be determined from knowledge of the heat capacities and the entropy changes during a *phase change* as the temperature rises from 0 K to T . The following equation shows S_T for a substance that undergoes two phase changes, melting (m) and vaporization (v):

$$S_T = \int_0^{T_m} \frac{C_P dT}{T} + \frac{\Delta H_m}{T_m} + \int_{T_m}^{T_v} \frac{C_P dT}{T} + \frac{\Delta H_v}{T_v} + \int_{T_v}^T \frac{C_P dT}{T}$$

where $S_0 = 0$ has been omitted. Each of these terms can be evaluated independently; in particular, the first integral is calculated numerically by plotting C_P/T versus T . Below 20 K few data are available, so that it is customary to apply the Debye approximation $C_P \propto aT^3$, joules/mole K in this region.

Free Energy Functions and Applications

The criterion for spontaneity given by the second law requires the knowledge of the entropy changes both in the system and the surroundings as stated in equation (3-43). It may be very useful, however, to have a property that depends only on the system and nevertheless indicates whether a process occurs in the natural direction of change.

Let us consider an *isolated system* composed of a closed container (i.e., the system) in equilibrium with a temperature bath (i.e., the surroundings) as illustrated in Figure 3-1d, then according to equations (3-42) and (3-43), the resulting equation is

$$\Delta S_{\text{isolated system}} = \Delta S_{\text{syst}} + \Delta S_{\text{surr}} \geq 0 \quad (3-50)$$

Equilibrium is a condition where the transfer of heat occurs reversibly; therefore, at constant temperature, $\Delta S_{\text{surr}} = -\Delta S_{\text{syst}}$ and

$$\Delta S_{\text{surr}} = -\frac{Q_{\text{rev}}}{T} \quad (3-51)$$

Now, renaming $\Delta S_{\text{syst}} = \Delta S$ and $Q_{\text{rev}} = Q$, we write equation as

$$\Delta S - \frac{Q}{T} \geq 0 \quad (3-52)$$

which can also be written in the following way:

$$Q - T\Delta S \leq 0 \quad (\text{at } T = \text{const}) \quad (3-53)$$

For a process at constant volume, $Q_v = \Delta E$, so equation (3-53) becomes

$$\Delta E - T\Delta S \leq 0 \quad (\text{at } T = \text{const}, V = \text{const}) \quad (3-54)$$

In the case of a process at constant pressure, $Q_p = \Delta H$, and

$$\Delta H - T \Delta S \leq 0 \quad (\text{at } T = \text{const}, P = \text{const}) \quad (3-55)$$

Equations (3-54) and (3-55) are combinations of the first and second laws of the thermodynamics and express both equilibrium (=) and spontaneity (<) conditions depending only on the properties of the system; therefore, they are of fundamental practical importance. The terms on the left of equations (3-54) and (3-55) are commonly defined as the *Helmholtz free energy or work function* A ,

$$A = E - TS \quad (3-56)$$

and the *Gibbs free energy* G ,

$$G = H - TS \quad (3-57)$$

respectively, which are two new state properties because they are composed of state variables E , H , T , and S . Thus, equilibrium and spontaneity conditions are reduced to only

$$\Delta A = 0 \quad (\text{at } T = \text{const}, V = \text{const}) \quad (3-58)$$

$$\Delta G = 0 \quad (\text{at } T = \text{const}, P = \text{const}) \quad (3-59)$$

Maximum Net Work

The second law of the thermodynamics expressed in equation (3-53) for an isothermal process can be combined with the conservation of energy by substituting $Q = \Delta E - W$, yielding

$$\Delta E - W - T \Delta S = 0 \quad (3-60)$$

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Table 3-3 Criteria for Spontaneity and Equilibrium				
Function	Restrictions	Sign of Function		
		Spontaneous	Nonspontaneous	Equilibrium
	Total system,			
$\Delta S_{\text{universe}}$	$\Delta E = 0, \Delta V = 0$	+ or >0	- or <0	0
ΔG	$\Delta T = 0, \Delta P = 0$	- or <0	+ or >0	0
ΔA	$\Delta T = 0, \Delta V = 0$	- or <0	+ or >0	0

In this case, W represents all possible forms of work available and not only PV work (i.e., expansion or compression of the system). The system does maximum work (W_{max}) when it is working under reversible conditions; therefore, only the equality in equation (3-60) applies. By including the definition for A in equation (3-60), we obtain

$$\Delta A - W_{\text{max}} = 0 \quad \text{or} \quad \Delta A = W_{\text{max}} \quad (3-61)$$

The former equation explains the meaning of the *Helmholtz* energy (which also explains why it is called a *work function*), that is, the *maximum work* produced in an isothermal transformation is equal to the change in the Helmholtz energy.

Now if W is separated into the PV work and all other forms of work excluding expansion or compression, W_a (also called *useful work*) for an isothermal process at constant pressure equation (3-60) can be written as

$$\Delta E - W_a = P \Delta V - T \Delta S = 0 \quad (3-62)$$

The definition of the Gibbs energy given in equation (3-60) can also be written as

$$G = E + PV - TS \quad (3-63)$$

For a reversible process equation, (3-62) transforms into

$$\Delta G - W_a = 0 \quad \text{or} \quad \Delta G = W_a \quad (3-64)$$

Equation (3-64) expresses the fact that the change in Gibbs free energy at constant temperature and pressure equals the *useful* or *maximum net work* (W_a) that can be obtained from the process. Under those circumstances in which the PV term is insignificant (such as in electrochemical cells and surface tension measurements), the free energy change is approximately equal to the maximum work.

Criteria of Equilibrium and Spontaneity

When net work can no longer be obtained from a process, G is at a minimum, and $\Delta G = 0$. This statement signifies that the system is at equilibrium. On the other hand, from equation (3-62) a negative free energy change written as $\Delta G < 0$ signifies that the process is a spontaneous one. If ΔG is positive ($\Delta G > 0$), it indicates that net work must be absorbed for the reaction to proceed, and accordingly it is not spontaneous.

When the process occurs isothermally at constant volume rather than constant pressure, ΔA serves as the criterion for spontaneity and equilibrium. From equation (3-58) it is negative for a spontaneous process and becomes zero at equilibrium.

These criteria, together with the entropy criterion of equilibrium and spontaneity, are listed in Table 3-3. The difference in sign between ΔG and $\Delta S_{\text{universe}}$ implies that the condition for a process being spontaneous has changed from an increase of the total entropy, $\Delta S_{\text{universe}} > 0$, to a decrease in Gibbs free energy, $\Delta G < 0$. However, Gibbs free energy is only a composite that expresses the total change in entropy in terms of the properties of the system alone. To prove that, let us combine equations (3-42) and (3-51) for a reversible isothermal process into

$$T \Delta S_{\text{universe}} = T \Delta S - Q_{\text{rev}} \quad (\text{at } T = \text{const}) \quad (3-65)$$

Then, if the pressure is constant,

$$T \Delta S_{\text{universe}} = T \Delta S - \Delta H \quad (\text{at } T = \text{const}, P = \text{const}) \quad (3-66)$$

For the same process,

$$\Delta G = \Delta H - T \Delta S \quad (3-67)$$

and therefore

$$\Delta G = -T \Delta S_{\text{universe}} \quad (3-68)$$

From the former equation it is clear that *the only criterion for spontaneous change is an increase of the entropy of the universe (i.e., the system and its surroundings)*. Chemical reactions are usually carried out at constant temperature and constant pressure. Thus, equations involving ΔG are of particular interest to the chemist and the pharmacist.

It was once thought that at constant pressure a negative ΔH (evolution of heat) was itself proof of a spontaneous reaction. Many natural reactions do occur with an evolution of heat; the spontaneous melting of ice at 10°C , however, is accompanied by absorption of heat, and a number of other examples can be cited to prove the error of this assumption. The reason ΔH is often thought of as a criterion of spontaneity can be seen from the familiar expression (3-67).

If $T \Delta S$ is small compared with ΔH , a negative ΔH will occur when ΔG is negative (i.e., when the process is spontaneous). When $T \Delta S$ is large, however, ΔG may be negative, and the process may be spontaneous even though ΔH is positive.

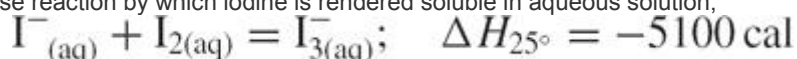
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The entropy of all systems, as previously stated, spontaneously tends toward randomness according to the second law, so that *the more disordered a system becomes, the higher is its probability and the greater its entropy*. Hence, equation (3-64) can be written as

$$\Delta G = \left[\begin{array}{c} \text{Difference in bond energies or} \\ \text{attractive energies between} \\ \text{products and reactants, } \Delta H \end{array} \right] - \left[\begin{array}{c} \text{Change in probability} \\ \text{during the process,} \\ T \Delta S \end{array} \right] \quad (3-69)$$

One can state that ΔG will become negative and the reaction will be spontaneous either when the enthalpy decreases or the probability of the system increases at the temperature of the reaction. Thus, although the conversion of ice into water at 25°C requires an absorption of heat of 1650 cal/mole, the reaction leads to a more probable arrangement of the molecules; that is, an increased freedom of molecular movement. Hence, the entropy increases, and $\Delta S = 6$ cal/mole deg is sufficiently positive to make ΔG negative, despite the positive value of ΔH .

Many of the complexes of Chapter 10 form in solution with a concurrent absorption of heat, and the processes are spontaneous only because the entropy change is positive. The increase in randomness occurs for the following reason. The dissolution of solutes in water may be accompanied by a *decrease* in entropy because both the water molecules and the solute molecules lose freedom of movement as hydration occurs. In complexation, this highly ordered arrangement is disrupted as the separate ions or molecules react through coordination, and the constituents thus exhibit more freedom in the final complex than they had in the hydrated condition. The increase in entropy associated with this increased randomness results in a spontaneous reaction as reflected in the negative value of ΔG . Conversely, some association reactions are accompanied by a decrease in entropy, and they occur in spite of the negative ΔS only because the heat of reaction is sufficiently negative. For example, the Lewis acid-base reaction by which iodine is rendered soluble in aqueous solution,



is accompanied by a ΔS of -4 cal/mole deg. It is spontaneous because

$$\begin{aligned} \Delta G &= -5100 - [298 \times (-4)] \\ &= -5100 + 1192 = -3908 \text{ cal/mole} \end{aligned}$$

In the previous examples the reader should not be surprised to find a negative entropy associated with a spontaneous reaction. The ΔS values considered here are the changes in entropy of the *substance alone*, not of the total system, that is, the substance and its immediate surroundings. As stated before, when ΔS is used as a test of the spontaneity of a reaction, the entropy change of the entire system must be considered. For reactions at constant temperature and pressure, which are the most common types, the change in free energy is ordinarily used as the criterion in place of ΔS . It is more convenient because it eliminates the need to compute any changes in the surroundings.

By referring back to Example 3-8, it will be seen that ΔS was negative for the change from liquid to solid water at -10°C. This is to be expected because the molecules lose some of their freedom when they pass into the crystalline state. The entropy of water plus its surroundings increases during the transition, however, and it is a spontaneous process. The convenience of using ΔG instead of ΔS to obtain the same information is apparent from the following example, which may be compared with the more elaborate analysis required in Example 3-8.

Example 3-10

ΔH and ΔS for the transition from liquid water to ice at -10°C and at 1 atm pressure are -1343 cal/mole and -4.91 cal/mole deg, respectively. Compute ΔG for the phase change at this temperature (-10°C = 263.2 K) and indicate whether the process is spontaneous. Write $\Delta G = -1343 - [263.2 \times (-4.91)] = -51$ cal/mole = -213 joules

The process is spontaneous, as reflected in the negative value of ΔG .

Pressure and Temperature Coefficients of Free Energy

By differentiating equation (3-63), one obtains several useful relationships between free energy and the pressure and temperature. Applying the differential of a product, $d(uv) = u dv + V du$, to equation (3-63), we obtain the following relationship:

$$dG = dE + P dV + V dP - T dS - S dT \quad (3-70)$$

Now, in a reversible process in which $dq_{\text{rev}} = T dS$, the first law, restricted to expansion work (i.e., $dE = dq_{\text{rev}} - P dV$), can be written as

$$dE = T dS - P dV \quad (3-71)$$

and substituting dE of equation (3-71) into equation (3-70) gives

$$dG = T dS - P dV + P dV + V dP - T dS - S dT$$

or

$$dG = V dP - S dT \quad (3-72)$$

At constant temperature, the last term becomes zero, and equation (3-72) reduces to

$$dG = V dP \quad (3-73)$$

or

$$\left(\frac{\partial G}{\partial P}\right)_T = V \quad (3-74)$$

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At constant pressure, the first term on the right side of equation (3-72) becomes zero, and

$$dG = -S dT \quad (3-75)$$

or

$$\left(\frac{\partial G}{\partial T}\right)_P = -S \quad (3-76)$$

To obtain the isothermal change of free energy, we integrate equation (3-73) between states 1 and 2 at constant temperature:

$$\int_{G_1}^{G_2} dG = \int_{P_1}^{P_2} V dP \quad (3-77)$$

For an ideal gas, the volume V is equal to nRT/P , thus allowing the equation to be integrated:

$$\Delta G = (G_2 - G_1) = nRT \int_{P_1}^{P_2} \frac{dP}{P}$$

$$\Delta G = nRT \ln \frac{P_2}{P_1} = 2.303nRT \log \frac{P_2}{P_1} \quad (3-78)$$

where ΔG is the free energy change of an *ideal gas* undergoing an *isothermal* reversible or irreversible alteration.

Example 3-11

What is the free energy change when 1 mole of an ideal gas is compressed from 1 atm to 10 atm at 25°C? We write

$$\Delta G = 2.303 \times 1.987 \times 298 \times \log \frac{10}{1}$$

$$\Delta G = 1364 \text{ cal}$$

The change in free energy of a solute when the concentration is altered is given by the equation

$$\Delta G = 2.303nRT \log \frac{a_2}{a_1} \quad (3-79)$$

in which n is the number of moles of solute and a_1 and a_2 are the initial and final activities of the solute, respectively.

Example 3-12

Borsook and Winegarden¹ roughly computed the free energy change when the kidneys transfer various chemical constituents at body temperature (37°C or 310.2 K) from the blood plasma to the more concentrated urine. The ratio of concentrations was assumed to be equal to the ratio of activities in equation (3-79). They found

$$\Delta G = 2.303 \times 0.100 \times 1.987 \times 310.2 \times \log \frac{0.333}{0.00500}$$

$$\Delta G = 259 \text{ cal}$$

The concentration of urea in the plasma is 0.00500 mole/liter; the concentration in the urine is 0.333 mole/liter. Calculate the free energy change in transporting 0.100 mole of urea from the plasma to the urine.

This result means that 259 cal of work must be done on the system, or this amount of net work must be performed by the kidneys to bring about the transfer.

Fugacity

For a reversible isothermal process restricted to PV work, the Gibbs energy is described by equation (3-73) or (3-74). Because V is always a positive magnitude, these relations indicate that at constant temperature the Gibbs energy varies proportional to the changes in P . Thus, from equation (3-73) it is possible to evaluate the Gibbs free energy change for a pure substance by integrating between P° and P :

$$\int_{P^\circ}^P dG = \int_{P^\circ}^P V dP$$

$$G - G^\circ = \int_{P^\circ}^P V dP \quad (3-80)$$

For pure solids or liquids the volume has little dependence on pressure, so it can be approached as constant, and equation (3-80) is reduced to

$$G = G^\circ + V(P - P^\circ) \quad (\text{for solids and liquids}) \quad (3-81)$$

On the other hand, gases have a very strong dependence on pressure; by applying the ideal gas equation $V = nRT/P$, we find that equation (3-80) becomes

$$\begin{aligned} G - G^\circ &= \int_{P^\circ}^P \frac{nRT}{P} dP \\ &= nRT \ln\left(\frac{P}{P^\circ}\right) \quad (\text{for ideal gas}) \quad (3-82) \end{aligned}$$

Relations (3-81) and (3-82) can be simplified by first assuming $P^\circ = 1 \text{ atm}$ as the reference state. Then, dividing by the amount of substance n gives a new property (G/n) called the *molar Gibbs energy* or *chemical potential*, defined by the letter μ ,

$$\mu = \left(\frac{G}{n}\right) \quad (3-83)$$

Thus, for an ideal gas we can write

$$\mu = \mu^\circ + RT \ln\left(\frac{P}{1 \text{ atm}}\right) \quad (3-84)$$

where the integration constant μ° depends only on the temperature and the nature of the gas and represents the chemical potential of 1 mole of the substance in the reference state where P° is equal to 1 atm. Note that P in equation (3-84) is a finite number and not a function. When a real gas does not behave ideally, a function known as the *fugacity* (f) can be introduced to replace pressure, just as activities are introduced to replace concentration in nonideal solutions (see later discussion).

Equation (3-84) becomes

$$\mu = \mu^\circ + RT \ln f \quad (3-85)$$

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Open Systems

The systems considered so far have been closed. They exchange heat and work with their surroundings, but the processes involve no transfer of matter, so that the amounts of the components of the system remain constant.

The term *component* should be clarified before proceeding. A phase consisting of w_2 grams of NaCl dissolved in w_1 grams of water is said to contain two independently variable masses or two *components*. Although the phase contains the species Na^+ , Cl^- , $(\text{H}_2\text{O})_n$, H_3O^+ , OH^- , and so on, they are not all independently variable. Because H_2O and its various species, H_3O^+ , OH^- , $(\text{H}_2\text{O})_n$, and so on, are in equilibrium, the mass m of water alone is sufficient to specify these species. All forms can be derived from the simple species H_2O . Similarly, all forms of sodium chloride can be represented by the single species NaCl, and the system therefore consists of just two components, H_2O and NaCl. The *number of components* of a system is the smallest number of independently variable chemical substances that must be specified to describe the phases quantitatively.

In an open system in which the exchange of matter among phases also must be considered, any one of the extensive properties such as volume or free energy becomes a function of temperature, pressure, and the number of moles of the various components.

Chemical Potential

Let us consider the change in Gibbs energy for an open system composed of a two-component phase (binary system). An infinitesimal reversible change of state is given by

$$dG = \left(\frac{\partial G}{\partial T}\right)_{P,n_1,n_2} dT + \left(\frac{\partial G}{\partial P}\right)_{T,n_1,n_2} dP + \left(\frac{\partial G}{\partial n_1}\right)_{T,P,n_2} dn_1 + \left(\frac{\partial G}{\partial n_2}\right)_{T,P,n_1} dn_2 \quad (3-86)$$

The partial derivatives $(\partial G/\partial n_1)_{T,P,N_2}$ and $(\partial G/\partial n_2)_{T,P,N_1}$ can be identified as the *chemical potentials* (μ) of the components n_1 and n_2 , respectively, so that equation (3-86) is written more conveniently as

$$dG = \left(\frac{\partial G}{\partial T}\right)_{P,n_1,n_2} dT + \left(\frac{\partial G}{\partial P}\right)_{P,n_1,n_2} dP + \mu_1 dn_1 + \mu_2 dn_2 \quad (3-87)$$

Now, relationships (3-74) and (3-76), $(\partial G/\partial P)_T = V$ and $(\partial G/\partial T)_P = -S$, respectively, for a closed system also apply to an open system, so we can write equation (3-87) as

$$dG = -S dT + V dP + \mu_1 dn_1 + \mu_2 dn_2 + \dots \quad (3-88)$$

The chemical potential, also known as the *partial molar free energy*, can be defined in terms of other extensive properties such as E , H , or A . However, what is most useful is the general definition given for Gibbs energy: At constant temperature and pressure, with the amounts of the other components (n_j) held constant, the chemical potential of a component i is equal to the change in the free energy brought about by an infinitesimal change in the number of moles n_i of the component:

$$\mu_i = \left(\frac{\partial G}{\partial n_i}\right)_{T,P,n_j} \quad (3-89)$$

It may be considered the change in free energy, for example, of an aqueous sodium chloride solution when 1 mole of NaCl is added to a large quantity of the solution so that the composition does not undergo a measurable change.

At constant temperature and pressure, the first two right-hand terms of equation (3-88) become zero, and

$$dG_{T,P} = \mu_1 dn_1 + \mu_2 dn_2 \quad (3-90)$$

or, in abbreviated notation,

$$dG_{T,P} = \sum \mu_i dn_i \quad (3-91)$$

which, upon integration, gives

$$G_{T,P,N} = \mu_1 n_1 + \mu_2 n_2 + \dots \quad (3-92)$$

for a system of constant composition $N = n_1 + n_2 + \dots$. In equation (3-92), the sum of the right-hand terms equals the total free energy of the system at constant pressure, temperature, and composition. Therefore, $\mu_1, \mu_2, \dots, \mu_n$ can be considered as the contributions per mole of each component to the total free energy. The chemical potential, like any other partial molar quantity, is an *intensive* property; in other words, it is independent of the number of moles of the components of the system.

For a closed system at equilibrium and constant temperature and pressure, the free energy change is zero, $dG_{T,P} = 0$, and equation (3-91) becomes

$$\mu_1 dn_1 + \mu_2 dn_2 + \dots = 0 \quad (3-93)$$

for all the phases of the overall system, which are closed.

Equilibrium in a Heterogeneous System

We begin with an example suggested by Klotz.² For a two-phase system consisting of, say, iodine distributed between water and an organic phase, the overall system is a closed one, whereas the separate aqueous and organic solutions of iodine are open. The chemical potential of iodine in the aqueous phase is written as μ_{Iw} and that in the organic phase as μ_{Io} . When the two phases are in equilibrium at constant temperature and pressure, the respective free energy changes dG_w and dG_o of the two phases must be equal because the free energy of the overall system is zero. Therefore, the chemical potentials of iodine in both phases are identical. This can be shown by allowing an infinitesimal amount of iodine to pass from the water to the organic phase, in which, at equilibrium, according to equation (3-93),

$$\mu_{Iw} dn_{Iw} + \mu_{Io} dn_{Io} = 0 \quad (3-94)$$

Now, a decrease of iodine in the water is exactly equal to an increase of iodine in the organic phase:

$$-dn_{Iw} = dn_{Io} \quad (3-95)$$

Substituting equation (3-95) into (3-94) gives

$$\mu_{Iw} dn_{Iw} + \mu_{Io}(-dn_{Iw}) = 0 \quad (3-96)$$

and finally

$$\mu_{Iw} = \mu_{Io} \quad (3-97)$$

This conclusion may be generalized by stating that the chemical potential of a component is identical in all phases of a heterogeneous system when the phases are in equilibrium at a fixed temperature and pressure. Hence,

$$\mu_{i\alpha} = \mu_{i\beta} = \mu_{i\gamma} = \dots \quad (3-98)$$

where $\alpha, \beta, \gamma, \dots$ are various phases among which the substance i is distributed. For example, in a saturated aqueous solution of sulfadiazine, the chemical potential of the drug in the solid phase is the same as its chemical potential in the solution phase.

When two phases are not in equilibrium at constant temperature and pressure, the total free energy of the system tends to decrease, and the substance passes spontaneously from a phase of higher chemical potential to one of lower chemical potential until the potentials are equal. Hence, the chemical potential of a substance can be used as a measure of the *escaping tendency* of the component from its phase. The concept of escaping tendency will be used in various chapters throughout the book. The analogy between chemical potential and electric or gravitational potential is evident, the flow in these cases always being from the higher to the lower potential and continuing until all parts of the system are at a uniform potential. For a phase consisting of a *single pure substance*, the chemical potential is the free energy of the substance per mole defined in equation (3-83).

For a two-phase system of a single component, for example, liquid water and water vapor in equilibrium at constant temperature and pressure, the *molar free energy* G/n is identical in all phases. This statement can be verified by combining equations (3-98) and (3-83).

Clausius–Clapeyron Equation

If the temperature and pressure of a two-phase system of one component, for example, of liquid water (l) and water vapor (v) in equilibrium, are changed by a small amount, the molar free energy changes are equal and

$$dG_l = dG_v \quad (3-99)$$

In a phase change, the free energy changes for 1 mole of the liquid vapor are given by equation (3-72),

$$dG = V dP - T dS$$

Therefore, from equations (3-99) and (3-72),

$$V_l dP - S_l dT = V_v dP - S_v dT$$

or

$$\frac{dP}{dT} = \frac{S_v - S_l}{V_v - V_l} = \frac{\Delta S}{\Delta V} \quad (3-100)$$

Now, at constant pressure, the heat absorbed in the reversible process (equilibrium condition) is equal to the molar heat of vaporization, and from the second law we have

$$\Delta S = \frac{\Delta H_v}{T} \quad (3-101)$$

Substituting equation (3-101) into (3-100) gives

$$\frac{dP}{dT} = \frac{\Delta H_v}{T \Delta V} \quad (3-102)$$

where $\Delta V = V_v - V_l$, the difference in the molar volumes in the two phases. This is the *Clapeyron equation*.

The vapor will obey the ideal gas law to a good approximation when the temperature is far enough away from the critical point, so that V_v may be replaced by RT/P . Furthermore, V_l is insignificant compared with V_v . In the case of water at 100°C , for example, $V_v = 30.2$ liters and $V_l = 0.0188$ liter.

Under these restrictive circumstances, equation (3-102) becomes

$$\frac{dP}{dT} = \frac{P \Delta H_v}{RT^2} \quad (3-103)$$

which is known as the *Clausius–Clapeyron equation*. It can be integrated between the limits of the vapor pressures P_1 and P_2 and corresponding temperatures T_1 and T_2 , assuming ΔH_v is constant over the temperature range considered:

$$\int_{P_1}^{P_2} \frac{dP}{P} = \frac{\Delta H_v}{R} \int_{T_1}^{T_2} T^{-2} dT \quad (3-104)$$

$$[\ln P]_{P_1}^{P_2} = \frac{\Delta H_v}{R} \left[\left(-\frac{1}{T_2} \right) - \left(-\frac{1}{T_1} \right) \right] \quad (3-105)$$

$$\ln P_2 - \ln P_1 = \frac{\Delta H_v}{R} \left(\frac{1}{T_1} - \frac{1}{T_2} \right) \quad (3-106)$$

and finally

$$\ln \frac{P_2}{P_1} = \frac{\Delta H_v(T_2 - T_1)}{RT_1 T_2} = 0$$

or

$$\log \frac{P_2}{P_1} = \frac{\Delta H_v(T_2 - T_1)}{2.303RT_1 T_2} = 0 \quad (3-107)$$

This equation is used to calculate the mean heat of vaporization of a liquid if its vapor pressure at two temperatures is available. Conversely, if the mean heat of vaporization and the vapor pressure at one temperature are known, the vapor pressure at another temperature can be obtained.

The Clapeyron and Clausius–Clapeyron equations are important in the study of various phase transitions and in the development of the equations of some colligative properties.

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Example 3-13

The average heat of vaporization of water can be taken as about 9800 cal/mole within the range of 20°C to 100°C . What is the vapor pressure at 95°C ? The vapor pressure P_2 at temperature $T_2 = 373$ K (100°C) is 78 cm Hg, and R is expressed as 1.987 cal/deg mole.

Write

$$\log \frac{78.0}{P_1} = \frac{9800}{2.303 \times 1.987} \left(\frac{373 - 368}{368 \times 373} \right)$$

$$P_1 = 65 \text{ cm Hg}$$

Activities: Activity Coefficients

If the vapor above a solution can be considered to behave ideally, the chemical potential of the solvent in the vapor state in equilibrium with the solution can be written in the form of equation (3-84),

$$\mu = \mu^\circ + RT \ln P$$

If Raoult's law is now introduced for the solvent, $P_1 = P_1^\circ X_1$, equation (3-84) becomes

$$\mu_1 = \mu_1^\circ + RT \ln P_1^\circ + RT \ln X_1 \quad (3-108)$$

Combining the first and second right-hand terms into a single constant gives

$$\mu_1 = \mu^\circ + RT \ln X_1 \quad (3-109)$$

for an ideal solution. The reference state μ° is equal to the chemical potential μ_1 of the pure solvent (i.e., $X_1 = 1$). For nonideal solutions, equation (3-109) is modified by introducing the "effective concentration" or *activity* of the solvent to replace the mole fraction:

$$\mu_1 = \mu^\circ + RT \ln a_1 \quad (3-110)$$

or, for

$$a = \gamma X \quad (3-111)$$

and γ is referred to as the *activity coefficient*, we have

$$\mu_1 = \mu^\circ + RT \ln \gamma_1 X_1 \quad (3-112)$$

For the *solute* on the mole fraction scale,

$$\mu_2 = \mu^\circ + RT \ln a_2 \quad (3-113)$$

$$\mu_2 = \mu^\circ + RT \ln \gamma_2 X_2 \quad (3-114)$$

Based on the practical (molal and molar) scales

$$\mu_2 = \mu^\circ + RT \ln \gamma_m m \quad (3-115)$$

$$\mu_2 = \mu^\circ + RT \ln \gamma_c c \quad (3-116)$$

Equations (3-110) and (3-113) are frequently used as definitions of activity.

Gibbs–Helmholtz Equation

For an isothermal process at constant pressure proceeding between the initial and final states 1 and 2, equation (3-57) yields

$$\begin{aligned} G_2 - G_1 &= (H_2 - H_1) - T(S_2 - S_1) \\ \Delta G &= \Delta H - T \Delta S \end{aligned} \quad (3-117)$$

Now, equation (3-76) may be written as

$$-\Delta S = -(S_2 - S_1) = \left(\frac{\partial G_2}{\partial T} \right)_P - \left(\frac{\partial G_1}{\partial T} \right)_P$$

or

$$-\Delta S = \left[\frac{\partial(G_2 - G_1)}{\partial T} \right]_P = \left[\frac{\partial(\Delta G)}{\partial T} \right]_P \quad (3-118)$$

Substituting equation (3-118) into (3-119) gives

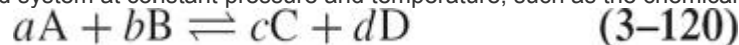
$$\Delta G = \Delta H + T \left[\frac{\partial(\Delta G)}{\partial T} \right]_P \quad (3-119)$$

which is one form of the Gibbs–Helmholtz equation

Standard Free Energy and the Equilibrium Constant

Many of the processes of pharmaceutical interest such as complexation, protein binding, the dissociation of a weak electrolyte, or the distribution of a drug between two immiscible phases are systems at equilibrium and can be described in terms of changes of the Gibbs free energy (ΔG).

Consider a closed system at constant pressure and temperature, such as the chemical reaction



Because G is a state function, the free energy change of the reaction going from reactants to products is

$$\Delta G = \sum \Delta G_{\text{products}} - \sum \Delta G_{\text{reactants}} \quad (3-121)$$

Equation (3-120) represents a closed system made up of several components. Therefore, at constant T and P the total free energy change of the products and reactants in equation (3-121) is given as the sum of the chemical potential μ of each component times the number of moles [see equation (3-83)]:

$$\Delta G = (c\mu_C + d\mu_D) - (a\mu_A + b\mu_B) \quad (3-122)$$

When the reactants and products are ideal gases, the chemical potential of each component is expressed in terms of partial pressure [equation (3-84)]. For nonideal gases, μ is written in terms of fugacities [equation (3-85)]. The corresponding expressions for solutions are given by equations (3-110) to (3-116). Let us use the more general expression that relates the chemical potential to the activity, equation

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(3-110). Substituting this equation for each component in equation (3-121) yields

$$\begin{aligned} \Delta G = & c(\mu_C^\circ + RT \ln a_C) + d(\mu_D^\circ + RT \ln a_D) \\ & - a(\mu_A^\circ + RT \ln a_A) - b(\mu_B^\circ + RT \ln a_B) \end{aligned} \quad (3-123)$$

Rearranging equation (3-123) gives

$$\begin{aligned} \Delta G = & c\mu_C^\circ + d\mu_D^\circ - a\mu_A^\circ - b\mu_B^\circ + RT(\ln a_C^c + \ln a_D^d) \\ & - RT(\ln a_A^a + \ln a_B^b) \end{aligned} \quad (3-124)$$

μ° is the partial molar free energy change or chemical potential under standard conditions. Because it is multiplied by the number of moles in equation (3-124), the algebraic sum of the terms involving μ° represents the *total standard free energy change of the reaction* and is called ΔG° :

$$\Delta G^\circ = c\mu_C^\circ + d\mu_D^\circ - a\mu_A^\circ - b\mu_B^\circ \quad (3-125)$$

or, in general,

$$\Delta G^\circ = \sum n\mu^\circ(\text{products}) - \sum n\mu^\circ(\text{reactants}) \quad (3-126)$$

Using the rules of logarithms, we can express equation (3-124) as

$$\Delta G = \Delta G^\circ + RT \ln \left[\frac{(a_C^c a_D^d)}{(a_A^a a_B^b)} \right] \quad (3-127)$$

The products of activities in brackets are called the reaction quotients, defined as

$$Q = \left[\frac{(a_C^c a_D^d)}{(a_A^a a_B^b)} \right] \quad (3-128)$$

or, in general,

$$Q = \frac{\sum a_{\text{products}}^n}{\sum a_{\text{reactants}}^n} \quad (3-129)$$

Thus, equation (3-127) can be written as

$$\Delta G = \Delta G^\circ + RT \ln Q \quad (3-130)$$

Because ΔG° is a constant at constant P and constant T , RT is also constant. The condition for equilibrium is $\Delta G = 0$, and therefore equation (3-130) becomes

$$0 = \Delta G^\circ + RT \ln K \quad (3-131)$$

or

$$\Delta G^\circ = -RT \ln K \quad (3-132)$$

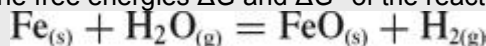
where Q has been replaced by K , the equilibrium constant.

Equation (3-132) is a very important expression, relating the standard free energy change of a reaction ΔG° to the equilibrium constant K . This expression allows one to compute K knowing ΔG° and vice versa.

The equilibrium constant has been expressed in terms of activities. It also can be given as the ratio of partial pressures or fugacities (for gases) and as the ratio of the different concentration expressions used in solutions (mole fraction, molarity, molality). The equilibrium constant is dimensionless, the ratio of activities or concentration canceling the units. However, the numerical value of K differs depending on the units used (activity, mole fraction, fugacity, etc.).

Example 3-14

Derive an expression for the free energies ΔG and ΔG° of the reaction



Because the chemical potential of a solid is constant (it does not depend on concentration), the equilibrium constant depends only on the pressures (or fugacities) of the gases. Using pressures, we obtain

$$\begin{aligned} \Delta G &= \mu^\circ_{\text{FeO}(s)} + \mu^\circ_{\text{H}_2(g)} - \mu^\circ_{\text{Fe}(s)} - \mu^\circ_{\text{H}_2\text{O}(g)} + RT \ln P_{\text{H}_2(g)} \\ &\quad - RT \ln P_{\text{H}_2\text{O}(g)} = 0 \\ \Delta G &= \Delta G^\circ + RT \ln P_{\text{H}_2(g)} - RT \ln P_{\text{H}_2\text{O}(g)} = 0 \end{aligned}$$

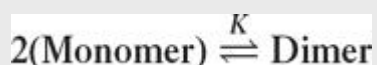
and

$$\Delta G^\circ = -RT \ln \frac{P_{\text{H}_2(g)}}{P_{\text{H}_2\text{O}(g)}}$$

The magnitude and sign of ΔG° indicate whether the reaction is spontaneous [see equation (3-59)], but only under *standard conditions*. When the reaction is not at equilibrium, $\Delta G \neq 0$ and the free energy change is described by equation (3-130), where Q , like K , is the ratio of activities [equation (3-129)], fugacities, or concentration units of the products and reactants but under different conditions than those of equilibrium. Q should not be confused with K , the ratio of activities, fugacities, and so on under *standard conditions at equilibrium*.

Example 3-15

Sodium cholate is a bile salt that plays an important role in the dissolution or dispersion of cholesterol and other lipids in the body. Sodium cholate may exist either as monomer or as dimer (or higher *n*-mers) in aqueous solution. Let us consider the equilibrium monomer–dimer reaction:



which states that two moles (or molecules) of monomer form 1 mole (or molecule) of dimer.

(a) If the molar concentration at 25°C of monomeric species is 4×10^{-3} mole/liter and the concentration of dimers is 3.52×10^{-5} mole/liter, what is the equilibrium constant and the standard free energy for the dimerization process? Write

$$\begin{aligned} K &= \frac{[\text{Dimer}]}{[\text{Monomer}]^2} = \frac{3.52 \times 10^{-5}}{(4 \times 10^{-3})^2} = 2.20 \\ \ln K &= 0.788 \\ \Delta G^\circ &= -RT \ln K = -(1.9872 \times 298 \times 0.788) \\ &= -466.6 \text{ cal/mole} \end{aligned}$$

The process is spontaneous under standard conditions.

(b) While keeping the concentration of monomer constant, suppose that one is able to remove part of the dimeric species by physical or chemical means so that its concentration is now four times less than the original dimer concentration. Compute the free energy change. What is the effect on the equilibrium?

The concentration of dimer is now

$$\frac{3.52 \times 10^{-5}}{4} = 8.8 \times 10^{-6} \text{ mole/liter}$$

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Because the conditions are not at equilibrium, equation (3-130) should be used. First calculate Q :

$$Q = \frac{[\text{Dimer}]}{[\text{Monomer}]^2} = \frac{8.8 \times 10^{-6}}{(4 \times 10^{-3})^2} = 0.550; \ln Q = -0.598$$

and from equation (3-130),

$$\begin{aligned} \Delta G &= 466.6 + [1.9872 \times 298 \times (-0.598)] \\ &= -820.7 \text{ cal/mole} \end{aligned}$$

ΔG is negative, Q is less than K , and the reaction shifts to the right side of the equation with the formation of more dimer.

If the monomer is removed from the solution, the reaction is shifted to the left side, forming monomer, and ΔG becomes positive. Suppose that monomer concentration is now 1×10^{-3} mole/liter and dimer concentration is 3.52×10^{-5} mole/liter:

$$\Delta G = -466.6 + (1.9872 \times 298 \times 3.561) = +1642 \text{ cal/mole}$$

The positive sign of ΔG indicates that the reaction does not proceed forward spontaneously.

The van't Hoff Equation

The effect of temperature on equilibrium constants is obtained by writing the equation

$$\ln K = \frac{\Delta G^\circ}{RT} \quad (3-133)$$

and differentiating with respect to temperature to give

$$\frac{d \ln K}{dT} = -\frac{1}{R} \frac{d(\Delta G^\circ/T)}{dT} \quad (3-134)$$

The Gibbs–Helmholtz equation may be written in the form (see one of the thermodynamics texts cited in the Recommended Readings section at the end of this chapter)

$$\frac{d(\Delta G/T)}{dT} = -\frac{\Delta H}{T^2} \quad (3-135)$$

Expressing equation (3-135) in a form for the reactants and products in their standard states, in which ΔG becomes equal to ΔG° , and substituting into equation (3-134) yields

$$\frac{d \ln K}{dT} = \frac{\Delta H^\circ}{RT^2} \quad (3-136)$$

where ΔH° is the standard enthalpy of reaction. Equation (3-136) is known as the *van't Hoff equation*. It may be integrated, assuming ΔH° to be constant over the temperature range considered; it becomes

$$\ln \frac{K_2}{K_1} = \frac{\Delta H^\circ}{R} \left(\frac{T_2 - T_1}{T_1 T_2} \right) \quad (3-137)$$

Equation (3-137) allows one to compute the enthalpy of a reaction if the equilibrium constants at T_1 and T_2 are available. Conversely, it can be used to supply the equilibrium constant at a definite temperature if it is known at another temperature. Because ΔH° varies with temperature and equation (3-137) gives only an approximate answer, more elaborate equations are required to obtain accurate results. The solubility of a solid in an ideal solution is a special type of equilibrium, and it is not surprising that the solubility can be written as

$$\ln \frac{X_2}{X_1} = \frac{\Delta H_f}{R} \left(\frac{T_2 - T_1}{T_1 T_2} \right) \quad (3-138)$$

which closely resembles equation (3-137). These expressions will be encountered in later chapters.

Combining equations (3-117) and (3-133) yields yet another form of the van't Hoff equation, namely

$$\ln K = -(\Delta H^\circ/R)1/T + \Delta S^\circ/R \quad (3-139)$$

or

$$\log K = -[\Delta H^\circ/(2.303)R]1/T + \Delta S^\circ/(2.303R) \quad (3-140)$$

where $\Delta S^\circ/R$ is the intercept on the $\ln K$ axis of a plot of $\ln K$ versus $1/T$.

Whereas equation (3-137) provides a value of ΔH° based on the use of two K values at their corresponding absolute temperatures T_1 and T_2 , equations (3-139) and (3-140) give the values of ΔH° and ΔS° , and therefore the value of $\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$. In the least squares linear regression equations (3-139) and (3-140), one uses as many $\ln K$ and corresponding $1/T$ values as are available from experiment.

Example 3-16

In a study of the transport of pilocarpine across the corneal membrane of the eye, Mitra and Mikkelsen⁴ presented a van't Hoff plot of the log of the ionization constant, K_a , of pilocarpine versus the reciprocal of the absolute temperature, $T^{-1} = 1/T$.

Using the data in Table 3-4, regress K_a versus T^{-1} . With reference to the van't Hoff equation, equation (3-139), obtain the standard heat (enthalpy), ΔH° , of ionization for pilocarpine and the standard entropy for the ionization process. From ΔH° and ΔS° calculate ΔG° at 25°C. What is the significance of the signs and the magnitudes of ΔH° , ΔS° , and ΔG° ?

Table 3-4 Ionization Constants of Pilocarpine at Various Temperatures*†

$T(^{\circ}\text{C})$	$T(\text{K})$	$1/T \times 10^3$	$K_a \times 10^7$	$\log K_a$
15	288	3.47	0.74	-7.13
20	293	3.41	1.07	-6.97
25	298	3.35	1.26	-6.90
30	303	3.30	1.58	-6.80
35	308	3.24	2.14	-6.67
40	313	3.19	2.95	-6.53
45	318	3.14	3.98	-6.40

*For the column headed $1/T \times 10^3$ the numbers are 1000 (i.e., 10^3) times *larger* than the actual numbers. Thus, the first entry in column 3 has the value 3.47×10^{-3} or 0.00347. Likewise, in the next column $K_a \times 10^7$ signifies that the number 0.74 and the other entries in this column are to be accompanied by the exponential value 10^{-7} , not 10^{+7} . Thus, the first value in the fourth column should be read as 0.74×10^{-7} and the last value 3.98×10^{-7} .

†From A. K. Mitra and T. J. Mikkelsen, *J. Pharm. Sci.* **77**, 772, 1988. With permission.

Answers:

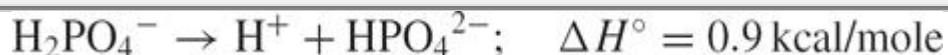
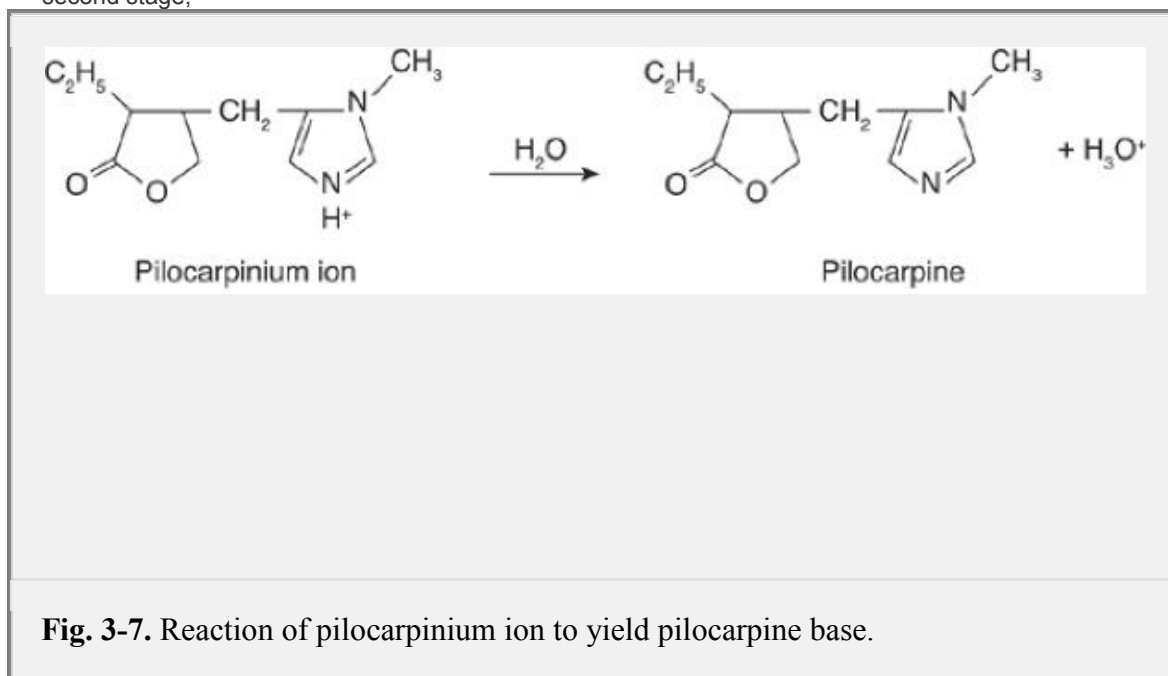
$$\begin{aligned}\Delta H^\circ &= 9784 \text{ cal/mole} \\ &= 40.94 \text{ kJ/mole} \\ \Delta S^\circ &= 1.30 \text{ cal/mole deg} \\ \Delta G^\circ_{25^\circ} &= \Delta H^\circ - T\Delta S^\circ = 9397 \text{ cal/mole}\end{aligned}$$

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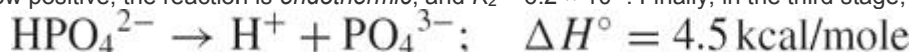
These thermodynamic values have the following significance. ΔH° is a large positive value that indicates that the ionization of pilocarpine (as its conjugate acid) should increase as the temperature is elevated. The increasing values of K_a in the table show this to be a fact. The standard entropy increase, $\Delta S^\circ = 1.30$ entropy units, although small, provides a force for the reaction of the pilocarpinium ions to form pilocarpine (Fig. 3-7). The positively charged pilocarpine molecules, because of their ionic nature, are probably held in a more orderly arrangement than the predominantly nonionic pilocarpine in the aqueous environment. This increase in disorder in the dissociation process accounts for the increased entropy, which, however, is a small value: $\Delta S^\circ = 1.30$ entropy units. Note that a positive ΔH° does not mean that the ionization will not occur; rather, it signifies that the equilibrium constant for the forward reaction (ionization) will have a small value, say K_a [congruent] 1×10^{-7} , as observed in Table 3-4. A further explanation regarding the sign of ΔH° is helpful here. Mahan⁵ pointed out that in the first stage of ionization of phosphoric acid, for example,



the hydration reaction of the ions being bound to the water molecules is sufficiently exothermic to produce the necessary energy for ionization, that is, enough energy to remove the proton from the acid, H_3PO_4 . For this reason, ΔH° in the first stage of ionization is negative and $K_1 = 7.5 \times 10^{-3}$ at 25°C . In the second stage,



ΔH° is now positive, the reaction is *endothermic*, and $K_2 = 6.2 \times 10^{-8}$. Finally, in the third stage,



ΔH° is a relatively large positive value and $K_3 = 2.1 \times 10^{-13}$. These ΔH° and K_a values show that increasing energy is needed to remove the positively charged proton as the negative charge increases in the acid from the first to the third stage of ionization. Positive ΔH° (endothermic reaction) values do

not signal nonionization of the acid—that is, that the process is nonspontaneous—but rather simply show that the forward reaction, represented by its ionization constant, becomes smaller and smaller.

Chapter Summary

In this chapter, the quantitative relationships among different forms of energy were reviewed and expressed in the three laws of thermodynamics. Energy can be considered as the product of an intensity factor and a capacity factor; thus, the various types of energy may be represented as a product of an intensive property (i.e., independent of the quantity of material) and the differential of an extensive property that is proportional to the mass of the system. For example, mechanical work done by a gas on its surroundings is $P dV$. Some of the forms of energy, together with these factors and their accompanying units, are given in Table 3-5.

Table 3-5 Intensity and Capacity Factors of Energy

Energy Form	Intensity or Potential Factor (Intensive Property)	Capacity or Quantity Factor (Extensive Property)	Energy Unit Commonly Used
Heat (thermal)	Temperature (deg)	Entropy change (cal/deg)	Calories
Expansion	Pressure (dyne/cm ²)	Volume change (cm ³)	Ergs
Surface	Surface tension (dyne/cm)	Area change (cm ²)	Ergs
Electric	Electromotive force or potential difference (volts)	Quantity of electricity (coulombs)	Joules
Chemical	Chemical potential (cal/mole)	Number of moles	Calories

Practice problems for this chapter can be found at thePoint.lww.com/Sinko6e.

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Chapter Legacy

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