CHAPTER 1

INTRODUCTION

> Of all the inorganic substances acting in their own proper nature, and without assistance or combination, water is the most wonderful. If we think of it as the source of all the changefulness and beauty which we have seen in clouds; then as the instrument by which the earth we have contemplated was modeled into symmetry, and its crags chiseled into grace; then as, in the form of snow, it robes the mountains it has made, with what transcendent light which we could not have conceived if we had not seen; then as it exists in the form of torrent, in the iris which spans it, in the morning mist which rises from it, in the deep crystalline pools which mirror its hanging shore, in the broad lake and glancing river; finally, in that which is to all human minds the best emblem of unwearied, unconquerable power, the wild, various, fantastic, tameless unity of the sea; . . . It is like trying to paint a soul.[1]

Aqueous chemistry is one of the oldest forces of change in the solar system. It started less than 20 million years after the gases of the solar nebula began to coalesce into solid objects.[2] Water is also the most abundant volatile molecule in comets. On the earth, the oceans alone contain about 1.4×10^{21} kilograms or 320,000,000 cubic miles of water. Another 0.8×10^{21} kilogram is held within the rocks of the earth's crust, existing in the form of water of hydration. The human

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body is roughly 65% water by weight. Some organs like the brain and lungs are composed of nearly 80% water.[3]

Water is the basis and bearer of life. For millions of years, water had been at work to prepare the earth for the evolution of life. It is the solvent in which numerous biochemical organic reactions (and inorganic reactions) take place. All these reactions affecting the living system have inevitably occurred in an aqueous medium. On the other hand, modern organic chemistry has been developed almost on the basis that organic reactions are often to be carried out in organic solvents. It is only within the last two decades or so that people have again focused their attention on carrying out organic reactions in water. This development is in large part due to the study by Breslow on the Diels-Alder reactions.[4] Since then, many organic reactions that are traditionally carried out exclusively in organic solvents, such as the Barbier-Grignard-type reaction, have been successfully performed in an aqueous medium. Furthermore, novel reactions have been discovered, for which the use of water as solvent is critical.

Why should we consider using water as a solvent for organic reactions? There are many potential advantages:

- *Cost.* Water is the cheapest solvent available on earth; using water as a solvent can make many chemical processes more economical.
- *Safety.* Many organic solvents are flammable, potentially explosive, mutagenic, and/or carcinogenic. Water, on the other hand, is none of these.
- *Synthetic efficiency.* In many organic syntheses, it may be possible to eliminate the need for the protection and deprotection of functional groups, and save many synthetic steps. Water-soluble substrates can be used directly. This will be especially useful in carbohydrate and protein chemistry.
- *Simple operation.* In large industrial processes, isolation of the organic products can be performed by simple phase-separation. It is also easier to control the reaction temperature, since water has the largest heat capacities of all substances.
- *Environmental benefits.* It may alleviate the problem of pollution by organic solvents since water can be recycled readily and is benign when released into the environment (when no harmful residue is present).
- *Potential for new synthetic methodologies.* Compared to reactions in organic solvents, the use of water as a reaction solvent has

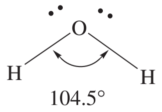
been explored much less in organic chemistry. There are many opportunities to develop novel synthetic methodologies that have not been discovered before.

This chapter will briefly survey some basic physical and chemical properties of water as well as the possible relevance of these properties to aqueous organic chemistry in terms of reactivity, selectivity (chemo-, regio-, and stereo-), and phase-separations.

1.1 THE STRUCTURE AND FORMS OF WATER[5]

In the 1780s, Cavendish and Lavoisier established that water is composed of hydrogen and oxygen. Gay-Lussac and Humboldt discovered in 1805 that the ratio of hydrogen and oxygen in a water molecule is two to one. And in 1842, Dumas found that the ratio of the combining weights of hydrogen and oxygen is very close to 2 to 16 in the molecule.

Water has two σ bonds, two lone pairs of electrons on oxygen, and a bond angle of 104.5° at oxygen.



Water exists in three basic forms: vapor, liquid, and solid. The relationship among the three forms of water is described by the pressure-volume-temperature phase diagram (Figure 1.1).

The structure of water in its liquid state is very complicated and is still a topic of current research. The structure of liquid water, with its molecules connected together by hydrogen bonds, gives rise to several anomalies when compared with other liquids.[6]

In its solid state, however, the basic structural features of ordinary hexagonal ice (ice I) are well established. In this structure (Figure 1.2), each water molecule is hydrogen bonded to four others in nearly perfect tetrahedral coordination. This arrangement leads to an open lattice in which intermolecular cohesion is large.

In its gaseous state, water molecules become dissociated from each other and can aggregate easily into small clusters. Increasing temperature and decreasing pressure help the dissociation; whereas increasing both the temperature and pressure increases the gasification of the liquid

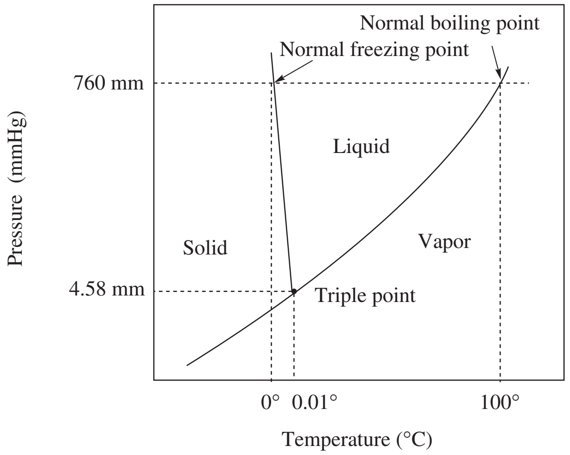


Figure 1.1 Phase diagram for water.

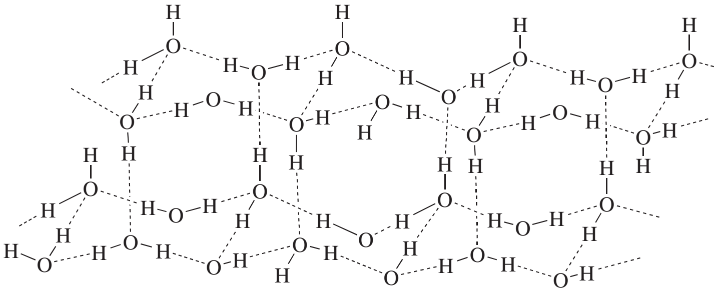


Figure 1.2 The structure of hexagonal ice.

phase as well as the aggregation of the gaseous phase. Under extremely high temperature and high pressure, water reaches a supercritical state in which the distinct gaseous phase and liquid phase no longer exist.

1.2 PROPERTIES OF WATER

The principal physical properties of water are shown in Table 1.1.[7]

Water has its highest density at 3.98°C and decreases as the temperature falls to 0°C. For this reason, ice is lighter than water and floats, which insulates deeper water from the cold and prevents it from freezing. This property has fundamental importance in nature. The density

TABLE 1.1 Principal Physical Properties of Water

Density, g/ml (3.98°C)	1.00
Melting point, °C (at 760 mm Hg)	0.00
Boiling point, °C (at 760 mm Hg)	100.00
Temperature at maximum density, °C	3.98
Heat of melting, (cal/g °C)	79.71
J/g °C	333.75
Heat of vaporization, cal/(g °C)(0°C)	595.40
(J/g °C)	2260.00
Specific heat, cal/(g °C)(15°C)	1.00
(J/(g °C)	4.19
Surface tension, mN/m (20°C)	72.75
Dynamic viscosity, mN.s/m^2 (20°C)	1.00
Specific electrical conductivity, s/m (25°C)	5.10^{-6}
Critical temperature, °C	374.00
Critical density, g/cm^3	0.322
Critical specific volume, cm^3/g	3.110
Dielectric constant (20°C)	80.20

of water also decreases with the increase of temperature above 3.98°C. It reaches the density of ice at about 70°C.

The viscosity of water also changes with temperature. It decreases with an increase in temperature because of the reduction in the number of hydrogen bonds binding the molecules together. The viscosity of water has an influence on the movement of solutes in water and on the sedimentation rate of suspended solids.

Water has the highest value for the specific heat of all substances. The specific heat of water is the standard against which the values for all the other substances are determined. The high value for the specific heat of water is because of the great heat capacity of the water mass. This means that rapid changes in ambient temperature result in only slow changes in water temperature. Such an effect is important for aquatic organisms. It is also an important advantage in using water as solvent to control the temperature for both endo- and exothermic reactions, especially in large-scale industrial processes.

If the surface of a liquid is regarded as an elastic membrane, then the surface tension is the breaking force of this membrane. Water has one of the highest surface tensions of all liquids. For example, the surface tension of ethanol at 20°C is 22 mN/m, while that of water is 72.75 mN/m. The surface tension of water decreases with temperature.

The presence of surface active agents, such as detergents, also decreases the surface tension of water.

1.3 SOLVATION

Water is a very good solvent for many substances, which is of fundamental importance in nature. The solubility of a chemical substance is dependent upon the temperature. The solubility of gases such as oxygen, nitrogen, and carbon dioxide in water usually decreases with a rise in temperature. However, there are some gases whose solubility increases with an increase in temperature. An example of such is helium. Similarly, there is variation in the relation between the solubility of solids in water and the temperature. For example, the solubility of $AgNO_3$ rapidly increases with an increase in temperature, but for NaCl there is only a slight increase in solubility with a rise in temperature. On the other hand, when temperature increases there is a decrease in solubility for Li_2CO_3. The influence of the temperature on the solubility of substances is dictated by the heat of solution of the substance, which is the heat emitted or absorbed during the dissolution of one mole of a substance in one liter of water.

Metal ions in aqueous solution exist as complexes with water. The solubility of organic compounds in water depends primarily on their polarity and their ability to form hydrogen bonds with water. Organic compounds with a large part of polar components such as acetic acid, “dissolve” in water without limit. In such cases, the polar part dominates. By contrast, soaps and detergents have a polar “end” attached to a relatively large nonpolar part of the molecule. They have limited solubility and the molecules tend to coalesce to form micelles.

1.4 HYDROPHOBIC EFFECT

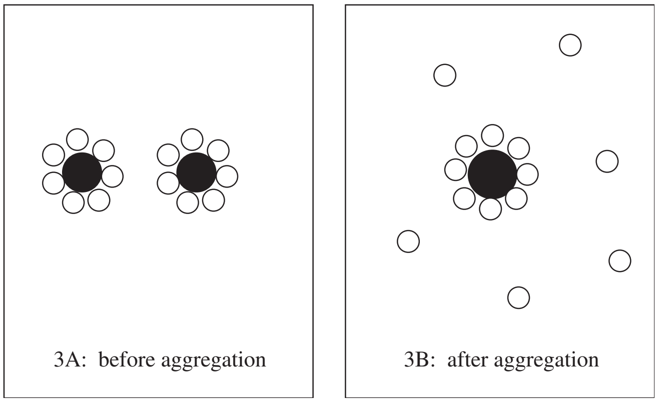
Polar compounds and compounds that ionize can dissolve readily in water. These compounds are said to be hydrophilic. In contrast to hydrophilic substances, hydrocarbons and other nonpolar substances have very low solubility in water because it is energetically more favorable for water molecules to interact with other water molecules rather than with nonpolar molecules. As a result, water molecules tend to exclude nonpolar substances, forcing them to associate with themselves in forming drops, thereby minimizing the contact area between water and the organic substance. This phenomenon of repulsion of nonpolar substances by water is referred to as the hydrophobic effect.[8] The hydrophobic effect plays a critical role in biological systems. For example, it is the primary force in determining the folding patterns of proteins and the self-assembly of biological membranes.

Hydrophobic interaction, the association of a relatively nonpolar molecule or group in water with other nonpolar molecules, is not due to the mutual attraction of the nonpolar molecules. Rather, it is due to the large *cohesive energy density* (c.e.d.) of water. Cohesive energy density of a liquid is the energy of vaporization in calories per cubic centimeter of the liquid, which reflects the van der Waals forces holding the molecules of the liquid together, whereas the internal pressure of a liquid describes the sensitivity of energy to a change in volume and reflects the strength of intermolecular forces. The large cohesive energy density causes the polar water molecules surrounding the nonpolar compounds to associate with each other. Internal pressure of water, however, may also play a role in hydrophobic interaction. Table 1.2 contains the internal pressure and cohesive energy density for some common solvents at 25°C.

In thermodynamic terms, solutes can be divided into two classes. For hydrophobic solutes in dilute solution in water, the partial Gibbs free energy of solution is positive. This is because water molecules that surround a less polar molecule in solution are more restricted in

TABLE 1.2 Internal Pressures and Cohesive Energy Densities for Some Common Solvents (25°C)[9]

Solvent	c.e.d. (cal cm^{-3})	Internal pressure (cal cm^{-3})
Water	550.2	41.0
Formamide	376.4	131.0
Methanol	208.8	70.9
Dimethyl sulfoxide	168.6	123.7
Dimethylformamide	139.2	114
Acetonitrile	139.2	96
Acetone	94.3	79.5
Benzene	83.7	88.4
Carbon tetrachloride	73.6	80.6
Diethyl ether	59.9	63.0
Hexane	52.4	57.1



3A: before aggregation

3B: after aggregation

Figure 1.3 (● nonpolar solute; ○ water).

their interactions with other water molecules, and these restricted water molecules are relatively immobile and ordered (3A, Figure 1.3). However, water molecules in the bulk solvent phase are much more mobile and disordered. Thermodynamically, there is a net gain in the combined entropy of the solvent and the nonpolar solute when the nonpolar groups aggregate and water is freed from its ordered state surrounding the nonpolar groups (3B, Figure 1.3).

Hydrophobic interaction, however, is a relatively weak interaction. For example, the energy required to transfer a $-CH_2-$ unit from a hydrophobic to an aqueous environment is about 3 kJ mol^{-1}.

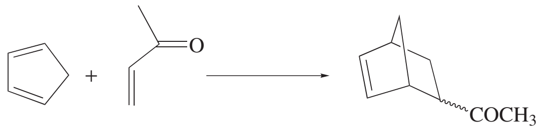
Thus, the transfer of a hydrophobic molecule from a pure state to an aqueous solution is an unfavorable process due to the large decrease of entropy resulting from the reorganization of the water molecules surrounding the solutes. By contrast, the partial Gibbs free energy for dissolving a hydrophilic solute in water is negative. This is because hydrophilic solutes can bind water molecules through hydrogen bonding.

1.5 SALT EFFECT

The effect of dissolved hydrophilic electrolytes on the interaction between organic solutes and water can be described by the salting-in and salting-out effects. Dissolved electrolytes usually increase the internal pressure in water, through a volume-reducing process that involves polarization and attraction of solvent molecules around the ionic species (electrostriction). For example, a 3 M aqueous solution of sodium bromide has an internal pressure of around 75 cal cm^{-3}, whereas the internal pressure of water at 25°C is only 41 cal cm^{-3}.

When the dissolved salt increases the internal pressure of aqueous solution to a certain extent, the nonelectrolyte is squeezed out (salting out). On the other hand, when the dissolved salt reduces the internal pressure of the solution, more of the nonelectrolyte is able to dissolve (salting in). All the electrolytes except perchloric acid increase the internal pressure of water and cause a salting out of organic species. For example, saturated sodium chloride is used to separate organic compounds from water.

Water's internal pressure acts on the volume of activation ($\Delta V^{\neq}$) of a reaction in the same way as an externally applied pressure does. Thus, the internal pressure of water influences the rates of nonpolar reactions in water in the same direction as external pressures. Nonpolar reactions with a negative volume of activation will thus be accelerated by the internal pressure of water, whereas nonpolar reactions with a positive volume of activation will be slowed by the internal pressure. For example, at 20°C the rate of Diels-Alder reaction between cyclopentadiene and butenone, which is known to have a negative volume of activation, in a 4.86 M LiCl solution is about twice as that of the reaction in water alone (Eq. 1.1).[4]



(1.1)

Solvent	$k_2 \times 10^5$, ($M^{-1}s^{-1}$)
H_2O	4400 ± 70
H_2O + LiCl (4.86 M)	10800

1.6 WATER UNDER EXTREME CONDITIONS[3,10]

Ordinary water behaves very differently under high temperature and high pressure. Early studies of aqueous solutions under high pressure showed a unique anomaly that was not observed with any other solvent.[11] The electrolytic conductance of aqueous solutions increases with an increase in pressure. The effect is more pronounced at lower temperatures. For all other solvents, the electrical conductivity of solutions decreases with increase in pressure. This unusual behavior of water is due to its peculiar associative properties.[12]

Thermal expansion causes liquid water to become less dense as the temperature increases. At the same time, the liquid vapor becomes more dense as the pressure rises. For example, the density of water varies from 1.0 g/cm^3 at room temperature to 0.7 g/cm^3 at 306°C. At the critical point, the densities of the two phases become identical and they become a single fluid called *supercritical fluid*. Its density at this point is only about 0.3 g/cm^3 (Figures 1.4 and 1.5).

In the region of supercritical point, most properties of supercritical water vary widely. The most prominent of these is the heat capacity at constant pressure, which approaches infinity at the critical point. Even 25°C above T_c, at 80 bar away from P_c, the heat capacity of water is an order of magnitude greater than its value at higher or lower pressure.

The dielectric constant of dense, supercritical water can range from 5 to 20 simply upon variation of the applied pressure.

As the temperature increases from ambient to the critical point, the electrolytic conductance of water rises sharply and is almost independent of the pressure. Macroscopically, this is due to the decrease in water viscosity over this range. The primary cause for the fall in viscosity is a disintegration of water clusters.

However, the conductances (being as much as tenfold greater than at room temperature) begin to drop off after entering the supercritical

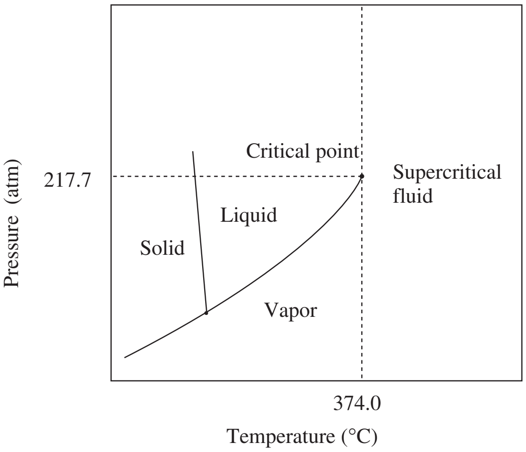


Figure 1.4 Phase diagram of water around the supercritical region.

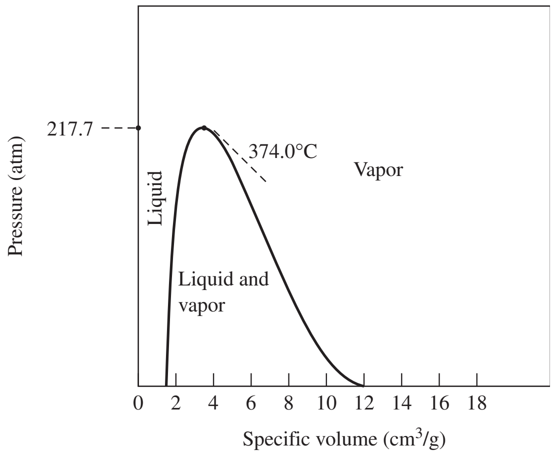


Figure 1.5 Pressure-volume diagram for water around the supercritical region.

region. The degree of drop is dependent on the pressure. Low pressures bring about a sharp drop, while at high pressures the decline is much less severe. Dissolved salts associate with themselves and behave as weak electrolytes.

On the other hand, water, itself an extremely weak electrolyte at room temperature, dissociates to a greater extent as the temperature rises (Eq. 1.2). For example, K_w increases to about 10^{-6} at 1000°C and a density of 1.0 g/ml.

$$2\ H_2O \rightleftharpoons H_3O^+ + {}^-OH \tag{1.2}$$

The increased dissociation of water in conjunction with the increased association of the electrolyte in the supercritical region has a fundamental influence on chemical reactions. Some reactions such as hydrolysis become faster in supercritical water. For example, there are at least eight species (KCl, KOH, HCl, HOH, K^+, Cl^-, H^+, and OH^-) for potassium chloride in supercritical water.

On the other hand, the increase in temperature decreases the intermolecular interaction (hydrogen bonding) between water molecules, which lessens the squeezing-out effect for nonpolar solutes. At the supercritcal state, water exhibits an "antiaqueous property." For example, water at high temperatures exhibits considerable, and sometimes complete, miscibility with nonpolar compounds.

Because oxygen, carbon dioxide, methane, and other alkanes are completely miscible with dense supercritical water, combustion can occur in this fluid phase. Both flameless oxidation and flaming combustion can take place. This leads to an important application in the treatment of organic hazardous wastes. Nonpolar organic wastes such as polychlorinated biphenyls (PCBs) are miscible in all proportions in supercritical water and, in the presence of an oxidizer, react to produce primarily carbon dioxide, water, chloride salts, and other small molecules. The products can be selectively removed from solution by dropping the pressure or by cooling. Oxidation in supercritical water can transform more than 99.9 percent of hazardous organic materials into environmentally acceptable forms in just a few minutes. A supercritical water reactor is a closed system that has no emissions into the atmosphere, which is different from an incinerator.

Quantum chemistry calculations suggest that supercritical water can provide new reaction pathways by forming structures with the reacting molecule that lower the activation energies for bond breakage and formation.[10b] The calculation shows that the more water molecules participate in the reaction, the lower the activation energy of the reaction is. For example, calculation on the following gas-shift reactions (Eq. 1.3) shows that the activation energy for the first step of the reaction is 61.7 kcal/mol if no additional water molecules participate in the reaction ($n = 0$); whereas the participation of an additional water molecule ($n = 1$) would lower the activation energy to half of its original value (35.6 kcal/mol). A similar decrease in activation energy by the participation of an additional water molecule was found for the second step, and the participation of more water molecules in the reaction would further reduce the activation energy.

$$\mathrm{CO} + (n+1)\mathrm{H_2O} \xrightarrow[\text{Step 1}]{} \mathrm{HCOOH} + n\mathrm{H_2O} \xrightarrow[\text{Step 2}]{} \mathrm{CO_2} + \mathrm{H_2} + n\mathrm{H_2O} \tag{1.3}$$

In this case water is effectively acting as a catalyst for the reaction by lowering the energy of activation. These catalytic water molecules are more likely to participate in the reaction under supercritical conditions because their high compressibility promotes the formation of solute-solvent clusters.

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