Control of Chemical Equilibrium by Solvent: A Basis for Teaching Physical Chemistry of Solutions

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The main concern of chemists is the control of product yields and reaction rates, but the number of ways we can influence the outcome of a particular reaction is surprisingly small. Moreover, the methods that are available have limited applicability owing to the physical properties of the system under study. Temperature, for example, is one of the most commonly controlled parameters, but the temperature range available for monitoring is often severely limited by the stability and phase of reacting substances. Changes in pressure are effective only in systems with at least one gaseous component. Other perturbations, including radiation, mechanical and acoustic actions, and so forth, have limited applicability and are specific to the process under investigation. Any additional method that can be used to control chemical reactivity is particularly welcome.

Solvent-control of chemical reactions is one method that has gained popularity in recent years, since a judiciously selected solvent can alter the equilibrium or kinetics of a reaction, even changing its direction entirely. Also, since the overwhelming majority of known chemical processes take place in solution or liquid phase, solvent-control is a convenient means of influencing reactions. The comprehensive development of solution chemistry has allowed chemists to put forward and prove the idea that the solvent acts simultaneously as a medium and a reactive agent in a chemical system (1–3).

A number of books (4–9) are devoted to detailing the power that solvents have over the kinetics of chemical processes (10, 11) and the issue is also addressed in nearly every physical chemistry textbook. The influence of solvents on chemical equilibria—particularly the role of solvent in altering product yields and reaction branching—has received less attention (12–18) and consequently is not included in many textbooks. The didactic presentation of solvent effects on chemical equilibria given below is intended to provide the basis for teaching physical chemistry of solutions. Following a general review of equilibrium thermodynamics and quantification of the universal and specific solute–solvent interactions, the solvent-control is illustrated with examples from homo- and hetero-molecular associations and conformational equilibria.

The material given in this article is appropriate for presentation following a review of the general ideas underlying chemical equilibrium and an introduction of different types of solvent effects. The students should be familiar with the equilibrium constant and its relationship to the equilibrium free energy (Gibbs energy at constant pressure and temperature); then the concepts of universal and specific solvation may be introduced. Solvents such as hexane and carbon tetrachloride are excellent examples of universal solvents, since they provide inert environments for carboxylic acid dimerization. The specific solvents such as water and dioxane are capable of hydrogen bonding with the acid. The concept of a dielectric medium that screens electrostatic solute–solvent interactions should be discussed in terms of the dielectric constant.

Examples of nonpolar solvents with small dielectric constants, such as hexane, and polar solvents with large dielectric constants, such as acetonitrile and water, should be considered. The instructor may elect to quiz the students on chemical equilibrium and the types of solute–solvent interactions at this point. At this point, the discussion of solvent effects on chemical equilibrium may be terminated in a general chemistry curriculum. A physical chemistry class can further explore the detailed examples included below and in the Supplemental Material. These descriptions of homom- and hetero-molecular association and conformer equilibria could be used to develop illustrative laboratory experiments. In such case, and especially if the laboratory experiment does not follow the lecture immediately, the instructor can provide a “to-review list” in the week preceding the lab. The “to-review list” should be based on the lecture material and should give several examples of solute–solvent pairs and types of interactions. Finally, students should be required to hand in a complete laboratory report.

General Considerations

Chemical equilibrium (15) in solution can be represented in general as

\[ A \rightleftharpoons B \]  (1)

where A are reactants and B are products formed from the reactants as a result of a chemical reaction. Consideration of the thermodynamic cycle gives the Gibbs energy of the reaction

\[ \Delta G = \Delta G_{\text{solvB}} - \Delta G_{\text{solvA}} + \Delta G_v \]  (2)

where \( \Delta G_{\text{solvA}} \) and \( \Delta G_{\text{solvB}} \) are the Gibbs solvation energies of reactants and products, respectively, and \( \Delta G_v \) is the Gibbs energy of the reaction in vacuum.

The solute–solvent interactions can be separated into universal and specific components, giving a sum (19):

\[ \Delta G_{\text{solv}} = \Delta G^{(\text{univ})} + \Delta G^{(\text{spec})} \]  (3)
In $\Delta G^{(\text{univ})}$ the solvent acts as an inert medium, whereas $\Delta G^{(\text{spec})}$ includes chemically active interactions such as hydrogen bonding. Substituting eq 3 in eq 2 leads to a general equation that describes the effect of a solvent on chemical equilibrium:

$$
\Delta G = \Delta G^v + \left[ \Delta G_{\text{solvB}}^{(\text{univ})} - \Delta G_{\text{solvA}}^{(\text{univ})} \right] + \left[ \Delta G_{\text{solvB}}^{(\text{spec})} - \Delta G_{\text{solvA}}^{(\text{spec})} \right]
$$

(4)

$\Delta G^v$, of course, does not depend on the solvent. The difference in the first bracket in eq 4 characterizes universal solvation, and the difference in the second bracket accounts for specific solvation. Thus, the solvent effect on chemical equilibrium is determined by the solvation energies of each of the chemical species involved. Note that for universal, chemically-inert solvents where $\Delta G^{(\text{univ})} \gg \Delta G^{(\text{spec})}$, we may rewrite eq 4 as

$$
\Delta G = \Delta G^v + \left[ \Delta G_{\text{solvB}}^{(\text{univ})} - \Delta G_{\text{solvA}}^{(\text{univ})} \right]
$$

(5)

The equilibrium Gibbs energy is directly related to the equilibrium constant, $K$, at temperature $T$. As in eq 4 for the Gibbs energy, one can distinguish between the universal and specific contributions of a solvent to the magnitude of $K$

$$
\ln K = -\frac{\Delta G^v}{RT} + \frac{\left[ \Delta G_{\text{solvB}}^{(\text{univ})} - \Delta G_{\text{solvA}}^{(\text{univ})} \right]}{RT} \left( \delta_\beta_{\text{univ}}^{\text{univ}} \right) + \frac{\left[ \Delta G_{\text{solvB}}^{(\text{spec})} - \Delta G_{\text{solvA}}^{(\text{spec})} \right]}{RT} \left( \delta_\beta_{\text{spec}}^{\text{spec}} \right)
$$

(6)

or

$$
\ln K = -\frac{\Delta G^v}{RT} + \frac{\delta_\beta_{\text{spec}}^{\text{spec}}}{RT} + \frac{\delta_\beta_{\text{univ}}^{\text{univ}}}{RT}
$$

(6a)

As before (cf. eq 5), the equations simplify for universal solvents:

$$
\ln K^{(\text{univ})} = -\frac{\Delta G^v}{RT} + \frac{\left[ \Delta G_{\text{solvB}}^{(\text{univ})} - \Delta G_{\text{solvA}}^{(\text{univ})} \right]}{RT}
$$

(7)

or

$$
\ln K^{(\text{univ})} = -\frac{\Delta G^v}{RT} + \frac{\delta_\beta_{\text{univ}}^{\text{univ}}}{RT}
$$

(7a)

We can develop a practical representation for $\delta_\beta_{\text{spec}}^{\text{spec}}$ by considering the screening of the electrostatic solute–solvent interactions in terms of solvent dielectric permittivity, $\varepsilon$. Then eq 6a may be expressed (17) as

$$
\ln K = -\frac{1}{RT} \left[ \Delta G^v + \frac{\delta_\beta_{\text{spec}}^{\text{spec}}}{\varepsilon} \right] + \frac{\beta_{\text{solvB}} - \beta_{\text{solvA}}}{\varepsilon}
$$

$$
= -\frac{1}{RT} \left[ \Delta G^v + \frac{\delta_\beta_{\text{spec}}^{\text{spec}}}{\varepsilon} \right]
$$

(8)

where the $\beta_i$ represent the main types of electrostatic interactions, such as dipole–dipole, ion–dipole, ion–ion interactions, and so forth. Equation 8 simplifies for the case of a universal solvent to

$$
\ln K^{(\text{univ})} = -\frac{1}{RT} \left( \Delta G^v + \frac{\delta_\beta_{\text{solv}}^{\text{spec}}}{\varepsilon} \right)
$$

(9)

where $\delta_\beta_{\text{solv}}^{\text{spec}}$ equals the universal solvation component extrapolated to vacuum ($\varepsilon = 1$), that is, $\delta_\beta_{\text{solv}}^{\text{spec}} = \delta_\beta_{\text{solv}}^{\text{univ}}$. In addition to characterizing a solvent, the permittivity $\varepsilon$ provides a convenient handle for hypothetically turning the solute–solvent interaction on and off. For instance, in the limit of perfect screening, $\varepsilon \to \infty$ and the $1/\varepsilon$ interaction terms in eqs 8 and 9 disappear.

An analysis of eq 8 allows us to draw essential conclusions about the influence of solvent on the thermodynamic characteristics of chemical processes taking place in solution. It follows from eq 8 that at fixed temperature, the equilibrium constant changes with solvent properties because of a change in either a specific interaction, $\delta_\beta_{\text{solv}}^{\text{spec}}$, or a universal electrostatic interaction, $\delta_\beta_{\text{solv}}^{\text{univ}}$. This leads to several scenarios for the functional dependence of $\ln K$ on $1/\varepsilon$, depending on the behavior of $\delta_\beta_{\text{solv}}^{\text{spec}}$ and $\delta_\beta_{\text{solv}}^{\text{univ}}$.

Generally, if both $\delta_\beta_{\text{solv}}^{\text{spec}}$ and $\delta_\beta_{\text{solv}}^{\text{univ}}$ vary between the solvents, $\ln K = f(1/\varepsilon)$ is a nonlinear function. Even in solvents where the specific interaction $\delta_\beta_{\text{solv}}^{\text{spec}}$ is constant, and only the universal interaction $\delta_\beta_{\text{solv}}^{\text{univ}}$ changes, $\ln K = f(1/\varepsilon)$ is still nonlinear in general. If both the $\delta_\beta_{\text{solv}}^{\text{spec}}$ and $\delta_\beta_{\text{solv}}^{\text{univ}}$ values are constant for different solvents, that is, in a "conditionally universal medium" (16), the $\ln K = f(1/\varepsilon)$ dependence becomes linear (cf. eq 9)

$$
\ln K^{(\text{univ})} = a + \frac{b}{\varepsilon}
$$

(10)

where $a$ and $b$ are the coefficients of the linear equilibrium equation. In the absence of specific solute–solvent interactions $\delta_\beta_{\text{solv}}^{\text{spec}} = 0$, the $\ln K = f(1/\varepsilon)$ dependence is also linear and is described by eq 10.

Extrapolation of the $\ln K = f(1/\varepsilon)$ dependence to $\varepsilon \to \infty$, that is, putting the system in a hypothetical medium in which there are no electrostatic interactions, reduces eq 8 for a solvent with specific interactions to

$$
\ln K_{\varepsilon \to \infty} = -\frac{1}{RT} \left[ \Delta G^v + \delta_\beta_{\text{spec}}^{\text{spec}} \right]
$$

(11)

Similarly, eq 9 becomes

$$
\ln K_{\varepsilon \to \infty}^{(\text{univ})} = -\frac{\Delta G^v}{RT}
$$

(12)

from which we can find the vacuum component of the Gibbs energy of a chemical equilibrium process:

$$
\Delta G^v = -RT \ln K_{\varepsilon \to \infty}^{(\text{univ})}
$$

(12a)

Finally, we can determine the energy of specific solvation by comparing the equilibrium constants of chemical processes taking place in specific and universal solvents with approximately the same dielectric constant $\varepsilon^{(\text{spec})} = \varepsilon^{(\text{univ})}$.

$$
-RT \left[ \ln K^{(\text{spec})} - \ln K^{(\text{univ})} \right] = \delta_\beta_{\text{solv}}^{\text{spec}}
$$

(13)
Thus, analysis of the \( \ln K = f(1/\varepsilon) \) dependence allows one to characterize all three basic components of Gibbs energy of a chemical process in solution: \( \Delta G^\circ \), \( \delta \Delta G_{\text{solv}}^{(\text{spec})} \), and \( \delta \Delta G_{\text{solv}}^{(\text{univ})} \).

To compare the equilibrium constants of eq 1 in two solvents \( S^{(1)} \) and \( S^{(2)} \), we start by writing eq 8 for each solvent:

\[
\ln K_{S^{(1)}} = -\frac{1}{RT} \left[ \Delta G^\circ + \delta \Delta G_{\text{solv}}^{(\text{spec})} + \frac{\delta \beta_{\text{solv}}^{(1)}}{\varepsilon} \right] \tag{14a}
\]

\[
\ln K_{S^{(2)}} = -\frac{1}{RT} \left[ \Delta G^\circ + \delta \Delta G_{\text{solv}}^{(\text{spec})} + \frac{\delta \beta_{\text{solv}}^{(2)}}{\varepsilon} \right] \tag{14b}
\]

Solving eqs 14a and 14b for \( \varepsilon \) and equating the results, we obtain

\[
\ln K_{S^{(1)}} = \text{const}_1 + \text{const}_\Pi \ln K_{S^{(2)}} \tag{15}
\]

where

\[
\text{const}_1 = -\frac{1}{RT} \left[ \Delta G^\circ + \delta \Delta G_{\text{solv}}^{(\text{spec})} + \frac{\delta \beta_{\text{solv}}^{(1)}}{\varepsilon} \right] \tag{15a}
\]

\[
\text{const}_\Pi = \frac{\delta \beta_{\text{solv}}^{(1)}}{\delta \beta_{\text{solv}}^{(2)}} \tag{15b}
\]

An examination of eq 15 leads to two important conclusions. First, the logarithm of the equilibrium constant of a chemical process in solution:

\[
\ln \frac{K_{S^{(1)}}}{K_{S^{(2)}}} = \text{const}_1 + \text{const}_\Pi \ln \frac{K_{S^{(2)}}}{K_{S^{(1)}}}
\]

Second, if const1 > 1, as represented in Figure 1, the equilibrium constant in solvent \( S^{(1)} \) is increased relative to solvent \( S^{(2)} \). Solvent \( S^{(1)} \) shifts the equilibrium towards products, so it can be thought of as having a “differentiating” effect with respect to solvent \( S^{(2)} \). Conversely, solvent \( S^{(2)} \) has a “leveling” effect with respect to solvent \( S^{(1)} \), since it tends to shift the equilibrium towards the middle.

In this section we have shown that solvent contributions to the equilibrium constant produce two major factors that affect chemical equilibrium: the Gibbs energies of specific and universal solvation. The former occurs by a donor–acceptor interaction between solute and solvent. The latter originates due to universal electrostatic interactions between solute and solvent molecules and is often taken into account by considering dielectric permittivity of the solvent.

Several methodologically interesting examples of solvent influence on chemical equilibrium are presented in the following sections. The examples cover a wide range of phenomena, including homo- and hetero-molecular association and conformational equilibrium.

### Homo-Molecular Association Processes

Dimerization is the most common homo-molecular association process:

\[
2A \rightleftharpoons A_2 \tag{16}
\]

The solvent dependence of the equilibrium constant for the dimerization process (eq 16) can be obtained through application of eq 8:

\[
\ln K_{\text{dim}}^{(\text{univ})} = -\frac{1}{RT} \left[ \Delta G_{\text{dim}}^\circ + \delta \Delta G_{\text{dim}}^{(\text{univ})} \right] \tag{18}
\]

We can specify the form of \( \delta \Delta G_{\text{dim}}^{(\text{univ})} \) in terms of dielectric permittivity as in eq 9

\[
\ln K_{\text{dim}}^{(\text{univ})} = -\frac{1}{RT} \left( \Delta G_{\text{dim}}^\circ + \frac{\beta_{\text{solv}} A_2 - 2 \beta_{\text{solv}} A_2}{\varepsilon} \right) \tag{19}
\]

obtaining a linear relationship

\[
\ln K_{\text{dim}}^{(\text{univ})} = a + \frac{b}{\varepsilon} \tag{20}
\]

where \( \Delta G_{\text{dim}}^\circ = -RTa \) and \( \Delta G_{\text{dim}}^{(\text{univ})} = -RTb/\varepsilon \).

Equation 20 agrees well with experimentally determined \( K_{\text{dim}} \) values, as illustrated in Table 1 for solutions of carboxylic acids. The correlation coefficient \( r \) presented in the table is close to one. The linear correlation between the logarithm

<table>
<thead>
<tr>
<th>Acid</th>
<th>10^a</th>
<th>10^b</th>
<th>10^r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetic</td>
<td>4.62</td>
<td>5.10</td>
<td>0.982</td>
</tr>
<tr>
<td>Monochloroacetic</td>
<td>3.91</td>
<td>5.15</td>
<td>0.997</td>
</tr>
<tr>
<td>Dichloroacetic</td>
<td>3.35</td>
<td>5.97</td>
<td>0.998</td>
</tr>
<tr>
<td>Trichloroacetic</td>
<td>5.60</td>
<td>4.35</td>
<td>0.998</td>
</tr>
</tbody>
</table>

Figure 1. Dependence of the equilibrium constants, \( K \), of processes taking place in a solvent \( S^{(1)} \) on the equilibrium constants of the same processes taking place in another solvent \( S^{(2)} \).
of the equilibrium constant and the polarity parameter \((20, 21) E_T\), which is directly related to the solvent dielectric permittivity \(\varepsilon\), gives reasonable estimates for \(K_{\text{dim}}\) in universal media (Figure 2).

Table 2 presents the vacuum and universal solvent interaction components of the equilibrium Gibbs energy of carboxylic acid dimerization. The data show that in the series from acetic to trichloroacetic acid, the vacuum interaction component \(\Delta G_{\text{dim}}^{\nu}\) decreases and the solvent interaction component \(\delta \Delta G_{\text{dim}}^{(\text{univ})}\) increases. While the \(\Delta G_{\text{dim}}^{\nu}\) and \(\delta \Delta G_{\text{dim}}^{(\text{univ})}\) values are comparable in weakly-polar solvents (small \(\varepsilon\)), the \(\delta \Delta G_{\text{dim}}^{(\text{univ})}\) component rapidly decreases with increasing \(\varepsilon\); in chlorobenzene \(\delta \Delta G_{\text{dim}}^{(\text{univ})}\) drops to about 20–30% of \(\Delta G_{\text{dim}}^{\nu}\). This trend is even more pronounced in the highly-polar nitrobenzene. Thus, the dependence of \(\ln K\) (or \(\Delta G\)) on \(1/\varepsilon\) in universal media provides important information about the thermodynamics of homo-molecular association.

The \(\ln K_{\text{dim}} = f(\varepsilon, T)\) dependence for acetic acid dimerization (CH\(_3\)COOH, Figure 3) in a mixture of the universal solvents CCl\(_4\) and C\(_6\)H\(_5\)Cl can be approximated (22) by the following

\[
\ln K_{\text{dim}} = -1.72 + \frac{1817.1}{T} - \frac{0.92}{\varepsilon} + \frac{1553.4}{\varepsilon T}
\]

The dimer concentration \((x, \text{mol L}^{-1})\) is related to initial concentration of the monomer \((c)\) and the equilibrium constant \((K_{\text{dim}})\) by

\[
x = \frac{4 K_{\text{dim}} c + 1 - \sqrt{8 K_{\text{dim}} c + 1}}{8 K_{\text{dim}}}
\]

Equation 21 predicts that the concentration of the acetic acid dimer in hexane \((n\text{-C}_6\text{H}_{14}, K_{\text{dim}} \approx 1.5 \times 10^3)\) equals half that of the monomer, whereas the dimer concentration in nitrobenzene \((C_6H_5NO_2, K_{\text{dim}} \approx 10^2)\) equals one third. Using selected mixtures of the two solvents, one can adjust the acetic acid dimer content from 33 to 50%. Similarly, dissolving phenol in mixtures of CCl\(_4\) and C\(_6\)H\(_5\)NO\(_2\) with varying composition one can control the concentration of the phenol dimer within a 2-to-12% interval relative to the monomer concentration. More examples can be found in refs 17, 23–25.

In a specific medium, the interaction between some participants of a chemical equilibrium and solvent molecules can be exceptionally strong. In such a case, homo-molecular dimerization is described by

\[
2A \rightleftharpoons A_2 + (S)
\]

which assumes that the dimer is solvated to a lesser degree than the monomer. In order to relate the homo-molecular dimerization in the presence of specific solute–solvent interaction (eq 22) to that in a universal solvent (eq 16), we must consider the solvation process

\[
A + S \rightleftharpoons AS
\]

Figure 2. Dependence of the dimerization constants for acetic acid (solid line) and trichloroacetic acid (dashed line) on the polarity parameter \((E_T)\) of the following solvents: 1–n-C\(_6\)H\(_{14}\); 2–CCl\(_4\); 3–CS\(_2\); 4–CHCl\(_3\); 5–C\(_6\)H\(_5\)Cl; and 6–C\(_6\)H\(_5\)NO\(_2\).

Figure 3. Molecular models of the acetic acid dimers: (A) cyclic dimer and (B) linear dimer.

### Table 2. Components of Gibbs Energies of Dimerization of Carboxylic Acids in Universal Solvents at 298.15 K

<table>
<thead>
<tr>
<th>Solvent</th>
<th>(\varepsilon)</th>
<th>(-\Delta G_{\text{dim}}^{\nu}) / [kJ mol(^{-1})]</th>
<th>(-\Delta G_{\text{dim}}^{(\text{univ})}) / [kJ mol(^{-1})]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Acetic acid</td>
<td>Monochloroacetic acid</td>
</tr>
<tr>
<td>Hexane</td>
<td>1.89</td>
<td>6.7</td>
<td>6.8</td>
</tr>
<tr>
<td>Tetrachloromethane</td>
<td>2.23</td>
<td>5.7</td>
<td>5.7</td>
</tr>
<tr>
<td>Carbon disulfide</td>
<td>2.62</td>
<td>4.8</td>
<td>4.9</td>
</tr>
<tr>
<td>Chloroform</td>
<td>4.72</td>
<td>2.7</td>
<td>2.7</td>
</tr>
<tr>
<td>Chlorobenzene</td>
<td>5.62</td>
<td>2.2</td>
<td>2.3</td>
</tr>
<tr>
<td>Nitrobenzene</td>
<td>34.8</td>
<td>0.36</td>
<td>0.37</td>
</tr>
<tr>
<td>Vacuum</td>
<td>11.4</td>
<td>9.7</td>
<td>8.3</td>
</tr>
</tbody>
</table>

Note: The Gibbs energy for the vacuum is expressed as \(-\Delta G_{\text{dim}}^{\nu}\) / [kJ mol\(^{-1}\)].
Comparing eqs 22 and 23 with eq 16 indicates that homo-molecular association in a specific medium is complicated by the necessity to break the A···S bond first. The energy required to break the bond is subtracted from the energy gained during dimerization, resulting in a decrease of $K_{\text{dim}}$ compared to the corresponding value in a universal medium with the same dielectric permittivity. Mathematically, the decrease in $K_{\text{dim}}$ follows from eq 17: the $[\Delta G_{\text{solvA}}^{\text{(spec)}}, - 2\Delta G_{\text{solvA}}^{\text{(spec)}}]$ term becomes negative in a specific medium, thereby lowering the total energy of the association process relative to the Gibbs energy for a universal medium, eq 19. This analysis is supported by the experimental data presented in Table 3, which shows a comparison of $K_{\text{dim}}$ values for dimerization of acetic acid in various universal and specific solvents.

The role of specific solvation is illustrated particularly well through consideration of $K_{\text{dim}}$ values in specific and universal solvents with similar dielectric primitivities. We consider here the specific solvents benzene and 1,4-dioxane, and the universal solvent CCl$_4$, which all have $\varepsilon \sim 2.5$. The $K_{\text{dim}}$ value for acetic acid dimerization in benzene is an order of magnitude lower than in CCl$_4$. The role of specific solvation is even more dramatic in 1,4-dioxane, where the equilibrium constant is almost three orders of magnitude lower than its value in CCl$_4$. 1,4-Dioxane shows significantly stronger specific solvation than benzene because it is much more basic. Equations 8 and 9 were used to calculate the energies of specific solvation of acetic acid by benzene and 1,4-dioxane, giving $-5.8$ and $-16.6$ kJ mol$^{-1}$, respectively.

| Table 3. Equilibrium Constants for Dimerization of Acetic Acid in Various Solvents at 298.15 K |
|-----------------------------------------------|---------------|-----------------|
| **Universal Solvents**                       | $\varepsilon$ | $K_{\text{dim}}$ |
| Hexane                                        | 1.88          | 1250            |
| Tetrachloromethane                            | 2.23          | 990             |
| Carbon disulfide                              | 2.62          | 700             |
| Chloroform                                    | 4.72          | 290             |
| Chlorobenzene                                 | 5.62          | 240             |
| Nitrobenzene                                  | 34.8          | 110             |
| **Specific Solvents**                         |               |                 |
| Benzene                                       | 2.3           | 95              |
| 1,4-Dioxane                                   | 2.2           | 1.2             |
| Water                                         | 78.3          | 0.05            |

In water, the Gibbs energies of both specific and universal solvation of acetic acid are large. Owing to water’s high dielectric permittivity, the $K_{\text{dim}}$ value is insignificant.

Binary mixtures of universal and specific solvents allow one to control the degree of homo-molecular association over a wide range of concentrations (17). For instance, by varying the composition of the $n$-hexane/1,4-dioxane mixture it is possible to change the content of the acetic acid dimers from 50% to 8%. The dimer concentration can be further decreased below the 8% mark, all the way down to 0.5%, by using a mixture of 1,4-dioxane and water.

It happens quite often that suitable solvent selection provides the only practical mechanism for changing the degree of molecular association.

**Solvent Effect on Conformer Equilibrium**

A conformational equilibrium process can be expressed in general as

$$\text{conformer I } \rightleftharpoons \text{conformer II} \quad (24)$$

or for the special case of cis–trans isomerization as

$$\text{cis-isomer } \rightleftharpoons \text{trans-isomer} \quad (25)$$

The experimental approaches for determining conformer concentrations are not always sufficiently accurate (17); as a rule the difference in conformer energies is relatively small, ranging from 0.1 to 10–12 kJ/mol. This is similar to the energies of dipole–dipole interaction and specific solvation in moderately active solvents, so it is difficult to discriminate between the conformer equilibrium and other processes.

Since dipole moments are often very different between the conformers (26), dielectric permittivity of the solvent plays a crucial role in the equilibrium processes (22, 25). The conformer transformation energies are inversely proportional to permittivity in universal solvents

$$\Delta G_{\text{conf}} = A + \frac{B}{\varepsilon} \quad (26)$$

where $A$ and $B$ are the coefficients of the linear energy equation. Correspondingly, ln $K_{\text{conf}}$ depends on $1/\varepsilon$ linearly

$$\ln K_{\text{conf}} = a + \frac{b}{\varepsilon} \quad (27)$$

and the equilibrium constant shows an exponential dependence on $1/\varepsilon$. Here, $a = -A/RT$ and $b = -B/RT$, cf. eq 6. These equations are sufficiently accurate to describe experimental data for conformation and isomerization equilibria.

We will illustrate the argument above with the isomerization of 1,2-disubstituted ethane: XCH$_2$–CH$_2$Y. The potential energy of the molecule depends on a number of geometric parameters, the most important of which is the torsion angle $\Theta$ (Figure 4). Stable conformers include the synclinal (sc) conformation characterized by $\Theta_{sc}$ and the anti-periplanar (ap) conformation characterized by $\Theta_{ap}$ which exactly equals 180$^\circ$ owing to symmetry. The key parameters of the potential energy profile include the difference $\Delta G^0$ in the Gibbs free energies of the isomers and the heights of the two types of maxima $\Delta G^0_1$ and $\Delta G^0_2$. Given an explicit form
for the shapes of the minima and the maxima, for instance, a cosine function, one can uniquely determine the values of the angles $\Theta_{ac}$ and $\Theta_{op}$. The Gibbs energy difference $\Delta G^\circ$ between the stable rotamers follows the inverse dependence on solvent dielectric permittivity. For example, eq 26 for 1-fluoro-2-chloroethane in mixtures of alkane and chloralkane solvents becomes (27)

$$\Delta G_{\text{conf}} = \left( -2.86 + \frac{8.69}{\varepsilon} \right) \quad r = 0.963$$

Considering eq 5 in the context of eq 26, it is clear that an increase in solvent dielectric permittivity decreases the absolute value of the electrostatic components of the conformer transformation free energies in universal solvents. This stabilizes the isomerization equilibrium. For instance, the $\Delta G_{\text{conf}}$ for bromocyclohexanone in cyclohexane ($\varepsilon = 2$) is 5.2 kJ/mol, while in acetonitrile ($\varepsilon = 36$) the energy equals ~0.3 kJ/mol.

The stabilization of polar conformers offered by solvents with higher dielectric permittivity affects not only the final equilibrium composition of the conformer mixture, but also the rate of approach to equilibrium. When the transition state between the conformers is more polar than the stable conformers—as is often the case—equilibration occurs faster in polar solvents. We see this phenomenon, for instance, with the rotation around the formally double C=C bond in substituted ethylenes

![Image](image94x175 to 248x245)

In this example, the isomerization transition state (II) is significantly more polar than the stable conformer (I) (28).

The influence of specific solvation on conformational equilibrium is widely known for solvents capable of intermolecular hydrogen bonding. A good illustration is given by the tautomerization of imidazoletetrahydropyran (III), which can form a hydrogen bond or even abstract a proton (IV) in such solvents as chloroform (28):

![Image](image94x349 to 248x402)

However, correlating specific solvation effects on conformational equilibrium with the physical and chemical properties of the solvent is extremely difficult. Attempts to determine simple and reliable connections between $\Delta G$ and $\ln K_{\text{conf}}$ values and the donor and acceptor energy levels do not succeed in general. Significantly better results have been obtained with pairwise solute–solvent interaction parameters (29).

As in the molecular association example above, often times the solvent effect is the only method available to effect drastic change in the relative concentrations of different conformational forms. Consider, for example, dichloroacetaldehyde conformers in cyclohexane and DMSO solvents. At room temperature, the axial rotamer is favored in cyclohexane; the equilibrium constant for the formation of this rotamer is $K_{\text{conf}} = 0.79$. However, the corresponding $K_{\text{conf}}$ value in DMSO is just 0.075. To obtain a similar equilibrium in cyclohexane, one would have to cool the solution to 64 K (−209 °C); this is entirely impossible experimentally, since cyclohexane freezes at +6.5 °C. Similarly, to achieve $K_{\text{conf}} = 0.79$ in DMSO, one would have to heat the solution to 435 K (162 °C).

**Conclusions**

We have presented a didactic description of solvent effects on chemical equilibria, illustrated by several examples of basic processes occurring in solution. This material is intended to provide the basis for teaching physical chemistry of solutions, assuming the students are familiar with the general ideas underlying chemical equilibrium: the equilibrium constant and equilibrium free energy. The universal and specific types of solvation have been introduced, followed by detailed examples of homomolecular association and conformer equilibrium. Further examples involving heteromolecular association may be found in the Supplemental Material. This article shows the students that solvent can be used to influence chemical equilibrium, thereby altering the yield of reaction products.

To determine the influence of solvent on chemical equilibrium, it is necessary to consider the donor–acceptor properties of the solvent as well as its polarity (i.e., permittivity as a microscopic property or the dipole moment and polarizability as a molecular property). Using mixed solvents allows one to widely vary these properties.

We have not considered chemical processes taking place in water, because they have been studied more extensively than those taking place in nonaqueous environments. Moreover, owing to its singular physical-chemical properties, water in no way provides a representative system for the study of nonwater solvents. It is certainly necessary to give attention to mixtures of water and nonwater solvents, which find greater application in research and in industry (dyeing, electrochemical processing of materials, etc.). However, areas of science and engineering based on nonwater solvents are advancing no less intensely. Clearly the development presented in this article is urgently needed and will provide a valuable addition to the physical chemistry curriculum.

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**Supplemental Material**

Mathematical derivation of the temperature dependence of the Gibbs energy as well as a detailed example of the solvent effect on heteromolecular association are available in this issue of *JCE Online*.
Literature Cited