# Thermodynamics of Solvation in Mixed Solvents

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In the development of chemical processes chemists have traditionally made use of a wide range of solvents; however, it is often startling to realize just how profound the effect of changes in solvent can be on chemical systems. Figure 1, which shows the variation in the equilibrium constant for the simple disproportionation of cuprous ions (reaction E1) as a function of solvent composition in aqueous acetonitrile mixtures,[1] provides one illustration of this.

$$2Cu^{+} \leftrightarrow Cu^{0} + Cu^{2+} \qquad (E1)$$

Thus in water the text book disproportionation reaction occurs but, on transferring the reaction to acetonitrile, there is a change in the equilibrium constant of some 26 powers of ten ($10^{6}$ to $10^{-20}$); moreover this change is a markedly non-linear function of solvent composition, with a change of twelve orders of magnitude occurring between pure water and an acetonitrile mole fraction of 0.05.

Confronted by results such as this, it is only natural to ask how the replacement of one clear colourless liquid by another can cause such a dramatic change in the chemistry of simple reactions. It is also obvious that the ability to predict such changes in chemical reactivity would be of considerable importance in the optimization of chemical processes.

In the early 1970s the available quantitative solvation theories simply could not account for such effects. There were, however, a number of important qualitative observations. Among these were Parker's[2] demonstration that poor anion solvation resulted in the marked increases in the rates of nucleophilic reactions in aprotic solvents, Reichardt's[3] and Gutmann's[4] work showing that the solvation could be correlated with parameters which gave a measure of the solvent's acidity or basicity, and Strehlow's[5] studies showing the existence of preferential solvation in mixed solvent systems.

All of this work pointed to the dominance of solute to near neighbour solvent molecule interactions in determining the chemical changes which result from changes in solvent. Simply, if these interactions were strong the solute would be well solvated, while it was poorly solvated (and hence more reactive) if they were weak. In mixed solvents, the solute was preferentially solvated by the component with which it interacted more strongly.

The observation of preferential solvation in mixed solvents was particularly striking and suggested that solvation in these media was analogous to complexation, with the better solvent taking the role of the ligand. This analogy was supported by the isolation of crystalline solvates of a number of electrolytes and by the determination of stability constants for the complexation of a number of cations by common solvents.[1]

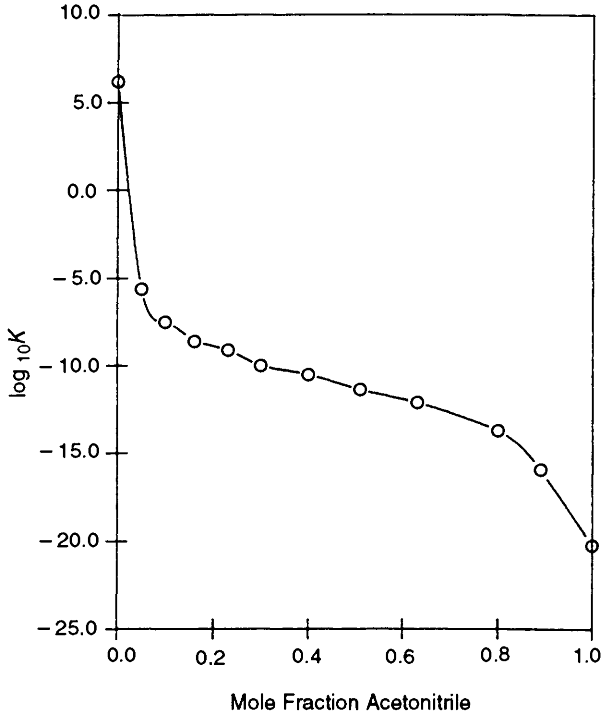

**Figure 1** Variation in the logarithm of the equilibrium constant for the disproportionation of cuprous ions (equilibrium, E1) in aqueous acetonitrile mixtures.

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These results raised the obvious question as to the extent to which changes in the thermodynamics of solvation result simply from changes in the composition of the solute's coordination, or inner solvation, sphere.

The simple coordination model, which results from this,[1,6,7] assumes that *all* of these thermodynamic changes result from the successive replacement of the molecules of one solvent, say A, by those of a second solvent, B, in the coordination sphere of the solute. Thus it takes no account of changes in solvent – solvent interactions, nor of changes in the interactions of coordinated solvent molecules with the surrounding medium. It also takes no account of the effect of changes in the permittivity of the solvent system, although this contribution could be included.

This leads to a set of relatively simple equations for the thermodynamic transfer parameters of a solute. Thus the free energies of transfer of a solute, $\Delta_t G^{\ominus}$, from some solvent, A, to some second solvent, B, and to mixtures of A and B are given by equations 1 and 2 respectively.

$$\Delta_t G^{\ominus} = -RT\ln\beta'_n \qquad (1)$$

$$\Delta_t G^{\ominus} = -RT\ln x_A - RT\ln\left\{1 - \sum_{i=1}^{n}\beta'_i\left(\frac{x_B}{x_A}\right)^{i}\right\} \qquad (2)$$

Throughout, $n$ is the coordination number of the solute, $n_i$ the number of molecules of $i$ in the coordination sphere and the $\beta'_i$'s are the equilibrium products for the equilibria:

$$\mathrm{MA}_n + i\mathrm{B} \leftrightarrow \mathrm{MA}_{n-i}\mathrm{B}_i + i\mathrm{A} \qquad \text{(E2)}$$

written in terms of the mole fractions of A and B ($x_A$ and $x_B$ respectively) These equations are formally identical to those derived by Covington *et al*[8] except that the latter include a term to take account of changes in the solvent permittivity

The composition of the coordination sphere of the solute is similarly calculable from the $\beta_i'$ values *via*

$$\frac{n_B}{n} = \frac{1}{n}\left\{ \sum_{i=1}^{n} i\beta_i'\left(\frac{x_B}{x_A}\right)^{i}\left[1 + \sum_{j=1}^{n}\beta_j'\left(\frac{x_B}{x_A}\right)^{j}\right]^{-1}\right\} \qquad (3)$$

Clearly relationships for the enthalpies and entropies of transfer, $\Delta_t H^\ominus$ and $\Delta_t S^\ominus$ can be derived by the appropriate differentiation of equation 2 with respect to temperature More directly, if the enthalpy changes for the successive replacement of A by B can be taken to be constant, $\Delta_t H^\ominus$ is given by

$$\Delta_t H^\ominus = \left\{\frac{n_B}{n}\right\}\overset{\mathrm{A}\rightarrow\mathrm{B}}{\Delta_t} H^\ominus \qquad (4)$$

which requires the determination of the enthalpy of transfer from A to B, $\overset{\mathrm{A}\rightarrow\mathrm{B}}{\Delta_t} H^\ominus$, as well as the $\beta_i'$ values

A more elegant route to these parameters comes from the recognition that $\Delta_t S^\ominus$ simply reflects the fact that preferential solvation results in a non-random distribution of solvent molecules within the system[6] Thus the proportions of A and B molecules in the solute's coordination sphere differ from those in the bulk solvent Clearly the compositions of the bulk solvent and coordination sphere are the same ($x_i = n_i/n = 1$) in the single component solvent systems and the corresponding entropy is zero in these Thus $\Delta_t S^\ominus$ to mixtures of A and B is given by

$$\Delta_t S^\ominus = -n_A R\ln\left(\frac{n_A}{n x_A}\right) - n_B R\ln\left(\frac{n_B}{n x_B}\right) \qquad (5)$$

while that to pure solvents is zero

$\Delta_t H^\ominus$ is calculable as

$$\Delta_t H^\ominus = \Delta_t G^\ominus + T\Delta_t S^\ominus \qquad (6)$$

with $\Delta_t H^\ominus$ between pure solvents equal to the corresponding $\Delta_t G^\ominus$

Thus this simple coordination model leads to a self-consistent set of equations for the composition of the coordination sphere of the solute and the transfer free energies, enthalpies and entropies, moreover, the only parameters required for these calculations are the $\beta_i'$ and $n$ for the system

This model is formally restricted to solvent systems which form ideal liquid mixtures, since it assumes that the observed changes result *solely* from changes in the composition of coordination sphere of the solute It is, of course, possible to modify equations 2 and 3 to take account of non-ideality of the solvent system by replacing the $x_i$ values by the corresponding Raoult's law activities, however, additional factors have to be included in the relationship for the transfer enthalpies and entropies (see below)

Testing this model requires experimental values of the appropriate $\beta_i'$ and of the transfer parameters, or some measure of the variation of the composition of the coordination sphere, of the solute in a reasonably ideal mixed solvent system Dimethylsulfoxide (DMSO) and the propylene carbonate (PC) form almost ideal liquid mixtures and have the advantages that there is a large difference between their basicities The latter leads to large changes in cation solvation, and experimentally accessible values of $\beta_i'$ for the complexation of several cations by DMSO in PC Additionally, since both solvents are aprotic, changes in anion solvation should be minimal This approximation is supported by the fact that the transfer parameters for the silver halides in these media are, within experimental error, independent of the anion

Figure 2 shows the experimental $\Delta_t G^\ominus$, $\Delta_t H^\ominus$, and $\Delta_t S^\ominus$ (as $-T\Delta_t S^\ominus$) values for the transfer of AgCl and NaCl from PC to DMSO + PC mixtures along with the corresponding values for $Ag^+$ and $Na^+$, calculated *via* equivalents 1—6 using the experimental $\beta_i'$ values for $Ag^+$–DMSO and $Na^+$–DMSO complexes in PC[1,6,9] The results for LiCl are similar and have been omitted for clarity

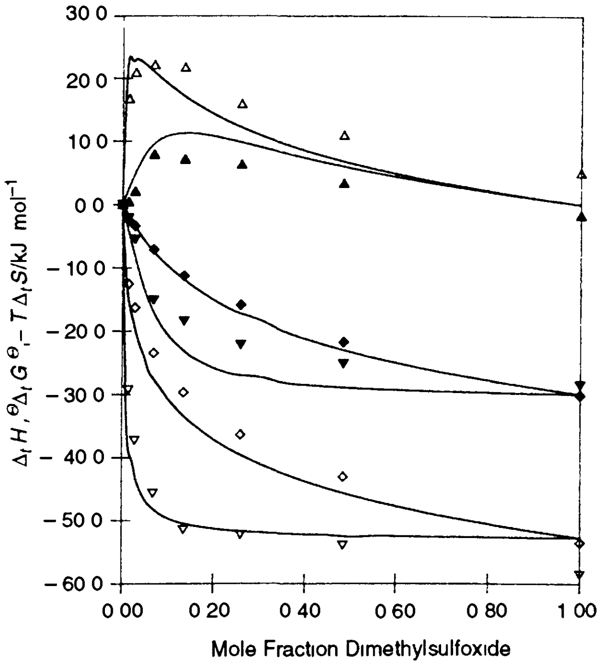

**Figure 2** Comparison of calculated (lines) and experimental (points) transfer free energies (◇) enthalpies (▽) and entropies (as $-T\Delta_t S^\ominus$) (△) of sodium (open symbols) and silver (filled symbols) chloride from propylene carbonate to propylene carbonate + dimethylsulfoxide mixtures

The agreement between the calculated and experimental transfer parameters is, in all cases, close to the limits of experimental precision and provides striking support for the simple coordination model Thus the cations are preferentially solvated by DMSO leading to monotonic decreases in $\Delta_t G^\ominus$ and $\Delta_t H^\ominus$, with the latter decreasing more rapidly at low DMSO mole fractions and the values converging for transfer from PC to DMSO Preferential solvation also accounts for the relatively large maxima in $-T\Delta_t S^\ominus$ (minima in $\Delta_t S^\ominus$) which result from the differences in the compositions of the coordination sphere and bulk solvent These provide an obvious marker for significant preferential solvation in mixed solvents

Unfortunately there are no data which provide direct information about the composition of the coordination spheres of the ions in these media, although the agreement shown in Figure 2 strongly argues for the applicability of equation 3 There are, however, $^{23}$Na-NMR chemical shift data available in a number of mixed solvent systems, and these do provide a method for estimating these changes[10] The DMSO + acetonitrile, MeCN, system is one for which there are NMR data and, although there are no directly determined $B_i'$ values available, there are $\Delta_t G^\ominus$ data[1] Assuming that the $\beta_i'$ values are related statistically it is straightforward to recover a value of $\beta_n'^{(1/n)}$ This in turn can be used to calculate the individual $\beta_i'$ values, provided that the coordinating number, $n$, is available, a value of six, consistent with the results of molecular dynamics calculations,[11] was chosen in this case

Figure 3 shows the corresponding plots of the experimental and calculated values of $n_D/n$, the fraction of the coordination sites occupied by DMSO, and $\Delta_t G^\ominus$, for $Na^+$, as a function of solvent composition in this system Again the agreement between the calculated and experimental results is excellent

Thus, for these relatively simple solvent systems, we arrive at a simple, predictive model for the effect of changes in solvent in

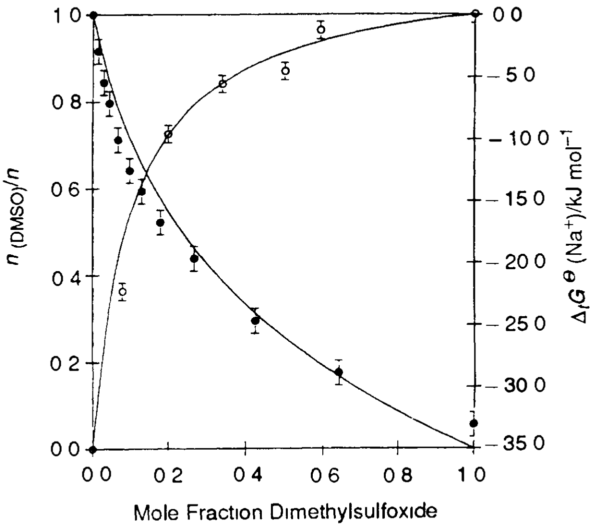

**Figure 3** Comparison of calculated (lines) and experimental (points) values for the composition of the solvation shell (○), left hand scale) and transfer free energy (●, right hand scale) of the sodium ion in acetonitrile + dimethylsulfoxide mixtures

which the dominant interactions are those between the solute and its coordination sphere of solvent molecules The composition of the coordination sphere varies with solvent composition according to simple equilibrium process, with the component solvents acting as ligands, competing for coordination sites around the solute, and changes in solvent composition act by altering the relative concentrations of these ligands

The obvious response to the success of the simple coordination model is to test its applicability to more complex solvent systems, that is, those which do not form ideal liquid mixtures Initially this involved measuring $\beta_i'$ and $\Delta_t G^\ominus$ values for a range of systems Inconveniently, the measurement of $\beta_i'$ values for anions is relatively difficult, and these studies concentrated on cations, particularly $Ag^+$, and involved single ion $\Delta_t G^\ominus$ values estimated using an extrathermodynamic assumption [1 12]

The results of these studies were remarkable, in that equation 1 and 2 reproduced the $\Delta_t G^\ominus$ data, practically to experimental error, in a wide range of solvent systems However, when the studies were extended to the $\Delta_t H^\ominus$ and $\Delta_t S^\ominus$ data[9] there were systematic deviations between the experimental data and those predicted by equations 3–6 This was a much more interesting situation

Figure 4 shows the experimental and calculated transfer parameters for silver chloride from methanol, MeOH, to MeOH + MeCN mixtures, which is a good example of the situation In this system $Ag^+$ is preferentially solvated by MeCN, and $Cl^-$ by methanol The $\beta_i'$ values for the $Ag^+$–MeCN complexes are available from the literature,[13] however, these are unusual in that only three constants were recovered, while the coordination number of $Ag^+$ is generally found to be four Thus the fourth equilibrium constant was assumed to be unity, corresponding to random solvation at the fourth site (this gives $\beta_i'$ values of $2\ 51 \times 10^2$, $6\ 31 \times 10^4$, $1\ 00 \times 10^6$, and $1\ 00 \times 10^6$) The corresponding values for the $Cl^-$–MeOH complexes are not available and were estimated by first calculating the $\Delta_t G^\ominus$ values for $Ag^+$ *via* equations 1 and 2 and subtracting these from the experimental $\Delta_t G^\ominus$ data to give those for Cl, equation 1 was used to estimate $\beta_n'$ which was in turn used to calculate the $\beta_i'$ values, assuming that the coordination number of $Cl^-$ was four The $\beta_i'$ values recovered in this way were $1\ 04 \times 10^2$, $3\ 62 \times 10^3$, $4\ 18 \times 10^4$, and $4\ 18 \times 10^4$

There are several striking aspects to the results shown in Figure 4 First, despite the fact that the MeOH + MeCN mixtures form non-ideal liquid mixtures, the simple coordination model accurately predicts $\Delta_t G^\ominus$ for AgCl, and by implication those of the individual ions Moreover the predicted maxima in $-T\Delta_t S^\ominus$, and sharp changes in $\Delta_t H^\ominus$, at high and low MeCN mole fractions are clearly observed Thus the basic picture is similar to that in the simpler DMSO + PC system, with the $Ag^+$ and $Cl^-$ ions being preferentially solvated by MeCN and MeOH respectively in the mixed solvents

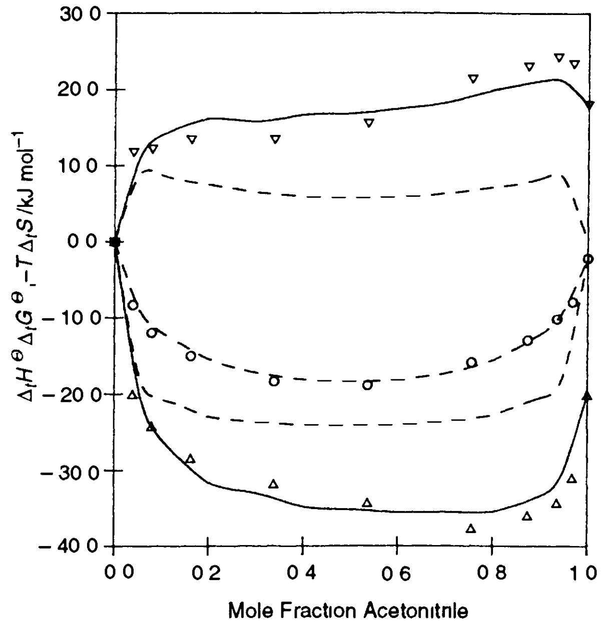

**Figure 4** Comparison of calculated (lines) and experimental (points) transfer free energies (○), enthalpies (△), and entropies (as $-T\Delta_t S^\ominus$) (▽) for silver chloride from methanol to methanol + acetonitrile mixtures Dashed lines are values calculated using equations 1 7 and solid lines those calculated using equations 8 and 7 (see text)

The most intriguing features of the results shown in Figure 4 are the systematic deviations between the experimental $-T\Delta_t S^\ominus$ and $\Delta_t H^\ominus$ data and those predicted by the simple coordination model Two things can be said immediately about these deviations (i) they reflect some factor not included in the simple coordination model and (ii) they compensate in each other exactly, or very nearly so, in $\Delta_t G^\ominus$

Now, the principal limitation imposed on the simple coordination model is that it takes no account of changes in solvent–solvent interactions Thus it is reasonable to ask whether these changes could result in the observed deviations It is also reasonable to ask whether the effects of changes in solvent–solvent interactions should contribute only to the $-T\Delta_t S^\ominus$ and $\Delta_t H^\ominus$ data and compensate each other in $\Delta_t G^\ominus$

This second question has been addressed by Ben-Naim,[14] who showed on the basis of statistical mechanical arguments that, provided the solute is at infinite dilution, solute-induced structural changes in the solvent will contribute to the enthalpies and entropies of solution but will cancel each other *exactly* in the free energy of solution Clearly any contributions which cancel in the free energies of solution will also cancel in $\Delta_t G^\ominus$ since this is simply the difference between the free energies of solution in the reference and target solvents Hence Ben-Naim's result supports the view that the observed deviations result from solvent–solvent interactions

Extension of the simple coordination model to take account of the effects of changes in solvent–solvent interactions is relatively straightforward and has been described in detail elsewhere [15 16] Briefly, the solute occupies a cavity in the solvent structure, surrounded by its coordination sphere of $n$ solvent molecules In order to complex to the solute each of these $n$ molecules will have broken some fraction, $\alpha$, of their bonds to other solvent molecules, resulting in an endothermic enthalpy change of $-\alpha n \Delta H^\circ_{11}$ where $\Delta H^\circ_{11}$ is the average enthalpy of solvent solvent bonding Additionally there may be a modification of solvent–solvent bonds around the coordination sphere, affecting $N$ (note $N \geq n$) solvent molecules By postulating that the resulting enthalpy change is proportional to $\Delta H^{0}_{11}$ we can set it equal to $-\beta N \Delta H^{0}_{11}$ where $\beta$ is the average proportionality constant for the modified bonds and is negative if the bonds are strengthened (leading to an exothermic contribution to the enthalpy of solution).

After introducing the approximation that the values of $\alpha$ and $\beta$ are constant over a range of solvent compositions, and some manipulation, this leads to

$$\Delta_t H^{\ominus} = \frac{p x_B}{(x_A + p x_B)} \Delta\Delta H^{\ominus}_{12} - \frac{(\alpha n + \beta N)}{(x_A + p x_B)}(x_A L_A + p x_B L_B) + \left\{\frac{p x_B}{(x_A + p x_B)}\right\}(\alpha n + \beta N)\Delta\Delta H^{0*} \qquad (7)$$

and

$$\Delta_t S^{\ominus} = \frac{p x_B}{(x_A + p x_B)} \Delta\Delta S^{\ominus}_{12} - \frac{NR}{x_A + p x_B}\left\{x_A \ln\left(\frac{1}{x_A + p x_B}\right) + p x_B \ln\left(\frac{p}{x_A + p x_B}\right)\right\} - \frac{(\alpha n + \beta N)}{(x_A + p x_B)}[x_A(s_A - R\ln x_A) + p x_B(s_B - R\ln x_B)] + \left\{\frac{p x_B}{(x_A + p x_B)}\right\}(\alpha n + \beta N)\Delta\Delta S^{0*} \qquad (8)$$

for the enthalpies and entropies of transfer.

In equations 7 and 8 $x_i$ are mole fractions, $L_i$ and $s_i$ the relative partial molar enthalpies and entropies of the components of the mixed solvent. The parameters $\Delta\Delta H^{0*}$ and $\Delta\Delta S^{0*}$ represent the differences between the enthalpies and entropies of interaction of the pure solvents and are calculable from the enthalpies and entropies of vaporization (the latter corrected for volume effects[16]).

The remaining model parameters reflect the solvation of the solute in the mixed solvent system. The parameter $p$, which is defined by

$$\left(\frac{n_A}{n_B}\right) \approx \left(\frac{N_A}{N_B}\right) = \frac{1}{p}\left(\frac{x_A}{x_B}\right) \qquad (9)$$

accounts for preferential solvation and, in the simplest case, is equal to the mean stability constants for the equilibria E2 [*i.e.*, $p = \beta_n^{(1/n)}$]

The effect of the solute on the solvent–solvent interactions is accounted for by the composite parameter $(\alpha n + \beta N)$ with $\alpha n$ resulting from the formation of the cavity to accommodate the solute and $\beta N$ from any further modification of the solvent structure around the cavity.

The parameters $\Delta\Delta H^{\ominus}_{12}$ and $\Delta\Delta S^{\ominus}_{12}$ represent the differences between the enthalpies, and entropies of solute–solvent interactions in the pure solvents **A** and **B**.

Thus equation 7 contains three model parameters, $\Delta\Delta H^{\ominus}_{12}$, $(\alpha n + \beta N)$, and $p$, and equation 8 the corresponding parameters $\Delta\Delta S^{\ominus}_{12}$, $(\alpha n + \beta N)$, and $p$ and the additional parameter $N$ which corresponds closely to the solvation number of the solute.

Clearly the value of $p$ is the same in each of these equations.

At first sight, it would appear that the values of $(\alpha n + \beta N)$ would also be common to the entropies and enthalpies, however this need not be the case. To see the reason for this we consider, for example, a water molecule which has hydrogen bonds to four near neighbour water molecules. If this molecule becomes the near neighbour of a solute it must break, initially, one of these bonds to allow the formation of the cavity, with an increase in enthalpy equal to 25% ($\alpha_H = 0.25$), however, the remaining three hydrogen bonds continue to restrict the motion of the solvent molecule, in particular its rotational freedom, leading to a much smaller increase in its entropy ($\alpha_S \ll 0.25$). Similar considerations apply to the $\beta$ values, which result from restructuring of the solvent around the cavity. We will consider the significance of this point in more detail below.

By now the reader will have formulated the obvious question as to whether these equations do, in fact, predict the experimental values of $\Delta_t H^{\ominus}$ and $\Delta_t S^{\ominus}$. Ultimately this is the only valid test of any theory.

We can address this question by considering again the data for AgCl in the MeOH–MeCN system. The necessary value of $p$ is simply calculated from the value of $\beta'_4$ as indicated above, and the values recovered are 17.8 and 0.0700 for $Ag^+$ and $Cl^-$ respectively, both written for coordination by MeCN in MeOH. (Note that the value for $Cl^-$ calculated this way is the inverse of that for the coordination by MeOH in MeCN.)

Using Ben-Niam's compensation principle we can set the value of $\Delta\Delta H^{\ominus}_{12}$ equal to that of $\Delta_t G^{\ominus}$, since the other contributions to $\Delta_t H^{\ominus}$ result from solvent–solvent interactions, and so disappear from $\Delta_t G^{\ominus}$. (The individual values fror $Ag^+$ and $Cl^-$, calculated *via* equation 1 are $-28.5$ and 26.3 kJ mol$^{-1}$ respectively.)

Thus, for $\Delta_t H^{\ominus}$ from MeOH to pure MeCN, equation 7 reduces to

$$\Delta_t H^{\ominus} = \Delta_t G^{\ominus} + (\alpha n + \beta N)\Delta\Delta \bar{H}^{0*} \qquad (10)$$

and, setting $\Delta\Delta \bar{H}^{0*}$ equal to the difference between the enthalpies of condensation of the pure solvents, we calculate a value of 2.45 for $(\alpha n + \beta N)$.

Thus we have values for all of the necessary model parameters, without recourse to the $\Delta_t H^{\ominus}$ values in the mixed solvents, except that we have no *a priori* method of separating $(\alpha n + \beta N)$ into its individual ionic contributions. This seems to be an acceptably small degree of flexibility.

The variation in $\Delta_t H^{\ominus}$ across the entire range of solvent compositions, calculated using $(\alpha n + \beta N)$ values of 1.00 and 1.45 for $Ag^+$ and $Cl^-$, and the values of $-T\Delta_t S^{\ominus}$ calculated from these and the calculated $\Delta_t G^{\ominus}$ values, are shown as solid lines in Figure 4. The agreement between these and the experimental data is satisfactory. Similar agreement is found between the predicted and calculated $\Delta_t H^{\ominus}$ data for the other silver halides in this solvent system.[9]

Given the success of this treatment, it is worth considering equations 7 and 8 in slightly more detail. The first point which can be made is that the model separates the direct solute–solvent and solvent–solvent contributions to $\Delta_t H^{\ominus}$ and $\Delta_t S^{\ominus}$, the latter residing entirely in those terms containing $(\alpha n + \beta N)$.

This separation allows the rigorous testing of Ben-Naim's compensation principle.[14] This has been anticipated slightly in the above, but warrants further comment. If we consider solvation in a mixed solvent which has a non-zero excess free energy, then two possibilities arise: (i) there is exact compensation of the solvent–solvent contributions to $\Delta_t G^{\ominus}$, in which case the values of $(\alpha n + \beta N)$ for the enthalpies and entropies must differ, or (ii) the $(\alpha n + \beta N)$ value is common to the two parameters, in which case exact compensation cannot occur.

This situation was investigated previously,[16] where the $\Delta_t H^{\ominus}$ and $\Delta_t S^{\ominus}$ data for the alkali metal halides in aqueous methanol systems were fitted to equations 7 and 8, giving the corresponding $(\alpha n + \beta N)$ values.

These results are shown, for LiCl and NaI (the best and worst cases respectively) in Figure 5. Again the agreement is good, but in these cases the calculated values reflect the ability of the model to reproduce, rather than predict, the data. The values of $(\alpha n + \beta n)$ recovered from the fits are listed in Table 1, along with the ratio of the $(\alpha n + \beta N)$ values obtained from the enthalpy and entropy data.

It is clear from the results listed in Table 1 that the values of $(\alpha n + \beta N)$ recovered from the entropy data are systematically lower than those from the entropy data, and that the ratio of these values is substantially the same for all of the electrolytes. Thus, in these systems at least, case (ii) does not obtain.

The solvation of these simple electrolytes in the aqueous methanol system is essentially random (*i.e.*, $p = 1$) and in this case $\Delta_t H^{\ominus}$ and $\Delta_t S^{\ominus}$ are simply related to the excess enthalpies and entropies of the solvent system since

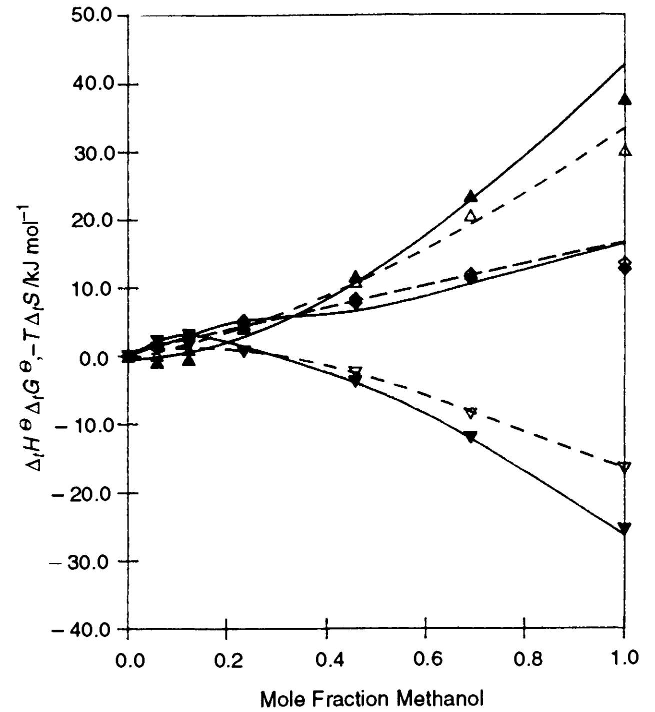

**Figure 5** Comparison of calculated (lines) and experimental (points) transfer free energies (◇), enthalpies (▽), and entropies (as $-T\Delta_tS^\ominus$) (△) for lithium chloride (open symbols) and sodium iodide (filled symbols) from water to water + methanol mixtures.

**Table 1** Values of $(\alpha n + \beta N)$ for alkali metal halides in aqueous methanol solvents from $\Delta_tH^\ominus$ and $\Delta_tS^\ominus$ data

| Electrolyte | $(\alpha n + \beta N)_H$ | $(\alpha n + \beta N)_S$ | $\frac{(\alpha n + \beta N)_H}{(\alpha n + \beta N)_S}$ |
|---|---|---|---|
| LiCl | 5.6 | 4.7 | 1.19 |
| NaCl | 6.1 | 4.7 | 1.30 |
| KCl | 5.7 | 4.3 | 1.33 |
| RbCl | 5.6 | 4.2 | 1.33 |
| CsCl | 5.9 | 4.7 | 1.26 |
| NaBr | 8.0 | 6.3 | 1.27 |
| NaI | 10.1 | 8.0 | 1.26 |
| Average | | | 1.28 |

$$x_A + px_B = 1 \qquad (11)$$

$$x_AL_A + px_BL_B = \Delta\bar{H}^E \qquad (12)$$

$$x_A(s_A - R\ln x_A) + px_B(s_B - R\ln x_B) = \Delta\bar{S}^E \qquad (13)$$

and exact compensation between the solvent–solvent contributions to $\Delta_tH^\ominus$ and $\Delta_tS^\ominus$ requires that the ratio of the corresponding $(\alpha n + \beta N)$ values is equal to that of $-T\Delta\bar{S}^E$ to $\Delta\bar{H}^E$. In the aqueous methanol system this ratio increases slightly across the range of solvent compositions (from 1.18 to 1.63) with an average value of 1.36 for the composition at which the experimental data were obtained. These values are in reasonable agreement with the ratio of the $(\alpha n + \beta N)$ values, lending support to the compensation principle [case (i) above] but more work is required to test this thoroughly.

Acceptance of Ben-Naim's compensation principle has one immediate consequence. Equations 7 and 8 are derived using the approximation that the $(\alpha n + \beta N)$ values are constant over a range of solvent compositions. If the compensation principle is to hold, this situation cannot obtain for the $(\alpha n + \beta N)$ from both enthalpies and entropies where there are varying ratios between the enthalpies and entropies of solvent–solvent interactions.

One goal of the development of theoretical models, such as those discussed above, is the prediction of the thermodynamic consequences of changes in the solvent system. A second approach is to use the model equations analytically, to obtain information about the fundamental solvation process. Thus, for example, $\Delta_tH^\ominus$ or $\Delta_tS^\ominus$ data may be fitted to equations 7 or 8 respectively and the corresponding model parameters recovered.

Enthalpy data are far more numerous in the literature, and, in general, are the more easily measured.

The application of equation 7 to $\Delta_tH^\ominus$ data for electrolytes is complicated by the fact that two solutes, the cation and anion, are involved, each with their own set of model parameters. This is simplified if, as in the aqueous methanol system, the $p$ values are similar for these, in which case one set of parameters referring to the whole electrolyte, are recovered. It is also tractable where the $p$ values are available from other measurements, as for AgCl in the MeOH–MeCN system, or where the solvation is dominated by one of the ions. In the main, however, six parameters provide rather too much flexibility for unambiguous information to be obtained from the simple fitting of experimental data to equation 7.

At first sight at least, this problem is simplified when considering solutes which are non-electrolytes, since only one set of model parameters is recovered from the analysis. Correspondingly the solvation of a number of simple non-electrolytes has been investigated in this way.

One example of this approach is shown in Figure 6, where the experimental $\Delta_tH^\ominus$ data for a series of non-electrolytes, from MeOH to MeOH–MeCN mixtures, are shown along with the corresponding fits to equation 7;[17] the parameters recovered from these analyses are listed in Table 2 (note that, for clarity, not all of the data are shown in Figure 6).

The first point to be made about the data shown in Figure 6 is that equation 7 satisfactorily reproduces all of the experimental data, across the whole range of solvent compositions, despite the marked variations in the $\Delta_tH^\ominus$ against composition profiles,

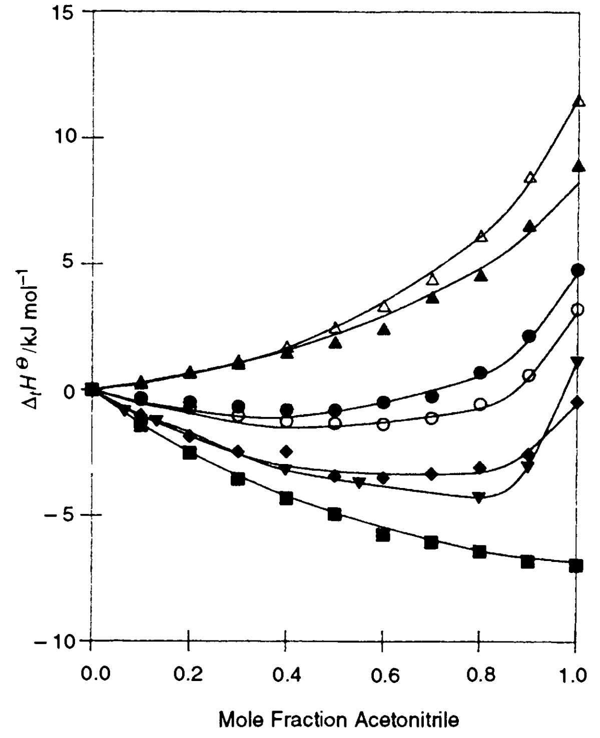

**Figure 6** Comparison of calculated (lines) and experimental (points) enthalpies of transfer of water (△), propan-1-ol (▲), formamide (●), *N*-methylformamide (○), *N,N*-dimethylformamide (◆), dimethylsulfoxide (▼), and propylene carbonate (■) from acetonitrile to acetonitrile + methanol mixtures.

**Table 2** Solvation parameters for solutes in acetonitrile–methanol mixtures[a]

| Solute[b] | $p$ | $(an + \beta N)$ | $\Delta\Delta H^{\circ}_{12}$ / kJmol$^{-1}$ |
|---|---|---|---|
| $H_2O$ | 1 8 ± 0 3 | 1 4 ± 0 3 | − 22 ± 5 |
| PrOH | 2 0 ± 0 5 | 0 8 ± 0 3 | − 16 ± 5 |
| TBA | 1 5 ± 0 3 | 0 7 ± 0 3 | − 14 ± 4 |
| OcOH | 2 0 ± 0 5 | 0 8 ± 0 6 | − 17 ± 5 |
| PC | 0 7 ± 0 2 | 0 8 ± 0 2 | 1 ± 3 |
| DMSO | 2 4 ± 0 4 | 4 0 ± 0 4 | − 30 ± 5 |
| DMA | 1 5 ± 0 3 | 4 1 ± 0 8 | − 33 ± 7 |
| DMF | 1 6 ± 0 3 | 2 8 ± 0 4 | − 21 ± 3 |
| NMF | 1 8 ± 0 4 | 2 5 ± 0 4 | − 20 ± 4 |
| Form | 1 6 ± 0 3 | 2 7 ± 0 3 | − 24 ± 4 |

Calculated using acetonitrile as the reference solvent, $p > 1$ indicates preferential solvation by methanol [b] Solutes are PrOH, propan-1-ol, TBA,2,2-dimethyhlpropan-2-ol, t-butyl alcohol, OcOH, octan-1-ol, Pc propylene carbonate, DMSO, dimethylsulfoxide, DMF, *N N*-dimethylformamide, NMF *N*-methylformamide, Form, formamide

again providing support for the extended coordination model

Consideration of the various solutes studied shows that the interpretation of the model parameters is somewhat less straightforward than the one, naively, first believed Thus, considering for example *N,N*-dimethylformamide, the solute presents a variety of different surfaces, including the basic −C=O carbonyl and the relatively non-polar −C−H and $N-CH_3$ groups, to the surrounding solvent, and the parameters recovered are the sums [$(an + \beta N)$ and $\Delta\Delta H^{\circ}_{12}$] or the weighted means ($p$) of those for these different groups

A second point which must be recognized is that these polyatomic solutes may undergo conformational changes with changing solvent composition, with corresponding intramolecular contributions to $\Delta_t H^{\ominus}$ To a first approximation, these intramolecular contributions will follow changes in the composition of the coordination sphere of the solute, paralleling the first term in equation 7 and appearing in $\Delta\Delta H^{\circ}_{12}$ This makes interpretation of this parameter relatively treacherous However, if the compensation principle holds, it may provide an opportunity to investigate these intramolecular effects, since the enthalpy of direct solute–solvent interaction may be equated to $\Delta_t G^{\ominus}$ leaving the intramolecular contribution as the difference between $\Delta_t G^{\ominus}$ and the measured $\Delta\Delta H^{\circ}_{12}$value

In the MeCN + MeOH system the interpretation of the model parameters is not difficult This has been discussed in detail elsewhere,[17] and we can restrict ourselves to the main features

The values of $(an + \beta N)$ reflect the contribution of solvent–solvent effects to $\Delta_t H^{\ominus}$, with positive values resulting from a net breaking, or weakening, of solvent–solvent bonds In the methanol–acetonitrile system these are positive for all of the solutes studied, moreover, these increase systematically in the order water, alcohols, propylene carbonate < formamides < *N,N*-dimethylacetamide, DMSO

The first point to be noted is that the values for the hydroxyl solutes are independent of the size of the alkyl group Thus, while, for example, the cavity required to accommodate the n-octyl group (octan-1-ol) must be larger than that for the propyl group (propan-1-ol) this does not affect $(an + \beta N)$

This can be understood by recognizing that $\Delta_t H^{\ominus}$ is sensitive only to those contributions to the enthalpy of solvent–solvent bonding which vary with solvent composition In this system the contribution from hydrogen bonding of the methanolic −OH group will be composition dependent, but those from interactions of the other, non-polar, surfaces of the solvent molecules may be much less so Thus the enthalpies of solvent–solvent bonding, reflected in the $L_i$ and $\Delta\Delta H^{\circ *}$ values, are likely to be dominated by the changes in the hydrogen bonding of the methanolic −OH groups, in which case the $(an + \beta N)$ values will indicate only the extent to which the solute disrupts these This suggests that these solutes are solvated with their −OH groups interacting with those of the methanol molecules and their alkyl residues accommodating in a cavity surrounded by acetonitrile molecules and the methanolic $-CH_3$ groups In this case formation of the cavity for the solute alkyl residue would make little contribution to $\Delta_t H^{\ominus}$, although it would make a significant, but composition independent, contribution to the enthalpy of solution

Support for this view comes from the relatively low value of $(an + \beta N)$ for PC which will not hydrogen bond strongly to methanol, and so not disrupt the methanol–methanol hydrogen bonds, in effect the solvation PC then would be similar to that of the alkyl groups

The insensitivity of the $(an + \beta N)$ values to the size of the alkyl groups greatly simplifies their interpretation, since they can reasonably be attributed to the effect of the polar groups on the hydrogen bonded network of methanol molecules

The interpretation is further simplified by noting that $(an + \beta N)$ is essentially the same for the three formamids, indicating that hydrogen bond formation to the amide −N−H protons doesn't involve disruption of this network This is easily understood since, at most, only half of the methanol oxygen lone pairs are involved in methanol–methanol hydrogen bonding, leaving a large reservoir of these basic sites available for hydrogen bonding to the −N−H protons

Thus we can focus on the $(an + \beta N)$ values for two types of functional groups, the R−OH of the hydroxylic solutes and the aprotic −C=O or −S=O of the amides or DMSO

Solvation of the R−O−H group can be accomplished by insertion into the hydrogen bonded network, without perturbing it significantly, and so results in a relatively small value of $(an + \beta N)$

In contrast, hydrogen bonding to the −C=O or −S=O groups involves breaking the network Now, hydrogen bonding in extended networks, such as that formed by MeOH in these systems, is cooperative and there is evidence that the hydrogen bonds to terminal molecules in such networks are weaker than the average hydrogen bonds in the network [18] Thus, solvation of these groups will involve not only a breaking of methanol–methanol hydrogen bonds ($an > 0$), but a weakening of hydrogen bonds near the point where the network is broken, giving a further endothermic contribution to $\Delta_t H^{\ominus}$ ($\beta N > 0$)

Support for this comes from considering the $(an + \beta N)$ values for the amides Infra-red studies indicate that the formamides form, on average, about 1 5 hydrogen bonds to their −C=O groups in pure methanol while the acetamides form close to 2 such bonds,[19 20] thus leading to an increase in $(an + \beta N)$ from 2 5 to 4 This increase in the extent of hydrogen bond formation is consistent with the extra basicity of the acetamides, relative to the formamides and, combined with the $(an + \beta N)$ values, suggests that DMSO also forms a maximum of two hydrogen bonds to methanol

Despite the earlier comment, one can cautiously note that the $\Delta\Delta H^{\circ}_{12}$values are entirely consistent with this interpretation Thus that of PC is close to zero, indicating roughly equal interaction enthalpies with methanol and acetonitrile, while those of the other solutes are negative, and those for the more basic DMA and DMSO significantly more so, indicating stronger interactions with methanol than acetonitrile

Thus, consideration of the model parameters leads to a remarkably detailed picture of the solvation of the species, with the non-polar alkyl groups surrounded by methanol $-CH_3$ groups and acetonitrile molecules and the polar groups hydrogen bonded to the methanol −OH group This latter interaction results in the preferential solvation by methanol, the variation in the $(an + \beta N)$ values and, arguably, that in $\Delta\Delta H^{\circ}_{12}$

The fact that the model allows the recovery of these insights into solvation, in what are relatively complex systems, from measurements effectively made with a Dewar flask and a thermometer, is both startling and gratifying However, the Holy Grail of all work in the area of solvation chemistry is to provide a

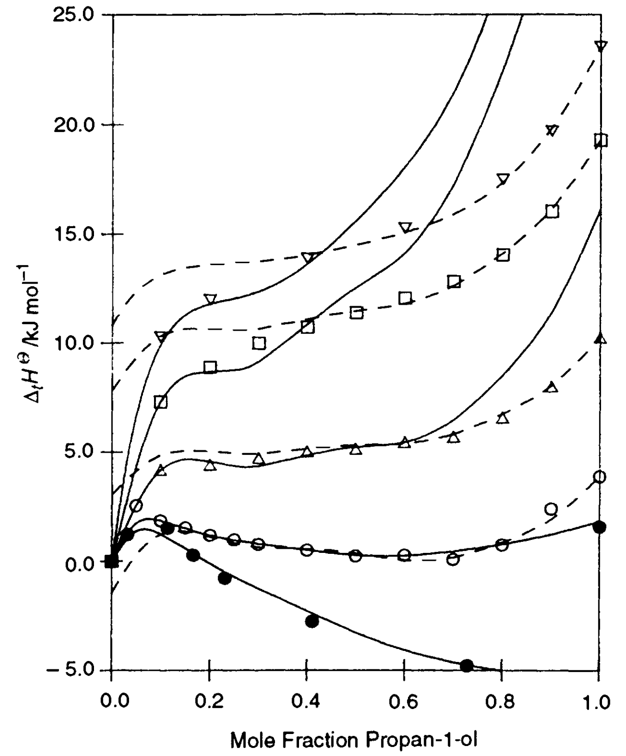

**Figure 7** Comparison of calculated (lines) and experimental (points) transfer enthalpies for *N*-methylpyrrolidinone (▽), *N*,*N*-dimethylformamide (□), *N*-methylformamide (△), formamide (○), and urea (●) from water to aqueous propan-1-ol mixtures. Solid lines represent the fits to the water rich domain, dashed lines those to the organic rich domain (see text).

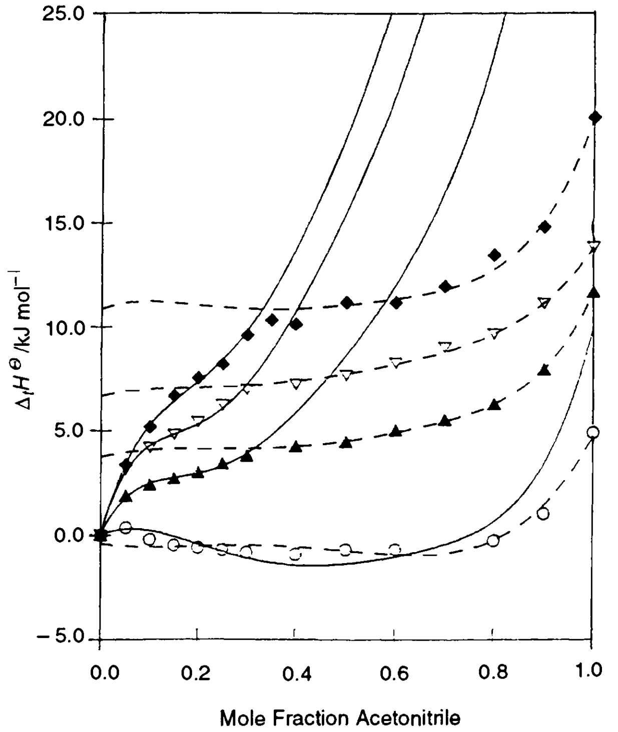

**Figure 8** Comparison of calculated (lines) and experimental (points) transfer enthalpies for *N*,*N*-dimethylacetamide (◆), *N*,*N*-dimethylformamide (▽), *N*-methylformamide (▲), and formamide (○) from water to aqueous acetonitrile mixtures. Solid lines represent the fits to the water-rich domain, dashed lines those to the organic-rich domain (see text).

better understanding of aqueous solutions. Correspondingly we can conclude by briefly considering some of the results obtained in mixed aqueous solvents.

Figures 7 and 8 show $\Delta_t H^\ominus$ for several amides, and related solutes, in aqueous mixtures with propanol[21] and acetonitrile.[22] The plots for the other aqueous alcohol systems are similar and are reported elsewhere.[21]

The most obvious feature of the results shown in Figures 7 and 8 is that two sets of model parameters are required to produce the experimental data, one in the water-rich mixtures and the other at higher concentrations of the organic co-solvent. This is also the case, for these solutes, in the aqueous methanol and ethanol systems;[20] however, as is clear from above, this transition in the solvation parameters is not found for the amides in the non-aqueous mixed solvents so far studied, nor for the alkali metal halides in aqueous methanol.

The parameters recovered for the water-rich and organic-rich composition ranges are listed in Table 3, those for the same solutes in the aqueous methanol, ethanol, and 2-methyl-2-propanol (TBA) systems show the same general features.

These results pose an obvious question. What change might occur in these aqueous solvent systems which could lead to the changes in their solvating properties?

Since no corresponding transitions are observed in the purely non-aqueous solvent systems, it is reasonable to assume that they reflect some change specific to the aqueous media.

The principal difference between the parameters for the water-rich and organic-rich domains lies in the $(\alpha n + \beta N)$ values. In the organic-rich regions these are similar to those in the purely non-aqueous systems; that is, they are relatively insensitive to the size of the solute. In contrast, the values in the water-rich domains increase systematically with the size of the non-polar alkyl residues on the solute and, for the bulkier solutes, are relatively large.

These results, combined with those from studies of aqueous-organic mixtures,[17] led us to attribute the change in the solvation parameters to a change in the solvent structure, from one based on the three-dimensional hydrogen-bonded water structure to one of lower order, based on that of the organic component.[21]

Thus, in the water-rich domain, introduction of the solute requires disruption of the hydrogen-bonded water structure, principally to create the cavity necessary to accommodate the solute, and this disruption will be greater for the larger solutes. Beyond the structural transition the solvent structure will more closely resemble those of the non-aqueous mixed solvents, and the non-polar surfaces of the solute will, correspondingly, make less contribution to $(\alpha n + \beta N)$.

The $\Delta_t H^\ominus$ against composition profiles of the amides are similar to those for a range of solutes, including the tetraalkylammonium halides,[24–26] and t-butyl alcohol[27] (as solute) in mixed aqueous solvents. Thus, in each case $\Delta_t H^\ominus$ rises markedly as the concentration of the organic component increases from zero, and then varies relatively gently over the remaining composition range. This is typical of solutes with significant non-polar surfaces; that is, those solutes which are commonly referred to as *hydrophobic*.

It is clear from Figures 7 and 8 that the initial rise in $\Delta_t H^\ominus$ becomes more extreme as the size of the non-polar surfaces increases, and from the parameters listed in Table 3 that it is associated with increases in $(\alpha n + \beta N)$. This is also the case for the tetraalkylammonium halides in aqueous propanol and t-butyl alcohol.[24]

Thus these variations in $\Delta_t H^\ominus$, in the water-rich domain, reflect a net disruption of the solvent structure $[(\alpha n + \beta N) > 0]$, with the extent of this disruption increasing with the size of the non-polar groups. This result doesn't preclude the possibility of rigidification of the water structure around these surfaces $(\beta N < 0)$ but shows that any such contribution to $\Delta_t H^\ominus$ is outweighed by that from the formation of the cavity required to accommodate the solute $(\alpha n > 0)$.

**Table 3** Solvation parameters for solutes in aqueous propan-1-ol and acetonitrile mixtures[a]

| Solute[b] | $p$ | $(\alpha n + \beta N)$ | $\Delta\Delta H^{\ominus}_{12}$/kJmol$^{-1}$ |
|---|---|---|---|
| | | **Water-Rich Region** | |
| | | Propan-1-ol + Water | |
| Urea | 1 0 ± 0 3 | 4 7 ± 0 5 | − 26 ± 3 |
| Form | 1 0 ± 0 3 | 4 5 ± 0 2 | − 14 ± 1 |
| NMF | 0 6 ± 0 3 | 7 8 ± 0 3 | − 12 ± 2 |
| DMF | 0 6 ± 0 3 | 12 1 ± 0 5 | − 5 ± 10 |
| NMPY | 0 6 ± 0 3 | 17 8 ± 0 9 | − 16 ± 10 |
| | | Acetonitrile + Water | |
| Form | 0 6 ± 0 2 | 6 ± 1 | 90 ± 20 |
| NMF | 0 7 ± 0 1 | 14 ± 1 | 244 ± 16 |
| DMF | 0 7 ± 0 1 | 23 ± 2 | 405 ± 20 |
| DMA | 0 4 ± 0 1 | 21 ± 2 | 413 ± 30 |
| | | **Organic-Rich Region** | |
| | | Propanol-1-ol + Water | |
| Form | 0 5 ± 0 2 | 5 9 ± 1 5 | − 15 ± 5 |
| NMF | 0 3 ± 0 1 | 2 3 ± 1 5 | − 1 ± 5 |
| DMF | 0 2 ± 0 1 | 0 7 ± 1 | 8 ± 5 |
| NMPY | 0 2 ± 0 1 | 0 0 ± 1 | 1 ± 10 |
| | | Acetonitrile + Water | |
| Form | 0 4 ± 0 2 | 2 ± 1 | 35 ± 10 |
| NMF | 0 4 ± 0 2 | 2 ± 1 | 36 ± 15 |
| DMF | 0 7 ± 0 1 | 2 ± 1 | 35 ± 10 |
| DMA | 0 5 ± 0 1 | 3 5 ± 0 5 | 60 ± 10 |

[a] Calculated using acetonitrile as the reference solvent $p > 1$ indicates preferential solvation by methanol or acetonitrile [b]Solutes as in Table 2 except NMPY *N*-methylpyrolidinone

It is interesting to note that the $(\alpha n + \beta N)$ values for the amidic solutes, in the water-rich domain, (Table 3) increase almost linearly with the area of the non-polar $-CH_n$ groups of the solute[21] This is consistent with independent solvation of these groups and suggests that it may be possible to develop a *group contributions* approach to predicting $\Delta_t H^{\ominus}$ However this needs further investigation, and the corresponding variations for the tetraalkylammonium bromides,[24] for which the $(\alpha n + \beta N)$ values are far larger, are markedly non-linear

A slightly surprising feature of the model parameters for these systems[21] is that the $p$ values indicate slight preferential hydration, with this increasing with the size of the non-polar $-CH_n$ groups This result has been observed consistently, for a range of solutes The origin of this isn't clear and requires further study, in particular by other techniques which can probe the solvation of these groups directly

It is clear, from these few examples, that analysis of the thermodynamic transfer parameters in this way can give remarkable insights into solvation in mixed solvents Combining these with the results of studies using other techniques, particularly those that probe the solvation of individual functional groups, will sharpen these images further This is particularly exciting in the study of complex solutes, where the solvation of different functional groups will differ markedly

The ultimate goal of formulating a complete, predictive theory for the thermodynamic changes which result from changes in solvent remains tantalizingly beyond our grasp However, the broad features of such a theory are clear The principal interactions of significance are the near neighbour solute–solvent and solvent–solvent interactions, with the former dominating the free energy and the latter contributing to the enthalpies and entropies Preferential solvation is the norm and, although in many cases it is relatively weak, it affects the variations in all of the transfer parameters in mixed solvent systems

The above has concentrated, for obvious reasons, on one series of developments Of course this isn't unique and other theoretical approaches have been, and continue to be, pursued[28] However, the basic picture of solvation which these paint is essentially similar to the above with the apparent differences reflecting differences in the mathematical, rather than the chemical, approach adopted

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