Free Energies, Enthalpies, and Entropies of Transfer of Non-electrolytes from Water to Mixtures of Water and Dimethyl Sulphoxide, Water and Acetonitrile, and Water and Dioxan

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The transfer of non-electrolytes from water to mixtures of water and dimethyl sulphoxide results in large increases in both enthalpy and entropy. The corresponding changes in free energy are relatively small. Similar behaviour was found for transfer to mixtures of water and acetonitrile and water and dioxan. The results are discussed in terms of the entropy and enthalpy changes occurring when non-electrolytes are dissolved in water.

RECENT studies of the effect of solvent upon the rate of many acid and base catalysed hydrolyses in mixed aqueous–organic solvents [1-7] have shown the rate variations to be strongly dependent on the mechanism of the reaction.

An analysis of the effect of solvent on reaction rate in terms of transition-state theory requires a knowledge of the variation of the thermodynamic properties of both the reactants and transition state in the solvent mixtures concerned.[8] In some kinetic studies [3-6] free energies of transfer of the substrates from water to the different solvent mixtures have been determined, but in general there are very little data available on the variation of thermodynamic properties of the substrates in the mixed solvents.

In this paper, free energies, enthalpies, and entropies of transfer from water to mixtures of water and dimethyl sulphoxide (DMSO) have been determined for a number of the more commonly studied substrates, together with several non-reactive solutes. The solutes have been

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chosen so as to give a fairly wide range in the total free energy of transfer from water to pure DMSO.

It is commonly observed that the free energy of transfer of solutes passes through a maximum in the region of 0·1 to 0·4 mole fraction of DMSO.[4,6] The behaviour of one such substrate, ethyl acetate, in DMSO–water mixtures has been compared with that in acetonitrile–water and dioxan–water mixtures, where no such maxima are observed.

TABLE 1

Henry's law constants of solutes in mixtures of water and dimethyl sulphoxide at 25 °C

x_{DMSO} [a]	Acetone	Ethyl vinyl ether	Benzene
0·00	33·3	1850	
0·104	40·1	2370	
0·212	56·6	1620	
0·320	56·8	1410	254
0·490	49·8	710	78
0·725	38·4	310	32
1·00	31·0	190	20

[a] Mole fraction of dimethyl sulphoxide.

TABLE 2

Henry's law constants of ethyl acetate in mixtures of water and acetonitrile and water and dioxan at 25 °C

x_{DIOX} [a]	0·00	0·090	0·210	0·310	0·460	0·700	1·00
h/l mmHg mol^{-1}	115	53	20	15	10·4	6·5	6·0
x_{AN} [b]	0·00	0·105	0·190	0·300	0·475	0·750	1·00
h/l mmHg mol^{-1}	115	67	32	20	12	8·7	8·6

[a] Mole fraction of dioxan. [b] Mole fraction of acetonitrile.

TABLE 3

Solubility of benzene in mixtures of water and dimethyl sulphoxide at 25 °C

x_{DMSO} [a]	0·00	0·104	0·212	0·320
10^2S/mol l^{-1} [b]	2·23 [c]	5·4	14·5	33·9

[a] Mole fraction of dimethyl sulphoxide. [b] S Is the solubility of benzene. [c] Ref. 11.

TABLE 4

Enthalpies (ΔH/kcal mol^{-1}) of solution [a] of solutes in mixtures of water and dimethyl sulphoxide at 23·5 °C

x_{DMSO} [b]	EtOAc [c]	t-BuOAc [c]	Acetal [c]	EVE [c]	Acetone	Benzene	TMP [c]	Water
0·00	−2·34	−2·24	−5·33	−1·7 [d]	−2·38	+0·72 [e]	−3·04	0·00
0·104	0·00	+0·80	−2·30	+1·12	−0·95	+2·35	−0·97	+0·08
0·212	+1·47	+2·13	+0·42	+2·20	+0·24	+2·66	+0·19	−0·24
0·312	+1·79	+2·62	+1·86	+2·23	+0·80	+2·20	+0·58	−0·60
0·490	+1·38	+2·10	+2·01	+1·49	+0·75	+1·32	+0·52	−1·13
0·725	+0·86	+1·43	+1·52	+0·94	+0·50	+0·79	+0·28	
1·00	+0·56	+1·08	+1·19	+0·73	+0·36	+0·65	+0·20	−1·28 [e]

[a] Estimated uncertainty ±0·03 kcal mol^{-1}. [b] Mole fraction of dimethyl sulphoxide. [c] EtOAc = Ethyl acetate, t-BuOAc = t-butyl acetate; Acetal = acetaldehyde diethyl acetal, EVE = ethyl vinyl ether, TMP = trimethyl phosphate. [d] ±0·3 kcal mol^{-1} because of slow solution of EVE in water. [e] From E. M. Arnett and D. R. McKelvey, *J. Amer. Chem. Soc.*, 1966, **88**, 2598.

EXPERIMENTAL AND RESULTS

Dimethyl sulphoxide was purified by drying over calcium hydride followed by distillation under reduced pressure. Dioxan was purified as described.[9] Acetonitrile was purified by drying and distilling over calcium hydride followed by fractional distillation from P_2O_5 and then again from calcium hydride. All organic solutes were commercial samples purified by standard procedures of drying and distillation.

The following solutes have been studied: ethyl acetate, t-butyl acetate, ethyl vinyl ether, acetaldehyde diethyl acetal, trimethyl phosphate, benzene, and acetone.

Free Energies of Transfer.—Except for benzene these were obtained from vapour pressure measurements using a previously described Henry's law apparatus.[10,11] All measurements were made at 25 °C. Henry's law constants were independent of solute concentration over the concentration range studied (0·1—1·0M).

The constants were found to be reproducible to ±10%, corresponding to an uncertainty of ±0·1 kcal mol^{-1} in the free energy of transfer of the various solutes [see equation (1)].

The solubility of benzene in mixtures of water and DMSO containing less than 0·3 mole fraction of DMSO was too low to allow accurate measurement of the vapour pressure. For this reason the free energy of transfer of benzene from water to solvents containing 0·1, 0·2, and 0·3 mole fraction of DMSO was obtained from the change in solubility and from 0·3 mole fraction of DMSO to pure DMSO from the change in Henry's law constants. Solubilities of benzene were obtained from the u.v. absorption of saturated solutions.[12] Measured Henry's law constants are recorded in Tables 1 and 2. The solubility of benzene is given in Table 3.

From the measured Henry's law constants, it is possible to obtain the free energy of transfer of the various solutes from water to a given solvent using equation (1) where

$$\Delta G_{\text{tr(A)}} = 2{\cdot}303RT \log(h_{\text{S}}M_0d_{\text{S}}/h_0d_0M_{\text{S}}) \qquad (1)$$

$\Delta G_{\text{tr(A)}}$ is the free energy of transfer of solute A at infinite dilution from the reference solvent water, to solvent S based on the standard state of the hypothetical ideal solution of unit mole fraction (*i.e.* the mole fraction concentration scale). d_{S} and d_0 are the densities of solvent S and water respectively, M_0 is the molecular weight of water and M_{S} is the molecular weight of solvent S. For a mixed solvent M_{S} is defined by equation (2) where x_1,M_1 are the

$$M_{\text{S}} = x_0M_0 + x_1M_1 \qquad (2)$$

mole fraction and molecular weight of the second component of the mixed solvent and x_0 is the mole fraction of water. h_0 and h_{S} are the Henry's law constants of solute A in water and solvent S respectively. The factor $M_0d_{\text{S}}/d_0M_{\text{S}}$

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TABLE 5

Enthalpies of solution[a] of ethylacetate in mixtures of water and dioxan and water and acetonitrile at 23·5 °C

x_{DIOX} [b]	0·00	0·09	0·210	0·310
ΔH_S/kcal mol^{-1}	−2·34	+0·28	+0·86	+0·68
x_{DIOX} [b]	0·460	0·700	1·0	
ΔH_S/kcal mol^{-1}	+0·56	+0·34	+0·19	
x_{AN} [c]	0·00	0·105	0·190	0·300
ΔH_S/kcal mol^{-1}	−2·34	−0·12	−0·00	+0·00
x_{AN} [c]	0·475	0·750	1·0	
ΔH_S/kcal mol^{-1}	+0·04	+0·12	+0·03	

[a] Estimated uncertainty ±0·03 kcal mol^{-1}. [b] Mole fraction of dioxan. [c] Mole fraction of acetonitrile.

for the various solvent mixtures was calculated from known densities at 25 °C.[13]

TABLE 6

Free energies (ΔG_{tr}/kcal mol^{-1}), enthalpies (ΔH_{tr}/kcal mol^{-1}), and entropy terms ($-298\Delta S_{\text{tr}}$/kcal mol^{-1}) of transfer of solutes from water to mixtures of water and dimethyl sulphoxide at 25 °C

		Mole fraction of DMSO							
Solute [c]		0·0	0·1	0·2	0·3	0·4	0·6	0·8	1·0
EtOAc	ΔG_{tr} [a]	0·0	0·0	−0·2	−0·4	−0·7	−1·1	−1·6	(−2·0) [b]
	ΔH_{tr}	0·0	+2·3	+3·7	+4·2	+4·0	+3·5	+3·1	+2·9
	$-298\Delta S_{\text{tr}}$	0·0	−2·3	−3·9	−4·6	−4·7	−4·6	−4·7	(−4·9) [b]
t-BuOAc	ΔG_{tr} [a]	0·0	−0·2	−0·4	−0·8	−1·1	−1·9	−2·5	(−3·0) [b]
	ΔH_{tr}	0·0	+3·0	+4·3	+4·9	+4·8	+4·0	+3·6	+3·3
	$-298\Delta S_{\text{tr}}$	0·0	−3·2	−4·7	−5·7	−5·9	−5·9	−6·1	(−6·3) [b]
Acetal	ΔG_{tr} [a]	0·0	0·0	0·1	0·1	−0·2	−0·8	−1·3	(−1·7) [b]
	ΔH_{tr}	0·0	+3·2	+5·5	+7·0	+7·4	+7·1	+6·7	+6·5
	$-298\Delta S_{\text{tr}}$	0·0	−3·2	−5·4	−6·9	−7·6	−7·9	−8·0	(−8·2) [b]
EVE	ΔG_{tr}	0·0	−0·1	−0·3	−0·5	−0·8	−1·4	−1·9	−2·2
	ΔH_{tr}	0·0	+2·2	+3·9	+4·0	+3·6	+2·9	+2·6	+2·4
	$-298\Delta S_{\text{tr}}$	0·0	−2·3	−4·2	−4·5	−4·4	−4·3	−4·5	−4·6
Acetone	ΔG_{tr}	0·0	0·0	0·0	−0·1	−0·2	−0·5	−0·7	−0·9
	ΔH_{tr}	0·0	+1·3	+2·5	+3·1	+3·3	+3·0	+2·8	+2·7
	$-298\Delta S_{\text{tr}}$	0·0	−1·3	−2·5	−3·2	−3·2	−3·5	−3·5	−3·6
Benzene	ΔG_{tr}	0·0	−0·7	−1·2	−1·9	−2·4	−3·2	−3·6	−3·9
	ΔH_{tr}	0·0	+1·5	+2·0	+1·6	+1·1	+0·3	0·0	−0·1
	$-298\Delta S_{\text{tr}}$	0·0	−2·2	−3·2	−3·5	−3·5	−3·5	−3·6	−3·8
TMP	ΔG_{tr} [d]	0·0	+0·7	+1·1	+1·5	+1·7	+2·0		
	ΔH_{tr}	0·0	+2·2	+3·2	+3·5	+3·7	+3·4	+3·3	+3·2
	$-298\Delta S_{\text{tr}}$	0·0	−2·5	−2·1	−2·0	−2·0	−1·4		

[a] Values from ref. 6. [b] Values obtained by extrapolation to pure DMSO. [c] Abbreviations as in Table 4. [d] Values from ref. 5.

TABLE 7

Free energies, enthalpies, and entropies of transfer of ethyl acetate from water to mixtures of water and acetonitrile and water and dioxan at 25 °C

x_{AN} [a]	0·0	0·1	0·2	0·3	0·4	0·6	0·8	1·0
ΔG_{tr}/kcal mol^{-1}	0·0	−0·4	−0·9	−1·3	−1·6	−1·9	−2·1	−2·2
ΔH_{tr}/kcal mol^{-1}	0·0	+2·2	+2·4	+2·4	+2·4	+2·4	+2·4	+2·4
$-298\Delta S_{\text{tr}}$/kcal mol^{-1}	0·0	−2·6	−3·3	−3·7	−4·0	−4·3	−4·5	−4·5
x_{DIOX} [b]	0·0	0·1	0·2	0·3	0·4	0·6	0·8	1·0
ΔG_{tr}/kcal mol^{-1}	0·0	−0·7	−1·3	−1·7	−1·9	−2·3	−2·6	−2·7
ΔH_{tr}/kcal mol^{-1}	0·0	+2·8	+3·2	+3·1	+2·9	+2·8	+2·6	+2·5
$-298\Delta S_{\text{tr}}$/kcal mol^{-1}	0·0	−3·5	−4·5	−4·7	−4·9	−5·1	−5·2	−5·2

[a] Mole fraction of acetonitrile. [b] Mole fraction of dioxan.

Enthalpies of Solution.—Heats of solution were obtained by conventional methods of calorimetry using a Gould calorimeter model 400 of design essentially as described.[14] Measured heats of solution were independent of solute concentration in the range 1×10^{-3} to *ca.* 2×10^{-2}M. The results are given in Tables 4 and 5. All measurements were made at 23·5 ± 0·5 °C.

From plots of the free energies of transfer of the solutes from water to the various solvent mixtures obtained from the application of equation (1) to the data in Tables 1 and 2, values of $\Delta G_{\text{tr(A)}}$ at selected mole fractions of the organic component of the solvent were obtained. These values, together with previously published values for acetaldehyde diethyl acetal, ethyl acetate, and t-butyl acetate in mixtures of DMSO and water,[6] can be combined with corresponding values of $\Delta H_{\text{tr(A)}}$ (the heat of transfer of solute A at infinite dilution from water to solvent S), similarly obtained from the data in Tables 4 and 5, to give the various entropies of transfer of A from water to solvent S ($\Delta S_{\text{tr(A)}}$) according to equation (3). It has been assumed that $\Delta H_{\text{tr(A)}}$ at 25 °C is the same as that at 23·5 °C, the temperature at which the

$$\Delta G_{\text{tr(A)}} = \Delta H_{\text{tr(A)}} - T\Delta S_{\text{tr(A)}} \qquad (3)$$

experimental heats were obtained. Values of $\Delta G_{\text{tr(A)}}$, $\Delta H_{\text{tr(A)}}$, and $-298\Delta S_{\text{tr(A)}}$ for various solutes A at selected

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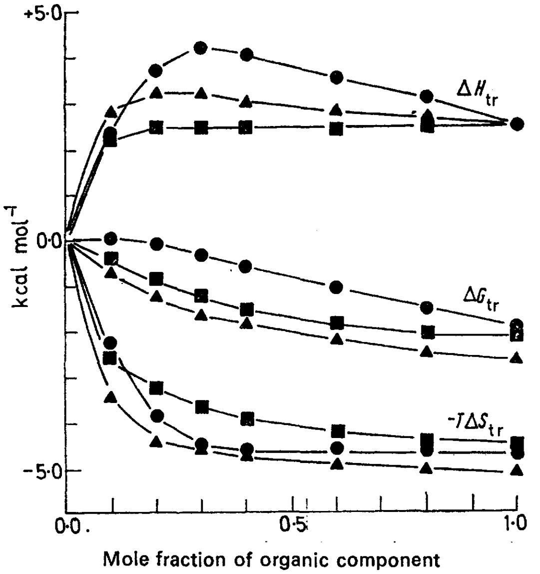
mole fractions of the solvent mixtures are listed in Tables 6 and 7. The Figure shows a comparison of the behaviours of ethyl acetate in mixtures of water with DMSO, acetonitrile, and dioxan.



Free energies (ΔG_{tr}), enthalpies (ΔH_{tr}), and entropy terms ($-T\Delta S_{tr}$) of transfer of ethyl acetate from water to mixtures of water and dimethyl sulphoxide (●), water and dioxan (▲) and water and acetonitrile (■) at 25 °C

DISCUSSION

(a) *Thermodynamics of Solute Transfer*.—The most striking feature of the results presented in Table 6 and the Figure is the very large increase in entropy terms and a corresponding, though smaller, increase in enthalpy accompanying the transfer of the various solutes from water to DMSO. The net result in most cases is a relatively small decrease in free energy. The major increase in both enthalpy and entropy occurs during the addition of the first 0·2—0·3 mole fraction of DMSO. Further addition of DMSO results in small decrease of both free energy and enthalpy with the entropy remaining approximately constant.

If one assumes that entropy changes caused by solution of the various solutes in DMSO are relatively small, then these changes are most simply explained by considering the effect of adding water to the solution of the solute in DMSO. DMSO, being larger and more polarisable than water, should have considerably larger dispersion force interactions with the solutes than does water. As DMSO is replaced by water in the solvent system the total dispersion force interaction between DMSO and the solute should decrease, this leading to an increase in both free energy and enthalpy as is observed. This trend should continue until there are appreciable quantities of water in the solvent. Up to this stage entropy changes would be expected to be quite small. When the mole fraction of water is sufficiently high for water to retain some of its structure, the behaviour of the solvent should start to resemble that of pure water. It is known that the solution of ' inert ' non-electrolytes in water often results in a large decrease in entropy.[15] This is commonly interpreted [15] as being due to an increase in the structure of water. Thus in water-rich solvent mixtures, the addition of the solute will cause a decrease in entropy (and hence an increase in $-T\Delta S$). Any increase in structure must result in a corresponding decrease in enthalpy because of the formation of a larger number of, or stronger, water–water hydrogen bonds. The net effect will be a decrease in both entropy and enthalpy in agreement with the results shown in Table 6 and the Figure. This effect will increase as the solvent approaches pure water. The results in Table 6 indicate that the structure of water has been destroyed in solvents containing $>$*ca*. 30 mole % of DMSO.

It is difficult to predict the variation of the free energy in solvents for which $0 < X_{\rm DMSO} < 0\cdot3$, and in fact the variation of free energy in this region is considerably less than that of both the enthalpy and entropy. The results in Table 6 show that there is generally either a very small increase or decrease in this region, apart from benzene which has a relatively large decrease.

A comparison of the behaviour of ethyl acetate in mixtures of water with DMSO, acetonitrile, and dioxan (Figure) shows that the variation of both the enthalpy and entropy is qualitatively the same for all three solvent systems. However the rate of decrease of free energy of transfer of ethyl acetate with increasing organic mole fraction of the solvent is greater in water-rich solvent mixtures for solvents containing both acetonitrile and dioxan than DMSO. Vapour pressure data show that mixtures of water and dioxan and water and acetonitrile [13] show positive deviations from Raoult's law behaviour whereas mixtures of water and dimethyl sulphoxide show large negative deviations and are known to interact strongly with each other.[16] Thus even at low mole fraction, both dioxan and acetonitrile are free to ' solvate ' ethyl acetate whereas solvation by DMSO in water-rich solvent mixtures is hindered by, or requires the disruption of, very stable water–DMSO bonds.

The behaviour of trimethyl phosphate, which shows a relatively large increase in free energy as the DMSO content of the solvent is increased, is consistent with the known stability of phosphate groups in water because of favourable hydrogen bond formation between water and the oxygen atoms of the phosphate group. DMSO is not capable of donating hydrogen bonds and, by accepting hydrogen bonds from water and so lowering the water activity, raises the free energy of the trimethyl phosphate.

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