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SOLUTE-SOLUTE-SOLVENT INTERACTIONS IN DILUTE TERNARY AQUEOUS SOLUTIONS OF UREA AND α,ω-ALIPHATIC DIOLS. EXCESS ENTHALPIES AND GIBBS ENERGIES

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ABSTRACT

The enthalpies of dilution and osmotic coefficients of ternary solutions of urea and α,ω-aliphatic diols in water have been determined at 298 K through microcalorimetric and vapour pressure osmometric measurements, respectively. The experimental virial coefficients of the power expansion series of the excess Gibbs energies and enthalpies have been evaluated and compared with the literature data for similar aqueous systems containing urea and alkanols, ketones and cyclic ethers. The following diols have been considered: propane-diol-1,3; butane-diol-1,4; pentane-diol-1,5. The results are discussed in terms of the hydrophilic and hydrophobic properties of the solutes, and in the light of previous data on the excess thermodynamic properties of binary water-aliphatic diol solutions.

INTRODUCTION

Thermodynamic studies of binary and ternary dilute solutions in water of urea and aliphatic diols are of some biochemical interest because of behaviour of these compounds towards proteins. Polyols, in fact, stabilize protein structure in water [1] and promote micellization [2], whereas monosubstituted alcohols act as protein denaturants, probably by means of intermolecular hydrophobic interactions competitive with the intramolecular ones [3]. Urea, on the other hand, acts as a denaturant through a mechanism not yet completely understood. There is evidence for the direct binding of urea to proteins [4] and at the same time for its chaotropic effect on the ordered macromolecular structures, due to perturbation of water organization by the concentrated urea

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[5].

In this contest, C_3 to C_5 α,ω-diols (x), that is propane-diol-1,3 (1,3-PD), butane-diol-1,4 (1,4-BD) and pentane-diol-1,5 (1,5-PeD), were chosen to test the influence of increasing chain hydrophobicity on the cross interactions with urea (y), account being also taken of previous results on binary water-diol [6,7] and ternary urea-water-monohydric alcohol solutions [8,9].

Our recent reports [7] and those of Barone and coworkers [10] show that α,ω-aliphatic diols, on the basis of the sign and magnitude of the second virial coefficient of their relevant excess thermodynamic functions (see below), may be considered as "hydrophobic structure maker solutes" with $Ts_{xx}>h_{xx}>0$ and $g_{xx}<0$. Only the head of the series, ethane-diol (ED), behaves (like glycerol and higher homologous polyols) as a hydrophilic solute ($g_{xx}>0$). The prevailing hydrophobic behaviour of α,ω-diols may be explained through a model based on the overlapping of the ordered-hydration-cospheres in the self-interactions of solutes [10-12]. Of the aliphatic compounds, this behaviour is typical of monohydric alcohols, too [11,13,14].

As is known, the excess thermodynamic properties of a solution (enthalpy, H^E; Gibbs energy, G^E; etc.) can be conveniently described as a virial expansion in the solute molality, m:

$$H^E = h_2 m^2 + h_3 m^3 + \dots\dots \qquad (1)$$

$$G^E = g_2 m^2 + g_3 m^3 + \dots\dots \qquad (2)$$

where h_2, h_3, g_2, g_3 ....., are the coefficients of interacion between the pair, triplet, etc., like solute molecules, in the case of binary solutions. These interaction coefficients also account for the changes that the solvent molecules undergo.

H^E is also related to the experimental enthalpies of dilution, $\Delta_{dil}H$. In effect:

$$\Delta_{dil}H \{m_i \rightarrow m_f\} = H^E\{m_f\} - (m_f/m_i)\, H^E\{m_i\} \qquad (3)$$

where subscripts i and f refer to the initial and final conditions. The combination of eqns. (1) and (3) gives:

$$\frac{\Delta_{dil}H \{m_i \rightarrow m_f\}}{m_i(m_f - m_i)} = h_2 + h_3 (m_f + m_i) + \dots\dots \qquad (4)$$

From the linear approximation of eqn. (4), valid in sufficiently dilute solutions, h_2 and h_3 can be deduced.

In ternary and more complex solutions, h_2 and h_3 represent particular combinations of self and cross interaction coefficients. In the case of ternary solutions equimolal in the solutes x and y, by indicating with $m_i=(m_{i,x}+m_{i,y})$ and $m_f=(m_{f,x}+m_{f,y})$ the total initial and final solute molalities, h_2 and h_3 embrace all pair and triplet interactions, respectively, and are given by [15]

$$h_2 = (1/4)(h_{xx} + 2h_{xy} + h_{yy}) \tag{5}$$

$$h_3 = (1/8)(h_{xxx} + 3h_{xyy} + 3h_{xxy} + h_{yyy}) \tag{6}$$

As the self-enthalpic interaction coefficients, h_{xx} and h_{yy} for diols [6,7] and urea [13] are known, the cross enthalpic coefficient, h_{xy}, can be obtained by least squares treatment of the experimental data in the linear portion of eqn. (4).

The excess Gibbs energy interaction coefficients in ternary solutions, g_2 and g_3, see eqn. (2), on the other hand, can be related to the osmotic coefficients , Φ, through the relationship [14,16] :

$$\Phi = 1 + (m/RT)(g_2 + 2mg_3 + ...) \tag{7}$$

Here m is again the total solute molality. When the ternary solution contains equimolal amounts of x and y, then

$$g_2 = (1/4)(g_{xx} + 2g_{xy} + g_{yy}) \tag{8}$$

$$g_3 = (1/8)(g_{xxx} + 3g_{xyy} + 3g_{xxy} + g_{yyy}) \tag{9}$$

The cross interaction coefficient, g_{xy}, can be obtained from the experimental Φ data of ternary solutions, if the corresponding self coefficients, g_{xx} [7] and g_{yy} [14,17] are known.

EXPERIMENTAL

The enthalpies of dilution of ternary aqueous solutions, $\Delta_{dil}H$ (J/kg of water in the final solution), determined by means of a LKB 2107 standard flow microcalorimeter at (298.15±0.02) K, are given by [6] :

$$\Delta_{dil}H\,\{(m_x,m_y)_i \rightarrow (m_x,m_y)_f\} = -(dQ/dt)/P_w \tag{10}$$

where dQ/dt is the heat evolved per time unit in steady-state conditions; P_w is the total mass flow rate of water.

A Knauer model 11.00 Vapour Pressure Osmometer (VPO) was used to evaluate Φ [7]. A drop of solution and a drop of solvent are suspended on the tips of two thermistors in a cell at constant temperature ($\pm 1\times10^{-3}$ K) saturated with solvent vapours. The differential solvent mass-transfer between the two drops and the vapour phase gives rise to a steady-state temperature difference, ΔT, which is proportional to the drop in vapour pressure, ΔP. ΔT is measured by a resistance change, ΔR, in the Wheatstone bridge circuit of the instrument. The relationship between ΔR and the solute molality, m, is:

$$\Delta R = k\Phi m \tag{11}$$

where k is the calibration constant.

Dilute solutions of sucrose, whose osmotic coefficients are known from accurate isopiestic measurements within ±0.1% [18], were used as the primary standard. At 298.15 K, k was 2943±5. Urea was used as secondary standard; Φ values calculated from experimental ΔR values measured in dilute urea solutions ($0.1<m<2$), with $k = 2943$ were in agreement to ±0.1% with reliable literature data [19,20].

Diols and urea (Fluka and Aldrich products) were purified according to the literature [6]. Solutions were prepared by weight before each set of measurements. Water was deionized and triply distilled.

RESULTS AND DISCUSSION

The enthalpies of dilution for each system are collected in Table 1. The linear least squares fits of the data in columns 4th and 5th, according to eqn. (4) are also given in a footnote with the standard deviations in brackets.

The pair cross coefficients h_{xy} and their 95% confidence limits (in brackets), as deduced from eqns. (4) and (5), are given in Table 2. Literature data concerning aqueous solutions of other prevailing hydrophobic solutes in the presence of urea are also reported for the sake of comparison.

Mean h_{xy} values calculated according to the empirical combining rule

$$h_{xy,mean} = (1/2)\,(h_{xx} + h_{yy}) \tag{12}$$

TABLE 1

Enthalpies of dilution for ternary aqueous solutions of various aliphatic diols (x) and urea (y) at 298.15 K.

m_i	m_f	$\Delta_{dil}H/m_f$[a]	$\Delta_{dil}H/m_f(m_f-m_i)$[b]	m_f+m_i
		x = 1,3-PD		
0.1936	0.0944	-13.5	136	0.2880
0.2443	0.1189	-17.7	141	0.3632
0.3627	0.1607	-71.1	146	0.4874
0.3500	0.1697	-25.1	139	0.5197
0.3995	0.1934	-30.0	146	0.5929
0.4000	0.1937	-28.7	139	0.5937
0.4308	0.2150	-30.7	142	0.6458
0.4627	0.2266	-32.6	138	0.6893
0.5392	0.2588	-39.1	140	0.7980
0.5792	0.2826	-45.2	152	0.8618
0.6923	0.3364	-52.0	146	1.0287
		x = 1,4-BD		
0.1729	0.0847	-20.9	237	0.2576
0.2009	0.0980	-24.7	240	0.2988
0.2191	0.1067	-26.2	233	0.3258
0.3397	0.1647	-40.6	229	0.5000
0.3663	0.1767	-43.4	229	0.5430
0.4380	0.2116	-52.1	230	0.6496
0.4659	0.2243	-56.4	233	0.6902
0.5804	0.2447	-61.8	234	0.7351
0.6488	0.3107	-76.4	226	0.9595
0.6868	0.3280	-79.7	222	1.0147
0.8048	0.3832	-92.4	219	1.1880
1.1456	0.5389	-131.6	217	1.6845
		x = 1,5-PeD		
0.1518	0.0760	-31.7	419	0.2278
0.2900	0.1426	-61.3	416	0.4326
0.3110	0.1500	-66.7	411	0.6165
0.3999	0.1957	-85.5	419	0.5956
0.4500	0.2198	-93.8	408	0.6698
0.4700	0.2294	-98.0	407	0.6994
0.4968	0.2422	-103.6	407	0.7391
0.5200	0.2533	-106.8	400	0.7733
0.6000	0.2913	-127.7	414	0.8913

[a] J mol^{-1}; [b] J kg mol^{-2}.

Eqn. (4): $\Delta_{dil}H/m_f(m_f-m_i)$ = 136(5)+10(7) (m_f+m_i) for 1,3-PD;
= 239(2)+14(2) (m_f+m_i) for 1,4-BD;
= 423(12)-20(17) (m_f+m_i) for 1,5 PeD.

TABLE 2

Enthalpic pairwise interaction coefficients for some α,ω-aliphatic diols, alcohols and ketones (x) with urea (y) in water at 298.15 K.

System	h_{xy}	h_{yy}	h_{xx}	$h_{xy,mean}$
Urea-1,3-ED	46(7)[a]	-350(11)[a]	362(4)[a]	6(7)
Urea-1,3-PD	185(23)	-350(11)[a]	523(18)[b]	86(15)
Urea-1,4-BD	259(10)	-350(11)[a]	787(4)[b]	218(6)
Urea-1,5-PeD	353(54)	-350(11)[a]	1335(50)[b]	492(26)
Urea-EtOH	319(9)[c]	-351(3)[d]	243(10)[e]	-54(5)
Urea-*n*-PrOH	424(5)[c]	-351(3)[d]	559(14)[e]	104(7)
Urea-*n*-BuOH	476(8)[c]	-351(3)[d]	1003(15)[e]	326(8)
Urea-*t*-BuOH	715[f]	-359[f]	680(4)[f]	161
Urea-DMK	50(8)[d]	-351(3)[d]	770(10)[d]	291(5)
Urea-MEK	121(15)[d]	-351(3)[d]	1188(20)[d]	419(10)
Urea-THF	295(40)[d]	-351(3)[d]	1182(30)[d]	416(15)

Unit: J kg mol^{-2}. In brackets the uncertainities given at 95% confidence limits.
DMK = Dimethylketone; MEK = Methylethylketone; THF=Tetrahydrofurane.
$h_{xy,mean} = (h_{xx}+h_{yy})/2$.
[a] From Ref. 13; [b] From Ref. 7; [c] From Ref. 8; [d] From Ref. 21; [e] From Ref. 11; [f] From Ref. 9.

taken as an estimate of an unperturbed ternary system, are given in Table 2, column 4th. Triplet enthalpic mixed coefficients do not play a significant role in the concentration range explored.

It can be seen that the h_{xy} values in urea-diol systems are intermediate between those of monohydric alcohol, and those of ketones- and cyclic ethers-urea systems.

In Fig.1, h_{xy} coefficients are plotted vs the number of carbon atoms, n_c, in the aliphatic diol chain. The corresponding data for urea-*n*-alkanol systems [8] are also shown. The trend is reasonably parallel to that of the *n*-alkanols-urea system, with a shift in the negative of about 230 J Kg mol^{-2}, due to the higher OH/CH_2 ratio in the diol molecule. In both cases, h_{xy} becomes more positive with increasing hydrocarbon length, with a contribution, per added CH_2 group, of about 30 J kg mol^{-2}, in agreement with the values reported for the enthalpic urea-CH_2 group contribution [22].

Preliminary data on the osmotic coefficient, Φ, for the three systems, evaluated according to eqn. (11), Table 3, were fitted to the following polynomial expansion in the total solute molality, m

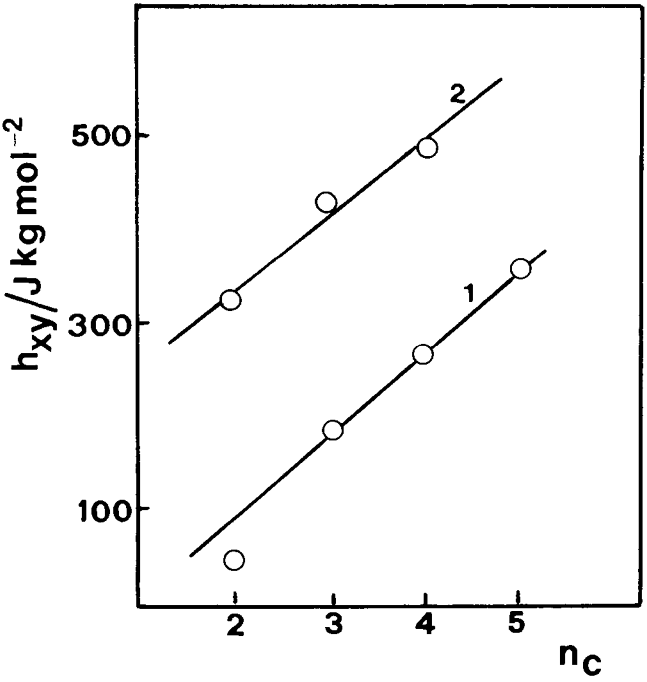

Fig.1. Enthalpic pairwise interaction coefficients, h_{xy}, for alcohols and urea vs. the number of carbon atoms n_c. Line 1: aliphatic diols, present work; Line 2: *n*-alkanols [8].

$$\Phi_{(298\ K,\ m)} = 1 + a_1\, m + a_2\, m^2 + ... \qquad (13)$$

where $a_1 = g_2/RT$ and $a_2 = 2g_3/RT$, see eqn. (7).

The a_1 coefficients for the three systems are set out in Table 3 (footnote), with their standard deviations in brackets. The mixed pair g_{xy} coefficients derived from the data of Table 3 through eqns. (7) and (8) are shown in Table 4 along with their 95% confidence limits.

Gibbs energy pairwise self interaction coefficients for urea and diols are also included together with g_{xy} mean values calculated according to an empirical combination rule, similar to eqn. (12). Due to the limited range of the total molality explored, triplet mixed interaction coefficients could not be evidenced.

Fig. 2 shows the dependence of the experimental g_{xy} coefficients on the number of carbon atoms, n_c, in the diol molecule (line 1). The trend of the mean values, $g_{xy,\,mean}$, is also reported for the sake of comparison (line 2).

Fig. 2 shows that g_{xy} decreases by about 175 J kg mol^{-2} per added CH_2 group in the diol molecule, i.e. about twice the value predicted from the trend

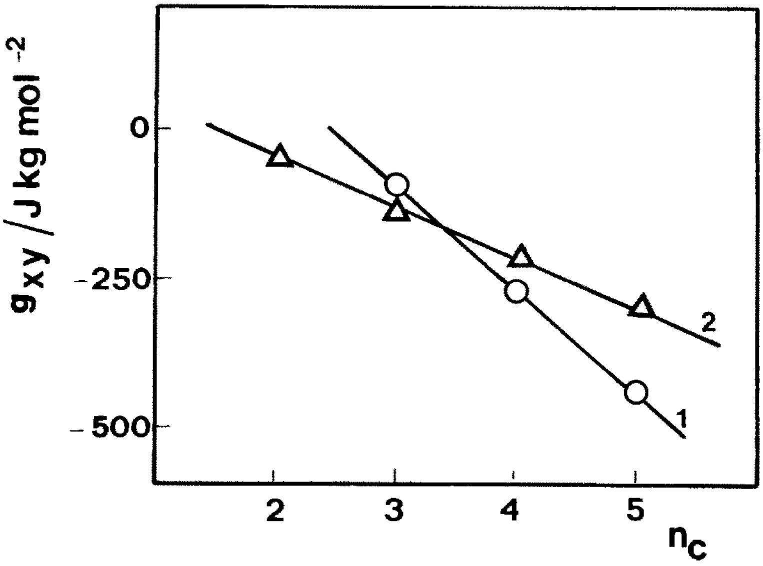

Fig. 2. Gibbs energy pairwise interaction coefficients, g_{xy}, between urea and α,ω-aliphatic diols vs. the number of carbon atoms n_C. Line 1: experimental data; line 2: mean values.

TABLE 3

Osmotic coefficients Φ for ternary aqueous solutions of various α,ω-aliphatic diols (x) and urea (y) at 298.15 K.

m	Φ	m	Φ	m	Φ
x = 1,3-PD		x = 1,4-BD		x = 1,5-PeD	
0.1499	0.992	0.0935	0.989	0.1102	0.989
0.1936	0.978	0.1729	0.980	0.2105	0.974
0.2442	0.974	0.2009	0.978	0.3999	0.953
0.3000	0.983	0.2191	0.974	0.4821	0.937
0.3266	0.998	0.2500	0.972	0.5875	0.914
0.3500	0.989	0.3000	0.971	0.7858	0.894
0.3634	0.989	0.3397	0.970	0.8173	0.884
0.3983	0.971	0.4659	0.957	0.8576	0.881
0.4625	0.975	0.4665	0.954	0.9516	0.864
0.5391	0.963	0.5000	0.945	1.1816	0.837
0.5972	0.978	0.5148	0.950		
0.6923	0.969	0.6000	0.941		
0.7051	0.966	0.6500	0.936		
0.8000	0.959	0.6848	0.931		
0.9652	0.952	0.6952	0.934		
1.0898	0.943	1.1456	0.890		

a_1 values of eqn. (13) in kg mol^{-1}: -0.045(7) for 1,3-PD; -0.095(3) for 1,4-BD; -0.146(4) for 1,5-PeD.

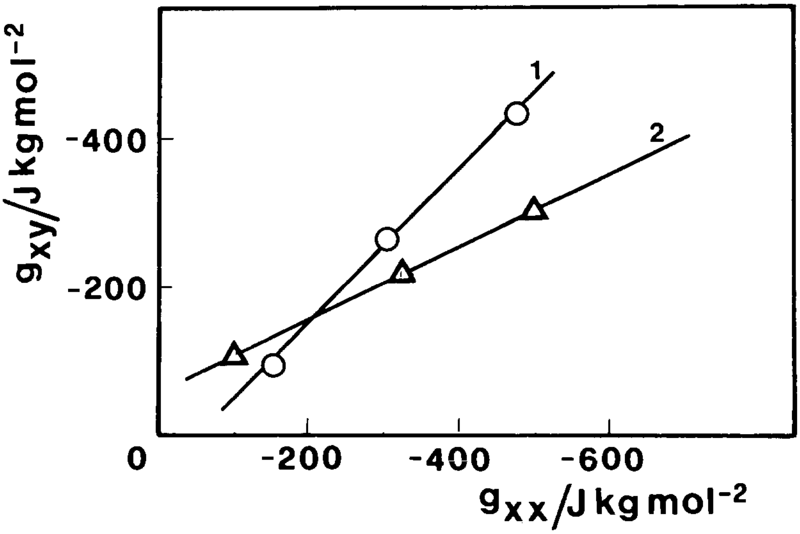

Fig. 3. Line 1: experimental g_{xy} values between α,ω-aliphatic diols and urea vs. the self interaction coefficients of diols, g_{xx}. Line 2: $g_{xy,mean}$ vs g_{xx}.

TABLE 4

Gibbs energy pairwise interaction parameter values for urea (y) and α,ω-diols (x) at 298.15 K.

System	g_{xy}	g_{yy}	g_{xx}	$g_{xy,mean}$	Ts_{xy}
Urea - 1,2-ED	-	-106[a]	11(7)[b]	-47	-
Urea - 1,3-PD	-94(35)	-106[a]	-155(8)[b]	-130(10)	279(42)
Urea - 1,4-BD	-262(20)	-106[a]	-311(21)[b]	-208(20)	521(30)
Urea - 1,5-PeD	-432(35)	-106[a]	-478(28)[b]	-292(30)	785(68)

Unit: J kg mol^{-1}. In brackets the uncertainities given at 95% confidence limits.
$g_{xy,mean} = (g_{xx} + g_{yy})/2$.
[a] From Ref. 17; [b] From Ref. 7.

of the mean values.

As the latter are those expected from an "ideal" mixing of two real solutes, the difference $g_{xy,exp} - g_{xy,mean}$ is a measure of the new perturbations as opposed in the ternary in respect to binary aqueous solutions. The negative value of this difference, as well as that of the overall experimental g_{xy} data, are

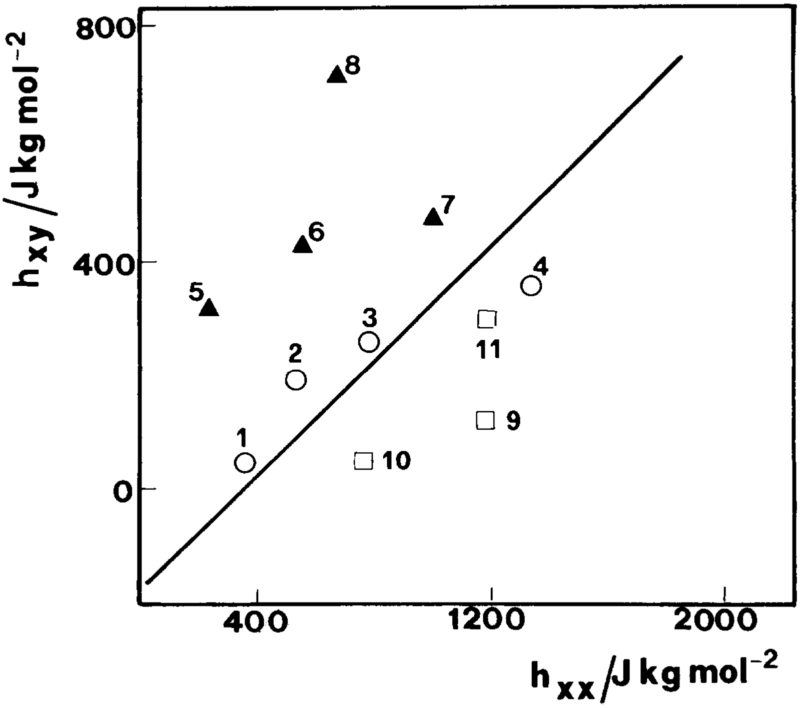

Fig. 4. Experimental h_{xy} coefficients between urea and various aliphatic compounds vs h_{xx}. 1: 1,2-ED; 2: 1,3-PD; 3: 1,4-BD; 4: 1,5-PeD [this work]; 5: EtOH; 6: PrOH; 7: *n*-BuOH; 8: *t*-BuOH [8,9]; 9: MEK; 10: DMK; 11: THF [21]. Line: $h_{xy,mean}$ vs h_{xx} (see Table 1).

mainly due to the positive increasing values of entropic contributions (Table 4, last column), defined as:

$$Ts_{xy} = h_{xy} - g_{xy} \tag{14}$$

The first important conclusion to be drawn is that this fact makes any model based on a direct urea-diol interaction, not involving the solvent at all due, for instance, to intermolecular H-bonding, unreal. The favourable urea-diol interactions seem more due to other water-mediated effects, as already proposed for urea-alkanols [8]: i) the desordering effect of urea and its cosphere on the weaker hydrophobic cospheres of the alkyl chains of diols; or ii) the enhancement of diol-diol hydrophobic interactions, again involving the alkyl chain cospheres. These two mechanisms are not in contrast each other. Both require the release of water molecules from the ordered cospheres to the bulk water.

In Figs. 3 and 4, the experimental g_{xy} and h_{xy} values are plotted against g_{xx} and h_{xx}. These plots compare the effectiveness of the urea-diol interaction with that of the diol-diol interaction in water in the light of the hypothesis set out above, assuming the lines of the mean values as an unperturbed reference system.

Fig. 3, indeed, suggests that the cosphere of diols are more destabilized the more hydrophobic the solute. This behaviour cannot be deduced from Fig. 4, which shows a generally opposite trend for the enthalpic contributions. The larger entropic contributions are responsible for the reversing of the trend (Table 4). This leads to a second important conclusion: the present results provide a strong case for the exercise of caution in interpreting the enthalpies in the absence of free-energy data. The subtle enthalpy-entropy balance involves compensation effects that cannot be easily predicted, and fallacious conclusions can be drawn.

However Fig. 4 by itself is reach in suggestions, as it shows the strict analogy between the enthalpic behaviour of all the known systems: in particular the quite similar values of the THF-urea and 1,5-PeD-urea systems and the curves characterizing the trends of the *n*-alkanols and diol families.

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REFERENCES

1 G. Di Paola and B. Belleau, Can. J. Chem., 55 (1977) 3825-3830.
2 L.G. Ionescu and D.S. Fung, J. Chem. Soc. Faraday Trans. I, 77 (1981) 2907-2912.
3 P.H. Van Hippel and K.Y. Wong, J. Biol. Chem., 240 (1965) 3909-3923.
4 M. Bloemendal and G. Somsen, J. Am. Chem. Soc., 107 (1985) 3426-3434.
5 F. Franks and D. Eagland, Crit. Rev. Biochem., 3 (1975) 165-174.
6 G. Borghesani, R. Pedriali, F. Pulidori and I. Scaroni, J. Solution Chem., 15 (1986) 397-408.
7 G. Borghesani, R. Pedriali and F. Pulidori, J. Solution Chem., in press.
8 G. Barone, G. Castronuovo and V. Elia, Adv. Mol. Relax. Inter. Processes, 23 (1982) 279-286.
9 J.E. Desnoyers, G. Perron, L. Avedikian and J.P. Morel, J. Solution Chem., 6 (1976) 631-644.

10 G. Barone, P. Cacace, G. Castronuovo and V. Elia, J. Chem. Soc. Faraday Trans. I, 77 (1981) 1569-1577.
11 F. Franks, M. Pedley and D.S. Reid, J. Chem. Soc. Faraday Trans. I, 72 (1976) 359-367.
12 H.L. Friedman and C.V. Krishnan, J. Solution Chem., 2 (1973) 119-128.
13 J.J. Savage and R.H. Wood, J. Solution Chem., 5 (1976) 733-750.
14 B.J. Okamoto, R.H. Wood and P.T. Thompson, J. Chem. Soc. Faraday Trans. I, 74 (1978) 1990-2007.
15 M. Blackburn, T.H. Lilley and E. Walmsley, J. Chem. Soc. Faraday Trans. I, 76 (1980) 915-922.
16 M. Blackburn, T.H. Lilley and E. Walmsley, J. Chem. Soc. Faraday Trans. I, 78 (1982) 1641-1665.
17 F. Franks and M.D. Pedley, J. Chem. Soc. Faraday Trans. I, 77 (1981) 1341-1349.
18 R.A. Robinson and R.H. Stokes, J. Phys. Chem., 65 (1961) 1954-1958.
19 G. Scatchard, W.J. Hamer and S.E. Wood, J. Am. Chem. Soc., 60 (1938) 3061-3070.
20 H.D. Ellerton and P.J. Dunlop, J. Phys. Chem., 70 (1966) 1831-1837.
21 G. Barone, V. Elia and E. Rizzo, J. Solution Chem., 11 (1982) 687-698.
22 V. Abate, G. Barone, G. Castronuovo, V. Elia and V. Savino, J. Chem. Soc. Faraday Trans. I, 80 (1984) 759-768.