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EXCESS THERMODYNAMIC PROPERTIES OF *myo*-INOSITOL AND POLYHYDRIC ALCOHOLS IN WATER AT 25°

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ABSTRACT

The excess thermodynamic properties of aqueous solutions of *myo*-inositol have been determined at 25° and differ remarkably from those of pyranosides. New excess-enthalpy data for aqueous solutions of *myo*-inositol and acyclic polyhydric alcohols are treated by a group-contribution approach that reveals subtle, but probably significant, differences in the parameters characterising the same functional groups in both sugars and polyhydric alcohols.

INTRODUCTION

The excess thermodynamic properties at 25° of some polyhydric alcohols in water have been reported[1–4]. The limiting properties depend on solute–solvent interactions, whereas excess properties depend on solute–solute interactions and on the changes in solute–solvent and solvent–solvent interactions as the concentration is varied. For solutions of simple non-electrolytes in water, none of these interactions prevails and controversy has arisen about the interpretation of the data. We have hypothesised that the behaviour of polyhydric alcohols in aqueous solution is very different from that of monofunctional alcohols, which are mainly hydrophobic solutes[5]. Preliminary data[1,2,6–8] suggested that polyhydric alcohols can be compared with hydrophilic monosaccharides. On the other hand, polyhydric alcohol molecules are simpler than those of sugars, since they lack the hemiacetal group and show less-complex conformational equilibria. However, examination of the excess enthalpies of the polyhydric alcohols shows that they differ appreciably from those of the sugars[3], and that only the first terms of the series are comparable. As molecular weight increases, the behaviour of polyhydric alcohols changes drastically.

We now show that this is also true for *myo*-inositol which, in spite of the structural analogy with the pyranosides, has a completely different behaviour. These conclusions arise from the excess free energies, enthalpies, and entropies of aqueous solutions of *myo*-inositol, whereas the limiting properties do not reveal these differences[9,10]. We report also the excess enthalpies of some ternary aqueous solutions of isomeric polyhydric alcohols. The properties of the corresponding bi-

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nary solutions differ remarkably if the solutes are not enantiomers. However, the excess enthalpies of the ternary solutions can be evaluated as combinations of the properties of the two binary solutions[11]. This excludes the occurrence of new interactions in the ternary solutions. Since enthalpic data are more numerous than those for other thermodynamic properties, another approach, namely, the group-contribution method can be used[1-2]. This approach is based on the application of the additivity principle at a molecular level, and allows predictions to be made concerning unknown binary and ternary solutions. Given the limits of the approach, it is not possible to distinguish the behaviour of *myo*-inositol from that of the acyclic polyhydric alcohols. *myo*-Inositol, then, can be classified as a different, or as an extreme, case among the members of this family of solutes. However, the group-contribution approach shows subtle but significant differences between the enthalpic behaviour in water of the same functional groups in the polyhydric alcohols and in the saccharides.

EXPERIMENTAL

Materials. — *myo*-Inositol, D-mannitol, galactitol, and D- and L-arabinitol were recrystallised from 1:1 ethanol–water[3], and solutions were freshly prepared by weight, using doubly distilled and degassed water, and protected from bacterial contamination.

Isopiestic gravimetric measurements were performed at 25 ±0.02° by a known precedure[12-14]. Osmotic coefficients were obtained from the known molalities and isopiestic osmotic coefficients of the KCl reference solutions:

$$\phi = 2\phi_{KCl} m_{KCl}/m, \qquad (1)$$

where m is the mean molality of three or four sample solutions at the end of each equilibrium experiment. The data of Stokes and Robinson[15] were used for KCl. The enthalpies of dilution of the binary and ternary solutions were determined[16] using an LKB 10700-1 flow microcalorimeter at 25 ±0.02°. The values of the heats of dilution ΔH^{dil} for binary solutions from the initial (m_i) to the final molality (m) were obtained from the total mass flow-rate of water, P_w, and the normalised heat-flux, dQ/dt, using Eq. 2.

$$\Delta H^{dil}\,[(m_i \rightarrow m)] = -\,(dQ/dt)/P_w \qquad (2)$$

Repeated electrical calibrations were carried out for each set of runs. In an analogous manner, the heats of dilution for the ternary aqueous solutions, from the initial (m_{xi} and m_{yi}) to the final aquo-molalities (m_x and m_y), were obtained from Eq. 3.

$$\Delta H^{dil}\,[(m_{xi}), (m_{yi}) \rightarrow (m_x, m_y)] = -\,(dQ/dt)/P_w \qquad (3)$$

The ΔH^{dil} values are expressed in $J.kg^{-1}$ of water in the final solutions

THERMODYNAMICS

The excess thermodynamic properties, at constant temperature and pressure, of a binary solution of a non-electrolyte x in the solvent w can be expressed by virial expansions[4–6] as a function of the molality[5,16–19]:

$$G^{E}(\mathrm{m}) = g_{xx}\mathrm{m}^{2} + g_{xxx}\mathrm{m}^{3} + \cdots, \tag{4}$$

$$H^{E}(\mathrm{m}) = h_{xx}\mathrm{m}^{2} + h_{xxx}\mathrm{m}^{3} + \cdots, \tag{5}$$

$$\mathrm{T}S^{E}(\mathrm{m}) = \mathrm{T}s_{xx}\mathrm{m}^{2} + \mathrm{T}s_{xxx}\mathrm{m}^{3} + \cdots, \tag{6}$$

where G^{E}, H^{E}, and $\mathrm{T}S^{E}$ are the excess free energy, enthalpy, and entropy, respectively.

The coefficients of Eqs. *4* and *5* were obtained by interpolation of the experimental osmotic coefficients[14] and heats of dilution[5,16–20], respectively.

The excess properties for ternary solutions are defined similarly to those for the binary solutions[5,18,21]. The virial expansion for the enthalpy is

$$\begin{aligned} H^{E}(\mathrm{m}_x, \mathrm{m}_y) = h_{xx}\mathrm{m}_x^2 + 2h_{xy}\mathrm{m}_x\mathrm{m}_y + h_{yy}\mathrm{m}_y^2 + h_{xxx}\mathrm{m}_x^3 + \\ + 3h_{xxy}\mathrm{m}_x^2\mathrm{m}_y + 3h_{xyy}\mathrm{m}_x\mathrm{m}_y^2 + h_{yyy}\mathrm{m}_y^3 + \cdots \end{aligned} \tag{7}$$

To evaluate $H^{E}(\mathrm{m}_x, \mathrm{m}_y)$ and the polynomial coefficients of Eq. *7*, the heats of dilution of the binary solutions were determined, or calculated through the values of h_{xx}, h_{yy}, *etc.*, where known. The heats of mixing of two binary solutions can then be measured. In this instance, an auxiliary function ΔH^{**} can be introduced, as defined[21] in Eq. *8*.

$$\begin{aligned} \Delta H^{**} = \Delta H^{\mathrm{dil}}\,[(\mathrm{m}_{xi}), (\mathrm{m}_{yi}) \rightarrow (\mathrm{m}_x, \mathrm{m}_y)] - \Delta H^{\mathrm{dil}}\,(\mathrm{m}_{xi} \rightarrow \mathrm{m}_x) \\ - \Delta H^{\mathrm{dil}}\,(\mathrm{m}_{yi} \rightarrow \mathrm{m}_y) \end{aligned} \tag{8}$$

It is possible to show[21] that

$$\begin{aligned} \Delta H^{**} = 2h_{xy}\mathrm{m}_y(\mathrm{m}_x - \mathrm{m}_{xi}) + 3h_{xxy}\mathrm{m}_y(\mathrm{m}_x^2 - \mathrm{m}_{xi}^2) \\ + 3h_{xyy}\mathrm{m}_y(\mathrm{m}_x - \mathrm{m}_{xi})(\mathrm{m}_y + \mathrm{m}_{yi}) + \cdots \end{aligned} \tag{9}$$

By changing the x and y indices, a symmetrical expression is obtained. The ΔH^{**} values, calculated using Eq. *8*, are interpolated according to Eq. *9*, giving the values of the cross coefficients.

RESULTS AND DISCUSSION

Aqueous solutions of myo-*inositol.* — Table I contains the experimental osmotic coefficients, the molalities of the relative solutions, and the data for the reference solutions at isopiestic equilibrium. The heats of dilution, as a function of the initial and final molalities, are given in Table II. The coefficients obtained are reported in Table III together with their 95% confidence limits. The interpolating polynomials of highest degree, the coefficients of which still exceed their own 95% confidence limits, were chosen. The reported values of h_{xx} and h_{xxx} are in good agreement with those found independently by Tasker and Wood[4] [-818 ± 17 and 205 ± 25 J.mol^{-1} (mol.kg^{-1})$^{-1}$, respectively]. On the other hand, we have shown[3] that the known h_{xx} values for the acyclic polyhydric alcohols vary from +362 for ethylene glycol to −299 for perseitol (D-*glycero*-D-*galacto*-heptitol). The enthalpic data indicate that *myo*-inositol is an extreme case among the polyhydric alcohols, but that its behaviour is partially similar to that of other more-flexible hexaols and heptaols. All of the polyhydric alcohols are characterised by a negative contribution to h_{xx}, which becomes increasingly important as the molecular weight increases and also depends on the stereochemistry and on the separation of hydrophilic and hydrophobic domains on the solute molecules[3,4]. In fact, D-glucitol, galactitol, and perseitol (as does *myo*-inositol) show negative values for h_{xx}, whereas D-mannitol behaves in the same way as the homologues of lower molecular weight[3].

TABLE I

OSMOTIC COEFFICIENTS FOR *myo*-INOSITOL IN WATER AT 25°

m_{KCl}	ϕ_{KCl}	m_{myo}	ϕ_{myo}
0.3375	0.9045	0.6378	0.9571
0.3699	0.9029	0.7054	0.9469
0.4172	0.9011	0.7948	0.9460
0.4646	0.8996	0.8845	0.9451
0.4982	0.8989	0.9511	0.9417
0.5154	0.8986	0.9772	0.9479
0.5194	0.8986	0.9897	0.9432

TABLE II

HEATS OF DILUTION OF BINARY AQUEOUS SOLUTIONS OF *myo*-INOSITOL AT 25°

m_i	m	$(1/m_i)\Delta H^{dil}$ (J mol^{-1})
0.1011	0.0540	44.4
0.3153	0.1689	106.3
0.3994	0.2070	132.7
0.5155	0.2659	161.9
0.6087	0.3127	184.4
0.6688	0.3426	197.5
0.5013	0.1667	220.5
0.8541	0.4332	235.9
0.6293	0.2244	262.8
0.7015	0.2490	282.9
0.7939	0.2813	303.3
0.9071	0.3171	339.4

TABLE III

COEFFICIENTS[a] OF THE EXCESS FREE ENERGY, ENTHALPY, AND ENTROPY FOR AQUEOUS SOLUTIONS OF *myo*-INOSITOL AT 25°

g_{xx}[b]	h_{xx}[b]	Ts_{xx}[b]
−260 (55)	−800 (29)	−540
g_{xxx}[c]	h_{xxx}[c]	Ts_{xxx}[c]
120 (61)	188 (28)	68

[a] The numbers in parentheses are the 95% confidence limits. [b] Units. $J.mol^{-1}$ $(mol.kg^{-1})^{-1}$. [c] Units: $J.mol^{-1}$ $(mol.kg^{-1})^{-2}$.

The negative values of the excess free energies and entropies (determined by the second coefficients, in the explored range of molalities) amplify the large differences between the aqueous solutions of *myo*-inositol and those of the monosaccharides[16]. Such differences suggest that different kinds of molecular interaction rule the behaviour of these solutions. The negative value of g_{xx} [and the enthalpic and entropic contributions (h_{xx} and Ts_{xx})] can be explained by two different processes, namely, formation of water-mediated pairs of solute and (analogous to the explanation proposed for urea[21–24]) coalescence of "distorted" hydration cospheres with relaxation of water to the bulk, which is less rich in enthalpy and entropy. The first hypothesis is based on the fact that, in the McMillan–Mayer theory[5,14,16,19,25,26], g_{xx} is not only a measure of the interaction of pairs of solute particles, but includes, implicitly, the variations of the solute–solvent and solvent–solvent interactions occurring in the concentration process[5,14]. The formation of "contact pair" interactions cannot be excluded *a priori*, but the small value of the second coefficient and the strong solute–solute interactions[9,10] make this occurrence unlikely. In changing from monosaccharides (a maximum of four equatorial hydroxyl groups for β-D-xylopyranose and β-D-glucopyranose) to *myo*-inositol (five equatorial hydroxyl groups[27]), the possibility of interactions among solute molecules in water seems to increase remarkably, in spite of the increasing strength of the solute–solvent interactions (comparable to an ionic hydration, as suggested by the limiting compressibility[9,10]). For *scyllo*-inositol, the presence of six equatorial hydroxyl groups makes it easier to assemble the molecules into the crystal and to establish a network of hydrogen bonds. This could explain the very poor solubility of *scyllo*-inositol[4]. However, the poor solubility cannot be assumed to be an indication of the formation of a contact pair, because of the different, highly cooperative, nature of the crystallisation process.

The other cited process, namely, the coalescence of the "distorted" hydration cospheres, which is favoured for acyclic polyhydric alcohols, seems to be less probable, the similarities of the properties of *myo*-inositol with those of the acyclic homologues being fortuitous. The hypothesis of water-mediated pairs must be tested further. Even this interaction probably has some steric requirements. A more complex explanation would involve the first and second hydration shells, in order to ascertain the total number of water molecules perturbed, their energy states, and their preferential reciprocal orientations. This would explain how, for *myo*-inositol, relatively strong hydration can dynamically aid the solute–solute, water-mediated interactions ("water-enhanced pairing"[4]) and how, for pyranosides, weaker hydration can prevent the same process.

The differences in the behaviour of the functional groups in polyhydric alcohols and monosaccharides: the group-contribution approach. — In Tables IV and V, the heats of dilution of ternary aqueous solutions of D-mannitol, galactitol, and D- and L-arabinitol are reported, together with the ΔH^E values, the literature values of h_{xx} and h_{yy}, and the h_{xy} values with the 95% confidence limits found in the present study. It can be seen that, within experimental error, the solutions of enentiomers have almost equal values for the h coefficients. The solutions of the polyhydric alcohols examined have values of h_{xy} intermediate between those of the pairwise interaction coefficients h_{xx} and h_{yy}. This situation was also found for solutions containing a polyhydric alcohol and cyclohexanol[4]. These results indicate that no other particular interaction occurs in the ternary solutions with respect to the binary ones[11,21]. Then, apart from the process that determines the values observed, the excess enthalpies of the alcohols, polyhydric alcohols, and cyclitols can be used to evaluate, for instance, the mean contributions of the functional groups to the second coefficients h_{xx}, h_{xy}.

The additivity principle is often used in chemical thermodynamics for separating the contributions of groups of atoms, arbitrarily chosen, to the molecular properties. When applied to solution properties, the theoretical basis of this principle is not well established. However, for the limiting properties in solution (as well as for pure substances), a simple sum or a linear combination over all the groups is sufficient[28]. Using the McMillan–Mayer approach, Wood and his col-

TABLE IV

HEATS OF DILUTION OF TERNARY AQUEOUS SOLUTIONS OF D-ARABINITOL (D) AND L-ARABINITOL (L) AT 25°[a]

m_{Di}	m_{Df}	m_{Li}	m_{Lf}	ΔH^{dil} ($J\ kg^{-1}$)	ΔH^E ($J\ kg^{-1}$)
0.3370	0.1603	0.3039	0.1445	-18.9	-9.4
0.1792	0.0849	0.5225	0.2477	-23.9	-9.8
0.3119	0.1475	0.4423	0.2091	26.7	-13.1
0.3314	0.1562	0.4699	0.2215	-31.2	-15.9
0.3501	0.1649	0.4964	0.2339	-34.7	-17.7
0.2996	0.1388	0.8732	0.4047	-65.5	-26.3
0.5768	0.2608	0.5202	0.2417	-54.9	27.0
0.3194	0.1474	0.9311	0.4297	-73.4	-28.8
0.3381	0.1558	0.9847	0.4537	-83.0	-33.1
0.6143	0.2846	0.5540	0.2567	-65.0	-33.3
0.6506	0.3009	0.5868	0.2714	-72.0	-36.5

[a] h_{DL} 195(4), h_{DD} 187(3)[3], h_{LL} 185(3)[3]

TABLE V

HEATS OF DILUTION OF TERNARY AQUEOUS SOLUTIONS OF MANNITOL (M) AND GALACTITOL (G) AT 25°

m_{M_i}	m_M	m_{G_i}	m_G	ΔH^{dil} $(J.kg^{-1})$	ΔH^{**} $(J.kg^{-1})$
0.5866	0.2750	0.2102	0.0985	−8.8	−2.3
0.6287	0.2941	0.2253	0.1054	−10.9	−3.3
0.6765	0.3154	0.2425	0.1131	−13.1	−4.1
0.7648	0.3541	0.2741	0.1269	−16.5	−4.5
0.7168	0.3330	0.2569	0.1193	−15.0	−4.7
0.8102	0.3753	0.2904	0.1345	−19.7	−5.9

[a] h_{MG} 47.5(4), h_{MM} 66(12)[3], h_{GG} −132(50)[3]

leagues obtained an expression for the second virial coefficients of the excess enthalpy[1] and free energy[2]. The h_{xy} coefficients, for instance, are given by the sum of all the contributions $\{H_{kl}\}$ obtained by coupling each group k of the solute molecule x with each group l of the solute molecule y (of the same or different species), as in Eq. *10*.

$$h_{xy} = \sum_{kl} n_k^x n_l^y \{H_{kl}\}, \tag{10}$$

where n_k^x and n_l^y are the numbers of identical groups of atoms on each molecule. This sum is a formal procedure. As for the h_{xy} coefficients, the values of the $\{H_{kl}\}$ contributions can also be due to very different mechanisms. In the discussion, the expression "group interaction" indicates that the interaction can be solvent-mediated, or due exclusively to changes in the state of the solvent in the hydration cospheres, *etc.* Moreover, the arbitrary choice of the groups and the formal separation leads to unknown contributions, due to the nearest-neighbour interactions, to each $\{H_{kl}\}$ value. The discussion on the physical meaning of the $\{H_{kl}\}$ values then requires care, as exemplified in the following.

In a preceding paper[3], this method was applied to monohydric and polyhydric alcohols using -CHOH and -CH_2- as representative groups (which generates three possible contributions $\{H_{kl}\}$). According to Wood and his colleagues, the relationships CH ≡ 0.5 CH_2 and CH_3 ≡ 1.5 CH_2 were assumed, but tetrasubstituted carbons were not considered. We have sought to refine the group contributions by considering our data and also those of Tasker and Wood[4], and to compare these group contributions with those obtained for saccharides and their derivatives[29,30]. The preferred representative groups are pure hydrophobic (-CH_2-) and pure hydrophilic (-OH); the contributions due to the CHOH–CHOH and CHOH–CH_2 interactions can be obtained by an appropriate linear combination[31] of the contributions CH_2–OH, OH–OH, and CH_2–CH_2.

In Table VI, the values of h_{xy} used to evaluate the $\{H_{kl}\}$ contributions (by interpolation of Eq. *10*) are given, together with the numbers of each functional

TABLE VI

VALUES OF THE COEFFICIENTS OF THE EXCESS ENTHALPIES USED TO DERIVE $\{H_{\mathrm{KI}}\}$

Solute (x)	$n_{CH}^{x\,a}$	$n_{OH}^{x\,a}$	$h_{xx}^{exp\,b}$	$h_{xx}^{calc\,b}$
MeOH	1.5	1	247[c]	113
EtOH	2.5	1	243[c]	317
^{n}PrOH	3.5	1	559[c]	597
^{i}PrOH	3.5	1	330[c]	597
^{n}BuOH	4.5	1	1003[d]	952
^{s}BuOH	4.5	1	916[e]	952
^{i}BuOH	4.5	1	1008[e]	952
^{t}BuOH	4.5	1	656[e]	952
^{t}PnOH	5.5	1	1758	1382
Cyclohexanol	5.5	1	1405	1382
Ethylene glycol	2	2	362[c]	156
Glycerol	2.5	3	251[e]	166
Erythritol	3	4	358[g]	144
Pentaerythritol	4	4	395[g]	623
Ribitol	3.5	5	198	89
D-Arabinitol	3.5	5	187[f]	89
L-Arabinitol	3.5	5	185[g]	89
Xylitol	3.5	5	88[g]	89
D-Mannitol	4	6	66[g]	2
D-Glucitol	4	6	11	2
Galactitol	4	6	−132	2
Perseitol	4.5	7	299[g]	118
myo-Inositol	3	6	800	−655

Solutes x	y	$n_{CH}^{x\,a}$	$n_{CH}^{y\,a}$	$n_{OH}^{x\,a}$	$n_{OH}^{y\,a}$	$h_{xy}^{exp\,b}$	$h_{xy}^{calc\,b}$
EtOH	^{n}PrOH	2.5	3.5	1	1	372[c]	438
EtOH	^{n}BuOH	2.5	4.5	1	1	464[f]	550
EtOH	^{t}BuOH	2.5	4.5	1	1	368[e]	550
^{n}PrOH	^{n}BuOH	3.5	4.5	1	1	718[f]	755
^{n}PrOH	^{t}BuOH	3.5	4.5	1	1	660[e]	755
^{n}BuOH	^{t}BuOH	4.5	4.5	1	1	903[e]	952
Ethylene glycol	Pentaerythritol	2	4	2	4	131	311
D-Arabinitol	L-Arabinitol	3.5	3.5	5	5	195	89
D-Mannitol	Galactitol	4	4	6	6	[illegible]	2
myo-Inositol	D-Mannitol	3	4	6	6	220[g,h]	−310
Cyclohexanol	D-Mannitol	5.5	4	1	6	1267[g]	1510
Cyclohexanol	*myo*-Inositol	5.5	3	1	6	1487[g,h]	1276

[a] Numbers of CH and OH groups in the molecule [b] J mol^{-1} (mol kg^{-1})$^{-1}$ [c] Ref 1 [d] Ref 5 [e] Ref 8 [f] Ref 4 [g] Ref 3 [h] The h_{xy} values were recalculated, using the h_{xx} values of this work and of ref 3

group on each molecule and the calculated h_{xx} values. Table VII contains the interpolated $\{H_{\mathrm{KI}}\}$ values; the agreement with the values obtained by Tasker and Wood[4], and with those we obtained previously, is good. Even excluding *myo*-inositol from the interpolation, the evaluated contributions do not change remarkably (sixth column of Table VII). In the last two columns are reported the contribu-

TABLE VII

GROUP CONTRIBUTIONS $\{H_{kl}\}$ TO THE EXCESS ENTHALPY COEFFICIENTS FOR OXYGENATED COMPOUNDS IN WATER AT 25°

Groups		$\{H_{kl}\}$ $[J.mol^{-1}\,(mol.kg^{-1})^{-1}]$					
k	*l*	*This work*	*Ref 3*	*Ref. 4*	*Ref. 4*	*Refs 1 and 31*	*Ref 29*
CH_2	CH_2	38(4)[a]	35(6)	40(33)[b]	34(8)[c]	40(8)	43(4)
OH	OH	−53(6)	−59[d]	−53[b,d]	−50[c,d]	−26[d]	−1(8)
CH_2	OH	27(5)	32[d]	26[b,d]	27[c,d]	14[d]	10(8)
O	O	—	—	—	—	−116(102)[e]	−138(27)
OH	O	—	—	—	—	—	−95(10)
CH_2	O	—	—	—	—	71(32)[e]	78(9)
σ		±163	±163	±247		±220 ±155[d]	±149

[a] The numbers in parentheses are the 95% confidence limits. In ref 1, it was assumed that CHO ≡ CHOH; in refs 29 and 31, the disubstituted oxygen was assumed to be equivalent in ethers, sugars, and the carbonyl groups of the ketones. [b] Only D-mannitol, *myo*-inositol, and cyclohexanol included. [c] *myo*-Inositol and some of the polyhydric alcohols reported here and in ref 3 were excluded, because the data are not yet published. [d] Evaluated by linear combination of other coefficients: see text. [e] Ref. 31

tions evaluated from those of Wood and colleagues[1,31] (considering all the known data for aqueous solutions of non-electrolytes[1]) and by us [29] (aqueous solutions of saccharides and derivatives, monohydric alcohols, ketones, and cyclic ethers). Other functional groups have also been considered, namely, peptide[1] and disubstituted oxygen[29,31]. In Table VII, only the contributions involving the latter group are reported. It can be seen that the most important differences concern the $\{H_{OH,OH}\}$ contributions, the values calculated by Wood and co-workers being intermediate, since the few data for polyhydric alcohols were not separated from those for the sugars. From the present data concerning polyhydric alcohols and sugars, a worst interpolation [σ ±220 $J.mol^{-1}\,(mol.kg^{-1})^{-1}$] and systematic deviations of the calculated h_{xx} values are obtained*. It is then assumed that the differences between the $\{H_{OH,OH}\}$ contributions in the two sets of data are significant. The value [$-53 \pm 6\ J.mol^{-1}\,(mol.kg^{-1})^{-1}$] of $\{H_{OH,OH}\}$ for the polyhydric alcohols, compared to that (-1 ± 8) for the sugars, provides support for the hypothesis discussed above. In fact, the group-contribution approach seems to indicate that hydroxyl groups (and their cospheres) are mainly responsible for the differences between sugars and polyhydric alcohols. Moreover, the $\{H_{OH,OH}\}$ value is almost ideal for sugars, suggesting that there are neither contributions to the solute–solute interactions nor concentration-dependent perturbations in the solvent promoted by the presence of pairs of hydroxyl groups. The negative value for $\{H_{OH,OH}\}$ found for the set of solutes including polyhydric alcohols and cyclitols does not contradict the above hypotheses.

**Note added in proof.* The same conclusion can be inferred from one of the interpolations reported in the recent paper of I. R. Tasker and R. H. Wood. *J. Solution Chem.*, 11 (1982) 469–480.

A positive value for $\{H_{CH_2,CH_2}\}$ is expected for hydrophobic interactions[5,17–19,27] and is in substantial agreement with the value found by Wood and co-workers[1,31]. The positive value for $\{H_{OH,CH}\}$ (as well as for $\{H_{O,CH}\}$) is in agreement with the positive values usually found for the overall, second enthalpic coefficients for pairs of co-solutes, one predominantly hydrophobic (monohydric alcohols, ketone, *etc.*) and one predominantly hydrophilic (*e.g.*, urea)[32–34]. Finally, the negative value of $\{H_{O,O}\}$ should be noted, which demonstrates that polar groups, unable to interact directly *via* a H-bond, show a favourable enthalpic contribution to the intermolecular interactions[29–31].

The group-contribution approach is useful for making approximate predictions about the properties of unknown simple systems, but it must be carefully employed when speculations on the mechanism involved are made. In fact, the $\{H_{kl}\}$ values are averages for different steric situations that cannot be distinguished on the basis of limited data. Moreover, the separation into the various contributions can depend on the particular set of systems considered. The nearest-neighbour effects can be significant and attributed, in an uncontrollable manner, to each $\{H_{kl}\}$ by the interpolation procedure. The contribution due to each group interacting with a group in another molecule can depend on the intramolecular perturbation affecting both. The nearest-neighbour effect could occur through inductive effects or through interactions involving the solvent cospheres of the nearest groups. Recently, this aspect has been discussed in detail[4].

It is concluded that the results obtained for these systems, which strongly depend on the stereochemistry of the solutes, are not worse than those concerning the aqueous solutions of other simple organic compounds. Hence, the differences found among the same functional groups on similar classes of substances (*e.g.*, sugars and polyhydric alcohols) can be assumed to be significant, even though averaged for different stereochemical environments.

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