Thermodynamic Studies of Dilute Aqueous Solutions of Cyclic Ethers and Simple Carbohydrates

F. Franks,¹ J. R. Ravenhill,¹ and D. S. Reid¹

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Apparent molal volumes and compressibilities are reported for dilute aqueous solutions of cyclic ethers, simple carbohydrates, and related polyhydroxy compounds. The results for carbohydrates are considered in the light of two theoretical descriptions of such systems, i.e., the semiideal solution approach of Stokes and Robinson, and the McMillan-Mayer theory type of approach as employed by Kozak, Knight, and Kauzmann. It is concluded that neither model is satisfactory, and that for these solutions a specific hydration model, described in more detail in another paper, is more satisfactory.

KEY WORDS: Aqueous; cyclic ethers; carbohydrates; inositols; apparent molal volume; apparent molal compressibility; density.

1. INTRODUCTION

The properties of aqueous solutions of nonelectrolytes pose several interesting problems which so far have received little systematic attention. Most effort in the past has been devoted to ionic solutions, no doubt because an acceptable theory existed against which experimental results could be tested, even though this theory takes no direct account of the solvent other than ascribing to it a bulk permittivity. Of the nonionic solutes most attention has been paid to apolar, or substantially apolar molecules, following the classic work of Frank and Evans⁽¹⁾ which first postulated the effects which solutes seem to exert on water–water interactions. This eventually led to the concepts of structure making and breaking and hydrophobic bonding in aqueous solutions.⁽²⁾

¹ Unilever Research Laboratory Colworth/Welwyn, Colworth House, Sharnbrook, Bedford, England.

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solutions of monofunctional solutes, such as alcohols, amines, and ethers, are now available and have shed some light on the nature of the interactions between water and apolar moieties.⁽³⁾

This is, however, not the case for solutions of solutes possessing several functional groups capable of hydrogen bonding to the solvent. Whereas apolar hydration is probably fairly nonspecific,² hydration effects due to solute-solvent hydrogen bonding would be expected to be highly orientation-dependent and therefore the conformation of the solute molecule might be one of the factors determining such hydration effects. In order to obtain the necessary experimental information, we have studied some physical properties (those which we believe to be most relevant to an understanding of solute-solvent interactions) of dilute aqueous solutions of a series of related polyhydroxy compounds, mainly simple carbohydrates. This communication describes measurements of the thermodynamic properties.

2. METHODOLOGY

The limiting partial molal volumetric properties of solutes in aqueous solution are a useful measure of solute-solvent interactions and, in particular, of solvent "structural" changes. As has been discussed previously⁽⁴⁾ it is difficult to separate the interaction term from the measured limiting partial molal volume \vec{V}^{o} since this operation requires a somewhat arbitrary assessment of the intrinsic volume of the solute molecule. Various attempts have been made to achieve this for ionic solutions, but the uncertainties increase with the complexity of the ion under consideration. Some useful information can, however, be derived from comparisons of \overline{V}^o of series of closely similar molecules, e.g., isomers and anomers. The temperature and pressure derivatives of \vec{V}^o are of more immediate interest, since they will reflect directly changes in hydration behavior, if it is assumed that the solute molecules are incompressible. We have therefore determined densities, expansibilities, and compressibilities of dilute (<0.2 mole-kg⁻¹) solutions of tetrahydrofuran (THF) and tetrahydropyran (THP) derivatives, sugars, sugar esters, and some other related polyhydroxy derivatives.

3. EXPERIMENTAL

3.1. Materials

THF, THP, tetrahydrofurfuryl alcohol (THFA), tetrahydropyran-2carbinol (THPA), and 1,4-dioxane (DI) were purified as previously described.⁽⁴⁾ Glucose, galactose, mannose and ribose, mannitol, sorbitol, and

² For example, the molecular geometry of clathrates is dependent solely on the size of the apolar residue, and not its detailed molecular conformation.

 α - and β -methyl-D-glucosides were obtained from Sigma and checked for purity by gas-liquid chromatography.

 α -Methyl-D-galactopyranoside was prepared according to the method of Frahn and Mills.⁽⁵⁾ The β -anomer was prepared by allowing D-galactose to react with a methanolic solution of trimethyl orthoformate in the presence of BF₃. The ester was purified and recrystallized from ethanol (mp 177°C) and its purity checked by T.L.C. Scyllo-inositol was prepared from scyllo-meso-inosose by treating its sodium diborate complex with HCl⁽⁶⁾ and recrystallizing the reaction product (mp 355°C). Water was purified by a method previously described.⁽⁷⁾

3.2. Volumetry

Density determinations were performed using a magnetic-float technique previously described⁽⁸⁾ and capable of precisions higher than one part in 10⁶ required for the meaningful extrapolation of data in the evaluation of \vec{V}^{o} .

3.3. Acoustic Interferometry

The simplest accurate determination of the compressibility of liquids is based on the Laplace equation and involves measurements of the velocity of sound in the liquid.

The ultrasonic interferometer method is a simple and yet accurate method for measuring the velocity of sound in a liquid. A relatively simple system yields reasonable reproducibility, i.e., $\pm 0.015\%$, and since the apparent molal compressibility is obtained by a difference method, useful results can be achieved.

The interferometer system used for these experiments⁽⁹⁾ was fitted with an Archimedian screw stirring attachment similar to that used in the magnetic-float densimeter.⁽⁸⁾ This attachment enabled aliquots of concentrated solution to be rapidly mixed with the solution in the interferometer, thus reducing the interval between separate determinations to approx. 2 h.

The apparatus was constructed from a high grade of stainless steel, with polished internal surfaces. The position of the polished reflector plate was adjusted by means of a micrometer (periodic error $\pm 0.03 \times 10^{-4}$ cm). A 2.54-cm-diameter quartz crystal was mounted in the bottom section of the interferometer, and was continuously driven by a crystal-controlled 4 MHz sine-wave generator. The standing wave node positions were detected by a simple voltage comparator. Provision was made for the generation of pulsed sine waves which could be propagated through the sample. The reflected waves could then be examined on an oscilloscope for asymmetry, and the reflector and crystal surfaces adjusted until the surfaces were accurately parallel, thus minimizing asymmetry and diffraction errors.

The apparatus provided the halfwave lengths of the sound wave in the liquid, and from these measurements and a knowledge of the signal frequency

the velocity of sound and hence the adiabatic compressibility were calculated.

Typically the concentration range 0–0.15 mole-kg⁻¹ was covered in ten concentration steps. The velocity of sound in water measured by the above method was within 0.3 m-sec⁻¹ of the result by Barlow and Yazgan, 1496.58 m-sec⁻¹.⁽¹⁰⁾

3.4. Data Processing and Errors

The processing of density data to yield apparent molal volumes ϕ_v and the estimation of errors have been previously described.⁽⁸⁾ Since the concentration range which can be covered with a given float is inversely proportional to its size, but the sensitivity of the technique is directly proportional to the size of the float, a compromise had to be struck in order to obtain the necessary precision required for extrapolation of the data to infinite dilution. The experimental concentration range was therefore limited to 0–0.05 mole-kg⁻¹. In order to obtain ϕ_v at higher concentrations, such as had to be employed for the compressibility studies, a cubic extrapolation equation was used.⁽⁹⁾ This could be justified by checking the computed densities against pyknometrically determined values or literature data for several systems. Also it had been shown previously that at the concentrations under discussion, i.e., > 0.005 mole-kg⁻¹, small errors in the density do not materially affect ϕ_v .

From the experimentally determined densities and sound velocities in solutions and water, the apparent molal compressibility ϕ_{κ} was evaluated by means of a computer program, which also included estimates of errors arising from the following sources: frequency (± 5 Hz), permanent and periodic micrometer errors (± 0.2 and $\pm 0.03 \ \mu$ m), temperature ($\pm 0.01^{\circ}$ C), diffraction and concentration. Of these, errors due to diffraction and permanent error in the micrometer were the most significant, each giving rise to an uncertainty of ± 0.2 m-sec⁻¹ in the measured sound velocity.

The computer program also provided for a smoothing procedure which enabled ϕ_K^{α} , the limiting apparent molal compressibility, to be evaluated by extrapolation of the data. The experimental technique and method of data processing were tested by a series of experiments with aqueous solutions of NaCl. The results were in excellent agreement with published data.⁽¹¹⁾³

³ The compressibilities which are obtained from sound-velocity measurements are adiabatic compressibilities. While for the purposes of interpretation, isothermal compressibilities, related to adiabatic compressibilities by the equation $\phi_{KS} = \phi_{KT} - \phi_{\alpha}^2 T/C_p$, where C_p is the molar heat capacity, are to be preferred, the requisite heat capacities are not available. It should be remembered that the corrections required for cyclic ethers and for sugars might be quite different. Most compressibilities reported in the literature are also adiabatic compressibilities, due to the paucity of C_p data, and the difficulty of direct determination of ϕ_{KT} .

4. RESULTS

Figures 1 and 2 show a representative selection of experimental $\phi_v(m)$ results for sugars and their derivatives. The corresponding values for the cyclic ethers can be found in ref. 4. Table I lists the coefficients in the density interpolation equation $d = d_o + Am + Bm^2 + Cm^3$ which provides a close fit to the experimental data in the concentration range employed. Figures 3 and 4 summarize the $\phi_K(m)$ results at 5 and 25°C, respectively. Actual experimental determinations are shown for THP and ribose and the lines represent the smoothed data with error limits as indicated. Limiting values of ϕ_v^o and ϕ_K^c are summarized in Table II. Because the errors tend to increase at low concentrations, a linear extrapolation procedure has been employed from the points at higher concentrations. A further reason for employing this extrapolation procedure is the possibility of systematic errors at low concentrations, due to the presence of dissolved air in the solution.⁽⁸⁾ Only two of the results here presented can be compared with data in the literature, namely, ϕ_v^o for glucose⁽¹²⁾ and Me- α -glucoside.⁽¹³⁾ In both cases the agreement is excellent.



Fig. 1. Apparent molal volumes of carbohydrates in solution at 5 and 25°C. The numbers refer to the solutes as identified in Table II. Triangles indicate data at 25°C; circles, data at 5°C. Error bars are shown for solute 9 at 25°C. These error bars are representative for all solutes.



Fig. 2. Apparent molal volumes of carbohydrate derivatives in solution at 5°C. The numbers refer to the solutes as identified in Table II. The filled-in circles refer to solute 11 at 5°C, the triangles to solute 11 at 25°C.

5. DISCUSSION

Examination of the P-V-T data presented in Figs. 1–4 and in Table II reveals the following interesting features:

1. For the series of cyclic ethers ϕ_v^o is, as a first approximation, a function of molecular size with constant ϕ_v increments due to additional CH₂ groups. Ether O and OH groups, although isoelectronic with CH₂ and CH₃, respectively, do not contribute markedly to ϕ_v^o . This is borne out by a comparison of ϕ_v^o for the pairs THFA-ribose and THPA-glucose (mannose, galactose); in both cases the additional four OH groups in the sugar hardly contribute to ϕ_v^o . This minimal volume contribution of OH groups is also evident in solutions of polyols and, in particular, of inositol.

2. Within the hexose series ϕ_v^o differs significantly for different conformers. An interpretation of this observation must be obscured by the different equilibrium anomeric ratios, but this complicating factor can be eliminated by a consideration of the four methyl pyranosides included in this study. It is seen that

		5°C			25°C			
	$d_o = 0.999965$				$d_o = 0.997048$			
	A	В	Ċ		A	В	С	
THF	0.00364	0.0026	-0.004		- 0.00460	0.0039	-0.015	
THP	-0.00444	0.0085	-0.055		-0.00559	0.0157	-0.123	
DI	0.00929	-0.0011	0.004		0.00730	0.0002	-0.002	
t-BuOH	-0.01381	0.0054	-0.002					
THFA	0.00986	-0.0008	0.013		0.00859	0.0010	-0.005	
THPA	0.00941	0.0058	-0.040		0.00765	0.0145	-0.098	
Ribose (αβ)	0.05764	-0.0280	0.462		0.05471	0.0137	-0.324	
Glucose $(\alpha\beta)$	0.07017	0.0114	-0.236		0.06830	-0.0040	-0.058	
Galactose $(\alpha\beta)$	0.07229	0.0034	-0.145		0.06981	-0.0125	0.072	
Mannose $(\alpha\beta)$	0.07097	-0.0931	-0.006					
a-Methylglucoside	0.06315	0.0020	-0.118		0.06107	0.0012	-0.101	
β-Methylglucoside	0.05978	-0.0173	0.107		0.05891	-0.0121	0.077	
α-Methyl galactoside	0.06780	-0.2040	2.393					
β-Methyl galactoside	0.06748	0.0425	-0.830					
Scyllo-inositol	0,10735	-0.8733	9.462					
Myo-inositol	0.08344	-0.0307	0.283					
Mannitol	0.06548	-0.0513	0.525					
Sorbitol	0.06569	0.0090	-0.294					

Table I. Coefficients of Density Interpolation Equation $d = d_0 + Am + Bm^2 + Cm^3$

 ϕ_v^o is larger for compounds which have the OCH₃ group as an equatorial substituent, compared to those anomers which have an axial OCH₃ substituent. Although these differences are small, they are nevertheless highly significant.

3. Whereas ϕ_v of all the ethers exhibits a marked concentration dependence, this is not the case for the polyhydroxy derivatives.

4. Mean limiting apparent expansibilities $\phi_{\alpha}^{o}(=\partial \phi_{\nu}^{o}/\partial T)$, nominally at 15°C, are very low for all the simple derivatives, but increase with the degree of hydroxyl substitution. Low, or indeed negative values of ϕ_{α}^{o} have been identified with the property possessed by simple monofunctional compounds of raising the temperature of maximum density of water.^(14,15) Highly polar compounds, such as sugars, exhibit the normal effect of lowering the temperature of maximum density.

5. The trends in $\phi_K(m)$ are not as clear cut as those for $\phi_v(m)$, because of the magnitude of the errors at low concentrations. Since the errors in the sound velocity measurements, etc., are already as small as one could reasonably hope for, a reduction of this error is not at present feasible. No significance is therefore attached to variations in the slopes of the $\phi_K(m)$ plots. However, if it is assumed that the solute molecules are incompressible, then the observed ϕ_K^o reflects intermolecular effects only. Table II shows that the introduction of

		Mol	ϕ_{v}^{O} , cm ³ -mole ⁻¹		$\phi^o_{\alpha},$ cm ³ -mole ⁻¹ -deg ⁻¹	$10^4 \phi_{K}^{O}$, cm ³ -mole ⁻¹ -bar ⁻¹	
		wt.	5°C	25°C	15°C	5°C	25°C
1.	THF	72	75.7 ^a	76.9 ^a	0.06	-11.4	+7.7
2.	THP	86	90.6 ^a	91.8 ^a	0.06	-20.1	+6.4
3.	DI	88	78.9 ^a	81.1 ^a	0.11	-9.9	+9.3
4.	t-BuOH	74	87.9 ^b	87.8 ^b	-0.005	-20.5	-
5.	THFA	102	92.4 ^a	93.8 ^a	0.07	-22.7	+4.4
6.	THPA	116	106.8 ^a	108.1 ^a	0.065	-28.6	-2.0
7.	Ribose (\alpha\beta)	150	93	95.3	0.115	-33.5	-13.0
8.	Glucose (ab)	180	109.5	111.9	0.120	-38.8	-16.0
9.	Galactose (ab)	180	107.7	110.7	0.150	-	_
10.	Mannose $(\alpha\beta)$	180	109.2	~		_	_
11.	a-Methyl glucoside	194	130.9	133.2	0.115	-35.3	-13.0
12.	B-Methyl glucoside	194	134.6	135.5	0.045	-29.2	-5.9
13.	a-Methyl galactoside	194	130.8			-	_
14.	β-Methyl galactoside	194	132.8			-	_
15.	Scyllo-inositol	180	98	_		-	-
16.	Mvo-inositol	180	97	_		-61.1	-
17.	Mannitol	182	117.1			_	_
18.	Sorbitol	182	117.0	_		-	-
19.	NaCl	_ • •	14.2 ^c	16.7 ^c	0.125	-67.3 ^d	50.5 ^đ

Table II. Limiting Volumetric Properties of Cyclic Ethers and Carbohydrates inSolution at 5 and 25°C

^a See ref. 4.

^b Franks and Smith, Trans. Faraday Soc. 64, 2962 (1968).

^c See ref. 8.

^d See ref. 11.

successive OH groups into the ether ring renders ϕ_K^o more negative but that there are again small but significant differences between the effects of equatorial and axial substituents. Since ϕ_K^o is a measure of the protection against compression which the solute molecule imparts to water, the large negative values would suggest that polyhydroxy compounds act as structure preservers. The effect produced by myo-inositol (five equatorial OH groups) is particularly striking and almost of the same magnitude as that produced by electrolytes which derive their negative ϕ_K^o from electrostrictive hydration (as evidenced, for instance, by the low ϕ_K^o).

6. The mean temperature dependence of $\phi_K^o(=\partial \phi_K^o/\partial T)$ is large and positive and within the experimental precision the same for all compounds studied, ca. 1×10^{-4} cm³ (mole-bar-deg)-1. This suggests that the structural effects of the solutes respond similarly to the general structure-breaking effect of temperature. The very accurate data of Owen and Kronick⁽¹¹⁾ (see Table II) suggest that for NaCl $\partial \phi_K/\partial T$ is somewhat lower than for the nonelectrolytes



Fig. 3. Apparent molal compressibilities of cyclic ethers and carbohydrates in solution at 5° C. The numbers refer to the solutes as identified in Table II. The indicated points refer to lines 2 and 7. Error bars are shown for solute 7. These errors are representative for all solutes.



Fig. 4. Apparent molal compressibilities of cyclic ethers and carbohydrates in solution at 25° C. The numbers refer to the solutes as identified in Table II. The indicated points refer to lines 2 and 7. Error bars are shown for solute 2. These error bars are representative for all solutes.

and it is likely that more accurate data could resolve differences in $\partial \phi_{\kappa}^{o}/\partial T$. Finally, the sign of $\partial \phi_{\kappa}/\partial T$ is surprising in view of the fact that over the same range of temperature (5–25°C) the adiabatic compressibility of water *decreases* by about 10%.

6. THE THERMODYNAMICS OF AQUEOUS SOLUTIONS OF POLY-FUNCTIONAL SOLUTES

The results on infinitely dilute solutions of simple ether derivatives have been previously discussed in terms of an interstitial, or clathrate type of hydration.^(4,6) Such an interpretation is consistent with both NMR proton chemical shift data⁽¹⁶⁾ and rotational diffusion times.^(17,18) The concentration profiles of heats, heat capacities, and volumes of mixing,⁽¹⁹⁾ although more difficult to interpret, because of marked solute–solute interactions in such systems, are also consistent with this type of hydration. Not much useful information could previously be adduced as to the part played by the polar portion of the solute molecule in determining the solution behavior. That the number and positions of the ether O atoms do not affect the solvent interactions can be seen from a comparison of the solution behavior of the structurally and electronically almost identical molecules, 1,3-dioxane, 1,4-dioxane, and THP.^(4,19)

Previous thermodynamic studies on solutions of simple carbohydrates have been interpreted in terms of two seemingly contradictory models. A thermodynamic study of aqueous solutions of glucose and their comparison with aqueous sucrose⁽²⁰⁾ led Taylor and Rowlinson⁽¹²⁾ to the conclusion that these solutions resembled water $-H_2O_2$ rather than water–alcohol mixtures. Thus it was suggested that solute–water hydrogen bonds were more abundant and/or stronger than water–water bonds. Using the concept of the semiideal solution Stokes and Robinson⁽²¹⁾ have suggested that the observed concentration dependence of thermodynamic quantities is due to the solute–water interactions and can be expressed in terms of a series of hydration equilibria

$$S_{i-1} + H_2O \xrightarrow{K_{i-1}} S_i \qquad i = 1, 2, \ldots, n$$

where *n* is the number of potential hydration sites. An average hydration number can be derived which depends only on the water activity. Using this approach Stokes and Robinson could fit the experimental activity data for glucose $(n = 6, K_{i-1} = K_i = ..., K_n = 0.786)$ to saturation concentrations and for sucrose (n = 11, K = 0.994) up to 6 M.

Spectroscopic evidence in support of the simple hydration approach is provided by a study of the effect of increasing concentrations of sucrose on the $152-175 \text{ cm}^{-1}$ Raman band, assigned to a water hydrogen stretching mode.⁽²²⁾ If I_o and I are the total integrated band intensities in pure water and in 2 M

sucrose, respectively, and M'_o and M' the corresponding molar concentrations of water, then it is found that the ratio $IM'/I_oM'_o = 1.6$, although the band shape does not change with the addition of sucrose. This suggests that intramolecular hydrogen bonds are ruled out and that the solute-water hydrogen bonds resemble those in water, although hydrogen bonding is more extensive in the sucrose solution. Further support for a simple hydration approach is provided by viscometrically determined hydration numbers of glucose and THPA.⁽²³⁾ The hydration determined for glucose decreases slowly with temperature, while THPA hydration decreases more rapidly. This would suggest that glucose has a specific hydration, whereas THPA hydration is hydrophobic in nature, and hence decreases more rapidly.

The interpretation of activity coefficient data in terms of simple hydration processes may be a useful first approximation, but closer examination of more recent data, including those described in this account, suggest that as a result of enthalpy-entropy compensating effects, free energies are fairly insensitive in discriminating between alternative models. For example, $\Delta G^E(x_2)$ curves for most aqueous liquid mixtures look quite similar, symmetrical about $x_2 = 0.5$, and can approximately be fitted by simple Scatchard type equations, a procedure which is certainly not possible for the temperature or pressure derivatives of ΔG^E . It has also been shown that in the case of sucrose $\partial \ln \gamma / \partial T$ and $\partial \ln \gamma / \partial P$ can no longer be fitted by the simple mean hydration number model.⁽²⁴⁾

The effects of conformation on solvent participation in reactions are clearly demonstrated by the thermodynamic functions associated with the mutarotation of sugars. Thus, standard entropies of mutarotation ($\alpha \rightarrow \beta$) range from -0.52 eu for xylose to +0.70 eu for maltose.⁽²⁵⁾ An interpretation of these data in terms of differences in the hydration behavior of axial and equatorial OH groups has been attempted⁽²⁶⁾ and recent NMR relaxation studies performed at this laboratory⁽²⁷⁾ support the view that energetically, the hydration of equatorially substituted groups is favored. It has also been speculated that anomer specificity of some enzyme-catalyzed reactions involving sugars may be related to facilitated solvent participation in the case of β -sugars.⁽²⁸⁾

The problem of accounting for the concentration dependence of activity coefficients of aqueous carbohydrate solutions has been approached in a more rigorous manner by Kozak *et al.*⁽²⁹⁾ In their comprehensive study they have analyzed freezing point, osmotic pressure, enthalpy, and heat capacity data of a wide range of aqueous solutions in terms of the Flory–Huggins lattice model and the McMillan–Mayer theory⁽³⁰⁾ which relates the osmotic pressure of a solution to solute pair, triplet, etc., interactions without explicitly taking into account the nature of the solvent, i.e., it accounts for the thermodynamics solely in terms of solute–solute effects in the presence of the solvent. The use-

fulness of these theories when applied to aqueous solutions can be gauged by comparing the predicted and experimental concentration and temperature dependence of the coefficients in the virial equations

$$\ln \gamma_1 = B x_2^2 + C x_2^3 \dots \tag{1}$$

$$\pi/kT = \rho + B^* \rho^2 + C^* \rho^3 \dots$$
 (2)

where γ_1 is the solvent activity coefficient, π is the osmotic pressure, and ρ is the number density of the solution. Thus, according to the lattice solution model, strong solute interactions are identified by positive *B* and negative *C* values, whereas intercomponent association (hydration) leads to a reduction of both *B* and *C*. When one deals with a homologous series the position is further complicated by the fact that an increase in the solute size leads to more negative *B* but more positive *C* values. The application of the above predictions to the available experimental data for the lower alcohols leads to inconclusive results: except for methanol, *B* values are positive and increase with the number of carbon atoms, while *C* are negative. Insufficient data are available for sugars, but it appears that *B* is generally negative and depends on solute size.⁽²⁹⁾ This suggests that the solution behavior is dominated by solvation rather than by solute association.

According to the McMillan–Mayer formalism the second virial coefficient B^* of the osmotic pressure equation can yield the attractive contribution to the pair potential function $U^{(2)}(r)$. This can also be obtained more indirectly from B, provided that V_1^o and ϕ_v^o are known. According to Kozak *et al.* the attractive contribution to $U^{(2)}(r)$ increases in magnitude for the series urea \approx lactamide \approx glycerol < mannitol < sucrose < raffinose and is therefore said to be simply related to the number of functional groups in the molecule. It is suggested that the concentration dependence of the thermodynamic properties of solutions of polyfunctional compounds is best accounted for in terms of solute–solute pairwise interactions.

Our own results for the polyfunctional molecules do not support the conclusion arrived at by the application of the McMillan–Mayer treatment, since the ϕ_v data show a zero concentration dependence, and the spectroscopic results discussed in ref. 27 show an absence of marked solute–solute interactions. On the other hand, monofunctional solutes give $\phi_v(x_2)$ curves with negative slopes, the magnitudes of which depend on the size of the hydrophobic residue.⁽⁴⁾ This type of behavior can be well reconciled with the McMillan– Mayer prediction of pair, triplet, etc., interactions increasing with the rise in temperature. Indeed, low-angle x-ray scattering studies on *tert*-butanol–water mixtures have identified concentration fluctuations of a considerable magnitude.⁽³¹⁾

The thermodynamic data here described for sugars and polyhydric alcohols, particularly when seen in the context of complementary NMR and

dielectric relaxation studies,⁽²⁷⁾ suggest an absence of solute-solute interactions even at relatively high concentrations. Instead we favor the specific hydration model with emphasis not only on the number of potential solute hydration sites, but their relative conformations.⁴ This type of model will satisfactorily explain many of the observations set out at the beginning of the Discussion section. The small effect of hydroxyl groups on ϕ_n^o can be understood if one considers that the oxygen spacings in many of these solute molecules^(26,32) are compatible with the second nearest neighbor distance of the oxygens in liquid water, as obtained from the x-ray radial distribution function.^(33,34) This would suggest that any specific hydration is likely to be compatible with the structures already existing in liquid water, and so, unlike hydrophobic hydration, this type of interaction will not affect the volume of the system to any marked extent. Also, due to the structural compatibility, one would not expect any long-range effects to be apparent, so that no concentration dependence would be expected. Since it is equatorial OH groups which possess this favorable spacing, axial OH groups would not be expected to contribute so much to specific hydration, and the effect of equatorial OCH₁ substitutions on ϕ_v^o should be larger than that of axial OCH₃ substitutions, as is the case.

The specific-hydration model also enables us to understand better the trends observed in the ϕ_{k}^{o} data. Increasing OH substitution should result in increasing hydration, the amount being dependent on the relative proportions of axial and equatorial OH substituents. Since it is reasonable to expect this specific-hydration structure to be less compressible than bulk water, ϕ_{k}^{o} should decrease with increasing OH substitution. Myo-inositol, with five equatorial OH groups, would be expected to have strong hydration, and therefore have a large negative ϕ_{k}^{o} , as is in fact observed.

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⁴ A possible hydration model is discussed in more detail in another paper.⁽²⁷⁾

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