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EXCESS ENTHALPIES OF AQUEOUS SOLUTIONS OF MONO- AND OLIGO-SACCHARIDES AT 25°

GUIDO BARONE, PASQUALE CACACE, GIUSEPPINA CASTRONUOVO, AND VITTORIO ELIA
Istituto Chimico, University of Naples, Via Mezzocannone 4, 80134 Naples (Italy)

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ABSTRACT

The heats of dilution in water of D-xylose, D-fructose, D-galactose, D-mannose, lactose, and raffinose have been determined calorimetrically at 25°. The calorimetric data, expressed in terms of excess enthalpy, lead to an evaluation of pair- and triplet-interaction coefficients. Osmotic data, where known, permit the analogous coefficients of the excess free energy to be obtained and thence those of the excess entropy. Analysis of the excess functions and comparison with spectroscopic properties permits some qualitative hypotheses to be formulated on the molecular interactions occurring in these solutions.

INTRODUCTION

The study of aqueous solutions of polar non-electrolytes is interesting both from a biological and from a physicochemical point of view. For simple saccharides and their derivatives, many efforts have been directed to the elucidation of their conformations in solution. Information provided in turn by X-ray diffractometry (on crystals)[1] and spectroscopy[2,3], together with conformational analysis calculations and polarimetric and n.m.r. investigations of mutarotation[3-5], gives a detailed picture of the behaviour of these substances. There has been much recent interest in the interaction of saccharides with the solvent water, involving spectroscopic[6] or n.m.r. and dielectric[7-13] investigations. By contrast, systematic, thermodynamic studies have concerned only the limiting properties (specific heats, compressibilities, and molar volumes)[8,14-16]. There are few data on the excess thermodynamic-properties of concentrated or moderately concentrated solutions[17-21]. However, an analysis of the properties of these systems is useful for formulating at least qualitative hypotheses on the molecular interactions occurring in solutions of such natural macromolecules as polysaccharides and glycoproteins. In these cases, concentrated solutions are more realistic models than infinitely dilute solutions.

We now report on a preliminary, calorimetric study of some simple mono- and oligo-saccharides. The heats of dilution and then the excess enthalpies in water at 25° have been determined for D-xylose, D-fructose, D-galactose, D-mannose, and raffinose. Also reported are the heats of dilution of lactose; these were slightly

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different from the data given in the literature, whereas the agreement for D-glucose and sucrose[22,23] is very good. The data on excess enthalpies, when compared with those for excess free energies and entropies, permit a qualitative discussion on the molecular properties of aqueous solutions of the oligosaccharides.

THERMODYNAMICS

The excess enthalpy $H^E(m_x)$ of a solution containing m_x moles of the solute x per kg of water is defined as:

$$H^E(m_x) = H(m_x) - H_w^0 - m_x \bar{H}_x^\circ, \tag{1}$$

where $H(m_x)$ is the enthalpy of the solutions, H_w^0 is the enthalpy of one kg of water in its standard state, and $\bar{H}_x^\circ$ is the partial molal enthalpy of the solute in its standard state (hypothetical state at $m_x = 1$ having the same properties as the infinitely dilute solution). The excess properties, then, are a measure of the deviations from the standard states, and their numerical values depend only on the choice of the standard states. The properties of the standard state of the solute, in turn, referring to the infinitely dilute solution, are determined by the perturbation induced by the introduction of the solute into the solvent. Hence, the excess properties, which are also a measure of the non-ideality of the solution, take account of the changes for all the interactions solute–solute, solute–solvent, and solvent–solvent.

The excess enthalpy is related to the other excess properties through relationships *2* and *3*.

$$H^E = \left[\frac{\partial (G^E/T)}{\partial (1/T)} \right]_{P,m} \tag{2}$$

$$H^E = G^E + TS^E \tag{3}$$

It can be expressed in the virial form[24–26] as

$$H^E(m_x) = h_{xx} m_x^2 + h_{xxx} m_x^3 + \cdots . \tag{4}$$

Similar relations[26] can be used for G^E and TS^E.

$$G^E(m_x) = g_{xx} m_x^2 + g_{xxx} m_x^3 + \cdots \tag{4'}$$

$$TS^E(m_x) = Ts_{xx} m_x^2 + Ts_{xxx} m_x^3 + \cdots \tag{4''}$$

The McMillan–Mayer theory of solutions[27] allows a formal separation of the effects caused by the interactions of pairs, triplets, *etc.* of solute particles. The coefficients g_{xx}, g_{xxx} and the relative enthalpic and entropic contributions, h_{xx}, h_{xxx}, and Ts_{xx}, Ts_{xxx}, characterise these interactions. However, the values of the coefficients implicitly allow for the change of the solute–solvent interactions and for the overall change of the state of the solvent.

The coefficients of Eq. *4* can be obtained from the experimental heats of dilution from the molality m_i to the molality m_f, according to the following relations[26,28,29]:

$$\Delta H^{dil}(m_i \to m_f) = H^E(m_f) - (m_f/m_i)\, H^E(m_i) = \\ = h_{xx} m_f(m_f - m_i) + h_{xxx} m_f(m_f^2 - m_i^2) + \cdots, \qquad (5)$$

where ΔH^{dil} is given in $J.kg^{-1}$ of solvent in the final solution.

EXPERIMENTAL

D-Xylose, D-fructose, D-galactose, D-mannose, lactose, and raffinose were commercial products (Sigma), and were used without further purification.

The heats of dilution, except for D-galactose, were determined by using an LKB 10700-1 standard flow-microcalorimeter, according to the procedure previously described[26,29]. The values of ΔH^{dil} were obtained from

$$\Delta H^{dil}(m_i \to m_f) = -(dQ/dt)_{exp}/P_w, \qquad (6)$$

where $(dQ/dt)_{exp}$ is the heat evolved per time unit (evaluated from the instrumental deviation, normalised by electrical calibration), and P_w is the total, mass flow-rate of water per time unit.

The heats of dilution for D-galactose were obtained by using an LKB 2107/112 standard batch-microcalorimeter. In this case, the heats of dilution were obtained from:

$$\Delta H^{dil}(m_i \to m_f) = -Q/w, \qquad (6')$$

where Q is the heat produced (evaluated by integrating the area of the thermogram, normalised by an electrical calibration for the same experimental conditions), and w is the weight of water (in kg) in the final solution.

RESULTS AND DISCUSSION

The experimental heats of dilution and the initial and final molalities for each experiment are reported in Tables I–VI. The enthalpic interaction coefficients were obtained by a smoothed interpolation of a modified form of Eq. 5, using a least-squares method. The quantity interpolated as a function of the molality was $\Delta\phi_L = \Delta H^{dil}/m_f$. The values of the h coefficients are summarised in Table VII, together with the 95% confidence limits; the h values are also compared with literature values for other saccharides. For each case, the interpolating polynomial of highest degree, for which all the coefficients still exceed their own 95% confidence limits, was chosen.

The following are the main features of the data obtained. (*a*) The pair-interaction coefficients, h_{xx}, were always positive, whereas h_{xxx} values were negative, the values of the latter being at least one order of magnitude smaller than those of h_{xx}. (*b*) The values of h_{xx} depended on the nature of the solute and on its stereochemistry. For instance, large differences were found within the hexose class. (*c*) The h_{xx} values of the di- and tri-saccharides are given approximately by the sum of the

TABLE I

HEATS OF DILUTION OF D-XYLOSE IN WATER AT 25°

m_i	m_f	$-\Delta\phi_L\ (m_i \rightarrow m_f)$ $(J.mol^{-1})$
4.8379	2.0791	577.0
4.8379	1.8386	633.8
2.9512	1.3658	429.8
2.9512	1.2205	476.7
2.1467	1.3800	184.7
2.1467	1.6634	109.1
2.1436	1.8078	93.8
2.1436	1.2717	262.4
2.1436	1.5665	159.1
2.0797	0.9941	286.8
2.0027	0.9570	308.4
2.0027	0.8650	345.2
1.8386	0.8029	303.4
1.3658	0.6703	202.8
1.2205	0.6190	192.2
0.9941	0.4915	135.6
0.9570	0.4732	123.8
0.8029	0.4089	119.9
0.6703	0.3415	99.4
0.6703	0.3415	100.7
0.6110	0.3144	87.9
0.4915	0.2513	63.6
0.4723	0.2433	57.8
0.4098	0.2038	62.7
0.3415	0.1764	42.7
0.2513	0.1300	34.7

h_{xx} values of the monomers. This behaviour, however, is to be expected, on the basis of the additivity principle, for a limiting, rather than for an excess, property. The introduction of new functional groups would be expected to increase very rapidly the number of possible interactions between two solute-molecules (whatever the nature of the main molecular processes). A very large increase in the values of the thermodynamic parameters must then be expected on going from a given solute to the higher homologues of the same family[23].

Moreover, for raffinose, the prediction largely exceeds the statistical uncertainty of the group contribution method[23,30-32]. For raffinose and other oligosaccharides, the effectiveness in determining the value of h_{xx} for the groups involved in the glycosidic linkages (as well as that of the nearest groups) is probably not the same as that of the corresponding groups in each of the constituent monosaccharides, because of steric hindrance. Otherwise the larger the molecule of a solute, the smaller would be the effectiveness of the contribution of each functional group to the overall intermolecular interactions.

TABLE II

HEATS OF DILUTION OF D-FRUCTOSE IN WATER AT 25°

m_i	m_f	$-\Delta\phi_L$ $(m_i \rightarrow m_f)$ ($J.mol^{-1}$)
4.5392	1.7342	613.8
2.9577	1.4000	354.0
2.9577	1.0804	448.7
2.1613	1.2249	208.9
2.1613	0.5646	383.9
1.8046	0.6953	309.9
1.8046	0.9042	251.1
1.4000	0.7279	144.7
1.3891	0.9104	89.8
1.2087	0.9389	65.0
1.2087	0.9389	66.5
1.7342	0.7600	247.1
1.0804	0.4872	138.7
0.9042	0.4743	113.1
0.7279	0.3038	96.4
0.7279	0.3847	76.1
0.6953	0.2987	113.1
0.7600	0.3628	97.7
0.4872	0.2158	66.2
0.4743	0.2323	55.2
0.3628	0.1769	42.9

TABLE III

HEATS OF DILUTION OF D-GALACTOSE IN WATER AT 25°

m_i	m_f	$-\Delta\phi_L$ $(m_i \rightarrow m_f)$ ($J.mol^{-1}$)
0.7141	0.0756	79.2
0.7141	0.1767	67.2
0.7141	0.0910	74.0
0.7141	0.1669	62.5
0.7141	0.3748	48.3
0.7141	0.3197	57.0
0.7141	0.2356	62.9
1.4954	0.8565	97.0
1.4954	0.6703	120.1
1.4954	0.5946	134.1
1.4954	0.4829	135.9
1.4954	0.4379	122.4
2.0095	0.2357	202.6
2.0095	0.4881	209.3
2.0095	0.5371	231.0
2.0095	0.8120	162.7
2.0095	1.4278	78.6

TABLE IV

HEATS OF DILUTION OF D-MANNOSE IN WATER AT 25°

m_i	m_f	$-\Delta\phi_L\ (m_i \rightarrow m_f)$ $(J.mol^{-1})$
2.2581	0.7374	251.7
2.2581	1.4720	120.2
2.2581	1.1061	185.6
2.2581	1.6470	90.3
0.9691	0.3926	110.0
0.9691	0.3926	108.5
0.9691	0.7046	57.6
0.9691	0.5583	81.4
0.9691	0.7856	34.2
0.7046	0.4112	48.3
0.6301	0.4773	26.0
0.6301	0.3838	43.8
0.5583	0.3276	39.3

TABLE V

HEATS OF DILUTION OF LACTOSE IN WATER AT 25°

m_i	m_f	$-\Delta\phi_L\ (m_i \rightarrow m_f)$ $(J.mol^{-1})$
0.5720	0.3742	93.9
0.5706	0.3007	132.0
0.4747	0.2382	129.5
0.4757	0.2512	130.4
0.4381	0.2372	103.8
0.3620	0.2298	70.3
0.3585	0.1890	68.9
0.3327	0.1980	59.1
0.3327	0.1603	76.5
0.3113	0.1663	84.5
0.3113	0.1511	67.5
0.2635	0.1361	69.6
0.1890	0.1121	37.5
0.1663	0.0841	52.6
0.1604	0.0870	54.2
0.1980	0.1113	38.8

TABLE VI

HEATS OF DILUTION OF RAFFINOSE IN WATER AT 25°

m_i	m_f	$-\Delta\phi_L$ ($m_i \rightarrow m_f$) (J.mol^{-1})
0.8472	0.3826	374.0
0.8472	0.3568	443.6
0.8472	0.3568	386.3
0.5865	0.2442	260.7
0.5865	0.0959	357.0
0.3568	0.1637	171.2
0.3228	0.1478	154.5
0.3826	0.1819	182.9
0.2442	0.0435	162.6
0.2442	0.0435	145.5
0.1478	0.0700	116.2

TABLE VII

COEFFICIENTS OF THE EXCESS ENTHALPY FOR AQUEOUS SOLUTIONS OF MONO- AND OLIGO-SACCHARIDES

	h_{xx}[a]	h_{xxx}[b]	h_{xx} *calc.*[c]
D-Xylose	339 ±16	−19 ±3	
D-Fructose	264 ±18	− 7 ±4	
D-Galactose	133 ±8		
D-Mannose	207 ±14	−14 ±5	
D-Glucose	343.2 ±9.6[d]	−12.8	
Lactose	506 ±32 556.6[e]		476
Sucrose	577.1 ±5.9[d]	−33.8	607
Raffinose	811 ±50		740

[a] Units: J.mol^{-1} (mol.kg^{-1})$^{-1}$. [b] Units: J.mol^{-1}(mol.kg^{-1})$^{-2}$. [c] Values obtained by summing the values of h_{xx} for the monomers. [d] Ref. 23. [e] Ref. 22.

TABLE VIII

COEFFICIENTS OF THE EXCESS ENTHALPY, FREE ENERGY, AND ENTROPY FOR AQUEOUS SOLUTIONS OF MONO- AND OLIGO-SACCHARIDES

	h_{xx}[a]	g_{xx}[a]	$(-Ts_{xx})$[a]
D-Xylose	339	34[b]	−266
D-Glucose	343	70[c]	−273
Sucrose	577	183[d]	−394
Raffinose	811	331[e]	−480

[a] Units: J.mol^{-1}(mol.kg^{-1})$^{-1}$. [b] Evaluated from ref. 21. It is also possible to obtain $g_{xxx} = 2.8$ and $g_{xxxx} = 0.2$, in the concentration range reported (0–3.46 molal). [c] Evaluated from ref. 39. Also obtained: $g_{xxx} = -0.8$, in the concentration range 0–7.5 molal). [d] Evaluated from ref. 19. The authors gave two interpolations of their data: we chose the one relative to the more restricted range of molalities 0–2 molal. Also obtained: $g_{xxx} = 49.4$. [e] From ref. 20.

The difference found among the h_{xx} values of isomeric monosaccharides cannot be easily explained, as well as the origins of all the h_{xx} values determined. In fact, many effects and equilibria combine in determining the excess properties of these apparently simple, binary systems, namely: changes in the hydration of each solute molecule; interactions among solute particles (eventually involving the hydration water); changes in the overall state of the bulk water at increasing concentrations; shift of the anomeric equilibria (except for such non-reducing oligosaccharides as sucrose and raffinose); shift of the equilibria between pyranoid and furanoid forms; shift of conformational equilibria (*e.g.*, the $^4C_1$–$^1C_4$ interconversion of pyranose rings or rotation about glycosidic linkages).

Some of the equilibria considered above are probably little influenced by the concentration changes. On the other hand, despite the large differences in the population of every isomeric or conformational state for each compound examined, all of the excess properties are grossly similar to the same properties of the binary, aqueous solutions of other simple non-electrolytes, which do not undergo similar transformations.

A hint can be provided by the analysis of the whole of the excess properties. In Table VIII, the values of the coefficients of the excess free energy, enthalpy, and entropy for the four known cases are reported. The g_{xx} coefficients are positive, because of the positive values of the excess enthalpies which are large enough to balance the positive contribution of the entropic terms. The sign of g_{xx} suggests that there are no favourable interactions between pairs of saccharide molecules, in agreement with spectroscopic and n.m.r. data[5,6]. Solute–solute interactions are then prevented by the more favourable solute–solvent interactions, and they will not contribute to the values of h_{xx}. It should be emphasised that, especially for the smaller solutes of this group, the enthalpic and entropic terms are very large with respect to g_{xx}. This is a case of enthalpy–entropy compensation, a phenomenon well known in biophysical chemistry and in the physical chemistry of aqueous solutions[33].

However the compensation is only partial, as with the excess properties of other simple, binary, aqueous solutions[26,29,34,35]. The predominance of the enthalpic over the entropic contributions characterises hydrophilic solutes in water[36,37]. However, the signs of the coefficients of each term lead to the classification of the oligosaccharides in a characteristic group that is different from such hydrophilic substances as the urea-like[29] or self-associating solutes. The remarkable enthalpy–entropy compensation (peculiar to aqueous systems) and the unfavourable solute–solute interactions led us to consider the changes in the state of the water in the cosphere of the saccharides upon the concentration processes. All of the limiting, thermodynamic properties[8,14–16], as well as the spectroscopic ones[5–14], suggest that, in dilute solutions, the saccharide molecules are extensively hydrated. The extent of the hydration depends on the temperature, the number and nature of the substituents, and the stereochemistry of the solute molecule. The functional groups that seem to be more extensively hydrated are those entering easily into the structure of water without appreciable orientational distortion. The intensities of the solute–water and water–water hydrogen bonds are quite similar[6].

Scatchard *et al.*[38] and Stokes and Robinson[39] proposed a model for aqueous solutions of sucrose and D-glucose, based on a semi-ideality approach. This model rationalises the osmotic coefficients, assuming that, as dilution increases, a stepwise hydration-equilibrium takes place. The model is really too simple, since it takes into account only the change of the hydration number with the concentration. Every step of the hydration process is assumed to be characterised by a unique value of the equilibrium constant. However, the partial molar volumes and the heats of dilution cannot be explained on the basis of the same assumptions[25,40]. On the other hand, the free energy data by themselves do not permit discrimination of one model among others, because of the enthalpy–entropy compensation. Taylor and Rowlinson[17] observed that the similarity between the properties of aqueous solutions of D-glucose and those of the mixtures H_2O–H_2O_2 suggests that the former are more "structured" than pure water. In other words, the hydrogen bonds for solute–water and water–water (in the neighbourhood of the solute) are more numerous and/or stronger than those for water–water in the same volume. The results of Raman spectroscopy seem to indicate that aqueous solutions of sucrose are more structured for an increase of the number, rather than the intensity, of the hydrogen bonds with respect to pure water[6,14]. Nevertheless, every water molecule, because of favourable steric correlations, experiences a higher average-number of hydrogen bonds in the cosphere of the solute than in the bulk. It lies, then, in an enthalpic and entropic, less-rich state.

On the basis of the preceding considerations, it is concluded that the signs and values of h_{xx}, g_{xx}, and $(-Ts_{xx})$ for the compounds reported in Table VIII suggest, or are not in conflict with, the hypothesis that the saccharide solutions become more "structured" at increasing concentrations. However, a partial retrogradation of hydration occurs, due to the partition of water between the bulk and the cospheres, which determines the signs and the values of the excess properties. It is probable that the "compatibility"[5] of these solutes with the structure of water means that only the solvent molecules of the specific hydration domain constitute the "structured cosphere". Thus, the relaxation of the water depends specifically on the ratio between the number of equatorial and axial hydroxyl groups of the solute, and on their reciprocal positions and hydration states. For this reason, the Stokes and Robinson model is too simple. However, Harvey and Symons[13], on the basis of proton chemical-shift data, concluded that the number of water molecules interacting with saccharides is larger than that predicted by relaxation methods and other approaches. In fact, each hydroxyl group of the solute is involved in two hydrogen bonds with the solvent. The nearest layers of water molecules are in a dynamic field of forces, not different from that acting in the bulk; hence, they are not important for the present discussion. (If the hydrated polar groups of a solute have a geometry and a symmetry different from those of water, the solvated molecules influence the nearest layers of the solvent with their particular orientations[29].)

Another suggestion arises from the observation that aqueous solutions of D-glucose and sucrose can be mixed without "extra" enthalpic effects; the excess enthalpy of the ternary solution is a weighted average of the excess enthalpies of the two binary solutions. In other words, the cross-interaction coefficient h_{GS} is related to the two self-interaction coefficients, h_{GG} and h_{SS}, by the simple rule[41] $h_{GS} = (h_{GG}.h_{SS})^{\frac{1}{2}}$. It then emerges that the specific sets of equilibria characterising the separate solutions of D-glucose and sucrose do not appreciably disturb each other, and that the h_{GS} value is mainly due to the same kind of processes that determine h_{GG} and h_{SS}. The collection of more data is necessary for an understanding of the origins of the difference in the values of the coefficients h_{xx}, g_{xx}, *etc.* for sets of isomeric monosaccharides. Moreover, it is necessary to ascertain whether large differences also exist for di- and tri-saccharides.

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