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EXCESS ENTHALPIES OF AQUEOUS SOLUTIONS OF METHYL α-D-ALDOPYRANOSIDES AT 25°

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ABSTRACT

The excess enthalpies of four methyl α-D-aldopyranosides were determined at 25° by calorimetry and expressed as virial expansion of the molality, according to the McMillan–Mayer approach. The signs and the values of the pair-interaction coefficients were attributed to the release of water from the hydration cospheres during the concentration process. The influence of the stereochemistry of the solutes on this release is discussed.

INTRODUCTION

The molecular structures and conformations of monosaccharides have been studied widely by X-ray and neutron diffractometry[1], and n.m.r. and dielectric relaxation spectrometry[2–4]. Some of these investigations have been concerned with the state of hydration of sugars. By contrast, there have been few studies of the thermodynamic properties of sugars in solution, and the more systematic ones have dealt with the limiting properties (specific heats, compressibility, and molar volumes)[5–8].

We have reported on the excess enthalpies[9–12] and free energies[10,11] for aqueous solutions at 25° of some oligosaccharides and 2- and 6-deoxy derivatives. The excess thermodynamic properties, at constant temperature and pressure, of a binary solution of a non-electrolyte x can be represented[9–16] by a virial expansion of the molality m:

$$Y^{E}(m) = y_{xx}m^2 + y_{xxx}m^3 + \cdots, \qquad (1)$$

where $Y^{E}(m)$ is the excess thermodynamic property, referred to a solution containing m mol of solute and 1 kg of water. The standard states and all the other quantities employed in the following are defined according to the current literature[9–16]. The coefficients of the excess free energy, given in the form of Eq. *1*, are usually considered as a measure of the interactions among pairs, triplets, *etc.*, of solute particles. Generally, however, they account implicitly for all the changes in the intermolecular interactions occurring during the concentration process.

For reducing sugars, the occurrence of equilibria variously involving acyclic and α- and β-pyranose and -furanose forms can make the interpretation of data

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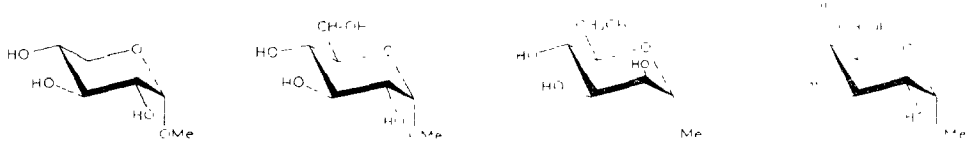
uncertain. Such equilibria cannot occur for glycosides and for this reason we have studied aqueous solutions at 25 of methyl α-D-xylopyranoside (αMeXyl*p*, **1**), methyl α-D-glucopyranoside (αMeGlc*p*, **2**), methyl α-D-mannopyranoside (αMeMan*p*, **3**), and methyl α-D-galactopyranoside (αMeGal*p*, **4**). The data are compared with those for the corresponding monosaccharides and other sugars, and with the other physicochemical properties of these solutions.



1 2 3 4

EXPERIMENTAL

Materials. — Each glycoside (Sigma products) was crystallised from aqueous ethanol to constant m.p., and dried *in vacuo* at room temperature. The solutions for study were freshly prepared by weight using doubly distilled and degassed water, and protected from bacterial contaminations.

The heats of dilution $\Delta H^{dil}(m_i \rightarrow m)$, from the initial ($m_i$) to the final molality (m), were determined[10] at 25 ±0.02° using an LKB 2107-112 batch microcalorimeter. The experimental heat Q, given by the integration and normalisation of the thermogram, was converted into the heat of dilution ΔH^{dil} (reported as J . kg^{-1} of solvent in the final solution) by the relation:

$$-Q/w = \Delta H^{dil}(m_i \rightarrow m), \tag{2}$$

where w is the total number of kilograms of solvent. For αMeGlc*p*, an LKB 10700-1 flow microcalorimeter was used[9]. The values of ΔH^{dil} were obtained, in this case, from the total mass flow-rate P_w of water:

$$\Delta H^{dil}(m_i \rightarrow m) = -(dQ/dt)/P_w, \tag{3}$$

and dQ/dt was evaluated from the instrumental deviations, normalised by electrical calibrations for each set of runs. The reproducibility of the data obtained by the two techniques was established as in previous work[9].

RESULTS

The enthalpic coefficients are obtained by the interpolation of the heats of dilution as follows[9,17]:

$$(1/m)\Delta H^{dil}(m_i \rightarrow m) = (1/m)H^E(m) - (1/m_i)H^E(m_i) =$$
$$= h_{xx}(m - m_i) + h_{xxx}(m^2 - m_i^2) + \cdots \tag{4}$$

TABLE I

HEATS OF DILUTION IN WATER OF METHYL α-D-XYLOPYRANOSIDE (**1**) AT 25°

m_i	m	$-\Delta H^{dil}/m$ ($J.mol^{-1}$)
1.3779	0.4156	1018.2
1.3779	0.8682	533.4
1.3315	0.8275	528.1
1.0029	0.3153	735.5
1.0029	0.6658	354.1
0.8682	0.2777	644.3
0.8275	0.5491	295.3
0.6658	0.1883	529.2
0.6658	0.4344	251.6
0.3824	0.0557	357.2
0.3824	0.2497	147.5
0.2782	0.1677	125.1

TABLE II

HEATS OF DILUTION IN WATER OF METHYL α-D-GALACTOPYRANOSIDE (**4**) AT 25°

m_i	m	$-\Delta H^{dil}/m$ ($J.mol^{-1}$)
1.3991	0.4124	806.0
1.3991	0.8661	426.2
1.3763	0.4048	788.8
1.3763	0.6959	562.2
1.3763	0.8446	438.5
1.3763	0.9636	332.9
0.9636	0.6597	252.2
0.8661	0.2732	500.5
0.8446	0.2545	518.3
0.8446	0.5004	293.5
0.6959	0.3394	307.5
0.5104	0.2199	248.9
0.4124	0.2683	124.3
0.3954	0.1186	245.6
0.3954	0.2496	127.1
0.3070	0.0788	199.3

The degree of the interpolating polynomial was chosen so that the highest coefficients still exceeded their own 95% confidence limit. According to this criterion only, values of h_{xxx} significant in the explored molality range were found in some cases. The heats of dilution, as a function of the initial and final molalities, are given in Tables I–IV. The coefficients obtained by the interpolation of Eq. *4* are reported in Table V, together with their 95% confidence limits, and compared with the values of the virial

TABLE III

HEATS OF DILUTION IN WATER OF METHYL α-D-GLUCOPYRANOSIDE (2) AT 25

m_i	m	$-\Delta H^{dil}/m$ ($J.mol^{-1}$)
0.9121	0.7719	144.9
0.9121	0.7383	197.6
0.7719	0.6543	127.8
0.7383	0.5919	166.4
0.7383	0.5919	165.4
0.6543	0 5559	104.0
0.6367	0.5376	108.3
0.6183	0.1205	511.1
0.5919	0.4810	131.4
0.5752	0.1126	476 7
0.5559	0.4732	87.0
0.4810	0.3918	103.9
0.4767	0.3736	123.3
0.4767	0.0942	447 4
0.4732	0.4034	75.3
0.4034	0.3449	64.5
0.3982	0.2191	244.1
0.3617	0.0723	334.0
0.3449	0.0807	288.4
0.3449	0.1295	205.8
0.2027	0.0413	211.9
0.1964	0.0400	178.2
0.1933	0.0394	199 0

TABLE IV

HEATS OF DILUTION IN WATER OF METHYL α-D-MANNOPYRANOSIDE (3) AT 25

m_i	m	$-\Delta H^{dil}/m$ ($J.mol^{-1}$)
1.3702	0.4158	973.2
1.3702	0.8401	516.0
0.9982	0.3033	745 1
0.9971	0.3083	740.0
0.9971	0.6338	370.8
0.8401	0.5244	333.8
0.6338	0.1939	496.1
0.6338	0.3986	258.6
0.4158	0.1310	320.7
0.4158	0.2706	163.8
0.3083	0.1017	237.4
0.3083	0.1997	127.4
0.3033	0.1950	125.9

TABLE V

COEFFICIENTS OF THE VIRIAL EXPANSION OF THE EXCESS ENTHALPIES AND THEIR 95% CONFIDENCE LIMITS FOR AQUEOUS SOLUTIONS OF SOME MONOSACCHARIDES AND THEIR METHYL α-GLYCOSIDES AT 25°

Compound	h_{xx}[a]	h_{xxx}[b]	*Anomeric form (%)*	*Orientation of non-hydrogen substituents*[f]
αMeMan*p*	1206 ±14	−105 ±10	100	1*a*2*a*3*e*4*e*5*e*
αMeXyl*p*	1126 ±5	−38 ±3	100	1*a*2*e*3*e*4*e*—
αMeGlc*p*	1097 ±39	—	100	1*a*2*e*3*e*4*e*5*e*
αMeGal*p*	900 ±25	−42 ±14	100	1*a*2*e*3*e*4*a*5*e*
α-D-Glucose	343 ±10[c]	−13[c]	~36	1*a*2*e*3*e*4*e*5*e*
β-D-Glucose			~64	1*e*2*e*3*e*4*e*5*e*
α-D-Xylose	339 ±16[d,e]	−19 ±3[d,e]	~33	1*a*2*e*3*e*4*e*—
β-D-Xylose			~67	1*e*2*e*3*e*4*e*—
α-D-Mannose	207 ±14[d]	−14 ±5[d]	~67	1*a*2*a*3*e*4*e*5*e*
β-D-Mannose			~33	1*e*2*a*3*e*4*e*5*e*
α-D-Galactose	133 ±8[d]	—	~27	1*a*2*e*3*e*4*a*5*e*
β-D-Galactose			~73	1*e*2*e*3*e*4*a*5*e*

[a] J.mol^{-1} (mol.kg^{-1})$^{-1}$. [b] J.mol^{-1} (mol.kg^{-1})$^{-2}$. [c] Ref. 14. [d] Ref. 9. [e] h_{xx} = 336 for L-xylose[11]. [f] All of these compounds assume the $^4C_1$ conformation[4]. The reported pairs of axial substituents lie on opposite sides of the ring.

coefficients for the corresponding monosaccharides. It is seen that the methyl aldopyranosides have values of h_{xx} much larger than those of the monosaccharides, and that the sequence of the h_{xx} values of the monosaccharides is maintained by the methyl α-aldopyranosides with the exception of αMeMan*p*. Galactose and αMeGal*p* have the smallest values of h_{xx} in the respective groups; xylose and glucose, as αMeXyl*p* and αMeGlc*p*, have similar values of h_{xx}. The value of h_{xx} for mannose is intermediate between that of galactose and those of the other two sugars, whereas the value for αMeMan*p* is somewhat larger than those of αMeXyl*p* and αMeGlc*p* (mannose, of the foregoing sugars, is the only one in which the α-pyranoid form preponderates, see Table V). The parallelism between the excess properties of the monosaccharides and those of the methyl glycosides suggests that these properties depend on the stereochemistry of the solutes, not on the shifts of the anomeric equilibria at varying concentrations.

DISCUSSION

The enthalpic pair-interaction coefficients for the four methyl aldopyranosides examined are positive. An old value[18] for αMeGlc*p* and preliminary data from our laboratory for the other solutes[11] demonstrate also that the corresponding free-energy coefficients g_{xx} are positive or at least zero, as for other sugars[9-12], and that $h_{xx} \geqslant Ts_{xx} > 0$.

The methylation of only one hydroxyl group is not enough to change completely the hydrophilic character. The saccharides show an inversion of the signs of the three reported coefficients as compared to the urea-like hydrophilic solutes[16]. For this reason, we recently proposed the classification of non-electrolytes in water according to the sign and the relative values of these coefficients, making a distinction between hydrophobic, hydrophilic sucrose-like, and hydrophilic urea-like solutes[16]. The self-associating solutes undergoing strong interactions (stacking, complexation, *etc.*) differ from the last ones essentially because their g_{xx} coefficients (and h_{xx} too) have negative but very large values, 10^4–10^5 or more, instead of 10^2–10^3 J mol^{-1} (mol . kg^{-1})$^{-1}$. The positive sign of the g_{xx} coefficients suggests that no favourable interactions occur for pairs of hydrated methyl pyranoside molecules. The solute solute interactions are probably prevented by the more favourable solute–solvent interactions, as for the sugars. This characteristic of aqueous solutions of simple saccharides presumably can explain why they do not crystallise easily from water, but often form supersaturated solutions[19,20].

The hydrophilic, sucrose-like solutes show excess enthalpies and entropies comparable (for the signs and values) with those of the hydrophobic solutes in water (alcohols, alkylamides, alkylureas, ketones, ethers, *etc.*). As with the hydrophobic solutes, this suggests that, at increasing concentration, some processes occur that are opposite to the perturbations induced by the solute in the infinitely dilute solution. The water molecules could return from a more "structured" state to the bulk state, richer in enthalpy and entropy. This return will be due only to the partition of water between the bulk and the cospheres surrounding the solute molecules. (For hydrophobic solutes, a further process, namely an overlap of the cospheres, has been suggested[13,15]; this should be the cause of the negative sign of g_{xx}, which differentiates these compounds from the sugars.) We have discussed[9] in detail the indications favouring this hypothesis. In particular, the Raman data suggest that, in aqueous solutions of sucrose, the hydrogen bonds increase in number, rather than in intensity, in comparison with pure water[21].

According to the preceding hypothesis, the values of the pair-interaction coefficients g_{xx} and of their enthalpic part h_{xx} will probably depend on the quantity of water released into the bulk, on the extent of the changes in the energy and degrees of freedom experienced by these water molecules, and on the kind and extent of the hydration. In fact, the values of h_{xx} seem to increase primarily with hydrophobic substitution [*cf.* the values of 700 and 450–600 J . mol^{-1} (mol . kg^{-1})$^{-1}$, respectively, for the 6-deoxy and 2-deoxy derivatives[10,12]]. Further, there is a correlation with the specific hydrophilic hydration[19], which in turn depends on the stereochemistry and conformation of the solute.

It must be emphasised that the various polar groups have different affinities for water, and it is possible to distinguish the anomeric, more acidic, hydroxyl groups from other hydroxyl groups (all acting as both donors and acceptors of hydrogen bonds) and the ring oxygen atom. Moreover, the reciprocal distances and orientations of these groups are important in the simultaneous, co-operative interactions of two

or more of them with one or more water molecules. A hypothesis for rationalising some properties of the sugars is based on correlations between pairs of alternate, equatorial hydroxyl groups, the distances and reciprocal orientations of which correspond to those of the same two groups in a tetrahedral arrangement of water molecules[2]. The O–O distances of these hydroxyl groups fall in the range 0.451–0.528 nm, which determines the limits of the second peak in the radial distribution function of liquid water at 25°. A pair of these hydroxyl groups could induce the formation of a ring structure involving three water molecules (two from the first shell, one from the second). The equatorial hydroxymethyl group of the hexopyranoses can also be involved in some of these interactions (*cf.* Fig. 2 of ref. 2). The possibility of forming these labile structures is drastically reduced if HO-4 is axial, as in D-galactose. In Table V, the sequences of all the equatorial and axial non-hydrogen substituents in the $^4C_1$ pyranose conformations (assumed by these compounds in aqueous solutions) are reported, together with percentages of α and β anomers.

However, the number of equatorial hydroxyl groups does not explain the differences among the isomers. Thus, D-mannose, and the sterically related pentose D-lyxose[12], having two axial hydroxyl groups in the $^4C_1$ form of the α anomers, have values of h_{xx} intermediate between those of D-glucose and D-xylose and those of D-galactose and its sterically related pentose L-arabinose[9,11], the α anomers of which have only one axial hydroxyl group in the $^4C_1$ form. For the methyl α-aldopyranosides, however, the stereochemistry at C-1 is fixed and the value of h_{xx} for αMeMan*p* is larger than those of αMeXyl*p* and αMeGlc*p*. This fact suggests that the axial HO-2 in αMeMan*p* does not disturb the hydration, and it can be considered in the same way as an equatorial hydroxyl group concerning the effects on the thermodynamic properties (see also the values of the limiting properties[5,6,15,19]).

The data for mannose and sterically similar compounds suggest that the hydration models must be treated on a more-rigorous theoretical basis. Specific solute–solvent interactions could characterise mannose and its derivatives, making them more similar to glucose and related sugars than to galactose and its derivatives. In particular, steric correlations between the axial hydroxyl group and the other oxygen atoms must play a role. We conclude that the differences in the excess thermodynamic properties of the stereoisomers depend on the differences in the specific, solute–solvent co-operative interactions. These determine the small differences in the stability of the bonded water molecules and the possibility of forming a large number of labile solvent-aggregates, without relevant orientational distortions. The more extended are these "structures", the longer is the time during which water remains involved in a network of interactions. Hence, the changes of enthalpy and entropy will be larger (and positive) when, at increasing concentration, these structures will be diminished.

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