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Inclusion compounds in water: calorimetric and spectroscopic studies of the interaction of cyclomaltohexaose (α-cyclodextrin) with alkanols at 25°

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ABSTRACT

A study of the interaction in water of some alkanols and alkanediols with cyclomaltohexaose (α-cyclodextrin, αCD), by calorimetry and ^{1}H-n.m.r. spectroscopy at 25°, indicates that the alkyl chains are included in the cavity of αCD, that 1:1 complexes are formed, and that the formation constants and enthalpies are markedly dependent on the number and position of the hydroxyl groups in the chain. For α,ω-alkanediols, the interaction is more complex than a simple inclusion.

INTRODUCTION

Cyclomalto-oligosaccharides (cyclodextrins, CDs) can interact, in solution or in the solid state, with various organic compounds[1,2] to form complexes that have technological, pharmaceutical, and biological applications[3]. However, several aspects of the forces involved in this interaction still need to be clarified[4,5]. It is important to know the changes in the hydration cospheres of the interacting substances, the role of the conformational changes of the CD during complexation, and the kinetics of the inclusion processes.

In the solid state, the smallest of the cyclodextrins, cyclomaltohexaose (αCD), has two molecules of water in the cavity, hydrogen-bonded to each other and to two glucopyranose residues[6]. When an inclusion complex is formed, these water molecules are displaced and the conformation of the αCD relaxes[7]. In turn, the guest molecule may be included in the cavity with modification of the solvent in its hydration cosphere.

We have studied binary, aqueous solutions of αCD[8] and the interaction with normal and branched alcohols[8], alkylureas[9], amino acids[10,11], and other organic molecules[12,13]. We now report on the interaction of αCD with 1-, 2-, and 3-pentanol, 1-, 2-, and 3-hexanol, 4-heptanol, 1,2- and 1,3-propanediol, 1,2- and 1,4-butanediol, 1,2- and 1,5-pentanediol, 1,2-, 1,6-, 1,5-, and 2,5-hexanediol, using calorimetry and ^{1}H-n.m.r. spectroscopy at 25°.

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EXPERIMENTAL

Materials. — αCD (Sigma) was dried under vacuum at 70° for 3 h. The alkanols employed (Aldrich) were of the highest purity available commercially and were used without further purification. Solutions were prepared freshly by weight, using doubly distilled water. The concentration of αCD was determined from the reported $[\alpha]_D$ value[3].

Calorimetry.— An LKB 10700-1 flow microcalorimeter was used at 25°. The values of the experimental heats were obtained from

$$\Delta H = -(\mathrm{d}Q/\mathrm{d}t)/P_w, \qquad (1)$$

where $\mathrm{d}Q/\mathrm{d}t$ is the heat flux and P_w is the total mass-flow rate of the water through the calorimeter. Details of the calorimetric experiments have been reported extensively[8–10,14–19].

Quantitative n.m.r. spectroscopy. — Solutions of αCD (5×10^{-3}–13×10^{-2}M), in the presence of a constant concentration of alkanol (2×10^{-3}M for the C_3 and C_4 alkanols, 5×10^{-3}M for C_4 and C_5 alkanols), were prepared in D_2O (Carlo Erba, 99.8% isotopic purity).

Spectra were recorded with a Bruker WH-400 spectrometer. The HDO signal was pre-irradiated in order to reduce the intensity of its signal. Chemical shifts of the resonances of the probe protons were obtained from the spectra of the alkanols in solution in D_2O prior to, and after, the addition of αCD. The resulting changes in chemical shift and the extrapolated values to infinite concentration of αCD were used to evaluate the association constant.

Treatment of the data. — The enthalpy of formation of a 1:1 complex (αCD-L) between αCD and a guest molecule (L) or, in general, the enthalpy of interaction between solutes[20] (ΔH^*) is related to the heat of mixing of two binary solutions (ΔH^{mix}) and to the heats of dilution experienced by the two solutes x and y, (ΔH^{dil}), as follows[14].

$$\Delta H^* = \Delta H^{\mathrm{mix}}[(m_{ix})\,(m_{iy}) \rightarrow (m_x, m_y)] - \Delta H^{\mathrm{dil}}(m_{ix} \rightarrow m_x) - \Delta H^{\mathrm{dil}}\,(m_{iy} \rightarrow m_y). \qquad (2)$$

The values of the heats of dilution of the binary aqueous solutions were calculated from

$$(1/m)\,\Delta H^{\mathrm{dil}}\,(m_i \rightarrow m) = h_{xx}(m - m_i) + h_{xxx}(m^2 - m_i^2) + \ldots, \qquad (3)$$

where ΔH^{dil} (J per kg of solvent in the final solution) is the heat of dilution from the initial (m_i) to the final (m) molality. Knowledge of the coefficients of Eq. *3* is necessary in order to determine the contributions to the total changes in enthalpy from the dilution of each of the solutes during the mixing of the two binary solutions.

The standard molar enthalpy of inclusion (ΔH°_I) of the guest molecule is obtained from the relation

$$\Delta H^\circ_I = \Delta H^*/m_{\alpha\mathrm{CD\text{-}L}}, \qquad (4)$$

where $m_{x\mathrm{CD}\cdot\mathrm{L}}$ is the aquomolality of the adduct formed. In the presence of a large excess of the guest molecule $m_{x\mathrm{CD}\cdot\mathrm{L}} \rightarrow m_{x\mathrm{CD}}$, and at saturation,

$$\Delta H^{\circ}_{\mathrm{I}} = (\Delta H^{*}/m_{x\mathrm{CD}})_{\mathrm{sat}}. \tag{5}$$

ΔH^{*}, normalised for the total molality ($m_{x\mathrm{CD}}$), can be related to the actual molality of the guest molecule ($m^{\mathrm{f}}_{\mathrm{L}}$), to the saturation value of ΔH^{*}, and to the apparent association constant (K'_{I}) through the relationship[21]

$$\frac{m_{x\mathrm{CD}}}{\Delta H^{*}} = \frac{1}{\Delta H^{\circ}_{\mathrm{I}}} + \frac{1}{\Delta H^{\circ}_{\mathrm{I}} K'_{\mathrm{I}} m^{\mathrm{f}}_{\mathrm{L}}}. \tag{6}$$

For each value of ΔH^{*}, the concentration of the guest molecule is given by

$$m^{\mathrm{f}}_{\mathrm{L}} = m_{\mathrm{L}} - [\Delta H^{*}/\Delta H^{*}(\mathrm{sat})]m_{x\mathrm{CD}}, \tag{7}$$

where m_{L} is the total stoichiometric molality of the guest. $\Delta H^{\circ}_{\mathrm{I}}$ and K'_{I} are obtained from Eqs. *3* and *7* by an iterative least-squares method. The condition of best fit was assumed to be achieved when the difference between two successive values of $\Delta H^{\circ}_{\mathrm{I}}$ was $<2\%$. The values of $\Delta G^{\circ}_{\mathrm{I}}{}'$ and $T\Delta S^{\circ}_{\mathrm{I}}{}'$ were then obtained from the usual relations

$$\Delta G^{\circ}_{\mathrm{I}}{}' = -RT\ln K'_{\mathrm{I}} \text{ and } T\Delta S^{\circ}_{\mathrm{I}}{}' = \Delta H^{\circ}_{\mathrm{I}} - \Delta G^{\circ}_{\mathrm{I}}{}'. \tag{8}$$

In the absence of any information about the activity coefficients, only an apparent constant can be determined.

For some systems, equilibrium constants were also evaluated using the change in chemical shifts of the resonances of the probe protons of the alkanols in relation to that of the signal for HDO. For a titration carried out at constant concentration of alkanol (m_{L}), the observed chemical shift (δ_{o}) is given by

$$\begin{aligned}\delta_{\mathrm{o}} &= (m^{\mathrm{f}}_{\mathrm{L}}/m_{\mathrm{L}})\delta_{\mathrm{L}} + (m_{x\mathrm{CD}\cdot\mathrm{L}}/m_{\mathrm{L}})\delta^{\mathrm{sat}}_{x\mathrm{CD}\cdot\mathrm{L}} = \\ &= \delta_{\mathrm{L}} - (m_{x\mathrm{CD}\cdot\mathrm{L}}/m_{\mathrm{L}})\delta_{\mathrm{L}} + (m_{x\mathrm{CD}\cdot\mathrm{L}}/m_{\mathrm{L}})\delta^{\mathrm{sat}}_{x\mathrm{CD}\cdot\mathrm{L}},\end{aligned} \tag{9}$$

where $m^{\mathrm{f}}_{\mathrm{L}} = (m_{\mathrm{L}} - m_{x\mathrm{CD}\cdot\mathrm{L}})$ is the concentration of the free alkanol, δ_{L} is the chemical shift of the resonance of the probe proton of the alkanol in the binary solution at the same molality (m_{L}), and $\delta^{\mathrm{sat}}_{x\mathrm{CD}\cdot\mathrm{L}}$ is the chemical shift of the resonance of the probe proton in the complex at saturation. Equation *9* can be rewritten as

$$\Delta = (m_{x\mathrm{CD}\cdot\mathrm{L}}/m_{\mathrm{L}})\,\Delta_{\mathrm{o}}, \tag{10}$$

where $\Delta = (\delta_{\mathrm{o}} - \delta_{\mathrm{L}})$ and $\Delta_{\mathrm{o}} = (\delta^{\mathrm{sat}}_{x\mathrm{CD}\cdot\mathrm{L}} - \delta_{\mathrm{L}})$. Considering the equilibrium constant relative to the 1:1 complex, Eq. *10* gives

$$\Delta = \frac{K'_I m^f_{\alpha CD} \Delta_o}{1 + K'_I m^f_{\alpha CD}}, \tag{11}$$

or, in a linear form,

$$\frac{1}{\Delta} = \frac{1}{\Delta_o} + \frac{1}{K'_I m_{\alpha CD} \Delta_o} \tag{12}$$

For each value of Δ, the concentration of αCD is given by

$$m^f_{\alpha CD} = m_{\alpha CD} - (\Delta/\Delta_o)m_L, \tag{13}$$

where $m_{\alpha CD}$ is the total stoichiometric molality. The K'_I values were obtained through the same program used to process the calorimetric data.

RESULTS

Table I lists the h coefficients reported in the literature for binary aqueous solutions of αCD and of the hydroxylated compounds studied[22-25]. It was necessary to subtract the heats of dilution of the binary solutions from the heats of mixing. The h values for alkanols and alkanediols are positive, increase with increase of molecular weight, and depend on the position of hydroxyl groups.

Table II contains the thermodynamic parameters for the interaction of αCD with the alkanols and also data from the literature. The heptanols were not studied by calorimetry due to their low solubility. Hence, the association constant for 4-heptanol was determined on the basis of n.m.r. data.

Table III contains the thermodynamic parameters for the interactions of αCD with alkanediols. The ΔH°_I and K'_I values were evaluated through the iterative least-squares method (see Experimental).

In order to prove that 1:1 complexes were formed for the higher alkanols, the calorimetric experiments involved constant concentrations of αCD or of the guest molecule. The equality of the saturation enthalpies was considered as evidence of a 1:1 complex.

The enthalpies are negative and, for homologous series, they increase with increase in the length of the alkyl chain. For α,ω-alkanediols, they are higher than for 1,2-alkanediols. The association constants are largest for the higher normal alcohols and decrease when the hydroxyl group occupies a non-terminal position.

In Fig. 1, $\Delta G^\circ_I{}'$ is plotted against the total number of carbon atoms for 1-alkanols, 1,2-alkanediols, and α,ω-alkanediols. The three curves show that the affinity of the alkanols toward αCD follows the order: 1-alkanols > 1,2-alkanediols > α,ω-alkanediols. Moreover, when the upper curve reaches a plateau at n_{C_I} between 5 and 6 carbon atoms, the lowest curve, for α,ω-diols, is still rising. The difference in the abscissa between curves 1 and 2, relative to 1-alkanols and 1,2-alkanediols, respectively, corresponds almost to 1 carbon atom.

TABLE I

Values of the coefficients of the excess enthalpies of binary aqueous solutions of αCD, alkanols, and alkanediols at 25°

Solute	h_{xx}[a]	h_{xxx}[b]
αCD[8]	−3920 (65)[c]	
1-Pentanol[22]	1766 (68)	
2-Pentanol[22]	1502 (113)	1666 (543)
3-Pentanol[22]	1290 (125)	1549 (301)
1-Hexanol[22]	$\Delta H^{dil}=0$	
2-Hexanol[22]	2064 (88)	
3-Hexanol[22]	2224 (112)	
1,2-Propanediol[23]	589 (1)	6 (1)
1,3-Propanediol[23]	523 (9)	5 (2)
1,2-Butanediol[24]	923 (5)	60 (3)
1,4-Butanediol[24]	787 (2)	−8 (2)
1,2-Pentanediol[25]	1777 (30)	
1,5-Pentanediol[25]	1335 (25)	−20 (10)
1,2-Hexanediol[25]	2955 (55)	
1,6-Hexanediol[25]	2402 (35)	−65 (28)
1,5-Hexanediol[25]	1939 (68)	
2,5-Hexanediol[25]	1769 (51)	

[a] $J.kg.mol^{-2}$. [b] $J.kg^2.mol^{-3}$. [c] Figures in parentheses are the 95% confidence limits.

TABLE II

Thermodynamic parameters for the association between αCD and alkanols at 25°

Guest	K'_I[a,b]	ΔH°_I[b,c]	$\Delta G^{\circ\prime}_I$[c,d]	$T\Delta S^{\circ\prime}_I$[c,e]
1-Ethanol[8]	6.7	2.5	4.7	2.2
1-Propanol[8]	27.0	6.1	8.2	2.1
1-Butanol[8]	99.9	9.9	11.4	1.5
2-Butanol[8]	28.4	9.0	8.3	−0.7
1-Pentanol	275(15)	11.8(0.2)	13.9(0.2)	2.1(0.4)
2-Pentanol	101(8)	13.4(0.4)	11.4(0.2)	−2.0(0.6)
3-Pentanol	70(4)	12.8(0.3)	10.5(0.2)	−2.3(0.5)
1-Hexanol	379(51)	17.5(0.8)	14.7(0.3)	−2.8(1.1)
2-Hexanol	285(13)	15.5(0.2)	14.0(0.2)	−1.5(0.3)
3-Hexanol	156(24)	13.8(0.6)	12.5(0.4)	−1.3(1)
4-Heptanol	188(40)[f]		13.0(0.6)	

[a] $kg.mol^{-1}$. [b] Figures in parentheses are the standard deviations as obtained by fitting the data to equation 6. [c] $kJ.mol^{-1}$. [d] Errors are half the range of $\Delta G^{\circ}{}_I{}'$ calculated from the upper and lower error in K'_I. [e] Errors are the sum of the errors on free energy and enthalpy. [f] Association constant determined on the basis of n.m.r. data. Calorimetric measurements were not possible for the small solubility of the alkanol.

TABLE III

Thermodynamic parameters for the association between αCD and various alkanediols at 25°

Alkanediol	$K'^{a,b}_{I}$	$-\Delta H^{\circ\,b,c}_{I}$	$-\Delta G^{\circ\,\prime c,d}_{I}$	$T\Delta S^{\circ\,\prime c,e}_{I}$	K'^{f}_{sp}
1,2-Propanediol	3 (2)	2 (1)	2.7(2)	0.7(3)	
1,3-Propanediol	4.3(0.4)	6.7(0.5)	3.6(0.2)	−3.1(0.7)	7(3)
1,2-Butanediol	12.8(0.4)	7.7(0.1)	6.3(0.1)	−1.4(0.2)	
1,4-Butanediol	8 (1)	10 (1)	5.2(0.3)	−4.8(0.2)	2(3)
1,2-Pentanediol	78 (5)	11.5(0.2)	10.8(0.2)	−0.7(0.4)	
1,5-Pentanediol	31 (1)	14.3(0.3)	8.5(0.1)	−5.8(0.4)	26(9)
1,2-Hexanediol	185 (43)	14.0(0.4)	12.9(0.6)	−1.1(1)	174(68)
1,6-Hexanediol	94 (7)	16.1(0.4)	11.3(0.2)	−4.8(0.6)	
1,5-Hexanediol	35 (5)	13 (1)	8.8(0.4)	−4.2(1.4)	
2,5-Hexanediol	26 (7)	2.1(0.4)	8.1(0.7)	6 (1.1)	

[a] kg.mol^{-1}. [b] Figures in parentheses are the standard deviations as obtained by fitting the data to equation *6*. [c] kJ.mol^{-1}. [d] Errors are half the range of $\Delta G^{\circ}_{I}{}'$ calculated from the upper and lower error in K'_{I}. [e] Errors are the sum of the errors on free energy and enthalpy. [f] Association constants calculated from the n.m.r. chemical shift data.

The ^{1}H-n.m.r. spectra of solutions of αCD in D_2O at various concentrations in the presence of a constant concentration of alkanol revealed a regular and significant behaviour. The signal of the probe proton of the alkanols was shifted to higher frequencies (up to a maximum of 0.17 p.p.m. for a ratio of 20:1 for the concentrations of αCD and alkanols). Also, the resonance of H-3 of αCD was shifted to higher field (to a maximum of 0.06 p.p.m.) consistent with its position in the hydrophobic cavity of the αCD. The shifts increased in the sequences 1,2-propanediol to 1,2-hexanediol and from 1,6-hexanediol to 1,2-hexanediol. Table III contains the association constants calculated from the n.m.r. data together with those obtained by calorimetry.

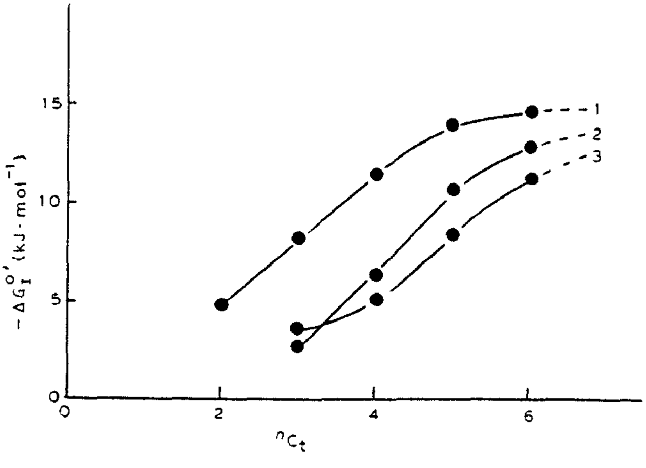

Fig. 1. Values of the free energy of inclusion versus the total number of carbon atoms (n_{C_t}) for 1-alkanols (curve 1), 1,2-alkanediols (curve 2), and α,ω-alkanediols (curve 3).

In Fig. 2, the ^{1}H-n.m.r. spectra are reported for solutions of 1,2-hexanediol in D$_2$O in the absence (*a*) and in the presence (*b*) of αCD.

DISCUSSION

The important finding is the discrimination of positional isomers of alkanols by αCD. The affinity is dependent on the length of the alkyl chain as reflected by the thermodynamic parameters for the interaction of αCD with the isomeric hexanediols. Therefore, it is important to analyse the forces that regulate the association process.

It has been inferred[8-10] that it is the alkyl chain of the guest molecule that penetrates the cavity of αCD. When the chain is short, the association is least effective since, statistically, the guest molecule is disordered in the cavity. As the length of the alkyl chain increases, the cavity is filled more effectively, and the resulting complex is characterised by larger association constants and enthalpies. In the present work, the association constants and the enthalpies for the 1-alkanols follow the order expected. The association constants follow the sequence 1- > 2- > 3-alkanol. The data in Table II

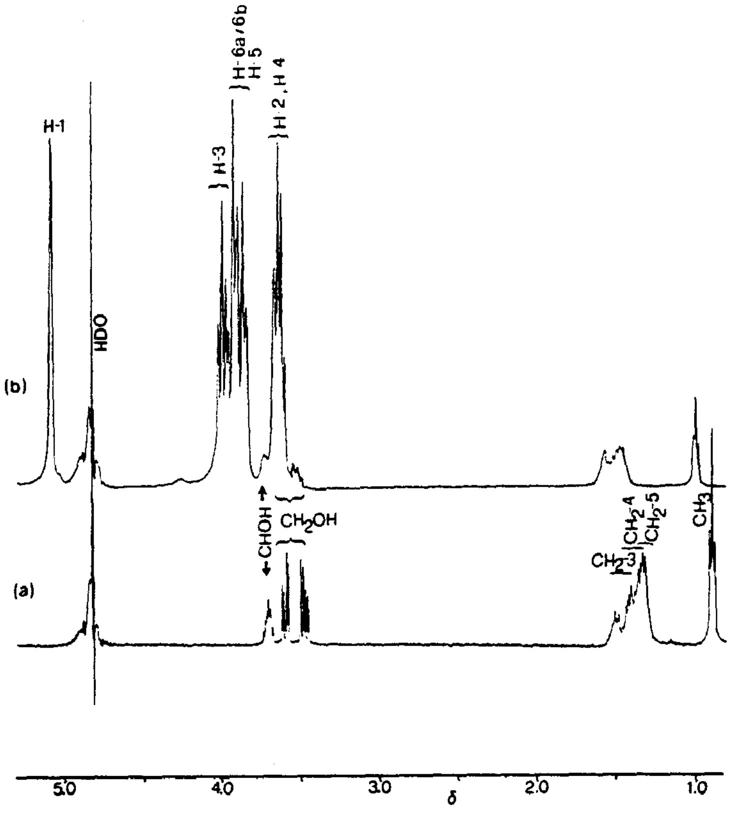

Fig. 2. ^{1}H-N.m.r. spectra (400 MHz) of 1,2-hexanediol (1.4 × 10^{-2}M) (*a*) and in the presence of αCD (4.0 × 10^{-2}M) (*b*) in D$_2$O at 25°.

show that the association constants of the 2-alkanols are equal to those of the corresponding 1-alkanols that have one carbon atom less, which indicates that the association with αCD involves primarily the free and longer alkyl chains. The hydroxyl group prevents the remainder of the molecule from penetrating the cavity. For the 3-alkanols and 4-heptanol, the values of the association constants are not equal to those of the normal alcohols with two less carbon atoms. In fact, they are consistently larger and reflect an increased probability of association[26] due to the presence of two alkyl residues in each alkanol molecule. For the 2-alkanols, the interaction of the methyl group with αCD is weak[8] and does not affect the association constant which is determined by the longer alkyl chain.

1,2-Alkanediols have almost the same free energy values as the corresponding 1-alkanols that have one carbon atom less (Fig. 1, and Tables II and III). The mechanisms of interaction for these two classes of substances must be similar, namely, more effective inclusion as the length of the alkyl chain increases, leaving the primary hydroxyl group of the 1,2-diols outside the cavity. The interaction of αCD with α,ω-diols is more complex. The formation of a complex by penetration of one of the terminal hydroxyl groups into the cavity is unlikely. The smaller values of the association constants, the higher values of the enthalpies, and the negative and constantly larger entropies for the 1,2-diols can be explained in terms of an interaction that involves mainly the exterior of the αCD. Probably, the molecule of an α,ω-diol caps the αCD with the alkyl chain pointing towards the cavity and the hydroxyl groups hydrogen-bonded to two primary hydroxyl groups on the exterior of the αCD. The association constants become larger as the alkyl chain becomes longer, probably due to improved hydrophobic interactions within the cavity. This capping of αCD is similar to that found for the interaction of these macrocycles with other bifunctional compounds[27].

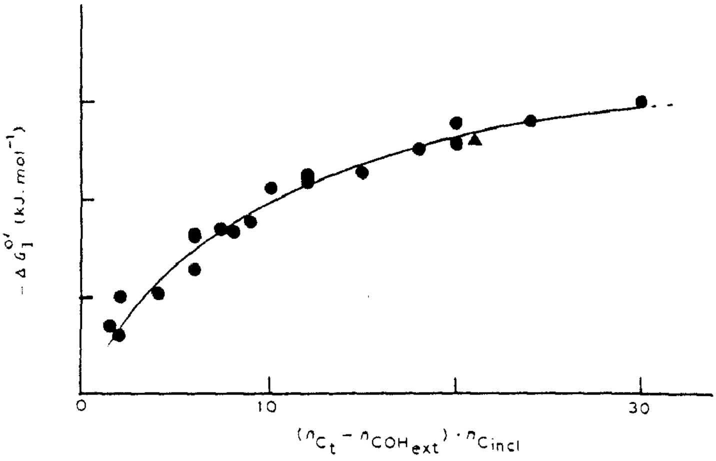

Fig. 3. Plot of the free energy of inclusion (ΔG°_{I}) against $(n_{C_t} - n_{COH_{ext}})\cdot n_{C_{incl}}$, where n_{C_t} is the total number of carbon atoms, $n_{COH_{ext}}$ is the number of carbon atoms that bear hydroxyl groups, and $n_{C_{incl}}$ is the number of carbon atoms included in the cavity. For α,ω-diols, 1,5-hexanediol, and 2,5-hexanediol, $n_{C_{incl}}$ was considered to be half of the chain between the hydroxyl groups.

On the basis that it is the length of the alkyl chain which regulates the formation of the complexes with αCD in aqueous solutions, a unifying representation was attempted. In Fig. 3, $\Delta G^{\circ}{}_{\mathrm{I}}{}'$ is plotted against $(n_{\mathrm{C_t}} - n_{\mathrm{COH_{ext}}}) \cdot n_{\mathrm{C_{incl}}}$, which shows the effects of the total number of carbon atoms ($n_{\mathrm{C_t}}$), the number of carbon atoms ($n_{\mathrm{COH_{ext}}}$) that bear hydroxyl groups which are left outside the cavity, and the number of carbon atoms ($n_{\mathrm{C_{incl}}}$) in the alkyl chain in the 1-alkanols and 1,2-alkanediols or the alkyl chain between the hydroxyl groups in α,ω-diols. The free energies of inclusion of all of these systems fall on the same curve (only half of the number of carbon atoms in the alkyl chain between the hydroxyl groups of α,ω-diols and of 1,5- and 2,5-hexanediol are considered). The validity of this assumption is further evidence that, for these compounds, the alkyl chain bends in order to be included in the cavity of the αCD. The above plot is useful for discriminating between 1,2- and α,ω-alkanediols that have the same number of carbon atoms. In fact, it permits the hydroxyl groups of the 1,2-diols to be distinguished since the most external hydroxyl group does not participate in the inclusion process. Moreover, the dependence on $n_{\mathrm{C_t}}$ reflects the probability of association through both the alkyl groups.

An analogous representation for the enthalpies is reported in Fig. 4. The values of $\Delta H^{\circ}{}_{\mathrm{I}}$ for all the systems fall on the lower curve with the exception of those for the α,ω-diols and 1,5-hexanediol, which are described by the upper curve. For these latter compounds, the involvement of both the hydroxyl groups in hydrogen bonding with the exterior of the αCD could be responsible for the higher values of $\Delta H^{\circ}{}_{\mathrm{I}}$. 2,5-Hexanediol is markedly outside the two trends, probably because the two terminal methyl groups sterically hinder the interaction of the hydroxyl groups with the αCD. The $\Delta H^{\circ}{}_{\mathrm{I}}$ that characterises the formation of these inclusion complexes is negative and small, as for most of the complexes reported in the literature[28]. It is the sum of several and contrasting effects that are determined primarily by the changes of water during the interaction process. For αCD, water molecules in the cavity are displaced to the bulk, whereas there

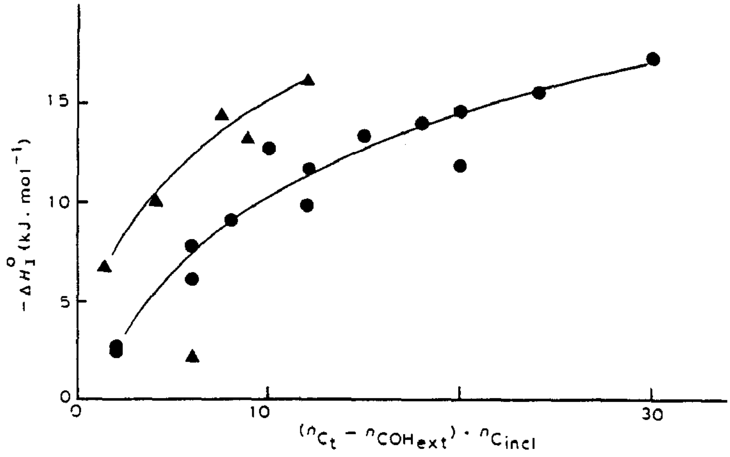

Fig. 4. Plot of the enthalpies of inclusion ($\Delta H^{\circ}{}_{\mathrm{I}}$) against $(n_{\mathrm{C_t}} - n_{\mathrm{COH_{ext}}}) \cdot n_{\mathrm{C_{incl}}}$ for α,ω-diols (upper curve) and for alkanols and alkanediols (lower curve). The isolated point on the bottom of the figure refers to 2,5-hexanediol; $n_{\mathrm{C_t}}$, $n_{\mathrm{COH_{ext}}}$, and $n_{\mathrm{C_{incl}}}$ are as defined in Fig. 3.

are rearrangements in the external hydration cosphere. At the same time, the hydration shell of the hydrophobic part of the guest molecule loses some water molecules on entering the cavity. These two effects are endothermic. However, the reconstitution of the hydration shell of the complex, dipole-induced dipole and "host–guest" interactions, hydrogen bonds, and the decrease in energy when a hydrophobic residue fills the cavity make the value of the enthalpy negative. The role of water is also indicated by the observation that the association constant depends on the hydration of the guest molecule. In fact, $\Delta G^{\circ}{}_{\mathrm{I}}{}'$ varies with the values of the limiting partial molal volume $(\bar{V}^{\circ}_{\mathrm{X}})$ of the guest molecule[29], in a manner similar to that reported in Fig. 1, again indicating that 1-alkanols interact the most effectively with αCD.

The results obtained by ^{1}H-n.m.r. spectroscopy accord with those obtained by calorimetry. The magnitude of the shifts to higher frequencies of the resonances of the probe proton of each alkanol, and of that of αCD, suggests mutual deshielding[5,30,31]. In each complex, the aliphatic part of the alkanols is included in the hydrophobic cavity of αCD and the interaction strengthens progressively on going from the propanols to the hexanols. However, differently from the 1,2-diols, the n.m.r. spectra of the aliphatic protons of α,ω-diols changed as the concentration of αCD was increased, consistent with a change in the conformation of the alkanol. This finding supports the hypothesis of capping of the αCD cavity by the aliphatic chain which is bent to point towards the interior.

Thus, there are several effects involved in the formation of these complexes. Hydrophobic interactions do not always play the major role, as evidenced by the positive or negative values of the entropies. There is an enthalpy–entropy compensation[32,33], a phenomenon frequently observed in water, and ascribed to the modifications experienced by the solvent in the hydration cospheres of the interacting substances. This compensation leads to the same free energy for different compounds, even though the enthalpies and entropies are different (see the data for the 1- and 2-alkanols). This means that the affinities are determined primarily by the contributions of the parts that are included in the cavity, whereas the other parts of the molecules affect only the enthalpies and entropies.

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