

Enthalpy and entropy changes on molecular inclusion of 1-heptanol into α - and β -cyclodextrin cavities in aqueous solutions

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Abstract

The enthalpies of transfer of 1-heptanol from aqueous to aqueous α - or β -cyclodextrin (CD) solutions have been determined by microcalorimetry at various mole fractions at 298.15 K. 1-Heptanol greatly stabilized in enthalpy in an α -CD cavity, accompanying a large entropy decrease. On the other hand, the enthalpy changes on inclusion into a β -CD cavity is too large and exothermic. This is the first case in a series of the system of β -CD + *n*-alkane-1-ols.

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1. Introduction

In liquid phase a vast crowd of molecules gather closely, oscillating and rotating violently. Colliding with each other, they distinguish a kind of molecules from another ones. In particular, stereospecific interactions due to neighboring surfaces may play the leading role in, e.g., enzyme–substrate reactions, antigen–antibody reactions, some kinds of mechanisms of senses of smell and taste, and so on. Therefore, elucidating the role of asymmetric intermolecular interactions owing to the stereospecific structures of molecules is really important for understanding the mechanisms of chemical and biochemical reactions.

The accumulation of accurate and quantitative values of the changes in thermodynamic functions on molecular inclusion of alcohol into the cavities of α - and β -cyclodextrins (CD) in aqueous solutions has been carried out systematically by microcalorimetry [1,2], in order to clarify the mechanisms of molecular recognition and discrimination in aqueous solutions.

In this paper, the thermodynamic functions were determined systematically for the molecular inclusion of

1-heptanol into α - and β -CD cavities in aqueous solutions in order to know the existence of any correlation between the molar enthalpy and entropy of inclusion and the number of carbon atoms in *n*-alkane-1-ols.

2. Experimental

2.1. Materials

1-Heptanol (GR grade, Kishida Chemical Co.) was fractionally distilled over freshly activated molecular sieves 4A through a spinning-band column under reduced pressure. The coulometric Karl Fischer's method on a Mitsubishi Moisture Meter model CA-02 gave the water content of the 1-heptanol to be 0.002 mass%.

Details of the careful purification used for the α -CD [3], β -CD [4], water [5] and mercury [6] were described earlier. The mercury used was freshly distilled in vacuo before each measurement. All solutions were prepared by mass.

2.2. Apparatus and procedures

A rocking twin-microcalorimeter of a heat-conduction type, laboratory designation RMC, was used for the determination of enthalpies of dilution and mixing. All the measurements were carried out at 298.15 K under the atmospheric

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Table 1

Experimental enthalpies of dilution $\Delta_{\text{dil}}H$ of dilute aqueous 1-heptanol solutions with water at 298.15 K

$10^6 n_3$ (mol)	$10^5 x_i$	$10^5 x_f$	$-\Delta_{\text{dil}}H$ (mJ)	$\delta(\Delta_{\text{dil}}H)^a$ (mJ)
2.4732	6.007	1.192	3.3 ₈	0.05
2.4730	6.007	1.378	3.0 ₅	0.3
2.4568	6.007	1.187	3.5 ₂	-0.1
2.4306	6.007	1.180	2.8 ₇	0.5
2.3686	6.007	1.168	4.0 ₆	-0.8
2.0542	4.941	0.9838	2.0 ₅	-0.1
1.8147	4.324	0.8146	1.3 ₀	0.02
1.6904	4.061	0.8090	1.3 ₀	-0.2
1.6517	4.032	0.8104	0.6 ₂	0.4
0.3833 ₂	0.9264	0.1847	0.2 ₈	-0.3
0.2621 ₁	0.6312	0.1259	0.2 ₇	-0.3
0.0782 ₃	0.1946	0.03823	0.02 ₉	-0.03

^a Difference from the smoothed values.

pressure. Enthalpy changes were measured automatically with an online system described elsewhere [7]. Details of the apparatus and procedures, including the mixing vessels [8], are similar to those described previously [9].

3. Results and discussion

3.1. Enthalpy of dilution

The experimental results for the enthalpy changes on diluting the dilute aqueous 1-heptanol solutions ranging from 1.9×10^{-6} to 6.0×10^{-5} in mole fraction to final solutions from 3.8×10^{-7} to 1.2×10^{-5} at 298.15 K under the atmospheric pressure are given in Table 1, where n_3 denotes the amount of 1-heptanol in the solutions and x_i and x_f , respectively, are the mole fractions before and after the dilution.

Table 2

Parameters a and b and the calculated standard deviations of the fit s_f for least-squares representation by equation of $\Delta_{\text{dil}}H_m$ for dilute aqueous solutions of alcohols at 298.15 K

Alcohol	a (kJ mol ⁻¹)	b (kJ mol ⁻¹)	s_f (mJ)
1-Heptanol	-752	-3.89×10^8	0.39

The results were fitted to Eq. (1) by the least-squares calculation:

$$\Delta_{\text{dil}}H = an_3(x_i - x_f) + bn_3(x_i^2 - x_f^2) + \dots \quad (1)$$

The best-fit values for the parameters in Eq. (1) are listed in Table 2, as well as the calculated standard deviation of the fit s_f . The last column of Table 1 shows the differences in $\Delta_{\text{dil}}H$ between the experimental results and the corresponding smoothed values. The molar enthalpy of dilution of aqueous 1-heptanol solution having a mole fraction x to $x = 0$ can be obtained by Eq. (2) with the parameters a and b listed in Table 2:

$$\Delta_{\text{dil}}^\infty H_m = ax + bx^2 \quad (2)$$

Once the explicit expression of the Eq. (2) is obtained, the enthalpy of dilution per mole of alcohol from x_i to x_f may be calculated using the following equation:

$$\Delta_{\text{dil}}H_m = \Delta_{\text{dil}}^\infty H_m(x_i) - \Delta_{\text{dil}}^\infty H_m(x_f) \quad (3)$$

3.2. Enthalpy of transfer

The experimental enthalpies of mixing and the related quantities are summarized in Table 3. The average values of $z = (n'_1 + n''_1)/n_2$ [3,4] were $(17.1 \pm 0.9) \times 10^3$ and $(18.01 \pm 1.7) \times 10^3$, respectively, for α -CD and β -CD. The

Table 3

Experimental enthalpies of mixing $\Delta_{\text{mix}}H$ and molar enthalpies of transfer $\Delta_{\text{trf}}H_m$ of 1-heptanol from dilute aqueous solutions to dilute aqueous α - or β -cyclodextrin (CD) solutions at 298.15 K, where n'_1 , n''_1 , n_2 and n_3 represent, respectively, amounts of water in the CD solution, amounts of water in the 1-heptanol solution, amounts of CD in the aqueous solution and amounts of 1-heptanol in the aqueous solution

f^a	$10^2 n'_1$ (mol)	$10^2 n''_1$ (mol)	$10^5 n_2$ (mol)	$10^6 n_3$ (mol)	$\Delta_{\text{mix}}H$ (mol)	$\Delta_{\text{trf}}H_m$ (kJ mol ⁻¹)
H ₂ O(1) + α -CD(2) + 1-heptanol(3)						
0.0499 ₅	16.408	4.221	1.250	0.6572	-13.30	-20.20
0.1241 ₁	16.372	4.221	1.254	1.777	-36.17	-19.69
0.1316 ₁	17.428	4.276	1.202	1.821	-36.84	-19.54
0.1405 ₇	16.573	4.225	1.295	2.119	-42.84	-19.27
0.1488 ₂	16.331	4.115	1.269	2.218	-46.60	-19.91
0.1833 ₈	16.684	4.036	1.150	2.246	-44.38	-18.58
0.1862 ₉	16.674	4.112	1.172	2.682	-53.98	-18.51
0.1882 ₀	16.661	4.161	1.171	2.714	-55.82	-18.95
H ₂ O(1) + β -CD(2) + 1-heptanol(3)						
0.0434 ₅	16.506	4.091	1.099	0.4993	-3.63	-3.99
0.0575 ₆	16.320	4.136	1.087	0.6637	-4.44	-4.17
0.1034 ₂	16.337	4.095	1.088	1.255	-6.60	-3.613
0.1459 ₈	16.399	4.128	1.092	1.867	-10.76	-4.116
0.1593 ₀	16.579	4.151	1.428	2.761	-14.00	-2.954
0.1852 ₁	16.434	4.141	1.094	2.488	-12.78	-3.113

^a $f = n_3/(n_2 + n_3)$.

Table 4

Equilibrium constants for the formation of 1:1 inclusion complexes, ratios of water molecules over the cyclodextrin molecules, limiting molar enthalpies of transfer of alcohol and the limiting molar ratios y_{\max} of 1-heptanol included to the whole at 298.15 K

System	$\log_{10} K$	$10^{-4}z$	$\Delta_{\text{trf}}^{\infty} H_m$ (kJ mol ⁻¹)	y_{\max}
α -CD + 1-heptanol	4.38	1.71	-20.18	0.583
β -CD + 1-heptanol	4.23	1.81	-3.85	0.486

experimental enthalpies of transfer of 1-heptanol from dilute aqueous solutions to dilute aqueous α - or β -CD solutions determined by Eq. (4) [3,4] are also summarized in the last column of Table 3. In the calculation through Eq. (4), the enthalpy of dilution of aqueous 1-heptanol solution is

$$\Delta_{\text{trf}} H = \Delta_{\text{mix}} H - \Delta_{\text{dil}} H_{12} - \Delta_{\text{dil}} H_{13} \quad (4)$$

$\Delta_{\text{dil}} H_{13}$ was determined by Eqs. (2) and (3) with the parameters given in Table 2. Those of α -CD solution [9] and β -CD solution [4], $\Delta_{\text{dil}} H_{12}$, were obtained from our earlier papers.

By the least-squares treatment of the experimental values of $\Delta_{\text{trf}} H_m$ as a function of z and the mole fraction of 1-heptanol, $f = n_3/(n_2 + n_3)$, according to the Eq. (9) described in the earlier paper of this series [10], limiting molar enthalpies of transfer at infinite dilution, $\Delta_{\text{trf}}^{\infty} H_m$, were determined, as well as the equilibrium constants K of 1:1 inclusion complex formation and limiting ratios y_{\max} of 1-heptanol included over the total 1-heptanol in the systems at infinite dilution. These quantities thus determined are summarized in Table 4. The smoothed values of $\Delta_{\text{trf}}^{\infty} H_m$ for mean values of z are drawn in Fig. 1 against the mole fraction f .

The molar enthalpies of transfer of 1-heptanol were negative values for the both of α - and β -CD solutions.

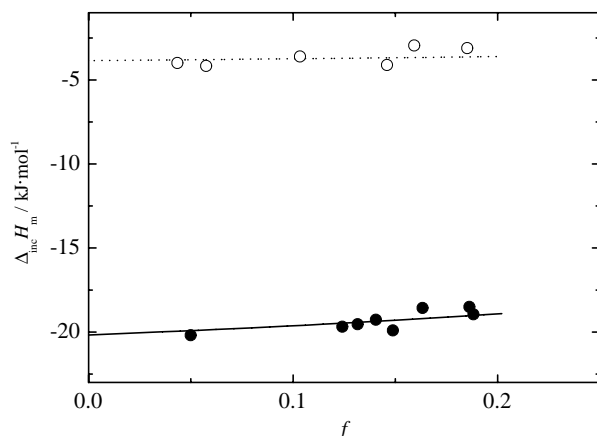


Fig. 1. Molar enthalpies of transfer of 1-heptanol from aqueous to aqueous (●) α -CD and (○) β -CD solutions at 298.15 K as a function of $f = n_3/(n_2 + n_3)$. The solid curve represents α -CD solutions. The dash-dotted curve represents β -CD solutions.

Table 5

The changes of thermodynamic functions on 1:1 inclusion of n -alkane-1-ols into α - and β -cyclodextrin cavities in dilute aqueous solutions at 298.15 K

Alcohol	$\Delta_{\text{inc}} H$ (kJ mol ⁻¹)	$\Delta_{\text{inc}} G$ (kJ mol ⁻¹)	$-T\Delta_{\text{inc}} S$ (kJ mol ⁻¹)	$\Delta_{\text{inc}} S$ (J (K mol) ⁻¹)
α -Cyclodextrin				
Methanol ^a	0	–	–	–
Ethanol ^a	-0.9	-22.0	-21.0	70.5
1-Propanol ^b	-6.6	-17.8	-11.2	37.5
1-Butanol ^b	-7.9	-22.6	-14.7	49.5
1-Pentanol ^b	-13.9	-24.4	-10.4	34.9
1-Hexanol ^b	-29.1	-22.2	6.9	-23.1
1-Heptanol	-34.6	-25.0	9.6	-32.2
β -Cyclodextrin				
Methanol ^a	0	–	–	–
Ethanol ^a	1.1	-17.8	-18.9	63.2
1-Propanol ^b	1.9	-17.5	-19.4	65.0
1-Butanol	3.0	-18.0	-21.0	70.5
1-Pentanol ^b	2.2	-22.6	-24.8	83.2
1-Hexanol ^b	0.6	-21.5	-22.1	74.1
1-Heptanol	-7.9	-24.2	-16.3	54.5

^a See [2].

^b See [1].

3.3. Enthalpy and entropy of inclusion

From the thermodynamic functions listed in Table 4, the molar enthalpies, molar Gibbs energies and molar entropies of inclusion of 1-heptanol at infinite dilution into α - and β -CD cavities in aqueous solutions at 298.15 K under the atmospheric pressure were determined and are summarized in Table 5, as well as the reported values [1,2] for the sake of comparison. The enthalpies of inclusion of 1-heptanol with α -CD are exothermic and large. Also, Hallén et al. obtained -22.8 kJ mol⁻¹ as the change in enthalpy of inclusion of 1-heptanol with α -CD in water at 298.15 K by the careful microcalorimetric titration [11]. The molar enthalpies of inclusion are plotted in Fig. 2 against the number of carbon atoms (N_C) in alcohol molecules. The molar enthalpies of

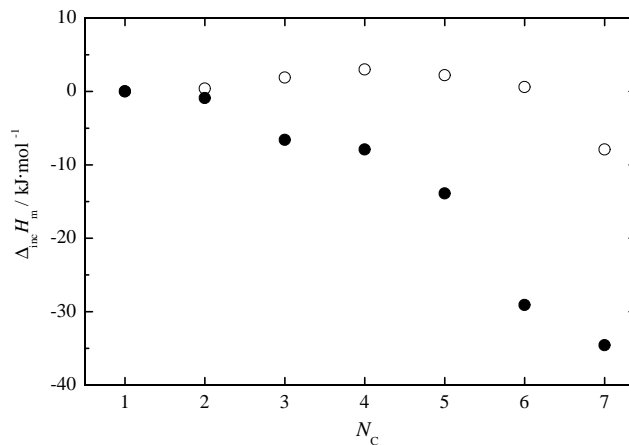


Fig. 2. Molar enthalpies of inclusion of n -alkane-1-ols into (●) α -CD and (○) β -CD cavities at 298.15 K.

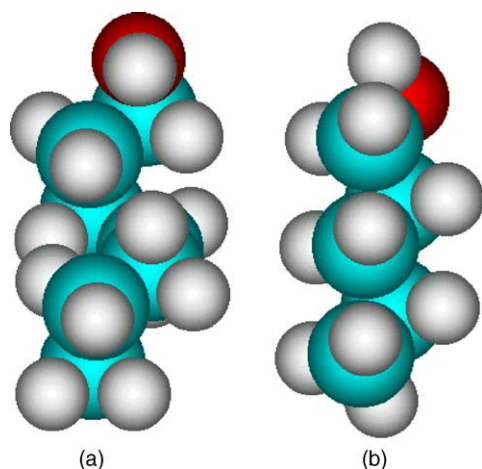


Fig. 3. Comparison of molecular shapes: (a) heptanol in gauche-gauche conformation; (b) pentanol in trans-trans conformation.

inclusion of 1-heptanol with β -CD is exothermic, whereas those for the systems of other *n*-alkane-1-ols are endothermic.

As shown in Fig. 2, heptanol molecules are stabilized largely on inclusion into α -CD cavities in aqueous solution, accompanying a large entropy decrease. To explain these situations, we proposed that heptanol molecules take gauche-gauche conformation (Fig. 3) in the cavities instead of ordinary trans-trans conformation, by inspection of the molecular fit by using molecular modeling tool [12]. Moreover, when 1-heptanol molecules take gauche-gauche conformation, OH groups are exported in water. Such conformations may result in some tight inclusion complexes in which the heptanol molecules cannot rotate around molecular axis. When a 1-heptanol molecule has a gauche-gauche conformation, its molecular length is almost equal to that of 1-pentanol having an ordinary trans-trans conformation. On the other hand, the enthalpy changes on inclusion into a β -CD cavity is too large though is exothermic. It is considered that 1-heptanol molecules take gauche-gauche conformation in a β -CD cavity; moreover, the space of the extent that 1-heptanol can rotate exists around molecular axis. Molar Gibbs energies of inclusion are plotted against N_C in Fig. 4. Fig. 4 shows that 1-heptanol molecules cannot discriminate α - and β -CDs. However, the largest stabilization in Gibbs energy is obtained by the inclusion of 1-heptanol. The stabilization has almost same value of $\Delta_{inc}G_m$ as that

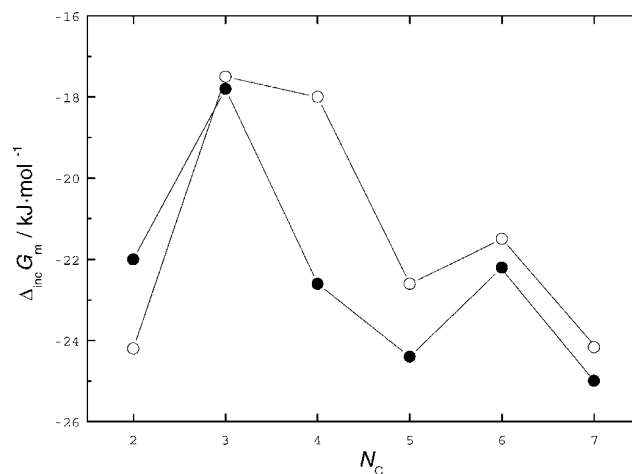


Fig. 4. Molar Gibbs energies of inclusion of *n*-alkane-1-ols into (●) α -CD and (○) β -CD cavities at 298.15 K.

of the system α -CD + 1-pentanol + H_2O . Inspection of the molecular fit by the use of molecular modeling tool showed that the best fitting was obtained for 1-heptanol with the cavity of β -CD. 1-Heptanol molecules must change their conformations to make the closest contacts with the atoms on the wall of α -CD cavities or those on the wall of β -CD cavities and the remaining water molecules in β -CD cavities. These inclusion processes are advantageous energetically.

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