

Enthalpy and entropy changes on molecular inclusion of 1,3-butanediol into α - and β -cyclodextrin cavities in aqueous solutions *

Sadao Takagi, Masao Fujisawa and Takayoshi Kimura

Department of Chemistry, Faculty of Science and Technology, Kinki University, 3-4-1 Kowakae, Higashi-Osaka 577 (Japan)

(Received 14 September 1990)

Abstract

The enthalpies of transfer of 1,3-butanediol (BD) from aqueous solutions to aqueous α - or β -cyclodextrin (CD) solutions have been determined by microcalorimetry at various mole fractions at 298.15 K. The enthalpy changes on inclusion of 1,3-BD in aqueous solutions determined for α -CD and β -CD are exothermic and small. However, those from the ideal gas phase are large. Comparison with other alcohols shows that 1,3-BD molecules in the CD cavities must be changing their conformation according to the size of the cavities. The enthalpies of dilution of dilute aqueous CD solutions having a mole fraction smaller than 0.0015 are also determined.

INTRODUCTION

Molecular recognition and discrimination may be caused by the interactions among contacting surfaces of colliding molecules in solutions and mixtures. In particular, stereospecific interactions due to neighbouring surfaces may play the leading role in, for example, enzyme–substrate reactions, antigen–antibody reactions, some kinds of mechanisms of the senses of smell and taste, etc. Therefore it is vital to elucidate the role of asymmetric intermolecular interactions due to the stereospecific structure of a molecule in order to understand the mechanisms of reactions in chemistry and biochemistry.

To clarify the mechanism of molecular recognition and discrimination in aqueous solutions, the authors have determined systematically thermodynamic functions for the molecular inclusion of monohydric alcohols into α - and β -cyclodextrin (CD) cavities in aqueous solutions [1–9]. The importance of the increase in entropy was discovered from the quantitative consideration of these thermodynamic functions [3,4,8,9].

* Paper presented at the Second Japan–China Joint Symposium on Calorimetry and Thermal Analysis, 30 May–1 June 1990, Osaka, Japan.

In this paper, new results for the dihydric alcohol, 1,3-butanediol (1,3-BD), are described.

EXPERIMENTAL

Materials

1,3-BD (Tokyo Kasei Co.) was dried with K_2CO_3 and fractionally distilled twice under reduced pressure through a 1 m column over helices. It was further fractionally distilled under a reduced pressure of 0.4 kPa through a spinning-band column over freshly activated molecular sieves 4A. Application of the coulometric Karl–Fischer method on a Mitsubishi moisture meter model CA-02 (Mitsubishi Chemical Ind.) gave the water content of the 1,3-BD as 0.004 mass per cent.

Details of the careful purification processes used for the α -CD [1], β -CD [2], water [10] and mercury [11] are described elsewhere. All solutions were prepared using the masses of the components.

All the aqueous 1,3-BD mixtures prepared were stirred for 20 min at room temperature using a magnetic stirrer. Then they were stirred vigorously for about 15 min at room temperature with a supersonic washer (Taga Electric Co., Ltd., model UW-25; out-put frequency, 38 kHz; 45 W).

Apparatus and procedures

The enthalpies of mixing of aqueous 1,3-BD solutions and aqueous CD solutions and those of dilution of the aqueous solutions were measured with a rocking twin-microcalorimeter of heat conduction type, laboratory designation RMC-III, which was made with some modification of the RMC-II [11] as the third stage of development [5]. The details of the automatic measuring on-line system are similar to one already reported [12] although a d.c. amplifier, a Keithley 148 nanovoltmeter, was used here.

The mixing vessels used were the same as that described in Fig. 1 of ref. 5; about 3.0 g of aqueous CD solution and about 0.75 g of aqueous BD solution were mixed for the mixing measurement. In the dilution measurements, about 3.0 g of water and 0.75 g of aqueous solution were loaded. Rocking was carried out ten times in each run.

Enthalpies of transfer of 1,3-BD from dilute aqueous solutions to dilute aqueous CD solutions were obtained from the equation

$$[\Delta_{tr}H = \Delta_{mix}H - \Delta_{dil}H(CD) - \Delta_{dil}H(BD)] \quad (1)$$

according to the procedures already reported [1,4]. All the measurements of enthalpies of transfer were carried out at the molar ratio of water to CD,

$z = (n_1' + n_1'')/n_2$, of approximately 5116 for α -CD of approximately 7936 for β -CD.

In order to use the enthalpies of dilution at very small mole fractions, those of aqueous α -CD solutions were redetermined at $x = 1.5 \times 10^{-3}$ – 1.3×10^{-4} , although they had already been determined at $x = 2.4 \times 10^{-3}$ – 2×10^{-4} [1]. The enthalpies of dilution of aqueous 1,3-BD solutions were also determined at $x = 2.8 \times 10^{-3}$ – 2×10^{-4} .

RESULTS AND DISCUSSION

Enthalpy of dilution

The experimental results for dilute aqueous solutions of α -CD are summarised in Table 1, where n_2 denotes the amount of CD in the solutions, and x_i and x_f are respectively the mole fractions before and after dilution. The results were fitted to eqn. (2) by the least-squares calculation

$$[(\Delta_{\text{dil}}H)/n_2 = a(x_i - x_f) + b(x_i^2 - x_f^2)] \quad (2)$$

The enthalpy of dilution of a solution having a mole fraction x to infinite dilution can be obtained from

$$[\Delta_{\text{dil}}^\infty H_m = ax + bx^2] \quad (3)$$

The parameters a and b and the standard deviation of the fit are summarised in Table 3, and a comparison with the experimental results is illustrated in Fig. 1. Details of the above treatment will be given separately [13].

TABLE 1

Experimental enthalpies of dilution, $\Delta_{\text{dil}}H$, of dilute aqueous α -cyclodextrin solutions with water at 298.15 K in the range $x < 0.0015$

$n_2 \times 10^5$ (mol)	$x_i \times 10^4$	$x_f \times 10^4$	$\Delta_{\text{dil}}H$ (mJ)	$\delta(\Delta_{\text{dil}}H)$ (mJ)
17.91	14.65	10.54	21.8	0.04
5.282	9.736	4.726	6.43	-0.4
4.460	8.012	3.941	4.72	0.2
4.029	8.012	3.726	4.45	0.2
3.822	8.012	3.647	3.92	-0.2
3.152	5.663	2.764	2.51	0.4
3.106	5.663	2.773	1.74	-0.4
1.585	2.737	1.375	0.68	0.2
1.523	2.737	1.351	0.65	0.2
1.509	2.769	1.347	0.89	0.4

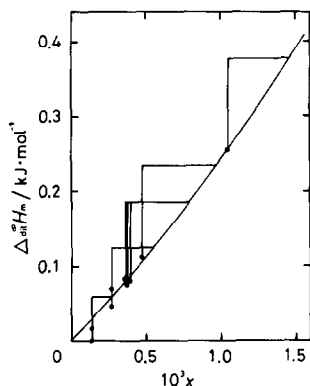


Fig. 1. Enthalpy of dilution of dilute aqueous solution ($x < 0.0015$) of α -CD to infinite dilution at 298.15 K plotted against the mole fraction x of α -CD in the solution, where the curve represents smoothed values given by eqn. (3) with a and b values from Table 3. The lengths of the vertical lines show the experimental enthalpies of dilution.

The experimental enthalpies of dilution for dilute aqueous 1,3-BD solutions are listed in Table 2, and the parameters and the standard deviations are also given in Table 3.

Figure 2 shows the deviation of the individual experimental values from the smoothed ones.

TABLE 2

Experimental enthalpies of dilution, $\Delta_{\text{dil}}H$, of dilute aqueous 1,3-butanediol solutions with water at 298.15 K

$n_3 \times 10^4$ (mol)	$x_i \times 10^3$	$x_f \times 10^4$	$-\Delta_{\text{dil}}H$ (mJ)	$\delta(\Delta_{\text{dil}}H)$ (mJ)
1.037	2.779	5.199	24.1	0.9
0.9337	2.400	4.577	21.7	-1.4
0.8523	2.291	4.363	19.1	-1.1
0.8169	1.947	3.896	15.0	0.1
0.7163	1.719	3.477	10.7	1.3
0.6816	1.618	3.293	6.82	4.0
0.6259	1.492	3.074	12.1	-2.8
0.4094	0.9933	2.043	5.80	-1.5

TABLE 3

Parameters a and b in eqn. (2) and the calculated standard deviations of the fit, S_f

	a (kJ mol $^{-1}$)	b (kJ mol $^{-1}$)	S_f (mJ)
1,3-Butanediol	-147.0	12210	2.1
α -Cyclodextrin	202.9	36953	0.29

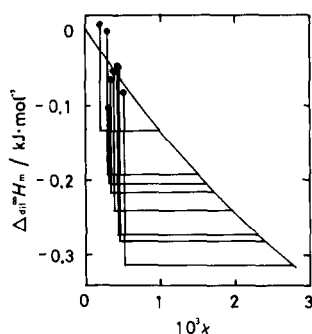


Fig. 2. Comparison of the experimental enthalpies of dilution with the smoothed values for aqueous 1,3-butanediol mixture at 298.15 K. The curve represents eqn. (3) with a and b values from Table 3.

Enthalpy of transfer

Molar enthalpies of transfer, $\Delta_{tr}H_m$, of BD from dilute aqueous solutions to dilute aqueous α - and β -CD solutions at 298.15 K under atmospheric pressure are listed in Table 4 and in Fig. 3 they are plotted against the mole fraction, $f = n_3/(n_2 + n_3)$, where n_2 refers to the amount of CD and n_3 to

TABLE 4

Experimental enthalpies of mixing, $\Delta_{mix}H$, and molar enthalpies of transfer, $\Delta_{tr}H_m$, of 1,3-butanediol from dilute aqueous solutions to dilute aqueous α - or β -cyclodextrin solutions at 298.15 K

f^a	$n'_1 \times 10^2$ (mol)	$n'_1 \times 10^2$ (mol)	$n_2 \times 10^5$ (mol)	$n_3 \times 10^5$ (mol)	$\Delta_{mix}H$ (mJ)	$\Delta_{tr}H_m$ (kJ mol ⁻¹)
H₂O(1) + α-CD(2) + 1,3-BD(3)						
0.1557 ₅	14.759	3.804	4.081	0.7530	-7.75	-1.08
0.1938 ₃	16.373	4.373	3.954	0.9506	-9.26	-1.00
0.2219 ₄	17.124	4.402	3.962	1.130	-12.0	-1.07
0.3041 ₉	15.893	4.071	3.876	1.694	-15.5	-0.895
0.3720 ₅	16.391	4.020	3.892	2.306	-18.0	-0.735
0.5383 ₀	16.504	3.922	4.025	4.693	-34.9	-0.627
0.6530 ₅	16.195	3.800	3.908	7.355	-46.4	-0.450
H₂O(1) + β-CD(2) + 1,3-BD(3)						
0.1568 ₇	16.195	4.127	2.556	0.4755	-4.80	-1.00
0.1587 ₆	16.395	4.108	2.527	0.4769	-4.51	-0.932
0.1959 ₈	15.936	4.207	2.356	0.5743	-5.13	-0.878
0.3210 ₅	15.373	4.224	2.566	1.214	-9.58	-0.757
0.3249 ₃	16.211	4.223	2.670	1.285	-5.25	-0.374
0.3393 ₉	15.897	4.264	2.628	1.350	-7.25	-0.501
0.4017 ₂	15.696	3.999	2.520	1.692	-8.10	-0.431
0.4378 ₅	15.834	4.206	2.475	1.928	-9.64	-0.449

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

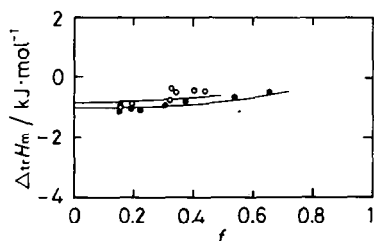


Fig. 3. Molar enthalpies of transfer, $\Delta_{tr}H_m$, of 1,3-butanediol from aqueous to aqueous α -CD (●) and β -CD (○) solutions at 298.15 K as a function of $f = n_3/(n_2 + n_3)$.

that of 1,3-BD. In Fig. 3, each curve was obtained by the least-squares method as already reported [3], determining the values of the equilibrium constant K of 1:1 inclusion complex formation, the limiting molar ratio of included 1,3-BD, y_{max} , and the limiting molar enthalpy of transfer, $\Delta_{tr}H_m^\infty$, at $f = 0$. The values obtained are summarised in Table 5.

Enthalpy and entropy of inclusion

The enthalpy, Gibbs energy and entropy changes on 1:1 molecular inclusion of 1,3-BD into α - and β -CD in aqueous solutions were determined and are listed in Table 6, together with the reported values [4] for the sake of comparison. The enthalpic stabilisation on molecular inclusion of 1,3-BD by α -CD in aqueous solution at 298.15 K is very small.

To compare the enthalpy changes on 1:1 molecular inclusion, preventing any confusion which may arise from the difference in stabilisation of alcohols in aqueous solutions, the molar enthalpies of inclusion of some alcohols into the CD cavities in aqueous solutions from an ideal gas phase were determined and are listed in Table 7. These enthalpies of inclusion are composed of the enthalpy changes due to (1) the liberation of water molecules already included in the CD cavity into the bulk water and (2) the inclusion of an alcohol molecule into the empty cavity from the ideal gas phase at 298.15 K. Because the former enthalpy change may be similar for different alcohols, especially in the case of inclusion into α -CD cavities, the

TABLE 5

Equilibrium constants for the formation of 1:1 inclusion complexes, the limiting molar enthalpies of transfer of 1,3-butanediol and the limiting molar ratios, y_{max} , of 1,3-butanediol included at 298.15 K

System	$\text{Log}_{10} K$	$\Delta_{tr}H_m^\infty$ (kJ mol^{-1})	y_{max}
1,3-BD + α -CD	4.21	-1.02	0.761
1,3-BD + β -CD	4.08	-0.83	0.600

TABLE 6

The changes in thermodynamic functions on 1:1 inclusion of an alcohol in aqueous solutions at 298.15 K

Alcohol	$\Delta_{\text{inc}}H_m$ (kJ mol ⁻¹)	$\Delta_{\text{inc}}G_m$ (kJ mol ⁻¹)	$-T\Delta_{\text{inc}}S_m$ (kJ mol ⁻¹)	$\Delta_{\text{inc}}S_m$ J (K ⁻¹ mol ⁻¹)
<i>α</i> -Cyclodextrin				
1-Propanol ^a	-6.6	-17.8	-11.2	37.5
1-Pentanol ^a	-13.9	-24.4	-10.4	34.9
2-Propanol ^a	-0.4	-19.2	-18.8	63.0
1,3-Butanediol	-1.3	-24.0	-22.7	76.1
Cyclohexanol ^a	-7.9	-23.8	-15.9	53.3
<i>β</i> -Cyclodextrin				
1-Propanol ^a	1.9	-17.5	-19.4	65.0
1-Pentanol ^a	2.2	-22.6	-24.8	83.2
2-Propanol ^a	1.2	-19.7	-20.9	70.1
1,3-Butanediol	-1.4	-23.3	-21.9	73.4
Cyclohexanol ^a	-7.0	-24.9	-17.9	60.1

^a Ref. 4.

differences in the values of $\Delta_{\text{inc}}H_m^g$ show the difference in the molecular interaction between an alcohol molecule and the inner wall of the cavity of the CD molecule. Figure 4 shows that 1,3-BD has the largest stabilisation of the alcohols in both *α*- and *β*-CD cavities. The fact that the stabilisation of 1,3-BD in both *α*- and *β*-CD cavities is larger than that of cyclohexanol

TABLE 7

The enthalpies of inclusion of alcohols into the cavities of cyclodextrin in dilute aqueous solution from ideal gas phase at 298.15 K and values of the molar enthalpies of evaporation and solution of the alcohols used in their calculation

Alcohol	$-\Delta_{\text{vap}}H_m$ (kJ mol ⁻¹)	$\Delta_{\text{sol}}H_m^\infty$ (kJ mol ⁻¹)	$\Delta_{\text{inc}}H_m$ (kJ mol ⁻¹)		$\Delta_{\text{inc}}H_m^g$ (kJ mol ⁻¹)	
			<i>α</i> -CD	<i>β</i> -CD	<i>α</i> -CD	<i>β</i> -CD
Methanol	-37.43 ^a	-7.33 ^c	0 ^f	0 ^f	-44.76	-44.76
1-Propanol	-47.32 ^a	-10.12 ^c	-6.6 ^f	1.9 ^f	-64.0	-55.5
1-Pentanol	-56.94 ^a	-7.72 ^c	-13.9 ^f	2.2 ^f	-78.6	-62.5
2-Propanol	-45.52 ^a	-13.10 ^c	-0.4 ^f	1.2 ^f	-59.0	-57.4
1,3-Butanediol	-67.78 ^b	-12.77 ^d	-1.3	-1.4	-81.9	-82.0
Cyclohexanol	-62.01 ^a	-9.01 ^e	-7.9 ^f	-7.0 ^f	-78.9	-78.0

^a Riddick and Bunger [14].

^b Ducros, Gruson and Sannier [15].

^c Rouw and Somsen [16].

^d Takagi, Nishino and Kimura [17].

^e Arnett, Kover and Carter [18].

^f Takagi and Maeda [4].

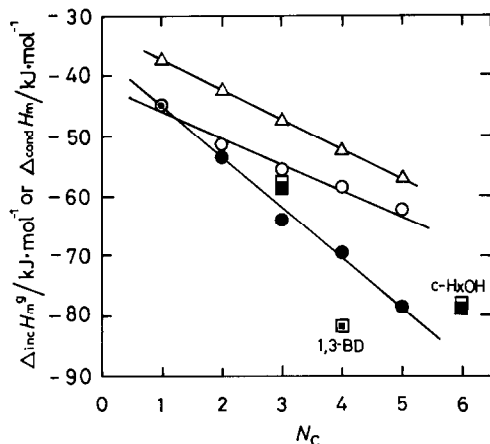


Fig. 4. Enthalpies of inclusion of alcohols into the cavities of cyclodextrin in dilute aqueous solution from ideal gas phase plotted against the number of carbon atoms in each alcohol, N_c , at 298.15 K: ●, ■, enthalpy of inclusion into α -CD cavities; ○, □, enthalpy of inclusion into β -CD cavities; \triangle , enthalpy of condensation of alcohols. Circles and triangles refer to linear alcohols. The values for the alcohols, except 1,3-butanediol, are cited in refs. 2–4 and 9.

indicates that the 1,3-BD molecules in the cavities may have a bulky conformation in order to achieve close contact with the atoms on the cavity wall and to get the maximum contact between them: the molecules of 1,3-BD must be changing their conformation according to the size of the cavities. Intramolecularly hydrogen-bonded 1,3-BD and cyclohexanol have similar molecular shapes, but the latter cannot change its shape drastically. Cyclohexanol cannot fit the α -CD cavities completely and it fits loosely into the β -CD cavities, as can be seen by inspection with CPK (Corey, Pauling, Koltum) precision molecular models (The Ealing Corporation) which represent precise van der Waals radii, bond angles and bond lengths [4]. The small enthalpy change, $\Delta_{\text{inc}} H_m$, suggests that one of the hydroxyl groups of 1,3-BD is trapped in the cavity.

Figure 4 also tells us that straight-chain alcohols in the α -CD cavities are largely stabilised (the $-\text{CH}_2-$ increment of enthalpic stabilisation is -8.4 kJ mol^{-1}) but in the β -CD cavities, stabilisation ($-\text{CH}_2-$ increment, -4.2 kJ mol^{-1}) is less than that ($-\text{CH}_2-$ increment, -4.9 kJ mol^{-1}) of the liquid state of the corresponding alcohols, indicating the existence of larger vacancies in the β -CD cavities than in the liquid state of pure alcohols at 298.15 K under atmospheric pressure. Thus the alcohol molecules must be moving actively in the β -CD cavities at 298.15 K. This is consistent with the large increase in the entropy on molecular inclusion shown in Table 6.

ACKNOWLEDGEMENTS

The authors wish to thank Mr. Makoto Inagaki for assistance in the measurement of the enthalpy of dilution of aqueous α -CD solutions.

The present work was supported partially by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture of Japan.

REFERENCES

- 1 M. Maeda and S. Takagi, *Nippon Kagaku Kaishi*, (1983) 188 (contains an adequate English summary).
- 2 M. Maeda and S. Takagi, *Netsu Sokutei*, 10 (1983) 43.
- 3 M. Maeda and S. Takagi, *Netsu Sokutei*, 10 (1983) 103 (in English).
- 4 S. Takagi and M. Maeda, *J. Inclusion Phenom.*, 2 (1984) 775.
- 5 S. Takagi, T. Kimura and M. Maeda, *Thermochim. Acta*, 88 (1985) 247.
- 6 M. Fujisawa, T. Kimura and S. Takagi, *Netsu Sokutei*, 18 (1991), in press.
- 7 S. Takagi, T. Kimura and M. Fujisawa, in W.-H. Yen (Ed.), *Abst. of Sino-Jpn. Joint Symp. on Calor. and Therm. Anal.*, Hangzhou, November 1986, pp. 70–73.
- 8 S. Takagi, T. Kimura, M. Maeda and M. Fujisawa, *Abst. of Int. Symp. on Bioorg. and Bioinorg. Chem.*, The Chemical Society of Japan, Kyoto, July 1987, pp. 89–90.
- 9 S. Takagi, T. Kimura, M. Maeda and M. Fujisawa, in J.L. Atwood (Ed.), *Abst. of 5th Int. Symp. on Inclusion Phenom. and Mol. Recognition*, Orange Beach, Alabama, September 1988, p. H4.
- 10 T. Kimura and S. Takagi, *J. Chem. Thermodyn.*, 11 (1979) 119.
- 11 T. Kimura and S. Takagi, *J. Chem. Thermodyn.*, 10 (1978) 495.
- 12 T. Kimura and S. Takagi, *Thermochim. Acta*, 123 (1988) 293.
- 13 M. Maeda and S. Takagi, *J. Chem. Thermodyn.*, to be published.
- 14 J.A. Riddick and W.B. Bunger, *Organic Solvents*, Wiley-Interscience, New York, 1970.
- 15 M. Ducros, J.F. Gruson and H. Sannier, *Thermochim. Acta*, 36 (1980) 39.
- 16 A.C. Rouw and G. Somsen, *J. Chem. Thermodyn.*, 13 (1981) 67.
- 17 S. Takagi, H. Nishino and T. Kimura, to be published.
- 18 E.M. Arnett, W.B. Kover and J.V. Carter, *J. Am. Chem. Soc.*, 91 (1969) 4028.