3718 © *1989 The Chemical Society of Japan* NOTES *Bull. Chem. Soc. Jpn.*, ***62***, *3718—3720 (1989)* [Vol. 62, No. 11

Association of Carbon Tetrachloride, Chloroform, and Dichloromethane with Cyclodextrins in Aqueous Medium

Makoto Nishimura, Toshio Deguchi, and Isao Sanemasa*
Department of Chemistry, Faculty of Science, Kumamoto University, Kurokami 2-39-1, Kumamoto 860

(Received June 14, 1989)

Synopsis. The 1 : 1 host (cyclodextrin, CyD)–guest (CCl_4, $CHCl_3$, and CH_2Cl_2) association constants at 25 °C have been determined by making use of the volatilization rate of guest from aqueous into gaseous phase. No association was observed between γ-CyD and the three guests and between β-CyD and CH_2Cl_2.

Cyclodextrins (CyDs) are cyclic oligomers forming distinctive cavity; α-, β-, and γ-CyD are composed of 6, 7, and 8 glucoses, respectively. While the outside of the CyD molecule is hydrophilic, the cavity inside is a hydrophobic environment, and various hydrophobic substances in aqueous medium can be included therein as the guest, when they are spatially fitted in the cavity. Owing to this unique property of CyD, much interest has been drawn to its applications such as catalysts in organic syntheses or a modifier in solvent extraction.

Intermediates such as trichloromethyl cation and dichlorocarben derived in situ in CyD with the suitable cavity size from CCl_4 and $CHCl_3$, respectively, play a predominant role in the selective reaction of phenolates.[1] CyDs were also used to modify partition of hydrophobic solutes between organic and aqueous phase.[2,3] In these applications, association constants of CyD with CCl_4, $CHCl_3$, and CH_2Cl_2 in water are essential information to be needed, because the complexation in the aqueous medium plays an important role. On the other hand, when water-insoluble CyD derivatives are used in organic solvent,[4] knowledge of the extent of affinity of the organic solvent molecule with the cavity of parent CyD is required.

A wide variety of guest compounds have been known to be accepted in CyD cavities, but there are no available data concerning carbon tetrachloride, chloroform, and dichloromethane. This is probably due to the lack of suitable methods to detect the free- or associated-guest species in water. UV absorption and fluorescence methods, which are generally used to evaluate the CyD–guest association, cannot be applied to these guests, because they have neither absorption peaks in the ordinary accessible ultraviolet region, nor fluorescence. We have recently proposed a method which can be applied to such guests without any UV absorption and fluorescence.[5] The only requirement is the guest volatility. The guests dealt with in this study are highly volatile and hence ideal objects for our method to be applied.

Experimental

Materials and Preparation of Sample Solutions. Distilled deionized water was used throughout this work. Carbon tetrachloride, chloroform, and dichloromethane (Wako Pure Chemicals Co.) used as guests and cyclodextrins (α-, β-, and γ-CyD, Nakarai Chemical Co.) used as hosts were all of analytical reagent grade and were used as received. An aqueous solution saturated with each guest was prepared by a vapor-circulation method using an apparatus described in the previous paper.[6] The saturated guest concentration was not determined, but taken from the literature.[7] By diluting the saturated aqueous solution with water, each 1.60×10^{-4} M (M≡mol dm^{-3}) solution was prepared. A suitable portion (10 cm^3 for CCl_4 and CH_2Cl_2, 20 cm^3 for $CHCl_3$) was transferred into a $2.5\phi\times25$ cm cylindrical glass tube and diluted with water, with or without addition of CyD aqueous solution, to 50 cm^3 for CCl_4 and CH_2Cl_2 or to 90 cm^3 for $CHCl_3$. CyD aqueous solutions were prepared daily by dissolving suitable amounts of CyD which had been dried over phosphorus pentaoxide under vacuum.

Apparatus and Procedures. Nitrogen gas was blown at a constant flow rate of 15 cm^3 min^{-1} into the aqueous guest solution placed with or without CyD in the cylindrical glass tube immersed in a bath thermostated at 25±0.1 °C. The N_2 gas leaving the sample solution was passed through a collector (a tapered glass tube of $0.5\phi\times17$ cm, packed with Tenax GC resin beads of 60—80 mesh in 10 cm length) for a fixed time. The amount of guest collected at definite time intervals, ΔQ_ϕ, and that collected during a sufficiently long time (1 h in most cases, during which almost all guest molecules were to be driven out of the sample solution), Q_ϕ, were determined by a Shimadzu GC-12A gas chromatograph. An injection port of the chromatograph was connected with a furnace (Shimadzu flush sampler FLS-3) to feed the guest sample; a collector tube was heated to above 200 °C in one min. A SE-30 (60—80 mesh) column of 2 m long was used at 80 ° and a flame ionization detector was used. A Shimadzu Chromatopac C-R6A was used to determine the peak areas.

Results and Discussion

Under the present experimental condition that host molecules are always excessive over guest molecules, the possible host–guest association reactions are:

$$\mathrm{CyD} + \phi \rightleftharpoons \mathrm{CyD}\cdot\phi, \quad K_1, \tag{1}$$

$$\mathrm{CyD}\cdot\phi + \mathrm{CyD} \rightleftharpoons \mathrm{CyD}_2\cdot\phi, \quad K_2, \tag{2}$$

and

$$\phi(\mathrm{aq}) \longrightarrow \phi(\mathrm{gas}), \quad k, \tag{3}$$

where ϕ refers to a guest molecule, K_1 and K_2 are the corresponding stepwise association constants, and k is the rate constant for the transfer of guest molecules from aqueous to gaseous phase.

We assume that the release of guest molecules at a constant N_2 flow rate is of first-order with respect to the concentration of free species present at any time t in the solution as follows:

$$\mathrm{d}Q_\phi V^{-1}/\mathrm{d}t = k[\phi], \tag{4}$$

Table 1. The 1:1 (Host:Guest) Formation Constant at 25 °C[a)]

	Concentration of CyD	Formation constant
	10^{-2} mol dm^{-3}	dm^3 mol^{-1}
Carbon tetrachloride		
α-CyD	2.07—8.25	42±17
β-CyD	0.414—1.13	150±35
γ-CyD	8.11	b)
Chloroform		
α-CyD	1.11—7.05	42±10
β-CyD	1.07	24[c)]
γ-CyD	5.56	b)
Dichloromethane		
α-CyD	2.65—8.32	28±14
β-CyD	1.11	b)
γ-CyD	8.33	b)

a) In the present runs, the concentration of each guest in the aqueous solution before aeration was set at constant, 1.60×10^{-4} mol dm^{-3}. b) The host-guest association was not observed at the given CyD concentration. c) C_{CyD} was not changed, and the formation constant was determined on the assumption of 1:1 association.

where V is the volume of aqueous solution.

An equation to estimate K_1 and K_2 can be derived using the total concentrations of host (C_{CyD}) and guest (C_ϕ) and the total amount of guest released, Q_ϕ (the sum of ΔQ_ϕ from time 0 to t), in the same way as described in the previous paper[5)] as follows:

$$\ln(C_\phi - Q_\phi V^{-1}) = -kt/(1 + K_1C_{CyD} + K_1K_2C_{CyD}^2) + \ln C_\phi$$

$$= -k't + \ln C_\phi, \qquad (5)$$

where

$$k' = k/(1 + K_1C_{CyD} + K_1K_2C_{CyD}^2). \qquad (6)$$

Rearrangement of Eq. 6 yields:

$$1/k' = K_1K_2C_{CyD}^2/k + K_1C_{CyD}/k + 1/k. \qquad (7)$$

For each host-guest combination, plots according to Eq. 5 at a constant C_{CyD} gave a similar straight line to that shown in our previous papers.[5)] From inclination of the straight line, k' (and k) was determined and plotted according to Eq. 7. The $1/k'$ vs. C_{CyD} plots appeared to be linear, showing that K_2 can be neglected. In the case of $CHCl_3$–β-CyD, the CyD concentration was not changed, and K_1 was estimated on the assumption that this host–guest forms a 1:1 complex. When γ-CyD was used as the host, $1/k'$ values for the three guests were found to be in accordance with $1/k$ within experimental error. It was thus assumed that γ-CyD does not associate with each of guests studied. This is also the case for β-CyD–CH_2Cl_2. The K_1 value evaluated in this work for each combination is given in Table 1.

Molecular sizes of both host and guest being taken into account, the inclusion models are illustrated in Fig. 1; the guest molecule is oriented so that it enters as deeply as possible into the CyD cavity. CCl_4 molecule is only partly included in α-CyD, and a part of $CHCl_3$ molecule protrudes out of the α-CyD cavity, while the CH_2Cl_2 is completely accomodated in the cavity. Contrary to our expectation, however, the association constant of the α-CyD–CH_2Cl_2 complex is rather small. This is probably relevant to the polarity of the guest molecule.

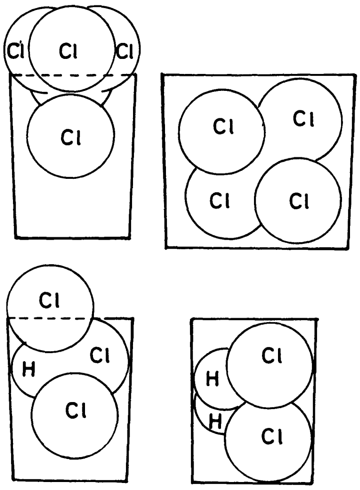

Fig. 1. Inclusion model. The larger cage refers to β-CyD ($CHCl_3$–β-CyD model is omitted).

The guest has to loose surrounding water molecules before it enters the CyD cavity. The free-energy change associated with this process can be estimated from Henry's law constant, K_H, as follows: $\Delta G_{dehyd} = -RT \ln K_H$. Using K_H values reported in the literature,[8)] $-\Delta G_{dehyd}$ at 25 °C are evaluated to be 18.4 (CCl_4), 13.2 ($CHCl_3$), and 11.9 kJ mol^{-1} (CH_2Cl_2). The ΔG_{dehyd} is a quantitative measure of guest hydrophobicity: a guest with larger $-\Delta G_{dehyd}$ can be more easily transferred from aqueous into gaseous phase.

CCl_4 molecule is suitably accomodated in the β-CyD cavity. This accounts for larger K value of the β-CyD complex than that of the α-CyD complex. On the other hand, β-CyD is a little large for $CHCl_3$ and too large for CH_2Cl_2 to be fitted in with the cavity. In addition, relatively high polarity of CH_2Cl_2 may also be responsible for unobserved association of this guest with β-CyD. The large cavity of γ-CyD seems to explain the cause of the results that any association between this host and the three guests studied in this work has not been observed.

The association constant of CCl_4 with β-CyD is comparable to that of benzene with β-CyD. Molecular volume of CCl_4 (86.82×10^{-3}) is similar to that of benzene (80.33×10^{-3} nm^3),[9)] and benzene also suitably fits with the β-CyD cavity. When we consider that $-\Delta G_{dehyd}$ for CCl_4 is much larger than that of benzene, 14.4 kJ mol^{-1}, a much larger association of CCl_4 with β-CyD will be expected. This may indicate that stabilization such as van der Waals does not work, or even it works, to a lesser extent for CCl_4 than benzene.

It is generally observed that CyDs dissolved in water in relatively high concentrations precipitate upon shaking with some organic solvents; γ-CyD easily precipitates with chloroform. Some workers believe that this arises from the organic solvent molecule forming stable complexes with CyDs.[2] It is not true because γ-CyD does not form any complex with $CHCl_3$. The precipitation seems to occur through the change in the polarity of aqueous solution caused by organic solvent dissolving in water.

It is now rationalized why the selective syntheses of benzoic acids and benzaldehydes from phenolates using CyDs as catalysts can be performed;[1] α-CyD–dichlorocarben, α- and β-CyDs–chroloform, and β-CyD–carbon tetrachloride are successful combinations but γ-CyD cannot be used for the purpose.

It should be mentioned that the present study does not necessarily exclude the possibility of formation of a CyD complex with more than one guest molecules, because such an association cannot take place under our experimental condition that C_{CyD} is much higher than C_ϕ.

References

1) M. Komiyama and H. Hirai, *Bull. Chem. Soc. Jpn.*, **54**, 2053 (1981); *J. Am. Chem. Soc.*, **105**, 2018 (1983); **106**, 174 (1984).

2) L. A. Blyshak, T. M. Rossi, G. Patonay, and I. M. Warner, *Anal. Chem.*, **60**, 2127 (1988).

3) K. Matsunaga, M. Imanaka, T. Ishida, and T. Oda, *Anal. Chem.*, **56**, 1980 (1984); J. Harangi and P. Nánási, *Anal. Chim. Acta*, **156**, 103 (1984).

4) M. Komiyama, H. Yamamoto, and H. Hirai, *Chem. Lett.*, **1984**, 1081; H. Takahashi, Y. Irinatsu, S. Kozuka, and W. Takagi, *Mem. Fac. Eng., Osaka City Univ.*, **26**, 93 (1985).

5) I. Sanemasa and Y. Akamine, *Bull. Chem. Soc. Jpn.*, **60**, 2059 (1987); M. Fujiki, T. Deguchi, and I. Sanemasa, *ibid.*, **61**, 1163 (1988); I. Sanemasa, T. Takuma, and T. Deguchi, *ibid.* **62**, 3098 (1989).

6) I. Sanemasa, M. Araki, T. Deguchi, and H. Nagai, *Bull. Chem. Soc. Jpn.*, **55**, 1054 (1982).

7) M. J. Kamlet, R. M. Doherty, M. H. Abraham, P. W. Carr, R. F. Doherty, and R. W. Taft, *J. Phys. Chem.*, **91**, 1996 (1987).

8) J. M. Gossett, *Environ. Sci. Technol.*, **21**, 202 (1987).

9) R. D. Cramer, III, *J. Am. Chem. Soc.*, **99**, 5408 (1977).