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Association of Naphthalene and Its Methyl Derivatives with Cyclodextrins in Aqueous Medium

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(Received September 5, 1987)

Formation constants of naphthalene and its (1- and 2-)methyl and (1,4-, 1,5-, and 1,8-)dimethyl derivatives with α-, β-, and γ-cyclodextrins (CyD) were determined in the aqueous medium in the presence of excess CyD. The technique used to study associations between host (CyD) and guest(hydrocarbon) is based on the facts that the guest molecules can be driven out to gaseous phase by introducing an inert gas at a constant flow rate into the aqueous solution and that the volatilization rate of guest decreases with increasing association with the host in aqueous solution. The 1 : 1 and 2 : 1 (host : guest) formation constants were evaluated at 25 °C. From the formation constant estimated, a host-guest spatial-fitting model for each association complex is presented.

We have recently reported a method useful for estimating association constants between volatile and nonvolatile solutes in aqueous medium.[1-2] The method is based on volatility of nonelectrolyte solute in water. Volatile molecules are driven out to gaseous phase by introducing an inert gas at a constant flow rate into the aqueous solution. The volatilization rate was measured with and without addition of nonvolatile solute which associates with the volatile solute and decreased with the degree of association between the solutes. The method is applicable to such systems where (a) one of the solute is volatile, (b) the concentration of nonvolatile solute is sufficiently high in comparison with that of volatile solute, and (c) the rate of association is rapid compared with the volatilization rate.

The method was applied to association of benzene and alkylbenzenes as guests with cyclodextrins (CyD) as hosts and 1 : 1 and 2 : 1 (host : guest) formation constants were evaluated.[3] The present work is concerned with an application of the method to association of naphthalene and its methyl derivetives with α-, β-, and γ-CyDs.

There have been reported several data concerning the naphthalene-CyD formation constant.[4-7] The data are, however, only on the β-CyD complex and little is known concerning naphthalene derivatives. The present study was undertaken to see whether or not the volatilization method is successfully applicable to naphthalene and its derivatives and to elucidate the effects of the cavity size of host and the steric hindrance of guest on the host-guest inclusion complex formation.

Experimental

Materials and Preparation of Sample Solutions. Distilled deionized water was used throughout the experiments. Aromatic hydrocarbons used as guest were of analytical reagent grade (the purity is listed in Table 1). Cyclodextrins (α-, β-, and γ-CyD) used as host were of guaranteed grade from Nakarai Chemical Co. Both guest and host reagents were used without further purification. An aqueous solution of each guest was prepared by adding an excess solid or liquid hydrocarbons to water and stirring for at least 24 h. After standing the mixture for at least 24 h, a portion of the saturated guest solution was transferred into a separatory funnel and the UV absorption of its chloroform extract was measured to determine the guest concentration, and another portion was transferred into a 2.5ϕX25 cm cylindrical glass tube. A suitable amount of CyD, which had been dried over phosphorus pentaoxide under vacuum, was weighed and dissolved into the guest solution. The solution was then diluted to 100 cm^3 with water. Ranges of concentration of guest and host are given in Table 3.

Amberlite XAD-2 resin (Rohm and Hass) of 100—150 mesh size was used as an adsorbent of guest vapor.

Apparatus and Procedures. The apparatus and the experimental procedure were the same as those described in the previous paper with minor modifications.[3] Because the volatility of guest substances examined in this study is considerably lower than that of benzene and alkylbenzenes, a sintered glass ball was used as an N_2 bubbler to drive guest molecules effectively out of the aqueous solution at higher N_2 flow rates (Table 1). The N_2 gas leaving the sample solution was passed through an XAD resin column of 0.5ϕX10 cm and the guest hydrocarbon adsorbed on the resin for a fixed time was eluted out with $CHCl_3$ of 6 cm^3. The amount of guest collected in an XAD column, ΔQ_ϕ, was determined by UV spectroscopy at the optimum wavelength for each guest hydrocarbon (Table 1).

Table 1. Experimental Conditions

Guest substance	Purity	λ[a]	N_2 gas flow rate
	%	nm	cm^3 min^{-1}
Naphthalene	G.R.[b]	276.6	50, 150, 250
1-Methyl-naphthalene	97	283.0	350
2-Methyl-naphthalene	G.R.	277.2	350
1,4-Dimethyl-naphthalene	95	243.0	700
1,5-Dimethyl-naphthalene	98.0	289.0	700
1,8-Dimethyl-naphthalene	95.0	287.6	700

a) The wavelength for determining the concentration of guest molecules after $CHCl_3$ extraction. b) Guaranteed grade reagent (the purity is not specified).

Results and Discussion

Estimation of 1 : 1 and 2 : 1 (Host : Guest) Formation Constants. Under the present experimental conditions that host molecules are always excess over guest molecules, the possible host : guest stoichiometric ratios are 1 : 1 and 2 : 1. Then, the reactions that should be taken into account are:

$$\mathrm{CyD} + \phi \rightleftarrows \mathrm{CyD}\cdot\phi,\ (K_1), \tag{1}$$

$$\mathrm{CyD}\cdot\phi + \mathrm{CyD} \rightleftarrows \mathrm{CyD}_2\cdot\phi,\ (K_2), \tag{2}$$

and

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

where ϕ refers to a guest hydrocarbon molecule, K_1 and K_2 are the corresponding stepwise formation constants, and k is the rate constant for 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 in the solution as follows:

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

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 amount of guest released from aqueous solution during the aeration time (Q_ϕ, the sum of ΔQ_ϕ from time 0 to t), in the same way as described in the previous paper as follows:[3)]

$$\begin{aligned}\ln(C_\phi - Q_\phi V^{-1}) &= -kt/(1 + K_1 C_{\mathrm{CyD}} + K_1 K_2 C_{\mathrm{CyD}}{}^2) \\ &\quad + \ln C_\phi \\ &= -k't + \ln C_\phi,\end{aligned} \tag{5}$$

where

$$k' = k/(1 + K_1 C_{\mathrm{CyD}} + K_1 K_2 C_{\mathrm{CyD}}{}^2). \tag{6}$$

Rearrangement of Eq. 6 yields:

$$1/k' = K_1 K_2 C_{\mathrm{CyD}}{}^2/k + K_1 C_{\mathrm{CyD}}/k + 1/k. \tag{7}$$

Plots according to Eq. 5 for naphthalene-β-CyD are shown in Fig. 1. The plots give straight lines up to ca. 70% release of the guest hydrocarbon initially present in the solution. This linearity verifies the assumption that the volatilization of guest molecules follows a first-order reaction at a constant N_2 flow rate. The slopes of resulting straight lines, k' (and k), were evaluated using the least-squares method; the results for naphthalene are given in Table 2. Both k and k' values change with the N_2 flow rate, but their values

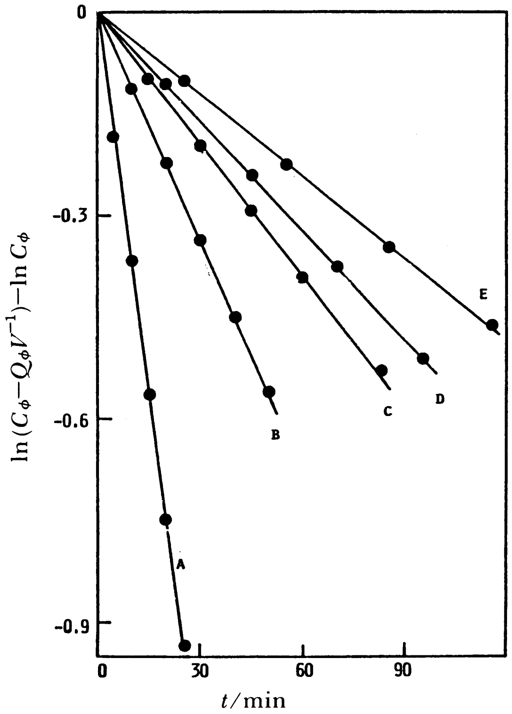

Fig. 1. Naphthalene-β-CyD system. The plots of $\ln(C_\phi - Q_\phi V^{-1}) - \ln C_\phi$ vs. t in the presence and absence of cyclodextrin. N_2 flow rate: 250 cm^3 min^{-1}; $C_{\mathrm{CyD}}/10^{-3}$ M: (A) 0, (B) 3.50, (C) 7.11, (D) 8.84, (E) 12.1; C_ϕ: 1.76×10^{-5} M.

Table 2. The Rate Constant for Transfer of Naphthalene from Aqueous to Gaseous Phase in the Presence and Absence of α-, β-, and γ-Cyclodextrin

k or k'[a)]	C_ϕ[b)]	Total concentration of		
		α-CyD	β-CyD	γ-CyD
10^{-2} min^{-1}	10^{-5} M	10^{-2} M	10^{-3} M	10^{-3} M
N_2 flow rate: 250 cm^3 min^{-1}				
3.53[c)]	0.86—1.71			
1.22	1.94	1.50		
0.625	1.94	3.00		
0.369	2.01	4.50		
0.180	1.94	7.50		
0.112	2.01	10.2		
0.0893	1.94	11.5		
1.12	1.76		3.50	
0.648	1.76		7.11	
0.538	1.76		8.84	
0.413	1.76		12.1	
2.31	2.02			2.62
2.00	2.02			5.24
1.78	2.02			7.45
1.30	1.95			9.44
0.694	1.95			24.9
0.437	1.95			44.9
0.385	1.95			52.8
N_2 flow rate: 50 cm^3 min^{-1}				
0.971[c)]	1.90			
0.439			1.90	
0.313			3.36	
0.219			5.38	
0.126			10.1	
N_2 flow rate: 150 cm^3 min^{-1}				
2.22[c)]	2.05			
0.714	2.05		3.35	
0.435	2.05		6.65	
0.326	2.05		9.40	

a) $k' = k/(1 + K_1 C_{\mathrm{CyD}} + K_1 K_2 C_{\mathrm{CyD}}{}^2)$, where C_{CyD} is the total concentration of cyclodextrin. b) The initial concentration of naphthalene. c) The average of four determinations.

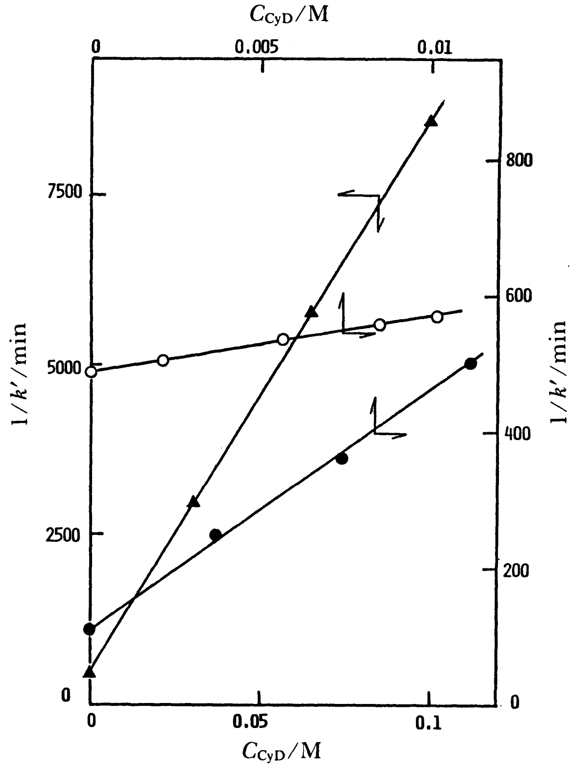

Fig. 2. The plots of $1/k'$ vs. C_{CyD}. Examples of straight line. 1-Methylnaphthalene-β-CyD (●), 1,8-dimethylnaphthalene-β-CyD (○), 1,8-dimethylnaphthalene-γ-CyD (▲).

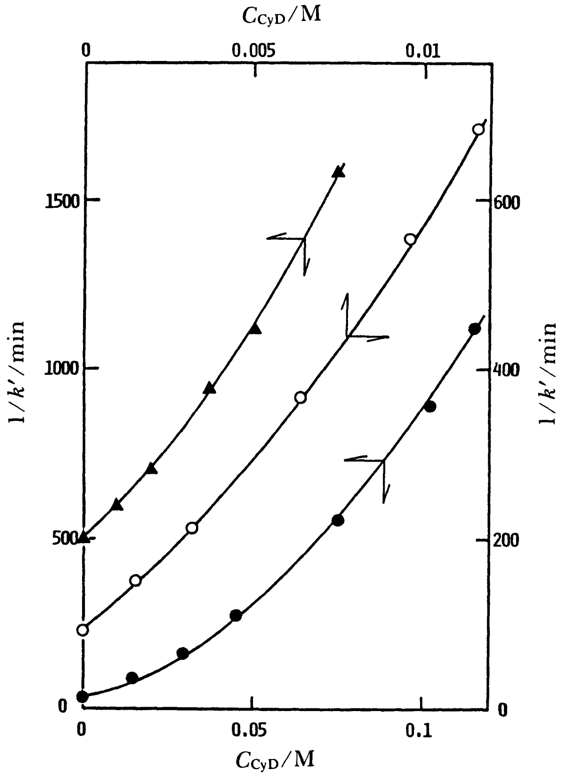

Fig. 3. The plots of $1/k'$ vs. C_{CyD}. Examples of parabolic curve. Naphthalene-α-CyD (●), 1,4-dimethylnaphthalene-β-CyD (○), 1,8-dimethylnaphthalene-α-CyD (▲).

are not significant when the N_2 flow is set at the same rate for two runs in the presence and absence of CyD. The K values determined for naphthalene-β-CyD at three different N_2 flow rates of 50, 150, and 250 cm^3 min^{-1} are found to be (6.6, 6.2, and 6.3)$\times 10^2$ M^{-1} ($M \equiv mol\,dm^{-3}$), respectively. Relatively large deviation inherent in the present method being considered, these K values for naphthalene-β-CyD seem to be in a reasonable agreement. This suggests that the rate of association is rapid compared with the volatilization rate; the essential requirement of the present method is fulfilled.

Figures 2 and 3 show some typical results plotted by a curve-fitting method with the aid of Eq. 7. The $1/k'$ vs. C_{CyD} plots appear to be linear (Fig. 2) or parabolic (Fig. 3) depending on the host-guest combination. The K_1 and K_2 values determined in this work are summarized in Table 3. As was pointed out in our previous paper,[3)] the deviation of formation constant is relatively large, which arises from uncertainty in determining the amount of released guest; the overall error in Q_{ϕ} becomes large due to the accumulation of errors in ΔQ_{ϕ}.

The K value estimated here for naphthalene-β-CyD of 6.3×10^2 M^{-1} is consistent with the literature values,

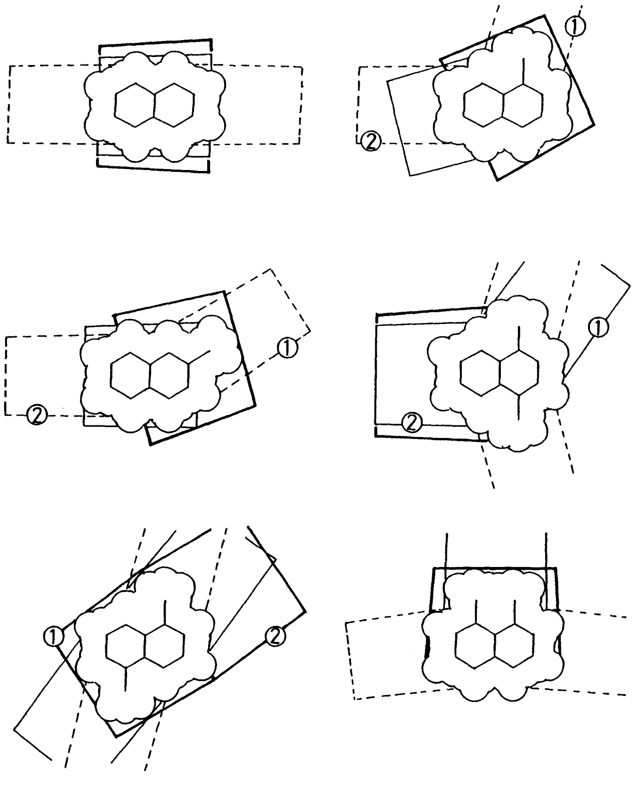

Fig. 4. Host-guest inclusion model. α-, β-, and γ-cyclodextrin cavities are drawn by dotted, thin solid, and thick solid lines, respectively. In the case of 2:1 (host:guest) complex being formed, the binding sites corresponding to K_1 and K_2 are, when necessary, are indicated respectively by the numbers, 1 and 2, in the circle.

Table 3. Concentration Ranges of Host and Guest and the Formation Constants, $K_1(1:1)$ and K_2 (2 : 1) of (Host : Guest) Complexes at 25.0 °C

	Concentration		Formation constant[a)]	
	C_{ϕ} [b)]	C_{CyD} [c)]	K_1	K_2 [d)]
	10^{-5} M	10^{-2} M	M^{-1}	M^{-1}
Naphthalene				
α-CyD	1.94—2.02	1.50 —11.5	83±3	23±6
β-CyD	1.76—2.05	0.190— 1.21	$(6.3\pm0.4)\times10^2$	—
γ-CyD	2.08	0.260— 9.06	$(1.3\pm0.4)\times10^2$	—
1-Methylnaphthalene				
α-CyD	2.61	2.62 —11.8	40±1	17±1
β-CyD	2.62	0.372— 1.32	$(3.1\pm0.3)\times10^2$	—
γ-CyD	2.61	1.04 —13.3	$(1.3\pm0.5)\times10^2$	—
2-Methylnaphthalene				
α-CyD	1.95	1.51 —11.1	22±5	12±4
β-CyD	1.93	0.377— 1.36	$(7\pm1)\times10^2$	—
γ-CyD	1.88	2.60 —11.7	$(1.5\pm0.2)\times10^2$	—
1,4-Dimethylnaphthalene				
α-CyD	0.482	1.91 — 9.52	43±8	17±7
β-CyD	0.478	0.161— 1.16	$(3.5\pm0.2)\times10^2$	50±8
γ-CyD	0.524	2.24 — 8.96	10±2	—
1,5-Dimethylnaphthalene				
α-CyD	0.181	2.47 —11.2	28±3	16±4
β-CyD	0.366	0.249— 1.12	$(2.0\pm0.2)\times10^2$	$(1.1\pm0.4)\times10^2$
γ-CyD	0.395	2.47 —11.2	$(1.00\pm0.04)\times10^3$	5±1
1,8-Dimethylnaphthalene				
α-CyD	1.37	1.01 —10.2	20±1	6±2
β-CyD	1.42	0.211— 1.01	17±1	—
γ-CyD	1.45	3.06 — 9.95	$(1.7\pm0.1)\times10^2$	—

a) The confidence level is set at 95%. b) The initial concentration of guest substance. c) The total concentration of cyclodextrin. d) The dash-sign indicates that K_2 was not evaluated, because $1/k'$ vs. C_{CyD} plots by Eq. 7 gave nearly straight line only.

685,[4] 730,[4] and 850 M^{-1},[6] determined by fluorescent method (the enhancement of guest fluorescence intensity in the presence of host). The UV absorption measurement, on the other hand, seems to give a lower value, 186 M^{-1}.[7]

For the naphthalene-β-CyD system, Hamai proposed 2 :2 complex formation:[4]

$$\beta\text{-CyD}\cdot\phi+\beta\text{-CyD}\cdot\phi \rightleftarrows (\beta\text{-CyD}\cdot\phi)_2. \qquad (8)$$

The equilibrium constant is reported to be 4000 M^{-1}. If the 2 :2 complex exists, a 5% of the 1 : 1 complex is to be converted into the 2 : 2 form, when the initial concentration of naphthalene is 10^{-5} M and that of β-CyD is 10^{-2} M. Under the present experimental conditions, where the contribution of Reaction 8 is small, we have ignored the equilibrium of 2 : 2 complex formation in determining K.

Host-Guest Spatial-Fitting Model. The following data in Å unit were used for guests; bond length: 1.40 for the average C-C in naphthalen,[8] 1.54 for C-C in alkyl group, 1.08 for C-H in naphthalene and alkyl group, van der Waals radius:[9] 1.0 for H and 1.7 for C. Concerned with hosts, we used the values; the inner diameter of cavity:[10] 4.7—5.2 for α-CyD, 6.0—6.4 for β-CyD, and 7.5—8.3 for γ-CyD (the smaller value is for the primary hydroxyl group and the larger is for the secondary hydroxyl group), the cavity depth:[11] 6.7 for α-CyD and ca. 7 for β- and γ-CyD.

By taking into account the magnitude of K_1 and K_2, inclusion models for all the host-guest combinations studied in this work are depicted in Fig. 4. When two hosts share a single guest, unambiguous assignment of K_1 and K_2 to the corresponding binding site is difficult. Then, we assumed that alkyl group is included in CyD cavity preferentially to naphthalene ring if the cavity entrance radius admits. Another assumption was made that a guest enters into CyD through wider secondary hydroxyl side.

It has been suggested that, if K_2 is large or nearly equal to K_1, the cross-section of secondary hydroxyl group sides of two CyDs are situated in parallel to each other in a suitable distance to form hydrogen bond.[12] In view of the K_2 values for the present 2 : 1 complexes being smaller than the corresponding K_1, we speculate that the distance along a naphthalene molecule is too long for two α-CyDs to cooperate with each other to form hydrogen bonds, while the distance is suitable for the second α-CyD to act to stabilize the 1 : 1 complex for benzene and also for p-xylene.

The cavity size of γ-CyD is sufficiently large to include naphthalene ring, while the diameter of β-CyD cavity seems small to include a whole naphthalene molecule.[13] The cavity of β-CyD is, however, considered to suitably fit the naphthalene molecule, because K of β-CyD is larger than that of γ-CyD. The inner diameter of β-CyD we employed should be larger by 10%. According to this modification, 2-methylnaphthalene can enter the β-CyD cavity from methyl substituent. It seems, however, that 1-methyl derivative cannot be included from this substituent side due to the steric hindrance. The bulky 1,8-dimethyl groups obviously hinder the guest from entering deeply into β-CyD, but seem to exert no hindrance effect on γ-CyD. The 1,4-dimethyl groups, on the other hand, have a hindrance effect on γ-CyD. The size of γ-CyD fits most suitably 1.5-dimethylnaphthalene, and a large van der Waals stabilization works.

For benzene, alkylbenzenes, naphthalene, and its methyl derivatives, the largest formation constants observed are as follows; propylbenzene for α-CyD ($5.9\times10^2\,M^{-1}$), isopropylbenzene for β-CyD ($1.2\times10^3\,M^{-1}$), and 1,5-dimethylnaphthalene for γ-CyD ($1.00\times10^3\,M^{-1}$). From these observations, the alkyl chain seems to contribute to form more stable complexes with CyDs than an additional condensed ring does. This implies that the hydrophobic nature of guest is an important factor when the host-guest spatial-fitting requirement meets.

It should be emphasized that the inclusion models presented here are highly speculative because they are made based only on the magnitude of K_1 and K_2. Other information such as NMR, CD, and X-ray crystallographic data and thermodynamic and kinetic studies are necessary to confirm the inclusion model.

References

1) I. Sanemasa, Y. Nishimoto, A. Tanaka, and T. Deguchi, *Bull. Chem. Soc. Jpn.*, **59**, 1459 (1986).

2) I. Sanemasa, Y. Nishimoto, A. Tanaka, and T. Deguchi, *Bull. Chem. Soc. Jpn.*, **59**, 2269 (1986).

3) I. Sanemasa and Y. Akamine, *Bull. Chem. Soc. Jpn.*, **60**, 2059 (1987).

4) S. Hamai, *Bull. Chem. Soc. Jpn.*, **55**, 2721 (1982).

5) K. Kano, B. Zhou, M. Sakaguchi, H. Matsumoto, and S. Hashimoto, *Sci. Eng. Rev. Doshisha Univ.*, **25**, 33 (1985).

6) S. Hashimoto and J. K. Thomas, *J. Am. Chem. Soc.*, **107**, 4655 (1985).

7) N. Kobayashi, S. Minato, and T. Osa, *Makromol. Chem.*, **184**, 2123 (1983).

8) K. B. Lipkowitz, A. M. Naylor, and W. B. Melchior, *Tetrahedron Lett.*, **25**, 2297 (1984).

9) A. Bondi, *J. Phys. Chem.*, **68**, 441 (1964).

10) W. Saenger, *Angew. Chem., Int. Ed. Engl.*, **19**, 344 (1980).

11) M. L. Bender and M. Komiyama, "Cyclodextrin Chemistry," Springer-Verlag, New York (1978).

12) W. C. Cromwell, K. Byström, and M. R. Eftink, *J. Phys. Chem.*, **89**, 326 (1985).

13) The CyD cavity size differs from literature to literature. According to F. Cramer, W. Saenger, and H.-Ch. Spatz, *J. Am. Chem. Soc.*, **89**, 14 (1967), the inner diameter of α-, β-, and γ-CyD is 6, 7.5, and 9—10 Å, respectively. The data we employed in this paper are considerably small compared with these values.