Association of Some Polynuclear Aromatic Hydrocarbons with Cyclodextrins in Aqueous Medium

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Complex formation using cyclodextrins (CyDs) as hosts and anthracene, phenanthrene, and naphthacene as guests has been studied in aqueous medium at 25 °C by measuring the guest volatilization rate. The results obtained are compared with those previously determined for benzene and naphthalene. Factors governing the host-guest association are discussed based on the dehydration energy of the guest derived from the Henry's law constant. It was suggested that van der Waals force is the main factor to stabilize the polynuclear aromatic hydrocarbons in the CyD cavity and that the contribution of hydrophobic interaction is less important. The additional van der Waals stabilization does not work fully for naphthacene of the longest molecular axis among the guests studied.

Cyclodextrins (CyDs) consist of glucopyranose units, forming cyclic oligosaccharides with different cavity size: α-, β-, and γ-CyD composed of 6, 7, and 8 units has the cavity diameter, 4.5—6.0, 6.0—8.0, and 8.0—10.0 Å, respectively. The interior of cavity is thought to be of hydrophobic environment, and, in aqueous medium, a wide variety of substances can be included therein as guests, if they are more or less hydrophobic in nature.[1]

In order to elucidate the CyD-guest binding forces and the complex formation process, many investigations have been made using hydrocarbons with polar derivatives.[2-5] In such studies, the use of hydrophobic guest substances without any polar group is desirable, because the presence of polar group in the guest molecule makes the contribution of hydrophobic effect uncertain.

Hydrophobic substances are in general only sparingly soluble in water and, moreover, some are volatile, so that it is difficult to use these solutes as guests. We have recently proposed a method that can be applied to such guests. The method 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 medium. This method is applicable to such a system that the host-guest association rate is rapid compared with the guest volatilization rate. We have applied this method to benzene and alkylbenzenes,[6] and naphthalene and its methyl derivatives.[7] The host-guest spatial fitting was discussed on the basis of their association constants determined.

The present work is concerned with a further application of the method to such guests as anthracene, phenanthrene, and naphthacene. By combining the present results with the previous ones on benzene and naphthalene, we will get a better insight into the inclusion mechanism for polynuclear aromatic hydrocarbons.

Experimental

Materials and Preparation of Sample Solutions. Distilled deionized water was used throughout the experiments. Anthracene (Wako Pure Chemicals Co.), phenanthrene (Kodak Co.), and naphthacene (Tokyo Kasei Co.) as guests and cyclodextrins (α-, β-, and γ-CyD, Nakarai Chemical Co.) as hosts were of analytical reagent grade and used as received. An aqueous stock solution of each guest was prepared by adding an excess of each solid hydrocarbon to water and stirring for at least 24 h in the dark. After standing the mixture for at least 24 h, a portion of the saturated guest solution was transferred to a separatory funnel and the fluorescence of its chloroform extract was measured to determine the guest concentration using the following wavelengths: emission; 383, 367, and 479.1 nm, excitation; 260, 260, and 446.7 nm, for anthracene, phenanthrene, and naphthacene, respectively. Another portion of anthracene or phenanthrene aqueous solution was transferred to a 2.5 ϕ×25 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, and then the solution was diluted to 50

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

	Concentration of CyD / 10^{-2}mol dm^{-3}	Fraction(%) of guest volatilized	Formation constant / dm^3 mol^{-1}
Anthracene			
α-CyD	0.808—4.00	43	40±20
β-CyD	0.151—0.602	18	(2.3±0.2)×10^3
γ-CyD	1.50 —4.50	9	(1.5±0.2)×10^3
Phenanthrene			
α-CyD	1.82 —9.00	47	16±5
β-CyD	0.193—0.934	15	(1.5±0.3)×10^3
γ-CyD	0.800—3.20	8	(7.7±0.1)×10^2
Naphthacene			
β-CyD	0.100	3	3.4×10^3
γ-CyD	0.120	7	1.7×10^3

a) The concentration ranges of guest are, (5.00—17.8)×10^{-8} for anthracene, (5.7—19.1)×10^{-7} for phenanthrene, and (4.6—9.6)×10^{-9} for naphthacene, in mol dm^{-3}.

cm^3 with water. In the case of naphthacene, a 450 cm^3 portion of the guest aqueous solution was transferred to a round-bottom flask of 1 dm^3 capacity and diluted with water to 500 cm^3 after addition of CyD. The host and guest concentration ranges are given in Table 1.

Amberlite XAD-2 resin (Rohm and Hass) of 80—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.[7] Nitrogen gas was blown at a constant flow rate of 600 $cm^3\,min^{-1}$ into the aqueous guest solution placed with or without CyD in the cylindrical glass tube or the round-bottom flask immersed in a bath thermostated at 25.0±0.1 °C. The N_2 gas leaving the sample solution was passed through a glass column of 0.5 ϕ×23 cm filled with XAD resin beads of 8 cm in length and the guest adsorbed on the resin within a fixed time was eluted out with $CHCl_3$ of 4 cm^3, and the amount of guest, ΔQ_ϕ, was determined by fluorescence measurement.

Results

Under the present experimental conditions that host molecules are always excess over guest molecules, the possible host:guest stoichiometric ratios are assumed to be 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 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:

$$dQ_\phi V^{-1}/dt = k[\phi], \tag{4}$$

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.[7]

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

where

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

Rearrangement of Eq. 6 yields:

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

The plots according to Eq. 5 for anthracene-β-CyD are shown in Fig. 1. The plots give straight lines over the aeration time employed; the volatilization rates of guest molecules dealt with in this work are much slower than those previously studied,[6,7] and hence the fraction of the amount of guest released

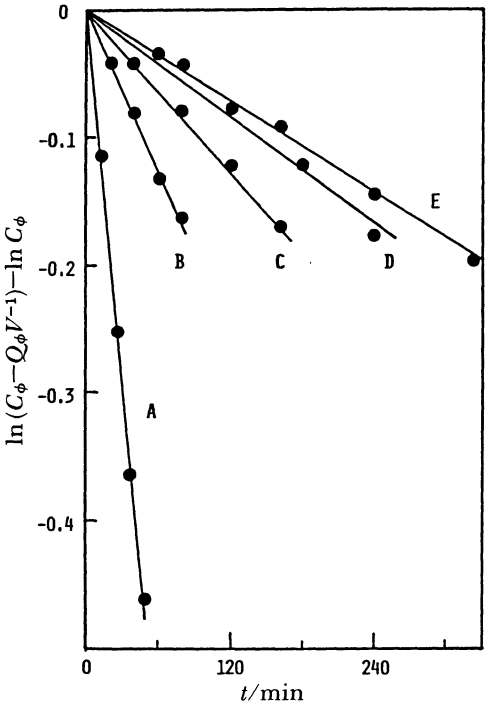

Fig. 1. Anthracene-β-CyD system. The plots of $\ln(C_\phi - Q_\phi V^{-1}) - \ln C_\phi$ vs. t with and without cyclodextrin. $C_{CyD}/10^{-3}$ mol dm^{-3}: (A) 0, (B) 1.51, (C) 3.01, (D) 4.49, (E) 6.02; C_ϕ: (5.00—17.8)×10^{-8} mol dm^{-3}.

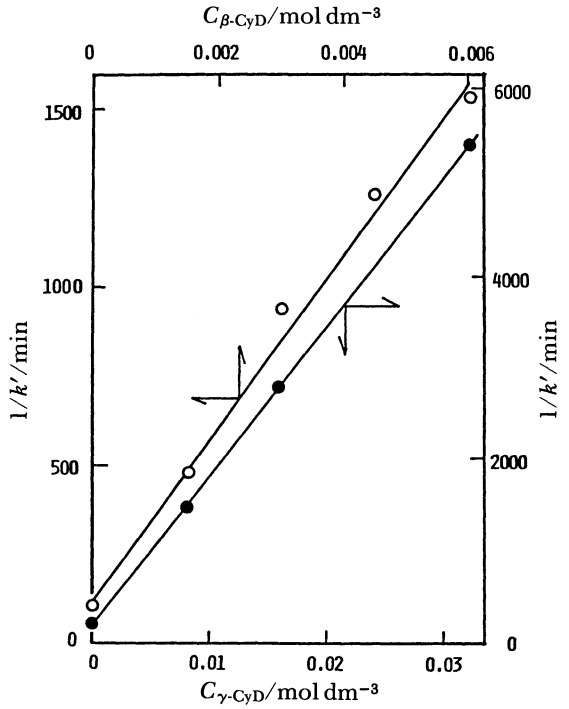

Fig. 2. The plots of $1/k'$ vs. C_{CyD}. Anthracene-β-CyD (○), phenanthrene-γ-CyD (●).

during the aeration is small (see Table 1). This linear relationship verifies the assumption that the volatilization of guest molecules follows a first-order reaction at a constant N_2 flow rate. Slopes of the resulting straight lines, k'(and k), were evaluated using the least-squares method. Typical $1/k'$ vs. C_{CyD} plots are shown in Fig. 2. The plots appeared to be linear for each host-guest combination studied; the K_2 can be neglected. In the case of naphthacene, measurements were made at a constant CyD concentration and the K_1 values were estimated from the average of three (for β-CyD) and two (for γ-CyD) runs. The K_1 values for this guest are, therefore, less reliable. The K_1 values determined in this work are summarized in Table 1. It should be noted that the K_1 values for α-CyD are less reliable because the difference between k and k' is small.

Discussion

Comparison of Association Constants with Literature Values. Vapor pressure,[8] fluorescence,[9-13] UV absorption,[14] and thin-layer chromatographic[15] methods have been used to evaluate CyD association constants with guests relevant to the present study. These are listed in Table 2. Our measurement provides reasonable values for benzene and naphthalene, while, for the other three guests, there is very large disagreement between ours and literature values. These differences probably arise from low solubility of guest substances in water. It is difficult to maintain the guest concentration in water constant owing to the adsorption of guest solute on the walls of glasswares including the cell.[16] Our method is suitable for these guests, because the accurate knowledge of the guest concentration in the aqueous medium is not essential, but what is required is the relative volatilization rate of the guest with and without CyD. While we have no criterion to judge which are more reliable, between ours and literature values, it seems to be helpful to clarify what factors govern the CyD-guest association.

The Inclusion Models. Since the cavity size of α-CyD is relatively small, a benzene ring associates only partly with the host. On the other hand, the other two hosts have sufficiently large cavity to accept linear-condensed benzene-ring compounds. Some water-soluble anthracene derivatives have been demonstrated to be accommodated in γ-CyD as dimer.[17] It seems probable, therefore, that γ-CyD with large internal cavity size includes two anthracene molecules. In this work, however, we have analyzed γ-CyD-anthracene system as a 1 : 1 complex according to the preceding stoichiometric study.[18] We simply postulate that naphthalene, anthracene, phenanthrene, and naphthacene are all axially included in β- and γ-CyD cavities. Inclusion models for anthracene are depicted in Fig. 3.

Factors Governing the Stability of Inclusion Complex. Hydrogen bonding, van der Waals forces, and hydrophobic interaction are generally accepted to be responsible for bonding of guest molecules to CyD

Table 2. Association Constants of 1 : 1 (Host : Guest) Complexation at 25 °C, Comparison with Those in Literatures

Guest-Host	Association constant/dm³ mol⁻¹	
	Our studies	Literature
Benzene-α-CyD	17[6]	31.6[8]
-β-CyD	1.2×10^2[6]	169,[8] 196[9]
-γ-CyD	12[6]	9.1[8]
Naphthalene-α-CyD	83[7]	
-β-CyD	6.3×10^2[7]	685,[10] 730,[11] 850,[12] 186[14]
-γ-CyD	1.3×10^2[7]	
Anthracene-β-CyD	2.3×10^3	420,[14] 32.39[15]
-γ-CyD	1.5×10^3	9.41[15]
Phenanthrene-β-CyD	1.5×10^3	170[13]
Naphthacene-β-CyD	3.4×10^3	221[14]

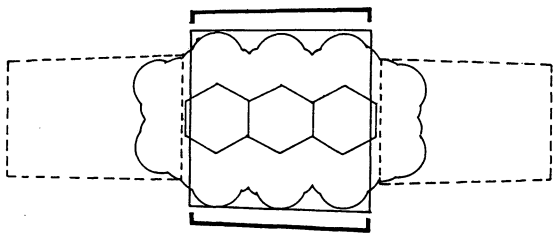

Fig. 3. Anthracene-CyD inclusion model. α-, β-, and γ-cyclodextrin cavities are drawn by dotted, thin solid, and thick solid lines, respectively.

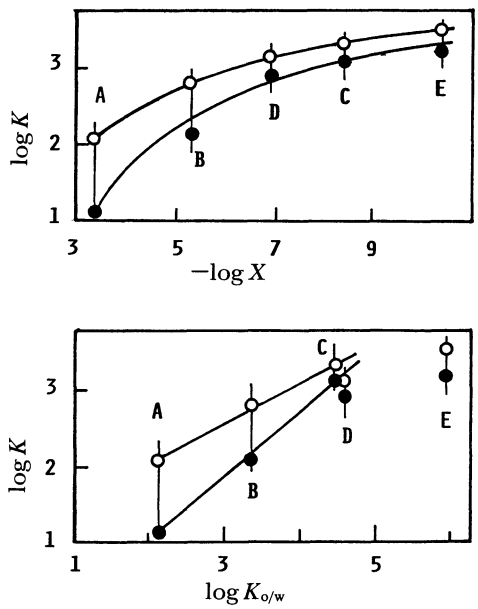

Fig. 4. The dependence of association constant (K) on the mole fraction solubility (X) of guest substance in water (upper), on the partition coefficient ($K_{o/w}$) of guest in 1-octanol/water (lower). Guest: benzene (A), naphthalene (B), anthracene (C), phenanthrene (D), naphthacene (E); β-CyD(○), γ-CyD (●).

cavity. The first one can be excluded in the present case because the guests under consideration have no ability to form hydrogen-bond with CyDs. Hydrophobic interaction has been thought to occur in an aqueous environment between the CyD interior wall and the guest molecule which has lower affinity with water.

It is a problem what should be chosen for an indication of guest hydrophobicity. For some homologous guest series, their solubility in water or their partition coefficient between 1-octanol (or chloroform) and water has been used as a measure of hydrophobicity: logarithmic values vs. $\log K$ plots give fairly good linear relationships.[19-21] Such plots are shown in Fig. 4, from which we can see that the association constant, K, increases with decreasing guest solubility in water or increasing partition coefficient in 1-octanol/water, $K_{o/w}$. A simple interpretation of the phenomena is that the more hydrophobic guest forms the more stable complex with CyD, but we need real reason.

Is a solute with lower solubility in water or larger $K_{o/w}$ value more hydrophobic? The partition coefficient is defined as the ratio of solute concentration in organic solvent to that in water at equilibrium. This coefficient has been measured for a wide variety of chemicals to relate it theoretically to the solute aqueous solubility or to predict the distribution of hydrophobic pollutants in aquatic environments.[22,23] For instance, chemicals with a large partition coefficient are liable to be accumulated into fish body.[24] The partition coefficient is often taken as a measure of the hydrophobic character of a solute,[25] but in a strict sense it is a measure of the relative solubility of the solute in organic solvent and in water, that is, a relative affinity of the solute between surrounding organic and water molecules.

An image of the host-guest association process is that a guest molecule is transferred from water to the hydrophobic environment leaving behind a structured cavity which collapses and redistributes.[26] The free-energy change associated with this process can be easily evaluated, if the hydrophobic environment is substituted for the gaseous phase. Using the Henry's law constant, K_H, $\Delta G_{dehyd}=-RT \ln K_H$. The K_H value is estimated for each guest from its partial vapor pressure and the mole fraction solubility in water at 25 °C. The free-energy change in the 1 : 1 complex formation, $\Delta G_{complex}$ ($=-RT \ln K_1$), is plotted against ΔG_{dehyd} in Fig. 5; a dotted line indicates that $\Delta G_{complex}=\Delta G_{dehyd}$.

For volatile solutes, the most suitable parameter of the hydrophobicity is K_H, a measure of free-energy necessary to carry a solute from aqueous medium to gaseous phase. According to $-\Delta G_{dehyd}$ values, benzene is more hydrophobic than naphthalene, and the latter is more hydrophobic than anthracene. This statement may be strange from the fact that the solubility of naphthalene in water (2.35×10^{-4} M at 25 °C; 1M=1 mol dm^{-3}) is lower two orders of magnitude than that of benzene (2.07×10^{-2} M), and that the solubility of anthracene (2.5×10^{-7} M) is lower three orders of magnitude than that of naphthalene. Such differences in the solubility arise from the difference in the saturated vapor pressure of the solute. The vapor pressure of benzene (1.26×10^{4} Pa at 25 °C) is higher three orders of magnitude than that of naphthalene (10.98 Pa), and the vapor pressure of the latter is higher four orders of magnitude than that of anthracene (8.31×10^{-4} Pa). This is also the case for phenanthrene and anthracene. The former is a little more hydrophobic than the latter in spite of the former aqueous solubility being thirty times larger than the latter.

It can be seen from Fig. 5 that the guests except benzene have considerably larger $-\Delta G_{complex}$ than $-\Delta G_{dehyd}$. If we postulate that a guest molecule is fully embraced in the CyD cavity and that the environment around the guest is a gaseous phase, $-\Delta G_{dehyd}$ for the guest will contribute fully to the $-\Delta G_{complex}$, that is, $-\Delta G_{dehyd}$ estimated from K_H is to be taken as the upper limit of the hydrophobic contribution.

For the guest substances studied here, hydrophobic interaction as a driving force of CyD complexation is not significant, because $-\Delta G_{complex}$ does not increase with $-\Delta G_{dehyd}$. It is van der Waals force that plays the major role to stabilize the complex for the guest of large size. The plots of $\log K$ vs. the total surface area of associating guest are shown in Fig. 6. Nearly

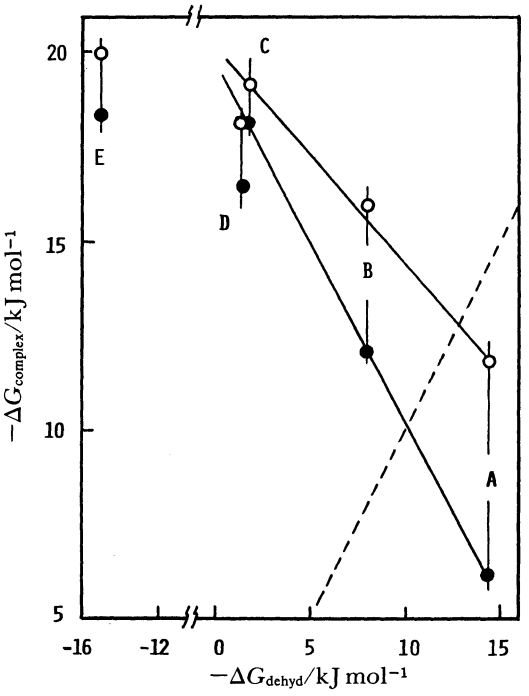

Fig. 5. Free energy changes of CyD-guest complexation and dehydration of guest. Signs and symbols are the same as those shown in Fig. 4.

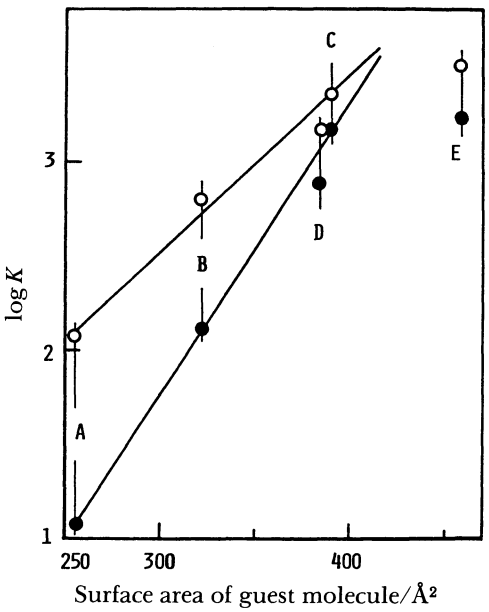

Fig. 6. The dependence of association constant on the surface area of guest molecule. The signs and symbols are the same as those shown in Fig. 4. Values of surface area are taken from Ref. 27.

linear relationships can be seen for β- and γ-CyD except phenanthrene and naphthacene. The increase in the axial length of guest molecule increases the host-guest contact area, leading to the increase in net stabilization. For naphthacene, however, the additional stabilization does not serve to any significant extent, probably because a considerable part of the molecule protrudes out of the CyD cavity. Anthracene and phenanthrene have approximately the same surface area, but the latter forms less stable complexes with CyDs. The reason cannot be fully given at present. Less favorable contact of phenanthrene to the CyD cavity wall may be partially responsible.

The tendency that a guest with the large partition coefficient forms more stable complex with CyD has been observed for guests of homologous series. The tendency is not due to the guest hydrophobicity, but due to the relative strength of guest-water and guest-organic solvent interactions. Intermolecular forces acting between the solute (or guest) and the surrounding solvent molecules (or CyD cavity wall) are similar in its character to each other, that is, the van der Waals forces.

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