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Cyclodextrin Precipitates with Normal Alcohols in an Aqueous Medium and Their Stability on Being Left Standing in Air

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Cyclodextrin (CyD) precipitates with normal alcohols (guests, 1-butanol to 1-decanol) were prepared at 25 °C by introducing an alcohol vapor into an aqueous CyD solution and circulating it in a closed system. The guest/CyD molar ratio of the precipitates was measured immediately after preparation and after having been allowed to stand in air at room temperature for 30 or 40 d. Precipitates were obtained with alcohols higher than 1-pentanol for α-CyD, 1-hexanol for β-CyD, and 1-butanol for γ-CyD. The reason that CyD does not precipitate with lower alcohols could be explained in terms of the solubility product. There was a linear relationship between the apparent solubility (derived from the solubility product) of the CyD precipitates in water and the guest–CyD association constant. Upon drying in air, the guest/CyD molar ratio in the precipitates gradually decreased with days allowed to stand. In the cases of α- and γ-CyDs, the ratio remained constant after one week.

Cyclodextrins (CyD's), cyclic oligosaccharides consisting of six (α-), seven (β-), or eight (γ-CyD) glucopyranose units, act as hosts and form inclusion complexes with various guest substances in an aqueous medium. Precipitation of the complex occurs in some cases, where, as was pointed out in a preceding paper,[1] the product, $[\mathrm{CyD}]\,[\phi]^n$, exceeds the K_{sp} value that is characteristic to the precipitate. Here, [CyD] and $[\phi]$ are the concentrations of free CyD (not associated with guest) and free guest in the supernatant aqueous solution, respectively, and n refers to the guest/CyD molar ratio in the precipitate.

The purity of the CyD precipitates is an important factor used to determine their guest/CyD molar ratios. A method, called "shake-flask," has been used to prepare various CyD precipitates in water.[2,3] After an excess quantity of a guest substance, which exists either in the solid or liquid state at room temperature, is added to a CyD aqueous solution, the mixture is mechanically shaken. The thus-prepared precipitates must be washed, after separation from the aqueous phase, with an organic solvent to remove any excess guest substance adsorbed on the precipitate. Wash-water cannot be used, because, even if cooled, it more or less dissolves the precipitates. The choice of detergents is important. Washing with some organic solvents may partly extract the guest molecules included in CyD, and the solvent molecules, themselves, may be included instead.[3]

We recently proposed an alternative method, called "vapor-circulation," to prepare CyD precipitates.[1,4—7] This method involves the vaporization of a guest substance and the continuous supply of guest molecules to an aqueous CyD solution by circulating the guest vapor in a closed system. Relatively pure CyD precipitates were obtained by this method without any washing operation, because the thus-formed precipitates were not in direct contact with an excess guest phase.

In this work, the vapor-circulation method was applied to prepare CyD precipitates with normal alcohols, 1-butanol to 1-decanol, and the (alcohol/CyD) molar ratio in the precipitates was determined. It would be interesting to determine whether or not the concept of solubility product, which was recently proposed concerning CyD precipitates,[1] is applicable to the CyD–alcohol system. We also studied the stability of CyD precipitates, isolated from water, on being left standing in air. It would also be interesting to understand how alcohol molecules are lost from the CyD precipitates during storage in air.

Experimental

Reagents. All of the reagents used were of analytical reagent grade. Deionized distilled water was used throughout the experiments. α-, β-, and γ-CyD's of guaranteed grade (Nacalai Tesque Co.), dried over phosphorus pentaoxide under vacuum, were used as received. Alcohols (Wako Pure Chemical Co.) of the highest commercially available purity were used without further purification.

Preparation of CyD Precipitates. The procedure used to prepare CyD precipitates was described in a previous paper.[5] α-CyD (0.100 M, $1\ \mathrm{M}\equiv 1\ \mathrm{mol\,dm^{-3}}$), β-CyD (0.0100 M), and γ-CyD (0.0500 and 0.100 M) aqueous solutions were used. The temperature of the CyD solution was held at 25.0±0.1 °C and that of alcohol at 24.5±0.1 °C. The alcohol vapor was introduced into the CyD solution and circulated in a closed system with the aid of a Viton diaphragm air pump (Iwaki Co., AP-032Z). Vapor-circulation was continued until a milky turbidity of the CyD solution no longer increased. In the case of γ-CyD, precipitates were also prepared by the direct addition of methanol, ethanol, and 1-propanol into the CyD solution.

Determination of Molar Ratio of Precipitate. A turbid CyD solution of less than 10 cm^3 was transferred to a conical-type centrifuge tube of 10 cm^3 capacity, centrifuged for 10 min at 4000 rpm, and the supernatant was removed. Three of these centrifuge tubes were immediately treated, and the rest were reserved and allowed to stand in air at room temperature (around 20 °C) for 1 to 30 or 40 d. The content of the centrifuge tube was transferred with 50 cm^3 of water into an extraction funnel, in which a 5 cm^3 portion of an extractant had been placed in advance. Two kinds of extractants were used, one being dichloromethane for 1-pentanol to 1-decanol and the other being 1-hexanol for methanol to 1-butanol.

The extracted alcohols were analyzed with a Shimadzu GC-14B gas chromatograph: a fused silica capillary column of 0.53 mm × 60 m, coated with SPB-1. Calibration curves were prepared using the same volumes of CyD-free water and extractant as those used for sample analyses. As the internal standard, *m*-xylene was used in the dichloromethane extractant, while an unidentified impurity contained in 1-hexanol (the retention time of which was shorter than that of 1-hexanol) was used in the 1-hexanol extractant.

After extraction with dichloromethane or 1-hexanol, a 12.0 cm^3 portion of the aqueous phase in the extraction funnel was transferred to a teat tube, diluted with water, and N_2 gas was bubbled through the solution to expel the dissolved extractant. The solution was then applied to a JASCO RI-930 differential refractometer, and the amount of CyD in the precipitate was determined.

Determination of CyD in Supernatant Aqueous Solution. A 2.00 cm^3 portion of the supernatant aqueous solution was removed from the centrifuge tube, diluted with water to 50.0 cm^3, and shaken with dichloromethane (5 cm^3) to extract any dissolved alcohol molecules. The aqueous phase was diluted with water, aerated with N_2 to expel the dissolved extractant, and applied to the refractometer. In cases where alcohols lower than 1-pentanol were used as guests, the CyD concentrations of the supernatant solutions were not determinable; it was difficult to completely remove such alcohols from aqueous solutions.

Results and Discussion

General Considerations of Guest/CyD Molar Ratio of CyD Precipitates. In determining the guest/CyD molar ratio of the CyD precipitates with various guests, it is important to choose an appropriate method to prepare the precipitates. The shake-flask method is both simple and versatile, while vapor-circulation is only applicable to volatile guest substances. It can be seen from Table 1, where the guest/CyD molar ratio of some CyD precipitates prepared by Cramer and Henglein (shake-flask)[2] and ourselves (vapor-circulation)[5] are shown, that the results are quite different between the two. It is a reasonable expectation that the guest/CyD molar ration for a given guest be larger, in accordance with an increase in the inside diameter of the CyD cavity α : 4.7—5.3, β : 6.0—6.5, γ : 7.5—8.3 Å).

Table 1. Comparison of (Guest/CyD) Molar Ratio in CyD Precipitates Obtained by Shake-Flask and Vapor-Circulation Methods for Some Guest Substances

Guest substance	(Guest/CyD) molar ratio					
	Shake-flask method[a]			Vapor-circulation method[b]		
	α	β	γ	α	β	γ
Fluorobenzene	0.47	0.32	0.55	1.1	1.9	3.0
Chlorobenzene	1	0.42	0.54	0.94	2.0	2.3
Bromobenzene	0.92	1	0.44	0.91	2.0	2.3
Iodobenzene	0.8	1.0	1	0.90	1.6	2.3
Benzene	0.12	0.2	0.3	1.1	1.9	2.7
Naphthalene	—[c]	0.77	0.27	0.30	1.3	1.9

a) Taken from Ref. 2. b) Taken from Ref. 5. c) Precipitation was not observed.

Usually, but not always, the shake-flask method gives a smaller guest/CyD ratio. This may arise from a washing process, indispensable for improving the purity, because the precipitates prepared by this method coexist with the excess guest phase. Cramer and Henglein used diethyl ether as a detergent.[2] Although this detergent has been proven not to affect the molar ratio of such a stable inclusion complex as I_2–α-CyD,[6,8] it is not clear whether or not this is also the case for the other complexes. Moreover, when volatile guests are concerned, the stability of the CyD precipitates should be considered. The guest/CyD molar ratio of precipitates may quickly change upon separating from water, or gradually on standing thereafter in air.

The guest/host molar ratio of a CyD complex may depend on whether the precipitated complex exists in a crystalline or amorphous form. Moreover, it should be taken into account whether the precipitation results from the formation of an inclusion complex, or only decreases in the solubility of CyD, itself, in water in the presence of guest substance due to a change in the physical properties of water.

Experimental Conditions for Preparing CyD Precipitates. As pointed out in a previous paper,[5] in applying the vapor-circulation method, the temperature of the liquid guest phase should be kept slightly lower than that of the CyD solution. It can be seen from Table 2 that, if both temperatures were set to be equal (Condition B in Table 2), the guest/CyD molar ratio of the precipitate gradually increased as the guest vapor-circulation was continued. This was due to the adsorption of the liquid guest phase, which might appear in the CyD solution as a consequence of condensation of the alcohol vapor.

The effects of the initial CyD concentration ($[CyD]_i$) on the guest/CyD molar ratio and the CyD concentration in the supernatant aqueous solution ($[CyD]_s$) were studied on β-CyD using 1-heptanol and 1-octanol as guests (Table 3). The $[CyD]_i$ had, as a matter of course, a direct influence on the amount precipitated, but almost no effect on both the guest/CyD molar ratio and the $[CyD]_s$. It should be noted that

Table 2. (1-Heptanol/β-CyD) Molar Ratio in the Precipitate (Prepared Under Two Different Conditions)[a] as a Function of Alcohol Vapor-Circulation Time

Vapor-circulation time/h	Molar ratio in precipitate	
	Condition A	Condition B
5	0.85	0.87
10	0.85	0.89
15	0.85	0.92
20	0.85	0.94
25	0.85	0.95

a) The temperature of 1-heptanol phase was set at 24.5 °C (Condition A) or at 25.0 °C (Condition B), while the temperature of β-CyD solution was set at 25.0 °C in both conditions.

Table 3. Effect of Initial Concentration of β-CyD on the Amount of Precipitate Observed and the (Guest/β-CyD) Molar Ratio in the Precipitate[a)]

Alcohol (Guest)	Concentration of β-CyD/10^{-3} M		Observed amount of precipitate	Guest/β-CyD molar ratio in the precipitate
	$[\mathrm{CyD}]_i$[b)]	$[\mathrm{CyD}]_s$[c)]		
1-Heptanol	4.00	—	No ppt.	
	6.00	—	No ppt.	
	8.00	7.02	Small	0.85
	10.0	7.00	Large	0.85
	12.0	7.11	Very large	0.84
1-Octanol	4.00	—	No ppt.	
	6.00	—	No ppt.	
	8.00	5.62	Small	0.99
	10.0	5.63	Large	0.98
	12.0	5.65	Very large	0.97

a) The guest vapor was circulated for 15 (C_7) or 10 h (C_8). b) In the initial solution. c) In the supernatant solution.

precipitation rarely occurred, when the $[\mathrm{CyD}]_i$ was slightly above the $[\mathrm{CyD}]_s$.

Table 4 shows how CyD precipitation occurred after the beginning of guest vapor-circulation. It took a longer time at a lower $[\mathrm{CyD}]_i$ to obtain sufficient amounts of precipitates for the measurement. In this work we used considerably high CyD concentrations, as shown in Table 4. In the case of α-CyD–1-hexanol, a strange phenomenon was observed. That is, the precipitate once formed dissolved completely when the alcohol vapor-circulation was allowed to continue for 100 min. Although the change in the form of the precipitate may be responsible for this phenomenon, we cannot explain this phenomenon at the present time.

Table 4. Precipitation Observed on Alcohol Vapor-Circulation

Precipitation with α-CyD (0.100 M)
1) Any ppt. was not observed for 1-butanol, even after 10 h.
2) 1-Pentanol: A small amount of ppt. was obtained after 10 h.
3) 1-Hexanol: Ppt. appeared after 30 min and increased gradually with time, then, after 90 min, the aq soln. began to be clear and the ppt. became completely dissolved after 100 min. The data obtained at 80 min was listed in Table 5.
4) 1-Heptanol, 1-octanol, and 1-nonanol: Ppts. appeared after 20 (C_7, C_8) or 30 min (C_9) and increased gradually with time.
5) 1-Decanol: Ppt. appeared after 1 h and increased a little with time.
Precipitation with β-CyD (0.0100 M)
1) Any ppts. were not observed for the lower alcohols, 1-butanol to 1-hexanol, even after 20 h.
2) 1-Heptanol and 1-octanol: Ppts. appeared after 1 h (C_7) or 30 min (C_8) and increased gradually with time.
3) 1-Nonanol and 1-decanol: Ppts. appeared after 2 h and increased a little with time.
Precipitation with γ-CyD (0.0500 M for C_4 to C_8 and 0.100 M for C_9 and C_{10})
Ppts. appeared after 10 (C_5, C_6), 20 (C_4, C_7, C_8), or 30 min (C_9, C_{10}) and increased gradually with time.

Alcohol/CyD Molar Ratio in Precipitate. The guest/CyD molar ratio of the precipitates measured immediately after preparation and the $[\mathrm{CyD}]_s$ are given in Table 5. The concentration of "free" CyD not associated with the guest ([CyD]) was estimated to be

$$[\mathrm{CyD}]_s = [\mathrm{CyD}] + K[\mathrm{CyD}][\phi], \qquad (1)$$

where K is the 1 : 1 (CyD : guest) association constant and $[\phi]$ refers to the free-guest concentration. For the alcohols studied here, although the K values have been reported for α- and β-CyDs,[9)] the data for γ-CyD as well as that for 1-nonanol and 1-decanol are not available at the present time. The solubility of the alcohols in water at 25 °C, taken from the literature,[10)] was used as $[\phi]$: 1-butanol (0.98), 1-pentanol (0.24), 1-hexanol (5.8×10^{-2}), 1-heptanol (1.5×10^{-2}), 1-octanol (4.5×10^{-3}), 1-nonanol (9.8×10^{-4}), and 1-decanol (2.5×10^{-4} M).

The errors associated with measurement of the guest/CyD molar ratio mainly arise from the water content in the precipitate, because it is impossible, as a matter of fact, to remove water (supernatant solution) completely from the precipi-

Table 5. (Guest/CyD) Molar Ratio in the Precipitate and the Concentration of CyD in the Supernatant Aqueous Solution

Alcohol (Guest)	Type of CyD	Amount in precipitate/10^{-2} mmol		Concentration of CyD/10^{-3} M		n[c)]
		Alcohol	CyD	$[\mathrm{CyD}]_s$[a)]	$[\mathrm{CyD}]$[b)]	
Methanol	γ	426	$17._3$			25
Ethanol	γ	170	$10._9$			16
1-Propanol	γ	$37._0$	4.9_0			7.6
1-Butanol	γ	$14._8$	3.6_0			4.1
1-Pentanol	α	4.4_6	6.2_3			0.72
	γ	3.3_5	2.2_7			1.5
1-Hexanol	α	1.9_8	3.9_0	$74._5$	1.4_2	0.51
	γ	3.3_5	2.9_5	6.0_0		1.1
1-Heptanol	α	0.86	2.9_6	$33._2$	0.95_1	0.29
	β	2.6_8	3.1_5	7.0_0	0.61_0	0.85
	γ	1.9_9	2.6_6	7.8_7		0.75
1-Octanol	α	1.6_0	5.0_4	8.2_5	0.28_2	0.32
	β	2.6_0	2.6_5	5.6_3	0.74_0	0.98
	γ	2.0_5	3.1_0	8.4_5		0.66
1-Nonanol	α	3.1_4	8.3_3	7.3_2		0.38
	β	5.1_2	5.6_5	3.1_5		0.91
	γ	2.9_8	3.9_6	8.2_5		0.75
1-Decanol	α	1.6_8	4.9_4	9.5_0		0.34
	β	1.5_5	2.0_0	6.6_5		0.78
	γ	1.5_7	2.5_0	8.9_5		0.63

a) Concentration of CyD in the supernatant aqueous solution was difficult to measure in the presence of the lower alcohols, methanol to 1-pentanol. b) Concentration of free CyD, not associated with a guest molecule, estimated from Eq. 1; the K value for the other alcohol–CyD systems is not available. c) Guest/CyD molar ratio in the precipitate.

tate by centrifugation. A rough estimation shows that the guest/CyD molar ratio determined immediately after precipitation is overestimated by ca. 30% for 1-pentanol, ca. 10% for 1-hexanol and a few percent for the other higher alcohols. As for CyD, on the other hand, the $[\mathrm{CyD}]_s$ lies in the range of $(3.2—9.5)\times10^{-3}$ M with two exceptions, (1-hexanol, 1-heptanol)–α-CyD (see Table 5). Even in these two exceptional cases, the contribution of CyD in the supernatant solution to the guest/CyD molar ratio in the precipitates was estimated to be a few percent.

Stability on Drying Precipitates. The alcohol–CyD precipitates were separated from the supernatant aqueous solution by centrifugation, stored in centrifuge tubes, and left in air at room temperature for 30 or 40 d. Tables 6 and 7 show how the alcohol/CyD molar ratio in the precipitates changed as a function of the standing time.

The guest/CyD molar ratio in the γ-CyD–1-butanol precipitate just after preparation was extremely high. Such an inclusion complex is unlikely, even for γ-CyD, having the largest cavity size. The observed high molar ratio, which decreased rapidly upon standing in air, was a consequence of the adsorption of 1-butanol molecules on the precipitate. To make this sure, we prepared γ-CyD precipitates with methanol to 1-propanol by directly adding these alcohols to the CyD solution until clear precipitation occurred. The results given in Table 7 indicate that the precipitation with these lower alcohols was not due to complex formation, but to a change in the bulk solvent properties. It has been reported that the solubility of β-CyD decreases in a mixture of water–(methanol or ethanol).[11] 1-Propanol, which was used to purify CyD's by precipitation,[12] seems to fall in the same category.

In the case of α-CyD, the precipitates with 1-heptanol to 1-decanol were quite stable, while those with 1-pentanol and 1-hexanol lost, upon standing, a part of the guest molecules which were probably adsorbed on the precipitate. In contrast, the guest/CyD molar ratio in the β-CyD precipitates was observed to gradually decrease upon standing. The difference in the stability observed for α- and β-CyD precipitates may be explained, after Matsui and Mochida,[9] as follows: "straight-chain alkanols are closely fitted to the relatively small α-CyD cavity, whereas they are too small in size to be in close contact with the relatively large cavity of β-CyD." The same logic, however, cannot be applied to the case of γ-CyD, because the cavity of γ-CyD is larger than that of β-CyD. We assume, in order to explain the experimental results, that there is a room in this cavity to accept water molecule(s) together with a guest alcohol molecule. The water molecule(s) may act as a space-filler and/or a stabilizer through hydrogen bonding to the guest. It has been clarified by X-ray crystallography that water molecules are included in the "empty" cavity of a CyD (α—γ) molecule.[13]

Table 7. Change in (Alcohol/CyD) Molar Ratio of γ-CyD Precipitates as a Function of Days Allowed to Stand in Air

Days	(Alcohol/γ-CyD) molar ratio									
	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}
0	24	16	7.6	4.1	1.5	1.1	0.75	0.66	0.75	0.63
1	10	7.4	4.8	2.8	1.3	1.1	0.73	0.67	0.75	0.65
2	2.6	2.9	2.2	2.0	1.1	0.97	0.72	0.66	0.75	0.63
4	1.8	1.6	1.3	1.4	1.0	0.94	0.69	0.66	0.74	0.63
8	0.07	0.09	0.54	1.1	0.96	0.88	0.68	0.66	0.74	0.62
16	—[a]	—[a]	0.23	1.0	0.89	0.85	0.68	0.66	0.74	0.62
30	—[a]	—[a]	0.12	1.0	0.89	0.85	0.68	0.66	0.74	0.62
40			0.11	1.0	0.89	0.85				

[a] The amount of alcohol in the precipitates was not measurable to a reliable extent.

Hydrogen bonding plays an important role in the CyD–alcohol system. There are three kinds of evidence to support this. First, the association between CyD and alcohol in water is extremely larger than that between CyD and the corresponding alkane.[14] Second, the CyD–alcohol precipitates are quite stable upon standing in air. This is in sharp contrast to other CyD–guest precipitates: an α-CyD–iodine precipitate is most stable among precipitates we have studied,[6] and the present CyD–alcohol precipitates are comparable to the precipitate. Third, more direct evidence has been obtained from X-ray crystallography, though the data are limited to the lower alcohols, such as methanol, ethanol, and 1-propanol.[15,16]

Solubility Product and Solubility of CyD–Alcohol Precipitates. In the preceding paper,[1] we reported on the solubility product (K_{sp}) for various CyD–guest precipitates. The precipitation equilibrium is as follows:

Table 6. Change in (Alcohol/CyD) Molar Ratio of α- or β-CyD Precipitates as a Function of Days Allowed to Stand in Air

Days	(Alcohol/α-CyD) molar ratio						(Alcohol/β-CyD) molar ratio			
	C_5	C_6	C_7	C_8	C_9	C_{10}	C_7	C_8	C_9	C_{10}
0	0.72	0.51	0.29	0.32	0.38	0.34	0.85	0.98	0.91	0.78
1	0.68	0.48	0.29	0.32	0.38	0.34	0.84	0.97	0.88	0.73
2	0.64	0.45	0.29	0.32	0.38	0.34	0.82	0.95	0.87	0.71
4	0.61	0.43	0.29	0.31	0.38	0.33	0.82	0.91	0.85	0.68
8	0.59	0.40	0.29	0.32	0.38	0.33	0.80	0.84	0.79	0.60
16	0.57	0.39	0.29	0.31	0.38	0.33	0.75	0.79	0.69	0.57
30	0.57	0.39	0.29	0.31	0.37	0.33	0.68	0.73	0.65	0.55
40	0.57	0.39								

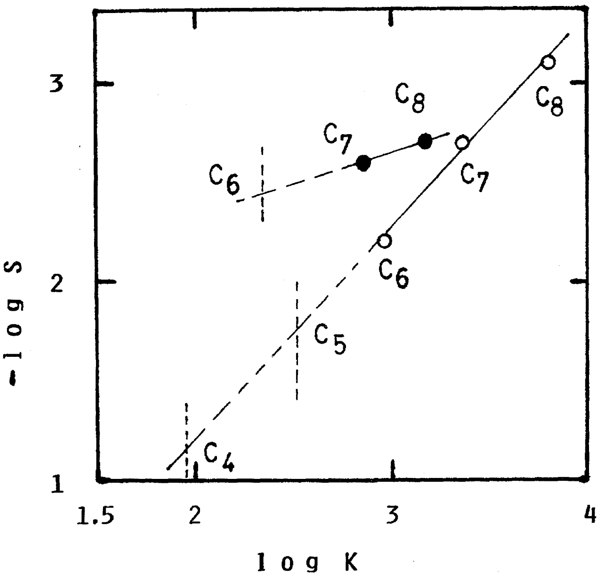

Fig. 1. Plots of $-\log S$ vs. $\log K$ for α-CyD (○) and β-CyD (●). The solubility (S) in water at 25 °C was derived from the solubility product. The 1 : 1 association constant (K) was taken from Ref. 9.

$$\mathrm{CyD} + n\phi \rightleftharpoons \mathrm{CyD}\cdot\phi_n(\mathrm{s}), \tag{2}$$

where ϕ refers to a guest molecule. The solubility product is then expressed as

$$K_{\mathrm{sp}} = [\mathrm{CyD}][\phi]^n. \tag{3}$$

We introduced an apparent solubility (S) for the solubility of a CyD precipitates in water; [CyD] and $[\phi]$ are equal to S and nS, respectively. We then obtained the following equation:

$$K_{\mathrm{sp}} = S(nS)^n. \tag{4}$$

For α- and β-CyD precipitates with some homologeous guest series, a linear relationship was observed between $-\log S$ and $\log K$,[1] where K is the 1 : 1 (CyD : guest) association constant. In Fig. 1, for the present CyD–guest systems, where the K value is available,[9] $-\log S$ is plotted against $\log K$.

Extrapolation of this linear line to the point ($\log K$=) 2.51 for α-CyD–1-pentanol gives a value of 0.016 M as S. Here, n being 0.72 for this precipitate, we obtain 6.4×10^{-4} for K_{sp} from Eq. 4. Precipitation occurs under the condition that the product, [CyD] $[\phi]^n$, is larger than 6.4×10^{-4}, where $[\phi]$ is the solubility of 1-pentanol in water (0.24 M). Thus, since [CyD] is estimated to be 1.8×10^{-3} M, $[\mathrm{CyD}]_\mathrm{s}$ is 0.14 M (from Eq. 1). This value is slightly greater then $[\mathrm{CyD}]_\mathrm{i}$ (0.1 M). This conflict seems not to be very significant when we consider the uncertainties in the experimentally determined K, n, and $[\mathrm{CyD}]_\mathrm{s}$.

The same calculations were undertaken for the α-CyD–1-butanol system; here, we postulated n to be unity (if we employed 0.5—0.7 as n, almost same results were obtained). Using 0.98 M as $[\phi]$ and 1.95 as $\log K$, $[\mathrm{CyD}]_\mathrm{s}$ was estimated to be 0.23 M, which is considerably larger than $[\mathrm{CyD}]_\mathrm{i}$.

We also made a calculation for the case of the β-CyD–1-hexanol system. Extrapolating the line shown in Fig. 1 gives 2.4 as $-\log S$ at the point ($\log K$=) 2.34. Here, we postulated n to be 0.9, if such a precipitation really occurred. Then, $[\mathrm{CyD}]_\mathrm{s}$ was estimated to be 0.004 M. If n was varied over the range of 0.8 to unity, the estimated $[\mathrm{CyD}]_\mathrm{s}$ was not greatly changed. In the case of β-CyD, a large uncertainty is caused by such an extrapolation based on only two plots. If we employ 2.3 as $-\log S$, $[\mathrm{CyD}]_\mathrm{s}$ becomes 0.007 M. This is slightly lower then $[\mathrm{CyD}]_\mathrm{i}$ (0.01 M). Under such conditions, precipitation, if it occurs, takes a much longer time. Now, since the K values for γ-CyD and those for 1-nonanol and 1-decanol are not available, we cannot further discuss the precipitation of such alcohol–CyD complexes based on the solubility product and the hypothentical (or apparent) solubility.

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