In the formalism developed for molecular similarity analysis, "corresponding" atoms (points) from two similar structures are matched in pairs. In contrast, chirality measures, by their very essence, compare *different*, rather than similar, structures: in fact, one can view the most chiral object as the one that differs from its mirror image as much as possible. It is therefore not feasible, in general, to find an unambiguous match of "corresponding" points in enantiomorphs. Take, for example, an asymmetric tetrahedron, $Q = abcd$, and its mirror image, Q'. Identifying points a/a' and b/b' as matched pairs in Q and Q' mismatches c/d' and d/c', and this is true of all six possible pairwise matches, since each produces a different mismatch of the remaining pairs. By the same token, pairwise matching of *all* points that are related by mirror reflection symmetry, i.e., a/a', ..., d/d', results in a similarity measure that does not vanish for achiral tetrahedra. It is therefore not surprising that this approach may yield contradictory results, and it follows that the methodology of rms similarity analysis is unsuitable as a measure of chirality. In contrast, the Hausdorff chirality measure does not require identification and matching of "corresponding" points and is therefore free from any ambiguity arising from the need to define such points. Moreover, the method described in this paper not only can be used to calculate the degree of chirality but also may prove to be valuable as a tool in molecular similarity analysis.

Acknowledgment. We are grateful to Victor Klee and Thomas Auf der Heyde for stimulating discussions and to the National Science Foundation for support of this research.

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Inclusion of Azulene and Alcohol by β-Cyclodextrin in Aqueous Solution

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Abstract: β-Cyclodextrin (β-CD) has been found to form a ternary inclusion complex with alcohol and azulene, with a stoichiometry of 2:2:1. By means of a fluorescence method, equilibrium constants for the formation of the ternary inclusion complex have been evaluated for alcohols from ethanol to 1-pentanol. Induced circular dichroism studies suggest that in the ternary inclusion complex azulene slightly extrudes from the β-CD cavity compared with a 1:1 inclusion complex between β-CD and azulene. From an analysis of a ^{1}H-NMR spectrum for azulene in D_2O containing both β-CD and 1-propanol, 1-propanol incorporated into the β-CD cavity is deduced to be in close proximity to H-2 and H-6 of azulene in the ternary inclusion complex.

β-Cyclodextrin (β-CD) is a cyclic oligosaccharide consisting of seven glucose units. Because of the characteristic doughnut-like shape of β-CD, various kinds of organic compounds are incorporated into the β-CD, forming inclusion complexes. The ability of β-CD to form inclusion complexes is highly affected by the size, shape, and hydrophobicity of guest molecules. Usually, a single guest molecule is accommodated into the β-CD cavity, with a host/guest stoichiometry of 1:1. However, inclusion complexes of 1:2, 2:1, or 2:2 stoichiometry are also known.[1-9] In addition to these binary inclusion complexes, there are ternary inclusion complexes that contain β-CD(s) and two different kinds of guests.[10-18] Recently, Munoz de la Pena et al. have revealed that in a β-CD–alcohol–pyrene system a ternary inclusion complex has a stoichiometry of not 1:1:1 but 2:2:1 β-CD/alcohol/pyrene.[19] Owing to the complicated nature of ternary complexes, however, molecular structures (relative dispositions of component molecules) of ternary complexes are not fully understood. Spectroscopic studies involving absorption and fluorescence spectra and fluorescence lifetime measurements have preferentially been performed for the characterization of the ternary inclusion complexes.

We found that azulene forms a ternary inclusion complex with β-CD and alcohol. Fortunately, azulene is relatively soluble in water. Thus, we could investigate the nature and structure of the ternary inclusion complex of azulene by means of induced circular dichroism (ICD) and ^{1}H-NMR measurements in addition to absorption and fluorescence spectral techniques. Our results demonstrated that the ternary inclusion complex is composed of two β-CD, two alcohol, and one azulene molecule(s), and that,

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[†] Miyazaki Medical College.
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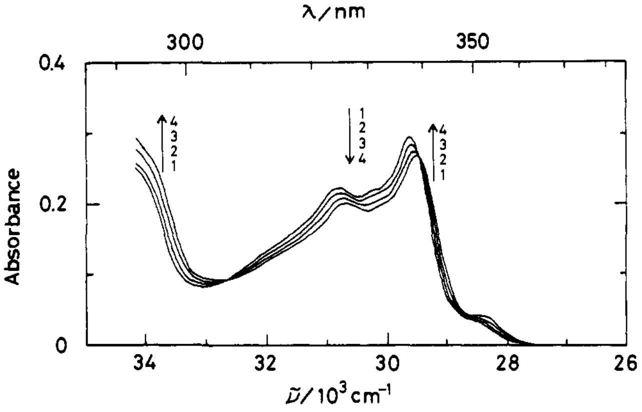

Figure 1. Absorption spectra (340-nm band) of azulene aqueous solutions containing varying concentrations of β-CD. Concentration of β-CD: (1) 0, (2) 5.0×10^{-4}, (3) 2.0×10^{-3}, and (4) 5.0×10^{-3} mol dm^{-3}.

in the ternary inclusion complex of β-CD–1-propanol–azulene, a propyl group of 1-propanol is located in the vicinity of the H-2 and H-6 of an azulene molecule within the β-CD cavity.

Experimental Section

Absorption spectra were recorded on a Shimadzu UV-3100 or UV-260 spectrophotometer. Fluorescence spectra were measured with a Hitachi 850 fluorescence spectrophotometer or a Shimadzu RF-501 fluorometer equipped with a cooled Hamamatsu R-943 photomultiplier. Fluorescence spectra were corrected for the spectral sensitivity of the fluorometers. Induced circular dichroism (ICD) spectra were obtained with a JASCO J-600 spectropolarimeter. ^{1}H-NMR spectra were run on a Varian VXR-500S spectrometer, operating at 500 MHz. At least 800 transients were collected for each ^{1}H-NMR spectrum. Chemical shifts were expressed in parts per million (ppm) relative to an external standard of sodium 3-(trimethylsilyl)-1-propanesulfonate-d_4 in D_2O.

Spectroscopic measurements were made at 25 °C, except for ICD spectra which were taken at room temperature.

β-Cyclodextrin (β-CD) purchased from Nacalai Tesque Inc. was recrystallized from water three times. Azulene purchased from Tokyo Kasei Inc. was chromatographed by a silica gel column. Alcohols from Wako Pure Chemical Industries, Ltd. were distilled under atmospheric or reduced pressure. Deuterium oxide (99.9%) was obtained from E. Merck. Azulene aqueous solution used for the preparation of sample solutions was prepared by allowing azulene crystals to plunge into water for a few days. The concentration of azulene in the sample solutions was about 7×10^{-5} or 1.4×10^{-5} mol dm^{-3} for absorption and ICD measurements and about 7×10^{-6} mol dm^{-3} for fluorescence measurements. For ^{1}H-NMR measurements, the concentration of azulene was about 7×10^{-5} mol dm^{-3}.

Results and Discussion

Inclusion Complex of β-CD with Azulene. Figure 1 shows absorption spectra of the 340-nm band ($S_0 \rightarrow S_2$ band) of azulene in aqueous solutions containing varying concentrations of β-CD. With a progressive increase in the β-CD concentration, the absorption peak is slightly red shifted, accompanied by isosbestic points at 306 and 339 nm, indicating the formation of a 1:1 inclusion complex of β-CD with azulene. From a ^{1}H-NMR study, Fornasier et al. have demonstrated the existence of a 1:1 inclusion complex of β-CD with azulene.[20] Their result for the formation of the 1:1 β-CD–azulene inclusion complex is consistent with our conclusion obtained from the absorption spectra. Figures 2 and 3 depict absorption spectra of the 270-nm ($S_0 \rightarrow S_4$ band) and the 570-nm band ($S_0 \rightarrow S_1$ band) of azulene in the absence and the presence of β-CD, respectively. Upon the addition of β-CD, the 270-nm band in Figure 2 is also red shifted, with concomitant isosbestic points at 245 and 280.5 nm. Similarly, a red shift of the 570-nm band occurs by the addition of β-CD (Figure 3). Figure 4 shows fluorescence spectra of azulene aqueous solutions containing varying concentrations of β-CD. When the β-CD concentration is increased, the fluorescence intensity is enhanced and a slight red shift of the fluorescence peak is observed. This fluorescence spectral change is also due to the formation of the 1:1 β-CD–azulene inclusion complex (CD·Az).

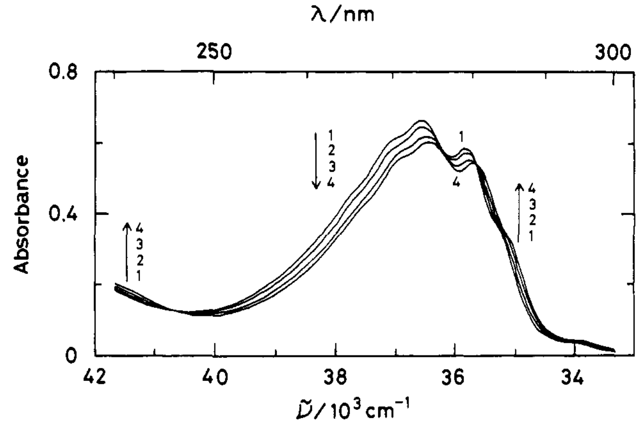

Figure 2. Absorption spectra (270-nm band) of azulene aqueous solutions containing varying concentrations of β-CD. Concentration of β-CD: (1) 0, (2) 5.0×10^{-4}, (3) 2.0×10^{-3}, and (4) 5.0×10^{-3} mol dm^{-3}.

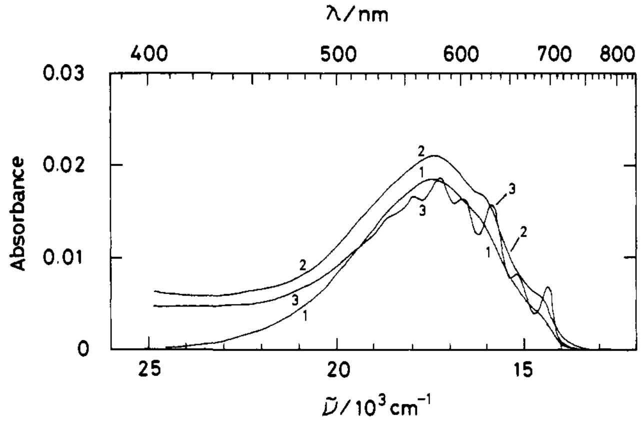

Figure 3. Absorption spectra (570-nm band) of azulene: (1) in aqueous solution, (2) in aqueous solution containing 5×10^{-3} mol dm^{-3} of β-CD, and (3) in aqueous solution containing 5×10^{-3} mol dm^{-3} of β-CD and 0.134 mol dm^{-3} of 1-propanol.

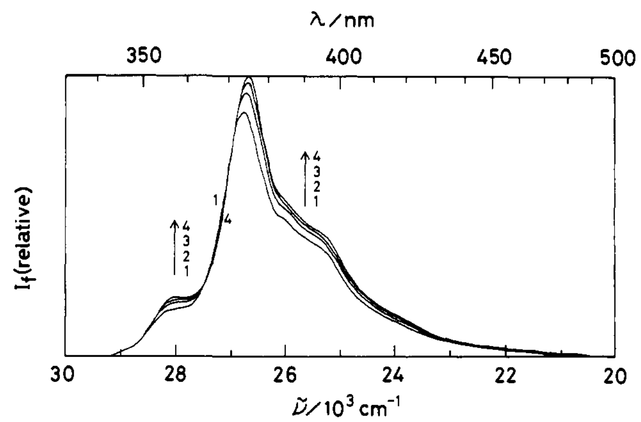

Figure 4. Fluorescence spectra of azulene aqueous solutions containing varying concentrations of β-CD. Concentration of β-CD: (1) 0, (2) 2.0×10^{-3}, (3) 5.0×10^{-3}, and (4) 1.0×10^{-2} mol dm^{-3}. $\lambda_{ex} = 280.5$ nm.

$$\beta\text{-CD} + \mathrm{Az} \overset{K_1}{\rightleftharpoons} \mathrm{CD{\cdot}Az} \tag{1}$$

Here, Az represents azulene and K_1 is an equilibrium constant for the formation of CD·Az. Based on a double reciprocal analysis, K_1 could be determined. From the intensity change in the fluorescence excited at 280.5 nm that is an isosbestic point shown in Figure 2, K_1 was evaluated to be 520 ± 100 mol^{-1} dm^3.

Ternary Inclusion Complex of β-CD with Alcohol and Azulene. When 1-propanol is added to an azulene aqueous solution containing 5×10^{-3} mol dm^{-3} of β-CD, the absorption maxima un-

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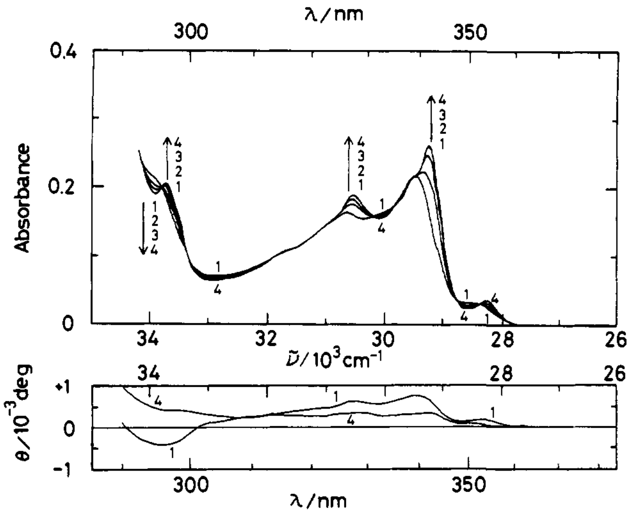

Figure 5. (Top) Absorption spectra (340-nm band) of azulene aqueous solutions containing 5×10^{-3} mol dm^{-3} of β-CD and varying amounts of 1-propanol. Concentration of 1-propanol: (1) 0, (2) 4.01×10^{-2}, (3) 8.03×10^{-2}, and (4) 1.34×10^{-1} mol dm^{-3}. (Bottom) ICD spectra (340-nm band) of azulene aqueous solutions (spectrum 1) containing 5×10^{-3} mol dm^{-3} of β-CD alone and (spectrum 4) both 5×10^{-3} mol dm^{-3} of β-CD and 1.34×10^{-1} mol dm^{-3} of 1-propanol.

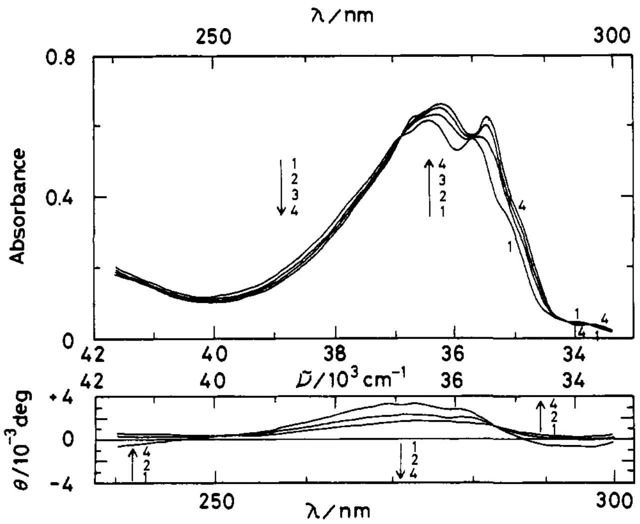

Figure 6. (Top) Absorption spectra (270-nm band) of azulene aqueous solutions containing 5×10^{-3} mol dm^{-3} of β-CD and varying amounts of 1-propanol. Concentration of 1-propanol: (1) 0, (2) 4.01×10^{-2}, (3) 8.03×10^{-2}, and (4) 1.34×10^{-1} mol dm^{-3}. (Bottom) ICD spectra (270-nm band) of azulene aqueous solutions containing 5×10^{-3} mol dm^{-3} of β-CD and varying amounts of 1-propanol. Concentration of 1-propanol: (1) 0, (2) 4.01×10^{-2}, and (4) 1.34×10^{-1} mol dm^{-3}.

dergo red shifts accompanied by isosbestic points at 271, 292, 296, 331, 339, 348, and 353 nm (Figures 5 and 6). At the same time, the absorption bands are sharpened with an increase in the 1-propanol concentration. Addition of 1-propanol to an azulene solution containing β-CD results in an emergence of distinct vibronic bands belonging to the 570-nm band (Figure 3). These findings clearly provide evidence for the formation of a ternary inclusion complex consisting of β-CD, 1-propanol, and azulene. As the 1-propanol concentration is increased, the azulene fluorescence is intensified without any discernible shift of the 376-nm band (Figure 7). In addition, the fluorescence bands as well as the absorption bands for an azulene solution containing both β-CD and 1-propanol are much more structured than those for an azulene solution containing β-CD alone. Such absorption and fluorescence spectral changes were found to take place for normal-chain 1-alcohols from ethanol to 1-pentanol.

Under the conditions that the sum of the initial concentrations of β-CD and 1-pentanol was fixed at 8×10^{-3} mol dm^{-3}, keeping

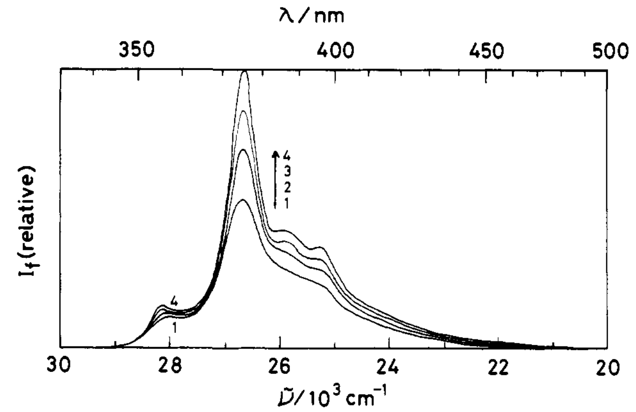

Figure 7. Fluorescence spectra of azulene aqueous solutions containing 5×10^{-3} mol dm^{-3} of β-CD and varying concentrations of 1-propanol. Concentration of 1-propanol: (1) 0, (2) 2.68×10^{-2}, (3) 5.36×10^{-2}, and (4) 1.34×10^{-1} mol dm^{-3}. $\lambda_{ex} = 271$ nm.

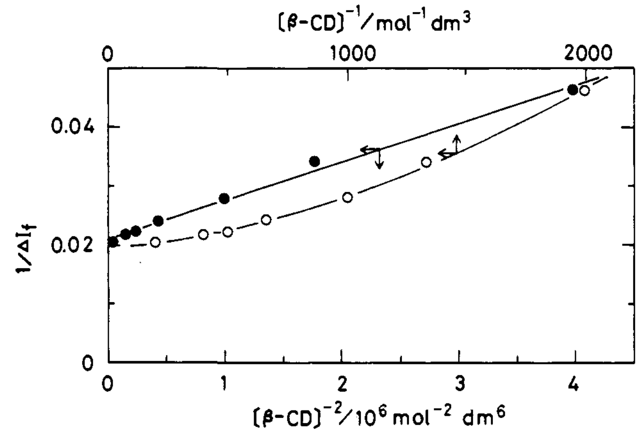

Figure 8. Plots of $1/\Delta I_f$ against $1/[\beta\text{-CD}]$ (○) and $1/[\beta\text{-CD}]^2$ (●) for azulene solutions containing β-CD and 2.68×10^{-1} mol dm^{-3} of 1-propanol. $\lambda_{ex} = 274$ nm.

the azulene concentration constant, the continuous variation method was applied for monitoring the fluorescence intensity. The result for the ternary inclusion complex containing 1-pentanol indicated a 1:1 stoichiometry of β-CD and 1-pentanol (not shown). Munoz de la Pena et al. have reported a ternary β-CD/alcohol/pyrene inclusion complex of a 2:2:1 stoichiometry.[19] For the γ-CD–methanol–coronene system, we proposed a ternary 2:2:1 inclusion complex of γ-CD–methanol–coronene.[21] However, there is the possibility of a 1:1:1 inclusion complex of β-CD–alcohol–azulene. Thus, we investigated how many β-CD molecules are included in the relevant ternary inclusion complex. When n molecules of β-CD are contained in the ternary inclusion complex, the number of alcohols in the inclusion complex is n according to the 1:1 stoichiometry of β-CD and alcohol. Under the conditions of a large excess of alcohol, the following equilibrium is applicable:

$$n(\beta\text{-CD}) + n(\text{alcohol}) + \text{Az} \overset{K}{\rightleftharpoons} (\text{CD})_n\cdot(\text{alcohol})_n\cdot\text{Az} \quad (2)$$

Here, $(\text{CD})_n\cdot(\text{alcohol})_n\cdot\text{Az}$ is the ternary inclusion complex including n molecules of β-CD and alcohol, and K is an equilibrium constant for the formation of $(\text{CD})_n\cdot(\text{alcohol})_n\cdot\text{Az}$. On the basis of eq 2, the following equation regarding the azulene fluorescence intensity is derived:

$$1/\Delta I_f = 1/a + 1/(aK[\text{alcohol}]^n[\beta\text{-CD}]^n) \quad (3)$$

where ΔI_f is an intensity difference of the azulene fluorescence in the presence and the absence of β-CD, and a is a constant. If a single β-CD molecule is contained in the ternary inclusion complex, i.e., $n = 1$, a plot of $1/\Delta I_f$ against $1/[\beta\text{-CD}]$ should be

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Table I. Equilibrium Constants K_3 and K_4 in the β-CD–Alcohol–Azulene Systems[a]

alcohol	K_3/mol^{-3} dm^9	K_4/mol^{-2} dm^6
ethanol	$(3.5 \pm 0.8) \times 10^2$	$(2.1 \pm 0.5) \times 10^5$
1-propanol	$(8.6 \pm 1.9) \times 10^4$	$(3.2 \pm 0.7) \times 10^6$
1-butanol	$(1.3 \pm 0.3) \times 10^6$	$(2.5 \pm 0.6) \times 10^6$
1-pentanol	$(5.2 \pm 1.1) \times 10^6$	$(6.8 \pm 1.4) \times 10^5$

[a] The fixed alcohol concentrations used for the determination of K_3 and K_4 were 1.70, 2.68×10^{-1}, 4.37×10^{-2}, and 2.78×10^{-2} mol dm^{-3}, for ethanol, 1-propanol, 1-butanol, and 1-pentanol, respectively.

linear under the conditions of a large excess of alcohol. Incorporation of two β-CD molecules in the ternary inclusion complex, i.e., $n = 2$, leads to a linear plot of $1/\Delta I_f$ versus $1/[\beta\text{-CD}]^2$ under the same conditions. These plots for 1-propanol (2.68×10^{-1} mol dm^{-3}) are given in Figure 8. The plot of $1/\Delta I_f$ versus $1/[\beta\text{-CD}]$ exhibits a concave upward curve. On the other hand, the plot of $1/\Delta I_f$ versus $1/[\beta\text{-CD}]^2$ is linear, indicative of $n = 2$. From the plot of $1/\Delta I_f$ versus $1/[\beta\text{-CD}]^2$ for 1-propanol, a value of $(4.5 \pm 0.2) \times 10^7$ mol^{-4} dm^{12} is evaluated as K. The K values of other alcohols from ethanol to 1-pentanol were similarly determined. The overall equilibrium of eq 2 can be divided into some stepwise equilibria:

$$\beta\text{-CD} + \text{CD}\cdot\text{Az} + 2(\text{alcohol}) \overset{K_3}{\rightleftharpoons} (\text{CD})_2\cdot(\text{alcohol})_2\cdot\text{Az} \quad (4)$$

or

$$\beta\text{-CD} + \text{alcohol} \overset{K_2}{\rightleftharpoons} \text{CD}\cdot\text{alcohol} \quad (5)$$

$$2(\text{CD}\cdot\text{alcohol}) + \text{Az} \overset{K_4}{\rightleftharpoons} (\text{CD})_2\cdot(\text{alcohol})_2\cdot\text{Az} \quad (6)$$

where K_3 is an equilibrium constant for the formation of the ternary inclusion complex $(\text{CD})_2\cdot(\text{alcohol})_2\cdot\text{Az}$ from β-CD, CD·Az, and alcohol, CD·alcohol is an inclusion complex between β-CD and alcohol, and K_2 and K_4 are an equilibrium constant for the formation of CD·alcohol and that for the formation of $(\text{CD})_2\cdot(\text{alcohol})_2\cdot\text{Az}$ from CD·alcohol and Az, respectively. Using relationships of $K_3 = K/K_1$ and $K_4 = K_1K_3/K_2^2$, K_3 and K_4 for all the alcohols examined were estimated from K's which were obtained previously, and summarized in Table I. A glance at Table I reveals that, on going from ethanol to 1-pentanol, K_3 monotonously increases. Since K_1K_3 equals K, K similarly behaves. On the other hand, K_4 passes through a maximum at 1-propanol on going from ethanol to 1-pentanol. Although the alcohol having the greatest value for K_3 is different from the one for K_4, the alcohol chain length plays an important role in the formation of the ternary inclusion complex. Such an alcohol size effect seems to arise from the steric factor that is related to the facility for occupation of the void space inside the two β-CD cavities accommodating azulene by alkyl groups of two alcohol molecules.

In the β-CD–alcohol–Az system, the fluorescence intensity of azulene, I_f, can be approximated:

$$I_f = b[\text{Az}] + c[\text{CD}\cdot\text{Az}] + d[(\text{CD})_2\cdot(\text{alcohol})_2\cdot\text{Az}] \quad (7)$$

with $b = f\phi_0\epsilon_0$, $c = f\phi_1\epsilon_1$, and $d = f\phi_2\epsilon_2$, where f is an experimental constant, ϕ_0, ϕ_1, and ϕ_2 are the fluorescence quantum yields of Az, CD·Az, and $(\text{CD})_2\cdot(\text{alcohol})_2\cdot\text{Az}$, respectively, and ϵ_0, ϵ_1, and ϵ_2 are molar absorption coefficients, at the excitation wavelength (271 nm) that is an isosbestic point in the β-CD–alcohol–Az system (Figure 6), of Az, CD·Az, and $(\text{CD})_2\cdot(\text{alcohol})_2\cdot\text{Az}$, respectively. Since the initial concentration of azulene is much less than that of β-CD, the latter can be represented as the sum of [β-CD] and [CD·alcohol]. Consequently, using K_1 and K_3, eq 7 is re-formed:

$$I_f = (b + cK_1[\beta\text{-CD}] + dK_1K_3[\beta\text{-CD}]^2[\text{alcohol}]_0^2) \times [\text{Az}]_0/(1 + K_1[\beta\text{-CD}] + K_1K_3[\beta\text{-CD}]^2[\text{alcohol}]_0^2) \quad (8)$$

with $[\beta\text{-CD}] = [\beta\text{-CD}]_0/(1 + K_2[\text{alcohol}]_0)$. Here, suffix 0 stands for the initial concentration. We measured I_f as a function of 1-propanol concentration, and the experimental data are displayed in Figure 9, together with a simulation curve which was best fitted with parameters $b = 178$, $c = 0.816$, $d = 77.1$, and $K_3 = 1.14 \times 10^5$ mol^{-3} dm^9.[22] This K_3 value reasonably agrees with a K_3 value of $(8.6 \pm 1.9) \times 10^4$ mol^{-3} dm^9 that is estimated from K experimentally determined. However, a relationship $b < c < d$, which is expected from the fluorescence intensities of Az, CD·Az, and $(\text{CD})_2\cdot(\text{alcohol})_2\cdot\text{Az}$, is not reproduced, probably because nearly the same simulation curves are obtained if b and c satisfy the relation $b + cK_1[\beta\text{-CD}]_0 = 180$ and appropriate K_3 and d are selected. In this case, K_3 and d were found to show weak dependences on the values of b and c.

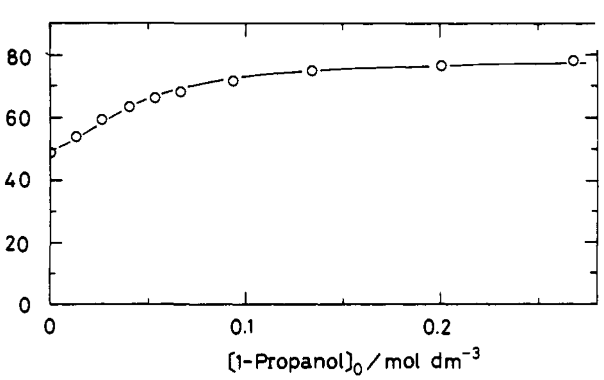

Figure 9. Plot of I_f against $[\text{1-propanol}]_0$ for azulene solutions containing 1-propanol and 5×10^{-3} mol dm^{-3} of β-CD. $\lambda_{ex} = 271$ nm.

Induced Circular Dichroism Study of the Ternary Inclusion Complex. Figures 5 and 6 illustrate ICD spectra of azulene aqueous solutions containing β-CD alone and both β-CD and 1-propanol. The directions of the transition moments of the 270-nm ($S_0 \rightarrow S_4$ absorption band) and 340-nm band ($S_0 \rightarrow S_2$ absorption band) in azulene are parallel to the long axis of azulene.[23,24] On the contrary, the transition moments of the $S_0 \rightarrow S_3$ band (about the 290- to 300-nm region) and the $S_0 \rightarrow S_5$ band (about the 240-nm region) are directed perpendicularly to the long axis of azulene.[23,24] The signs in the ICD spectrum of an azulene solution with β-CD alone are positive for the $S_0 \rightarrow S_2$ and $S_0 \rightarrow S_4$ band as shown in Figures 5 and 6. By contrast, negative ICD curves are observed for the $S_0 \rightarrow S_3$ and $S_0 \rightarrow S_5$ band. These findings can be interpreted in terms of the axial inclusion of azulene into the β-CD cavity.[25] Our conclusion of the axial inclusion is the same as the result obtained by Ikeda and Yamaguchi.[26] When 1-propanol is added to the azulene solution containing 5×10^{-3} mol dm^{-3} of β-CD, the sign of the ICD curve varies from negative to positive in the wavelength regions of the $S_0 \rightarrow S_3$ and $S_0 \rightarrow S_5$ bands (Figures 5 and 6). The ICD curve in the other band regions remains positive in sign but has smaller ellipticity values compared with that for the β-CD–azulene system. The ICD sign for a guest within the CD cavity changes from negative to positive when an angle between the electronic transition moment of a guest and the symmetry axis of CD becomes more than about 35° or when a guest extrudes from the cavity to some extent.[27-29] Similarly, the increase in the angle or the extrusion of the guest from the cavity brings about the reduction of the ellipticity.[27-29] It is unlikely that azulene deeply penetrating within the β-CD cavity rotates to such a large degree. Therefore, both the change in sign of the ICD curves corresponding to the $S_0 \rightarrow S_3$ and $S_0 \rightarrow S_5$ absorption bands and the decrease in ellipticity for the other absorption bands are most likely to be caused by the slight extrusion of azulene from the β-CD cavity.[28,29] However, there may be the possibility that the slight extrusion of azulene out of the cavity occurs accompanied by a slight tilt in an orientation of azulene.

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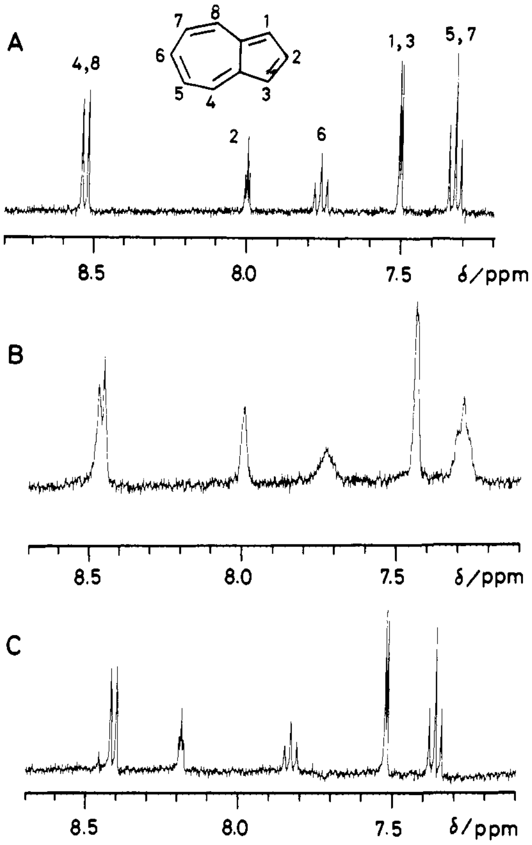

Figure 10. ^{1}H-NMR spectra of azulene (spectrum A) in D_2O, (spectrum B) in D_2O containing 5×10^{-3} mol dm^{-3} of β-CD, and (spectrum C) in D_2O containing 5×10^{-3} mol dm^{-3} of β-CD and 1.34×10^{-1} mol dm^{-3} of 1-propanol.

^{1}H-NMR Study of Inclusion Complexes of Azulene. Figure 10 shows ^{1}H-NMR spectra of azulene (spectrum A) in a D_2O solution, (spectrum B) in a D_2O solution containing 5×10^{-3} mol dm^{-3} of β-CD, and (spectrum C) in a D_2O solution containing both 5×10^{-3} mol dm^{-3} of β-CD and 0.134 mol dm^{-3} of 1-propanol. Upon the addition of β-CD in a D_2O solution of azulene (spectrum B), all the proton signals of azulene are higher-field shifted. The higher-field shifts of the H-2 and H-6 signals are, however, considerably small compared with those of the other proton signals. The H-2 and H-6 seem to be exposed to a bulk water molecule(s) to some extent because of the axial inclusion of azulene into the cavity. Therefore, the H-2 and H-6 of azulene within the cavity are most likely affected by the field of the bulk water molecule(s), resulting in nearly the same resonance positions as those of azulene in D_2O. In the presence of β-CD, the proton signals of azulene are broadened relative to those in a D_2O solution without β-CD. This finding seems to show that the rotation around the long axis of azulene is restricted to some extent because of the deep penetration of azulene into the β-CD cavity. In sharp contrast to spectrum B, the proton signals of an azulene solution with both β-CD and 1-propanol (spectrum C) exhibit lower-field shifts ($\Delta\delta$) relative to spectrum A except for the H-4 and H-8 signals. The most drastic lower-field shift ($\Delta\delta = 0.19$ ppm) is observed for H-2. In a D_2O–1-propanol (2:8) mixture, it was found that the proton signals of azulene are lower-field shifted by 0.15–0.2 ppm relative to those in D_2O. This solvent effect on the proton chemical shifts of azulene can be ascribed to the presence of 1-propanol having a hydrophobic alkyl chain in the mixture. Inoue et al. have shown that ^{13}C chemical shifts for benzoic acid, *p*-hydroxybenzoic acid, and *p*-nitrophenol are linearly dependent on $(\epsilon - 1)/2\epsilon$, where ϵ is the dielectric constant of the solvent.[30] As in the case of the ^{13}C chemical shifts for benzoic acid, etc., a variation of the solvent dielectric constant may be mainly responsible for the solvent effect of the proton chemical shifts of azulene. In addition to the solvent effect of 1-propanol on the proton chemical shifts of azulene, the CD cavity favorably accommodates a hydrophobic moiety of a guest molecule. Consequently, the remarkable lower-field shift of the H-2 resonance of spectrum C leads us to a conclusion that a propyl group of 1-propanol is located in the neighborhood of the H-2 of azulene inside the cavity; a hydrophobic propyl chain enters the cavity in the ternary inclusion complex. The $\Delta\delta$ values of the signals of neighboring H-1 and H-3 are estimated to be 0.02 ppm. The lower-field shifts for H-1 and H-3 are consistent with our conclusion. The $\Delta\delta$ values are 0.03, 0.03, and 0.07 ppm for H-5, H-7, and H-6, respectively. As evidenced by the lower-field shifts of the H-5, H-7, and H-6 signals, another 1-propanol molecule exists near the H-6 of azulene in the ternary inclusion complex. That is, in the ternary inclusion complex, there is an alcohol molecule in close proximity to each end of the long axis of azulene. A similar result has been pointed out for a ternary inclusion complex of γ-CD–methanol–coronene; in this case, an alkyl part of methanol intrudes the cavity.[21] Judging from the higher-field shifts of the H-4 and H-8 signals, an environment around H-4 and H-8 of azulene in the β-CD–alcohol–azulene ternary inclusion complex is not too different from that in the 1:1 β-CD–azulene inclusion complex: the H-4 and H-8 protons of azulene are fully buried inside the cavity, being remote from an alkyl chain of alcohol bound into the cavity. The proton signals in spectrum C are sharpened compared with those in spectrum B. This sharpening can be explained in terms of the shallow penetration of azulene into the β-CD cavity in the ternary inclusion complex compared with the 1:1 β-CD–azulene inclusion complex. The intrusion of the alkyl moiety of alcohol into the cavity is responsible for the shallow penetration of azulene, which is also deduced from the ICD spectral change in the presence of alcohol. The shallow penetration affords a large degree of rotational freedom to azulene within the cavity, resulting in the narrow signal width.

Our proposed model, for the ternary inclusion complex, which is built on the basis of NMR and ICD spectra, well elucidates the absorption and fluorescence spectral changes. In the ternary inclusion complex, the partial occupation of the void of the β-CD cavity by the alkyl chain of alcohol induces a decrease in polarity around azulene. The decrease in polarity causes the sharpening in the absorption and fluorescence spectra of an azulene solution containing both β-CD and alcohol.

Registry No. β-CD, 7585-39-9; 2β-CD·2ethanol·azulene, 141707-89-3; 2β-CD·(1-propanol)$_2$·azulene, 141707-90-6; 2β-CD·(1-butanol)$_2$·azulene, 141707-91-7; 2β-CD·(1-pentanol)$_2$·azulene, 141707-92-8; azulene, 275-51-4; ethanol, 64-17-5; 1-propanol, 71-23-8; 1-butanol, 71-36-3; 1-pentanol, 71-41-0.

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