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Excimer Formation and Intramolecular Self-Complexation of Double-Armed γ-Cyclodextrin

Fumio Hamada,[†] Koichi Murai,[†] Akihiko Ueno,* Iwao Suzuki, and Tetsuo Osa*
Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980
[†]Department of Fuel Chemistry, Mining College, Akita University, Gakuen-cho, Tegata, Akita 010

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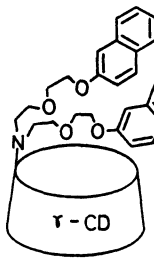
Synopsis. Circular dichroism and fluorescence studies of γ-cyclodextrin bearing two naphthyl moieties (**1**) suggest that **1** exists as two intramolecular self-complexation forms in water-rich solutions with one or two of the naphthyl moieties included in its cavity. Upon addition of (−)-borneol as a guest, **1** forms a 1 : 1 host-guest complex, exhibiting slightly diminished excimer and circular dichroism bands. Ethylene glycol converts the intramolecular complexes into a relaxed form, in which two naphthyl moieties dangle outside the cavity.



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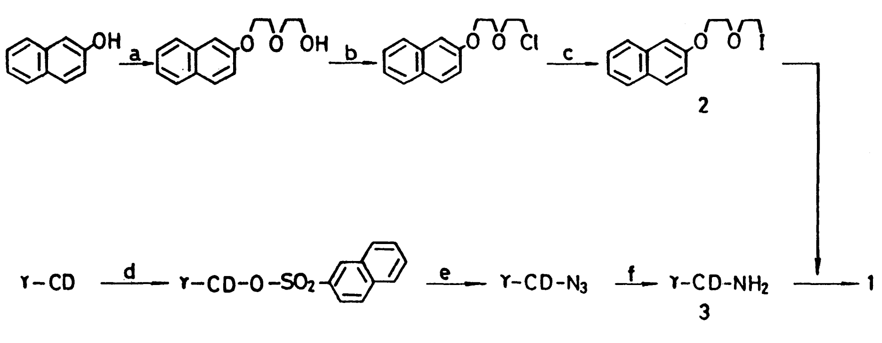
Many spectroscopic studies have shown that γ-cyclodextrin (γ-CD, cyclooctaamylose) can include two guest molecules in its large cavity.[1)] When an aromatic moiety is covalently linked to γ-CD, it was suggested to enable γ-CD to form 1 : 1 host-guest complexes by narrowing the large cavity as a spacer.[2)] When γ-CD has two naphthyl moieties located apart on its rim, the host accommodates one guest molecule in its cavity by moving the two naphthyl moieties outward from the interior of the cavity.[3)] We describe here fluorescence and circular dichroism properties of another type of bi-chromophoric γ-CD (**1**), in which two naphthyl moieties are branched out from the nitrogen atom of amino-γ-CD.

The double armed γ-CD **1** was prepared as shown in Scheme 1. Since the reaction of γ-CD with 2-naphthalenesulfonyl chloride in pyridine is known to give a γ-CD derivative sulfonated regiospecifically at a primary hydroxyl, the amino moiety bearing two naphthalene rings is located at the narrower mouth of the primary hydroxyls of γ-CD.

Figure 1 shows the circular dichroism spectra of **1** in an aqueous 10% ethylene glycol solution. The spectrum of **1** at 8.42×10^{-5} mol dm^{-3} exhibits peaks around 220 nm and 280 nm and a trough around 240 nm. The dichroism intensities of the peak and the trough below 250 nm were reduced with decreasing concentration of **1**, and the spectrum, which has no trough around 240 nm, is eventually obtained. This concentration-dependency suggests that **1** associates with each other at its high concentrations. The change in the dichroism sign from negative to positive from the longer wavelength side below 250 nm may be related to the exciton coupling of S-helicity[4)] arising from the electronic interaction between two naphthalene rings involved in the associated forms of **1**. Since no concentration-dependency was observed at lower concentrations than 2×10^{-5} mol dm^{-3} (Fig. 1 (B)), **1** is likely to exist as a monomer species in the concentration range. Upon addition of (−)-borneol to a dilute solution of **1**, the intensity of the positive peak around 218 nm was found to diminish, but the spectrum obtained in the presence of excess (−)-borneol still has the peak with a considerable intensity (Fig. 1). The analysis of the (−)-borneol-induced circular dichroism variations gave 720 mol^{-1} dm^3 as the binding constant.[3)]

Figure 2 shows the fluorescence spectra of **1** in an aqueous 10% ethylene glycol solution, alone or in the presence of (−)-borneol. It is noted that the fluorescence pattern is hardly dependent on the concentration of **1**. The spectra exhibit a broad band around 410 nm in addition to the normal fluorescence around 358 nm. Since the broad band was observed even in acidic solu-



a, $ClCH_2CH_2OCH_2CH_2OH$, NaOH, 1-BuOH; b, $SOCl_2$; c, NaI, DMF; d, 2-$C_{10}H_7SO_2Cl$, pyridine; e, NaN_3; f, H_2/Pd-C

Scheme 1.

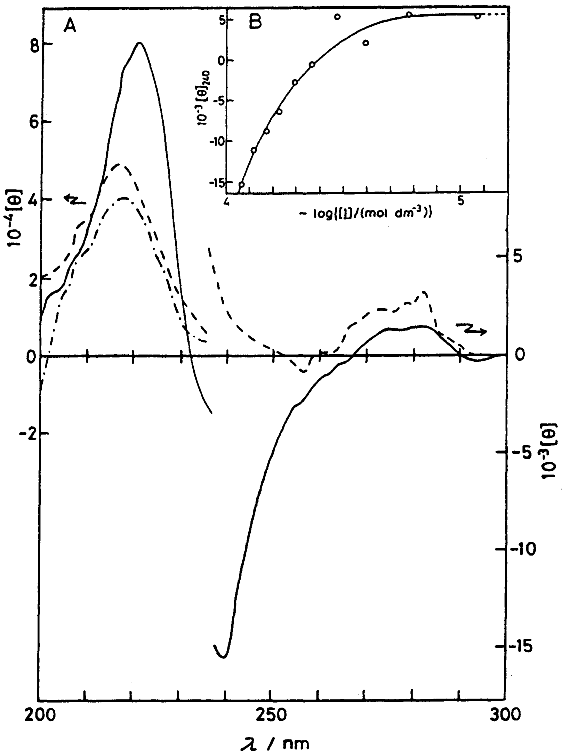


Fig. 1. Circular dichroism spectra of **1**, alone (——, 8.42×10^{-5} mol dm^{-3}; ----, 1.68×10^{-5} mol dm^{-3}) or in the presence of (−)-borneol (-·-: **1**, 1.68×10^{-5} mol dm^{-3}; (−)-borneol, 2.17×10^{-4} mol dm^{-3}) in an aqueous 10% ethylene glycol solution. The concentration-dependency of 240-nm dichroism intensity is shown in B.

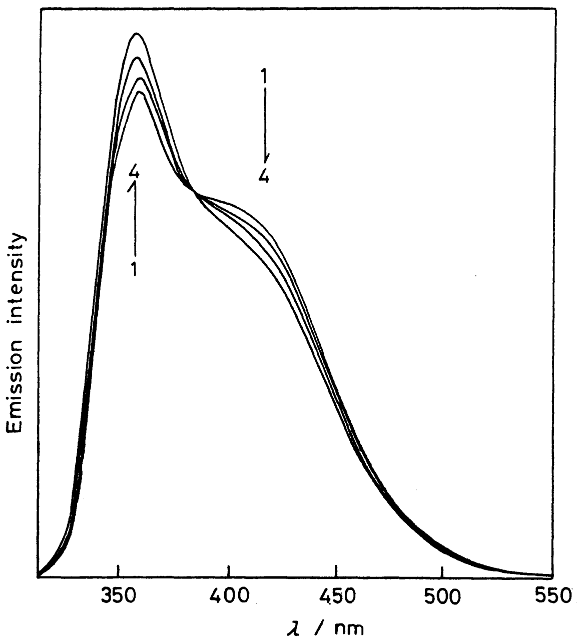
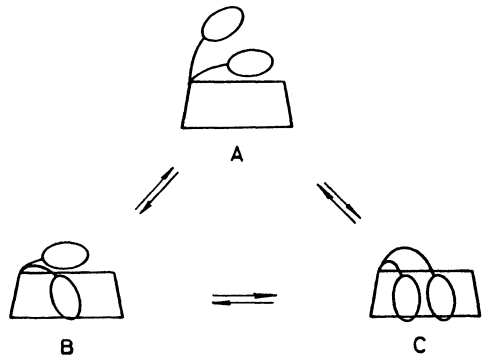


Fig. 2. Fluorescence spectra of **1** (7.68×10^{-6} mol dm^{-3}) in an aqueous 10% ethylene glycol solution at various (−)-borneol concentrations (1, 0; 2, 5.0×10^{-4}; 3, 2.0×10^{-3}; 4, 4.0×10^{-3} mol dm^{-3}).

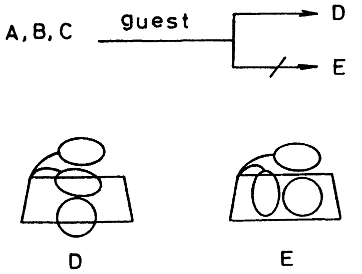
tions, it was assigned to excimer emission, in other words, the band cannot be assigned to exciplex emission, which might have been caused by excited-state electronic interaction between the naphthyl chromophore and the nitrogen atom.[5] With increasing (−)-borneol concentration, the excimer intensity decreases while the monomer intensity increases. These (−)-borneol-induced variations are slight and suggest that excimer formation is possible even in the complexes.

When fluorescence spectra of **1** were measured at various ethylene glycol contents, the relative intensity of the excimer emission diminished with increasing ethylene glycol, and almost pure monomer fluorescence band was obtained in ethylene glycol. The absence of the excimer emission in ethylene glycol indicates that the two naphthyl moieties of **1** are separated from each other outside the cavity in the organic solvent.

Compound **1** may take three equilibrium forms **A**, **B**, and **C** in its dilute solutions as shown in Scheme 2. In **B** and **C**, **1** accommodates one or two of the pendant naphthyl moieties in its own cavity (intramolecular self-complexation). Since **1** exhibits induced circular dichroism in the naphthalene absorption regions, the naphthyl moiety is likely to be involved in the chiral CD cavity, and **B** and **C** forms are candidates for predominant species in water-rich solutions. In **B**, one of two naphthyl moieties acts as a cap[6] for another naphthyl moiety, which is included in the cavity, stabilizing the intramolecular complex. In **C**, the two naphthyl moieties are involved into the cavity together. The excimer emission observed in water-rich solutions confirms that **1** can take **C** form with two naphthyl moieties included in the cavity. On the other hand, the considerable intensity of the monomer emission suggests that **1** can also take **B** form, in which excimer is hardly formed because of the difficulty in face-to-face interactions between the two naphthyl moieties.[7] In ethylene glycol, **1** exhibits no excimer emission and may take **A** form due to weak hydrophobic interactions. The complex formation with (−)-borneol may convert **1** from intramolecular self-complexation forms **B** and **C** to an intermolecular complexation form **D** as shown in Scheme 3. Since excimer emission of **1** was still observed in the presence of (−)-borneol, the two naphthyl moieties are likely to be closely located in complex **D**. Examination of molecular



Scheme 2.



Scheme 3.

models indicates that complex form **E**, in which one of the two naphthyl moieties acts as a typical spacer for (−)-borneol, cannot be formed due to bulky size of (−)-borneol. The fact that the circular dichroism intensity of **1** is still large in the presence of excess (−)-borneol, suggests that one or two of the naphthyl moieties are likely to be involved partly in the γ-CD cavity in complex **D**, acting as flexible caps for the included guest.

Experimental

The circular dichroism and fluorescence spectra were measured at 25 °C using a JASCO J-400X spectrodichrometer and a Shimadzu RF-500 spectrofluorophotometer, respectively. The circular dichroism intensities were expressed as molar ellipticity (in degree $cm^2 dmol^{-1}$) on the basis of the total concentration of **1**. Due to the poor solubility of **1** in pure water, an aqueous 10% ethylene glycol solution was used as the solvent. 2-Naphthylsulfonyl-γ-CD was prepared according to the reported method.[2b)] Azido and amino derivatives of γ-CD were prepared by the methods similar to those reported by Melton et al.[8)] for preparation of the corresponding α-CD derivatives.

Synthesis of 1. A mixture of the iodide **2** (2.7 g, 7.5 mmol), amino-γ-CD **3** (1.2 g, 0.93 mmol), K_2CO_3 (0.98 g), and *N*,*N*-dimethylformamide (40 ml) was heated at 80 °C for 40 h under nitrogen. After cooling, the reaction mixture was filtered and the filtrate was poured into 500 ml of acetone. The precipitates were collected by filtration, dissolved in water, and subjected to CM-Sephadex C-50 column chromatography with water as the eluting solvent. Recrystallization from methanol gave the desired product (0.202 g, 12%): R_f=0.46 (*n*-BuOH, EtOH, H_2O 5 : 4 : 3); ^{1}H NMR (DMSO-d_6) δ=2.6—3.8 (m, 64H), 4.50 (m, 7H, O_6H), 4.88 (m, 8H, C_1H), 5.63—5.96 (br. s, 16H, O_2H, O_3H), 7.13—7.88 (m, 14H, Ar); IR (KBr): 1628, 1600 cm^{-1}. Found: C, 50.76; H, 6.25; N, 0.76%. Calcd for $C_{76}H_{109}NO_{43} \cdot 4H_2O$: C, 50.80; H, 6.56; N, 0.78%.

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