

# Supramolecular assembly system depended on guest species based on bis-naphthalene modified $\beta$ -cyclodextrin dimer

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Received: 27 September 2006 / Accepted: 7 May 2007 / Published online: 3 August 2007  
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**Abstract** The supramolecular assembly system based on bis naphthalene modified  $\beta$ -cyclodextrin dimer linked with ethylenediamine unit was studied. The synthesis of the titled compound ( $\beta$ -1) was succeeded in a 7% synthetic yield. It was observed that  $\beta$ -1 showed monomer emission, which was decreased concurrently with appearance of excimer emission in an addition of guest species such as 1-adamantanol or ursodeoxycholic acid. When  $\gamma$ -CyD was added to the system, two types of fluorescent spectra were obtained, which was depended on guest species. It was indicated that both of naphthalene units of  $\beta$ -1 were included in the  $\gamma$ -CyD cavity in the presence of 1-adamantanol in a fashion of 2:1 complex. On the other hand, an addition of ursodeoxycholic acid gave disappearance of the excimer emission as well as increase of monomer emission. In the system, each of the appended units was trapped by the each of two  $\gamma$ -CyDs, which is 2:2 complex formation.

**Keywords** Supramolecular assembly · Cyclodextrin dimer · Naphthalene · Excimer emission · Monomer emission

## Introduction

There are several reports concerning hetero association complexes formation or recognition system based on cyclodextrin (CyD) derivatives as supramolecular

assembly [1–5]. These reports described two components such as assembly based on monomer CyD and assembly based on modified CyD.

On the other hand, multiple CyD such as linked CyD dimer and polymeric CyD derivatives have attracted much interest because these CyDs have multi complexation sites which forms multiple complexation of guest molecule. For a last decade, we have studied host-guest complexation systems based on fluorescent CyD dimer such as dansyl modified  $\gamma$ -CyD [6] and pyrene modified  $\gamma$ -CyD [7], which can complex with steroidal framework compound such as ursodeoxycholic acid.

Recently, we have reported hetero supramolecular formation based on bis-pyrene modified  $\beta$ -CyD dimer [8]. For further an extension of the work, we would like to report another type of supramolecular assembly based on bis-naphthalene modified  $\beta$ -CyD dimer.

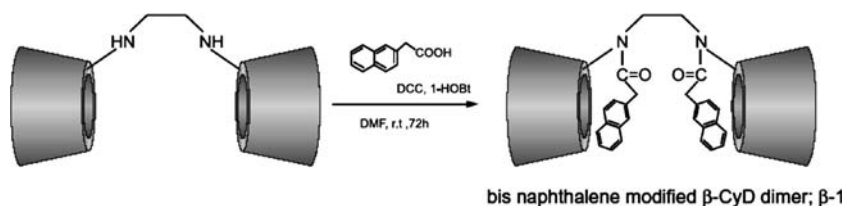
## Experimental

Preparation of bis naphthalene modified  $\beta$ -cyclodextrin dimer linked with ethylenediamine ( $\beta$ -1)

Dicyclohexylcarbodiimide (DCC, 0.195 g, 0.95 mmol) was added to a cooled solution ( $-20\text{ }^{\circ}\text{C}$ ) of 2-naphthalene acetic acid (0.166 g, 0.89 mmol) and 1-hydroxybenzotriazole (1-HOBt, 0.128 g, 0.95 mmol) in 20 ml of DMF. The reaction mixture was stirred at  $-20\text{ }^{\circ}\text{C}$  for 2 h. To a stirred solution was added portion wise 6-(2-aminoethyl)-amino-6-deoxy-bis- $\beta$ -CyD ( $\beta$ -CyD dimer, 0.600 g, 0.26 mmol), the solution was stirred for another 1 h at  $-10\text{ }^{\circ}\text{C}$ , and then the reaction mixture was stirred at room temperature for 2 days. After stirring, the reaction mixture was concentrated under reduced pressure. The residue was

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**Scheme 1** Preparation of bis naphthalene modified  $\beta$ -CyD dimer



poured into ca. 300 ml of acetone. The resulting precipitates were filtrated and dried. The water soluble fraction was applied to a reversed-column (Lobar column LiChro-prep RP-18, Merck Ltd.,  $310 \times 10$  mm). Stepwise elution with 200 mL of 10–30 vol.%, 300 mL of 40 vol.% aqueous MeOH and 400 mL of 50 vol. % aqueous MeOH gave bis naphthalene-modified  $\beta$  CyD dimer ( $\beta$ -1) as a white powder, 7.0%.  $R_f$  0.43 (1-butanol-ethanol-water 5:4:3 by volume, TLC, silica gel 60F<sub>254</sub>).

<sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  = 3.2–3.8 (84 H, m, C<sup>2</sup>–C<sup>6</sup> of CyD) 4.8–5.0 (12 H, m, O<sup>6</sup>H of CyD), 5.7–6.0 (28 H, m, O<sup>2</sup>H and O<sup>3</sup>H of CyD), 7.96–8.25 (14H, m, aromatic–H of naphthalene). Calcd for C<sub>110</sub>H<sub>160</sub>O<sub>70</sub>N<sub>2</sub>•11H<sub>2</sub>O: C 46.71; H 6.48 ; N 0.99 %. Found: C 46.55; H 6.32; N 1.72%. TOF-MS(*m/z*):2652 ([M + Na]<sup>+</sup>).

## Measurements

Fluorescence and induced circular dichroism (ICD) spectra were measured at 25 °C using a Perkin–Elmer LS 40B fluorescence spectrophotometer and JASCO J-700 spectropolarimeter, respectively. ICD spectra were taken in a 10 vol.% DMSO aqueous solution at the concentration of  $\beta$ -1 was  $5.0 \times 10^{-5}$  M. For fluorescence measurements, the excitation wavelength of the fluorescence spectra was 295 nm and excitation and emission slits were 5 nm. For spectroscopic measurements, dimethyl sulfoxide (DMSO) aqueous solution (10 vol.%) was used as a solvent, because the solubility of  $\beta$ -1 in pure water is poor. Five  $\mu$ L of guest species of 0.05 M in DMSO or MeOH were injected into a 10 vol.% DMSO aqueous solution of the host (2.5 mL) to make a sample solution with a host concentration of  $1.0 \times 10^{-6}$  M and guest concentration of  $1.0 \times 10^{-4}$  M.

## Results and discussion

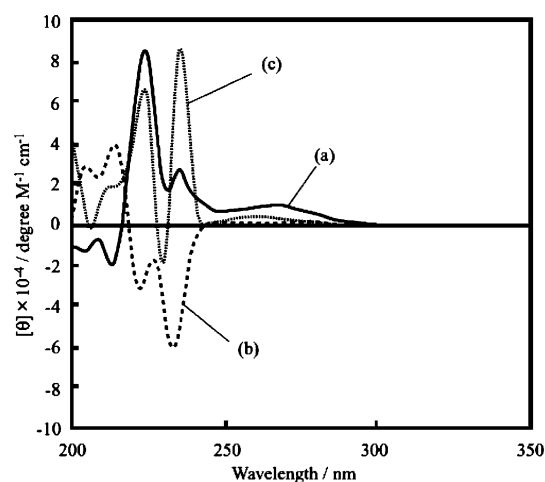
### Preparation of $\beta$ -1

Bis naphthalene-modified  $\beta$ -CyD dimer ( $\beta$ -1) was prepared from  $\beta$ -CyD dimer [6] (6-(2-aminoethyl)-amino-6-deoxy-bis- $\beta$ -CyD) with an excess of 2-naphthalene acetic acid in the presence of DCC and 1-HOBT as shown in Scheme 1, and a crude product containing  $\beta$ -1 was purified with

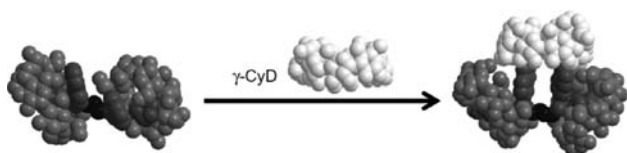
reverse phase column chromatography (RP-18 column chromatography).

### Circular dichroism spectra

Figure 1 shows ICD spectra of  $\beta$ -1 in 10 vol. % DMSO aqueous solution at 25°C, alone (a), in the presence of 1-adamantanol (b), coexistence of  $\gamma$ -CyD (c). The ICD spectrum of  $\beta$ -1 exhibits three positive Cotton peaks at around 225, 235 and 280 nm. When 1-adamantanol was added to the  $\beta$ -1 solution, the both positive peaks at 225 and 235 nm were altered to negative ones. It is suggested that the appended units came out from the CyD cavity, of which a long axis of naphthalene is taking a position to parallel to the CyD cavity [9] as illustrated in Scheme 2. When  $\gamma$ -CyD was added to the  $\beta$ -1 solution containing with 1-adamantanol, those negative Cotton peaks were alternated to positive Cotton ones, again. It is estimated that the appended units of  $\beta$ -1 were included in the  $\gamma$ -CyD cavity perpendicularly [10] as illustrated in Scheme 2. This observation was evidence for a formation of hetero association consisted with three components, such as  $\beta$ -1, 1-adamantanol and  $\gamma$ -CyD. Figure 2 shows ICD spectra of  $\beta$ -1 in 10 vol.% DMSO aqueous solution at 25°C, alone



**Fig. 1** Induced circular dichroism spectra of  $\beta$ -1 in 10 vol.% DMSO aqueous solution ( $5.0 \times 10^{-5}$  M) with added species (a) [1-adamantanol] = 0, [ $\gamma$ -CyD] = 0, (b) [1-adamantanol] =  $2.0 \times 10^{-4}$ , [ $\gamma$ -CyD] = 0, (c) [1-adamantanol] =  $2.0 \times 10^{-4}$ , [ $\gamma$ -CyD] =  $1.0 \times 10^{-3}$  M

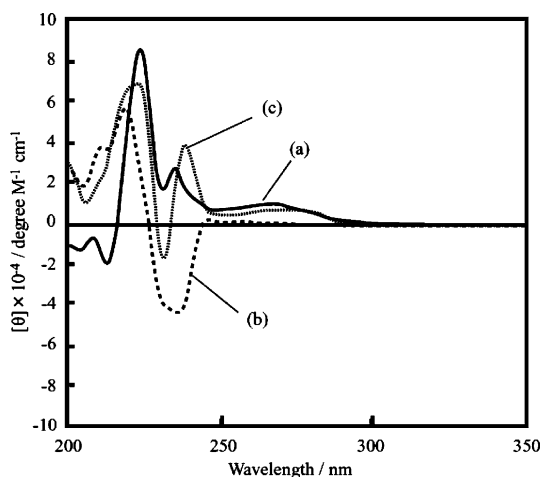


**Scheme 2** Supramolecular assembly among  $\beta$ -1, 1-adamantanol, and  $\gamma$ -CyD

(a), in the presence of ursodeoxycholic acid (b), coexistence of  $\gamma$ -CyD (c). The ICD pattern obtained from  $\beta$ -1 with an addition of ursodeoxycholic acid shows a different from that of the case when 1-adamantanol was used as a guest. When ursodeoxycholic acid was added to the  $\beta$ -1 solution,  $\beta$ -1 exhibits exciton coupling bands in the naphthalene  ${}^1B_u$  transition region (220–260 nm) [11]. It means that bis appended units came out the CyD cavity, which made counterclockwise (*S*-helicity) configuration with a locating near the CyD cavity. When  $\gamma$ -CyD was added to the  $\beta$ -1 solution containing ursodeoxycholic acid, the exciton coupling was cancelled, which resulted in coming back to similar original spectrum of  $\beta$ -1. It is estimated that the each appended units of  $\beta$ -1 was included in the each  $\gamma$ -CyD cavity perpendicularly, because twisting of appended units would be easy to be trapped by each  $\gamma$ -CyD cavity, not both naphthalene units were trapped by one  $\gamma$ -CyD cavity.

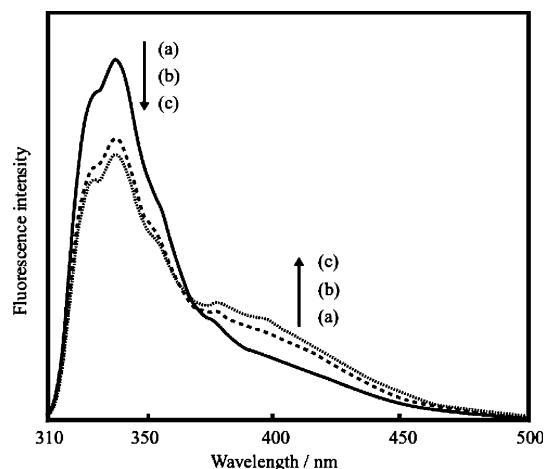
#### Fluorescence spectra

Figures 3 and 4 show the fluorescence spectra of  $\beta$ -1 in 10 vol.% DMSO aqueous solution at 25 °C, alone and in the

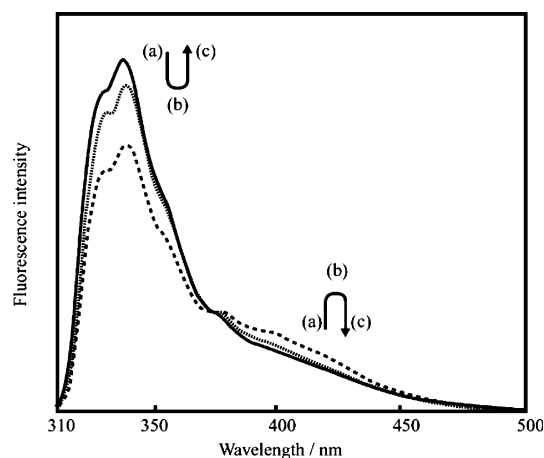


**Fig. 2** Induced circular dichroism spectra of  $\beta$ -1 in 10 vol.% DMSO aqueous solution ( $5.0 \times 10^{-5}$  M) with added species. (a) [ursodeoxycholic acid] = 0, [ $\gamma$ -CyD] = 0, (b) [ursodeoxycholic acid] =  $2.0 \times 10^{-4}$ , [ $\gamma$ -CyD] = 0, (c) [ursodeoxycholic acid] =  $2.0 \times 10^{-4}$ , [ $\gamma$ -CyD] =  $1.0 \times 10^{-3}$  M

presence of 1-adamantanol (a) or ursodeoxycholic acid (b) as a guest and coexisting of  $\gamma$ -CyD (c). The  $\beta$ -1 alone exhibits only strong monomer emission at 340 nm, which suggests each naphthalene unit was mostly included in each the CyD cavity. In this case, an intermolecular interaction such as excimer formation between two naphthalene units seems to be impossible because two naphthalene units were locating as not so close. When 1-adamantanol was added, monomer emission was decreased and the relative weak excimer emission was appeared. It was suggested that naphthalene moieties were moved out from the cavity, 1-adamantanol was included in



**Fig. 3** Fluorescence spectra of  $\beta$ -1 in 10 vol.% DMSO aqueous solution ( $1.0 \times 10^{-6}$  M) with added species. (a) [1-adamantanol] = 0, [ $\gamma$ -CyD] = 0, (b) [1-adamantanol] =  $2.0 \times 10^{-4}$ , [ $\gamma$ -CyD] = 0, (c) [1-adamantanol] =  $2.0 \times 10^{-4}$ , [ $\gamma$ -CyD] =  $1.7 \times 10^{-3}$  M



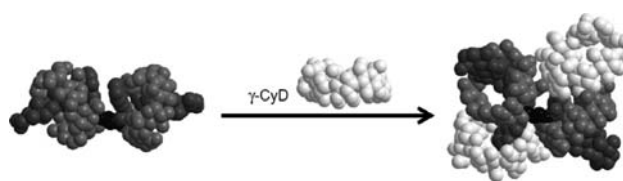
**Fig. 4** Fluorescence spectra of  $\beta$ -1 in 10 vol.% DMSO aqueous solution ( $1.0 \times 10^{-6}$  M) with added species. (a) [ursodeoxycholic acid] = 0, [ $\gamma$ -CyD] = 0, (b) [ursodeoxycholic acid] =  $2.0 \times 10^{-4}$ , [ $\gamma$ -CyD] = 0, (c) [ursodeoxycholic acid] =  $2.0 \times 10^{-4}$ , [ $\gamma$ -CyD] =  $6.0 \times 10^{-4}$  M

the CyD cavity, simultaneously. When  $\gamma$ -CyD was added to the  $\beta$ -1 solution containing 1-adamantanol, the monomer emission was decreased and the excimer emission was additionally increased. This phenomenon suggested that two naphthalene units were trapped in  $\gamma$ -CyD cavity. Therefore, assembly consisted with three components such as  $\beta$ -1, two 1-adamantanols and  $\gamma$ -CyD was constructed, which are 1:2:1 complex as shown in scheme 2.

On the other hand, when ursodeoxycholic acid was added to the  $\beta$ -1 solution, the decrease of monomer intensity and increase of excimer intensity were observed. It is suggested that appended units such as two naphthalene moieties were come out from the  $\gamma$ -CyD cavity as shown in the case of 1-adamantanol used. When  $\gamma$ -CyD was added to the  $\beta$ -1 solution containing ursodeoxycholic acid, the increase of monomer intensity together with decrease of excimer intensity was recognized. This is not same phenomena shown as case of 1-adamantanol was used as a guest. This observation suggested that each naphthalene unit was included in each  $\gamma$ -CyD cavity, resulted in making 1:1 complex between naphthalene and  $\gamma$ -CyD, because ursodeoxycholic acid is larger size molecule than that of 1-adamantanol, which makes a different movement of appended units. Consequently, the complexation between  $\beta$ -1, ursodeoxycholic acid and two  $\gamma$ -CyDs was 1:2:2 as shown in scheme 3. These results suggested that such an assembly of 1:2:1 or 1:2:2 systems are controlled by guest species.

## Conclusion

We succeeded to make two kinds of CyD hetero association systems consisted with bis naphthalene-modified  $\beta$ -CyD dimer, guest molecules and  $\gamma$ -CyD, which are 1:2:1 and 1:2:2 complexes. These assemblies are subject to guest species. It might be unsuitable to apply chemosensory system using  $\beta$ -1, because a drastic change of fluorescent intensity was not observed when a guest was added to the  $\beta$ -1 solution, which was different from that of bis-pyrene modified  $\beta$ -CyD system [8]. Although,  $\beta$ -1 system is very interesting phenomena because the molecular recognition system is variable depended on the guest species, which the first example in the supramolecular assembly.



**Scheme 3** Supramolecular assembly among  $\beta$ -1, ursodeoxycholic acid, and  $\gamma$ -CyD

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