Pergamon

Tetrahedron 57 (2001) 9317–9324

TETRAHEDRON

Synthesis of bis dansyl-modified β-cyclodextrin liner trimer having multi-recognition sites and high hydrophobic environment

Tohru Kikuchi, Miyuki Narita and Fumio Hamada*

Department of Materials-process Engineering and Applied Chemistry for Environments, Faculty of Engineering and Resource Science, Akita University, Tegata, Akita 010-8502, Japan

Received 6 July 2001; accepted 17 September 2001

Abstract—Fluorescent β-cyclodextrin (CyD) trimer linked with amine, which are (6^A,6^D-bis-deoxy-dansylamino-β-CyD)6-deoxy-bis-β-CyDs (β-1), has been synthesized in order to investigate their sensing ability for organic compounds such as bile acids. Host β-1 showed pure monomer fluorescence, exhibiting a decrement in fluorescence intensity on complexation of bile acid. The extent of fluorescence variation with a guest was employed to evaluate the sensing ability of β-1. The guest-induced variation in the fluorescence (ΔI) was used to describe the sensing ability of β-1. Host β-1 could detect ursodeoxycholic acid and chenodeoxycholic acid with remarkable sensitivities, although, could not detect deoxycholic acid and cholic acid. The behaviors of the appended moieties of β-1 during a host–guest complexation were studied by induced circular dichroism (ICD), fluorescence and absorption spectra and MM2-energy-minimized structure. The guest-induced variations in the absorption, fluorescence, and ICD intensity suggest that the appended moieties work as a hydrophobic cap to elevate binding ability, and this fact was supported by three-dimension MM2-minimized structure while a host–guest complexation occurred.

1. Introduction

Cyclodextrins (CyDs), as a host, can make inclusion compounds by inducing various organic molecules as a guest into their chiral and hydrophobic cavities in an aqueous solution.[1,2] Since CyDs are spectroscopically inert, the inclusion phenomena have usually been observed by using spectroscopically active guest molecules. However, CyDs can be converted into spectroscopically active host by modification with fluorescent active units. Fluorescent modified CyDs show a fluorescence spectral change for guest-inclusion and this change is applied as a probe to demonstrate molecular recognition for the guest compounds.[3–9] Multiple CyDs such as linked CyD dimers and polymeric CyDs have attracted much interest over a decade,[10–36] because these CyD derivatives have fixed multi-recognition sites forming multiple complexation of guest species. Unfortunately, these multiple CyDs were spectroscopically inert and their molecular recognition were studied by using spectroscopically active guests. So now it is interesting to study complexing properties of large host molecules such as CyD dimers, trimers and polymers, because these CyD derivatives detect large molecules such as proteins.[37] Furthermore, nano-scale size host molecules such as dimeric cavitand and calixarene capsules are considered, because these host compounds will be used as supramolecules in the next generation.[38–41] In the previous report, we discussed fluorescent sensory system based on CyD dimers linked ethylenediamine such as bis dansyl-modified β- and γ-CyD dimers and bis pyrene-modified γ-CyD dimer for terpenoids and bile acids as guest molecules, because these guests are biologically significant substances produced by plants or animals and used for crude drugs. In this system, the variations of the guest-induced fluorescence can be used as sensitive and selective factors for the chemo-sensor.[42–44] As an extension of our previous work, we would like to report here results on a fluorescent sensory system for bile acids based on bis dansyl-modified CyD trimer linked with amine, which is (6^A,6^D-bis-deoxy-dansylamino-β-CyD)6-deoxy-bis-β-CyDs (β-1), as a new indicator bearing three molecular including sites, compared with that of mono-dansyl-modified β-CyD monomer (β-2) reported previously [45] (Scheme 1).

2. Results and discussion

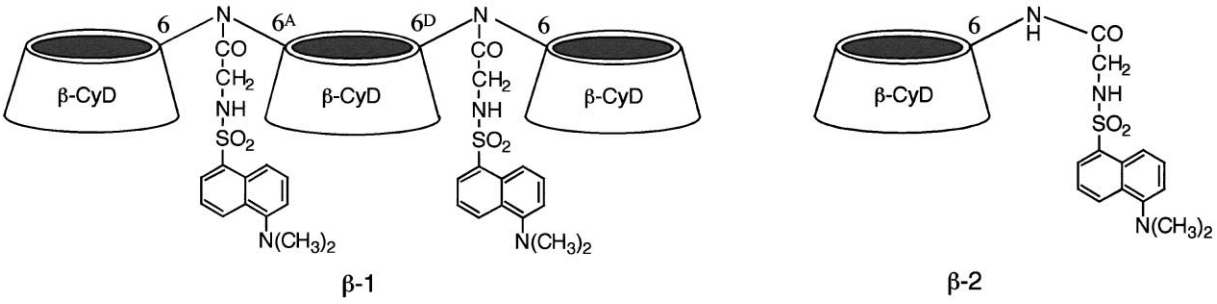
2.1. The preparation of (6^A,6^D-bis-deoxy-amino-β-CyD)6-deoxy-bis-β-CyDs (I) and (6^A,6^D-bis-deoxy-dansylamino-β-CyD)6-deoxy-bis-β-CyDs (β-1)

Compound **I** was prepared as β-CyD trimer from 6^A,6^D-di-iodo-β-CyD with excess of 6-deoxy-6-amino-β-CyD in DMF at 80°C. Compound **I** was purified with column chromatography using ion exchange resin. The fraction of compound **I** was eluted with 1 vol% NH_4OH. The central

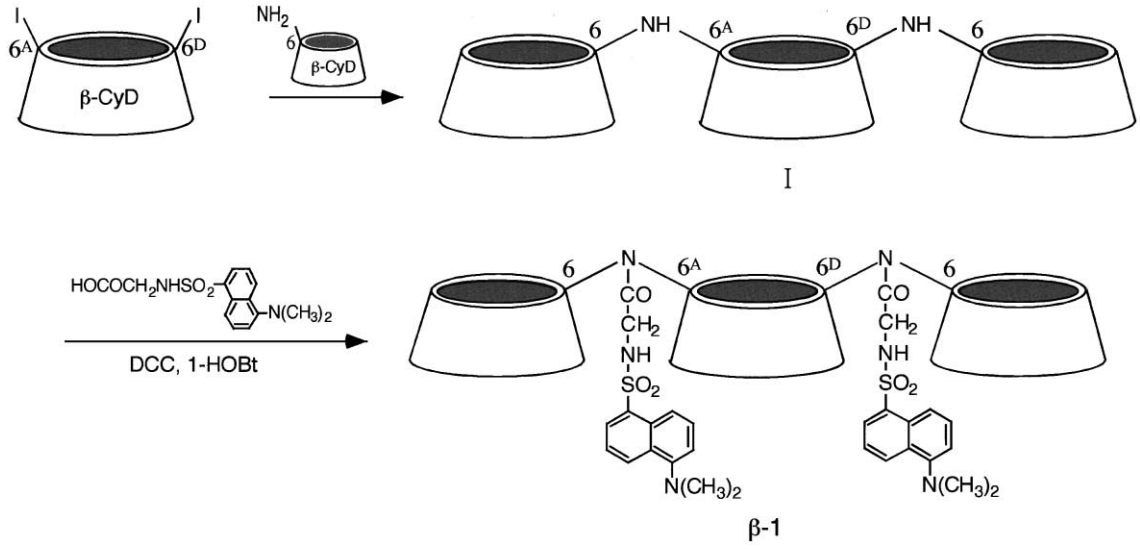
Keywords: β-cyclodextrin; trimer; dansyl.

* Corresponding author. Tel.: +81-18-889-2440; fax: +81-18-837-0404; e-mail: hamada@ipc.akita-u.ac.jp

0040–4020/01/$ - see front matter
PII: S0040-4020(01)00935-8



Scheme 1. Structures of β-1 and β-2.



Scheme 2. Preparation of β-1.

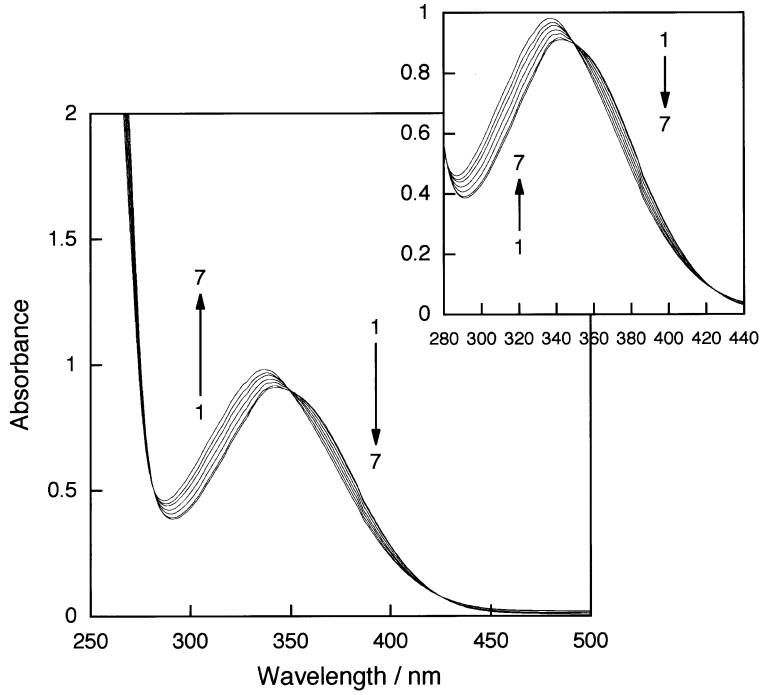


Figure 1. Absorbance spectra of β-1 in a 10 vol% ethylene glycol aqueous solution (1.0×10^{-4} M, 25°C) at various concentrations of ursodeoxycholic acid ((1) 0, (2) 2.0×10^{-5}, (3) 6.0×10^{-5}, (4) 1.0×10^{-4}, (5) 1.4×10^{-4}, (6) 1.8×10^{-4}, (7) 2.2×10^{-4} M).

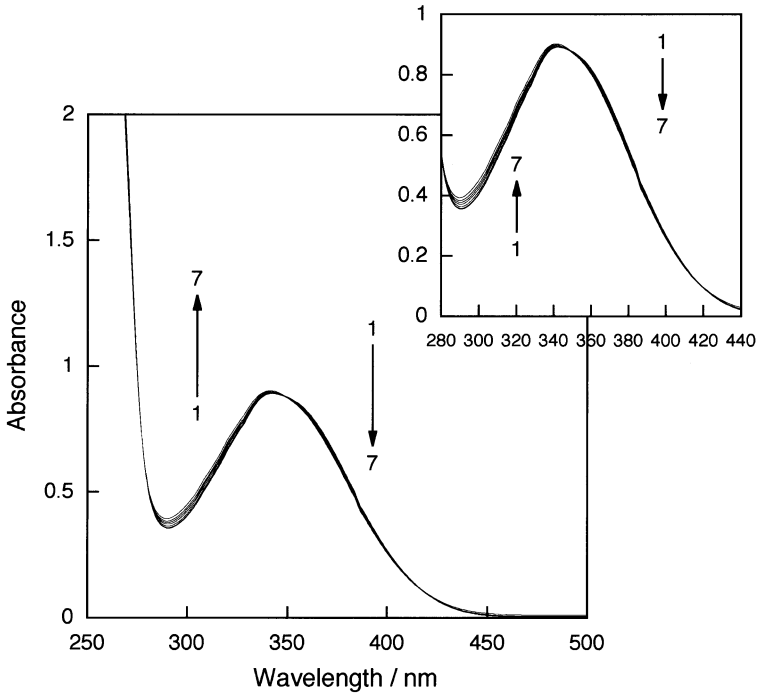
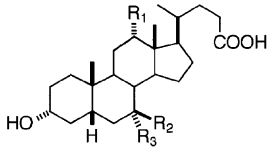


Figure 2. Absorbance spectra of β-1 in a 10 vol% ethylene glycol aqueous solution (1.0×10^{-4} M, 25°C) at various concentrations of cholic acid ((1) 0, (2) 2.0×10^{-5}, (3) 6.0×10^{-5}, (4) 1.0×10^{-4}, (5) 1.4×10^{-4}, (6) 1.8×10^{-4}, (7) 2.2×10^{-4} M).

CyD of compound **I** was linked with two CyDs at its A and D position, which are most distant from the glucopyranose units. Therefore, compound **I** is a liner trimer exhibiting few steric hindrances. Host β-1 was prepared form **I** with dansylglycine in the presence of dicyclohexyl carbodiimido (DCC) in DMF at 60°C, as shown in Scheme 2. Host β-1 was purified with reversed phase column chromatography in 10.8% yield.

2.2. Absorption and induced circular dichroism (ICD) spectra

Fig. 1 shows absorption spectra of β-1, alone, and in the presence of ursodeoxycholic acid in a 10 vol% ethylene glycol aqueous solution. The absorption spectra of β-1 in the presence of this guest change with isosbestic point at 282 and 349 nm. It means that the dansyl moieties move from the inside of CyD cavity to the outside of one when host–guest complexation is occurred. However, the variations in absorption spectra of β-1 on accommodation of cholic acid are hardly observed, as shown in Fig. 2. These results suggest that the moving of the dansyl moieties is depended on the guest species (Scheme 3). The ICD spectra of β-1 and β-2 in the absence and presence of ursodeoxycholic acid in a 10 vol% ethylene glycol aqueous solution are shown in Fig. 3. The ICD intensities of β-1 show positive and negative Cotton peaks around 265 and 365 nm, respectively. The ICD pattern of β-2 alone is similar to that of β-1, although, the intensity of β-2 is smaller than that of β-1. The ICD patterns of β-1 and β-2 are opposite to those of bis dansyl-modified β- and γ-CyD dimers.[43,44] It is reported that the ICD sings of the dansyl moiety of the CyD derivatives indicated a type of inclusion which is equatorial or axial self-inclusion, in which a positive and a negative Cotton peak around 250–280 and 320–400 nm, respectively,



	R_1	R_2	R_3
Lithocholic acid (**1**)	H	H	H
Chenodeoxycholic acid (**2**)	H	H	OH
Ursodeoxycholic acid (**3**)	H	OH	H
Deoxycholic acid (**4**)	OH	H	H
Cholic acid (**5**)	OH	H	OH

Scheme 3. Guest molecules.

indicated that the dansyl moiety was induced into the chiral CyD cavity with axial complexation, and reversal pattern indicated that the dansyl moiety was included into the CyD cavity with equatorial complexation.[46] The MM2-minimized structure, which was calculated by molecular mechanics using MM2 in CS Chem 3D,[49,50] supports that the type of the self-inclusion of β-1 is axial. As a result of the MM2-minimized calculation, the short and long axes at the upper rim of the central CyD are roughly 4.5 and 15.1 Å. In contrast, the short and long axes at the upper rim of the end CyD are roughly 7.7 and 11.2 Å. It seems that the upper rim on the central CyD as a linker of β-1 is distorted. Therefore, the upper rim on the central CyD is too narrow to include the dansyl moiety into its cavity. It is suggested that two dansyl moieties are included into both end CyD β-1, not the central CyD and another end CyD of β-1, as shown in Scheme 4. The ICD pattern and

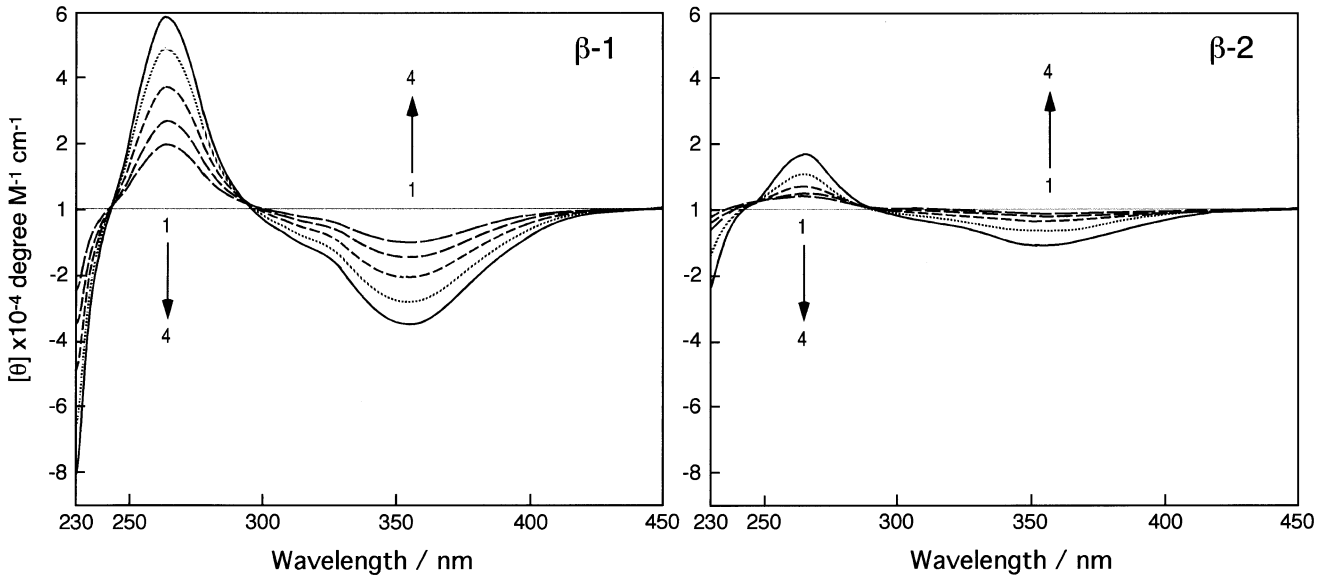
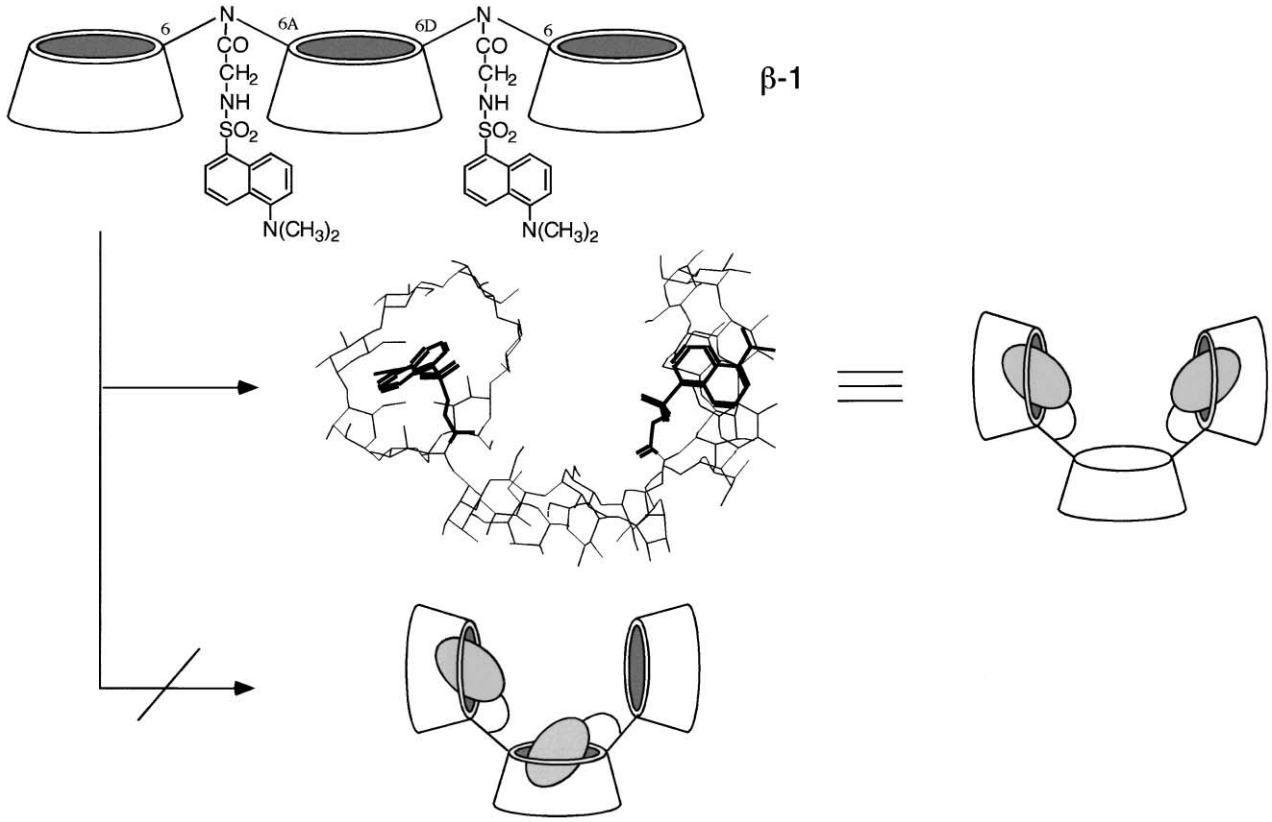


Figure 3. ICD spectra of β-1 and β-2 in a 10 vol% ethylene glycol aqueous solution (5.0×10^{-5} M: —) at various concentration of ursodeoxycholic acid (5.0×10^{-5} M: - - - , 1.0×10^{-4} M: – – –, 1.5×10^{-4}: — — —, 2.0×10^{-4} M: — – —).

MM2-minimized structure of β-1 suggests that the dansyl moieties are included into the chiral CyD cavity with parallel to the both end CyD axial. The ICD intensity of β-1 was decreased with increasing guest concentration, in which the extent of the change in the ICD intensities of β-1 was twice larger than that of β-2, whereas β-1 has two dansyl moieties and β-2 has one dansyl moiety. It is suggested that the binding ability of β-1 is larger in comparison with that of β-2 and the dansyl moieties of β-1 move from the interior of the chiral CyD cavity toward the achiral outside of the CyD cavity while simultaneously a guest is included into the CyD cavity. If the dansyl moieties of β-1 were included into the central and one end CyDs, the guest-induced ICD spectra of β-1 would be completely changed, which was shift of the peak. Since the guest-induced ICD spectral pattern of β-1 is simple, it is supported that two



Scheme 4. Energy-minimized structures of β-1 obtained by using molecular mechanics in CS Chem 3D (MM2).

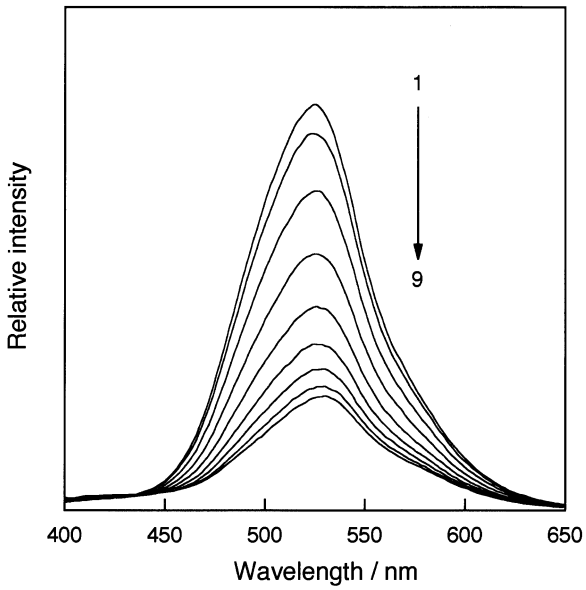


Figure 4. Fluorescence spectra of β-1 in a 10 vol% ethylene glycol aqueous solution (1.0×10^{-6} M, 25°C, excitation wavelength: 340 nm) at various concentration of ursodeoxycholic acid ((1) 0, (2) 4.0×10^{-6}, (3) 1.2×10^{-5}, (4) 2.4×10^{-5}, (5) 4.0×10^{-5}, (6) 6.0×10^{-5}, (7) 8.3×10^{-5}, (8) 1.1×10^{-4}, (9) 1.4×10^{-4} M).

dansyl moieties are included into the both end CyD of β-1, as illustrated in Scheme 4, and then two appended moieties are excluded from the both end CyD of β-1 when the guest is added.

2.3. Fluorescence spectra

Fig. 4 shows fluorescence spectra of β-1 alone and in the presence of ursodeoxycholic acid in a 10 vol% ethylene glycol aqueous solution. Increasing concentration of this guest resulted in decrement of the intensities. It is reported that the decrement of the guest-responsive fluorescence intensities indicates that the appended moiety is moving from the hydrophobic environment into the hydrophilic one.[8] These guest-induced ICD and fluorescence decrements of β-1 suggest that the dansyl moieties are moving out of the CyD cavity and act as a hydrophobic residue, as illustrated in Scheme 5. To display the sensing ability of β-1, ΔI was used as a sensitivity parameter. Here, ΔI is I^0-I, where I^0 and I are the fluorescence intensities at 526 nm for the host alone and a mixture of complex and uncomplexed host in equilibrium, respectively. Fig. 5 shows the parameter values of β-1 and β-2 with bile acids at 0.1 mM except for lithocholic acid (**1**), which was examined at 0.01 mM because 0.1 mM of **1** is not soluble in a 10 vol% ethylene glycol aqueous solution. Among the steroidal guests, host β-1 detects ursodeoxycholic acid (**3**), which bears two hydroxyl groups on C-3 and C-7 of the steroidal framework, with greatest sensitivity, exhibiting a value of 268. Chenodeoxycholic acid (**2**), which is the diastereoisomer of **3**, is detected with the next highest sensitivity, exhibiting a value of 192. These sensing parameters of β-1 are higher than those of β-2 and bis dansyl-modified β-CyD dimer.[48] Guest **1**, which bears only one hydroxyl group on C-3 of the steroidal framework, is detected with a value of 83, however, this sensing parameter is lower than that of bis-dansyl-modified β-CyD dimer.[47] Deoxycholic acid (**4**) and cholic acid (**5**), which bear two hydroxyl groups on C-3 and C-12 of the steroidal framework and three hydroxyl groups

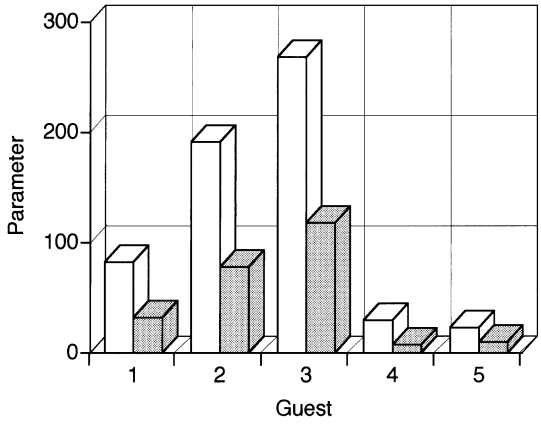
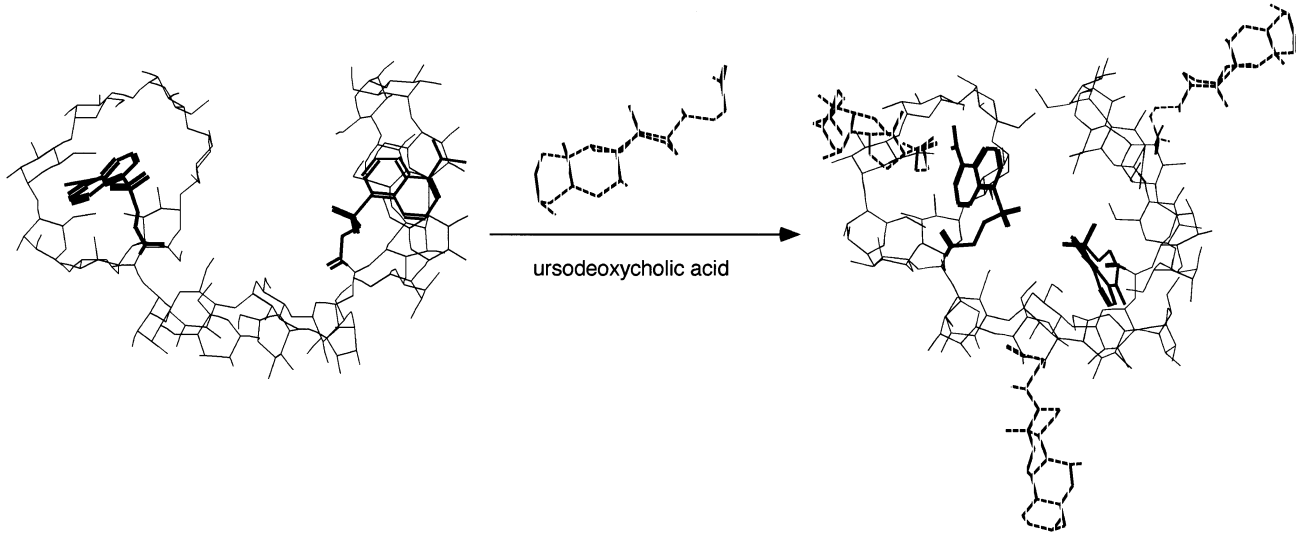


Figure 5. Sensitivity factors of β-1 (□) and β-2 (▨) in a 10 vol% ethylene glycol aqueous solution (1.0×10^{-6} M, 25°C) for all guests examined.



Scheme 5. One of the estimations of host–guest complexation mechanism of β-1 obtained as MM2-minimized structure.

on C-3, C-7 and C-12 of the steroidal one, respectively, are detected with low sensitivity, exhibiting that these values are almost negligible. The results obtained as sensing parameters indicated that β-1 can more sensitively and selectively detect the guests, which bear hydroxyl groups on C-3 and C-7 of the steroidal framework, than β-2 and bis dansyl-modified β-CyD dimer. This qualitative fluorescent molecular sensing ability of β-1 is speculated to be caused by three binding sites and large hydrophobic domain enclosed by three CyDs.

In order to examine the composition of β-1 with the guest, the binding constants obtained as the guest-induced fluorescent spectral variation were investigated. The guest-induced fluorescence variation at 526 nm was employed to calculate the binding constants of β-1 using a Benesi–Hildebrand type Eq. (1) for a 1:1 complex formation as reported previously

$$\frac{1}{I_f - I_{f0}} = \frac{1}{a[\mathrm{CD}]} + \frac{1}{b[\mathrm{CD}]K}\frac{1}{[G]} \quad (1)$$

Here, I is the fluorescence intensity at 526 nm (I_f for complex, I_{f0} for the host alone), [CD] is the total host concentration, [G] is the total guest concentration, and a and b are constants. A computer simulation using fluorescent intensity at 526 nm as a function of guest concentration proved that experimental data could fit to linear equations, indicating a 1:1 complex formation. The host–guest complex formation seems to be 1:3, although it is obvious that the formation is a 1:1 type, because β-1 has three cavities which can include a guest into each cavity. The binding constants of β-1 are $153,000 \pm 10,700$, 5300 ± 600, $21,600 \pm 1000$, 4450 ± 790, and 1830 ± 210, for guests **1**, **2**, **3**, **4**, and **5**, respectively. The order of binding constants of β-1 for the guests is not parallel with the order of the sensing factors. This means that the sensitivity value gives a relative but not absolute sensing ability. It is assumed that when a guest concentration is varied, the sensing ability of β-1 is also changed.

3. Conclusion

Bis dansyl-modified β-CyD trimer has been synthesized to examine its fluorescent molecular sensory system for bile acids. This trimer shows pure monomer fluorescence, of which the guest-induced variations were used as a sensing parameter to discuss the molecular sensing ability. It is clarified that this trimer exhibits qualitative molecular sensing ability for bile acids such as chenodeoxycholic acid and ursodeoxycholic acid, which have hydroxyl groups on C-3 and C-7 in the steroidal framework. During host–guest complexation, the dansyl moieties play a role as a hydrophobic cap to elevate the binding ability. In this system, three binding sites and a large hydrophobic domain enclosed three CyDs of β-1 are estimated to contribute the qualitative molecular recognition. This study can lead the speculation that the fluorescent polymeric CyDs will be a much more selective and sensitive molecular recognition system based on fixed multi-inclusion sites and large hydrophobic domain enclosed by hydrophobic CyD cavities.

4. Experimental

4.1. General

4.1.1. Preparation of (6^A,6^D-bis-deoxy-amino-β-CyD)6-deoxy-bis-β-CyDs (I). A mixture of 6^A,6^D-di-iodo-β-CyD[7] (150 mg, 0.11 mM) and 6-deoxy-6-amino-β-CyD[48] (317 mg, 0.28 mM) in 10 mL of DMF was heated at 80°C for 12 h. After cooling, the reaction mixture was poured into 300 mL of acetone. The resulting precipitates were filtered and dried. The water soluble fraction was applied on a CM-Sephadex C-50 column (7×35 cm). Stepwise elution from 2 L of water and 1 L of 1 vol% ammonia aqueous solution were applied to give compound **I**. The fractions containing **I** were collected and evaporated in vacuo; they were poured into 200 mL of acetone. The resulting precipitates were filtered and dried to afford 49 mg (13.6%, isolated yield) of pure **I**.

R_f: 0.27 (methyl ethyl ketone–methanol–acetic acid 12:3:5 by volume; TLC: silica gel $60F_{254}$). ^{1}H NMR (DMSO-d_6) δ=3.2–3.8 (126H, m, C^2–C^6H), 4.4–4.5 (17H, m, O^6H), 4.8–4.9 (21H, m, C^1H), 5.6–5.8 (42H, m, O^2H and O^3H).

4.1.2. Peparation of (6^A,6^D-bis-deoxy-dansylglycine-amido-β-CyD)6-deoxy-bis-β-CyDs (β-1). To a cooled solution (−10°C) of dansylglycine (18.5 mg, 0.06 mM) in 5 mL of DMF were added dicyclohexyl carbodiimido (DCC, 12.4 mg, 0.06 mM) and 1-hydroxytribenzothiazole (1-HOBt, 8.1 mg). The reaction mixture was stirred at −10°C for 30 min. To a stirred solution was added portion-wise compound **I** (40.0 mg, 0.012 mM), and the solution was stirred at −10°C for another 30 min, and then the reaction mixture was stirred at 60°C for 24 h. After cooling, the reaction mixture was concentrated under reduced pressure. The residue was poured into 200 mL of acetone. The resulting precipitates were filtered and dried. The water soluble fraction was applied on a reversed-column (Lobar column LiChroprep RP-18, MerckLtd. 240×10 mm). Stepwise elution from 200 mL of 10 vol% CH_3CN-aqueous solution and 200 mL of 20 vol% CH_3CN-aqueous solution was applied to give β-1. The fractions containing β-1 were collected and evaporated in vacuo, and then they were poured ino 200 mL of acetone. The resulting precipitates were filtered and dried to afford 5 mg of pure β-1 (10.8%, isolated yield).

R_f: 0.51 (butanol–ethanol–water 5:4:3 by volume; TLC; silica gel $60F_{254}$) and 0.72 (methanol–water 2:1 by volume; TLC; RP-18 F_{254S}). ^{1}H NMR (DMSO-d_6): δ=3.2–3.8 (126H, m, C^2–C^6H), 4.4–4.6 (17H, m, O^6H), 4.8–4.9 (21H, m, C^1H), 5.6–5.8 (42H, m, O^2H and O^3H), 7.26 (2H, d, J=7.8 Hz, aromatic-H), 7.59 (4H, quintet, J=8.4 Hz, aromatic-H), 8.12 (2H, d, J=7.5 Hz, aromatic-H), 8.28 (2H, d, J=8.7 Hz, aromatic-H), 8.46 (2H, d, J=8.7 Hz, aromatic-H). Calcd for $C_{154}H_{236}O_{107}N_6S_2{\cdot}5H_2O$: C, 45.81; H, 6.14; N, 2.08%. Found: C, 45.77; H, 6.36; N, 2.19%. TOF-MS (m/z): 3948, ($[M]^+$).

4.2. Measurements

Fluorescence and circular dichroism spectra were measured at 25°C, with a Perkin–Elmer LS 40B fluorescence

spectrophotometer and a JASCO J-700 spectropolarimeter, respectively. For the fluorescence measurements, the excitation wavelength of the fluorescence spectra was 340 nm and excitation and emission slits were 6 nm. Ethylene glycol aqueous solution (10 vol%) was used as a solvent for host for the spectroscopic measurements because the solubility of the host in pure water is poor. Five microliters of guest species (0.05 and 0.005 M) in dimethyl sulfoxide (DMSO) or MeOH were injected into 10 vol% ethylene glycol aqueous solution of the host 2.5 mL to make a sample solution with a host concentration of 1.0×10^{-6} M and guest concentration of and 0.01 mM, respectively. For the circular dichroism measurements, 5 μL of guests species (0.05 M) in dimethyl sulfoxide (DMSO) were injected into a 10 vol% ethylene glycol aqueous solution of host (2.5 mL) to make a sample solution with the host concentration of 5.0×10^{-5} M and the guest concentrations of 5.0×10^{-5}, 1.0×10^{-4}, 1.5×10^{-4}, and 2.0×10^{-4} M.

4.3. Energy-minimized structures

Energy-minimized structures were calculated by molecular mechanics using MM2 in CS Chem 3D. The parameters of MM2 are improved ones obtained from studies by Allinger[49] based on TIKER system researched by Ponder.[50]

Acknowledgements

This study was supported by a Grant-in-Aid for Specially Promoted Research (No. 404: Molecular Synchronization for Design of New Materials System) from the Ministry of Education Science, Sports and Culture of Japan.

References

1. Lehn, J.-M. *Supramolecular Chemistry*; VCH: Weinheim, 1995 23.
2. Szejtli, J. *Cyclodextrin Technology*; Kluwer: Dordrecht, 1988.
3. Narita, M.; Hamada, F.; Suzuki, I.; Osa, T. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2751.
4. Narita, M.; Hamada, F.; Sato, M.; Suzuki, I.; Osa, T. *J. Inclusion. Phenom. Macrocycl. Chem.* **1999**, *34*, 421.
5. Narita, M.; Koshizaka, S.; Hamada, F. *J. Inclusion. Phenom. Macrocycl. Chem.* **1999**, *35*, 605.
6. Ito, S.; Narita, M.; Hamada, F. *Int. J. Soc. Mater. Engng Resour.* **1999**, *7*, 156.
7. Sato, M.; Narita, M.; Ogawa, N.; Hamada, F. *Anal. Sci.* **1999**, *15*, 1199.
8. Narita, M.; Hamada, F. *J. Chem. Soc., Perkin Trans. 2* **2000**, 823.
9. Hamada, F.; Narita, M.; Kinoshita, K.; Makabe, A.; Osa, T. *J. Chem. Soc., Perkin Trans. 2* **2001**, 388.
10. Tabushi, I.; Kuroda, Y.; Shimokawa, K. *J. Am. Chem. Soc.* **1979**, *101*, 1614.
11. Fujita, K.; Ejima, S.; Imoto, T. *J. Chem. Soc., Chem. Commun.* **1984**, 1277.
12. Fujita, K.; Ejima, S.; Imoto, T. *Chem. Lett.* **1985**, 11.
13. Breslow, R.; Greenspoon, N.; Guo, T.; Zarzycki, R. *J. Am. Chem. Soc.* **1989**, *111*, 8296.
14. Kuroda, Y.; Hiroshige, T.; Sera, T.; Shiroiwa, Y.; Tanaka, H.; Ogoshi, H. *J. Am. Chem. Soc.* **1989**, *111*, 1912.
15. Breslow, R.; Chung, S. *J. Am. Chem. Soc.* **1990**, 9659.
16. Petter, C. T.; Sikorski, C. T.; Waldeck, D. H. *J. Am. Chem. Soc.* **1991**, *113*, 2325.
17. Breslow, R.; Zhang, B. *J. Am. Chem. Soc.* **1992**, *114*, 5882.
18. Zhang, B.; Breslow, R. *J. Am. Chem. Soc.* **1993**, *115*, 9353.
19. Kuroda, Y.; Ito, M.; Sera, T.; Ogoshi, H. *J. Am. Chem. Soc.* **1993**, *115*, 7003.
20. Kuroda, Y.; Egawa, Y.; Seshimo, H.; Ogoshi, H. *Chem. Lett.* **1994**, 2361.
21. Jiang, T.; Sukumaran, D. K.; Soni, S.-D.; Lawrence, D. S. *J. Org. Chem.* **1994**, *59*, 5149.
22. Deschenaux, R.; Greppi, A.; Ruch, T.; Kriemler, H.-P.; Raschdorf, F.; Ziessel, R. *Tetrahedron Lett.* **1994**, *35*, 2165.
23. Sikorski, C. T.; Petter, R. C. *Tetrahedron Lett.* **1994**, *35*, 4275.
24. Okabe, Y.; Yamamura, H.; Obe, K.; Ohta, K.; Kawai, M.; Fujita, K. *J. Chem. Soc., Chem. Commun.* **1995**, 581.
25. Breslow, R.; Halfon, S.; Zhang, B. *Tetrahedron* **1995**, *51*, 377.
26. Breslow, R.; Zhang, B. *J. Am. Chem. Soc.* **1996**, *118*, 8495.
27. Ishimura, Y.; Masuda, T.; Ida, T. *Tetrahedron Lett.* **1997**, *38*, 3743.
28. Ruebner, A.; Kirsch, D.; Andrees, S.; Decker, W.; Roeder, B.; Spengler, B.; Kaufmann, R.; Moser, J. G. *J. Inclusion Phenom. Mol. Recognit. Chem.* **1997**, *27*, 69.
29. Harada, A.; Furue, M.; Nozakura, S. *Macromolecules* **1976**, *9*, 701.
30. Harada, A.; Furue, M.; Nozakura, S. *Macromolecules* **1976**, *9*, 705.
31. Harada, A.; Furue, M.; Nozakura, S. *Macromolecules* **1977**, *10*, 676.
32. Harada, A.; Furue, M.; Nozakura, S. *Polym. J.* **1981**, *13*, 777.
33. Suh, J.; Lee, S. H.; Zoh, K. D. *J. Am. Chem. Soc.* **1992**, *114*, 7916.
34. Xu, W.; Demas, J. N.; DeGraff, B. A.; Whaley, M. *J. Phys. Chem.* **1993**, *97*, 6546.
35. Werner, T. C.; Warner, I. M. *J. Inclusion Phenom. Mol. Recognit. Chem.* **1994**, *18*, 385.
36. Hollas, M.; Chung, M.-A.; Adams, J. *J. Phys. Chem. B* **1998**, *102*, 2947.
37. Hamada, F.; Narita, M.; Makabe, A.; Itoh, H. *J. Inclusion. Phenom. Macrocycl. Chem.* **2001**, *40*, 83.
38. Rudkevich, D. M.; Rebek Jr., J. *Eur. J. Org. Chem.* **1999**, 1991.
39. Lücking, U.; Tucci, F. C.; Rudkevich, D. M.; Rebek, Jr., J. *J. Am. Chem. Soc.* **2000**, *122*, 8880.
40. Jacopozzi, P.; Dalcanale, E. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 613.
41. Cuminetti, N.; Ebbing, M. H. K.; Prados, P.; de Mendoza, J.; Dalcanale, E. *Tetrahedron Lett.* **2001**, 527.
42. Narita, M.; Hamada, F. *Anal. Sci.* **2000**, *16*, 865.
43. Narita, M.; Itoh, J.; Kikuchi, T.; Hamada, F. A high sensitivity fluorescent chemo-sensory system based on β-cyclodextrin dimer modified with dansyl moieties. *J. Inclusion. Phenom. Macrocycl. Chem.* **2001** in press.
44. Narita, M.; Mima, S.; Ogawa, N.; Hamada, F. *Anal. Sci.* **2000**, *16*, 865.
45. Ueno, A.; Minato, S.; Suzuki, I.; Fukushima, M.; Ohkubo, M.; Osa, T.; Hamada, F.; Murai, K. *Chem. Lett.* **1990**, 605.
46. Corradini, R.; Dossena, A.; Galaverna, G.; Marchelli, R.; Panagia, A.; Sartor, G. *J. Org. Chem.* **1997**, *62*, 6283.
47. In the case of bis dansyl-modified β-CyD dimer, ΔI for

guests **1**–**5** were 88.81, 176.98, 257.20, 31.13, and 39.45, respectively.
48. Hamada, F.; Murai, K.; Ueno, A.; Suzuki, I.; Osa, T. *Bull. Chem. Soc. Jpn* **1988**, *61*, 3758.
49. Burkert, U.; Allinger, N. L. *Molecular Mechanics*; *ACS Monograph*, 177; American Chemical Society: Washington, DC, 1982.
50. Dudek, M. J.; Ponder, J. W. *J. Comput. Chem.* **1995**, *16*, 791.