Facile Dimerization and Circular Dichroism Characteristics of 6-*O*-(2-Sulfonato-6-naphthyl)-*β*-cyclodextrin

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A monofunctional derivative of *β*-cyclodextrin (*β*-CD) containing a 2-sulfonato-6-naphthyl group at the primary face (**1**: *β*-CD-NS) was prepared. The concentration dependences of fluorescence, circular dichroism (c.d.), and NMR spectra of **1** have been investigated and compared with the spectral changes associated with complexation of 6-methoxy-2-naphthalenesulfonate (MNSS) with *β*-CD. When the concentration of **1** was increased, the following were observed: the enhancement of the concentration-normalized fluorescence intensity; an increase in molar ellipticities of the negative band around 280 nm; a more pronounced exciton coupling band around 230 nm in c.d. spectra; and an upfield shift of NMR signals from aromatic protons. The concentration dependent fluorescent intensity and molar ellipticity data fitted well to the monomer−dimer equilibrium of **1** with the dimerization constant of 9700 ± 2500 M^{-1}. The dimerization constant is much larger than the association constants of MNSS with *β*-CD (510 ± 40 M^{-1}) and **1** with *β*-CD (430 ± 50 M^{-1}). The naphthyl groups in the dimer do not show an excimer band in fluorescence spectra but exhibit exciton coupling bands around 230 and 330 nm. These indicate that **1** forms a head-to-head type dimer, which is stabilized by mutual inclusion of the 2-sulfonato-6-naphthyl moieties deeply into *β*-CD cavities of counter molecules. The naphthyl moiety of the monomer of **1** is in a similar environment to that in a **1**/*n*-octyl sulfate complex and appears to cap the primary face of *β*-CD loosely. Compared to the c.d. spectrum of the MNSS/*β*-CD complex, the spectrum of the **1**/*β*-CD complex is similar in shape, but the rotational strengths of the c.d. bands are much greater.

Introduction

Cyclodextrins (CDs) possess hydrophobic cavities capable of forming inclusion complexes with a variety of organic molecules in aqueous solution. Because of this characteristic, CDs have been widely used as biomimetic microreactors, sensors, novel media for photophysical and photochemical studies, and building blocks for supramolecular structures and functional units.[1,2] Photoactive and fluorescent groups have been attached to obtain fluorescent hosts for sensors or photochemical microreactors.[3−13] When the pendant group has a proper size, the group is usually self-included into the cavity of a CD where it is attached or of a counter molecule. Inclusion of a guest molecule results in a large fluorescence change by displacing the pendant fluorophore from a CD cavity.[9−12] When the guest molecule is an energy or electron acceptor, the inclusion complexation of the guest facilitates efficient excitation transfer to the guest.[3−8]

The mono- and multi-naphthalene-substituted *β*-CDs have drawn a great amount of interest as antennas in photochemical molecular devices and as fluorescent molecular sensors.[5−8,13] The naphthalene-substituted *β*-CDs can form dimers in water, as suggested for 3-*O*-(2-methylnaphthyl)-*β*-CD[8] and *β*-CD-6-*O*-2-naphthoate.[14] The dimerization affects the guest binding properties of the fluorescent hosts. However, there is ambiguity about the structures of the dimers. For quantitative analysis of the guest binding equilibria and to characterize the host/guest complexes of the naphthalene-substituted *β*-CDs, detailed information on the dimerization equilibrium and the structural characteristics of the monomer and dimer is required.

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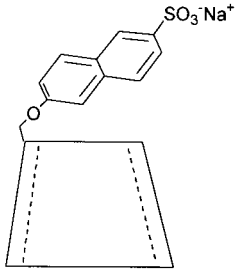
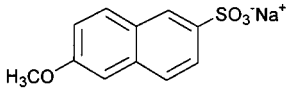
In this paper, we present the results of our studies on a highly water-soluble naphthyl-substituted *β*-CD, mono-6-*O*-(2-sulfonato-6-naphthyl)-*β*-CD (**1**: *β*-CD-NS), with various spectroscopic methods including fluorescence, circular dichroism, and ^{1}H NMR. The spectral properties of **1** are compared with those of the intermolecular complex of 6-methoxy-2-naphthalenesulfonate (**2**: MNSS) with *β*-CD. From the concentration dependence of the spectroscopic properties, the monomer−dimer equilibrium constant and the characteristics of the monomer and dimer of **1** are obtained. In addition, this work provides circular dichroism (c.d.) spectra of the monomer and dimer of **1** as well as **1**/*β*-CD and **2**/*β*-CD complexes and discusses the c.d. characteristics in view of their structures.



1: β-CD-NS



2: MNSS

Experimental Section

Materials. *β*-CD (Aldrich) was recrystallized from water and vacuum-dried. 2-Naphthol (Junsei) was purified by sublimation

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at reduced pressure. Sodium 6-hydroxy-2-naphthalenesulfonate (Aldrich) was purified by silica gel column chromatography using methanol−chloroform (1:2 v/v) as an eluent and then recrystallized from water. 6-Mono-tosylated β-CD (β-CD-OTs) was prepared according to a literature procedure.[15] Sodium *n*-octyl sulfate (SOS) was obtained from Aldrich and used as received. Compounds **1** and **2** were synthesized according to the following procedures.

Mono-6-*O*-(2-sulfonato-6-naphthyl)-β-CD (1: β-CD-NS). β-CD-OTs (2.7 g, 2.1 mmol) and 1.0 g of sodium 6-hydroxy-2-naphthalenesulfonate (4.2 mmol) were reacted in 25 mL of dry DMF containing 0.17 g of NaOH for 80 h at 65 °C under N_2 atmosphere. After precipitation with acetone, the precipitate was dissolved in water and purified by anion exchange chromatography on Sephadex DEAE A-25 using a linear gradient of NaCl (0.0−0.3 M). UV and β-CD active fractions were concentrated to dryness. The salt was removed by filtration after selective solubilization of the product in DMF. After DMF was evaporated off, the product was dissolved in water, ultrafiltrated through a MWCO 500 cellulose membrane, and finally freeze-dried to obtain 0.43 g (yield 30%) of the desired product. UV(H_2O) λ_{max}/nm (log ϵ) 278 (3.78), 314 (3.08), 328 (3.06); mp 260 °C(dec); ^{1}H NMR (D_2O, 5 mM) δ 7.16 (s, 1H), 7.31 (d, 1H), 7.8−7.9 (m, 2H), 7.97 (d, 1H), 8.31 (s, 1H), and β-CD resonances; FAB-MS *m*/*z* 1363.3555, $[M + H]^+$ calcd for $C_{52}H_{76}O_{38}SNa$ 1363.3633.

Sodium 6-Methoxy-2-naphthalenesulfonate (2: MNSS). MNSS was synthesized by a procedure reported by Gravett and Guillet.[6] The product was recrystallized from ethanol. The ^{1}H NMR spectrum was consistent with the structure. UV(H_2O) λ_{max}/nm (log ϵ) 278 (3.70), 314 (3.02), 328 (2.95).

Spectroscopic Measurements. ^{1}H NMR spectra were obtained by using a Varian 400 MHz instrument, and FAB-MS data were collected at the Korea Basic Science Institute using a JEOL JMS-HX110A/110A mass spectrometer. Steady-state fluorescence spectra (λ_{ex} = 326 nm) were obtained with a Hitachi F-3010 spectrofluorimeter. The time-resolved fluorescence spectroscopy was carried out with a picosecond time-resolved single photon counting system assembled at the Korea Basic Science Institute. Circular dichroism (c.d.) spectra were recorded on a JASCO J-810 spectropolarimeter. The cell path length was varied from 0.010 to 10.0 cm, depending on the concentration and wavelength region. The solution of MNSS was used as a blank for c.d. spectral measurement of β-CD-NS and titration of MNSS with β-CD. The bandwidth was set at 2 nm, and the response time was 2 s. Spectra were scanned 10 times at the speed 50 nm/min, averaged, and then smoothed using JASCO software. All spectroscopic measurements were done at 25 °C, using an appropriate temperature controller. Unless otherwise specified, the ionic strength of the solutions was fixed at 0.1 M with NaCl.

Determination of Dimerization Constant. The dimerization constant (K_D) of β-CD-NS was determined from the dependence of fluorescence intensity, molar ellipticity, and ^{1}H NMR chemical shift on the concentration of the compound by nonlinear-least-squares fitting to appropriate equations. For example, the concentration-normalized fluorescence intensity (I_{obs}) data was fitted to eq 1, where C_{tot} is the total concentration

$$I_{obs} = I_{mon}\frac{\sqrt{8K_DC_{tot}+1}-1}{4K_DC_{tot}} + I_{dimer}\frac{(4K_DC_{tot}+1)-\sqrt{8K_DC_{tot}+1}}{4K_DC_{tot}} \quad (1)$$

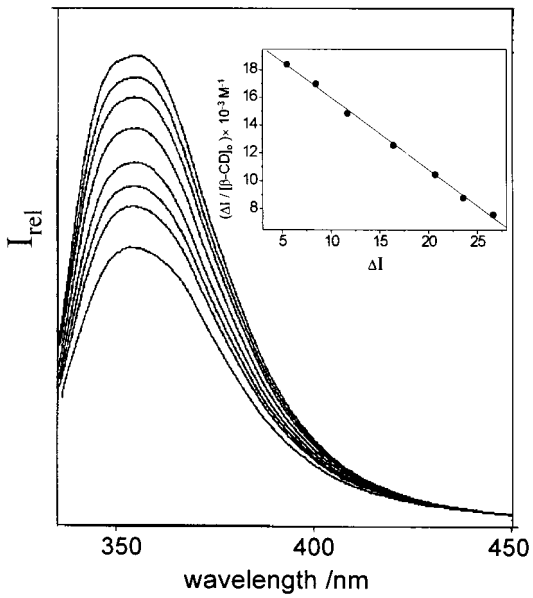


Figure 1. Variation of fluorescence spectra of 1.0×10^{-5} M MNSS at various concentrations of β-CD. The concentrations of β-CD are the following: 0.00, 0.30×10^{-3}, 0.50×10^{-3}, 0.79×10^{-3}, 1.3×10^{-3}, 2.0×10^{-3}, 2.7×10^{-3}, and 3.5×10^{-3} M (from bottom to top). The inset shows the Benesi−Hildebrand type plot (eq 2) of the fluorescence titration data taken at 355 nm.

of β-CD-NS; I_{obs} is the fluorescence intensity per naphthyl group (I_F/C_{tot}); and I_{mon} and I_{dimer} represent the expected fluorescence intensity when all of the molecules are present as the monomeric and dimeric species, respectively. For c.d. and ^{1}H NMR data, the I' values in eq 1 were substituted with the molar ellipticity ($[\theta]$) per naphthyl group and chemical shift (δ) of a given proton, respectively. To fit the spectral data taken at various concentrations of β-CD-NS to eq 1, the K_D and characteristics of dimeric species were set as fitting parameters, and the spectral data taken at a high concentration of sodium *n*-octyl sulfate (SOS) were used as those of a β-CD-NS monomer.

Results and Discussion

Reaction of 6-hydroxy-2-naphthalenesulfonate with β-CD-OTs in DMF containing NaOH afforded the mono-naphthalene derivative of β-CD, β-CD-NS, in which a 2-sulfonatonaphthyl group is attached to the primary face of β-CD. ^{1}H NMR and FAB-MS data were in good agreement with the structure. To obtain information on the intermolecular associating properties and the structural features of the monomer and aggregate of this compound, we followed the concentration dependence of fluorescence, c.d., and ^{1}H NMR spectra. In all cases, strong concentration dependence of the spectra was observed (vide infra), suggesting intermolecular association of the compound. Details are described in following sections.

Fluorescence Studies. β-CD-NS as well as MNSS exhibits strong naphthyl fluorescence around 350 nm. To correlate the intermolecular association of β-CD-NS with the inclusion of a naphthyl group into the cavity of β-CD, we first titrated a 1.0×10^{-5} M MNSS solution with β-CD fluorometrically (Figure 1). As the concentration of β-CD was increased, a large enhancement of the fluorescence intensity was observed. This reflects the transfer of the naphthyl moiety of MNSS from the aqueous medium to the apolar β-CD cavity by inclusion complexation. For 1:1 complexation, the increase in fluorescence intensity (ΔI) is related to the association constant K by a

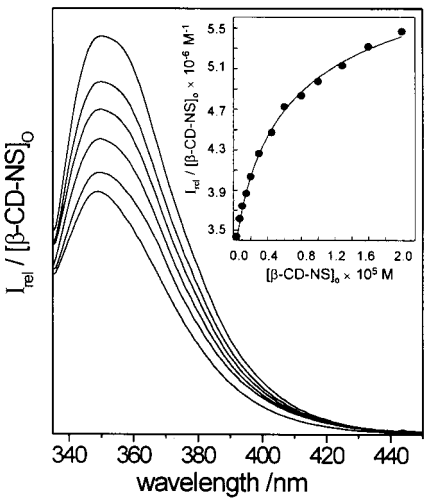


Figure 2. Concentration dependence of fluorescence spectra of β-CD-NS. The total β-CD-NS concentrations ([β-CD-NS]$_0$) are the following: 2.0×10^{-4}, 1.0×10^{-4}, 0.50×10^{-4}, 0.25×10^{-4}, 0.10×10^{-4}, and 2.0×10^{-4} M (from top to bottom). The bottom spectrum was taken in the presence of 1.5×10^{-2} M sodium *n*-octyl sulfate. Note that the fluorescence intensity is normalized to concentration. The inset shows the plot of the concentration-normalized fluorescence intensity (I/[β-CD-NS]$_0$) at 350 nm against [β-CD-NS]$_0$. The solid line is the fitted curve to eq 1.

Benesi−Hildebrand type equation[16]

$$\Delta I/[\beta\text{-CD}] = K\Delta I_\infty - K\Delta I \qquad (2)$$

where ΔI_∞ is the maximum change in fluorescence intensity when all of the MNSS molecules form the complex. The plot of experimental data according to eq 2 gave a good straight line, ensuring 1:1 complexation (Figure 2, inset). The K value and the ratio of the fluorescence intensities of β-CD-complexed and -uncomplexed MNSS, $I_{CD}/I_w = \Delta I_\infty/I_{[\beta-CD]=0} + 1$, were obtained as 530 ($\pm$ 20) M^{-1} and 2.1, respectively. The K value is similar to the reported association constants of 2-naphthalenesulfonate,[17] 2-naphthol,[18] and 3-(2-naphthoxyl)-1-aminopropane[19] with β-CD.

Figure 2 shows the concentration dependence of the concentration-normalized fluorescence spectra of β-CD-NS. The concentration-normalized fluorescence intensity increases as the concentration of β-CD-NS becomes higher. This closely resembles the effect of added β-CD on the spectra of MNSS shown in Figure 1. The addition of SOS to a given concentration of β-CD-NS solution decreases the emission intensity. The effect of *n*-octyl sulfate (SOS), whose association constant with β-CD was reported as 2560 M^{-1},[16] was leveled off when the concentration of SOS exceeded 1×10^{-2} M, indicating that the β-CD-NS aggregates are almost completely dissociated at the high SOS concentration.

The concentration dependence of the concentration-normalized fluorescence intensity is shown in the inset of Figure 2: we corrected for the inner filter effect on the measured emission intensity by $I_{corr} = I_{meas} \times 10^{(A_{ex}+A_{em})/2}$ where A_{ex} and A_{em} are absorbances at exciting and emitting wavelengths, respectively. Assuming a dimerization equilibrium, the I/[β-CD-NS]$_0$ versus [β-CD-NS]$_0$ curve was fitted to eq 1, using the intensity in the presence of 1.5×10^{-2} M SOS as that of the monomer. Excellent fitting was obtained, and the K_D value and I_{dimer}/I_{mon} ratio were obtained as 9000 ($\pm$ 900) M^{-1} and 2.2, respectively. The I_{dimer}/I_{mon} value is close to the value of I_{CD}/I_w of MNSS, 2.1. This indicates that the change of the environment of the naphthyl moiety of β-CD-NS by dimerization is similar to that of MNSS by complexation with β-CD. This suggests that the naphthyl moiety of the β-CD-NS dimer is included deeply inside the β-CD cavity, whereas that in the monomer is outside the cavity.

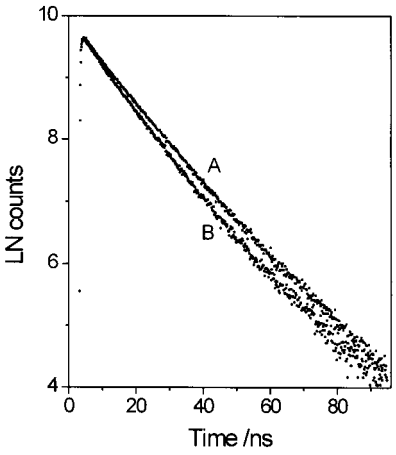


Figure 3. Fluorescence decay profiles of 1.0×10^{-4} M (A) and 1.0×10^{-5} M (B) β-CD-NS. Both profiles are fitted to $I(t) = A_1 \exp(-t/\tau_1) + A_2 \exp(-t/\tau_2)$, where τ_1 is 8.5 ns and τ_2 is 14.5 ns; the A_1/A_2 ratio values are 1.4 for A and 3.0 for B.

We also investigated the dimerization of β-CD-NS by fluorescence lifetime measurements. The fluorescence decay profile of MNSS fitted well to a single-exponential function with lifetime $\tau = 9.5 \pm 0.5$ ns ($\chi^2 = 1.1$), which is in good agreement with the reported lifetime.[6] However, the decay profiles of β-CD-NS (Figure 3) required a sum of two exponential terms to give a satisfactory fit. The lifetimes obtained from the fitting were $\tau_1 = 8.5 \pm 1.0$ ns and $\tau_2 = 14.5 \pm 2.0$ ns with χ^2 values less than 1.2. The pre-exponential factor of the longer component becomes greater as the concentration of β-CD-NS is higher. Thus, the short lifetime is attributed to the β-CD-NS monomer and the longer one to the β-CD-NS dimer. These results agree reasonably well with the results of steady-state fluorescence measurements.

Circular Dichroism Studies. β-CD is a chiral molecule, and thus a chromophore complexed with or appended to β-CD exhibits circular dichroism. The β-CD-induced c.d. spectra of MNSS consist of a strong positive band at around 235 nm and a negative band at 328 nm, and the ellipticities (θ) increase as the β-CD concentration increases (spectra not shown). The dependence of ellipticity on the concentration of β-CD fitted well to a 1:1 complexation, and the fitting gave the association constant (K) of MNSS with β-CD as 500 ($\pm$ 30) M^{-1}. The K value is in good agreement with that obtained from aforementioned fluorescence studies.

β-CD-NS shows intrinsic c.d., and the molar ellipticity ([θ]) depends highly on the concentration of β-CD-NS (Figure 4). As in fluorescence studies, the addition of SOS to a given β-CD-NS solution caused a spectral change similar to that observed when the solution is diluted. Again, the SOS-induced spectral change was leveled off when [SOS] $> 1 \times 10^{-2}$ M. The concentration dependence of the [θ] data of β-CD-NS was fitted to eq 1 to obtain the K_D value as 10 400 ($\pm$ 1700) M^{-1} (Figure 4, inset). The K_D value agrees well with the value obtained from the fluorescence intensity data described in the previous section.

The addition of β-CD to a β-CD-NS solution resulted in a large change in the c.d. spectrum (Figure 5). This reflects inclusion of the β-CD-appended naphthyl moiety into the cavity of the added β-CD to form a β-CD-NS/β-CD complex. The

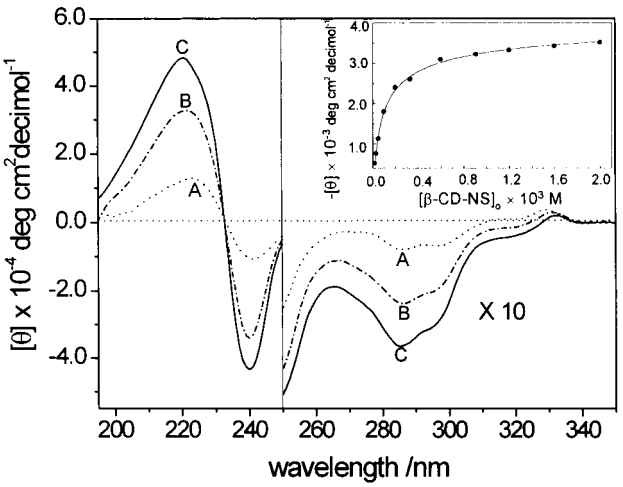


Figure 4. C*o*ncentration dependence of circular dichroism spectra of β-CD-NS. The concentrations of β-CD-NS are 2.0×10^{-5} (A), 2.0×10^{-4} (B), and 2.0×10^{-3} M (C). The inset shows the dependence of the molar ellipticity of β-CD-NS at 286 nm on its concentration. The solid line is the fitted curve to eq 1.

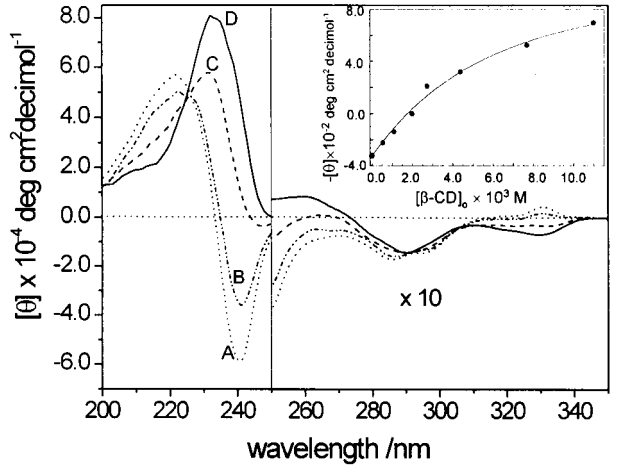


Figure 5. Effect of β-CD on the circular dichroism spectra of 1.0×10^{-4} M β-CD-NS. The concentrations of β-CD are 0.0 (A), 1.1×10^{-3} (B), 4.4. $\times 10^{-3}$ (C), and 11×10^{-3} M (D). The inset shows the dependence of molar ellipticity at 333 nm on the concentration of β-CD. The solid line is the fitted curve to eq 4.

observed molar ellipticity $[\theta]$ per naphthyl group is given by the weighted average of the molar ellipticities of contributing species and becomes

$$[\theta] = [\theta]_{mon} f_{mon} + [\theta]_{dimer} f_{dimer} + [\theta]_{complex} f_{complex} \quad (3)$$

where f's are the fraction of naphthyl moiety in each respective species. From the expressions of equilibrium constants and mass balance relationships, eq 3 can be rewritten as eq 4, where K_C

$$[\theta] = [\theta]_{mon} f_{mon} + 2K_D[\theta]_{dimer} f_{mon}^2 [\beta\text{-CD-NS}]_0 + K_C[\theta]_{complex} f_{mon} [\beta\text{-CD}] \quad (4)$$

is the association constant of the β-CD-NS monomer with β-CD. The fraction of the β-CD-NS monomer (f_{mon}) is related to the concentration of β-CD and the total concentration of β-CD-NS, $[\beta\text{-CD-NS}]_0$, by eq 5.

$$f_{mon} = \frac{\sqrt{(1 + K_C[\beta\text{-CD}])^2 + 8K_D[\beta\text{-CD-NS}]_0} - (1 + K_C[\beta\text{-CD}])}{4K_D[\beta\text{-CD-NS}]_0} \quad (5)$$

We used ellipticity data at 333 nm, which is an isoellipticity point for the monomer−dimer equilibrium with $[\theta]_{mon} = [\theta]_{dimer} = 360$ deg cm^2 dmol^{-1}, to fit the $[\theta]$ versus $[\beta$-CD] curve to eq 4 under the restriction of eq 5 and obtained K_C and $[\theta]_{complex,333\ nm}$ values: a K_D value of 10 700 M^{-1} was used, and $[\beta$-CD] was taken as the total concentration of β-CD, as it is much greater than $[\beta\text{-CD-NS}]_0$. The K_C and $[\theta]_{complex,333\ nm}$ values were found to be 430 ($\pm$ 50) M^{-1} and -900 deg cm^2 dmol^{-1}, respectively. The K_C value is close to the association constant of MNSS with β-CD, supporting the idea that the naphthyl moiety of the β-CD-NS monomer is outside the β-CD cavity.

^{1}H NMR Studies. Figure 6 shows the concentration dependence of ^{1}H NMR spectra of β-CD-NS. As the concentration of β-CD-NS is increased, the signals from aromatic protons of β-CD-NS move to upfield. This is reminiscent of an observation with 3-*O*-(2-methylnaphthyl)-β-CD.[8] Similar NMR spectral changes are observed when β-CD is added to MNSS (spectra not shown) and 2-naphthalenesulfonate[17] solutions. Furthermore, the addition of SOS resulted in a downfield shift of the aromatic protons and a large modification of the spectrum in the CD region (Figure 6). These results provide further evidences of the intermolecular association of β-CD-NS and the displacement of the naphthyl group from the β-CD cavity by SOS.

Since no separate signals for the monomer and the aggregate were observed, the dynamic equilibrium between a monomer and an aggregate is within the NMR time scale. In this situation, the observed chemical shift is determined by the weighted average of the shifts of contributing species.

We attempted to determine the K_D value by nonlinear least-squares fitting of the concentration dependent ^{1}H NMR chemical shifts to eq 1. The K_D value was found to be in the range 2 000−15 000 M^{-1}, depending on the experimental set and the choice of protons. The practical limit of the low concentration end in NMR measurements seems to be too high to give a reliable K_D value, which is ~10 000 M^{-1}, as determined from fluorescence and c.d. studies: the fractions of the β-CD-NS monomer are calculated to vary from 0.05 to 0.33 when the 20×10^{-3} M solution is diluted to 0.3×10^{-3} M.

Structure of the β-CD-NS Dimer and Thermodynamic Consideration of the Dimerization. So far, we have shown that β-CD-NS exhibits a strong tendency for intermolecular association in water, and the association behavior fits well to a dimerization equilibrium. The schematic structures of possible dimers of β-CD-NS are presented in Chart 1.[20]

The HT-1 dimer can be formed by inclusion of the naphthyl moiety of a β-CD-NS molecule into a β-CD cavity of a counter β-CD-NS molecule from the secondary face. The dimerization is the first step for the formation of higher head-to-tail aggregates. Since the association constant of the β-CD-NS monomer with β-CD is 430 $\pm$ 50 M^{-1} (vide supra), the formation of the HT-1 type dimer as well as higher aggregates should be insignificant at a low concentration of β-CD-NS, for example $[\beta\text{-CD-NS}]_0 < 10^{-4}$ M, used in this work. The HT-2 dimer, in which two naphthyl moieties are included in a β-CD cavity, is similar to that proposed for β-CD-6-*O*-2-naphthoate.[14] Formation of such a type of dimer is also unlikely because the cavity volume of β-CD is not large enough to accommodate two naphthyl groups and we failed to observe excimer fluores-

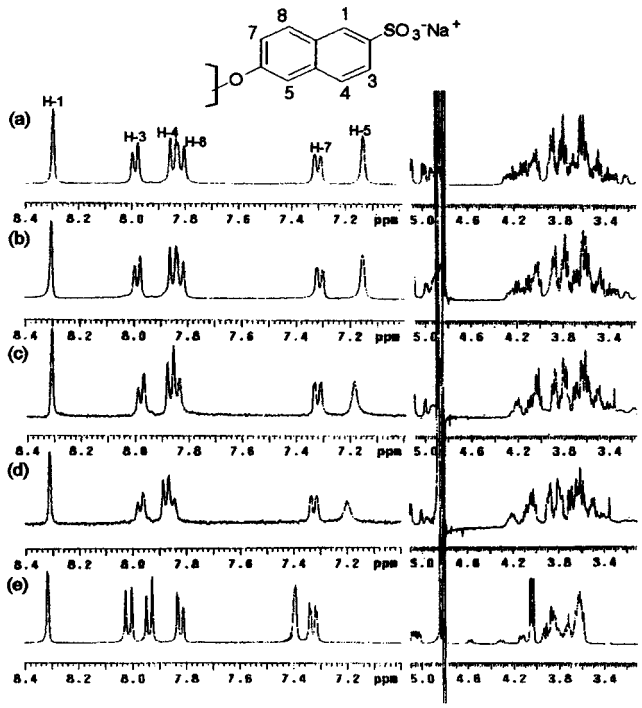
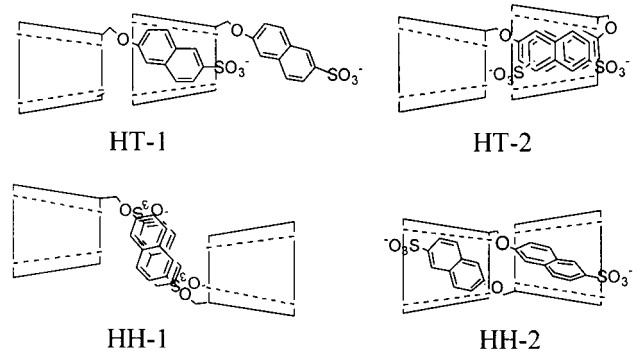


Figure 6. ^{1}H NMR (D_2O) spectra of naphthalene and CD regions of β-CD-NS: (a) 20×10^{-3} M, (b) 3.0×10^{-3} M, (c) 0.6×10^{-3} M, (d) 0.3×10^{-3} M, (e) 5.0×10^{-3} M β-CD-NS + 25×10^{-3} M sodium *n*-octyl sulfate. Assignments of the aromatic protons of the 2-sulfonato-6-naphthyl group were made with COSY spectra and are given in spectrum a. The peak at 4.07 ppm in spectrum e is from sodium *n*-octyl sulfate.

CHART 1: Structurally Feasible Dimers of β-CD-NS: Among These, HH-2 Is Consistent with Thermodynamic Data and Fluorescence and Circular Dichroism Spectra (see text)



cence: it was reported that coinclusion of two naphthyl moieties in the γ-CD cavity exhibits a strong excimer band near 400 nm.[21] We also rule out the possibility of the formation of a HH-1 type dimer, which was suggested as a possible dimer for 3-*O*-(2-methylnaphthyl)-β-CD,[8] as the observed dimerization constant is too large to attribute to the interaction between sulfonatonaphthyl groups and no excimer fluorescence was observed. The HH-2 dimer is thermodynamically feasible, as it is stabilized through mutual inclusion of naphthyl groups into the cavities of β-CD moieties of counter molecules. Such stabilization of dimers of pendant β-CDs by mutual inclusion of pendant groups has been demonstrated for one-electron reduced mono-6-(1-alkyl-4,4′-bipyridino)-β-CDs.[22] The similarity of the fluorescence change for MNSS/β-CD complexation to that for dimerization of β-CD-NS also supports the dimer structure. Also, the separation of two naphthyl groups in the structure is consistent with the absence of excimer fluorescence.

The dimerization constant (K_D) of β-CD-NS is best estimated as 9700 ($\pm$ 2500) M^{-1} from two independent methods, that is, fluorescence and c.d.. The K_D value is comparable to the dimerization constant of 3-*O*-(2-methylnaphthyl)-β-CD, ~5000 M^{-1}.[7] Since the HH-2 dimer is stabilized by cooperative inclusion of two naphthyl groups into β-CD cavities, the association constant for the inclusion of a naphthyl group into a β-CD cavity is estimated as 100 ($\pm$ 15) M^{-1}, that is, the square root of the K_D value. This is much smaller than the association constants of a β-CD-NS monomer or MNSS with β-CD. But it is reasonable when one considers that the HH-2 dimer is formed by the inclusion of a naphthyl moiety into a β-CD cavity of a counter β-CD-NS molecule from the narrower primary face, whereas the MNSS/β-CD and β-CD-NS/β-CD complexes are formed by inserting the naphthyl group into both openings of a β-CD cavity.

The estimated width of a naphthyl group is ~0.68 nm, while the cavity diameter of β-CD is 0.7−0.95 nm. Because of such a size difference, the long axis of the naphthyl group could be slightly oblique with the β-CD axis, as depicted by others.[17,27] Also, the transition dipole moments of the groups in the dimer would be in an oblique orientation with each other, resulting in exciton coupling in c.d. spectra. The H-5 proton shows the most prominent upfield shift in ^{1}H NMR spectra upon dimerization (Figure 6). The shift of 0.26 ppm is about twice the shift (0.13 ppm) calculated from data reported on the complexation of 2-naphthalene sulfonate with β-CD.[17] One plausible explanation for this is that the H-5 proton is closer to the naphthyl group of the counter molecule and experiences the largest ring current effect. This was supported by the downfield shift of the signal by the addition of a large excess of β-CD to β-CD-NS solution (spectrum not shown).

Circular Dichroism Spectral Characteristics of the Monomer and Dimer of β-CD-NS, and the MNSS/β-CD Complex. The c.d. spectrum of a chiral compound or a chiral complex depends highly on the structure of the compound or complex.[23−25] For a complex between a chiral macrocyclic host, for example cyclodextrins, and an achiral guest bearing a chromophore, the sign and ellipticity of the induced c.d. spectra are related to the relative position and orientation of the chromophore with respect to the macrocycle.

To correlate c.d. spectra of existing species with their structures, we generated the spectra of each species from mixture spectra, using the determined equilibrium constants and a relationship that the c.d. spectrum of a mixture is the sum of those of the contributing species. The spectra of a monomer and dimer of β-CD-NS are generated from the spectra taken at two different concentrations of the compound by using eqs 6 and 7 where the subscripts 1 and 2 denote the concentrations 1

$$[\theta]_{mon} = (f_{dimer,2}[\theta]_1 - f_{dimer,1}[\theta]_2)/(f_{dimer,2} - f_{dimer,1}) \quad (6)$$

$$[\theta]_{dimer} = (f_{mon,2}[\theta]_1 - f_{mon,1}[\theta]_2)/(f_{mon,2} - f_{mon,1}) \quad (7)$$

and 2. Fractions of the monomer and dimer at each concentration, f_{mon} and $f_{dimer} = 1 - f_{mon}$, are calculated from the K_D and the total concentration of β-CD-NS from eq 5. The monomer and dimer spectra generated at various sets of concentrations were averaged: the monomer spectrum matched well with the spectrum of β-CD-NS in the presence of 2.5×10^{-2} M SOS in the limit of spectral resolution. The spectra were shown in Figure 7.

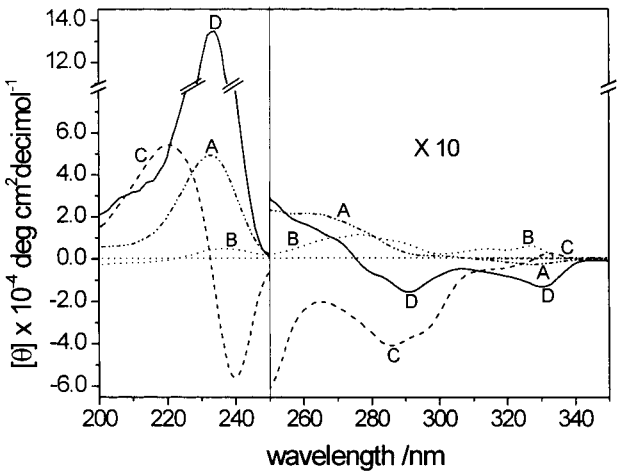


Figure 7. Circular dichroism spectra of the MNSS/β-CD complex (A), β-CD-NS monomer (B), β-CD-NS dimer (C), and β-CD-NS/β-CD complex (D). The molar ellipticity of spectrum A was corrected from the association constant of MNSS with β-CD, $K = 500$ M^{-1}. For generation of spectra B−D, see text. The spectrum of the β-CD-NS/SOS complex coincides with that of the β-CD-NS monomer in the limit of spectral resolution.

The spectrum of the β-CD-NS/β-CD complex, $[\theta]_{complex}$, was generated from spectra of β-CD-NS taken in the presence of various concentrations of β-CD. For this, the fraction of the β-CD-NS monomer, f_{mon}, was calculated at each concentration of β-CD from eq 5, using the determined equilibrium constants and $[\beta\text{-CD-NS}]_0$. Then the spectrum of the β-CD-NS/β-CD complex was calculated from eq 4, using the monomer and dimer spectra of β-CD-NS. Again, the spectra obtained from various concentrations of β-CD were averaged and included in Figure 7, together with the spectrum of the MNSS/β-CD complex.

Harata et al.[23] and Shimazu et al.[24] derived a rule that the sign of induced c.d. for a chromophore inside the β-CD cavity is positive when the electric transition moment is parallel to the axis of β-CD while the one perpendicular to the axis is negative. Kodaka extended this rule to derive a general rule that the sign of induced c.d. is reversed when the guest moves from inside of the cavity to outside and the direction of the transition is fixed, and it changes at the angle between the transition moment and the β-CD axis 54.7°.[25] The major UV transitions of the naphthyl group are ^1B_b (~230 nm), ^1L_a (~275 nm), and ^1L_b (~320 nm): the directions of the ^1B_b and ^1L_b transition moments are nearly parallel and perpendicular, respectively, to the long axis of naphthalene while that of the ^1L_a transition is tilted about 10−40° from the short axis.[26,27] On the basis of the rules, the induced c.d. spectrum of the MNSS/β-CD complex (spectrum A in Figure 7) agrees well with axial inclusion complexation. The c.d. spectra of the β-CD-NS monomer and the β-CD-NS/SOS complex (spectrum B in Figure 7) show a small ellipticity value for the ^1B_b transition and positive c.d. for ^1L_a and $1L_b$ transitions. These imply that the c.d. spectrum of a chromophore covalently attached to β-CD exhibits similar c.d. characteristics as those for the chromophore in the β-CD complex and that the angle between the β-CD axis and the long axis of naphthyl groups in the β-CD-NS monomer as well as the β-CD-NS/SOS complex is about 60°, indicating loosely capped structures.

The c.d. spectrum of the β-CD-NS dimer (spectrum C in Figure 7) shows an intense exciton coupling band in the ^1B_b transition region and a less distinct one in the ^1L_b region. The couplet in the c.d. spectrum was also reported for β-CD-6-*O*-2-naphthoate,[14] 3-*O*-(2-methylnaphthyl)-β-CD,[8] and a 2:2 complex between anthracene-2-sulfonic acid and per-6-amino-β-CD associated at the primary face of the β-CD derivative.[28,29] Gao et al. attributed the c.d. couplet as evidence of the formation of an HT-2 type dimer.[14] However, it was shown that a strongly split c.d. also can arise from a long-range effect[30] and that the exciton-split c.d. curves between chromophores 40−45 Å could still be expected for chromophores with molar absorptivity (ϵ) values of ~20 000 M^{-1} cm^{-1} (ref 31): the ϵ value of the naphthyl group is 21 000 at 234 nm. The oblique orientation of the naphthyl groups in the dimer, as discussed in the previous section, would allow transition. On the basis of these findings, together with our conclusion in the previous section that the prevailing dimer of β-CD-NS is HH-2 type and the expectation that the similar structural and thermodynamic factors should be applied to both β-CD-NS and β-CD-6-*O*-2-naphthoate dimers, we propose that β-CD-6-*O*-2-naphthoate would also form the HH-2 type dimer and the exciton coupling band is characteristic of the dimer.

The c.d. spectrum of the β-CD-NS/β-CD complex differs from that of the MNSS/β-CD complex, exhibiting much larger c.d. signals for ^1B_b (~230 nm) and ^1L_b (~320 nm) transitions. A plausible explanation for this is that the 2-sulfonatonaphthyl moiety of β-CD-NS is included into the secondary face of β-CD, as the face is wider and the protruded sulfonate group interacts favorably with the positive potential field of the primary face.[32] The parallel arrangement of the two β-CD moieties in the complex is expected in enhanced helical charge circulation to give greater rotational strength to the naphthyl moiety than to the MNSS/β-CD complex.

Conclusions

A monofunctional derivative of β-CD having a 2-sulfonato-6-naphthyl group (β-CD-NS) was prepared. The fluorescence, circular dichroism (c.d.), and ^{1}H NMR spectra of β-CD-NS depend highly on the concentration, indicating intermolecular association of the compound accompanied by inclusion of a naphthyl moiety into a β-CD cavity. The concentration dependent fluorescence and c.d. data are fitted well to the monomer−dimer equilibrium of β-CD-NS with the dimerization constant (K_D) of 9700 ± 2500 M^{-1}. The K_D value is much greater than the association constant of 2-methoxy-6-naphthalenesulfonate (MNSS) with β-CD, 500 ± 30 M^{-1}, and the association constant of β-CD-NS with β-CD, 430 ± 50 M^{-1}. These results indicate that β-CD-NS molecules form a head-to-head type dimer, which is stabilized by mutual inclusion of the naphthyl moieties deeply into the β-CD cavities of counter molecules. The dimer does not exhibit an excimer band in the fluorescence spectrum but shows exciton coupling bands in the ^1B_b (~230 nm) and ^1L_b (~320 nm) transition regions. The c.d. spectra of the MNSS/β-CD complex and β-CD-NS monomer agree well with general rules developed for induced c.d. of β-CD complexes. The naphthyl moiety of the β-CD-NS monomer appears to cap the primary face loosely. Compared to the c.d. spectrum of the MNSS/β-CD complex, the c.d. spectrum of the β-CD-NS/β-CD complex is similar in shape, but the rotational strengths of the bands are much greater. The results reported here would provide guidance for understanding the host−guest chemistry of aromatic group-tethered β-CD, excitation transfer in the host−guest complexes, and the relationship between the structure and c.d. characteristics of cyclodextrin complexes and derivatives

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References and Notes

(1) For compilations of recent research on cyclodextrins, see: (a) *Comprehensive Supramolecular Chemistry;* Szejtli, J., Osa, T., Eds.; Pergamon Press: Oxford, 1996; Vol. 3. (b) *Chem. Rev.* **1998**, *98*, 1741−2076.

(2) Wenz, G. *Angew. Chem., Int. Ed. Engl*. **1994**, *33*, 803.

(3) (a) Gonzalez, M. C.; McIntosh, A. R.; Bolton, J. R.; Weedon, A. C. *J. Chem. Soc., Chem. Commun*. **1984**, 1138. (b) Kuroda, Y.; Ito, M.; Sera, T.; Ogosi, H. *J. Am. Chem. Soc.* **1993**, *115*, 7003. (c) Hubbard, B. K.; Beilstein, L. A.; Heath, C. E.; Abelt, C. J. *J. Chem. Soc., Perkin Trans. 2* **1996**, 1005.

(4) Acquavella, M. F.; Evans, M. E.; Farraher, S. W.; Nevoret, C. J.; Abelt, C. J. *J. Chem. Soc., Perkin Trans. 2* **1995**, 385.

(5) (a) Berberan-Santos, M. N.; Canceill, J.; Brochon, J. C.; Jullien, L.; Lehn, J.-M.; Pouget, J.; Tauc, P.; Valeur, B. *J. Am. Chem. Soc*. **1992**, *114*, 6427. (b) Berberan-Santos, M. N.; Pouget, J.; Valeur, B.; Canceill, J.; Jullien, L.; Lehn, J.-M. *J. Phys. Chem*. **1993**, *97*, 11376. (c) Jullien, L.; Canceill, J.; Valeur, B.; Bardez, E.; Lehn, J.-M. *Angew. Chem., Int. Ed. Engl*. **1994**, *33*, 2438. (d) Berberan-Santos, M. N.; Canceill, J.; Gratton, E.; Jullien, L.; Lehn, J.-M.; So, P.; Sutin, J.; Valeur, B. *J. Phys. Chem*. **1996**, *100*, 15. (e) Jullien, L.; Canceill, J.; Valeur, B.; Bardez, E.; Léfèvre, J.-P.; Lehn, J.-M.; Marchi-Artzner, V.; Pansu, R. *J. Am. Chem. Soc*. **1996**, *118*, 5432. (f) Wang, P. F.; Jullien, L.; Valeur, B.; Filhol, J.-S.; Canceill, J.; Lehn, J.-M. *New J. Chem*. **1996**, *20*, 895. (g) Nowakowska, M.; Loukine, N.; Gravett, D. M.; Burke, N. A. D.; Guillet, J. E. *J. Am. Chem. Soc*. **1997**, *119*, 4364. (h) Berberan-Santos, M.; Choppinet, P.; Fedorov, A.; Jullien, L.; Valeur, B. *J. Am. Chem. Soc.* **1999**, *121*, 2526.

(6) Gravett, D. M.; Guillet, J. E. *J. Am. Chem. Soc*. **1993**, *115*, 5970.

(7) McAlpine, S. R.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **1996**, *118*, 2750.

(8) McAlpine, S. R.; Garcia-Garibay, M. A. *J. Am. Chem. Soc*. **1998**, *120*, 4269.

(9) (a) Ikeda, H.; Nakamura, M.; Ise, N.; Oguma, N.; Nakamura, A.; Ikeda, T.; Toda, F.; Ueno, A. *J. Am. Chem. Soc.* **1996**, *118*, 10980. (b) Ikeda, H.; Nakamura, M.; Ise, N.; Toda, F.; Ueno, A. *J. Org. Chem*. **1997**, *62*, 1411. (c) Saviano, M.; Lombardi, A.; Pavone, V. *Chem.—Eur. J*. **1996**, *2*, 373. (d) Ueno, A.; Ikeda, A.; Ikeda, H.; Ikeda, T.; Toda, F. *J. Org. Chem*. **1999**, *64*, 382.

(10) Corradini, R.; Dossena, A.; Galaverna, G.; Marchelli, R.; Panagia, A.; Sartor, G. *J. Org. Chem*. **1997**, *62*, 6283.

(11) Narita, M.; Hamada, F.; Suzuki, I.; Osa, T. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2751.

(12) Liu, Y.; Han, B.-H.; Sun, S.-X.; Wada, T.; Inoue, Y. *J. Org. Chem*. **1999**, *64*, 1487.

(13) McAlpine, S. R.; Garcia-Garibay, M. A. *J. Org. Chem*. **1996**, *61*, 8307.

(14) (a) Gao, X.-M.; Tong, L.-H.; Zhang, Y.-L.; Hao, A.-Y.; Inoue, Y. *Tetrahedron Lett*. **1999**, *40*, 969. (b) Gao, X.-M.; Zhang, Y.-L.; Tong, L.-H.; Ye, Y.-H.; Ma, X.-Y.; Liu, W.-S.; Inoue, Y. *J. Inclusion Phenom. Macrocyclic Chem*. **2001**, *39*, 77.

(15) Petter, R. C.; Sallek, J. S.; Sikorski, C. T.; Kumaravel, G.; Lin, F.-T. *J. Am. Chem. Soc*. **1990**, *112*, 3866.

(16) Park, J. W.; Song, H. J. *J. Phys. Chem*. **1989**, *93*, 6454.

(17) Nishijo, J.; Ushiroda, Y. *Chem. Pharm. Bull*. **1998**, *46*, 1790.

(18) (a) Yoruzu, T.; Hoshino, M.; Imamura, M.; Shizuka, H. *J. Phys. Chem*. **1982**, *86*, 4422. (b) Park, H. R.; Mayer, B.; Welschann, P.; Kohler, G. *J. Phys. Chem*. **1994**, *98*, 6158.

(19) Park, J. W.; Park, S. H.; Lee, B. A.; Lee, S. Y. *Chem. Lett*. **1997**, 1043.

(20) A reviewer suggested a possibility of another head-to-head dimer in which a naphthyl group is included into a β-CD cavity and the other group is sandwiched between two β-CD rings. It appeared that the dimer structure is less feasible sterically than the HH-2 dimer from CPK modeling.

(21) Ueno, A.; Moriwaki, F. M.; Osa, T.; Hamada, F.; Murai, K. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 465.

(22) Park, J. W.; Choi, N. H.; Kim, J. H. *J. Phys. Chem*. **1996**, *100*, 769.

(23) Harata, K.; Uedaira, H. *Bull. Chem. Soc. Jpn*. **1975**, *48*, 375.

(24) (a) Shimizu, H.; Kaito, A.; Hatano, M. *Bull. Chem. Soc. Jpn*. **1979**, *52*, 2678. (b) Shimizu, H.; Kaito, A.; Hatano, M. *Bull. Chem. Soc. Jpn*. **1981**, *54*, 513. (c) Shimizu, H.; Kaito, A.; Hatano, M. *J. Am. Chem. Soc.* **1982**, *104*, 7059.

(25) (a) Kodaka, M.; Fukaya, T. *Bull. Chem. Soc. Jpn*. **1989**, *62*, 1154. (b) Kodaka, M. *J. Phys. Chem*. **1991**, *95*, 2110. (c) Kodaka, M. *J. Am. Chem. Soc*. **1993**, *115*, 3702.

(26) The directions of the transition moments of naphthalene derivatives depend little on substituents. We took the directions from the results of Kodaka in ref 27.

(27) Kodaka, M. *J. Phys. Chem. A* **1998**, *102*, 8101.

(28) Tamagaki, S.; Fukuda, K.; Maeda, H.; Mimura, N.; Tagaki, W. *J. Chem. Soc., Perkin Trans. 2* **1995**, 389.

(29) The chirality of the β-CD-NS dimer is the opposite of that of other dimers. Clarification of the origin of the different chirality is beyond the scope of this work.

(30) Chen, S. L.; Harata, N.; Nakanishi, K. *J. Am. Chem. Soc*. **1974,** *96*, 7352.

(31) Nakanishi, K.; Berova, N. In *Circular Dichroism. Principles and Applications*; Nakanishi, K., Berova, N., Woody, R. W., Eds.; VCH: New York, 1994; p 376.

(32) Sakurai, M.; Kitagawa, M.; Hoshi, H.; Inoue, Y.; Chujo, R. *Chem. Lett*. **1988**, 895.