Face Selectivity of Inclusion Complexation of Viologens with β-Cyclodextrin and 6-O-(2-Sulfonato-6-naphthyl)-β-cyclodextrin

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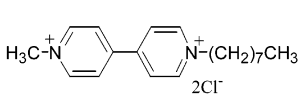
Face selectivity in binding of methyloctyl viologen ($C_1C_8V^{2+}$: **1**) and adamantylmethyl viologen ($AdaC_1V^{2+}$: **2**) with β-CD and 6-O-(2-sulfonato-6-naphthyl)-β-CD (β-CD-NS: **4**) has been investigated. Circular dichroic titration of **1** and **2** with β-CD gave the binding constants and the molar ellipticities $[\theta]_{254nm}$ of the β-CD complexes as 890 M^{-1} and −2000 deg cm^2 $dmole^{-1}$ for **1**, and as 7300 M^{-1} and −3600 deg cm^2 $dmole^{-1}$ for **2**. The $[\theta]$ values of the complexes are much less negative than −8500 deg cm^2 $dmole^{-1}$ of β-CD−viologen compound **3** in which the viologen is covalently bonded to the primary face of β-CD. Fluorescence quenching of the naphthyl group of **4** by **1** and **2** is much more efficient than that of 6-methoxy-2-naphthalenesulfonate (MNSS), but residual fluorescence was observed even at high viologen concentration. The binding constants of the viologens with **4** and the fractions of the residual fluorescence with respect to fully monomeric **4** were determined as 4700 M^{-1} and 0.09 for **1** and 10 400 M^{-1} and 0.15 for **2**. Comparing the steady-state fluorescence quenching and time-resolved fluorescence studies, it appeared that the bipyridinium moiety of **2** is predominantly on the secondary side of β-CD of **4**, whereas that of **1** favors the primary side, mainly due to the direct charge transfer interaction between the naphthyl and bipyridinium groups: without the interaction, it would prefer the secondary face 14 times more favorably to the primary face. The rate constants of the photoinduced electron-transfer reactions between the bipyridinium group on the secondary face and the naphthyl group are 1.9×10^8 s^{-1} for the **1**/**4** complex and 7.9×10^8 s^{-1} for the **2**/**4** complex.

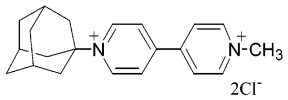
Introduction

Cyclodextrins (CDs) are torus-like cyclic oligosaccharides with hydrophobic cavities capable of forming inclusion complexes with a variety of organic molecules in aqueous solution. Because of these characteristics, CDs have been widely used as biomimetic microreactors, novel media for photophysical and photochemical studies, and building blocks for supramolecular structures and functional units as well as in various fields of industries.[1,2] Guest molecules can be included from both ends of CD cavities. The face selective inclusion complexation with CDs is believed to be important in molecular recognition and chemical reactions mediated by CDs as the size of opening, acidity of hydroxyl groups, and electrostatic potential of the ends are different. There has been much effort to determine the structures, and thus the face selectivity, of CD-inclusion complexes: NMR[3−5] and circular dichroic[6−8] spectroscopic methods have been widely utilized for this purpose. Molecular modeling[9] and the nonlinear free energy relationship model[10] have been also used to determine and/or predict the guest orientation in the CD complexes. However, there is a paucity of experimental evidence on the face selectivity of the complexes. Long alkyl chains are a typical part of guest molecules that are included into CD cavities.[11−14] Inclusion complexation of alkyl viologens, 1,1′-dialkyl-4,4′-bipyridinium salts, with CDs has been a subject of numerous studies.[6,7,14,15] On the basis of the negative induced circular dichroism (ICD) of diheptyl viologen/CD complexes and rules for ICD derived from the Kirwood−Tinoco equation, Kodaka suggested that the bipyridinium moiety of the viologen is placed above the narrower primary side of CDs.[6,7] However, as the ICD of a chromophore gives the same sign on the both sides of CDs,[6,7] the negative ICD cannot be taken as an unequivocal evidence for the location of the bipyridinium group with respect to CD cavities. Also, the conclusion is in conflict with an expectation that the bipyridinium group would prefer the wider secondary side by ion−dipole interaction as the electrostatic potential outside the secondary rim is negative.[16]

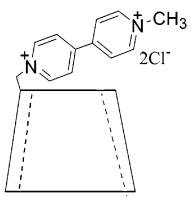
In this paper, we reexamined the face selectivity of the inclusion complexation of alkyl viologen through the studies on the complexation of methyloctyl viologen ($C_1C_8V^{2+}$: **1**) and adamantylmethyl viologen ($AdaC_1V^{2+}$: **2**) with native β-CD and 6-O-(2-sulfonato-6-naphthyl)-β-CD (β-CD-NS: **4**) by a combination of a variety of spectroscopic techniques. From these studies and comparison of ICD spectra of the viologen/β-CD complexes with that of a β-CD-viologen compound **3**, it was



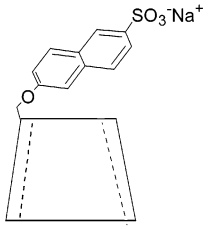
1: $C_1C_8V^{2+}$



2: $AdaC_1V^{2+}$



3: β-CD-$V^{2+}C_1$



4: β-CD-NS

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shown that the bipyridinium moieties of **1** and **2** are preferentially placed on the secondary side of β-CD in their complexes with native β-CD. The rate constants of photoinduced electron-transfer reactions in the viologen/**4** complexes were also obtained.

Experimental Section

Materials. Chemicals were obtained from Aldrich. β-CD and 4,4′-bipyridine were recrystallized from water and vacuum-dried. The chloride salts of methyloctyl viologen **1** and mono-6-(1-methyl-4,4′-bipyridino)-β-CD **3** were prepared as reported in a previous paper.[14] The synthesis and characterization of 6-O-(2-sulfonato-6-naphthyl)-β-CD **4** were reported elsewhere.[17] The compound **2** was prepared as described below.

Synthesis of 1-Adamantyl-1′-methyl-4,4′-bipyridinium Dichloride, 2. To a solution of 4,4′-bipyridine (6.0 g, 38 mmol) in ethanol (15 mL) at 40 °C was added a solution of dinitrochlorobenzene (3.8 g, 20 mmol) in 15 mL of ethanol dropwise, and stirring was continued for 40 h at the same temperature. After evaporating off the solvent, the residue was washed with dry diethyl ether and recrystallized from ethanol to obtain 2.3 g (6.4 mmol; 32% yield) of 1-(2,4-dinitrophenyl)-4,4′-bipyridinium chloride, **5**. The compound **5** (1.0 g, 2.8 mmol) and 1-adamantanamine (0.63 g, 4.2 mmol) were dissolved in 10 mL of methanol and refluxed for 3 h under N_2 atmosphere. After evaporating off the methanol solvent, 40 mL of water was added and then filtered. The filtrate was evaporated to dryness, and the resulting solid was recrystallized in 2-propanol to obtain 0.67 g (75% yield) of white crystalline 1-adamantyl-4,4′-bipyridinium chloride, **6**. The compound **2** was obtained by reacting **6** with large excess of CH_3I in ethanol, followed by counterion exchange through stirring the aqueous viologen solution in the presence of AgCl, in nearly quantitative yield.[14] Recrystallization from 2-propanol/ethanol (10:1 v/v) gave the analytically pure **2**.

Data for **5**: ^{1}H NMR (D_2O) δ 9.44 (d, 1H), 9.30 (d, 2H), 8.99 (dd, 1H), 8.88 (dd, 2H), 8.74 (d, 2H), 8.34 (d, 1H), 8.07 (dd, 2H).

Data for **6**: ^{1}H NMR (D_2O) δ 9.25 (d, 2H), 8.79 (d, 2H), 8.42 (d, 2H), 7.93 (d, 2H), 2.30 (s, 9H), 1.88 (t, 6H).

Data for **2**: UV(H_2O) λ_{max}/nm (logϵ), 264(4.31); mp 270 °C (dec); ^{1}H NMR (D_2O) δ 9.37 (d, 2H), 9.06 (d, 2H), 8.54 (d, 4H), 4.52 (s, 3H), 2.41 (s, 9H), 1.86 (t, 6H); Anal. Calcd for $C_{21}H_{26}N_2Cl_2 \cdot 3H_2O$: C, 58.47; H, 7.47; N, 6.49; Found: C, 58.75; H, 7.84; N, 6.51.

Spectral Measurements. ^{1}H NMR spectra were obtained on a Bruker 250 MHz spectrometer. Absorption spectra were recorded with a GBC Cyntra 20 spectrophotometer. Difference spectra for charge-transfer complexation were taken from mixing tandem double cells. Steady-state fluorescence spectra were obtained with a Hitachi F-3010 spectrofluorimeter. Fluorescence lifetime measurements were performed using a time-correlated single photon counting setup assembled at Pohang University. Circular dichroism spectra were taken with a JASCO J-810 spectropolarimeter. The bandwidth was set at 2 nm and the response time was 2 s. The β-CD-free solutions having the same concentration of viologens were used as blanks. Spectra of 10 repetitive scans taken at the scan speed of 50 nm per min were averaged and smoothed using JASCO software. All measurements were carried out at 25 °C using an appropriate temperature controller. Unless otherwise specified, ionic strength of solutions was maintained as 0.10 M with NaCl.

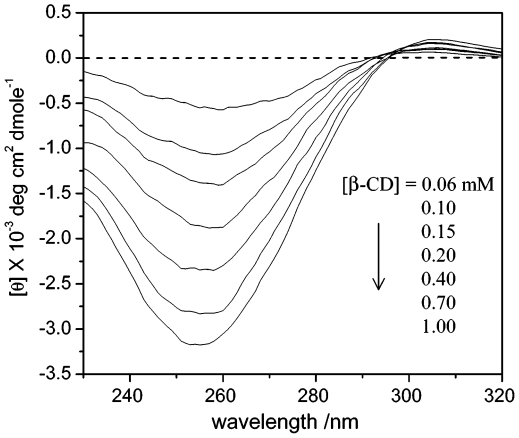


Figure 1. Induced circular dichroism spectra of **2** in the presence of β-CD. The concentration of **2** was 1.0×10^{-4} M. The concentrations of β-CD are shown in the figure.

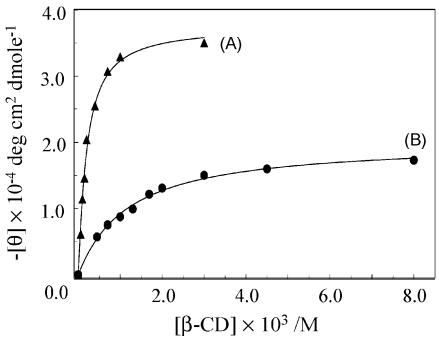


Figure 2. Dependence of the apparent molar ellipticity of **2** (A) and **1** (B) on the concentration of β-CD.

Results and Discussion

Binding of Viologens with β-CD and Circular Dichroic Properties of the β-CD Complexes. Both $C_1C_8V^{2+}$ (**1**) and $AdaC_1V^{2+}$ (**2**) are achiral molecules and do not show circular dichroism. However, in the presence of β-CD, they exhibited virtually identical negative induced circular dichroism (ICD) around 255 nm. This is due to the complexation of the viologens with the chiral host. The ICD spectra grow as the concentration of β-CD becomes higher (Figure 1). The dependences of ellipticity at 254 nm on the concentration of β-CD are presented in Figure 2.

If we assume 1:1 complexation between the viologen (V^{2+}) and β-CD (eq 1), the apparent molar ellipticity ([θ]) of a spectrum taken at an initial viologen concentration $[V]_0$ and β-CD concentration $[\beta\text{-CD}]_0$ is expressed as eq 2.

$$V^{2+} + \beta\text{-CD} \rightleftharpoons V^{2+}-\beta-\text{CD}; \qquad K = [V^{2+}-\beta-\text{CD}]/[V^{2+}][\beta\text{-CD}] \quad (1)$$

$$[\theta] = ([\theta]_{\text{complex}}\{([V^{2+}]_0 + [\beta-\text{CD}]_0 + 1/K) - \sqrt{([V^{2+}]_0 + [\beta-\text{CD}]_0 + 1/K)^2 - 4[V^{2+}]_0[\beta-\text{CD}]_0}\})/2[V^{2+}]_0 \quad (2)$$

where $[\theta]_{\text{complex}}$ is the molar ellipticity of the complex at the measured wavelength. The [θ] versus $[\beta\text{-CD}]_0$ data fitted well to eq 2, and the determined K and $[\theta]_{\text{complex}}$ are given in Table 1. The binding constants of **1** (890 ± 60 M^{-1}) and **2** (7300 ± 400 M^{-1}) with β-CD are close to the reported binding constants of *n*-octylammonium (750 M^{-1})[13] and 1-adamantanammonium (8430 M^{-1})[4] chlorides with β-CD, implying that the bindings

TABLE 1: Association Constants and the Characteristics of the Complexes of Viologens with β-CD and β-CD-NS 4 in 0.1 M Aqueous NaCl Solutions at 25 °C

	β-CD		β-CD-NS	
viologen	K/M^{-1}	$[\theta]_{complex}$/ deg cm^2 dmole^{-1}[a]	K_C/M^{-1}[b]	$I_{complex}/I_{mon}$[c]
1: $C_1C_8V^{2+}$	890 ± 60	−2000 ± 100	4700 ± 200	0.09 ± 0.01
2: $AdaC_1V^{2+}$	7300 ± 400	−3600 ± 100	10400 ± 400	0.15 ± 0.05

[a] λ = 254 nm. The $[\theta]$ value of β-CD-$V^{2+}C_1$ **3** which bears covalently bonded viologen at the primary face of β-CD is −8540 deg cm^{2}dmole^{-1}. [b] Apparent binding constants with monomeric **4**. [c] The ratio of the fluorescence intensities of 1:1 complex and monomeric **4**.

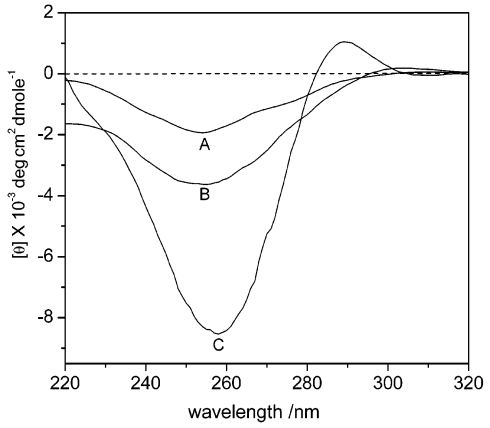


Figure 3. Circular dichroism spectra of **1**/β-CD (A), **2**/β-CD (B) complexes, and **3** (C). The spectra of the complexes were calculated from ICD spectra using measured complexation constants.

of the viologens are mainly driven by inclusion of the hydrophobic groups into β-CD cavity.

We calculated the concentration of the viologen/β-CD complexes using the determined binding constants and then generated the ICD spectra of **1**/β-CD and **2**/β-CD complexes. The spectra were compared with that of a β-CD-tethered viologen **3** in Figure 3. Kodaka derived a general rule for circular dichroism induced by a chiral macrocycle including CDs.[6,7,18] The rule predicts that the absolute value of ICD is larger when a chromophore is placed on the narrower-rim side of the macrocycle than on the wider-rim side. The rule also predicts that the sign and magnitude of ICD depend on the angle (Φ) between the axis of macrocycle and the direction of transition moment of the chromophore: the sign changes at Φ = 54.7°, and the magnitude becomes greater as the deviation of Φ from 54.7° is larger. The major transition of a viologen is the A → B_3 transition near 260 nm which is directed along the long axis of the viologen.[6] The negative circular dichroism of **3** near 260 nm suggests that the angle between CD axis and the long axis of viologen in **3** is less than 54.7°. This differs from the conclusion drawn from a NMR study that the long axis of viologen in a β-CD-viologen compound directs approximately perpendicular to the CD axis.[19] The estimation of the orientation of the viologen moiety with respect to β-CD in **3** is beyond the scope of this work. However, the smaller ellipticity of the β-CD complexes than that of **3** can be regarded as an evidence that the bipyridinium groups in the viologen/β-CD complexes are placed on the secondary side of β-CD cavity rather than the primary side claimed by Kodaka.[6,7] Other conclusive evidences for this were obtained from the binding studies of **1** and **2** with **4** described below.

Binding of Viologens with β-CD-NS and Intracomplex Quenching Studied by Fluorescence. Viologens quench the naphthalene fluorescence via electron transfer from the excited

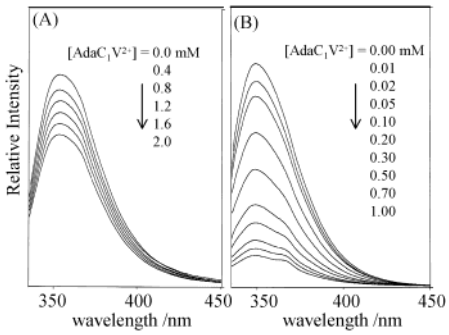


Figure 4. Quenching of the fluorescence of 1.0×10^{-5} M solutions of MNSS (A) and **4** (B) by **2**. The concentrations of **2** are shown in the figures.

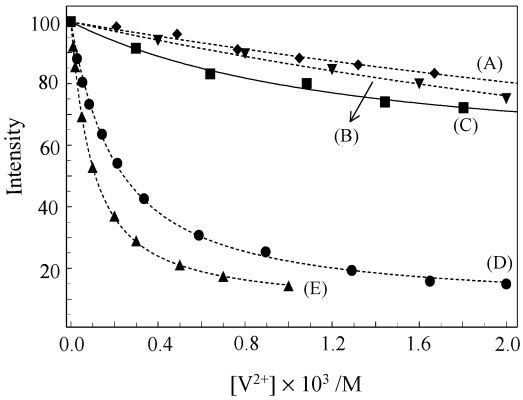


Figure 5. Dependence of the fluorescence intensity of 1.0×10^{-5} M solutions of MNSS and **4** on the concentration of viologens: (A), MNSS + $C_1C_1V^{2+}$; (B), MNSS + **2**; (C), **4** + $C_1C_1V^{2+}$; (D), **4** + **1**; (E), **4** + **2**.

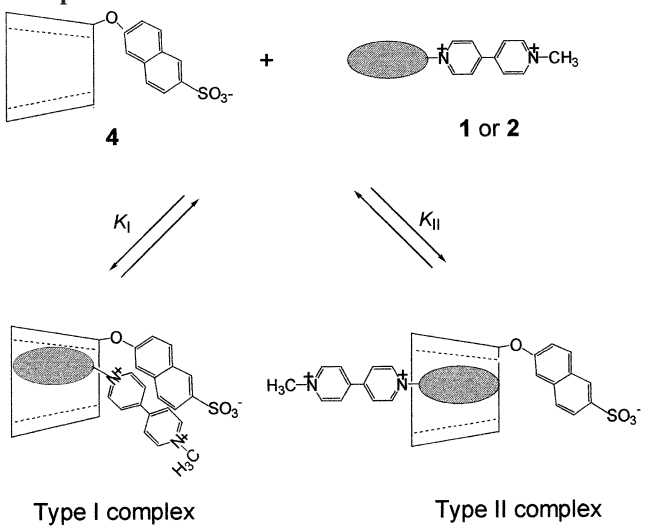
naphthalene to viologen.[20−22] The fluorescence quenching of β-CD-NS (**4**) and 2-methoxy-6-naphthalenesulfonate (MNSS) by **2** is compared in Figure 4. The dependences of the fluorescence intensity of **4** and MNSS on the concentrations of the viologen quenchers are shown in Figure 5. Figures 4 and 5 show that the fluorescence quenching of **4** by **1** and **2** is much more efficient than that of MNSS. In contrast to this, the quenching by dimethyl viologen ($C_1C_1V^{2+}$), which has little binding affinity to β-CD, was less efficient for both fluorophores. These results indicate clearly that the efficient quenching of the fluorescence of **4** by **1** and **2** is facilitated by the inclusion complexation of the quenchers with the β-CD-tethered fluorophore. Such inclusion-facilitated efficient quenching was demonstrated with other β-CD-tethered fluorophores and quenchers.[21,23] Even at high concentrations of **1** and **2**, the fluorescence of **4** was not completely quenched, and residual fluorescence was observed (Figure 5). This is an indication that the complexes between the quenchers and **4** are still fluorescent.

We have shown in a previous report[17] that the fluorescent host **4** forms a dimer with the dimerization constant (eq 3) of 9700 M^{-1} via mutual inclusion of the naphthyl groups into β-CD cavities of counter molecules and the fluorescence intensity of a naphthyl group in the dimer is 2.2 times greater than that in the monomer.

$$2\beta\text{−CD−NS} \rightleftarrows (\beta\text{−CD−NS})_2;$$
$$K_D = [(\beta\text{−CD−NS})_2]/[\beta\text{−CD-NS}]^2 \quad (3)$$

As β-CD cavities in the dimer of **4** are occupied by naphthyl groups, the dimer cannot form inclusion complexes with the viologen guests, but the monomer of **4** forms the complex with

CHART 1: Possible Structures of the Complexes between β-CD-NS 4 and a Viologen with a Hydrophobic Group



a guest and the monomer−dimer equilibrium is shifted by the complexation.

As shown in Chart 1, two types of **4**/viologen complexes are possible. One is that the bipyridinium moiety is placed on the primary side of **4** (type I complex), and the other is that it is placed on the secondary side (type II complex). The proximity of naphthyl and bipyridinium groups in a type I complex would result in a charge-transfer interaction (vide infra) and a static-like quenching.[22] The distance between naphthyl and bipyridinium groups in the type II complex appears to be not short enough to show the static quenching as evidenced by the residual fluorescence.

When we consider the apparent complexation (eq 4) and the weight-averaged fluorescence intensity of the complexes ($I_{complex}$), the K_C and $I_{complex}$ are related to the microscopic binding constants, K_I and K_{II}, defined in Chart 1 by eqs 5 and 6:

$$\beta\text{−CD−NS} + V^{2+} \rightleftarrows \text{complex};$$

$$K_C = [\text{complex}]/[\beta\text{−CD−NS}][V^{2+}] \quad (4)$$

$$K_C = K_I + K_{II} \quad (5)$$

$$I_{complex} = \frac{K_I I_I + K_{II} I_{II}}{K_I + K_{II}} \quad (6)$$

where the subscripts I and II represent the type I and II complexes, respectively.

An equation relating the observed fluorescence intensity of a given solution of **4** to the concentration of the viologen quencher **1** or **2** was derived as a function of K_D, K_C, and the ratio (γ) of fluorescence intensities of the complex and monomeric **4** and shown in the Appendix. The K_C and γ values obtained by the fitting of the experimental data (Figure 5) to the equation are listed in Table 1.[24]

We also investigated the fluorescence decay profiles of **4** both in the absence and in the presence of the viologens, **1** and **2**. In the absence of viologens, the decay curve fitted a biexponential function with lifetimes of $\tau_1 = 8.5$ (±1.0) ns and $\tau_2 = 14.5$ (±2.0) ns, which correspond to those of monomer and dimer of **4**, respectively.[17] However, the decay profiles in the presence of **1** and **2** exhibit a shorter component of which lifetimes are 3.3 (±0.2) ns for **1** and 1.1 (±0.2) ns for **2**, together with a long component having lifetime of ca. 9 ns (Figure 6): the

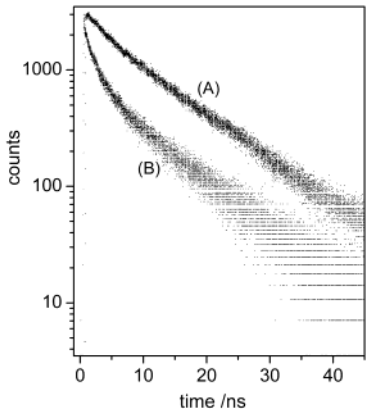


Figure 6. Fluorescence decay profiles of 3.0×10^{-4} M **4** in the absence of viologen (A) and in the presence of 1.0×10^{-3} M **2** (B). The decay profile of **4** in the presence of **1** was omitted for clarity.

decays of uncomplexed monomer and dimer of **4** were resolved poorly. The shorter component can be attributed to the complexes of the viologens with **4**.

In the absence of static quenching, i.e., in case when the type I complex is not formed, the ratio ($\tau_{complex}/\tau_{mon}$) of lifetimes of the complex and the monomeric **4** is expected to be the same as the ratio (γ) of fluorescence intensities of the respective species. The quenching by **2** seems to belong to this case as the ratio of lifetimes is 0.13 (±0.05), whereas γ was observed as 0.15 (±0.02). On the other hand, in case of **1**, the ratio of lifetimes is 0.39 (±0.05), which is much greater than the γ value of 0.09 (±0.01). This suggests that **1** forms the type I complex as well as the type II complex.

As the type I complex of the **1**/**4** system is not fluorescent, the ratio of fluorescence lifetimes of the type II complex and monomeric **4**, 0.39 (±0.05), is equal to the ratio (γ_{II}) of the fluorescence intensities of the corresponding species. Thus $K_{II}/(K_I + K_{II})$ becomes equal to γ_{II}/γ, which is 0.23 (±0.06), from eq 6 after putting $I_I = 0$ and dividing both sides by $I_{monomer}$. This corresponds to K_I/K_{II} ratio of ca. 3.3. As $K_I + K_{II}$ is determined as 4700 M^{-1} (Table 1), K_I and K_{II} are estimated as 3600 and 1100 M^{-1}, respectively.

The rate constant of the intracomplex electron-transfer reaction (k_{et}) in the type II complex is related to the fluorescence lifetimes of monomeic **4** and the complex by eq 7:

$$k_{et} = \frac{1}{\tau_{complex}} - \frac{1}{\tau_{mon}} \quad (7)$$

From the lifetime data, k_{et}'s were calculated as 1.9×10^8 s^{-1} for **1**/**4** and 7.9×10^8 s^{-1} for the **2**/**4** complexes. These values are the through-space/solvent electron-transfer rate constants from the excited naphthyl to bipyridinium groups in the respective complexes. As k_{et} varies exponentially with the donor−acceptor distance,[25] the result suggests that the bipyridinium group of **1** in its type II complex with **4** locates farther from the wider secondary rim of β-CD than that of **2** in the corresponding complex.

Charge-Transfer Interaction between Naphthyl and Bipyridinium Groups in the Complexes of 4 with Viologens. The addition of the viologen **1** or **2** to a solution of **4** results in a diffused absorption above 350 nm (Figure 7). This is due to the ground-state charge-transfer interaction between a naphthyl group and the bipyridinium moiety of viologens.[20−22] The shape of the spectra was virtually identical for both viologens, but the dependence of the absorbance on the concentration of the viologen was quite different (see inset of Figure 7). The fitting

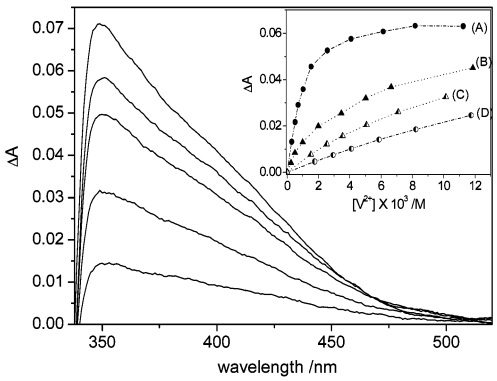


Figure 7. Absorption spectra of 0.50 mM **4** at various concentrations of **1** (the blank was 0.50 mM **4**). The concentrations of **1** are 0.30, 0.70, 1.54, 2.57, and 11.25 mM (from bottom to top). The inset shows the dependence of the charge-transfer band absorption of 0.5 mM **4** at 362 nm on the concentration of **1** (A, D) and **2** (B, C). The data in C and D were taken in the presence of 50 mM $AdaNH_3^+$.

of the charge-transfer absorption versus $[V^{2+}]$ relationship to the 1:1 complexation scheme was not successful, presumably because of the complication from the monomer−dimer equilibrium of **4**. To simulate the interaction between a naphthyl group of the monomeric **4** and viologens, we induced the monomer by the addition of 1-adamantanammonium ($AdaNH_3^+$) to the solution of **4** and titrated the solution with viologens (see inset of Figure 7).[26] The titration data fitted well to a Benesi−Hildebrand equation (eq 8) and the K_{CT} values were found to be 26 (±1) M^{-1} for **1** and 77 (±2) M^{-1} for **2**. We also determined the charge-transfer complexation constant of **1** with MNSS as 48 (±2) M^{-1}:

$$\Delta A_{CT}/[V^{2+}] = K_{CT}\Delta\epsilon_{CT}[\beta\text{-CD-NS}] - K_{CT}\Delta A_{CT} \quad (8)$$

In contrast to the gradual increase of the charge-transfer absorption in the titration of **4** with **1** or **2** in the presence of $AdaNH_3^+$ (curves C and D in Figure 7), the titration in the absence of $AdaNH_3^+$ showed a sharp rise of absorption reflecting binding of the viologens with CD cavity of **4**. However, the trends of the two viologens are quite different. In the titration with **2** (curve B), the initial absorption rise is small, and the absorption increases gradually as the concentration of **2** becomes higher and the titration curve is nearly parallel to that taken in the presence of $AdaNH_3^+$ (curve C). We explain this in terms of the formation of the type II complex between **2** and **4** giving the initial small absorption rise and the interaction of the naphthyl group expelled by **2** with another **2**, in similar fashion with that expelled by $AdaNH_3^+$. The difference of absorbance of curves B and C at high concentration of **2** is about 0.01. This can be ascribed to the long-range charge-transfer absorption between the naphthyl and bipyridinium groups separated by β-CD cavity.[22] Unlike **2**, the titration with **1** shows a large increase in charge-transfer absorption, and the absorption becomes almost leveled off at $[\mathbf{1}] > 4 \times 10^{-3}$ M (curve A). This can be taken as an evidence that the **1**/**4** exists predominantly as the type I complex in which the naphthyl and bipyridinium groups can interact directly.

Structures of the Complexes between 4 and viologens and the Face Selectivity of Binding. The studies on the charge-transfer interaction in the preceding section indicate clearly that the bipyridinium moiety of **2** in its complex with **4** is on the secondary face of β-CD (type II complex), whereas that of **1** is mainly on the primary face (type I complex). These are in good agreement with the results of fluorescence study.

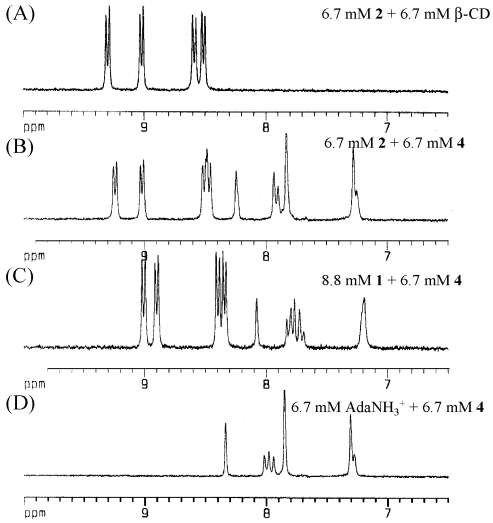


Figure 8. ^{1}H NMR spectra of the aromatic region: (A), 6.7 mM **2** + 6.7 mM β-CD; (B), 6.7 mM **2** + 6.7 mM **4**; (C), 8.8 mM **1** + 6.7 mM **4**; (D), 6.7 mM $AdaNH_3^+$ + 6.7 mM **4**.

To confirm the different complexation behaviors of **1** and **2** with **4**, we took NMR spectra of the complexes and compared them with that of the $AdaNH_3^+$/**4** complex (Figure 8). The chemical shifts of the bipyridinium protons of **2** are little affected by the binding with **4**. Also the chemical shifts of naphthyl protons of **4** are similar in **2**/**4** and $AdaNH_3^+$/**4** complexes. In contrast to this, the chemical shifts of the protons of both groups move to upfield upon complexation between **1** and **4**. Such upfield shifts were observed in aromatic donor−viologen dyad molecules and ascribed to the intramolcular charge-transfer complexation causing ring current effect.[27]

The fluorescence studies showed that the microscopic binding constants, K_I and K_{II}, between **1** and **4** are 3600 and 1100 M^{-1}, respectively. The inclusion of the hydrophobic octyl chain into the β-CD cavity of **4** and the intracomplex charge-transfer interaction between the bipyridinium and naphthyl groups contribute to the stability of the type I complex. If we assume independent contribution of the two factors to the microscopic binding constant for the formation of the type I complex, K_I can be represented as $K_I = K_{octyl,I} \cdot K_{CT}$, where $K_{octyl,I}$ is the contribution from the inclusion of the octyl group and thus the expected binding constant in the absence of the charge-transfer interaction. As the charge-transfer complexation constant of **1** with MNSS, 48 M^{-1}, is approximated for the K_{CT} value, the $K_{octyl,I}$ is calculated as 75 M^{-1}. This value is much smaller than the K_{II} value, 1100 M^{-1}. Thus, we can soundly conclude that the preference of the bipyridinium group of **1** for the primary face of **4** is mainly due to the charge-transfer interaction, and without the interaction, the group would prefer the secondary face about 14 times to the primary face.

The bipyridinium groups of the viologen guests **1** and **2** in their complexes with native β-CD can also be placed on both sides of β-CD as in the complexes with **4**. The formation of a complex between a viologen with a hydrophobic group and native β-CD is mainly driven by the inclusion of the hydrophobic group into the β-CD cavity. The difference in the binding constants of a viologen with native β-CD and **4** forming the type II complexes would reflect the contribution of the electrostatic effect to the stability of the complex with **4**. The small difference in the binding constants of **2** with β-CD and **4**, compared to the complexes of **1**, strongly suggests that the bipyridinium moiety in the **2**/β-CD complex is mainly placed on the secondary face: the electrostatic free energy in the type

II complex of **2** with **4** is estimated as -0.9 kJ mol^{-1} from the ratio of binding constants of the complexes **2**/β-CD and **2**/**4**.

The microscopic binding constant ($K_{I,CD}$) of **1** with native β-CD from the primary side would be the same as $K_{octyl,I}$, 75 M^{-1}, the binding constant of **1** with **4** forming the type I complex. Thus, the microscopic binding constant ($K_{II,CD}$) of **1** with native β-CD from the secondary side is calculated as 810 M^{-1} from the apparent binding constant of 890 M^{-1}. The $K_{II,CD}$ value can also be estimated as 790 M^{-1} from the K_{II} value of the type II complex between **1** and **4** by correcting the electrostatic contribution. These results indicate that the binding of **1** with native β-CD from the secondary side placing the bipyridinium group on the secondary side is about 10 times more favored than the binding from the primary side. This agrees well with the tentative conclusion drawn from ICD studies. A theory of ICD predicts that the magnitude of ICD becomes smaller as the chromophore is farther apart from the rim of the cavity of the chiral macrocyclic host.[6,7] Based on this, the smaller ICD of the **1**/β-CD complex than **2**/β-CD can be taken as an evidence that the bipyridinium group in the former complex locates farther from the secondary rim than that of the latter complex. This is consistent with the difference in the intracomplex electron-transfer rate in the type II complex of the viologens with **4**.

The result obtained in this work that the bipyridinium group of **2** is exclusively placed on the secondary face in the complexes with native β-CD as well as with **4** is reminiscent of a report that the ammonium group of the β-CD complex of $AdaNH_3^+$ is on the secondary face of β-CD.[4] A plausible explanation for this is that the opening of the primary side of β-CD is not large enough to accommodate the adamantyl group inside the narrower rim of the β-CD cavity, while protruding the substituted hydrophilic groups through the rim. The origin of the face selectivity in the complexation of **1** with β-CD is not certain at this point. However, it is noted that a CNDO/2 calculation showed that the electrostatic potential outside the primary face of CDs is positive, whereas it is negative outside the secondary face.[16] The bipyridinium dication would favor the secondary face by ion−dipole interaction. This is in line with a suggestion by Davies et al.[28] that the electronic effect plays a decisive role for guest orientation in CD complexes and that the electron withdrawing group of a guest molecule locates in the primary rim of CDs.

Conclusions

From the induced circular dichroic study on the complexation of methyloctyl viologen **1** and adamantylmethyl viologen **2** with β-CD and comparison of the ICD spectra with the circular dichroic spectra of a β-CD-viologen compound **3** and fluorescence and NMR studies on the complexation of **1** and **2** with 6-O−(2-sulfonato-6-naphthyl)-β-CD **4**, we obtained the following conclusions. (1) The bipyridinium group of **1** is placed on the secondary side of the β-CD cavity 10 times more favorably than the primary side in its complex with native β-CD. (2) In the complex of **1** with **4**, the bipyridinium group is placed on the primary side 3.3 times more favorably than the secondary side because of the charge-transfer interaction between the bipyridinium and 2-sulfonatonaphthyl groups: without the interaction, the secondary side would be favored by 14 times. (4) The adamantyl group of **2** is placed on the secondary side in the complexes with native β-CD as well as **4**. (5) The magnitude of the induced circular dichroism of the viologen **1** in the complexation with native β-CD is smaller than that of the viologen **2**, and the intracomplex electron-transfer rate constant is slower in the complex of **1** with **4** than in the corresponding complex of **2**, because the bipyridinium group of **1** is farther apart from the secondary rim of β-CD cavity than that of **2**. We believe that the results of this work would be very important in interpreting various CD-mediated chemical reactions and designing CD-based supramolecules.

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Appendix

Analysis on the Binding of Viologen Guests with β-CD-NS by Fluorescence Measurements. The fluorescence quenching of β-CD-NS (**4**) fluorescence by viologens (V^{2+}) with hydrophobic groups is mainly due to the inclusion complexation, and the dynamic quenching is negligible at low concentrations of V^{2+}. The observed fluorescence intensity of a solution containing β-CD-NS and V^{2+} is the sum of the contributions from β-CD-NS monomer and dimer, and the complex β-CD-NS/V^{2+}:

$$I_{obs} = I_{mon}[\beta\text{−CD−NS}] + 2\,I_{dimer}[(\beta\text{−CD−NS})_2] + I_{complex}[\text{complex}] \quad \text{(A-1)}$$

where I's denote the fluorescence intensities per naphthyl group expected when all of the β-CD-NS molecules are present as the respective species. Using eqs 3 and 4 in the text, eq A-1 can be rewritten as eq A-2:

$$I_{obs} = I_{mon}[\beta\text{−CD−NS}] + 2K_D I_{dimer}[\beta\text{−CD−NS}]^2 + K_C I_{complex}[\beta\text{−CD−NS}][V^{2+}] \quad \text{(A-2)}$$

From the mass balance of V^{2+}, $[V^{2+}]$ is given as $[V^{2+}] = [V^{2+}]_0/(1+ K_C[\beta\text{-CD-NS}])$ and is approximated as $[V^{2+}] = [V^{2+}]_0(1 - K_C[\beta\text{-CD-NS}])$ as $K_C[\beta\text{-CD-NS}] \ll 1$. From a mass balance equation with respect to the total concentration (C_{tot}) of [β-CD-NS] and the above relationship, the concentration of monomeric β-CD-NS is expressed as eq A-3:

$$[\beta\text{-CD-NS}] = \frac{\sqrt{(1 + K_C[V^{2+}]_0)^2 + 4C_{tot}(2K_D - K_C{}^2[V^{2+}]_0)} - (1 + K_C[V^{2+}]_0)}{2(2K_D - K_C{}^2[V^{2+}]_0)} \quad \text{(A-3)}$$

Putting $[V^{2+}] = [V^{2+}]_0(1 - K_C[\beta\text{-CD-NS}])$ and then eq A-3 into eq A-2, we get an equation relating the fluorescence intensity as a function of $[V^{2+}]_0$ and C_{tot}. From the equation, the fluorescence intensity in the absence of a viologen, I_0, is expressed as eq A-4, and the ratio of fluorescence intensities in the presence and in the absence of V^{2+} is given as eq A-5:

$$I_0 = \frac{(I_{dimer} - I_{mon})(1 - \sqrt{1 + 8K_D C_{tot}}) + 4I_{dimer}K_D C_{tot}}{4K_D} \quad \text{(A-4)}$$

$$\frac{I}{I_0} = (4K_D\{[\beta\text{-CD-NS}] + 2K_D\beta[\beta\text{-CD-NS}]^2 + K_C\gamma[\beta\text{-CD-NS}][V^{2+}]_0(1 - K_C[\beta\text{-CD-NS}])\})/[(1 - \beta)(\sqrt{1 + 8K_D C_{tot}} - 1) + 4\beta K_D C_{tot}] \quad \text{(A-5)}$$

where β and γ represent I_{dimer}/I_{mon} and $I_{complex}/I_{mon}$, respectively.

Nonlinear least-squares fitting of the I/I_0 data taken at various $[V^{2+}]_0$ keeping constant C_{tot} (Figure 5) yields the parameters in eq A-3: to reduce the fitting parameters, we used K_D and β values from a previous study,[17] and K_C and γ values were determined from the fitting.

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