

# Synthesis of Diaza-18-Crown-6-Functionalized $\beta$ -Cyclodextrin Derivatives at the Secondary Side and Induced Circular Dichroism Studies of Their Complexes with (2-Naphthoxy)alkylammonium Ions

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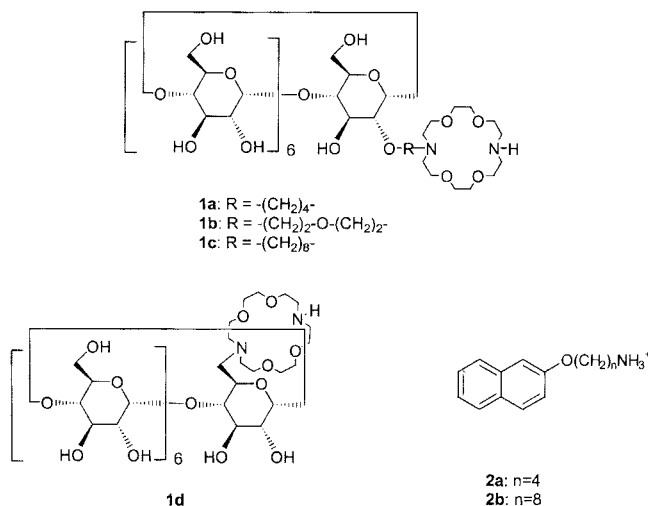
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$\beta$ -Cyclodextrin derivatives connected with diaza-18-crown-6 through flexible bridges (R) at the secondary face **1a-c** (**1a**: R =  $-(\text{CH}_2)_4-$ ; **1b**: R =  $-\text{CH}_2\text{CH}_2\text{OCH}_2\text{CH}_2-$ ; **1c**: R =  $-(\text{CH}_2)_8-$ ) have been prepared. The association constants of **1** with (2-naphthoxy)alkylammonium ions (**2a**: alkyl = butyl; **2b**: alkyl = octyl) were determined by induced circular dichroism (ICD) spectroscopy and it was found that the derivatization of  $\beta$ -CD with the diazacrown resulted in enhanced binding with **2**, compared to the native  $\beta$ -CD. ICD Characteristics of the host-guest complexes indicate that a part of the alkylammonium moiety of **2** is protruded from the secondary side of the  $\beta$ -CD cavity, and the guest molecules **2a** and **2b** move to the secondary and primary side, respectively, to make the binding of the ammonium group with the diaza-18-crown-6 moiety more feasible. The energy accompanied by the relocation of the guest molecules inside  $\beta$ -CD moiety is compensated by the interaction energy between the ammonium ion and diazacrown ether.

## Introduction

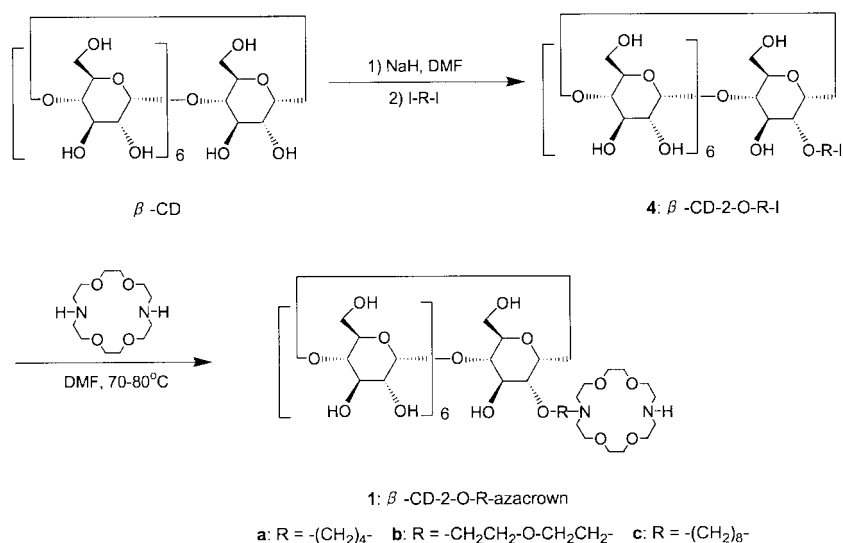
Cyclodextrins (CDs) are cyclic oligosaccharides and have hydrophobic cavities capable of forming inclusion complexes with a variety of organic molecules in aqueous solution. They have attracted widespread interest as hosts in supramolecular chemistry.<sup>1</sup> One of drawbacks in utilizing CDs in various applications is low binding constant with most guest molecules. Much efforts have been exercised to modify CDs to provide non-covalent interactions to improve the guest binding characteristics of CDs.<sup>2</sup> In contrast to CDs, crown ethers and related macrocycles bind with metal ions by coordination and ammonium ions *via* hydrogen bonding mostly in organic media.<sup>3,4</sup> To improve the molecular recognition characteristics of the macrocycles, particularly for biologically important amine compounds, a wide variety of derivatives of crown ethers have been prepared and subjected to extensive investigation.<sup>4</sup> However, characteristics of CDs and crown ethers were rarely combined to obtain a receptor with multiple recognition sites: Willner and Goren first reported the synthesis of the  $\beta$ -CD derivative modified with diaza-18-crown-6 at the primary face and showed its enhanced binding of alkali metal salts of *p*-nitrophenolates in DMF.<sup>5</sup> Recently, we found that the  $\beta$ -CD derivative functionalized with diaza-18-crown-6 at the primary face, **1d** shows 7-10 fold greater binding constants for aromatic ammonium ions in aqueous media than the unmodified  $\beta$ -CD due to the cooperative binding of the aromatic group to  $\beta$ -CD and ammonium group to crown ether moiety.<sup>6</sup> It is known that  $\beta$ -CD derivatives functionalized with the same group but at different sides could exhibit quite contrasting properties,<sup>7</sup> but the  $\beta$ -CD derivatives functionalized at the secondary side are less common than the derivatives modified at the primary face, presumably due to greater difficulty

in synthesis. Here, we report the synthesis of  $\beta$ -cyclodextrin derivatives linked with diaza-18-crown-6 at the secondary side through flexible bridges, **1a-c** and induced circular dichroism (ICD) studies of their complexes with (2-naphthoxy)alkylammonium ions **2a-b**. The dependences of the host-guest association constants and ICD pattern on the connecting linkages in the hosts and the alkyl chains in the guest molecules were investigated.



## Results and Discussions

**Syntheses of Diaza-18-Crown-6-Functionalized  $\beta$ -Cyclodextrin Derivatives at the Secondary Side and (2-Naphthoxy)alkylammonium Chloride.** The synthesis of  $\beta$ -cyclodextrin derivatives connected with diaza-18-crown-6 at the secondary face through flexible chains, **1a-c** is outlined in Scheme 1. Reaction of  $\beta$ -CD with equimolar amount of

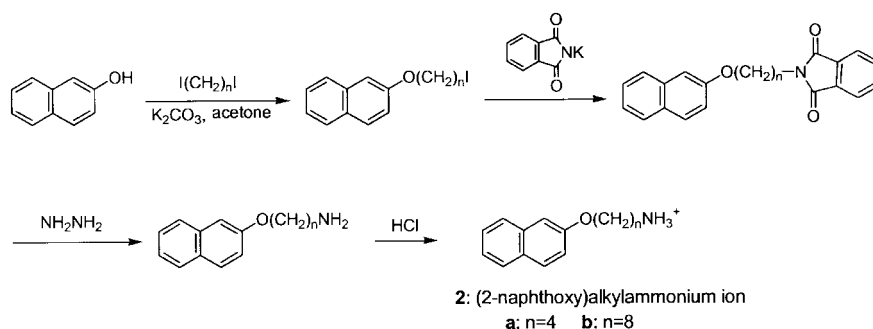


**Scheme 1.** Synthesis of Diaza-18-crown-6-functionalized  $\beta$ -Cyclodextrins at the Secondary Side.

NaH results in mono-deprotonation of the hydroxyl groups at the 2-position,<sup>8</sup> which are more acidic. The alkoxide reacts with  $\omega,\omega'$ -diiodoalkane to give mono-2-O-( $\omega$ -iodoalkyl)- $\beta$ -CD **4**. Higher hydrophobicity of the product **4**, compared to native  $\beta$ -CD, enables one to purify the product by reverse-phase column chromatography. The compound **4** was reacted with diaza-18-crown-6 in dry DMF at 70–80 °C for 3 h. Product **1** is partially purified by cation exchange chromatography after acidification. Further purification and removal of NaCl contained in the crude product by reverse-phase column chromatography provides analytically pure **1a-c**. The compounds **1a** and **1b** are fairly soluble in water, but **1c** is only sparingly soluble in water. Because of this, only **1a** and **1b** are subjected to guest binding studies in aqueous media.

$\omega$ -(2-Naphthoxy)alkylammonium chlorides are prepared by the procedure outlined in Scheme 2. 2-( $\omega$ -Iodoalkoxy)naphthalene was obtained by refluxing 2-naphthol with  $\omega,\omega'$ -diiodoalkane in the presence of  $\text{K}_2\text{CO}_3$  in acetone. The reaction product was transformed to  $\omega$ -(2-naphthoxy)alkylamine by following Gabriel amine synthesis procedure.<sup>9</sup> The amine was transformed to its salt by adding conc HCl to the solution in absolute ethanol.

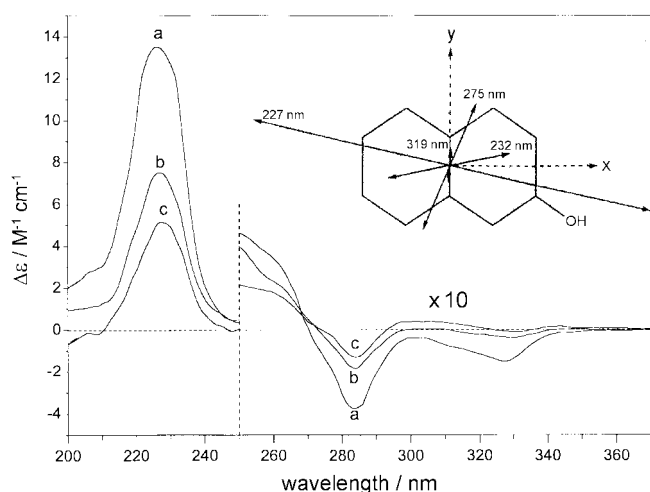
#### Induced Circular Dichroism Studies of (2-Naphthoxy)-



**Scheme 2.** Synthesis of (2-Naphthoxy)alkylammonium Ions.

**alkylammonium Ion Complexes with  $\beta$ -Cyclodextrin Derivatives.** Induced circular dichroism (ICD) spectroscopy is one of the useful methods for the observation of the complexation behavior of chromophoric guests with cyclodextrins, since cyclodextrins are inherently chiral and ICD spectral changes caused by the inclusion of guest molecules in cyclodextrins are often more sensitive than other spectra. We measured the ICD spectra of 0.20 mM solution of (2-naphthoxy)alkylammonium ions **2** in the presence of various concentrations (0–5.0 mM) of  $\beta$ -CDs. The spectra of **2a** and **2b** in the presence of 5.0 mM of  $\beta$ -CD and the spectra of **2a** in the presence of 2.0 mM of the azacrown-modified  $\beta$ -CD **1a** are shown in Figure 1 as representative examples.

ICD Spectra of the ammonium ions **2a** and **2b** exhibit similar pattern of peaks in the presence of either  $\beta$ -CD or the azacrown-modified  $\beta$ -CD derivatives studied here. The spectra comprise of three peaks: a large positive peak at 227 nm, a medium negative peak at 284 nm and a small negative peak at 331 nm. The ICD spectral pattern is similar to that of 2-naphthol,<sup>10</sup> 2-naphtholate<sup>11</sup> and 2-naphtholamine<sup>11</sup> in  $\beta$ -CD solution and the peaks are assigned as  $^1\text{L}_b$  (331 nm),  $^1\text{L}_a$  (284 nm), and  $^1\text{B}_b$  (227 nm) transitions of naphthyl group which is axially included into the cavity of  $\beta$ -CD.<sup>10</sup> The direction and the magnitude of the transition dipole of 2-

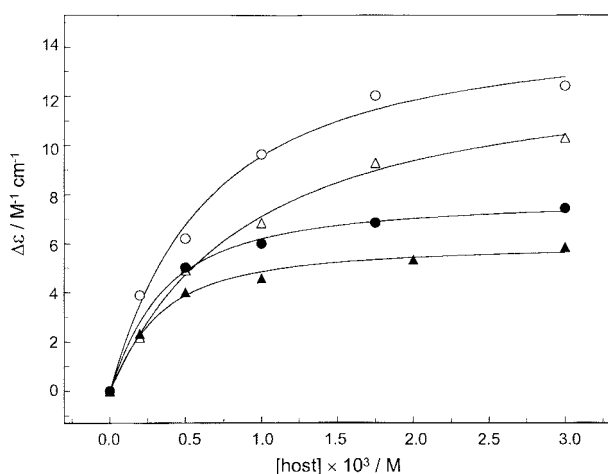


**Figure 1.** Circular dichroism spectra of 0.20 mM solution of 4-(2-naphthoxy)butylammonium ion **2a** in the presence of 5.0 mM  $\beta$ -CD (a) or 2.0 mM 2-O-{4-(azacrown)butyl}- $\beta$ -CD **1a** (b), and 8-(2-naphthoxy)octylammonium ion **2b** in the presence of 5.0 mM  $\beta$ -CD (c) at 25 °C. The spectra were taken with 0.10 cm path-length cell up to 250 nm and 1.0 cm cell above 250 nm. Inset is the direction and magnitude of the transition dipole moments of 2-naphthol (ref. 10).

naphthol are shown in Figure 1: note that  $\lambda_{\max}$  of  $^1L_a$  and  $^1L_b$  transitions of **2a** and **2b** are slightly different from those of 2-naphthol.

The magnitude of the ICD spectra<sup>12</sup> is getting greater as the concentration of the host is higher, although the absorption spectra remain unchanged, and becomes leveled off at high concentration of the host. However, for a given guest-host pair, the ratio of the peaks does not depend on the concentration of  $\beta$ -CDs. This implies that the average structure of the complex does not change in the concentration range of the hosts studied here. The dependence of  $\Delta\epsilon$  value at 227 nm on the concentration of the hosts is presented in Figure 2.

Assuming 1 : 1 host-guest stoichiometry, the complex-



**Figure 2.** Variation of ICD signals at 227 nm of 0.20 mM **2a** ( $\circ$ ,  $\triangle$ ) and **2b** ( $\bullet$ ,  $\blacktriangle$ ) on the concentration of the host. Hosts are  $\beta$ -CD ( $\circ$ ,  $\bullet$ ) or **1a** ( $\triangle$ ,  $\blacktriangle$ ). The lines are fitted to equation (2) and the obtained parameters are given in Table 1.

ation between the host (H) and the guest (G) is expressed by equation (1).



The ICD signal ( $\Delta\epsilon$ ) of a guest solution in the presence of a host is related to the initial concentrations of the guest  $[G]_0$  and the host  $[H]_0$  and the association constant  $K$  by Eq. (2),<sup>13</sup>

$$\Delta\epsilon = (\Delta\epsilon_c/[G]_0)[G]_0 + [H]_0 + 1/K - \{([G]_0 + [H]_0 + 1/K)^2 - 4[G]_0[H]_0\}^{1/2}/2 \quad (2)$$

where  $\Delta\epsilon_c$  is the ICD expected when all of the guest molecules form the complex, *i.e.* ICD of the complex. The  $K$  and  $\Delta\epsilon_c$  values were obtained from the non-linear-least-square fitting of the dependence of  $\Delta\epsilon$  on the host concentration  $[H]_0$  to Eq. (2) (Figure 2). The experimental data fit well with the equation and the obtained  $K$  and  $\Delta\epsilon_c$  values are summarized in Table 1.

Table 1 shows that the  $K$  value between **2b** and  $\beta$ -CD is about 4 times greater than that between **2a** and  $\beta$ -CD. Such dependence of  $K$  value on the length of the aliphatic linkage between the 2-naphthoxyl and the ammonium groups is reminiscent of the similar dependence observed in the binding between 2-naphthoxyalkyl-viologen compounds and  $\beta$ -CD.<sup>14</sup> This indicates that the complexation between **2a** and  $\beta$ -CD is mainly inclusion of 2-naphthoxy group into the  $\beta$ -CD cavity, while the aliphatic linkage is the primary portion contributing to the binding of **2b** with  $\beta$ -CD.<sup>14</sup> As the electrostatic potential of the secondary face of  $\beta$ -CD is negative,<sup>15</sup> the cationic ammonium group of the guest molecule would favor the secondary face.

Table 1 indicates that the functionalization of  $\beta$ -CD with diaza-18-crown-6 at the secondary face enhances the binding affinity of (2-naphthoxy)alkylammonium guests. The attachment of diaza-18-crown-6 to  $\beta$ -CD by tetramethylene bridge (**1a**) results in 1.5 times enhancement of the binding for naphthoxyalkylammonium ions **2a** and **2b**, compared to native  $\beta$ -CD. Diaza-18-crown-6-attached  $\beta$ -CD at the secondary face through ethoxyethyl group, **1b** shows *ca.* 1.3 times stronger binding for naphthoxybutylammonium ion **2a**, but no significantly enhanced binding for naphthoxyoctylammonium ion **2b**. This result clearly indicates that, with a possible exception of **1b/2b** system, the azacrown-appended  $\beta$ -CD derivatives behave as hosts with two recog-

**Table 1.** The Association Constants ( $K$ ) and Induced Circular Dichroism of the Complexes between (2-Naphthoxy)alkylammonium Ions and  $\beta$ -CD or its Diaza-18-crown-6 Derivatives at the Secondary Face in  $H_2O$  at 25 °C

Guest	Host	$K/M^{-1}$	$\Delta\epsilon_c/M^{-1}cm^{-1}$ at 227 nm	$-\Delta\epsilon_{331} : -\Delta\epsilon_{284} : \Delta\epsilon_{227}$
<b>2a</b>	$\beta$ -CD	$950 \pm 70$	$15.3 \pm 0.4$	1.0 : 2.7 : 88
	<b>1a</b>	$1430 \pm 120$	$13.3 \pm 0.6$	1.0 : 2.4 : 78
	<b>1b</b>	$1260 \pm 150$	$13.9 \pm 0.5$	1.0 : 2.4 : 68
<b>2b</b>	$\beta$ -CD	$3970 \pm 310$	$7.9 \pm 0.2$	1.0 : 5.1 : 190
	<b>1a</b>	$5980 \pm 710$	$6.1 \pm 0.2$	1.0 : 10 : 350
	<b>1b</b>	$3970 \pm 520$	$7.6 \pm 0.8$	1.0 : 7.2 : 220

nition sites for (2-naphthoxy)alkylammonium compounds in aqueous media.

According to a theoretical work by Harata and Uedaira,<sup>11</sup> the rotational strength of  ${}^1B_b$  transition of naphthyl group, which appears near 227 nm, is maximum when the naphthyl group is at the center of the  $\beta$ -CD cavity and becomes less as the chromophore moves to the outside. Much smaller  $\Delta\epsilon$  for the complexes of **2b** than that for **2a** complexes indicates that the naphthalene moiety of **2b** locates near a rim of  $\beta$ -CD. The theory also suggests that, in contrast to the  ${}^1B_b$  transition, the rotational strength of the  ${}^1L_b$  transition near 330 nm becomes less negative when the chromophore moves to the narrow primary side, but becomes more negative when it moves to the wide secondary face. The smaller ratio of  $\Delta\epsilon_{227}/\Delta\epsilon_{331}$  of **2a** complexes than that of **2b** complexes indicates that the naphthalene moiety in **2b** complexes resides near the primary face of  $\beta$ -CD. This agrees with our aforementioned expectation from the larger  $K$  values for **2b** and the preference of the ammonium group for the secondary side of  $\beta$ -CD.

The magnitude of the ICD signal at 227 nm, as well as the ratio of  $\Delta\epsilon_{227}/\Delta\epsilon_{331}$ , of **2a** and **2b** complexes with the modified  $\beta$ -CDs is significantly different from that of  $\beta$ -CD and depends on the linkage between  $\beta$ -CD and diaza-18-crown-6. This implies that the position of the naphthyl chromophore with respect to  $\beta$ -CD cavity varies upon binding of the ammonium group with the appended diaza-18-crown-6 moiety of the  $\beta$ -CD derivative. The increasing order of the ratio  $\Delta\epsilon_{227}/\Delta\epsilon_{331}$  for **2a** is **1b** < **1a** <  $\beta$ -CD. This suggests that the naphthyl group move to the secondary face of  $\beta$ -CD to facilitate the binding between the ammonium group of naphthoxybutylammonium ion and the appended diaza-18-crown-6-moiety of the  $\beta$ -CD derivative. The extent of the movement is more significant for the complex with **1b** than for the complex with **1a**, presumably due to the longer linkage between the azacrown moiety and the  $\beta$ -CD cavity of **1b**. A different trend for the order of the ratio  $\Delta\epsilon_{227}/\Delta\epsilon_{331}$ ,  $\beta$ -CD < **1b** < **1a**, is observed for the complexes of **2b**, indicating that the naphthyl group of **2b** moves further to the primary face of  $\beta$ -CD to make the binding between the ammonium group and azacrown moiety more feasible. This implies that, though a part of the octamethylene linkage of **2b** is inside the  $\beta$ -CD cavity, the protruded part of the linkage is too long for the ammonium group to bind with the azacrown moiety. Obviously, the mismatch between the protruded octyl ammonium group of **2b** and the  $\beta$ -CD-pendent diazacrown is greater for **1a** than **1b**. Contrary to this, the

protruded part of the butylammonium moiety of **2a** in its complex with  $\beta$ -CD is not long enough for the ammonium group to bind with the azacrown ether moiety. Based on the  $K$  values and the ICD characteristics of the complexes, the structures for the  $\beta$ -CD complexes of **2a** and **2b** are represented in Scheme 3.

The relocation of naphthyl group inside the  $\beta$ -CD cavity would be energetically disfavored, but it could be compensated by the energetically favored interaction between the ammonium group and diaza-18-crown-6 moiety. The energetic disfavor for the relocation of naphthyl group would be a reason why the binding constants of the naphthoxyalkylammonium ion with the diazacrown-modified  $\beta$ -CDs are less than twice of that with  $\beta$ -CD, though both  $\beta$ -CD and diazacrown moieties bind cooperatively the guest molecules.

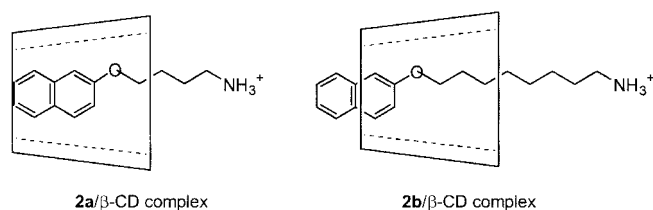
In conclusion, we synthesized  $\beta$ -cyclodextrin derivatives connected with diaza-18-crown-6 through flexible bridges at the secondary face **1a-c** and have demonstrated that the derivatization results in enhanced binding with (2-naphthoxy)alkylammonium ions (**2a**: alkyl = butyl; **2b**: alkyl = octyl), compared to the native  $\beta$ -CD. Induced circular dichroism characteristics of the host-guest complexes were measured. A part of the alkylammonium moiety of **2** is protruded from the secondary side of the  $\beta$ -CD cavity. To make the binding of the ammonium group with the diaza-18-crown-6 moiety feasible, **2a** and **2b** move to the secondary and primary side, respectively. The energy accompanied by the relocation of the guest molecules inside  $\beta$ -CD moiety is compensated by the interaction energy between the ammonium ion and diazacrown ether.

## Experimental Section

${}^1H$  NMR spectra were recorded on a Varian Unity INOVA 400 spectrometer at the Center for Research Facilities at Chungnam National University. Mass spectra were taken at Korea Basic Science Center. Circular dichroism spectra were taken with a JASCO J-810 spectropolarimeter.

**Mono-2-O-( $\omega$ -iodoalkyl)- $\beta$ -CD 4a-c.** This was prepared by modifying the reported procedure.<sup>8</sup> Dried  $\beta$ -CD (7.0 g, 6.2 mmol) was dissolved in 70 mL of dry DMF, to which equimolar amount of NaH was added and the mixture was stirred overnight until the solution became clear. To this solution was added equimolar amount of  $\omega,\omega'$ -diiodoalkane or 1-iodo-2-(2-iodoethoxy)ethane<sup>16</sup> and stirred at rt for 6-30 h (8 h for **4a**, 30 h for **4b**, and 6 h for **4c**). The precipitates obtained by addition of acetone (500 mL) to ca. 10 mL of the concentrated reaction mixture were purified by reverse-phase column chromatography (Licroprep Rp-18, Merck) eluting with water/acetonitrile gradient (for **4b** and **4c**) or water/methanol gradient (for **4a**). The title compounds were obtained in the yields of 10-15%.

**Mono-2-O-( $\omega$ -azacrown-alkyl)- $\beta$ -CD 1a-c.** 1.5 Molar excess of 4,13-diaza-18-crown-6 (1,4,10,13-tetraoxa-7,16-diazacyclooctadecane, 197 mg, Aldrich) in 1 mL of dry DMF was added to a solution of mono-2-O-( $\omega$ -iodoalkyl)- $\beta$ -CD **4** (0.50 mmol) in 4 mL of dry DMF and the reaction



**Scheme 3.** Schematic Representation of the Structures of **2a**/ $\beta$ -CD and **2b**/ $\beta$ -CD Complexes.

mixture was heated at 70-80 °C for 3 h. The precipitates obtained by the addition of acetone to the concentrated reaction mixture (ca. 1-2 mL) was dissolved in water, acidified to pH 3 with 0.5 M HCl, and then purified by cation exchange chromatography (Sephadex-CM C-25, Aldrich) using 0-0.5 M NaCl gradient as eluent. The fractions containing the product was concentrated under reduced pressure and basified to pH 9 with 0.5 M NaOH. Further purification and removal of NaCl contained in the crude product by reverse-phase column chromatography (eluent: water/methanol gradient) provided analytically pure **1a-c** with the yields of ca. 40%.

**1a:** mp. 240 °C (dec);  $^1\text{H-NMR}$  ( $\text{D}_2\text{O}$ )  $\delta$  1.62 (broad s, 4H,  $\beta$ -CD-OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>N-), 2.65 (broad s, 2H,  $\beta$ -CD-OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>N-), 2.85 (broad s, 8H, two -CH<sub>2</sub>NCH<sub>2</sub>- of diazacrown ether moiety), 3.50-4.10 (m, 60H,  $\beta$ -CD moiety + nine -OCH<sub>2</sub>-), 5.09 (broad s, 6H, anomeric H of  $\beta$ -CD moiety), 5.21 (broad s, 1H, anomeric H1A of  $\beta$ -CD moiety);  $^{13}\text{C-NMR}$  ( $\text{D}_2\text{O}$ )  $\delta$  20.10, 25.49, 46.15, 51.25, 52.05, 58.8, 66.80, 67.84, 68.12, 68.22, 70.17, 70.38, 70.54, 70.62, 70.94, 71.35, 71.69, 78.56, 79.75, 80.33, 99.05, 100.47; mass (positive ion FAB) 1451.6 (calculated for  $\text{C}_{58}\text{H}_{102}\text{O}_{39}\text{N}_2+\text{H}^+$ : 1451.6).

**1b:** mp 255 °C (dec);  $^1\text{H-NMR}$  ( $\text{D}_2\text{O}$ )  $\delta$  2.82-2.96 (m, 10H, five -NCH<sub>2</sub>-), 3.53-4.10 (m, 64H,  $\beta$ -CD moiety + eleven -OCH<sub>2</sub>-), 5.06-5.10 (m, 6H, anomeric H of  $\beta$ -CD moiety), 5.21 (d,  $J = 4$ , 1H, anomeric H1A of  $\beta$ -CD moiety);  $^{13}\text{C-NMR}$  ( $\text{D}_2\text{O}$ )  $\delta$  49.94, 50.14, 54.45, 56.36, 62.91, 63.07, 67.94, 68.30, 68.41, 72.30, 72.44, 72.50, 72.69, 73.58, 74.25, 74.38, 74.59, 74.74, 74.79, 75.69, 75.99, 83.08, 84.06, 84.55, 103.16, 104.67; mass (positive ion FAB) 1467.6 (calculated for  $\text{C}_{58}\text{H}_{102}\text{O}_{40}\text{N}_2+\text{H}^+$ : 1467.6).

**1c:** mp 245 °C (dec);  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$  1.23 (broad s, 8H,  $\beta$ -CD-OCH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>4</sub>CH<sub>2</sub>CH<sub>2</sub>N-), 1.33 (broad s, 2H,  $\beta$ -CD-OCH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>4</sub>CH<sub>2</sub>CH<sub>2</sub>N-), 1.48 (broad s, 2H,  $\beta$ -CD-OCH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>4</sub>CH<sub>2</sub>CH<sub>2</sub>N-), 2.38 (t,  $J = 7$  Hz, 2H,  $\beta$ -CD-CH<sub>2</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>4</sub>CH<sub>2</sub>CH<sub>2</sub>N-), 2.61 (broad s, 8H, two -CH<sub>2</sub>NCH<sub>2</sub>- of diazacrown ether moiety), 3.18-3.76 (m,  $\beta$ -CD moiety + nine -OCH<sub>2</sub>, overlapped with H<sub>2</sub>O peak), 4.81 (broad s, 6H, anomeric H of  $\beta$ -CD moiety), 4.93 (d, broad s, 1H, anomeric H1A of  $\beta$ -CD moiety);  $^{13}\text{C-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$  25.38, 27.00, 29.09, 29.17, 29.49, 48.90, 49.15, 53.66, 55.00, 60.05, 69.64, 69.82, 70.00, 70.29, 71.99, 72.28, 72.53, 73.18, 80.79, 81.76, 82.52, 100.63, 102.18; mass (positive ion FAB) 1507.7 (calculated for  $\text{C}_{62}\text{H}_{110}\text{O}_{39}\text{N}_2+\text{H}^+$ : 1507.7).

**$\omega$ -(2-Naphthoxy)alkylammonium Chloride 2a-b.** 2-( $\omega$ -Iodoalkoxy)naphthalene was obtained in ca. 70% yield by refluxing the equimolar mixture of 2-naphthol,  $\omega$ , $\omega'$ -diiodoalkane and K<sub>2</sub>CO<sub>3</sub> in acetone for 10 h. 2-( $\omega$ -Iodoalkoxy)naphthalene was then reacted with potassium phthalimide in DMF at 90 °C for 3 h to give 2-[ $\omega$ -(2-naphthoxy)alkyl]-isoindole-1,3-dione in ca. 80% yield. Two molar excess of hydrazine hydrate was added to the solution of 2-[ $\omega$ -(2-naphthoxy)alkyl]-isoindole-1,3-dione in methanol or ethanol. The reaction mixture was heated at reflux for 2 h, acidified to pH 1 with 1 M HCl, refluxed for 1.5 h, adjusted to pH 11 with 1 M NaOH, and then extracted with chloroform.

The amine obtained by concentration of the organic layers was dissolved in absolute ethanol and transformed to HCl salt **2** by adding conc HCl. The yields of the amine salt **2** from 2-[ $\omega$ -(2-naphthoxy)alkyl]-isoindole-1,3-dione were ca. 75%.

**2a:** mp 223 °C;  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$  1.72-1.88 (m, 4H, -OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NH<sub>3</sub><sup>+</sup>), 2.84-2.92 (m, 2H, -OCH<sub>2</sub>CH<sub>2</sub>-CH<sub>2</sub>CH<sub>2</sub>NH<sub>3</sub><sup>+</sup>), 4.08 (t,  $J = 6$  Hz, 2H, -OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-NH<sub>3</sub><sup>+</sup>), 7.13 (dd,  $J = 9$  & 2 Hz, 1H), 7.28-7.35 (m, 2H), 7.41-7.47 (m, 1H), 7.76-7.83 (m, 3H), 8.04 (broad s, 3H, NH<sub>3</sub><sup>+</sup>).

**2b:** mp 169 °C;  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$  1.30-1.40 (m, 6H, -O(CH<sub>2</sub>)<sub>3</sub>(CH<sub>2</sub>)<sub>3</sub>-), 1.45 (quintet,  $J = 7$  Hz, 2H, -OCH<sub>2</sub>CH<sub>2</sub>-CH<sub>2</sub>-), 1.56 (quintet,  $J = 7$  Hz, 2H, -CH<sub>2</sub>CH<sub>2</sub>NH<sub>3</sub><sup>+</sup>), 1.77 (quintet,  $J = 7$  Hz, 2H, -OCH<sub>2</sub>CH<sub>2</sub>-), 2.70-2.80 (m, 2H, -CH<sub>2</sub>NH<sub>3</sub><sup>+</sup>), 4.07 (t,  $J = 6$  Hz, 2H, -OCH<sub>2</sub>-), 7.14 (dd,  $J = 9$  & 2 Hz, 1H), 7.28-7.35 (m, 2H), 7.42-7.46 (m, 1H), 7.77-7.83 (m, 3H), 8.00 (broad s, 3H, NH<sub>3</sub><sup>+</sup>).

**Circular Dichroism Spectroscopy.** Induced circular dichroism measurements were performed at 25.0  $\pm$  0.2 °C on a JASCO J-810 spectropolarimeter equipped with a temperature controller. The concentration of (2-naphthoxy)alkylammonium chloride was  $2.0 \times 10^{-4}$  M and conventional quartz cells of light path-lengths of 1.0 cm and 0.10 cm were used for 250-370 nm and 200-250 nm wavelength regions, respectively. The solution of (2-naphthoxy)alkylammonium ion without  $\beta$ -CD or its derivative was used for baseline measurement.

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## References and Notes

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12. Circular dichroic signal is usually measured as ellipticity  $\theta$  in degree unit. The dichroism ( $\Delta\epsilon = \epsilon_L - \epsilon_R$ ) is related by  $\Delta\epsilon = 4\pi\theta/180 \times 2.303 c l$ , where  $c$  is the concentration (mol/L) and  $l$  is the light path-length (cm).
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  16. 1-Iodo-2-(2-iodoethoxy)ethane was prepared in 84% yield by reacting diethylene glycol ditosylate with 10-fold excess of sodium diiodide in refluxing acetone for 2 h. The product was purified by silica gel column chromatography using hexane as eluent.
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