Formation of Inclusion Complexes of Monodisperse Oligo(ethylene glycol)s with α-Cyclodextrin

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ABSTRACT: Monodisperse oligo(ethylene glycol)s (OEG) have been prepared by stepwise synthesis coupled with preparative size-exclusion chromatography (SEC). Complex formation between α-cyclodextrin (α-CD) and the oligo(ethylene glycol)s was studied. α-CD was found to form complexes with tetrakis(ethylene glycol) (TEG) and larger oligo(ethylene glycol)s. The yields of the complexes increase with an increase in the degree of polymerization. Eicosakis(ethylene glycol) and larger oligo(ethylene glycol)s formed complexes with α-CD almost quantitatively. The ^{1}H NMR spectra of the complexes show that the stoichiometry of the complexes is 2:1 (two ethylene glycol units and one α-CD) when the degree of polymerization is higher than 6. The stoichiometry of the complexes of α-CD with tetrakis(ethylene glycol) and pentakis(ethylene glycol) (PEG) is 2:1 (CD:OEG). The X-ray powder patterns of the α-CD–OEG complex show that α-CDs form channels. The ^{13}C CP/MAS NMR spectra of the complexes suggest that an OEG chain is included in the channel formed by α-CDs. β-CD did not form complexes with any OEG. Cyclic oligomers of ethylene glycol (crown ethers, 15-crown-5, and 18-crown-6) did not form complexes with α-CD, except for 12-crown-4 which gave complexes with α-CD in low yield. The modes of the complexes are discussed.

Introduction

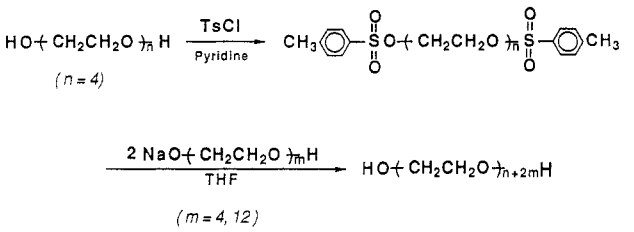
Cyclodextrins (CDs) are cyclic molecules consisting of six to eight glucose units linked by α-1,4-glycosidic linkages. They are called α-, β-, and γ-cyclodextrins with six, seven, and eight glucose units, respectively, and are known to form inclusion complexes with various low molecular weight compounds.[1] Since the discovery of cyclodextrins, there have been many reports on complex formation of cyclodextrins with small molecules and ions.[2] The X-ray diffraction studies of the complexes show that guest molecules are included in the cavities of cyclodextrins.[3]

Recently, we found that α-CD formed complexes with poly(oxyethylene) (POE) of various molecular weights to give stoichiometric compounds in high yields in the crystalline state.[4] β-CD did not form complexes with POE. However, β-CD formed complexes with poly(propylene glycol) (PPG),[5] although α-CD did not form complexes with PPG. Previously, we used commercially available poly(oxyethylene)s which are polydisperse. Therefore, the complexes obtained were polydisperse and heterogeneous. We also found that α-CD did not form complexes with low molecular weight analogues, such as ethylene glycol and bis(ethylene glycol). In order to make clear the chain-length selectivity and obtain pure monodisperse complexes, we prepared monodisperse oligo(ethylene glycol)s and studied the interactions between α-CD and the pure oligo(ethylene glycol)s. We also studied the complex formation between α-CD and cyclic oligomers of ethylene glycol (crown ethers) to test the shape selectivity and the effects of the end groups on the complex formation.

This paper describes the preparation and properties of the inclusion complexes of monodisperse oligo(ethylene glycol)s with α-CD in detail, and the modes of the complexation are discussed.

Previously, we[6a] and Wenz et al.[6b] prepared polyrotaxanes in which many α-CDs are threaded on a polymer chain. Rotaxanes containing a single cyclodextrin have also been reported.[7] Bodanov et al. reported on the inclusion complexes between poly(oxyethylene) and urea.[8] Shen and Gibson reported on the preparation of polyrotaxanes consisting of crown ethers and polymers.[9] After submission of this paper, molecular nanotube aggregates of cyclodextrins by diphenylhexatrienes have been reported.[10]

Scheme 1



Results and Discussion

Synthesis of Monodisperse Oligo(ethylene glycol)s. Oligo(ethylene glycol)s HO(-$CH_2CH_2O)_n$-) OH (n = 8, 12, 18, 20, 28, 36, 44) were prepared by stepwise reactions starting from α,ω-tetrakis(ethylene glycol) ditosylate and the monosodium tosylate using Bomer's method[11] as shown in Scheme 1. The products were purified by preparative size-exclusion chromatography (SEC) repeatedly. Bomer et al. reported that it took 50 days to obtain nonakis(ethylene glycol) from tris(ethylene glycol). Marshall et al. used tetrahydrofuran (THF) as the solvent instead of glycol and reported that the nonakis(ethylene glycol) was obtained in 30% yield in 4–5 days.[12a] Teo et al. reported that the pentadecakis(ethylene glycol) was obtained in 84% yield in 2 weeks using THF as the solvent.[12b] We obtained dodecakis(ethylene glycol) from tetrakis(ethylene glycol) using THF in 82% in 3 days by raising the reaction temperature to 45 °C.

Figure 1 shows the GPC charts of the monodisperse OEGs separated from the reaction mixtures. OEGs with the degree of polymerization of 8, 12, 18, 20, and 28 are pure, and those of 36 and 44 are almost pure samples.

Complex Formation between Monodisperse OEG and α-CD. Previously, we found that α-cyclodextrin forms complexes with poly(oxyethylene) to give crystalline compounds in high yields, although α-CD did not form complexes with the low molecular weight analogs, such as ethylene glycol and bis(ethylene glycol). In order to make

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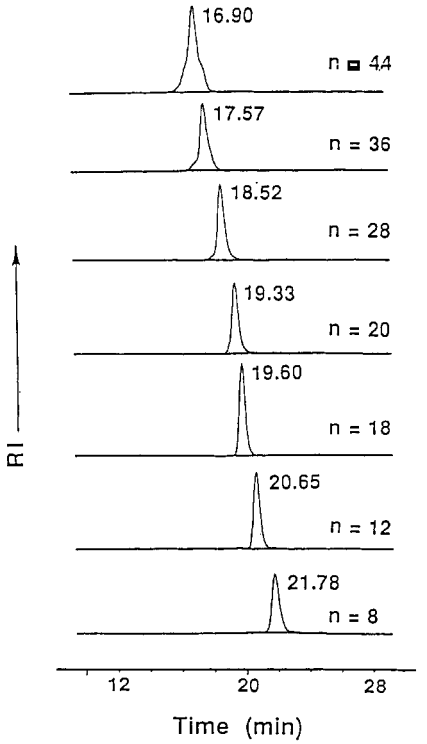

Figure 1. GPC charts of the monodisperse OEG separated from the reaction mixtures of stepwise synthesis followed by the preparative GPC. *n* is the degree of polymerization.

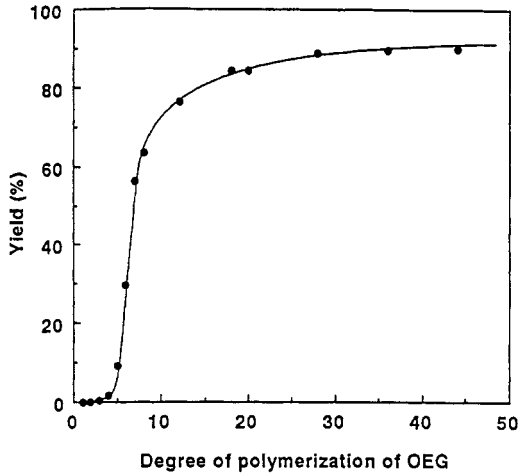

Figure 2. Yields of the complexes of α-CD with OEG as a function of the degree of polymerization of OEG.

clear a minimum PEG length required for the formation of stable cyclodextrin complexes and the effects of chain length on the formation of the complexes, we have studied interactions between α-CD and the monodisperse OEGs.

We found that α-CD forms complexes with OEG in a crystalline state when the degree of polymerization is higher than 3. When saturated aqueous solutions of α-CD were added to OEG or aqueous solutions of OEG at room temperature, the solution became turbid and complexes were formed as crystalline precipitates. The complexes were isolated by filtration or centrifugation, washed with water, and dried. Figure 2 shows the yields of the complexes of α-CD with OEG as a function of the degree of polymerization of OEG. The yields are calculated on the bases of 2:1 (ethylene glycol unit:α-CD) stoichiometry which will be discussed in the next section when the degree of polymerization is over 6. α-CD did not form complexes with ethylene glycol,[13] bis(ethylene glycol), and tris(ethylene glycol). α-CD formed complexes with TEG and larger OEG. The yields increase sharply with an increase

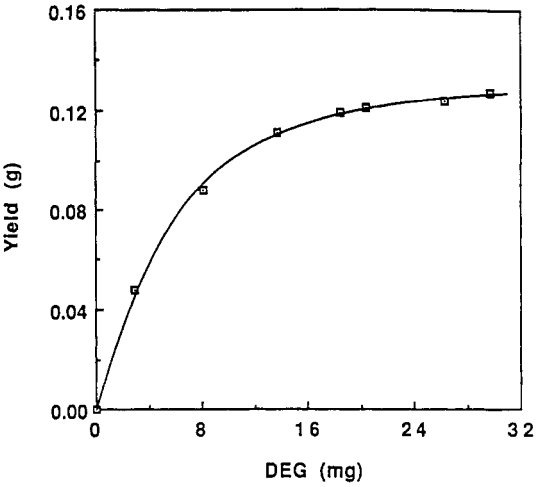

Figure 3. Yields of α-CD–OEG complexes as a function of added DEG.

in the degree of polymerization from 5 to 12. The complexes were obtained almost quantitatively with eicosakis(ethylene glycol) and larger OEG. β-CD did not form complexes with any OEG.

Stoichiometries of the Complexes. The complex formation of α-CD with dodecakis(ethylene glycol) (DEG) was studied quantitatively. Figure 3 shows the plots of the amount of the complexes obtained as a function of DEG added. The amounts of the complex formed increased with an increase in DEG added to the aqueous solution of α-CD and approach to saturation. These results indicate that the complex formation is stoichiometric. The saturation values show that more than 80% of the α-CD was consumed by complex formation with DEG. The initial slope and the amount of OEG at the saturation suggest that two ethylene glycol units $(CH_2CH_2O)_2$ were bound in each α-CD cavity. The continuous-variation plots for the complex formation of α-CD with DEG show that the maximum was reached at the molar ratio of 0.33 (α-CD fraction), which suggests that α-CD forms a complex with a 2:1 ratio. The stoichiometries were confirmed by the ^1H NMR spectrum. Figure 4 shows the ^1H NMR spectrum of the complex of DEG with α-CD. It should be noted that the stoichiometries of the complexes are 2:1 even if α-CD and DEG are treated each other in any ratio. The length of two ethylene glycol units corresponds to the depth of the cavity of α-CD. Figure 5 shows the ^1H NMR spectrum of the complexes of α-CD with TEG and PEG. The stoichiometries of the complexes of α-CD with TEG and PEG are both 2:1 (CD:OEG).

Properties of the Complexes. The complexes of α-CD with OEG of degree of polymerization lower than 8 are soluble in water. The complexes of α-CD with OEG of degree of polymerization higher than 12 can be dissolved in water by heating. The solubilities of the complexes of OEG with CD in water are less than those of the complexes of CD with PEG (polydisperse) of corresponding average molecular weight, indicating that crystallinity of the complexes of CD with pure OEG is higher than that of the complexes of CD with polydisperse PEG. The addition of an excess amount of propanol to the suspension of the complex resulted in solubilization of the complex. OEG might be replaced by the low molecular weight guest. The formation of the complex is reversible, and complexes are in equilibrium between the complex and its component. The addition of urea results in solubilization of the complexes. The results indicate that hydrogen bonding plays an important role in forming the complexes between OEG and α-CD. Preliminary results on the microcalo-

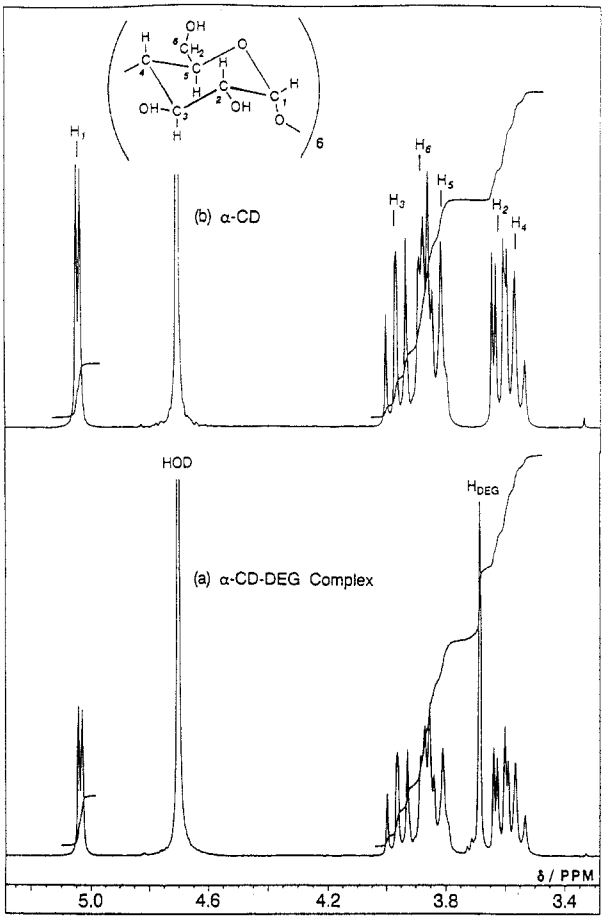

Figure 4. 270-MHz ^{1}H NMR spectra of the complex of DEG with α-CD (a) and α-CD (b) in D_2O.

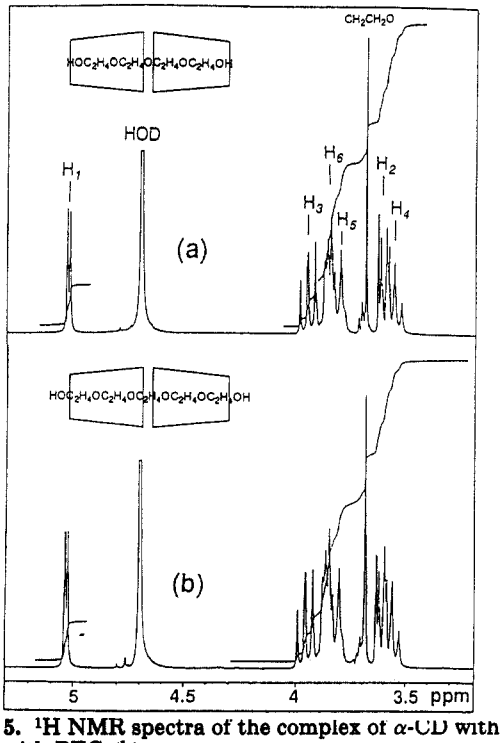

Figure 5. ^{1}H NMR spectra of the complex of α-CD with PEG (a) and with PEG (b).

rimetry for complex formation between three α-CDs and hexakis(ethylene glycol) show that the complexation process is highly exothermic, −117.4 kJ/mol, indicating strong hydrogen-bond formation between neighboring α-CDs in the complex.

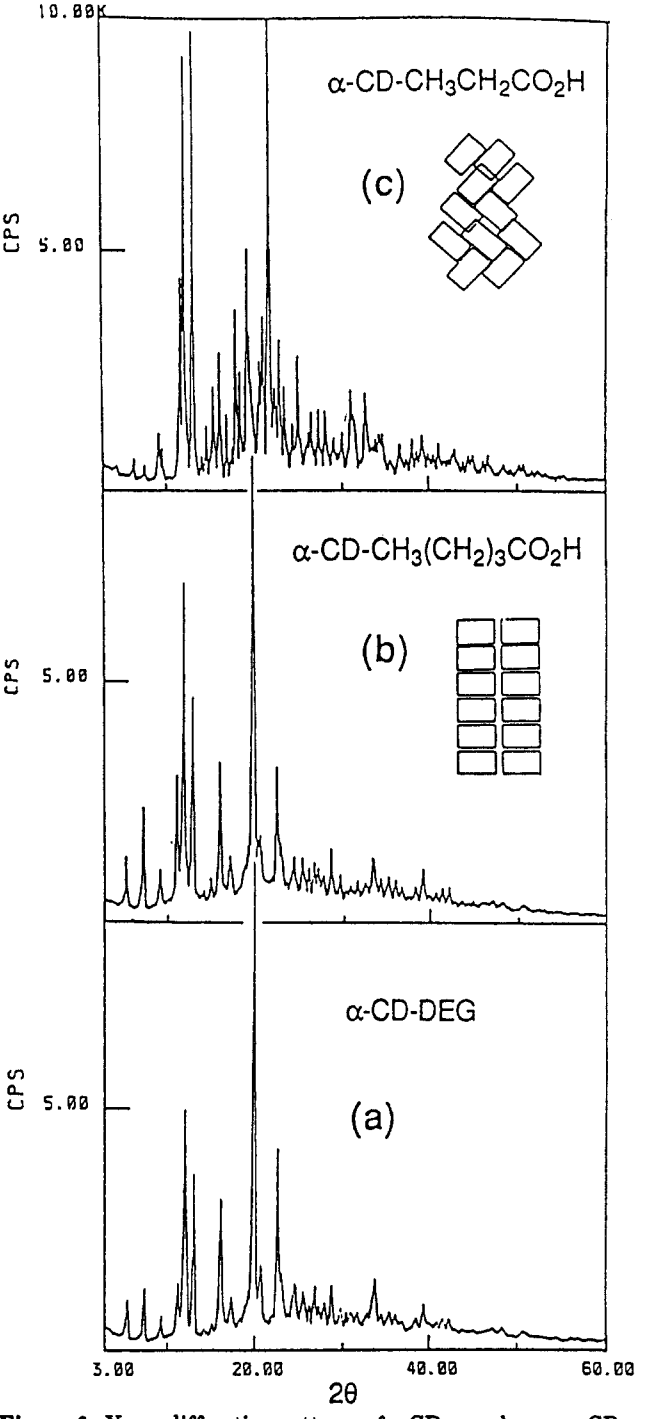

Figure 6. X-ray diffraction patterns of α-CD complexes. α-CD–DEG (a), α-CD–valeric acid (b), and α-CD–propionic acid (c).

The inclusion complexes are thermally stable. The decomposition points of the complexes are a little higher than that of each component. The complexes of α-CD with DEG decompose above 300 °C, although α-CD melts and decomposes below 300 °C. DEG stabilized α-CD.

Binding Mode of the Complex. Figure 6 shows the X-ray powder patterns of the complex of α-CD with DEG and with other low molecular weight compounds. The X-ray powder pattern of α-CD–DEG complex shows that the complex is crystalline. There are no amorphous patterns, which could be observed in the freeze-dried sample of α-CD and the complexes of α-CD with high molecular weight poly(ethylene glycol). The patterns are similar to those of the complex of α-CD with valeric acid or octanol, which have been reported to have extended column structure,[14] and different from those of α-CD and

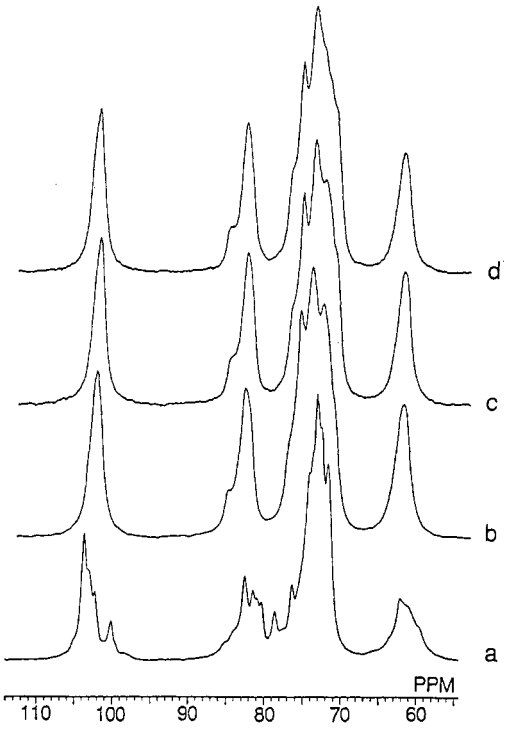

Figure 7. ^{13}C CP/MAS NMR spectra of α-CD, (a) that of the α-CD–HEG (OEG(6)) complex (b), that of α-CD–DEG (OEG-(12)) (c), and that of the α-CD–OEG(20) complex (d).

the complexes with small molecules, such as acetic acid and propanol, which have a cage structure. These results indicate that the complexes of α-CD and OEG have channel type structure and not "cage" type structure.

Molecular model studies show that OEG chains are able to penetrate α-CD cavities, while the poly(propylene glycol) chain cannot pass through the α-CD cavity due to the steric hindrance. These views are in accordance with our results that α-CD formed complexes with OEG but not with poly(propylene glycol). β-CD did not form complexes with any OEG. An OEG chain is too thin to fit in a β-CD cavity. However, β-CD forms complexes with poly-(propylene glycol) as we reported previously in a paper.[5] Model studies also show that the single cavity of α-CD (depth 6.7 Å) accommodates two ethylene glycol units (6.6 Å) when ethylene glycol units assume planar zigzag conformation.

The complexes between α-CD and OEG have been examined in the solid state by ^{13}C-CP/MAS-NMR spectroscopy, and representative spectra are shown in Figure 7. α-CD assumes a less symmetrical conformation in the crystal when it does not include a guest in the cavity. In this case, the spectrum shows the fine splitting of the C-1 and C-4 lines from each of the six α-(1–4)-linked glucose residues. Especially C-1 and C-4 adjacent to a conformationally strained glycosidic linkage are observed at 79.5 and 100 ppm, respectively.[15] On the other hand, in the spectrum of the α-CD–OEG complex the peaks at 79.5 and 100 ppm disappeared. Each carbon of glucose can be observed in a single peak. These results indicate that α-CD adopts a symmetrical conformation and each glucose unit of CD is in a similar environment and an OEG chain is included in a tunnel. We can observe systematic changes in the peaks around 70–75 ppm in the spectra. The peak at 72 ppm became broad and the peak at 74 ppm became sharp as the chain length of OEG increased. We cannot explain this phenomenon right now.

Table 1 shows the results of complex formation between α-CD and cyclic oligomers of ethylene glycol together with those of linear OEG for comparison. It is interesting that the yields of the complexes of α-CD with cyclic OEG decreased with an increase in the size of the guest, and those of the complexes of α-CD with linear OEG increased with an increase in the chain length. Dioxane gave complexes with α-CD in a moderate yield (21%), and small crown ether, 12-crown-4, gave complexes in low yield (9%). The stoichiometries of these complexes are 2:1 (cyclic ether: α-CD). Large crown ethers, 15-crown-5 and 18-crown-6, did not form complexes with α-CD at all. These results indicate that these crown ethers are too large to fit in the α-CD cavity and α-CDs are not able to penetrate the chain due to the absence of the chain ends.

Table 1. Yields (%) for the Complex Formation of Linear and Cyclic Oligo(ethylene glycol) with α-CD[a]

	number of $-CH_2CH_2O-$							
	2	3	4	5	6	7	8	12
linear	0	0	2	9	30	56	64	76
cyclic	21		9	0	0			

[a] Complexes formed at 25 °C.

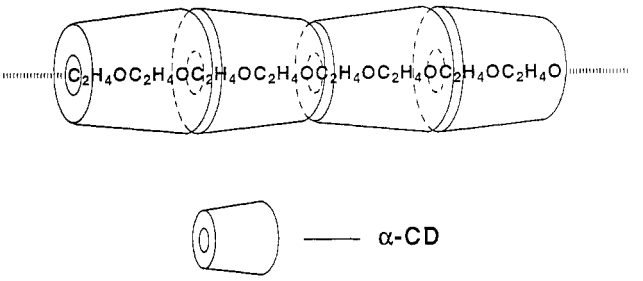

Figure 8. Proposed structure of the α-CD–OEG complex.

Figure 8 shows a proposed structure of the complex of OEG with α-CD. The inclusion complex formation of OEG in a α-CD channel is entropically unfavorable. However, formation of the complexes is thought to be promoted by hydrogen-bond formation between cyclodextrins. Therefore, head-to-head and tail-to-tail arrangement is thought to be the most probable structure.

In conclusion, α-cyclodextrin forms complexes with oligo(ethylene glycol) to give crystalline complexes, although β-CD did not form complexes with OEG.

Experimental Section

Materials. α-Cyclodextrin and β-cyclodextrin were obtained from Nakarai Tesque Inc. and used after drying under vacuum with P_2O_5. Ethylene glycol and bis(ethylene glycol) were obtained from Nakarai Tesque Inc. Tris(ethylene glycol) and tetrakis-(ethylene glycol) were purchased from Tokyo Kasei Inc. Pentakis(ethylene glycol), hexakis(ethylene glycol), and heptakis(ethylene glycol) were purchased from Aldrich Chemicals. *p*-Toluenesulfonyl chloride and sodium were obtained from Nakarai Tesque Inc. Pyridine and methanol (Nakarai Tesque Inc.) were stirred over CaH_2, heated with reflux, and then fractionally distilled under a nitrogen atmosphere and stored over a type 4A molecular sieve. Tetrahydrofuran (THF; Nakarai Tesaque Inc.) was stirred over CaH_2, refluxed, and then fractionally distilled and stored over sodium wire under a nitrogen atomsphere. D_2O and $CDCl_3$ used as solvent in the NMR measurements were obtained from Aldrich.

Preparation of Oligo(ethylene glycol). Tetrakis(ethylene glycol) Ditosylate (TEG-Ts2). Tetrakis(ethylene glycol) (13.86 g, 0.173 mol), which had been previously dried in vacuum with P_2O_5, was dissolved in dry pyridine (38 mL). *p*-Toluenesulfonyl chloride (36 g) was added to this solution, and the mixture was stirred under a nitrogen atmosphere at 0 °C for 4 h. The resultant mixture was added to ice–water (800 mL) with vigorous stirring, and the mixture was extracted with dichloromethane (4 × 200 mL). The dichloromethane solution was washed successively

with hydrochloric acid (3 N, 2 × 250 mL), saturated aqueous ammonium chloride (2 × 250 mL), and distilled water (4 × 250 mL) and dried with Na_2SO_4. Distillation of the solution followed by rotary evaporation yielded a viscous oil which was subsequently dried completely in a vacuum desiccator with P_2O_5 (33.15 g, 92%). The IR spectrum showed a band at 1160 cm^{-1} ($-CH_3C_6H_4SO_3-$) and no bands at 3200–3600 cm^{-1} (–OH). The ^1H NMR spectrum ($CDCl_3$) showed resonances at δ 2.24 ($-CH_3$), 3.55–4.16 ($-CH_2-CH_2O-$), and 7.31–7.80 (Ar–H) with associated integration in accord with the expected structure. Anal. Calcd for $C_{23}H_{30}O_9S_2$: C, 52.12; H, 6.00; S, 12.76. Found: C, 52.58; H, 6.02; S, 12.76.

Oligo(ethylene glycol) (I). Dry methanol (23.3 g, 0.728 mol) was added to Na (1.844 g, 0.0819 mol) under dry N_2. The mixture was gently refluxed for 0.7 h and then cooled in ice–water. Tetrakis(ethylene glycol) (50.71 g, 0.261 mol) was poured into the vigorously stirred sodium methoxide solution at 0 °C. After the mixture was stirred at room temperature for 1 h, the methanol was distilled off in a stream of dry N_2. To the residual liquid was added a solution of TEG-Ts_2 (20.9 g, 0.0416 mol) in dry THF (100 mL). The flask was shielded from light, and the mixture was stirred at 45 °C for 3 days. The white precipitate of sodium tosylate was filtered off. THF was removed with rotary evaporation, and a clear yellow liquid resulted. The crude product was separated with gel filtration for at least 10 times. A Sephadex LH-20 column (120 × 2.2 cm) with methanol as the elution solvent was used. Oligo(ethylene glycol)s were obtained as follows: A, 0.09 g (n = 8); B, 18.5 g (n = 12); C, 1.90 g (n = 20); D, 0.55 g (n = 28). Total, 21.04 g, 92.7% recovery. GPC determination and FAB-MS spectra for these oligo(ethylene glycol)s show each fraction is a monodisperse pure sample.

Oligo(ethylene glycol)s (II). Dry methanol (1.58 g, 0.049 mol) was added to Na (0.141 g, 6.13 × 10^{-3} mol) under dry N_2. The mixture was gently refluxed for 0.7 h and then cooled in ice–water. Dodecakis(ethylene glycol) (5.22 g, 9.55 × 10^{-3} mol) was poured into the sodium methoxide solution at 0 °C. After reaction with TEG-Ts_2 (1.49 g, 2.96 × 10^{-3} mol) in THF at 45 °C for 3 days, the products were purified as described above. Oligo(ethylene glycol)s were obtained as follows: A, 0.140 g (n = 20); B, 1.384 g (n = 28); C, 0.430 g (n = 36); D, 0.128 g (n = 44). Total 2.082 g, 56% yield.

The main product of the reaction between tetrakis(ethylene glycol) ditosylate and TEG monoanion is dodecakis(ethylene glycol) which is the trimer of TEG. The main product of the reaction between hexakis(ethylene glycol) ditosylate (HEG) and HEG anion is eicosakis(ethylene glycol). The main product of the reaction between tetrakis(ethylene glycol) ditosylate and dodecakis(ethylene glycol) anion is 28-mer.

Measurements. GPC determination was carried out with a Tosoh CCP &8010 system (columns: G3000HXL and G2000-HXL). Mass spectra were recorded with a JEOL JMS SX-102 mass spectrometer by the fast atom bombardment (FAB) method. ^1H NMR spectra were recorded at 270 MHz in $CDCl_3$ and D_2O on a JEOL JNM GXS-270 spectrometer. Chemical shifts were referenced to the solvent values (δ 7.26 for $CHCl_3$ and δ 4.70 for HOD). Powder X-ray diffraction patterns were taken by using Cu Kα radiation with a Rigaku RAD-ROC diffractometer. ^{13}C CP/MAS NMR spectra were measured on a JEOL EX-270 NMR spectrometer with a single contact line of 1 ms and spinning rates of 5.5 and 6.4 kHz.

Preparation of Inclusion Complexes. Reaction of Oligo(ethylene glycol) with α-Cyclodextrin. Oligo(ethylene glycol) (15 mg) was added to a saturated aqueous solution of α-CD (1 mL) containing α-CD (145 mg). The product precipitated was collected by centrifugation or filtration and washed with water and dried.

α-CD–OEG(4) (TEG): yield 1.5%; mp (dec) 300–305 °C; ^1H NMR (D_2O, 270 MHz) σ 5.03 (d, 6H, C(1)H of α-CD), 3.96 (t, 6H, C(3)H of α-CD), 3.85 (m, 12H, C(6)H of α-CD), 3.81 (m, 6H, C(5)H of α-CD), 3.69 (m, 8H, CH_2 of OEG), 3.61 (m, 6H, C(2)H of α-CD), 3.56 (t, 6H, C(4)H of α-CD); ^{13}C NMR (D_2O, 67.8 MHz) δ 103.96 (C(1) of α-CD), 83.76 (C(4) of α-CD), 75.86 (C(3) of α-CD), 74.56 (C(5) of α-CD), 74.24 (C(2) of α-CD), 72.03–72.24 (CH_2 of OEG), 62.97 (C(6) of α-CD); IR (KCl, cm^{-1}) 3398 (vs, ν_{OH}), 2923 (s, ν_{CH}), 1154, 1078, 1027 (vs, ν_{CO}), 573. Anal. Calcd for $C_{80}H_{138}O_{65}\cdot 4H_2O$: C, 43.44; H, 6.65. Found: C, 43.17; H, 6.75.

α-CD–OEG(5) (PEG): yield 9.2%; mp (dec) 300–305 °C; ^1H NMR (D_2O, 270 MHz) δ 5.03 (d, 6H, C(1)H of α-CD), 3.96 (t, 6H, C(3)H of α-CD), 3.85 (m, 12H, C(6)H of α-CD), 3.81 (m, 6H, C(5)H of α-CD), 3.69 (m, 10H, CH_2 of OEG), 3.61 (m, 6H, C(2)H of α-CD), 3.56 (t, 6H, C(4)H of α-CD); ^{13}C NMR (D_2O, 67.8 MHz) δ 104.04 (C(1) of α-CD), 83.86 (C(4) of α-CD), 75.96 (C(3) of α-CD), 74.68 (C(5) of α-CD), 74.34 (C(2) of α-CD), 72.13–72.33 (CH_2 of OEG), 63.05 (C(6) of α-CD); IR (KCl, cm^{-1}) 3386 (vs, ν_{OH}), 2923 (s, ν_{CH}), 1153, 1078, 1030 (vs, ν_{CO}), 571. Anal. Calcd for $C_{82}H_{142}O_{66}\cdot 4H_2O$: C, 43.66; H, 6.70. Found: C, 43.63; H, 6.66.

α-CD–OEG(6): yield 30%; mp (dec) 300–305 °C; ^1H NMR (D_2O, 270 MHz) δ 5.03 (d, 6H, C(1)H of α-CD), 3.96 (t, 6H, C(3)H of α-CD), 3.85 (m, 12H, C(6)H of α-CD), 3.81 (m, 6H, C(5)H of α-CD), 3.69 (m, 8H, CH_2 of OEG), 3.61 (m, 6H, C(2)H of α-CD), 3.56 (t, 6H, C(4)H of α-CD); ^{13}C NMR (D_2O, 67.8 MHz) δ 103.92 (C(1) of α-CD), 83.74 (C(4) of α-CD), 75.86 (C(3) of α-CD), 74.56 (C(5) of α-CD), 74.24 (C(2) of α-CD), 72.01–72.23 (CH_2 of OEG), 62.95 (C(6) of α-CD); IR (KCl, cm^{-1}) 3386 (vs, ν_{OH}), 2921 (s, ν_{CH}), 1153, 1078, 1028 (vs, ν_{CO}), 573. Anal. Calcd for $C_{120}H_{206}O_{97}\cdot 6H_2O$: C, 43.55; H, 6.64. Found: C, 44.03; H, 6.56.

α-CD–OEG(7): yield 56%; mp (dec) 300–305 °C; ^1H NMR (D_2O, 270 MHz) δ 5.03 (d, 6H C(1)H of α-CD), 3.96 (t, 6H, C(3)H of α-CD), 3.86 (m, 12H, C(6)H of α-CD), 3.81 (m, 6H, C(5)H of α-CD), 3.69 (m, 9H, CH_2 of OEG), 3.61 (m, 6H, C(2)H of α-CD), 3.57 (t, 6H, C(4)H of α-CD); ^{13}C NMR (D_2O, 67.8 MHz) δ 103.91 (C(1) of α-CD), 83.73 (C(4) of α-CD), 75.82 (C(3) of α-CD), 74.22 (C(5) of α-CD), 74.36 (C(2) of α-CD), 72.00–72.21 (CH_2 of OEG), 62.94 (C(6) of α-CD); IR (KCl, cm^{-1}) 3386 (vs, ν_{OH}), 2923 (s, ν_{CH}), 1153, 1077, 1029 (vs, ν_{CO}), 574. Anal. Calcd for $C_{122}H_{210}O_{98}\cdot 6H_2O$: C, 43.70; H, 6.67. Found: C, 44.13; H, 6.67.

α-CD–OEG(8): yield 64%; mp (dec) 300–305 °C; ^1H NMR (D_2O, 270 MHz) δ 5.03 (d, 6H, C(1)H of α-CD), 3.96 (t, 6H, C(3)H of α-CD), 3.86 (m, 12H, C(6)H of α-CD), 3.81 (m, 6H, C(5)H of α-CD), 3.69 (m, 8H, CH_2 of OEG), 3.61 (m, 6H, C(2)H of α-CD), 3.57 (t, 6H, C(4)H of α-CD); ^{13}C NMR (D_2O, 67.8 MHz) δ 104.08 (C(1) of α-CD), 83.09 (C(4) of α-CD), 75.99 (C(3) of α-CD), 74.68 (C(5) of α-CD), 74.36 (C(2) of α-CD), 72.25 (CH_2 of OEG), 63.05 C(6) of α-CD); IR (KCl, cm^{-1}) 3386 (vs, ν_{OH}), 2924 (s, ν_{CH}), 1153, 1078, 1031 (vs, ν_{CO}), 575. Anal. Calcd for $C_{160}H_{274}O_{129}\cdot 8H_2O$: C, 43.62; H, 6.63. Found: C, 43.70, H, 6.63.

α-CD–OEG(12): yield 76%; mp (dec) 300–305 °C, ^1H NMR (D_2O, 270 MHz) δ 5.03 (d, 6H, C(1)H of α-CD), 3.96 (t, 6H, C(3)H of α-CD), 3.86 (m, 12H, C(6)H of α-CD), 3.81 (m, 6H, C(5)H of α-CD), 3.68 (m, 8H, CH_2 of OEG), 3.61 (m, 6H, C(2)H of α-CD), 3.57 (t, 6H, C(4)H of α-CD); ^{13}C NMR (D_2O, 67.8 MHz) δ 104.41 (C(1) of α-Cd), 83.84 (C(4) of α-CD), 75.96 (C(3) of α-CD), 74.68 (C(5) of α-CD), 74.34 (C(2) of α-CD), 72.25 (CH_2 of OEG), 63.07 (C(6) of α-CD); IR (KCl, cm^{-1}) 3384 (vs, ν_{OH}), 2923 (s, ν_{CH}), 1152, 1077, 1031 (vs, ν_{CO}), 575. Anal. Calcd for $C_{240}H_{410}O_{193}\cdot 12H_2O$: C, 43.68; H, 6.63. Found: C, 43.62; H, 6.72.

α-CD–OEG(20): yield 85%; mp (dec) 300–305 °C; ^1H NMR (D_2O, 270 MHz, δ 5.03 (d, 6H, C(1)H of α-CD), 3.96 (t, 6H, C(3) of α-CD), 3.86 (m, 12H, C(6)H of α-CD), 3.81 (m, 6H, C(5)H of α-CD), 3.68 (s, 8H, CH_2 of OEG), 3.61 (m, 6H, C(2)H of α-CD), 3.56 (t, 6H, C(4)H of α-CD); ^{13}C NMR (D_2O, 67.8 MHz) δ 104.02 (C(1) of α-CD), 83.84 (C(4) of α-CD), 75.96 (C(3) of α-CD), 74.66 (C(5) of α-CD), 74.34 (C(2) of α-CD), 72.25 (CH_2 of OEG), 63.05 (C(6) of α-CD); IR (KCl, cm^{-1}) 3384 (vs, ν_{OH}), 2923 (s, ν_{CH}), 1152, 1077, 1031 (vs, ν_{CO}), 571. Anal. Calcd for $C_{400}H_{682}O_{321}\cdot 20H_2O$: C, 43.72; H, 6.62. Found: C, 43.96; H, 6.71.

α-CD–OEG(28): yield 88%; mp (dec) 300–305 °C; ^1H NMR (D_2O, 270 MHz) δ 5.03 (d, 6H, C(1)H of α-CD), 3.96 (t, 6H, C(3)H of α-CD), 3.86 (m, 12H, C(6)H of α-CD), 3.81 (m, 6H, C(5)H of α-CD), 3.68 (s, 8H, CH_2 of OEG), 3.61 (m, 6H, C(2)H of α-CD), 3.56 (t, 6H, C(4)H of α-CD); ^{13}C NMR (D_2O, 67.8 MHz) δ 104.02 (C(1) of α-CD), 83.84 (C(4) of α-CD), 75.96 (C(3) of α-CD), 74.66 (C(5) of α-CD), 74.34 (C(2) of α-CD), 72.25 (CH_2 of OEG), 63.07 (C(6) of α-CD); IR (KCl, cm^{-1}) 3384 (vs, ν_{OH}), 2925 (s, ν_{CH}), 1154, 1078, 1032 (vs, ν_{CO}), 573. Anal. Calcd for $C_{560}H_{954}O_{449}\cdot 28H_2O$: C, 43.74; H, 6.62. Found: C, 43.33; H, 6.79.

α-CD–OEG(36): yield 89%; mp (dec), 300–305 °C; ^1H NMR (D_2O, 270 MHz) δ 5.03 (d, 6H, C(1)H of α-CD), 3.96 (t, 6H, C(3)H of α-CD), 3.85 (m, 12H, C(6)H of α-CD), 3.81 (m, 6H, C(5)H of α-CD), 3.68 (s, 8H, CH_2 of OEG), 3.61 (m, 6H, C(2)H of α-CD), 3.56 (t, 6H, C(4)H of α-CD); ^{13}C NMR (D_2O, 67.8 MHz) δ 103.91 (C(1) of α-CD), 83.71 (C(4) of α-CD), 75.82 (C(3) of α-CD), 74.53

(C(5) of α-CD), 74.21 (C(2) of α-CD), 72.12 (CH_2 of OEG), 62.92 (C(6) of α-CD); IR (KCl, cm^{-1}) 3386 (vs, ν_{OH}), 2925 (s, ν_{CH}), 1153, 1078, 1032 (vs, ν_{CO}), 574. Anal. Calcd for $C_{720}H_{1226}O_{577}\cdot 36H_2O$: C, 43.76; H, 6.62. Found: C, 43.46; H, 6.65.

α-CD–OEG(44): yield 89%; mp (dec) 300–305 °C; ^1H NMR (D_2O, 270 MHz), δ 5.03 (d, 6H, C(1)H of α-CD), 3.96 (t, 6H, C(3)H of α-CD), 3.85 (m, 12H, C(6)H of α-CD), 3.81 (m, 6H, C(5)H of α-CD), 3.68 (s, 8H, CH_2 of OEG), 3.61 (m, 6H, C(2)H of α-CD), 3.56 (t, 6H, C(4)H of α-CD); ^{13}C NMR (D_2O, 67.8 MHz) δ 104.08 (C(1) of α-CD), 83.09 (C(4) of α-CD), 75.99 (C(3) of α-CD), 74.68 (C(5) of α-CD), 74.36 (C(2) of α-CD), 72.25 (CH_2 of OEG), 63.05 (C(6) of α-CD); IR (KCl, cm^{-1}) 3386 (vs, ν_{OH}), 2923 (s, ν_{CH}), 1154, 1078, 1029 (vs, ν_{CO}), 573. Anal. Calcd for $C_{880}H_{1498}O_{705}\cdot 44H_2O$: C, 43.76; H, 6.62. Found: C, 43.37, H, 6.80.

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