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Selection between Pinching-Type and Supramolecular Polymer-Type Complexes by α-Cyclodextrin−β-Cyclodextrin Hetero-Dimer and Hetero-Cinnamamide Guest Dimers

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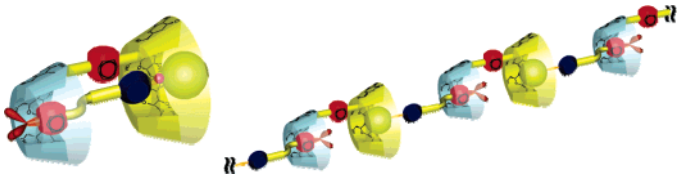

Novel supramolecular complexes have been prepared from an α-cyclodextrin−β-cyclodextrin hetero-dimer (α-CD−β-CD hetero-dimer) and hetero-cinnamamide guest dimers, G-*t*-Boc and G-NH_2, having adamantyl groups in aqueous solutions. On addition of the competitive guest, the supramolecular structure formed by a mixture of the α-CD−β-CD hetero-dimer and G-*t*-Boc was found to be different from that of a mixture of the α-CD−β-CD hetero-dimer and G-NH_2 by the ^{1}H NMR spectroscopy, the ROESY NMR spectroscopy, and the circular dichroism spectroscopy. The size of the supramolecular complex from the mixture of the α-CD−β-CD hetero-dimer and G-NH_2 is larger than that from the mixture of the α-CD−β-CD hetero-dimer and G-*t*-Boc, which was proved by the pulse field gradient spin−echo NMR and the atomic force microscopy. These results suggest that the mixture of the α-CD−β-CD hetero-dimer and G-*t*-Boc formed a pinching-type complex, and the mixture of the α-CD−β-CD hetero-dimer and G-NH_2 formed a supramolecular polymer-type complex.

Introduction

Biological systems offer several excellent examples of supramolecular polymers including double- and triple-helical DNA, as well as protein β-sheet and tobacco mosaic virus.[1] Microtubles are supramolecular polymers consisting of hetero-dimers of α-tubulin and β-tubulin with alternating structures.[2] Chemists have challenged the formation of supramolecules based on host-dimers as supramolecular architectures of artificial assemblies.[3] Cyclodextrins (CDs) have been used frequently as a component of supramolecular complexes. CD dimers, used for molecular recognition and drug delivery, possess the structural characteristics to completely encapsulate a guest molecule. CD dimers were prepared by some researchers to increase the association constants with CDs, because association constants for complexations of appropriate guests with CDs show 10^4 M^{-1}, whereas the corresponding values for complexations of substrates with antibody are more than 100 times larger.[4,5] Many researchers are actively working on producing enzyme models based on CD dimers that strongly bind appropriate substrates to both CD cavities such as a pinching-type structure.[6,7] Although there are some papers on the cooperative binding of guests by CD hetero-dimers,[8,9] there are

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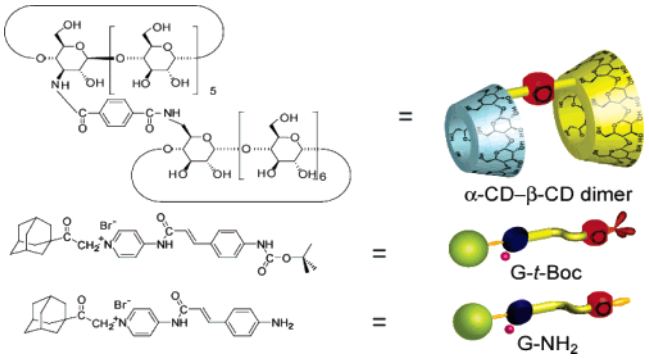


FIGURE 1. Chemical structures of α-CD−β-CD dimer, G-*t*-Boc, and G-NH_2 guest dimers.

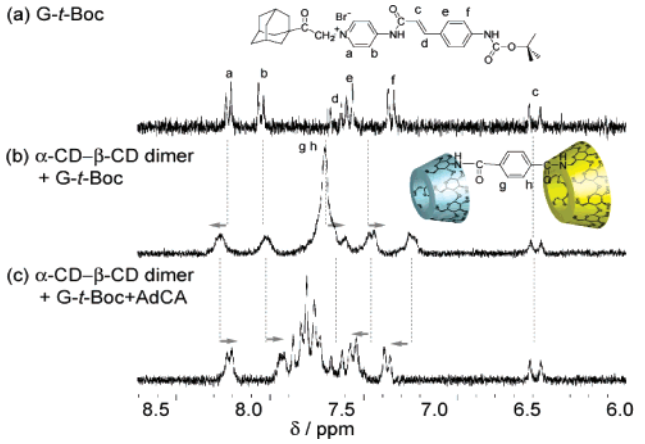


FIGURE 2. ^{1}H NMR spectra of the G-*t*-Boc dimer (a), the mixture of the α-CD−β-CD dimer and G-*t*-Boc in 3 mM (b), and the mixture of the α-CD−β-CD dimer and G-*t*-Boc in the presence of 5 equiv of AdCA in D_2O at 30 °C (c).[12]

few on the formation of supramolecular complexes of CD hetero-dimers with hetero-guest dimers. Previously, we reported that a CD dimer formed supramolecular polymers with ditopic guest molecules and did not form a 1:1 inclusion complex.[10] In the present paper, we describe the synthesis of an α-CD−β-CD hetero-dimer and formation of supramolecular complexes from the α-CD−β-CD hetero-dimer and hetero-cinnamamide guest dimers. Our purpose was the construction of a new supramolecular polymer consisting of the CD hetero-dimer and hetero-cinnamamide guest dimers. However, we found the selection between the pinching-type structure and the supramolecular polymer-type structure in these systems, depending on the combination of an α-CD−β-CD hetero-dimer and a hetero-cinnamamide guest dimer.

Results and Discussion

Preparation of α-CD−β-CD Hetero-Dimer and Hetero-Guest Dimers. The α-CD−β-CD hetero-dimer was prepared by the reaction of 6-amino-α-CD and 6-*O*-(4-carboxylphenylamide)-β-CD using DCC (dicyclohexyl carbodiimide) and HOBT (1-hydroxybenzotriazole) in DMF. Hetero-guest dimers, G-*t*-Boc and G-NH_2 were prepared by aminocinnamate, aminopyridine, and 1-adamantyl bromomethyl ketone. Two kinds of hetero-guest dimers were prepared: one with an adamantyl group and *tert*-butyl group (*t*-Boc) and the other with an adamantyl group and both having an amino cinnamate group as a spacer (Figure 1). The *t*-Boc group and an amino group are included in the α-CD cavity, while an adamantyl group is not included in the α-CD cavity because of the steric hindrance.

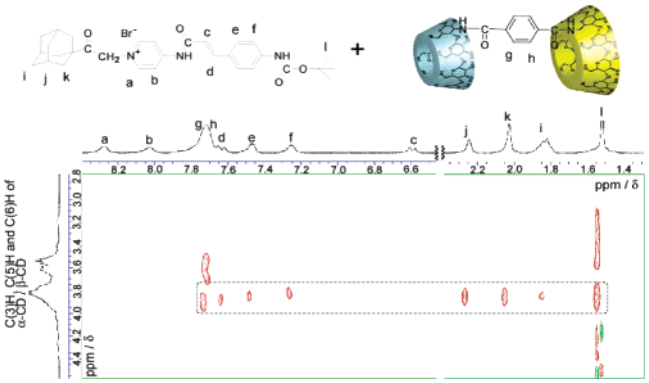
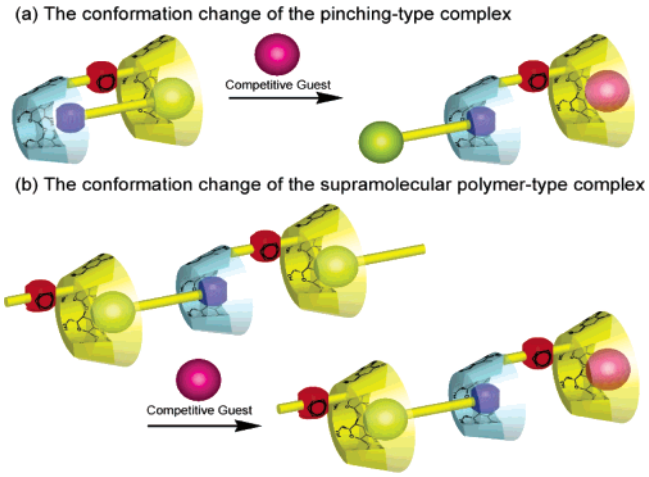


FIGURE 3. ROESY spectrum of the mixture of the G-*t*-Boc dimer and the α-CD−β-CD dimer in D_2O at 30 °C.

SCHEME 1



Formation of Supramolecular Complexes from α-CD−β-CD hetero-dimer and hetero-guest dimers. The supramolecular complexes from the α-CD−β-CD hetero-dimer with G-*t*-Boc or the α-CD−β-CD hetero-dimer with G-NH_2 were expected to form two types, a pinching-type and a supramolecular polymer-type. The NMR spectroscopy was used to reveal the mode of these supramolecular complexes. Figure 2 shows the ^{1}H NMR spectra of the mixtrue of the α-CD−β-CD hetero-dimer and the G-*t*-Boc guest dimer in D_2O. The peaks of phenyl, pyridinium, and *t*-Boc protons showed the peak shifts with an increase in the concentration (Figure 2b and S3). The two-dimensional ROESY NMR spectrum showed that the peaks of the cinnamamide protons, adamantane protons, and *t*-Boc protons were correlating with inner protons (C(3)−H and C(5)−H) of CDs (Figure 3), but the correlation peaks between the peaks of pyridinium protons and inner protons of CDs were not observed.[11] Considering the molecular size of the adamantyl

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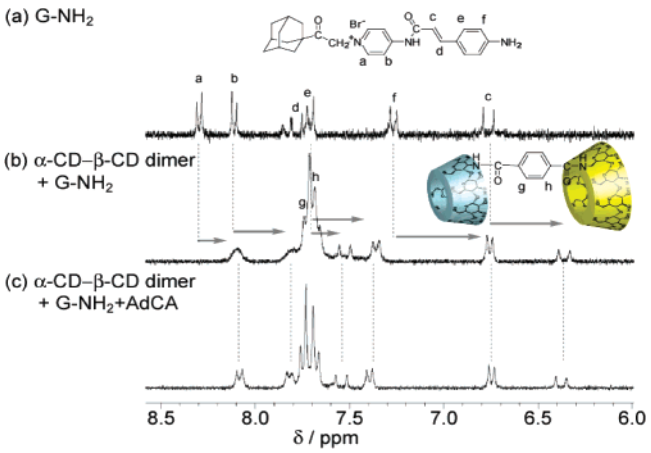


FIGURE 4. ^{1}H NMR spectra of the G-NH_2 dimer (a), the mixture of the α-CD−*β*-CD dimer and G-NH_2 in 3 mM (b), and the mixture of the α-CD−*β*-CD dimer and G- NH_2 on addition of 5 equiv of AdCA in D_2O at 30 °C (c).[12]

group and the *t*-Boc group, the *t*-Boc group is included in the α-CD cavity, and the adamantyl group is included in the *β*-CD cavity, because the adamantyl group is too large to fit the adamantyl group in the α-CD cavity. These data indicate the formation of inclusion complexes, but it is difficult to determine a pinching-type or a supramolecular polymer-type.

The direction of the cinnamamide group in the pinching-type supramolecular complex is supposed to change on addition of excessive amounts of the competitive guest, which is included in the *β*-CD cavity. The direction of the cinnamamide group in the supramolecular polymer-type did not change on addition of excessive amounts of adamantane carboxylic acid (AdCA; Scheme 1).

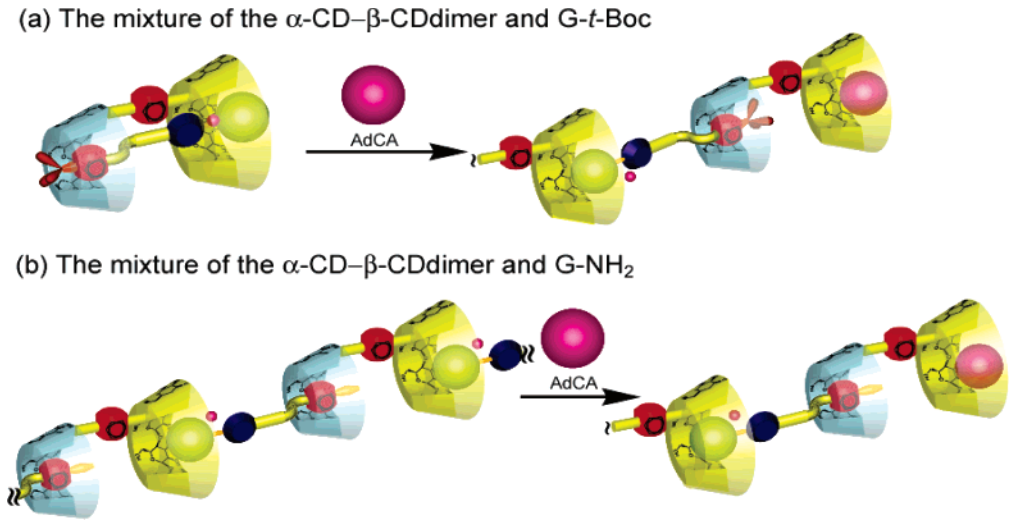
When 5 equiv of AdCA, which is strongly bound to the *β*-CD cavity, were added to the solution of the α-CD−*β*-CD hetero-dimer and G-*t*-Boc, the peaks of the aromatic protons and the *t*-Boc protons showed the peak shifts (Figure 2c and S4). These results showed that the inclusion complex was dissociated or that the mode of the inclusion complex changed on addition of AdCA. The ROE correlation between cinnamamide protons, adamantly protons, *t*-Boc protons, AdCA and inner protons (C(3)−H and C(5)−H) of CDs were observed (Figure S7), indicative of the formation of the supramolecular complex. The mixture of α-CD−*β*-CD dimer, G-*t*-Boc guest dimer, and AdCA were thought to form four possible supramolecular complexes (Scheme S1). These results of one-dimensional (1D) ^{1}H NMR and ROESY NMR showed that the supramolecular structure, shown in Scheme 1a, was formed by the mixture of α-CD−*β*-CD dimer, G-*t*-Boc guest dimer, and AdCA.

The mixture of the α-CD−*β*-CD hetero-dimer and G-NH_2 showed the same behavior in the ^{1}H NMR (Figure 4b) and showed that the peaks of cinnamamide protons and adamantly protons were correlating with inner protons (C(3)−H and C(5)−H) of CDs (Figure S6), indicative of the formation of the inclusion complex. However, upon addition of AdCA to the solution of the α-CD−*β*-CD hetero-dimer with G-NH_2, the peak shifts of G-NH_2 protons were not observed (Figure 4c). We supposed that AdCA was not included in the *β*-CD cavity or that the conformation of the inclusion complex does not change on addition of AdCA. The cinnamamide protons and adamantyl protons were correlating with inner protons (C(3)−H and C(5)−H) of CDs (Figure S8). Moreover, the ROE correlation between AdCA and inner protons (C(3)−H and C(5)−H) of CDs was observed. These results of 1D ^{1}H NMR and ROESY NMR showed that the supramolecular structure from the mixture of α-CD−*β*-CD dimer and G-NH_2 guest dimer was different from that from the mixture of α-CD−*β*-CD dimer, G-*t*-Boc guest dimer and AdCA.

The protons of the cinnamamide group in the mixture of the α-CD−*β*-CD hetero-dimer and G-*t*-Boc showed the peak shifts by addition of AdCA in the ^{1}H NMR spectroscopy. On the contrary, the protons of the cinnamamide in the mixture of the α-CD−*β*-CD hetero-dimer and G-NH_2 did not show any peak shifts. These mixtures of the α-CD−*β*-CD hetero-dimer and guest dimers showed the ROE correlation between the inner protons of CDs and guest parts. On the basis of these data, we suppose that the mixture of the α-CD−*β*-CD hetero-dimer and G-*t*-Boc formed the pinching-type complex, and the mixture of the α-CD−*β*-CD hetero-dimer and G-NH_2 formed the supramolecular polymer-type complex (Scheme 2).

Calculation of the Molecular Sizes of Supramolecular Complexes. The pulsed field gradient spin−echo NMR was measured to determine diffusion coefficients of the supramolecular complex between the α-CD−*β*-CD hetero-dimer and

SCHEME 2



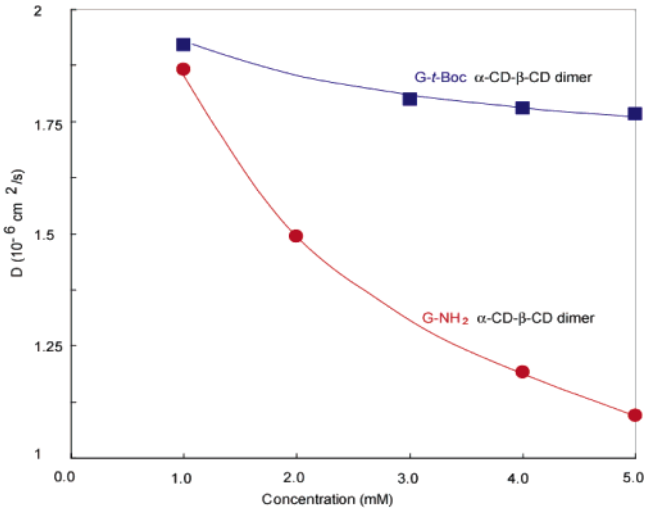


FIGURE 5. Concentration dependence of the diffusion coefficient values (*D*) of supramolecular polymers formed between the α-CD−*β*-CD dimer and the G-*t*-Boc dimer (filled square) and the α-CD−*β*-CD dimer and the G-NH_2 dimer (filled circle) in D_2O at 30 °C by NMR.

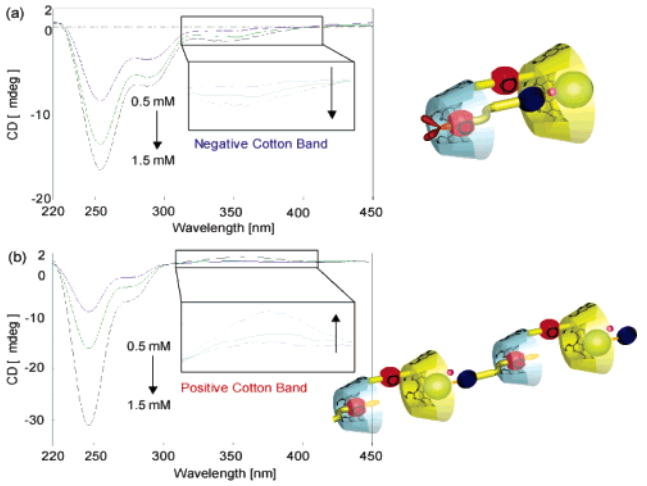


FIGURE 6. Circular dichroism spectra of the mixture of the G-*t*-Boc dimer and the α-CD−*β*-CD dimer (a) and the mixture of the G-NH_2 dimer and the α-CD−*β*-CD dimer (b) as a fraction of the concentration in H_2O at 25 °C.

hetero-guest dimers. Figure 5 shows that the apparent diffusion coefficient (*D*) of the mixture of the α-CD−*β*-CD hetero-dimer and G-*t*-Boc slightly decreased with an increase in the concentration. *D* of the mixture of the α-CD−*β*-CD hetero-dimer and G-*t*-Boc was comparable to *D* of the α-CD−*β*-CD hetero-dimer, indicative of the formation of the pinching-type complex. However, *D* of the supramolecular complex from the α-CD−*β*-CD hetero-dimer and G-NH_2 largely decreased with an increase in the concentration. The hydrodynamic volume of the supramolecular complex from the α-CD−*β*-CD hetero-dimer and G-NH_2 is larger than that of the supramolecular complex

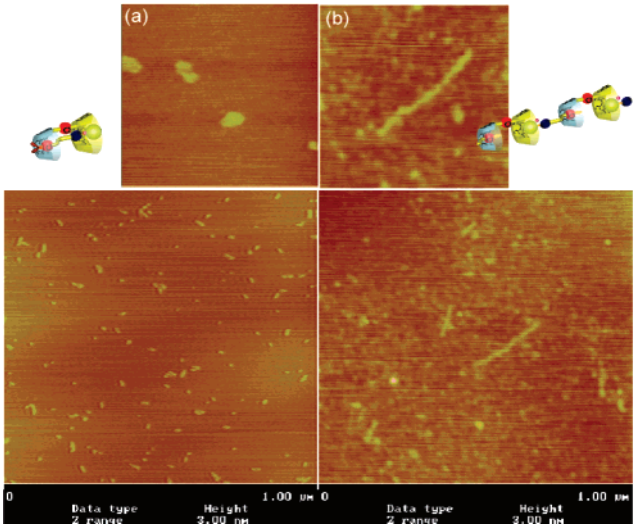


FIGURE 7. AFM images of a 1:1 mixture of the G-*t*-Boc dimer and the α-CD−*β*-CD dimer (a) and the G-NH_2 dimer and the α-CD−*β*-CD dimer (b).

from the α-CD−*β*-CD hetero-dimer and G-*t*-Boc at 5mM, indicating that the mixture of the α-CD−*β*-CD hetero-dimer and G-NH_2 guest dimer formed the supramolecular polymer. These data support the formation of a pinching-type complex from the α-CD−*β*-CD hetero-dimer and G-*t*-Boc and the formation of a supramolecular polymer-type complex from the α-CD−*β*-CD hetero-dimer and G-NH_2 by NMR studies.

Circular Dichroism Spectra. The achiral compounds located in the CD cavity produce induced circular dichroism signals in the corresponding transition bands.[11,12] To confirm the different conformations of the complex of the α-CD−*β*-CD hetero-dimer with G-*t*-Boc and that of the α-CD−*β*-CD hetero-dimer with G-NH_2, their circular dichoism spectra were measured at 25 °C. The mixture of the α-CD−*β*-CD hetero-dimer and G-*t*-Boc showed a negative Cotton band at 240 nm and a negative Cotton band at 350 nm, while the mixture of the α-CD−*β*-CD hetero-dimer and G-NH_2 showed a negative Cotton band at 240 nm and a positive Cotton band at 350 nm in Figure 6. These results indicate that the location of cinnamamide moiety of G-*t*-Boc in the cavity of the α-CD−*β*-CD hetero-dimer is different from that of G-NH_2.

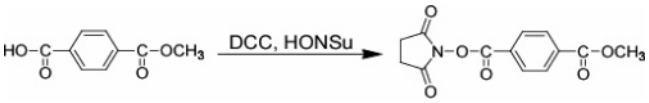
Direct Observation by Atomic Force Microscopy. To confirm the nanometer-sized molecular assemblies, the supramolecular dimer or polymer, atomic force microscopy (AFM) measurements were performed. When the sample was made from a 1:1 mixture of the α-CD−*β*-CD hetero-dimer and G-*t*-Boc, only a small object that was approximately 20 nm in overall length could be detected. The size of the small object from the α-CD−*β*-CD hetero-dimer and G-*t*-Boc was as large as that of the α-CD−*β*-CD hetero-dimer. However, nanometer-sized supramolecular wires that were approximately 250 nm in overall length were observed on the mica substrate (Figure 7).

Conclusion. We studied the preparation of the supramolecular complex using the α-CD−*β*-CD hetero-dimer and hetero-guest dimers. The mixture of the α-CD−*β*-CD hetero-dimer and hetero-guest dimers, G-*t*-Boc and G-NH_2, had been expected to form supramolecular polymers. However, it is concluded that a 1:1 mixture of the α-CD−*β*-CD hetero-dimer and G-*t*-Boc

(11) Generally, the cationic compounds are not included in the CD cavity. Previously, we have studied the formation inclusion complexes between the viologen polymers and the *a*-CD. These results indicated that the cationic groups play a rule in the electron stopper and were not included in the α-CD caviry. (a) Kawaguchi, Y.; Harada, A. *J. Am. Chem. Soc*. **2000**, *122*, 3797−3798. (b) Kawaguchi, Y.; Harada, A. *Org. Lett*. **2000**, *2*, 1353−1356.

(12) Excess amounts of AdCA, which exceeded the limit of the solubility in D_2O, were added to the solution of the mixture of α-CD−*β*-CD dimer and G-*t*-Boc guest dimer.

SCHEME 3



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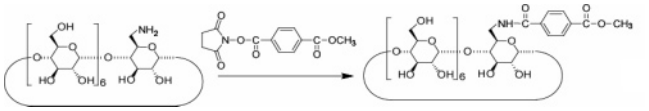
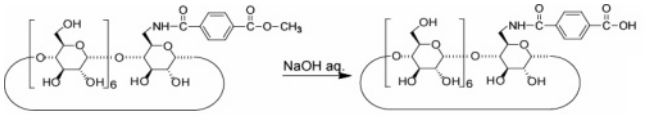


SCHEME 5



guest dimer forms a pinching-type dimer structure and that a 1:1 mixture of the α-CD−*β*-CD hetero-dimer and the G-NH_2 guest dimer forms a supramolecular polymer-type structure. The selection of supramolecular complexes is caused by the steric effect, the association constants, and some interactions such as the hydrophobic interaction, the hydrogen bond interaction, and so on. This is the first example of the selection of supramolecular complexes between a pinching-type complex and a supramolecular polymer-type complex. These results are important from a viewpoint of not only supramolecular chemistry, but of the formation of specific structures in biological systems.

Experimental Section

Preparation of Terephthalic Acid Methyl ONSu Ester (Scheme 3). Terephthalic acid monomethyl ester (2.2 g, 12.0 mmol), dicyclohexyl carbodiimide (DCC; 3.7 g, 18.0 mmol), and *N*-hydroxylsuccinimide (2.4 g, 18.0 mmol) were allowed to react in THF (30 mL) at room temperature. After a day, the precipitate, dicyclohexylurea, was removed by centrifuge. The supernatant solution was evaporated to dryness in vacuo. The residue was dissolved in 30 mL of 2-propanol and recrystallized at 2 °C as a white crystal in 50% yield.

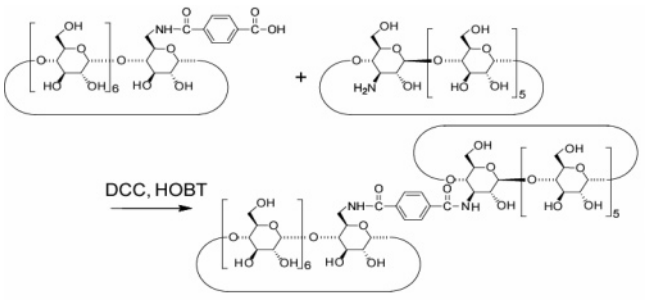
^{1}H NMR (DMSO-d_6, 30 °C, 270 MHz): *δ* 8.1 (d, 2H, 2-*Ph*), 8.2 (d, 2H, 3-*Ph*), 3.9 (s, 3H, *Me*), 2.9 (s, 4H, *ONSu*). Elem anal. Calcd for $C_{13}H_{11}NO_6$: C, 56.32; H, 4.00; N, 5.05. Found: C, 56.10; H, 3.96; N, 5.23.

Preparation of Methylterephthalamide *β*-CD (Scheme 4). To a solution of 6-NH_2-*β*-CD (1.0 g, 0.88 mmol) in 20 mL of DMF was added terephthalic acid methyl ONSu ester (0.3 g, 1.01 mmol). The reaction mixture was stirred at room temperature for 36 h. After the prescribed time, the reaction mixture was poured into 300 mL of acetone to precipitate methylterephthalamide *β*-CD. The crude methylterephthalamide *β*-CD was collected by centrifuge and washed with acetone to give methylterephthalamide *β*-CD in 87% yield.

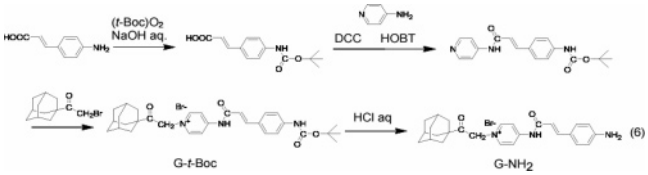
^{1}H NMR (DMSO-d_6, 30 °C, 270 MHz): *δ* 8.4 (t, 1H, −CON*H*−), 8.0 (d, 2H, 2-*Ph*), 7.9 (d, 2H, 3-*Ph*), 5.7 (m, 14H, O(2)*H* and O(3)*H*), 4.9 (d, 1H, C(1)′*H*), 4.8 (m, 6H, C(1)H), 4.2 (m, 4H, O(6)*H*), 4.15 (m, 1H, O(6)′*H*), 3.92 (s, 3H, *Me*), 3.6 (m, 21H, C(3)*H*, C(5)*H*, and C(6)*H*), 3.3 (m, 14H, C(2)*H*, and C(4)*H*).

Preparation of Terephthalamide *β*-CD (Scheme 5). Methylterephthalamide *β*-CD was dissolved in 10 mL of water and added to 0.2 mL of 1 M NaOH and stirred for an hour. After the prescribed time, the reaction mixture was neutralized by citric acid and evaporated to dryness under reduced pressure. The crude product was purified by column chromatography on DIAION HP-20 (eluted with water/methanol = 100/0 to 50/50). The 60/40 (water/methanol) eluent was concentrated to give terephthalamide *β*-CD in 88% yield.

SCHEME 6



SCHEME 7



^{1}H NMR (DMSO-d_6, 30 °C, 270 MHz): *δ* 8.4 (t, 1H, −CON*H*−), 8.0 (d, 2H, 2-*Ph*), 7.9 (d, 2H, 3-*Ph*), 5.7 (m, 14H, O(2)*H* and O(3)*H*), 4.9 (d, 1H, C(1)′*H*), 4.8 (m, 6H, C(1)H), 4.2 (m, 4H, O(6)*H*), 4.15 (m, 1H, O(6)′*H*), 3.6 (m, 21H, C(3)*H*, C(5)*H*, and C(6)*H*), 3.3 (m, 14H, C(2)*H* and C(4)*H*). Elem anal. Calcd for $C_{50}H_{75}NO_{37}\cdot 6.0H_2O$: C, 43.20; H, 6.31; N, 1.01. Found: C, 42.98; H, 6.22; N, 1.24. MALDI-TOF MS (*m*/*z*): 1306.4 ([M + Na]$^+$).

Preparation of α-CD−*β*-CD Hetero-Dimer (Scheme 6). To a solution of terephthalamide *β*-CD (0.12 mg, 0.09 mmol) in 10 mL of DMF was added the mixture solution of 3-NH_2-α-CD, DCC (0.37 mg, 0.18 mmol), and 1-hydroxylbenzotriazole (24 mg, 0.18 mmol) at 0 °C. After being stirred for an hour, it was allowed to warm to room temperature and stirred for 3 days. After the prescribed time, the precipitate, dicyclohexylurea, was removed by centrifuge. The supernatant solution was poured into 300 mL of acetone to precipitate the CD compounds. The crude product was purified by the size exclusion column chromatography on Tosoh TSKgel α-2500 and α-3000, eluted with water, to give the α-CD−*β*-CD hetero-dimer in 17% yield.

^{1}H NMR (DMSO-d_6, 30 °C, 270 MHz): *δ* 8.30 (b, 1H, −CON*H*−), 8.17 (d, 1H, −CON*H*−), 7.89 (s, 4H, 2,3-*Ph*), 5.90−5.19 (m, 26H, O(2)*H* and O(3)*H*), 4.93 (m, 1H, C(1)′*H*), 4.82 (s, 11H, C(1)*H*), 4.79 (s, 1H, C(1)″*H*), 4.67−4.29 (m, 11H, O(6)*H*), 4.04−3.50 (m, 39H, C(3)*H*, C(5)*H*, and C(6)*H*), 3.47−3.14 (m, overlaps with HOD, C(2)*H* and C(4)*H*). Elem anal. Calcd for $C_{86}H_{134}N_2O_{65}\cdot 11.0H_2O$: C, 42.43; H, 6.46; N, 1.15. Found: C, 42.25; H, 6.41; N, 1.35. MALDI-TOF MS (*m*/*z*): 2252.6 ([M + Na]$^+$).

Preparation of Hetero-Guest Dimers (Scheme 7).

(1) Preparation of *tert*-Boc-aminocinnamic Acid. *p*-Aminocinnamic acid was dissolved in 20 mL of dioxane and 10 mL of 1 M aq NaOH and stirred at 0 °C for 30 min. To the mixture solution was added a dioxane (10 mL) solution of (*tert*-Boc)$_2$O (2.4 g, 11 mmol) at 0 °C and stirred 12 h. The mixture solution was neutralized by the addition of hydrochloric acid solution (pH 3). The product was extracted with ethyl acetate, and the separated organic layer was washed with water three times. The separated organic layer was dried under sodium sulfate and evaporated under reduced pressure to give the product (0.61 g) in 23% yield.

^{1}H NMR (DMSO-d_6, 30 °C, 270 MHz): *δ* 9.5 (s, 1H, −CON*H*−), 7.6 (d, 1H, −CH═C*H*−), 7.5 (d, 2H, 2-*Ph*), 7.4 (d, 2H, 3-*Ph*), 6.38 (d, 1H, −C*H*═CH−), 1.5 (s, 9H, *t-Bu*).

(2) Preparation of Boc-aminocinnamamide Pyridine. 4-Aminopyridine (1.20 g, 12.7 mmol) and *tert*-Boc-aminocinnamic acid (2.80 g, 10.6 mmol) were allowed to react with DCC (2.19 g, 10.6 mmol) and HOBt (1.43 g, 10.6 mmol) in 30 mL of DMF at 0 °C

for an hour. After stirring for an hour, it was allowed to warm to room temperature and stir for 2 days. After the prescribed time, the precipitate, dicyclohexylurea, was removed by centrifuge. The supernatant solution was poured into 300 mL of acetone to precipitate the crude *tert*-Boc-aminocinnamamide pyridine. The product was washed with acetone three times and dissolved in 30 mL of ethyl acetate. The separated organic layer was washed with water three times and evaporated under reduced pressure to give the product (2.03 g) in 56% yield.

^{1}H NMR (DMSO-d_6, 30 °C, 270 MHz): δ 10.5 (s, 1H, −CON*H*−Py), 9.55 (s, 1H, −CON*H*−Ph), 8.4 (d, 2H, *Py*), 7.4−7.7 (m, 7H, *Ph*, *Py*, −CH═C*H*−Ph), 6.8 (d, 1H, −C*H*═CH−), 1.55 (s, 9H, *t-Bu*). FAB MS (*m*/*z*): 340.0 ([M + Na]$^+$).

(3) Preparation of Adamantyl-*N*-methyl Ketone *tert*-Boc-aminocinnamamide Pyridine (G-*t*-Boc). *tert*-Boc-aminocinnamamide pyridine (200 mg, 1.77 mmol) and 1-adamantyl bromomethyl ketone (455 mg, 1.77 mmol) were allowed to react in acetone (20 mL) at 60 °C for 3 h. After being cooled to room temperature, the yellow precipitate was collected by filtration and washed with diethyl ether three times to give the crude product. The resulting residue was recrystallized from 2-propanol/water (9/1) at 0 °C in 59% yield (181 mg).

^{1}H NMR (D_2O, 30 °C, 270 MHz): δ 8.22 (d, J = 7.8 Hz, 2H, *2-Py*), 8.04 (d, J = 7.7 Hz, 2H, *3-Py*), 7.65 (d, J = 15.1 Hz, 1H, −CH═C*H*−Ph), 7.58 (d, J = 8.4 Hz, 2H, *2-Ph*), 7.35 (d, J = 8.4 Hz, 2H, *3-Ph*), 6.59 (d, J = 15.9 Hz, 1H, −C*H*═CH−Ph), 2.01 (b, 3H, adamantane), 1.85 (b, 6H, adamantane), 1.72 (q, 6H, adamantane), 1.45 (s, 9H, *t-Bu*). Elem anal. Calcd. for $C_{31}H_{38}BrN_3O_4 \cdot 1.3H_2O$: C, 60.06; H, 6.60; N, 6.78. Found: C, 59.82; H, 6.25; N, 6.55. FAB MS (*m*/*z*): 517.3 ([M − Br]$^+$).

(4) Preparation of Adamantyl-*N*-methyl Ketone Aminocinnamamide Pyridine (G-NH_2). Adamantyl-*N*-methyl ketone Boc-aminocinnamamide pyridine (G-*t*-Boc) (66.6 mg, 0.19 mmol) was dissolved in 20 mL of 6 M HCl and 1,4-dioxane and stirred at room temperature for an hour. After an hour, the mixture was evaporated to dryness under reduced pressure, and the crude product was washed with acetone and diethyl ether three times. The precipitate was dried in vacuo to give the crude product. The resulting residue was recrystallized from 2-propanol/water (9/1) at 0 °C in 52% yield (42 mg).

^{1}H NMR (D_2O, 30 °C, 270 MHz): δ 8.30 (d, J = 7.3 Hz, 2H, *2-Py*), 8.11 (d, J = 7.6 Hz, 2H, *3-Py*), 7.78 (d, J = 15.1 Hz, 1H, −CH═C*H*−Ph), 7.71 (d, J = 8.9 Hz, 2H, *2-Ph*), 7.27 (d, J = 8.6 Hz, 2H, *3-Ph*), 6.76 (d, J = 15.7 Hz, 1H, −C*H*═CH−Ph), 5.65 (s, 2H, CO−CH_2−), 2.00 (b, 3H, adamantane), 1.89 (b, 6H, adamantane), 1.72 (q, 6H, adamantane). Elem anal. Calcd for $C_{26}H_{30}BrN_3O_2 \cdot 0.4H_2O$: C, 62.00; H, 6.16; N, 8.34. Found: C, 61.97; H, 6.19; N, 8.30. MALDI-TOF MS (*m*/*z*): 416.2 ([M − Br]$^+$).

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Supporting Information Available: ROESY NMR spectra for the α-CD−β-CD hetero-dimer and adamantane hetero-cinnamate guests (G-*t*-Boc and G-NH_2) are shown. This material is available free of charge via the Internet at http://pubs.acs.org.

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