Supporting Information for:

Formation of Supramolecular Polymer with Alternating α-, β-Cyclodextrin Units Using Conformational Change Induced by Competitive Guests

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Methods

General. The $^1$H NMR spectra were recorded on a 270 MHz JEOL JNM EX-270 spectrometer at 30 °C. Chemical shifts were referenced to the external standard in the solvent ($\delta$=1.96 ppm for acetonitrile in D$_2$O). 2D NMR (mixing time for each modified CDs and 1:1 complexes are 600 msec and 200 msec respectively) and pulsed gradient NMR experiments (PFG NMR) were obtained with D$_2$O as the solvent at 30 °C on a 600 MHz VARIAN-UNITY-600 NMR spectrometer. BPPSTE pulse sequence is applied for PFG NMR measurements and the pulsed gradient strength was increased from 300 to 25,000 (gauss/cm). The time separation between pulsed field gradients and their duration were applied the values of 0.10 and 1.1 x $10^{-3}$ (s). FT-IR measurements were performed on a JASCO FT/IR-410 spectrometer. KBr was used as the dispersant. The analytical size exclusion chromatography and preparative size exclusion chromatography were carried out with TOHSO CCP&8010 system (column: TSKgel $\alpha$-2500 and TSKgel $\alpha$-3000; elution: methanol/water=40/60). The Circular dichroism spectra and UV spectra were recorded on a JASCO J820 spectrometer in water with 0.1 cm cell at room temperature. Positive-ion matrix assisted laser desorption ionization time of flight (MALDI-TOF) mass spectrometry experiments were performed using a Shimadzu/KRATOS Axima CFR V2.2.1 mass spectrometer. $\alpha$-cyano-4-hydroxycinnamic acid and insulin were used as the standard materials. Vapor pressure osmometry measurements were used KNAUER No. A0280 vapor osmometer at 40 °C. NaCl aqueous solution and $\alpha$-CD were used as the instruments standard. The second virial coefficients were neglected due to rough estimation of the molecular weight. Dynamic Light Scattering measurements are
performed in water with cylindrical quartz cell on ALV/DLS/SLS-5000 light scattering system equipped by an ALV-5000 multiple $\tau$ digital correlator by using vertically polarized light with the wavelength $\lambda_0$ of 532 nm emitted from a Nd:YAG laser (model 532, Cohrent) at 30 °C.

**Materials.**

$\alpha$-CD, sodium hydroxide (NaOH), dicyclohexyl carbodiimide and 1-hydroxybenzotriazole were obtained from Nacalai Tesque, Inc. *trans*-p-Aminocinnamic acid, 1-adamanetane carbonyl chloride and 6-aminoheXanoic acid were obtained by Tokyo Kasei Kogyo, CO., Lmd. Di-tert-butyl-dicarbonate, dimethyl sulfoxide (DMSO)-$d_6$, and D$_2$O were purchased from Aldrich.

**Synthesis.**

**1-Adamantanamid hexanoic acid (AdHex-OH).** 1-Adamanetane carbonyl chloride (3.0 g, 1.5 x 10$^{-2}$ mol) in THF (10ml) was added to 1.27 M NaOH aqueous solution (30ml) of 6-aminoheXanoic acid (3.0 g, 2.3 x 10$^{-2}$ mol). The solution was stirred for 2 h at 0 °C. The solution was adjusted pH = 3 with a few drops of 2N HCl aqueous solution. After the extraction with Et$_2$O, the Et$_2$O solution was dried with sodium sulfate and evaporated to give 3.9 g of the desired product. (Yield 98%). $^1$H-NMR (DMSO-$d_6$, 270MHz): $\delta$ 7.52(t, 1H, -NH-), $\delta$ 3.00 (q, 2H, $\varepsilon$-H), 2.16 (t, 2H, $\alpha$-H), 1.93 (s, 3H, adamantane), 1.72 (s, 6H, adamantane), 1.64 (s, 6H, adamantane), 1.47 (s, 2H, $\delta$-H), 1.36 (s, 2H, $\beta$-H), 1.20 (s, 2H,
γ-H). m.p.: 118 °C.

**p-tert-Butoxy cinnamic acid (p-tert-BocCiOH).** *trans-p*-Aminocinnamic acid (1.63 g, 1.0 x 10^{-2} mol) in dioxane (10 ml) was added to 0.5 M NaOH aqueous solution (10 ml). Di-tert-butyl-dicarbonate (2.37 g, 1.1 x 10^{-2} mol) was added to the solution at 0 °C. The reaction was carried out with stirring for 6 h at 0 °C. Then, the solution was added citric acid and ethyl acetate (30 ml). After the extraction three times, the ethyl acetate was dried with sodium sulfate and evaporated under vacuum to give 2.80 g of the desired product. (Yield: 98 %). ¹H NMR (DMSO-d$_6$, 270 MHz): δ 9.54 (s, 1H, -NH-), δ 7.56 (d, 1H, 3-H of phenyl), 7.48 (d, 1H, Ph=CH-), 7.48 (d, 1H, 2-H of phenyl), 6.36 (d, 1H, =CH-CO), 1.47 (s, 1H, CH$_3$-). M.p. 204 °C.

**Mono-6-deoxy-6-amino-β-CD (6-NH$_2$-β-CD), Mono-3-deoxy-6-amino-α-CD (3-NH$_2$-α-CD).** These compound were prepared according to the literature previously reported.$^{1,2}$
$^1$H NMR spectra

Figure S1 shows the 270MHz $^1$H NMR spectrum of 3-AdHexNH-α-CD in DMSO-$d_6$ solution.

Figure S1. 270MHz $^1$H NMR spectrum of 3-AdHexNH-α-CD in DMSO-$d_6$. 
Figure S2 shows the 270MHz $^1$H NMR spectrum of 6-$p$-BocCiNH-β-CD in DMSO-$d_6$ solution.

*Figure S2. 270MHz $^1$H NMR spectrum of 6-$p$-BocCiNH-α-CD in DMSO-$d_6$.***
2D ROESY NMR spectra

Figure S3 shows the 600MHz 2D ROESY NMR spectrum of 3-AdHexNH-α-CD in D$_2$O solution at 5 mM. Only the correlations of glucose unit in CD were observed. Since no concentration dependency was observed in the $^1$H NMR spectra, 3-AdHexNH-α-CD does not form intermolecular complexes in D$_2$O solution.

**Figure S3.** 600MHz 2D ROESY NMR spectrum of 3-AdHexNH-α-CD (5 mM) in D$_2$O (mixing time = 600 msec).
Figure S4 shows the 2D ROESY NMR spectrum of 6-\textit{p}-\textit{t}BocCiNH-\textit{β}-CD in D\textsubscript{2}O solution at 5 mM. The correlations between the phenyl ring of the cinnamoyl part and inner protons of CD were observed. The observed C(1)H protons are widely dispersed in the range from 4.8 ppm to 5.2 ppm. Ikeda and Ueno et al. reported that if the substituent part at 6-positions of \textit{β}-CD is included or fixed near the rim of its CD cavity, the dispersed anomeric protons are observed due to the reduction of the sevenfold symmetry of the modified \textit{β}-CD respectively.\textsuperscript{3} Since no concentration dependency was observed in the \textsuperscript{1}H NMR spectra (Figure 1), 6-\textit{p}-\textit{t}BocCiNH-\textit{β}-CD was found to form intramolecular complexes in D\textsubscript{2}O solution.

![Figure S4](image)

**Figure S4.** 600MHz 2D ROESY NMR spectrum of 6-\textit{p}-\textit{t}BocCiNH-\textit{β}-CD (5 mM) in D\textsubscript{2}O (mixing time = 600 msec).
Figure S5 shows the 600MHz 2D NMR spectrum of 3-AdHexNH-α-CD (5 mM) in D$_2$O solution with 6-\textit{p}-BocCiNH-β-CD (5 mM). The correlations of adamantane protons–inner protons of CD part and \textit{t}Boccinamoyl part–inner protons CD part were observed.

\textbf{Figure S5.} 600MHz 2D ROESY NMR spectrum of 3-AdHexNH-α-CD (5 mM) and 6-\textit{p}-BocCiNH-β-CD (5 mM) in D$_2$O (mixing time = 200 msec).
VPO measurements

Figure S6 shows the molecular weight of the complexes as a function of concentration estimated by vapor pressure osmometry measurements. The molecular weight of the complexes increased with an increase in the concentrations, and reached about 10,000 at 10 mM.

![Figure S6](image)

**Figure S6.** Effects of concentrations on the molecular weight of 3-AdHexNH-α-CD and 6-p'-BocCiNH-β-CD complexes at 40 °C.

Circular dichroism spectroscopy

Figure S7a shows the circular dichroism spectrum of 6-p'-BocCiNH-β-CD at 0.5 mM in an aqueous solution. The spectrum shows an induced circular dichroism (ICD) signals with a negative Cotton effect peak (-23.9 mdeg) in 250-350 nm wavelength range, corresponding to the 1L_a (long axis) transition bands of p'-BocCi part. Since intrinsic Cotton effects of cyclodextrins are observed below 220 nm wavelength, the observed circular dichroism bands in 220-350 nm wavelength region essentially can be assigned to
the circular dichroism bands induced by the inclusion of the \( p\)-BocCi part with \( \beta\)-CD. According to the theoretical treatment by Kodaka et al., the observed negative Cotton effect peak is ascribable to the fact that the \( ^1\)La transition moment (long axis) of \( p\)-BocCi part is at a considerably tilt from a \( \beta\)-CD axis to form self-inclusion complexes (Figure S7b).

When an excess amount of 1-AdCA is added to this 0.5 mM aqueous solution of 6-\( p\)-BocCiNH-\( \beta\)-CD, the negative Cotton effect peak decreased (from -23.9 mdeg to -7.98 mdeg), indicating that the \( p\)-BocCi part is exposed into water to be parallel to the CD axis by inclusion with 1-AdCA \((K_a = 10^5)\) (Figure S7c). Moreover, after an addition of an excess amount of \( \alpha\)-CD to 6-\( p\)-BocCiNH-\( \alpha\)-CD–1-AdCA aqueous solution, the observed negative Cotton effect peak increased (from -7.98 mdeg to -12.8 mdeg), indicating that the \( p\)-BocCi part is included in \( \alpha\)-CD cavity with a slantwise state to form 6-\( p\)-BocCiNH-\( \beta\)-CD–1-AdCA–\( \alpha\)-CD heterocomplexes (Figure S7d). The ICD signal of 6-\( p\)-BocCiNH-\( \beta\)-CD at 0.5 mM with 3-AdHexNH-\( \alpha\)-CD at 0.5 mM in aqueous solution showed a negative Cotton effect peak (–35.8 mdeg), which obviously indicates the fact that the \( \text{Boccinnamoyl} \) part is exposed to water by the inclusion of the adamantane part of 3-AdHexNH-\( \alpha\)-CD is included in another \( \alpha\)-CD cavity.
Figure S7. Circular dichroism spectra of 6-p-^2^BocCiNH-β-CD in water at 0.5 mM (blue line), 0.5 mM of 6-p-^2^BocCiNH-β-CD + 1-AdCA (brown line), 0.5 mM of 6-p-^2^BocCiNH-β-CD + 1-AdCA + α-CD (green line) and 6-p-^2^BocCiNH-β-CD at 0.5 mM + 3-AdHexNH-α-CD at 0.5mM (red line) (a), schematic structure of 6-p-^2^BocCiNH-β-CD (b), 6-p-^2^BocCiNH-β-CD + 1-AdCA complex (c), 6-p-^2^BocCiNH-β-CD + 1-AdCA + α-CD complex (d) and 6-p-^2^BocCiNH-β-CD + 3-AdHexNH-α-CD complex (e).
The $^1$H NMR spectra of 6-$p$-BocCiNH-β-CD with competitive guest and host molecules.

The 270MHz $^1$H NMR spectrum of 6-$p$-BocCiNH-β-CD in D$_2$O solution is shown in Figure S8a. The observed spectrum shows the broadened signals of $p$-BocCi part in comparison with that of DMSO-$d_6$ solution in Figure S2, indicating that the substitution part is included in CD cavity in D$_2$O solution. When 1-AdCA was added to D$_2$O solutions of 6-$p$-BocCiNH-β-CD (5.0 mM), the $^1$H NMR spectrum of the cinnamoyl part and the Boc part of 6-$p$-BocCiNH-β-CD showed peak-shifts and a well resolved peaks, indicating that the cinnamoyl group was exposed to D$_2$O solution (Figure S8b). When an excess amount of α-CD was added into this solution, the $^1$H NMR spectra of the cinnamoyl group showed shifts and broadening (Figure S8c), although there are no changes when an excess amount of α-CD was added to a D$_2$O solution of 6-$p$-BocCiNH-β-CD in the absence of 1-AdCA (Figure S8d). These results strongly indicate that the $p$-BocCi part was included in α-CD cavity. As can be seen in Figure S8d, the spectrum is extremely similar to that of 3-AdHexNH-α-CD and 6-$p$-BocCiNH-β-CD mixture solution in Figure 1c, indicating the alternating supramolecular complexes formed by 6-$p$-BocCiNH-β-CD and 3-AdHexNH-α-CD in D$_2$O solution.

When a twice as large amount of 6-$p$-BocCiNH-β-CD (10.0 mM) was added to 3-AdHexNH-α-CD (5.0 mM) in D$_2$O solution, the signals of adamantane part showed no change, indicating that all adamantane groups are included in β-CD cavities with a 1:1 ratio at 5.0 mM (Figure S9).
Figure S8. 270MHz $^1$H NMR spectra of 6-p-tert-BocClOH (a), 6-p-tert-BocClOH + 1-AdCA (b), 6-p-tert-BocClOH + 1-AdCA + $\alpha$-CD complex (c) and 6-p-tert-BocClOH + $\alpha$-CD complex (d) in D$_2$O.

Figure S9. 270MHz $^1$H NMR spectra of 3-AdHexNH-$\alpha$-CD (5.0 mM) + 6-p-tert-BocClOH-$\beta$-CD (5.0 mM) (a) and 3-AdHexNH-$\alpha$-CD (5.0 mM) + 6-p-tert-BocClOH-$\beta$-CD (10.0 mM) (b) in D$_2$O solution.
These data strongly support the results of VPO measurements, which showed the formation of supramolecular polymers formed by 6-p'-BocCiNH-β-CD and 3-AdHexNH-α-CD.

When the aqueous solution of supramolecular polymers at 40 mM was evaporated, the white powder was stably isolated. This white powder would be a high-ordered supramolecular polymer formed in the solid state. Now we investigate the detailed structure of this supramolecular polymer in the solid state.

References

