Formation of supramolecular isomers; poly[2]rotaxane and supramolecular assembly†

Atsuhisa Miyawaki, Masahiko Miyauchi, Yoshinori Takashima, Hiroyasu Yamaguchi and Akira Harada*

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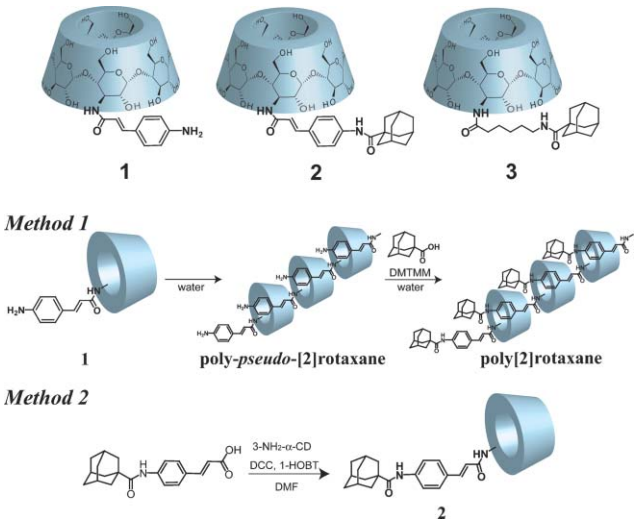
Poly[2]rotaxane and supramolecular assembly have been prepared by modified cyclodextrins bearing an adamantyl group in an aqueous medium.

Cooperative interaction plays an important role in controlling the process of molecular recognition and the formation of supramolecular structures.[1,2] Controlling the process of molecular recognition and the formation of supramolecular structures provides useful applications for developing unique functions. There are many reports on controlling the formation of supramolecular structures using external stimuli such as pH,[3] redox,[4] light[5] *etc.*, by adjusting the space between recognition moieties,[6] stoichiometry[7] or by chemical modification.[8] Cyclodextrins (CDs) are known to form complexes with organic compounds in aqueous solutions.[9] Especially, adamantane derivatives form 2 : 1 inclusion complexes with α-CD[10] and are often utilized as steric stoppers for rotaxanes having α-CD.[11] To control the formation of supramolecular structures between supramolecular assembly and poly[2]rotaxane, adamantane derivatives are suitable for α-CD derivatives as a guest and a sterically hindered group, respectively.

Previously, formation of supramolecular complexes using host–guest interactions of CDs was reported.[12] However, to the best of our knowledge, there are no reports on the formation of CD based self-assembled supramolecular complexes and mechanically locked supramolecules consisting of the same components. Herein, we report our successful efforts to control the formation of poly[2]rotaxane and novel supramolecular assembly from the same components under different reaction conditions.

After synthesizing cinnamamide-α-CDs (**1**,**2** and **3**), we investigated the formation of supramolecular complex in aqueous solutions. Cinnamamide-α-CDs (**1**,**2** and **3**) showed concentration dependent peak shifts by ^{1}H NMR studies, indicating the formation of supramolecular complexes in aqueous solutions. After detailed characterization by 2D NMR studies, it was found that compound **1** forms linear poly-*pseudo*-[2]rotaxane.[13] To prepare a stable supramolecular complex, poly[2]rotaxane was synthesized by the reaction of preorganized poly-*pseudo*-[2]rotaxane with adamantane carboxylic acid as a sterically hindered group as shown in Method 1 (Scheme 1). The MALDI-TOF mass spectrum of poly[2]rotaxane showed polymeric species up to approximately 10,000 (Fig. 1). The interval between signals



Scheme 1

corresponds to the molecular weight of **1** with the adamantyl group as a monomer. On the other hand, the compound **2** prepared by Method 2 did not show polymeric species. These results indicate that poly[2]rotaxane forms a stable supramolecular complex due to the adamantyl groups.

As previously mentioned, although the adamantane derivatives are sterically hindered groups for the cavity of α-CD, they form inclusion complexes with α-CD. Therefore, compound **2** may form a supramolecular assembly in aqueous solutions. To determine the properties and structure of the supramolecular assembly of **2**, circular dichroism (cd) measurements were carried out. Fig. 2(a) shows the cd spectra of **2** in aqueous solution and in methanol. A

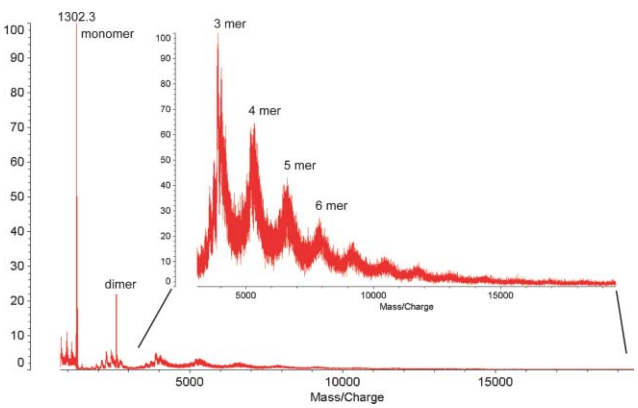


Fig. 1 MALDI-TOF mass spectrum of poly[2]rotaxane.

Department of Macromolecular Science, Graduate School of Science, Osaka University, Toyonaka, Osaka 560-0043, Japan.
E-mail: harada@chem.sci.osaka-u.ac.jp; Fax: +81 6 6850 5445; Tel: +81 6 6850 5445

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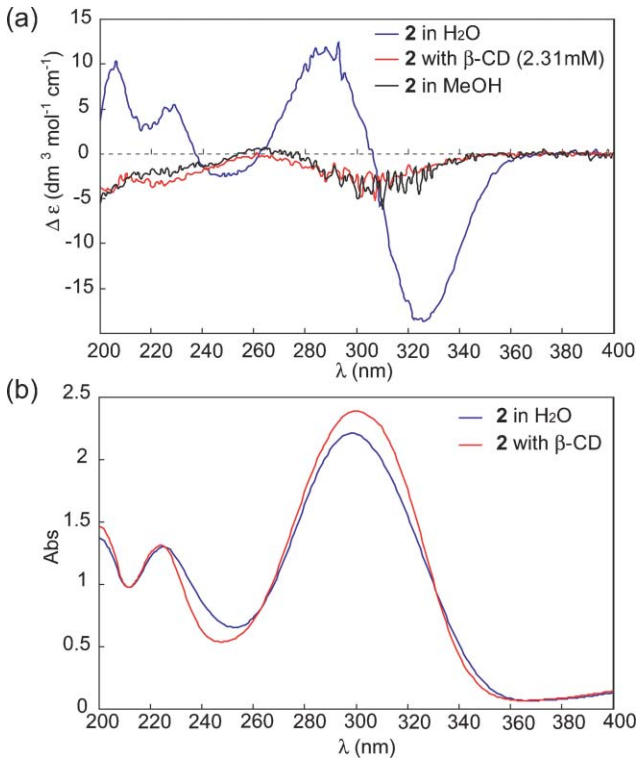

Fig. 2 Circular dichroism spectra (a) and UV-vis spectra (b) of **2** in water (blue), addition of β-CD (red) and in methanol (black).

negative–positive Cotton band around 300 nm corresponding to the ^{1}La transition band of the cinnamamide moiety was observed in aqueous solution (blue line). This Cotton band is assigned to the exciton–coupling interaction. It is noted that two or more excitons are located in relatively close distance, indicating the formation of helical supramolecular assembly with negative chirality. On the other hand, no significant Cotton band was observed in methanol (black line) because of the dissociation of this supramolecular assembly. On addition of β-CD as a competitive host for an adamantyl group[9] to the aqueous solution of **2**, the Cotton band disappeared as shown by the red line (Fig. 2 (a)) and the absorption band around 300 nm showed a hyperchromic effect (Fig. 2(b)). We suppose that the cooperativity effect between hydrophobic host–guest interaction and π–π stacking interaction plays an important role in the formation of the supramolecular assembly of **2**.

The ^{1}H NMR spectra of **2** showed that the protons of the adamantyl group and the cinnamamide group shifted to upfield with an increase in the concentrations. After addition of β-CD, the protons of an adamantyl group shifted to upfield (protons a and c) and downfield (proton b), and the protons of the cinnamamide group significantly shifted to downfield. These resonance shifts suggest that the adamantyl group is included in the β-CD cavity and that π–π stacking interaction between cinnamamide moieties disappeared. The ROESY NMR spectrum indicated the formation of a supramolecular assembly. The inner protons C3(H) of α-CD, which are located in the wider rim, showed the ROEs correlations to protons a, b and c of the adamantyl group, whereas the inner protons C5(H) of α-CD, which are located in the narrower rim, showed the ROEs correlations to protons a and b

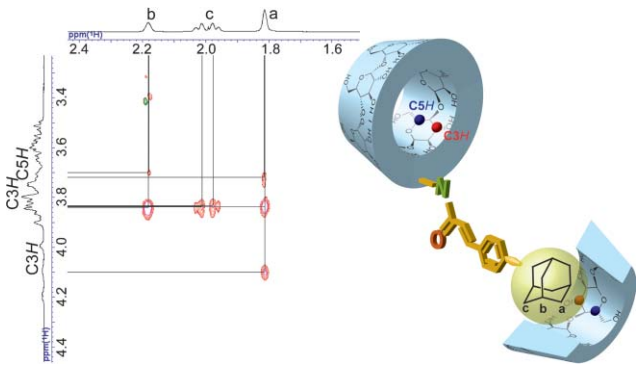

Fig. 3 Partial 2D ROESY NMR spectrum of **2** in D_2O at 30 °C (600 MHz, mixing time 200 ms).

(Fig. 3). These observations indicate that the adamantyl group is shallowly included from the wider rim of α-CD cavity. These results are in agreement with the data from cd spectrometry measurement.

To estimate the hydrodynamic volume of the supramolecular assembly, self-diffusion coefficients (D_s) were determined by the pulsed field gradient spin-echo NMR measurement.[14] Compound **3**, which has no aromatic group, was used as a reference. Although the D_s of **3** slightly decreased with an increase in the concentrations and reached 2.37×10^{-6} cm^2 s^{-1} at 40 mM, that of **2** significantly decreased and reached 1.36×10^{-6} cm^2 s^{-1} at 40 mM. It should be noted that the hydrodynamic radius (R_h) of **2** is larger than that of **3** over the whole concentration range. It is thought that the formation of the larger supramolecular complex from **2** is caused by not only the host–guest interaction between the adamantyl group and the α-CD cavity but also the π–π stacking interaction between the cinnamamide group. The D_s of 2-cinnamoyl-α-CD (2-CiO-α-CD), which formed a double threaded dimer determined by single crystal X-ray analysis showed saturation and reached 2.30×10^{-6} cm^2 s^{-1} (R_h = 0.96 nm) in the lower concentration region (10–30 mM).‡ On the other hand, the D_s of **2** continuously decreased with the concentrations, showing 1.36×10^{-6} cm^2 s^{-1} (R_h = 1.67 nm) at 40 mM. These results suggest that compound **2** does not form dimeric assembly but oligomeric assembly in an aqueous solution. The electrospray ionization (ESI) mass spectrum provides direct evidence to support the formation of supramolecular assembly (Fig. 4). It shows polymeric species up to approximately 5 mer. Intervals between signals corresponding to the molecular weight of **2** as a monomer unit are observed.

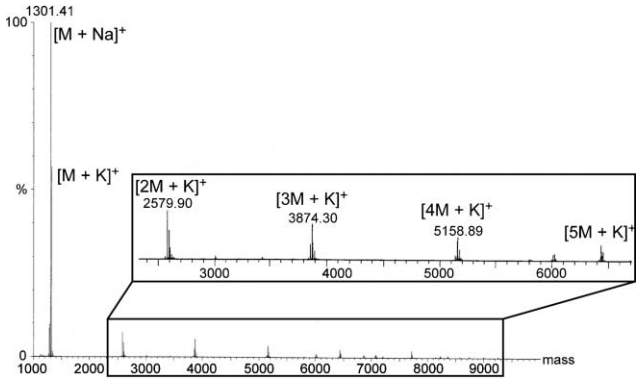

Fig. 4 ESI-TOF mass spectrum of **2** (positive mode).

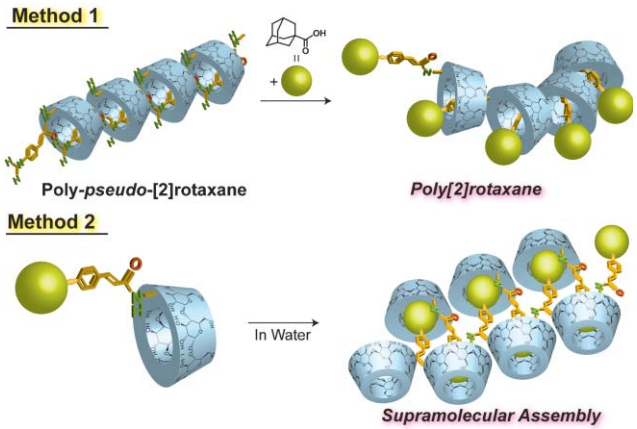

Fig. 5 Proposed supramolecular structures formed by cinnamamide α-CD bearing an adamantyl group prepared by Method 1 and Method 2.

Consequently, the proposed supramolecular structures formed by cinnamamide-α-CD bearing an adamantyl group prepared by Method 1 or Method 2 are illustrated in Fig. 5.

In conclusion, we have prepared poly[2]rotaxane and supramolecular assemblies formed from the same building blocks using different preparation methods in an aqueous medium. Although each unit of poly[2]rotaxane and supramolecular assembly is the same building block, the structure of each supramolecular complex was revealed to be quite different. This methodology should be applicable to control the process of molecular recognition and the formation of supramolecular structures.

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Notes and references

‡ The R_h value was calculated using the Stokes–Einstein equation. The D value for 2-CiO-α-CD was only observed up to 32 mM because above this concentration powder crystal was formed. The D value corrected by viscosity is listed in the supporting information† (Table S1).

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