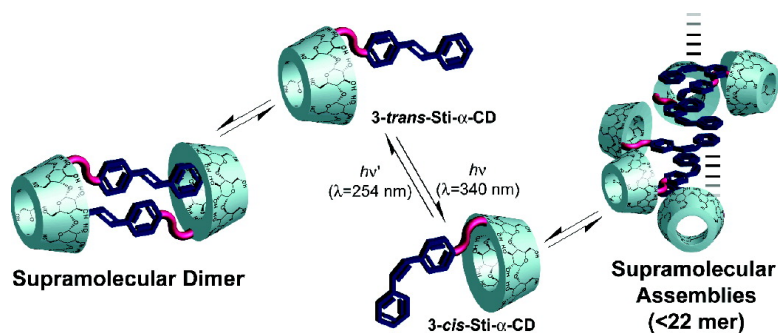


## Switching between Supramolecular Dimer and Nonthreaded Supramolecular Self-Assembly of Stilbene Amide- $\beta$ -Cyclodextrin by Photoirradiation

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## Switching between Supramolecular Dimer and Nonthreaded Supramolecular Self-Assembly of Stilbene Amide- $\alpha$ -Cyclodextrin by Photoirradiation

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In biological systems, protein localization and assembly are controlled by reversible interactions of specific controlled elements, which have been exploited with supramolecular interactions for the study of signal transduction,<sup>1,2</sup> tubulin stabilization,<sup>3</sup> and transcription factors.<sup>4,5</sup> In the field of supramolecular chemistry, some research groups demonstrated that molecular recognition for small guest molecules was controlled by structural changes of host molecules.<sup>6–8</sup> More sophisticated supramolecular assemblies have been achieved by controlling assembly and disassembly using external stimuli such as light, environment, and exogenous ligands.<sup>9–15</sup> We have undertaken the structural control of supramolecular complexes by photoirradiation.<sup>16</sup> Stilbene derivatives are well-known to show the photoinduced isomerization, which are isomerized from the *trans* form to the *cis* form and from the *cis* form to the *trans* form under irradiation with UV and visible light, respectively.<sup>17</sup> We have chosen stilbene compounds because the association constant of  $\alpha$ -cyclodextrin (CD) for *trans*-stilbene is larger than that for *cis*-stilbene (*trans*-stilbene,  $K_a = 1260 \text{ M}^{-1}$ ; *cis*-stilbene,  $K_a = 360 \text{ M}^{-1}$ ).<sup>18</sup> Herein, we have demonstrated photochemical switching of supramolecular structures of 3-stilbene amide- $\alpha$ -CD (3-Sti- $\alpha$ -CD).

The  $^1\text{H}$  NMR spectra of 3-*trans*-Sti- $\alpha$ -CD showed that the peaks of protons of 3-*trans*-Sti- $\alpha$ -CD shifted with an increase in the concentration, indicating the formation of supramolecular complexes in aqueous solutions. However, no peak shift was observed in organic media due to the dissociation of supramolecular complexes. The 2D ROESY NMR of 3-*trans*-Sti- $\alpha$ -CD in an aqueous solution showed that the protons (a–d) of the stilbene amide group correlated to inner protons (C(3)-H and C(5)-H) of  $\alpha$ -CD (Figure 1). We have obtained a single crystal of 3-*trans*-Sti- $\alpha$ -CD that is suitable for X-ray crystallographic analysis. The X-ray crystallographic analysis showed the formation of a double-threaded dimer (Figure 2). This result is in an agreement with the 2D ROESY NMR experiments.

After photoirradiation with visible light ( $\lambda = 340 \text{ nm}$ ), 85% of 3-*trans*-Sti- $\alpha$ -CD isomerized to 3-*cis*-Sti- $\alpha$ -CD (*trans*:*cis* = 15:85). Although we had expected that 3-*cis*-Sti- $\alpha$ -CD would not show peak shifts because the supramolecular complex of 3-*cis*-Sti- $\alpha$ -CD is supposed to decompose, the protons of 3-*cis*-Sti- $\alpha$ -CD actually showed the peak shifts with an increase in the concentration. The 2D ROESY NMR spectra of 3-*cis*-Sti- $\alpha$ -CD did not show the correlation peaks between inner protons (C(3)H and C(5)H) of  $\alpha$ -CD and protons of the stilbene amide group in aqueous solutions. The UV spectra of 3-*cis*-Sti- $\alpha$ -CD showed a red shift with an increase in the concentration, indicative of the formation of nonthreaded supramolecular self-assembly. The circular dichroism (cd) spectra showed the negative–positive Cotton band around

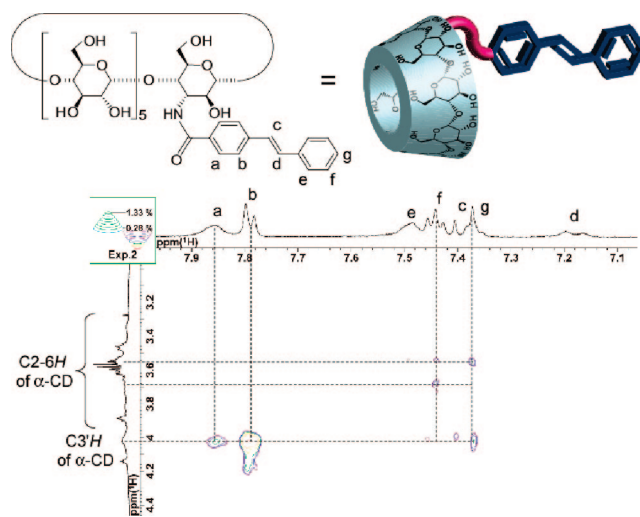


Figure 1. Partial 2D ROESY NMR spectrum of 3-*trans*-Sti- $\alpha$ -CD in  $\text{D}_2\text{O}$  at  $30^\circ\text{C}$  (500 MHz, mixing time = 200 ms).

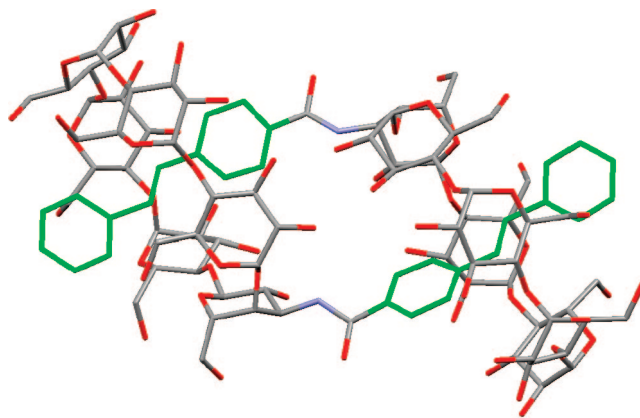
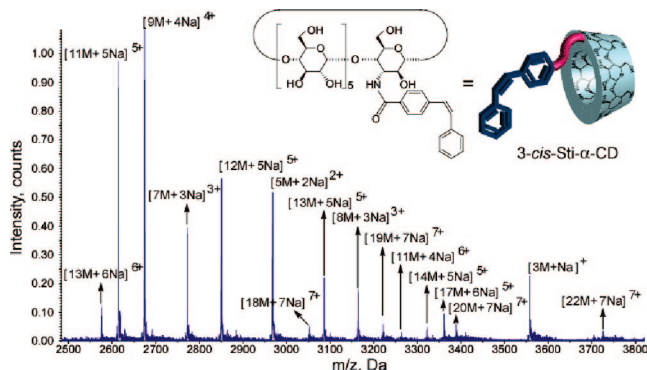


Figure 2. Crystal structure of a double-threaded dimer consisting of 3-*trans*-Sti- $\alpha$ -CD. Carbon and oxygen of  $\alpha$ -CD are shown in gray and red, respectively. Carbon and oxygen of stilbene amide groups are shown in light green.

300 nm in aqueous solutions, corresponding to the transition band of the stilbene amide group. This Cotton band is assigned to the exciton coupling interactions between stilbene amide groups. This result suggests that two or more excitons are located in relatively close distance. In contrast, 3-*cis*-Sti- $\alpha$ -CD did not exhibit the Cotton band in methanol because of the dissociation of these supramolecular assemblies. The mixture of 3-*cis*-Sti- $\alpha$ -CD and  $\beta$ -CD in an aqueous solution showed the positive Cotton band because the *cis*-stilbene amide group is strongly included in the  $\beta$ -CD cavity.<sup>19</sup> These results indicate that 3-*cis*-Sti- $\alpha$ -CD forms nonthreaded



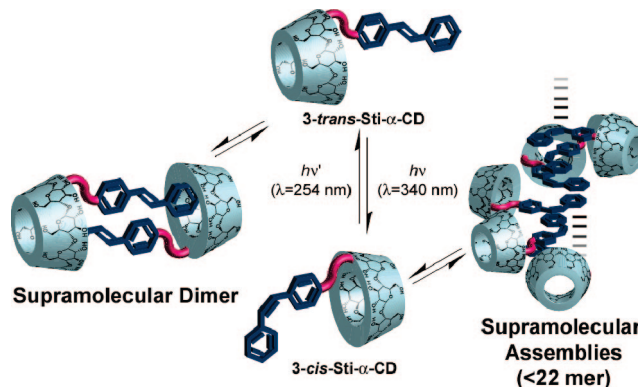
**Figure 3.** Turbo ion spray TOF mass spectrum of 3-*cis*-Sti- $\alpha$ -CD in an aqueous solution.

supramolecular self-assembly by  $\pi$ - $\pi$  stacking interactions between stilbene amide groups.

To estimate the molecular size of the nonthreaded supramolecular self-assembly from 3-*cis*-Sti- $\alpha$ -CD, self-diffusion coefficients ( $D_s$ ) were determined by the pulsed field gradient spin-echo NMR measurements. We have chosen 2-cinnamoyl- $\alpha$ -CD (2-CiO- $\alpha$ -CD) as a reference compound because 2-CiO- $\alpha$ -CD formed a double-threaded dimer, which was proved by single-crystal X-ray analysis. The  $D_s$  of 2-CiO- $\alpha$ -CD showed  $0.23 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1}$  in the lower concentration region (10–30 mM). We are not able to determine the  $D_s$  of 3-*trans*-Sti- $\alpha$ -CD because of a high crystallinity and a low-water solubility. The  $D_s$  of 3-*cis*-Sti- $\alpha$ -CD significantly decreased with an increase in concentration (<60 mM). It should be noted that the hydrodynamic radius of 3-*cis*-Sti- $\alpha$ -CD is larger than that of 2-CiO- $\alpha$ -CD at the whole region of the concentration (see Supporting Information). These results suggest that the size of nonthreaded supramolecular self-assembly from 3-*cis*-Sti- $\alpha$ -CD was larger than that of a double-threaded dimer in aqueous solutions.

The turbo ion spray TOF mass spectrum provides direct evidence of the formation of nonthreaded supramolecular self-assembly. Mass spectrum of 3-*trans*-Sti- $\alpha$ -CD exhibited dimeric species as a major peak, whereas that of 3-*cis*-Sti- $\alpha$ -CD showed polymeric peaks with multivalent species in aqueous solutions (Figure 3). These results indicate that 3-*trans*-Sti- $\alpha$ -CD formed a double-threaded dimer, and 3-*cis*-Sti- $\alpha$ -CD formed a nonthreaded supramolecular self-assembly with around 15mer in 1 mM aqueous solution.

In conclusion, we have succeeded in controlling formation of a double-threaded dimer and that of nonthreaded supramolecular self-assembly consisting of stilbene amide- $\alpha$ -CD by photoirradiation as shown in Figure 4. First, we thought that 3-*trans*-Sti- $\alpha$ -CD would form a supramolecular polymer and then 3-*cis*-Sti- $\alpha$ -CD would decompose it after photoirradiation. The facts are contrary to what we expected. Formations of these supramolecular complexes might be due to  $\pi$ - $\pi$  stacking interactions between stilbene amide groups. These interactions are presumed to inhibit the formation of a supramolecular polymer. Instead, it created a more interesting supramolecular system, in other words, “switching between supramolecular dimer and nonthreaded supramolecular self-assembly”. The unit of  $\alpha$ -CD and the *cis*-stilbene group play important roles to form supramolecular assembly as a hydrophilic and hydrophobic part, respectively. These interactions and environment promote the  $\pi$ - $\pi$  stacking of the *cis*-stilbene group and affect cooperatively the formation of the supramolecular assembly. Now, the photoresponsive properties of supramolecular structures are under investigation.



**Figure 4.** Schematic illustration of switching between supramolecular dimer and nonthreaded supramolecular self-assembly consisting of 3-Sti- $\alpha$ -CD with photoirradiation.

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**Supporting Information Available:** Selected NMR data (1D NMR and ROESY spectrum), the determination of the diffusion coefficient, UV spectra, cd spectra, and turbo ion spray mass spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

## References

- (1) Spencer, D. M.; Wandless, T. J.; Schreiber, S. L.; Crabtree, G. R. *Science* **1993**, *262*, 1019–1024.
- (2) Belshaw, P. J.; Spencer, D. M.; Crabtree, G. R.; Schreiber, S. L. *Chem. Biol.* **1996**, *3*, 731–738.
- (3) Nicolaou, K. C.; Roschangar, F.; Vourloumis, D. *Angew. Chem., Int. Ed.* **1998**, *37*, 2015–2045.
- (4) Minter, A. R.; Brennan, B. B.; Mapp, A. K. *J. Am. Chem. Soc.* **2004**, *126*, 10504–10505.
- (5) Kwon, Y.; Arndt, H. D.; Mao, Q.; Choi, Y.; Kawazoe, Y.; Dervan, P. B.; Uesugi, M. *J. Am. Chem. Soc.* **2004**, *126*, 15940–15941.
- (6) Raymo, F. M.; Stoddart, J. F. Switchable Catenanes and Molecular Shuttles. In *Molecular Switches*; Feringa, B. L., Ed.; Wiley-VCH: Weinheim, Germany, 2001; Sec. 7.
- (7) Shinkai, S.; Shigematsu, K.; Sato, M.; Manabe, O. *J. Chem. Soc., Perkin Trans. 1* **1982**, 2735–2745.
- (8) Mulder, A.; Jukovic, A.; van Leeuwen, F. W. B.; Kooijman, H.; Spek, A. L.; Huskens, J.; Reinhoudt, D. N. *Chem.—Eur. J.* **2004**, *10*, 1114–1123.
- (9) Yang, W.-Y.; Ahn, J.-H.; Yoo, Y.-S.; Oh, N.-K.; Lee, M. *Nat. Mater.* **2005**, *4*, 399–402.
- (10) Sidhaye, D. S.; Kashyap, S.; Sastry, M.; Hotha, S.; Prasad, B. L. V. *Langmuir* **2005**, *21*, 7979–7984.
- (11) Rakotonradany, F.; Whitehead, M. A.; Lebus, A.-M.; Sleiman, H. F. *Chem.—Eur. J.* **2003**, *9*, 4771–4780.
- (12) (a) Hirose, T.; Matsuda, K.; Irie, M. *J. Org. Chem.* **2006**, *71*, 7499–7508.
- (13) (a) Mueller, M.; Zentel, R. *Macromolecules* **1994**, *27*, 4404–4406. (b) Maxein, G.; Zentel, R. *Macromolecules* **1995**, *28*, 8438–8440. (c) Mueller, M.; Zentel, R. *Macromolecules* **1996**, *29*, 1609–1617. (d) Mayer, S.; Maxein, G.; Zentel, R. *Macromolecules* **1998**, *31*, 8522–8525.
- (14) Ciardelli, F.; Fabbri, D.; Pieroni, O.; Fissi, A. *J. Am. Chem. Soc.* **1989**, *111*, 3470–3472. (b) Pieroni, O.; Fissi, A.; Viegi, A.; Fabbri, D.; Ciardelli, F. *J. Am. Chem. Soc.* **1992**, *114*, 2734–2736.
- (15) Ajayaghosh, A.; Praveen, V. K. *Acc. Chem. Res.* **2007**, *40*, 644–656.
- (16) (a) Inoue, Y.; Kuad, P.; Okumura, Y.; Takashima, Y.; Yamaguchi, H.; Harada, A. *J. Am. Chem. Soc.* **2007**, *129*, 6396–6397. (b) Tomatsu, I.; Hashidzume, A.; Harada, A. *J. Am. Chem. Soc.* **2006**, *128*, 2226–2227. (c) Kuad, P.; Miyawaki, A.; Takashima, Y.; Yamaguchi, H.; Harada, A. *J. Am. Chem. Soc.* **2007**, *129*, 12630–12631.
- (17) (a) Irie, M. *Chem. Rev.* **1999**, *100*, 1685–1716. (b) Takeshita, K.; Irie, M. *J. Org. Chem.* **1998**, *63*, 6643–6649. (c) Takeshita, K.; Irie, M. *J. Chem. Soc., Chem. Commun.* **1996**, 1807–1808.
- (18) Herrmann, W.; Wehrle, S.; Wenz, G. *Chem. Commun.* **1997**, 1709–1710.
- (19) Harata, K.; Uedaira, H. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 375–378.

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