J|A|C|S
COMMUNICATIONS

External Stimulus-Responsive Supramolecular Structures Formed by a Stilbene Cyclodextrin Dimer

Paul Kuad, Atsuhisa Miyawaki, Yoshinori Takashima, Hiroyasu Yamaguchi, and Akira Harada*

Department of Macromolecular Science, Graduate School of Science, Osaka University,
1-1 Machikaneyama Toyonaka, Osaka 560-0043, Japan

Received July 11, 2007; E-mail: harada@chem.sci.osaka-u.ac.jp

Stilbene derivatives undergo a reversible trans−cis photoisomerization of their C═C double bond and thus are expected to provide useful applications for optical switching, image storage devices, or molecular function regulation, because of the induced changes of various chemical and physical properties such as absorption spectrum, refractive index, or viscosity. Additionally, cyclodextrins (CD) are known to form inclusion complexes with a variety of organic compounds in aqueous solutions. Therefore, in the field of nanoscience and nanotechnology, CD stilbene derivatives may open the way to machine-like light-switching compounds,[1] where the photoisomerization of the stilbene group can control the inclusion and exclusion of guest molecules.

Some researchers[2,3] reported the preparation of analogue azobenzene bridged bis(β-CD) and studied its photoisomerization and its binding behavior for small guests. However, to the best of our knowledge, bridged bis(β-CD) with a stilbene linker preparation and formation of supramolecular complexes based on this dimer have not been reported yet. Previously, we discussed the formation of supramolecular polymers based on homo- and hetero-CD dimer and various ditopic guests,[4] but these supramolecular structures could not be controlled by an external stimuli. In this Communication, we synthesized a stilbene bridged bis(β-CD) dimer and investigated its photoisomerization in aqueous solutions. Then, the conformational change of supramolecular complexes (pinching-type supramolecular dimer to supramolecular polymer and vice versa) has been controlled by photoirradiation.

β-Cyclodextrin were bound to a stilbene moiety by the reaction of 6-amino-β-CD with trans stilbene-4,4′-dicarboxylic acid disuccinimide ester in DMF to give the trans stilbene bis(β-CD) dimer (Figure 1). Guest dimer, C3, has two adamantyl groups linked by a pyridinium derivative and has been prepared as previously described.[4b] Adamantyl derivatives were chosen since these groups have high association constants with β-CD.[5]

The UV−vis spectra of the trans stilbene bis(β-CD) dimer displayed a strong absorption maximum at 330 nm. Upon irradiation with a monowavelength handy lamp ($\lambda = 365$ nm), the absorption at 330 nm decreased, indicating the isomerization from the trans to the cis form (see Supporting Information, Figure S1). Irradiation at 254 nm of the compound allowed recovering mainly the trans form. The photoisomerization of the stilbene bis(β-CD) dimer is reversible and quantitative: at saturated state, the cis/trans ratios are 88/12 and 15/85.

The ROESY spectrum of the mixture of the trans stilbene bis(β-CD) dimer (2 mM) and the guest dimer C3 (2 mM) showed that the signals of adamantyl protons were correlating with the signals of inner protons of the β-CD (Figure 2). This result indicated the formation of the inclusion complex between CD and adamantyl moiety. The same measurements were carried out with the cis stilbene bis(β-CD) dimer and concluded to a similar host−guest inclusion behavior with C3 guest.

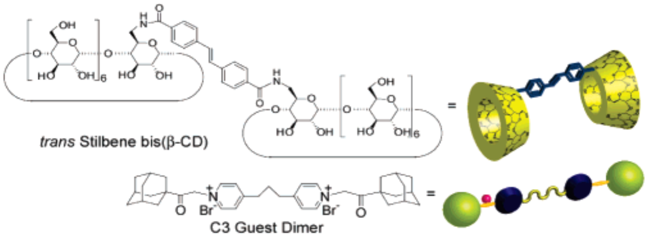


Figure 1. Structures of stilbene bis(β-CD) dimer and C3 guest dimer.

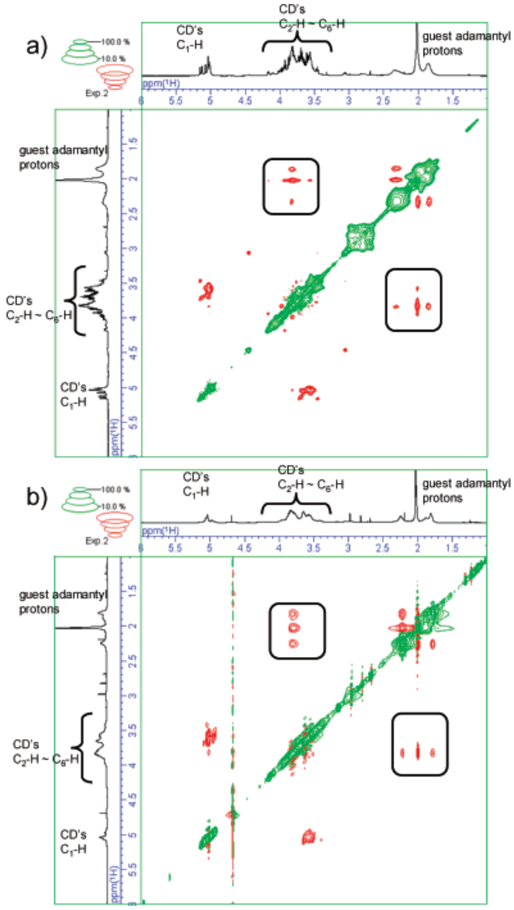


Figure 2. Partial 2D ROESY ^{1}H NMR spectrum of a 1:1 mixture of the C3 guest and the trans (a) and cis (b) β-CD dimer in D_2O at 2 mM at 30 °C.

To get some insight on the structure of the host−guest complex, we determined diffusion coefficients (D) by pulse field gradient (PFG) NMR. Figure 3 shows the D of the trans and cis forms of the host, alone and mixed with the guest. D of the mixture of C3 with trans isomer complex slightly decreased with an increased in

10.1021/ja075139p CCC: $37.00

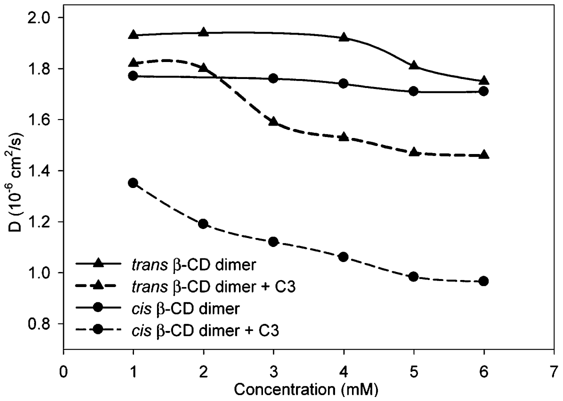


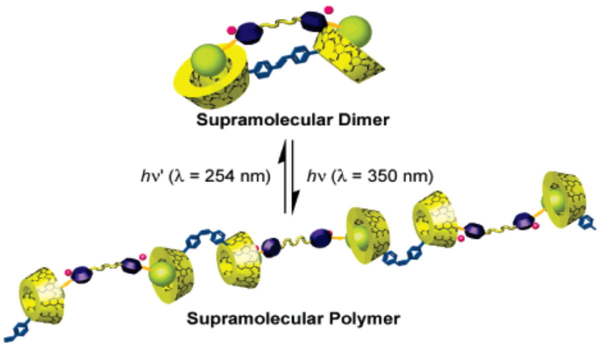
Figure 3. Concentration dependence of the diffusion coefficient values (*D*) of free CD dimer guest (solid line) and 1−1 mixtures of guest C3 dimer with host CD dimer (dash line) in D_2O at 30 °C by NMR. The cis and trans isomers of the guest are respectively represented in blue and red lines.

the concentration, and this value was comparable to that of the host alone, indicative of the formation of 1:1 complexes or small assemblies (hydrodynamic radius, $R_h = 1.51$ nm at 6.0 mM). However, *D* of the guest and cis host mixture was significantly lower than that with the trans isomer at high concentration, indicating a higher R_h (2.39 nm at 6.0 mM)[6] and that cis stilbene bis(*β*-CD) dimer and C3 guest formed a supramolecular polymer. In the ^{1}H NMR spectra, broad proton signals also indicated the formation of supramolecular structure. Remarkably, the upfield shift of the C3 pyridinium protons when mixed with trans host pointed out electron donor−acceptor type interactions and supported the formation of a dimer-type structure. (see Supporting Information, Figure S5)

Association constants between host and guest dimers are in agreement with the PFG NMR measurements. Isothermal titration calorimetry (ITC) experiments have been carried out in aqueous solutions. With three monotopic model guest molecules,[4b] it was shown that the trans and cis CD dimers have similar affinity for these adamantyl derivatives. But concerning the ditopic C3 guest, the association constants were $(1.45 \pm 0.2) \times 10^6$ M^{-1} and $(4.18 \pm 0.3) \times 10^5$ M^{-1}, respectively, for the trans and cis stilbene dimer (see Supporting Information, Table S3). The higher constant for the trans isomer (about three times higher) resulted from a cooperative effect:[7] the ditopic guest is complexed simultaneously by both CD residues of the same host dimer, forming a 1:1 complex. In the case of the cis isomer, a ditopic guest is complexed by two cyclodextrins belonging to two dimers, and it forms a linear and higher-order supramolecular entity with a lower association constant.

To confirm the nanometer-sized molecular assembly, supramolecular dimer or polymer, atomic force microscopy (AFM) measurements were performed. When the sample was made from a 1:1 mixture of trans host and C3 guest, only small objects that were approximately 30 nm in overall length could be detected. In contrast, nanometer-sized supramolecular wires, that were about 350 nm in overall length, were observed on mica substrate in the case of the cis isomer (see Supporting Information, Figure S2). Therefore, the AFM measurements also pointed out different supramolecular structures for the trans and cis stilbene bis(*β*-CD) dimer mixed with C3 guest. Consequently, the proposed conformation change of cis stilbene bis(*β*-CD) dimer and C3 adamantyl dimer in aqueous solutions stimulated by light was illustrated schematically in Scheme 1.

Scheme 1



In conclusion, we prepared a stilbene bis(*β*-CD) dimer and controlled its trans−cis conformation by photoirradiation in aqueous solutions. With a ditopic adamantyl guest molecule, in trans conformation, it formed dimer or small supramolecular assemblies (oligomers), whereas in cis conformation, supramolecular linear polymers with high molecular weight were observed. The control of the structure of the supramolecular polymers by an external stimulus may open the way to various applications. Now we are studying the properties of the supramolecular polymers and the interaction of the stilbene CD dimer with different guests.

Acknowledgment. P.K. gratefully acknowledges the Japanese Society for the Promotion of Science (JSPS) for a JSPS Postdoctoral Fellowship for Foreign Researchers (Grant PE07064). This work has been partially supported by Grant in-Aid No. A19205014 for Scientific Research and has been conducted with financial support from the “Stress and Symbiosis on Supramolecules” program of the Ministry of Education, Culture, Sports, Science and Technology, Japan.

Supporting Information Available: Synthesis, UV−vis spectra, ITC titrations, and AFM measurements. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) Koumura, N.; Zijlstra, R. W. J.; van Delden, R. A.; Harada, N.; Feringa, B. L. *Nature* **1999**, *401*, 152−155. (b) Brouwer, A. M.; Frochot, C.; Gatti, F. G.; Leigh, D. A.; Mottier, L.; Paolucci, F.; Roffia, S.; Wurpel, G. W. H. *Science* **2001**, *291*, 2124−2128. (c) Shinkai, S.; Nakaji, T.; Nishida, Y.; Ogawa, T.; Manabe, O. *J. Am. Chem. Soc.* **1980**, *102*, 5860−5865. (d) Murakami, H.; Kawabuchi, A.; Kotoo, K.; Kunitake, M.; Nakashima, N. *J. Am. Chem. Soc.* **1997**, *119*, 7605−7606. (e) Muraoka, T.; Kinbara, K.; Kobayashi, Y.; Aida, T. *J. Am. Chem. Soc.* **2003**, *125*, 5612−5613. (f) Inoue, Y.; Kuad, P.; Okumura, Y.; Takashima, Y.; Yamaguchi, H.; Harada, A. *J. Am. Chem. Soc.* **2007**, *129*, 6396−6397. (g) Yu, Y.; Nakano, M.; Ikeda, T. *Nature* **2003**, *425*, 145−145. (h) Tomatsu, I.; Hashidzume, A.; Harada, A. *J. Am. Chem. Soc.* **2006**, *128*, 2226−2227.
(2) Aoyagi, T.; Ueno, A.; Fukushima, M.; Osa, T. *Macromol. Rapid. Commun.* **1998**, *19*, 103−105.
(3) Lui, Y.; Kang, S.; Chen, Y.; Yang, Y.-W.; Huskens, J. *J. Inclusion Phenom. Macrocyclic Chem.* **2006**, *56*, 197−201.
(4) (a) Takahashi, H.; Takashima, Y.; Yamaguchi, H.; Harada, A. *J. Org. Chem.* **2006**, *71*, 4878−4883. (b) Ohga, K.; Takashima, Y.; Takahashi, H.; Kawaguchi, Y.; Yamaguchi, H.; Harada, A. *Macromolecules* **2005**, *38*, 5897−5904. (c) Hasegawa, Y.; Miyauchi, M.; Takashima, Y.; Yamaguchi, H.; Harada, A. *Macromolecules* **2005**, *38*, 3724−3730.
(5) Lott, P. F.; Millich, F. *J. Chem. Educ.* **1966**, *43*, A191.
(6) The moderate value for the supramolecular polymer is due to the relatively low concentration of the measurement and to the dynamic exchange in solutions. Indeed, in solutions, the supramolecular structure is constantly in fast equilibrium between the polymer and the monomers in the NMR time scale (as confirmed by the broad signals). This explains the relatively high measured diffusion coefficient.
(7) (a) Soto Tellini, V. H. S.; Jover, A.; Garcia, J. C.; Galantani, L.; Meijide, F.; Tato, J. V. *J. Am. Chem. Soc.* **2006**, *128*, 5728−5734. (b) Zhang, B.; Breslow, R. *J. Am. Chem. Soc.* **1993**, *115*, 9353−9354.

JA075139P