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Thermal and Photochemical Switching of Conformation of Poly(ethylene glycol)-Substituted Cyclodextrin with an Azobenzene Group at the Chain End

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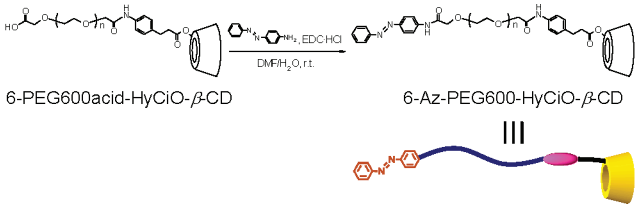
Controlling the conformations and dynamics of molecules or supramolecules by external stimuli is one of the great concerns in the field of nanosciene and nanotechnology. There are numerous external stimuli such as pH,[1] redox,[2] light,[3] etc. that can be utilized, of which light is especially of interest because it works rapidly, remotely, and cleanly. The conformations of molecules incorporating photoactive groups can be altered reversibly by the controlled isomerization of the photoactive sites. These conformational changes can be exploited to modulate the physical and chemical properties of such molecules. Azobenzene is one of the most widely employed photoactive groups for such systems because of its superior characteristic of reversible photoisomerization.[3e−l] Previously, we have reported conformations and conformational changes of poly(ethylene glycol) (PEG)-substituted cyclodextrins (CDs) (6-PEG-acid-HyCiO-β-CDs) in aqueous solutions in the presence of a competitive guest.[4] In this Communication, we synthesized PEG-substituted CD with an azobenzene group at the terminal of the PEG chain (6-Az-PEG600-HyCiO-β-CD) according to Scheme 1, and the thermally and photochemically induced conformational changes in aqueous solutions were studied by 1D and 2D NMR analyses.

Scheme 1



We investigated the conformation of 6-Az-PEG600-HyCiO-β-CD in aqueous solution. Figure 1a shows the partial 2D ROESY ^{1}H NMR spectrum of 6-Az-PEG600-HyCiO-β-CD at 1 mM at 30 °C after heating at 60 °C for 1 day. In the 1D ^{1}H NMR spectrum of the aromatic region, the signals of the *trans*-isomer (6-*trans*-Az-PEG600-HyCiO-β-CD) were only observed in the azobenzene part. In the 2D ROESY NMR spectrum, the correlation signals between the protons of the CD cavity and both of the hydrocinnamoyl aromatic protons and the azobenzene protons were observed. In the pulsed field gradient (PFG) NMR measurement, the diffusion coefficient was obtained as a single molecule (see Supporting Information). These results indicate that 6-*trans*-Az-PEG600-HyCiO-β-CD forms a self-inclusion complex, where the CD cavity alternatively includes the hydrocinnamoyl aromatic part and the azobenzene part.

The temperature dependence of the conformation of 6-*trans*-Az-PEG600-HyCiO-β-CD at low concentration was investigated. Figure 1b shows the 2D ROESY NMR spectrum at 1 mM at 1 °C. The correlation signals between the protons of the CD cavity and

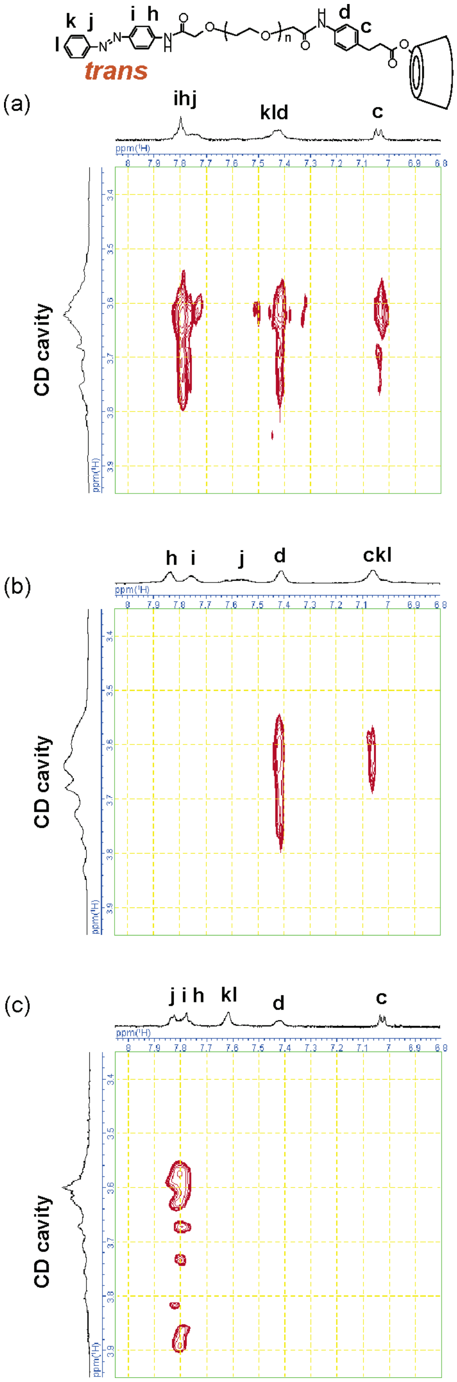


Figure 1. Partial 2D ROESY ^{1}H NMR spectra of 6-*trans*-Az-PEG600-HyCiO-β-CD in D_2O at 1 mM at (a) 30 °C, (b) 1°C, and (c) 60 °C.

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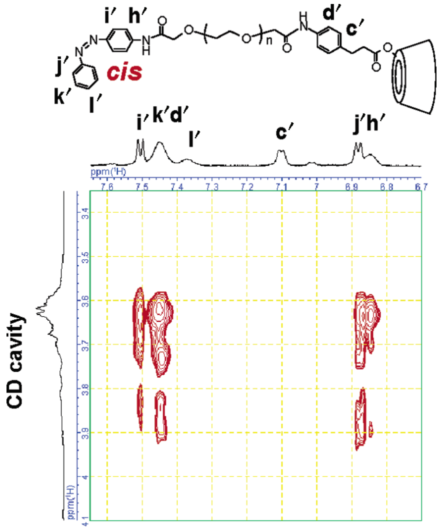

Figure 2. Partial 2D ROESY ^{1}H NMR spectrum of 6-*cis*-Az-PEG600-HyCiO-β-CD in D_2O at 1 mM at 30 °C.

only those of the hydrocinnamoyl aromatic part were observed. This result suggests that 6-*trans*-Az-PEG600-HyCiO-β-CD forms a self-threading complex, where the CD cavity includes the hydrocinnamoyl aromatic part. Meanwhile, in the spectrum at 60 °C (Figure 1b), the correlation signals between the protons of the CD cavity and only those of the azobenzene part were observed. These findings suggest that 6-*trans*-Az-PEG600-HyCiO-β-CD forms a self-inclusion complex, where the CD cavity includes the azobenzene part. Furthermore, correlation signals between the protons of the CD cavity and both of the hydrocinnamoyl aromatic protons and the azobenzene protons were not observed at 80 °C, suggesting that it exists in a dethreading form.[5] The 1D NMR spectrum of 6-*trans*-Az-PEG600-HyCiO-β-CD showed a concentration dependency. The diffusion coefficient decreases as the concentration increases in the PFG NMR measurement (see Supporting Information). Threse results indicate that 6-*trans*-Az-PEG600-HyCiO-β-CD forms intermolecular complexes at high concentration.

The conformational change of 6-*trans*-Az-PEG600-HyCiO-β-CD by irradiating with UV light was investigated. Figure 2 shows the 2D ROESY NMR spectrum at 30 °C after irradiating with UV light (ca. 340 nm) for 2 h. In the 1D NMR spectrum, the signals of the *cis*-isomer (6-*cis*-Az-PEG600-HyCiO-β-CD) were mainly observed. In the 2D NMR spectrum, the correlation signals between the protons of the CD cavity and only those of the azobenzene part were observed, while those between the protons of the CD cavity and the hydrocinnamoyl aromatic protons were not observed. These results indicate that the CD cavity includes only the azobenzene part. The same results were obtained at 1 °C (see Supporting Information). In contrast to 6-*trans*-Az-PEG600-HyCiO-β-CD, the 1D NMR spectrum and the diffusion coefficient of 6-*cis*-Az-PEG600-HyCiO-β-CD did not show a concentration dependency (see Supporting Information). These results indicate that 6-*cis*-Az-PEG600-HyCiO-β-CD did not form an intermolecular complex but formed a self-inclusion complex where the CD cavity includes the azobenzene part regardless of the concentration. Inclusion of the azobenzene part by the CD cavity in *trans*- and *cis*-isomers was confirmed by circular dichroism spectroscopy (see Supporting Information). Consequently, the proposed conformational changes of 6-Az-PEG600-HyCiO-β-CD in aqueous solutions by external stimuli were illustrated schematically in Figure 3.

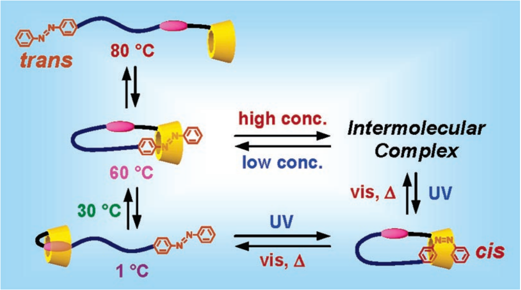

Figure 3. Proposed conformational changes of 6-Az-PEG600-HyCiO-β-CD in aqueous solutions by external stimuli.

In conclusion, we thermally and photochemically controlled the conformation of 6-Az-PEG600-HyCiO-β-CD in an aqueous solution. At low concentration, 6-*trans*-Az-PEG600-HyCiO-β-CD forms different types of self-inclusion complexes or exists in a dethreading form depending on the temperature, while at high concentration, an intermolecular complex is formed. Moreover, UV-light irradiation causes the conformation to change to a self-inclusion complex where the CD cavity includes the azobenzene part regardless of the concentration.

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Supporting Information Available: Materials, measurements, synthesis, and additional experiments. This material is available free of charge via the Internet at http://pubs.acs.org.

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(5) It was confirmed that 6-*trans*-Az-PEG600-HyCiO-β-CD existed in a single molecule in aqueous solution at low concentration regardless of the temperature by PFG NMR measurement. The variation of the diffusion coefficient of 6-Az-PEG600-HyCiO-β-CD owing to the solution viscosities were corrected with those of HOD.

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