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Self-Threading of a Poly(ethylene glycol) Chain in a Cyclodextrin-Ring: Control of the Exchange Dynamics by Chain Length

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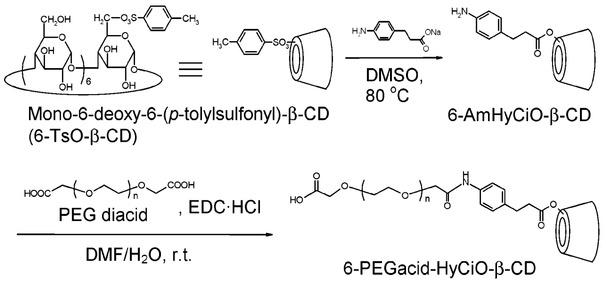
Design and control of dynamics of supramolecular complexes are actively worked on to develop unique and valuable properties in recent years.[1] When a guest part is covalently attached to a cyclic host, it may form intramolecular or intermolecular complexes.[2] We chose cyclodextrins (CDs) as cyclic hosts, because CDs are able to form complexes with guest compounds in aqueous solutions. Although there are some reports on CDs with a small guest forming intramolecular complexes, which are useful for molecular recognition sensors,[3] an artificial enzyme[4] in aqueous solutions, there are few on polymer-substituted CDs.[5] Previously, we reported that 6-hydrocinnamoyl-β-CD (6-HyCiO-β-CD) formed a self-inclusion complex in aqueous solutions.[2e] Now, we have synthesized poly(ethylene glycol) (PEG)-substituted CDs with different chain lengths (6-PEG600acid-HyCiO-β-CD from PEG 600 diacid, 6-PEG3000acid-HyCiO-β-CD from PEG 3000 diacid; Scheme 1).

Mono-6-deoxy-6-(4-aminohydrocinnamoyl)-β-CD (6-AmHyCiO-β-CD) and 6-PEGacid-HyCiO-β-CDs have also been found to form intramolecular complexes in aqueous solutions by 1D and 2D NMR analysis, circular dichroism spectroscopy, and vapor pressure osmometry (VPO). When 1-adamantane carboxylic acid (AdCA) was added to aqueous solutions of 6-PEGacid-HyCiO-β-CD as a competitive guest ($K_a = 10^5$ for β-CD), the substituent (PEG chain and hydrocinnamoyl part) was found to be exposed to water. The exchange dynamics of 6-PEGacid-HyCiO-β-CDs were found to be regulated by their chain lengths.

Figure 1a shows the partial ^{1}H NMR spectra of 6-PEG600acid-HyCiO-β-CD in D_2O. The signals of the aromatic protons of the substituent were observed at 7.02 and 7.59 ppm, respectively. The 2D ROESY NMR spectrum of 6-PEG600acid-HyCiO-β-CD shows the rotational nuclear overhouser effects (ROEs) between the aromatic protons of the substituent and the inner protons of the CD, indicating that the aromatic of the substituent is included in the CD cavity (see Supporting Information). The molecular weight of 6-PEG600acid-HyCiO-β-CD, measured by VPO, showed about 1900 in aqueous solutions, which is consistent with that of a monomer. These results indicate that 6-PEG600acid-HyCiO-β-CD formed a self-inclusion complex in aqueous solutions. 6-PEG3000-acid-HyCiO-β-CD also was found to form a self-inclusion complex in aqueous solutions (see Supporting Information).

Scheme 1



Our next interest moved to the structural change of 6-PEG600acid-HyCiO-β-CD by external stimulus. In the presence of a half amount of AdCA in aqueous solutions of 6-PEG600acid-HyCiO-β-CD, the signals of the aromatic protons were shifted and broadened with small signals[6] (Figure 1b), suggesting that the rate of the formation of the self-inclusion complex is modestly slow because of its long chain. Indeed, in the case of 6-AmHyCiO-β-CD with a small substituent, such broadening was not observed under the same conditions (see Supporting Information). In the presence of an equal amount of AdCA in aqueous solutions of 6-PEG600acid-HyCiO-β-CD, the signals of the aromatic protons largely shifted without broadening (Figure 1c). The 2D ROESY NMR spectrum showed no correlation between the aromatic protons of the substituent and the inner protons of CD, indicating that the substituent was completely exposed to water by inclusion of AdCA into the CD cavity (see Supporting Information). The circular dichroism spectrum of 6-PEG600acid-HyCiO-β-CD in aqueous solutions shows an induced positive band around 245 nm, corresponding to the ^{1}La transition band of the substituent. According to the rules of Harata

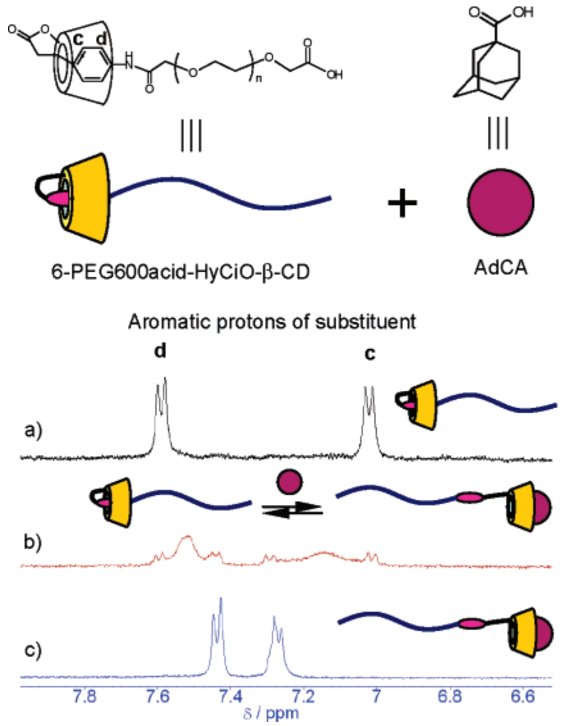


Figure 1. NMR spectra and proposed structures of 6-PEG600acid-HyCiO-β-CD in D_2O at 30 °C (a) in the absence of AdCA, (b) in the presence of a half amount of AdCA, and (c) in the presence of an equal amount of AdCA.

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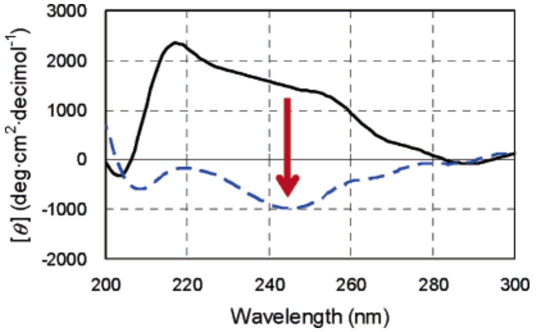

Figure 2. Circular dichroism spectra of 6-PEG600acid-HyCiO-β-CD in aqueous solutions (solid line) and in the presence of an equal amount of AdCA (dashed line).

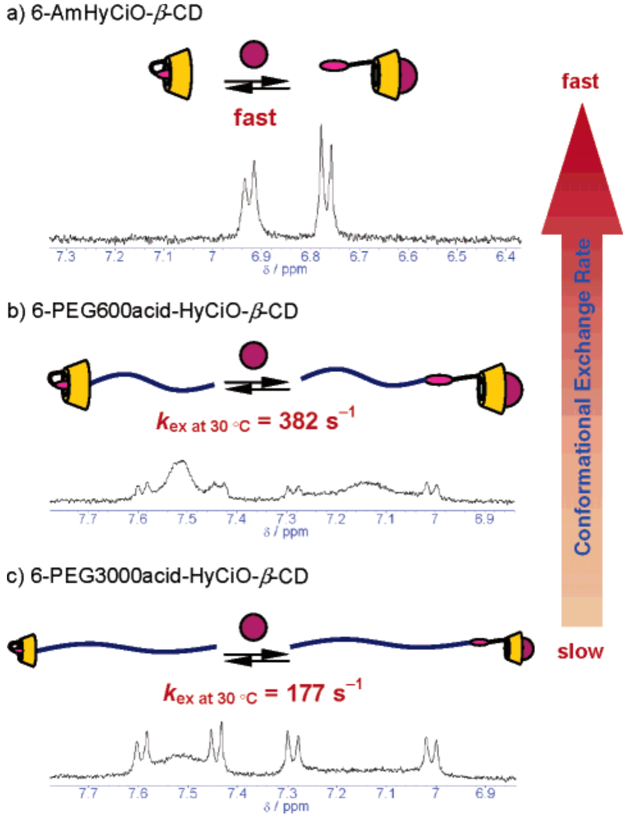

Figure 3. NMR spectra of the aromatic protons of the substituted CDs and conformational exchange rates in the presence of a half amount of AdCA at 30 °C.

and Uedaira,[7] the substituent is included in its CD cavity and is parallel to the axis of CD. On the contrary, the circular dichroism spectrum of 6-PEG600acid-HyCiO-β-CD with AdCA showed an induced negative band in the same wavelength region. According to the theoretical treatment by Kodaka,[8] the exposed substitution part in water exists nearly parallel to its CD axis (Figure 2).

6-PEG3000acid-HyCiO-β-CD with a longer PEG chain showed similar results to 6-PEG600acid-HyCiO-β-CD. In contrast, the NMR spectrum in the presence of a half amount of AdCA is quite different from that of 6-PEG600acid-HyCiO-β-CD. The signals of the aromatic protons of 6-PEG3000acid-HyCiO-β-CD were split in the presence of a half amount of AdCA (Figure 3c). From the variable-temperature NMR measurement, the conformational exchange rate constants of 6-PEG600acid-HyCiO-β-CD and 6-PEG3000acid-HyCiO-β-CD were estimated to be 382 s^{-1} and 177 s^{-1} at 30 °C, respectively (see Supporting Information). It was revealed that the conformational exchange of 6-PEG600acid-HyCiO-β-CD was more than twice as fast as that of 6-PEG3000acid-HyCiO-β-CD. These results indicate that the rate of the self-threading complex formation depends on the length of the PEG chain in the substituent.

This is the first report on the self-threading complex of polymer-substituted CD, and the observation of the difference of self-threading behavior, depending on polymer chain length. Moreover, there is a possibility that this self-threading of polymer-substituted CD leads to novel properties of polymer. The detailed self-threading behaviors of these complexes are now under investigation.

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Supporting Information Available: Synthesis and characterization of 6-AmHyCiO-β-CD, 6-PEG600acid-HyCiO-β-CD, and 6-PEG3000-acid-HyCiO-β-CD. Variable-temperature measurement. This material is available free of charge via the Internet at http://pubs.acs.org.

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(6) It was found that the broad signals came from the species that participate in conformational exchange because these signals coalesced; in contrast, the small signals came from the species that did not participate in conformational exchange because these signals did not coalesce in the variable-temperature NMR measurement (see Supporting Information).

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