Supramolecular Chemistry

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Cyclodextrin-Based Side-Chain Polyrotaxane with Unidirectional Inclusion in Aqueous Media**

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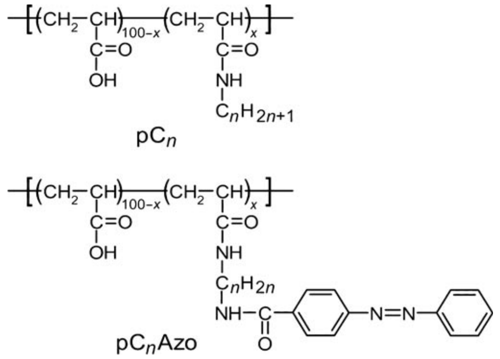
Recently, polyrotaxanes have attracted much interest from researchers from the viewpoint of nanotechnological applications.[1] In particular, well-defined polyrotaxanes that consist of simple components are becoming important for the construction of more sophisticated molecular machines. There are a number of designs and strategies for the preparation of polyrotaxanes.[2] Among these approaches, the side-chain polyrotaxane is one of the simplest architectures, but there are only a few examples of side-chain polyrotaxanes that contain cyclodextrin (CD),[3] apart from those of Ritter and co-workers.[4] Extensive studies by Ritter[4] demonstrated the successful synthesis of side-chain polyrotaxanes primarily in organic media from methylated β-CD and various polymers.

Over the past decade, we have been studying the interaction of cyclodextrins with polymer side chains attached to water-soluble polymers.[5] Herein, we report an example of the successful construction of CD-based side-chain polyrotaxanes in aqueous media, in which CD includes polymer side chains preferentially from the side with the secondary hydroxy functionality, by using a combination of simple components, α-CD and hydrophobically modified poly(acrylic acid) (pAA).

We have reported that CD interacts with polymer side chains and forms inclusion complexes.[5] For example, α-CD forms 1:1 inclusion complexes with alkyl side chains attached to the pAA backbone in aqueous media at lower α-CD concentrations.[6] The structure of 1:1 complexes of α-CD with hexyl- and dodecyl-modified pAAs (pC_n, $n=6$ and 12, respectively; Scheme 1) were investigated in detail by 2D NOESY analysis (Figure 1). Both the spectra exhibit clear correlation peaks between the inner protons in the α-CD cavity and protons in the alkyl side chains, indicative of the formation of inclusion complexes of α-CD with the alkyl side chains. It is of note that both the spectra also exhibit significant correlation peaks between the protons at the 5-position in α-CD and the protons of the terminal methyl group in the alkyl side chains. These data indicate that α-CD includes the side chains preferentially from the side of the secondary hydroxy group. In other words, we have success-



Scheme 1. Structures of the polymers used in this study.

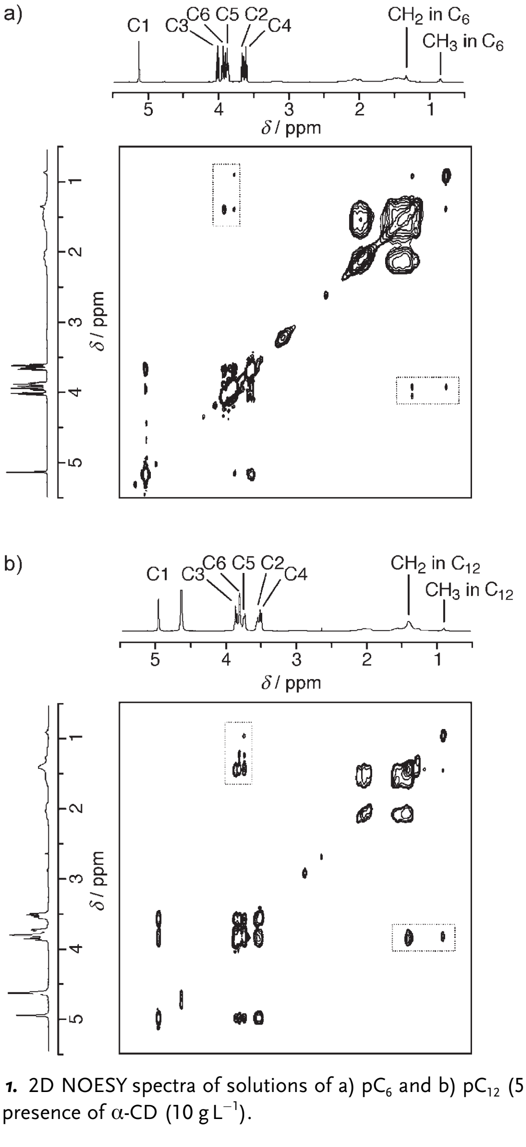


Figure 1. 2D NOESY spectra of solutions of a) pC_6 and b) pC_{12} (5 gL^{-1}) in the presence of α-CD (10 gL^{-1}).

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fully obtained unidirectionally included side-chain polypseudorotaxanes by using a combination of simple components. At present, we are not sure of the driving force for the unidirectional inclusion, but it should be thermodynamically driven: certain interactions between the hydroxy groups in α-CD and the carboxylate groups in the pAA backbone may lead to a stronger interaction between the side of the secondary hydroxy group that bears more hydroxy groups with the pAA backbone. Thus, this observation may be in contrast to the cases of kinetically driven unidirectional inclusion reported recently.[7,8]

These observations motivated us to construct unidirectionally included side-chain polyrotaxanes in aqueous media. For this purpose, we prepared two azobenzene-carrying pAAs, namely, pAAs modified with azo moieties through hexamethylene and dodecamethylene linkers (pC$_n$Azo, $n=6$ and 12, respectively; Scheme 1). As azobenzene derivatives are isomerized from *trans* to *cis* under irradiation with UV light,[9] it is expected that side-chain polyrotaxanes can be controlled by utilizing photoisomerization of the azo moiety in pC$_n$Azo.[10]

The formation of inclusion complexes of α-CD with pC$_n$Azo was confirmed by UV/Vis absorption spectroscopy (see the Supporting Information). The structure of inclusion complexes of α-CD with pC$_n$Azo was also explored by 2D NOESY analysis. The spectrum for the α-CD/pC$_6$Azo mixture exhibits correlation peaks between the inner protons in the α-CD cavity and protons in the azo and C$_6$ moieties, thus indicating that α-CD includes both the moieties in the polymer side chain (Figure 2a). The correlation peaks between α-CD and the azo moiety are stronger than those between α-CD and the C$_6$ linker, thus indicating that α-CD interacts with the azo moiety more favorably than with the C$_6$ linker. The spectrum for the α-CD/pC$_{12}$Azo mixture also indicates that α-CD included both the azo and C$_{12}$ moieties (Figure 3a). The correlation peaks between α-CD and the C$_{12}$ linker are much stronger than those between α-CD and the azo moiety, thus indicating that α-CD interacts with the C$_{12}$ linker much more favorably than with the azo moiety.

When we irradiated the α-CD/pC$_n$Azo mixtures with UV light, more than 75 % of the azo moieties were isomerized into the *cis* form. The formation of the side-chain polyrotaxane was investigated by 2D NOESY analysis. The spectrum for the α-CD/pC$_6$Azo mixture after UV irradiation exhibits no significant correlation peaks between the protons in α-CD and those in the azo moiety and in the C$_6$ linker, thus indicating that the inclusion complex of α-CD with the side chain is dissociated by *trans*-to-*cis* photoisomerization (Figure 2b). This observation implies that the C$_6$ linker is so short that side-chain polyrotaxanes are not formed. On the other hand, the spectrum for the α-CD/pC$_{12}$Azo mixture after UV irradiation exhibits correlation peaks between the inner protons in α-CD and those in the C$_{12}$ linker (Figure 3b). This observation means that α-CD stays on the C$_{12}$ linker, even after *trans*-to-*cis* photoisomerization of the azo moiety, which is indicative of the formation of the side-chain polyrotaxane. The formation of the side-chain polyrotaxane was confirmed by pulsed-field-gradient NMR spectroscopy, which demonstrated two diffusion modes of the signals as a result of α-CD with diffusion constants 6.8×10^{-12} (complexed α-CD) and 1.7×10^{-10} (free α-CD) m^{2}s^{-1} (see the Supporting Information). As shown in Figure 4a, the expanded 2D NOESY spectrum for the α-CD/pC$_{12}$Azo mixture exhibits a weak but clear correlation peak between protons of the 5-position in α-CD and the proton e of the *cis* azo moiety. This spectrum indicates that the C$_{12}$ linker is included by α-CD, in which the primary hydroxy side is close to the azo moiety (Figure 4b).

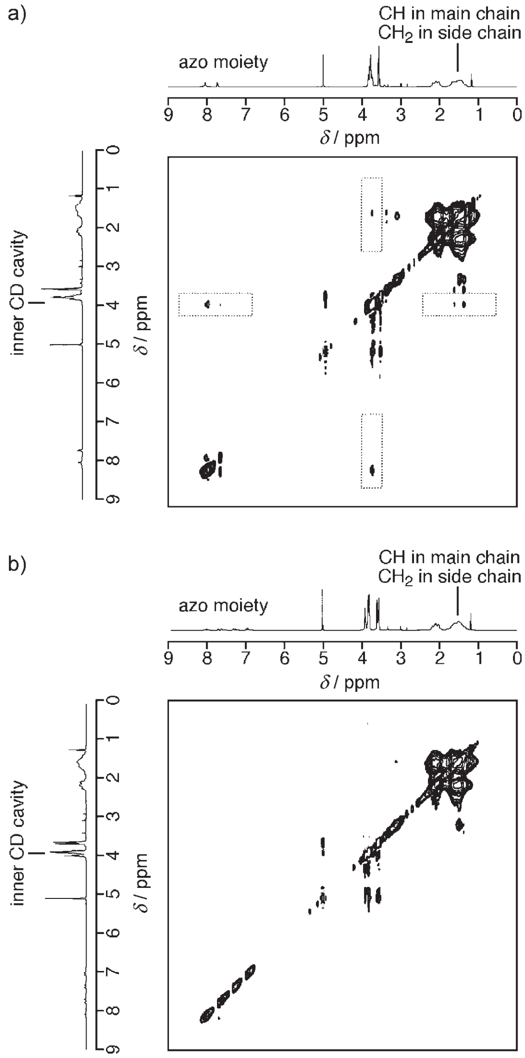

Figure 2. 2D NOESY spectra of a solution of pC$_6$Azo (10 g L^{-1}) in the presence of α-CD (10 g L^{-1}) measured a) before and b) after UV irradiation.

In conclusion, we have successfully constructed a CD-based side-chain polyrotaxane with unidirectional inclusion in aqueous media by using a combination of the simple components, α-CD and pC$_{12}$Azo. We are investigating the driving force for the unidirectional inclusion.

Experimental Section

Materials: Poly(acrylic acid) (pAA; Wako Pure Chemical Industries, Ltd.) was used as supplied. The average molecular weight of pAA was reported to be 250000 by the supplier. α-Cyclodextrin (α-CD) was

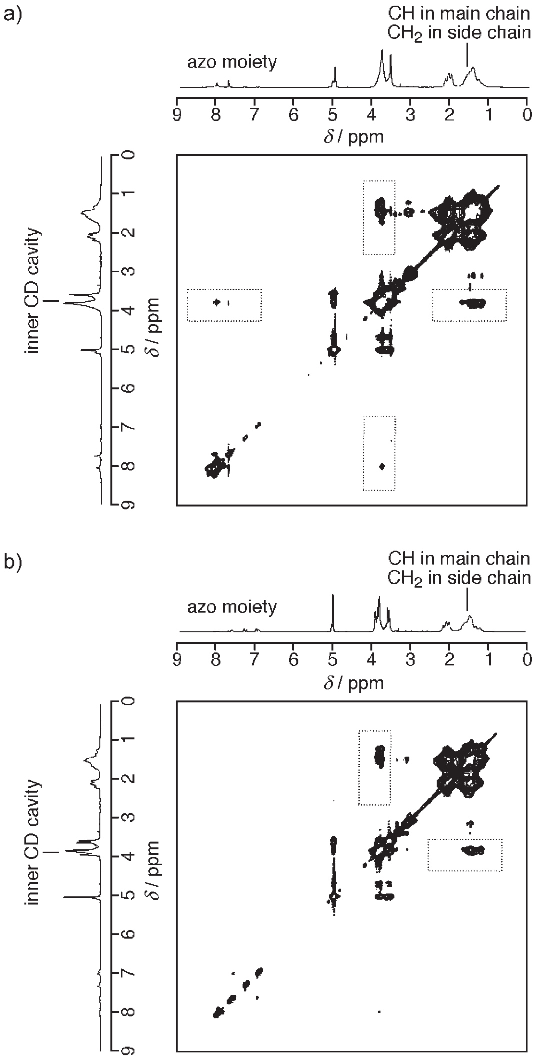

Figure 3. 2D NOESY spectra of a solution of $pC_{12}Azo$ (10 g L^{-1}) in the presence of α-CD (10 g L^{-1}) measured a) before and b) after UV irradiation.

recrystallized twice from water. Milli-Q water was used for preparation of aqueous solutions. Other reagents were used as received.

Preparation of hydrophobically modified pAAs: Alkyl-modified pAAs (pC_n, n = number of carbon atoms in the alkyl chain) were prepared from pAA and respective amines in the presence of *N,N'*-dicyclohexylcarbodiimide (DCC) according to the procedure of Iliopoulos and co-workers.[11] The preparation details are described elsewhere.[6] The degrees of modification (x) were determined to be 5.4 and 5.2 mol% for pC_6 and pC_{12}, respectively, by ^1H NMR spectroscopic analysis. Azobenzene-modified pAAs (pC_nAzo, n = number of carbon atoms in the alkylene linker) were also prepared by the same procedure. The preparation details are described elsewhere.[12] The degrees of modification (x) were determined to be 3.8 and 2.7 mol% for pC6Azo and pC12Azo, respectively, by ^1H NMR spectroscopic analysis.

NMR: Two-dimensional NOESY NMR spectra were recorded with a VARIAN UNITY INOVA PLUS 600 NMR or JEOL JNM LA500 NMR spectrometer at 30 °C. Sample solutions were prepared with D_2O containing 0.05 M sodium carbonate and 0.05 M sodium bicarbonate. Sample solutions were heated at 60 °C for 1 day, and then the solution was irradiated with UV light for 12 h. Pulsed-field-gradient NMR measurements were performed on a VARIAN UNITY INOVA 750 NMR spectrometer at 25 °C. Diffusion constants were calculated using the direct exponential curve resolution algorithm and the maximum entropy method. The experimental details are described elsewhere.[13]

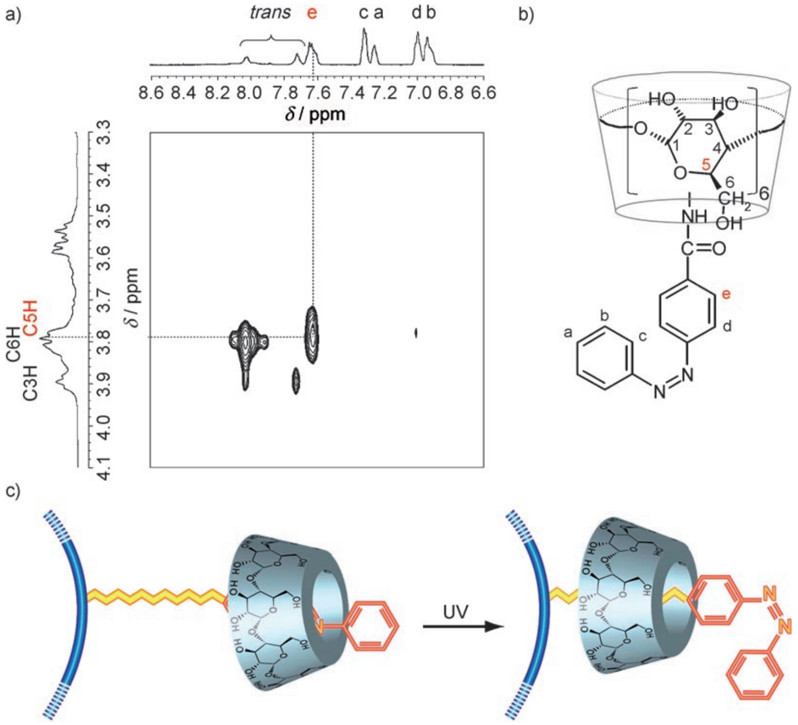

Figure 4. Expanded 2D NOESY spectra of a solution of $pC_{12}Azo$ (10 g L^{-1}) in the presence of α-CD (10 g L^{-1}) measured after UV irradiation (a). Schematic representation of side-chain polyrotaxane with unidirectional inclusion (b) and (c).

UV/Vis absorption spectroscopy: UV/Vis absorption spectra were recorded with a Shimadzu UV-2500PC spectrophotometer using a 1-cm path length quartz cuvette. Sample solutions were prepared with a carbonate buffer solution containing 0.05 M sodium carbonate and 0.05 M sodium bicarbonate, and the solution was heated at 60 °C for 1 day.

Photoisomerization: pC_6Azo and $pC_{12}Azo$ were isomerized from *trans* to *cis* isomers by UV irradiation with a 500-W Xe lamp (Ushio Inc.) equipped with a cutoff filter (Hoya UV34) and a band-pass filter (Hoya U340). The distance between the sample cell and the lamp was fixed at 40 cm.

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