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pH Responsive [2]Rotaxanes with 6-Modified-α-Cyclodextrins

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Rotaxanes are considered to be prototype molecular machines bearing a rotor and an axis within a molecule. In our study on complex formation of modified α-CDs as host molecules for guest molecules consisting of an alkyl chain with pyridyl end caps, we observed control of complex formation and dissociation by pH responses of functional groups on modified α-CDs.

In a biological system, external stimuli control catalytic functions and structures. Recently, supramolecular structures[1] have been controlled using external stimuli such as pH,[2] redox changes,[3] and light.[4] In our research, we have selected cyclodextrins (CDs)[1b,5] as a ring component to construct rotaxanes due to the rigidity, well-defined nonsymmetric ring structures, and hydrophobic cavities of CDs. Previously, we have reported the formation of a pseudo[2]rotaxane consisting of α-CD and 1,10-di(1-pyridyl)decane axis molecules[6] as well as face-direction control of CDs in the construction of pseudo-rotaxane with an alkyl chain bearing pyridyl end caps.[7] One characteristic of dipyridyldecane axis molecules is that the rotor on the axle is entrapped by the repulsion between α-CD and the cationic end group.[8,9] Herein, we report a study on complex formation and dissociation by pH responses of the basic functional groups in modified α-CDs.

We chose NH_2-α-CD and Py-α-CD, which have substituents at the C3 and C6 positions, as pH-responsive host molecules. Mixing modified CD with a dipyridinium axis molecule caused the protons of the axis molecule to split in an aqueous solution (pH 7). This splitting is related to the formation of [2]rotaxane (Figure 1). 2D ROESY NMR spectroscopy characterized the formation of [2]rotaxane with 6-Py-α-CD and an axis. The inner protons of 6-Py-α-CD and protons of an axis were correlated, suggesting the formation of [2]rotaxane (Figure S4[11]). The ratio of complex formation using 6-modified α-CD (6-Py-α-CD and 6-NH_2-α-CD) was slightly smaller than that of α-CD at pH 7 (Table 1). The steric repulsion between the substituents and an electric stopper affected the ratio of the complex formation. The ratio of complex formation of 6-modified α-CD was significantly larger than that of 3-modified α-CD (Figure S12[11]) because the structural stability of 3-modified α-CD changed when the glucopyranose unit was modified to an altrose unit.[10]

We investigated the dependence of [2]rotaxane formation on the pH using 6-modified α-CD, which effectively formed [2]rotaxane under neutral conditions. Figure 1 shows the ^{1}H NMR spectra of the dipyridinium axis molecule with 6-Py-α-CD at 5 mM. The pH of the solution was adjusted using NH_3 (aq) or D_2SO_4. Change in the pH of the solution of 6-Py-α-CD with the axis solution from 7 to 3 caused the integral value of the e′ and e″ proton to decrease. On the other hand, neutralizing the acid solution with NH_3 (aq) caused the integral value of the e

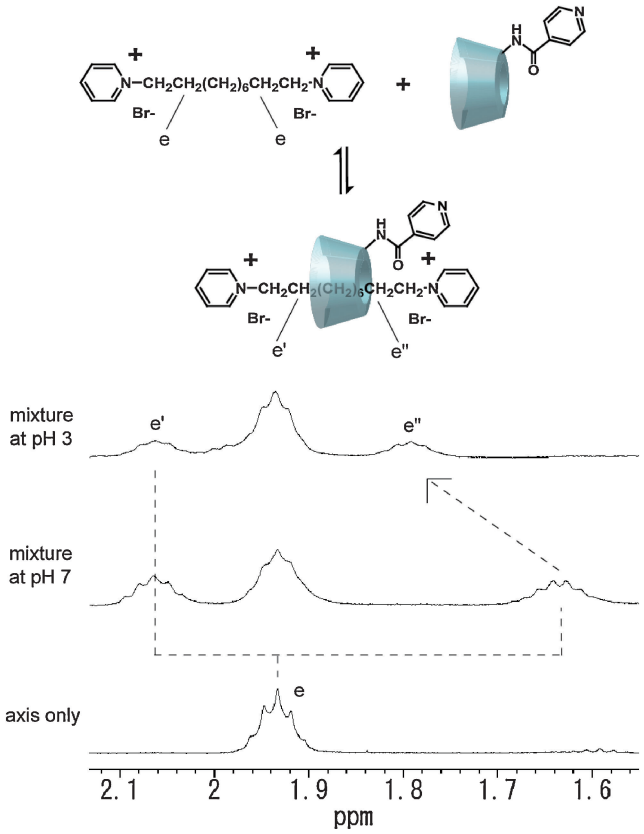
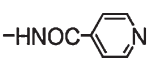


Figure 1. ^{1}H NMR spectra of the axis (5 mM) in the absence and presence of 6-Py-α-CD (5 mM) at pH 3 or 7 in D_2O at 30 °C.

Table 1. Ratios of complex formation and association constants for mixtures of axis (5 mM) and several 6-modified α-CDs (5 mM) at pH 7 and 3 in D_2O at 30 °C

	R	pD	Ratio of complex[a]/%	Association constant/M^{-1}
6-Py-α-CD	–HNOC– 	7	49	380
		3	31	130
6-NH_2-α-CD	–NH_2	7	51	430
		3	12	30
α-CD	–OH	7	79	3600
		3	75	2400

[a]The ratio of complex was calculated by the integral values of complex (e′ and e″ protons) and uncomplex (e proton).

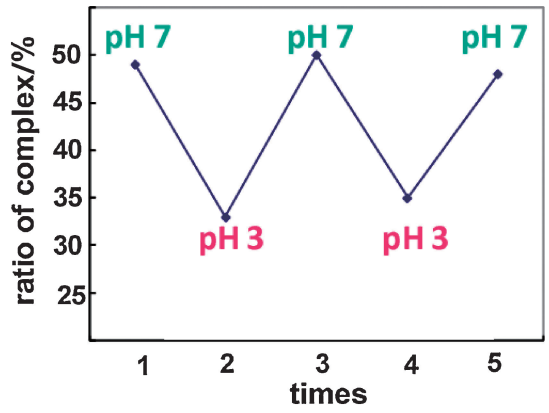


Figure 2. pH response of the [2]rotaxane axis (5 mM) and 6-Py-α-CD (5 mM) in D_2O at 30 °C.

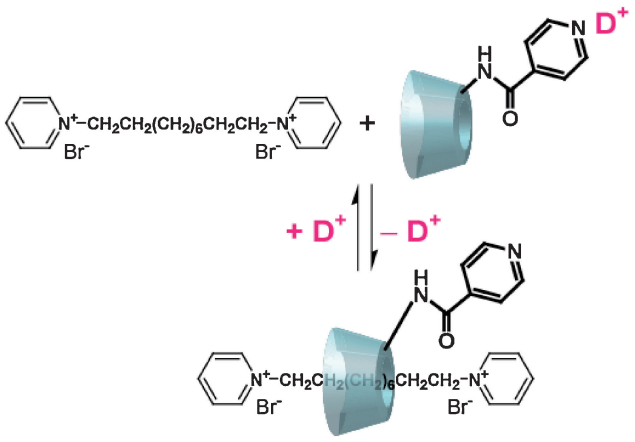


Figure 3. Chemical structure for switching of [2]rotaxane using the pH response of 6-Py-α-CD.

proton to recover the value at the neutral state, indicating [2]rotaxane is re-formed. We hypothesize that the decreasing ratio of complex formation is due to electric repulsion between the pyridyl group of 6-Py-α-CD at pH 3 and the pyridinium group of the axis under the acidic conditions.

Changing the pH of the solution of 6-NH_2-α-CD from 7 to 3 using D_2SO_4 decreased the complex ratio from 50 to 10% (Table 1). Although this decline is an interesting behavior, 6-NH_2-α-CD was irreversible because 6-NH_2-α-CD was not deprotonated by NH_3 (aq). On the other hand, [2]rotaxane with 6-Py-α-CD indicated the reversibility for complex formation depends on pH. Figure 2 shows the repetition of pH dependency for the formation of [2]rotaxane with 6-Py-α-CD. The formation (threading) and deformation (dethreading) cycle of [2]rotaxane could be repeated at least four times by adjusting the pH.

In conclusion, we have studied complex formation of [2]rotaxane with α-CD derivatives. Using 6-Py-α-CD or 6-NH_2-α-CD, we observed the pH dependency of the complex formation of [2]rotaxane (Figure 3). Our results suggested that [2]rotaxane on a polymer side chain can be used to prepare a supramolecular hydrogel. Although we were unable to find another report on complex formation of CD–[2]rotaxane controlled by pH, we believe these stimulus-responsive properties may eventually be applied to stimulus-responsive sol–gel supramolecular materials and stretchable materials.

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