

## Rotaxane-like Characteristics of [2]Pseudorotaxane Complexes of $\alpha$ -Cyclodextrin and Dodecamethylene Threading Chain Derivatives with Cationic End Groups

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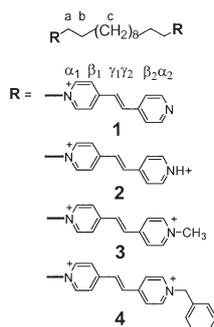
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(Received September 25, 2001; CL-010945)

We have prepared several threading chain molecules that are capable of producing [2]pseudorotaxane complexes with  $\alpha$ -CD. The free energy of activation of site exchange ( $\Delta G^\ddagger$ ) of [2]pseudorotaxanes indicates that the [2]pseudorotaxanes have increasingly rotaxane-like characteristics as the number of cationic end groups and the steric hindrance of end groups of an axle increase.

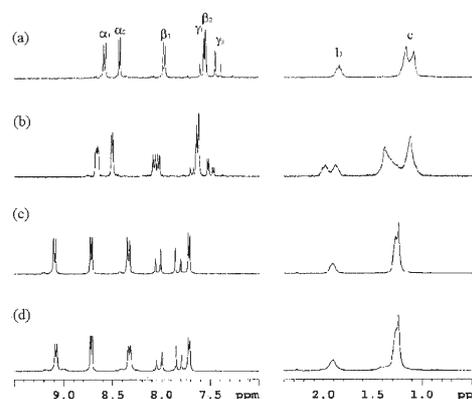
The construction of interlocked molecules, such as rotaxanes, catenanes, knots and polyrotaxanes has fascinated chemists not only because of their unique structure and properties but also because of their potential applications to molecular devices.<sup>1</sup> A large number of rotaxanes have been prepared by the imprisonment of a ring molecule in a dumbbell structure using the steric hindrance of bulky stoppers.<sup>2,3</sup> Recently, Harada and co-workers have demonstrated a new method for entrapping cyclodextrin (CD) in the formation of a series of pseudorotaxanes by using electrostatic repulsion between the end groups and CD.<sup>4</sup> We were prompted to extend that study to clarify the role of both the repulsive interaction and steric hindrance between end groups of an axle and CD. Several dodecamethylene-bearing threading chains (**1**, **2**, **3** and **4**) were designed by adjusting the number of cationic end groups and the end group sizes.

The threading chain **1** was prepared by reaction of *trans*-1,2-bis(4-pyridyl)ethylene with 1,12-dibromododecane in DMF at 80 °C for 12 h.<sup>5</sup> Other threading chains **2**, **3** and **4** can be easily prepared from **1**. In addition, all the counter-anions used were exchanged to Cl<sup>-</sup> to increase solubility of each ligand in water. All the threading chains were fully characterized by <sup>1</sup>H NMR and <sup>13</sup>C NMR spectroscopy, and FAB-MS spectrometry.



**Figure 1.** Structures of the threading chains **1**, **2**, **3** and **4**.

The <sup>1</sup>H NMR spectra of **1** in the presence of  $\alpha$ -CD in D<sub>2</sub>O show new splitting patterns in the methylene region as well as the pyridyl regions indicating the formation of the stable [2]pseudorotaxane containing  $\alpha$ -CD (Figure 2a, b). The splitting peaks are



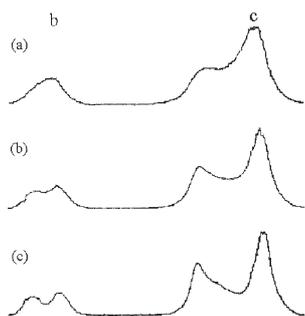
**Figure 2.** <sup>1</sup>H NMR spectra (300 MHz) of (a) **1** in D<sub>2</sub>O (b) **1** with 2 equiv  $\alpha$ -CD in D<sub>2</sub>O (c) **1** in DMSO-*d*<sub>6</sub> (d) **1** with 2 equiv  $\alpha$ -CD in DMSO-*d*<sub>6</sub> ([**1**]=10 mM).

reasonably well explained on the basis of the anisotropy produced by asymmetric  $\alpha$ -CD.

However, the phenomenon is not observed in DMSO-*d*<sub>6</sub> (Figure 2c, d) as a result of the lack of hydrophobic interaction between  $\alpha$ -CD and the threading chain **1**. All the other threading chains **2**, **3** and **4** showed similar behavior with the addition of  $\alpha$ -CD, exhibiting the formation of stable [2]pseudorotaxanes in D<sub>2</sub>O. The stability of [2]pseudorotaxanes is largely dependent on the hydrophobic interaction between the dodecamethylene chain and  $\alpha$ -CD. Therefore, all the threading chains with uniform dodecamethylene chains should have the same order of stability constant ( $K_a \geq 10^3$ ) as observed in [2]pseudorotaxane **1** ·  $\alpha$ -CD.<sup>6</sup>

In addition, we measured the kinetic parameters during the site exchange process to investigate the effect of different end groups on the process of threading and dethreading. To elucidate these characteristics, the free energy of activation for the site exchange process ( $\Delta G^\ddagger$ ) was determined from temperature-dependent <sup>1</sup>H NMR experiments. Temperature effects on the peak shapes showed the dynamic features of **1** ·  $\alpha$ -CD as depicted in Figure 3. The coalescence temperatures ( $T_c$ ) were measured from the b-proton signals of the dodecamethylene chains (Table 1).

$\Delta G^\ddagger$  was evaluated from Eyring's equation<sup>7</sup> which suggests that the rate of dethreading slows down with increasing  $\Delta G^\ddagger$ , indicating that the more stable [2]pseudorotaxane has been formed. The differences in  $\Delta G^\ddagger$  between **1** and other chains imply that the multi-charged end groups act as a trap in keeping  $\alpha$ -CD in [2]pseudorotaxanes from dethreading. In addition, we examined the size effect of end groups with different steric demand. Comparison between  $\Delta G^\ddagger$ 's of **2**, **3** and **4** suggests that  $\Delta G^\ddagger$  gradually rises with increasing steric bulkiness of end groups. With different numbers of cationic terminal groups,  $\alpha$ -CD must



**Figure 3.** Partial  $^1\text{H}$  NMR spectra (300 MHz) of [2]pseudorotaxane **1**· $\alpha$ -CD in methylene regions at three different temperatures: (a) 45 °C ( $T_c$ ) (b) 40 °C (c) 30 °C.

**Table 1.** Kinetic data of each threading chains with  $\alpha$ -CD

	$\Delta\nu/\text{Hz}^a$	$T_c/^\circ\text{C}^b$	$K_c/\text{Hz}^c$	$\Delta G^\ddagger/\text{KJmol}^{-1d}$
<b>1</b>	35.6	45	79.1	$66.5 \pm 0.1$
<b>2</b>	31.9	52	70.9	$68.2 \pm 0.1$
<b>3</b>	32.5	55	72.2	$69.0 \pm 0.1$
<b>4</b>	31.0	67	68.9	$72.0 \pm 0.1$

<sup>a</sup>b-Protons of the dodecamethylene chains were calculated at 303 K. <sup>b</sup> $T_c$  was measured at 5 mM of the threading chains with 20 equiv of  $\alpha$ -CD. <sup>c,d</sup>From Eyring' equation,  $K_c = (\pi\Delta\nu)/(2)^{1/2}$ ,  $\Delta G^\ddagger = 19.1T_c(10.32 + \log(T_c) - \log(K_c))$ .

experience different energy barriers of dehydration around cationic end groups during the site exchange process. Therefore, slow dethreading as well as threading in  $\text{D}_2\text{O}$  was attributed to the increased repulsive interactions between  $\alpha$ -CD and the hydrated charged end groups. The steric factors also play an important role in the course of threading and dethreading. This is in good agreement with our expectation that by increasing the charge density and steric hindrance of the cationic end groups, [2]pseudorotaxanes develop more rotaxane-like characteristics.

In conclusion, we have developed [2]pseudorotaxane complexes between several threading chain molecules and  $\alpha$ -CD which have increasingly rotaxane-like characteristics in the order

**1 < 2 ≤ 3 < 4**. We have found that the complexes between  $\alpha$ -CD and dodecamethylene-bearing threading chains with cationic end groups are stabilized as the number of cationic species and the degree of steric hindrance increase. Therefore, multi-cationic terminal groups with appropriate sizes could be used to develop more rotaxane-like characteristics in pseudorotaxane structures. Further study on the photoresponsiveness of end groups is currently in progress.

This work was supported by the CMDS (KOSEF). B.-S. K thanks the Ministry of Education for the award of the BK 21 fellowship.

#### References and Notes

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- Selected spectral data for **1**:  $^1\text{H}$  NMR (300 MHz,  $\text{D}_2\text{O}$ )  $\delta$  8.68 (d,  $J = 6.7$  Hz, 4H), 8.55 (d,  $J = 6.1$  Hz, 4H), 8.09 (d,  $J = 6.7$  Hz, 4H), 7.66 (d,  $J = 16.5$  Hz, 2H), 7.65 (d,  $J = 6.5$  Hz, 4H), 7.51 (d,  $J = 16.5$  Hz, 2H), 4.46 (t,  $J = 7.2$  Hz, 4H), 1.9–1.7(m, 4H), 1.3–1.1(m, 16H)  $^{13}\text{C}$  NMR (75 MHz,  $\text{D}_2\text{O}$ )  $\delta$  152.7, 149.0, 144.8, 144.4, 137.5, 128.8, 125.4, 123.0, 61.6, 30.7, 28.8, 28.7, 28.3, 25.5; FAB-MS (m-NBA):  $m/z$  568  $[\text{M}-\text{Cl}]^+$ ; UV  $\lambda_{\text{max}}$  315 nm,  $\epsilon = 58000 \text{ M}^{-1}\text{cm}^{-1}$  in water.
- Assuming 1 : 1 binding, the stability constant,  $K_a$  of [2]pseudorotaxane **1**· $\alpha$ -CD can be obtained from the ratio of free and complexed species to be about  $4,500 \text{ M}^{-1}$ .  $[\mathbf{1}] = 10 \text{ mM}$ .
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