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A Molecular Reel: Shuttling of a Rotor by Tumbling of a Macrocycle

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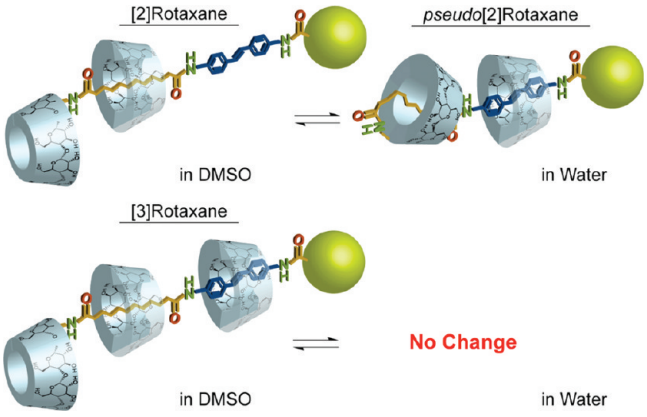

A molecular shuttle is a prototype of molecular machines capable of shuttling a part back and forth in the molecule. To control the shuttling of a macrocycle, we studied the reeling of an axis molecule into a macrocyclic host molecule located at the end of the axis. [2]Rotaxane and [3]rotaxane are composed of α-cyclodextrin (α-CD) rotors, a decamethylene chain, and a stilbene unit as axes and an *altro*-α-CD stopper containing one altropyranose unit and five glucopyranose units. The α-CD rotor of [2]rotaxane includes the decamethylene chain in DMSO-d_6 and moves to include the stilbene group in D_2O. It should be noted that the *altro*-α-CD stopper group reorients to include the decamethylene chain in D_2O. The mechanism for tumbling was elucidated with 2D ROESY NMR measurements and kinetic studies. These studies showed that an altropyranose unit of the *altro*-α-CD stopper tumbles to form a self-inclusion complex in aqueous solution. The *altro*-α-CD stopper of [2]rotaxane reels an axis molecule into its cavity and then pushes the α-CD rotor onto the stilbene group, resulting in conversion to pseudo[2]rotaxane in D_2O. In contrast, the rotors of [3]rotaxane did not show shuttling because there was insufficient space not only for the rotors to shuttle but also for the *altro*-α-CD stopper to include an axis after tumbling. The decamethylene chain and the stilbene group are already included in the rotors of [3]rotaxane. The tumbling of the *altro*-α-CD stopper was found to play a critical role in controlling the shuttling of rotors. We successfully controlled the shuttling of a rotor by reeling the axis molecule into a host molecule at the end of an axis.

Introduction

The X-ray crystal structures of RNA polymerase, DNA polymerase, and λ-exonuclease have shown that these enzymes have a cylindrical cavity for the substrate-binding site to form rotaxanes.[1−3] Prior to the determination of the crystal structures of biological rotaxanes and reports of the

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linear movement of enzymes, rotaxanes[4,5] were studied as candidates for artificial molecular machines[6−8] in supramolecular chemistry. Rotaxanes are good examples of molecules capable of controlling molecular movement because a distinction between the linear motion[9] and the rotary motion[10] of rotors in dumbbell molecules can be made. Several research groups have demonstrated that the shuttling of rotors can be controlled by external stimuli, such as chemical,[11] electrical,[12] or photochemical stimuli.[13] The stimuli-mediated structural changes of host or axis molecules were shown to restrict the position or the shuttling motion of rotors.[14−19] We have previously reported the control of shuttling of rotors and supramolecular structures by external stimuli.[20] However, to our knowledge, there have been no reports of controlling the shuttling of rotors by reeling an axis molecule into the cavity of a host molecule.

Herein, we report the preparation of precisely designed [2]rotaxane and [3]rotaxane with α-cyclodextrin (α-CD) functioning as not only a stopper but also as a rotor. We initially thought that the conformation of rotaxanes would be nearly independent of solvent polarity. We found that [3]rotaxane did not change conformation when solvent and temperature were changed, but [2]rotaxane showed solvent dependency for shuttling of the α-CD rotor. [2]Rotaxane was found to form pseudo[2]rotaxane in D_2O by tumbling of an altropyranose unit of the *altro*-α-CD stopper. The conformational change of [2]rotaxane resembles the action of a "reel" which rotates to reel in the decamethylene chain into the cavity of the *altro*-α-CD stopper. The control of supramolecular structures by tumbling of host molecules has been mostly unexplored in artificial molecular machines. In our study, we observed the movement of an α-CD rotor by the reeling of an axis molecule into the *altro*-α-CD stopper in [2]rotaxane.

Results and Discussion

Preparations of [2]Rotaxane and [3]Rotaxane. [2]Rotaxane and [3]rotaxane were prepared as outlined in Scheme 1. The starting material is an axis molecule having an *altro*-α-CD group (*altro*-α-CD stopper)[21] and a stilbene unit linked

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(21) The *altro*-α-CD stopper is composed of one altropyranose unit and five glucopyranose units. The stopper is formed during the course of synthesis of mono(3-amino-3-deoxy)-α-CD.

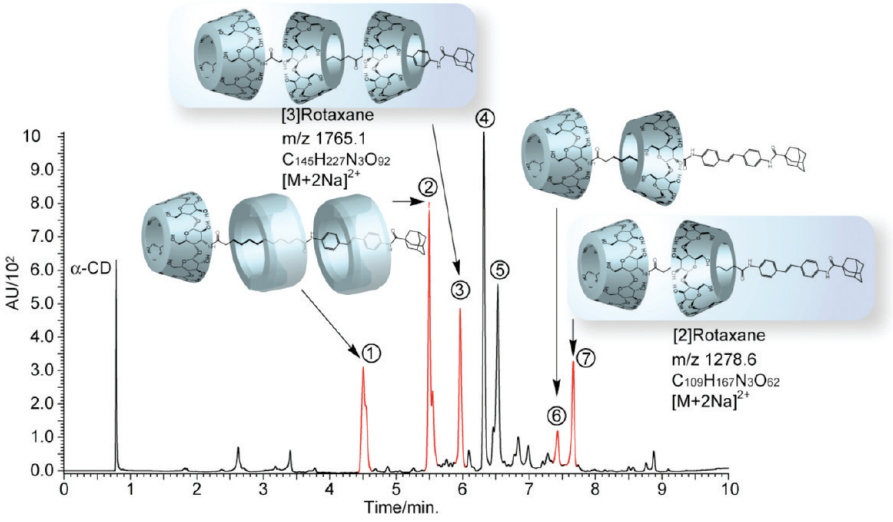
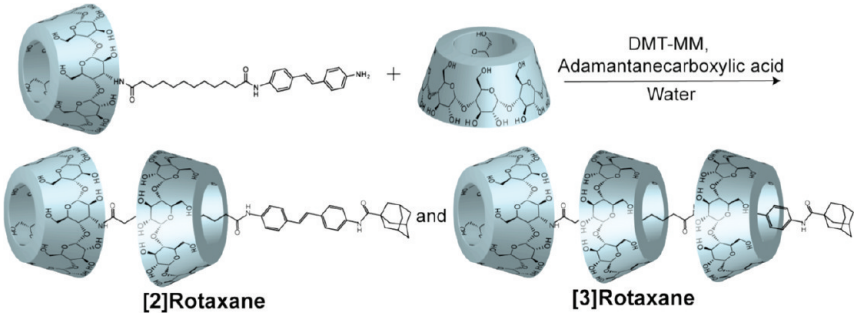


FIGURE 1. Liquid chromatography of the reaction mixture containing [2]rotaxane and [3]rotaxane. The direction of α-CD rotors on [3]rotaxane at peaks 1 and 2 cannot be determined by 2D NMR techniques.

SCHEME 1. Preparation of [2]Rotaxane and [3]Rotaxane[a]



[a]DMT-MM = (4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride.

through a decamethylene group. This axis molecule was condensed with adamantane carboxylic acid in the presence of α-CD (α-CD rotor) in aqueous solution to afford the rotaxane products. The reaction mixture was characterized by reverse phase liquid chromatography-electrospray mass spectrometry (Figures S3 and S4, Supporting Information).

Figure 1 shows the liquid chromatogram of the reaction mixture. Analysis of the corresponding mass spectra showed that the reaction mixture contained the starting materials (peaks "α-CD", 4, and 5), [2]rotaxane (peaks 6 and 7), and [3]rotaxane (peaks 1−3). Three peaks with the same mass number were found to correspond to four isomers of [3]rotaxane. The isomers of [3]rotaxane differed in the direction of the rotors, which had head-to-head, head-to-tail, tail-to-head, or tail-to-tail orientations relative to each other. We cannot determine the structure of isomers (the direction of α-CD rotors) at peaks 1 and 2 even though we made full use of 2D NMR techniques because peak 2 is the mixed isomer. Peaks 6 and 7 were found to correspond to [2]rotaxane isomers with the α-CD rotor having two possible orientations relative to the *altro*-α-CD stopper. The orientation of an α-CD rotor on [2]rotaxane at peak 7 was determined by 2D NMR techniques, whereas that of another [2]rotaxane at the peak 6 was not yet determined because another [2]rotaxane at peak 6 overlapped into raw materials. [3]Rotaxane (peak 3) and [2]rotaxane (peak 7) were each isolated as a single species by preparative reversed-phase chromatography. The conformations of these pure rotaxane isomers in solution were investigated.

Conformational Change of [2]Rotaxane with Solvent Polarity. The location and the direction of the rotor on an axis were determined by 2D NOESY and 2D ROESY NMR spectroscopy. The resonance peaks of the rotaxanes were assigned by COSY, TOCSY, and ROESY measurements (Figures S9−S11, Supporting Information). When the 1D NMR spectra of [2]rotaxane and a dumbbell molecule in DMSO-d_6 were compared, only the protons of the decamethylene group of [2]rotaxane showed peak shifts. The protons of the stilbene group and the adamantyl group of [2]rotaxane did not shift in this solvent (see Figure S7, Supporting Information). A dumbbell molecule without a rotor molecule does not show ROE correlation peaks between the inner protons of the *altro*-α-CD stopper and the protons of an axis group. The 2D ROESY NMR spectrum of [2]rotaxane in DMSO-d_6 showed no correlation peaks between the protons of the stilbene group and the inner protons (C_3H, C_5H, and C_6H) of the α-CD rotor (Figure 2). The protons of the decamethylene group strongly correlated to the protons of the α-CD rotor. These results indicate that the decamethylene group was included within the α-CD rotor when [2]rotaxane was dissolved in DMSO-d_6.

The 2D NOESY NMR spectrum of [2]rotaxane in D_2O showed that the C_3H inner proton of the α-CD rotor clearly correlated to protons A and B of the stilbene group adjacent to a decamethylene group (Figure 3). However, there was only a weak correlation between the C_3H proton and protons C−F of the stilbene group. The C_5H proton clearly correlated to protons C−E, and the C_6H proton correlated to proton E. Further, a correlation between proton F and protons on the adamantyl group was observed. These results suggest that the α-CD rotor is located on the stilbene group and the narrow rim of the α-CD rotor is directed toward the adamantyl stopper. It should be noted that the inner protons of the *altro*-α-CD stopper showed strong correlation peaks to the protons of the decamethylene group. These results provide evidence that [2]rotaxane forms pseudo[2]rotaxane in D_2O through tumbling of the *altro*-α-CD stopper to include the decamethylene axis.

Conformation of [3]Rotaxane. The 2D ROESY NMR spectrum of [3]rotaxane in D_2O showed correlation peaks between the axis protons and the protons of α-CD groups (Figure 4). Because of the stilbene group's shielding effect, the protons of the rotor CD on the stilbene axis could be distinguished from the protons on the rotor on the decamethylene group. The C_3H inner proton of α-CD rotor 1 but not of α-CD rotor 2 correlated to the stilbene group. The C_3H inner proton of α-CD rotor 2 but not of α-CD rotor 1

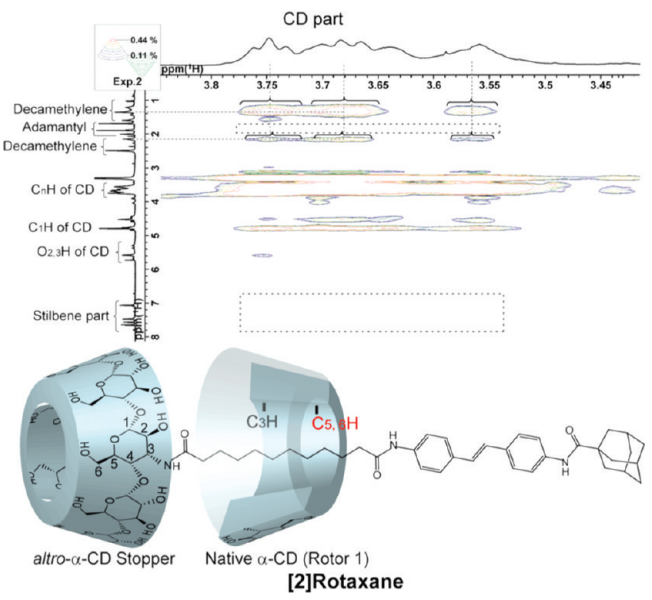


FIGURE 2. 2D NOESY NMR spectrum of [2]rotaxane in DMSO-d_6 at 30 °C (600 MHz, mixing time = 800 ms).

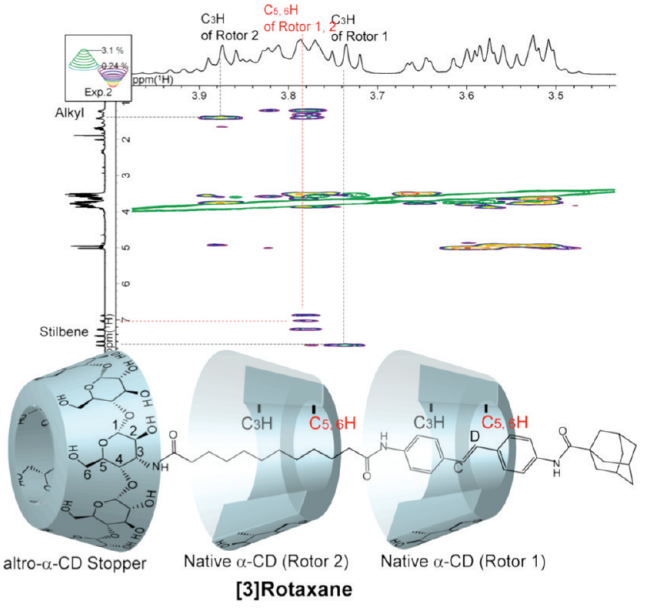


FIGURE 4. 2D ROESY NMR spectrum of [3]rotaxane in D_2O at 30 °C (600 MHz, mixing time = 200 ms).

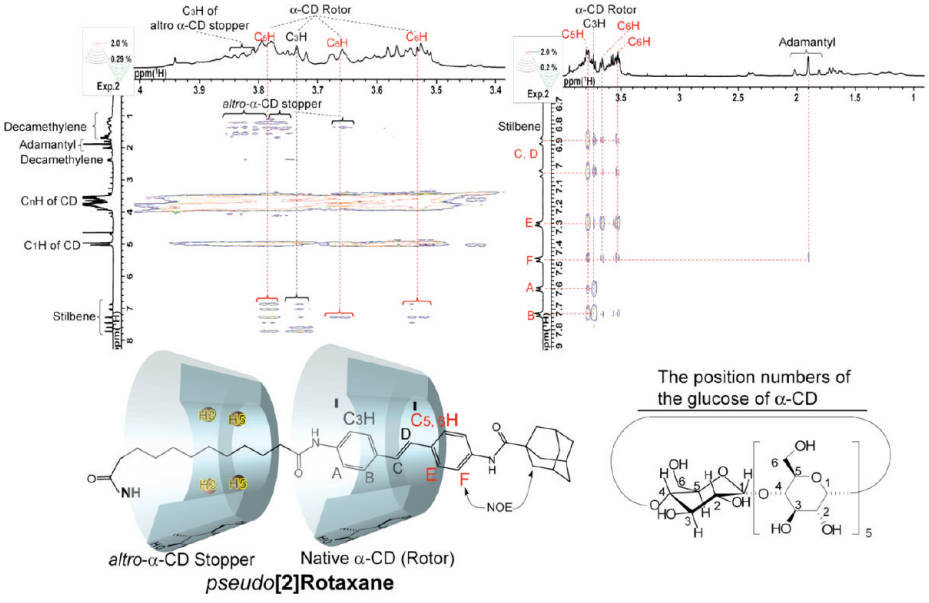


FIGURE 3. 2D NOESY NMR spectrum of pseudo[2]rotaxane converted from [2]rotaxane in D_2O at 30 °C (600 MHz, mixing time = 800 ms). The NOE correlation peak between the proton F and the adamanthyl proton showed the revalidation assignment. Protons of the stilbene group are assigned by the correlation peak between the proton F and the adamantyl protons and by COSY spectroscopy measurements.

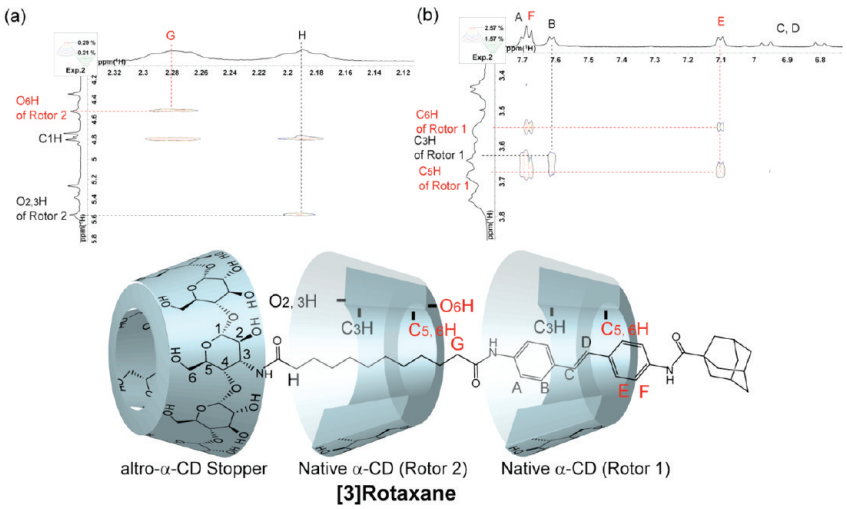
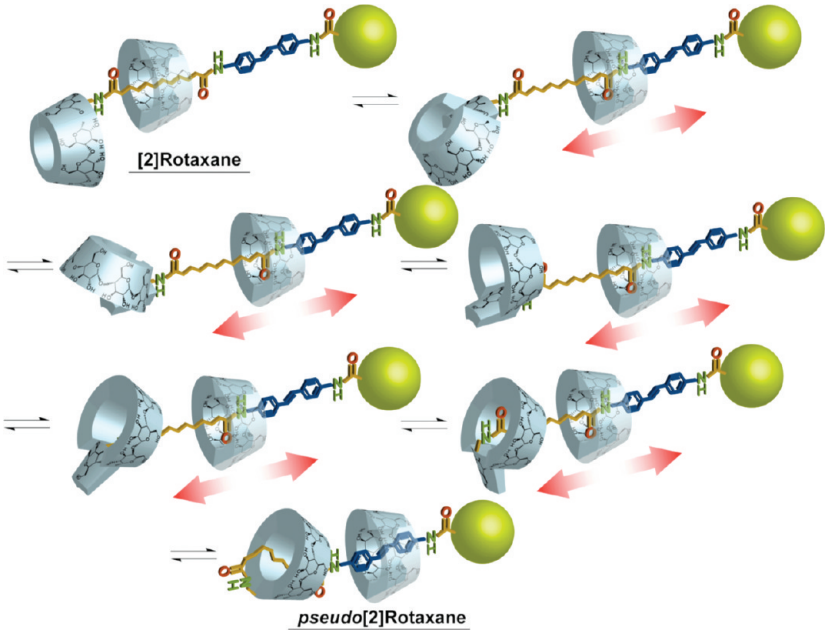


FIGURE 5. 2D NOESY NMR spectra of [3]rotaxane in DMSO-d_6 at 30 °C (600 MHz, mixing time = 800 ms).

SCHEME 2. Formation of Pseudo[2]rotaxane from [2]Rotaxane via Tumbling an Altropyranose Unit



correlated to the decamethylene group. The direction of the rotors on the axes was determined by 2D NOESY NMR studies in DMSO-d_6 because the hydroxyl groups ($O_{2,3,6}H$) of the α-CD rotors were clearly observed in this solvent. Figure 5a shows correlation peaks between the hydroxyl groups of the α-CD rotor 2 and the decamethylene group. Proton G correlated to O_6H of the rotor 2, but not to $O_{2,3}H$ of rotor 2, while proton H correlated to $O_{2,3}H$ of rotor 2 but not to O_6H of rotor 2. The α-CD rotor 1 showed correlation peaks between the $C_{5,6}H$ protons and protons E and F and between the C_3H protons and protons A and B. A correlation peak between the C_6H proton and the proton B was not observed (Figure 5b). The structure of [3]rotaxane in DMSO-d_6 was similar to that observed in D_2O or methanol-d_4. Results of the NMR studies indicated that the narrow rims of both rotors of [3]rotaxane are directed toward the adamantyl stopper group. However, no solvent dependency was observed for the inclusion sites of the rotors in [3]rotaxane. The rotors of [3]rotaxane did not show the shuttling effect observed in [2]rotaxane because there was insufficient space not only for the rotors to shuttle but also for the *altro*-α-CD stopper to enclose an axis after tumbling. [3]Rotaxane forms a relatively stable conformation in D_2O because the two available axes are already included in rotors.

Kinetics: [2]Rotaxane to Pseudo[2]rotaxane. The conformational change of [2]rotaxane through tumbling of an altropyranose unit[22] is shown in Scheme 2. The activation

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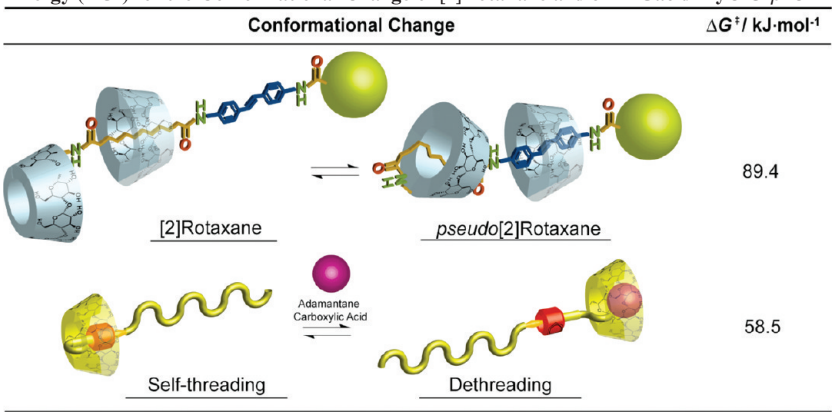
TABLE 1. Activation Free Energy ($\Delta G^{\ddagger}$) for the Conformational Change of [2]Rotaxane and 6-DEGacid-HyCiO-β-CD[a]



[a]The $\Delta G^{\ddagger}$ value for the conformational change of 6-DEGacid-HyCiO-β-CD was calculated by the kinetic rate reported in ref 24b.

free energy ($\Delta G^{\ddagger}_{288K}$) for the conformational change from [2]rotaxane to *pseudo*[2]rotaxane was determined by observing the time-resolved UV spectral change for the process in D_2O at 288 K (Figure S14, Supporting Information). Assuming a two-site exchange process, the $\Delta G^{\ddagger}_{288K}$ value was calculated to be 89.4 kJ·mol^{-1} using a single exponential fitting. The calculated $\Delta G^{\ddagger}$ value for tumbling of the altropyranose residue is higher than the reported value for calix[4]arene tumbling ($\Delta G^{\ddagger}$ = 65.7 kJ·mol^{-1}).[23] The glucopyranose unit of permethylated CDs can easily tumble because hydrogen bonds between neighboring permethylated glucopyranose units cannot form from deprotonation of hydroxyl groups. On the other hand, the normal glucopyranose and altropyranose units are unable to tumble easily due to the formation of hydrogen bond between neighboring units. In any case, the $\Delta G^{\ddagger}$ value for this tumbling process has yet to be revealed.

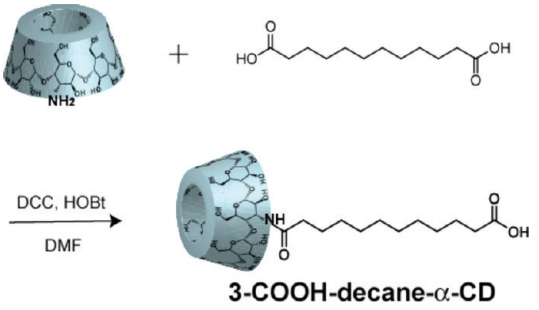
Activation Free Energy of Tumbling and Self-Threading. We have previously studied the self-threading and dethreading dynamics of poly(ethylene glycol) (PEG)-substituted β-CDs with different chain lengths.[24] In these studies, we reported an exchange rate (k_{ex}) of 521 s^{-1} and a $\Delta G^{\ddagger}$ value of 58.5 kJ·mol^{-1} for mono-6-*O*-[4-diethylene glycol acid−hydrocinnamoyl]-β-CD (6-DEGacid-HyCiO-β-CD). This $\Delta G^{\ddagger}$ value is smaller than the calculated $\Delta G^{\ddagger}$ values for tumbling of [2]rotaxane. The k_{ex} and ΔG values of PEG-substituted β-CDs showed a dependence on chain-length because the self-threading process is the main energy barrier. However, a potential explanation for the greater $\Delta G^{\ddagger}$ values in the tumbling process is that the main energetic barrier is the breakage of the hydrogen bond network in the *altro*-α-CD (Table 1). These results indicate that the $\Delta G^{\ddagger}$ value calculated for the conformational change from [2]rotaxane to pseudo[2]rotaxane can be regarded as a reasonable quantity.

Conclusion

We prepared [2]rotaxane and [3]rotaxane bearing an *altro*-α-CD stopper and studied the conformations of these molecules in different solvents. [2]Rotaxane showed a conformational change to pseudo[2]rotaxane depending on the solvent polarity. In contrast, the conformation of [3]rotaxane did not depend on solvent polarity. 2D NOESY and kinetic analyses indicated that [2]rotaxane forms pseudo-[2]rotaxane in D_2O through tumbling of the *altro*-α-CD stopper. Our studies provide evidence for a "molecular reel" mechanism in which the *altro*-α-CD stopper in pseudo-[2]rotaxane reels the decamethylene chain into its cavity and the α-CD rotor reorients to enclose the stilbene group. We successfully controlled the shuttling of a rotor, which enabled a macrocyclic host molecule to reel in an axis molecule and generate a new conformer.

Experimental Section

Preparation of 3-COOH-decane-α-CD.



1,10-Decanedicarboxylic acid (0.11 g, 0.50 mmol), *N*,*N*′-dicyclohexylcarbodiimide (DCC) (0.32 g, 1.6 mmol) and 1-hydroxybenzotriazole acid (HOBt) (0.097 g, 0.72 mmol) were added to dried *N*,*N*-dimethylformamide (DMF) (5.0 mL) at 0 °C. After 1 h, a solution of 3-NH_2-α-CD (0.49 g, 0.50 mmol) in dried DMF (50 mL) was added to the reaction mixture, and the mixture was stirred at 0 °C for 2 h. It was allowed to warm to room temperature and stirred for 60 h. The solution was evaporated and washed with acetone (50 mL × 3) to give crude product of 3-COOH-decane-α-CD (0.20 g, 33%). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 7.64 (d, J = 8.8 Hz, 1H, −N*H*−), 5.87−5.07 (m, 12H, $O_{2,3}H$ of CD), 4.86−4.73 (m, 6H, C_1H of CD), 4.61−4.44 (m, 5H, O_6H of CD), 4.05−3.24 (m, 36H, others of CD), 2.24 (t, J=7.6 Hz, 2H, −CH_2COOH), 2.18 (t, J=7.4 Hz, 2H, −CH_2CONH−), 1.47 (b, 4H, alkyl), 1.25 (b, 12H, alkyl). ^{13}C NMR (150 MHz, DMSO-d_6): δ 24.7, 25.2, 29.4, 29.7, 30.6, 32.3, 33.6, 34.7, 35.9, 36.7(decamethylene), 49.6, 59.3, 60.0, 70.7,

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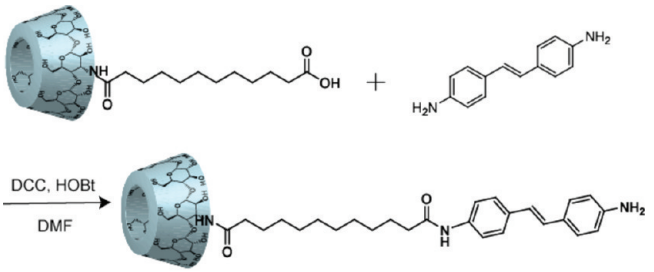
(24) (a) Inoue, Y.; Miyauchi, M.; Nakajima, H.; Takashima, Y.; Yamaguchi, H.; Harada, A. *Macromolecules* **2007**, *40*, 3256–3262. (b) Inoue, Y.; Miyauchi, M.; Nakajima, H.; Takashima, Y.; Yamaguchi, H.; Harada, A. *J. Am. Chem. Soc.* **2006**, *128*, 8994–8995.

71.5, 71.8, 72.1, 72.7, 72.9, 73.2, 73.5, 76.5, 79.6, 80.7, 81.7, 82.8, 101.1, 101.5, 102.0, 102.2, 102.4, 104.7 (C(1−6) of CD moiety), 171.2 (−NH-*C*=O), 174.2 (−O-*C*=O). ESI-MS: calcd for $C_{48}H_{80}NO_{32}$ 1182.5 ([M − H]$^-$), found 1182.6. ESI-TOF MS (high resolution MS): calcd for $C_{48}H_{81}NO_{32}Na$ 1206.4639 ([M + Na]$^+$), $C_{48}H_{82}NO_{32}$ 1184.4820 ([M + H]$^+$), $C_{48}H_{80}NO_{32}$ 1182.4663 ([M − H]$^-$), found 1206.4690 ([M + Na]$^+$), 1184.4844 ([M + H]$^+$), 1182.4674 ([M − H]$^-$). Mp: 260−265 °C dec.

Preparation of 4-NH_2Sti-decane-α-CD.



4-NH_2Sti-decane-α-CD

3-COOH-decane-α-CD (0.24 g, 0.20 mmol), DCC (0.044 g, 0.22 mmol), and HOBt (0.029 g, 0.21 mmol) were added to dried DMF (5 mL) at 0 °C. After 1 h, a solution of diaminostilbene (0.40 g, 1.9 mmol) in dried DMF (50 mL) was added to the reaction mixture, and the mixture was stirred at 0 °C for 2 h. It was allowed to warm to room temperature and stirred for 7 days. The solution was evaporated and washed with acetone (50 mL × 3) to give yellow powder. The precipitate was washed with water (50 mL) to give 4-NH_2Sti-decane-α-CD (yellow powder, 44 mg, 16%). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 9.81 (s, 1H, amido of stilbene side), 7.64−7.62 (d, J=8.1 Hz, 1H, amido proton of α-CD side), 7.53−7.52 (d, J = 8.6 Hz, 2H, 2-position of stilbene), 7.40−7.39(d, J=8.9 Hz, 2H, 3-position of stilbene), 7.24−7.22 (m, J=8.3 Hz, 2H, 3′-position of stilbene), 6.95−6.79 (d, J=17 Hz, 2H, olefin of stilbene), 6.55−6.53 (d, J= 8.6 Hz, 2H, 2′-position of stilbene), 5.86−5.06 (m, 12H, $O_{2,3}H$ of CD), 4.85−4.78 (m, 6H, C_1H of CD), 4.67−4.42 (m, 5H, O_6H of CD), 4.00−3.21 (m, overlaps with HOD, 36H, others of CD), 2.29−2.26 (t, J = 7.3 Hz, 2H, alkyl), 1.61−1.47 (m, 4H, alkyl), 1.28−1.24(m, 12H, alkyl). ^{13}C NMR (DMSO-d_6 30 °C, 150 MHz): δ 26.1, 29.6, 37.3 (decamethylene), 56.2, 57.5, 60.3, 67.9, 68.2, 72.9, 80.8, 82.7, 88.9, 103.0, 103.2 (CD moiety), 114.9 (−*C*H=CH-Ph), 120.2 (−CH=CH-2,6-*Ph*), 126.9 (−CH=CH-3,5-*Ph*), 128.3 (−CH=CH-4-*Ph*), 128.6 (−CH=CH-1-*Ph*), 148.1 (−CH=*C*H-Ph). ESI-MS: calcd for $C_{62}H_{93}N_3O_{31}$ 1398.5691 ([M + Na]$^+$), 1376.5871 ([M + H]$^+$), found 1398.6 1376.6; calcd for $C_{62}H_{92}N_3O_{31}$ 1374.5715 ([M − H]$^-$), found 1374.6. ESI-TOF MS (high resolution MS): calcd for $C_{62}H_{93}N_3O_{31}$ 1398.5691 ([M + Na]$^+$), 1376.5871 ([M + H]$^+$),1374.5715 ([M − H]$^-$), found 1398.5627 ([M + Na]$^+$), 0.1376.5834 ([M + H]$^+$), 1374.5750 ([M − H]$^-$). Anal. Calcd for $C_{62}H_{93}N_3O_{31}\cdot 8.10H_2O$: C, 48.92; H, 7.23; N, 2.76. Found: C, 48.46, H, 6.75; N, 2.72.

Preparation of [2]Rotaxane and [3]Rotaxane. 4-NH_2Sti-decane-α-CD (10 mg, 7.3 μmol), α-CD (50 mg, 5.1 μmol), adamantanecarboxylic acid (320 mg, 1.6 mmol), and DMT-MM (97 mg, 720 μmol) were added to water (5 mL) at room temperature for 7 days. The insoluble residue was filtered, and the solution was purified by preparative reversed-phase high-performance liquid chromatography to give pure [2]rotaxane (white powder, 0.75 mg, 4.1%) and [3]rotaxane (white powder, 2.1 mg, 8.2%).

[2]Rotaxane. ^{1}H NMR (600 MHz, CD_3OD) δ_H 7.59 (d, J=8.7 Hz, 4H, 2-position of stilbene), 7.53 (d, J = 8.7 Hz, 4H, 2-position of stilbene), 7.50−7.40 (m, 4H, 3-position of stilbene), 7.06 (s, 2H, olefin of stilbene), 4.98−4.79 (m, 12H, C_1H of CD), 4.01−3.79 (m, 36H, $C_{3,5,6}H$ of CD), 3.63−3.46 (m, 24H, $C_{2,4}H$ of CD), 2.36 (t, J=7.3 Hz, 4H, α methylene in decamethylene), 2.07 (s, 3H, adamantane part), 2.00 (s, 6H, adamantane part), 1.81 (s, 6H, adamantane part), 1.78 (b, 2H, others of decamethylene), 1.67 (b, 2H, others of decamethylene), 1.52−1.28 (m, 12H, others of decamethylene). ESI-MS: calcd for $C_{109}H_{167}N_3Na_2O_{62}$ 1277.8 ([M + Na]$^{2+}$), found 1278.6; calcd for $C_{109}H_{165}N_3O_{62}$ 1253.993 ([M − 2H]$^{2-}$), found 1254.8. ESI-TOF MS (high resolution MS): calcd for $C_{109}H_{167}N_3O_{62}$ 2532.9905 ([M + Na]$^+$), 1278.4918 ([M + 2Na]$^{2+}$), found 2532.9993 ([M + Na]$^+$), 1278.4974, ([M + 2Na]2$^+$).

[3]Rotaxane. ^{1}H NMR (600 MHz, DMSO-d_6): δ_H 9.83 (s, 1H, amido proton of stilbene side), 9.15 (s, 1H, amido proton of adamantane side), 7.83 (d, J = 6.2 Hz, 1H, amido proton of modified CD), 7.70−7.65 (m, 4H, 2-position of decamethylene side of stilbene, 2-position of adamantane side of stilbene), 7.61 (d, 2H, 3-position of decamethylene and side of stilbene), 7.10 (m, 4H, 3-position of adamantane side of stilbene), 6.96 (d, J=17.1 Hz, 1H, decamethylene side of olefin of stilbene), 6.80 (d, J = 16.3 Hz, 1H, adamantane side of olefin of stilbene), 6.05−5.01 (m, $O_{2,3}H$ of CD), 4.85−4.74 (m, C_1H of CD), 4.59 (s, 6H, C_1H of *altro*-α-CD stopper), 4.52−4.34 (m, O6H of CD), 4.06 (s, C_3H of *altro*-α-CD stopper), 3.92−3.30 (m, $C_{2-6}H$ of CD), 2.28 (s, 2H, α methylene in decamethylene), 2.19 (s, 2H, α methylene in decamethylene), 2.02 (s, 3H, adamantane part), 1.93 (s, 6H, adamantane part), 1.70 (s, 6H, adamantane part), 1.61−1.08 (m, 16H, others of decamethylene). ^{13}C NMR (DMSO-d_6 30 °C, 150 MHz): δ 27.6, 28.9, 29.7, 35.0, 36.0 (decamethylene), 59.1, 59.9, 71.7, 72.1, 73.1, 73.3, 78.7, 81.6, 102.0, 104.5 (CD moiety), 119.2, 125.6, 127.3, 128.6(−CH=CH-Ph), 146.9 (−NH-*C*=O), 151.5 (−NH-*C*=O), 164.3 (−NH-*C*=O). ESI-MS: calcd for $C_{145}H_{227}N_3O_{92}$ 1764.7 ([M + 2Na]$^{2+}$), 1740.2 ([M − 2H]$^{2-}$), found 1765.1 ([M + 2Na]$^{2+}$), 1740.9 ([M − 2H]$^{2-}$). ESI-TOF MS (high resolution MS): calcd for $C_{145}H_{227}N_3O_{92}$ 1764.6503 ([M + 2Na]$^{2+}$), 1753.6593 ([M + H + Na]$^{2+}$), 1742.6683 ([M + 2H]$^{2+}$), 1763.6425 ([M + 2Na − 2H]$^{2-}$), 1740.6527 ([M−2H]$^{2-}$), found 1764.6503 ([M+2Na]$^{2+}$), 1753.6617 ([M + H + Na]$^{2+}$), 1742.6621 ([M + 2H]$^{2+}$), 1763.6495([M + 2Na − 2H]$^{2-}$), 1740.6542 ([M − 2H]$^{2-}$).

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Supporting Information Available: Selected NMR data (variable-temperature NMR and time-resolved NMR spectrometry, 2D gCOSY, TOCSY, ROESY, 2D NOESY, and gHSQC) and Eyring plots are shown. This material is available free of charge via the Internet at http://pubs.acs.org.