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Relative Rotational Motion between α-Cyclodextrin Derivatives and a Stiff Axle Molecule

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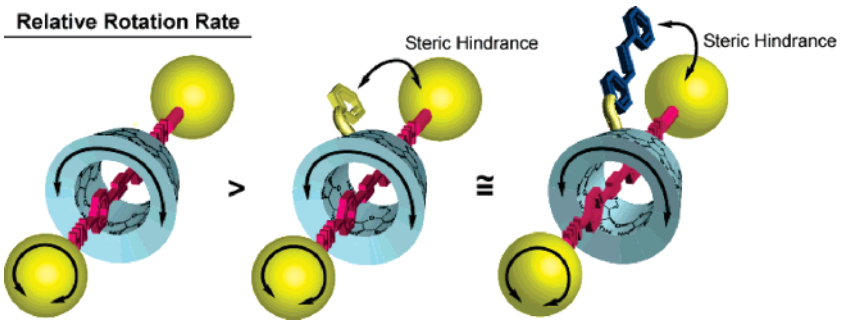

Novel [2]rotaxanes bearing α-cyclodextrin (α-CD) derivatives and a diphenylacetylene axis molecule with trinitrobenzene as a bulky stopper have been prepared to investigate the relative rotary movement of a ring relative to an axis molecule and that of an axis molecule in a ring by NMR techniques. [2]-Rotaxanes **2** and **3** were composed of α-CD derivatives (**2**: 6-phenyl-amide-α-CD; **3**: 6-stilbene-amide-α-CD). The protons of α-CDs in rotaxanes were thoroughly assigned by the two-dimensional NMR techniques (TOCSY, COSY, ROESY, HMQC, and HMBC). The protons of α-CD in rotaxane **1** did not show splitting, whereas the resonance peak shifts and splitting for the corresponding protons of α-CD derivatives in rotaxanes **2** and **3** were observed by the shielding and deshielding effects from a diphenylacetylene axis molecule. The splitting of resonance peaks was closely related to the rotary movements of α-CDs and an axis molecule. We supposed that α-CD in rotaxane **1** rotates freely around a diphenylacetylene axis molecule, and vice versa, whereas the rotary movement of α-CD derivatives and the axis molecules of rotaxanes **2** and **3** were restricted by the steric repulsion between the substituent group of α-CD and the stopper group of an axis molecule. To estimate the relative rotary movement of CDs and an axis molecule in rotaxanes, the rotational correlation time (τ_c) of rotaxanes was measured by ^{13}C NMR. The results indicate that the corresponding rotary movement of the modified α-CD and the axis molecules in rotaxanes **2** and **3** depends on the size of the substituent group.

Introduction

Molecular motors in biological systems are roughly distinguished between linear molecular motors, such as myosin, kinesin, dynein, etc.,[1−4] and rotary motors, such as F_0F_1-ATP synthase, F_1-ATPase, etc.[5−6] Rotaxanes are considered to be a good example of controlled molecular movement in both linear and rotary molecular motor systems. Recently, excellent studies

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on controlled synthetic linear[7,8] and rotary molecular motors have been reported by using rotaxane as building blocks, which were achieved by controlling rotary movement.[9−12] We previously reported that the linear movement of α-cyclodextrin (α-CD) on pseudo-[2]rotaxane with dicationic axle molecules showed controlled direction of faces of α-CD depending on the axle terminal groups.[13] In the present report, we have focused on the rotary movement of α-CD derivatives around a diphenylacetylene axle molecule in suitably designed rotaxanes. NMR studies of CD rotors with an axle molecule were reported by some research groups.[14−18] Now we have investigated the relationship between the structure of substituent groups in modified CDs and the rotational motion of CDs and/or an axis molecule. Three kinds of α-CD on [2]rotaxane have been prepared (Figure 1). The effect of a substituent group of α-CD on the rotary movement was investigated by variable temperature NMR spectroscopy and the rotational correlation time (τ_c).

Results and Discussion

Preparation of Rotaxanes and Crystal Structure of Rotaxane 1. [2]Rotaxanes (**1**, **2**, and **3**) were prepared by the reaction of diaminodiphenylacetylene with sodium 2,4,6-trinitrobenzene-1-sulfonate in aqueous solutions of CD derivatives as outlined in Scheme 1. The crude products were subjected to a reversed phase HPLC to give [2]rotaxanes (**1**, **2**, and **3**) in 65%, 67%, and 8% yield, respectively. The sodium adducts of molecular ion of rotaxanes were observed by MALDI-TOF mass spectroscopy. Pseudo-rotaxanes, which do not have end stoppers, showed no such molecular ion peaks of pseudo-rotaxane because of their dissociations. We have obtained a single crystal of rotaxane **1** suitable for X-ray crystallography analysis (Figure 2). The crystal structure of rotaxane **1** shows that the wider rim (secondary hydroxyl group side) of α-CD is located close to the trinitrobenzene end group. The distance between secondary hydroxyl groups of α-CD and the nitro group showed an average of 2.95−3.85 Å, whereas the distance between primary hydroxyl groups of α-CD and the nitro group showed an average of 3.85−4.60 Å. These results indicate that we succeeded in obtaining interlocked molecules, rotaxanes (**1**, **2**, and **3**).

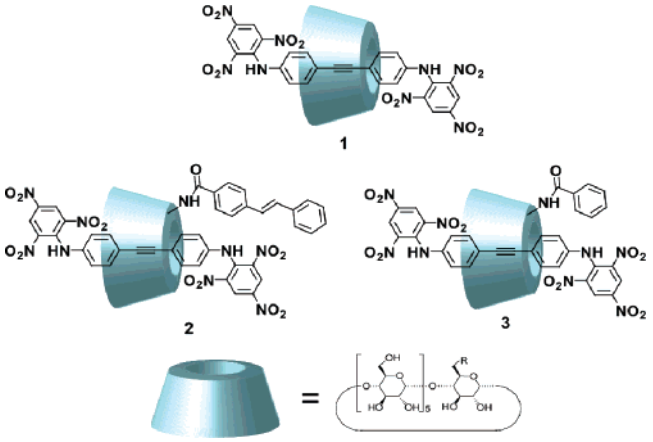


FIGURE 1. Chemical structures of α-CD-based rotaxanes.

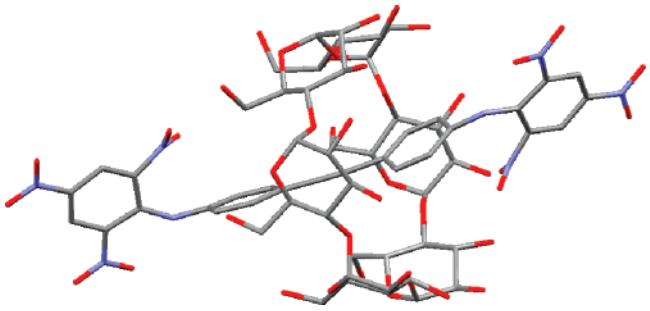
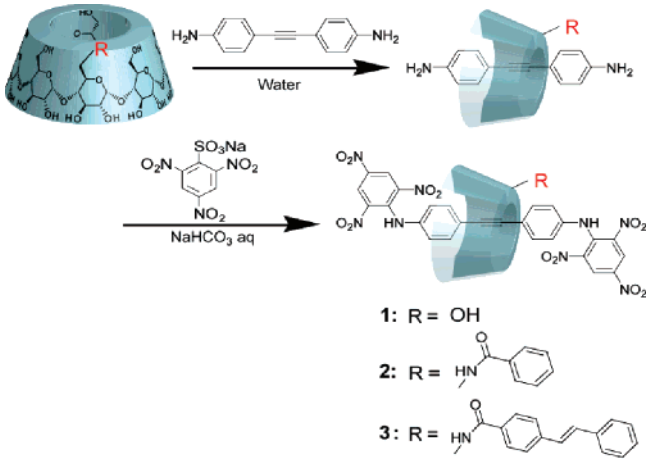


FIGURE 2. Crystal structure of rotaxane **1**. Carbon, oxygen, and nitrogen are shown in gray, red, and purple, respectively.

SCHEME 1. Preparation of [2]Rotaxanes



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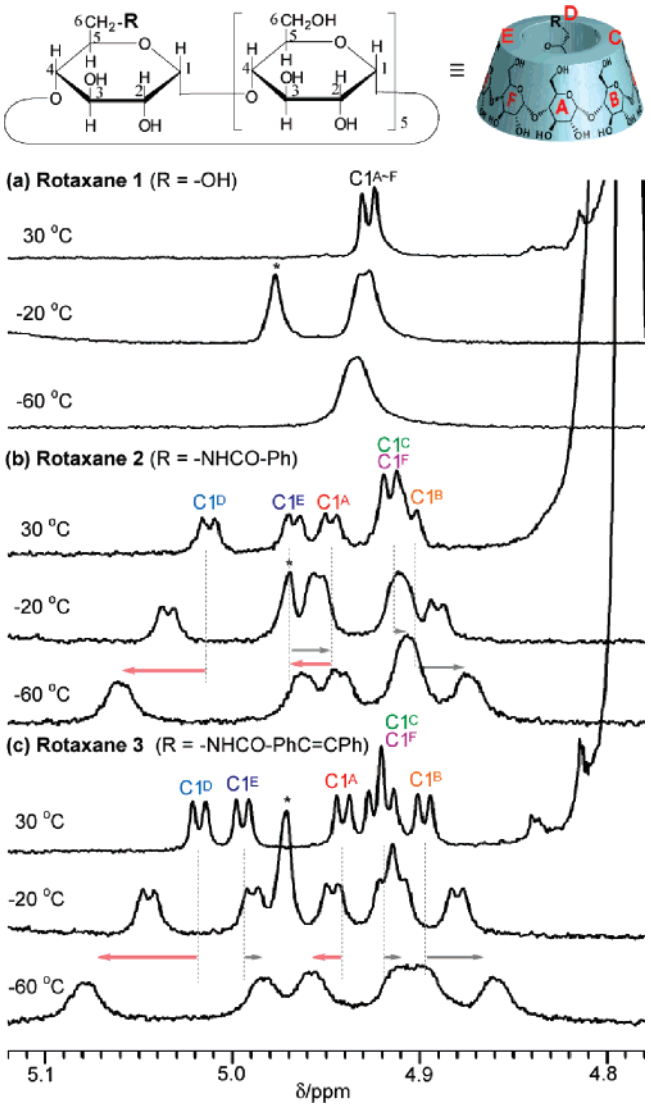

FIGURE 3. ^{1}H NMR spectra of rotaxanes **1** (a), **2** (b), and **3** (c) in methanol-d_4 (0.6 mM) under variable temperature. *: Exchange peak between H_2O and methanol-d_4.

^{1}H NMR Analyses of Rotaxanes. Temperature Variation. The ^{1}H NMR spectra of [2]rotaxanes **1**, **2**, and **3** at varying temperatures are shown in Figure 3. The resonance peaks of these rotaxanes have been thoroughly assigned by COSY, TOCSY, HMQC, HMBC, and ROESY measurements. The C1*H* protons of the glucopyranose unit of A−F in α-CD, hereinafter called C1^{A-F}*H*, in rotaxane **1** exhibited a peak shift downfield with a decrease in temperature, whereas the corresponding protons in rotaxane **1** did not split because α-CD is not modified (Figure 3a). The C1^{A-F}*H* peaks in rotaxanes **2** and **3** were split by the introduction of a substituent group to α-CD and an anisotropic effect from a diphenylacetylene axle molecule. The C1^{A}*H* and C1^{D}*H* peaks in rotaxanes **2** and **3** shifted downfield with decrease in temperature, respectively, whereas the C1^{B}*H*, C1^{C}*H*, and C1^{F}*H* peaks of rotaxanes **2** and **3** shifted upfield, respectively (Figures 3b,c). Figure 4 summarizes the peak shifts of the inner protons of modified α-CDs (C3*H* and C5*H*) for rotaxanes **2** and **3** at 30 °C and −60 °C, respectively. For rotaxane **2**, C3^{B,C,F}*H* and C5^{B,C,E}*H* peaks showed the upfield shifts with a decrease in temperature by the shielding effect from a diphenylacetylene axis molecule on the glucopyranose

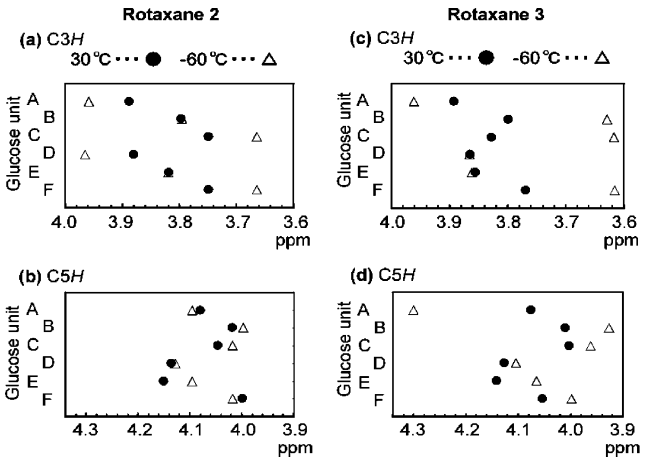

FIGURE 4. Results of the peak shifts of inner protons (C3*H* and C5*H*) of modified α-CDs from 30 °C to −60 °C. (a and b) Protons of C3*H* and C5*H* in rotaxane **2**, respectively. (c and d) Protons of C3*H* and C5*H* in rotaxane **3**, respectively. A vertical scale (A−F) represents the glucopyranose unit.

units of B, C, and E, whereas the downfield shifts of C3^{A,D}*H* and C5^{A}*H* peaks were observed as shown in Figure 4a,b. For rotaxane **3**, C3^{B,C,F}*H* and C5^{B,C,E,F}*H* peaks showed upfield shifts at −60 °C. The downfield shifts of C3^{A}*H* and C5^{A,F}*H* peaks with a decrease in temperature were caused by the deshielding effect (Figure 4c,d). The glucopyranose units of A and D in rotaxanes **2** and **3** are located adjacent to the edge of a diphenylacetylene axis molecule at −60 °C. It should be noted that the corresponding signals of rotaxane **3** showed larger peak shifts and splitting than those of rotaxane **2** (Figure 4). Steric repulsion between the substituent group of α-CD and the stopper group (trinitrophenyl group) of an axis molecule is supposed to restrict the rotary movement between modified α-CDs and axis molecules.

ROESY Spectra of Rotaxanes Measured under Varying Temperatures. The detailed conformations of rotaxanes **2** and **3** were determined by using ROESY NMR measurements. The ROESY NMR spectra of rotaxanes **2** and **3** at 30 °C showed correlation peaks between inner protons (C3*H* and C5*H*) of modified α-CD and the protons (i and k) of the diphenylacetylene axis molecule (Figure 5a,c). For rotaxane **2**, the correlation peaks between C5*H* and k proton and between C3*H* and i proton were observed. On the other hand, no correlation peak between C5*H* and i proton was observed because rotaxanes form asymmetric structures due to the bucket structure of α-CDs. The correlation intensities between C5^{A-F}*H* and k proton (or j proton) and between C3^{A-F}*H* and i (or j proton) proton showed equivalent intensities at 30 °C, indicating that modified CDs freely rotate around a diphenylacetylene axis molecule on the NMR relaxation time scale ($<10^{-3}$ s)[19] at 30 °C. Rotaxane **3** showed similar inclusion and rotation behavior at 30 °C.

For rotaxane **2** at −60 °C, correlation peaks between C3^{A,B,D,E}*H* and i proton were observed, as well as those between C5^{A,B,D,E}*H* and k proton, whereas C3^{C,F}*H* did not show the correlation peaks with i proton, as well as between C5^{C,F}*H* and k proton. For rotaxane **3** at −60 °C, C3^{A,D,E}*H* and C5^{D,E}*H* of 6-stilbene-amide-α-CD were correlated with i and k protons of the axis molecule, respectively. Neither C3^{B,C,F}*H* nor C5^{B,C,F}*H*

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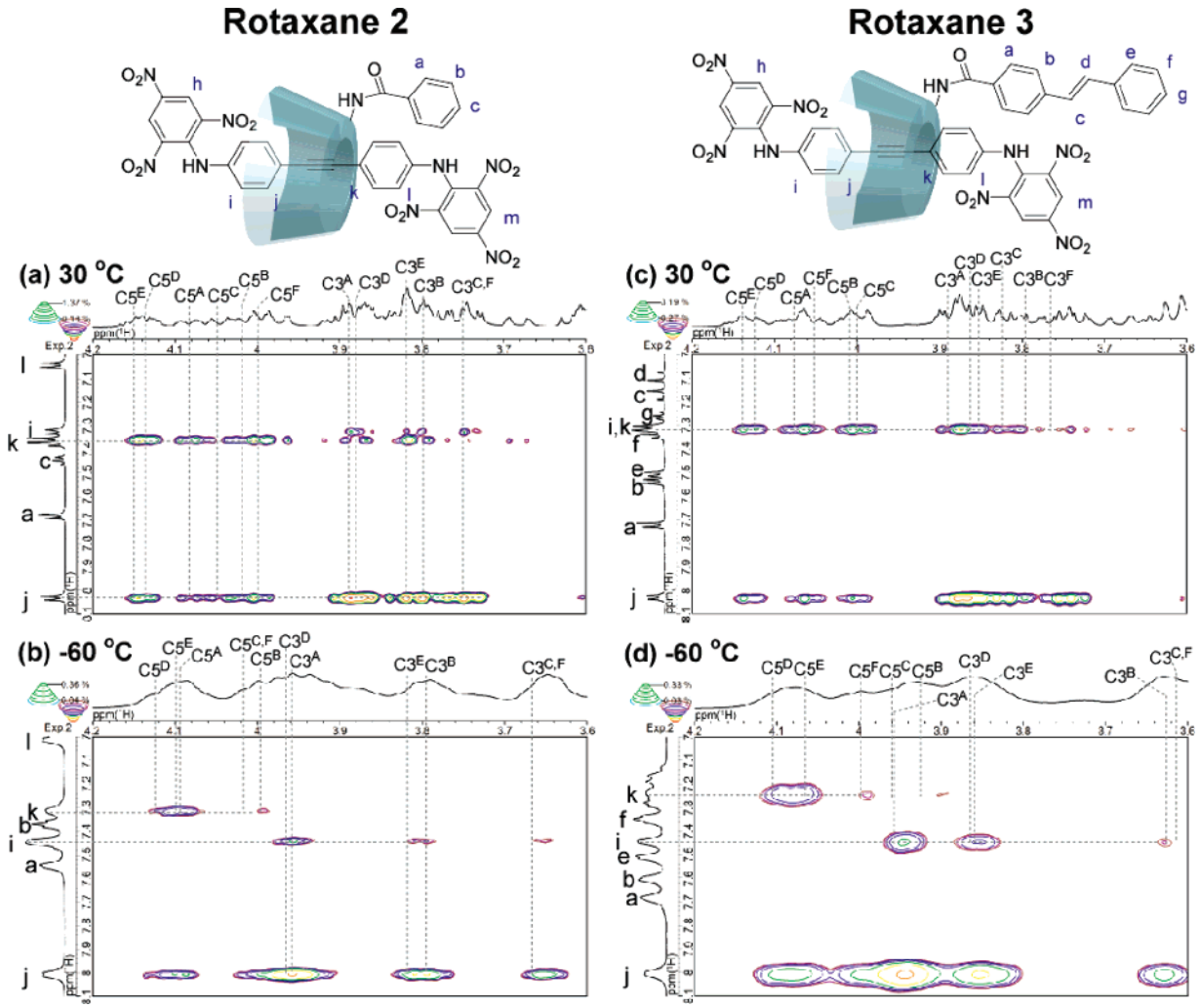


FIGURE 5. ROESY NMR spectra of rotaxanes **2** (a and b) and **3** (c and d) in methanol-d_4 (5 mM) under variable temperature.

showed the correlation peaks with k proton. The distance between C3^{A-F}*H* and i proton and between C5^{A-F}*H* and k proton in rotaxane **1** was 2.698−4.643 Å and 2.575−3.928 Å, respectively, which were measured with the data of single X-ray analysis. These results indicate that the relative rotational movements between modified α-CDs and axis molecules are significantly decreased at −60 °C.[20] The rotation behavior of rotaxane **3** is different from that of rotaxane **2** as represented schematically in Figure 6.

Rotational Relaxation Time Measurement for [2]Rotaxanes. Longitudinal relaxation times (T_1) of ^{13}C NMR for [2]-rotaxanes were measured in DMSO-d_6[21] at 30 °C to estimate the average time scale for molecular motions of α-CDs. In the observation of the motion of rotaxanes, it is necessary to distinguish the motion of axis molecules and α-CD molecules. We have measured the T_1 for ^{13}C of the 2′-position in a diphenylacetylene group and ^{13}C of C1, C2, and C4 in α-CDs by using 270, 400, 500, and 600 MHz NMR spectrometers, respectively, corresponding to 67.77, 100.4, 125.5, and 150.6 MHz resonance frequencies for ^{13}C, respectively (Table 1). Figure 7 shows the relationship between the obtained T_1 data and the resonance frequency for rotaxane **1**. Curve fitting was performed on these plots by using eq 1 to determine a rotational correlation time (τ_c) showing the molecular fluctuation (Table 2). The relative movements between α-CDs and axis molecules were estimated by $\Delta(1/\tau_c)$. τ_c of the axis molecules were shorter than those of α-CDs in each rotaxane, indicating that the relative rotation rates of axis molecules are faster than that of α-CDs. The order of $\Delta(1/\tau_c)$ is rotaxanes **1** > **2** ≅ **3**. The relative rotary movements of CDs and/or axis molecules in rotaxanes **2** and **3** were restricted relative to that of rotaxane **1**. There is a slight difference in motion between rotaxanes **2** and **3**. This result is in excellent agreement with the 2D ROESY NMR experiments.

Conclusion

We have observed the rotary movement of α-CDs as a rotor on the rotaxanes by NMR measurements. ROESY measurements showed that α-CDs rotate around an axis molecule faster on the NMR time scale at 30 °C; however, rotaxanes **2** and **3**

(20) The torsion angle between phenyl rings of diphenylacetylene was 8.68 Å in rotaxane **1**, measured by single crystal X-ray analysis. However, the diphenylacetylene did not show a disordered structure. If the nonspecific glucopyranose units show the correlation peaks for the phenyl ring, the phenyl ring should show a flip of more than 60°. On the basis of these data, we supposed that the flipping phenyl rings did not occur during the 2D ROESY NMR measurement.

(21) We have to adjust the concentration of the solution to measure τ_c by ^{13}C NMR spectroscopy because these rotaxanes have high solubility for DMSO-d_6.

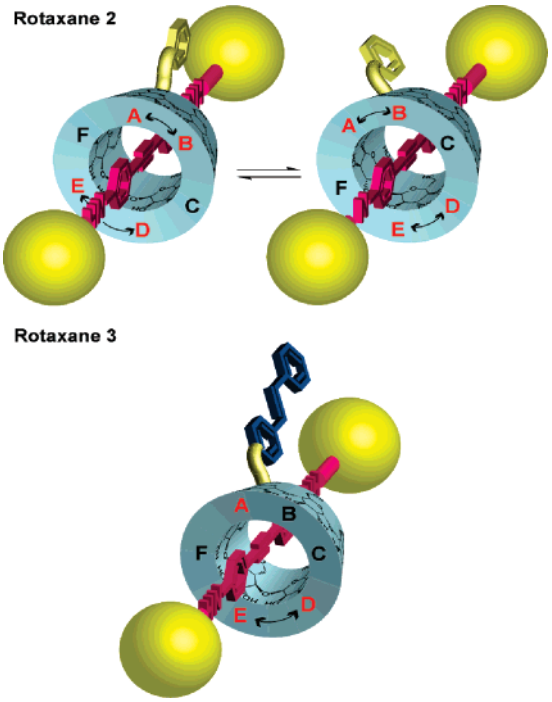


FIGURE 6. Schematic illustration of rotary movement of rotaxanes **2** and **3**. The rotary movement of axis molecules were omitted to clarify the rotation behavior of axis molecules and modified α-CDs.

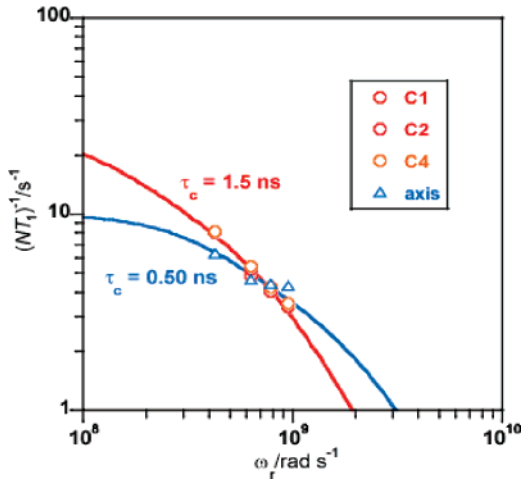


FIGURE 7. Dependency of $(NT_1)^{-1}$ on ω_r for C1, C2, and C5 nuclei in rotaxane **1** in DMSO-d_6 at 30 °C. See Figures S16 and S17 for rotaxanes **2** and rotaxanes **3**, respectively.

showed nonequivalent correlation peaks between the protons of an axis molecule and inner protons of α-CDs, indicating that the rotational motion of the α-CDs and the axis molecules are slowed down at −60 °C. To estimate the significant difference in rotary movement between rotaxans **2** and **3**, we have measured a rotational correlation time (τ_c) for an axis molecule and α-CDs, respectively. Comparing rotaxanes **1**, **2**, and **3** on the basis of an axis molecule, the rotational rates of modified α-CDs in rotaxanes **2** and **3** were slower than that of the α-CD in rotaxane **1** (Figure 8). We suppose that the steric hindrance between the substituent group of the α-CDs and the end group

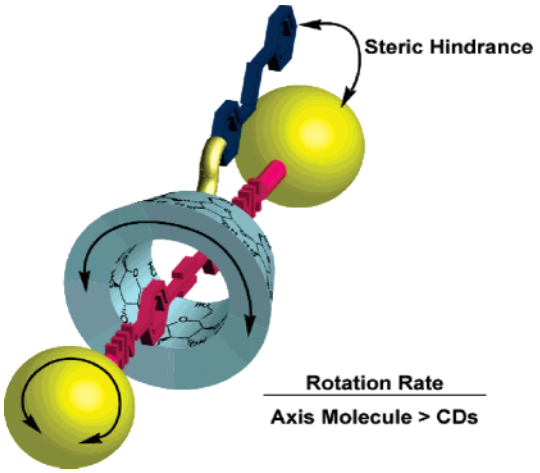


FIGURE 8. Schematic illustration of rotation behavior of [2]rotaxanes. This figure shows a typical result, [2]rotaxane with 6-stilbene-amide-α-CD.

of an axis molecule triggered the restriction of rotary movement of the α-CDs around the axis molecule. Now we are preparing novel [2]rotaxanes, without acceptor molecules (trinitrobenzene group), to control the rotary movement by photoirradiation.

Experimental Section

Longitudinal Relaxation Time Measurements. ^{13}C NMR measurements were performed to determine the longitudinal relaxation time, T_1, by using JEOL EX-270 (resonance frequency for ^{13}C: $\omega_r = 67.77$ MHz), JEOL GSX-400 (resonance frequency for ^{13}C: $\omega_r = 100.4$ MHz), JEOL Lambda-500 (resonance frequency for ^{13}C: $\omega_r = 125.5$ MHz), and Varian Unity plus-600 (resonance frequency for ^{13}C: $\omega_r = 150.6$ MHz) spectrometers at 30 °C via a conventional inversion recovery pulse sequence, 90°−τ−180°, under the deuterium lock mode. The rotational correlation time, τ_c, for each ^{13}C nucleus in the rotaxanes was determined via eq 1 with obtained T_1 values at different resonance frequencies.[22]

$$\frac{1}{NT_1} = \left(\frac{\mu_0}{4\pi}\right)\frac{\gamma H^2 \gamma C^2 h^2}{40\pi^2 r_{CH}^6}\left(\frac{\tau_c}{1+9(\omega_r\tau_c)^2} + \frac{3\tau_c}{1+(\omega_r\tau_c)^2} + \frac{6\tau_c}{1+25(\omega_r\tau_c)^2}\right) \quad (1)$$

where N, μ_0, g_H, γ_C, h, and r_{CH} are the number of ^1Hs directly bound to ^{13}C, permeability of free space ($4\pi \times 10^{-7}$ H·m^{-1}), gyromagnetic ration of ^1H (2.675×10^8 rad·T^{-1}·s^{-1}), gyromagnetic ratio of ^{13}C (0.688×10^8 rad·T^{-1}·s^{-1}), Planck's constant (6.626×10^{-34} J·s), and distance between ^1H and ^{13}C, respectively, 0.1102 nm for a diphenlyacetylene group and 0.112 nm for C1-H, C2-H, C4-H of the α-CDs. These distances were calculated by Spartan '04 using the Hartree−Fock method.

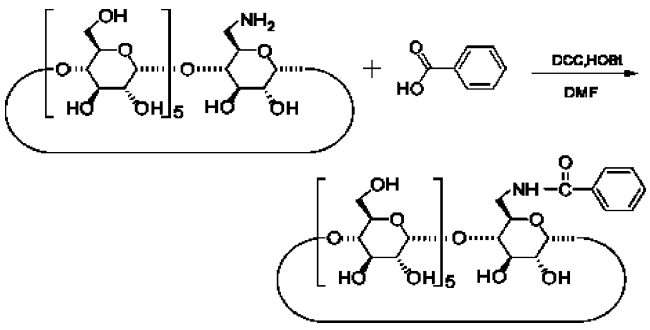


TABLE 1. Dependency of Longitudinal Relaxation Time (T_1) on ^{13}C of the 2′-Position in a Diphenylacetylene Group and ^{13}C of C1, C2, and C4 in α-CDs in [2]Rotaxanes (1, 2, and 3) by Using 67.77, 100.4, 125.5, and 150.6 MHz in Resonance Frequencies for ^{13}C

	T_1 of rotaxane **1**, s				T_1 of rotaxane **2**, s				T_1 of rotaxane **3**, s			
resonance		CD unit				CD unit				CD unit		
frequency, MHz	axis	C1	C2	C4	axis	C1	C2	C4	axis	C1	C2	C4
67.77	0.16	0.12	0.12	0.12	0.15	0.13	0.13	0.14	0.15	0.10	0.12	0.12
100.4	0.22	0.21	0.19	0.18	0.21	0.18	0.21	0.20	0.19	0.21	0.19	0.19
125.5	0.23	0.24	0.25	0.24	0.24	0.27	0.26	0.25	0.22	0.26	0.26	0.26
150.6	0.23	0.30	0.30	0.29	0.24	0.30	0.30	0.29	0.25	0.35	0.35	0.33

[a] Concentration of rotaxanes: rotaxane **1**; 20.4 mM, rotaxane **2**; 20.6 mM, rotaxane **3**; 20.6 mM.

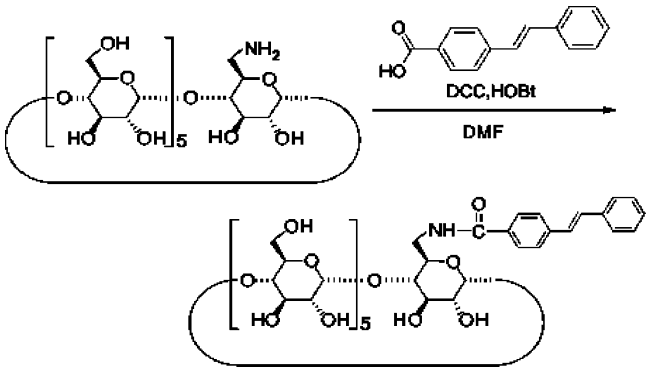
TABLE 2. Rotational Correlation Time (τ_c) of Axis Molecules and α-CD in DMSO-d_6

	axis		CD		
	τ_c, 10^{-10} (s)	$1/\tau_c$, 10^8 (s^{-1})	τ_c, 10^{-10} (s)	$1/\tau_c$, 10^8 (s^{-1})	$\Delta 1/\tau_c$
rotaxane **1**	5.0	20	15	6.8	13
rotaxane **2**	5.5	18	14	7.3	11
rotaxane **3**	6.0	17	18	5.7	11

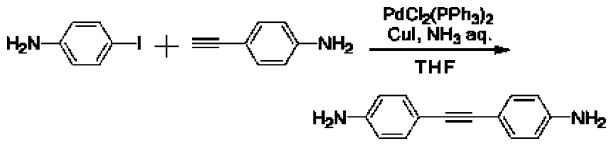
$\Delta 1/\tau_c = 1/\tau_c$ (axis) $- 1/\tau_c$(CD)

Preparation of 6-Phenyl-amide-α-CD. Benzoic acid (52.4 mg, 0.429 mmol), dicyclohexyl carbodiimide (DCC; 126 mg, 0.612 mmol), and 1-hydroxybenzotriazole (HOBt; 95.4 mg, 0.622 mmol) were added to dried DMF (10 mL) at 0 °C. After 1 h, a solution of 6-NH_2-α-CD (374.1 mg, 0.379 mmol) in dried DMF (20 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 5 days. The mixture was poured into acetone (1 L). The precipitate was collected and dissolved in water. The solution was applied to a DIAION HP-20 column. The column was flushed with water (2 L) and then eluted with a water/methanol = 20/80 (v/v). The fraction was concentrated under reduced pressure, and pure 6-phenyl-amide-α-CD was obtained (white powder, 348 mg, 85.4%). ^1H NMR (500 MHz, DMSO-d_6) δ_H 8.32 (t, J = 5.8 Hz, 1H, amido), 7.80 (d, J = 7.2 Hz, 2H, ortho H of phenyl), 7.51 (t, J = 7.4 Hz, 1H, *p*-Ph), 7.43 (t, J = 7.4 Hz, 2H, *m*-Ph), 5.57−5.36 (m, 12H, O2,3*H* of CD), 4.93−4.73 (m, 6H, C1*H* of CD), 4.56−4.34 (m, 5H, O6*H* of CD), 3.83−3.22 (m, overlaps with HOD, others of CD). TLC (*n*-butanol/ethanol/water 5:4:3): R_f = 0.56 (relative to the solvent front). MALDI TOF−MS, *m*/*z* (%), 1098.5-(100) $[M + Na]^+$, 1114.0(55) $[M + K]^+$. Mp 285−286 °C (decomp). Anal. Calcd for $C_{43}H_{65}O_{30}N{\cdot}7.73H_2O$: C, 42.50; H, 6.67; N, 1.15; Found: C, 42.37; H, 6.48; N, 1.35.

Preparation of 6-Stilbene-amide-α-CD. (a) Preparation of 4-Stilbenecarboxylic Acid. Styrene (1.56 g, 14.9 mmol) and 4-iodobenzoic acid (3.97 g, 15.9 mmol) were dissolved in tetrahydrofran (THF; 17 mL) and triethylamine (20 mL). The solution was refluxed in the presence of triphenylphosphine (0.124 g, 0.473 mmol) and palladium(II) acetate (0.100 g, 0.445 mmol) for 24 h. After the removal of the solvent, ethyl acetate (150 mL) was added, and the soluble part was washed with three portions of water (60 mL). The organic layer was concentrated under reduced pressure, and recrystallization from hexane and ethyl acetate afforded pure 4-stilbenecarboxylic acid (pale brown powder, 472 mg, 14.1%). ^1H NMR (270 MHz, DMSO-d_6) δ_H 12.8 (br, 1H, OH), 7.92 (d, J = 8.5 Hz, 2H, 3-*H* of stilbene), 7.71 (d, J = 8.4 Hz, 2H, 2-*H* of stilbene), 7.63 (d, J = 7.1 Hz, 2H, 2′-*H* of stilbene), 7.44−7.27 (m, 5H, 3′,4′-*H* of stilbene, olefin of stilbene). TLC (ethyl acetate/hexane 1:1): R_f = 0.30 (relative to the solvent front). IR (KBr), ν 3300−2500 (O−H), 1680 (C=O), 1425 (O−H), 1290 (C−O) cm^{-1}. FAB-MS, *m*/*z*, 224 (M^+), 207, 178, 154, 135, 107. Mp. 254−255 °C. Anal. Calcd for $C_{15}H_{12}O_2{\cdot}0.35H_2O$: C, 78.14; H, 5.55. Found: C, 78.05; H, 5.22.



(b) Preparation of 6-Stilbene-amide-α-CD. 6-Stilbene-amide-α-CD was prepared by the same method as 6-phenylamide-α-CD, using 4-stilbene carboxylic acid (224 mg, 1.00 mmol), DCC (248 mg, 1.20 mmo), HOBt (184 mg, 1.20 mmol), and 6-NH_2-α-CD (987 mg, 1.00 mmol). 6-Stilbene-amide-α-CD was obtained (white powder, 664 mg, 56.3%). ^1H NMR (270 MHz, DMSO-d_6) δ_H 8.31 (t, J = 5.8 Hz, 1H, amido), 7.83 (d, J = 8.3 Hz, 2H, 3-*H* of stilbene), 7.66 (d, J = 8.4 Hz, 2H, 2-*H* of stilbene), 7.63 (d, J = 7.1 Hz, 2H, 2′-*H* of stilbene), 7.42−7.26 (m, 5H, 3′,4′-*H*, olefin of stilbene), 5.58−5.38 (m, 12H, O2,3*H* of CD), 4.94−4.74 (m, 6H, C1*H* of CD), 4.59−4.34 (m, 5H, O6*H* of CD), 3.84−3.21 (m, overlaps with HOD, others of CD). TLC (*n*-butanol/ethanol/water 5:4:3): R_f = 0.58 (relative to the solvent front). MALDI TOF−MS, *m*/*z* (%), 1200.7 (100) $[M + Na]^+$, 1177.3 (24) $[M]^+$, 1217.4 (15) $[M + K]^+$. Mp 284−286 °C (decomp). Anal. Calcd for $C_{51}H_{71}O_{30}N{\cdot}0.3DMF{\cdot}4.35H_2O$: C, 48.76; H, 6.45; N, 1.48. Found: C, 48.76; H, 6.44; N, 1.47.



Preparation of 4,4′-Diaminodiphenylacetylene. $PdCl_2(PPh_3)_2$ (35.9 mg, 0.0511 mmol), CuI (19.5 mg, 0.102 mmol), and *p*-iodoaniline (1.10 g, 5.02 mmol) were dissolved in THF (30 mL) at room temperature under an argon atmosphere. *p*-Ethynylaniline (589 mg, 5.03mmol) was added, and a 0.5 M solution of aqueous ammonia (20 mL) was added dropwise. The mixture was stirred for 4 h at room temperature and extracted with diethyl ether (3 × 50 mL). The organic layer was concentrated under reduced pressure. Ethyl acetate (150 mL) was added to the residue, and the soluble

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part was poured into hexane (1 L). The precipitate was collected and washed with hexane to afford pure 4,4′-diaminodiphenylacetylene (pale brown powder, 420 mg, 40.1%). ^{1}H NMR (500 MHz, DMSO-d_6) δ_H 7.09 (d, J = 8.5 Hz, 4H, 2,2′-position of phenyl), 6.51 (d, J = 8.5 Hz, 4H, 3,3′-*H* of Ph), 5.37 (s, 4H, amino). TLC (ethyl acetate/hexane 1:1): R_f = 0.38 (relative to the solvent front). Mp 208−210 °C. Anal. Calcd for $C_{14}H_{12}N_2$·0.35H_2O: C, 78.37; H, 5.97; N, 13.06; Found: C, 78.46; H, 5.61; N, 12.70.

Preparation of [2]Rotaxanes. Rotaxane 1. α-CD (972 mg, 1.00 mmol) and sodium hydrogen carbonate ($NaHCO_3$; 394 mg, 4.69 mmol) were dissolved in water (20 mL). 4,4′-Diaminodiphenylacetylene (42.3 mg, 0.203 mmol) was added to the mixture and stirred at room temperature. After 48 h, 2,4,6-trinitrobenzenesulfonic acid sodium salt dehydrate (TNBS; 143 mg, 0.406 mmol) was added to the mixture and stirred for 48 h at room temperature. The resultant solution was washed with ethyl acetate (5 × 25 mL) and concentrated under reduced pressure. The residue was dissolved in water, and the solution was applied to a DIAION HP-20 column (eluted with water/methanol = 100/0 to 70/30). The rotaxane **1** was obtained when the column was eluted with 30−70% methanol (orange powder; 210 mg, 64.6%). ^{1}H NMR (500 MHz, methanol-d_4) δ_H 9.15 (s, 2H, 3-*H* and 3′-*H* trinitrophenyl), 9.07 (s, 2H, 3-*H* and 3′-*H* trinitrophenyl), 8.02 (d, J = 8.5 Hz, 2H, 2-*H* of diphenylacetylene), 7.41 (d, J = 8.5 Hz, 2H, 2′-*H* of diphenylacetylene), 7.32 (d, J = 8.5 Hz, 2H, 3-*H* of diphenylacetylene), 7.23 (d, J = 8.5 Hz, 2H, 3′-*H* of diphenylacetylene), 4.91 (d, J = 3.5 Hz, 6H, C1*H* of CD), 4.03 (dt, J = 2.2, 9.1 Hz, 6H, C5*H* of CD), 3.85 (dd, J = 3.1, 12 Hz, 6H, C6H^B of CD), 3.80 (t, J = 9.3 Hz, 6H, C3*H* of CD), 3.67 (dd, J = 1.9, 12 Hz, 6H, C6H^A of CD), 3.57 (t, J = 9.2 Hz, 6H, C4*H* of CD), 3.44 (dd, J = 3.3, 9.8 Hz, 6H, C2*H* of CD). TLC (*n*-butanol/ethanol/water 5:4:3): R_f = 0.65 (relative to the solvent front). MALDI TOF−MS, *m*/*z* (%), 1609.6 (100) $[M + Li]^+$, 1595.6 (82) $[M + Li - N \text{ or } O]^+$, 1579.6 (52) $[M + Li - 2N \text{ or } O]^+$, 1563.6 (30) $[M + Li - 3N \text{ or } O]^+$, 1625.6 (28) $[M + Na]^+$, 1547.6 (16) $[M + Li - 4N \text{ or } O]^+$. Mp: 296−297 °C (decomp). Anal. Calcd for $C_{62}H_{74}O_{42}N_8$·8.03H_2O: C, 42.60; H, 5.19; N, 6.41; Found: C, 42.37; H, 4.96; N, 6.34.

(b) Rotaxane 2. Rotaxane **2** was prepared by the same method as that used for rotaxane **1** except for the method of purification, using 6-Phe-α-CD (156 mg, 0.145 mmol), $NaHCO_3$ (255 mg, 3.03 mmol), water (30 mL), 4,4′-diaminodiphenylacetylene (30.1 mg, 0.145 mmol), and TNBS (107 mg, 0.304 mmol). The crude product was dissolved in water, and the solution was applied to a DIAION HP-20 column (eluted with water/methanol = 100/0 to 80/20). The rotaxane **2** was obtained when the column was eluted with 80% methanol (orange powder, 164 mg, 66.5%). ^{1}H NMR (500 MHz, methanol-d_4) δ_H 9.15 (s, 2H, 3-*H* and 3′-*H* trinitrophenyl H), 9.04 (s, 2H, 3-*H* and 3′-*H* trinitrophenyl H), 8.03 (d, J = 8.6 Hz, 2H, 2-*H* position of diphenylacetylene), 7.69 (d, J = 7.1 Hz, 2H, ortho H of phenyl), 7.45 (t, J = 7.5 Hz, 1H, *p*-Ph), 7.39−7.32 (m, 6H, 3, 2′-*H* of diphenylacetylene and *m*-Ph), 7.04 (d, J = 8.6 Hz, 2H, 3′-*H* of diphenylacetylene), 5.02−4.90 (m, 6H, C1$^{A\sim F}H$ of CD), 4.14−3.37 (m, 30H, others of CD). TLC (*n*-butanol/ethanol/water 5:4:3): R_f = 0.76 (relative to the solvent front). MALDI TOF−MS, *m*/*z* (%), 1683.9 (100) $[M + Na - 3N \text{ or } O]^+$, 1668.3 (95) $[M + Na - 4N \text{ or } O]^+$, 1653.9 (75) $[M + Na - 5N \text{ or } O]^+$, 1697.6 (75) $[M + Na - 2N \text{ or } O]^+$, 1635.2 (50) $[M + Na - 6N \text{ or } O]^+$, 1715.9 (50) $[M + Na - N \text{ or } O]^+$. Mp: 278−279 °C (decomp). Anal. Calcd for $C_{69}H_{79}O_{42}N_9$·5.74H_2O: C, 44.23; H, 4.87; N, 6.73; Found: C, 44.46; H, 5.10; N, 6.73.

(c) Rotaxane 3. Rotaxane **3** was prepared by the same method as that used for rotaxane **1** except for the purification method, using 6-stilbene-α-CD (252 mg, 0.214 mmol), $NaHCO_3$ (168 mg, 14.1 mmol), water (22 mL), 4,4′-diaminodiphenylacetylene (29.4 mg, 0.141 mmol), and TNBS (103 mg, 0.293 mmol). The crude product was dissolved in water and subjected to reversed phase preparative HPLC. Fractions containing the rotaxane **3** were concentrated under reduced pressure, and pure rotaxane **3** was obtained (red powder, 19.7 mg, 7.72%). ^{1}H NMR (500 MHz, methanol-d_4) δ_H 9.12 (s, 2H, 3-*H* and 3′-*H* trinitrophenyl), 8.91 (s, 2H, 3-*H* and 3′-*H* trinitrophenyl H), 8.03 (d, J = 8.5 Hz, 2H, 2-*H* of diphenylacetylene), 7.72 (d, J = 8.5 Hz, 2H, 3-*H* of stilbene), 7.54 (d, J = 8.4 Hz, 2H, 2-*H* of stilbene), 7.51 (d, J = 7.3 Hz, 2H, 2′-*H* of stilbene), 7.36−7.25 (m, 7H, 3′, 4′-*H* of stilbene and 3, 2′-*H* of diphenylacetylene), 7.17 (d, J = 16 Hz, 1H, olefin of stilbene), 7.10 (d, J = 16 Hz, 1H, olefin of stilbene), 6.90 (d, J = 8.6 Hz, 2H, 3′-*H* of diphenylacetylene), 5.02−4.89 (m, 6H, C1^{A-F}H of CD), 4.16−3.36-(m, 30H, others of CD). TLC (*n*-butanol/ethanol/water 5:4:3): R_f = 0.71 (relative to the solvent front). MALDI TOF−MS, *m*/*z* (%), 1795.7 (100) $[M - N]^+$, 1780.2 (90) $[M - 2N \text{ or } O]^+$, 1810.7 (50) $[M]^+$, 1764.8 (40) $[M - 3N \text{ or } O]^+$, 1833.5 (18) $[M + Na]^+$. Mp: 290−292 °C (decomp). Anal. Calcd for $C_{77}H_{85}O_{42}N_9$·7.74H_2O: C, 47.48; H, 5.19; N, 6.47; Found: C, 47.45; H, 5.13; N, 6.39.

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Supporting Information Available: Selected NMR data (1D NMR and ROESY spectrum). The determination of association constants and the diffusion coefficients are shown. This material is available free of charge via the Internet at http://pubs.acs.org.

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