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Face-Selective [2]- and [3]Rotaxanes: Kinetic Control of the Threading Direction of Cyclodextrins

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Abstract: New [2]- and [3]pseudorotaxanes containing α-cyclodextrin (α-CDs) molecules as rotors and alkyl pyridinium derivatives as axles were prepared by a slipping process. The inclusion behavior of these rotaxanes was investigated by using one- and two-dimensional NMR spectroscopy. The methyl group at the 2-position of the pyridinium moiety at the end of each axle molecule was found to control the rates of threading of the α-CD onto the axle molecules. α-CD can approach axle molecules from a particular direction to form inclusion complexes. Axle molecules that contain a 2-methylpyridinium moiety at one end and a bulky stopper at the other end can regulate the direction of approach to give a [2]pseudorotaxane such as **2b**–α-CD. A [3]pseudorotaxane in which two α-CD molecules are arranged facing in the same direction at two stations of the tetracationic axle molecule was also obtained. These face-selective behaviors are dominated by kinetic processes rather than thermodynamic processes.

Keywords: cyclodextrins · kinetics · rotaxanes · supramolecular chemistry · unidirectional

Introduction

Control of the direction of incorporation of a guest into a host and the relative molecular motion that takes place within the complexes is of importance for the construction of molecular machines.[1–3] For instance, in living organisms, muscle stretching and shrinking[4] is caused by the relative motion of actin and myosin filaments in the manner of an accurately designed and controlled molecular motor. Recently, much attention has been focused on interlocked molecules[5] such as rotaxanes and catenanes, because of their unique structures and properties. A rotaxane is an interlocked molecule that consists of a ring with a dumbbell-shaped axle bound together by noncovalent bonds. The ring encircles the linear portion of the axle and is trapped mechanically around it by two bulky stoppers. In contrast, in a pseudorotaxane, in which at least one of the stoppers on the axle component is absent, the ring component can be dissociated from the axle component by external forces, such as dilution and heating in solution. Crown ethers,[6] cyclodextrins (CDs),[1,7] calixarenes,[8] and cucurbituril[9] have been used as the ring components of rotaxanes. We chose CD as the ring component for the construction of our rotaxanes, because CD molecules have a rigid, well-defined nonsymmetric ring structure and a hydrophobic cavity. Although a series of [*n*]rotaxanes with CD molecules have been reported, most of them are thermodynamically stable complexes and their ring components have randomly oriented structures.[10]

Previously, we reported that α-CD can form stable rotaxanes with α,ω-alkanediyl compounds in D_2O by a slipping process.[11] The ^{1}H NMR spectra of cationic α,ω-alkanediyl compounds in the presence of α-CD showed new splitting signals that indicated that the exchange between the free species and the complex was slower than the ^{1}H NMR timescale. In addition, the rotaxane structure of the molecular shuttle was retained for several hours in a diluted solution. Rotaxane structures were stabilized by an increase in the number of cationic species (Figure 1). Recently, we also re-

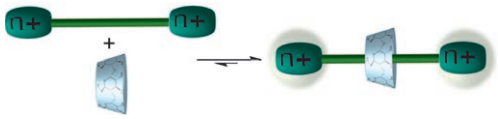

Figure 1. Schematic representation of a rotaxane structure stabilized by electric traps.

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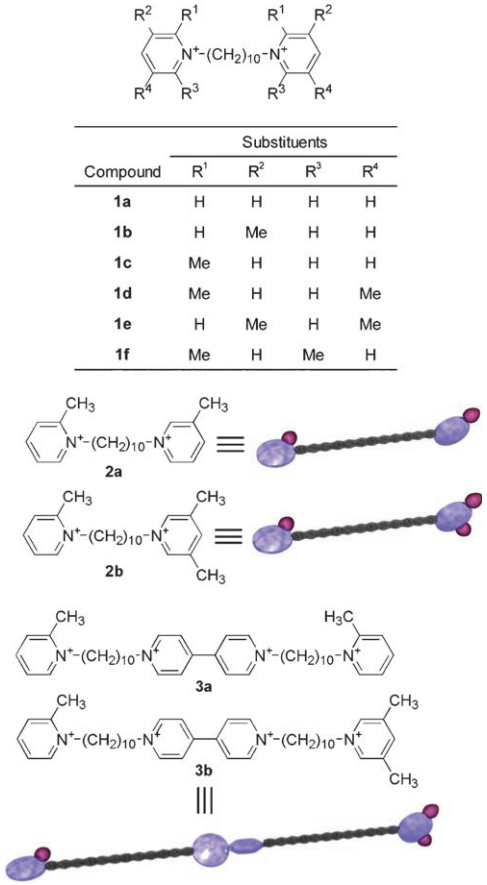
Supporting information for this article is available on the WWW under http://www.chemeurj.org/ or from the author. It contains the NMR spectra of complexes and association constants of *N*-methylpyridinium salts as terminal analogues.

ported the face selective threading of a CD molecule onto an axle compound.[12] A [2]pseudorotaxane was obtained with a α-CD molecule located in a unique direction at the recognition site of the dicationic axle molecule **2b** (Scheme 1). The face direction of threading α-CD was kinetically controlled.



Scheme 1. Structures of axle molecules.

In this paper, we report in detail the face-selective threading of a CD molecule onto an axle compound with one or two station moieties to give kinetically preferred [2]- and [3]pseudorotaxanes. The axle molecules have decamethylene units as their recognition sites for CD molecules, and pyridinium units as electric and steric trap moieties. Scheme 1 shows the structures of the various kinds of axle molecules made for this study.

Results and Discussion

Synthesis of the axle molecules: The axle molecules were prepared by the stepwise reaction of α,ω-dihalodecane with pyridine derivatives. Pyridinium ions at each end of the axle molecules were used to improve the solubility in water and to entrap α-CD molecules. The decamethylene moiety was chosen as a recognition site for α-CD molecules. Alkylation of the pyridinium moiety was carried out by a similar method to that reported previously:[12] two reactants were heated in acetonitrile, acetone, or dimethylformamide. The products were purified by reprecipitation in diethyl ether. The counteranion (of the pyridinium cation) in some compounds was changed to hexafluorophosphate or chloride to improve the solubility of the complexes in organic solvents or water, respectively.

Complexation of 1 with α-CD: A sample of dicationic axle molecules (**1**) was added to a solution of α-CD (4 mol excess) in D_2O. Table 1 shows the degree of complex formation at an equilibrium state, the time required to reach the equilibrium state, and the rate constant of formation for each of the inclusion complexes. Changes in the number and position of the methyl groups on the pyridinium moiety were found to govern the degree of complex formation. The ^{1}H NMR spectrum of **1a** in the presence of α-CD showed splitting in all signals of **1a** and no signals related to free **1a** (Figure 2). This indicates that **1a** is located in a nonsymmetrical environment, induced by complexation of a CD that

Table 1. Degree of complex formation of axle molecules with α-CD at an equilibrium state and the rate constants of the inclusion complexes.[a]

Axle	Degree of complex formation at equilibrium	Time to reach equilibrium	$k_1\times10^5$ [$M^{-1}s$][b]	$k_{-1}\times10^8$ [s][c]
1a	1.00	<10 min	n.d.[d]	n.d.[d]
1b	1.00	<10 min	n.d.[d]	n.d.[d]
1c	0.96	≈1 month	9.3	19
1d	0.94	≈1 month	7.3	17
1e	none	none	none	none
1f	none	none	none	none
2a	0.91	<10 min	n.d.[d]	n.d.[d]
2b	0.89	>2 months	2.9	8.3

[a] At 298 K. Axle molecule/α-CD, 6.25:25 mM. [b] Association rate constant of inclusion complex. [c] Dissociation rate constant of inclusion complex. [d] These values could not be determined, because the reactions occurred too fast.

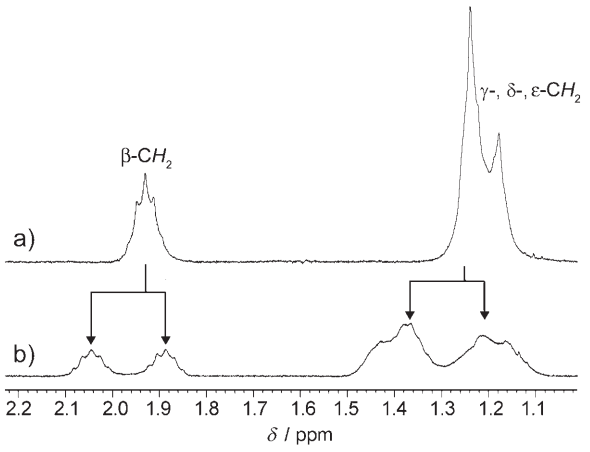


Figure 2. Partial ^{1}H NMR spectra of **1a** in D_2O a) without α-CD and b) with α-CD.

contains nonsymetrical primary and secondary hydroxyl groups.[13] After one day, the ^{1}H NMR spectrum of the complex **1a**–α-CD did not show any changes, indicating that the equilibrium of the complexation was reached immediately after the addition of α-CD. In the case of **1b**, which has a methyl group at the 3-position of the pyridinium moiety, the complexation behavior is similar to that of the **1a**–α-CD complex. However, in the case of **1c**, which has a methyl group at 2-position of the pyridinium moiety, the complex formation showed time dependency. It took about one month for the complexation of **1c** with α-CD to reach an equilibrium state. These results indicate that the inclusion of **1c** to α-CD was extremely slow. The complexation between α-CD and **1d**, which has methyl groups at the 2- and 5-positions of the pyridinium moiety, showed similar behavior to that of α-CD with **1c**. These results show that the methyl group at the 2-position of the pyridinium moiety clearly plays an important role in controlling the rate of the complex formation. Conversely, the methyl group at the 3- or 5-position of the pyridinium moiety does not affect the rate of complex formation.

A solution of α-CD with **1c** or **1d** in D_2O was diluted five times, and both of the complexes formed (**1c**–α-CD and **1d**–α-CD) were found to dissociate gradually. The degree of complex formation of the axle molecules **1c** and **1d** with α-CD after the dilution, determined by the change of the signals in the ^{1}H NMR spectra, is shown in Figure 3a. It took about 20 days for the complexes to reach an equilibrium state. After the solvent had evaporated, the residue was dissolved in [D_6]DMSO. Although the **1c**–α-CD complex gradually dissociated, ≈10% of the axle molecules were still included in the α-CD cavity (Figure 3b). These results indicate that the dissociation of α-CD from the pseudorotaxane is retarded by the methyl group at the 2-position of the pyridinium moiety. The ^{1}H NMR spectra of **1e** and **1f** showed no changes upon mixing with α-CD, indicating that these axle molecules cannot form inclusion complexes with α-CD, because the two methyl groups at the 3- and 5-positions or 2- and 6-positions of the pyridinium moiety prevent α-CD from dethreading.

These slipping processes over the end group of the axle molecules are significantly sensitive to steric effects. The number and position of methyl groups on the pyridinium moiety directly affect the formation of pseudorotaxanes. We have found that the methyl group at the 2-position of the pyridinium moiety at the end of the axle molecule controls the formation and dissociation of the inclusion complexes. The sensitivity of this system may be caused by the rigid cavity of α-CD.

Complexation of 2 with α-CD: The axles of the dicationic molecules **2a** and **2b** have different stoppers. The nonsymmetric axle molecule **2a** bears a 2-methylpyridinium moiety at one end and a 3-methylpyridinium moiety at the other end. The ^{1}H NMR spectrum of **2a**–α-CD, shows that both of the signals that represent the methylene groups in the vicinity of the pyridinium moieties (2-methylpyridinium and 3-methylpyridinium) in the complex have shifted. The spectra also indicate that each end group is located in a nonsymmetrical environment, hence the α-CD was able to form a complex with **2a** in a random direction (Figure 4a). The rate of formation of the **2a**–α-CD complex immediately reached

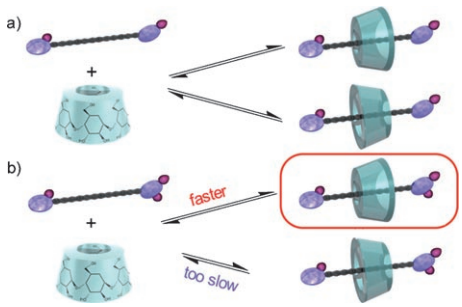


Figure 4. Proposed structures of [2]pseudorotaxanes a) **2a**–α-CD and b) **2b**–α-CD at room temperature.

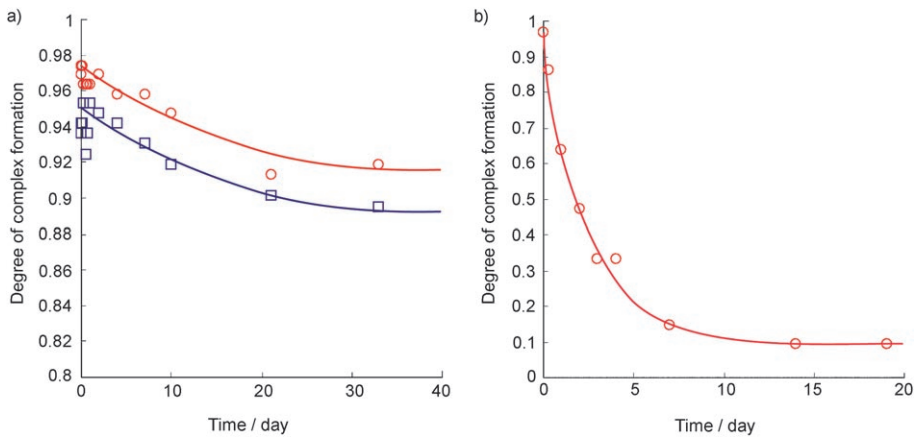


Figure 3. Degree of the complex formation of axle molecules **1c** (○) and **1d** (□) with α-CD as a function of time in the a) dilute solution and in b) [D_6]DMSO.

equilibrium after the addition of α-CD. This would indicate that α-CD can pass easily over the 3-methylpyridinium moiety. In contrast, the ^{1}H NMR spectrum of **2b** in the presence of α-CD in D_2O showed an upfield shift for the methylene group in the vicinity of the 2-methylpyridinium moiety and a downfield shift for the signals in the vicinity of the 3,5-dimethylpyridinium moiety. In addition, 2D ROESY measurements and the ^{1}H spin-lattice relaxation time revealed that α-CD formed an inclusion com-

plex with **2b** in a unique direction; the primary hydroxyl groups of α-CD face the 2-methylpyridinium moiety, and the secondary side faces the 3,5-dimethylpyridinium moiety. Figure 4b shows the proposed structures of **2b**–α-CD complex with face selectivity.

Figure 5a shows the degree of complex formation of **2b** with α-CD as a function of time at room temperature. Even after 70 days, the complex formation of **2b** with α-CD did not reach an equilibrium state. An estimation of the dissociation behavior, after dilution of the D_2O solution five times, was achieved after more than 50 days (Figure 5b). The complex **2b**–α-CD gradually dissociated to reach an equilibrium in [D_6]DMSO. However, the ^{1}H NMR signals of the complex in the rotaxane structure were still observed after 20 days. These results indicate that both the inclusion and the dissociation of complex **2b**–α-CD require about twice as much time to reach an equilibrium state compared with complex **1c**–α-CD, because α-CD can only enter from the 2-methylpyridinium side. α-CD cannot pass over **1e**, because the 3,5-dimethylpyridinium at the end of axle acts as a stopper as mentioned above. Therefore, α-CD forms complexes with **2b** only from the 2-methylpyridinium side. The number and position of methyl groups at the end group of the axle clearly contributes to the inclusion and dissociation processes of complexing α-CDs with axle molecules.

Complexation of 3 with α-CD: Tetracationic axle molecules **3**, which bear two decamethylene moieties as stations and a bipyridinium as a linker, were mixed in D_2O with α-CD (4 mol equiv) at 70 °C. Complex **3a**–α-CD bears a 2-methylpyridinium moiety at both ends. The ^{1}H NMR spectra of **3a**–α-CD shows that the methylene signals in the vicinity of the 2-methylpyridinium end and the bipyridinium linker split upfield and downfield, respectively (Figure 6). This result indicates that CDs can locate each station from both directions. This behavior can be explained as follows: α-CD threads over the 2-methylpyridinium end, the secondary hydroxyl group side facing the bipyridinium moiety, and afterwards the CD passes over the bipyridinium linker to face the 2-methylpyridinium moiety.

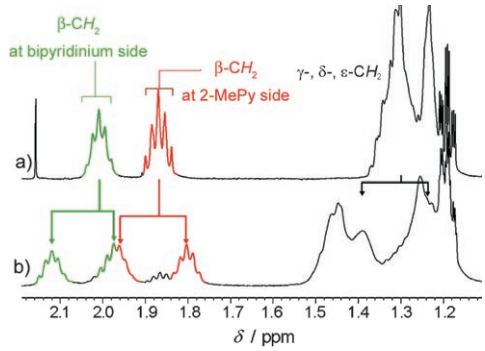


Figure 6. Partial ^{1}H NMR spectra of **3a** in D_2O a) without α-CD and b) with α-CD.

In the case of **3b**, which bears a 2-methylpyridinium moiety at one end and a 3,5-dimethylpyridinium moiety at the other end, the ^{1}H NMR signal that represents the methylene group in the vicinity of the 2-methylpyridinium side is shifted upfield, and the opposite methylene group in the vicinity of the 3,5-dimethylpyridinium side is shifted downfield. In the ^{1}H NMR spectrum of **3b**–α-CD the signal in the vicinity of the bipyridinium side is split both upfield and downfield (Figure 7). This result means that α-CDs are arranged in the same direction at two stations of **3b**.

Figure 8 shows the 2D ROESY spectrum of a solution of the axle molecule **3b** with α-CD in a D_2O. The spectrum shows negative ROE correlations between the protons in the 3-position of the α-CD and the downfield-shifted methylene protons of 3,5-dimethylpyridinium and bipyridinium, and between the protons in the 5- and 6-position of α-CD and the upfield-shifted methylene proton of 2-methylpyridinium, respectively. These results indicate that the methylene moieties are included in the α-CD cavity, and that the primary hydroxyl groups of the α-CD face the 2-methylpyridinium moiety. Figure 9 shows a proposed structure of pseudorotaxane **3b**–α-CD with the head-to-tail structure.

The degree of complex formation of **3a** or **3b** with α-CD has been derived from the integrated-intensity ratio established by their respective ^{1}H NMR spectra and is shown in

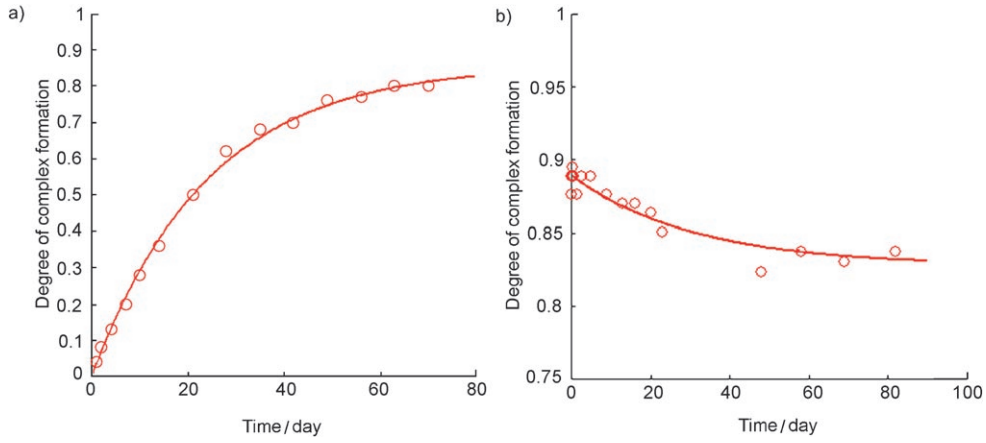


Figure 5. Degree of the complex formation of axle molecule **2b** (6.25 mM) with α-CD (25 mM) as a function of time in a) D_2O. and b) after dilution 5 times.

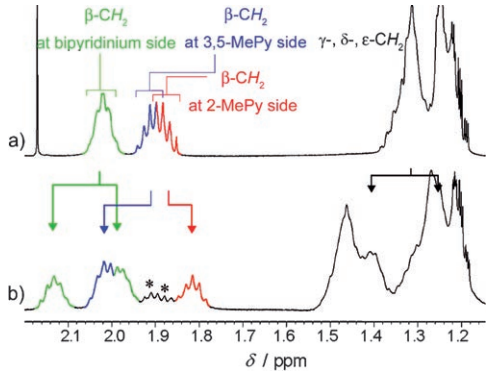


Figure 7. Partial ^{1}H NMR spectra of **3b** in D_2O a) without α-CD, and b) with α-CD. Asterisks indicate signals of uncomplexed guests.

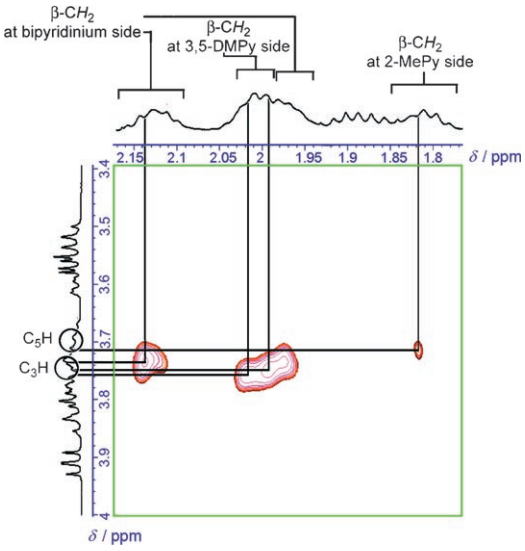


Figure 8. ROESY spectrum of **3b** with α-CD in D_2O.

Figure 9. Proposed structure of [3]pseudorotaxane **3b**–α-CD.

Figure 10. The red circles in Figure 10a show the degree of included decamethylene moieties of **3a** by α-CD with its primary hydroxyl groups facing the 2-methylpyridinium moiety, and the blue squares show the degree of inclusion of decamethylene by α-CD in the opposite direction. Both isomers increased soon after mixing **3a** and α-CD. The degree of included decamethylene moieties in which the primary hydroxyl groups of α-CD were facing the 2-methylpyridinium moiety was constantly higher than that of the other isomer. Furthermore, the ratio of the two isomers showed the same value in the early phase of the complexation.

In Figure 10b, the red circles show the degree of included decamethylene moieties of **3b** in the vicinity of the 2-methylpyridinium moiety, and the blue squares show the degree of included decamethylene in the vicinity of the 3,5-dimethylpyridinium moiety. Both isomers increased after the addition of α-CD to **3b**. The degree of included decamethylene moieties in the vicinity of the 2-methylpyridinium moiety was also proportionately higher than that of the other isomer and grew at a constant rate in the early phase of the complexation. The ratios of the inclusion complexes in which the α-CD faces in the opposite direction are shown as orange diamonds and green triangles and are clearly small during the experiment. This indicates that the rate of threading of α-CD from the narrow side of the cavity is very slow. The threading to **3b** shows a 7:1 selectivity for one orientation one day after the addition of α-CD at 70 °C.

Thermodynamic investigations: As mentioned above, it became clear that the 2-methylpyridinium moiety has a significant kinetic effect on the complexation between the axle molecules and the α-CD molecules. In this section, we elucidate the thermodynamic contributions derived from the number or the position of methyl groups on the pyridinium moiety.

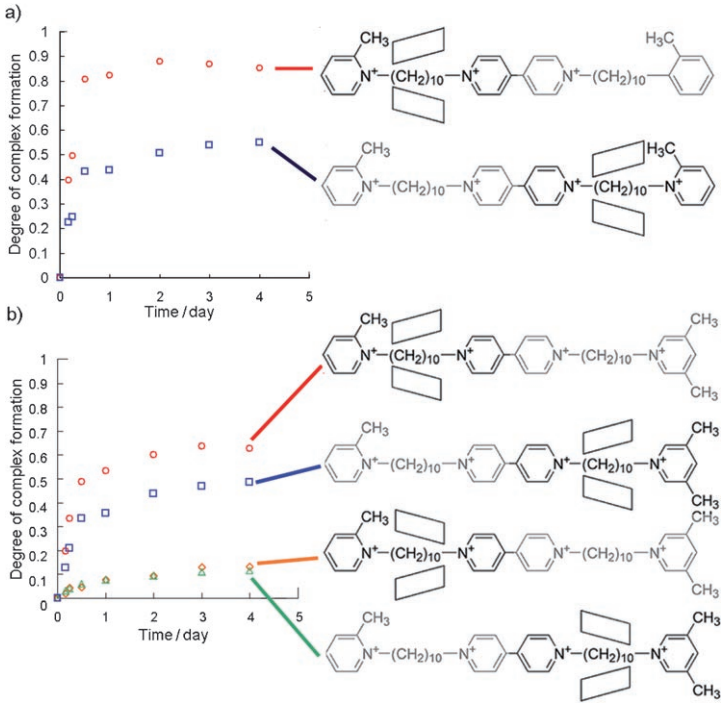


Figure 10. Degree of complex formation of a) **3a** and b) **3b** with α-CD as a function of time at 70 °C, in D_2O. a) The complex in which the primary hydroxyl groups of α-CD face the 2-methylpyridinium moiety (○) and the bipyridinium moiety (□). b) The degree to which the primary hydroxyl groups of the α-CD at the left station face the 2-methylpyridinium moiety (○) or the bipyridinium moiety (◇), and the degree to which the primary hydroxyl groups of α-CD at the right station face the bipyridinium moiety (□) or the 3,5-dimethylpyridinium moiety (△).

The thermodynamic parameters of the complex formation of CD molecules with a series of axle molecules **1a**–**1d** were investigated by NMR measurements at various temperatures. Enthalpy changes ($\Delta H°$) and entropy changes ($\Delta S°$) of the complexation were obtained from the slopes and the intercepts of van't Hoff plots (Figure 11). These thermodynamic parameters are listed in Table 2. The complex formations have favorable negative enthalpy changes ($\Delta H° < 0$) and unfavorable negative entropy changes ($T\Delta S° < 0$). These complex formations are driven by enthalpy changes. Negative enthalpy changes are thought to represent van der Waals interactions due to fitting sizes and shapes between CD and axle molecules. Negative entropy changes were ascribed to the reduction of the translational and conformational freedom of CD and axle molecules.

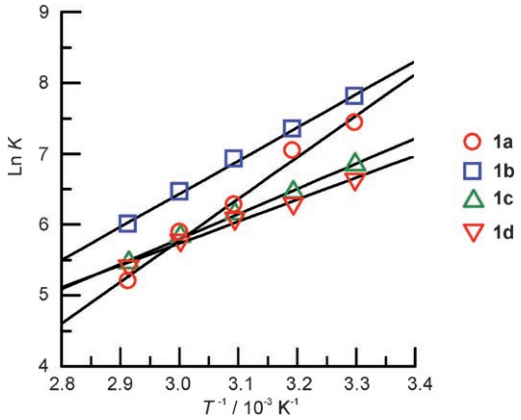


Figure 11. A van't Hoff plot for the complexation of **1a**–**1d** with α-CD.

Table 2. Thermodynamic parameters of complexation of axle molecules at 298 K.

Axle molecule	$\Delta H°$ [kJ mol^{-1}]	$\Delta S°$ [J mol^{-1} K^{-1}]	$\Delta G°$ [kJ mol^{-1}]
1a	−48.7	−98.1	−19.4
1b	−40.1	−68.4	−19.7
1c	−29.3	−40.0	−17.3
1d	−25.8	−31.7	−16.4

The differential enthalpy changes ($\Delta\Delta H°$) were plotted against the differential entropy changes ($\Delta\Delta S°$). The plots[14] gave a straight line with a slope (=0.746) that represents to what extent the enthalpic gain is canceled by the accompanying entropic loss, and the intercept (=9.85 kJ mol^{-1}) represents the complex stability obtained at $\Delta H° = 0$ (Figure 12). These four complexes participate in similar thermodynamic processes and the enthalpic contributions have been found to be large.

Furthermore, α-CD barely interacts with the terminal groups of the axle molecules, because the association constants related to the complex formation between α-CD and *N*-methylpyridinium salts of **1** are very small (<25 M^{-1}). These results suggest that, for the threading of α-CD molecules, methyl group substituents on the pyridinium moiety clearly affect the kinetic processes more significantly than the thermodynamic processes.

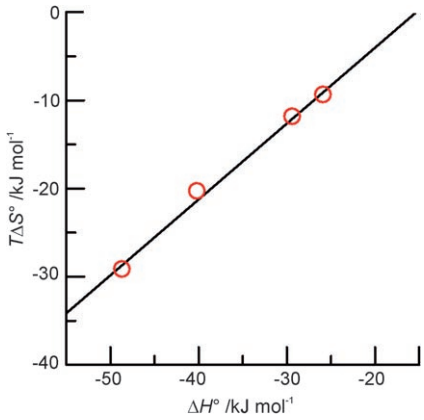


Figure 12. Enthalpy–entropy compensation plots for the complexation of **1a**–**1d** with α-CD.

Conclusion

The pseudorotaxanes of α-CD in combination with various kinds of cationic axle molecules possessing pyridinium end groups (**1**–**3**) were prepared by the slipping process. The 2-methylpyridinium moiety has a large energy barrier for the threading and dethreading of α-CD, and maintains rotaxane structures over long periods. Thermodynamic investigations revealed that the complex formation of α-CD with these axle molecules was driven by enthalpic changes.

α-CD formed a face selective [2]pseudorotaxane with axle molecule **2b** at room temperature. [3]pseudorotaxane was obtained with α-CD arranged in one direction at two recognition sites of tetracationic axle molecule **3b**. The 2D ROESY NMR measurements made it clear that the primary hydroxyl groups in α-CD faced the 2-methylpyridinium end group, and the secondary side faced the 3,5-dimethylpyridinium terminal in these [2]- and [3]pseudorotaxanes. The end group of the axle molecules was found to clearly control the direction in which the ring components faced in the pseudorotaxane structure.

Control of the direction in which a ring component faces is important for the construction of molecular devices or machines. Face-selective threading of CD molecules through axle molecules can be expected to lead to one-way movement of CD molecules on a rotaxane owing to its nonsymmetric structure.

Experimental Section

Materials: α-CD was obtained from Nacalai Tesque and used after recrystallization followed by drying at 80°C under vacuum. 3-Picoline, 2-picoline, 2,6-lutidine, and ammonium hexafluorophosphate were also obtained from Nacalai Tesque. 3,5-Lutidine, 1,10-dibromodecane, 1,10-

diiododecane, 4,4′-bipyridine, and tetraethylammonium chloride were obtained from Tokyo Kasei Kogyo 2,5-Lutidine was purchased from Aldrich.

Synthesis of axle molecules: Compounds **1** and **2** were prepared according to our previous report.[12]

[2-MePy-$(CH_2)_{10}$-bpy-$(CH_2)_{10}$I][I]$_3$ (Py: pyridinium, bpy: bipyridinium): The solution of [2-MePy-$(CH_2)_{10}$I][I] (1.10 g, 2.25 mmol) and 4,4′-bipyridine (3.15 g , 20.2 mmol) in acetone (50 mL) was heated at reflux for 3 days. The solution was poured into diethyl ether to give [2-MePy-$(CH_2)_{10}$-bpy][I]$_2$ as a yellow solid. This was dissolved in acetonitrile (5 mL), to which 1,10-diiododecane (9.8 g, 25 mmol) was added, and then the solution was heated at reflux for 2 days. The mixture was filtered, and the solid was collected and washed with CH_3CN and diethyl ether to give [2-MePy-$(CH_2)_{10}$-bpy-$(CH_2)_{10}$I][I]$_3$ (1.93 g, 82.6 %). ^{1}H NMR (500 MHz, D_2O) $\delta = 9.39$–9.38 (d, 4H; 2,2′-position of bpy), 8.98–8.97 (dd, 1H; 6-position H of 2-MePy), 8.78–8.77 (d, 4H; 3,3′-position of bpy), 8.48–8.45 (dt, 1H; 4-position of 2-MePy), 8.04–8.03 (d, 1H; 3-position of 2-MePy), 7.99–7.95 (t, 1H; 5-position of 2-MePy), 4.96–4.67 (t, 4H; α-methylene in decamethylene in the vicinity of the bpy side), 4.53–4.50 (t, 2H; α-methylene in decamethylene in the vicinity of the 2-MePy side), 3.28–3.24 (t, 2H; α-methylene in decamethylene in the vicinity of iodide side), 2.83 (s, 3H; 2-methyl), 2.00–1.95 (m, 4H; β-methylene in decamethylene in the vicinity of the bpy side), 1.86–1.80 (m, 2H; β-methylene in decamethylene in the vicinity of the 2-MePy side), 1.76–1.70 (m, 2H; β-methylene H in decamethylene in the vicinity of the iodide side), 1.35–1.24 ppm (m, 24H; γ-, δ-, ε-methylene H in decamethylene).

Compound 3a ([2-MePy-$(CH_2)_{10}$-bpy-$(CH_2)_{10}$-2-MePy][Cl]$_4$): A solution of [2-MePy-$(CH_2)_{10}$-bpy-$(CH_2)_{10}$I][PF_6]$_3$ (412 mg, 0.378 mmol) and 2-picoline (1.0 mL , 10 mmol) in acetone (12 mL) was heated at reflux for 2 days. The solution was poured into diethyl ether to give [2-MePy-$(CH_2)_{10}$-bpy-$(CH_2)_{10}$-2-MePy][PF_6]$_3$[I] as a red solid.

A solution of [2-MePy-$(CH_2)_{10}$-bpy-$(CH_2)_{10}$-2-MePy][PF_6]$_3$[I] in acetone was poured into a solution of tetraethylammonium chloride in acetone (18.5 mmol, 100 mL) and the solution was stirred overnight at room temperature. The precipitate was washed with acetone to give of **3a** as a red-brown solid (128 mg, 38.9 %). ^{1}H NMR (500 MHz, D_2O) $\delta = 9.05$–9.04 (d, 4H; 2,2′-position of bpy), 8.64–8.63 (dd, 2H; 6-position of 2-MePy), 8.49–8.47 (d, 4H; 3,3′-position of bpy), 8.32–8.28 (dt, 2H; 4-position of 2-MePy), 7.85–7.84 (d, 2H; 3-position of 2-MePy), 7.80–7.76 (t, 2H; 5-position of 2-MePy), 4.63–4.46 (t, 4H; α-methylene in decamethylene in the vicinity of the bpy side), 4.50–4.46 (t, 4H; α-methylene in decamethylene in the vicinity of the 2-MePy side), 2.79 (s, 6H; 2-methyl), 2.06–1.99 (m, 4H; β-methylene in decamethylene in the vicinity of the bpy side), 1.91–1.85 (m, 4H; β-methylene in decamethylene in the vicinity of the 2-MePy side), 1.38–1.25 ppm (m, 24H; γ-, δ-, ε-methylene in decamethylene); ^{13}C NMR (125.5 MHz, D_2O): see the Supporting Information for details; elemental analysis calcd (%) for $C_{42}H_{62}N_4Cl_4 \cdot 8.4\,H_2O$: C 55.06, H 8.67, N 6.12; found: C 54.90, H 8.77, N 6.32.

Compound 3b ([2-MePy-$(CH_2)_{10}$-bpy-$(CH_2)_{10}$-3,5-DMPy][Cl]$_4$) (DMPy: dimethylpyridinium): Compound **3b** was prepared in the same way as **3a**. Starting with [2-MePy-$(CH_2)_{10}$-bpy-$(CH_2)_{10}$I][PF_6]$_3$ (412 mg) and 3,5-lutidine (1.0 mL) produced **3b** ([2-MePy-$(CH_2)_{10}$-bpy-$(CH_2)_{10}$-3,5-DMPy][Cl]$_4$) (128 mg 43.6 %) as a red-brown solid. ^{1}H NMR (500 MHz, D_2O) $\delta = 9.05$–9.04 (d, 4H; 2,2′-position of bpy), 8.64–8.63 (dd, 1H; 6-position of 2-MePy), 8.49–8.47 (d, 4H; 3,3′-position of bpy), 8.41 (s, 2H; 2- and 6-position of 3,5-DMPy), 8.32–8.28 (dt, 1H; 4-position of 2-MePy), 8.12 (s, 1H; 4-position of 3,5-DMPy), 7.85–7.84 (d, 1H; 3-position of 2-MePy), 7.80–7.76 (t, 1H; 5-position of 2-MePy), 4.50–4.46 (t, 2H; α-methylene in decamethylene in the vicinity of the 2-MePy side), 4.63–4.46 (t, 4H; α-methylene in decamethylene in the vicinity of the bpy side), 4.44–4.40 (t, 2H; α-methylene in decamethylene in the vicinity of the 3,5-DMPy side), 2.79 (s, 3H; 2-methyl), 2.73 (s, 6H; 3,5-methyl), 2.06–1.99 (m, 4H; β-methylene in decamethylene in the vicinity of the bpy side), 1.94–1.88 (m, 2H; β-methylene in decamethylene in the vicinity of the 3,5-DMPy side), 1.91–1.85 (m, 2H; β-methylene in decamethylene in the vicinity of the 2-MePy side), 1.38–1.25 ppm (m, 24H; γ-, δ-, ε-methylene in decamethylene); ^{13}C NMR (125.5 MHz, D_2O): see the Supporting Information for details; elemental analysis calcd (%) for $C_{43}H_{64}N_4Cl_4 \cdot 3.5\,H_2O$: C 61.48, H 8.49, N 6.67; found: C 61.44, H 8.22, N 6.78.

Measurements: The ^{1}H NMR spectra were recorded by using a JEOL JNM EX-400 or a JEOL JNM-GX500 NMR spectrometer. Chemical shifts were determined with reference to solvent values ($\delta = 2.49$ ppm for [D_6]DMSO and 4.65 ppm for D_2O) or the external standard ($\delta =$ 3.75 ppm for dioxane in D_2O). Proton-decoupled broadband ^{13}C NMR spectra were recorded at 100.4 MHz on a JEOL JNM EX-400 NMR spectrometer or at 125.5 MHz on a JEOL JNM-GX500 NMR spectrometer. Chemical shifts were referenced to the solvent values ($\delta = 39.50$ ppm for [D_6]DMSO) or the external standard ($\delta = 67.19$ ppm for dioxane in D_2O). Determination of the thermodynamic parameters was achieved by the variable-temperature NMR method. The NMR spectra of solutions of α-CD with axle molecules in D_2O were measured at 30, 40, 50, 60 and 70 °C after reaching equilibrium.

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