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Rotaxanes with unidirectional cyclodextrin array

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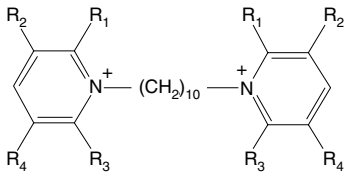
Abstract

We report here construction of *pseudo*-rotaxanes of α-cyclodextrin (α-CD) with axle molecules bearing pyridyl end caps via kinetic control of threading of α-CD onto axle molecules. A single substituted pyridyl group attached to the ends of the axle molecule regulates the rate for α-CD passing them. Two methyl substituents can clearly govern the degree of complex formation of α-CD with guest molecules and result in the distinction of face direction of CD molecules entering the axle ends. α-CDs are arranged in one direction at two station units of the axle molecule to give a face-selective *pseudo*-[3]rotaxane.

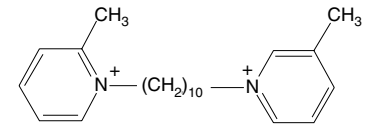
(Some figures in this article are in colour only in the electronic version)

1. Introduction

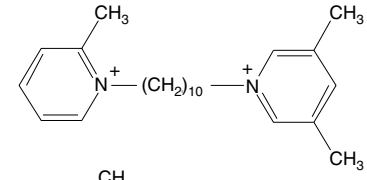
Recently, much attention has been paid to constructing machine-like supramolecules. Mechanically interlocked molecules, such as rotaxanes and catenanes, are suitable candidates for the construction of molecular machines [1]. Especially, rotaxanes are considered to be a typical prototype of molecular machines bearing a rotor and an axle in the molecule [2–10]. Crown ethers [11, 12], cyclodextrins (CDs) [13–18], calixarenes [19–21], and cucurbituril [22] have been used as ring components of rotaxanes. We chose CD as a ring component of supramolecular assemblies, because CD has a rigid, well defined 'non-symmetric' ring structure. Previously, we found that CDs form complexes not only with nonionic polymers but also with ionic polymers such as linear polymers consisting of bipyridinium bridged by polymethylene chains [23]. Furthermore, we have designed a 'molecular shuttle' by using CD as a ring and water-soluble polymers bearing two polymethylene chains as stations, bipyridinium units as linkers, and dinitrophenyl groups as stoppers [24, 25]. The shuttling behaviour of the molecular shuttle was solvent or temperature sensitive and could be controlled by double interactions: hydrophobic interaction between a CD ring and a station, and a repulsive interaction between a CD ring and a linker. If we can control the face direction of CDs over their threading process in the complex formation between CDs and axle molecules with multi-stations, a CD molecule can be oriented in one direction among the axle molecule. As an expected result, the movement of CD molecules on the axle molecule



Compound	Substituents			
	R_1	R_2	R_3	R_4
1a	H	H	H	H
1b	H	CH_3	H	H
1c	CH_3	H	H	H
2a	CH_3	H	H	CH_3
2b	H	CH_3	H	CH_3
2c	CH_3	H	CH_3	H



3a



3b

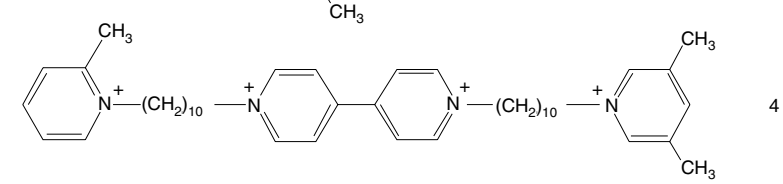


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Figure 1. Structures of axle molecules.

can be regulated. Although there are a few reports on the isolation of unidirectional *pseudo*-[2]rotaxane composed of CDs and axle molecules [26–29], there are no reports on the kinetic control of the face direction of CDs in the complex forming step. We report here the face-direction control of CD in the construction of *pseudo*-rotaxane with an alkyl chain bearing pyridyl end caps. The yields of complexes of CDs with guest alkyl derivatives were controlled by the simple change of the position and the number of methyl groups bound to the pyridyl moiety [30]. A single substituted pyridyl group attached to the ends of the axle molecule regulated the rate for CDs passing them. Two methyl substituents could clearly govern the degree of complex formation of CDs with the axle molecules and resulted in the distinction of the face direction of CD molecules entering the axle ends.

2. Complex formation between α-CD and axle molecules with various end groups

Figure 1 shows structures of various kinds of axle molecules **1**–**4**. These axle molecules have decamethylene units as the recognition site of CDs and pyridinium units as the electric and steric trap moieties. Compound **4** has two station units. Axle molecules were prepared by the reaction of α, ω-dihalodecane with pyridine derivatives [30]. Dicationic symmetrical axle molecules, **1a**–**c** and **2a**–**c**, were mixed with four molar excess amounts of α-CD in D_2O. One day after mixing α-CD with each axle molecule at room temperature, the ^{1}H NMR spectra were recorded in D_2O as shown in figure 2. The ^{1}H NMR spectrum of **1a** in the presence of α-CD (four molar excess) showed the split in all peaks of **1a** and no peaks of free **1a** (figure 2(B)). This result indicates that **1a** is included in α-CD completely. In the case of **1b** with a methyl group at the 3-position of a pyridinium part, the complexation mode was similar to that of the

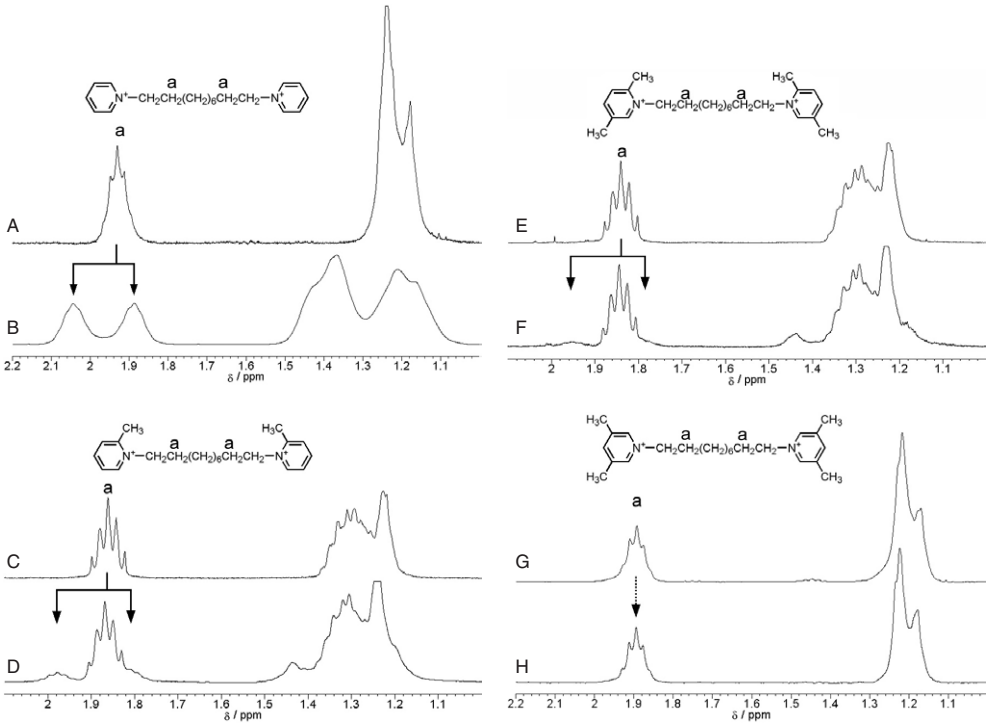

Figure 2. Partial ^{1}H NMR spectra of **1a** ((A) and (B)), **1c** ((C) and (D)), **2a** ((E) and (F)), and **2b** ((G) and (H)) in D_2O without α-CD ((A), (C), (E), and (G)) and with α-CD ((B), (D), (F), and (H)). The spectra of the samples containing α-CD were recorded one day after mixing with axle molecules at room temperature.

α-CD-**1a** complex. α-CD could pass through the end caps with methyl groups at the 3-position of a pyridinium part. The complexation of **1c** with α-CD showed time dependence. The rate of inclusion of **1c** in α-CD was extremely slow.

Figure 3 shows the time dependence of the complex formation between α-CD and axle molecules (**1b**, **1c**, and **2a**–**2c**). The complexation between α-CD and **2a**, which has methyl groups at 2- and 5-positions of the pyridinium group, showed a similar behaviour to that of α-CD with **1c**. These results show that the methyl group at the 2-position of the pyridinium part obviously plays an important role to control the rate of the complex formation. The methyl group at the 2-position of the pyridinium part was found to retard the threading of α-CD. The ^{1}H NMR spectra of **2b** and **2c** showed no changes on mixing with α-CD (figure 2(H)), indicating that axle molecules **2b** and **2c** cannot form inclusion complexes with α-CD. The two methyl groups at 3-, 5-positions or 2-, 6-positions of the pyridinium part prevented α-CD from passing. It became clear that the 2-methylpyridine moiety affected the kinetics of the complexation between the axle molecules and CDs.

Thermodynamic parameters on the complex formation of α-CD with a series of axle molecules **1a**–**1c** and **2a** were determined by variable temperature NMR measurements. Enthalpy changes (ΔH^0) and entropy changes (ΔS^0) of the complexation were obtained from the slopes and the intercepts of the van't Hoff plot. The values of ΔH° for the complexes of α-CD with **1a**, **1b**, **1c**, and **2a** were -48.7, -40.1, -29.3, and -25.8 kJ mol^{-1}, respectively. The values of ΔS° of these complexes were found to be -98.1, -68.4, -40.0,

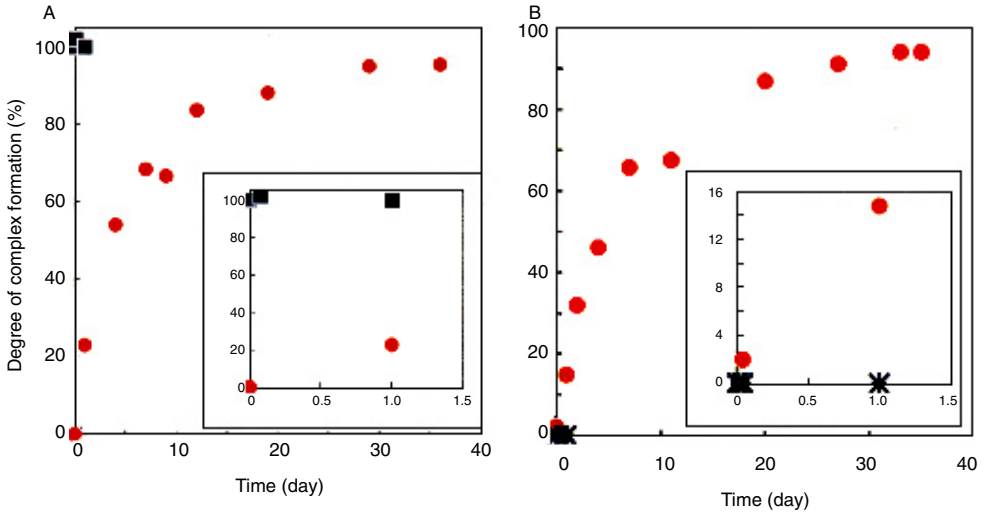

Figure 3. Correlation between time and degree of complex formations of α-CD with guest molecules capped by mono-methylated pyridyl groups (**1b** (■) and **1c** (●)) (A) or di-methylated pyridyl groups (**2a** (●), **2b** (♦), and **2c** (×)) (B). Inset graphs show the complex formation within a short time range.

and -31.7 J mol^{-1} K^{-1}, respectively. These complexations give favourable negative enthalpy changes and unfavourable negative entropy changes. These complexations were driven by the enthalpy changes. Negative enthalpy changes were thought to represent van der Waals interactions. Rekharsky and Inoue reported that large negative entropy changes are ascribable to the reduced translational and conformational freedoms of host and guest after complexation, while large positive entropy changes are due to the extensive desolvation from the hydrophilic moieties of host and guest or the release and restructuring of the water molecules inside and around CD's cavity [31]. Our system showed negative entropy changes, indicating the reduction of the translational and conformational freedoms of CD and axle molecules. From these values, the free energy changes (ΔG°) of these complex formations at 298 K were found to be -19.4 (**1a**), -19.7 (**1b**), -17.3 (**1c**), and -16.4 (**2a**) kJ mol^{-1}, respectively. It was indicated that these four complexations showed a similar thermodynamic process. These results suggested that methyl groups as substituents of the pyridinium group affect the kinetic processes on the threading of CD more effectively than the thermodynamic processes.

3. Complex formation of α-CD with axle molecules 3a and 3b

In the ^{1}H NMR spectrum of the axle molecule (**3a**), whose 2-position of one pyridyl end and 3-position of the other end were substituted by methyl groups (figure 4(A)), both signals of methylene groups in the vicinity of the 2-methylpyridine side and the 3-methylpyridine side of **3a** in the complex with α-CD shifted upfield and downfield (figure 4(B)), indicating that α-CD formed a complex with **3a** in the random direction. The ^{1}H NMR spectrum of **3b** in the presence of α-CD in D_2O showed the upfield split on the methylene groups in the vicinity of the 2-methylpyridine side and downfield split on the signals in the vicinity of the 3, 5-dimethylpyridine side, respectively (figure 4(D)). Even after 70 days, the complex formation of **3b** with α-CD did not reach an equilibrium state completely. α-CD was found to form

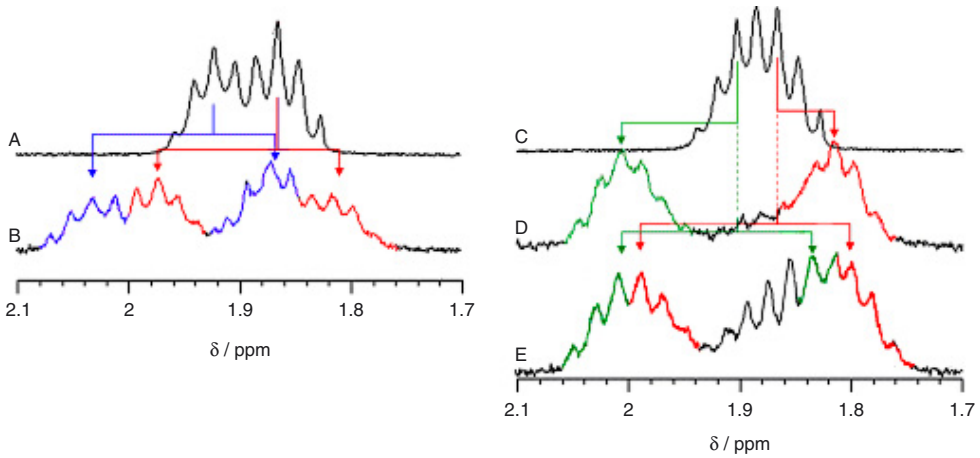

Figure 4. ^{1}H NMR spectra of axle molecules in D_2O. Axle molecule **3a** in the absence of CDs (A) and presence of α-CD after 1 day at 30 °C (B). Axle molecule **3b** in the absence of CDs (C), presence of α-CD after 70 days at 30 °C (D), and presence of α-CD after 2 days at 70 °C (E). The arrows indicate splitting behaviours of each signal on the complexations.

complexes with **3b** only from the 2-methylpyridine side and to give a unique supramolecular structure. The number and position of the methyl groups in the end cap of the axle molecule obviously contributed to the complexation with α-CDs.

The 2D ROESY spectrum of axle molecule **3b** with α-CD in D_2O showed a negative ROE correlation between 3-position protons of α-CD and downfield-shifted methylene protons of 3, 5-dimethyl pyridine [30]. A similar correlation was observed on the protons of the 5-position in α-CD. In addition, the ^{1}H spin–lattice relaxation time (T_1) of the methylene moiety in **3b**-α-CD was shorter than that of the pyridinium moiety in the free axle molecule. The T_1 values of upfield-shifted methylene protons of inclusion complexes were shorter than those of downfield-shifted signals. This result shows that the mobility of the upfield-shifted methylene proton was restricted by α-CD. The cavity size of the primary hydroxyl group side of α-CD is narrower than the secondary hydroxyl group side, so the primary hydroxyl side could strongly restrict mobility of guest molecules. These results indicate that α-CD form an inclusion complex with **3b** in a unique direction where the primary hydroxyl groups in the α-CD face the 2-methylpyridine moiety, and the secondary side faces the 3, 5-dimethylpyridine moiety.

Axle molecule **3b** and a four molar equivalents amount of α-CD were mixed in D_2O at 70 °C. The ^{1}H NMR showed new resonances (figure 4(E)). These signals are derived from α-CD facing the opposite direction. After many days, the signals of the two isomers had almost the same intensity. This phenomenon can be explained in the following way: at lower temperature, α-CD threads from the 2-methylpyridinium side of **3b** only from the secondary hydroxyl group side because of comparatively slow molecular dynamics. On the other hand, α-CD can thread from the terminal group from both hydroxyl sides of itself at high temperature because the molecular dynamics and equilibrium rate are faster. The complexation of **3b** with α-CD was controlled kinetically at low temperature and dominated by thermodynamics at high temperature. However, the rates of the complexation at 70 °C immediately after mixing were found to be significantly different between two isomers as shown in figure 5. Figure 6 shows kinetics on the complex formation of α-CD with axle molecule **3b** to give a face-selective *pseudo*-[2]rotaxane.

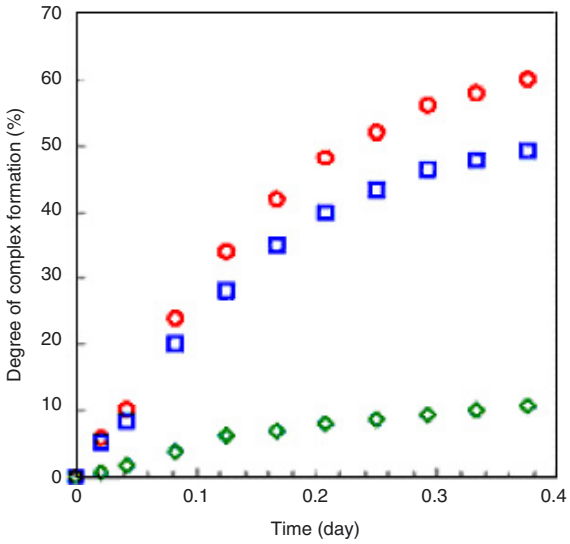

Figure 5. The correlation between time and degree of complex formations of α-CD with **3b** at 70 °C: the complex where the primary hydroxyl groups of α-CD face the 2-methylpyridine moiety (□) and that to the 3, 5-dimethylpyridine moiety (◇); the sum of two isomers (○).

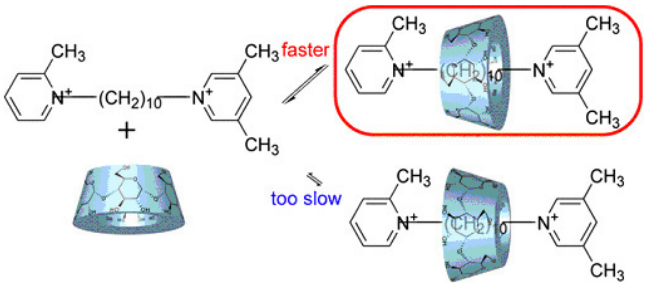

Figure 6. Kinetics of *pseudo*-[2]rotaxane prepared by axle molecule **3b** and α-CD.

4. Unidirectional threading of CD onto the axle molecule and construction of CD array

In the case of **4**, whose 2-position of one pyridyl end and 3- and 5-positions of the other end were substituted by methyl groups, the signal of the methylene group in the vicinity of the 2-methylpyridine side was shifted only upfield, that of the opposite methylene group in the vicinity of the 3, 5-dimethylpyridine side was shifted only downfield, and that in the vicinity of the bipyridinium side was split to upfield and downfield in the ^{1}H NMR spectrum of the **4**-α-CD complex. This result indicated that α-CD was placed in the same direction at two stations of **4**. Figure 7 shows the 2D ROESY spectrum of axle molecule **4** with α-CD in D_2O. The 2D ROESY spectrum of the complex between axle molecule **4** and α-CD showed a strong ROE correlation between 3-position protons of α-CD and downfield-shifted methylene protons of 3, 5-dimethyl pyridine. A similar correlation was observed on the protons of the 5- and 6-positions in α-CD with the upfield-shifted methylene proton of 2-methyl pyridine. These results indicate that the primary hydroxyl groups in α-CD face the 2-methylpyridine terminal, and the secondary side faces the 3, 5-dimethylpyridine terminal in *pseudo*-[3]rotaxane. Figure 8 shows

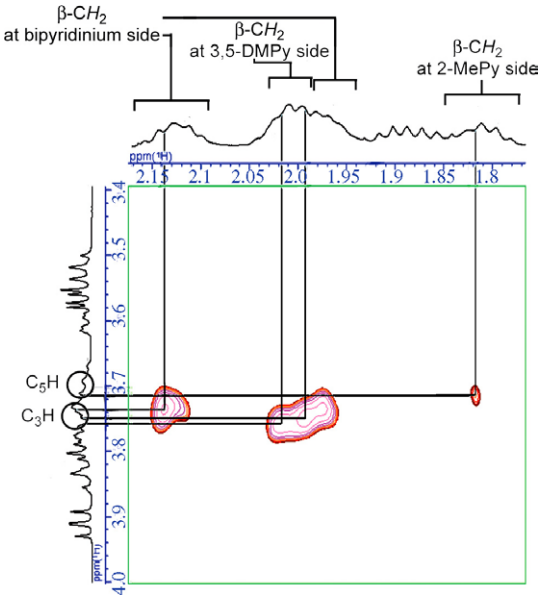

Figure 7. 2D-ROESY spectrum of **4** with α-CD in D_2O.

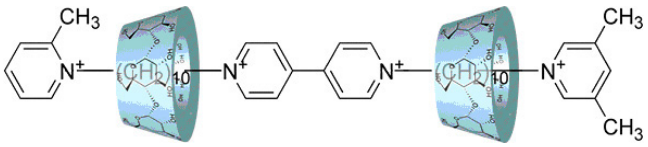

Figure 8. Proposed structure of *pseudo*-[3]rotaxane (**4**-α-CD).

the proposed structure of the complex between **4** and α-CD with the head-to-tail structure to give a *pseudo*-[3]rotaxane.

5. Conclusions

We obtained *pseudo*-[2]rotaxane with α-CD located in a unique direction at a recognition site of a dicationic axle molecule **3b** at room temperature. The methyl group at the 2-position of a pyridinium group on the end cap of the axle molecule was found to control the rates of threading of α-CD. The thermodynamic investigation revealed that the complex formations of α-CD with these axle molecules were driven by enthalpy changes. *Pseudo*-[3]rotaxane was also obtained with α-CD arranged in one direction at two stations of a tetracationic axle molecule **4**. The terminal group of axle molecules kinetically controlled the directions of faces of plural cyclodextrin molecules in the rotaxane structure. Controlling the face direction of the rings is expected to be efficient enough to regulate the direction of movement of the ring component in the rotaxane and to construct molecular devices.

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