REVIEW ARTICLE

Molecular brake systems controlled by light and heat

Keiji Hirose

Abstract   Machines at a molecular level are in perpetual Brownian motion even at an ambient temperature. One of the representative issues of researches on molecular machines is a development of technology, which can control Brownian motion. This review presents our efforts to achieve the first rationally designed molecular brake systems of threading/dethreading motions, a shuttling motion, and a rocking motion that work reversibly and quantitatively in response to external stimuli without producing any chemical wastes. These molecular brake systems were constructed from a dumbbell shaped secondary ammonium axle and a ring component having photo and thermally reactive moiety.

Introduction

There are idiosyncratic issues of research on molecular machines, which are not on miniaturizations of macroscopic machines, but specific for microscopic machines. One of the representative issues is a development of molecular brakes for Brownian motion. In this review the author presents an outline of the kinetic underpinnings of the concept and practical issues for a construction of molecular brakes from each molecular component using a

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technology based on a host–guest chemistry and an evaluation of the brake functions.

Host–guest chemistry as a key technology for the fabrication of molecular machines

The discoveries of a crown ether itself and a stable complex formation of a crown ether with a metal cation in 1967 by Pedersen [1–4], following avocation of the Host–guest chemistry by Cram [5, 6], and that of the Supramolecular chemistry by Lehn [7–9] showed an importance of interaction between molecules, initiated huge amount of researches on a relation between a physical property of a complex and a structural complimentarity between a host and a guest, and contributed to construct technologies for molecular assemblies.

A fundamental criterion of a host molecule is a binding constant for a guest molecule. That of supramolecule is a stability constant for a complex. Quantitative treatment of complex formation provides a way to compare between different molecular recognition phenomena, which can be useful for further development and application. In addition to cation recognition molecules [10–12] and anion recognition host molecules [11, 12], host molecules for a recognition of neutral molecules is still been developing [12, 13]. Guest molecules having large difference in size and/or in the position of binding sites were well differentiated. In addition subtle structural differences in shape such as chirality of guest molecule have also been able to be recognized clearly by using well-designed chiral host molecules [14], in which the author worked intensively [15–50].

There are many industrialized crops from this field such as ion sensors, ion selective membranes and electrodes [51–62] which were contributed by ion recognition

initiated by Pedersen and chiral stationary phases for chiral chromatography [46–49, 63–72] initiated by the contribution of Cram's chirality recognition technology [73–75]. Moreover, there are many other researches which have not been industrialized yet but have fascinated many researchers for a long term such as chiral shift reagents for the determination of enantiomeric excess of chiral substance [32] besides the reagents for the determination of absolute configuration [25, 34], chiral indicators [15, 17, 19–21, 26, 27, 29, 76–78], and fast chirality detection method using chiral hosts by means of mass spectrometry [23, 24, 36–40, 42] as well as many other researches for selective guest capture using intermolecular interaction are extensively spread out in different areas.

In the late 1980s researches for fabrication of molecular assemblies using inter- and/or intramolecular interactions of molecular components came under the spotlight. Typical examples are the syntheses of catenane, rotaxane, and molecular knot [79–82]. Emergence and large development of supramolecular methods make syntheses of supramolecules much easier with higher chemical yield [83–95] than before [96]. At the same time, covalent methods [97, 98], which were not thought to be versatile for the synthesis of interlocked molecules, were also well developed. By the covalent methods several interlocked molecules were synthesized with practical number of steps and chemical yields [99–102], including 100% rotaxane selective synthesis [103].

Furthermore, a devise for a reversible switching of an extent of an interaction between components of a rotaxane or a catenane was developed [104]. For example, rotaxane based molecular devices whose ring component shuttles back and forth in response to external stimuli was reported [105]. Stoddart and Heath have demonstrated that memory constructed with well-designed switchable rotaxane of their structure as fundamental component can work as electronic devices with high density [106–110]. This research got a lot of attention by providing concrete, exemplified application of molecular machines.

In general, the difficulty of development of molecular machines lies mainly on the fabrication process from molecular components. With the knowledge of host–guest chemistry, it will be possible to construct machines at the molecular scale easily using intercomponent interaction.

Molecular machines

The first time the topic of molecular machines was seriously contemplated was in 1959 by Feynman, Nobel Laureate in Physics, in his historic address "There is *Plenty* of Room at the Bottom" to the American Physical Society. At that time, it was impossible to construct molecular machines practically. After his address, technologies

concerns have proceeded. Now, it's high time to come up with practical solution, to create molecular machines with desired functions and to find the answers of his following questions: "What would be the utility of such machines? Who knows?… I cannot see exactly what would happen, but I can hardly doubt that when we have some control of the arrangement of things on a molecular scale we will get an enormously greater range of possible properties that substances can have, and of the different things we can do" [111–113].

The development of nanotechnologies and nanomaterials is believed to be capable of catalyzing dramatic breakthroughs for the industrial revolution of the twenty-first century. Molecular machines are one of the nanomaterials, which is an important application of nanotechnologies. To promote researches on molecular machines contributes not only to sophisticate microfabrication technology or patterning technique on a nanometer scale but also to create innovative material object, which realize large density growth of functional unit. For a functionalization, some of structural units (e.g. a field effect transistor (FET) or a single-molecular transistor), which are obtained by physical microfabrication technology or prospective chemical technology, should be combined directly or connected by wires. Both of such combination method and the wire method must require much more development of highly advanced microfabrication techniques. Therefore, these methods will face readily with difficulties to realize such logical assemblies or with a rising cost of production.

On the other hand, an introduction method of a function into a smallest structural unit is promising, because an integration of the structural units nor connections of the structural units by wires in logical ways are not required. Each structural unit itself works as a functional unit. Molecular machines are the structural units with function at the molecular level. Therefore, chemical approaches, which create molecular machines, are getting lots of attention because of realistic expectations.

Definition of a molecular machine and essential features of a machine

Balzani et al. defined a molecular machine and molecular device as follows: "A molecular machine is a particular type of molecular device in which the component parts change their relative positions as a result of an external stimulus. A molecular device is an assembly of a discrete number of molecular components designed to perform a specific function [111, 112]." A molecular machine can be defined more concisely as a supramolecule in which a mechanical movement of the component parts is related to perform a specific function as a result of an external stimulus. The energy of movement has to be derived from an energy transduction

process from fuel and/or an external stimulus because of the conservation law of energy. A function can be generated by a well controlled and ordered movement. For example, a gasoline engine used extensively in motor vehicles is now a reciprocating engine. The engine is a heat engine that converts pressure generated by combustion of fuel into a reciprocating linear movement of a piston. The linear movement is well controlled therefore can be converted into unidirectional rotating movement. In general, an energy conversion into a mechanical movement and a control of the movement into orders are scale-independent fundamentals of machines. Kelly, who reported the first molecular brake, had the same ways of thinking and taking on a molecular machine. He described: "Both the arrest and the creation of movement are fundamental aspects of dynamics on macroscopic as well as microscopic levels. Brakes and motors dominate the operation of machines." Certainly there are scale-independent essential features of machines.

There must be scale-dependent essential features of machines. The author believes that projects directly concerned to the "scale-dependent" essential features of machines are important in addition to a miniaturization of a macroscopic machine. One of the projects is a development of technology for a control of Brownian motion. Thermal energy at an ambient temperature is small to make macroscopic machine move, however, is large enough to have microscopic machine move. The method, which uses thermal energy for a power of motion and uses extra energy for a control of movements, can be applicable for machines at the molecular level. Therefore, the creation of molecular machines which work at an ambient temperature by thermal energy and the control of the dynamism of the molecular machines are inherent and promising research issues. Especially, molecular machines, which control the mechanical movements by an external stimulus without producing chemical wastes such as light and/or heat, are "advanced molecular machines".

Control of mechanical movement of molecular machine

There are two types of control methods of mechanical movement of molecular machine, a thermodynamically controlled method and a kinetically controlled method. A thermodynamically controlled method is a method that changes an energy difference between ground states of isomers having different positions of molecular components, which results in a change of ratio of the isomers. Therefore, an equilibrium reaction is the intended reaction for a thermodynamically controlled method as premise. Otherwise, a thermodynamically controlled method requires very long period of time for a switching function. On the other hand, a kinetically controlled method is a method that changes activation energy between ground states of isomers, which results in a change of a rate of the isomerization. Therefore, switching by a kinetically controlled method is generally quick at least in principle.
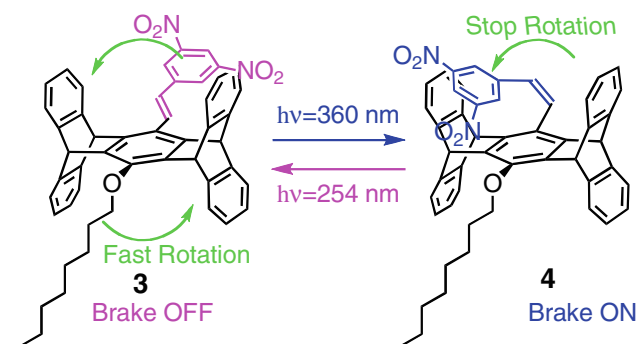
Molecular brake systems

In phase to the given situations with the current view of a molecular machine, author started projects to develop a novel arrest system of mechanical movements for molecular machines, because of the importance of the control of Brownian motion at the molecular level.

The first molecular brake system published in the literature was for a rotary movement around a single bond between triptycene and bipyridine components reported in 1994 by Kelly (Scheme 1) [114]. This system functions reversibly by the addition and removal of metal ion as external stimulus using complexation reaction. There are many other examples [115–121]. However, the addition of metal ion or other chemicals produces chemical wastes that are difficult to remove at the molecular level. Therefore, photochemical, electrochemical and/or thermal controls are ideal for molecular brake systems, which can function preferably at an ambient temperature.

In 2008, Yang et al. reported the first example of a room-temperature light-driven molecular brake that displays distinct rates of rotation in the brake-on versus brake-off states (Scheme 2) [122]. However, the interconversion between brake ON states (*cis*-form) and brake OFF states (*trans*-form) was not switched sufficiently.
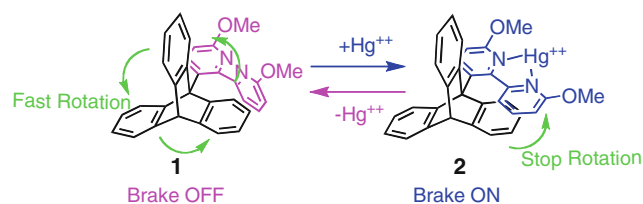
Scheme 1 Kelly's first molecular brake system

Scheme 2 Yang's first light-driven molecular brake that displays distinct rates of rotation in the brake-on versus brake-off states at room temperature

In view of the given situation, we designed an ideal molecular brake system for a frequency of molecular motions in response to physical stimuli and works quantitatively, reversibly, and without producing chemical wastes at an ambient temperature. In this paper, we report a switching in a frequency of molecular motions, threading/dethreading, shuttling, and rocking motions of pseudorotaxane and rotaxane systems by changing the size of ring component in response to physical stimuli [123–126].

Creation of ideal molecular brake systems

The purpose of this project is to create molecular brake systems whose (pseudo)rotaxane specific motions can be controlled by using clean energy.

Control of threading/dethreading motion

The first purpose of this project is to switch a frequency of molecular threading and dethreading motions reversibly and quantitatively by changing the size of ring component in response to physical stimuli without producing any chemical wastes. The concept and energy diagram of switching between fast and slow threading/dethreading in pseudorotaxane system [127] are shown in Fig. 1. The pseudorotaxane system is composed of a dumbbell shaped axle and a ring component. The dumbbell shaped axle has two stoppers and one station. Interactions between the axle and the ring components involve (1) an attractive interaction between the station and a ring and (2) a repulsive interaction between the ring and a stopper. The pseudorotaxane system with a large size ring involves fast threading and dethreading motions as shown in Fig. 1a. On the other

hand, the pseudorotaxane system with a small size ring molecule shown in Fig. 1b has slower threading/dethreading. Threading/dethreading rates depend on the balance of the changes of a stabilization (a ring on a station) and a destabilization (a ring on a stopper). Both the stabilization at the station and destabilization on the stopper act synergistically to enhance the activation energies Ea of threading motion as shown in Fig. 1b.
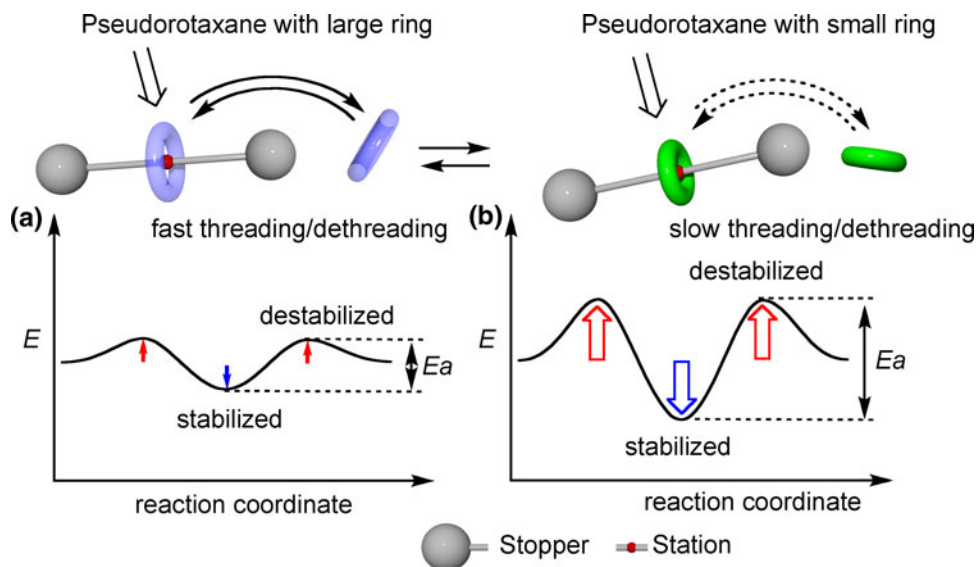
Design of switching system

Selection of switching units

The first step for the construction of molecular brakes is a selection of switching unit. As a key component of switching unit, we chose dianthrylethane derivatives which were known to be one of the famous photochromic compounds. The photodimerization and thermal reversion of some of these derivatives undergo quantitatively and reversibly. The reactivities can be tuned in large extent by using different substituents. For example, the half-life of dianthrylethane **5** (X = H) in Scheme 3 is 385 year whereas 2 h for methoxy derivative at 25 °C. This unit has a potential feasibility [128].
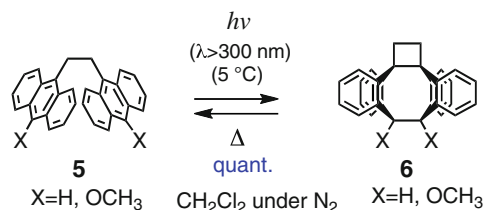
Scheme 3 Quantitative and reversible isomerization of dianthrylethane

Fig. 1 The concept and energy diagram of switching between fast and slow threading/ dethreading in pseudorotaxane

Selection of axle and ring

The next step is a selection of an axle and a ring components. The pseudorotaxane system that we designed for a switching of a frequency of threading/dethreading motion consists of secondary ammonium axle and crown ether ring components. Complexations of crown ethers with primary ammonium cations are well investigated, especially 18-crown-6 ethers with primary ammonium cations having large binding constants. On the other hand, a secondary ammonium cation is not bound in 18-crown-6 ethers well, even though a secondary ammonium cation is suitable as an axle component in shape. In the literature, it is reported that relatively large crown ethers form stable complexes with secondary ammonium cations [129–131], which can be used to differentiate chirality of the secondary ammonium cations [30, 31]. Then, the combination of secondary ammonium axle and crown ether ring with 24-crown-8 or 27-crown-9 structure was selected.

Design of pseudorotaxane system for the control of threading/dethreading motion

We designed molecule 7 as a key ring component to include a photocontrollable threading functionality. With this ring component we designed pseudorotaxane system (DBA@7o and DBA@7c) composed of dibenzylammonium hexafluorophosphate (DBA) and open form ring molecule 7o or closed-form ring molecule 7c (Scheme 4a). The photodimerization and the thermal reversion of the anthracene units of 7 would cause substantial change of the cavity size reversibly. [132–135] Because the cavity size of closed form 7c should be similar to that of dibenzo-24-crown-8, 7c would form a stable complex with a secondary ammonium salt [130]. In addition to the stabilization of

closed form crown ether and ammonium moiety, destabilization at transition state, which is presumably when the crown ether is placed on the bulky group at the ends, is also important, because the energy difference between these strategies correspond to activation energy (Ea) as shown in Fig. 1. Consequently, it is expected that the photocontrollable threading motion would be achieved using crown ether 7o as the key ring component and DBA as the proper axle-like component. For comparison, the rotaxanes A1@7o and A1@7c composed of the same crown ether 7 as ring component and axle-like component A1 with bulky stopper moieties (3,5-bis(triisopropylsilyl)phenyl group) at the both ends were also prepared, where the threading/dethreading motion was completely stopped.

Preparation and switching behavior of ring component 7

Preparation of macrocycle 7o

An introduction of dianthrylethane unit into crown ether ring was reported to be difficult, however, possible even with low chemical yield. The previously reported preparation of the photocontrollable 15-crown-5- and 12-crown-4-type compounds [136, 137] containing a dianthrylethane moiety from 1,2-bis(10-hydroxy-9-anthryl)ethane 8 [138] and corresponding oligoethyleneglycol ditosylates in the presence of sodium hydroxide resulted in low yields of the macrocyclization, partly because of the lability of diol 8. Even though diol 8 is relatively stable in form of crystals, it decomposes rapidly in solution. For this reason, high dilution conditions, which are common for macrocyclization, could not be applied. Therefore, diol 8 obtained as fine crystals was converted to stable bis(trimethylsilyl)ether 9 using N,O-bis(trimethylsilyl)acetamide (BSA) in 74% yield. Then in

Scheme 4 A concept of switching between fast and slow threading/dethreading in pseudorotaxane by using an anthracene-based 24-crown-8 type macrocycle and DBA (a), ideal non-threadable supramolecular system (b)
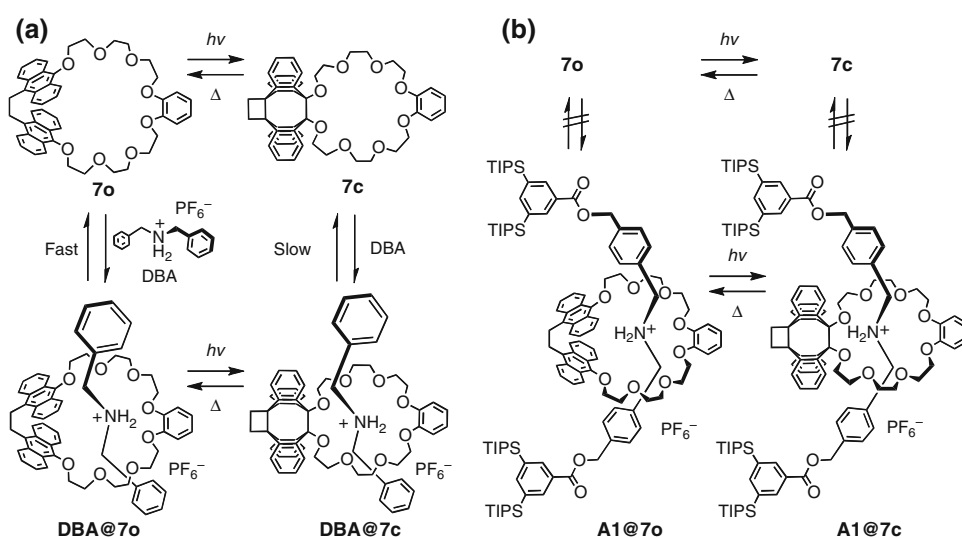
situ deprotection and coupling of **9** with ditosylates **10** furnished macrocycle **7o** with considerably improved yield (27%) compared to the previous syntheses of related molecules as shown in Scheme 5 [136] .

*Quantitative interconversion between ring components **7o** and **7c***

The photoisomerization of ring component **7o** to the corresponding closed-form molecule **7c** proceeded quantitatively. The solution of **7o** in well-degassed CD_3CN was placed in a Pyrex NMR tube at 285 K and irradiated with a high-pressure mercury lamp for 10 min. After the irradiation, the solution was kept under 273 K in order to avoid significant thermal reversion of **7c**. In the ^1H NMR spectra, a sharp singlet signal assigned to the benzylic protons (H_a) of **7o** at 4.1 ppm disappeared and a singlet signal assigned to the aliphatic protons appeared at 2.9 ppm after the irradiation as shown in Fig. 2. In the aromatic region, the characteristic signals at δ 8.12 and 7.55 ppm disappeared after irradiation and the corresponding aromatic protons (H_b, H_c) appeared at d 6.8–7.0 ppm. The thermal reversion of **7c**–**7o** involved appreciable spectral change observed in UV–

visible spectroscopy. The half-life of **7c** in acetonitrile was obtained based on the increase of absorbance at 383 nm by means of UV–visible spectroscopy: 10 min at 303 K, whereas 148 min at 283 K. Because of the long half-life at low temperature, the closed-form molecule **7c** could be conveniently isolated and then converted reversibly at room temperature to the open-form molecule **7o**. The photoirradiation and subsequent thermolysis were performed repeatedly using the sample solution prepared in quartz cell for absorption spectra in well-degassed CH_3CN (0.1 mm). Photoreaction was carried out using a 500-W high-pressure mercury lamp through Pyrex filter for 30 s cooling with water bath, then thermal reversion was carried at 313 K for 45 min monitoring absorbance at 383 nm by means of UV/Vis spectrometer. The change of the absorbance is shown in Fig. 3. After 10 times repetition, 97.4% durability is obtained based on the difference in absorbance.

Effect of the existence of ammonium station in the ring on the switching behavior

In order to obtain an information of the effect of the existence of ammonium station in the ring on the switching behavior,

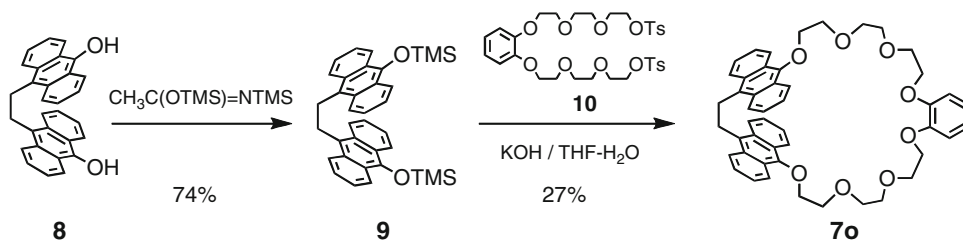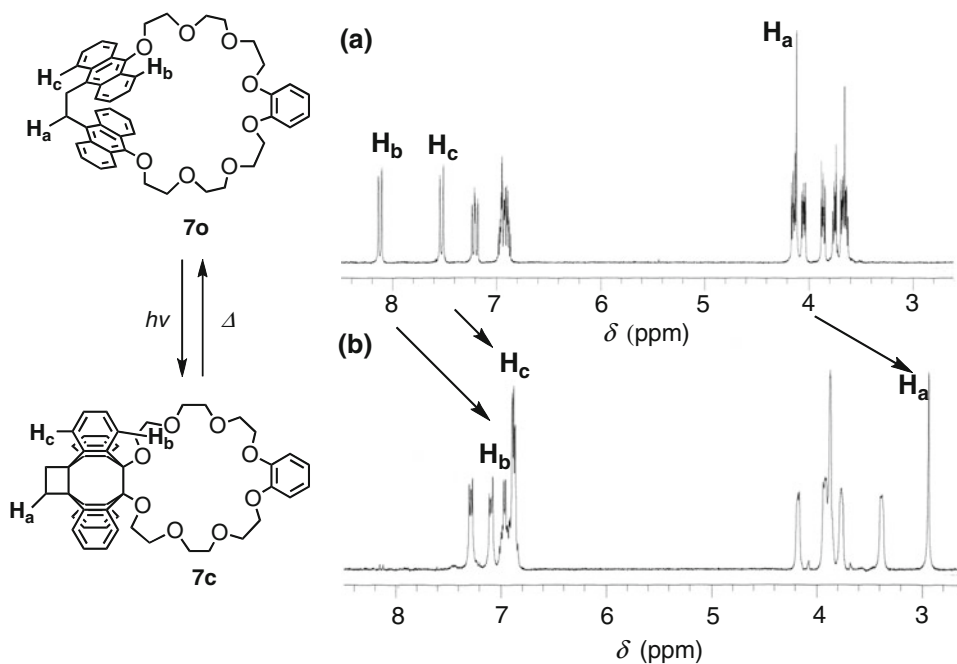Scheme 5 Synthesis of the photochromic ring component **7o**

Fig. 2 Partial ^1H NMR spectra (270 MHz) of open-form macrocycle **7o** (a) and closed-form **7c** (b) recorded in CD_3CN at 243 K
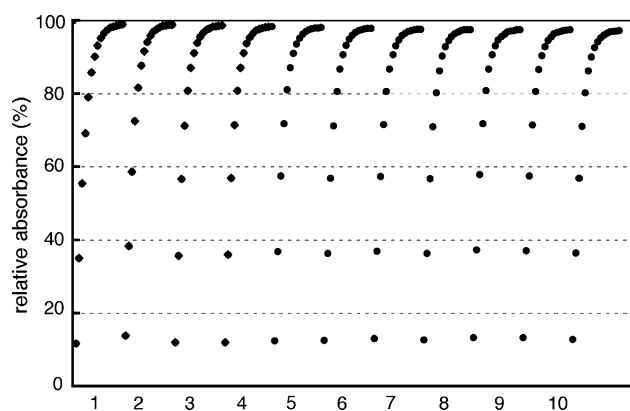
Fig. 3 Ten continuous cyclical changes in relative absorbance at 383 nm during photoreaction and thermal reversion cycles between open form **7o** and closed form **7c** recorded in CD$_3$CN at 313 K

the interconversion between open-form [2] rotaxane **A1@7o** and closed form [2] rotaxane **A1@7c** was investigated.

Preparation of rotaxane A1@7o

The synthesis of rotaxane **A1@7o** is summarized in Scheme 6. The closed-form **7c** was prepared from **7o** in benzene by irradiation with a 500-W high-pressure mercury lamp followed by evaporation of the solvent with cooling. Because the closed-form **7c** is stable enough at low temperature to handle, the freshly prepared **7c** and secondary ammonium hexafluorophosphate **11** were dissolved in CH$_2$Cl$_2$/CH$_3$CN. The resulting pseudorotaxane **11@7c** was treated with acid anhydride **12** in the presence of 40 mol% of n-Bu$_3$P under ice cooling [86]. Thermal reversion of the rotaxane **A1@7c**–**A1@7o** occurred during the post-treatment. The open-form [2] rotaxane **A1@7o** was obtained in 57% yield (three steps from **11**).

Quantitative interconversion between rotaxane A1@7o and A1@7c

The photoisomerization of **A1@7o**–**A1@7c** proceeded also quantitatively. The ^{1}H NMR spectra of **A1@7o** at 273 K are
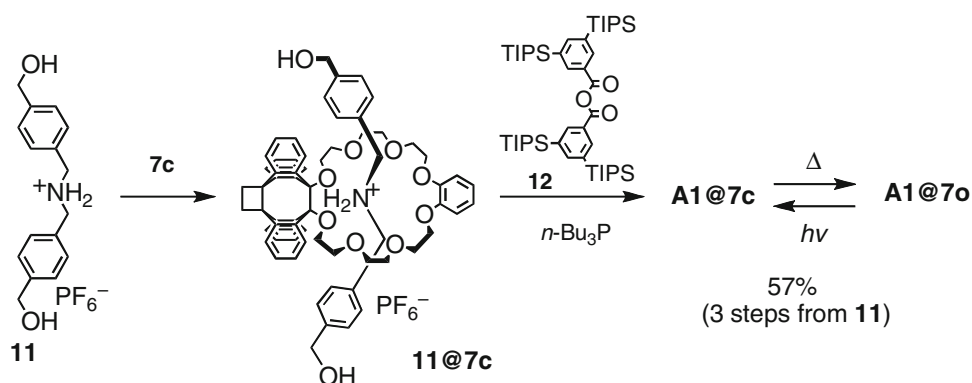
shown in Fig. 4. In the ^{1}H NMR spectra, characteristic changes for the signals of the ring component protons are observed. A sharp singlet signal assigned to the benzylic protons (H$_a$) of **A1@7o** at δ 4.05 ppm disappeared and corresponding signal of an aliphatic proton (H$_a$) appeared at 2.84 ppm after the irradiation, the aromatic signals (H$_b$, H$_c$) at 8.12 and 7.55 ppm shifted to 6.92–6.75 ppm after irradiation. The signal assigned to the benzylic protons of axle-like component (H$_d$) of **A1@7o** at 4.42 ppm shifted to 5.08 ppm after the irradiation. The thermal reversion of **A1@7c**–**A1@7o** was observed by the ^{1}H NMR spectra and the UV–visible spectra. The photoirradiation for 30 s and following thermolysis at 313 K for 60 min was performed repeatedly. The change of the absorbance at 383 nm by means of UV/Vis spectrometer is shown in Fig. 5. After 10 times repetition, 97.5% durability is obtained based on the difference in absorbance. The half-life of **A1@7c** in acetonitrile was determined based on the increase of absorbance at 383 nm by means of UV–visible spectroscopy: 18 min at 303 K, whereas 222 min at 283 K (Table 1). Half-lives of the rotaxanes **A1@7c**–**A1@7o** are significantly longer than those of the ring components **7c**–**7o**. It seems very likely that the presence of the ammonium station will increase the stability of the crown ether and slow down its retrophotodimerization.

Switching behavior of pseudorotaxane system (DBA@7)

Characterization of pseudorotaxanes

The apparent half-life of **7c** in the presence of DBA in acetonitrile was obtained based on the increase of absorbance at 383 nm by means of UV–visible spectroscopy. Although the half-lives of corresponding rotaxane **A1@7c** to **A1@7o** are appreciably longer than those of **7c**–**7o** (half-lives are 18 min at 303 K and 222 min at 283 K, whereas those of ring component **7c** are 10 and 148 min, respectively), apparent half-lives of **7c**–**7o** in the presence of **DBA** are slightly longer than

Scheme 6 Synthesis of the [2] rotaxanes **A1@7c** and **A1@7o**

Fig. 4 Partial ^{1}H NMR spectra (270 MHz) of open-form macrocycle **A1@7o** (**a**) and closed-form **A1@7c** (**b**) recorded in CD$_3$CN at 243 K
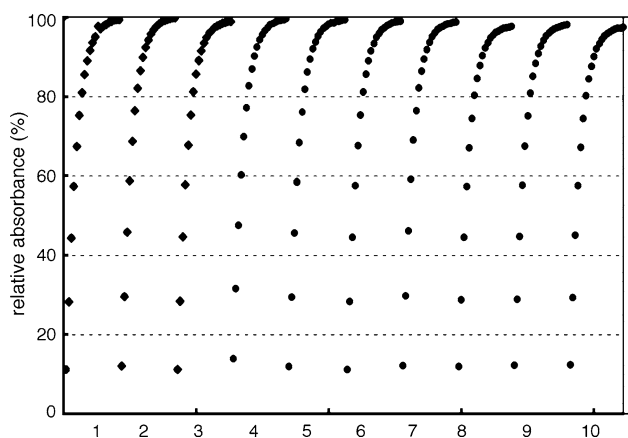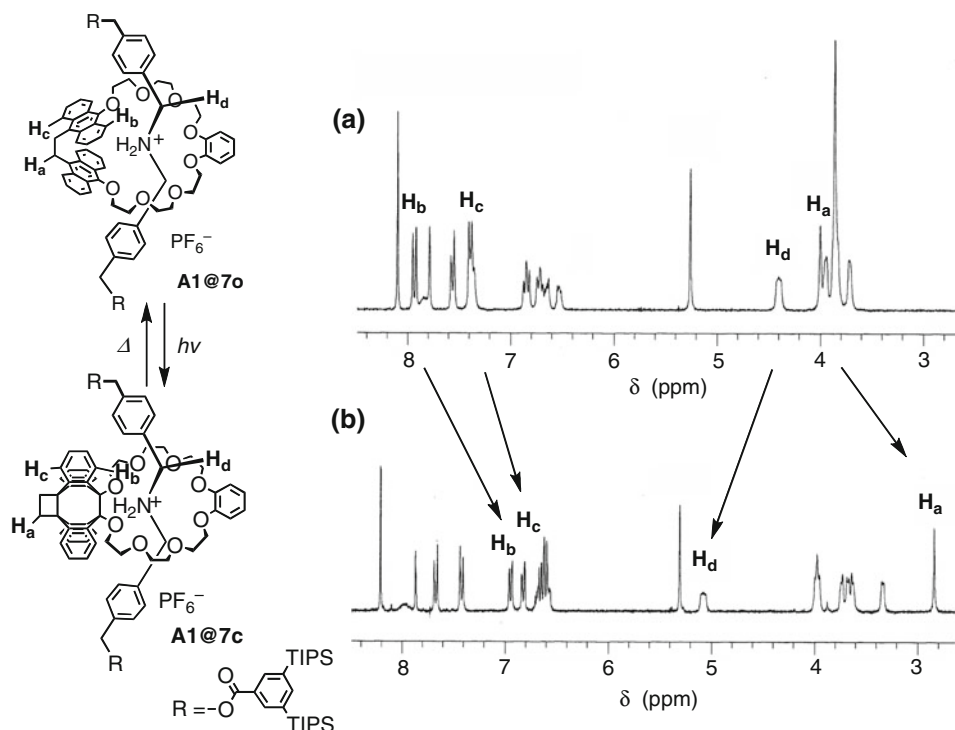

Fig. 5 Ten continuous cyclical changes in relative absorbance at 383 nm during photoreaction and thermal reversion cycles between open form **A1@7o** and closed form **A1@7c** recorded in CD$_3$CN at 313 K

Table 1 Apparent half lives of the thermal reversion of **7c**, **A1@7c** and pseudorotaxane system (**7c** with **DBA**) in CH$_3$CN obtained based on UV–visible spectral changes

T (K)	$t_{1/2}$ (min)		
	7c	**7c** with **DBA**	**A1@7c**
283	148	160	222
303	10	11	18

those of the ring components **7c**–**7o** itself (apparent half-life is 11 min at 303 K, whereas it is 160 min at 283 K) (Table 1).

Complexation behavior of 7 with DBA

In order to characterize the pseudorotaxane formation of the ring component **7c** or **7o** with the axle-like ammonium salt component, ^{1}H NMR titration experiments were performed. Although kinetic and thermodynamic data at high temperatures were not obtainable because of the less thermal stability of closed-form complex, ^{1}H NMR spectroscopy at room temperature gave information both on thermodynamic stability of pseudorotaxane and kinetic information of threading and dethreading rate. The addition of **DBA** to a solution of **7o** in CD$_3$CN formed a crown ether–ammonium cation complex. The complexation equilibrium was fast on the NMR time scale and gave signals at weight averaged chemical shifts of the free and complexed host. The binding constants of this system were obtained based on the chemical shift change by the titration experiment followed by non-linear least-square data treatment method. The binding constants are listed in Table 2 in a temperature range from 273 to 233 K. In addition to the binding constants, information on the frequency of molecular motions was obtained from this experiment. Even at a low temperature of 233 K, the host–guest complexation equilibrium has a fast exchange rate compared with the NMR time scale.

In contrast, the host–guest complexation equilibrium of the closed-form complex **7c** with **DBA** in CD$_3$CN has a slow exchange rate compared with the NMR time scale so that the peaks due to the complexed host and the free host

Table 2 Association constants of crown ethers **7o** and **7c** with **DBA** in CD$_3$CN determined by non linear least-squares method and single point measurement, respectively

T (K)	K (M^{-1})	
	7o	**7c**
273	23	67
263	30	82
253	42	126
243	53	184
233	63	286

are observed individually in an NMR spectrum. The ^{1}H NMR spectrum of a mixture of **7c** and **DBA** is shown in Fig. 6 together with those of **7c** (**c**) and **DBA** (**a**). In Fig. 6b, the signals with asterisks (*) are assigned to the pseudorotaxane and others are due to the free **DBA** and free **7c**. Based on the ^{1}H NMR spectra, the binding constants of **7c** with **DBA** were obtained by the integration of the complexed and free host signals. The results are listed in Table 2 together with those of **7o** with **DBA**. The binding constants of **7c** are two to four times larger than those of the open form **7o**. The stable binding between **7c** and DBA may explain the elongation of apparent half-lives of **7c** and slow exchange in the presence of **DBA**.

Summary of the molecular brake system of threading/dethreading motions

The anthracene-based photochromic molecules **7o** and **7c** are interconverted reversibly by photoirradiation and

thermolysis. The binding constants of **7o** and **7c** with DBA differ considerably. In addition, considerable differences in half-lives of thermal reversions of pseudorotaxane **DBA@7c** and rotaxane **A1@7c** are observed. The significant difference in frequencies of threading motions of DBA with ring components **7o** or **7c** in pseudorotaxane system is observed by ^{1}H NMR spectroscopy. The rate constant of **7o** is higher than the NMR time scale, however, the rate constant of **7c** is smaller within the temperature range between 233 and 303 K. The switching frequency of the molecular motion by the structural change of ring component is possible to produce promising new switching devices.

Control of shuttling motion

The second purpose of this project is to switch a frequency of shuttling motion and to appreciate the rate of the motion. Our concept for the control of shuttling motion is shown in Fig. 7 which includes models of [2] rotaxanes capable of changing the size of ring components and the corresponding potential energy diagrams. Figure 7a shows the larger ring (open-form) rotaxane and Fig. 7b shows the smaller ring (closed-form) state, which are reversibly interconverted. The rotaxanes possess the identical axle component having a symmetrical structure, which is composed by two stoppers, two stations, and one spacer. The potential energy of the individual rotaxane depends on the position of the ring component. The steric barrier between the ring component and the spacer is larger in the closed-form than in the open-form. Moreover, through the attractive interactions between the ring components and the

Fig. 6 Partial ^{1}H NMR spectra (270 MHz, CD$_3$CN, 243 K) of a 1:1 mixture (20 mM) (**b**) of closed-form macrocycle **7c** (**c**) and DBA (**a**). The descriptors "*" refer to signals representing protons of pseudorotaxane
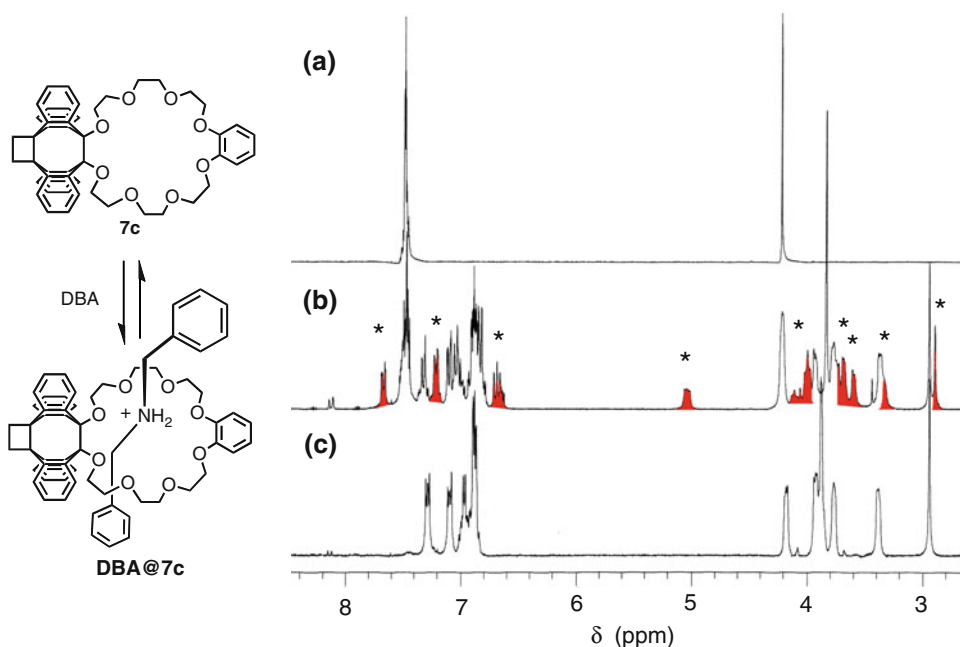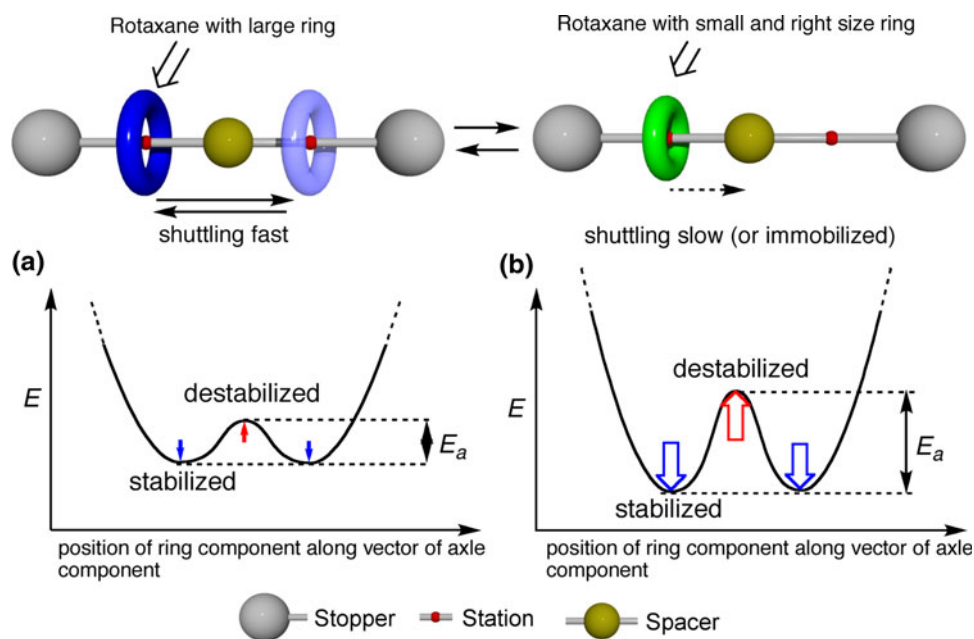
Fig. 7 Models of [2] rotaxanes and the corresponding energy diagrams of a shuttling machine with effective brake function

stations, the closed-form rotaxane can be more stabilized than the open-form. Consequently, the shuttling rate of the closed-form rotaxane would be reduced effectively than that of the open-form.

Design, preparation and switching of the brake system for shuttling motion

To build a prototype of the shuttling molecular machine with the reversible brake function, following structural requirements should be fulfilled; (1) a size-changeable ring component which responses to external stimuli, (2) an appropriate spacer which acts as a small barrier to the open-form ring and a large barrier to the closed-form ring, and (3) a station which interacts more strongly with the closed form ring molecule than the open-form. As a rotaxane system which meets these requirements, we designed rotaxanes **A2@7o** and **A2@7c** consisting of a photochromic dianthrylethane-based ring component **7o** and a dumbbell shaped axle molecule **A2** with a phenylene group and two secondary ammonium sites (Scheme 7). As the stopper, 3,5-bis(triisopropylsilyl)phenyl group was selected, because the stoppers were known to be large enough to prevent deslipping of the axle component from the open-form ring molecule.

Preparation of rotaxane A2@7o

Diester **13**, which was prepared according to the literatures [139], and the photocontrollable macrocycle **7** were used as starting materials. As shown in Scheme 7, ammonium hexafluorophosphate **16** was prepared from diester **13** by mono-protection of amino group to afford **14**, reduction

with LAH followed by salt formation with gaseous HCl and anion exchange with NH_4PF_6. The closed-form ring molecule **7c** freshly prepared from the open-form compound **7o** by UV irradiation was treated with **16** in CH_2Cl_2–CH_3CN (2.4:1) at 273 K, producing pseudorotaxane **16@7c**. Addition of anhydride **12** and n-Bu$_3$P at 273 K, followed by purification with preparative HPLC furnished the open-form rotaxane **A3@7o** (61%). Deprotection of the Boc group of **A3@7o** followed by treatment with NH_4PF_6 afforded open-form rotaxane **A2@7o**.

Interconversion between open- and closed-form rotaxanes A2@7o and A2@7c

The ^1H NMR spectra of **A2@7o** and **A2@7c** in THF-d_8 at 303 K are shown in Fig. 8. When a solution of **A2@7o** in THF-d_8 immersed in an ice bath was irradiated with a high pressure mercury lamp, the sharp singlet signal assigned to the benzylic proton (H_i) of **A2@7o** at 4.12 ppm disappeared and corresponding signal of the aliphatic proton of **A2@7c** appeared at 2.90 ppm indicating that the ring closure proceeded efficiently. In addition, the signal assigned to the benzylic protons of the axle component (H_g, H_h, H_j, and H_k) of **A2@7o** appeared as a broad signal at 4.36 ppm, which was averaged on the NMR time-scale. After the irradiation, the signal split into several signals including those of H_g and H_h at 5.10 and 5.28 ppm. The signals of H_j and H_k of **A2@7c** overlapped with the ethereal signals of the ring component. The spectrum of **A2@7c** reverted to that of **A2@7o** completely when the NMR solution of **A2@7c** was stood at room temperature overnight, implying that the thermal reversion of **A2@7c**– **A2@7o** proceeded quantitatively. Hence, the reversible

Scheme 7 Synthesis of the [2] rotaxanes **A2@7o**
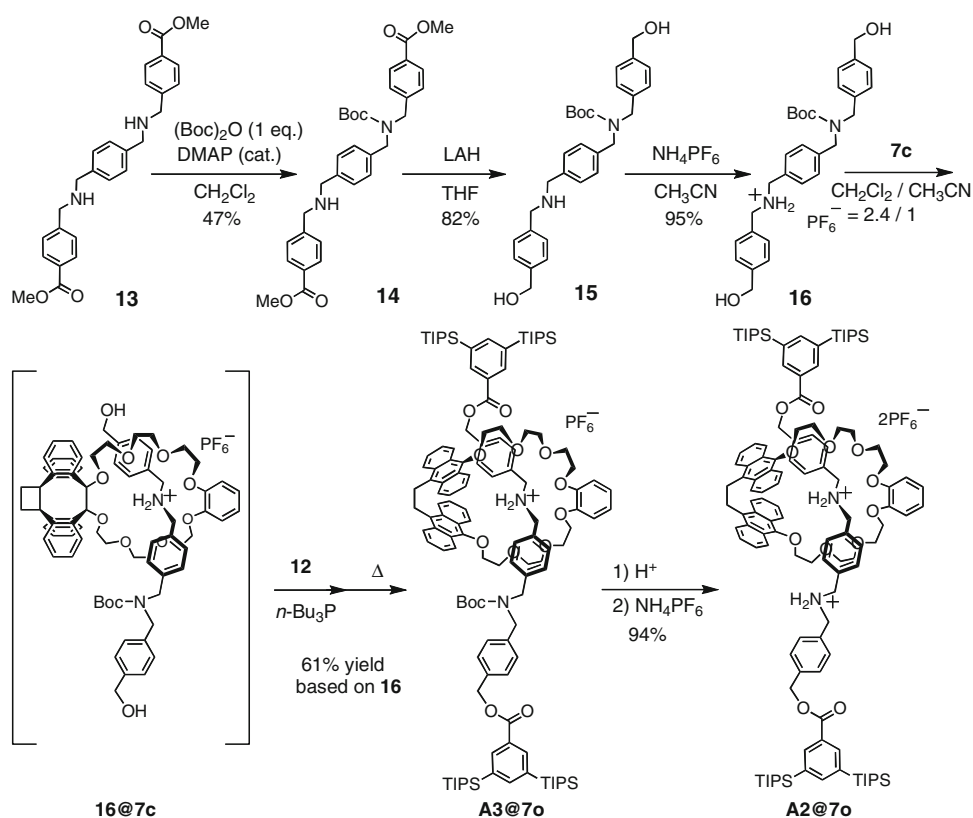
Fig. 8 Partial ^{1}H NMR spectra (400 MHz, THF-d_8, 303 K) of open- (**7o**, **a**) and closed-form (**7c**, **b**) rotaxanes
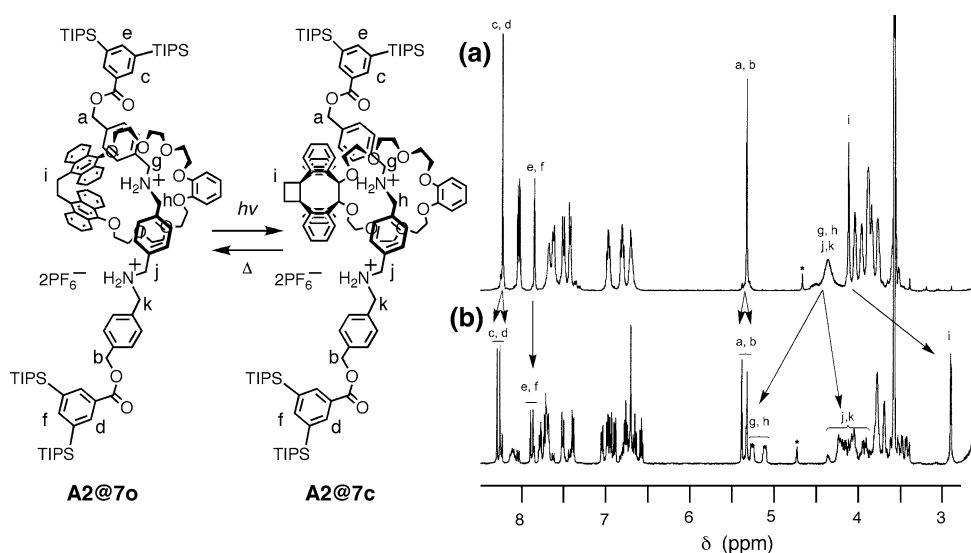
switching between **A2@7o** and **A2@7c** by external stimuli, photoirradiation and thermal heating, was established.

Determination of shuttling rates of open-form rotaxane A2@7o and closed-form rotaxane A2@7c

In order to determine the rates of the shuttling motion of rotaxane **A2@7o.** VT-NMR spectra were recorded. The rates of the shuttling motion of rotaxane **A2@7o** were determined by the line-shape analysis of their VT-NMR spectra in toluene-d_8 and THF-d_8 [140]. Figures 9 and 10 show partial experimental ^{1}H NMR spectra of the benzylic protons (H$_a$, H$_b$) on the axle component of open-form rotaxane **A2@7o** at different temperatures together with the simulated spectra assuming the rates shown. The kinetic parameters were determined from the Eyring plot as listed in Table 3. On the other hand, the shuttling rates of closed-form rotaxane **A2@7c** could not be determined in the same
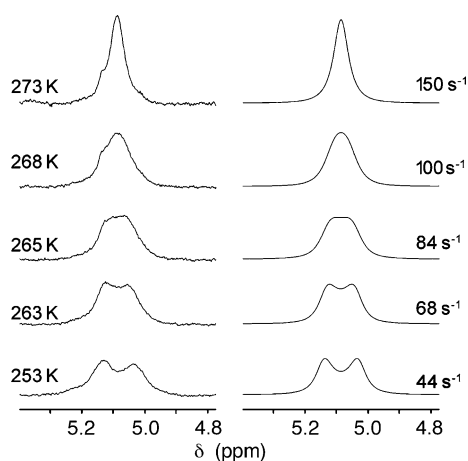
Fig. 9 Experimental (*left*) and simulated (*right*) partial VT-NMR (270 MHz) spectra of protons H_a and H_b of **A2@7o** in toluene-d_8. The corresponding temperatures and exchange rates are indicated

Fig. 10 Experimental (*left*) and simulated (*right*) partial VT-NMR (270 MHz) spectra of protons H_a and H_b of **A2@7o** in THF-d_8. The corresponding temperatures and exchange rates are indicated

manner. The room temperature spectra of **A2@7c** indicate that the shuttling motion is slow on the NMR time scale and the coalescence of the split signals was not observed when the solutions were heated to 303 K in toluene-d_8 and to 323 K in THF-d_8, respectively [141]. Therefore, the maximum rates of shuttling motions ($k_{303\ K}$ ands $k_{323\ K}$) were estimated to be <19 and <86 s^{-1}, respectively, from the Gutowski's equation using observed Δv, the smallest difference between the resonance frequencies of exchangeable protons (H_a and H_b in both solvents) of **A2@7c**, as shown in Table 3.

As shown in Table 3, the rate of shuttling of open-form rotaxane **A2@7o** ($k_{303\ K} = 860$ s^{-1}) is at least 45 times faster than that of closed-form rotaxane **A2@7c** ($k_{303\ K} < 19$ s^{-1}) in toluene-d_8. The switching ratio in THF-d_8 is about 50 ($k_{323\ K} = 4500$ s^{-1} vs. $k_{323\ K} < 86$ s^{-1}). These results clearly demonstrate that the shuttling motion was controlled very effectively by changing the ring size of the rotaxanes using photochemical cycloaddition and thermal reversion. In addition, the solvents used here did not affect significantly the ratio of shuttling rates.

In order to obtain more information, saturation transfer NMR experiments were carried out, which are useful to obtain the information of slow chemical exchange, because a saturation transfer is observed when chemically
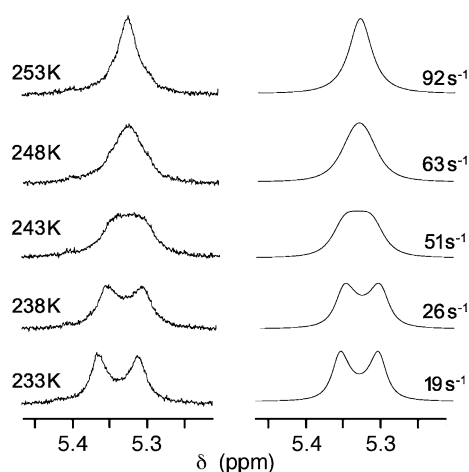
exchanging nucleus is observed as individual signals at different frequencies (v_a and v_b), however, the lifetime (τ) is shorter than the spin–lattice relaxation time (T_1). Namely, these factors satisfy the following Eq. 1.

$$1 \Big/ \left(\pi^{1/2} \cdot \Delta v \right) < \tau < T_1 \tag{1}$$

where, $\Delta v = v_a - v_b$, T_1 is spin–lattice relaxation time, τ is lifetime.

The information of the rate of shuttling of closed-form **A2@7c** was obtained by these experiments. As shown in Fig. 11, signals of H_a and H_b of **A2@7c** appeared at 5.35 and 5.40 ppm, respectively (303 K, THF-d_8). When the signal of H_a was irradiated, the intensity of H_b remained unchanged as shown with red line in Fig. 11, indicating that the lifetime (τ) is longer than the spin–lattice relaxation time T_1. Then, the T_1 value was determined by the null point method. NMR signals were measured at 273 K by changing the intervals between 180° and 90° pulse from 250 to 500 ms (Fig. 11). The null point, where the signal intensity is minimum, was obtained when the interval was 300 ms (Fig. 12). T_1 value defined as 1.44 times of the null point, was determined to be 430 ms (=300 × 1.44 ms). Therefore the oscillation frequency of rotaxane **A2@7c** at 273 K is slower than 2.3 Hz (=1/430 ms).

Table 3 Rates of shuttling and the corresponding kinetic parameters of **A2@7o** and **A2@7c**

	Solvent	T_c (K)	Δv (Hz)	ΔH (kJ mol^{-1})	ΔS (J K^{-1} mol^{-1})	k (s^{-1})
A2@7o	Toluene-d_8	266	–	37 ± 4	–65 ± 17	860 ± 270[b]
A2@7c	Toluene-d_8	>303	8.4	ND[a]	ND[a]	<19[b, c]
A2@7o	THF-d_8	243	–	36 ± 2	–65 ± 8	4500 ± 300[d]
A2@7c	THF-d_8	>323	39	ND[a]	ND[a]	<86[c, d]

[a] Not determined. [b] At 303 K. [c] Maximum rates estimated from the Gutowski's equation, assuming that the coalescence was observed at each temperature. [d] At 323 K

Fig. 11 Partial ^{1}H NMR spectra of **A2@7c** with and without irradiation at 5.35 ppm for the saturation experiment (400 MHz, THF-d_8, 303 K)
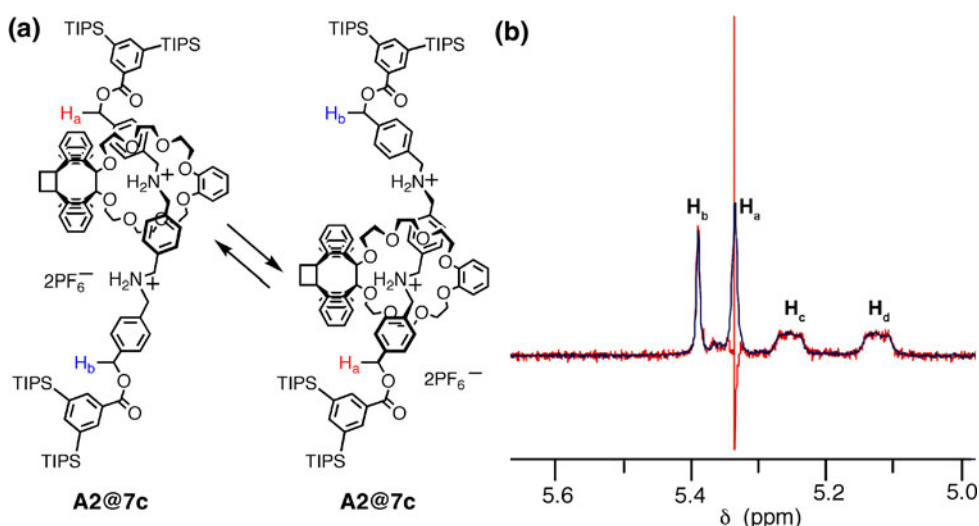
As a result, the shuttling rate of rotaxane **A2@7c** at 273 K in THF-d_8 was estimated to be <2.3 s^{-1}. The rate constant of **A2@7o** at the same temperature $k_{273\ K}$ in THF-d_8 was calculated from the kinetic parameters obtained from the VT-NMR shown in Table 3 to be 340 s^{-1}. These results also demonstrate that the rate of shuttling was reduced substantially to less than 1% (from 340 to <2.3 s^{-1}) by changing the size of the ring component.

Summary of the molecular brake system of shuttling motion

We synthesized 2-station [2] rotaxanes having a dianthrylethane moiety in the ring unit of which size was

Fig. 12 Partial ^{1}H NMR spectra of **A2@7c** with different intervals between 180° and 90° pulses (400 MHz, THF-d_8, 273 K)

changed reversibly and quantitatively by intramolecular photochemical cycloaddition and thermal reversion. Substantial difference between the shuttling rates of open- and closed-form rotaxanes was observed, demonstrating that the shuttling motion was controlled effectively by the external stimuli. These results clearly demonstrate the potential of the brake function of the present system for application to the control of shuttling and other motions directed toward the construction of artificial molecular machines.

Control of rocking motion

The third purpose of this project is to switch a frequency of rocking motion and to appreciate the rate of the motion.

Our concept for the control of rocking motion is shown in Fig. 13 which includes models of [2] rotaxanes capable of changing the size of ring components and the corresponding potential energy diagrams. Figure 13a shows the larger ring (open-form) rotaxane and Fig. 13b shows the smaller ring (closed-form) state, which are reversibly interconverted. The rotaxanes possess the identical axle component having a symmetrical structure, which is composed by two stoppers, one station. The potential energy of the individual rotaxane depends on the angle of the pendular moiety. The steric barrier between the axle component and the pendular moiety is larger in the closed-form than in the open-form. Moreover, through the attractive interactions between the ring components and the station, the closed-form rotaxane can be more stabilized than the open-form. Consequently, the shuttling rate of the closed-form rotaxane would be reduced effectively than that of the open-form.
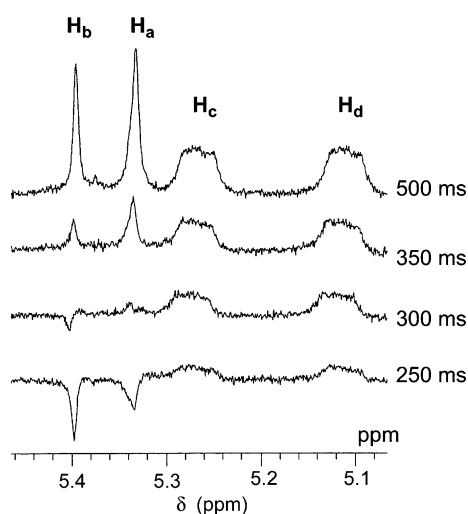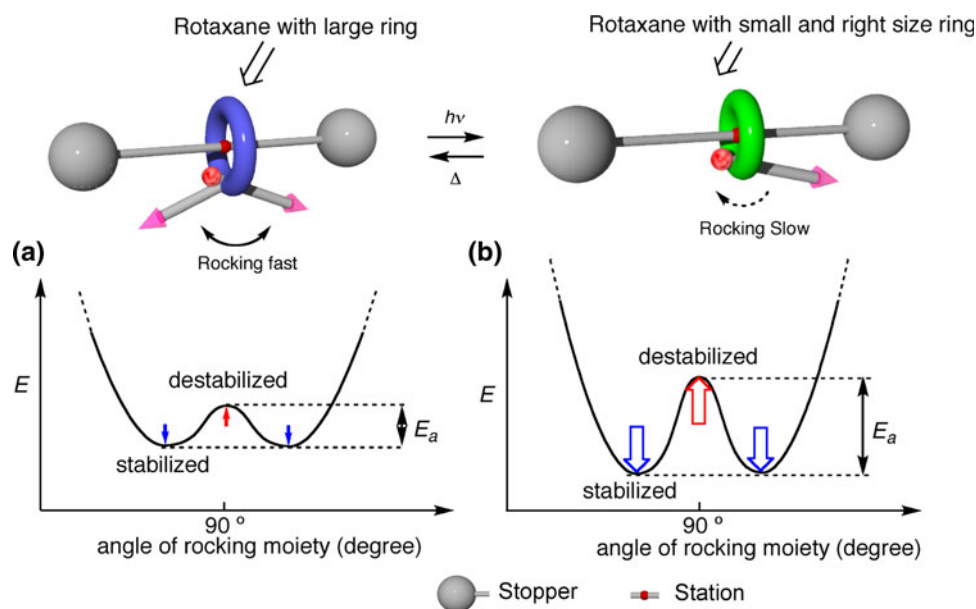
Fig. 13 Models of [2] rotaxanes and the corresponding energy diagrams of a rocking machine with effective brake function

Design, preparation and switching of the brake system for rocking motion

In Scheme 8, rotaxanes **A1@17o**, **A1@18o**, **A1@17c**, and **A1@18c** that we designed are shown. We planned to switch the rates of rocking motion of the metaphenylene unit, by changing the size of the ring component. We expected that the barrier to the pseudo rotation of the phenylene moiety would change between the open- (**A1@17o**, **A1@18o**) and closed-forms (**A1@17c**, **A1@18c**) rotaxanes. In order to induce appropriate steric barrier to switching of rocking frequencies between the open- and closed-forms, a methoxy or an isopropoxy group was attached at the flanked position of the meta-phenylene unit (pendular unit). Dibenzyl ammonium cation was used as the station which interacts more strongly with the closed-form ring molecule than the open-form. Finally, 3,5-bis(triisopropylsilyl)phenyl group was employed as the stopper component because it is bulky enough to prevent the dethreading of the axle in the open-form.

Preparation of rotaxanes A1@17o, A1@18o

The synthetic route of rotaxanes **A1@17o**, **A1@18o** is shown in Scheme 9. According to the literature [142], 2,6-bis(bromomethyl)-4-bromoanisole (**19**) was prepared from 4-bromophenol. Corresponding isopropyl derivative **20** was prepared by a similar procedure. Condensation of these halides **19**, **20** with two equivalents of triethylene glycol in the presence of NaOH gave **21**, **22**. Subsequent tosylation gave **23**, **24**. On the other hand, 1,2-bis [10-(trimethylsilyloxy)-9-anthryl]ethane (**9**) [138] was deprotected in situ

and coupled with ditosylates **23**, **24** under high dilution conditions to furnish crown ethers **17o**, **18o**, in 18% and 14% yields from **19**, **20**, respectively.

By photoirradiation of solutions of **17o**, **18o** in benzene with a high pressure mercury lamp, the corresponding closed-forms **17c**, **18c** were formed. After the solvent was changed to a mixture of dichloromethane and acetonitrile (10:1), pseudorotaxanes **11@17c**, **11@18c** were formed by complexation of **17c**, **18c** with secondary ammonium salt **11** at −10 °C. The acylation capping reaction [86] of **11@17c**, **11@18c** with anhydride **12** catalyzed by n-Bu$_3$P afforded the corresponding rotaxanes **A1@17c**, **A1@18c** which then reverted to the respective open-form rotaxanes **A1@17o**, **A1@18o** during the work-up and isolation procedures. The yields of rotaxanes **A1@17o**, **A1@18o** from crown ethers **17o**, **18o** (four steps) were 46% and 50%, respectively.

Interconversion between open- and closed-form crown ethers

The photoisomerization of the open-form ring molecule **17o** to the corresponding closed-form molecule **17c** proceeded quantitatively. A solution of **17o** in CD$_3$CN was placed in a Pyrex NMR tube and degassed by bubbling dry argon, and subsequently irradiated with a 500-W high-pressure mercury lamp for 30 min in a water bath. After the photoirradiation, the solution was kept under 273 K in order to avoid significant thermal reversion of **17c**. In the ^{1}H NMR spectra, a sharp singlet signal assigned to the benzylic protons (H$_a$) of anthracene unit of **17o** at 4.10 ppm disappeared and a singlet signal assigned to the aliphatic protons of **17c** appeared at 2.95 ppm after the

Scheme 8 Switching of the rocking rates (k) of rotaxanes **A1@17o**, **A1@18o**, **A1@17c**, and **A1@18c** based on the change in the size of the ring component
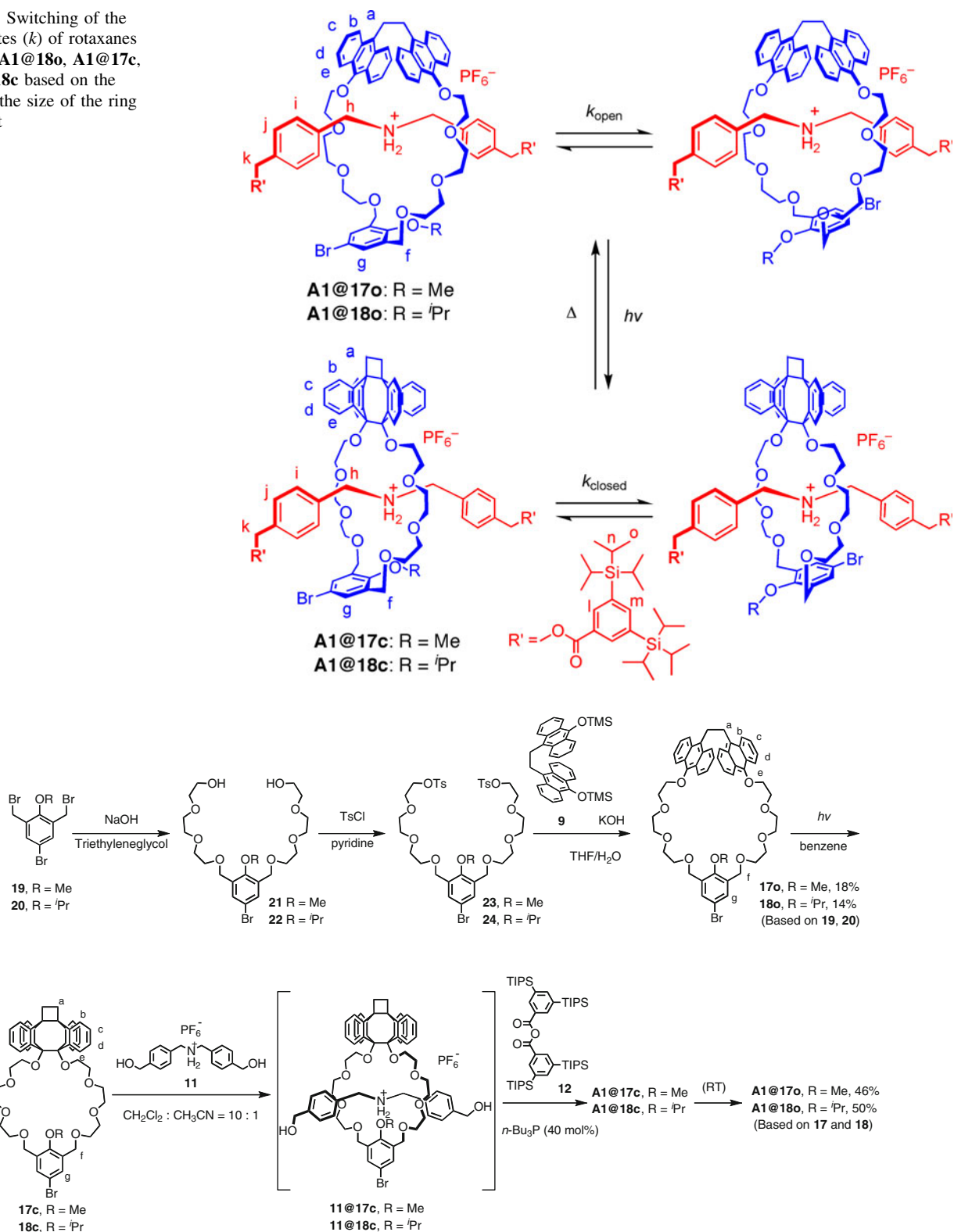
Scheme 9 Syntheses of ring molecules **17o**, **18o** and rotaxanes **A1@17o** and **A1@18o**. TsCl = tosyl chloride

irradiation as shown in Fig. 14. In the aromatic region, the characteristic signals of anthracene at 8.12 and 7.55 ppm (H_e and H_b, respectively) shifted to 7.23 and 7.10 ppm,

respectively, after irradiation. When the NMR solution of **17c** was stood at room temperature overnight, the spectrum of **17c** reverted to that of **17o**, implying that the thermal
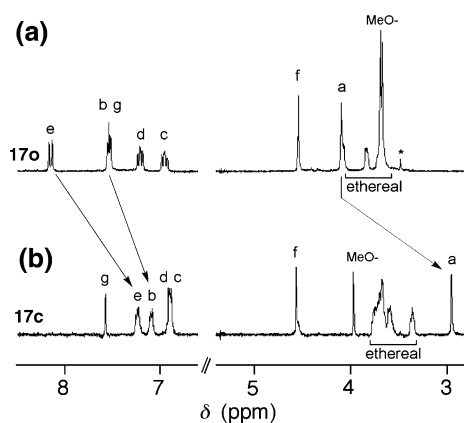
Fig. 14 Partial ^{1}H NMR spectra (270 MHz, CD$_3$CN, 273 K) of open-form macrocycle **17o** (**a**) and closed-form **17c** (**b**). The assignments of the protons refer to those indicated in Scheme 9

reversion **17c–17o** proceeded quantitatively. Reversible transformation between the isopropyl derivatives **18o** and **18c** was also observed as shown in Fig. 15.

Interconversion between open- and closed-form rotaxanes

The photochemical ring closure and the thermal reversion of the anthracene units took place reversibly between the open-form rotaxanes **A1@17o**, **A1@18o** and closed-forms **A1@17c**, **A1@18c**, respectively. As shown in Fig. 16, the photoreaction of rotaxane **A1@17o** in THF-d_8 was monitored by ^{1}H NMR spectroscopy in a similar manner as that for ring molecules **17o**, **18o**.

Upon irradiation, the singlet peak at 4.12 ppm assigned to the ethylene protons (H$_a$) of the dianthrylethane unit of **A1@17o** disappeared and a characteristic signal of the cyclobutane protons of **A1@17c** appeared at 2.94 ppm, indicating that the ring closure proceeded efficiently. In contrast to the photoisomerization of crown ether **17o**, the signal of the benzyl protons of the ring component (H$_f$)
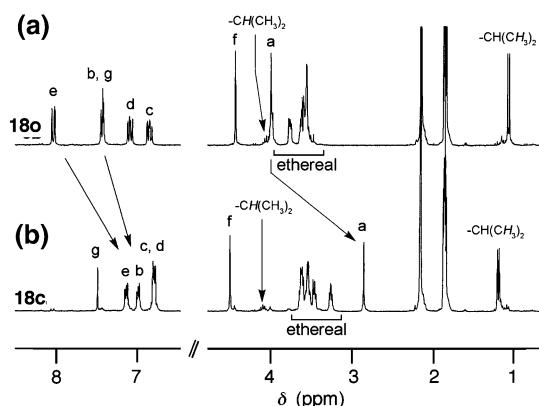

Fig. 15 Partial ^{1}H NMR spectra (270 MHz, CD$_3$CN, 273 K) of open-form macrocycle **18o** (**a**) and closed-form **18c** (**b**). The assignments of the protons refer to those indicated in Scheme 9
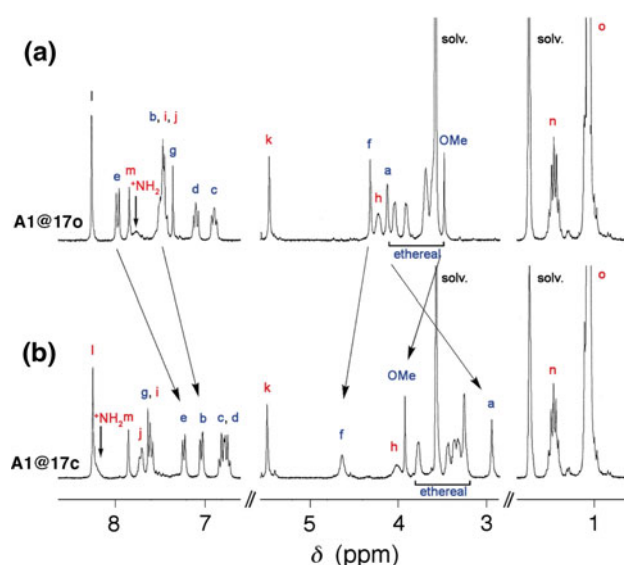

Fig. 16 Partial ^{1}H NMR spectra (270 MHz, THF-d_8, 273 K) of open-form rotaxane **A1@17o** (**a**) and closed-form **A1@17c** (**b**). The assignments of the protons refer to those indicated in Scheme 8

shifted to downfield and appeared as a broad singlet (from 4.31 to 4.64 ppm). The signals assigned to the protons (H$_l$, H$_k$) of the terminal part of the axle component did not shift significantly by photoisomerization (from 8.27 and 5.45 to 8.25 and 5.48 ppm, respectively), as shown in Fig. 16. These results indicate that ring contraction did not affect significantly the magnetic environment of the terminal part of the axle component. The spectrum of **A1@17c** reverted to that of **A1@17o** when the NMR solution of **A1@17c** was stood at room temperature overnight, implying that the thermal reversion **A1@17c–A1@17o** also proceeded quantitatively.

Reversible transformation between the isopropyl derivatives **A1@18o** and **A1@18c** was also observed as shown in Fig. 17. In contrast to the photoisomerization of rotaxane **A1@17o**, the photoirradiation of the corresponding isopropyl rotaxane **A1@18o** gave rise to additional difference in the appearance of the ^{1}H NMR spectra. For example, the signals assigned to the protons (H$_l$, H$_k$) of the axle component of **A1@18c** appeared as a pairs of singlets (8.26 and 8.24 ppm, 5.51 and 5.45 ppm, respectively). Moreover, the benzylic protons (H$_f$) of the ring component appeared as a double doublet at 4.97 and 4.37 ppm. These results indicate that the rate of the rocking motion of isopropyl derivative **A1@18c** is slower than the NMR time scale.

Rates of thermal reversions of crown ethers 17c, 18c and rotaxanes A1@17c, A1@18c

The thermal reversions of closed-forms **17c**, **18c**, **A1@17c**, and **A1@18c** to the corresponding open-forms **17o**, **18o**, **A1@17o**, and **A1@18o** gave rise to remarkable spectral
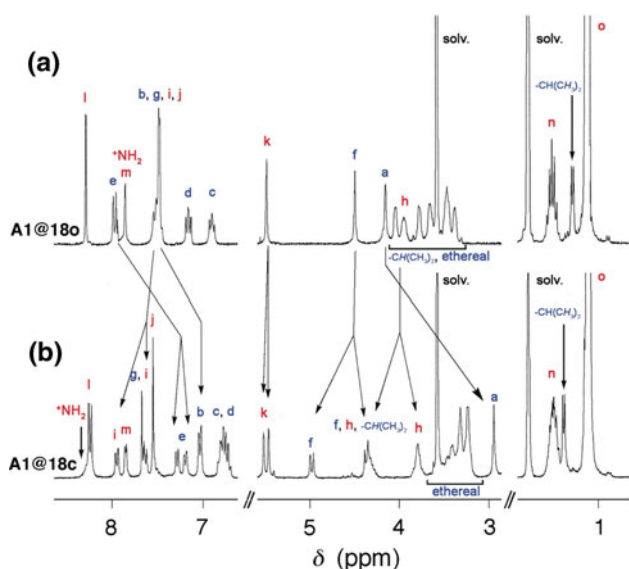
Fig. 17 Partial ^{1}H NMR spectra (270 MHz, THF-d_8, 273 K) of open-form rotaxane **A1@18o** (**a**) and closed-form **A1@18c** (**b**). The assignments of the protons refer to those indicated in Scheme 8

changes in UV–visible spectroscopy in CH$_3$CN. Based on the increase of absorbance at 383 nm, the first-order rate constants of the thermal reversion were determined. The rate constants of the thermal reversions of **17c**, **18c**, **A1@17c**, and **A1@18c** at 303 K were 1.36×10^{-3}, 1.33×10^{-3}, 4.97×10^{-4}, and 2.85×10^{-4} s^{-1} (the corresponding half lives: 9, 9, 23, and 41 min), respectively. As shown in Table 4, the rates of reversion of **A1@17c**, and **A1@18c** were slower than those of the corresponding crown ethers **17c**, **18c**. These results indicate that the closed-form rotaxanes **A1@17c**, and **A1@18c** are more stabilized than crown ethers **17c**, **18c** by the ion–dipole interactions between the crown ether ring and the secondary ammonium ion. In addition, it should be noted that the rates of **17c**, **18c** were almost identical (950×10^{-5} vs. 933×10^{-5} s^{-1}), whereas that of **A1@17c** was two times as large as that of **A1@18c** (3.00×10^{-5} vs. 1.47×10^{-5} s^{-1}) in spite of the greater steric hindrance in **A1@18c**. This suggests that the ion–dipole interactions in **A1@18c** are stronger than that in

Table 4 Reversion rates constants and half-lives of **17c**, **18c** and **A1@17c**, **A1@18c** in CH$_3$CN

	k (10^{-5} s^{-1})		$\tau_{1/2}$ (min)	
	$T = 283$ (K)	$T = 303$ (K)	$T = 283$ (K)	$T = 303$ (K)
17c	9.50	136	121	9
18c	9.33	133	124	9
A1@17c	3.00	49.7	385	23
A1@18c	1.47	28.5	784	41

A1@17c owing to the stronger basicity of the isopropoxybenzene than that of the methoxybenzene [143].

Complexation constants of crown ethers 17c, 18c with bis(3,5-dimethylbenzyl)ammonium hexafluorophosphate (25)

The relative strength of the ion–dipole interactions of closed-form crown ethers **17c**, **18c** with a secondary ammonium ion were estimated by determining their complexation constants with bis(3,5-dimethylbenzyl)ammonium hexafluorophosphate (**25**) using the ^{1}H NMR spectroscopy in a mixture of solvent consisting of CD$_2$Cl$_2$:CD$_3$CN = 2:1. Because of the lability of the closed-form ring molecules, the titration method could not be used. Instead, the complexation constants were determined by the relative integration of the signals of the free and complexed ring components in the ^{1}H NMR spectra [144]. Then, slightly bulky **25** was employed as a guest molecule because the slipping/deslipping rates between **17c**, **18c** and **25** were slow enough to observe the respective signals of the components (Scheme 10). As a result, **18c** bearing an isopropoxy substituent exhibits larger complexation constants by about five times than those of **17c** bearing a methoxy substituent [145], the result consistent with the observed rate retardation of the thermal reversion of closed-form rotaxanes **A1@17c**, **A1@18c** (Table 5).

Evaluation of the rates of rocking motions

The rates of the rocking motions of the rotaxanes **A1@18o** and **A1@18c** were determined by the line-shape analysis of their VT-NMR spectra in THF-d_8. Figure 18a shows partial experimental ^{1}H NMR spectra of H$_k$ on the axle component of **A1@18o** between 178 and 188 K and the simulated spectra assuming the rate constants shown. Similarly, the rates of rocking of **A1@17c** were estimated on the basis of the line-shape analysis [146] of the VT-NMR spectra for H$_f$ as shown in Fig. 18b. The kinetic parameters were determined from the Eyring plots as listed in Table 6.

In contrast to **A1@18o**, in the case of **A1@17o**, the room temperature spectrum indicates that the rocking motion of the phenylene unit is rapid on the NMR time scale and the spectrum did not change even when the solution was cooled down to 165 K. Therefore, the minimum rate of rocking ($k_{303\ K}$) of **A1@17o** was estimated to be 4.0×10^4 s^{-1}, assuming that the rocking frequency of **A1@17o** at the coalescence temperature is same as that of **A1@18o** and that the temperature dependence of their rocking frequencies is also identical. By contrast, in the

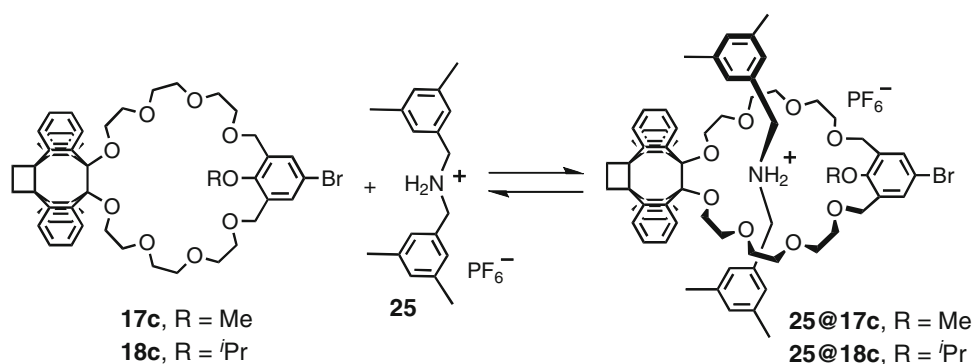**Scheme 10** Complexation process of **17c** and **18c** with **25** (CD$_2$Cl$_2$:CD$_3$CN = 2:1)

17c, R = Me
18c, R = ^{i}Pr

25

25@17c, R = Me
25@18c, R = ^{i}Pr

Table 5 Complexation constants of **17c** and **18c** with **25**, respectively

T (K)	K (M^{-1})[a]	
	17c	**18c**
273	30	150
263	40	250
253	100	440
243	150	750
233	350	1200

[a] Reactions performed in CD$_2$Cl$_2$/CD$_3$CN 2:1. It was confirmed that the complexation abilities of open-form crown ethers **17o**, **18o** were negligible by ^{1}H NMR spectroscopy

Table 6 Rocking rates and kinetic parameters of **A1@17o**, **A1@18o** and **A1@17c**, **A1@18c** in THF-d_8

	Tc (K)	ΔH (kJ mol^{-1})	ΔS (J K^{-1} mol^{-1})	k_{303}[b] (s^{-1})
A1@17o	ND[a]	ND[a]	ND[a]	>4.0 × 10^{4c}
A1@18o	186	17 ± 3.0	−113 ± 15	8.9 × 10^{3d}
A1@17c	241	32 ± 5.0	−59 ± 21	1.0 × 10^{4d}
A1@18c	ND[a]	ND[a]	ND[a]	<3.5[e]

[a] Not determined. [b] Rocking rate at 303 K. [c] Minimum estimate (see text). [d] Estimated by extrapolation of the Eyring plot. [e] Maximum value estimated on the basis of the saturation transfer experiment

case of **A1@18c**, the ^{1}H NMR spectrum at 273 K indicates that the rocking motion is slow on the NMR time scale. In contrast to **A1@17c**, coalescence of the signals, however, was not observed when the temperature was elevated to 303 K, indicating that the rocking rate of **A1@18c** is much slower than that of **A1@17c**.

The rate of rocking of closed-form rotaxane **A1@18c** was also estimated by saturation transfer experiments [147]. The saturation transfer experiment indicated that the rocking rate ($k_{303\ K}$) of **A1@18c** was slower than 3.5 s^{-1}. Table 6 summarizes the kinetic parameters and the rocking

frequencies at 303 K of rotaxanes **A1@17o**, **A1@18o**, **A1@17c**, and **A1@18c**.

For rotaxanes **A1@17o** and **A1@17c** with a methoxy substituent, the rate of rocking of open-form **A1@17o** ($k_{303\ K} > 4.0 × 10^4$ s^{-1}) should be at least four times faster than that of closed-form **A1@17c** ($k_{303\ K} = 1.0 × 10^4$ s^{-1}). On the other hand, for rotaxanes **A1@18o** and **A1@18c** with the isopropoxy substituent, the difference between the rocking rates should be more than 10^3 times (**A1@18o**; $k_{303\ K} = 8.9 × 10^3$ s^{-1}, **A1@18c**; $k_{303\ K} < 3.5$ s^{-1}). These results demonstrate clearly that the rocking rate is switched by the external stimuli. Moreover, the observed remarkable difference in the ratio of the rocking

Fig. 18 Experimental (*left*) and simulated (*right*) partial VT-NMR (270 MHz, THF-d_8) spectra of protons **a** H$_k$ of **A1@18o** and **b** H$_f$ of **A1@17c**

(a)
188 K   88 s^{-1}
186 K   73 s^{-1}
184 K   64 s^{-1}
181 K   52 s^{-1}
178 K   45 s^{-1}
5.8   5.4   5.8   5.4
δ (ppm)

(b)
283 K   5900 s^{-1}
263 K   2300 s^{-1}
243 K   410 s^{-1}
223 K   95 s^{-1}
203 K   23 s^{-1}
5.0 4.6 4.2   5.0 4.6 4.2
δ (ppm)
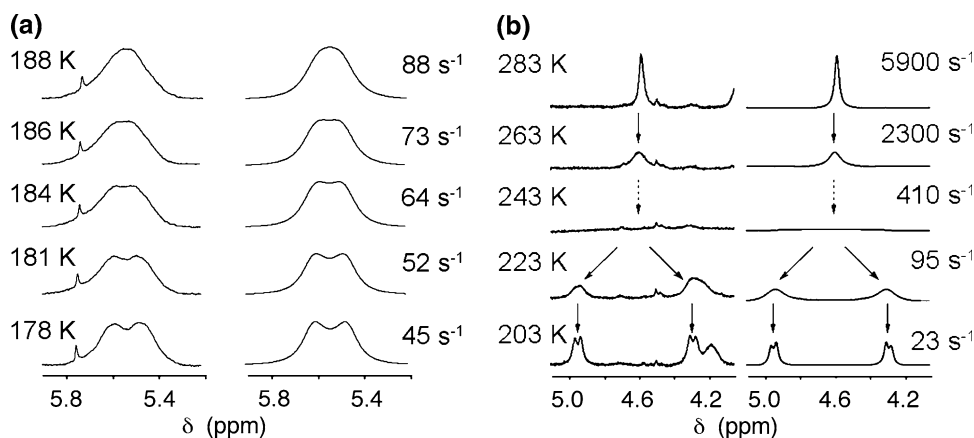
frequencies between open- and closed-form rotaxanes (**A1@17o/A1@17c** vs. **A1@18o/A1@18c**) is ascribed to the small rate of rocking of **A1@18c** as can be seen from Table 6. The reason for the slow rocking rate can be attributed to the destabilization of the transition state of the rocking due to large steric hindrance of the bulkier isopropoxy substituent. On the other hand, it can also be attributed by the stabilization of the ground state, since the crown ether unit of **A1@18c** with an isopropoxy substituent bears larger interaction with the secondary ammonium cation than that of **A1@17c** with a methoxy substituent due to stronger electron-releasing ability of the isopropylbenzene. These two effects may contribute to increase the activation energy of the rocking motion of **A1@18c**, thereby decelerating the rocking rate substantially.

Summary of the molecular brake system of rocking motion

The rotaxanes having the dianthrylethane moiety in the ring unit of which ring size was changed reversibly by photochemical cycloaddition and thermal reversion. The rates of rocking motion of the rotaxanes were determined on the basis of the NMR experiments. Fair to substantial differences between the rocking rates of the open- and closed-form rotaxanes were observed, demonstrating that the rocking motions were switched by the external stimuli. In addition, it was found that the difference of the rocking frequencies between the open- and closed-form rotaxanes varies considerably depending on the steric and electronic properties of the inside substituent. The rate of rocking motion was proved to be reduced to less than 0.1% (from 8.9×10^3 to <3.5 s^{-1}) by reducing the size of the ring component upon photoirradiation.

Perspective

Following the developments of synthetic methods for interlocked molecules, functionalization into interlocked molecules has been important issues in this field of chemistry. We have created novel brake systems of rotaxanes which operate by changing the sizes of ring components. Threading/dethreading, shuttling, and rocking motions were reduced by these brake systems. The rate of shuttling motion was proved to be reduced to less than 1%. The rate of rocking motion was proved to be reduced to less than 0.1%. Our brake systems were proved to function well. By a simple modification of the pendular moiety of the rotaxane with a high dipole moiety, it is possible to expect large changes of dipole moments accompanying rocking motions. Therefore, the brake system, which control rocking motion, is promising for the development of molecular devices.

Since Aviram and Ratner presented the first principle of molecular rectifiers [148], many constructions of simple electronic devices based on single organic molecules were investigated. In order to meet the integration requirement of electronic devices, a single molecule or a single supramolecule should work as a logic gate [149] or as a device with more complex functions. As an example, the author reported an idea of an impetus-responsible dipole switching system based on a control of rocking motion [126], which is shown in Scheme 11. The ring component in the rotaxane possesses a dipolar unit undergoing pendular motion. When the dipolar moiety flips rapidly, the net dipole moment should be negligible (Scheme 11, situation (a)). By applying an external electric (E) or magnetic field (H) to this system (Scheme 11, process a), the rocking motion can be stopped or decelerated owing to the interaction of the dipole with the external field (Scheme 11, situation (b)) [150]. At this stage, if the size of the ring component is contracted by an external stimulus (Scheme 11, process b), the rocking motion would be frozen because of increased steric hindrance between the ring and axle components, thereby locking the dipole moment (Scheme 11, situation (c)). This system corresponds to a memory system which can be constructed by a logical combination of several transistors. From more futuristic vista of this field, smaller and more ecological

Scheme 11 Schematic model of the switching system using rocking motion. **a** Application of an external electric (E) or magnetic field (H), resulting in alignment of the dipolar unit. **b** Contraction of the size of the ring moiety, thereby fixing the rocking motion in the absence of the external field. *Red arrow*: dipolar moiety in the ring component
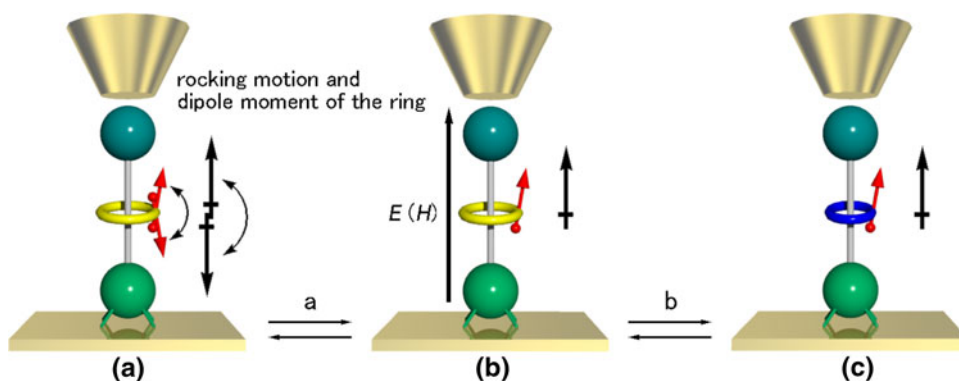
functional units shall be required and constructed. Then the arrest of movements becomes important. The arrest technique will create the nanoworld afresh.

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