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Reversible Photoswitching of Rotaxane Character and Interplay of Thermodynamic Stability and Kinetic Lability in a Self-Assembling Ring–Axle Molecular System

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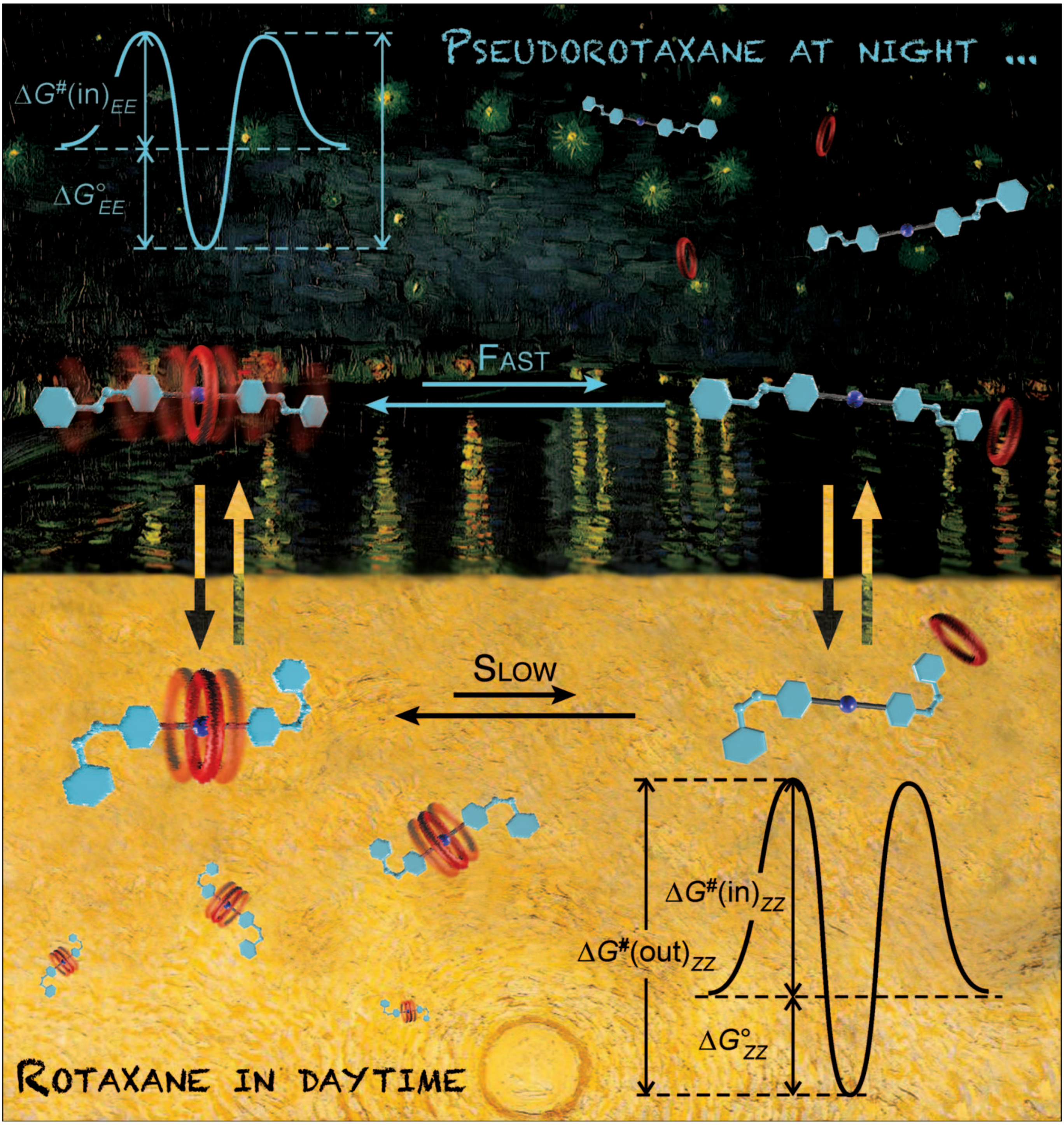
Dedicated to Professor Luigi Fabbrizzi, recipient of the 2010 International Izatt–Christensen Award in Macrocyclic Chemistry



Abstract: We have designed, synthesized, and investigated a self-assembling system that can be reversibly interconverted between thermodynamically stable (pseudorotaxane) and kinetically inert (rotaxane) forms by light irradiation. The system is composed of a dibenzo[24]crown-8 ring and an axle comprised of a dibenzylammonium recognition site and two azobenzene end groups. The isomeric form of the azobenzene units of the axle has a little influence on the stability constants of the respective pseudorotaxanes but greatly affects the threading–dethreading rate constants. In fact, equilibration of the ring and the axle in its *EE* isomeric form occurs within seconds in acetonitrile at room temperature, whereas the *ZZ* axle threads–dethreads the ring at least four orders of magnitude slower. Moreover, we show that a change in the stability of the complex, achieved by deprotonating the dibenzylammonium recognition site on the axle, affects its kinetic behavior. We compare the results of these experiments with those observed upon dethreading the (pseudo)rotaxane by using a competitive guest for the ring, an approach which does not inherently destabilize the ring–axle interaction. This study outlines a general strategy for the reversible photochemical control of motion kinetics in threaded and interlocked compounds and constitutes a starting point for the construction of multicomponent structures that can behave as photochemically driven nanomachines.

Keywords: azo compounds • crown compounds • hydrogen bonds • molecular devices • supramolecular chemistry

Introduction

Pseudorotaxanes are supramolecular complexes minimally composed of an axle-like molecule surrounded by a macrocycle. These complexes can be rendered kinetically inert, that is, transformed into rotaxanes, by attaching bulky groups at the extremities of the axle to prevent dethreading.[1,2] Therefore, the pseudorotaxane or rotaxane behavior of a given axle–macrocycle pair is determined by the threading–dethreading rate constants that in turn depend on the temperature and the energy barriers associated with these processes.[3]

Rotaxanes and related species are primarily interesting for the construction of molecular machines.[4,5] The operation of most rotaxane-type machines is based on classical switching processes between thermodynamically stable states. It has become clear, however, that functional molecular motors will only be realized if the reaction rates between states can also be controlled,[6] thus enabling the implementation of ratchet-type mechanisms.[7,8] In this context, the ability of adjusting the threading–dethreading kinetics[9] by modulating the corresponding energy barriers through external stimulation is an important goal.

A previously explored approach to convert a pseudorotaxane into a rotaxane by using light was based on a stilbene derivative as the photoswitchable capping group at one end of the molecular axle.[10,11] Qualitative observations indicate that the shape change of the stilbene end group brought about by $E \rightarrow Z$ photoisomerization is sufficient to hamper the dethreading of a dibenzo[24]crown-8 ring from the axle. However, these experiments were conducted at 0 °C under nitrogen and an external photosensitizer had to be used. Moreover, the $E \rightarrow Z$ conversion was not complete and reversibility was not demonstrated; in fact it is known[12] that, besides isomerization, irradiation of stilbene causes cyclization and dimerization. Thus, stilbene derivatives do not appear to be optimally suited for the reversible photochemical control of motion kinetics in threaded and interlocked compounds. Conversely, *E*-azobenzene can be converted to the *Z* form by direct UVA irradiation with yields exceeding 95 % and virtually no side products. The process is fully photochemically or thermally reversible.[13]

Herein we describe a self-assembling system based on the known[2,3a,14] dialkylammonium–crown ether recognition motif, which can be switched between thermodynamically stable (pseudorotaxane) and kinetically inert (rotaxane) forms by light irradiation owing to the presence of photoisomerizable azobenzene units at the extremities of the axle.[15] The structural formulas of the molecular components, namely the bis-azobenzylamine axle *EE*-**1**H$^+$ and the dibenzo[24]crown-8 ether ring **2**, are shown in Scheme 1. We present a quantitative investigation into the effect of the isomeric state of the azobenzene end groups on both the association equilibrium constant and the threading–dethreading rate constants of the molecular components. Furthermore, we report how a change in the ring–axle intercomponent interactions affects the kinetic behavior of the complex.

Results and Discussion

The dibenzo[24]crown-8 ring is commercially available. The axle was synthesized in good yield by using Mill's coupling of bis(4-aminobenzyl)amine and 4-nitrosotoluene in acetic acid, followed by anion exchange with NH_4PF_6 (Scheme 2). The *EE*-**1**H·PF_6 salt was fully characterized by using ^{1}H (Figure 1c) and ^{13}C NMR, DQF-COSY, ESI-MS, and UV/Vis absorption spectroscopies.[16] The ^{1}H NMR spectrum of

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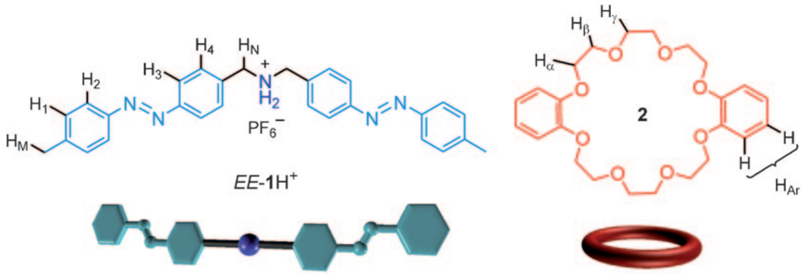
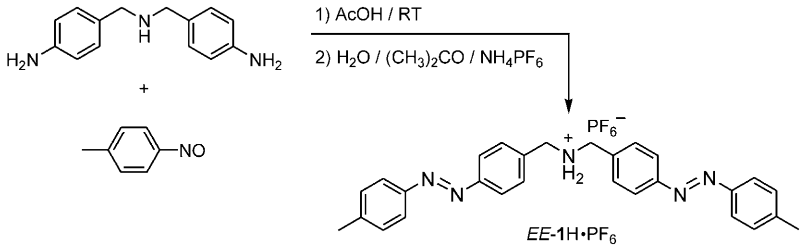


Scheme 1. Structure of the ring and axle components, showing the atom-numbering system.



Scheme 2. Synthesis of the EE-**1**H•PF$_6$ axle.

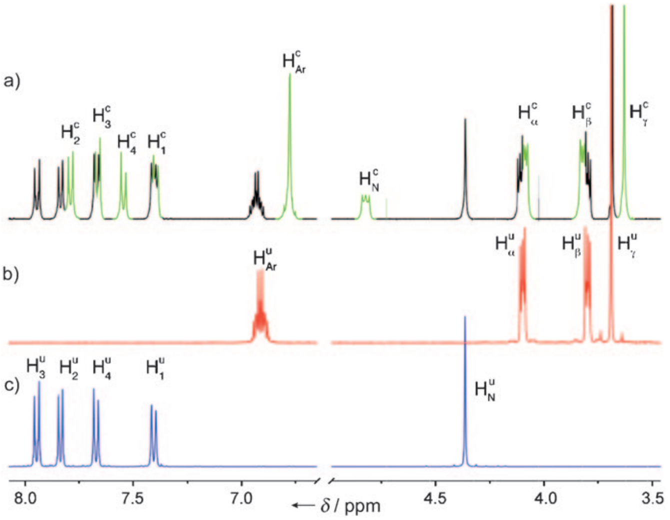


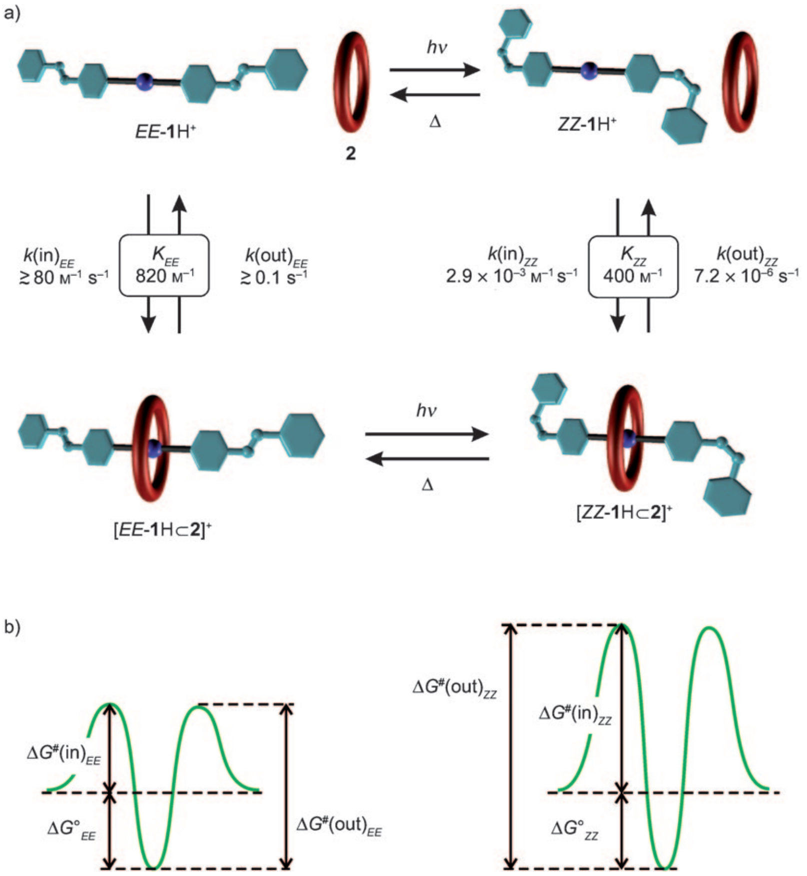
Figure 1. ^{1}H NMR spectra (400 MHz, 298 K, CD$_3$CN) of a) an equimolar solution of EE-**1**H•PF$_6$ and **2** (3 mM; about 50 % association), b) a solution of **2** (3 mM), and c) a solution of EE-**1**H•PF$_6$ (3 mM). Resonances associated with the complex [EE-**1**H⊂**2**]$^+$ are highlighted in green. For proton descriptors see Scheme 1; u = uncomplexed, c = complexed.

a freshly prepared 1:1 mixture of EE-**1**H$^+$ and **2** in CD$_3$CN shows sharp and well-resolved signals associated with 1:1 complex [EE-**1**H⊂**2**]$^+$ and with the free axle and ring components (Figure 1a). The NMR data[16] are fully consistent with a pseudorotaxane structure in which the crown ether surrounds the ammonium center of the axle (Scheme 3), in agreement with previous studies.[3a,14] The spectra also show that the threading–dethreading reactions are slow on the ^{1}H NMR timescale.

The stability constant of [EE-**1**H⊂**2**]$^+$ (K_{EE}) was obtained in acetonitrile at 298 K by using single-point determination from the ^{1}H NMR spectra, and was found to be $K_{EE}=820\,\text{M}^{-1}$. The equilibrium between the complex and its free components was established within the time necessary for mixing and recording the NMR spectrum. We could estimate a lower-limiting value for the threading rate constant $k(\text{in})_{EE}$ of $80\,\text{M}^{-1}\,\text{s}^{-1}$ and, accordingly, $k(\text{out})_{EE} \geq 0.1\,\text{s}^{-1}$ (see the Experimental Section). Because $k(\text{in})_{EE}$ was estimated at a concentration of $5\times10^{-3}\,\text{M}$, the corresponding pseudo first-order kinetic constant is $>0.4\,\text{s}^{-1}$. This value can be compared with that of the intramolecular shuttling rate constant ($40\,\text{s}^{-1}$) in a rotaxane[6c] in which a dibenzo[24]crown-8 ring moves onto a dialkylammonium site by slipping through a 1,4-phenylene unit, considering that the steric hindrance of the latter unit should be lower than that of E-azobenzene.

Photoirradiation of EE-**1**H$^+$ at $\lambda = 365$ nm afforded almost quantitative (>95 %) isomerization to the ZZ isomer, as shown by ^{1}H NMR and UV/Vis spectra (Figure 2).[16] The values determined for the $E\rightarrow Z$ photoisomerization quantum yield (0.095) and rate constant for the $Z\rightarrow E$ dark isomerization ($1.4\times10^{-6}\,\text{s}^{-1}$) are typical of the azobenzene unit[13a,17] and are virtually unaffected by the presence of ring **2**. Thus, both the end groups of **1**H$^+$ (either alone or surrounded by **2**) can be effectively switched between the E and Z isomers (Figure 3a). Cycling between EE and ZZ states could be performed with no sign of degradation. The ^{1}H NMR spectra also showed that ZZ-**1**H$^+$ remains complexed by **2**.

The inspection of molecular models (Figure 4) suggested that the Z-azobenzene unit could exert a stronger steric hindrance than E-azobenzene for the threading of **2** on **1**H$^+$. Indeed, no sign of complexation was observed by ^{1}H NMR soon after 1:1 mixing of **2** and ZZ-**1**H$^+$ in CD$_3$CN (Figure 3b). However, changes consistent with the formation of the [ZZ-**1**H⊂**2**]$^+$ complex took place on a much slower time scale (Figure 5). A kinetic analysis of the NMR spectra afforded a rate constant $k(\text{in})_{ZZ}=2.9\times10^{-3}\,\text{M}^{-1}\,\text{s}^{-1}$ while the stability constant, determined at equilibrium, resulted to be $K_{ZZ}=400\,\text{M}^{-1}$. From these data we calculated a dethreading rate constant for the ZZ isomer, $k(\text{out})_{ZZ}=7.2\times10^{-6}\,\text{s}^{-1}$. Therefore, the disassembly of the [ZZ-**1**H⊂**2**]$^+$ complex is at least four orders of magnitude slower than that of [EE-**1**H⊂**2**]$^+$ and takes place on the same timescale as the $Z\rightarrow E$ thermal isomerization. In other words, light irradiation



Scheme 3. a) Representation of the chemical equilibria and photochemical reactions involving components **1**H$^+$ and **2**. b) Simplified potential energy curves (free energy vs. ring–axle distance) for the threading–dethreading of the ring and the axle in its *EE* (left) and *ZZ* (right) isomeric forms.

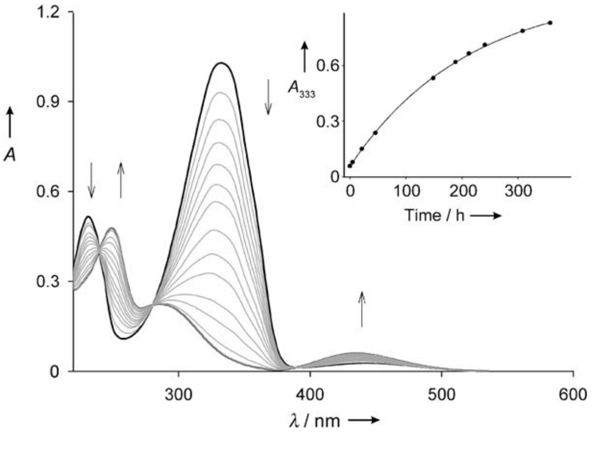


Figure 2. Absorption spectra at RT of an air-equilibrated solution of *EE*-**1**H·PF$_6$ (20 μM) in CH$_3$CN upon exhaustive irradiation at $\lambda=365$ nm. These spectral changes are reversed upon equilibration of the irradiated solution in the dark. The inset shows the time profile of the absorption changes at $\lambda=333$ nm, which corresponds to the thermal $Z\rightarrow E$ isomerization, and the data fitting (solid line) according to a first-order kinetic equation that gives $k_{Z\text{-}E}=1.4\times10^{-6}$ s^{-1}.

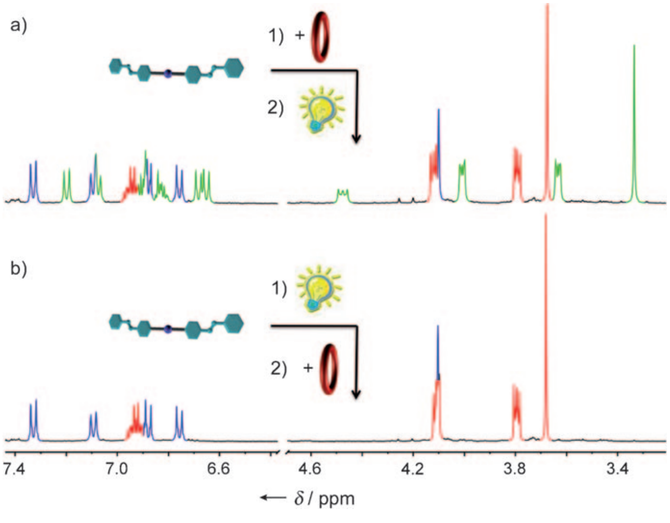


Figure 3. ^{1}H NMR spectra (400 MHz, CD$_3$CN, 298 K, 3 mM) of *EE*-**1**H$^+$ after a) the addition of one equivalent of **2** followed by exhaustive irradiation at $\lambda=365$ nm and b) the same inputs in reverse order. The resonances associated with *ZZ*-**1**H$^+$, **2**, and [*ZZ*-**1**H⊂**2**]$^+$ are colored in blue, green and red, respectively.

transforms the [*EE*-**1**H⊂**2**]$^+$ pseudorotaxane into a rotaxane species that remains kinetically interlocked for days (Scheme 3). This result is particularly surprising in view of the fact that *Z*-stilbenes were not considered large enough to prevent dethreading of **2**.[18] It is also worth noting that the $E\rightarrow Z$ photoisomerization of an azobenzene-type unit located on the axle was shown to block ring shuttling in rotaxanes with either α-cyclodextrin[6e] or cyclobis(paraquat-*p*-phenylene)[6l] as the macrocyclic components, which, however, are both considerably more rigid than crown ether **2**.

Now an interesting question arises: Can *Z*-azobenzene end units prevent dethreading if the intercomponent interactions between the ring and the axle are removed? Our system is particularly appropriate for investigating this aspect because such interactions can be virtually cancelled by deprotonating the ammonium center of the axle with a base, that is, using a stimulus orthogonal to that employed for switching the azobenzene end units. As expected,[14f,19] ^{1}H NMR spectroscopy experiments showed that deprotonation of the ammonium center of [*EE*-**1**H⊂**2**]$^+$ with a

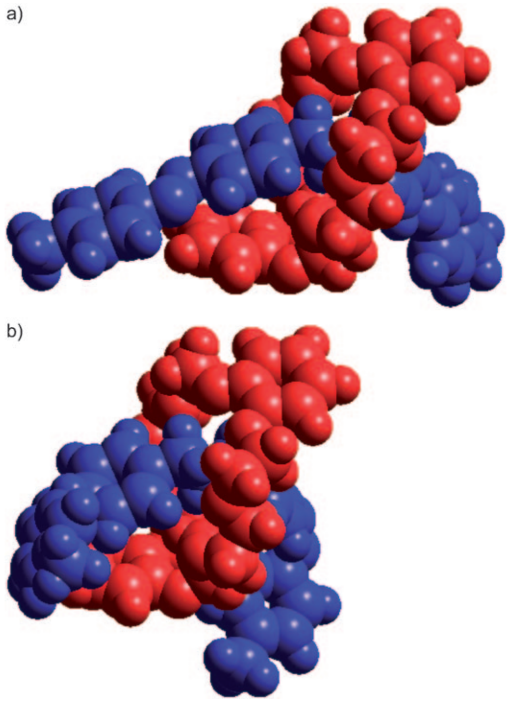


Figure 4. AMBER force-field optimized structures of a) $[EE\text{-}\mathbf{1}\mathrm{H}\subset\mathbf{2}]^{+}$ and b) $[ZZ\text{-}\mathbf{1}\mathrm{H}\subset\mathbf{2}]^{+}$.

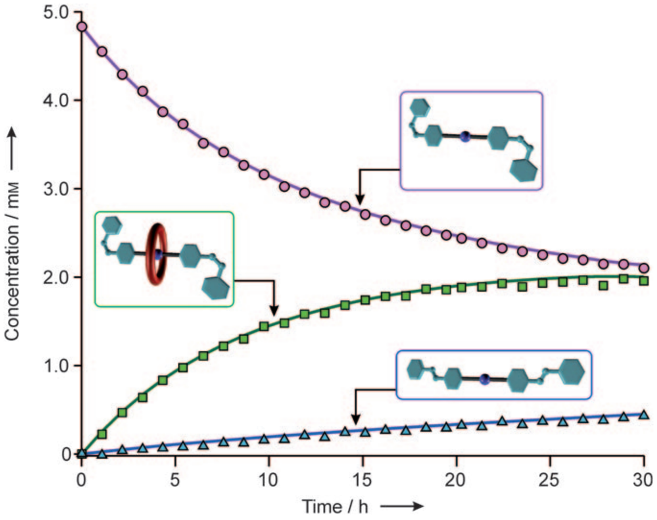


Figure 5. Concentration–time profiles, obtained from ^{1}H NMR spectroscopic data (CD_3CN, 298 K), of free (circles) and complexed (squares) $ZZ\text{-}\mathbf{1}\mathrm{H}^{+}$ upon mixing $ZZ\text{-}\mathbf{1}\mathrm{H}^{+}$ (4.8 mM) and **2** (5.4 mM). The thermal regeneration of $EE\text{-}\mathbf{1}\mathrm{H}^{+}$ is also shown (triangles). The solid lines represent the data fitting according to the model shown in Scheme 3a.

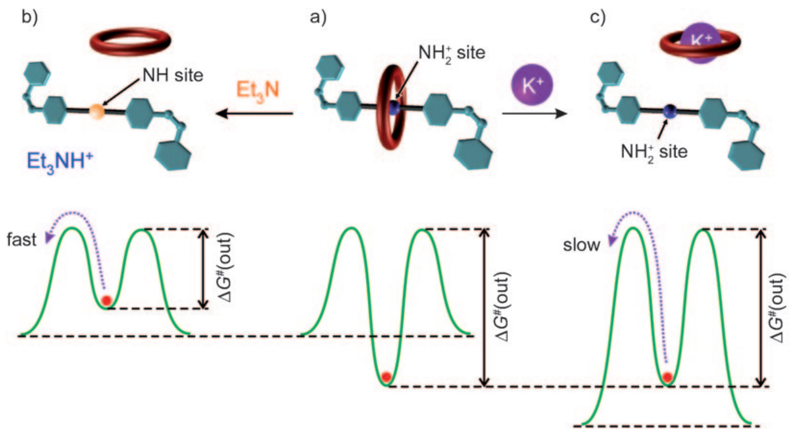
stoichiometric amount of triethylamine causes quantitative dethreading of the pseudorotaxane. This process occurs on a timescale faster than that required to add the base and record the NMR spectrum. Interestingly, the same behavior was observed upon addition of triethylamine to $[ZZ\text{-}\mathbf{1}\mathrm{H}\subset\mathbf{2}]^{+}$, that is, deprotonation of the ammonium site resulted in a quantitative and fast dethreading. This observation suggests that the barrier experienced by the ring upon dethreading is substantially lowered because of the destabilization of the energy level corresponding to the ring encircling the amine center of the axle, as schematically represented in Scheme 4a→b. Such an effect is a consequence of the proximity of the ammonium recognition site and azobenzene pseudo-stoppers.

To probe the hampering effect of the azobenzene end groups in a dethreading experiment, the self-assembly equilibrium of $\mathbf{1}\mathrm{H}^{+}$ and **2** should be displaced towards the free components without weakening their intermolecular interactions. One possibility is to cause the dethreading of the axle from the ring by using a competitive guest for the latter.[20] Potassium ions are ideal candidates[21] because they bind **2** in acetonitrile with a stability constant of $7.6\times10^{3}\,\mathrm{M}^{-1}$,[22] are spectroscopically silent, and should not interact with the axle. Simple calculations[23] show that under our conditions >90% of $[EE\text{-}\mathbf{1}\mathrm{H}\subset\mathbf{2}]^{+}$ and >94% of $[ZZ\text{-}\mathbf{1}\mathrm{H}\subset\mathbf{2}]^{+}$ would be disassembled in the presence of three equivalents of K^{+} ions. Indeed, the addition of 2.9 equivalents of KPF_6 to the $[EE\text{-}\mathbf{1}\mathrm{H}\subset\mathbf{2}]^{+}$ pseudorotaxane caused its complete and fast disassembly (Figure 6).

Conversely, no changes were observed in the ^{1}H NMR spectrum of $ZZ\text{-}\mathbf{1}\mathrm{H}^{+}\subset\mathbf{2}$ recorded soon after the addition of 2.9 equivalents of KPF_6.[16] This observation indicates that K^{+} ions do not cause an appreciable disassembly of $[ZZ\text{-}\mathbf{1}\mathrm{H}\subset\mathbf{2}]^{+}$ on a time scale of minutes. The NMR spectra recorded at longer times, however, demonstrate that dethreading eventually takes place. The time-dependent NMR spectral changes (Figure 7) show that the K^{+}-induced dethreading of $[ZZ\text{-}\mathbf{1}\mathrm{H}\subset\mathbf{2}]^{+}$ occurs on a timescale comparable to that observed in the absence of K^{+} (see the value of $k(\mathrm{out})_{ZZ}$ calculated from the threading rate constant and equilibrium constant). This behavior can be interpreted on the basis of the simplified potential energy curves shown in Scheme 4a→c. The energy of the potential well that represents the attractive ring–axle interactions is not perturbed because such interactions are not affected by the presence of K^{+}. Therefore, the barrier that the ring has to overcome to escape from the axle (Scheme 4c) is similar to that experienced in the absence of K^{+} (Scheme 4a).

Conclusion

We have shown that azobenzene units can be effectively employed as end groups in a molecular axle to exert photocontrol on the threading–dethreading rate of a crown ether ring. Both the *E*-azobenzene units can be rapidly and quantitatively isomerized to the *Z* form by light irradiation and fully converted back to the *E* isomer in the dark on a timescale of days. In acetonitrile at room temperature, the *EE*-axle is complexed by the ring in a pseudorotaxane fashion, according to a self-assembly equilibrium that is established in seconds. $E\rightarrow Z$ photoisomerization of the end groups of the axle slows down the threading–dethreading of the ring by at least four orders of magnitude, practically turning the pseudorotaxane into a kinetically inert rotaxane.



Scheme 4. Simplified potential energy curves (free energy vs. ring–axle distance) representing the dethreading of the *ZZ* axle from the ring, induced by external stimuli, that is, dethreading caused by deprotonation of the ammonium center of the axle with triethylamine (a→b) or by sequestration of the ring with K^+ as a competitive guest (a→c).

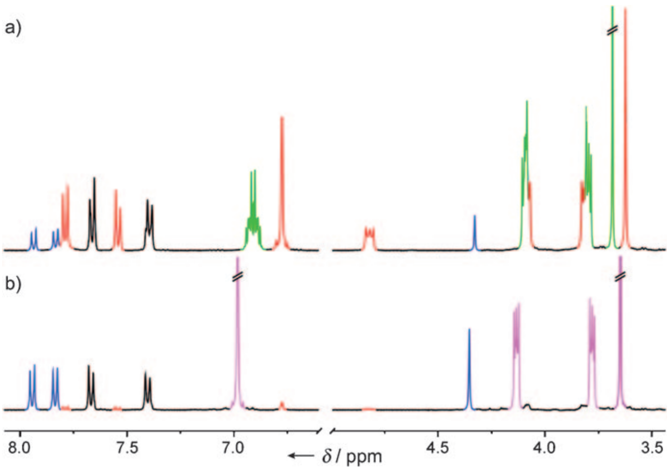


Figure 6. ^{1}H NMR spectra (400 MHz, 298 K, CD_3CN) of a) a solution containing *EE*-**1**H·PF_6 (5.2 mM) and **2** (6.9 mM; about 70 % complexation of the axle molecules). b) Solution (a) immediately after the addition of 2.9 equivalents of KPF_6. The resonances associated with *EE*-**1**H$^+$, **2**, [K·**2**]$^+$, and [*EE*-**1**H⊂**2**]$^+$ are colored in blue, green, purple, and red, respectively, and the resonances shown in black represent overlapping signals of free and complexed *EE*-**1**H$^+$ (see Figure 1). These data show that K^+ ions cause a fast disassembly of [*EE*-1H⊂**2**]$^+$.

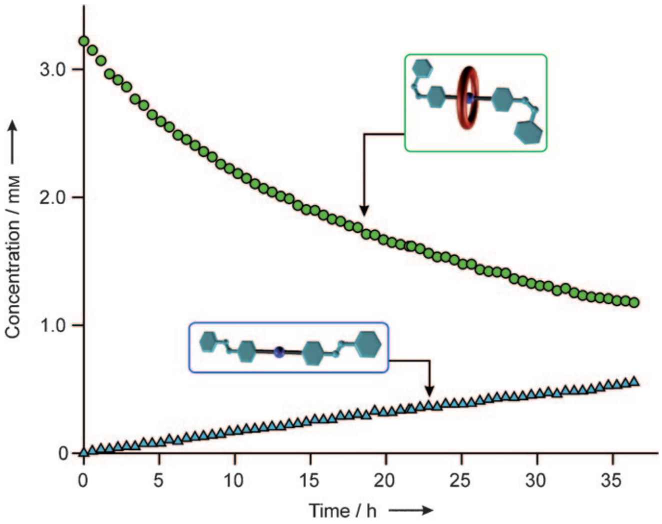


Figure 7. Concentration–time profiles, obtained from ^{1}H NMR data (298 K, CD_3CN), of [*ZZ*-**1**H⊂**2**]$^+$ (circles) upon addition of KPF_6 (16.7 mM) to a solution containing *ZZ*-**1**H$^+$ (4.8 mM) and **2** (7.6 mM; about 65 % complexation of the axle molecules). The thermal regeneration of *EE*-**1**H$^+$ is also shown (triangles).

We have also investigated the effect of switching off the ring–axle interaction on the self-assembly and disassembly kinetics. Our results show that the dethreading barrier is dramatically lowered by the thermodynamic destabilization of the threaded state as expected because of the close distance between the recognition site and the pseudo-stoppers. Conversely, the hampering effect of the *Z*-azobenzene unit can be clearly appreciated if the pseudorotaxane is dethreaded by competitive binding, an approach that does not require structural changes in the molecular components and thus does not affect the intrinsic thermodynamic stability of the complex.

In summary, the present system exhibits several advantages with respect to previously investigated ones[9c,10] because 1) it can be controlled by direct light irradiation (no photosensitizer required), 2) it exhibits a clear-cut behavior, 3) it is fully reversible, and 4) it is easy to make. Owing to the outstanding photochemical behavior of azobenzene and the simplicity of our design, the present study outlines a general strategy for the reversible photochemical control of motion kinetics in threaded and interlocked compounds. We are currently exploiting these results to develop nonsymmetric axle–ring systems in which the threading direction[9b] is controlled by light irradiation.

Experimental Section

Materials: 4-Nitrosotoluene[24] and bis(4-aminobenzyl)amine[25] were synthesized according to previously published procedures. Commercially available compounds, including dibenzo[24]crown-8 (Aldrich, 98 %), were reagent-grade quality and were used without further purification. Solvents were dried according to literature procedures. NBu_4PF_6 (Fluka) was dried at 70 °C and then by vacuum prior to use.

***EE*-1H·PF$_6$**: A solution of 4-nitrosotoluene (3.63 g, 30.0 mmol) and bis(4-aminobenzyl)amine (3.41 g, 15 mmol) in acetic acid (about 50 mL) was stirred under argon at RT for 12 h in the dark. Water was added to the reaction mixture to form a dark red precipitate that was collected by filtration and washed with water. The product was recrystallized from boiling DMF, filtered, and washed with diethyl ether. The isolated salt was dissolved in acetone and a saturated aqueous solution of NH_4PF_6 was added to precipitate the PF_6 salt as a brown-orange powder that was dried under vacuum to give *EE*-1H·PF_6 (yield: 6.3 g, 72 %). M.p. > 210 °C (decomp.); ^{1}H NMR (400 MHz, CD_3CN): $\delta=7.95$ (d, $J=8.3$ Hz, 4H), 7.84 (d, $J=8.4$ Hz, 4H), 7.67 (d, $J=8.4$ Hz, 4H), 7.41 (d, $J=8.3$ Hz, 4H), 4.36 (s, 4H), 2.44 ppm (s 6H); ^{13}C NMR (100.5 MHz, CD_3CN): $\delta=154.2$, 151.6, 143.8, 133.8, 132.4, 131, 123.9, 123.8, 52.1, 21.5 ppm; MS (ESI): *m/z* calcd: 434.2345; found 434.2346 $[M-PF_6]^+$ (100).

Instruments and methods: The ^{1}H and ^{13}C NMR spectra were recorded at 298 K in CD_3CN by using a Varian Mercury 400 spectrometer with the deuterated solvent as the lock and the residual solvent as the internal standard. All chemical shifts (δ) are quoted in ppm and all coupling constants (J) are expressed in Hertz (Hz). Melting points were determined by using a Büchi 510 series apparatus and are uncorrected. Absorption spectra were recorded by using a Varian Cary 50Bio spectrophotometer with air-equilibrated acetonitrile (Uvasol, Merck) solutions at RT (298 K), with concentrations ranging from 1×10^{-5}–1×10^{-3} mol L^{-1}. Solutions were examined in 1 cm spectrofluorimetric quartz cells. The experimental error on the wavelength values was estimated to be ±1 nm. Photochemical reactions were performed on thoroughly stirred air-equilibrated acetonitrile solutions at RT by using a Hanau Q400 medium pressure Hg lamp (150 W). ^{1}H NMR photochemical isomerization experiments were performed in air-equilibrated deuterated acetonitrile solutions irradiated directly inside the NMR tube by using a Hanau Q400 medium pressure Hg lamp (150 W). The selection of the desired irradiation wavelength ($\lambda=365$ nm) was accomplished by the use of an appropriate interference filter. The number of incident photons, as determined by ferrioxalate actinometry in its micro version,[26] was 2.6×10^{-7} $Nh\nu$ min^{-1}. The $E\rightarrow Z$ photoisomerization quantum yield ($\lambda_{irr}=365$ nm) was determined from the disappearance of the π–π^* absorption band of the azobenzene unit of the reactant at low conversion percentages (<10%; extrapolation to $t=0$ was made). The fraction of light transmitted at the irradiation wavelength was taken into account in the calculation of the yields. The experimental error on the quantum yield values was estimated to be 10%. Thermal $Z\rightarrow E$ isomerization was performed at 293 K in the dark; the experimental data were fitted by using the SPECFIT fitting program[28] with a first-order kinetic equation. Molecular modeling was performed by using HyperChem Professional software.[29]

Determination of stability and rate constants: The stability constant K_{EE} was obtained from the ^{1}H NMR spectra of equimolar solutions (1×10^{-3} mol L^{-1}, about 50% association) of *EE*-**1**H•PF$_6$ and **2** at 298 K by using the single-point method.[27] The concentration of all species at equilibrium was determined by using the initial concentrations and the integration of the resonances of the methylene protons adjacent to the NH_2^+ center of the complexed and uncomplexed species: H_N^c and H_N^u, respectively (see Figure 1). The stability constant K_{EE} was calculated by using Equation (1).

$$K_{EE}=\frac{C_{[EE\text{-}\mathbf{1}H\subset\mathbf{2}]^+}}{C_{EE\text{-}\mathbf{1}H^+}C_{\mathbf{2}}} \tag{1}$$

The experimental error on the value of the stability constant was estimated to be ±20%. The formation kinetics of $[EE\text{-}\mathbf{1}H\subset\mathbf{2}]^+$ and $[ZZ\text{-}\mathbf{1}H\subset\mathbf{2}]^+$ were investigated by using ^{1}H NMR spectroscopy (400 MHz) in CD_3CN at 298 K. In the case of the *EE* axle, *EE*-**1**H•PF$_6$ and **2** were rapidly mixed and subjected to NMR spectroscopic analysis (the final concentration was 5 mM for both components). Under our best operating conditions, we estimated that the time required for mixing and starting a meaningful NMR data acquisition is 10 s. The ^{1}H NMR spectrum recorded 10 s after mixing shows the signals of the $[EE\text{-}\mathbf{1}H\subset\mathbf{2}]^+$ complex (Figure 1 and Figure S3 in the Supporting Information) and does not show any further changes over time. Taking the safe value of 20% as the error on the concentrations determined by NMR spectroscopy, our results indicate that in 10 s the reaction has proceeded by at least 80% of its course. Assuming a second-order kinetic law [Eq. (2)] and taking $C^{\circ}_{EE-\mathbf{1}H^+}=5\times10^{-3}$ M, $C_{EE-\mathbf{1}H^+}=0.2\,C^{\circ}_{EE-\mathbf{1}H^+}$, and $t=10$ s, we calculated a lower-limiting value for the threading rate constant $k(\text{in})_{EE}$ of 80 M^{-1}s^{-1}.

$$\frac{1}{C_{ZZ\text{-}\mathbf{1}H^+}}=\frac{1}{C^{\circ}{}_{ZZ\text{-}\mathbf{1}H^+}}+k(\text{in})_{EE}\times t \tag{2}$$

Accordingly, the lower-limiting value for the dethreading rate constant $k(\text{out})_{EE}$ was determined to be $k(\text{in})_{EE}/K_{EE}=1\times10^{-1}$ s^{-1}. In a typical experiment for the *ZZ* axle, an equimolar mixture of **2** (3 mM) and the *ZZ*-**1**H•PF$_6$ salt (3 mM) was prepared in CD_3CN. ^{1}H NMR spectra of the solutions were recorded at 298 K at regular time intervals until equilibrium was reached, that is, until no further changes in the spectra could be detected. By evaluating the relative intensities of the probe protons identified in Figure S10 in the Supporting Information, the concentrations of all the species at time *t* could be calculated for each spectrum. The stability constant K_{ZZ} was calculated from the equilibrium concentrations by using Equation (3).

$$K_{ZZ}=\frac{C_{[ZZ\text{-}\mathbf{1}H\subset\mathbf{2}]^+}}{C_{ZZ\text{-}\mathbf{1}H^+}C_{\mathbf{2}}} \tag{3}$$

The concentration–time profiles were fitted by using the SPECFIT fitting program.[28] The following kinetic scheme was employed to model the threading experiments (Figure 5 and Figure S7 in the Supporting Information):

$$ZZ\text{-}\mathbf{1}H+\mathbf{2}\underset{\text{k(out)}_{ZZ}}{\overset{k(\text{in})_{ZZ}}{\rightleftarrows}}[ZZ\text{-}\mathbf{1}H\subset\mathbf{2}]^+ \tag{4}$$

$$ZZ\text{-}\mathbf{1}H^+\xrightarrow{k_{Z-E}}EZ\text{-}\mathbf{1}H^+ \tag{5}$$

$$[ZZ\text{-}\mathbf{1}H\subset\mathbf{2}]^+\xrightarrow{k_{Z-E}}[EZ\text{-}\mathbf{1}H\subset\mathbf{2}]^+ \tag{6}$$

in which $K_{ZZ}=k(\text{in})_{ZZ}/k(\text{out})_{ZZ}$ was fixed at 400 M^{-1} (see the main text), and k_{Z-E} was fixed at 1.4×10^{-6} s^{-1} (see Figure 2).

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