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Using "Threading Followed by Shrinking" to Synthesize Highly Stable Dialkylammonium-Ion-Based Rotaxanes

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Abstract: Herein, we report a "threading followed by shrinking" approach for the synthesis of rotaxanes by using an "oxygen-deficient" macrocycle that contained two arylmethyl sulfone units and the dumbbell-shaped salt bis(3,5-dimethylbenzyl)ammonium tetrakis(3,5-trifluoromethylphenyl)borate as the host and guest components, respectively. The extrusion of SO_2 from both of the arylmethyl sulfone units of the macrocyclic component in the corresponding [2]pseudorotaxane resulted in a [2]rotaxane that was sufficiently stable to maintain its molecular integrity in CD_3SOCD_3 at 393 K for at least 5 h.

Keywords: rotaxanes · shrinking · supramolecular chemistry · synthetic methods · threading

Introduction

The potential applicability of rotaxanes as molecular actuators and switches within mesoscale molecular electronic devices has driven the development of new methods and procedures for their synthesis.[1] Over the past two decades, "threading followed by stoppering",[2] "clipping",[3] and "slippage"[4] have been the most widely used approaches for the construction of interlocked molecules that perform various functions (Figure 1). Although "threading followed by swelling"[5] and "threading followed by shrinking"[6] strategies have conceptually been suggested for many years, their experimental realization was only recently demonstrated after several practical difficulties had been resolved. For example, balancing the sizes of the macrocyclic component and the termini of the dumbbell component—a major challenge when developing new "slippage" systems—is also a requirement for successful "threading followed by swelling" and "threading followed by shrinking" strategies, such that the macrocyclic component can thread onto, but not slip off from, the rod-like portion of the dumbbell-shaped component prior to the onset of specific reactions to enlarge the termini of the threadlike component ("swelling") or to shrink the size of the macrocyclic component ("shrinking").

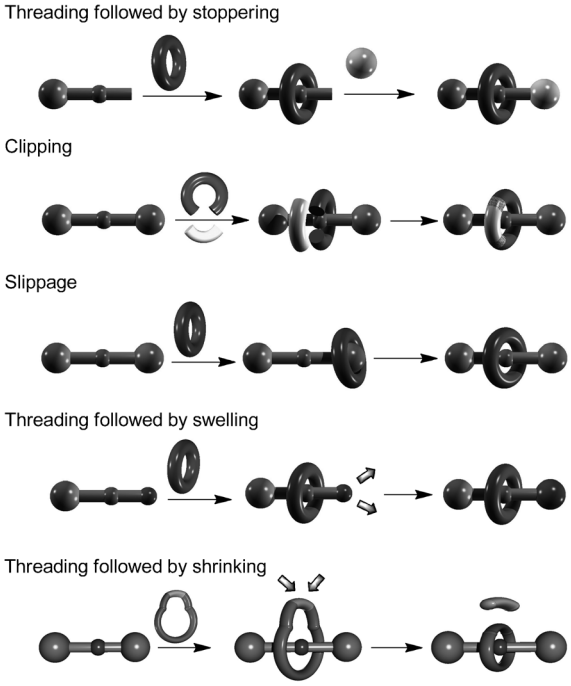

Figure 1. Schematic representation of various approaches for the synthesis of rotaxanes.

The "shrinking" approach was first realized by employing a Pd^{2+} ion to chelate a salophen moiety in the macrocyclic unit of a corresponding [2]pseudorotaxane, thereby decreasing the amount of free space in the complexed macrocycle and interlocking the components of the [2]rotaxane.[6a] To demonstrate the "shrinking" concept, which involves decreasing the number of atoms in the skeleton of the macrocyclic component, it was necessary to solve several other problems in addition to that of balancing the sizes of the macrocyclic and terminal components. When designing such a system, the non-shrinking portion of the macrocycle

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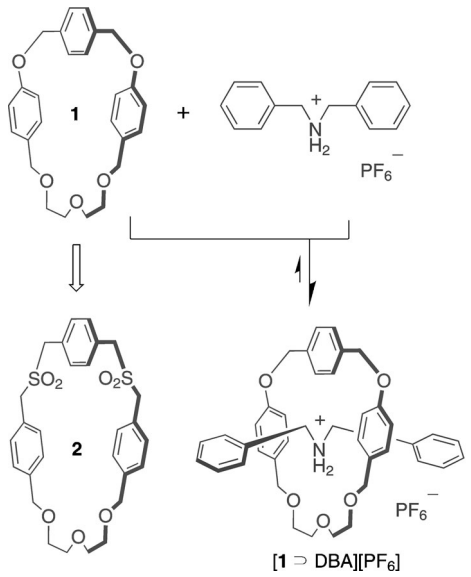
should be the primary source of stabilizing interactions toward the threadlike component; if so, the variation in the structure of the shrinking motif in the macrocyclic unit would not significantly disrupt the stabilizing interactions in the host/guest complex. In addition, the rate of shrinking of the macrocycle in its complexed state should not be much slower than that in its free state, thereby ensuring that the pseudorotaxanes that are generated in solution do not dissociate to overcome the decrease in concentration of the free macrocycle. Moreover, because the recognition of the components relies on weak noncovalent interactions, a mild chemical reaction would be preferred for shrinking the ring skeleton of the macrocyclic component to ensure that the [2]pseudorotaxane does not undergo significant dissociation in the presence of any undesired side products that may be generated during the transformation.

Previously, we reported the preparation of a [2]rotaxane by using a "threading follow by shrinking" approach that involved the photoextrusion of SO_2 from an arylmethyl sulfone motif in a penta(ethylene glycol)-containing macrocycle.[6b] We suspected that performing the same photoextrusion reaction twice on a single macrocyclic component would decrease the size of the resulting macrocycle even further and, hence, result in [2]rotaxanes that were structurally much more robust. Nevertheless, situating two arylmethyl sulfone motifs in a single macrocycle would presumably hinder its binding ability to an ammonium-ion-containing dumbbell-shaped component. Because we have previously developed a successful "threading followed by swelling" approach toward [2]rotaxanes, by using an "oxygen-deficient" macrocycle (**1**)/dibenzylammonium ion molecular recognition system with a *cis*-1-[(*Z*)-alk-1′-enyl]-2-vinylcyclopropane motif as the swellable terminal group,[5] we were interested in realizing a "shrinking" approach that employed macrocycle **1** (Scheme 1).



Scheme 1. Design of "shrinking" macrocycle **2** from macrocycle **1**.

Herein, we report the use of an "oxygen-deficient" macrocycle that contains two arylmethyl sulfone units for successful "threading follow by shrinking" in conjunction with a dumbbell-shaped salt, bis(3,5-dimethylbenzyl)ammonium tetrakis(3,5-trifluoromethylphenyl)borate; the resulting [2]rotaxane that is formed after SO_2 has been extruded from both of the arylmethyl sulfone motifs of the macrocyclic component is sufficiently stable to maintain its molecular integrity in CD_3SOCD_3 at 393 K for at least 5 h.

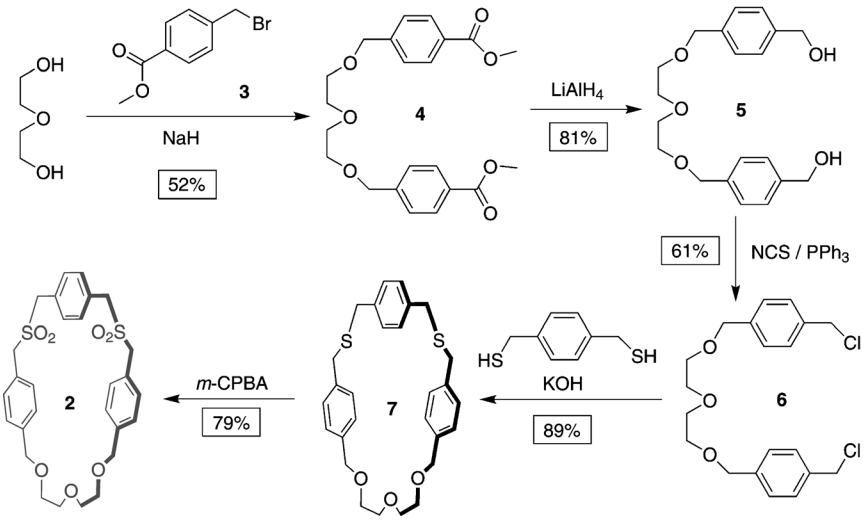
Results and Discussion

Previously, we have demonstrated that "oxygen-deficient" macrocycle **1** is capable of forming a complex with dibenzylammonium hexafluorophosphate ([DBA][PF_6]) in CD_3NO_2 with an association constant (K_a) as high as 15000 M^{-1} (Scheme 1).[7] Because the complexation of the DBA^+ ion with macrocycle **1** is mainly based on [N^+–H···O] and [N^+C–H···O] hydrogen bonds and on [N^+–H···π] and [N^+C–H···π] interactions between the $CH_2NH_2^+CH_2$ moiety and the di(ethylene glycol) loop and its adjacent phenolic units, respectively, in macrocycle **1**, we suspected that introduction of arylmethyl sulfone motifs into the *para*-xylene motif of compound **1**—a motif that is not involved significantly in the stabilization of the complex—would result in the formation of macrocycle **2**, which would also be capable of binding to the DBA^+ ion.

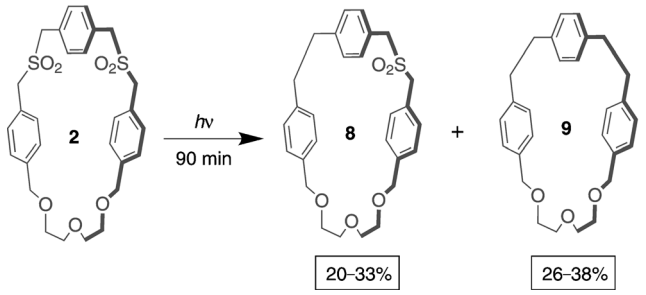
We synthesized macrocycle **2** from di(ethylene glycol) in five steps (Scheme 2). Alkylation of di(ethylene glycol) with methyl 4-(bromomethyl)benzoate (**3**) gave diester **4**, which we reduced into the corresponding diol (**5**) by using $LiAlH_4$. We obtained dichloride **6** after treating diol **5** with *N*-chlorosuccinimide (NCS) and triphenylphosphine (PPh_3); then, dichloride **6** underwent macrocyclization with 1,4-benzenedimethanethiol under basic conditions to afford macrocycle **7**. The use of *meta*-chloroperbenzoic acid (MCPBA) to oxidize the two sulfide motifs of macrocycle **7** into sulfone units gave macrocycle **2** (18% overall yield).

We irradiated (254 nm) a degassed solution of compound **2** in C_6H_6/CH_2Cl_2 (1:1) at 298 K for 90 min to confirm that the shrinking of the ring skeleton of macrocycle **2**, through the extrusion of SO_2, was possible. After four repeat experiments, we isolated macrocycles **8** and **9**, which resulting from one and two successful photoextrusions, in 20–33% and 26–38% yield, respectively, after column chromatography on silica gel (Scheme 3). Having demonstrated that the shrinking of the macrocyclic ring of compound **2** was possible under these conditions, we tested whether macrocycle **2** had reasonable binding affinity toward the DBA^+ ion—a necessity if the shrinking reaction were to be applied to the synthesis of rotaxanes.

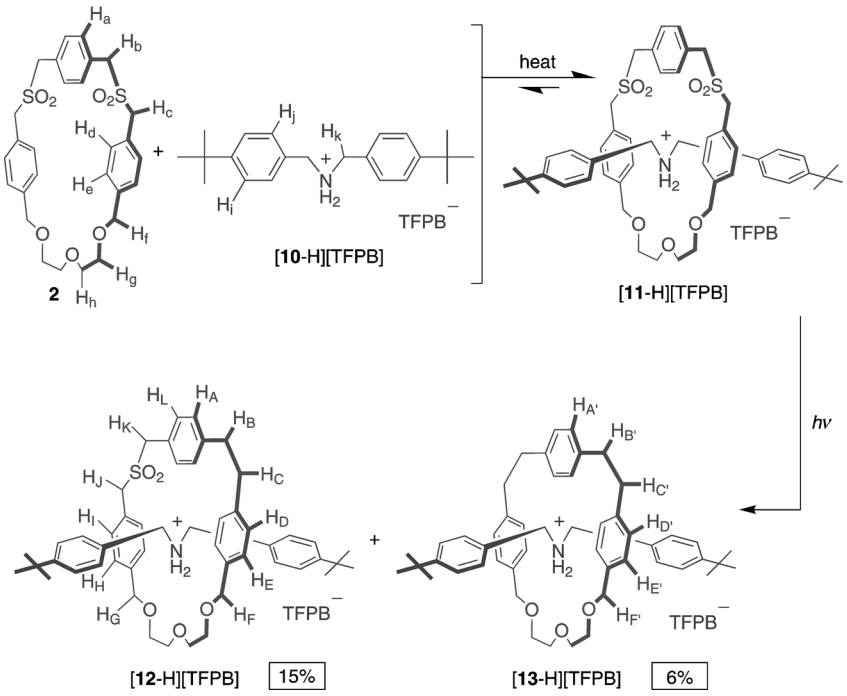
We observed no evidence for the threading of [DBA][PF_6] through macrocycle **2** in CD_3CN or CD_3NO_2; because of the poor solubility of this salt in less polar solvents ($CDCl_3$, CD_2Cl_2), we instead tested whether bis(*para-tert*-butyl)benzylammonium hexafluorophosphate[8] ([**10**-H][PF_6]) would



Scheme 2. Synthesis of macrocycle **2**.



Scheme 3. Shrinking of macrocycle **2** into macrocycles **8** and **9**.



Scheme 4. Slippage synthesis of the [2]rotaxane [**11**-H][TFPB], followed by photoextrusion to give [2]rotaxanes [**12**-H][TFPB] and [**13**-H][TFPB].

recognize macrocycle **2** in $CDCl_3$. However, the solubility of compound [**10**-H][PF_6] in $CDCl_3$ remained limited, even in the presence of an equimolar amount of compound **2**. The complexation of compound [**10**-H][PF_6] with macrocycle **2** was weak in $CDCl_3$/CD_3CN (8:2), with only negligible changes in the ^{1}H NMR spectrum of their equimolar (10 mM) mixture, even after heating at 318 K for several hours. We replaced the counteranion of the threadlike cation with an even more weakly associated anion, tetrakis(3,5-trifluoromethylphenyl)-borate (TFPB), with the expectation that the salt would be more soluble in $CDCl_3$ or CD_2Cl_2 and, therefore, that there would be stronger binding between the [**10**-H]$^+$ cation and macrocycle **2**.[9] The ^{1}H NMR spectrum of an equimolar (10 mM) mixture of macrocycle **2** and threadlike salt [**10**-H][TFPB] (Scheme 4) in $CDCl_3$ at room temperature showed a migration of the signals of the free salt [**10**-H][TFPB] and the free macrocycle **2** (Figure 2a–c). These shifted signals were presumably the result of face-to-face association between the DBA$^+$ and sulfone units of the threadlike salt and the macrocycle, respectively, rather than from a rapidly exchanging threading/dethreading process, because we observed the latter after heating the solution at 318 K for 12 h (Figure 2e). The intensity of these new signals increased with time, at the expense of those of the free compounds [**10**-H][TFPB] and **2**, becoming predominant after 72 h. The upfield shift of the signal of the methylene protons adjacent to the NH_2^+ center and the signals of the OCH_2CH_2 protons of the macrocycle, relative to the respective signals of their free species, were similar to those observed for the [2]pseudorotaxanes that were prepared from macrocycle **1** and DBA$^+$ ions, thus suggesting that the product was a [2]rotaxane that had formed through slippage (Scheme 4). When we repeated this slippage experiment on a larger scale and allowed the mixture

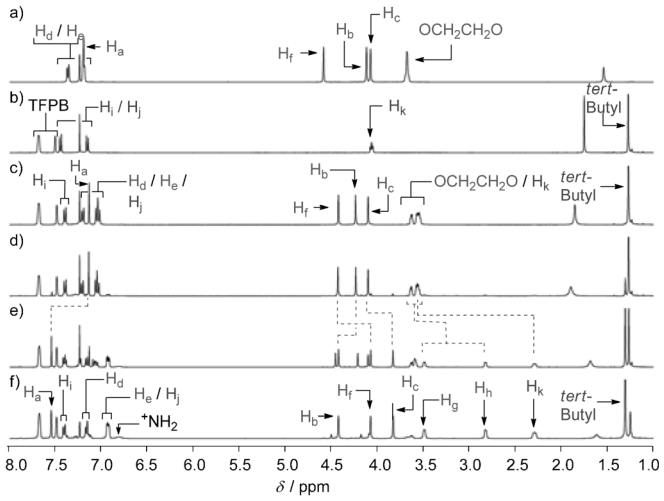


Figure 2. Partial ^{1}H NMR spectra (400 MHz, $CDCl_3$, 298 K) of: a) macrocycle **2**, b) threadlike salt [**10**-H][TFPB]; and their equimolar (10 mM) mixture after treatment at 298 K for: c) 0 h, and d) 6 h; or at 318 K for: e) 12 h, and f) 72 h.

to equilibrate for three days, we obtained the corresponding [2]rotaxane, [**11**-H][TFPB], in 58% yield after column chromatography on silica gel.

We grew single crystals that were suitable for X-ray crystallography through the liquid diffusion of hexanes into a solution of compound [**11**-H][TFPB] in CH_2Cl_2. The solid-state structure in Figure 3[10,11] shows the expected [2]rotaxane geometry, in which the rod-like portion of the dumbbell-shaped component penetrates through the cavity of the macrocyclic component, with the $CH_2NH_2^+$ unit interacting with the oxygen atoms and the aromatic rings of the macrocyclic unit through possible [N^+–H···O] and [N^+C–H···π] hydrogen bonds. Notably, although we only performed the crystallization of the purified slippage [2]rotaxane [**11**-H][TFPB], the crystals featured a 1:1 mixture of [2]rotaxane [**11**-H][TFPB] and free macrocycle **2**. Thus, the slippage

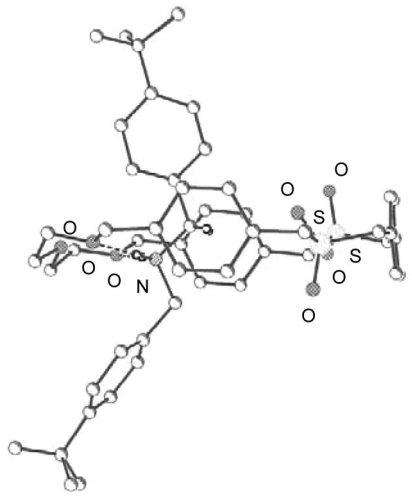


Figure 3. Ball-and-stick representation of the solid-state structure of the slippage [2]rotaxane [**11**-H]$^+$.

[2]rotaxane [**11**-H][TFPB] was not stable under the crystallization conditions, with its dissociation accelerated (in part) by one of its components being needed for crystal packing.

After dissolving the slippage [2]rotaxane [**11**-H][TFPB] in a mixture of C_6H_6 and CH_2Cl_2 (1:1), we irradiated (254 nm) the solution at 273 K. As expected, we obtained [2]rotaxanes [**12**-H][TFPB] and [**13**-H][TFPB], in 15 and 6% yield, respectively, after column chromatography on silica gel; in these interlocked molecules, the macrocyclic component had been "shrunk" to give smaller macrocycles that corresponded to compounds **8** and **9**, after the extrusion of SO_2 from one and two of the sulfone units, respectively (Scheme 4). The downfield and upfield shifts of the signals of the methylene protons adjacent to the NH_2^+ centers in the ^{1}H NMR spectra of [2]rotaxanes [**12**-H][TFPB] and [**13**-H][TFPB], relative to that in the spectrum of [**11**-H][TFPB], respectively (Figure 4), suggested that the [N^+C–H···π] interactions of

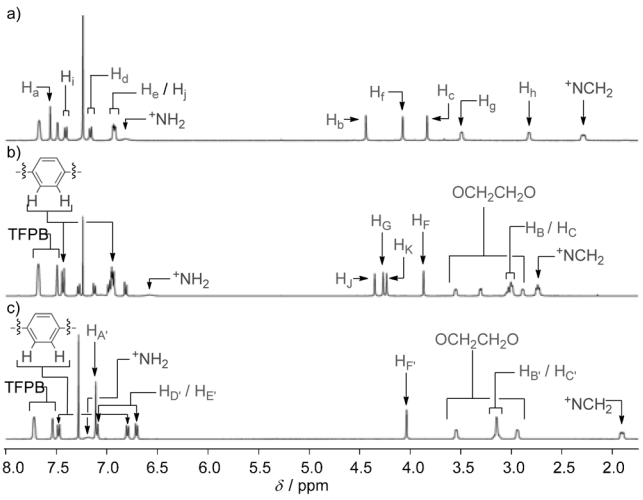


Figure 4. Partial ^{1}H NMR spectra (400 MHz, $CDCl_3$, 298 K) of: a) slippage [2]rotaxane [**11**-H][TFPB], and "shrinking" b) [2]rotaxanes [**12**-H][TFPB], and c) [**13**-H][TFPB].

the methylene protons adjacent to the NH_2^+ ions first weakened and then strengthened with each sequential extrusion of a SO_2 unit. We observed a similar trend in the migration of the signal for the NH_2^+ center, thus implying that the strength of its [N^+–H···O] hydrogen-bonding interactions with the di(ethylene glycol) motif of the macrocyclic component decreased in [2]rotaxane [**12**-H][TFPB] but increased in [**13**-H][TFPB]. Thus, conformational preorganization appears to be as important as the rigidity or ring size of the macrocycles in their binding to the $CH_2{}^+NH_2CH_2$ center. Our observation of reasonable ($K_a = 160\ M^{-1}$) binding affinity of macrocycle **9** to [DBA][PF_6] in $CDCl_3/CD_3CN$ (1:1), but negligible binding affinities for macrocycles **2** and **8** to the same salt, together with association constants of macrocycles **2** and **8** for alkyl-substituted salt [DBA][TFPB] in $CDCl_3$ of 5800 and 220 M^{-1}, respectively, are consistent with the trends in the chemical-shift data for the signals of the main interacting units of the corresponding [2]rotaxanes.[12] Our suc-

cessful syntheses of [2]rotaxanes [**12**-H][TFPB] and [**13**-H][TFPB] were also supported by the electrospray ionization (ESI) mass spectra of these compounds, which revealed intense peaks at *m*/*z* 790.4567 and 726.4926 for ions [**12**-H]$^+$ and [**13**-H]$^+$, respectively. Thus, our spectroscopic data confirmed that it was indeed possible to shrink macrocycle **2** photochemically, whilst it encircled the NH_2^+ center of a DBA^+ ion. Nevertheless, because the precursor that we used to perform the "shrinking" process was slippage [2]rotaxane [**11**-H][TFPB], which was already a stable compound at room temperature, our synthetic process was technically "slippage followed by shrinking," rather than "threading followed by shrinking." To truly realize this latter concept, we required a suitable terminal group for the threadlike cation, that is, one that would allow macrocycle **2** to freely associate and disassociate, but not allow egress of its shrinking products (macrocycles **8** and/or **9**).

After some effort, we found that compound [**14**-H][TFPB],[13] which featured terminal 3,5-dimethylphenyl groups, could not penetrate through the internal cavities of "shrunk" macrocycles **8** and **9**, with no noticeable signals that corresponded to [2]pseudorotaxanes appearing in the ^{1}H NMR spectra of their equimolar mixtures (5 mM). In contrast, an equimolar mixture of macrocycle **2** and threadlike salt [**14**-H][TFPB] (5 mM) in $CDCl_3$ at 298 K displayed three sets of resonances (Figure 5b): One set for the free macrocycle **2** (Figure 5a), one for the free salt [**14**-H][TFPB] (Figure 5c), and one for the 1:1 complex that had formed between compounds **2** and [**14**-H][TFPB]. The similar resolution of the originally overlapping signals for the protons of the two methylene groups on the di(ethylene glycol) unit into two separate multiplets and the significant upfield shifts of the methylene protons adjacent to the NH_2^+ centers of the complex (Figure 5b) and of the slippage [2]rotaxane [**11**-H][TFPB] (Figure 4a) suggested the formation of [2]pseudorotaxane [**2**⊃**14**-H][TFPB] under these conditions. By using a single-point method,[14] we determined the association constant (K_a) for the interaction between macrocycle **2** and threadlike salt [**14**-H][TFPB] in $CDCl_3$ (1:1, 5 mM) to be 5800 M^{-1}.[15] The observation that 3,5-dimethylphenyl units could penetrate through the cavity of the macrocycle **2** at ambient temperature to form [2]pseudorotaxane [**2**⊃**14**-H][TFPB], but not through the smaller macrocyclic units of compounds **8** and **9**, suggested that threadlike salt [**14**-H][TFPB] would be an ideal component for demonstrating the "threading followed by shrinking" concept (Scheme 5).

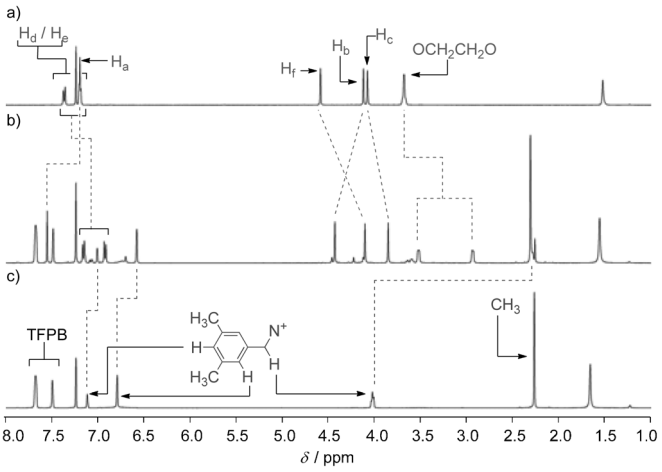
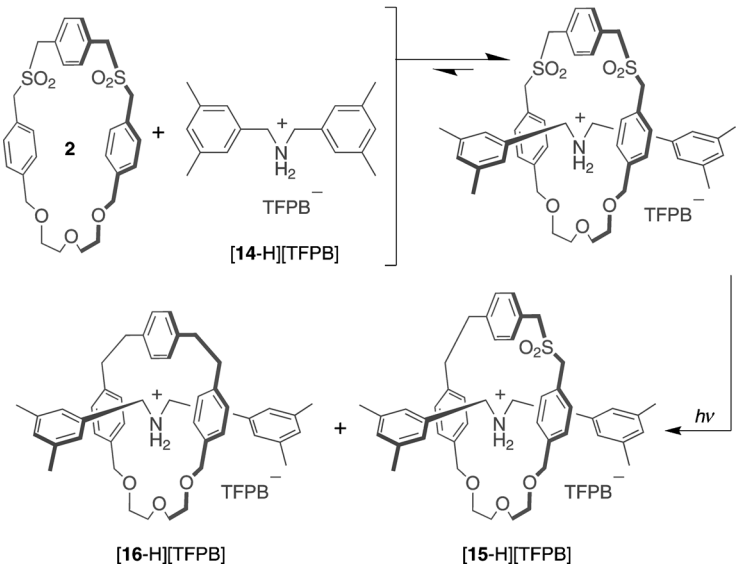


Figure 5. ^{1}H NMR spectra (400 MHz, $CDCl_3$, 298 K) of: a) macrocycle **2**, b) an equimolar mixture of macrocycle **2** and threadlike salt [**14**-H][TFPB] (5 mM), and c) [**14**-H][TFPB] alone.

Notably, the *tert*-butylphenyl and 3,5-dimethylphenyl moieties are "reasonable" and "true" stopper units for DB24C8, respectively, as evidenced from experimental observations that DB24C8 only dissociated from the corresponding "rotaxanes" that featured the former stoppering units after the NH_2^+ center had been acylated.[16] Based on those results, one might suspect that the 3,5-dimethylphenyl group would also be sterically bulkier and/or energetically less favorable than the *tert*-butylphenyl group when passing through the cavities of other macrocycles. However, in our case, we found that the *tert*-butylphenyl group was a slippage stopper for macrocycle **2**, whereas the 3,5-dimethylphenyl group could pass freely through it under similar conditions. We suspect that the different macrocycles that were applied in these two examples and the acylation of the NH_2^+ centers in the cases of [2]rotaxanes that featured DB24C8 components



Scheme 5. Synthesis of [2]rotaxanes [**15**-H][TFPB] and [**16**-H][TFPB] by the macrocycle "shrinking" approach.

resulted in different types and strengths of noncovalent interactions in the transition states for the dissociations of these two systems, thereby resulting in different activation energies for the same terminal functionality. For now, we merely suggest that the potential energy for the threading (or dethreading) of the terminus of a threadlike cation through a macrocycle is related in a complex way to the structures of the host and the guest and to the transition state for the passage event, the noncovalent interactions of which are hard to predict.[17]

To test whether we could perform a true "threading followed by shrinking" process, we prepared an equimolar (32 mM) solution of macrocycle **2** and threadlike salt [**14**-H][TFPB] in CH_2Cl_2/C_6H_6 (1:1) and then irradiated (254 nm) the solution at 273 K for 1 h. To our disappointment, we only isolated trace amounts of [2]rotaxane [**16**-H][TFPB] from the reaction mixture; instead, we isolated macrocycles **8** and **9** in 23 and 29% yield, respectively. We suspected that we were generating an insufficient amount of the [2]pseudorotaxane in solution; therefore, we performed the same reaction under similar conditions, but changed the stoichiometry of threadlike salt [**14**-H][TFPB] to macrocycle **2** to 2:1 (64 mM:32 mM). Gratifyingly, after reapplying the reaction conditions, we isolated the [2]rotaxanes [**15**-H][TFPB] and [**16**-H][TFPB], which resulted from the extrusion of one and two molecules of SO_2, respectively, from the arylmethylsulfone units of the macrocyclic component in 13 and 2% yield, respectively (Table 1).[18] Changing the ratio of the solvents in the "shrinking" reaction did not improve the yields, but increasing the amount of threadlike salt [**14**-H][TFPB] in the photoextrusion reaction mixture to up to four equivalents (128 mM) improved the yield of [2]rotaxane [**15**-H][TFPB] up to 17%. The addition of threadlike salt [**14**-H][TFPB] in several portions after various periods of time or extending the irradiation period did not significantly affect the efficiency of the synthesis of the [2]rotaxane through this "shrinking" process.

We grew single crystals suitable for X-ray crystallography through the liquid diffusion of diisopropyl ether into a $CHCl_3$ solution of compound [**16**-H][PF_6] (see below). The solid-state structure shows[19] the expected geometry of the [2]rotaxane, in which the dumbbell-shaped component is penetrated through the cavity of the macrocyclic component, with the $CH_2NH_2^+$ units hydrogen bonded to the aromatic rings and the oxygen atoms of the macrocyclic unit through possible [N^+–H···O] and [N^+C–H···π] hydrogen bonds (Figure 6).

To test their stability, we dissolved [2]rotaxanes [**15**-H][TFPB] and [**16**-H][TFPB] in CD_3SOCD_3 and then heated

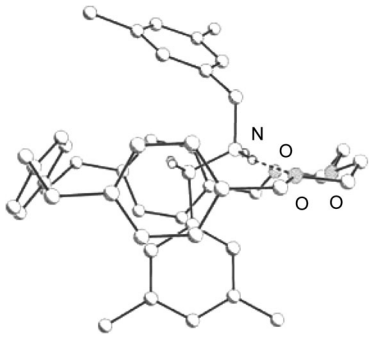


Figure 6. Ball-and-stick representation of the solid-state structure of the [2]rotaxane [**16**-H]$^+$.

the solutions at 343 K for 2 h whilst monitoring their ^{1}H NMR spectra. No signals were observed that corresponded to the free macrocycles or free dumbbell-shaped salt [**14**-H][TFPB], thus suggesting that the 3,5-dimethylphenyl group was a true stopper for both macrocycles **8** and **9** and that the two [2]rotaxanes were reasonably robust under these conditions. In contrast, we observed different behavior when subsequently heating these two solutions at 373 K. [2]Rotaxane [**15**-H][TFPB] quickly dissociated into macrocycle **8** and dumbbell-shaped salt [**14**-H][TFPB], whereas compound [**16**-H][TFPB] remained intact after 5 h (Figure 7c). We observed no dissociation in the ^{1}H NMR spectra of [2]rotaxane [**16**-H][TFPB] when we continued to heat its solution at 393 K for a further 5 h.[20] This result supports our original hypothesis that the shrinking of the ring twice could generate a more stable and robust rotaxane with an even smaller interlocked macrocyclic component (Scheme 6).

We suspect that the low yield of [2]rotaxane [**16**-H][TFPB] from the "shrinking" process was due to the inefficient production of its precursor, [**15**-H][TFPB]. The mechanism of the photoextrusion reaction proceeds through the photochemical cleavage of one of the C–S bonds of the arylmethylsulfone into two radicals, the extrusion of SO_2 by dissociating the other C–S bond in the same manner, and the recombination of the two benzylic radicals to form a new C–C bond.[21] Thus, if the time interval that is required for homolytic dissociation of the second C–S bond and the recombination of the two benzyl radicals after breaking the

Table 1. "Threading followed by shrinking" of macrocycle **2** and threadlike salt [**14**-H][TFPB] under various conditions.[a]

Entry	Thread [equiv]	Solvent system (CH_2Cl_2/C_6H_6)	t [min]	[**15**-H]$^+$ [%]	[**16**-H]$^+$ [%]
1	1	1:1	60	–	<1
2	2	1:1	60	13	2
3	2.2	3:2	60	7	3
4	2.2	2:3	60	3	2
5	3	1:1	60	13	4
6	4	1:1	60	17	4
7	5	1:1	60	14	3
8	4	1:1	120	10	3
9[b]	4 (=2+2)	1:1	60 (=30+30)	20	2
10[b]	4 (=2+1+1)	1:1	60 (=30+15+15)	19	2
11[b]	4 (=2+1+1)	1:1	60 (=20+20+20)	20	2
12[b]	4 (=2+2)	1:1	80 (=40+40)	19	3

[a] The concentration of macrocycle **2** was fixed at 32 mM. [b] The threadlike salt was added in portions; the solution was irradiated for the indicated time intervals.

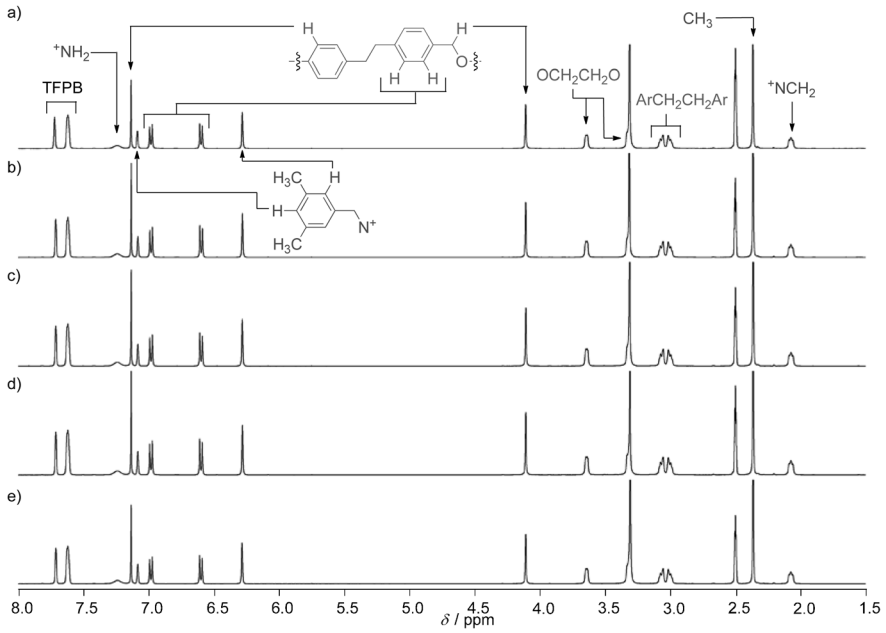
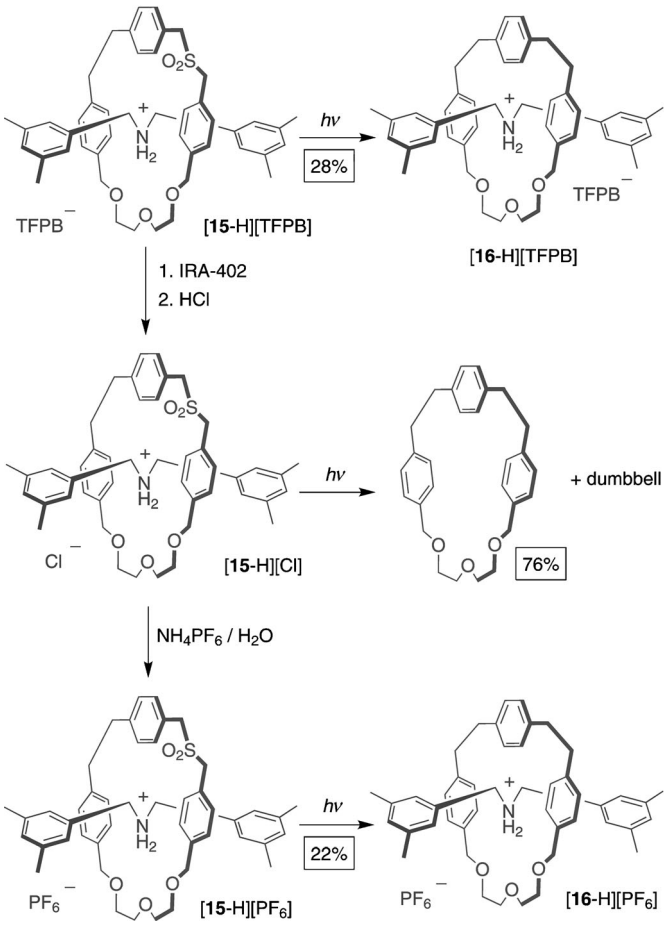


Figure 7. Partial ^{1}H NMR spectra (400 MHz, CD_3SOCD_3, 298 K) of: a) [2]rotaxane [**16**-H][TFPB], and the solution after sequential heating at: b) 343 K for 2 h, c) 373 K for 5 h, d) 383 K for 5 h, and e) 393 K for 5 h.



Scheme 6. Anion effect in transforming [2]rotaxane [**16**-H]$^+$ into [**15**-H]$^+$.

first C–S bond are sufficiently long enough to allow for the dissociation of the originally interlocked dumbbell-shaped ion from the open-chain podand-type host, recombination of the two radicals might result in the formation of the macrocycle in its free state. To verify this hypothesis, we exchanged the counteranion of [2]rotaxane [**15**-H][TFPB] for PF_6^- and Cl^-. We found that [2]rotaxanes [**15**-H][TFPB] and [**15**-H][PF_6] both underwent successful photoextrusions, with shrinkage of their originally interlocked macrocycles, thus giving their corresponding [2]rotaxanes, [**16**-H][TFPB] and [**16**-H][PF_6], in 28 and 22% yield, respectively. In contrast, the ^{1}H NMR spectrum of the irradiated [2]rotaxane [**15**-H][Cl] featured no detectable signals for the corresponding [2]rotaxane, [**16**-H][Cl]; indeed, we isolated its free macrocycle (**9**) in 76% yield after column chromatography on silica gel. This result suggests that strong ion-pairing of the NH_2^+ center with the Cl^- anion—an interaction that has previously been applied to operate a molecular switch that was comprised of a crown ether-like macrocycle and a dialkylammonium ion[22]—significantly decreases the stability of the complex between the dumbbell-shaped ion and the open-chain free radical intermediate that were formed from the macrocyclic component, thereby resulting in the dissociation of the complex, even though such ion-pairing would not dissociate the components of the interlocked [2]rotaxane [**15**-H][Cl] because of its bulky 3,5-dimethylphenyl stoppers. Although recombination of the two benzylic radicals that are generated from the extrusion of SO_2 from a diarylmethyl sulfone may be sufficiently rapid to retain a certain degree of chirality at the benzylic carbon atom,[21] we conclude that, when the counteranion is Cl^-, the total time interval between the cleavage of the first C–S bond and the formation of the C–C bond from the two benzylic radicals must be longer than the time that is required for the dissociation of the thread-like salt from the podand-like open-chain host, otherwise the reaction yield would not differ from those with TFPB and PF_6^- as the counteranions. In other words, this experiment supports an open-chain mechanism for the extrusion of SO_2 from diarylmethyl sulfones. Thus, the relatively low yields when synthesizing [2]rotaxane [**16**-H]$^+$ by using this approach presumably result from the difficulty of performing two successful extrusion and interlocking processes from the starting [2]pseudorotaxane. To enhance the efficiency of future rotaxane syntheses through such a "shrinking" ap-

proach (i.e., one in which cleavage of the macrocyclic structure of the complexed ring is unavoidable), it might be necessary to enhance the binding affinity of the corresponding open-chain podand to the guest unit or to decrease the lifetimes of the open-chain intermediates.

Conclusion

We have demonstrated that a "threading followed by shrinking" strategy can be applied to the synthesis of stable molecular rotaxanes from derivatives of macrocycle **1**. We obtained a relatively low yield of the [2]rotaxane [**16**-H][TFPB] as a result of the need to perform two open-chain SO_2-extrusion reactions with sufficiently long-living free-radical intermediates, thereby providing the weakly associated dumbbell-shaped cation and the open-chain podand-type host with sufficient time to dissociate. Nevertheless, by twice shrinking the size of the macrocyclic component, the resulting [2]rotaxane, [**16**-H][TFPB], incorporated the much smaller (25 atom) macrocycle **9** as one of its interlocked components, thereby providing a system that maintained its molecular integrity in CD_3SOCD_3 at 393 K for at least 5 h. We hope that this method will be added to the repertoire of reactions that are available to the synthetic chemist for the construction of complicated and robust interlocking structures.

Experimental Section

General: All glassware, stirrer bars, syringes, and needles were either oven- or flame-dried prior to use. All reagents were obtained from commercial sources, unless otherwise indicated. Anhydrous CH_2Cl_2 and MeCN were obtained by distillation from CaH_2 under N_2. The reactions were conducted under N_2 or Ar atmospheres. Thin layer chromatography (TLC) was performed on Merck 0.25 mm silica gel (Merck Art. 5715). Column chromatography was performed on Kieselgel 60 (Merck, 70–230 mesh). Melting points were determined on a Fargo MP-2D melting-point apparatus. For NMR spectroscopy, the deuterated solvent was used as the lock, whilst either the residual protons in the solvent or TMS were employed as an internal standard. Chemical shifts are reported in parts per million (ppm). Multiplicities are given as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or br (broad).

Diester 4: NaH (60%, 1.09 g, 27.3 mmol) was added to a solution of di(ethylene glycol) (1.11 g, 10.0 mmol) in THF (105 mL) and then the mixture was heated at reflux for 30 min before the addition of methyl 4-(bromomethyl)benzoate (5.27 g, 23.0 mmol). After heating at reflux for 16 h, the mixture was concentrated under reduced pressure and the yellow residue was partitioned between CH_2Cl_2 (50 mL) and water (30 mL). The organic layer was dried ($MgSO_4$), concentrated under reduced pressure, and purified by column chromatography on silica gel (EtOAc/hexanes, 3:7) to afford a colorless oil (2.09 g, 52% yield). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.60$–3.69 (m, 8H), 3.86 (s, 6H), 4.58 (s, 4H), 7.36 (d, $J = 8$ Hz, 4H), 7.95 ppm (d, $J = 8$ Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 51.9$, 69.8, 70.6, 72.5, 127.0, 129.2, 129.5, 143.5, 166.7 ppm; HRMS (ESI): m/z calcd for $C_{22}H_{26}NaO_7$: 425.1577 $[M+Na]^+$; found: 425.1533.

Diol 5: A solution of diester **4** (1.00 g, 2.48 mmol) in THF (10 mL) was slowly added to a suspension of LAH (0.24 g, 6.32 mmol) in THF (30 mL) at 0 °C and then the mixture was heated at reflux for 3 h. After cooling to RT, water (5 mL) and $MgSO_4$ (1 g) were added to the mixture, which was then filtered. The filtrate was concentrated under reduced pressure and purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 95:5) to afford a colorless oil (0.70 g, 81% yield). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.57$–3.71 (m, 8H), 4.55 (s, 4H), 4.65 (s, 4H), 7.28 (d, $J = 8$ Hz, 4H), 7.32 ppm (d, $J = 8$ Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 64.2$, 69.1, 70.3, 72.7, 126.7, 127.6, 137.0, 140.3 ppm; HRMS (ESI): m/z calcd for $C_{20}H_{26}NaO_5$: 369.1678 $[M+Na]^+$; found: 369.1675.

Dichloride 6: Diol **5** (0.7 g, 2.02 mmol), $NaHCO_3$ (1.71 g, 20.35 mmol), PPh_3 (1.6 g, 6.10 mmol), and NCS (0.81 g, 6.06 mmol) were mixed in CH_2Cl_2 (31 mL) at 0 °C and the mixture was stirred for 40 min before being quenched through the addition of a saturated aqueous solution of $NaHCO_3$ (10 mL). The organic layer was separated and the aqueous layer was extracted again with CH_2Cl_2 (30 mL). The organic layers were combined, dried ($MgSO_4$), concentrated under reduced pressure, and purified by column chromatography on silica gel (EtOAc/hexanes, 4:6) to afford a colorless oil (0.47 g, 61% yield). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.60$–3.69 (m, 8H), 4.55 (s, 4H), 4.56 (s, 4H), 7.31 (d, $J = 8.8$ Hz, 4H), 7.34 ppm (d, $J = 8.8$ Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 45.9$, 69.5, 70.6, 72.6, 127.8, 128.5, 136.6, 138.6 ppm; HRMS (ESI): m/z calcd for $C_{20}H_{25}Cl_2O_3$: 383.1181 $[M+H]^+$; found: 383.1144.

Macrocycle 7: A solution of KOH (0.24 g, 4.28 mmol) in EtOH (95%, 725 mL) was added to a solution of dichloride **6** (0.47 g, 1.20 mmol) and 1,4-benzenedimethanethiol (0.20 g, 1.20 mmol) in toluene (241 mL) over a period of 8 h. Then, the mixture was stirred at RT for 16 h. After concentrating under reduced pressure, the residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 98:2) to afford a white solid (0.50 g, 87% yield). M.p. 77–79 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.52$ (s, 4H), 3.58 (s, 4H), 3.60–3.68 (m, 8H), 4.54 (s, 4H), 7.06 (s, 4H), 7.06 (d, $J = 8$ Hz, 4H), 7.24 ppm (d, $J = 8$ Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 34.6$, 35.1, 69.4, 70.7, 72.5, 127.3, 129.0, 129.1, 136.6, 136.9, 137.2 ppm; HRMS (ESI): m/z calcd for $C_{28}H_{32}NaO_3S_2$: 503.1691 $[M+Na]^+$; found: 503.1638.

Macrocycle 2: MCPBA (1.05 g, 4.20 mmol) was added to solution of macrocycle **7** (0.50 g, 1.04 mmol) in CH_2Cl_2 (10 mL) at 0 °C and the mixture was stirred for 30 min. After partitioning between CH_2Cl_2 (40 mL) and a saturated aqueous solution of $NaHCO_3$ (2×20 mL), the organic phase was dried ($MgSO_4$) and concentrated under reduced pressure; the residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 98:2) to afford a white solid (0.45 g, 79% yield). M.p. 241–243 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 3.64$–3.72 (m, 8H), 4.08 (s, 4H), 4.12 (s, 4H), 4.59 (s, 4H), 7.16–7.22 (m, 8H), 7.37 ppm (d, $J = 8$ Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 58.0$, 58.2, 69.9, 70.7, 72.2, 126.4, 127.5, 129.0, 130.6, 131.2, 139.8 ppm; HRMS (ESI): m/z calcd for $C_{28}H_{32}NaO_7S_2$: 567.1487 $[M+Na]^+$; found: 567.1455.

General method for the photoextrusion process: The photoextrusion reaction was performed on a Rayonet RPR-200 photoreactor that contained 16 35 W, 254 nm lamps; the reaction mixture was placed in a quartz apparatus that was equipped with an internal cold finger.

Macrocycles 8 and 9: Macrocycle **2** (54 mg, 0.1 mmol) was dissolved in a degassed mixture of CH_2Cl_2 and benzene (1:1, 10 mL) and then irradiated (254 nm) for 1.5 h. The organic solvents were evaporated under reduced pressure and the residue was purified by column chromatography on silica gel (EtOAc/hexanes, 1:9 to 3:7) to afford macrocycle **8** as a white solid (15.8 mg, 33% yield) and macrocycle **9** as a white solid (14.2 mg, 34% yield).

Macrocycle ***8***: M.p. 131–133 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.87$–2.98 (m, 4H), 3.60–3.73 (m, 8H), 3.90 (s, 2H), 4.00 (s, 2H), 4.53 (s, 2H), 4.59 (s, 2H), 6.84–6.88 (m, 4H), 7.05–7.11 (m, 4H), 7.16 (d, $J = 8$ Hz, 2H), 7.33 ppm (d, $J = 8$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 37.1$, 56.4, 57.8, 69.2, 69.7, 70.4, 70.9, 71.8, 73.1, 125.4, 126.3, 127.2, 127.5, 128.9, 129.7, 129.9, 130.6, 136.0, 139.4, 139.6, 141.7 ppm (one signal is missing, possibly because of signal overlap); HRMS (ESI): m/z calcd for $C_{28}H_{32}NaO_5S$: 503.1868 $[M+Na]^+$; found: 503.1853.

Macrocycle ***9***: M.p. 110–112 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.79$–2.93 (m, 8H), 3.65–3.73 (m, 8H), 4.56 (s, 4H), 6.74 (d, $J = 8$ Hz, 4H), 6.75 (s, 4H), 7.13 ppm (d, $J = 8$ Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta =$ 37.0, 37.1, 69.5, 71.0, 72.9, 126.8, 128.8, 129.0, 135.7, 138.1, 140.0 ppm;

HRMS (ESI): *m/z* calcd for $C_{28}H_{32}NaO_3$: 439.2249 $[M+Na]^+$; found: 439.2175.

Dumbbell-shaped salt [10-H][TFPB]: Sodium tetrakis[3,5-bis(trifluoromethyl)phenyl] borate (NaTFPB, 444 mg, 0.501 mmol) was added to a solution of compound [**10**-H][PF_6] (228 mg, 0.501 mmol) in MeOH. The mixture was concentrated under reduced pressure and the residue was partitioned between CH_2Cl_2 (20 mL) and deionized water (10 mL). The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure to afford a yellow oil (563 mg, 96% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 (s, 18H), 4.07 (t, J = 6 Hz, 4H), 7.16 (d, J = 8.4 Hz, 4H), 7.45 (d, J = 8.4 Hz, 4H), 7.51 (s, 4H), 7.67 ppm (s, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.8, 34.9, 52.7, 117.6, 124.6, 124.6 (q, ^1J(C,F) = 271 Hz), 127.4, 128.9, 128.9 (q, ^2J(C,F) = 31 Hz), 134.8, 155.6, 161.7 ppm (q, ^1J(C,B) = 50 Hz); HRMS (ESI): *m/z* calcd for $C_{22}H_{32}N$: 310.2535 $[M]^+$; found: 310.2510.

[2]Rotaxane [11-H][TFPB]: A solution of macrocycle **2** (574 mg, 1.05 mmol) and dumbbell-shaped salt [**10**-H][TFPB] (585 mg, 0.498 mmol) in $CHCl_3$ (16 mL) was stirred at 45 °C for 3 days and then the organic solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2/hexanes, 9:1) to afford a white solid (499 mg, 58% yield). M.p. 97–99 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (s, 18H), 2.25–2.33 (m, 4H), 2.79–2.86 (m, 4H), 3.46–3.53 (m, 4H), 3.84 (s, 4H), 4.08 (s, 4H), 4.44 (s, 4H), 6.75–6.89 (br, 2H), 6.93 (d, J = 8 Hz, 4H), 6.93 (d, J = 8.4 Hz, 4H), 7.16 (d, J = 8 Hz, 4H), 7.41 (d, J = 8.4 Hz, 4H), 7.49 (s, 4H), 7.56 (s, 4H), 7.67 ppm (s, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.0, 34.7, 51.4, 56.9, 61.1, 69.0, 70.7, 74.1, 117.4, 124.5 (q, ^1J(C,F) = 271 Hz), 125.7, 127.0, 127.2, 127.9, 128.9 (q, ^2J(C,F) = 31 Hz), 128.8, 129.7, 131.8, 132.0, 134.8, 136.6, 153.2, 161.7 ppm (q, ^1J(C,B) = 50 Hz); HRMS (ESI): *m/z* calcd for $C_{50}H_{64}NO_7S_2$: 854.4124 $[M]^+$; found: 854.4101.

[2]Rotaxanes [12-H][TFPB] and [13-H][TFPB]: [2]Rotaxane [**11**-H][TFPB] (119 mg, 0.069 mmol) was dissolved in a degassed mixture of CH_2Cl_2 and benzene (1:1, 2 mL) and then irradiated (254 nm) at 273 K for 20 min. The organic solvents were evaporated under reduced pressure and the residue was purified by column chromatography on silica gel (CH_2Cl_2/hexanes, 1:4 to 1:1) to afford compound [**13**-H][TFPB] as a yellow oil (7.01 mg, 6% yield) and compound [**12**-H][TFPB] as a yellow oil (16.9 mg, 15% yield).

*Compound [**12**-H][TFPB]*: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (s, 18H), 2.74 (t, J = 6.6 Hz, 4H), 2.85–2.93 (m, 2H), 2.96–3.08 (m, 6H), 3.27–3.34 (m, 2H), 3.52–3.59 (m, 2H), 3.87 (s, 2H), 4.24 (s, 2H), 4.27 (s, 2H), 4.35 (s, 2H), 6.48–6.68 (br, 2H), 6.82 (d, J = 8 Hz, 2H), 6.91–7.01 (m, 10H), 7.13 (d, J = 8 Hz, 2H), 7.28 (d, J = 8 Hz, 2H), 7.44 (d, J = 8.4 Hz, 4H), 7.49 (s, 4H), 7.68 ppm (s, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.1, 34.8, 35.0, 35.8, 51.9, 58.3, 60.9, 69.2, 69.8, 70.6, 70.8, 74.1, 74.2, 117.4, 123.5, 124.5 (q, ^1J(C,F) = 271 Hz), 125.9, 126.9, 128.4, 128.9, 128.9 (q, ^2J(C,F) = 31 Hz), 129.2, 129.4, 129.7, 130.3, 130.3, 131.4, 133.1, 134.8, 137.1, 141.5, 141.8, 153.7, 161.7 ppm (q, ^1J(C,B) = 50 Hz); HRMS (ESI): *m/z* calcd for $C_{50}H_{64}NO_5S$: 790.4504 $[M]^+$; found: 790.4567.

*Compound [**13**-H][TFPB]*: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.34 (s, 18H), 1.83–1.91 (m, 4H), 2.87–2.94 (m, 4H), 3.04–3.16 (m, 8H), 3.47–3.54 (m, 4H), 4.00 (s, 4H), 6.67 (d, J = 8 Hz, 4H), 6.76 (d, J = 8 Hz, 4H), 7.06 (d, J = 8 Hz, 4H), 7.07 (s, 4H), 7.09–7.22 (br, 2H), 7.44 (d, J = 8 Hz, 4H), 7.50 (s, 4H), 7.68 ppm (s, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.2, 32.9, 33.3, 34.8, 50.9, 68.7, 70.6, 74.3, 117.4, 124.5 (q, ^1J(C,F) = 271 Hz), 125.7, 127.0, 127.5, 128.2, 128.9, 128.9 (q, ^2J(C,F) = 31 Hz), 129.2, 132.9, 134.8, 137.8, 142.3, 153.3, 161.7 ppm (q, ^1J(C,B) = 50 Hz); HRMS (ESI): *m/z* calcd for $C_{50}H_{64}NO_3$: 726.4886 $[M]^+$; found: 726.4926.

Dumbbell-shaped salt [14-H][TFPB]: NaTFPB (895 mg, 1.01 mmol) was added to a solution of compound [**14**-H][PF_6] (403 mg, 1.01 mmol) in MeOH, which was then concentrated under reduced pressure. The residue was partitioned between CH_2Cl_2 (20 mL) and deionized water (10 mL). The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure to afford a yellow solid (1.06 g, 94% yield). M.p. 134–135 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.27 (s, 12H), 4.01 (t, J = 6 Hz, 4H), 6.80 (s, 4H), 7.11 (s, 2H), 7.50 (s, 4H), 7.68 ppm (s, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.9, 52.9, 117.5, 124.6 (q, ^1J(C,F) = 271 Hz), 126.6, 127.7, 128.9 (q, ^2J(C,F) = 32 Hz), 133.1 (d, $^5J_{CF}$ = 1 Hz), 134.8, 140.6, 161.7 ppm (q, ^1J(C,B) = 50 Hz); HRMS (ESI): *m/z* calcd for $C_{18}H_{24}N$: 254.1909 $[M]^+$; found: 254.1879.

[2]Rotaxanes [15-H][TFPB] and [16-H][TFPB]: Macrocycle **2** (106 mg, 0.194 mmol) and dumbbell-shaped salt [**14**-H][TFPB] (432 mg, 0.387 mmol) were dissolved in a degassed mixture of CH_2Cl_2 and benzene (1:1, 6 mL) and then irradiated (254 nm) at 273 K for 40 min. After the addition of another portion of compound [**14**-H][TFPB] (432 mg, 0.387 mmol), the mixture was irradiated at 273 K for a further 40 min. The organic solvents were evaporated under reduced pressure and the residue was purified by column chromatography on silica gel (CH_2Cl_2/hexanes, 6:4 to 8:2) to afford [2]rotaxane [**15**-H][TFPB] as a yellow solid (58.4 mg, 19% yield). [2]Rotaxane [**16**-H][TFPB] was also obtained, after further purification by column chromatography on silica gel (CH_2Cl_2/hexanes, 2:8), as a white solid (8.5 mg, 3% yield).

*Compound [**15**-H][TFPB]*: M.p. 152–154 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.33 (s, 12H), 2.61–2.77 (m, 4H), 2.93–3.07 (m, 8H), 3.28–3.33 (m, 2H), 3.58–3.63 (m, 2H), 3.88 (s, 2H), 4.22 (s, 2H), 4.33 (s, 2H), 4.37 (s, 2H), 6.54–6.70 (br, 2H), 6.60 (s, 4H), 6.82 (d, J = 7.6 Hz, 2H), 6.91 (d, J = 7.6 Hz, 2H), 6.96 (d, J = 7.6 Hz, 2H), 6.98 (d, J = 7.6 Hz, 2H), 7.06 (s, 2H), 7.19 (d, J = 8 Hz, 2H), 7.32 (d, J = 7.6 Hz, 2H), 7.49 (s, 4H), 7.68 ppm (s, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.1, 35.2, 36.0, 52.2, 58.0, 61.0, 69.2, 69.9, 70.8, 70.9, 74.1, 74.4, 117.4, 123.6, 124.6 (q, ^1J(C,F) = 271 Hz), 126.7, 128.4, 128.9 (q, ^2J(C,F) = 31 Hz), 129.2, 129.4, 129.7, 130.0, 130.3, 130.3, 131.3, 131.4, 133.1, 134.8, 137.0, 138.8, 141.7, 141.7, 161.7 ppm (q, ^1J(C,B) = 50 Hz); HRMS (ESI): *m/z* calcd for $C_{46}H_{56}NO_5S$: 734.3874 $[M]^+$; found: 734.3854.

*Compound [**16**-H][TFPB]*: M.p. 170–172 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.86 (t, J = 6.4 Hz, 4H), 2.34 (s, 12H), 3.00–3.04 (m, 4H), 3.05–3.16 (m, 8H), 3.51–3.57 (m, 4H), 4.04 (s, 4H), 6.37 (s, 4H), 6.66 (d, J = 7.6 Hz, 4H), 6.99–7.19 (m, 12H), 7.50 (s, 4H), 7.69 ppm (s, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 32.9, 33.3, 51.2, 68.9, 70.7, 74.3, 117.4, 124.6 (q, ^1J(C,F) = 271 Hz), 125.5, 128.3, 128.8, 128.9 (q, ^2J(C,F) = 31 Hz), 129.2, 129.9, 130.9, 132.9, 134.8, 137.9, 138.6, 142.2, 161.7 ppm (q, ^1J(C,B) = 50 Hz); HRMS (ESI): *m/z* calcd for $C_{46}H_{56}NO_3$: 670.4260 $[M]^+$; found: 670.4203.

[15-H][Cl]: Amberlite@IR402 (Cl) resin was added to a solution of compound [**15**-H][TFPB] (48.2 mg, 0.030 mmol) in MeOH (5 mL) and the mixture was stirred at RT for 15 min before being filtered. This process was repeated a further nine times with each successive filtrate. An aqueous solution of HCl (1 M, 0.03 mL) was added to the final filtrate and the organic phase was separated and concentrated under reduced pressure. The residue was partitioned between CH_2Cl_2 (20 mL) and water (10 mL) and then the organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 92:8) to afford a colorless oil (22.9 mg, 98% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.37 (s, 12H), 2.66–2.86 (m, 4H), 2.93–3.03 (m, 4H), 3.06–3.13 (m, 2H), 3.13–3.20 (m, 2H), 3.38–3.47 (m, 2H), 3.67–3.74 (m, 2H), 3.92 (s, 2H), 4.37 (s, 2H), 4.63 (s, 2H), 4.82 (s, 2H), 6.66 (s, 4H), 6.79–6.86 (m, 4H), 6.95 (d, J = 8 Hz, 2H), 7.01–7.07 (m, 4H), 7.14 (d, J = 8 Hz, 2H), 7.59 ppm (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4, 35.4, 36.0, 52.1, 58.6, 61.0, 69.5, 70.0, 70.8, 71.2, 74.0, 74.6, 125.0, 127.0, 128.4, 128.8, 129.3, 130.0, 130.1, 130.5, 131.1, 131.9, 133.2, 136.2, 138.4, 140.6, 141.5 ppm (one signal was missing, possibly because of signal overlap); HRMS (ESI): *m/z* calcd for $C_{46}H_{56}NO_5S$: 734.3878 $[M]^+$; found: 734.3897.

[15-H][PF_6]: Amberlite@IR402 (Cl) resin was added to a solution of compound [**15**-H][TFPB] (46.6 mg, 0.029 mmol) in MeOH (5 mL) and the mixture was stirred at RT for 15 min before being filtered. This process was repeated a further nine times with each successive filtrate. An aqueous solution of HCl (1 M, 0.03 mL) and a saturated aqueous solution of NH_4PF_6 (5 mL) were added to the final filtrate and the organic phase was separated and concentrated under reduced pressure. The residue was partitioned between CH_2Cl_2 (20 mL) and water (10 mL) and then the organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 95:5) to afford a yellow solid (20.4 mg, 80% yield). M.p. 100–102 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.37 (s, 12H), 2.62–2.80 (m, 4H), 2.93–3.03 (m, 4H), 3.03–3.10 (m, 2H), 3.10–3.16 (m, 2H), 3.39–3.46

(m, 2H), 3.65–3.73 (m, 2H), 3.92 (s, 2H), 4.34 (s, 2H), 4.36 (s, 2H), 4.42 (s, 2H), 6.66 (s, 4H), 6.82 (d, $J=8$ Hz, 2H), 6.86 (d, $J=7.6$ Hz, 2H), 6.96 (d, $J=7.6$ Hz, 2H), 7.01 (d, $J=8$ Hz, 2H), 7.04 (s, 2H), 7.18 (d, $J=7.6$ Hz, 2H), 7.43 ppm (d, $J=7.6$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=21.2$, 35.4, 36.1, 52.1, 57.5, 60.9, 69.3, 69.8, 70.9, 71.2, 74.0, 74.4, 124.6, 126.8, 128.5, 129.0, 129.3, 129.9, 130.3, 130.3, 130.5, 131.1, 131.5, 133.3, 136.7, 138.6, 140.9, 141.5 ppm; HRMS (ESI): m/z calcd for $C_{46}H_{56}NO_5S$: 734.3878 $[M]^+$; found: 734.3896.

[16-H][PF$_6$]: Amberlite@IR402 (Cl) resin was added to a solution of compound [**16**-H][TFPB] (16.8 mg, 0.011 mmol) in MeOH (5 mL) and the mixture was stirred at RT for 15 min before being filtered. This process was repeated a further nine times with each successive filtrate. An aqueous solution of HCl (1 M, 0.01 mL) and a saturated aqueous solution of NH_4PF_6 (2 mL) were added to the final filtrate and the organic phase was separated and concentrated under reduced pressure. The residue was partitioned between CH_2Cl_2 (20 mL) and water (10 mL) and then the organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 95:5) to afford a white solid (4.59 mg, 51 % yield). M.p. 232–233 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=1.99$ (t, $J=6$ Hz, 4H), 2.38 (s, 12H), 3.01–3.15 (m, 8H), 3.25–3.35 (m, 4H), 3.64–3.74 (m, 4H), 4.09 (s, 4H), 6.31 (s, 4H), 6.61 (d, $J=7.6$ Hz, 4H), 6.95 (d, $J=7.6$ Hz, 4H), 7.03 (s, 2H), 7.08 (s, 4H), 7.20–7.30 ppm (br, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=21.4$, 33.2, 33.2, 50.9, 69.2, 71.0, 74.2, 125.7, 128.4, 128.6, 129.2, 130.2, 130.6, 133.2, 138.0, 138.3, 141.5 ppm; HRMS (ESI): m/z calcd for $C_{46}H_{56}NO_3$: 670.4260 $[M]^+$; found: 670.4283.

[16-H][TFPB] (through shrinking of the macrocyclic component of [15-H][TFPB]): [2]Rotaxane [**15**-H][TFPB] (28.6 mg, 0.018 mmol) was dissolved in a degassed mixture of CH_2Cl_2 and benzene (1:1, 1.8 mL) and then irradiated (254 nm) at 273 K for 30 min. The organic solvents were evaporated under reduced pressure and the residue was purified by column chromatography on silica gel (CH_2Cl_2/hexanes, 4:6) to afford compound [**16**-H][TFPB] (7.7 mg, 28 % yield).

[16-H][PF$_6$] (through shrinking of the macrocyclic component of [15-H][PF$_6$]): [2]Rotaxane [**15**-H][PF_6] (10 mg, 0.01 mmol) was dissolved in a degassed mixture of CH_2Cl_2 and benzene (1:1, 1 mL) and then irradiated (254 nm) at 273 K for 30 min. The organic solvents were evaporated under reduced pressure and the residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH, 95:5) to afford compound [**16**-H][PF_6] (2 mg, 22 % yield).

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[10] CCDC-917835 ([**11**-H][TFPB]) and CCDC-917836 ([**16**-H][PF_6]) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[11] Crystal data for [**11**-H][TFPB]: $[C_{50}H_{64}O_7NS_2][C_{28}H_{32}O_7S_2][C_{32}H_{12}BF_{24}][CH_2Cl_2]$; $M_r = 2347.95$; colorless columnar crystals; triclinic; space group $P\bar{1}$; $a = 14.4985(3)$, $b = 17.7566(3)$, $c = 24.1925(5)$ Å; $V = 5966.4(2)$ Å^3; $\rho_{calcd} = 1.307\ g\,cm^{-3}$; $\mu(Cu_{K\alpha}) = 1.134\ mm^{-1}$; $T = 200(2)$ K; 21747 independent reflections; F^2 refinement; $R_1 = 0.0906$ and $wR_2 = 0.2558$.

[12] The binding constants were determined based on an integration of the slowly exchanging signals in the ^{1}H NMR spectra of equimolar mixtures (5 mM) of macrocycle **2**/[bis(3,5-dimethylbenzylammonium)][TFPB] and macrocycle **8**/[bis(4-isopropylbenzylammonium)][TFPB].

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[18] From most of these reactions, we isolated macrocycles **8** and **9** as the major byproducts; the starting free macrocycle (**2**) was not completely consumed and we could recycle the dumbbell-shaped salt [**14**-H][TFPB] after ion-exchange and chromatography processes. However, increasing the irradiation time not only resulted in the recycling of much less of the free macrocycle (**2**) but also lower yields of the desired [2]rotaxanes; see Table 1, entries 7 and 8.

[19] Crystal data for [**16**-H][PF_6]: $[C_{46}H_{56}O_3N][PF_6][CHCl_3]$; $M_r = 935.26$; colorless columnar crystals; triclinic; space group $P\bar{1}$; $a = 11.5164(7)$, $b = 12.4216(6)$, $c = 17.7638(8)$ Å; $V = 2374.9(2)$ Å^3; $\rho_{calcd} = 1.308\ g\,cm^{-3}$; $\mu(Cu_{K\alpha}) = 1.134\ mm^{-1}$; $T = 200(2)$ K; 8625 independent reflections; F^2 refinement; $R_1 = 0.0851$ and $wR_2 = 0.2652$.

[20] We observed small and complicated signals when we heated the solution at 403 K for 5 h (see the Supporting Information), presumably because of decomposition of the [2]rotaxane, rather than its dissociation.

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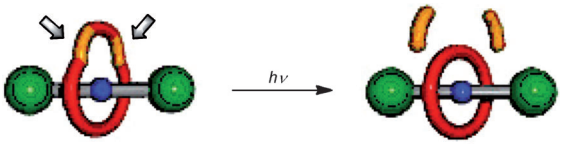
Rotaxanes

*L.-Y. Wang, J.-L. Ko, C.-C. Lai, Y.-H. Liu, S.-M. Peng, S.-H. Chiu** ..... ■■■■–■■■■

Using "Threading Followed by Shrinking" to Synthesize Highly Stable Dialkylammonium-Ion-Based Rotaxanes



Shrink wrap: A "threading followed by shrinking" method, which was used to extrude both arylmethyl sulfone motifs from the macrocyclic components of dialkylammonium-ion-based [2]pseudorotaxanes, afforded robust [2]rotaxanes that were sufficiently stable to maintain their molecular integrity in CD_3SOCD_3 at 393 K for at least 5 h (see figure).