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"Threading-Followed-by-Swelling": A New Protocol for Rotaxane Synthesis

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Rotaxanes have potential applicability as molecular actuators and switches within mesoscale molecular electronics devices.[1] Although many molecular rotaxanes have been synthesized using a range of recognition systems,[2] the protocols that are applied to the synthesis of these interlocked molecules remain limited in general to threading-followed-by-stoppering, slippage, and clipping approaches.[3] Although, in theory, rotaxanes could also be prepared through swelling of the terminal groups of the rod-like components of pseudorotaxane-like complexes (Figure 1), no "threading-followed-by-swelling" approaches have been demonstrated previously, most likely because of the difficulties in designing such systems, which would require the following features: (1) The "swelling" process should be conceptually unrelated to a "stoppering" process; ideally, the enlargement of the terminal group should be achieved without attaching any additional atoms or molecular motifs. (2) The macrocyclic unit must recognize the thread component with sufficient binding affinity while maintaining a delicate size balance with the terminal groups to ensure that it can pass over the terminal group prior to swelling, but not after. (3) The swelling of the terminal group must be initiated under controllable conditions. Herein, we describe the use of a threading-followed-by-swelling protocol to synthesize molecular rotaxanes by modifying our previously reported "oxygen-deficient" macrocycle **1**/dibenzylammonium ion (**1**/DBA^+) molecular recognition system[4] and using a *cis*-1-[(*Z*)-alk-1′-enyl]-2-vinylcyclopropane motif as the swellable terminal group.

Even when pseudorotaxanes are predominant species in solution, the chemical reactions that interlock their components to form rotaxanes often release undesired anions or other side products that may destabilize the pseudorotaxane and, thus, decrease the efficiency of the rotaxane synthesis.[5] We believed that pericyclic rearrangement of the carbon atom skeleton of a terminal group of a pseudorotaxane would be a clean and efficient means of interlocking the components because the size of the terminal group can be enlarged without the assistance of any other chemical reagents; that is, it is atom economical.[6] We chose the *cis*-1-[(*Z*)-alk-1′-enyl]-2-vinylcyclopropane group (Scheme 1) as the terminal group for the swelling process because it can be converted into a bulkier cycloheptadiene motif through a relatively slow Cope rearrangement under ambient conditions;[7] thus, we should be able to isolate the *cis*-1-[(*Z*)-alk-1′-enyl]-2-vinylcyclopropane-terminated thread-like ion at room temperature and then initiate the swelling process by elevating the temperature.

We reported previously that macrocycle **1** encircles dialkylammonium ions with high binding affinity in low-polarity solvents.[4] Thus, we prepared the racemic thread-like salt **3**-H·PF_6—featuring *p*-*tert*-butylphenyl and *cis*-1-[(*Z*)-alk-1′-enyl]-2-vinylcyclopropane units as its terminal groups—from *cis*-1,2-cyclopropanedimethanol **2** (see the Supporting Information) to pursue the threading-followed-by-swelling approach with macrocycle **1**.

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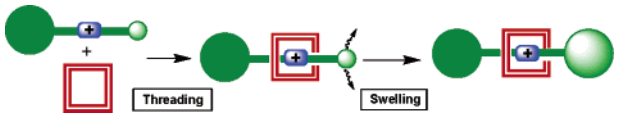
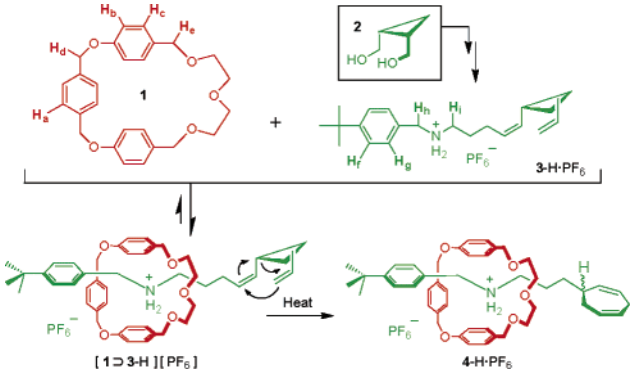


Figure 1. Cartoon representation of the threading-followed-by-swelling concept.

Scheme 1



An equimolar mixture of macrocycle **1** and thread **3**-H·PF_6 (8 mM) in CD_3CN displayed three sets of resonances (Figure 2b)—one set for the free macrocycle **1** (cf. Figure 2a), one for the free salt **3**-H·PF_6 (cf. Figure 2c), and one for the 1:1 complex formed between **1** and **3**-H·PF_6. Because the shifts of the signals in the ^{1}H NMR spectrum of the complex formed between macrocycle **1** and the thread-like cation **3**-H^+ are similar to those observed for the pseudorotaxane formed from DBA^+ and **1**,[4] we suspected that the former pair formed the [2]pseudorotaxane-like complex [**1**⊃**3**-H]-[PF_6] (Scheme 1). The ^{1}H NMR spectrum of an equimolar mixture of bis(*p*-*tert*-butylbenzyl)ammonium hexafluorophosphate and macrocycle **1** in CD_3CN (8 mM) exhibited no signals for any such complex, even after heating at 323 K for 24 h (see the Supporting Information); that is, under such conditions, macrocycle **1** lacks

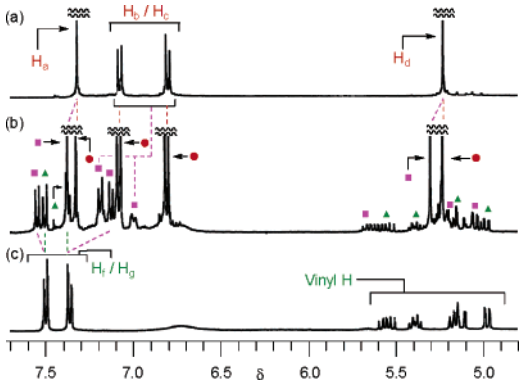


Figure 2. Partial ^{1}H NMR spectra (400 MHz, CD_3CN, 298 K) of (a) macrocycle **1**, (b) an equimolar mixture of **1** and **3**-H·PF_6 (8 mM), and (c) **3**-H·PF_6. The descriptors red circle, green triangle, and pink square refer to the signals of the uncomplexed states of macrocycle **1** and thread **3**-H·PF_6 and of their complex, respectively.

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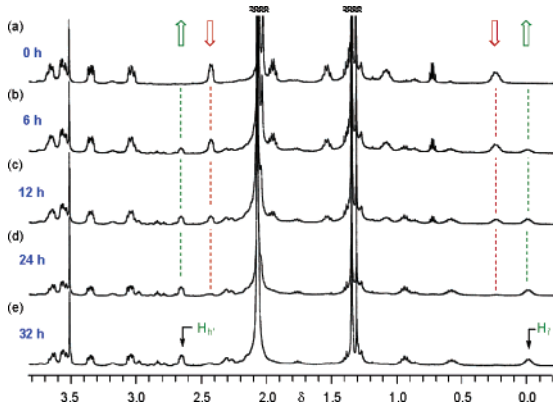

Figure 3. Partial ^{1}H NMR spectra (400 MHz, CD_3NO_2, 323 K) displaying the formation of [2]rotaxane **4**-H·PF_6 from the [2]pseudorotaxane [**1**⊃**3**-H][PF_6] over time: (a) 0, (b) 6, (c) 12, (d) 24, and (e) 32 h.

the ability to pass over *p-tert*-butylphenyl termini. Thus, the association and dissociation of the complex [**1**⊃**3**-H][PF_6] must occur via passage of only the *cis*-1-[(*Z*)-alk-1′-enyl]-2-vinylcyclopropane terminus of the thread-like component through macrocycle **1**. Using a single-point method,[8] we determined the association constant (K_a) for the interaction between macrocycle **1** and the thread-like salt **3**-H·PF_6 in CD_3CN to be 260 M^{-1}, which suggests that the *cis*-1-[(*Z*)-alk-1′-enyl]-2-vinylcyclopropane terminal group does not significantly affect the binding affinity between the two components.[9]

Because the macrocycle **1**/DBA^+ system forms a stronger complex in CD_3NO_2, which simplifies the ^{1}H NMR spectra by weakening the signals of the uncomplexed components to negligible levels, we used this solvent to monitor the progress of the swelling process.[10] From an equimolar mixture of macrocycle **1** and thread **3**-H·PF_6 (initial concentrations: 8 mM) in CD_3NO_2 at 323 K, Figure 3 displays the gradual consumption of the signals of the dialkenylcyclopropane-terminated [2]pseudorotaxane [**1**⊃**3**-H][PF_6] and the concomitant rise in the intensities of the signals of the cycloheptadiene-terminated [2]rotaxane **4**-H·PF_6. Thus, heating an equimolar mixture of **1** and **3**-H·PF_6 in CH_3NO_2 (70 mM) at 323 K for 48 h, followed by ion exchange (NH_4PF_6/H_2O) and chromatography processes, provided the [2]rotaxane **4**-H·PF_6 in an isolated yield of 86%.

Although the [2]rotaxane **4**-H·PF_6 was obtained as a racemic mixture, hydrogenation of the cycloheptadiene terminus converted each enantiomer into a single cycloheptane-terminated achiral [2]rotaxane **5**-H·PF_6 (Figure 4). No signals of the free components appeared in the ^{1}H NMR spectrum (see the Supporting Information) after heating a solution of the [2]rotaxane **5**-H·PF_6 in CD_3SOCD_3 at 343 K for 2 h, confirming the interlocked nature of its two components.

To prove the generality of this approach, based on the knowledge that *p-tert*-butylphenyl[11] and cycloheptane[12] moieties are effective stopper units for dibenzo[24]crown-8 (DB24C8),[13] we applied a similar complexation−swelling−hydrogenation sequence to an equimolar mixture of DB24C8 and **3**-H·PF_6; the corresponding [2]rotaxane was obtained in 64% yield after counterion exchange (see Supporting Information).

We have successfully demonstrated that a threading-followed-by-swelling protocol, with subsequent hydrogenation, can be used to synthesize achiral molecular rotaxanes. Because the interlocking of macrocycles through swelling of *cis*-1-[(*Z*)-alk-1′-enyl]-2-vinylcyclopropane termini is a mild and high-yielding method for synthesizing [2]rotaxanes, we believe that threading-followed-by-swelling protocols will be applicable for synthesizing more

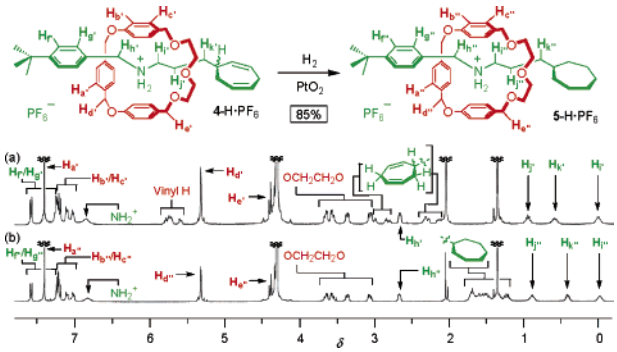

Figure 4. The hydrogenation reaction that converts the racemic [2]rotaxane **4**-H·PF_6 into the achiral [2]rotaxane **5**-H·PF_6, and ^{1}H NMR spectra (400 MHz, CD_3NO_2, 298 K) of (a) **4**-H·PF_6 and (b) **5**-H·PF_6.

complicated interlocked molecules, such as higher-order rotaxanes; related studies are currently under investigation in our laboratory.

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Supporting Information Available: Experimental procedures for the preparation of all new compounds and their characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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