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Magic Ring Catenation by Olefin Metathesis

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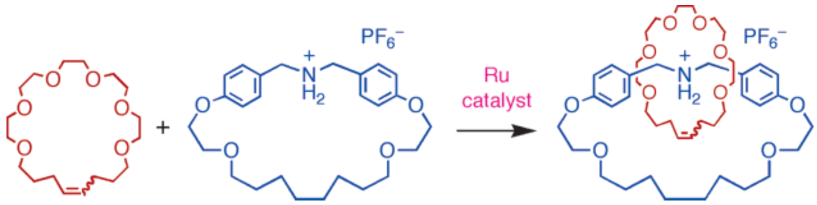
ABSTRACT



Olefin metathesis has been employed in the efficient syntheses of a [2]catenane with the templation being provided by the recognition between a secondary ammonium ion and a crown ether. In one approach, a crown ether precursor has been clipped around an NH_2^+ center situated in a macrocyclic ring, yielding the mechanically interlocked compound. In the other approach, the reversible nature of olefin metathesis allows for a magic ring synthesis to occur wherein two free macrocycles can be employed as the stationary materials, leading to the formation of the same [2]catenane.

Mechanically interlocked molecules[1] such as catenanes and rotaxanes have long been of interest to chemists because of their unique molecular structures. Furthermore, recent advances in the science of nanosystems has revealed that these molecules not only are aesthetically pleasing curiosities but also can function as the key components in active molecular electronic devices where bistable derivatives, for example, serve as volatile bistable switches in both memory and logic circuits.[2]

Although a vast number of syntheses of catenanes and rotaxanes have appeared in the chemical literature, most of the strategies employ kinetically controlled covalent bond formation as the final interlocking step.[3] This strategy does not always result in high yields of mechanically interlocked compounds because of the irreversible formation of unwanted noninterlocked byproducts. An alternative strategy, however, exploits dynamic covalent chemistry,[4] an approach that utilizes reversible reactions in which the product distribution depends on thermodynamic rather than kinetic control, i.e., the yield of a mechanically interlocked compound reflects its stability relative to those of any other noninterlocked byproducts with proof-reading and error-checking operating up until a final equilibrium state is reached. Examples of

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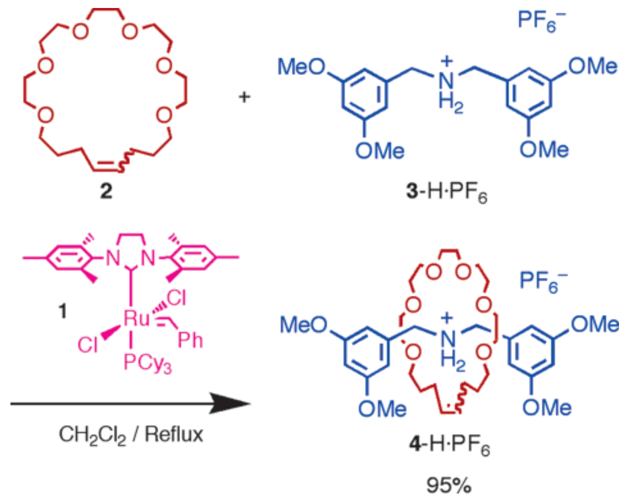
equilibrium reactions employed as the final bond-forming step in the synthesis of catenanes and rotaxanes include the reversible formation of imines,[5] disulfides,[6] and cyclic acetals,[7] as well as olefin metathesis mediated by functional group-tolerant ruthenium alkylidene catalysts.[8] This protocol has been applied successfully in the syntheses of both [2]catenanes[9] and [2]rotaxanes.[10] Recently, we have demonstrated[11] that the ring closing of certain olefin-containing polyether substrates around appropriately substituted secondary dialkylammonium ions results (Scheme 1) in the reversible formation of [2]rotaxanes. Thus, for example, by employing the ruthenium catalyst $(H_2IMes)(PCy_3)(Cl_2)Ru{=}CHPh$ (**1**),[12] the macrocyclic polyether **2** containing one olefinic double bond can be induced to undergo a magic ring synthesis in the presence of the dumbbell compound **3**-H·PF_6, wherein the NH_2^+ center acts as the template for the formation of the [2]rotaxane **4**-H·PF_6. Here, we show that two convenient, high-yielding methods for constructing [2]rotaxanes can be extended to the template-directed formation of [2]catenanes by (macrocyclic) polyether/secondary ammonium ion recognition[13] by using a cyclic rather than a linear template.

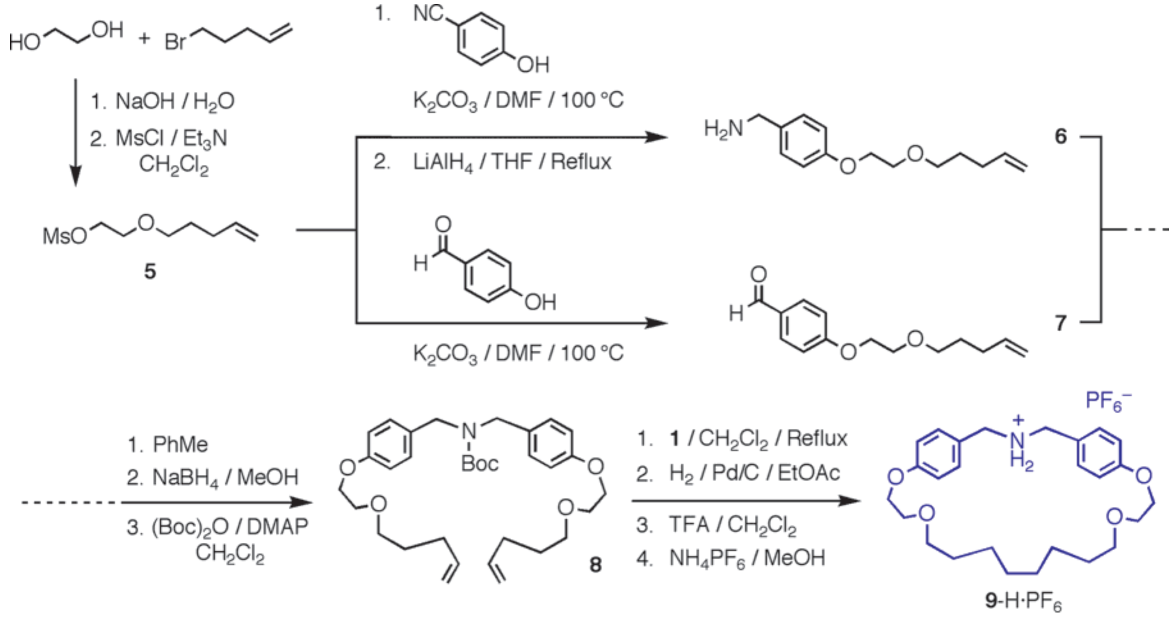
Scheme 1. Magic Ring Synthesis of a [2]Rotaxane (**4**-H·PF_6) Templated by a Linear Ammonium Ion-Containing Dumbbell-Shaped Component (**3**-H·PF_6)



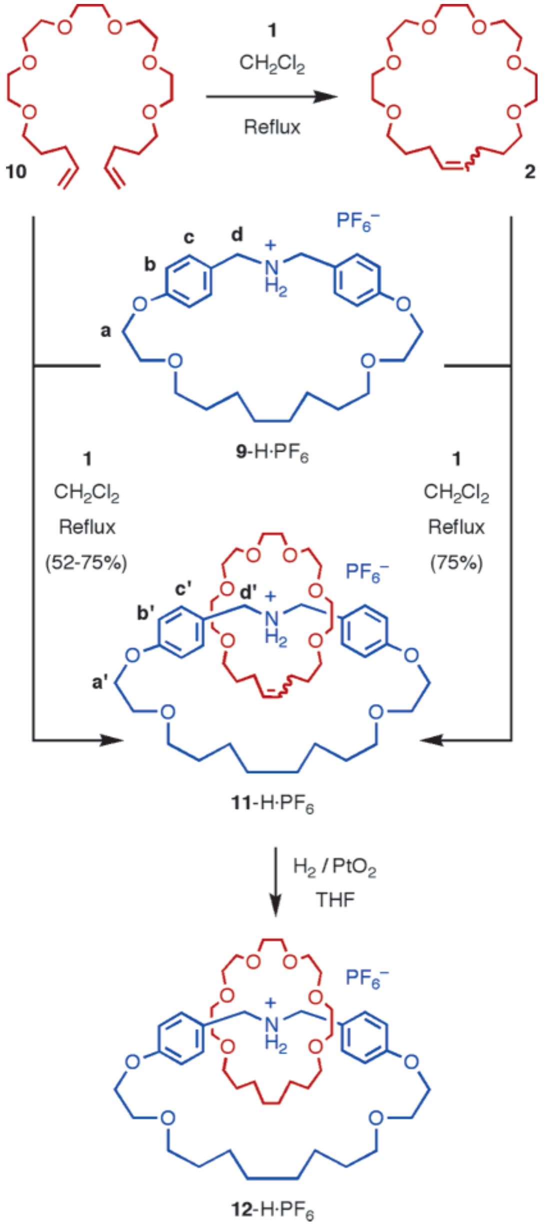
The formation of the [2]catenane requires that the dibenzylammonium-template-containing macrocycle is large enough to permit catenation by the polyether macrocycle. The 27-membered macrocyclic template **9**-H·PF_6, shown in Scheme 2, was identified as a suitable target for synthesis. As outlined in this scheme, 4-hydroxybenzaldehyde and 4-cyanophenol were both alkylated in separate reactions (K_2CO_3/DMF) with the mesylated ether **5**, prepared in two steps from ethylene glycol and 5-bromo-1-pentene. The cyano group in the second alkylation product was reduced to the primary amine **6** using $LiAlH_4$ in THF. Condensation of this amine with the aldehyde **7**, followed by reduction ($NaBH_4$/MeOH), yielded the macrocyclic precursor **8** after protection of the secondary amine function with a Boc group. Ring-closing metathesis (RCM) using the ruthenium catalyst **1** in a CH_2Cl_2 solution of **8** yielded the expected protected macrocycle, which was hydrogenated (H_2/Pd/C/EtOAc), deprotected (TFA/CH_2Cl_2), and subjected to counterion exchange (NH_4PF_6/MeOH) to yield the hexafluorophosphate salt **9**-H·PF_6 of the macrocycle.

Ring-closing of the terminal olefin functions in the acyclic polyether **10** in the presence of the macrocyclic template **9**-H·PF_6 and the catalyst **1** afforded (Scheme 3, lefthand route) the [2]catenane **11**-H·PF_6 in 52−75% isolated yield

Scheme 2. Synthesis of the Macrocyclic Template **9**-H·PF_6



Scheme 3. Dynamic Synthesis of a Catenane (**11**-H•PF$_6$) by Two Distinct, Yet Complementary, Routes[a]



[a] Either ring-closing (left) or ring-opening−ring-closing (right) metathesis protocols can be exploited.

as a mixture of (*E*)- and (*Z*)-isomers, as confirmed by ESI mass spectrometry[14] and both ^{1}H and ^{13}C NMR spectroscopy. Hydrogenation (H$_2$/PtO$_2$/THF) of the olefinic double bond in **11**-H•PF$_6$ results in the formation of a single species,[15] the [2]catenane **12**-H•PF$_6$.

To demonstrate further the reversible nature of the olefin metathesis reaction employed in the synthesis of the dynamic [2]catenane **11**-H•PF$_6$, the preformed macrocycle **2** was employed in the corresponding magic ring synthesis. When the two complementary macrocycles (**9**-H•PF$_6$ and **2**) are dissolved in CH$_2$Cl$_2$, catenation of these separate rings is, in the absence of any other species, not possible. Upon the addition of a catalytic amount of **1**, however, the formation of **11**-H•PF$_6$ is observed, by ^{1}H NMR spectroscopy (Figure 1), to occur within a matter of minutes. After only 2 minutes, signals are observed in the ^{1}H NMR spectrum at δ ~4.3 ppm, corresponding to the NH$_2^+$-adjacent methylene protons

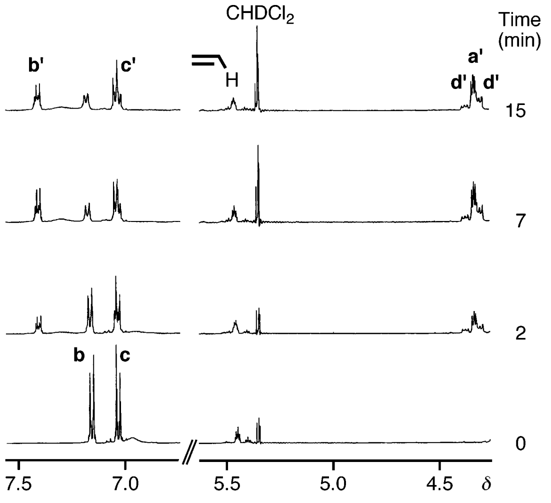


Figure 1. Partial ^{1}H NMR spectra showing the change over time during the magic ring synthesis of the dynamic [2]catenane **11**-H•PF$_6$. Peak labels are defined in Scheme 3.

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(**d′**) in an environment where they are encircled by a crown ether-like macrocycle; two sets of signals are observed, corresponding to the (*E*)- and (*Z*)-isomers of the [2]catenane. Furthermore, signals corresponding to "free" **9**-H•PF_6 (**b** and **c**) are observed to diminish in intensity, while others, corresponding to the [2]catenane **11**-H•PF_6, increase in intensity over the course of the observation, with equilibrium (75% interlocked product) being achieved after only 30 minutes. Formation of this interlocked compound presumably occurs via a process in which (i) the olefin **2** undergoes a ring-opening metathesis reaction to form a linear oligoether species, that (ii) subsequently threads through the ammonium ion-containing macrocycle **9**-H•PF_6 to form a [2]pseudorotaxane, prior to (iii) a ring-closing metathesis reaction that stitches the ends of the linear component back together, to reform a macrocycle with the same constitution as **2** that is now, however, wrapped around the NH_2^+ center of what was previously **9**-H•PF_6, resulting in the formation of a [2]catenane, namely, **11**-H•PF_6. In essence, catalyst **1** enables the topological isomerization of two noninterlocked rings into a catenated architecture, reminiscent of the conjurer's simple parlor trick, or, in a more scientific context, the action of topoisomerases[16] on circular double-stranded DNA.

In conclusion, the use of ruthenium-mediated reversible alkene metathesis has been applied to the synthesis of a [2]catenane based upon the secondary dialkylammonium ion/(macrocyclic) polyether recognition system. The synthesis, under thermodynamic control, of interlocked molecules allows for the efficient and high-yielding construction of complex molecular architectures. The extension of this methodology from simple catenanes and rotaxanes to larger macromolecular systems is currently under investigation.

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Supporting Information Available: Experimental procedures and characterization data for compounds **2**, **5**−**8**, and **9**-H•PF_6−**12**-H•PF_6. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) Peaks at m/z = 774 and 760 were observed in the mass spectrum of the [2]catenane **11**-H•PF_6. The lower mass peak arises from an impurity in the dibenzylammonium-based macrocycle **9**-H•PF_6, which is formed during the ring-closing metathesis (RCM) macrocyclization of the diolefin **8**. Olefin isomerization prior to the RCM reaction affords a macrocycle with one methylene deletion, resulting in a 26-membered ring, rather than the expected 27-membered one.

(15) Further confirmation of the interlocked nature of this [2]catenane (**12**-H•PF_6) was obtained following acylation of this compound under basic conditions. The acylated product, in which the mutual recognition expressed between the two mechanically interlocked rings has been removed, was proven to be a single species that had not fallen apart, as evidenced by both NMR spectroscopy and ESI mass spectrometry; see Supporting Information.

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