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Multivalency-Directed Magic-Ring [2](3)Catenane by Olefin Metathesis

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Multivalency,[1] as a way to compensate for the weak monovalent interactions in nature, has attracted considerable interest in recent years.[2] Chemists tried to discover the physical basis of multivalency effects based on a thermodynamic model combined with computational studies and found that thermodynamics play a key role as far as multivalent interactions is concerned.[3] The construction of supermolecules by the bottom-up approach to mimic biomacromolecules and their assemblies is one of the main aims for supramolecular chemists.[4] Although multivalency provides a fascinating inspiration for chemists seeking to transfer concepts from the biological world into supramolecular chemistry, there are still very few examples of multivalency in the noncovalent synthesis of various elaborate supermolecules.[5]

Mechanically interlocked molecules,[6] such as catenanes and rotaxanes, are not only aesthetically pleasing curiosities, but can function as the key components in future “intelligent” materials.[7] Although a vast number of syntheses of catenanes and rotaxanes have been reported, most of the strategies employ kinetically controlled covalent-bond formation as the final interlocking steps in which the product distribution relies on kinetic rather than thermodynamic control.[8] Therefore, chemists have exploited dynamic covalent chemistry (DCC)[9] as an alternative strategy that utilizes reversible reactions as the final interlocking step in which the product distribution relies on thermodynamic rather than kinetic control. Many reversible reactions, including the formation of imines, disulfides, and cyclic acetals, as well as olefin metatheses, have been employed as the final reaction steps to synthesize catenanes and rotaxanes.[10] Especially, the construction of magic-ring catenanes[5c] and magic-rod rotaxanes[11] by olefin metathesis has been recently reported. However, synthesis of more complex interlocked molecules by means of the DCC strategy is still a challenge.

In recent years, we became interested in developing new supramolecular systems based on triptycene-derived synthetic hosts.[12] As a result, we reported a highly efficient approach to synthesize [2](3)catenanes by threefold metathesis reactions of a triptycene-based tris[2]pseudorotaxane.[13,14] Herein, we report formation of a novel multivalency-directed complex **1**⋅**2**-3H⋅PF_6 composed of the trisdialkylammonium strand ions **2**-3H⋅PF_6 and the triptycene-based homotritopic host **1**,[13a] containing three dibenzo[24]crown-8 cavities, and the subsequent [2](3)catenane **4**-3H⋅3PF_6 by the olefin metathesis reaction. Moreover, we also designed and synthesized a trisdialkylammonium macrocycle ion, **3**-3H⋅PF_6, and found that it could form an interesting magic-ring [2](3)catenane with the homotritopic host **1** by reversible olefin metathesis (Scheme 1).

Scheme 2 outlines the synthesis of the trisdialkylammonium strand ions **2**-3H⋅PF_6. Condensation of the amine **10** with the aldehyde **9** gave the corresponding imine, which was reduced by $NaBH_4$ in methanol to give the amine **8**. Amine **8** was protected with Boc groups and then treated with TsCl in CH_2Cl_2 to give the compound **7**. The reaction of **7** with **6** in the presence of K_2CO_3 in CH_3CN gave the Boc-protected trisdialkylammonium ion precursor **2**. Finally, the Boc protective groups of **2** were removed with excess TFA, and the amines formed were simultaneously protonated. Subsequent counterion exchange with saturated NH_4PF_6 afforded **2**-3H⋅3PF_6 in 83% yield over two steps. The salt **2**-3H⋅3PF_6 has good solubility in acetone and acetonitrile.

We then investigated the multivalency-directed complexation between host **1** and trisdialkylammonium strand **2**-3H⋅3PF_6 in solution. Consequently, a mixture of **1** and **2**-3H⋅3PF_6 (1 mM each) in [D$_6$]acetone provided a complicated ^{1}H NMR spectrum (see the Supporting Information), which might be due to the swift structural exchange of the complex.[15] To assign the proton signals and further study

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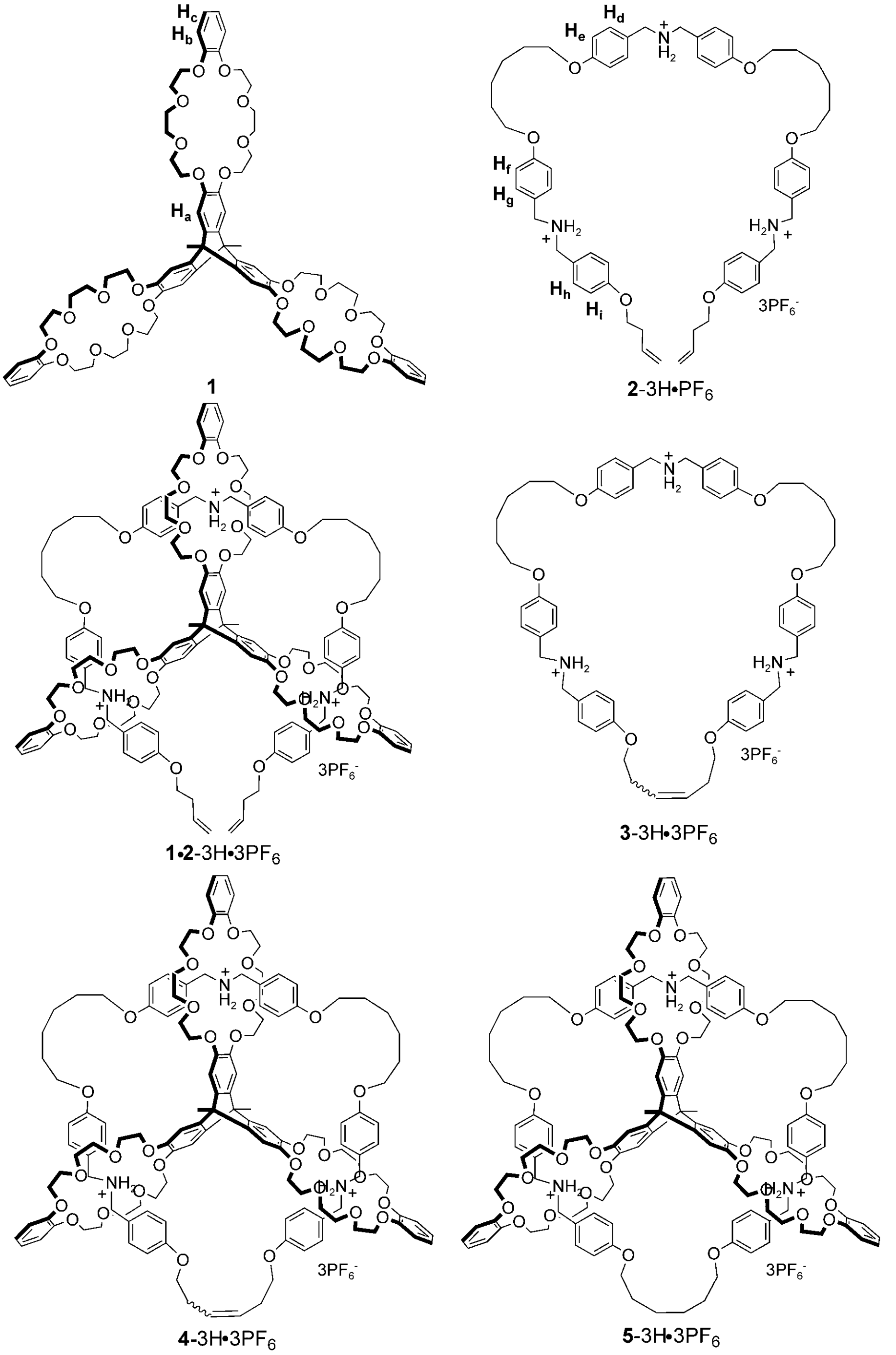
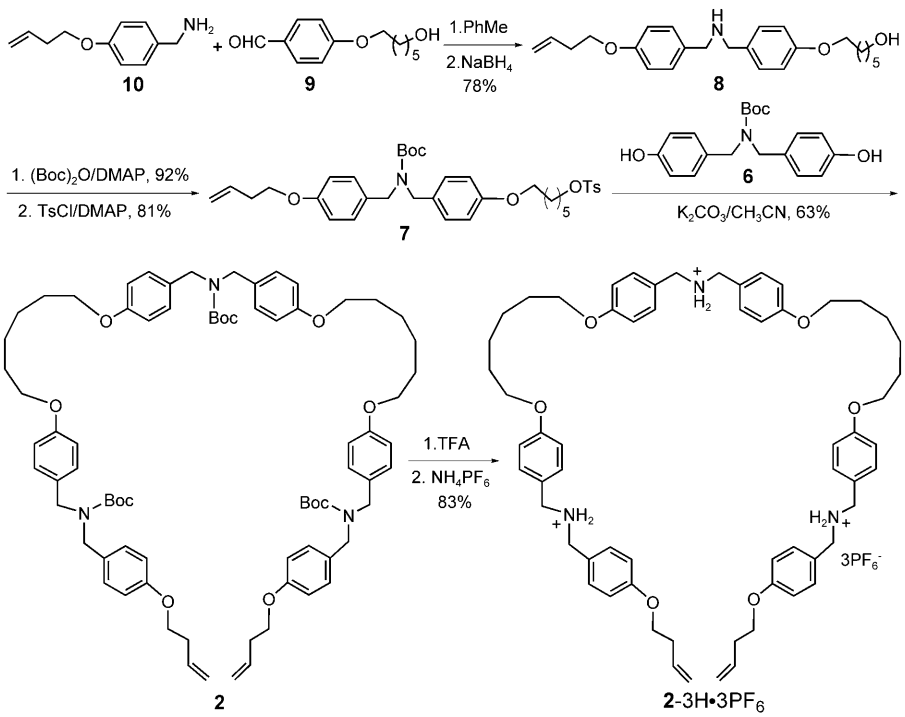


Scheme 1. Structures and proton designations of host **1**, trisdialkylammonium strand **2**-3H•PF$_6$, [2](3)pseudorotaxane **1**•**2**-3H•PF$_6$, trisdialkylammonium macrocycle **3**-3H•PF$_6$, and [2](3)catenanes **4**-3H·3PF$_6$ and **5**-3H·3PF$_6$.

the complexation between **1** and **2**-3H•3PF$_6$ in solution, the ^{1}H NMR spectroscopy experiments of complex **1**•**2**-3H•3PF$_6$ in [D$_6$]acetone at low temperatures were carried out.[14] The results showed that with lowering the temperature the aromatic proton signals changed gradually and revealed a dispersed array of well-defined resonances. The proton signals of **1** split into two groups at 228 K, which indicated that the structure of the complex was fixed slowly at low temperatures, and showed a C_{2v} symmetric structure in solution (Figure 1b). Moreover, it was found that the aromatic proton signals of **1** all shifted significantly downfield, and the aromatic proton signals of **2**-**3**H•3PF$_6$ shifted significantly upfield, which may be due to π–π stacking interactions between the phenyl groups in the salt and the catechol rings in the crown subunits. Furthermore, the formation of a stable 1:1 complex of **1**•**2**-**3**H•3PF$_6$ was evidenced by the MALDI-TOF mass spectrum (see the Supporting Information). As a result, the strong signal at *m*/*z* 2356.4 for [$M-3PF_6+H$]$^+$ was observed.

To further confirm the effect of multivalency, we performed an olefin metathesis reaction. As shown in Scheme 3, when a solution of **1**•**2**-3H•3PF$_6$ in dichloromethane (1.0 mM) was treated with the second-generation Grubbs catalyst (5 mol %), it was found that the reaction went smoothly and exclusively gave the threefold metathesis product **4**-**3**H•3PF$_6$ in 84 % yield. This high efficiency is due to the combination of multivalency and the reversible olefin metathesis. The ^{1}H NMR spectrum of **4**-3H•3PF$_6$ showed that the signals corresponding to terminal vinyl protons in the [2](3)pseudorotaxane disappeared instead of new ones at $\delta = 5.60$ ppm for $-CH{=}CH-$ protons in **4**-3H•3PF$_6$ as a *cis*/*trans* isomeric mixture. The ESI-HRMS showed a strong signal at *m*/*z* 1236.0826 for the [**4**-3H$-$PF$_6$]$^{2+}$ ion (see the Supporting Information), which is also consistent with formation of the [2](3)catanane. Moreover, as we previously described,[13a] hydrogenation of **4**-3H•3PF$_6$ with the Adam catalyst afforded [2](3)catenane **5**-3H•3PF$_6$ in quantitative yield.

Formation of complex **4**-3H•PF$_6$ provided us a chance to synthesize the magic-ring [2](3)catenane. First, we performed the ring-closing metathesis of **2** in CH$_2$Cl$_2$ in the presence of the Grubbs II catalyst to obtain the expected



Scheme 2. Synthesis of the trisdialkylammonium strand ions **2**-3H•PF$_6$. Boc = *tert*-butyloxycarbonyl, Ts = tosyl, DMAP = 4-dimethylaminopyridine, TFA = trifluoroacetic acid.

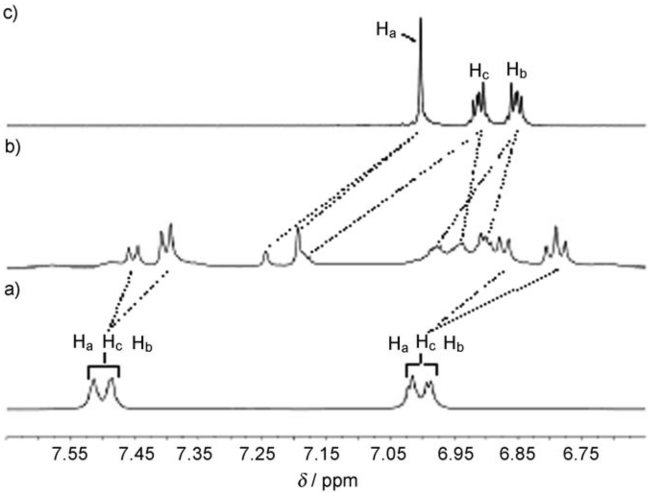


Figure 1. Partial ^{1}H NMR spectra (600 MHz, [D$_6$]acetone) of a) **2**-3H•3PF$_6$ (1.0 mM) at 228 K, b) **1** (1.0 mM) and 1 equiv of **2**-3H•3PF$_6$ at 228 K, and c) host **1** (1.0 mM) at 228 K. Resonance protons are labeled in Scheme 1.

57-membered macrocycle in 41 % yield, which was deprotected with TFA, and then subjected to counterion exchange (NH$_4$PF$_6$/MeOH) to yield the macrocycle **3**-3H•3PF$_6$. When **3**-3H•3PF$_6$ and host **1** were dissolved in CH$_2$Cl$_2$, catenation of the rings was not possible in the absence of the Grubbs catalyst. However, upon the addition of a catalytic amount of the Grubbs II catalyst, it was found that the reaction of **3**-3H•3PF$_6$ and **1** also went smoothly, and the metathesis product **4**-3H•3PF$_6$ could be isolated in 83 % yield. Formation of this magic-ring interlocked compound presumably occurred through a process in which the olefin **3**-3H•3PF$_6$ underwent a ring-opening metathesis reaction to form a strandlike trisdialkylammonium species that subsequently threaded the three [24]crown-8 cavities of **1** to form a multivalency-directed complex, followed by a ring-closing metathesis reaction that linked the ends of the strandlike component back together again (Scheme 4). This is an interesting example of the multivalency-directed magic-ring interlocked structures via olefin metathesis.

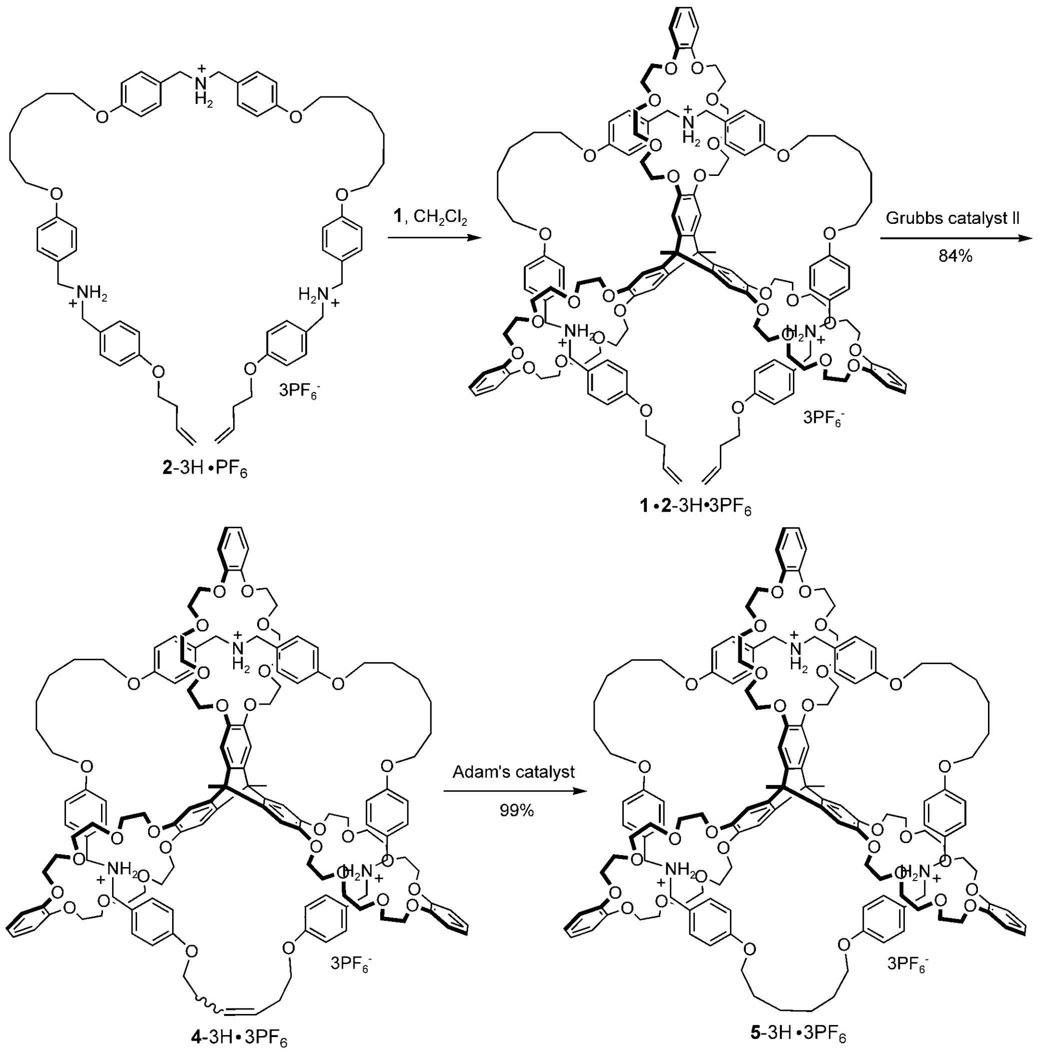
In conclusion, we have shown that a trisdialkylammonium strand **2**-3H•PF$_6$ threads the three [24]crown-8 cavities of a triptycene-derived host to form a novel multivalency-directed complex **1**•**2**-3H•PF$_6$, which resulted in the [2](3)catenane in high yield by the olefin metathesis reaction. Moreover, we have also found a trisdialkylammonium macrocycle ions **3**-3H•PF$_6$ forms an interesting magic-ring [2](3)catenane through reversible olefin metathesis. The presented results show that the combination of multivalency and olefin metathesis provides a powerful tool for the synthesis of complex interlocked molecules, which may find wide potential applications in molecular machines and supramolecular chemistry.

Experimental Section

Experimental details, including procedures for the synthesis of **2**-3H•3PF$_6$, **3**-3H•3PF$_6$, and characterization methods, are available in the Supporting Information.

Typical procedure A for the synthesis of 4-3H•3PF$_6$: The trisdialkylammonium strand ion **2**-3H•3PF$_6$ (0.02 mmol, 27.9 mg) and **1** (0.02 mmol, 27.8 mg) were dissolved in anhydrous, degassed CH$_2$Cl$_2$ (2.5 mM, 8 mL). After the mixture was stirred at room temperature for 24 h, the Grubbs II catalyst (0.85 mg, 0.001 mmol) was added under a dry Ar atmosphere and the mixture was heated at 40 °C for 12 h, allowed to cool to room temperature and quenched by addition of ethyl vinyl ether. The reaction was stirred for an additional 30 min. Solvent was removed under reduced pressure and the crude oil was purified by column chromatography (SiO$_2$: CH$_2$Cl$_2$/MeOH 200:1–160:1) to yield **4**-3H•3PF$_6$ (46 mg, 84 % yield).

Typical procedure B for the synthesis of 4-3H•3PF$_6$: The trisdialkylammonium macrocycle ions **3**-3H•3PF$_6$ (0.015 mmol, 20.9 mg) and **1** (0.015 mmol, 20.9 mg) were dissolved in anhydrous, degassed CH$_2$Cl$_2$ (2.5 mM, 6 mL). The Grubbs II catalyst (0.64 mg, 0.0075 mmol) was added under a dry Ar atmosphere and the mixture was heated at 40 °C for 24 h, allowed to cool to room temperature and quenched by addition



Scheme 3. Synthesis of the [2](3)catenane **5**-3H·3PF_6 via **1**·**2**-3H·3PF_6.

of ethyl vinyl ether. Solvent was removed under reduced pressure and the crude oil was purified by column chromatography (SiO_2: CH_2Cl_2/MeOH 200:1–160:1) to yield **4**-3H·3PF_6 (33.9 mg, 83% yield).

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Keywords: catenanes • dynamic covalent chemistry • macrocycles • multivalency

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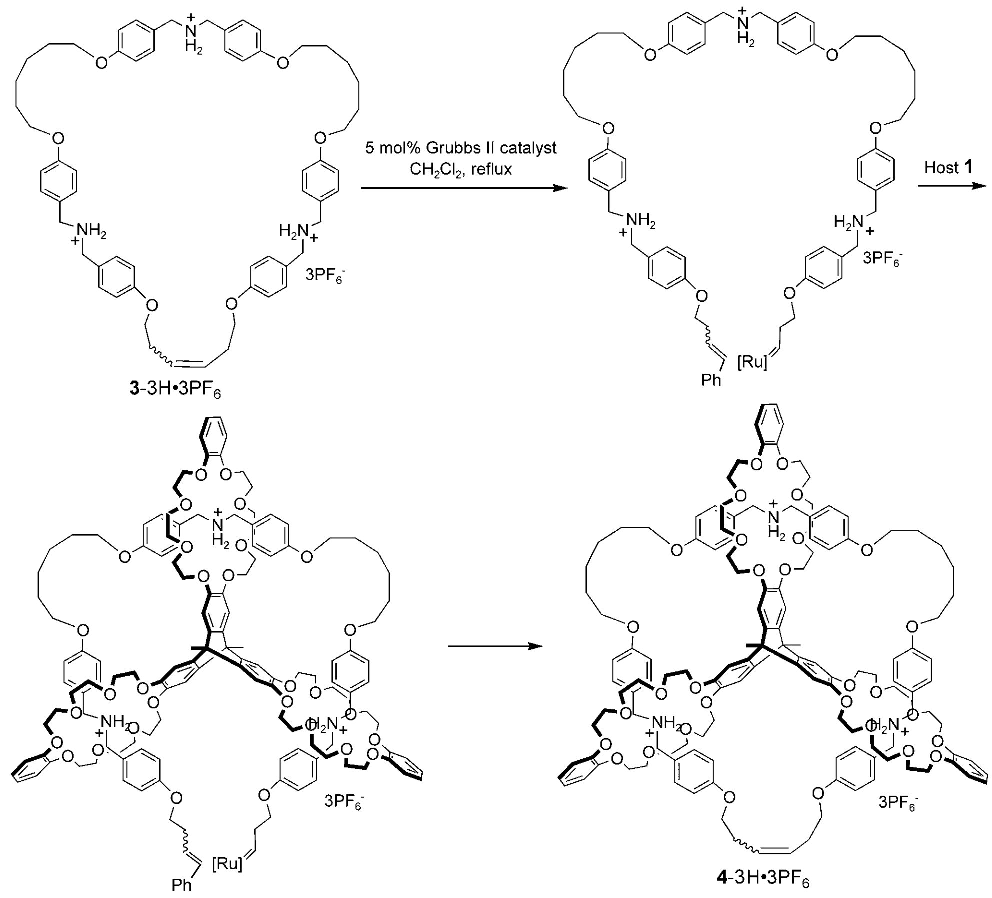

Scheme 4. A presumable process for formation of the magic-ring [2](3)catenane through two olefin metathesis steps.

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[14] We are grateful to one of the reviewers for the suggestions of nomenclature of the pseudorotaxanes and catenanes. Thus, **1·2**-3H·PF_6 was named as [2](3)pseudorotaxane, in which the number in brackets was used to indicate the number of molecular components, and after the bracket another number in parentheses could be designated the number of threadings involved. Similarly, **4**-3H·3PF_6 and **5**-3H·3PF_6 should be named as [2](3)catenanes.

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