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A double ring-closing olefin metathesis approach to [3]catenanes

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Abstract

A [3]catenane with peripheral olefinic macrocycles was conveniently synthesized via a double ring-closing olefin metathesis. Highlights of this work include the synthesis of a 65-membered macrocycle featuring two phenanthroline ligands, a Cu(I)-templated synthesis of a [3]pseudorotaxane, and the key double ring-closing olefin metathesis to afford the desired [3]catenane in 71% yield.

Keywords: Catenane; Macrocycle; Pseudorotaxane; Ring-closing metathesis

Catenanes and rotaxanes have long been of interest to chemists due, in part, to the various unique chemical and physical consequences of the fact that these types of compounds are composed of interlocking, but otherwise unbound, molecular-level species.[1] Over the last few decades, improved syntheses of interlocked structures based upon templation, molecular recognition, and host–guest interactions have finally allowed this field of study within supramolecular chemistry an opportunity to thrive.[2] More specifically, recent syntheses of [2]catenanes based upon supramolecular pre-organization in tandem with ring-closing olefin metathesis have been particularly fruitful, even allowing some of these methods to become preparatively useful.[3]

Beyond [2]catenanes, the synthesis of higher order [*n*]catenanes is significantly more challenging for a variety of reasons including the requirement for the central macrocycles to be doubly threaded. Nevertheless, several groups have achieved spectacular syntheses of [3], [4], and [5]catenanes.[4] In our own efforts to access polycatenanes and other polymers with interlocked components, we have developed a need for [3]catenanes that specifically feature peripheral macrocycles with olefin functionality. Our approach to [3]catenanes consists of a double clipping of two peripheral macrocycles onto a central macrocycle.[5] While a couple groups have accessed [3]catenanes in low yields via double olefin cross metatheses of [2]pseudorotaxanes, herein we describe a relatively high yielding synthesis of a [3]catenane via a related double ring-closing olefin metathesis of a [3]pseudorotaxane. Scheme 1 illustrates a pictorial representation of our complementary approach to [3]catenanes.

Our synthesis began with diol **1** which was prepared in three steps (61% overall yield) from 1,10-phenanthroline as described in the literature.[6] In Scheme 2, diol **1** was treated with allyl bromide to afford both the monoallylic species **2** and the diallylic species **6** in 67% and 15% yields, respectively. Two equivalents of monoallylic **2** were tethered in a diesterification reaction with isophthaloyl dichloride to provide diester **3** in 66% yield. Ring-closing olefin metathesis of diester **3** (5 mM) with 10 mol % Grubbs' 2nd generation pre-catalyst[7] afforded the olefinic macrocycle **4** in 85% yield. The internal olefin of macrocycle **4** was reduced upon treatment with 10 mass% palladium/carbon to provide macrocycle **5** in 91% isolated yield.

Macrocycle **5** possesses several useful structural features for [3]catenane synthesis. Most prominently **5** is large enough (65-membered ring) and it incorporates two phenanthroline ligands, inwardly directed, to enable a copper(I)-assisted double threading to access a [3]pseudorotaxane. Macrocycle **5** has one rigid aromatic tether

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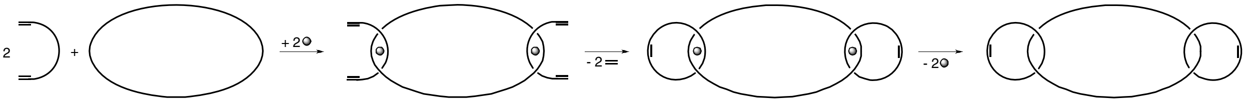
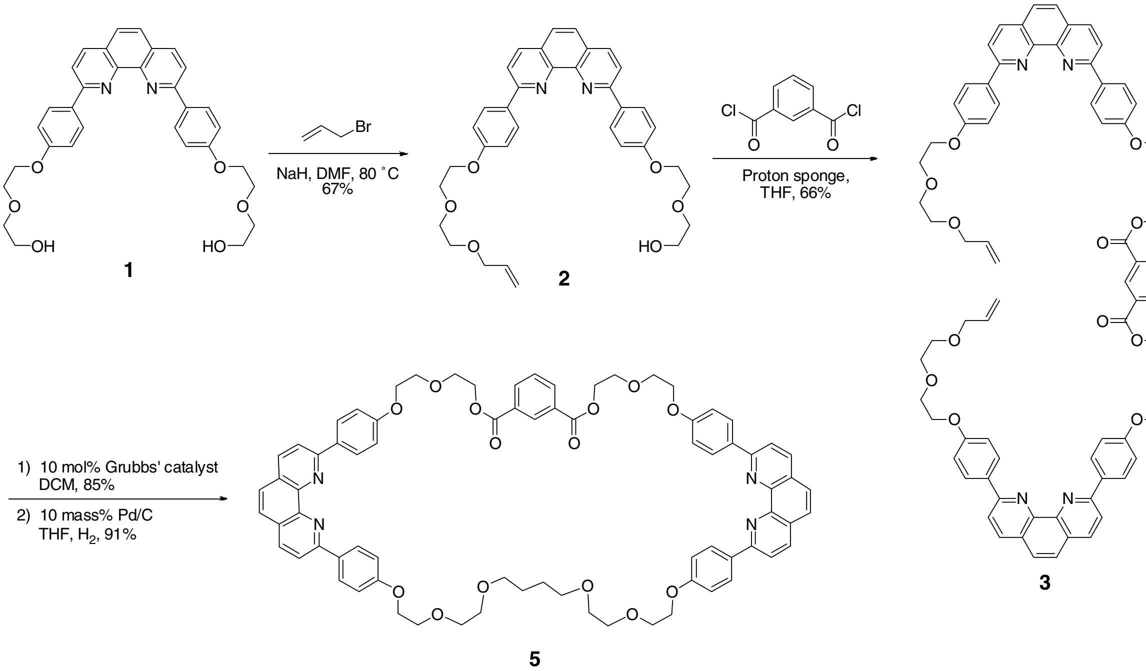
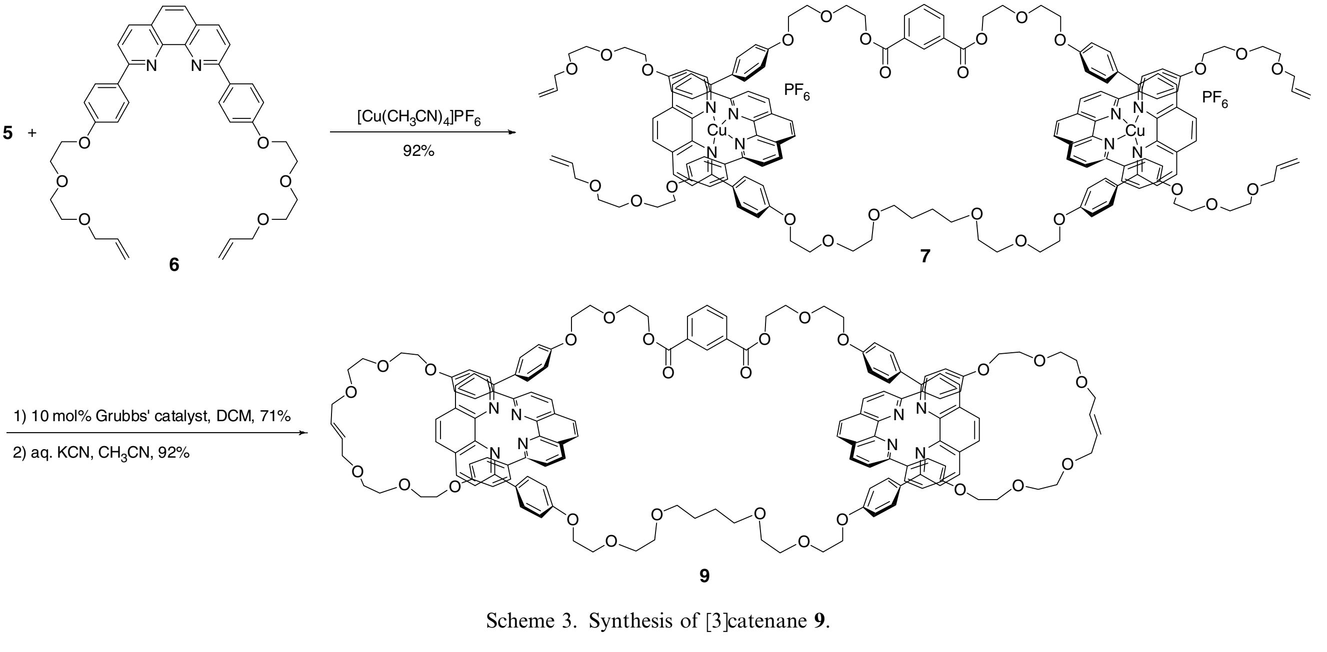


Scheme 1. Schematic representation of the [3]catenane synthesis.



Scheme 2. Synthesis of macrocycle **5**.

between the two 2,9-diaryl-1,10-phenanthroline moieties such that the two phenanthroline groups of **5** are unlikely to collapse, intramolecularly, onto a single copper(I) ion in a stable tetrahedral arrangement. Furthermore, the diethyleneglycol tethers between the 2,9-diaryl-1,10-phenanthrolines and the isophthaloyl group are short enough to prevent the phenanthrolines from twisting outward, thus precluding the formation of stable supramolecular oligomers in the presence of copper(I). Additionally, the more flexible fully aliphatic polyether linker between the two



Scheme 3. Synthesis of [3]catenane **9**.

2,9-diaryl-1,10-phenanthrolines functions as a solubilizing group for the compound in organic solvents. In comparison, a known, more symmetrical, bisphenanthroline macrocycle, similar to **5**, but with two aromatic linkers, was found to be poorly soluble in organic solvents.[8]

To access [3]catenane **9**, macrocycle **5** was briefly stirred with 2 equiv of copper(I), to form the Cu_2·**5** complex, and then treated with 2 equiv of diallyl **6** to provide the stable [3]pseudorotaxane **7** in 92% yield after column chromatography, Scheme 3. A minor byproduct, Cu·$\mathbf{6}_2$, was easily separable by column chromatography. A sharp ^1H NMR spectrum of **7** demonstrated formation of the tethered bisphenanthroline copper complexes from the characteristic upfield shift of the signals due to the 2,9-aryl substituents of the phenanthroline ligands.[9] The [3]pseudorotaxane **7** was also clearly inferred by MALDI-TOF-mass spectrometry from the distribution of peaks of the components of **7** as shown in Figure 1. Figure 1 shows that under the conditions of the MALDI-TOF-MS experiment, complex **7** undergoes some scrambling, for example to yield Cu·$\mathbf{6}_2$, which was not present in the purified sample of **7** (the R_f values of **7** and Cu·$\mathbf{6}_2$ differ greatly).

The [3]pseudorotaxane **7** was treated with 10 mol % Grubbs' 2nd generation pre-catalyst to perform the key double ring-closing olefin metathesis wherein two new 32-membered macrocycles were formed. Copper-complexed [3]catenane **8** was isolated in 71% yield (Scheme 3). The relatively high yield further demonstrates the remarkable nature of the bisphenanthroline–copper complex as an efficient pre-organizational element for the macrocyclic ring-closing olefin metathesis reaction.[3j] The ^1H NMR spectrum of the isolated product was consistent with the formation of the [3]catenane complex as judged by the disappearance of the signals due to the terminal olefin at 5.2 ppm and the appearance of a slightly broad signal at 6 ppm for the newly formed internal olefin.[9] MALDI-TOF-MS also clearly supported the formation of the [3]catenane structure (Fig. 2). As compared to **7**, the MALDI-TOF mass spectrum of **8** was simplified; no scrambling of the macrocyclic components was observed as would be expected for a covalently interlocked structure.

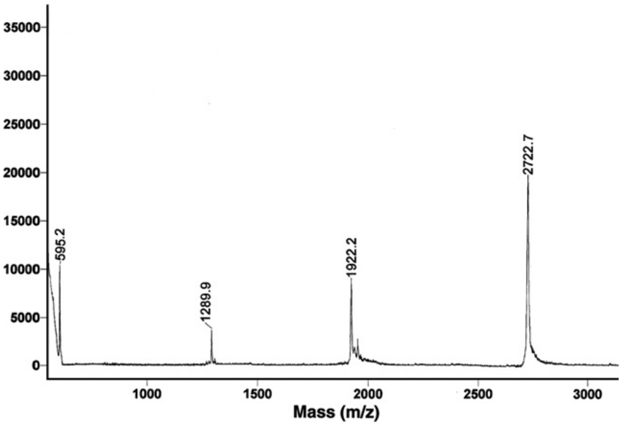


Fig. 2. MALDI-TOF-MS of **8**. Peak assignments (m/z): 2722.7, [$\mathbf{8}-PF_6$]$^+$; 1922.2, [$\mathbf{8}-2PF_6-Cu-(\mathbf{6}-CH_2{=}CH_2)$]$^+$; 1289.9, [$\mathbf{8}-2PF_6$]$^{2+}$; 595.2, [($\mathbf{6}-CH_2{=}CH_2$)+H]$^+$.

Lastly, the intermediate copper-complexed [3]catenane **8** was demetallated under mild conditions by the treatment with aq KCN in acetonitrile to provide the colorless, metal-free, and charge-neutral [3]catenane **9** in 92% yield, Scheme 3. The removal of copper was confirmed in the ^1H NMR spectrum by a return downfield shift of two diagnostic signals due to the 2,9-aryl substituents of the phenanthroline ligands from δ 6.03 and δ 7.29 to δ 7.10 and δ 8.40, respectively.[9] The MALDI-TOF mass spectrum of **9**, Figure 3, was simplified in comparison to the spectrum for **8** due to **9** being a neutral compound. Figure 3 shows three peaks in the mass spectrum that straightforwardly correspond to [3]catenane **9** (base peak, 2450.8) and two fragments. The two fragment peaks at 1859 and 595 are attributable to the [2]catenane and the smaller, peripheral (cleaved) macrocycle, respectively. Interestingly, under these MS experimental conditions, it appears that

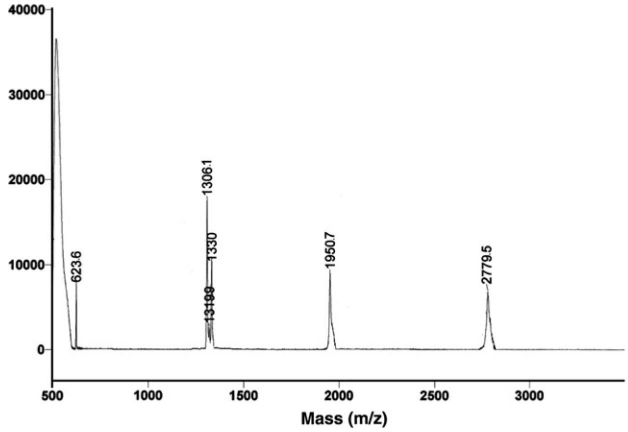


Fig. 1. MALDI-TOF-MS of **7**. Peak assignments (m/z): 2779.5, [$\mathbf{7}-PF_6$]$^+$; 1950.7, [$\mathbf{7}-\mathbf{6}-Cu-2PF_6$]$^+$; 1330, [$\mathbf{7}-2(\mathbf{6})-Cu-2PF_6$]$^+$; 1319.9, [$\mathbf{7}-2PF_6$]$^{2+}$; 1306.1, [$2(\mathbf{6})+Cu$]$^+$; 623.6, [$\mathbf{6}+H$]$^+$.

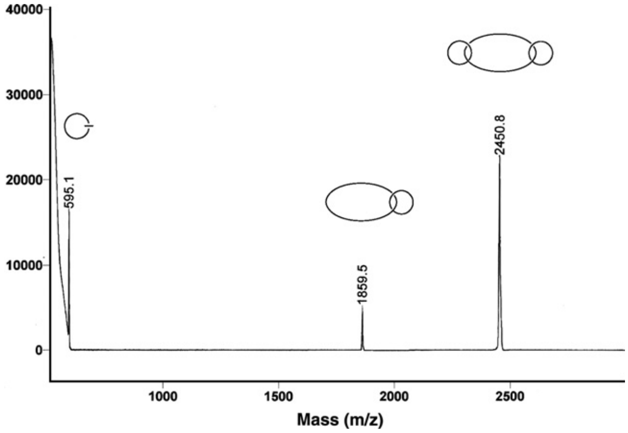


Fig. 3. MALDI-TOF-MS of **9**. Peak assignments (m/z): 2450.8, [$\mathbf{9}+H$]$^+$; 1859.6, [$\mathbf{9}-(\mathbf{6}-CH_2{=}CH_2)+H$]$^+$; 595.1, [($\mathbf{6}-CH_2{=}CH_2$)+H]$^+$.

fragmentary ring-opening occurs only within one of the smaller, peripheral macrocycles (derived from **6**) rather than from within the larger, central macrocycle. In general, the observation of a molecular ion, along with further peaks due to loss of rings from the parent catenane, without observation of peaks due to species of intermediary mass, is characteristic of mass spectra of catenanes.[4k]

Several unique byproducts that feature inter-threaded components could have arisen during the key double ring-closing metathesis, structures **A**–**C** in Figure 4. Byproduct **A** was anticipated as a result of a single templated intramolecular cross metathesis reaction between the diallyl **6** components of [3]pseudorotaxane **7**. However, we did not observe formation of such a species as determined by ^{1}H NMR spectroscopy (no terminal olefins) and MALDI-TOF-MS (no mass fragment at $m/z = 2748$, 1277, or 1214 corresponding to $[\mathbf{7}\text{–CH}_2\text{=CH}_2\text{–PF}_6]^+$, $[\text{Cu}\cdot\mathbf{6}_2\text{–CH}_2\text{=CH}_2]^+$, and $[\mathbf{6}_2\text{–CH}_2\text{=CH}_2\text{+H}]^+$, respectively). Two additional byproducts of interest could have arisen during the double ring-closing olefin metathesis of [3]pseudorotaxane **7**. A templated double cross-metathesis between two separate molecules of **6** (within **7**) could have occurred in two specific ways: that is, (1) to provide the simple ring-in-ring product **B** (not interlocked), and (2) to provide the racemic doubly interlocked [2]catenane product **C**. Neither of these byproducts were formed. Byproduct **B** was ruled out since demetallation released all noninterlocked components of **9** and no peak for the cyclic cross metathesis dimer of **6** (m/z: 1186 corresponding to $[\mathbf{6}_2\text{-}2(\text{CH}_2\text{=CH}_2)\text{+H}]^+$) was observed in the MALDI-TOF mass spectrum of the crude product. Byproduct **C** was ruled out since, under the MALDI-TOF-MS experimental conditions, we observed all species that are possible by a single fragmentary ring-opening of macrocycles containing an olefin. As can be seen in Figure 3, we did not observe a peak (again, m/z of 1186) for the cyclic cross metathesis dimer of **6** as would be expected if the doubly interlocked [2]catenane had been formed.

While we do not rule out byproduct **A** as a potential intermediate in the synthesis of **8**,[10] byproducts **B** and **C** were not formed. The resulting strain in the metal-complexed macrocycles of **B** and **C** (from **7**) would likely be too great, given the insufficient length of the flexible linker chains between the rigid segments, to allow a favorable conformation for macrocyclic ring-closure.

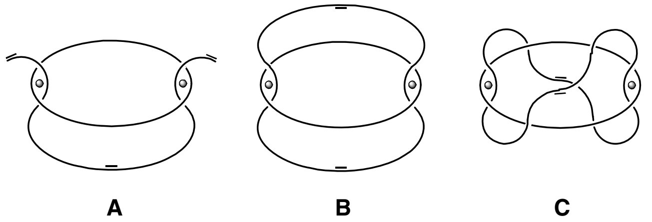


Fig. 4. Pictorial illustrations of possible byproducts arising from the key double ring-closing olefin metathesis.

In summary, the strategy presented here establishes a reasonably efficient approach to a [3]catenane via a double intramolecular ring-closing olefin metathesis reaction within a [3]pseudorotaxane. The yield of the one-pot, double ring-closing metathesis (71%) that creates the copper-complexed [3]catenane is among the highest reported yields to date for any process that creates a [3]catenane that consists of rings of all covalently bonded atoms.[11] The overall synthetic strategy is modular with respect to the template elements that enable the preorganized synthesis of the interlocked species as well as to the nature of the linkers between these elements. Upon modification or adoption of iterative sequences, this strategy may allow access to more elaborate interlocked oligomeric species and networks.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.03.012.

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