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Post-modification-induced supramolecular transformation of Hopf link to macrocycle

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ABSTRACT

Although supramolecular transformations have been emerged as a potent strategy for transitioning between various topologies, post-modification induced topological transformations have never been explored in the context of [2]catenane topologies. In this study, we present a novel supramolecular transformation between a Hopf link and a macrocycle, induced by the Diels–Alder click reaction. By strategically selecting the half-sandwich ruthenium binuclear fragment **B** as a rigid capping agent, we successfully integrated tetrazine moieties into the metalla[2]catenane structure. We demonstrated that the introduction of 2,5-norbornadiene (NBD) as an external stimulus allows for the transformation of the novel metalla[2]catenane, featuring reactive tetrazine sites, into the corresponding monomeric ring through post-modification for the first time. The synthetic results are corroborated by single-crystal X-ray diffraction analysis, ESI-TOF/MS, elemental analysis, and detailed solution-state NMR techniques.

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The synthesis of topologically complex knots, links, and entanglements has increasingly garnered attention in supramolecular chemistry over the past few decades [1–6]. Inspired by the profound relationship between topology and the functionality of molecular systems observed in nature, chemists have devoted significant efforts to harnessing topology to develop artificial molecular machines [7–12]. There has been a rapid rise in interest among scientists in mechanically interlocked structures composed of two or more interlocked rings, owing to their fascinating topological configurations and their potential applications as smart materials and nanoscale devices [13–21].

Among the various entities, [2]catenane, the simplest type of catenane with Hopf link topology, is particularly intriguing due to its unique topological features and properties [22–25]. A synthetic strategy that relies on component pre-orientation has been shown to be an effective method for constructing molecular [2]catenanes [26–28]. Sauvage and his colleagues pioneered the use of metal–ligand interactions through a metal-ion-templated approach to preorganize these components [29]. However, achieving the dynamic interconversion necessary for synthesizing [2]catenanes using metal-ion-templated assembly remains challenging. Self-assembly driven by various supramolecular interactions, including $\pi-\pi$ interactions, hydrogen bonds, and other weak secondary interactions, can serve as a significant driving force for catenation [30–35]. Compared to template methods, the self-assembly approach is more challenging to control due to the delicate nature of intermolecular interactions; however, it facilitates the realization of dynamic interconversion [36–44].

In addition to their intriguing structures and topological significance, [2]catenanes possess potential applications as smart materials, nanoscale devices, and molecular machines [45–52]. The stimuli-induced supramolecular transformations of [2]catenanes are crucial for achieving these functionalities and responsiveness. Over the past few decades, a variety of stimuli, including solvents, concentration changes, and guest molecules, have been effectively utilized to trigger the transformation processes of [2]catenanes [53–57]. Post-modification, which can be used to transform various initial self-assembled entities into new structures, has been rarely explored in the context of [2]catenane topologies.

The Diels–Alder (IEDDA) reaction between electron-rich dienophiles and electron-deficient tetrazines is considered a promising post-modification strategy, as it can generate desired products under mild conditions with minimal production of unwanted byproducts [58,59]. This reaction has been effectively

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employed to induce the supramolecular transformation of discrete supramolecular coordination complexes. Herein, a strategically chosen ligand 3,6-bis(4-pyridyl)-1,2,4,5-tetrazine (**L**) was synthesized and used as the bridge ligand. By utilizing ligand **L** as the linker and half-sandwich arene-Ru(II) binuclear fragments **B** as the rigid capping unit, a novel template-free ruthenium(II) metalla[2]catenane was realized. Moreover, taking advantage of the IEDDA reaction between these tetrazine moieties and electron-rich dienophiles, post-modification is shown to induce topological transformations from [2]catenanes to the corresponding component monomers.

We began our investigation into the potential of using IEDDA reactions as an effective method for triggering the transformation processes of [2]catenanes by synthesizing a metalla[2]catenane that incorporates tetrazine moieties. Given that the formation of metalla[2]catenanes featuring two identical interlocked rectangles is favored by π-π stacking and other non-covalent interactions that act as driving forces, we hypothesized that a binuclear building block length of approximately 7 Å would be suitable for generating two interlocked rings. Consequently, the treatment of the binuclear building block **B** with an equimolar amount of **L** resulted in the formation of metalla[2]catenanes **1** in a concentrated methanolic solution. When the reaction concentration exceeded 48.0 mmol/L (with respect to the Cp*Rh fragment), only one diffusion coefficient was observed in the DOSY NMR spectrum (Fig. S4 in Supporting information), indicating that the new self-assembled product was produced quantitatively.

The structure of the interlocked metalla[2]catenane **1** was unequivocally confirmed through single-crystal X-ray diffraction analysis. Single crystals of **1**, suitable for X-ray diffraction, were obtained with a yield of 91% by the diffusion of diethyl ether into a methanol solution of **1** over several days. The interlocked structural nature of **1** was verified upon structural refinement, which clearly illustrated the interlocked metalla[2]catenane (Fig. 1). The two metallarectangles in the refined X-ray crystal structure of **1** are mutually interpenetrated in a quadruple fashion. Strong π-π stacking interactions, observed in the range of 3.5–4.0 Å, occurred between the π-electron-rich thiophene moieties of **L1** from the two different macrocycles. Additionally, edge-to-face T-shaped C–H···π interactions were noted between one of the corner phenyl rings of the anthracene moiety and a corner phenyl ring of the naphthacenedione moiety, further stabilizing the interlocked structure. Thus, the π-π stacking and other weak interactions likely serve as the driving forces that lead to the preorientation of ligands **L**, facilitating the formation of the metalla[2]catenane. The ESI-MS spectrum of the interlocked **1** confirmed the $[M_4L_4]^{4+}$ composition, with a prominent signal at *m/z* 1575.453 ($[M\text{-}3OTf]^{3+}$; Fig. 2a). The

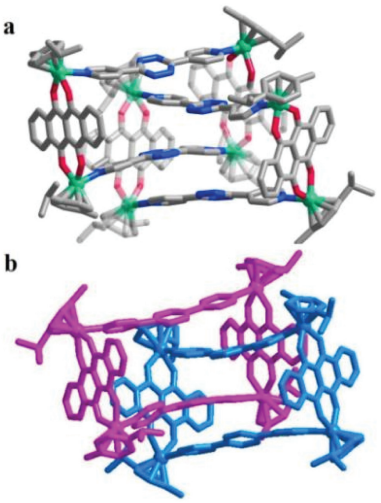


Fig. 1. Single-crystal X-ray structure of metalla[2]catenane **1**. Most hydrogen atoms, anions, solvent molecules, and disordered molecules are omitted for clarity (N, blue; O, red; C, gray; and Rh, green).

experimentally observed and theoretically calculated isotopic distributions showed excellent agreement. After determination of the solid-state molecular structure of **1**, relevant NMR spectroscopic experiments were carried out to further explore its behavior in solution (Fig. 3a). All ^{1}H NMR signal assignments were corroborated by ^{1}H–^{1}H COSY (Figs. S6 and S7 in Supporting information).

Recent investigations have demonstrated that coordination-driven self-assembled architectures provide an ideal platform for studying supramolecular transformations, primarily due to the inherently dynamic behavior of metal-ligand bonds and the weak interactions between subunits. In this study, we observed solvent-induced supramolecular transformations between metalla[2]catenane **1** and the corresponding monorectangle **2**. Upon dissolving crystals of metalla[2]catenane **1** in acetonitrile, the ^{1}H NMR spectral patterns of the solution changed. Electrospray ionization mass spectrometry (ESI-MS) supported the assignment of the monorectangle structure of **2** in acetonitrile solution, with a prominent signal at $m/z = 1144.612$ ($[\mathbf{2}\text{-}2OTf]^{2+}$), aligning well with the expected theoretical distribution (Fig. 2b).

To further investigate the interconversion between **1** and **2** induced by the solvent, a ^{1}H NMR titration experiment was conducted. Gradual addition of CD_3CN to a solution of complex **1** in CD_3OD facilitated the rapid conversion of complex **1** into **2**, as demonstrated by ^{1}H NMR spectroscopy. These results indi-

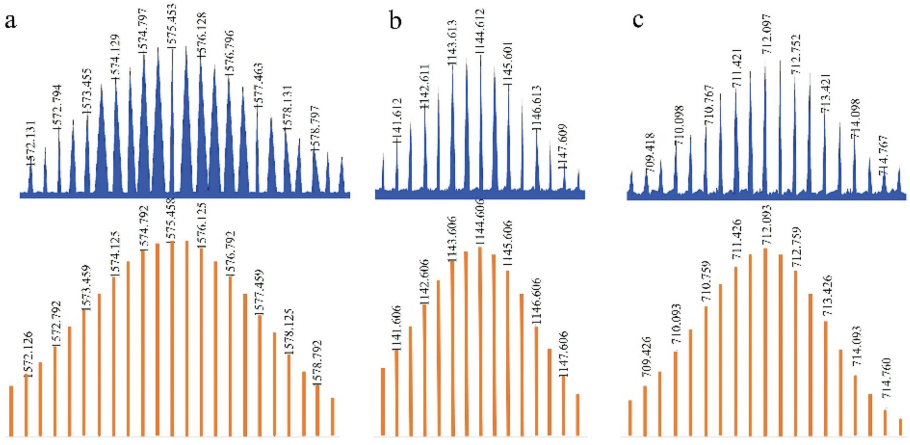


Fig. 2. Experimental (top, blue) and theoretical (bottom, pink) ESI-MS spectra of (a) $[\mathbf{1}\text{–}3OTf^-]^{3+}$, (b) $[\mathbf{2}\text{–}2OTf^-]^{2+}$ and (c) $[\mathbf{3}\text{–}3OTf^-]^{3+}$.

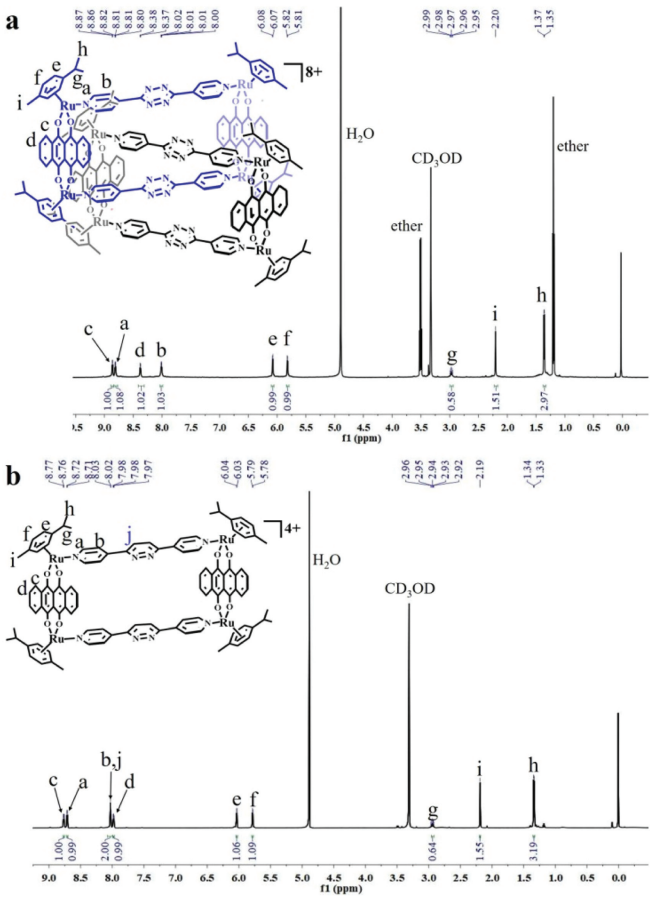
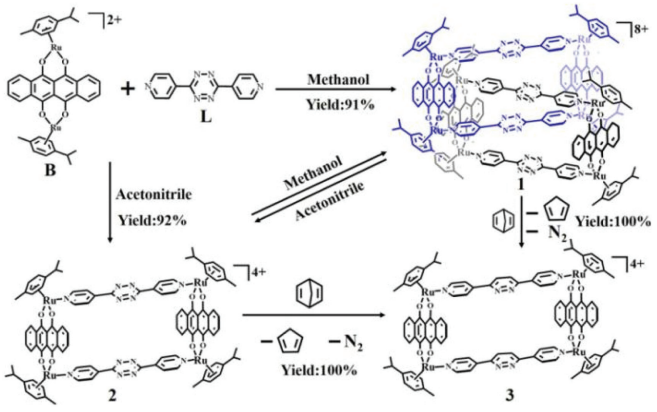


Fig. 3. ^{1}H NMR (600 MHz, CD_3OD, ppm) for (a) **1** and (b) **3**.



Scheme 1. Self-assembly of metalla[2]catenane and monorectangles and the topological transformation of metalla[2]catenane to monorectangles.

cate that the dynamic interconversion between metalla[2]catenane **1** and metallacycle **2** can be triggered by changes in solvent (Scheme 1). The ^{1}H NMR titration experiment revealed no transformation between the [2]catenane and the metallacycles solely through changes in concentration, suggesting that **1** remains stable in methanol solution.

The X-ray diffraction analysis unambiguously confirmed the formation of the monorectangle **2** (Fig. 4). Single-crystal X-ray crystallographic analysis revealed that the molecular structure of **2** is a single ring. Two di-Ru^{III} molecular clips are linked by two pyridyl ligands, thus forming a rectangle-like tetranuclear complex with the dimensions of 15.20 × 8.40 Å. Recorded NMR spectroscopic data

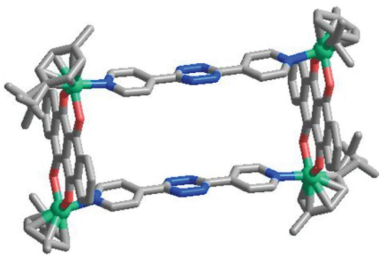


Fig. 4. Single-crystal X-ray structure of monorectangle **2**. Most hydrogen atoms, anions, solvent molecules, and disordered molecules are omitted for clarity (N, blue; O, red; C, gray; and Rh, green).

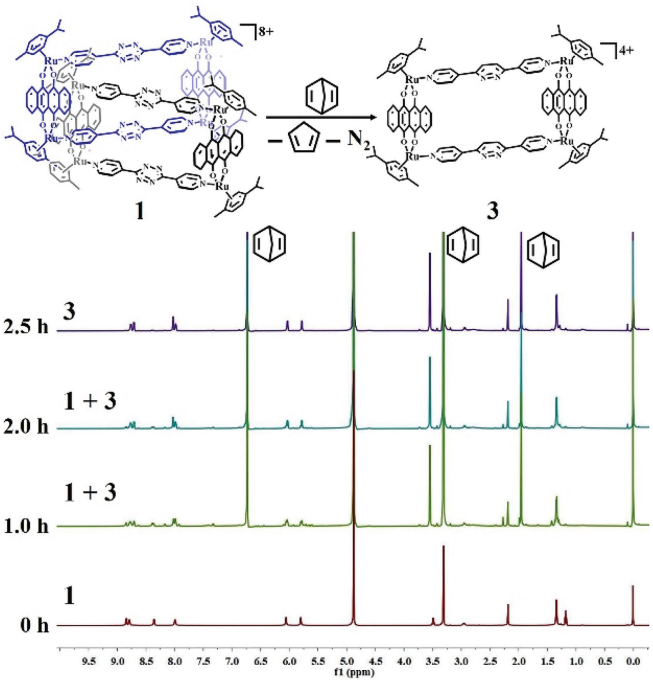


Fig. 5. *In situ* ^{1}H NMR monitoring of the reaction between metalla[2]catenane **1** and NBD (10 equiv. per tetrazine).

and elemental analysis confirmed the formation of **2**. The ^{1}H NMR spectrum of complex **2** exhibited two multiplets at δ 2.96 and 1.32, as well as a singlet at δ 2.19, which can be attributed to the protons of the Cp group. Moreover, the aromatic protons of **L** appeared at δ 8.72 and 8.25 ppm, while the protons of **B** resonated as two sets of multiplets at δ 8.76 and 7.97 ppm. The ^{1}H DOSY NMR spectra of **2** revealed a single diffusion coefficient for all aromatic and Cp proton signals, indicating that all resonances originate from a single assembly (Fig. S6).

The investigation was subsequently extended to explore the supramolecular transformation of metalla[2]catenanes induced by IEDDA reactions. Upon treating metalla[2]catenane **1** with NBD in methanol-d_4 at a concentration of 10 mmol/L, the ^{1}H NMR spectral patterns of the solution changed, revealing new proton resonances (Fig. 3b). Furthermore, the ESI-MS spectrum confirmed the metallacycle composition of the new product **3**, with a prominent signal at *m/z* 712.097 ([M-3OTf]$^{3+}$; Fig. 2c). The experimentally observed isotopic distribution agreed excellently with the theoretically calculated values.

To further investigate the interconversion between **1** and **3** induced by IEDDA reactions, a ^{1}H NMR monitoring experiment was conducted (Fig. 5). After the addition of ten equimolar amounts of NBD to a solution of **1** in methanol-d_4, the NMR data clearly demonstrated the gradual transformation of metalla[2]catenane **1**

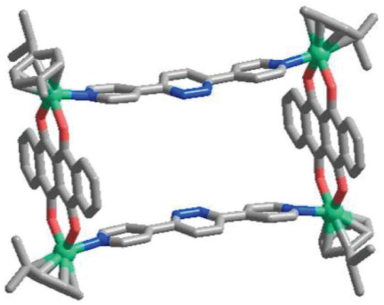


Fig. 6. Single-crystal X-ray structure of monorectangle **2**. Most hydrogen atoms, anions, solvent molecules, and disordered molecules are omitted for clarity (N, blue; O, red; C, gray; and Rh, green).

into the monorectangle **3**. As the reaction time increased, the signals corresponding to pyridine (H_a, H_b) and anthracene (H_c, H_d) shifted from 8.81, 8.01, 8.86, and 8.38 ppm to 8.71, 8.02, 8.76, and 7.98 ppm, respectively. Meanwhile, new proton resonances emerged, such as $\delta = 8.02$ ppm, which corresponded to pyridazine. The ^{1}H NMR spectra indicated that metalla[2]catenane **1** was completely transformed into monorectangle **3** after 2.5 h at 298 K. Additionally, upon adding NBD to a solution of rectangle **2** in CD_3CN, the NMR data showed a gradual transformation of rectangle **2** into monorectangle **3** over time (Fig. S10 in Supporting information).

We successfully obtained single crystals of compound **3** suitable for X-ray diffraction analyses by the slow diffusion of diethyl ether into a methanol solution of **3**. Single-crystal X-ray crystallographic analysis confirmed that **3** is a discrete tetranuclear metallarectangle with dimensions of 15.22×8.40 Å (Fig. 6). Compared to the pyridazine bridge ligand in **3**, the tetrazine ligand exhibits greater electron-donating behavior due to its higher electron density, resulting in stronger D-A stacking interactions between the tetrazine units and pyridine groups. This transformation is likely attributable to the comparatively weaker π-π stacking interactions of the pyridazine bridge ligand relative to those of the tetrazine ligand.

In conclusion, we successfully synthesized a novel metalla[2]catenane containing potentially reactive tetrazine sites by selecting the tetrazine-containing bridge ligand **L** as the linker and the half-sandwich ruthenium(II) dinuclear fragment **B** as a rigid capping unit. This metalla[2]catenane is stable in methanol solution, and no transformations occur between the [2]catenane and the metallacycles. However, dissolving crystals of metalla[2]catenane **1** in acetonitrile leads to its conversion into metallacycles. We observed solvent-induced linking and unlinking reactions of the metalla[2]catenane, with the dynamic interconversion between metalla[2]catenane **1** and metallacycle **2** being exclusively triggered by changes in solvent. Furthermore, the metalla[2]catenane was shown to undergo supramolecular structural transformations induced by rapid and efficient post-modification reactions, yielding the corresponding monorectangle. This demonstrated IEDDA reaction provides a valuable method for controlling intricate and adjustable topological transformations, offering new insights into the field of supramolecular transformation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Pan-Pan Hua: Writing – original draft, Data curation. **Hui-Jun Feng:** Writing – review & editing. **Shu-Ning Lan:** Investigation, Data curation. **Francisco Aznarez:** Supervision, Software. **Li-Fang Zhang:** Writing – review & editing.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.cclet.2024.110684.

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