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Dual Selectivity Expressed in [2+2+1] Dynamic Clipping of Unsymmetrical [2]Catenanes

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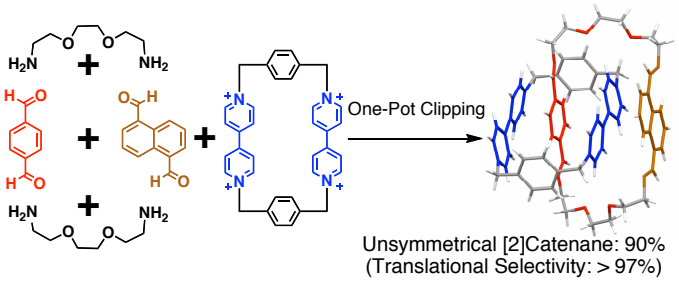
ABSTRACT

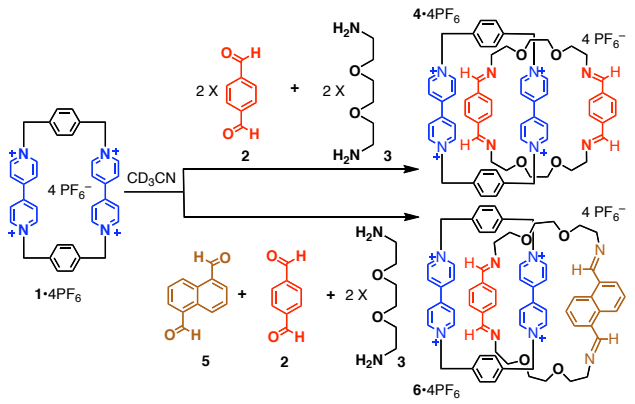


A π-templated dynamic [2+2+1] clipping protocol is established for the synthesis of [2]catenanes from two parts dialdehyde, two parts diamine and one part tetracationic cyclophane. It is further diversified for the selective formation of an unsymmetrical [2]catenane showing great translational selectivity by employing two different dialdehydes in a one-pot reaction. The dual selectivity and the dynamic nature are verified by ^{1}H NMR spectroscopy, X-ray single crystal structural studies and exchange experiments.

[2]Catenanes[1] have attracted much attention for their non-trivial topology and motor-like behavior at the nanoscale level.[2] In order to establish multi-stability, [2]catenanes have been desymmetrized by incorporating different recognition units in the interlocked ring components, giving rise to different translational conformations. A prerequisite for precise control of molecular motions is to achieve high translational selectivity between these conformations.[3] Although the synthesis of [2]catenanes has been substantially advanced with the advent of molecular recognition and self-assembly, it remains a challenging task to obtain unsymmetrical [2]catenanes with high translational selectivity, which requires the selection of appropriate recognition pairs and fitting assembly.[4] Prior examples of unsymmetrical catenane syntheses were based on an irreversible kinetic pathway through covalent bond formation.[5] Recent progress on reversible dynamic covalent chemistry (DCC) provides[6] a versatile approach for the synthesis of interlocked molecules. By virtue of thermodynamically controlled equilibria and templating effects,[7] the favorable product can be obtained in high yield from a multi-component system. One of the most widely used DCC reactions is reversible imine bond formation,[6,8] which has been adopted in a dynamic clipping protocol for the synthesis of numerous molecular

structures with increasing complexity.[8,9] This dynamic assembly protocol, although favorable for its simplicity, has not been demonstrated in the synthesis of unsymmetrical [2]catenanes. Here we report a π-templated [2+2+1] dynamic clipping of [2]catenanes using two parts dialdehyde, two parts diamine and one part of tetracationic cyclophane. Subsequently we have demonstrated its application in the selective formation of unsymmetrical [2]catenanes with high translational selectivity from a one-pot reaction involving two different dialdehyde precursors.

Scheme 1. Clipping of the Symmetric [2]Catenane **4**•4PF$_6$ and the Unsymmetrical [2]Catenane **6**•4PF$_6$



Recently it has been shown[8f] that the electron-deficient bipyridinium (BPY^{2+}) unit can template the formation of an imine-based cryptand host by a [3+2] dynamic clipping approach. This templated clipping strategy is validated in the assembly of [2]catenanes by a [2+2] macrocyclization. When dialdehyde **2**, diamine **3**, and a tetracationic cyclophane **1**•4PF$_6$[10] are mixed (Scheme 1) in a ratio of 2:2:1 in CD_3CN and stirred for 2 hours, a single species corresponding to [2]catenane **4**$^{4+}$ is formed, as indicated by ^{1}H NMR spectroscopy (Figure 1b). Two sets of the imine protons as well as the diiminobenzene (DIB) protons are observed, corresponding to their inside and alongside locations with respect to the tetracationic cyclophane. Characteristically, the inside DIB protons resonate at a high field around 4.1 ppm, as a result of being shielded by the surrounding cyclophane. The α- and β-protons of the BPY^{2+} unit concommitantly undergo upfield shifts when compared to the free cyclophane **1**$^{4+}$ (Figure 1a). Electrospray ionization mass spectrometry (ESI-MS) has identified a *m*/*z* peak at 651.2, corresponding to the doubly charged molecular ion after loss of two PF_6^- anions.

No [2]catenane is formed when **2** is replaced with 1,5-diformylnaphthalene (**5**). Instead a significant amount of insoluble polymeric species is formed. ^{1}H NMR spectroscopy and ESI-MS spectrum of the filtrate confirmed the absence of any catenane product (See Supporting Information). However, when equivalent **2** and **5** are mixed with diamine **3** (2 equiv) and cyclophane **1**$^{4+}$ (1 equiv) and stirred for 24 hours, a dominating species corresponding to the unsymmetrical [2]catenane **6**$^{4+}$ is observed, as confirmed by ^{1}H NMR spectroscopy (See Supporting Information). The symmetric [2]catenane **4**$^{4+}$ is also observed (~5%) in the equilibrated solution. Upon diffusing diisopropyl ether into the CD_3CN mixture, **6**$^{4+}$ is isolated as a yellow crystalline powder in 90% yield.[11] The well-resolved ^{1}H NMR spectrum of **6**$^{4+}$ (Figure 1c) indicates the presence of only one translational isomer, which can be unambiguously assigned to the conformation in which the DIB ring system is inside the cavity of the tetracationic cyclophane and the diiminonaphthalene (DINP) ring system sits alongside. The DIB protons resonate around4.0 ppm, consistent with being located inside the cavity. The DINP protons appear as a set of doublet, triplet and doublet signals at 8.5, 7.5 and 7.4 ppm, respectively. The absence of any high field doublets around 2–3 ppm, which is characteristic for the $H_{4/8}$ of the inside naphthalene ring system,[4] confirms the alongside location of the DINP ring system. To further determine if the spectrum is an averaged one from two fast exchanging isomers, variable temperature ^{1}H NMR experiments are conducted. As shown in Figure 1d, no new isomers appear at 233 K. The spectrum is consistent with the presence of one single isomer within the temperature range from 233 to 353 K (see Supporting Information), suggesting that the observed single resonance is not a result of site exchange and indeed the excellent translational selectivity is maintained throughout. Based on the detection limit of ^{1}H NMR spectroscopy, a selectivity greater than 97:3 can be estimated.

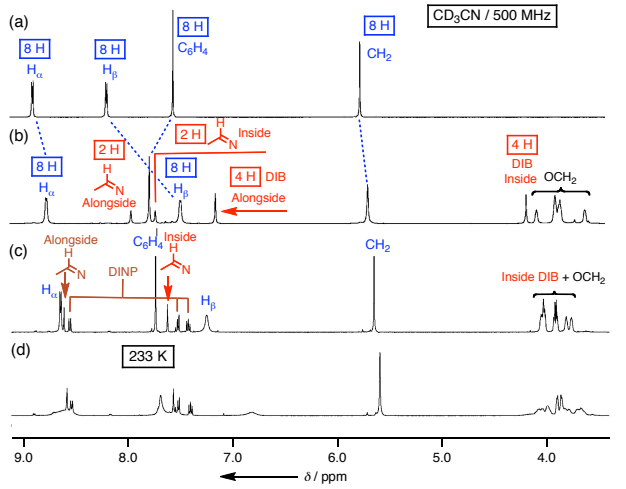


Figure 1. The ^{1}H NMR spectra of (a) **1**$^{4+}$ at 298 K, (b) **4**$^{4+}$ at 298 K, (c) **6**$^{4+}$ at 298 K and (d) **6**$^{4+}$ at 233 K.

A comparison of the single crystal X-ray structures[12] of these two [2]catenanes provides structural features that hint at the preferred formation of **6**$^{4+}$. As shown in Figure

2a, the solid state structure of $\mathbf{4}^{4+}$ contains two interlocking macrocycles, featured by alternating arrangement of π-surfaces with mean inter-plane separation around 3.4 Å. The imine bonds are almost coplanar with the conjugated phenylene ring in both DIB ring systems. The two imine protons of the inside DIB ring system adopt a *trans* conformation, while the outside imine protons are in a *cis* arrangement. The structure is stabilized by seven [C–H···O] hydrogen bonds[12] involving all four oxygen atoms on the ethylene glycol linkers. Noticeably, the centroid of the alongside DIB ring system is not aligned (Figure 2b) with the π-stacking axis. No intermolecular π-stacking is observed, presumably a consequence of weakened interactions due to the misalignment of π-surfaces. The solid state structure of the unsymmetrical [2]catenane $\mathbf{6}^{4+}$ confirms (Figure 2c and 2d) the translational selectivity, with the DIB ring system being included inside the cavity. Viewing along the π-stacking axis reveals (Figure 2d) a better overlap of the π-surfaces than that of $\mathbf{4}^{4+}$, suggesting a stronger alongside π-interaction between the DINP ring system and the BPY^{2+} unit. Correspondingly, intermolecular stacking is observed to give elongated π-stacks.[12] The four oxygen atoms on the ethylene glycol loops are placed in a geometry that is suitable to give up to eight [C–H···O] hydrogen bonds. It should be noted that even though the DIB and DINP ring systems are considerably more electron deficient than the oxylated π-donors such as hydroquinone or dioxynaphthalene,[13] the clipping still occurs efficiently. The strong collective [C–H···O] interactions in a molecular geometry with ideal preorganization presumably compensate for the weakened electronic interactions.

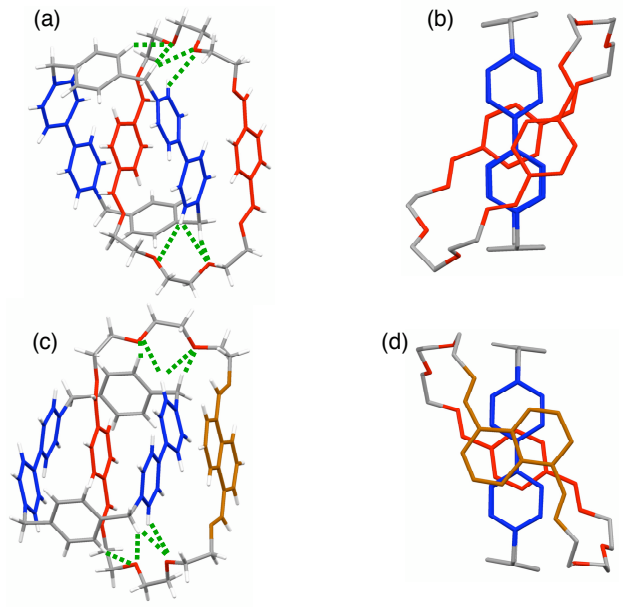


Figure 2. Stick representation of X-ray structures of (a) $\mathbf{4}^{4+}$ and (c) $\mathbf{6}^{4+}$ showing the [C–H···O] interactions (indicated by green dotted lines). (b) and (d) are views along the π-stacking directions showing the overlap of the π surfaces in $\mathbf{4}^{4+}$ and $\mathbf{6}^{4+}$. Solvent molecules and anions are omitted for clarity.

The selectivity in this dynamic clipping system is two-fold: the selective formation of an unsymmetrical [2]catenane as opposed to symmetric ones, and the translational selectivity expressed within the unsymmetrical [2]catenane. A balance between the inside and alongside interactions has to be fulfilled for such selectivity. It appears that the DIB ring system has stronger tendency than the DINP one for sitting inside the rigid tetracationic cyclophane, [14] probably a consequence of lesser steric hinderance — in the latter case, the imine groups directly conjugated onto the naphthalene ring system are rather space demanding when placed in the cavity of the tetracationic cyclophane. This is also suggested by the contrasting outcome of the two symmetric clipping reactions — the DINP-based one fails to give the corresponding symmetric [2]catenane. On the other hand, if placed alongside, the DINP ring system experiences less steric constraints from the tetracationic cyclophane. The large π-surface is suited for better stacking than the DIB ring system, which is confirmed by the comparison of the solid state structures of the two [2]catenanes (Figure 2b and 2d); the alongside DINP ring system is better aligned along the π-stacking axis than the DIB counterpart. The combined inside and alongside selectivities thus constitute the origin of the overall selectivity.

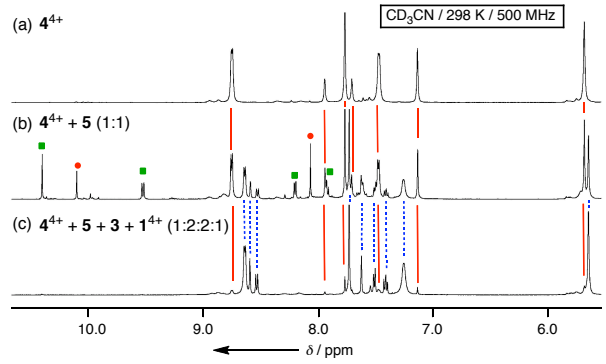


Figure 3. Exchange experiments monitored by ^{1}H NMR spectroscopy. The equilibrated solutions of (a) $\mathbf{4}^{4+}$, (b) after the addition of 1 equiv **5**, and (c) after the addition of **5**, **3**, and $\mathbf{1}^{4+}$ (2:2:1). The green squares and red dots indicate free **5** and **2** in the solution, respectively.

The thermodynamic nature of the [2]catenanes is verified by a few exchange experiments. Addition of **5** (1 equiv) to a pre-equilibrated CD_3CN solution containing symmetric [2]catenane $\mathbf{4}^{4+}$ (Figure 3a) results in the formation of unsymmetrical [2]catenane $\mathbf{6}^{4+}$ and free **2** that is displaced from $\mathbf{4}^{4+}$, as indicated by the ^{1}H NMR spectrum (Figure 3b). Similarly, addition of **2** (1 equiv) to a pre-equilibrated solution containing $\mathbf{6}^{4+}$ ends up with

the same spectrum as above, suggesting that the final equilibrium is irrelevant to the starting catenane, as long as the overall composition remains the same. The presence of excess dialdehyde **2** , however, drives the equilibrium towards $\mathbf{4}^{4+}$ at the expense of $\mathbf{6}^{4+}$. Thus another experiment is conducted to maintain the ideal stoichiometry. Upon addition of **5** (2 equiv), diamine **3** (2 equiv) and $\mathbf{1}^{4+}$ (1 equiv) to a pre-equilibrated CD_3CN solution containing $\mathbf{4}^{4+}$, $\mathbf{6}^{4+}$ is again generated as the dominating species (Figure 3c), confirming that the clipping is both dynamic and selective.

In conclusion, we present a dynamic clipping protocol that can be utilized for the highly selective formation of unsymmetrical [2]catenanes. The selectivity can be understood by the difference in the tendency of the DIB or DINP ring systems stacking inside or outside of a π-accepting cyclophane. This system coins a proof of principle in the asymmetric assembly of interlocked structures using DCC. The concise approach will not only enable a rapid screening of a library of dialdehyde precursors for the clipping reaction, but also opens up a window for the design and synthesis of more complex molecular systems.

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Supporting Information Available: Experimental details and X-ray crystallographic data of **5**, **4**•4PF_6 and **6**•4PF_6. Variable temperature ^{1}H NMR spectra of **6**•4PF_6. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) This is a cominbed yield taking into acount of $\mathbf{4}^{4+}$ (2%) and $\mathbf{1}^{4+}$ (3%) that cocrystallize with $\mathbf{6}^{4+}$.

(12) See Supporting Information for crystallographic information.

(13) In MeCN, the 1,5-dioxynaphthalene donor shows a preference in binding to **1**•4PF_6 over 1,4-dioxybenzene. See: Ashton, P. R.; Blower, M.; Philp, D.; Spencer, N.; Stoddart, J. F. Tolley, M. S.; Ballardini, R.; Ciao, M.; Balzani, V.; Gandolfi, M. T.; Prodi, L.; McLean C. H. *New. J. Chem.* **1993**, *17*, 689-695.

(14) DIB or DINP derivatives were synthesized by the condensation of either **2** or **5** with 2 equiv of *N*-Boc-2,2'-(ethylenedioxy)diethylamine, and subjected to binding studies towards $\mathbf{1}^{4+}$. For the DIB derivative, the binding event is slow on the ^{1}H NMR time scale and the binding constant is determined to be around 6.0 M^{-1} by integration. On the other hand, the DINP derivative doesn't show any binding towards $\mathbf{1}^{4+}$. More details will be published elsewhere.