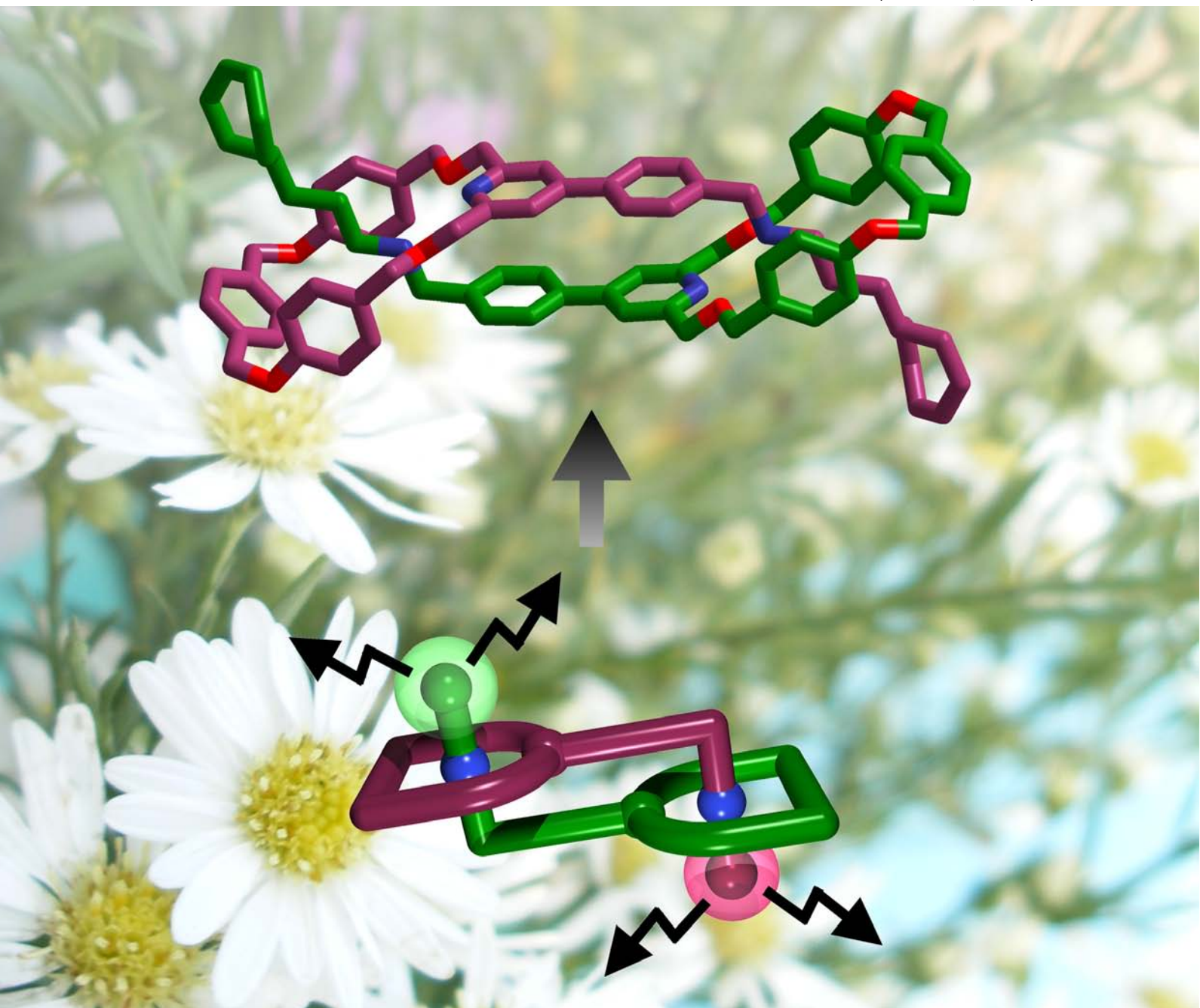


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Capturing a [c]daisy chain using the threading-followed-by-swelling approach

Capturing a [c2]daisy chain using the threading-followed-by-swelling approach†

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We have used the “threading-followed-by-swelling” approach to fix a daisy chain structure in solution, leading to the isolation of a captured [c2]daisy chain in 77% yield.

Interlocked molecules such as rotaxanes and catenanes have potential applicability as molecular actuators and switches within mesoscale molecular electronics devices.¹ Interest in extending their degree of mechanical interlocking and function into macromolecules has led to the development of a range of polyrotaxanes and polycatenanes, either through the polymerization of interlocked monomers or the stoppering of poly-pseudorotaxane complexes.² In the past decade or so, attempts have been made to construct linear and cyclic daisy chain-like supramolecular structures in both interwoven and interlocked forms because their unique molecular structures resemble prototypical molecular actuators and muscles.³ Because of entropic factors, however, [c2]daisy chains have usually predominated in solution.^{3e} Intuitively, the propensity of a pair of hermaphroditic monomers to form a [c2]daisy chain will be abated if the host and guest components are aligned orthogonally in their complex and are linked together (*i.e.*, within each monomer) through an inflexible spacer. In such a configuration, we might expect higher-order cyclic oligomers, such as [c3]- and [c4]daisy chains, to become predominant species in solution (Fig. 1). Herein, we report the preparation of an hermaphroditic daisy chain monomer comprising a macrocycle, a dibenzylammonium (DBA⁺) ion, and a dialkenylcyclopropane end group. Using the “threading-followed-by-swelling” approach,⁴ we heated a solution of the monomer to fix the daisy chain structure through efficient swelling of its reactive terminal groups to form cycloheptadiene stoppers, leading to isolation of—disappointingly—the captured [c2]daisy chain, albeit in a gratifyingly high yield of 77%.

Previously, we reported that the oxygen-deficient macrocycle **1** complexes DBA⁺ ions with high affinity in low-polarity solvents (Scheme 1).⁵ To obtain a symmetrical hermaphroditic daisy chain monomer—one that would not form

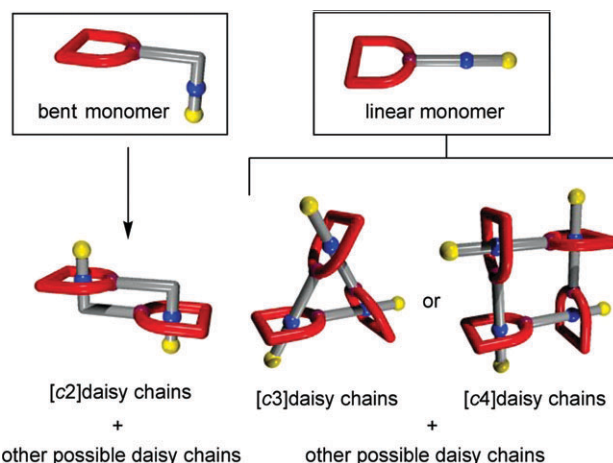
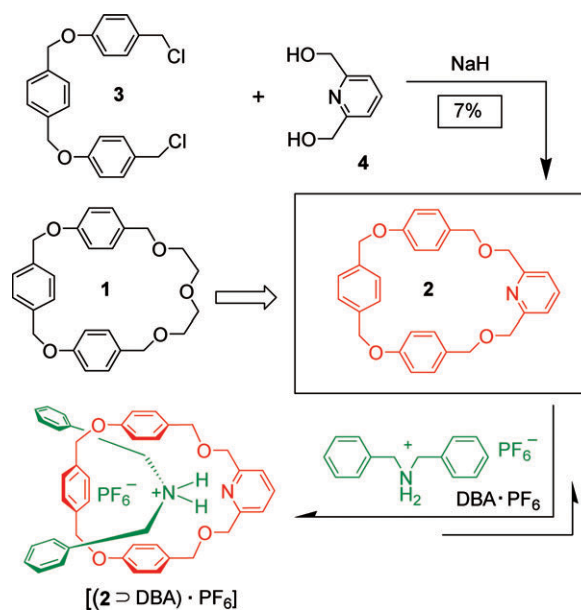


Fig. 1 Cartoon representation of the generation of higher-order cyclic daisy chains from a rigid linear monomer containing orthogonally complexing host and guest units.

diastereoisomeric daisy chain oligomers—we replaced the central diethylene ether motif of the macrocycle **1** with a pyridyl unit to allow substitution of a secondary ammonium



Scheme 1

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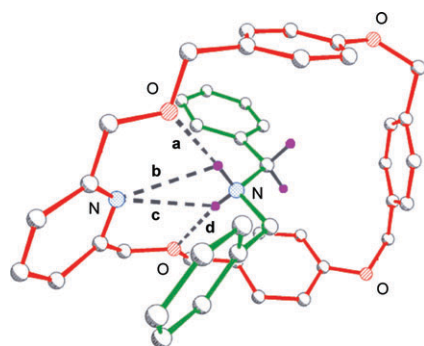


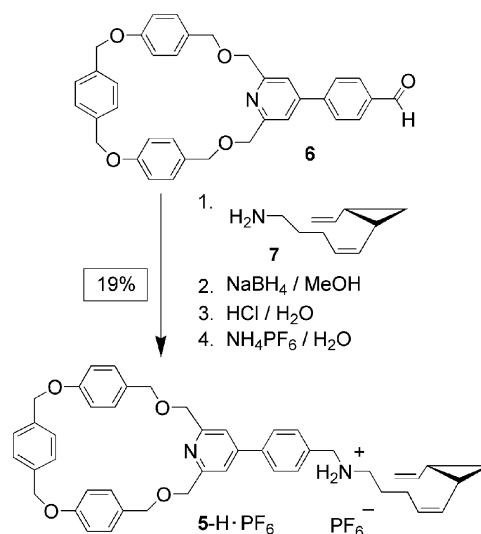
Fig. 2 Ball-and-stick representation of the solid state structure of the [2]pseudorotaxane-like complex $[2\supset\text{DBA}]^+$. Hydrogen bonding geometries, $\text{X}\cdots\text{N}$, $\text{X}\cdots\text{H}$ [\AA], and $\text{N-H}\cdots\text{X}$ [$^\circ$]: (a) 2.95, 2.05, 171.0; (b) 3.07, 2.66, 107.7; (c) 3.07, 2.64, 113.0; (d) 2.89, 2.07, 172.1.

ion at the 4-position; macrocyclization of the dichloride **3** and diol **4** gave the macrocycle **2** in 7% yield.

The ^1H NMR spectrum of an equimolar mixture of macrocycle **2** and $\text{DBA}\cdot\text{PF}_6$ in CD_3CN (10 mM) displays three sets of resonances: one set for the unthreaded macrocycle **2**, one for unthreaded $\text{DBA}\cdot\text{PF}_6$, and one for the 1 : 1 complex formed between macrocycle **2** and the DBA^+ ion (see the ESI †). Because the shifts in the signals of the complex formed between macrocycle **2** and DBA^+ are similar to those observed for the pseudorotaxane formed between **1** and DBA^+ , we suspected that the [2]pseudorotaxane-like complex $[2\supset\text{DBA}]^+$ formed in solution (Scheme 1).⁵ Using a single-point method,⁶ we determined the association constants (K_a) for this system in CD_3CN and CD_3NO_2 to be 40 and 770 M^{-1} , respectively. The binding affinity of macrocycle **2** toward the DBA^+ ion is substantially weaker than that of macrocycle **1**, possibly because of the reduced number of (or improperly positioned) lone pairs of electrons in the pyridine unit of **2** relative to those in the more-flexible diethylene oxide motif of **1**.⁷

Following vapor diffusion of isopropyl ether into a CH_3CN solution containing a 1 : 1 mixture of macrocycle **2** and $\text{DBA}\cdot\text{PF}_6$, we obtained single crystals that were suitable for X-ray crystallographic analysis, which revealed the [2]pseudorotaxane geometry of $[2\supset\text{DBA}]^+$ in the solid state (Fig. 2).⁸ \ddagger The presence of $[\text{N}^+-\text{H}\cdots\text{O}]$ and $[\text{N}^+-\text{H}\cdots\text{N}]$ ⁹ hydrogen bonds between the NH_2^+ center and pyridyl nitrogen atom and its adjacent oxygen atoms led us to hypothesize that an hermaphroditic daisy chain monomer derived from **2** might favor aggregation in a linear supramolecular structure because the pyridyl unit of the macrocycle would prefer to position its lone pair of electrons perpendicular to the orientation of the thread-like NH_2^+ unit to maintain these favorable hydrogen bonds.¹⁰ Our hope was that the structural rigidity of the hermaphroditic monomer would be sufficient to retard the formation of the entropically favored $[c2]$ daisy chain such that higher-order daisy chains would be generated in solution. Thus, we synthesized the hermaphroditic daisy chain monomer $5\text{-H}\cdot\text{PF}_6$.

To avoid unnecessary complications arising from stereoisomeric mixtures of daisy chains, we employed an optically pure dialkenylcyclopropane as the terminal swellable unit. In



Scheme 2 Synthesis of the hermaphroditic daisy chain monomer $5\text{-H}\cdot\text{PF}_6$.

contrast to our previously reported swelled-rotaxane synthesis,⁴ where we constructed the dialkenylcyclopropane motif in the final step, here we found that the chiral amine **7** was reasonably stable under ambient conditions so that we could perform the condensation (with aldehyde **6**), reduction, acidification, and ion exchange steps to give the desired hermaphroditic daisy chain monomer $5\text{-H}\cdot\text{PF}_6$ (Scheme 2).

The ^1H NMR spectrum of monomer $5\text{-H}\cdot\text{PF}_6$ in CD_3CN at room temperature displayed relatively broad resonances, which suggested the existence of intermolecular interactions between the monomers, most likely the formation of daisy chains. Heating this solution at 323 K and monitoring it using ^1H NMR spectroscopy indicated the gradual consumption of the signals of the putative supramolecular daisy chains and the concomitant rise in the intensities of the signals of the possible captured molecular daisy chains (Fig. 3). Subsequent ion exchange and chromatography of the reaction products provided the $[c2]$ daisy chain $8\text{-2H}\cdot 2\text{PF}_6$ in 77% yield (Scheme 3).¹¹

We grew single crystals suitable for X-ray crystallography by slowly evaporating a CD_3CN solution of $8\text{-2H}\cdot 2\text{PF}_6$. X-Ray crystallographic analysis¹² \ddagger of $8\text{-2H}\cdot 2\text{PF}_6$ revealed the $[c2]$ daisy chain structure stabilized by $[\text{N}^+-\text{H}\cdots\text{O}]$ and $[\text{N}^+-\text{H}\cdots\text{N}]$ hydrogen bonds (Fig. 4).¹³ Thus, the hermaphroditic monomer $8\text{-2H}\cdot 2\text{PF}_6$ was not sufficiently rigid to avoid the formation of the $[c2]$ daisy chain. We suspect that the structural flexibility of the $\text{ArCH}_2\text{NH}_2^+$ and $\text{OCH}_2(\text{C}_6\text{H}_3\text{N})\text{CH}_2\text{O}$ components of the hermaphroditic monomer was sufficient to deviate its molecular structure from linear upon complexation so that, once again, the entropically favored $[c2]$ daisy chain predominated.

We have demonstrated that macrocycle **2** recognizes DBA^+ ions with reasonable affinity and is capable of being derivatized into symmetrically monosubstituted compounds, increasing its potential for use as an anchor for appending such complexes onto the surfaces of solid supports or for building complicated supermolecules. Although the application of this threading-followed-by-swelling approach to the

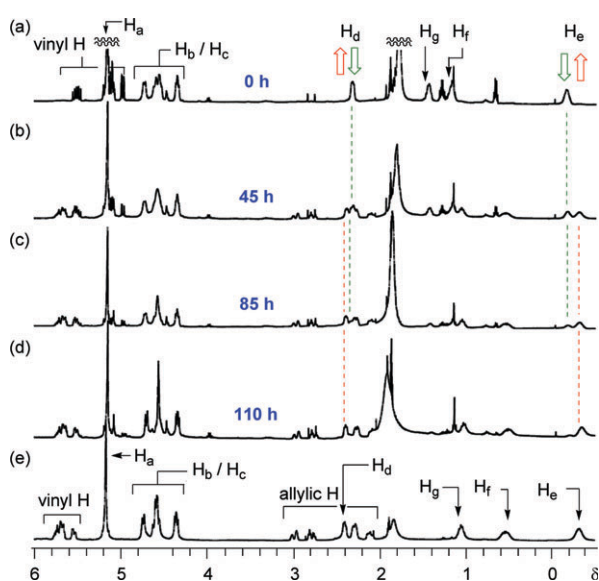
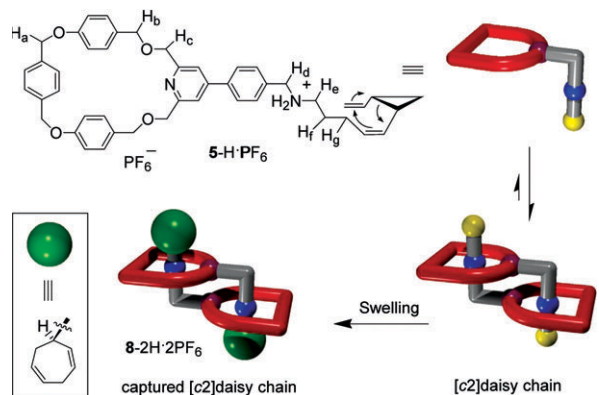


Fig. 3 Partial ^1H NMR spectra [400 MHz, $\text{CDCl}_3\text{-CD}_3\text{CN}$ (10 : 1), 323 K] displaying (a–d) the formation of the [c2]daisy chain **8-2H·2PF₆** from the monomer **5-H·PF₆** over time—(a) 0, (b) 45, (c) 85, and (d) 110 h—and (e) the purified **8-2H·2PF₆**.



Scheme 3 Fixing the [c2]daisy chain using the swelling approach.

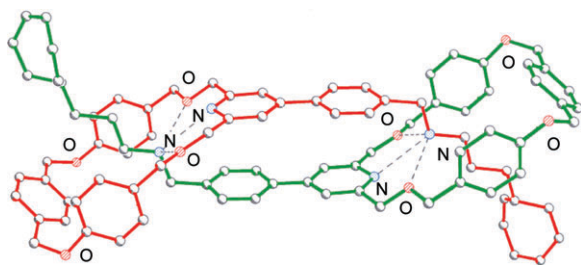


Fig. 4 Ball-and-stick representation of the solid state structure of the [c2]daisy chain [**8-2H**] $^{2+}$.

successful preparation of higher-order daisy chains will require the design of even-more-rigid hermaphroditic monomers, our efficient synthesis of this captured [c2]daisy chain suggests that this swelling protocol will be a useful means of fixing polymeric daisy chains.

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Notes and references

‡ CCDC 664527 and 664528 for **8-2H·2PF₆** and [**2**⊃DBA]·PF₆ respectively. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b716331b

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- Crystal data for [**2**⊃DBA]·PF₆: [$\text{C}_{43}\text{H}_{43}\text{O}_4\text{N}_2$][PF₆]; $M_r = 796.76$; orthorhombic; space group $P2_12_12_1$; $a = 12.50690(10)$; $b = 17.0522(2)$; $c = 18.6392(2)$ Å; $V = 3975.19(7)$ Å³; $\rho_{\text{calcd}} = 1.331$ g cm⁻³; $\mu(\text{MoK}\alpha) = 0.142$ mm⁻¹; $T = 295(2)$ K; colorless plates; 9055 independent measured reflections; F^2 refinement; $R_1 = 0.0546$; $wR_2 = 0.1510$.
- In this case, the [N $^+$ -H \cdots N] hydrogen bonds are relatively weak, as indicated by their longer bond lengths and smaller bond angles.
- The two phenolic rings sandwich the highlighted methylene protons adjacent to the NH₂ $^+$ center at distances (C \cdots phenolic ring centroid) of 3.53 and 3.66 Å, respectively, which agrees well with our previous computational finding (see ref. 5b) that such complexes might be stabilized partially by [N $^+$ C-H \cdots π] interactions. This arrangement explains the large upfield shifts of these protons in the NMR spectra.
- No higher-order cyclic daisy chains were observed in the crude product analyzed using electrospray mass spectrometry.
- Crystal data for **8-2H·2PF₆**: [$\text{C}_{16}\text{H}_{49}\text{O}_4\text{N}_2\cdot 4\text{CHCl}_3$][PF₆]; $M_r = 1315.31$; triclinic; space group $P1$; $a = 12.8645(4)$; $b = 13.4307(3)$; $c = 18.2973(5)$ Å; $V = 3010.00(14)$ Å³; $\rho_{\text{calcd}} = 1.451$ g cm⁻³; $\mu(\text{MoK}\alpha) = 0.640$ mm⁻¹; $T = 295(2)$ K; colorless cubes; 13743 independent measured reflections; F^2 refinement; $R_1 = 0.1094$; $wR_2 = 0.2561$.
- The phenyl and pyridyl rings in the solid state structure of [**8-2H**] $^{2+}$ were elegantly π -stacked with a centroid-to-centroid distance of 3.6 Å.