Supramolecular chemistry explores the effects of non-covalent interactions on the self-organization of matter.\cite{1} One strand of supramolecular enquiry has led to the creation of a variety of structurally and topologically nontrivial mechanically interlocked molecules.\cite{2} In the pursuit of deepening the complexity of such structures we report herein the formation of a new class of mechanically interlocked molecules in a system of three-dimensional tetrahedral catenanes.

Three distinct reversible processes were used in parallel to enable the formation of metal–organic tetrahedral polycatenanes, namely imine bond formation,\cite{20-23} metal–ligand coordination,\cite{24} and donor–acceptor interactions.\cite{25} A tetrahedral cage $M_{6}L_{6}$ (Scheme 1)\cite{26} was prepared through the reaction of a suspension (owing to poor solubility) of NDI diamine (6 equiv) with 2-formylpyridine (12 equiv) and iron(II) bis(trifluoromethane)sulfonimide (4 equiv) in acetonitrile.\cite{27}

This discrete metallosupramolecular architecture, capable of reversible catenation with an organic macrocycle, was designed to provide a pathway to polycatenated species.\cite{28} NDI moieties have been widely used in the self-assembly of mechanically interlocked molecules because of their planar, electron-poor aromatic surfaces, which engender favorable aromatic donor–acceptor interactions.\cite{29} A dynamic combinatorial library (DCL) of polycatenated cages was thus formed by allowing equilibration of the coordinatively dynamic $M_{6}L_{6}$ tetrahedral cage in the presence of an excess of bis-1,5-(dinaphtho)-[38]crown-10 (B; Scheme 1).\cite{30,31} 1H NMR analysis of equilibrated DCLs revealed the binding of B to the cage to be best described by a non-cooperative model,\cite{32} yielding a crown ether to cage-incorporated NDI binding constant of $794 \pm 34$ L mol$^{-1}$. Controlling crown ether and cage concentrations was found to determine the constitution of the library, and allowed the preparation of the fully-saturated tetrahedral $[7]$catenane.\cite{33}

The 1H NMR spectrum of cage A (Figure 1b) is consistent with the presence of a mixture of diastereomers with $T$, $S$, and $C_{3}$ point symmetries in solution, as has been previously observed for analogous cages.\cite{34} The superposition of diastereomer 1H resonances lead to broadened and overlapping signals, giving the overall appearance of a $T$-symmetric complex. The expected $M_{6}L_{6}$ type structure was confirmed by ESI-MS, COSY, and NOESY NMR spectroscopy (see Supporting Information).

For A to be catenated by B, we hypothesized a decoordination–threading–re-coordination mechanism to occur at the pyridylime metal chelate linkages (Supporting Information, Figure S11). An analogous mechanism is thought to operate in similar supramolecular hosts during the encapsulation of guests with larger radii than the hosts’ pores.\cite{35}

To investigate cage/crown ether binding, an excess of B (10 equiv) was allowed to equilibrate with A (1 equiv, Figure 1c); a minimum of 12 h was found necessary for equilibration (see the Supporting Information). Crown ether signals corresponding to catenation around an NDI axle of cage A were observed. The exchange between free and bound crown ether was observed to be slow on the NMR timescale at 298 K as peaks for the catenated complexes appeared as new resonances and did not shift with changes in crown ether concentration. The 1H resonances of bound crown ether molecules (Figure 1c, peaks H$^{'}, H_2^{'},$ and H$^{'})$ appeared upfield of resonances attributed to free crown ether (peaks H$^{'}, H_2^{'},$ and H$^{'})$ owing to the close proximity of the shielding aromatic NDI.\cite{36} We attribute the broadening of the 1H resonances of cage A in the DCL to loss of symmetry, with the exception of the new NDI peak (peak H$^{(10)}$ in Figure 1c). The NDI resonance (H$^{(10)}$), a singlet at 8.76 ppm in A, split into two signals in the DCL, one encompassing all free NDI binding sites (H$^{(10)}$ at 8.70 ppm and one assigned to all crown ether-bound NDI s (H$^{(10)}$)), the latter signal being split significantly upfield at 8.22 ppm. This peak was integrated relative to the resonances H$^{'}$, H$^{'}_2$, and H$^{'}$ of bound crown ether to confirm the expected one-to-one stoichiometry. Variable-temperature 1H NMR experiments on the DCL showed only small changes to line shapes and resonance shifts; however, specific catenated species and topological isomers of AB$_2$, AB$_3$, and AB$_4$ remained indistinguishable. In an attempt to drive the
DCL to the fully saturated [7]catenane, AB₆, the maximum amount of B soluble in CD₃CN/CDCl₃ 1:1 v/v, (38 equiv) was added to A and the mixture was allowed to equilibrate. ¹H NMR spectroscopy (Figure 1d) showed that all NDIs of cage A were threaded through a crown ether, and that the library had only a single member, the saturated [7]catenane AB₆.

NOESY analysis was consistent with the expected catedent motif, showing close contact between the bound NDI resonance and the bound macrocycle resonances. Diffusion-ordered spectroscopy (DOSY) was used to examine the constitution of a DCL made with 10 equivalents of B. The ¹H DOSY clearly distinguished two crown ether environments (Figure 2). Peaks corresponding to free crown ether B were observed at a diffusion coefficient of log(D) = 9.1, while all other resonances were observed at a coefficient of log(D) = 9.6. This second group of resonances includes peaks corresponding to all cage resonances as well as all of the resonances attributed to bound crown ether B. This observation highlights the tight binding between crown ether and cage, as would be expected in catedent structures. Despite the approximate 50% range in mass between catedent DCL constituents, polycatenation leads to an insufficient increase in radii to facilitate their separation in the diffusion dimension. Using the Stokes–Einstein equation, the above diffusion coefficients correspond to hydrodynamic radii of

![Scheme 1](image)

**Figure 1.** Partial ¹H NMR spectra (400 MHz, CD₃CN/CDCl₃ 1:1 v/v, 298 K) of a) crown ether B, b) cage A, c) a DCL formed following the mixture of A (5.4 x 10⁻⁴ M, 1 equiv) and B (10 equiv) after 12 h, and d) the [7]catenane obtained by the addition of B (38 equiv) to A (1 equiv) after 12 h. Signals H⁺, H⁻, and H⁺ are from crown ether protons threaded around an NDI, and peak H₁⁰⁺ is the corresponding catedent NDI proton. Peak H₁⁰⁻ corresponds to a noncatedent NDI edge of a cage. All other protons are assigned as indicated in Scheme 1.

![Figure 2](image)

**Figure 2.** DOSY spectrum (500 MHz, CD₃CN/CDCl₃ 1:1 v/v, 298 K) of a 1:10 cage/crown ether mixture.
6.2 Å and 19.7 Å for the free crown ether and the cage-crown ether adducts, respectively, which is in good agreement with the calculated radii (based on molecular-mechanics-minimized structures) of 7.4 Å and 23 Å respectively (see the Supporting Information). In a control experiment, 10 equivalents of an acyclic congener of B, 1,5-bis[2-(2-hydroxyethoxy)ethoxy]naphthalene, were added to the cage under identical conditions to crown ether/cage DCL formation. No interaction with A could be observed by 1H NMR spectroscopy (see the Supporting Information for all experimental and analytical details of polycatenane DCL experiments and the control study).

The electrospray Fourier-transform ion-cyclotron-resonance (ESI-FTICR) mass spectrum of A (Figure 3a) exhibited a signal at m/z 612 for the intact cage in its 8+ charge state. Isotope pattern analysis revealed a superposition with an [MLC]1+ fragment (peak spacing of 1/4 amu) which grew in at the expense of the [MLC]6+ parent ion (peak spacing of 1/8 amu) in an infrared multiphoton dissociation (IRMPD) tandem MS experiment (Figure 3a, insets), in which the mass-selected parent ion was irradiated with a CO2 laser at 10.6 μm wavelength. This dissociation was driven by charge repulsion and distributed the charges of the parent ion evenly over two fragments of identical size.17 After equilibration of A in the presence of B (1:10 ratio, respectively), the mass spectrum exhibited signals for the expected adducts [MLC]n+ (n = 0–6 and C = catenated crown ether), which were superimposed upon the corresponding [MLC]n+ ions for even values of n. Adducts carrying seven or eight crown ethers were also observed, indicating that unspecific binding can occur in the gas phase. Measurements of the control experiments with cage A and the acyclic naphthalene congener of B further confirmed non-specific binding to be possible in the gas phase, whereas no complexes between these two compounds were observed in solution. These observations raised questions as to whether the [MLC]n+ adducts with n ≤ 6 necessarily involve catenation, or whether these adducts could also result from nonspecific binding.

Confirmation of the specific formation of catenated complexes for [MLC]n+ with n = 1–6 came from IRMPD experiments. The fragmentation pathways for [MLC]n+ are indicated by the arrows in Figure 3c. [MLC]4+ fragmented preferentially into two identical [MLC]2+ fragments, which further decomposed by crown ether losses and the formation of [MLC2]+ and [MLC]4+. Competing with this fragmentation was the loss of one crown ether to yield [MLC]3+. In contrast, the dissociation of [MLC]3+ into the analogous [MLC]3+ and [MLC]4+ fragments was not observed, the latter of which would appear at an m/z higher than that of the parent ion (Figure 3d). Instead, the loss of the non-specifically bound crown ether was the only initial reaction of [MLC]3+, which formed [MLC]2+; the consecutive fragmentation of which explained all other fragments seen in the IRMPD spectrum of [MLC]3+. This observation indicated that the crown ether loss from [MLC]3+ occurred at significantly lower internal energies than that from [MLC]4+. It can be concluded from this analysis that the seventh crown ether is non-specifically bound in [MLC]3+ and that the major fraction of the [MLC]3+ ions have an intact tetrahedral structure with all six crown ether molecules threaded.

1H NMR spectroscopy was used to monitor speciation at increasing concentrations of crown ether B. As no one species of (poly)catenated cage could be distinguished (and thus quantified) owing to the overlap of signals, only information about the average degree of catenation could be obtained.

The fraction of bound NDI was calculated for several equilibrated samples with increasing crown ether concentration and plotted against crown ether concentration (Figure 4; for spectra, see the Supporting Information, Figure S26). The obtained binding isotherm fitted well to a one-to-one binding model, which assumes no cooperativity between the possible six binding events per cage. Our rationalization for this non-cooperative behavior is that cage A is spacious enough for the threading of 6 crown ether molecules, with little steric hindrance between bound crown ether molecules. This hypothesis was validated by geometrical information obtained from a molecular model of AB6 (see Supporting Information). An intrinsic binding constant for the NDI-crown ether interaction K_{chem} = 794 ± 34 L mol⁻¹ was thus determined and found to be consistent with reported studies.18

Assuming non-cooperative behavior, binding constants for the individual binding events of six consecutive crown ether molecules on to one cage could be calculated, taking into account the statistical factors.19 On the basis of these values it was possible to calculate and plot the fraction of each of the different AB₆ adducts as a function of crown ether concentration (Figure 4). To test the validity of our assumption of non-cooperativity, we calculated how the degree of
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