MOLECULAR TOPOLOGY

Star-crossed self-assembly

Interwoven supramolecular structures are often held up as examples of beauty in chemistry, but these assemblies can be fragile depending on the environments they are exposed to. Post-assembly covalent modification can, however, trap them in robust molecular form, and a triply entwined [2]catenane is one of the most sophisticated examples so far.

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Progress in the field of metal-templated self-assembly has made it possible to design and build supramolecular architectures with increasingly complex structures and topologies[1,2]. As well as the synthetic challenges and aesthetic appeal associated with such structures, current activities in this area are also driven by the desire to produce functional systems. This can be achieved in a number of different ways, such as through the incorporation of reactive sites or by building redox activity or photoswitchability into the resulting assemblies.

The reversible nature of intermolecular interactions such as hydrogen bonding, π–π-stacking and metal coordination allows for, in principle, very high yields of complex supramolecular architectures from relatively small (and simple) molecular building blocks. Such thermodynamically driven non-covalent approaches are in stark contrast with early syntheses of interlocked structures, which were based on statistically

controlled covalent protocols that resulted in poor yields[2]. Nevertheless, there is a downside to the inherent reversibility of the attractive interactions between the subcomponents of a self-assembled structure in that the stability of a system is not guaranteed when it is taken out of the environment in which it was formed.

A simple way to dismantle self-assembled structures that are based on metal cations and organic ligands is to dilute the system, thereby causing the position of the equilibrium to shift towards the side of the reactants rather than the product. Kinetic effects can help to stabilize self-assembled architectures from degradation under these circumstances, but problems arise when removal of the metal cations is desired or the complex is exposed to harsh conditions such as high temperatures, strong acids or bases, competing donors or other metal cations. In order to solve this dilemma, a few strategies have been developed. Fujita and co-workers have shown, for example, that coordination

bonds to kinetically stable platinum complexes can be temporarily weakened by slightly acidic solvents[3] or photoexcitation[4] to allow for reversible metal–ligand self-assembly to occur. Once the thermodynamic product has been obtained, the labilizing stimulus is removed and the product is rendered stable towards disassembly.

Another approach is one in which a multicomponent superstructure is fixed through a post-assembly covalent-modification step in which a supramolecular system is converted into a molecular one. Now, writing in *Nature Chemistry*, David Leigh and co-workers have shown[5] that a star-shaped supramolecular assembly comprising six tris-bipyridyl ligands and six Fe(II) cations can be locked together to form a triply entwined [2]catenane by ruthenium-mediated olefin–metathesis reactions (Fig. 1). The resulting molecular structure resembles a hexagram, a geometric shape that is known in many cultural and religious contexts such as Hinduism,
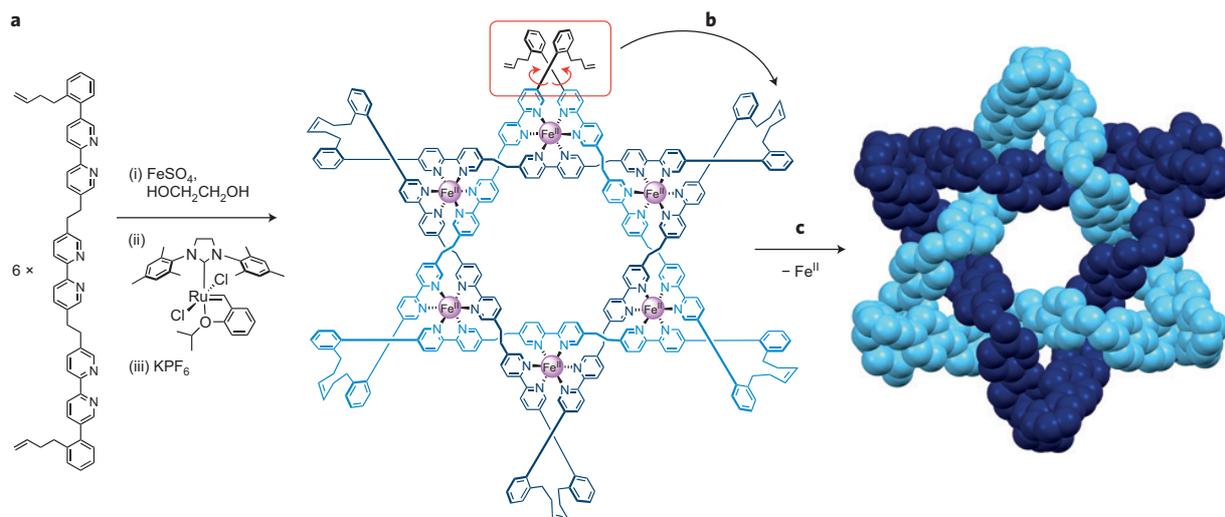

Figure 1 | Synthesis of a Star of David catenane made up of two triply entwined macrocycles. **a**, Iron(II) sulfate-mediated self-assembly of a cyclic [6]helicate and covalent trapping of the structure by olefin metathesis. **b**, High yields in the six metathesis reactions that are needed to close both intertwined macrocycles were achieved by constraining the conformational freedom of the olefin arms (highlighted by the red box on the structure; the black arrow shows the connection that is formed once the two olefins react with one another). **c**, The iron(II) cations can be removed by treatment with EDTA to give a wholly organic structure (image by G.H.C.).

Buddhism, Christianity, Islam and — most prominently — in Judaism. In the latter context it is known as the Star of David (also called the Shield of David or 'Magen David' in Hebrew) and it has become the sign of modern Jewish identity.

Although olefin metathesis has been used previously to fix metal-mediated self-assembled structures — such as octahedral capsules[6] — this method often suffers from poor yields because of the rather low probability of the flexible arms meeting up for the bond-forming reaction. In his early work on [2]catenanes, Jean-Pierre Sauvage described how the yield of ring-closing metathesis reactions could be increased by restricting the conformational freedom of olefin-containing arms that were held in place by non-covalent interactions[7]. Leigh and co-workers tackled the problem in a similar fashion, through careful design of the olefin-carrying portion of their ligands. Instead of flexible alkyl chains protruding distally from the ends, they introduced *ortho*-phenylene bridges, which resulted in kinks that oriented the olefins closer to one another. Using this strategy, the overall yield of the six metathesis reactions was increased to an impressive 92%. The reaction product was characterized by NMR spectroscopy, mass spectrometry and single-crystal X-ray analysis, which showed that two enantiomers of the interwoven structure — each containing a central PF_6^- anion — were formed as expected.

This current work follows on from a related study by Leigh and co-workers in which they made a pentafoil knot from five iron(II) cations, five linear multidentate ligands terminated by aldehydes, and five bridging diamines[8]. That synthesis was based on seminal studies by Jean-Marie Lehn carried out in the 1990s in which it was shown that chloride anions template the formation of a cyclic [5]helicate from Fe(II) cations and linear tris-bipyridyl ligands. Whereas Lehn's chloride-templated cyclic [5]helicate became so famous that it even illustrates the Wikipedia entry describing the term 'supramolecular chemistry', the related sulfate-templated cyclic [6]helicate hasn't garnered much attention outside of the original literature report[9]. No attempts at derivatizing this structure have been reported so far.

Nevertheless, Leigh and co-workers have now used this sulfate-templated [6] helicate as the basis for their synthesis of a triply entwined [2]catenane. In contrast to its pentagram-shaped progenitor, however, this interlocked compound consists of two interdigitated 114-membered rings rather than a single knotted molecular chain. Mathematically, this [2]catenane can be described as a 6_1^2 link and this is the first example of this particular topology being made in molecular form. This covalently captured cyclic helicate is also a very stable structure and the six metal centres can be removed by treatment with the chelating agent EDTA (ethylenediaminetetraacetic acid) to yield an entangled organic molecule.

Interlocked molecules and intertwined complexes are not just structural curiosities. Self-assembled helicates have been used for the molecular recognition of DNA three-way junctions[10], bistable rotaxanes can serve as valves for the controlled release of small molecules from nanoporous silica particles[11], various rotaxanes and catenanes have demonstrated catalytic activity[12] and transition metal-carrying grids have been studied in the context of electronically addressable quantum cellular automata[13]. The development of new strategies for the construction of ever more intricate structures, such as the approach demonstrated by Leigh and co-workers, may expand the potential of these systems for applications in technologies such as molecular machinery, chemical biology, supramolecular catalysis and information storage. ❒

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