

## INTERLOCKED MOLECULES

## One-pot pentaknot

The most complex non-DNA synthetic molecular knot so far has been made in a single step by combining a number of reversible chemical interactions, including metal-directed self-assembly, anion templation and imine bond formation.

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**K**nots are commonly encountered in everyday life, but their significance extends far beyond their obvious practical utility of being able to bind objects together. As well as serving as decorative motifs — most notably in some illuminated manuscripts such as the *Book of Kells* — the symbolism often associated with some knots' intricate interwoven structures has seen them used to represent countries, religious ideals and concepts such as unity. Knots have also long fascinated mathematicians with an interest in topology. Mathematically speaking, however, a knot is only considered to be a true knot if it cannot be undone without breaking it.

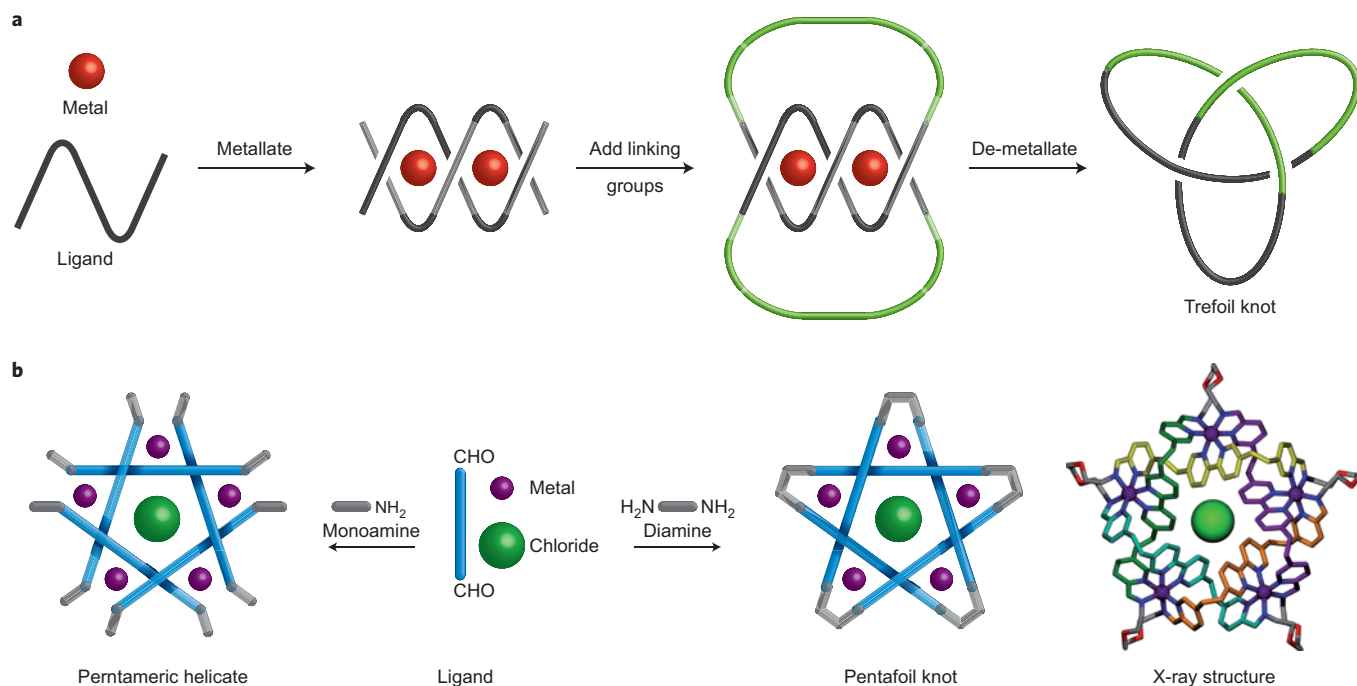
Chemists have long sought to tie molecules into knots<sup>1</sup>. This interest in making knots partly stems from the inherent beauty of such structures and the considerable synthetic challenge they represent. The appeal of knots goes well

beyond the aesthetic, however, because functional biomolecules including DNA and some proteins are known to form knotted structures. Both natural and synthetic polymers may form knots and this has a marked effect on their physical properties, with a knot weakening a polymer strand and making it more likely to break<sup>2</sup>.

Most examples of molecular knots made by chemists have been the simplest of the true knots, the trefoil knot. Now, writing in *Nature Chemistry*, David Leigh and his team report the synthesis of the first non-DNA molecular knot of higher order, namely the pentafoil or cinquefoil knot<sup>3</sup>. Their rational strategy for making a molecular pentafoil knot combines many aspects of modern supramolecular chemistry, including metal-directed assembly, anion templation and reversible covalent bond formation.

Using metal cations to direct how organic ligands come together has had a

rich recent history in creating topologically complex chemical architectures<sup>1</sup>. Such strategies require crossover points, either between different circuits, such as in a chain-like link (a catenane) or in the Borromean rings, or within a single circuit, such as in a knot. Researchers led by Jean-Pierre Sauvage demonstrated in the late 1980s that the three crossover points required to ultimately generate a trefoil knot can be introduced through a helicate<sup>4</sup>. Helicates consist of multiple ligand strands that wrap around metal cations in a helical fashion. Sauvage recognized that a two-stranded helicate with two metal centres will contain the three crossover points required for a trefoil knot. If the ends of the ligands in the helicate are linked together in the appropriate fashion a knot will ensue (Fig. 1a). Although extending the length of the ligand strands and increasing the number of metal cations should, in theory,



**Figure 1** | Making molecular knots. **a**, A schematic representation of Sauvage's step-wise synthesis of a trefoil knot. **b**, Leigh's one-pot synthesis of pentameric helicates (left) and a pentafoil knot (right) including X-ray crystallographic analysis that confirms the knotted topology.

result in more crossover points and hence lead to higher knots, such an approach has not proved successful in the laboratory.

Leigh and his team approached the problem of making a higher-order knot by using a special class of helicates, known as circular helicates, which were first reported by Lehn and co-workers<sup>5</sup>. Here, the twisted ligand strands form a disconnected ring by templation around an anion template. Chloride anions guide the formation of a circular pentameric helicate — comprising five ligands and five metal ions — that contains five crossover points, exactly the number required for a pentafoil knot. Connecting the ends of the ligand strands together in the correct manner would give the desired molecular pentafoil. Instead of doing this in a labour-intensive step-wise procedure, Leigh and colleagues pursued a one-pot method where all of the required chemical transformations occur in the same mixture.

Another crucial aspect of the design strategy was the choice of reversible bond-forming reactions. Reversible imine formation combined with labile metal–ligand bond formation has been previously shown by Leigh<sup>6</sup> and the groups of Stoddart<sup>7</sup> and Nitschke<sup>8</sup> to be a powerful approach to synthesizing highly complex architectures, including catenanes and Borromean rings. Unfortunately, imine bonds are not stable under the fairly harsh conditions that were originally used to make these circular helicates. To begin with, therefore, Leigh and co-workers showed that they could form circular helicates using a modified approach compatible with imine bond formation.

This new strategy required simultaneous formation of the metal-binding groups at the ends of the ligand strands along with

metal binding itself. This was achieved by reacting the aldehyde at each end of the ligand strands with a monoamine (Fig. 1b, left). Next the team tackled the even more challenging task of making the pentafoil knot using a similar one-pot procedure, but using diamine linkers to join the ligands together in a continuous strand (Fig. 1b, right). In a final complication, the choice of linking molecule proved crucial to ensure the correct conformational twist to enable complete closure of the cyclic structure. Ultimate proof of the success of this approach came from the crystal structure of the metallated pentafoil knot (Fig. 1b).

This chemistry is a beautiful illustration of the self-assembly processes that underpin many aspects of chemistry and biology. Many different products are possible, such as oligomers or simpler helicates, but the system continues to break and make chemical bonds until only a single product of the lowest energy is reached. The chemist designs the components, puts them together, and then allows the system to sort itself out, perhaps with a bit of encouragement through heating. With gentle heating, Leigh's circular helicates form themselves in around 24 hours from an initial complex mixture of products. The pentafoil knot, which requires the formation of ten imine bonds and fifteen metal–chelate interactions all in a specific pattern and with specific molecular conformations, took a mere two days to sort itself out.

For a number of decades, the trefoil knot was the highest-order knot that synthetic chemistry could lay claim to, but that is now beautifully superseded by the pentafoil knot. Given that larger anions such as sulfate can template even larger six-fold circular helicates, is a sexafoil now just round the corner? This

pentafoil knot contains five iron cations, but to be truly considered a knot — that is a self-entangled single circuit — it needs to be demonstrated that it can withstand removal of the metal centres. This has proved possible in other metal-templated systems.

More generally, two of the most complex synthetic chemical topologies to date, the Borromean rings and the pentafoil knot, have employed a convergent multi-reversible bond-formation strategy and the latter raises the bar by also including anion templation effects. This illustrates that supramolecular chemists are becoming more sophisticated in their approaches to complex architectures, and can successfully employ multiple and simultaneous bond-forming and structure-directing strategies. Although biology is said to use a small chemical 'toolbox' with a high degree of complexity, chemists have available a much larger chemical toolbox but are considerably less sophisticated in its use. Nevertheless, this is another step towards the chemist's control of very highly complex systems indeed. □

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## EXCITON DYNAMICS

# Electrons take an unexpected turn

Traditional wisdom suggests that excited electrons will move towards positively charged parts of a molecule. Advanced time-domain calculations show that the conventional picture breaks down in the ultrafast regime, providing key insights into photo-activated, attosecond processes.

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Decreasing resources and environmental concerns have turned the world's attention to alternative energy supplies. And with solar power expected to provide a major proportion of our energy in the future, chemists are taking a closer look at the photo-induced processes that drive the conversion of light into usable energy. Regardless of the

end product — electrical current, chemical fuel or biomass — photo-conversion relies on the generation and evolution of excitons. In a practical sense, an exciton is an electron–hole pair that is created on photo-excitation. They must be separated from one another to generate an electrical potential; however, negatively charged electrons and positively

charged holes interact, creating a barrier to such exciton dissociation. To best utilize photovoltaic and photosynthetic devices, one must understand the conditions that promote charge separation and exciton diffusion. However, truly understanding the evolution of excitons in molecular systems is far from trivial given their quantum mechanical