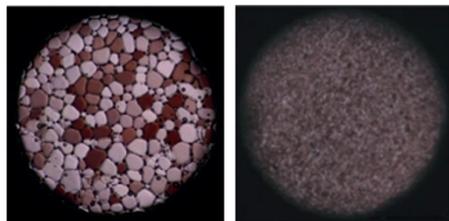


CRYOPRESERVATION

In the deep freeze

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Progress in regenerative medicine and organ transplantation has resulted in a constant pressure on supplies of donated blood and organs. Deep-freezing, or cryopreservation, is one method of mitigating fluctuations in supply and demand, but is not routinely undertaken due to the levels of cell death induced by ice crystal formation and growth during the freezing and thawing processes. The current state-of-the-art in cryopreservation is replacement of water with organic solvents, followed by rapid

freezing to achieve an ice-free state, known as vitrification. Issues with this process are the organic solvents used, which can be toxic to cells, and the possibility for devitrification — or ice formation — during thawing. However, the discovery of antifreeze proteins in Arctic fish has suggested that this vitrification process could be replaced by using compounds that mimic their action.

Now, Matthew Gibson and co-workers from the University of Warwick have demonstrated that poly(vinyl alcohol) (PVA) facilitates cryopreservation of both sheep and human blood. PVA is both non-toxic and widely available, and despite having few structural similarities to antifreeze proteins, still confers protection to cryopreserved red blood cells. Gibson and colleagues have also shown that only 0.1 wt% PVA is needed, in comparison with the 40 wt% organic solvents required in current vitrification-based cryopreservation processes.

Perhaps surprisingly, they also show that cryopreservation of the cells occurs

despite the formation of small extracellular ice crystals, precisely what vitrification aims to avoid. This suggests that the mere presence of ice crystals is not a barrier to cryopreservation, but that the growth of these crystals during thawing is in fact the cause of cell death. They suggest that the success of PVA is due to its ability to inhibit ice crystal growth (pictured, right) compared with untreated cells (left). In conjunction with rapid thawing to avoid ice crystal growth instead of melting, its use may preclude the use of organic solvents and vitrification for cryopreservation in the future.

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ASYMMETRIC CATALYSIS

Separation of powers

J. Am. Chem. Soc. **136**, 3020–3023 (2014)

Recently, Erick Carreira and co-workers from ETH Zürich introduced the idea of stereodivergent dual catalysis. This involves two reactants — each activated by a distinct chiral catalyst — reacting to form a product with two stereocentres;

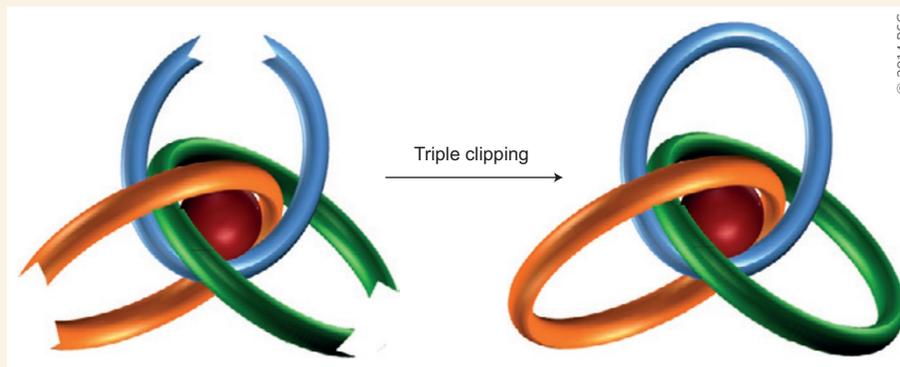
Chem. Commun. **50**, 2857–2860 (2014)

INTERLOCKED MOLECULES

Triple-clipped links

The simplest example of a catenane is one in which two macrocycles are mechanically interlocked with just a single link. Increasingly complicated structures result when the two rings are linked together more than once; for example, a doubly linked catenane has the same interwoven topology as the ancient motif known as Solomon's knot. When it comes to interlocked molecules made up of three macrocycles, the situation is even more complex. The most common arrangement is a catenane in which the three rings are (singly) linked together linearly to form a chain, but other topologies are possible.

Now, Thorfinnur Gunnlaugsson and co-workers at Trinity College Dublin have prepared a [3]catenane in which each ring in the structure is interlocked with the other two. Using an Eu(III) ion as a template, three copies of the same pyridyl diamide ligand can be brought together in a coordination complex. This acyclic ligand has an alkene group at each end and can, in isolation, undergo a ring-closing metathesis (RCM) reaction in the presence of a ruthenium catalyst to form a macrocycle. When three of these ligands are wrapped around a metal



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centre, however, the same RCM procedure can, in principle, yield a range of different products with interwoven topologies. If each ligand in the complex reacts with itself to form a macrocycle around the metal template — and the ligands are organized in the appropriate fashion — the result is a [3]catenane in which each ring is threaded through both of the others (pictured).

NMR spectroscopy, in addition to mass spectrometry, indicates that both [2]- and [3]catenanes are formed during the reaction, but other knotted structures could also

be produced by inter-ligand metathesis reactions. Although lanthanide ions have been used previously to make another class of interlocked compounds called rotaxanes, Gunnlaugsson and colleagues suggest that this is the first time that they have been used to template the formation of catenanes. Moreover, this particular arrangement of three interlocking rings is somewhat unusual and differs from the topologies observed in related systems, including linear [3]catenanes and molecular Borromean rings.

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