

Metal Ions in the Synthesis of Interlocked Molecules and Materials

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

James E. M. Lewis,^a Paul D. Beer,^b Stephen J. Loeb^c and Stephen M. Goldup^{*a}

The use of metal ions to template the synthesis of catenanes by Sauvage and co-workers was a pivotal moment in the development of the field of interlocked molecules. In this Review Article we shall examine the different roles metal-ligand interactions play in modern syntheses of interlocked molecules and materials, with a particular focus on seminal contributions and the advantages and disadvantages of employing metal ligand interactions.

Introduction

Species in which two or more covalent sub-components are held together not through direct covalent interactions but through the inability of bonds and atoms to pass through one another are referred to as mechanically interlocked molecules (MIMs). The archetypal examples of MIMs are catenanes - consisting of two or more mechanically interlocked macrocycles - and rotaxanes, which in their simplest form are described by a macrocyclic component threaded onto a linear axle, with dissociation of the subcomponents prevented by bulky "stopper" units at the axle termini (Fig 1).¹ Initially a curiosity, the exploration of MIMs for a variety of applications has increased dramatically over the last three decades, a trend inextricably associated with the development of high yielding methods for their synthesis. Many of these methodologies entail the use of metal ions to pre-organise the MIM precursors and, as such, metal ions have been used extensively in the synthesis of interlocked molecules.

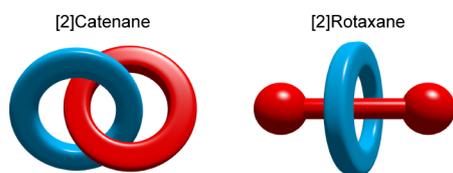


Fig. 1 Cartoon representations of a [2]rotaxane and a [2]catenane.

In this Review Article we discuss the different roles metal-ligand interactions play in the synthesis of interlocked molecules and materials, with a particular focus on seminal

contributions, along with key strategic and chemical considerations involved in employing metal ligand interactions and future directions. Where relevant the interested reader is referred to excellent recent comprehensive reviews on the various topics presented.²

Metal Ions in the Passive Template Synthesis of MIMs

Early syntheses of rotaxanes and catenanes relied either on Wasserman's statistical approach³ or Schill's covalent template directed methodology.⁴ These approaches led respectively to extremely low yields in the formation of the mechanical bond or laborious synthetic routes, again resulting in low overall yields of the target.

In 1983 Sauvage and co-workers revolutionised synthetic access to MIMs through the first demonstration of an efficient passive template (PT) approach. In their seminal work, the predictable tetrahedral coordination geometry of a Cu^I ion with phenanthroline ligands was exploited to arrange two precursor building blocks perpendicular to one another in such an orientation that intra-ligand cyclisation gave relatively facile and high yielding access to the catenane product (Fig 2a).⁵ Subsequently, Gibson and co-workers demonstrated that the introduction of bulky trityl stoppering units rather than a cyclisation reaction, using the same PT strategy, gave the corresponding rotaxane species (Fig 2b).⁶

Sauvage's demonstration of the PT approach was revolutionary because it relied on simple organic building blocks to assemble the required three-dimensional threaded structures that could be trapped to form interlocked molecules in high yield. This first high-yielding example of the PT philosophy also inspired the development of other approaches based on non-covalent interactions such as hydrogen bonding, π - π interactions, anion templation, solvophobic interactions and ion dipole interactions.

^aChemistry, University of Southampton, University Road, Southampton, SO17 1BJ, UK.

^bChemistry Research Laboratory, Department of Chemistry, University of Oxford, Mansfield Road, Oxford, OX1 3TA, UK.

^cDepartment of Chemistry and Biochemistry, University of Windsor, Windsor, Ontario, N9B 3P4, Canada.

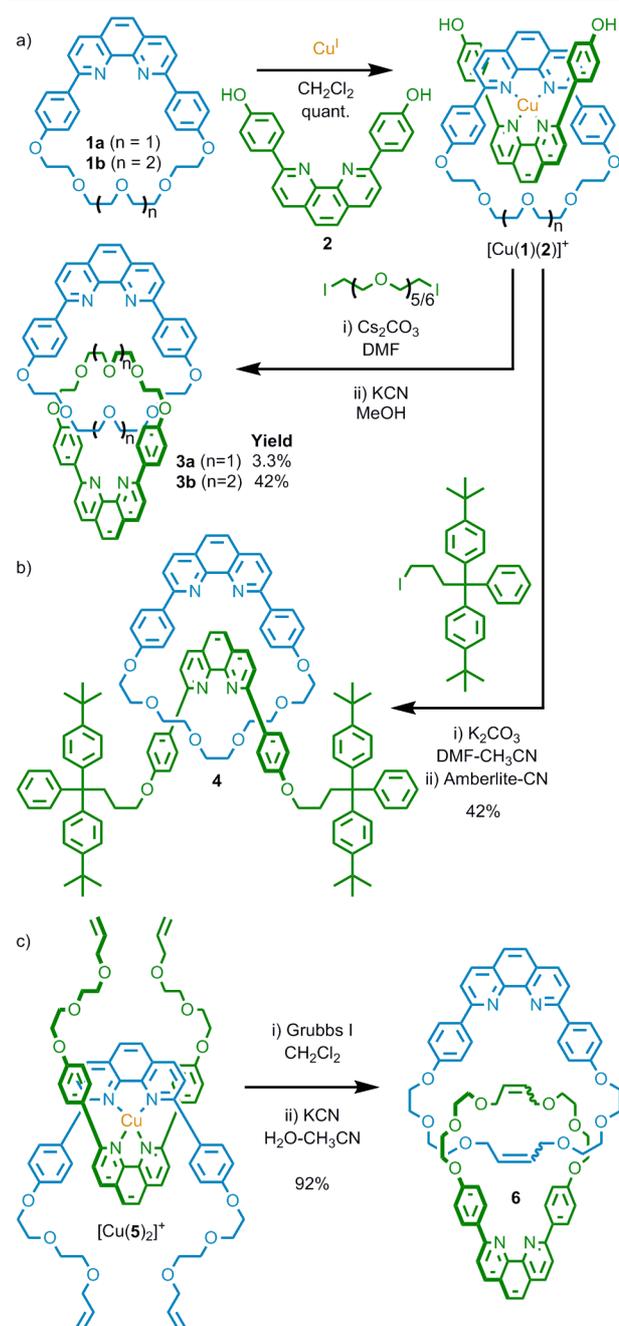


Fig. 2 a) Sauvage's original PT synthesis of a [2]catenane. b) Gibson's extension of the Sauvage PT approach to rotaxane synthesis. c) Sauvage's RCM approach to [2]catenanes.

More directly, Sauvage's seminal work inspired the development of a plethora of transition metal ion-ligand combinations of varying coordination geometry as templates in PT syntheses of MIMs (Fig 3a),⁷ including linear Au^I ,⁸ square planar Pd^{II} ,⁹ a variety of octahedral metal ions,^{10,11} as well as more kinetically inert templates including Ru^{II} ¹² and Co^{III} .¹³ Furthermore, it has proved possible to use the metal ion itself to drive formation of the ligand motif by subcomponent self-assembly as well as directing the formation of the threaded structure (Fig 3b).^{14,15}

We do not intend to provide a detailed overview of PT methodologies with metal ions as many excellent recent reviews cover this ground comprehensively.² Instead, below we highlight key points relating to this methodology, almost all of which can be exemplified using systems from the impressive work of the Sauvage group over the last three decades.

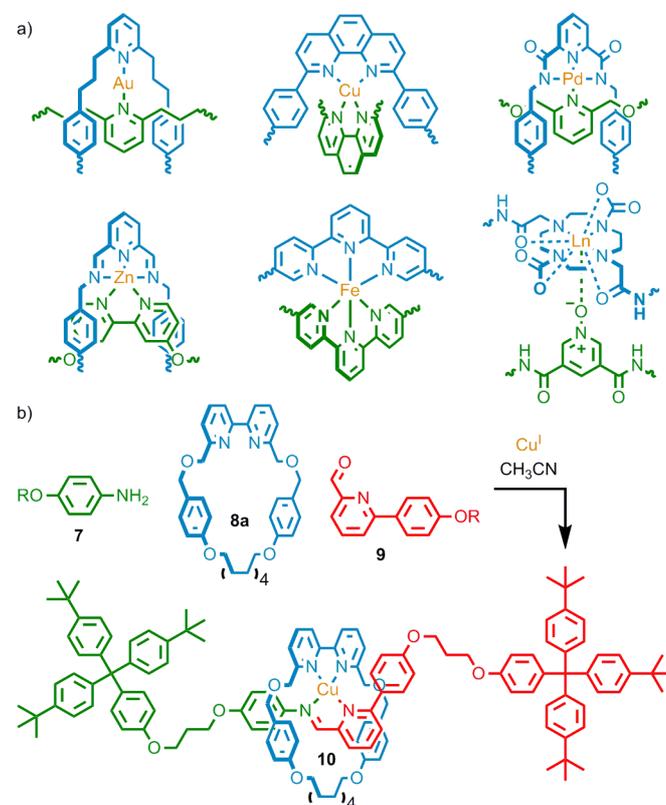


Fig. 3 a) Examples of PT motifs with varying ligand geometry. b) An example of subcomponent-self assembly in the synthesis of MIMs.

Choice of covalent bond-forming reaction

A key consideration of the PT approach, once the templating unit itself has been selected, is that the covalent bond forming reaction that captures the interlocked product must take place under conditions and using precursors that do not interfere with the template itself. Indeed, the correct choice of covalent bond forming reaction can have a dramatic effect on the yield of the target MIM. For example, the Williamson ether synthesis in the original synthesis of catenane **3** (Fig 2a) takes place in the presence of alkoxide and carbonate nucleophiles, produces iodide anions as a by-product and requires a coordinating solvent (DMF). Alternatively, a ring closing alkene metathesis (RCM) reaction (Fig 2c) takes place in the absence of coordinating solvents or by-products, resulting in a dramatic increase in the yield of the target catenane.¹⁶ This requirement has resulted in a relatively small number of bond forming reactions, Ru^{II} -mediated alkene metathesis, reactions of nucleophiles with isocyanates or activated esters, and cycloaddition reactions, particularly the Cu^I -mediated alkynyl azide cycloaddition (CuAAC) reaction, achieving privileged status in the synthesis of MIMs.

Role of Secondary Interactions

The PT approach requires the formation of a thermodynamically favourable complex that can adopt a suitable conformation for mechanical bond formation. Thus, secondary interactions (hydrogen bonding, π - π stacking, charge-charge and charge-dipole interactions) typically play a subtle and often overlooked role in determining the efficiency of mechanical bond formation, in addition to the primary template interaction. This is well exemplified in Sauvage's RCM catenane synthesis where C-H-O contacts between the back of the phenanthroline unit and the ethylene glycol chain have been invoked to rationalise the high yield of catenation versus macrocycle formation *via* an intercomponent cyclisation.¹⁶ Thus, the detailed covalent structure of the MIM precursor, as well as a suitable template geometry provided by ligand-metal interactions are essential.

Conversely, interactions that destabilise such productive conformations, principally steric repulsion, reduce or even prevent MIM formation. The key limitation this places on the PT approach is that the yield of the interlocked product typically falls once the cavity of the macrocycle component is reduced below a critical size, as the steric cost of including the metal ion and ligand moieties in the macrocycle cavity rises. For example, although Sauvage's original synthesis employing a 30-membered macrocycle gave catenane **3b** in 42% yield,⁵ reducing the macrocycle size to 27 atoms, while maintaining the same ligand-metal combination, led to just 3.3% yield of interlocked product **3a**.¹⁷ In the case of rotaxane synthesis, the requirement for larger macrocycles has the knock-on effect of requiring relatively large stopper units to prevent the macrocycle from escaping the axle.

Choice of Metal Ion – Beyond Transition Metals

The need for stable, well ordered complexes has led to the majority of metal-based PTs developed to date employing transition metal ions, typically in conjunction with pyridyl or other N-donor ligands. However, examples have been reported with less conventional metal ion templates. Indeed, as early as 1999 Sauvage and co-workers reported the assembly of a tris-phenanthroline precursor around three Li^I cations to synthesise a doubly interlocked isomer of a [2]catenane known as a Solomon link in 30% yield.¹⁸

Main group metal ions have recently begun to receive more attention as novel templates for MIMs. In 2013 Chiu and co-workers reported two new methods for the Na^I-templated synthesis of MIMs. In the first approach two orthogonal ethylene glycol moieties wrapped around a single Na^I ion direct the formation of the mechanical bond to produce interlocked target **14** (Fig 4a).¹⁹ The second approach employs the cooperative binding of a urea and Na^I ion by a crown ether macrocycle in which the metal ion coordinates to the urea and macrocycle oxygen donors.²⁰ Beer and co-workers have also demonstrated the synthesis of rotaxanes using a Na^I ion template using a different approach.²¹ In their system the Na^I cation is bound between the rim of a calix[4]diquinone in the macrocycle component and a pyridine *N*-oxide in the axle

component leading to a threaded complex. Subsequent stoppering using the CuAAC reaction led to rotaxane **17** in up to 50% yield (Fig 4b). Ba^{II} was also found to work as the templating cation, although this gave a lower yield of the desired rotaxane (28%). Using a double-CuAAC stoppering method, a similar heteroditopic rotaxane system was prepared via Na^I-templation in 62% yield.²²

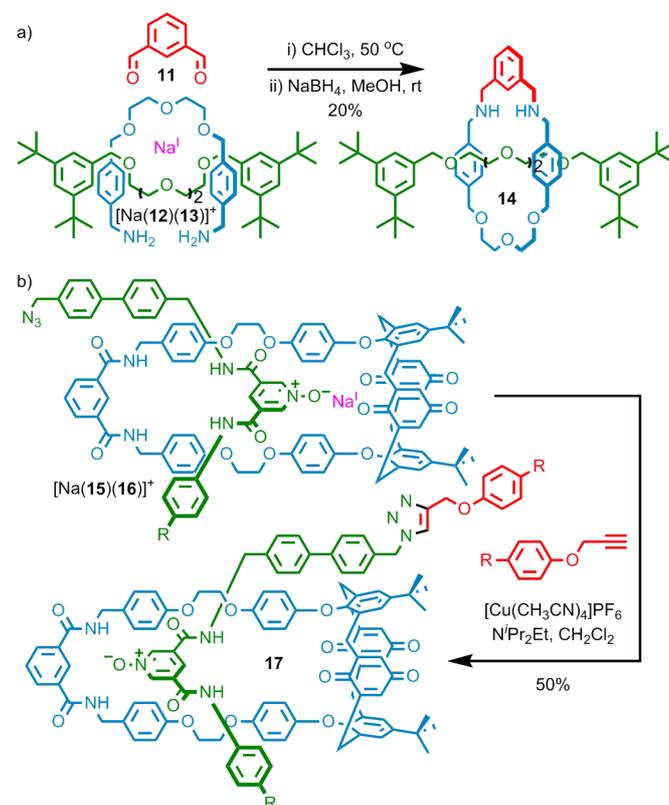


Fig. 4 Examples of rotaxane synthesis templated by Na^I ions from a) Chiu and b) Beer.

Beer and co-workers have since extended this approach to demonstrate the first example of lanthanide ions in the PT synthesis of MIMs.²³ Replacing the calix[4]diquinone with a DOTA derivative allowed the coordination of Lu^{III} or Eu^{III} and the interaction between this complex with a pyridine *N*-oxide axle produced a threaded complex that could once again be captured by CuAAC coupling (Fig 5). More recently, Gunnlaugsson and co-workers demonstrated the synthesis of a [3]catenane templated by Eu^{III}.^{24,25}

The Passive Template Approach to MIMs - Conclusions

Passive template approaches based on metal ions inspired by Sauvage's original contribution continue to drive a significant proportion of the research carried out on the synthesis and applications of MIMs. Recent efforts to expand the PT approach to less conventional metal ions increases the structural diversity of MIMs available, including structures that are not available using other approaches, and represents a relatively underexplored area of PT synthesis.

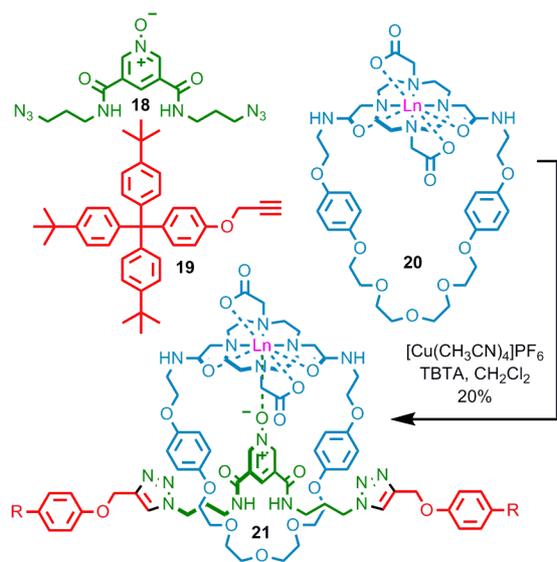


Fig. 5 Beer's lanthanide template synthesis of [2]rotaxanes.

Metal Ions in the Active Template Synthesis of MIMs

Although the power of the PT approach is hard to overstate, it is arguable that it fails to take full advantage of the properties of the metal ion; in addition to forming geometrically well-defined complexes suitable for directing mechanical bond formation, transition metal ions are often capable of mediating covalent bond formation in their own right. Indeed in later work, Sauvage and co-workers employed the same Cu^I source as the template and, by addition of an excess of the metal ion, the catalyst for a CuAAC stopping reaction.²⁶

In 2006, Leigh and co-workers introduced the active template (AT) approach to MIM synthesis in which both the catalytic and geometric properties of metal ions are harnessed in the formation of the mechanical bond.²⁷ As with many PT syntheses, a metal ion is first bound within the cavity of the macrocyclic component. However, whereas in the PT approach the second component also binds to the metal ion to form a threaded architecture which is subsequently stoppered (to form a rotaxane) or cyclised (in catenane synthesis), in the AT approach the mechanical bond is captured through the interaction of the metal ion with suitably functionalised reactive half-axle components (rotaxane synthesis) or macrocycle precursors (catenane synthesis) to form a new covalent bond through the cavity of the macrocycle (Fig 6a).

The AT approach was first demonstrated using the CuAAC reaction in which a Cu^I ion coordinated within the cavity of pyridine containing macrocycle **23**, mediated the CuAAC between bulky alkyne **19** and bulky azide **22** to give rotaxane **24** in 57% yield. Increasing the number of equivalents of half-axes **19** and **22** increased the yield of **24** to up to 94%. It even proved possible to use a sub-stoichiometric quantity of the Cu^I ion; with just 20 mol% of Cu^I the target rotaxane was produced in 82% yield (Fig 6b).

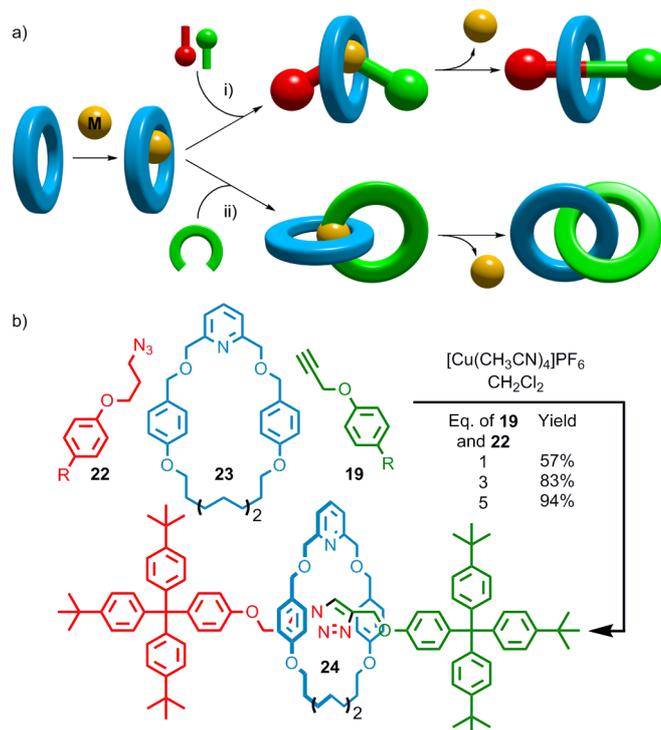


Fig. 6 a) Schematic representation of the active template approach for i) rotaxane formation, ii) catenane formation. b) Leigh's original AT-CuAAC reaction.

As much of the seminal work on the AT approach has been reviewed comprehensively elsewhere,²⁸ here we shall focus on the key features of this methodology, and in particular, how it differs from the PT approach discussed above.

Active vs Passive Templates

Whereas the PT approach can be considered being largely a thermodynamically driven approach,²⁹ the AT approach can be considered to be a kinetic template first and foremost; by immobilising the catalyst within the cavity of the macrocycle the reaction takes place faster through the ring than anywhere else in solution resulting in formation of the mechanical bond. The practical consequence of this is that, as opposed to PT products where, at least when they are initially formed, the interlocked product is both thermodynamically and kinetically more stable than the non-interlocked components, AT products often have no significant attractive intercomponent interactions and can even be significantly *less stable* due to repulsive steric interactions.

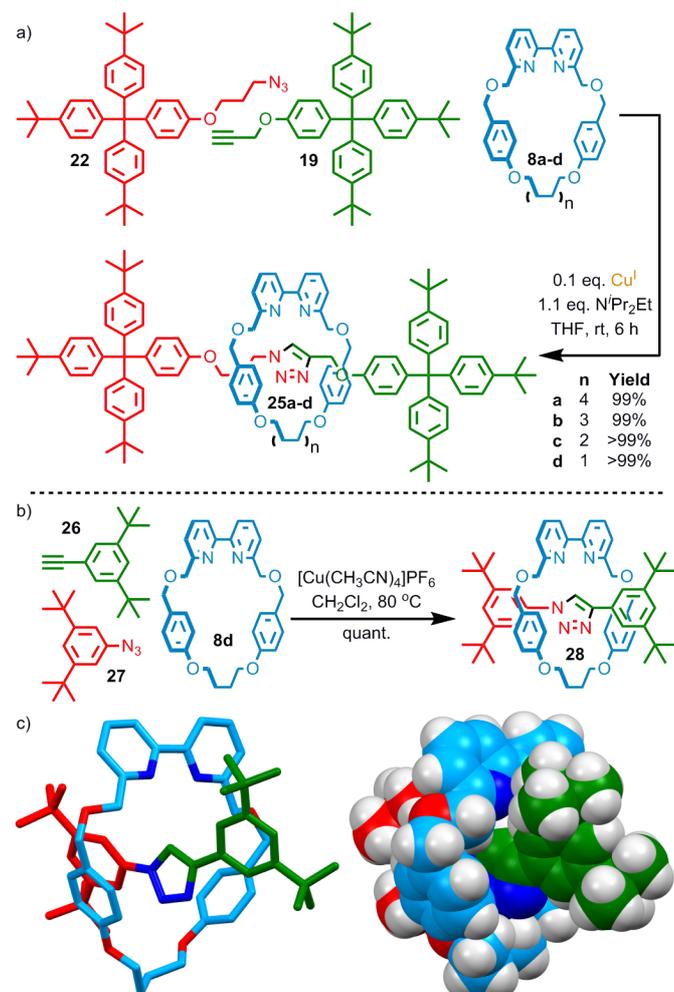


Fig. 7 a) Effect of macrocycle size on the AT-CuAAC reaction. b) Synthesis of crowded rotaxane **28**. c) X-ray crystal structure of **28**.

This is perhaps most starkly demonstrated in the effect of macrocycle size on the AT-CuAAC reaction. Goldup and co-workers found that, under optimised conditions, the yield of the AT-CuAAC coupling between azide **22** and alkyne **19** in the presence of bipyridine macrocycles of various sizes was essentially quantitative in all cases (Fig 7a).³⁰ It is worth noting that the smallest macrocycle is of a similar size to “small” phenanthroline macrocycle **1a** that proved ineffective in the PT synthesis of catenanes (Fig 2a). Using this small macrocycle, crowded rotaxane **28** could be synthesised in excellent yield despite the extremely hindered nature of the assembly, as demonstrated by the x-ray crystal structure obtained (Fig 7c).³¹ It should be noted that the steric crowding in **28** is not evident in the proposed intermediate that leads to its formation but builds up as the transition state for the CuAAC reaction is approached. Thus, as long as the driving force for covalent bond formation is high enough, crowded or otherwise thermodynamically disfavoured products can be formed in AT reactions. However, the nature of the bond forming reaction itself and the macrocycle also play a key role; Anderson and co-workers found that smaller bidentate macrocycles led to a reduced yield in the AT-Glaser reaction,³² while Crowley and

co-workers found that smaller pyridine macrocycles were less efficient than their larger counterparts in the AT-CuAAC reaction.³³ The origin of the conflicting effect of macrocycle size on the yield of the target MIM, which appear to depend on the ligand motif and reaction investigated, is poorly understood and warrants further investigation.

Generality of the AT Approach. The AT approach can in theory be extended to any metal mediated bond forming reaction simply by including the metal ion within the cavity of a suitably designed macrocycle. In reality the conditions for a successful AT reaction are more stringent as the resulting macrocycle-metal complex must adopt conformations in which the covalent bond formation is stereoelectronically biased towards forming the mechanical bond; if the reaction can take place on one face of the macrocycle then no rotaxane will be produced. Indeed in the case of the original AT-CuAAC reaction the yield of the interlocked product is less than quantitative despite complete conversion of **19** and **22** to triazole products, implying that macrocycle conformations are available that project the Cu^I centre in such a way that the reaction can take place exocyclically. Despite this relatively stringent requirement, the AT approach has been extended to a range of metal-mediated bond forming reaction including sp-sp homo-³⁴ and hetero-coupling,³⁵ Pd^{II}-mediated oxidative Heck reactions,³⁶ Diels-Alder reactions,³⁷ Ni-mediated sp³-sp³ couplings,³⁸ Ulmann couplings,^{34a, 39} Castro-Stephens reactions,⁴⁰ Pd-mediated Michael addition⁴¹ and the formation of iodo-triazoles.⁴²

Synthetic Advantages of the AT Approach. Whereas products formed through the PT approach using metal ions are synthetically required to contain ligand moieties in all covalent components, in the AT approach only the macrocycle component need bind to the metal ion and the only restriction on the other component is that it will contain the functional group produced in the AT bond forming reaction. This, in addition to the ability to form sterically crowded MIMs in high yield, increases the structural diversity of products available.

Furthermore, whereas PT products are typically better ligands for the template metal ion than their precursors due to the enforced association of the components (the “catenand effect”),⁴³ this is not true of AT products as the functional group produced in the AT bond forming step is not necessarily a good ligand for the metal ion. Thus, whereas in a PT synthesis the metal ion must be used stoichiometrically as it remains strongly bound by the product, in an AT synthesis only a substoichiometric amount of the metal ion is required as long as it can transfer from the interlocked product to the remaining non-interlocked macrocycle under the reaction conditions. This principle was demonstrated by Leigh and co-workers in the original AT-CuAAC report (Fig 6b).

A similar principle allows reactions to be driven to higher yield with respect to the macrocycle even when the bond forming reaction is not completely selective for the interlocked product. As demonstrated by Leigh and co-workers (Fig 6b), by increasing the equivalents of half-axle components, the macrocycle-metal complex resulting from “failed” AT bond

formation can be recycled into the reaction mixture because it does not associate strongly with the non-interlocked axle. In contrast, in the PT approach, unthreaded template conformations, once the final covalent bond formation is complete, will typically remain bound to the metal ion, limiting the yield of the process.

The Active Template Approach to MIMs - Conclusions

The features of the AT approach outlined above have led to its rapid development as an alternative to more established PT methodologies. Although it has yet to receive the same attention in terms of applications it has already been employed in the synthesis of molecular shuttles with reduced inter-component interactions,⁴⁴ so-called “impossible” interlocked molecules in which no obvious templating moiety is present,³⁸ complex molecular machines,⁴⁵ multiply-threaded species from a single template,^{32,46} separable mechanically epimeric rotaxanes,⁴⁷ mechanically stabilised organometallic species,⁴⁸ and rotaxane hosts for anions in which the anion-binding pocket is not determined by the requirements of a PT synthesis.^{42,49} The AT approach has also been extended to catenanes,⁵⁰ and molecules containing multiple mechanical bonds.⁵¹ Given the rapid progress in the area in the decade since the first report, it seems likely that further applications and innovations in the AT approach will be forthcoming in future.

Metal Ions as Structural Units Within MIM Sub-Components

Although the development of Sauvage’s PT approach to MIMs marked a turning point in their history, the use of metal ions as structural units in the synthesis of MIMs predates the work of Sauvage and co-workers, if only by a few years.

But first a cautionary note. In what follows metal-ligand interactions play a key structural role in the sub-components of the products presented and this raises a thorny problem: are metal ligand interactions covalent or non-covalent? This is important from the point of view of nomenclature because defining metal-ligand interactions as covalent would mean that the products below are true rotaxanes and catenanes whereas the non-covalent definition would lead them to be classified as pseudorotaxanes and inclusion complexes.

In practice, a hard and fast answer is difficult to come by, as some metal-ligand interactions are probably best considered as non-covalent (ion-dipole) while others clearly have a large degree of covalent character. In reality all metal-ligand bonds will sit somewhere on this continuum. It should also be noted that the dynamic nature of many metal-ligand interactions is not sufficient to solve the problem of classification; the same can be said of interlocked molecules assembled by dynamic covalent chemistry but no-one has to our knowledge, as yet, attempted to use this behaviour to disqualify them as “true” rotaxanes and catenanes.

We mention this to highlight the problem but do not seek to provide a definitive answer, preferring instead to leave the

line blurred. The reader is invited to decide for themselves what they consider to be “true” rotaxanes and catenanes.

Metal Complexes as Stoppers in Rotaxane Synthesis

Prosaically, bulky metal complexes such as ferrocene,⁵² or porphyrinoid macrocycles⁵³ have been employed as stoppers in rotaxane synthesis in which the metal-ligand bond is not formed during the key covalent bond forming step. However, metal-ligand bond formation to capture the interlocked product has a long and illustrious history in MIM synthesis that actually predates the development of PT reactions by Sauvage and co-workers.

In 1981, two years before Sauvage’s breakthrough, Ogino reported the formation of rotaxanes in “relatively high yield” (3-8%!) by stoppering the inclusion complex of an alkyl diamine with α - or β -cyclodextrin by reaction with Co^{III} complex **31** (Fig 8).^{54a} The efficiency of Ogino’s approach lies in the use of readily available starting materials to form the mechanical bond, but that this reaction was considered high yielding emphasises the difficulties encountered by researchers in the field at this time. In later work, Ogino demonstrated that, by tuning of the size of the cyclodextrin macrocycle and the length of the axle, it was possible to obtain a metallo-[2]-rotaxane in 19% yield.^{54b}

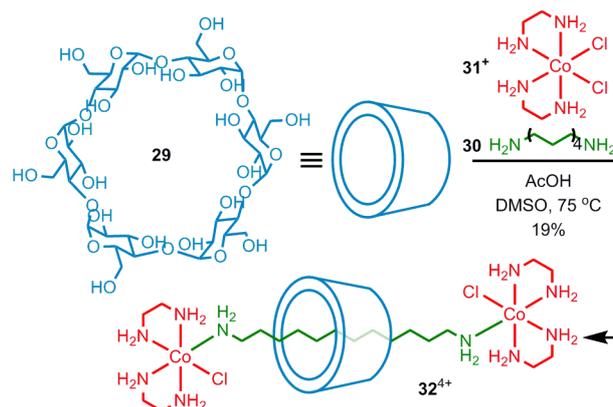


Fig. 8 Ogino’s templated synthesis of cyclodextrin rotaxanes stoppered by Co^{III} .

The choice of Co^{III} to stopper the inclusion complex was driven by the need for a mild bond forming reaction that would introduce a suitably bulky, kinetically stable unit without disrupting the solvophobic binding of the guest in the polar cyclodextrin macrocycle. Subsequent work has demonstrated the generality of this approach and various metal complexes have been employed as stoppers in the synthesis of rotaxanes assembled using a variety of templates.²

Recent work has highlighted an additional benefit of metal complexes as stoppers in rotaxane synthesis. By iteratively labilising ligands, a metal complex can be used not only as a stopper but also as a reactive handle for further synthesis. Yang and co-workers demonstrated the power of this approach by using iterative formation of Pt^{II} -acetylide bonds to produce metallo-dendrimer [n]rotaxanes with up to 45 macrocycles, the largest interlocked structure reported to date through an iterative approach (Fig. 9).⁵⁵

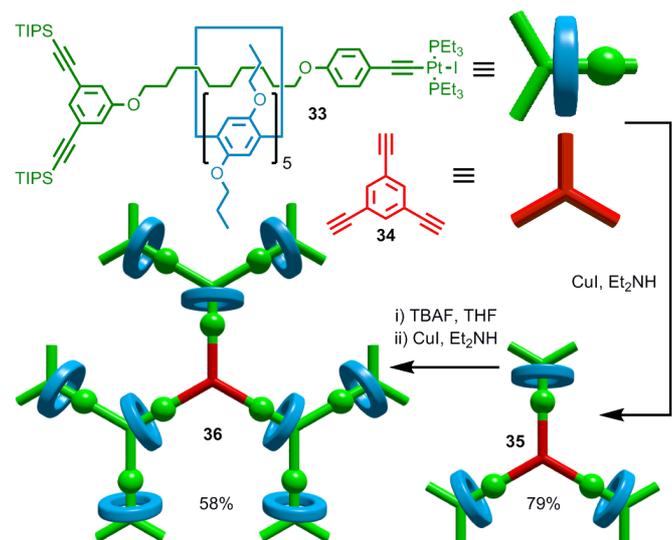


Fig. 9 Yang's metallo-[2]rotaxane monomer stoppered by a Pt^{II}(PEt₃)₂ stopper unit bearing a reactive Pt^{II}-I bond allowing iterative formation of rotaxane dendrimers.

Metal-ligand Bonds within the MIM Framework

Although Ogoni's stoppering reaction relied on the formation of a kinetically inert metal-ligand bond, one of the key advantages of using metal ligand bond formation in the synthesis of MIMs is the often reversible nature of metal-ligand interactions, similar to dynamic covalent bond formation,⁵⁶ allowing the MIM product to be formed under thermodynamic control, leading to extremely high yields of the interlocked product.

In 1994 Fujita and co-workers reported the formation of a simple M₂L₂ metallocycle [Pd₂(**37**)₂(en)₂] from the self-assembly of a bis-pyridyl ligand with ethylenediamine-capped Pd^{II} ion ([Pd(en)(NO₃)₂]) (Fig 10). However, when the metallocycle was dissolved in water at higher concentration, a second species was observed in equilibrium with [Pd₂(**37**)₂(en)₂] that was identified by mass spectrometry and ¹H NMR as catenane [Pd₄(**37**)₄(en)₄]. By increasing the concentration of the reaction to >50 mM, almost quantitative yields of the catenane were obtained.⁵⁷

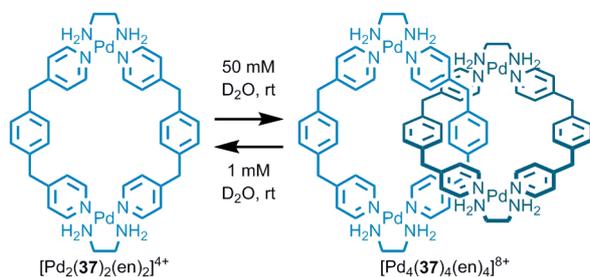


Fig. 10 Fujita's formation of a Pd^{II} catenane under thermodynamic control.

The high yield of catenane [Pd₄(**37**)₄(en)₄] was attributed to the higher thermodynamic stability of the catenated structure compared with metallocycle [Pd₂(**37**)₂(en)₂] due to π - π interactions and the hydrophobic effect, combined with reversible formation of Pd^{II}-pyridine bonds. The role of

reversible metal-ligand interactions in the excellent yield of [Pd₄(**37**)₄(en)₄] was underlined by comparison with the corresponding reaction with ([Pt(en)(NO₃)₂]). Under the same conditions, where the Pt^{II}-pyridine bond is known to form irreversibly, the corresponding catenane was not produced. Conversely, under conditions in which the Pt^{II}-pyridine bond is labilised (D₂O, 100 °C, excess NaNO₃) the Pt^{II}-metallacycle was converted quantitatively into the corresponding catenane.⁵⁸

Using this approach, Fujita and co-workers subsequently reported the formation of catenated triply-stranded Pd^{II} and Pt^{II} metallosupramolecular cages assembled from the same *cis*-protected [M(en)(NO₃)₂] (M = Pd^{II} or Pt^{II}) corner units and two different tripyridyl ligands (Fig 11a and b).⁵⁹ More recently Stang and co-workers reported the synthesis of a series of similarly structured hexa-ruthenium^{II} cages in which the identity of pillaring ligand employed controlled whether the monomeric cage or dimeric catenane structure was obtained (Fig 11c and d).⁶⁰

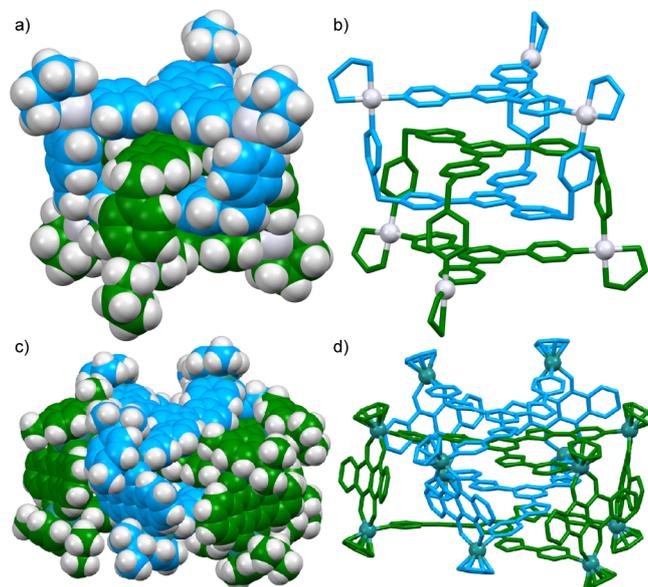


Fig. 11 X-ray crystal structures of Fujita's triply-interlocked catenated cage shown as a) space-filling and b) stick models, and Stang's doubly interpenetrated cage dimer shown as c) space-filling and d) stick models (arene ligand substituents omitted for clarity).

Whilst the examples discussed above are assembled through narcissistic self-association, typically driven by solvophobic interactions, it is possible to use reversible formation of metal-ligand bonds to direct the formation of complex heterocomponent assemblies in excellent yield by combining metal-based structural units and other, orthogonal templating interactions. Using this approach, Kim and co-workers reported a tri-Pt^{II} *molecular necklace* by the one-pot self-assembly of a bis-ammonium dipyridyl axle with a cucurbituril macrocycle and Pt^{II} ions (Fig 12).⁶¹ Similarly Stang and co-workers have pre-formed platinum^{II} rectangles, triangles and hexagons incorporating bipyridinium motifs which upon addition of a crown ether macrocycle⁶² or cryptand⁶³ form [3]-, [4]- and [7]-metallocatenanes, respectively.

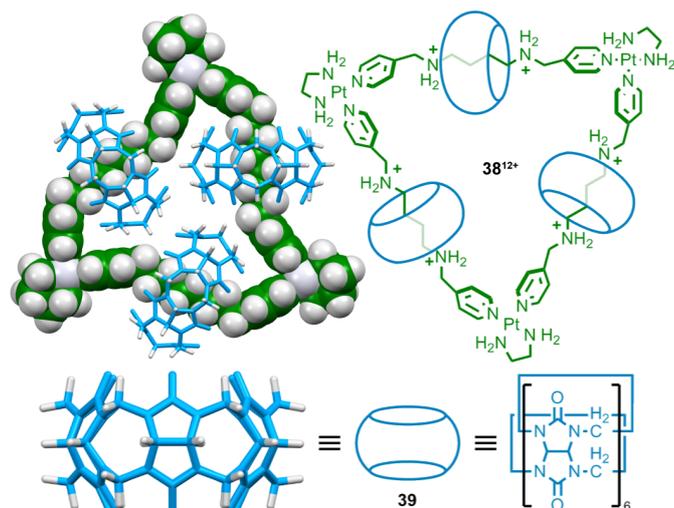


Fig. 12 X-ray crystal structure and chemical structure of Kim's triply interlocked tri-Pt^{II} molecular necklace.

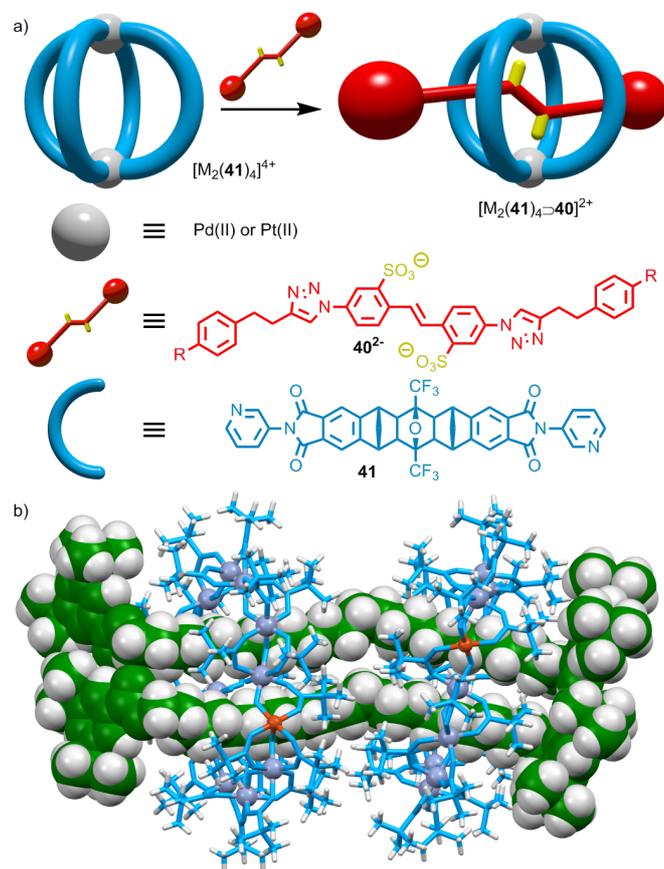


Fig. 13 Examples of self-assembling rotaxanes based on metallomacrocycles: a) Shionoya and Clever's M_2L_4 cage-based rotaxane, and b) Leigh and Winpenny's doubly threaded heterometallic [4]rotaxane.

Examples have also been reported in which a metallo-macrocycle is assembled around a preformed axle. Using this approach, Clever and Shionoya produced one of the largest rotaxanes reported to date (Fig 13a).⁶⁴ ¹H NMR studies indicated that $[M_2(41)4=40]^{2+}$ is formed by partial disassembly of the preformed cationic metallo-macrocycle to allow

incorporation of the anionic axle component with extremely large stoppers. Leigh and Winpenny and co-workers demonstrated the formation of an unusual [4]rotaxane comprised of two axles and two heterometallic rings. This remarkable process requires the self-assembly of 98 components to generate the doubly threaded product (Fig 13b)!⁶⁵

Complex three-dimensional structures have also been reported by combining metallo-cages with mechanically bonding units. Nitschke, Sanders, Schalley and co-workers reported a tetrahedral M_6L_4 hexa-iron^{II} cage assembled from ligands containing two bidentate pyridylimine units linked via a naphthalene diimide bridge. Addition of an excess of a crown ether macrocycle resulted in formation of the anticipated [7]catenane structure with the naphthalene diimide units threading through the macrocycles (Fig 14).⁶⁶ Interestingly, when a smaller tetrahedral cage was prepared, steric constraints prevented saturation of the naphthalene diimide sites, with evidence of only two macrocycles being incorporated into the assembly.⁶⁷

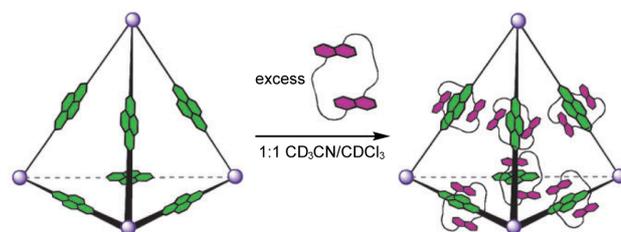


Fig. 14 A metallo-cage-based [7]catenane formed upon addition of an excess of naphthene-based macrocycle to a $Fe^II_6L_4$ cage with ligands containing naphthalene diimide cores. Adapted with permission from ref. 66. Copyright 2013 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

Stimuli Responsive Assembly and Disassembly of MIMs

An advantage of MIM formation under thermodynamic control, in addition to the excellent yields of product from simple reaction components, is the ability to generate stimuli responsive systems. Indeed, Fujita's Pd^{II} catenane can be said to demonstrate this as dilution of the reaction mixture leads to re-emergence of the simple $[Pd_2(37)_2(en)_2]$ metallocycle. More recently, Kuroda and co-workers synthesised a monomeric Pd_2L_4 cage that could be quantitatively converted to the catenated dimer upon heating.⁶⁸ Similarly, Clever and co-workers were able to control reversible catenation of metallosupramolecular cage structures through titration of halide anions, small enough to sit within the cavity of the cage dimer and negate the positive charges of proximal palladium ions. Surprisingly, addition of an excess of halide ions resulted in displacement of ligands to give a metallo-[3]-catenane composed of three interlocked dinuclear metallocycles (Fig 15).⁶⁹

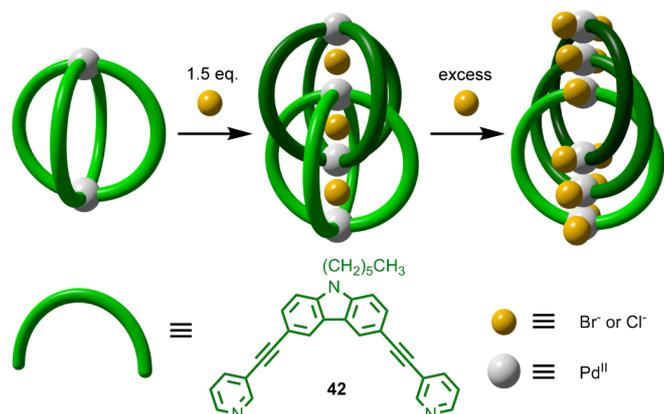


Fig. 15 Clever's anion-responsive catenane: addition of 1.5 equivalents of X (Br⁻ or Cl⁻) resulted in a quadruply-interpenetrated metallo-[2]catenane [Pd₄(**42**)₈-3X]⁵⁺; further addition yielded the neutral [3]catenane [Pd₆X₁₂(**42**)₆].

A Dual Role for Metal Ions in the Synthesis of MIMs – Structural Unit and Template

In the examples above the metal ions are a structural component of the MIM but are not directly involved in providing the thermodynamic driving force for mechanical bond formation. In 1987 Richey and Kushlan proposed the formation of a threaded complex from di-*p*-tolyl magnesium and 15-crown-5,⁷⁰ later corroborated by Bickelhaupt and co-workers, who obtained an x-ray crystal structure of a related diphenyl magnesium complex of xylyl-18-crown-5 (Fig 16a).⁷¹ Bickelhaupt and co-workers were also able to prepare and characterise the corresponding [2]catenane⁷² from organomagnesium building blocks (Fig 16b). The driving force for the formation of **43** and **44** is interactions between the Mg centre and the crown ether oxygen atoms that are largely electrostatic in nature. Wisner and co-workers reported a similar approach that takes advantage of metal-ligand bond formation to construct the axle of the rotaxane with threading driven by outer-sphere ligand interactions.⁷³

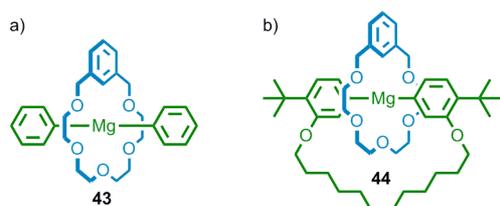


Fig. 16 Chemical structures of Bickelhaupt's organomagnesium a) rotaxane, and b) catenane.

Similarly, aurophilic interactions have been employed as the driving force for the formation of several Au-containing metallo-MIMs.⁷⁴ Mingos and co-workers observed that upon reaction of [Au(NH₃)₂](BF₄) with *tert*-butylacetylene a [2]-catenane composed of two interlocked hexa-gold^I macrocycles was formed.⁷⁵ The Puddephatt group have investigated the coordination of bis-(Au^I acetylide) species with diphosphine ligands. Through varying the spacer unit between the phosphines they were able to preferentially form [1+1]

metallocycle products or metallo-[2]-catenane architectures (e.g. Fig 17a),⁷⁶ and a *doubly braided* Solomon link (Fig 17b), in which the constituent metallocycles cross over twice, was also able to be isolated and characterised.⁷⁷

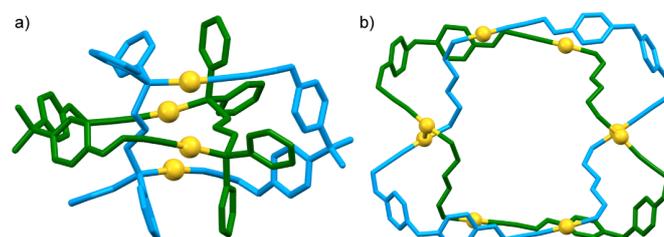


Fig. 17 X-ray crystal structures of MIMs assembled via aurophilic interactions: a) a [2]catenane, and b) a Solomon link (cyclohexyl units and phosphine substituents omitted for clarity).

Finally, Ruabenheimer and Barbour and co-workers reported a system that takes advantage of attractive Au^I-Au^I interactions to drive the formation of an unusual interlocked molecule in which both macrocycle and axle are composed of metal-ligand units. Reaction of a 1-propargyl-3-vinylimidazole carbene ligand with ClAuPMe₃ yielded a trimeric gold macrocycle with a [Au(PMe₃)₂]⁺ axle located through the annulus, stabilised by trifurcated aurophilic interactions. NMR and MS confirmed the persistence of the interlocked structure in solution (Fig 18).⁷⁸

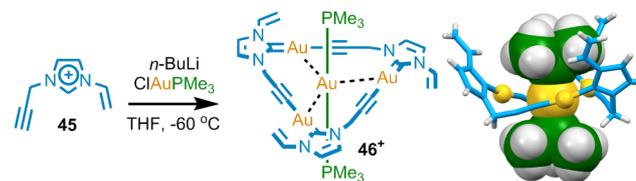


Fig. 18 Synthesis and X-ray crystal structure of a metallo-[2]rotaxane driven by aurophilic interactions.

Metal Ligand Interactions for Mechanically Interlocked Materials

Extended structures based on interlocked molecules have been discussed for many years in the context of smart materials. Indeed, one of the most successful commercial application of mechanical bonding relies on the presence of dynamic sliding links to produce polymers with enhanced mechanical properties.⁷⁹ Recently, combining the concept of metallo-supramolecular polymers with pseudorotaxane and rotaxane linkers has led to the development of rotaxane coordination polymer (RCP) and metal-organic rotaxane framework (MORF), as well as limited examples of catenane-based materials.⁸⁰ As a point of clarification it should be noted the term MORF/MOF will be applied exclusively to three dimensional coordination polymers of a porous nature in the discussion below.

The first rotaxane coordination polymers were reported by Kim and co-workers in the 1990s by employing metal ions to link and stopper pseudorotaxane monomers.⁸¹ Through careful choice of metal ion source it was possible to form complexes in which metal ions were shared between rotaxanes generating

polymeric materials. In the first example reported a pyridine stoppered pseudorotaxane was reacted with $\text{Cu}(\text{NO}_3)_2$ to generate a coordination polymer linked by *fac*- $[\text{Cu}(\text{H}_2\text{O})_3]$ nodes with rotaxanes binding *cis* to one another to complete the square pyramidal coordination geometry and create a zig-zag motif (Fig 19a). Alternatively, by mixing the pseudorotaxane with $\text{Ag}(\text{OTs})$ a 1D coordination polymer was also observed, with the Ag^{I} ions in a linear coordination environment.⁸² Furthermore, the geometry of the metal ions, and as a result the structure of the coordination polymer, was found to be highly dependent on the choice of anion; when AgNO_3 was employed in place of AgOTs the Ag^{I} ions adopted a heavily distorted trigonal bipyramidal geometry with three rotaxanes and a chelating NO_3 anion, generating a honeycomb-type 2D polymeric structure.

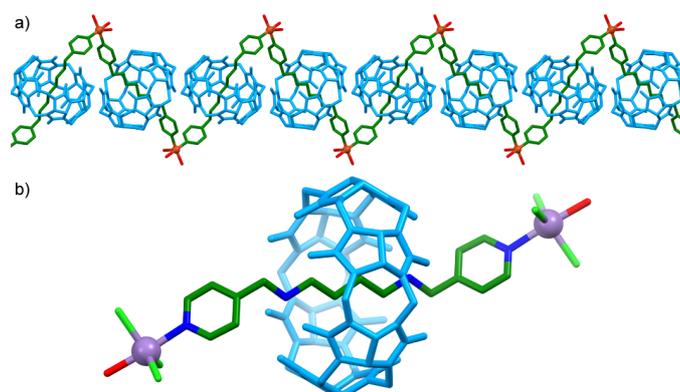


Fig. 19 X-ray crystal structures of Kim's a) 1D coordination polymer with $\text{Cu}(\text{H}_2\text{O})_3$ nodes, and b) a discrete [2]rotaxane with $\text{MnCl}_3(\text{H}_2\text{O})$ stoppers, both formed from the same *pseudo*-rotaxane precursor.

Extending this approach, Goldberg and co-workers were able to generate a 1D coordination polymer from pseudorotaxane **47** by use of what can be considered an extreme extension of Fujita's *cis*-protection strategy;⁸³ a porphyrin ligand was used to occupy the equatorial coordination sites of a Zn^{II} ion, leaving only the axial sites remaining (Fig 20). Thus, coordination with the linear bis-monodentate pseudorotaxane could not form polymers of higher dimensionality and a 1D CP was produced

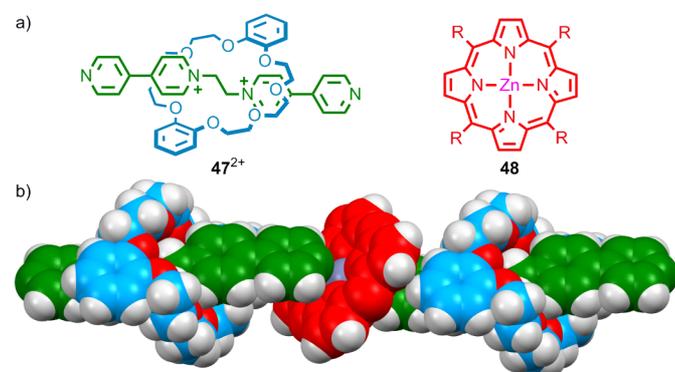


Fig. 20 a) Pseudo-rotaxane **47** and Zn^{II} -porphyrin complex **48** form 1D coordination polymers. b) Short fragment of X-ray crystal structure shown in space-filling model. Porphyrin substituents have been omitted for clarity.

Unsurprisingly, given the large effects that reaction conditions and counter-ion identity can have, regioisomerism of the pseudorotaxane structure (Fig 21a) was also found to greatly affect the structure of resultant coordination polymers. The polymer formed between Tb^{III} ions and a pseudorotaxane in which the thread was terminated by 4-carboxylatephenyl units formed a 2D network with three thread termini coordinated to a single Tb ion (Fig 21b). Conversely the 3-carboxylatephenyl isomer yielded the first 3D coordination network with an interlocked ligand. In this instance four equatorial rotaxane ligands formed a cluster with two Tb ions, with two axially coordinated ligands extending the network into three dimensions (Fig 21c).⁸⁴

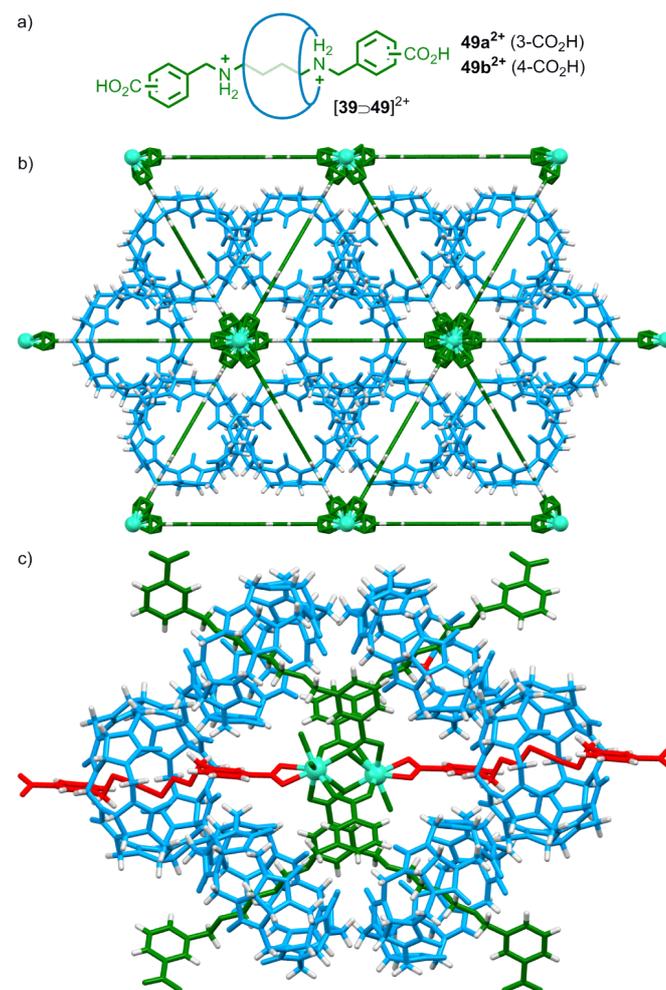


Fig. 21 a) Reaction of pseudo-rotaxanes formed between CB[6] and diammonium axes with Tb^{III} led to the formation of b) a 2D network with the 4-carboxylatephenyl isomer **49b**, and c) a 3D coordination polymer with the 3-carboxylatephenyl isomer **49a** (equatorially coordinated axles are shown in green, axially coordinated in red).

Similarly Loeb and co-workers were able to form 1D and 2D rotaxane coordination polymers utilising Co^{II} , Cu^{II} and Cd^{II} ions and pseudorotaxanes with a bis-pyridinium thread and crown ether macrocycles.⁸⁵ This motif was successfully extended to 3D coordination networks by replacing the thread with one containing pyridinium N-oxide termini. Isostructural polymers were formed with Sm^{III} , Eu^{III} , Gd^{III} and Tb^{III} in which six

rotaxane ligands were bound to a single metal ion in a distorted octahedral arrangement.⁸⁶ Use of smaller Yb^{III} ions resulted in formation of a unique polymer in which each Yb^{III} is coordinated to only five rotaxanes giving rise to 2D layers consisting of alternating square and triangular forms which are further pillared by rotaxanes bound to the axial site of the Yb^{III} centres.⁴¹

In the examples presented above, and the vast majority of RCPs, polymerisation is achieved by coordination of metal ions with ligand portions of the MIM ligand scaffold located on the thread component. Alternatively, incorporation of ligands into the macrocycle structure allows an increase in the diversity of assemblies that can be formed,⁸⁷ and also the preparation of coordination polymers based on catenane building blocks. Using this approach, Stoddart and Yaghi and co-workers prepared catenanes incorporating linear units of varying length, with carboxylate moieties at the termini. Upon self-assembly with Cu^{I} ions the catenane with the shorter bis-carboxylate (19 Å) was found to form a 2D CP,⁸⁸ whilst the longer unit (33 Å) yielded an interpenetrated 3D MOF (Fig 22).⁸⁹

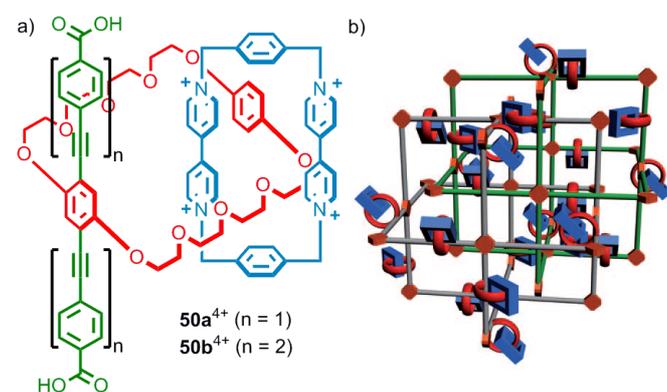


Fig. 22 a) Stoddart and Yaghi's catenane ligand and b) the MOF derived from ligand **50b**. Adapted with permission from ref. 89. Copyright 2010 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

Recently Loeb and co-workers have combined these two designs and prepared permanently interlocked [2]rotaxane ligands that have donor atoms on both the thread and macrocycle components (Fig 23a).⁹⁰ The resulting 3D materials generated using these multidentate interlocked ligands have unique poly-threaded topologies derived from the interpretation of independent lattices and the interlocked nature of the linker (Fig 23b). This strategy has the potential to create materials in which independent coordination polymers are interwoven (crosslinked) solely due to the threading of the mechanical bond of the ligand and may ultimately allow control over the relative positions of these frameworks in the solid state.

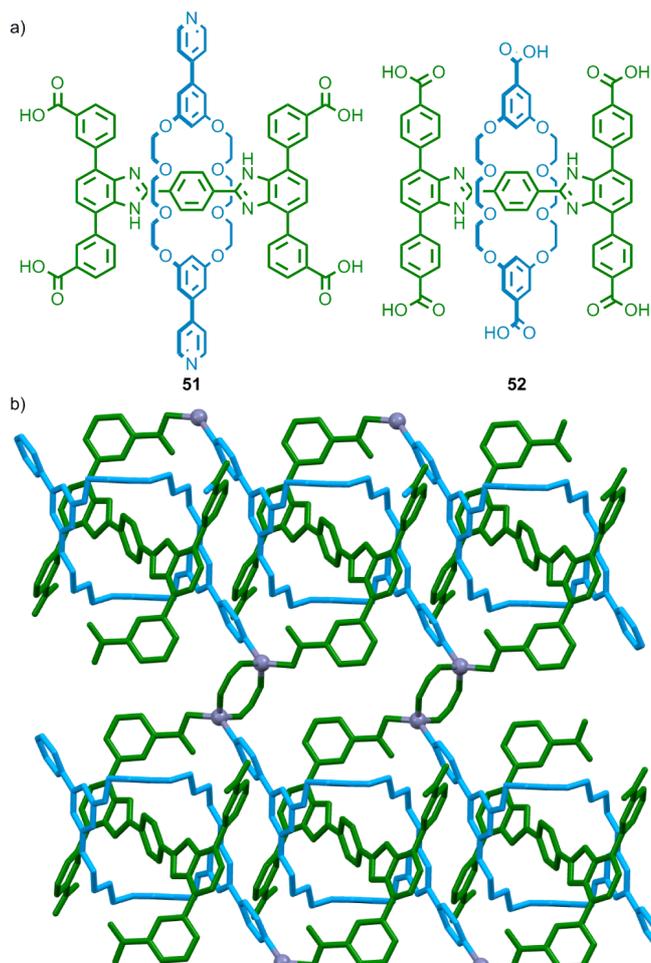


Fig. 23 a) Examples of rotaxane linkers for MORFs with donors on both the thread and macrocycle. b) X-ray crystal structure of MORF formed between ligand **49** and Zn^{II} .

MIM Coordination Polymers with Dynamic Components

Although the early examples of interlocked materials had unique and sometimes exotic solid-state structures with threaded ligands linking metal ions and clusters, none displayed the dynamic motion (rotation, shuttling) and switching properties that make interlocked molecules and related molecular machines so interesting and important.⁹¹ In 2012, Loeb and co-workers prepared the first MORF (UWDM-1) with a rotaxane linker that showed large amplitude motion of one of the components in the solid state (Fig 24a). Using an aniline-based thread and a crown ether macrocycle labelled with deuterium atoms it was demonstrated using variable temperature (VT) ^2H solid-state (SS) NMR that the macrocyclic ring was free to undergo rotation about the coordination polymer backbone.^{90d} This was followed by studies showing the effects upon rotation of changing the size and type of macrocycle.⁹¹ Recent studies have shown that this type of thermally driven motion can also be induced inside a Zn^{II} MORF in which the thread is an imidazolium ion (Fig 24b).⁹² Interestingly, it was also demonstrated, using a rotaxane pillared (Fig 24c) Zn^{II} MOF, that the rotation of the macrocycle could be turned ON and OFF by inducing a phase change in the material by alternately drying and re-soaking the solid with

solvent; the wet material did not show rotation due to trapping of the ring in the cavity of the lattice but upon drying the ring was free to rotate.⁹³

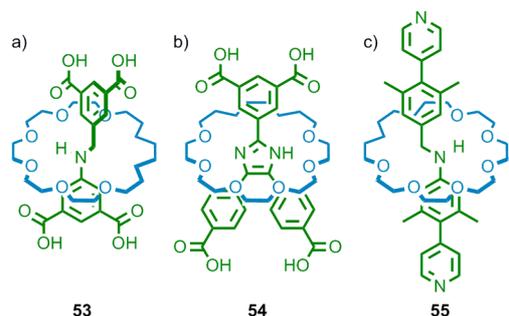


Fig. 24 Interlocked linkers used by Loeb and co-workers to demonstrate the rotation of rotaxane macrocycles inside MOF materials.

The concept of arraying switchable MIMs within an ordered network is an attractive extension of these polymeric systems that has begun to be explored,⁹⁴ offering the potential advantage of addressing the interlocked components individually. Inspired by the many sophisticated examples of molecular switches and machines based on interlocked molecules that operate beautifully in solution and to some extent in soft materials and on surfaces, it was further demonstrated that the fundamental to and fro motion of a degenerate molecular shuttle could be accomplished in the solid-state inside a MOF material. Using a ¹³C enriched sample of a Zn^{II} MOF constructed using a rigid H-shaped linker (Fig 25), it was demonstrated by VT ¹³C SSNMR and related EXSY experiments that a 24-crown-8 macrocycle could shuttle back and forth along a rigid track in a fashion analogous to what occurs in solution, albeit with a significantly higher energy barrier.⁹⁵

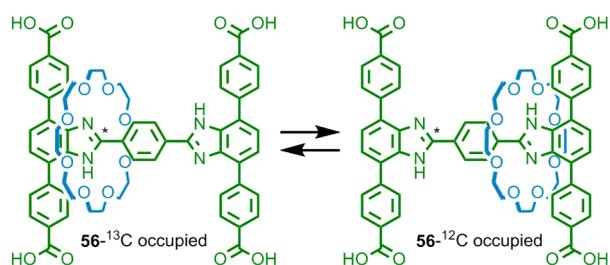


Fig. 25 The molecular shuttle linker used to demonstrate large amplitude translational motion (molecular shuttling) of a rotaxane macrocycle inside a MOF material.

Metal Ions as Structural Components of MIMs - Conclusions

The examples above demonstrate that metal-ligand structural units can provide access to a wide variety of complex MIMs by taking advantage of the properties of metal ligand interactions, in particular their reversible formation under mild conditions. More recently, it has been demonstrated that self-assembly via coordination chemistry provides a facile route to linking MIMs within ordered arrays as CPs and, perhaps most excitingly, MOFs. With the recent demonstration of dynamic behaviour, a key facet of MIMs, being retained in the solid

state these systems are beginning to demonstrate promise for materials applications in which individually addressable MIM units are a prerequisite. Although still in its infancy, the move towards real-world applications for these materials is inexorably gaining traction, with ongoing work continually advancing the state-of-the-art in the field.

Conclusions

The synthesis of MIMs has developed dramatically since the earliest attempts in the 1960s. Pre-dating the PT approach, metal-ligand interactions have been utilised as structural components within MIMs, both to kinetically trap non-covalently associated components, and also as reversible linkages that allow interlocked structures favoured by thermodynamics to self-assemble in high yield. However, beginning with Sauvage's seminal use of Cu^I ions to pre-organise components to favour formation of interlocked products, metal ion coordination has become one of the most versatile and commonly used templating motifs. This has since been extended with the development of the AT approach, in which the ability of metal ions to mediate covalent bond formation is also exploited. In this manner a thermodynamically favoured pseudo-interlocked precursor need not be prepared as with PMT, but rather the interlocked system is a product of kinetic mechanical trapping of the sub-components. In practice this leads to more stringent conditions for achieving successful mechanical bond formation, although it opens the door to the synthesis of MIMs in which at least one of the components does not require a coordinating moiety, nor do there have to be significant attractive interactions between the components.

Inevitably linked with the evolution of more rapid and higher yielding synthetic methodologies for an increasingly diverse range of structures is the move towards potential applications. In this sense metal ions also have an integral part to play as their predictable coordination geometry and reversible bond formation make them ideal components for linking MIMs together into designed, ordered arrays of varying dimensionality. Although still in the early stages, recent demonstration of switchable mechanical motion in the solid state indicates that this area of study has the potential to yield exciting new functional materials in the future.

Acknowledgements

SJL thanks the Natural Science and Engineering Research Council of Canada for support of his Canada Research Chair and the University of Windsor for financial support. PDB acknowledges funding from the European Research Council (Advanced Grant Agreement no. 267426). SMG acknowledges funding from the European Research Council (Consolidator Grant Agreement no. 724987). JEML is an EU Marie Skłodowska-Curie Fellow, receiving financial support from the EU's Horizon 2020 research and innovation programme under

Marie Skłodowska-Curie grant agreement No. 660731. SMG is a Royal Society Research Fellow.

Notes and references

- 1 Although catenanes and rotaxanes are the archetypal examples of interlocked molecules, other complex threaded and entangled molecular architectures are possible including higher order links (e.g. Borromean rings: J. C. Loren, M. Yoshizawa, R. F. Haldimann, A. Linden and J. S. Siegel, *Angew. Chem. Int. Ed.*, 2003, **42**, 5702–5705) and knots (e.g. J. J. Danon, A. Krüger, D. A. Leigh, J. Lemonnier, A. J. Stephens, I. J. Vitorica-Yrezabal and S. L. Woltering, *Science.*, 2017, **355**, 159–162). For more information the interested reader is directed to refs. 2.
- 2 For recent general reviews on the subject of interlocked molecules and molecular machines see: a) M. S. Vickers and P. D. Beer, *Chem. Soc. Rev.*, 2007, **36**, 211–225. b) J. F. Stoddart, *Chem. Soc. Rev.*, 2009, **38**, 1802–1820. c) J. E. Beves, B. A. Blight, C. J. Campbell, D. A. Leigh and R. T. McBurney, *Angew. Chem. Int. Ed.*, 2011, **50**, 9260–9327. d) E. A. Neal and S. M. Goldup, *Chem. Commun.*, 2014, **50**, 5128–5142. e) S. Erbas-Cakmak, D. A. Leigh, C. T. McTernan and A. L. Nussbaumer, *Chem. Rev.*, 2015, **115**, 10081–10206. f) M. Xue, Y. Yang, X. Chi, X. Yan and F. Huang, *Chem. Rev.*, 2015, **115**, 7398–7501. g) *The Nature of the Mechanical Bond: From Molecules to Machines*, C. J. Brunns and J. F. Stoddart, Wiley, 2016.
- 3 E. Wasserman, *J. Am. Chem. Soc.*, 1960, **82**, 4433–4434.
- 4 G. Schill and A. Lüttringhaus, *Angew. Chem. Int. Ed. Eng.*, 1964, **3**, 546–547.
- 5 C. O. Dietrich-Buchecker, J.-P. Sauvage and J. P. Kintzinger, *Tetrahedron Lett.*, 1983, **24**, 5095–5098; C. O. Dietrich-Buchecker, J.-P. Sauvage and J. M. Kern, *J. Am. Chem. Soc.*, 1984, **106**, 3043–3045.
- 6 C. Wu, P. R. Lecavalier, Y. X. Shen and H. W. Gibson, *Chem. Mater.*, 1991, **3**, 569–572.
- 7 J.-F. Ayme, J. E. Beves, C. J. Campbell and D. A. Leigh, *Chem. Soc. Rev.*, 2013, **42**, 1700–1712.
- 8 S. M. Goldup, D. A. Leigh, P. J. Lusby, R. T. McBurney and A. M. Z. Slawin, *Angew. Chem. Int. Ed.*, 2008, **47**, 6999–7003.
- 9 A.-M. Fuller, D. A. Leigh, P. J. Lusby, I. D. H. Oswald, S. Parsons and D. B. Walker, *Angew. Chem. Int. Ed.*, 2004, **43**, 3914–3918.
- 10 D. A. Leigh, P. J. Lusby, S. J. Teat, A. J. Wilson and J. K. Y. Wong, *Angew. Chem. Int. Ed.*, 2001, **40**, 1538–1543.
- 11 D. A. Leigh, R. G. Pritchard and A. J. Stephens, *Nat. Chem.*, 2014, **6**, 978–982.
- 12 J.-P. Sauvage and M. Ward, *Inorg. Chem.*, 1991, **30**, 3869–3874.
- 13 D. A. Leigh, P. J. Lusby, R. T. McBurney, A. Morelli, A. M. Z. Slawin, A. R. Thomson and D. B. Walker, *J. Am. Chem. Soc.*, 2009, **131**, 3762–3771.
- 14 a) D. A. Leigh, P. J. Lusby, S. J. Teat, A. J. Wilson and J. K. Y. Wong, *Angew. Chem. Int. Ed.*, 2001, **113**, 1586–1591. b) C. Browne, T. K. Ronson and J. R. Nitschke, *Angew. Chem. Int. Ed.*, 2014, **53**, 10701–10705. c) C. J. Campbell, D. A. Leigh, I. J. Vitorica-Yrezabal and S. L. Woltering, *Angew. Chem. Int. Ed.*, 2014, **53**, 13771–13774.
- 15 In a subcomponent-assembly ligand synthesis the ligand motif is assembled around the metal ion through dynamic covalent chemistry (e.g. imine formation as in Figure 3b). This is distinct from the active template approach as subcomponent-assembly is a thermodynamic template effect; if the metal ion is removed the molecule will slowly revert to its components and the mechanical bond will be lost.
- 16 B. Mohr, J.-P. Sauvage, R. H. Grubbs and M. Weck, *Angew. Chem. Int. Ed. English*, 1997, **36**, 1308–1310.
- 17 C. O. Dietrich-Buchecker, A. Edel, J. P. Kintzinger and J. P. Sauvage, *Tetrahedron*, 1987, **43**, 333–344.
- 18 C. Dietrich-Buchecker and J. Sauvage, *Chem. Commun.*, 1999, **1**, 615–616.
- 19 a) S. Te Tung, C. C. Lai, Y. H. Liu, S. M. Peng and S. H. Chiu, *Angew. Chem. Int. Ed.*, 2013, **52**, 13269–13272. b) Y.-W. Wu, P.-N. Chen, C.-F. Chang, C.-C. Lai and S.-H. Chiu, *Org. Lett.*, 2015, **17**, 2158–2161.
- 20 Y.-H. Lin, C.-C. Lai, Y.-H. Liu, S.-M. Peng and S.-H. Chiu, *Angew. Chem. Int. Ed.*, 2013, **52**, 10231–10236.
- 21 L. M. Hancock and P. D. Beer, *Chem. Commun.*, 2011, **47**, 6012–6014.
- 22 R. C. Knighton and P. D. Beer, *Chem. Commun.*, 2014, **50**, 1540–1542.
- 23 F. Zapata, O. A. Blackburn, M. J. Langton, S. Faulkner and P. D. Beer, *Chem. Commun.*, 2013, **49**, 8157–8159.
- 24 C. Lincheneau, B. Jean-Denis and T. Gunnlaugsson, *Chem. Commun.*, 2014, **50**, 2857–2860.
- 25 Recently, Leigh and co-workers have also utilised Lu^{III} and Eu^{III} ions to template the formation of trefoil knots: a) J.-F. Ayme, G. Gil-Ramírez, D. A. Leigh, J.-F. Lemonnier, A. Markevicius, C. A. Muryn and G. Zhang, *J. Am. Chem. Soc.*, 2014, **136**, 13142–13145. b) G. Zhang, G. Gil-Ramírez, A. Markevicius, C. Browne, I. J. Vitorica-Yrezabal and D. A. Leigh, *J. Am. Chem. Soc.*, 2015, **137**, 10437–10442.
- 26 P. Mobian, J.-P. Collin and J.-P. Sauvage, *Tetrahedron Lett.*, 2006, **47**, 4907–4909.
- 27 V. Aucagne, K. D. Hänni, D. A. Leigh, P. J. Lusby and D. B. Walker, *J. Am. Chem. Soc.*, 2006, **128**, 2186–2187.
- 28 J. D. Crowley, S. M. Goldup, A.-L. Lee, D. A. Leigh and R. T. McBurney, *Chem. Soc. Rev.*, 2009, **38**, 1530–1541.
- 29 Although the final covalent bond formation that captures the interlocked molecule is typically under kinetic control, the formation of thermodynamically stable precursors is a requirement of PT methodologies. For a discussion of these requirements and examples of PT synthesis under thermodynamic control see: W. R. Dichtel, O. S. Miljanić, W. Zhang, J. M. Spruell, K. Patel, I. Aprahamian, J. R. Heath and J. F. Stoddart, *Acc. Chem. Res.*, 2008, **41**, 1750–1761.
- 30 E. A. Neal and S. M. Goldup, *Chem. Sci.*, 2015, **6**, 2398–2404.
- 31 H. Lahlali, K. Jobe, M. Watkinson and S. M. Goldup, *Angew. Chem. Int. Ed.*, 2011, **50**, 4151–4155.
- 32 L. D. Movsisyan, M. Franz, F. Hampel, A. L. Thompson, R. R. Tykwinski and H. L. Anderson, *J. Am. Chem. Soc.*, 2016, **138**, 1366–1376.
- 33 A. Noor, W. K. C. Lo, S. C. Moratti and J. D. Crowley, *Chem. Commun.*, 2014, **50**, 7044–7047.
- 34 a) S. Saito, E. Takahashi and K. Nakazono, *Org. Lett.*, 2006, **8**, 5133–5136. b) J. Berná, J. D. Crowley, S. M.

- Goldup, K. D. Hänni, A.-L. Lee and D. A. Leigh, *Angew. Chem. Int. Ed.*, 2007, **46**, 5709–5713. c) J. D. Crowley, S. M. Goldup, N. D. Gowans, D. A. Leigh, V. E. Ronaldson and A. M. Z. Slawin, *J. Am. Chem. Soc.*, 2010, **132**, 6243–6248.
- 35 J. Berná, S. M. Goldup, A.-L. Lee, D. A. Leigh, M. D. Symes, G. Teobaldi and F. Zerbetto, *Angew. Chem. Int. Ed.*, 2008, **47**, 4392–4396.
- 36 J. D. Crowley, K. D. Hänni, A.-L. Lee and D. A. Leigh, *J. Am. Chem. Soc.*, 2007, **129**, 12092–12093.
- 37 J. D. Crowley, K. D. Hänni, D. A. Leigh and A. M. Z. Slawin, *J. Am. Chem. Soc.*, 2010, **132**, 5309–5314.
- 38 S. M. Goldup, D. A. Leigh, R. T. McBurney, P. R. McGonigal and A. Plant, *Chem. Sci.*, 2010, **1**, 383–386.
- 39 S. Hoekman, M. O. Kitching, D. A. Leigh, M. Papmeyer and D. Roke, *J. Am. Chem. Soc.*, 2015, **137**, 7656–7659.
- 40 K. Ugajin, E. Takahashi, R. Yamasaki, Y. Mutoh, T. Kasama and S. Saito, *Org. Lett.*, 2013, **15**, 2684–2687.
- 41 S. M. Goldup, D. A. Leigh, P. J. Lusby, R. T. McBurney and A. M. Z. Slawin, *Angew. Chem. Int. Ed.*, 2008, **47**, 3381–3384.
- 42 M. J. Langton, Y. Xiong and P. D. Beer, *Chem. Eur. J.*, 2015, **21**, 18910–18914.
- 43 A. M. Albrecht-Gary, Z. Saad, C. O. Dietrich-Buchecker and J. P. Sauvage, *J. Am. Chem. Soc.*, 1985, **107**, 3205–3209.
- 44 J. Berná, S. M. Goldup, A.-L. Lee, D. A. Leigh, M. D. Symes, G. Teobaldi and F. Zerbetto, *Angew. Chem. Int. Ed.*, 2008, **47**, 4392–4396.
- 45 B. Lewandowski, G. De Bo, J. W. Ward, M. Papmeyer, S. Kuschel, M. J. Aldegunde, P. M. E. Gramlich, D. Heckmann, S. M. Goldup, D. M. D'Souza, A. E. Fernandes and D. A. Leigh, *Science.*, 2013, **339**, 189–193.
- 46 a) H. M. Cheng, D. A. Leigh, F. Maffei, P. R. McGonigal, A. M. Z. Slawin and J. Wu, *J. Am. Chem. Soc.*, 2011, **133**, 12298–12303. b) J. J. Danon, D. A. Leigh, P. R. McGonigal, J. W. Ward and J. Wu, *J. Am. Chem. Soc.*, 2016, **138**, 12643–12647.
- 47 R. J. Bordoli and S. M. Goldup, *J. Am. Chem. Soc.*, 2014, **136**, 4817–4820.
- 48 J. Winn, A. Pinczewska and S. M. Goldup, *J. Am. Chem. Soc.*, 2013, **135**, 13318–13321.
- 49 J. Y. C. Lim, I. Marques, A. L. Thompson, K. E. Christensen, V. Félix and P. D. Beer, *J. Am. Chem. Soc.*, 2017, **139**, 3122–3133.
- 50 a) Y. Sato, R. Yamasaki and S. Saito, *Angew. Chem. Int. Ed.*, 2009, **48**, 504–507. b) S. M. Goldup, D. A. Leigh, T. Long, P. R. McGonigal, M. D. Symes and J. Wu, *J. Am. Chem. Soc.*, 2009, **131**, 15924–15929.
- 51 J. E. M. Lewis, J. Winn, L. Cera and S. M. Goldup, *J. Am. Chem. Soc.*, 2016, **138**, 16329–16336.
- 52 A. C. Benniston and A. Harriman, *Angew. Chem. Int. Ed.*, 1993, **32**, 1459–1461.
- 53 L. Flamigni, N. Armaroli, F. Barigelletti, J. Chambron, J. Sauvage and N. Sölladie, *New J. Chem.*, 1999, **23**, 1151–1158.
- 54 a) H. Ogino, *J. Am. Chem. Soc.*, 1981, **103**, 1303–1304. b) H. Ogino and K. Ohato, *Inorg. Chem.*, 1984, **23**, 3312–3316.
- 55 W. Wang, L.-J. Chen, X.-Q. Wang, B. Sun, X. Li, Y. Zhang, J. Shi, Y. Yu, L. Zhang, M. Liu and H.-B. Yang, *Proc. Natl. Acad. Sci.*, 2015, **112**, 5597–5601.
- 56 a) S. J. Rowan, S. J. Cantrill, G. R. L. Cousins, J. K. M. Sanders and J. F. Stoddart, *Angew. Chem. Int. Ed.*, 2002, **41**, 898–952. b) Y. Jin, C. Yu, R. J. Denman and W. Zhang, *Chem. Soc. Rev.*, 2013, **42**, 6634–6654.
- 57 M. Fujita, F. Ibukuro, H. Hagihara and K. Ogura, *Nature*, 1994, **367**, 720–723.
- 58 M. Fujita, F. Ibukuro, K. Yamaguchi and K. Ogura, *J. Am. Chem. Soc.*, 1995, **117**, 4175–4176.
- 59 M. Fujita, N. Fujita, K. Ogura and K. Yamaguchi, *Nature*, 1999, **400**, 52–55.
- 60 A. Mishra, A. Dubey, J. W. Min, H. Kim, P. J. Stang and K.-W. Chi, *Chem. Commun.*, 2014, **50**, 7542–7544.
- 61 D. Whang, K. Park, J. Heo, P. Ashton and K. Kim, *J. Am. Chem. Soc.*, 1998, **120**, 4899–4900.
- 62 S. Li, J. Huang, T. R. Cook, J. B. Pollock, H. Kim, K.-W. Chi and P. J. Stang, *J. Am. Chem. Soc.*, 2013, **135**, 2084–2087; S. Li, J. Huang, F. Zhou, T. R. Cook, X. Yan, Y. Ye, B. Zhu, B. Zheng and P. J. Stang, *J. Am. Chem. Soc.*, 2014, **136**, 5908–5911.
- 63 Y. Ye, S.-P. Wang, B. Zhu, T. R. Cook, J. Wu, S. Li and P. J. Stang, *Org. Lett.*, 2015, **17**, 2804–2807.
- 64 G. H. Clever and M. Shionoya, *Chem. Eur. J.*, 2010, **16**, 11792–11796.
- 65 C.-F. Lee, D. A. Leigh, R. G. Pritchard, D. Schultz, S. J. Teat, G. a Timco and R. E. P. Winpenny, *Nature*, 2009, **458**, 314–318.
- 66 S. P. Black, A. R. Stefankiewicz, M. M. J. Smulders, D. Sattler, C. A. Schalley, J. R. Nitschke and J. K. M. Sanders, *Angew. Chem. Int. Ed.*, 2013, **52**, 5749–5752.
- 67 S. P. Black, D. M. Wood, F. B. Schwarz, T. K. Ronson, J. J. Holstein, A. R. Stefankiewicz, C. A. Schalley, J. K. M. Sanders and J. R. Nitschke, *Chem. Sci.*, 2016, **7**, 2614–2620.
- 68 M. Fukuda, R. Sekiya and R. Kuroda, *Angew. Chem. Int. Ed.*, 2008, **47**, 706–710.
- 69 R. Zhu, J. Lübben, B. Dittrich and G. H. Clever, *Angew. Chem. Int. Ed.*, 2015, **54**, 2796–2800.
- 70 H. G. Richey and D. M. Kushlan, *J. Am. Chem. Soc.*, 1987, **109**, 2510–2512.
- 71 P. R. Markies, T. Nomoto, O. S. Akkerman, F. Bickelhaupt, W. J. J. Smeets and A. L. Spek, *J. Am. Chem. Soc.*, 1988, **110**, 4845–4846.
- 72 G. J. M. Gruter, F. J. J. de Kanter, P. R. Markies, T. Nomoto, O. S. Akkerman and F. Bickelhaupt, *J. Am. Chem. Soc.*, 1993, **115**, 12179–12180.
- 73 B. A. Blight, J. A. Wisner and M. C. Jennings, *Angew. Chem. Int. Ed.*, 2007, **46**, 2835–2838.
- 74 For a recent review on Au-containing MIMs see: R. J. Puddephatt, *J. Organomet. Chem.*, 2014, **792**, 13–24.
- 75 D. M. P. Mingos, J. Yau, S. Menzer and D. J. Williams, *Angew. Chem. Int. Ed. English*, 1995, **34**, 1894–1895.
- 76 C. P. McArdle, M. J. Irwin, M. C. Jennings and R. J. Puddephatt, *Angew. Chem. Int. Ed.*, 1999, **38**, 3376–3378.
- 77 C. P. McArdle, M. C. Jennings, J. J. Vittal and R. J. Puddephatt, *Chem. Eur. J.*, 2001, **7**, 3572–3583.
- 78 U. E. I. Horvath, J. M. McKenzie, S. Cronje, H. G. Raubenheimer and L. J. Barbour, *Chem. Commun.*, 2009, 6598–6600.
- 79 K. Ito, *Polym. J.*, 2007, **39**, 489–499.
- 80 a) S. J. Loeb, *Chem. Commun.* 2005, 1511–1518. b) S. J. Loeb, *Chem. Soc. Rev.* 2007, **36**, 226–235. c) V. N. Vukotic and S. J. Loeb, *Chem. Soc. Rev.* 2012, **41**, 5896–

5906. d) J. E. M. Lewis, M. Galli and S. M. Goldup, *Chem. Commun.*, 2017, **53**, 298–312.
- 81 D. Whang, Y. Jeon, J. Heo, K. Kim, *J. Am. Chem. Soc.*, 1996, **118**, 11333–11334.
- 82 D. Whang and K. Kim, *J. Am. Chem. Soc.*, 1997, **119**, 451–452.
- 83 Y. Diskin-Posner, G. K. Patra and I. Goldberg, *Eur. J. Inorg. Chem.*, 2001, 2515–2523.
- 84 E. Lee, J. Heo and K. Kim, *Angew. Chem. Int. Ed.*, 2000, **39**, 2699–2701.
- 85 a) G. J. E. Davidson and S. J. Loeb, *Angew. Chem. Int. Ed.* 2003, **42**, 74–77. b) D. J. Hoffart and S. J. Loeb, *Supramol. Chem.*, 2007, **19**, 89–93. c) L. K. Knight, V. N. Vukotic, E. Viljoen, C. B. Caputo and S. J. Loeb, *Chem. Commun.*, 2009, 5585–5587. d) V. N. Vukotic and S. J. Loeb, *Chem. Eur. J.* 2010, **16**, 13630–13637. e) D. J. Mercer, J. Yacoub, K. Zhu, S. K. Loeb and S. J. Loeb, *Org. Biomol. Chem.* 2012, **10**, 6094–6104.
- 86 D. J. Hoffart and S. J. Loeb, *Angew. Chem. Int. Ed.*, 2005, **44**, 901–904.
- 87 D. J. Mercer, V. N. Vukotic and S. J. Loeb, *Chem. Commun.*, 2011, **47**, 896–898.
- 88 Q. Li, W. Zhang, O. Š. Miljanić, C. B. Knobler, J. F. Stoddart and O. M. Yaghi, *Chem. Commun.*, 2010, **46**, 380–382.
- 89 Q. Li, C.-H. Sue, S. Basu, A. K. Shveyd, W. Zhang, G. Barin, L. Fang, A. A. Sarjeant, J. F. Stoddart and O. M. Yaghi, *Angew. Chem. Int. Ed.*, 2010, **49**, 6751–6755.
- 90 a) N. C. Frank, D. J. Mercer and S. J. Loeb, *Chem. Eur. J.* 2013, **19**, 14076–14080. b) G. Gholami, K. Zhu, J. S. Ward, P. E. Kruger and S. J. Loeb, *Eur. J. Inorg. Chem.* 2016, **27**, 4524–4529. c) G. Gholami, G. Baggì, K. Zhu and S. J. Loeb, *Dalton Trans.* 2017, **46**, 2462–2470. d) V. N. Vukotic, K. J. Harris, K. Zhu, R. W. Schurko and S. J. Loeb, *Nature Chem.*, 2012, **4**, 456–460.
- 91 V. N. Vukotic, C. A. O’Keefe, K. Zhu, K. J. Harris, C. To, R. W. Schurko and S. J. Loeb, *J. Am. Chem. Soc.* 2015, **137**, 9643–9651.
- 92 N. Farahani, K. Zhu, C. A. O’Keefe, R. W. Schurko and S. J. Loeb, *ChemPlusChem*, 2016, **81**, 836–841.
- 93 K. Zhu, V. N. Vukotic, C. A. O’Keefe, R. W. Schurko and S. J. Loeb, *J. Am. Chem. Soc.* 2014, **136**, 7403–7409.
- 94 H. Deng, M. A. Olson, J. F. Stoddart and O. M. Yaghi, *Nat. Chem.*, 2010, **2**, 439–443.
- 95 K. Zhu, V. N. Vukotic, C. A. O’Keefe, R. W. Schurko and S. J. Loeb, *Nature Chem.* 2015, **7**, 514–519.