DOI: 10.1002/anie.201007963

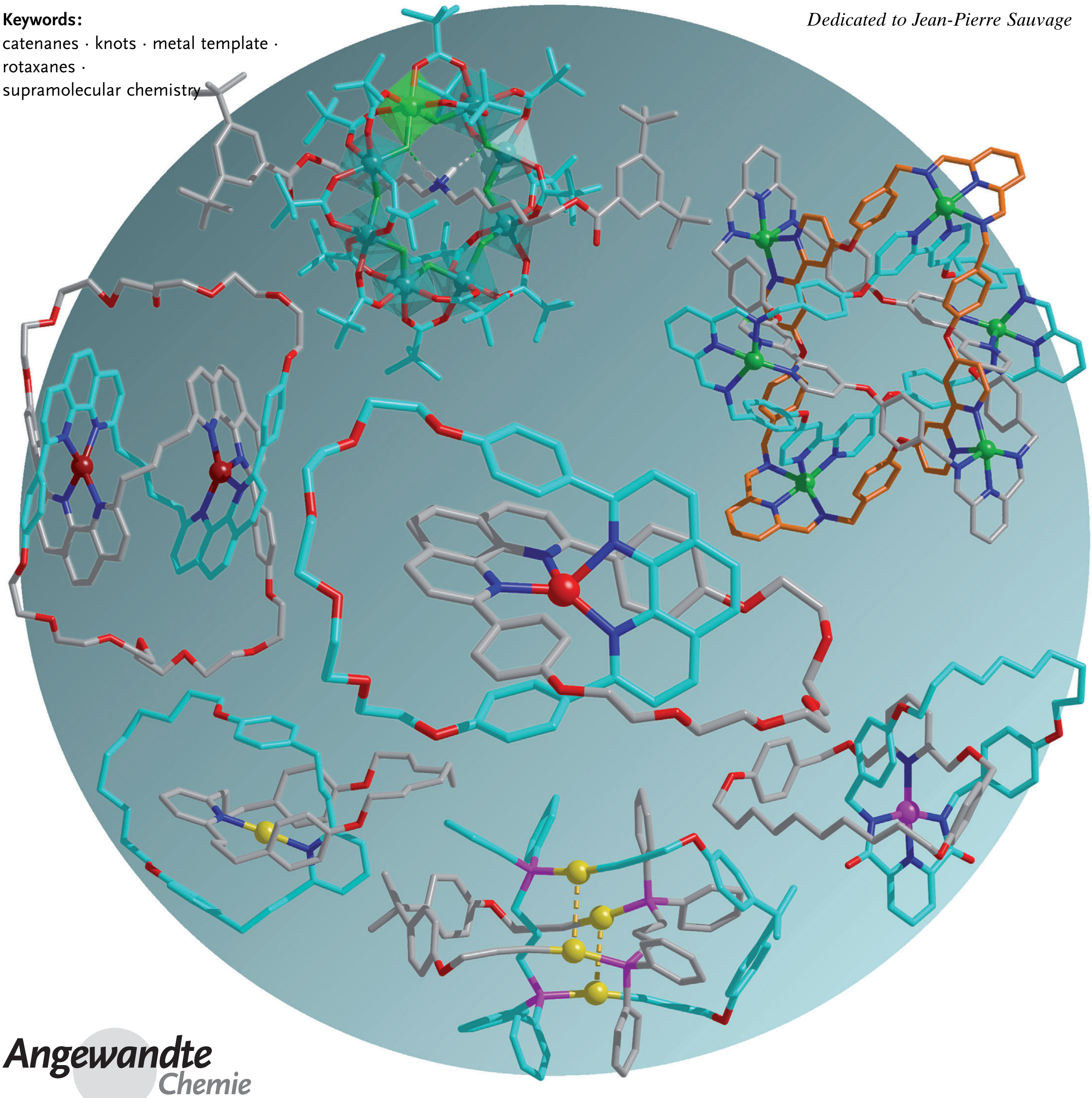
Interlocked Molecules

Strategies and Tactics for the Metal-Directed Synthesis of Rotaxanes, Knots, Catenanes, and Higher Order Links

Jonathon E. Beves, Barry A. Blight, Christopher J. Campbell, David A. Leigh, and Roy T. McBurney*

Keywords:
catenanes · knots · metal template · rotaxanes · supramolecular chemistry

Dedicated to Jean-Pierre Sauvage



© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

More than a quarter of a century after the first metal template synthesis of a [2]catenane in Strasbourg, there now exists a plethora of strategies available for the construction of mechanically bonded and entwined molecular level structures. Catenanes, rotaxanes, knots and Borromean rings have all been successfully accessed by methods in which metal ions play a pivotal role. Originally metal ions were used solely for their coordination chemistry; acting either to gather and position the building blocks such that subsequent reactions generated the interlocked products or by being an integral part of the rings or "stoppers" of the interlocked assembly. Recently the role of the metal has evolved to encompass catalysis: the metal ions not only organize the building blocks in an entwined or threaded arrangement but also actively promote the reaction that covalently captures the interlocked structure. This Review outlines the diverse strategies that currently exist for forming mechanically bonded molecular structures with metal ions and details the tactics that the chemist can utilize for creating cross-over points, maximizing the yield of interlocked over non-interlocked products, and the reactions-of-choice for the covalent capture of threaded and entwined intermediates.

From the Contents

1. Ordering Building Blocks about a Metal Ion Template 9261
2. Passive Metal-Ion-Template Synthesis of Rotaxanes and Catenanes 9272
3. Active Metal Template Synthesis 9285
4. Metal–Organic Interlocked Architectures 9292
5. Knots and Higher Order Links 9305
6. Conclusions and Outlook 9314
7. Addendum (August 2011) 9314

1. Ordering Building Blocks about a Metal Ion Template

The early metal ion template syntheses of catenanes, rotaxanes and knots has been reviewed by Sauvage and co-workers[1] with recent emphasis on the Strasbourg group's use of such structures as molecular machine prototypes.[2] Other types of statistical methods[3] and template routes[4] (π–π stacking,[5] hydrogen bonding,[6–8] ion pairing,[9] hydrophobic interactions,[10] anions,[11] radicals[12] and dynamic assembly[13]) to mechanically interlocked molecules have also been reviewed. Here we focus on the metal-ion-directed assembly of interlocked molecules in terms of synthetic strategies and tactics, a "tricks-of-the-trade" approach that encompasses the use of metal ions as templates, catalysts for mechanical bond formation, and as integral structural elements. X-Ray crystallography often plays a crucial role in the design and structural characterization of interlocked molecules. Here crystal structures are shown wherever possible, both for their aesthetic appeal and to illustrate the deviations from the idealized geometries of ligands, metal coordination geometries and noncovalent intercomponent interactions that are not always apparent from line drawings of chemical structures. All of the cap-and-stick structures shown in this Review are original representations produced from coordinates taken from the Cambridge Structural Database (CSD).[14]

1.1. Historical Background

The idea of using organic ligands coordinated to a metal ion to direct the assembly of mechanically interlocked molecules is almost as old as the field itself. While discussing possible strategies to catenane synthesis in their classic 1961 paper "Chemical Topology"[15] in the *Journal of the American Chemical Society*, Frisch and Wasserman include in a footnote that "*Another interesting suggestion has been that of W. Closson to utilize the geometry of the ligands about a metal atom as a core. Both approaches are being investigated in Dr. Lemal's laboratory at the University of Wisconsin (D. Lemal, private communication)*". In fact the experimental work carried out in the Lemal laboratories at that time focused on linking two macrocycles through a common quaternized nitrogen atom (derived from lutidine), with the intention of subsequently cleaving the two original C–N bonds to form a [2]catenane in which one of the rings was a secondary amine.[16] This was amongst the earliest attempts[17] to make interlocked molecules and is reminiscent in strategy to the directed syntheses of catenanes developed a few years later by Schill and Lüttringhaus.[3a,18] In 1973[19] Sokolov suggested that octahedral metal ions might be used as scaffolds for the assembly of both catenane-like structures and knots, and experimentally in 1981 Ogino succeeded in using metal complexes as stoppering groups to covalently capture a cyclodextrin threaded onto an axle to form one of the very first rotaxanes (see Section 4.1.2).[20] However, it is Sauvage's use of tetrahedral Cu^I ions to template the synthesis of a [2]catenane in 1983 (see Section 1.1.3),[1a,21,22] and the program[1,2] on topologically complex molecule synthesis sub-

---

[*] Dr. J. E. Beves, Dr. B. A. Blight, C. J. Campbell, Prof. D. A. Leigh, Dr. R. T. McBurney
School of Chemistry, University of Edinburgh
The King's Buildings, West Mains Road
Edinburgh EH9 3JJ (UK)
Fax: (+44) 131-650-6453
E-mail: david.leigh@ed.ac.uk
Homepage: http://www.catenane.net

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

sequently established by the Strasbourg team (joined, a few years later, by an influential program[5a,b,7a,b,12,13] from the Stoddart lab), that really sparked the development of the wide range of mechanically interlocked structures that we have today. In order to appreciate the diverse ways in which metal ions can be used in the synthesis of mechanically bonded molecules it is instructive to consider how the use of metals to direct the formation of particular types of architectures has evolved, from the metal ion template synthesis of simple macrocycles, to the assembly of entwined metal–ligand complexes and, ultimately, to the formation of mechanical bonds.

1.1.1. Template Effects: From Coordination Complexes to Macrocycles

Although the first examples of metal-template synthesis by chemists probably date from the 19th century,[23] the efficacy of metal ions in macrocycle synthesis only began to be appreciated following pioneering work carried out in the laboratories of Curtis[24] and Busch[25] in the early 1960s. The role that metal coordination geometries can play in organizing organic building blocks[26] during chemical reactions was formally recognized by Busch.[25,27–32] Several factors form the basis for the metal template[33] concepts introduced at that time:

a) *Stabilization/activation of the ligands:* The formation of a metal–ligand complex can either stabilize a ligand or activate it to further reaction (as occurs in metal catalysis). Both of these features have been exploited in interlocked molecule synthesis.

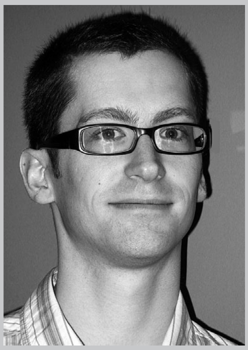
b) *Orientation of the ligands:* The coordination geometry of a metal ion is a “source of geometric information”[25a] and ligands bound to metal ions are often positioned in well-defined arrangements that can be used to direct chemical reactions.

c) *Effective concentration of the coordinated building blocks:* Due to proximity effects, the effective concentration of reactive groups that are part of the same complex is high, which reduces intermolecular reactions to form oligomeric or polymeric products.[25a]

From these ideas, Busch outlined[25] two template effects: the *thermodynamic template effect*[31] (or *equilibrium template*[27,31,34]) and the *kinetic template effect*[30,31] (or *proximity effect*[35]). In the former, the metal ion selectively sequesters one component from a dynamic, equilibrating, reaction mixture, thereby driving the composition towards that product through Le Châtelier’s principle.[34] The first example of Busch deliberately exploiting a template effect is shown in Scheme 1.[24,27] $\mathrm{Ni^{II}}$ promotes the formation of the Schiff base ligand **1** in high yield from reagents that form thiazolidines in the absence of the metal ion. Similarly, it was shown that although *o*-aminobenzaldehyde (**2**) undergoes a slow self-condensation reaction to form a trimer **3**,[36] in the presence of a range of metal ions a cyclic tetramer is preferentially formed as a square-planar complex **4-M$^{\mathbf{II}}$** ($\mathrm{M = Ni^{II}}$,[28,37] $\mathrm{Fe^{III}}$,[29d] $\mathrm{Co^{II}}$,[28a] $\mathrm{Co^{III}}$,[29c] $\mathrm{Cu^{II}}$,[28a,29a] $\mathrm{Zn^{II}}$[29e] and others,[29] Scheme 2a).

Jonathon Beves was born in Sydney (Australia) and obtained his BSc and MSc from the University of Sydney where he began working with metal-directed self-assembly under the supervision of Prof. Len F. Lindoy. He moved to Basel (Switzerland) in 2005 and completed his PhD under the supervision of Prof. Edwin Constable and Prof. Catherine Housecroft focusing on the use of terpyridine metal complexes for the formation of functional coordination polymers and photoaddressable devices. In 2009 he joined David Leigh’s group as a Swiss National Science Foundation Post-Doctoral Fellow.

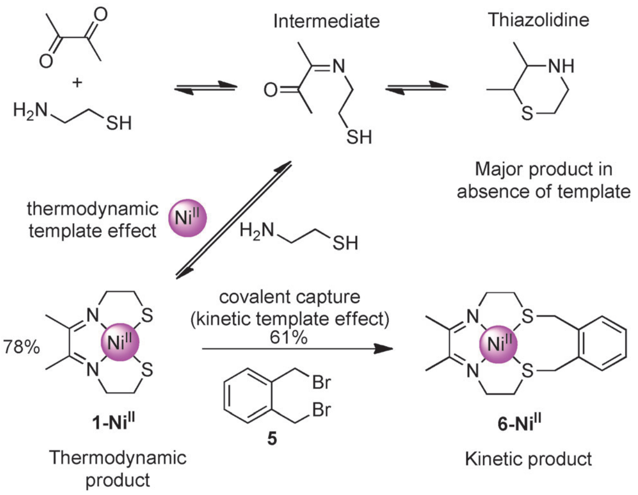
Chris Campbell was born in Cardiff (UK). He obtained an MChem degree from the University of Oxford where he was awarded a Stapledon Scholarship (2006–2009) and a Fitzgerald prize (2009) from Exeter College. His Masters research project was carried out under the guidance of Prof. Harry Anderson investigating the lasing applications of polyrotaxanes. He commenced his PhD in the group of Prof. David Leigh in 2009 and is currently working on new synthetic strategies towards topologically complex molecules.



Barry Blight was born in Bathurst, New Brunswick (Canada), and obtained his BSc at Mount Allison University in 2003. He completed his PhD with James Wisner at the University of Western Ontario in 2008. Following his doctoral studies he moved to the University of Edinburgh as a Marie Curie Postdoctoral Fellow in the group of David Leigh, studying new mechanisms of controlled molecular motion and novel hydrogen bonded materials. In 2010 he moved to Queen’s University (Canada) as an NSERC Postdoctoral Fellow developing luminescent triarylboron-containing materials with Suning Wang.

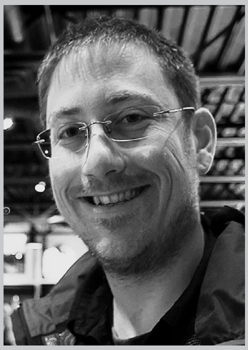
David Leigh was born in Birmingham (UK) and obtained his BSc and PhD from the University of Sheffield. After postdoctoral research in Ottawa (1987–1989) he returned to the UK as a lecturer at the University of Manchester Institute of Science and Technology. In 1998 he moved to the University of Warwick, and in 2001 he took up the Forbes Chair of Organic Chemistry at the University of Edinburgh. He was elected to the Fellowship of the Royal Society in 2009. His research interests include the development of new methods of interlocked molecule synthesis and synthetic molecular-level motors and machines.

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

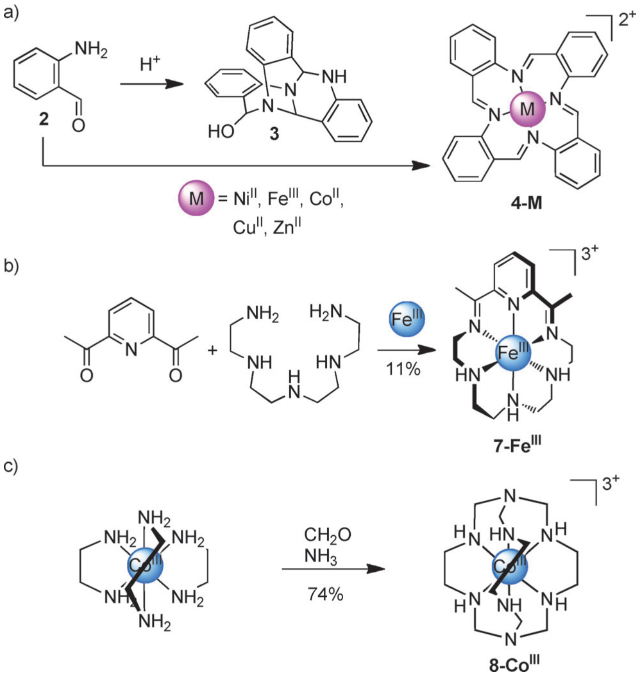


Scheme 1. The first rational use of metal ion templates through sequential thermodynamic[27] and kinetic[30] template effects. Reaction of α-diketones with β-mercaptoethylamine generally results in thiazolidines as the major products. However, in the presence of Ni^{II}, diimine complex **1-Ni**^{II} is formed in up to 78% yield.[27] Subsequent reaction of **1-Ni**^{II} with α,α′-dibromoxylene affords macrocycle complex **6-Ni**^{II} in 61% yield.[30,39]

In the kinetic template effect a metal ion constrains[30,31,38] ligands causing spatial (including geometric and/or topological) control of reactions between reactive functional groups similar to the proximity effects[35] observed in some enzyme catalysis. In Busch's original example (Scheme 1),[30,39] the conformation of the tetradentate ligand of **1-Ni**^{II} is controlled by the metal ion so as to bring the two reactive thiolate end-groups close together. Once one of these groups has reacted with *o*-xylylene dibromide **5** the preorganization favors intramolecular cyclization to form a small macrocycle **6-Ni**^{II}, rather than the intermolecular reaction which would result in larger macrocycles or oligomers.[30] The use of template effects was quickly extended to ligands with sufficient donor atoms to completely enclose a metal ion (**7-Fe**^{III}, Scheme 2b)[32] and three-dimensional cage structures[40] (e.g., **8-Co**^{III}, Scheme 2c).[41] Metal ion template effects[42] have subsequently been used to access many macrocyclic[43] and cage[44] structures and continue to be explored in many areas of synthesis.[45]



Roy McBurney grew up in Carnoustie (UK). He studied chemistry at the University of Edinburgh (Bader Bursary; MChem in 2005) and obtained his PhD with Prof. David Leigh on metal template strategies to interlocked architectures. In 2008 he took up a postdoctoral position in Durham with Prof. David Parker investigating responsive MRI probes, and in 2010 he joined the group of Prof. John Walton at the University of St Andrews. His research interests include semiconductors for use as photocatalysts in organic synthesis and free radical chemistry.

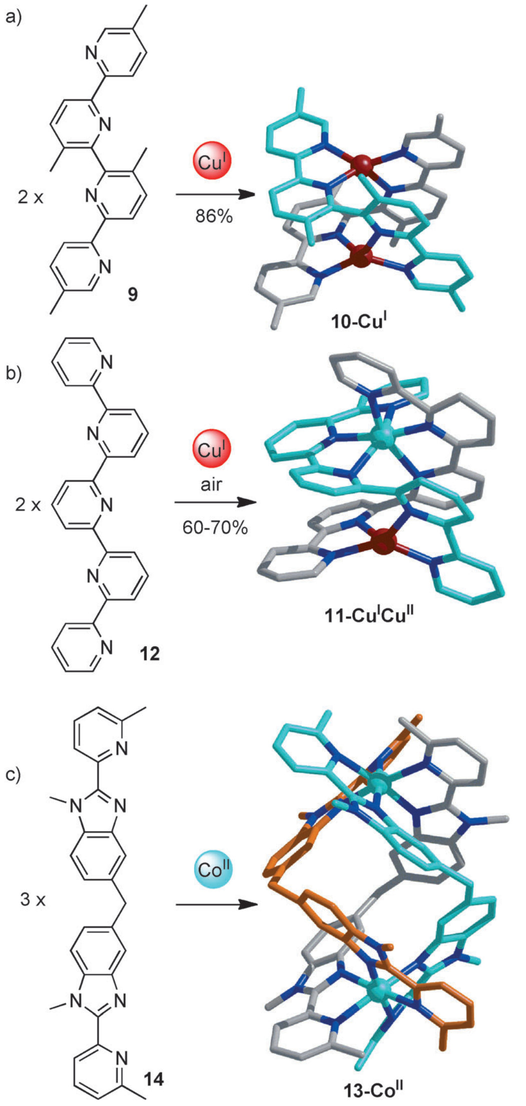


Scheme 2. The synthesis of 2D and 3D molecular structures by metal template effects. a) Busch's preparation of a tetradentate macrocycle using the thermodynamic template effect with square planar metal ions.[25a,28,29] In the presence of Ni^{II},[28] Fe^{III},[28d] Co^{II},[28a] Cu^{II},[29c] or Zn^{II}[29d] the cyclic tetramer is formed in good yield as square planar complex **4-M**^{II}.[28,29] Ni^{II} also templates the formation of a tridentate macrocycle by *fac*-octahedral coordination.[37] b) Busch's use of Fe^{III} in the synthesis of macrocycle **7-Fe**^{III} from 2,6-diacetylpyridine and tetraethylenepentaamine.[32] c) Sargeson's assembly of cage **8** around an octahedral Co^{III} center in a single step from $[Co^{III}(en)_3]^{3+}$, (en = 1,2-ethanediamine).[41]

1.1.2. *Entwining: Assembling Helicates*

The crucial additional feature required to access mechanically bonded structures rather than just topologically trivial macrocycles is for the metal ion coordination to hold extended ligands in positions that cause them to physically overlap, generating cross-over points. Some of the earliest examples of entwined metal–ligand complexes included triple-stranded bimetallic complexes containing Cu^{II} (Harris and McKenzie)[46] or Fe^{III} (Raymond)[47] and double-stranded bimetallic complexes based on Zn^{II} (Wester and Furlop)[48] or Ag^{I} (van Koten),[49] structures that would later become known as *helicates*.[50,51] Lehn initially made multi-ligand dimetal ion complexes for their potential electrochemical properties (the idea was that two-electron redox processes might take place within the dinuclear complexes), but he was quickly struck by the significance and beauty of their helical structures. His group demonstrated through many elegant examples that careful ligand design and metal ion selection can promote the self-assembly[52,53] of multinuclear entwined assemblies with well-defined structures under thermodynamic control.[54] An early example featured the complexation of two quaterpyridine ligands (**9**) to two tetrahedral Cu^{I} ions forming the dimetallic helicate complex **10-Cu**^{I} (Scheme 3).[50a] The steric and geometric demands of other oligopyridine ligands with a range of metal ions were established by forming helicates with

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 3. a) Lehn's helicate **10-Cu^{I}**, featuring Cu^{I} ions in a distorted tetrahedral geometry in the sold state. The N-Cu-N bond angles range from 80.6–81.3° for the ligand bite angle and 117.0–138.6° for the remaining ligand–metal–ligand bond angles.[50a] b) Constable's use of polypyridyl ligands to assemble multinuclear helicate **11-Cu^{I}Cu^{II}**.[55b] The N-Cu-N bond angles for the distorted tetrahedral Cu^{I} center range from 85.0(7)–142.4(7)° and for the Cu^{II} center *cis*-(N-Cu-N) from 74.8(7)–108.3(7)°, cf. 90° for an ideal octahedral geometry. c) Piguet and Williams' triple-stranded helicate **13-Co^{II}**, formed around two octahedral Co^{II} ions.[56] The ligand bite angles range from 74.1(6)–78.2(6) with the remaining *cis*-(N-Co-N) angles from 79.5(6)–106.8(6)°.

differing metal coordination geometries.[51a,55] A significant early example from the Constable group is shown in Scheme 3b, where a mixed Cu^{I}/Cu^{II} helicate (**11-Cu^{I}Cu^{II}**) was prepared using quinquepyridine **12**, taking advantage of the preferences of tetrahedral and octahedral coordination modes of Cu^{I} and Cu^{II}, respectively.[55b] One of the first triple stranded helicates (**13-Co^{II}**) was described by Piguet and Williams, assembled from octahedral Co^{II} ions and bis-bidentate ligand **14** (Scheme 3c).[56]

Lehn used extended oligo(bipyridine) units to form homo-duplex tri-,[52b,57] tetra-[52] and penta-nuclear[52] and hetero-duplex helicates,[58] and even circular assemblies[59] favored by secondary anion-template effects, such as five- (**15-Fe^{II}**)[59a] and six-membered circular double helicates (Scheme 4).[59b] As well as being exquisite examples of thermodynamically controlled self-assembly[53,54] the physical overlap of the extended ligands in these systems form well-defined "cross-over points". Linking cross-over points in the correct sequence, stereochemistry and connectivity is the key to generating mechanically linked molecular architectures.

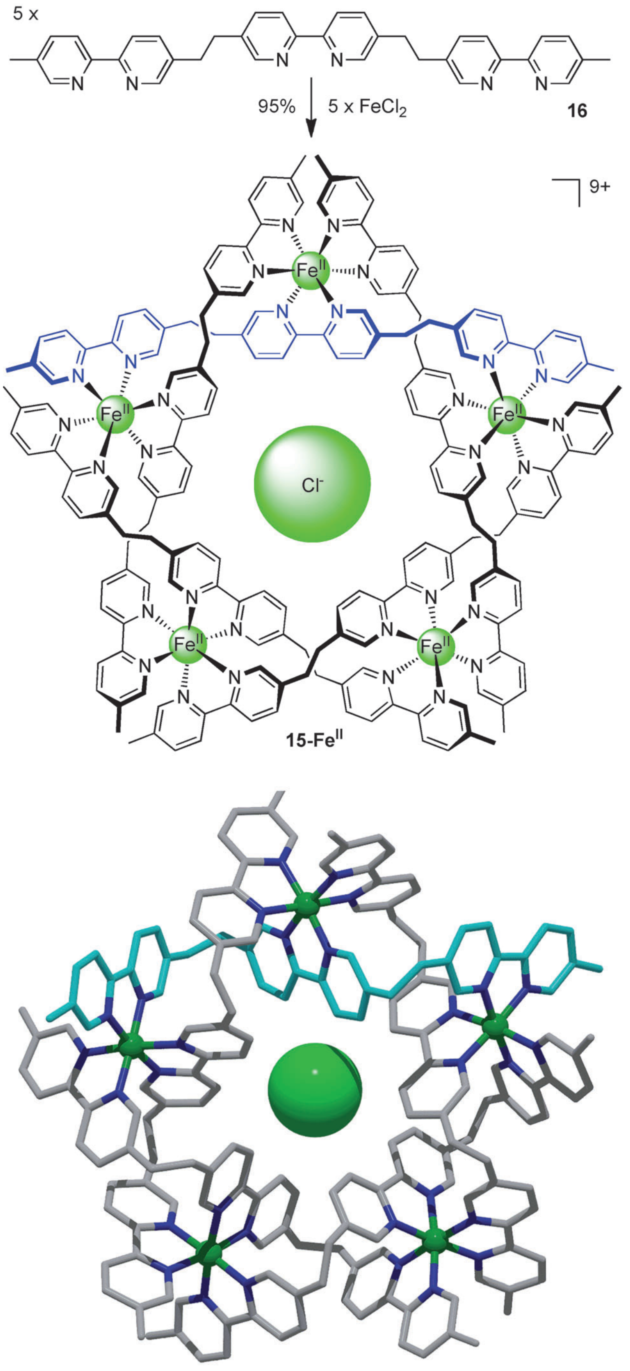
1.1.3. *Interlocking: Making Mechanical Bonds*

At the time that Lehn was developing the chemistry of self-assembled helicates, his former student Jean-Pierre Sauvage, also in Strasbourg, was investigating the use of hindered 1,10-disubstituted phenanthroline (phen) ligands[60,61] to encapsulate metal ions with the aim of improving the lifetime of photoexcited states.[60] Inspired by the elegant but lengthy "directed synthesis" of catenanes by Schill and others,[3a,b] Sauvage recognized that the shape and mutually orthogonal arrangement of such bidentate ligands in a tetrahedral Cu^{I} complex could generate the cross-over points necessary for catenane formation.

With Christiane Dietrich-Buchecker, who would become his long-term collaborator in this field, Sauvage introduced hydroxyl groups onto the phenyl substituents of a 2,9-diphenyl-1,10-phenanthroline (dpp) ligand (to form **17**), positioning them to undergo intracomponent (rather than intercomponent or intermolecular) Williamson ether macrocyclization reactions. Complex **18-Cu^{I}** was formed quantitatively from macrocycle **19** and ligand **17** from which the [2]catenate **20-Cu^{I}** was generated in 42% yield (Scheme 5).[1d,21,22] This was a remarkable result given that the statistical and directed synthesis routes to catenanes at the time typically took 6–20 steps to complete and often resulted in less than 1% overall yields of the interlocked products.[3a] The copper ion could be removed quantitatively from catenate **20-Cu^{I}** with potassium cyanide to afford metal-free catenand[62] **20** (Scheme 5).[22,63] Various combinations of the use of thermodynamic control (to self-assemble complicated multi-component architectures) and kinetic template effects (to direct reactions between ligands), featuring metal and non-metal templates, have been the basis for forming the vast majority of interlocked molecules ever since.

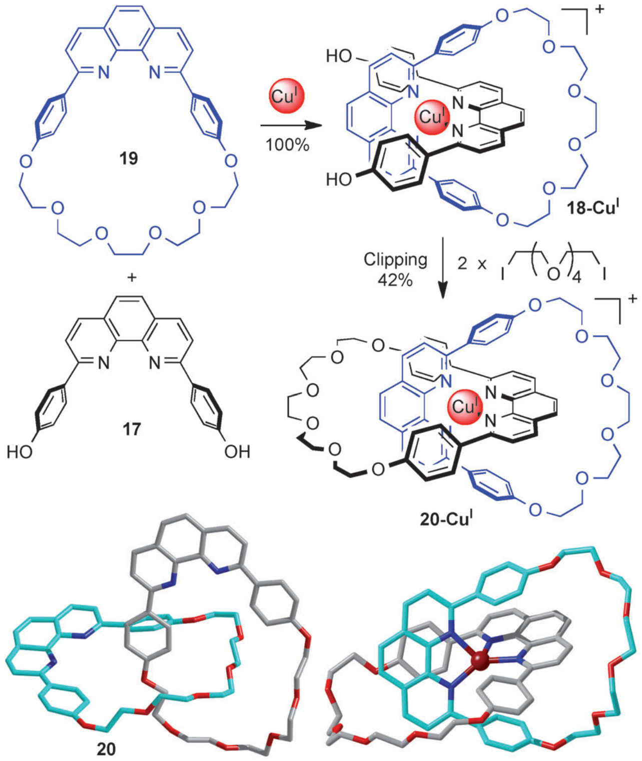
1.2. *Metal-Ion-Mediated Strategies to Interlocked Molecular Architectures*

The approach of using metal ions as templates has provided accessible pathways to topologically complex interlocked molecules that would be unobtainable by classical chemistry methods. In the absence of a metal template, such reactions generally result in the formation of oligomers and/or macrocycles of various sizes with negligible threading of one component through another. The key issues in the construction of interlocked structures are (i) the generation of



Scheme 4. Lehn's circular helicate assembly **15-Fe^{II}**, constructed using five Fe^{II} ions to organize five oligo(bipyridine) ligands **16**. The X-ray crystal structure shows a chloride ion in the center of the assembly that templates the size (in this case five strands of the ligand and five metal ions) of the cyclic helicate. The ligands are slightly too short to allow for an idealized circular array of octahedra around the chloride ion, resulting in the Fe^{II} geometries being amongst the most distorted [Fe^{II}(py)$_6$] complexes in the CSD database (*cis*-(N-Fe-N) bond angles 80.9(9)–99.0(10)°).[59a]

cross-over points and (ii) how these can be linked in a controlled manner to form mechanically bonded molecules.



Scheme 5. The first metal ion template synthesis of an interlocked molecule: Sauvage's Cu^I catenane synthesis using one preformed macrocycle.[21,22] Formation of **18-Cu^I** from **17** and **19** is quantitative because of the principle of maximal site occupancy; two macrocycles cannot bind to the same Cu^I ion (see Section 1.2.2.1). Subsequent ring closure by Williamson ether synthesis gives **20-Cu^I** in 42% yield. The X-ray crystal structures of catenate **20-Cu^I** (bottom right) and metal-free catenand **20** (bottom left) conclusively established the interlocked molecular structure.[62] Note that in the crystal structure of **20-Cu^I** one of the grey phenyl groups is actually close to planar with the grey diphenylphenanthroline (dpp) system (rather than orthogonal to it, as represented in the chemical drawing above) in order for it to π-stack with a phenyl group (blue) of the other macrocycle—a common feature in the crystal structures of this type of interlocked molecule. Most Cu^I(dpp)$_2$ catenate and rotaxane complexes have distorted tetrahedral metal ion geometries because of the steric requirements of the coordinated dpp components. For **20-Cu^I** the ligand bite angles are 82.7(7) and 84.4(8)° and the other N-C-N angles 88.0(8) and 136.6(7)°.

1.2.1. *Entwining or Threading Molecular Components: The Generation of Cross-Over Points*

A crucial design feature for the preparation of mechanically bonded structures is the creation of cross-over points (Figure 1), the points where the ligands physically overlap. In the metal ion template approach the metal ion acts to gather and organize the ligands (which are either cyclic or incorporate "turns" which bring the end-groups of particular ligands close together in space) in a well-defined geometry to generate the cross-over point. Subsequent ring closing or stoppering ("covalent capture"[64]) reactions form the mechanical bond.

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

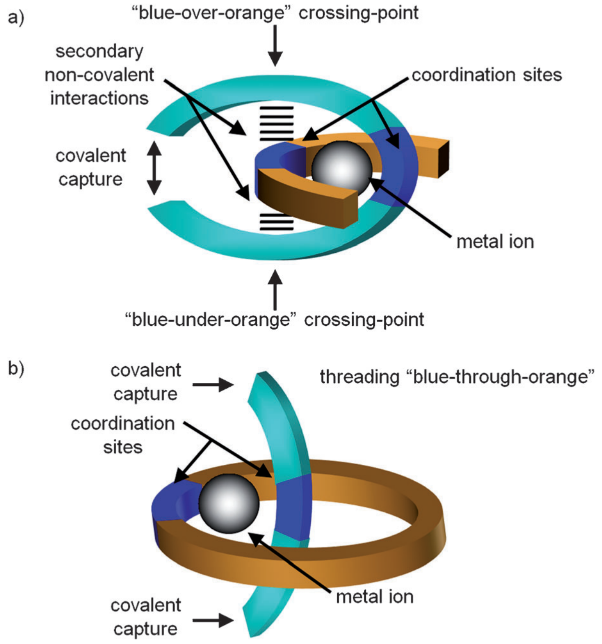


Figure 1. Using a metal ion to entwine or thread. The template metal ion (gray sphere) holds the ligands (blue and orange) in positions determined by the metal ion's preferred coordination geometry; the ligands physically cross to produce a "turn" around the metal center. a) Non-covalent interactions between the ligands can be used to control their relative orientations to generate cross-over points and promote interlocking. b) Threading forms cross-over points without the need for additional stabilizing interactions.

1.2.1.1. *Coordination Geometry and Metal Ion Selection*

The key role of the metal ion is to gather and organize ligands in the correct positions and orientations to promote the formation of a physical cross-over point. Metal ions with tetrahedral, trigonal bipyramidal and octahedral (Figure 2a–c) coordination geometries[65] are ideal candidates for forming cross-over points since bi- or tridentate ligands can be orientated orthogonally (see Sections 2.1, 2.2, and 2.3).[66]

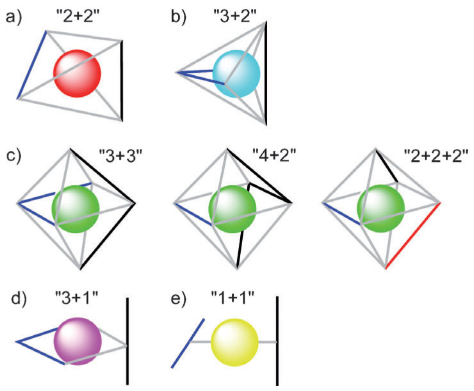


Figure 2. The range of simple (coordination number ≤ 6) metal–ligand coordination geometries utilized in the construction of catenanes, rotaxanes, knots, and higher order links: a–c) three-dimensional tetrahedral (a), trigonal bipyramidal (b), octahedral (c) with either "3+3", "4+2", or "2+2+2" sets of donor ligands, d) two-dimensional square planar, and e) one-dimensional linear motifs.

The two-dimensional arrangement of donor atoms in a square planar metal–ligand coordination geometry (Figure 2d) might superficially appear unsuitable for directing the assembly of a three-dimensional cross-over point. However, the steric requirements of the tridentate ligand in a "3+1" donor set can force the monodentate ligand into an orthogonal position such that the cross-over point can be efficiently generated (see Section 2.4). Indeed, a significant advantage of this "3+1" donor set is that the ligands must perforce be different (one tridentate, one monodentate) meaning heteroleptic complexes are formed which are required for the template assembly of rotaxanes or hetero-circuit (constitutionally different rings) catenanes. To efficiently form heteroleptic complexes with ligands that have the same number of donor atoms ("2+2" donor sets for tetrahedral complexes, "3+3" donor sets for octahedral complexes and "1+1" donor sets for linear complexes) requires additional tactics (see Section 1.2.2). Completing the range of simple metal–ligand coordination geometries (coordination number ≤ 6), one-dimensional linear coordination modes (Figure 2e) based on Au^{I} have also been used in catenane and rotaxane template synthesis (see Section 2.5).

A number of different transition metal ions[67] have been used to assemble stable[68] mechanically interlocked molecules (e.g. Cu^{I}, Cu^{II}, Zn^{II}, Pd^{II}, Fe^{II}, Ru^{II}, Rh^{II}, Mn^{II}, Ag^{I}, etc).[69] Some metal ions, such as Cu^{I}, Fe^{II}, Co^{III} and Pd^{II} are largely invariant in terms of their coordination number and geometry, organizing ligands in a largely predictable fashion. Others, such as Cu^{II}, Ag^{I} and Cr^{III}, adopt a range of coordination geometries making it more difficult to predict how they will position building blocks in template reactions. Metal ions which tend to form labile complexes with organic ligands (e.g. Cu^{I}, Zn^{II}, Ag^{I} etc) are usually best used in situ for template synthesis. Others, notably Pd^{II} and Ru^{II}, often form kinetically robust complexes that can be purified by column chromatography prior to being used in a subsequent catenane- or rotaxane-forming reaction. Metal ions that favor higher coordination numbers (>6) have rarely been utilized in the synthesis of mechanically interlocked molecules (for an exception, see the nine-coordinate Ba^{II} catenane in Figure 16) and the use of lanthanides or actinides as templates for interlocked molecules has yet to be reported.

An important feature of many interlocked molecules prepared by metal ion template reactions is that they often form very stable complexes with the ions used to template their assembly (the so-called "catenand effect").[22,70] This is because the three-dimensional structure of the interlocked ligand means that decomplexation of multiple donor atoms has to occur simultaneously, with limited access to solvent or other ligands, in order for demetalation of the interlocked ligand to occur.[22,70] Furthermore, the donor atom geometries in interlocked ligands are often so well-defined that they can sometimes be used to force other metal ions to adopt usually unfavored geometries,[71] or to stabilize complementary (low with neutral ligands),[72] or destabilize non-complementary,[73] oxidation states.

1.2.1.2. *Ligand Design—Introducing "Turns"*

In addition to metal ion coordination geometry and lability, another important factor for interlocking is the use of ligands that generate an appropriate "turn angle" about the metal ion. The substitution pattern of the ligands is often the most crucial issue; Figure 3 illustrates how 60, 120 and 180° turn angles can be formed around metal ions using differing substitution arrangements on commonly used ligands. 2,9-diphenyl-1,10-phenanthroline (dpp, **21**) and 5,5″-diphenyl-substituted tpy (tpy = 2,2″:6′,2″-terpyridine) (**22**) are both rigid ligands with the arms of the ligands orientated suitably to form crossing points in combination with tetrahedral and octahedral metal centers respectively. More flexible ligands (such as **23**–**25**) can be positioned by the metal ion to generate 180° turns. In addition to the turn angle, the degree of preorganization and the stability of conformations prior to linking significantly influence the successful formation of interlocked structures. Tactics to optimize and exploit these features are discussed in Section 1.2.2.

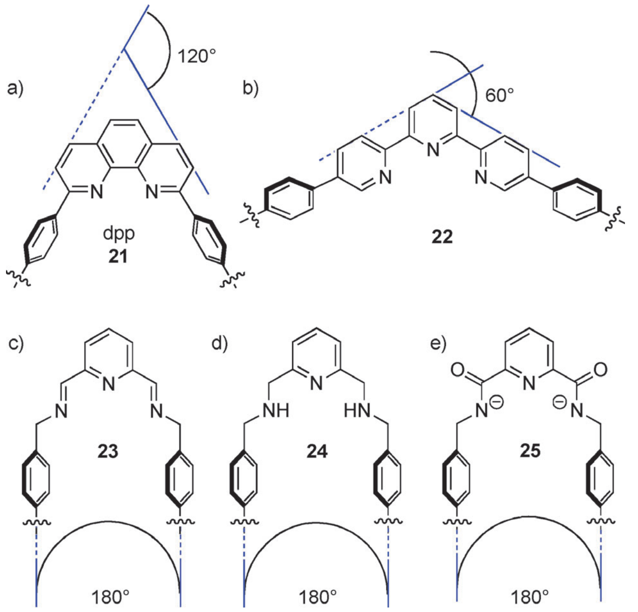


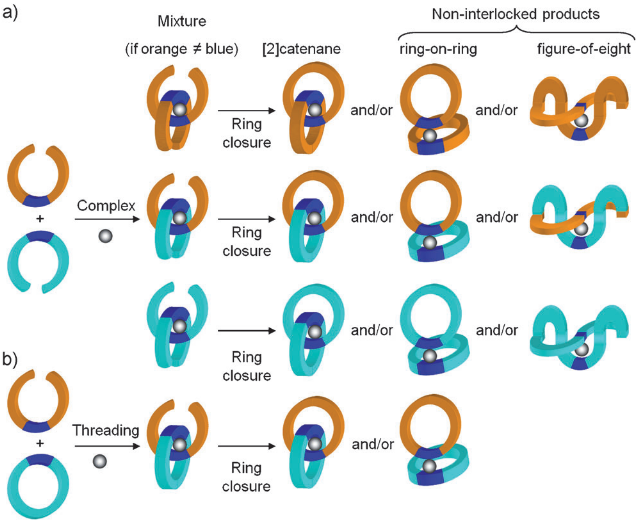
Figure 3. Some ligands and the turn angles that they complete around a metal ion template. Bipyridine-based ligands such as 2,9-diphenyl-1,10-phenanthroline (dpp, **21**) units generate a 120° turn; 5,5″-substituted-tpy (tpy = 2,2′:6′,2″-terpyridine) ligands (**22**) generate 60° turns and 2,6-substituted pyridine ligands (**23**-**25**) are able to complete 180° turns, particularly with the aid of secondary non-covalent interactions (see Scheme 10).

1.2.2. *Tactics for Forming Interlocked Structures*

When forming interlocked structures a number of tactics can be used to favor the formation of interlocked products over unwanted non-interlocked macrocycles, oligomers and polymers:

1.2.2.1. *Use of Topology to Favor Threading (Maximal Site Occupancy)*

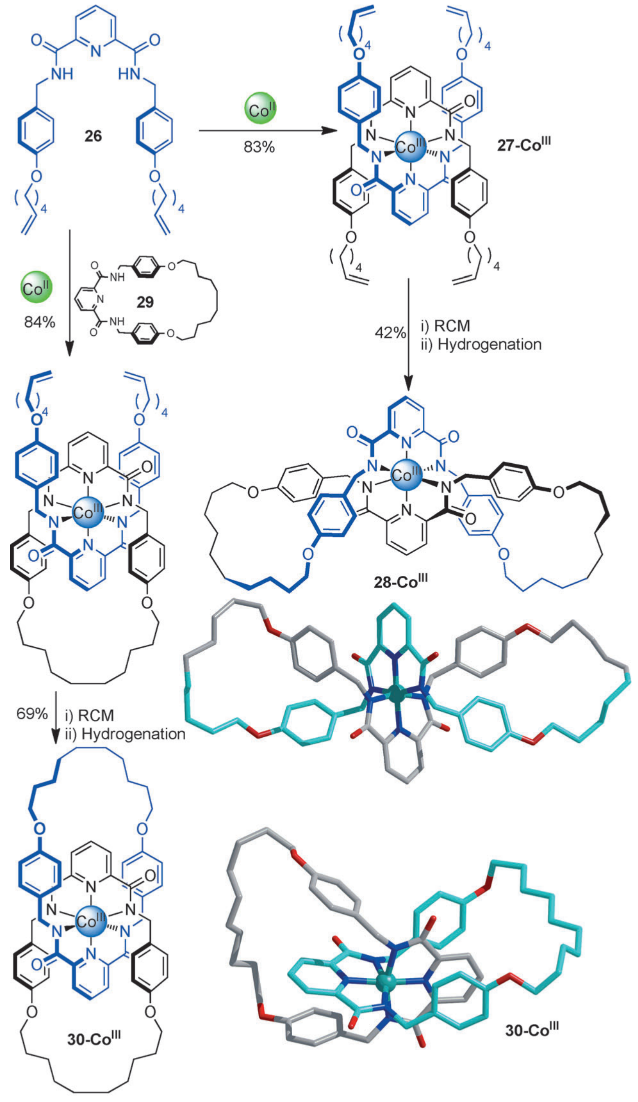
The principle of *maximal site occupancy*[52b] is that a system is thermodynamically driven toward the species with the highest occupancy of the binding sites available on both the ligand and the metal ions.[74] Introducing steric or topological restrictions can reduce the number of possible outcomes where maximum favorable interactions can be achieved and this can be exploited to favor the formation of interlocked structures. Scheme 6 shows different synthetic routes that could result in the formation of a [2]catenane. Using two different acyclic ligands with similar metal-ion binding modes (Scheme 6a) can lead to three different pre-catenane complexes which can be ring-closed to give [2]catenanes as well as non-interlocked figure-of-eight and ring-on-ring complexes, and higher order oligomers and polymers.[75] However, in many cases pre-forming one macrocycle (Scheme 6b) means that for steric reasons maximal site occupancy can only be achieved through a threaded complex and only one, mixed ligand, [2]catenane results. This tactic also prevents reactions between the different ligands (which could form figure-of-eight structures) and reduces the number of larger cyclic oligomers possible.



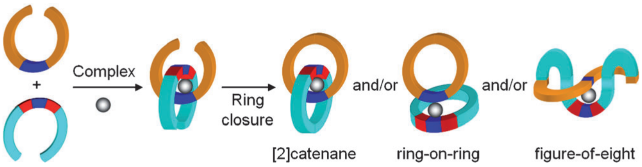
Scheme 6. Exploiting topology and the principle of maximal site occupancy[52b] in catenane synthesis. a) The use of equivalent binding motifs on both rings results in a mixture of homo- and heterolepitc complexes and products. b) The use of a pre-formed macrocycle prevents the formation of homo-ligand complexes to selectively give the mixed-ligand complex.

This principle was used in the first Cu$^{\text{I}}$ template catenane synthesis (Scheme 5) and has since been exploited in several other systems. For example, when octahedral Co$^{\text{III}}$ was employed as a template, attempted double-macrocyclization of two identical ligands (**26**) in **27-Co**$^{\text{III}}$ resulted in formation of the non-interlocked figure-of-eight complex **28-Co**$^{\text{III}}$ as the major product (Scheme 7). Pre-forming tridentate macrocycle (**29**) enabled the interlocked [2]catenane (**30-Co**$^{\text{III}}$) to be obtained in 84 % yield.[76]

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

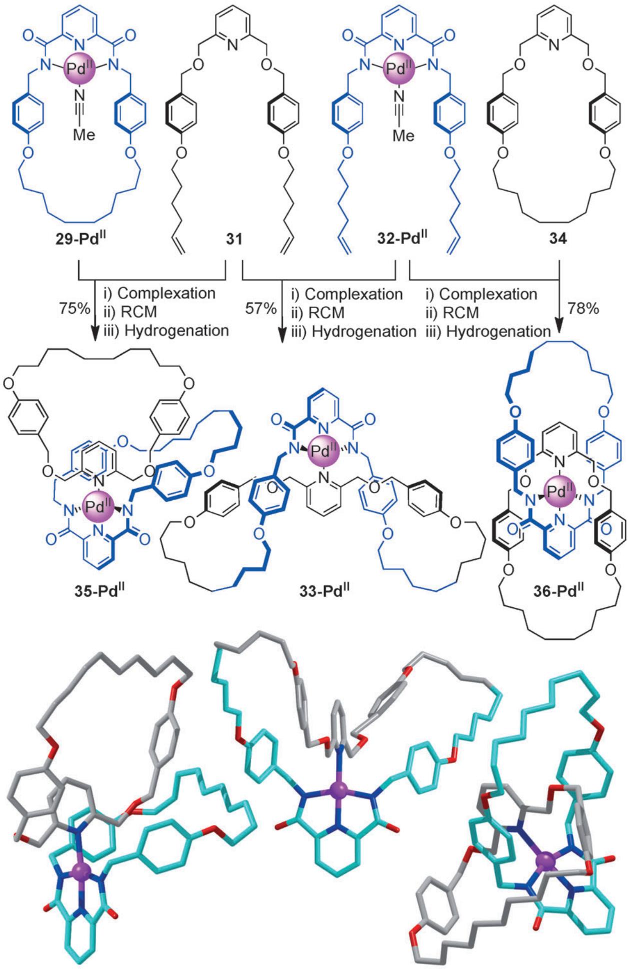


Scheme 7. The use of topological constraints to control the outcome of macrocyclization reactions. Double macrocyclization of **27-Co**^{III} led to the non-interlocked figure-of-eight complex (**28-Co**^{III}). Use of a pre-formed macrocycle (**29**) leads to the [2]catenane **30-Co**^{III}.[76] The X-ray crystal structures of **28-Co**^{III} and **30-Co**^{III} demonstrate their topologies and the orthogonal arrangement of the tridentate ligands. The metal–ligand bonds and angles are similar in both the catenate and figure-of-eight complex. Due to the bite angles of the ligands, the *cis*-(N-Zn-N) bond angles range from 81.2(1)–102.5(1)° but the two pyridyl groups remain close to orthogonal (85.7°) in both structures. Note the intercomponent π-stacking in the crystal structure of catenate **30-Co**^{III} (see Section 1.2.2.2 and Scheme 10).



Scheme 8. The use of unsymmetrical ligand donor sets prevents the formation of homoleptic complexes and promotes heterocircuit [2]catenane (or ring-on-ring complex) formation.

The advantages of this approach are even more pronounced for the synthesis of heterocircuit catenanes and rotaxanes, where mixed-ligand complexes are intrinsically required. For this reason "threading" approaches are often used for assembling such interlocked structures.[6f] An alternative approach is to employ a template system that utilizes different coordination modes on the two ligands bound to the metal ion (Scheme 8). This approach is a particular feature of the use of mono- and tri-dentate ligands with a square-planar metal center to give quantitative formation of mixed-ligand pseudorotaxanes[77] and catenanes.[78] In an early example, the double-cyclization of the mixed-ligand complex (**31** and **32-Pd**^{II}) led to the selective formation of a non-interlocked figure-of-eight complex **33-Pd**^{II} (Scheme 9). Instead, employing the pre-formed macrocycles (**29-Pd**^{II} and **34**) allowed the



Scheme 9. Three isomers **35-Pd**^{II}, **33-Pd**^{II} and **36-Pd**^{II} resulting from sequential or simultaneous metal-directed cyclization of acyclic tridentate and monodentate building blocks (a "3+1" donor set, see Section 2.4) about a Pd^{II} template.[78] In each of the X-ray crystal structures the Pd^{II} coordination geometry is distorted from perfectly square planar (the *cis*-(N-Pd-N) bond angles range from 80.1(1)–102.8(3)°) by the bite angle of the tridentate ligand. The pyridine rings are close to orthogonal in each complex (76.6–89.9°). Only in the [2]catenate, **36-Pd**^{II}, is intracomplex intercomponent π-stacking present.

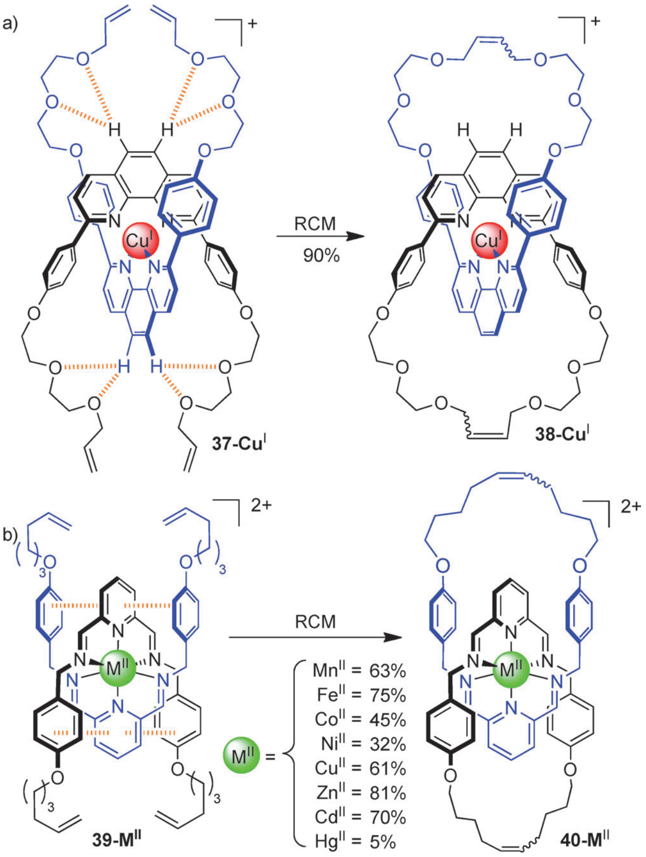
© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

selective synthesis of either the ring-on-ring (**35-Pd^{II}**) or [2]catenane (**36-Pd^{II}**) structures, depending on the order that the building blocks were assembled and cyclized, highlighting the subtleties involved in determining the reaction pathway with such systems.

1.2.2.2. *Use of Ligand–Ligand Interactions to Favor Mechanical Bond Formation*

Generally mechanically bonded molecules need to be formed in preference to alternative non-interlocked structures (macrocycles, threads, linear oligomers, polymers, etc.) that could be formed instead. In such reactions the outcome usually depends on the preferred spatial arrangement of the reactive functional groups. Pre-organization of stable conformations in which the reactive groups are positioned close together in space can greatly favor the desired product. Effective tactics for achieving this include sterically restricting the space explored by the reactive end groups of the ligands and/or the use of secondary interactions to stabilize desired conformations. Conformational restrictions are generally introduced most easily by using rigid ligands (such as the phenyl-substituted dpp groups popularized by Sauvage[1,2]), but stereoelectronic preferences for certain conformations,[79] such as the *gauche* effect[80] for glycol chains, can allow some conformational control with more flexible regions of a ligand.

Non-covalent interactions, such as hydrogen bonding and π–π stacking, have also proved useful in helping position ligand end-groups to promote ring closure to favor mechanical bond formation (Scheme 10). Aromatic-CH⋯O interactions[81] (and the *gauche* effect) in **37-Cu^{I}** probably play a significant role in favoring[82] intra-ligand ring closing metathesis (RCM)[83] to form **38-Cu^{I}** rather than inter-ligand RCM to form the topologically-trivial figure-of-eight isomer. Similarly, aromatic π–π interactions are used with 2,6-substituted pyridine ligands in **39-M^{II}**[84] to position the end-groups suitably for RCM to form [2]catenane **40-M^{II}**.



Scheme 10. The use of a) aromatic-CH⋯O hydrogen bonds[81] in **37-Cu^{I}** and b) π–π stacking[84] in **39-M^{II}** to orient the reactive arms of ligands to favor mechanical bond formation (see Scheme 26).

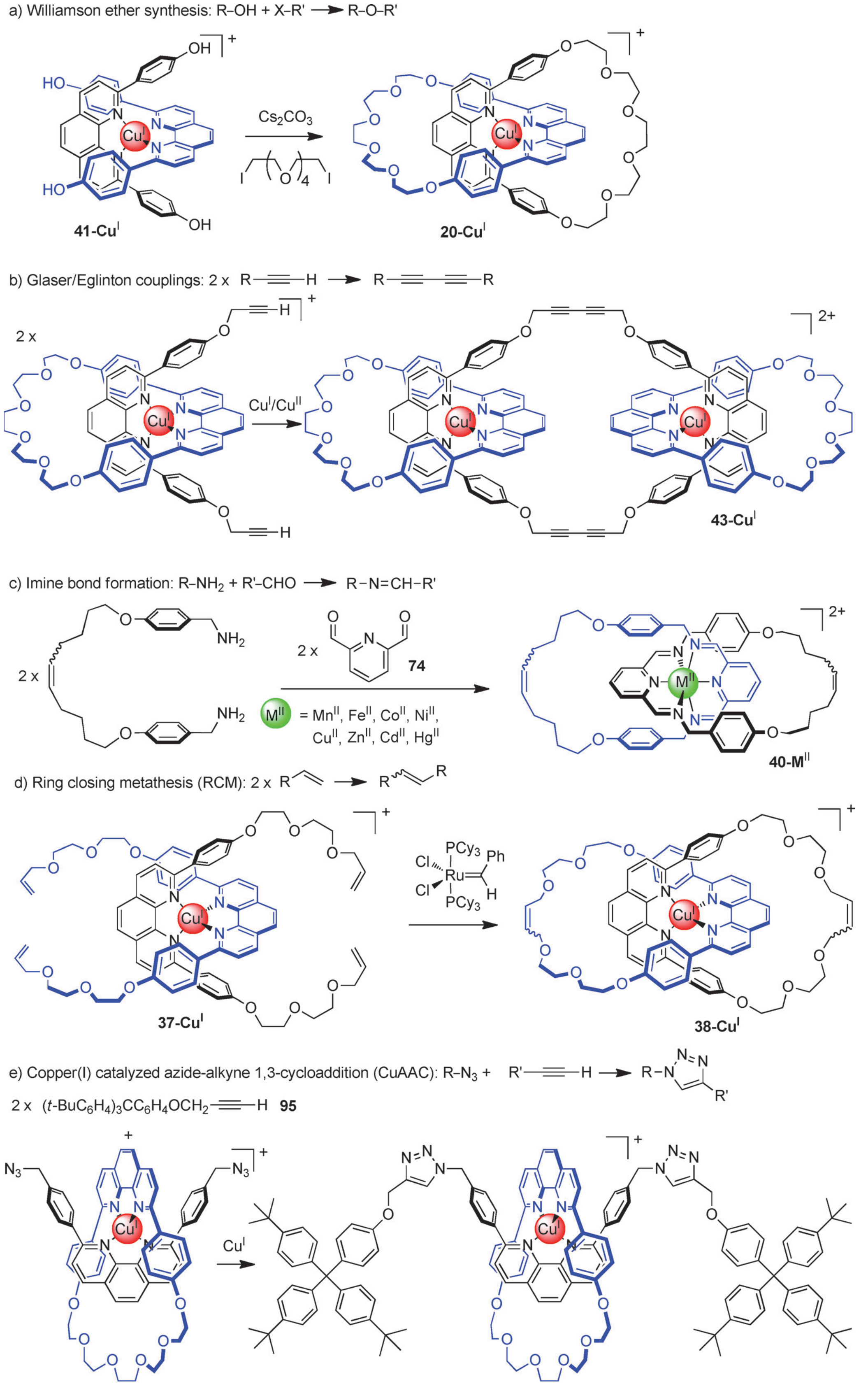
1.2.2.3. *Efficient Methods for Covalent Capture*[64]

Once ligands are appropriately orientated the entwined or threaded structure must be covalently captured to form the mechanical bond. A number of different types of reactions have been employed to accomplish this but amongst the most widely used in the early years of metal-ion-template catenane and rotaxane synthesis were Williamson ether synthesis (Scheme 11 a),[1,22] Glaser and Eglinton oxidative acetylene couplings (Scheme 11 b)[85] and imine-bond formation (a mild reaction under thermodynamic control, Scheme 11 c).[84] However, the invention of highly efficient ring-closing olefin metathesis[83] catalysts (Scheme 11 c)[82a] and the Huisgen–Meldal–Fokin Cu^{I}-catalyzed 1,3-cycloaddition of azides with terminal alkynes (the CuAAC "click" reaction,[86] Scheme 11 e)[87,88] have significantly increased the yields of many catenane and rotaxane template strategies. There are three principal reasons for the effectiveness of these two reactions for mechanical bond formation:

1. The intrinsic high functional group specificity of the reactions—they are highly selective and few other groups interfere with the reactions or are incompatible with the reaction conditions.
2. The reactions can be carried out in relatively non-polar solvents in which non-covalent interactions (often used to stabilize favorable conformations in the pre-interlocked architecture) are maximized.
3. The reactive end-groups are sufficiently stable, even when attached to a transition metal catalyst, that they react overwhelmingly in the desired fashion even when accessing the required reaction geometry is a rare event (as it is for the cyclization of large rings). The yield of interlocked versus non-interlocked products then depends on how effectively the template preorganizes the ring-closing reaction to take place while one component is threaded through the cavity of the other.

The CuAAC reaction is particularly functional group specific, substrate tolerant and high yielding and so it is unsurprising that its discovery and development has rapidly led to it becoming a reaction of choice for covalent capture to generate catenane and rotaxane architectures.[88] The use of RCM to form interlocked structures has also been reviewed.[89]

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 11. Methods for the covalent capture of interlocked structures: a) Williamson-ether reactions were often used in early metal-ion-template syntheses of catenanes and rotaxanes.[1,21] b) Glaser–Eglinton acetylene coupling.[85] c) Imine-bond formation[84] allows metal ion template catenanes, rotaxanes and links to be formed under thermodynamic control. d) Ring-closing-metathesis (RCM) macrocyclization[82,89] and e) Cu^I-catalyzed azide-alkyne 1,3-cycloadditions (CuAAC)[87,88] are amongst the most effective modern methods for covalent capture.

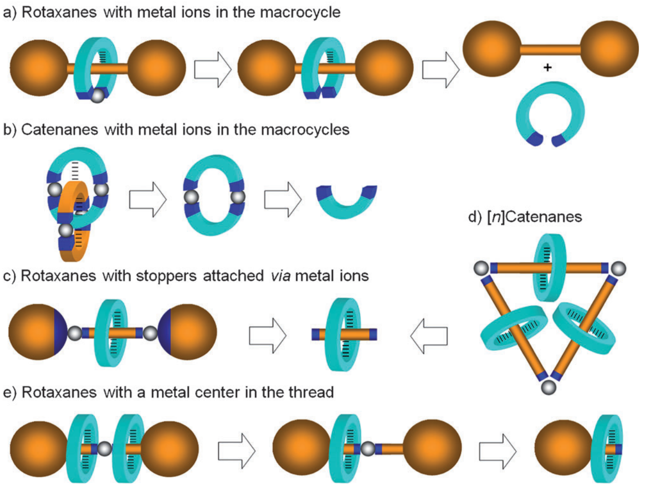
1.2.3. *Metal–Organic Structures: Forming Stoppers, Linkages, and Rings through Coordination Chemistry*

As well as acting as templates for crossing points, metal ions have been utilized in interlocked molecule synthesis by being incorporated within the backbone of the components themselves (see Section 4).[20,90,92,93] In such metal–organic systems the role of the metal ion is usually simply structural (Scheme 12; Figure 4).[94]

A range of different coordination motifs have been used as linear or angular connectors to connect threaded components (Figure 4 a,b) and to form, potentially functional, stopper units (Figure 4 c).

1.2.4. *Combining Coordination Chemistry and Transition Metal Catalysis: Active Metal Template Synthesis[100]*

Whilst the passive metal template approach has proved to be a highly successful strategy for catenane and rotaxane synthesis, it does not take full advantage of the rich chemistry of metal ions. Building on the principles of transition metal catalysis, a new strategy was recently introduced[101] in which the metal template ions play an additional active role in promoting the crucial final covalent bond forming reaction that captures the interlocked structure (i.e., the metal has a dual function; acting as a template for entwining the precursors and catalyzing covalent bond formation between the reactants). This "active metal template" approach relies upon the use of macrocycles that can bind metal ions endotopically within their cavities. The metal ion is chosen such that it is capable of promoting covalent bond formation between two suitably functionalized "half-thread" units (rotaxane synthesis) or to effect ring closure of a precursor to a macrocycle (catenane synthesis). As the catalytic species is immobilized within the cavity of the macrocycle the metal ion selectively mediates the formation of new covalent bonds through the ring, leading to the formation of a new mechanical bond. The active metal template process is shown schematically in Scheme 13 in both stoichiometric



Scheme 12. Metal–organic rotaxane and catenane structures. "Clipping" of an acyclic ligand by a metal ion can generate a) metal-coordinated-ring rotaxanes[90] or b) metal-coordinated-ring catenanes.[91] Metal ions can also be used to link pseudorotaxanes to form c) metal-complex-stoppered rotaxanes,[20] d) metal-coordinated-ring [*n*]catenanes[92] and e) metal-coordinated-thread rotaxanes.[93]

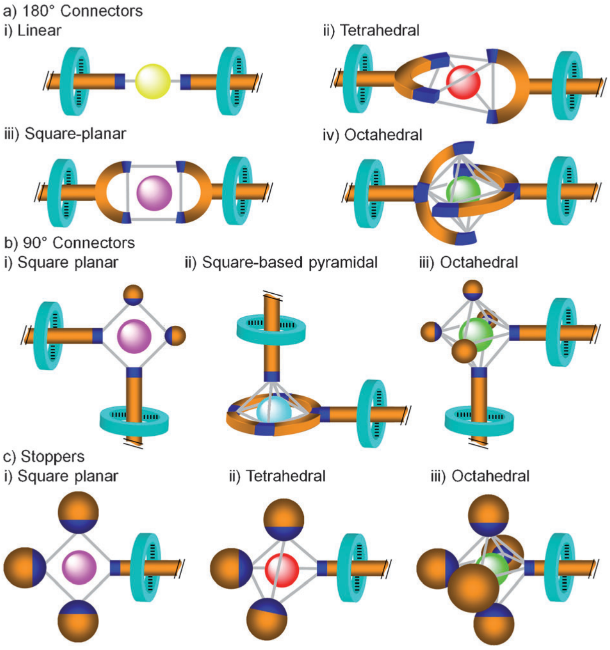
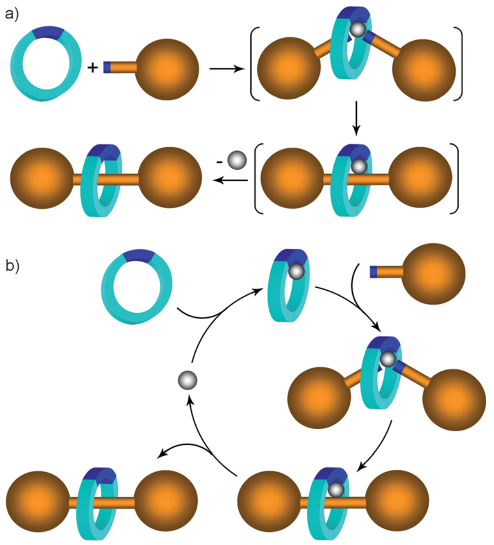


Figure 4. Metal ion coordination geometries incorporated into metal–organic interlocked structures. a) 180° connectors [using i) linear,[95] ii) tetrahedral, iii) square planar,[96] and iv) octahedral coordination geometries]; b) 90° connectors [using i) square planar,[91] ii) square-based pyramidal[90] and iii) octahedral[97] coordination geometries]; c) Coordination complexes have also been used as "stoppering" units [using i) square-planar,[98] ii) tetrahedral,[99] and iii) octahedral[20] coordination motifs].



Scheme 13. "Active" metal template strategy to interlocked molecules. a) The metal plays a dual role; gathering and positioning of the ligands as well as catalyzing covalent bond formation that captures the threaded structure. b) If the metal is able to turn over during the reaction cycle, sub-stoichiometric quantities of the template can be used, a feature that is normally not possible with passive template reactions.

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

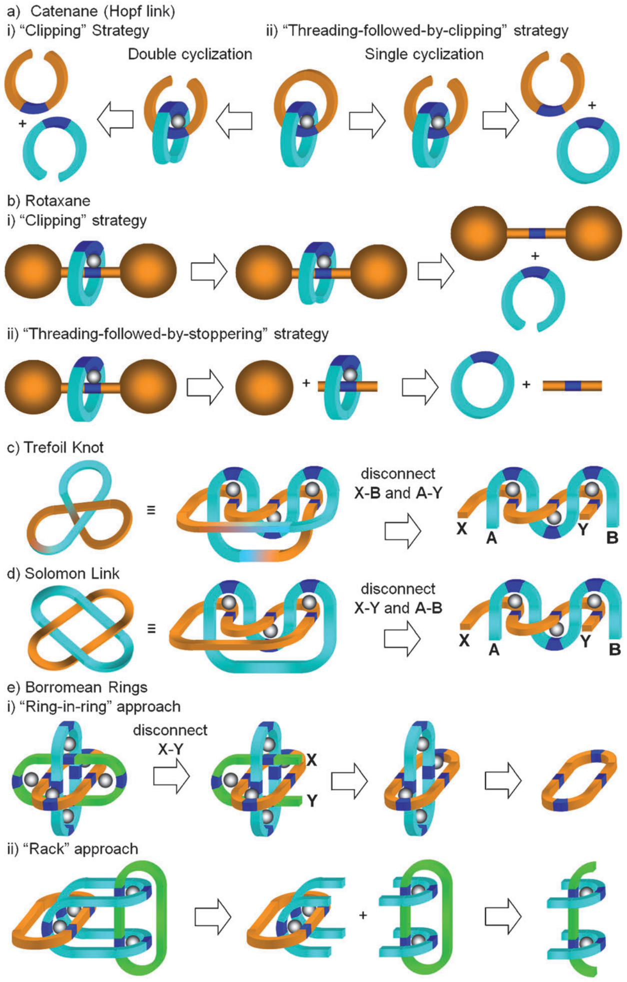
(one equivalent of the template is required) and catalytic (the active template turns over during the reaction) variants.

There are several potentially attractive features of such a synthetic approach to mechanically interlocked architectures: 1) the inherent efficiency and flexibility in having the macrocycle-metal complex perform multiple functions during the reaction; 2) the lack of requirement for permanent recognition elements on each component of the interlocked product, which increases the structural diversity possible in catenanes and rotaxanes and enables their formation to be "traceless"; 3) in some cases only sub-stoichiometric quantities of the active template are required (i.e., the catalytic active metal template variant, Scheme 13 b); 4) the strategy is applicable to many different types of well-known transition metal-catalyzed reactions; 5) reactions that only proceed through a threaded intermediate can allow access to currently inaccessible mechanically linked macromolecular architectures; 6) the coordination requirements during key stages of the catalytic cycle of active template reactions can provide insight into the mechanisms of the metal-catalyzed reactions; and the methodology can even act 7) as an effective conduit for the discovery of novel chemical reactions.

The first active metal template synthesis reaction was described[101] in 2006 using the copper(I)-catalyzed terminal alkyne–azide 1,3-cycloaddition (CuAAC) to assemble a [2]rotaxane. Since then the concept has been extended to other transition metal-mediated reactions such as Glaser,[102] Cadiot-Chodkiewicz[103] and Pd^{II}-mediated oxidative alkyne couplings,[104] oxidative Heck,[105] Pd^{II}-catalyzed Michael addition,[106] Zn^{II}- and Cu^{I}-catalyzed Diels–Alder,[107] Ni^{II}-Cu^{I} catalyzed alkyne homocoupling[108] and a Ni^{II}-catalyzed alkyl bromide sp^3–sp^3 carbon–carbon homocoupling,[109] as well as to the synthesis of molecular shuttles and catenanes (see Section 3).

1.3. Linking Cross-Over Points to Generate Different Mechanically Interlocked Architectures

The linking of crossing points in different ways (connecting "over" to "under" crossings and which reactive end-groups connect to which) determines the topology and structure of the product. An overview of the routes that have been used (or proposed) for the metal-ion directed synthesis of interlocked molecules is shown in Scheme 14. The most basic methods are the simple single or double cyclization routes to catenanes (Scheme 14 a) and the clipping or threading-followed-by-stoppering routes to rotaxanes (Scheme 14 b). More complex topologies, such as a trefoil knot or doubly interlocked [2]catenane (Solomon link), can in principle come from a common intermediate depending on how the end-groups are linked (Scheme 14 c and d).[110] Homocircuit (all the rings are constitutionally identical) Borromean links have been assembled by a remarkable one-pot assembly of all three rings with the required links and crossover points. Potential routes to homo- or heterocircuit Borromean links have been proposed based on "ring-in-ring" or "rack" approaches for linking threaded precursors (Scheme 14 e).[111]



Scheme 14. Passive metal template strategies to rotaxanes, catenanes, knots and links. In all cases metal ions are used to gather and organize the subcomponents prior to the interlocked architecture being captured by covalent bond formation. a) Catenanes can be obtained by either a single macrocyclization, using one pre-formed macrocycle and one acyclic ligand, or by a double macrocyclization, using two acyclic ligands. b) Rotaxanes can be accessed through a "threading-followed-by-stoppering" strategy in which an axle is threaded through and complexed to a macrocycle by coordination to a metal ion to generate a "pseudorotaxane", stopper units can then be introduced by covalent bond formation. c) Trefoil knots and d) Solomon links can, in principle, be formed from a common intermediate, with the outcome depending on which end-groups are linked to which.[110] e) Borromean rings could be accessed by "ring-in-ring" or "rack" approaches.[111]

2. Passive Metal-Ion-Template Synthesis of Rotaxanes and Catenanes

2.1. Tetrahedral Geometries

2.1.1. Sauvage's $Cu^{I}(dpp)_2$ System

The classic[1] Sauvage group strategy of complexing two dpp ligands to Cu^{I} so that they are held in orthogonal orientations by the tetrahedral coordination preference of the metal ion has been utilized in the synthesis of many types of mechanically interlocked molecules.[1,2] In addition to the original "threading" method (Scheme 5),[21,22] catenate **20-Cu^{I}**

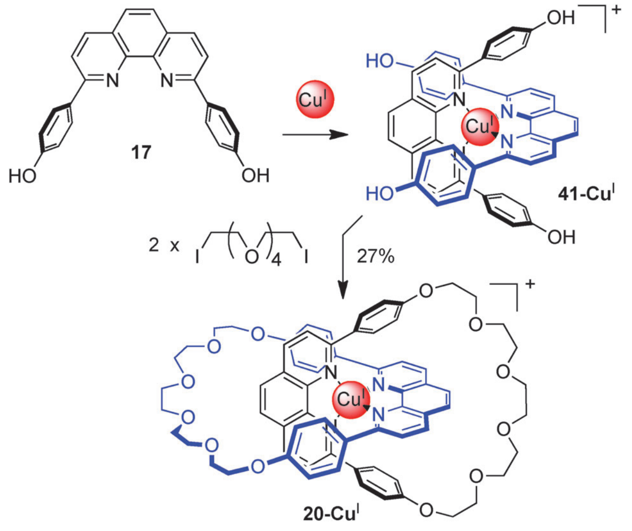
© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

was also accessed by double macrocyclization of **41-Cu^{I}**, albeit in lower yield (27 % cf. 42 %, Scheme 15).

The Cu^{I}(dpp)$_2$ motif has been used to make higher order interlocked compounds ([≥3]catenanes, [≥3]rotaxanes and knots) using two different strategies:

1. Assembling helicates with multiple Cu^{I}(dpp)$_2$ motifs (each Cu^{I}(dpp)$_2$ unit corresponds to a cross-over point (see Section 1.3)) and cyclizing the end-groups. Depending upon the number of cross-over points in the helicates, and which end groups react with which, single or multiply entwined catenanes and knots can be generated (Figure 5). Examples of this strategy are given in Section 5.
2. The linking of Cu^{I}-complexed threaded pseudorotaxane complexes to form [*n*]catenanes (Figure 6).

This latter strategy of linking pseudorotaxanes was used by Sauvage to form [3]catenanes, initially using Williamson ether synthesis,[116,117] and later by oxidative acetylene coupling (Figure 7),[85,118] in each case employing linkers that were too short to undergo intramolecular macrocyclization. These catenates could be demetallated using potassium cyanide and the X-ray crystal structures of a metal-free [3]catenand (**42**) was reported (Figure 7 a).[117] The yields of **42-Cu^{I}** and related structures prepared by William ether synthesis were modest at just 2–6 % but the use of the oxidative coupling of terminal acetylene groups afforded [3]catenane **43-Cu^{I}** in a yield of 58 % (Figure 7 b).[85,118–120] That synthesis also gave a tri-metallic complex, in 22 % yield, tentatively assigned as a [4]catenate consisting of a central hexayne 66-membered ring with three peripheral 30-membered rings. Higher order homologues of these catenates were also accessed by this synthetic approach and electrospray mass spectrometry of a crude reaction mixture provided evidence of multi-ring [*n*]catenates up to $n=7$.[121] A related approach by Vögtle and Sauvage employed a macrobicyclic ligand to form [4]catenanes.[122] Kim later used a similar strategy to form metal–organic “molecular necklaces”[92] (see Section 4.2.2).



Scheme 15. Sauvage’s double macrocyclization “clipping” of **41-Cu^{I}** to give catenate **20-Cu^{I}** in 27 % yield (for the single macrocyclization route, see Scheme 5).[22] Catenate **20-Cu^{I}** can be quantitatively demetallated with potassium cyanide (to give **20**) and a range of other mono- and divalent transition metal ions can be complexed by the catenand. The kinetics[70,112] of introduction of Li^{I}, Cu^{I}, Ag^{I}, Co^{II}, Ni^{II}, Cu^{II}, Zn^{II}, and Cd^{II} and their stabilities have been studied by electrochemical methods.[71a,113] The photophysical properties of many catenates of this type have been extensively studied.[114]

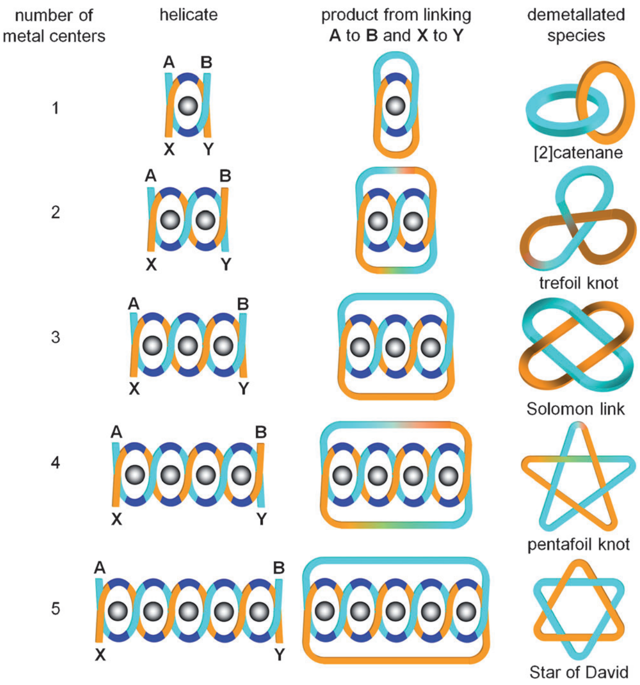


Figure 5. Sauvage’s strategy for forming catenanes and knots by linking the end groups of linear metal ion helicates with various numbers of turns. To date, only the first three ([2]catenane, trefoil knot and Solomon link) have been achieved experimentally.[115] Note added in revision: A pentafoil knot has recently been prepared through a cyclic helicate strategy.[373]

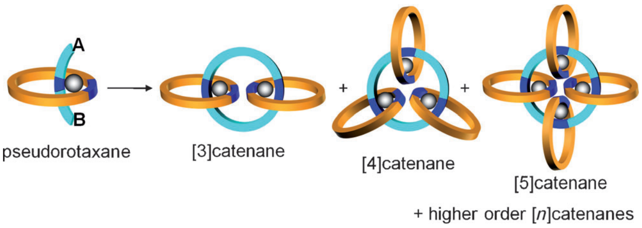


Figure 6. The linking of pseudorotaxane complexes to form higher order catenanes.

Gibson prepared rotaxanes through threaded pseudorotaxane complex **18-Cu^{I}** by replacing the macrocyclization reactions with a simple derivatization with bulky stoppering groups (Scheme 16 a).[123] Demetalation with solid-supported cyanide gave [2]rotaxane **44** in an overall 42 % yield. Sauvage prepared [2]rotaxane **45-Cu^{I}** in which the pseudorotaxane Cu^{I} complex was stoppered in 25 % yield by a reaction in which a second porphyrin unit was formed from the thread aldehyde (Scheme 16 b).[124] Higher order [3]-[125] and [5]rotaxanes[126] have also been synthesized by stoppering Cu^{I}(dpp)$_2$ pseudorotaxanes with porphyrin groups.[127]

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

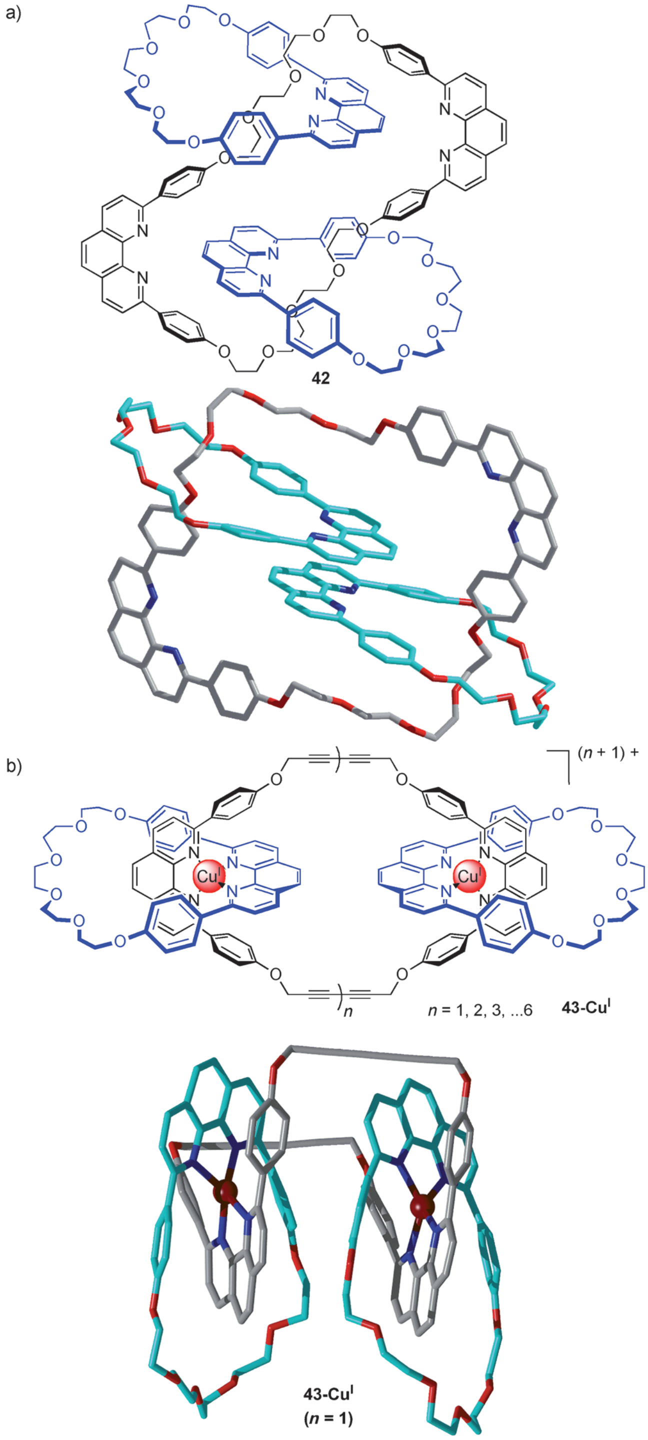
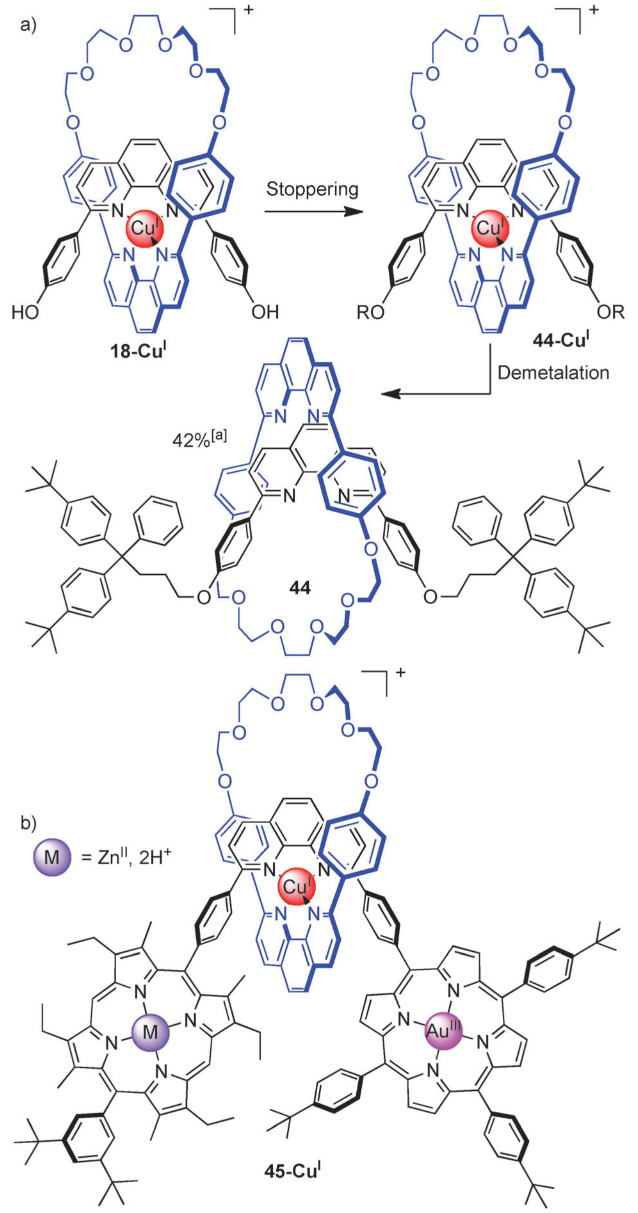


Figure 7. a) [3]Catenand (**42**) assembled by Sauvage by linking pseudorotaxanes through Williamson ether synthesis, followed by demetalation with KCN (2% overall yield).[116,117] A shorter chain analogue was formed in higher yield (6%) but proved difficult to demetallate.[117] In the X-ray crystal structure of **42** the two central phen groups π-stack with a separation of 3.40 Å. b) [3]Catenate **43-Cu**^{I} was formed by linking pseudorotaxanes through Glaser couplings in 58% yield.[85,119] Note the intercomponent π-stacking between various phenyl groups and the phenathroline units in the solid state structure. Using this synthetic methodology, higher order [*n*]catenanes (up to [7]catenates) were prepared, and detected by mass spectrometry.[121]

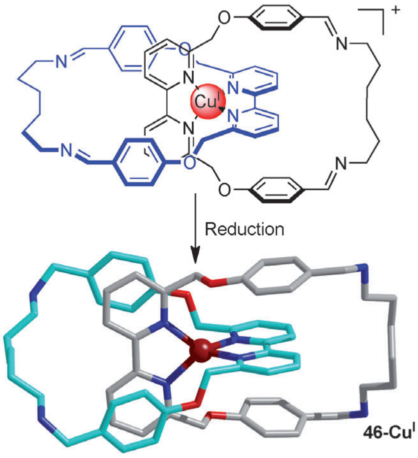


Scheme 16. a) Gibson's synthesis of the first metal template [2]rotaxane **44**, through a Cu^I template.[123] [a] Yield over 2 steps. b) Sauvage prepared a [2]rotaxane **45-Cu**^{I} through a similar "threading-followed-by-stoppering" approach using porphyrin formation as the stoppering reaction[124] and studied photoinduced electron transfer between the metallated porphyrin stoppers.[128]

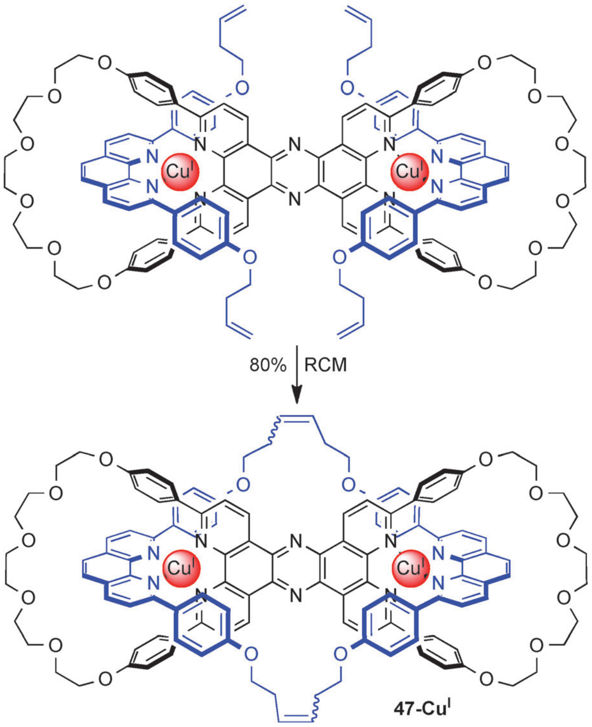
Alternative methods of covalent capture have also been used to access single Cu^I ion template interlocked structures. Lindoy and co-workers[129] employed reversible imine formation with a Cu^I(bpy)$_2$ (bpy = 2,2′-bipyridine) core (Scheme 17). Calculations were used to predict the likely outcome of ring-closing reactions (catenane or figure-of-eight) with diamines of variable lengths. The interlocked topology of **46-Cu**$^{\mathbf{I}}$ was confirmed by X-ray crystallography (Scheme 17).

As discussed in Section 1.2.2, the development of ring closing olefin metathesis dramatically improved the efficiency of assembling interlocked systems[89,130] by linking Cu^I-tem-

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 17. Lindoy's [2]catenate based on a single Cu^I ion template with bipyridyl ligands and assembled under thermodynamic control through imine bond formation. Although the catenane assembly appeared quantitative by ^1H NMR spectroscopy, the imine reduction was problematic resulting in a modest (7%) isolated yield. Reduction of the imine groups yielded [2]catenate **46-Cu^I** which was characterized by X-ray crystallography.[129] Unlike many of the $Cu^I(dpp)_2$ catenates, the two binding motifs of **46-Cu^I** are almost perfectly orthogonal (89.2°) in the solid state structure and the Cu^I center is, within the limits imposed by the ligand bite angles, close to idealized tetrahedral (N-Cu-N angles: ligand bite angles 82.0(2)°, 82.9(2)°; others 123.4(2)°, 126.0(2)°). Note also the intercomponent π-stacking between the bipyridine and phenyl rings (centroid-to-least-squares-plane distance 3.58–3.69 Å).



Scheme 18. Sauvage's "handcuff-like" bis-macrocyclic unit threads quantitatively with Cu^I due to the principle of maximal site occupancy (see Section 1.2.2). Subsequent RCM generated the doubly threaded catenate **47-Cu^I** in 80% yield.[131]

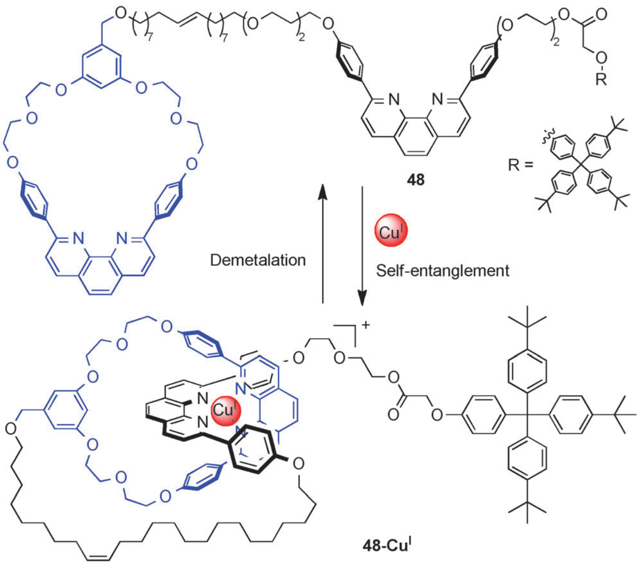
plate pseudorotaxanes (Figure 6). Sauvage exploited RCM to prepare increasingly complex structures, such as the bis-macrocyclic catenane "handcuff" **47-Cu^I** (Scheme 18)[131] where the double RCM reaction proceeds slowly (10 days) but in good yield (80%).

Mayer recently applied olefin metathesis to synthesize a [3]catenane in 71% yield[132] and a non-mechanically bonded but "self-entangled" lasso **48-Cu^I** that could be threaded and de-threaded by reversible complexation with Cu^I (Scheme 19).[133]

The CuAAC "click" reaction has proved a very effective method for stoppering Cu^I-complexed pseudorotaxane units (e.g. Scheme 11e).[87,134] This methodology has been adopted by Megiatto, Schuster and co-workers for the preparation of [2]rotaxanes decorated with porphyrin and [60]-fullerenes[135,136] and was recently extended to produce [2]-[137,138] and [3]catenanes[139] using a Cu^I-(dpp)$_2$ core in up to 92% yield (Scheme 20). This approach has allowed the preparation of non-symmetrical-functionalized [3]catenanes (e.g. **49-Cu^I**) in good yields (65–70% over three steps)[139] and the preparation of [2]catenanes with potentially useful functional groups on the periphery, such as **50-Cu^I**.[138]

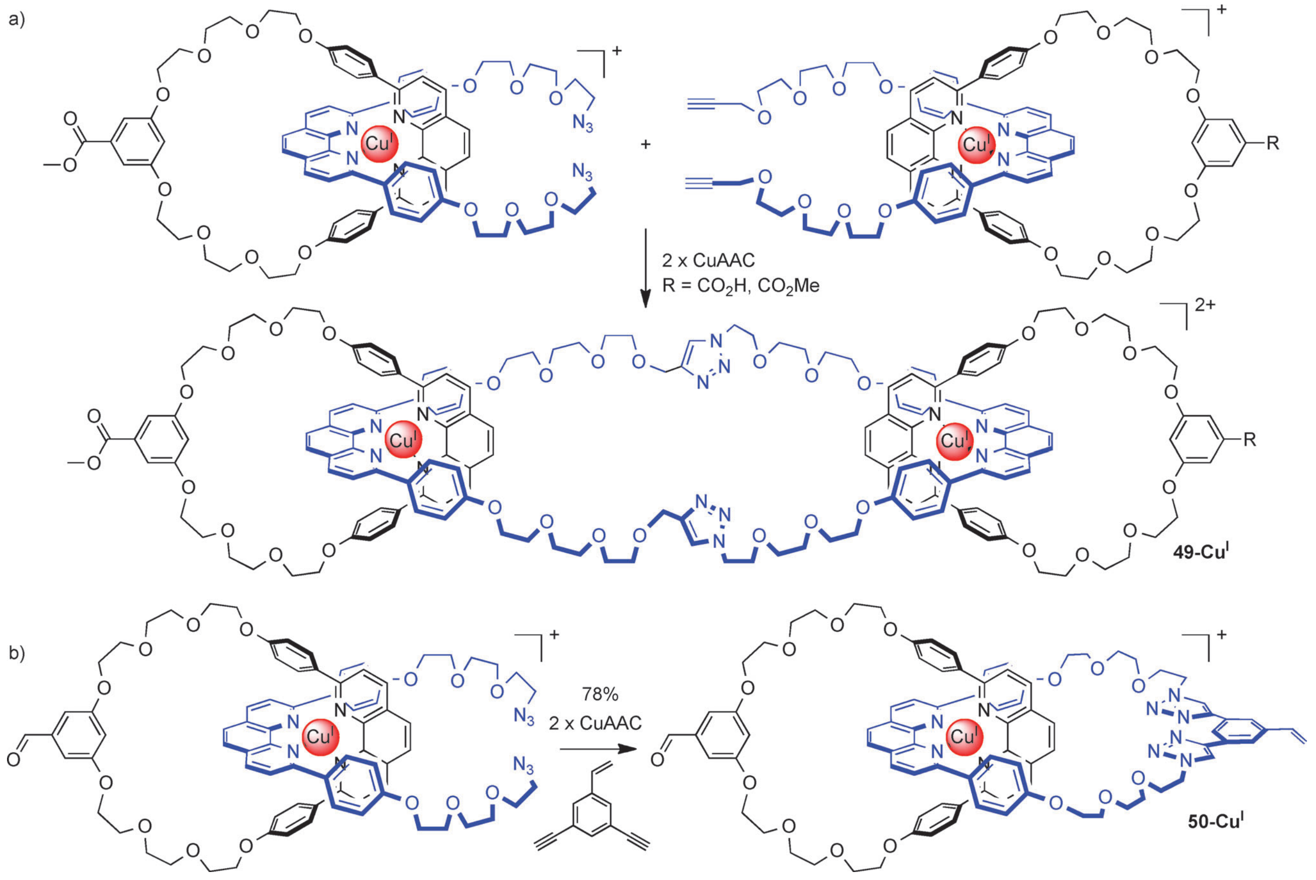
The Sauvage group have exploited the effectiveness of the CuAAC reaction for linking Cu^I-complexed pseudorotaxanes to make more complex structures such as a [3]rotaxane[134] and a cyclic [4]rotaxane (**51-Cu^I**)[140] (Figure 8).

The Sauvage $Cu^I(dpp)_2$ template has also been exploited by other groups using less common covalent-capture methods. Shinkai prepared chiral [2]catenanes by appending boronic acids to the dpp core and reacting them with carbohydrate derivatives.[141] A collaboration between Sauvage and Stoddart saw both groups trademark template motifs incorporated into a [2]catenate which used a $Cu^I(dpp)_2$ motif to organize the ligands prior to a "clipping" reaction through alkylation of the terminal pyridines to form the tetrapyridinium macro-



Scheme 19. Mayer's "self-entangled [1]rotaxane" **48-Cu^I** assembled about a Cu^I template.[133]

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 20. The use of CuAAC "click" reactions by Megiatto, Schuster, and co-workers to form catenanes. a) Non-symmetric [3]catenanes, such as **49-Cu**^{I}, have been prepared in 65–70% yield over three steps from the free ligands.[139] b) [2]Catenanes such as **50-Cu**^{I} have been prepared with useful functional groups on the periphery in up to 92% yield.[138]

cycle.[142] Swager's group synthesized [2]rotaxanes through esterification of a Cu^I-chelated bis-acyl chloride-bpy unit.[143] Saito explored the boundaries between rotaxanes and pseudorotaxanes by forming rotaxanes with a Cu^I(dpp)$_2$ template using large (33- to 45-membered) macrocycles.[144] Sauvage and Diederich covalently attached fullerenes through oxidative acetylene coupling (using the precursor in Scheme 11 b) to form [2]rotaxanes to study electrochemical and photo-induced processes.[145]

An interesting feature of interlocked molecules is the potential for forming topologically chiral structures.[146] Sauvage prepared a topologically chiral catenane through Cu^I template synthesis where the origin of chirality is the inability of the pentaethylene glycol chain to move from one side of the dpp ligand to the other.[147] Other topologically chiral catenanes[148] have been accessed through the use of unsymmetrical rings[149] (for example, **52-Cu**^{I}[149a]) and classically chiral catenanes have been formed by incorporating asymmetric carbon centers,[150] as in **53-Cu**^{I} (Figure 9).[150b]

The same type of Cu^I-complexed pseudorotaxane motif has also been used to assemble catenanes and rotaxanes containing other potential ligand sites, tailored for different coordination geometries. The utility of such systems is as prototypical molecular machine systems since the mechanically interlocked components can undergo large amplitude motions with respect to each other. By electrochemical switching between Cu^I and Cu^{II}, the geometry preference of the metal ion is switched between 4-coordinate tetrahedral and 5-coordinate trigonal bipyramidal, driving mechanical motion either by rotation of the macrocyclic ring (where two binding sites are on a ring) or translation along the thread (where multiple binding sites are on a thread). Examples of catenanes in which rotation of one ring with respect to the other can occur (**54-Cu**^{I}**/Cu**^{II})[151] and rotaxanes with two (**55-Cu**^{I}**/Cu**^{II})[152a] or three (**56-Cu**^{I}**/Cu**^{II})[152l] binding sites on the axle[152] are shown in Figure 10. A so-called "molecular muscle" **57-Cu**^{I}**/Zn**^{II} (Figure 11) that lengthens or contracts in response to chemical stimuli has also been described.[153] This chemistry has been extensively reviewed elsewhere.[2,153]

2.1.2. *A Two Cu^I-Ion Template Motif*

Using a diamine of carefully chosen length and shape, reversible imine bond formation has been used by the Nitschke group to assemble a catenane **58-Cu**^{I} based on a bimetallic bis-Cu^I helicate motif (Scheme 21).[154] Reduction of the imine groups afforded the kinetically stable [2]catenand **59**. The interlocked structure was established by careful mass spectrometry experiments. Using a shorter and more flexible diamine in the Cu^I-template imine-forming reaction

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

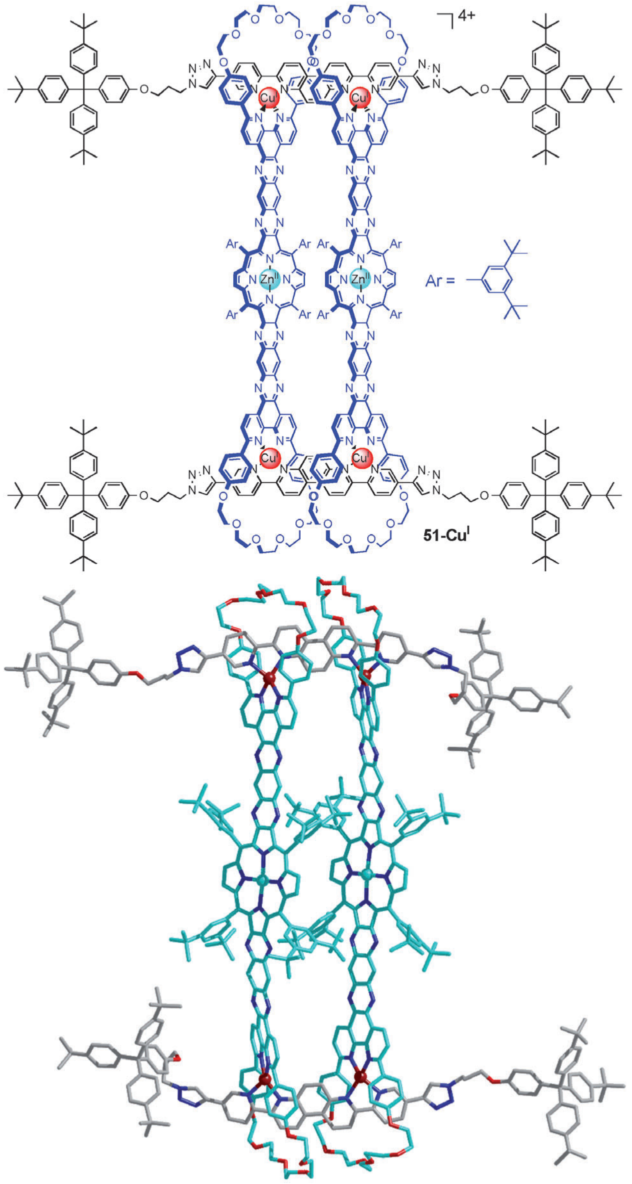


Figure 8. Sauvage's cyclic [4]rotaxane **51-Cu^I** in which metal centers are connected through long conjugated ligands. The quadruple stoppering CuAAC reaction proceeded slowly (5 days), but in excellent yield (95 %).[140] The Zn^{II} atoms of the porphyrins are 5-coordinate with axial water molecules (not shown). The Zn^{II}-Zn^{II} separation is 8.67 Å in the X-ray crystal structure and the molecule is over 64 Å in length.

gives rise to a non-interlocked macrocycle, illustrating again the crucial role that small changes in the structure of the ligand can have in mechanical bond formation (see Section 1.2.2).

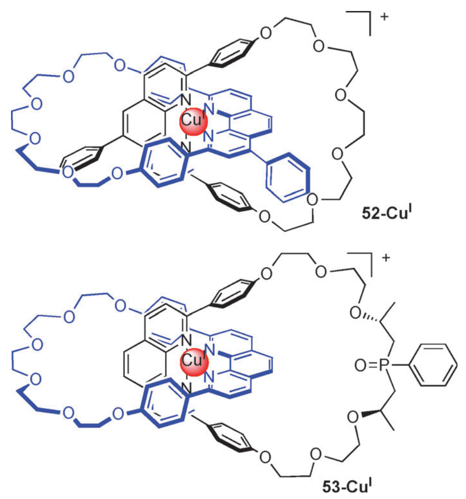
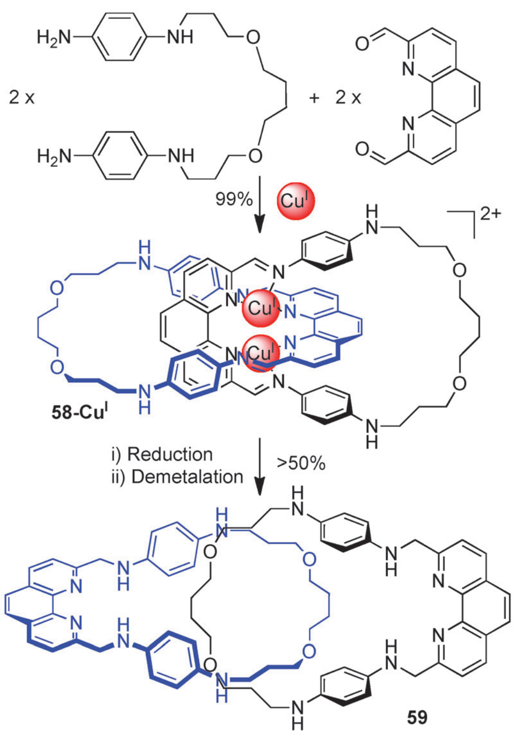


Figure 9. Chiral catenanes **52-Cu^I**[149] and **53-Cu^I**[150b] prepared by Cu^I-template synthesis.



Scheme 21. Nitschke's [2]catenate **58-Cu^I** based on a two Cu^I ion template and assembled under thermodynamic control through imine bond formation. Reduction of the imine groups and removal of the metal ions yielded [2]catenand **59**.[154]

2.2. Trigonal Bipyramidal Geometries

In contrast to the Cu^I(dpp)$_2$ motif, two ligands assembled about a five-coordinate metal ion must necessarily be different. Sauvage utilized Zn^{II}, which can form coordination complexes with 4–6 donor atoms, to assemble catenand **60** using a pair of tridentate and bidentate ligands (Scheme 22).[155]

Initial complexation of the tridentate terpyridine (tpy)-based macrocycle with Zn(OTf)$_2$, followed by binding of a bidentate dpp-based unit afforded pseudorotaxane complex **61-Zn^{II}**. RCM followed by hydrogenation of the olefin afforded the pentacoordinate Zn^{II} catenate **60-Zn^{II}**. The metal-free catenand could be obtained by treatment with aqueous base and the interlocked structure re-metallated with

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

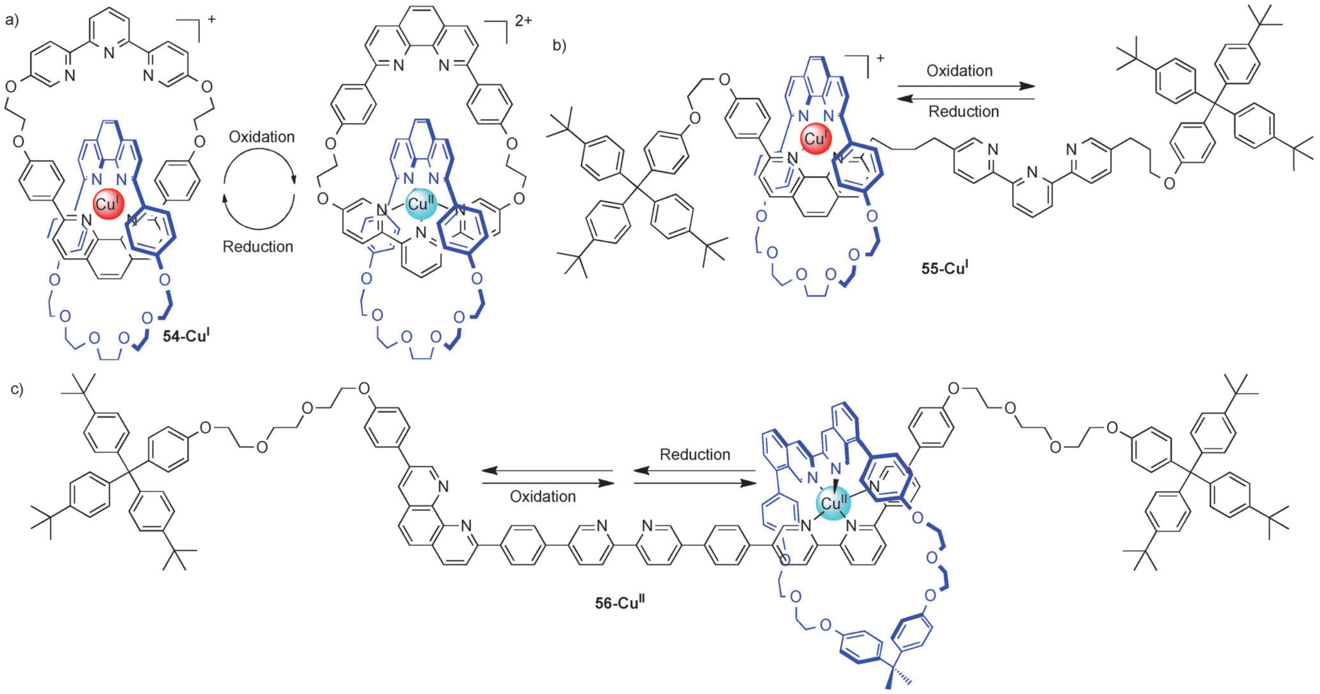


Figure 10. Rotaxanes and catenanes from the Sauvage group in which the redox chemistry of Cu^{I}/Cu^{II} is used to control the co-conformation of the macrocycle between tetradentate and pentadentate coordination modes. a) A Cu^{I}/Cu^{II} switchable [2]catenane **54-Cu^{I}/Cu^{II}**.[151a,b] b) A redox-switchable shuttle **55-Cu^{I}**.[152a] c) A Cu^{I}/Cu^{II} shuttle **56-Cu^{I}** with three binding sites on the axle which exhibits fast shuttling between the binding sites in response to electrochemical stimuli.[152l] For a recent review of these switchable systems, see Ref. [2i].

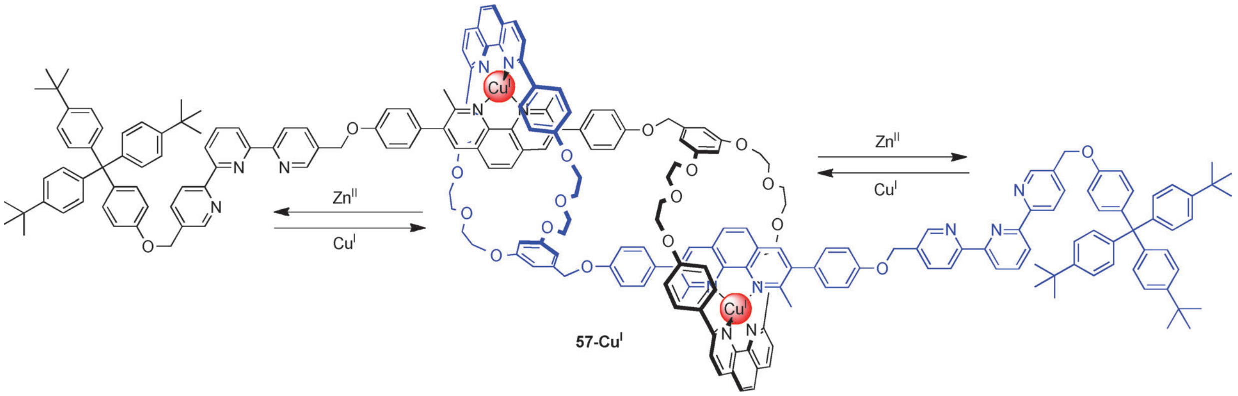


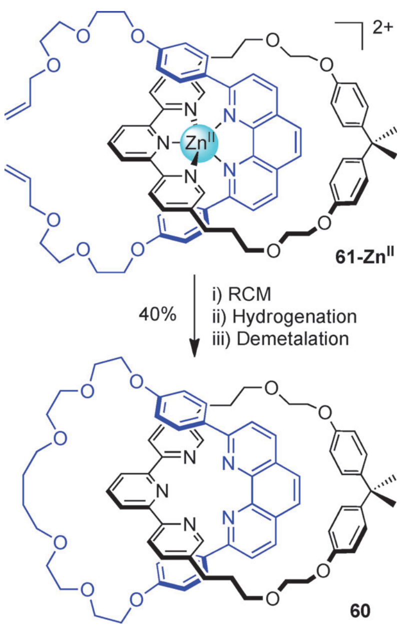
Figure 11. "Molecular muscle" **57-Cu^{I}**. The threaded ligand can be held in extended form by complexation of the phenanthroline units with tetrahedral Cu^{I} (as shown here) or a contracted form by decomplexation and subsequent binding of the terpyridine groups (and phenanthroline ligands of the macrocycle) to five-coordinate Zn^{II}.[153]

Zn^{II} or other metal ions that support a five-donor-atom ligand set, such as Cu^{II} and Fe^{II}. Recently five-coordinate Zn^{II} was used to template the formation of a pseudorotaxane from the classic dpp macrocycle **19** and a functionalized tpy ligand. From this structure a linear [5]rotaxane was formed in 75 % yield through CuAAC reactions with an appropriately functionalized [3]pseudorotaxane containing two Cu(dpp)$_2$ units.[156]

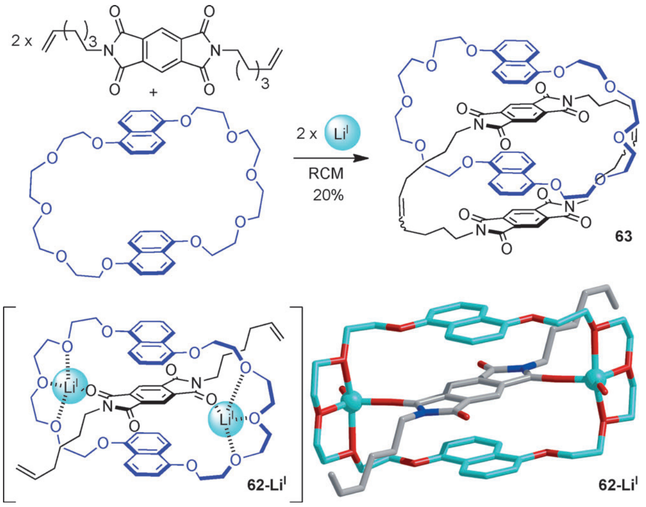
Another example of metal ions being used to direct mechanical interlocking while they are likely five coordinate comes from the Sanders group. Two Li^{+} ions enhanced the binding strength of components assembled predominantly by π–π stacking interactions in the construction of a pseudorotaxane **62-Li^{I}** that was cyclized by RCM to form a [2]catenane **63** (Scheme 23).[157] The X-ray structure of the pseudorotaxane showed four glycol oxygens coordinated to each Li^{+} ion with the fifth coordination site occupied by a water molecule. A collaboration between Sanders and Stoddart saw this motif used in the synthesis of [2]rotaxane molecular shuttles.[158]

Although there are few examples of interlocked structures being assembled through a five-coordinate metal ion template, a number of catenanes and rotaxanes containing a five-coordinate binding motif have been prepared using the

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 22. Sauvage's synthesis of [2]catenane **60** using a five-coordinate Zn^{II} ion as the template with tpy- and dpp-based ligands. Both Cu^{II} and Fe^{II} form stable five-coordinate complexes with **60**.[155]



Scheme 23. Sanders' use of five-coordinate Li^{I} ions to help template the synthesis of [2]catenane **63**. A ligand with improved π donor-acceptor interactions was used to assemble a similar catenane in 60% yield.[157] The X-ray crystal structure shown is that of the pseudorotaxane precursor **62-Li^{I}**. Note the intercomponent π-stacking (3.23 Å) in the solid state.

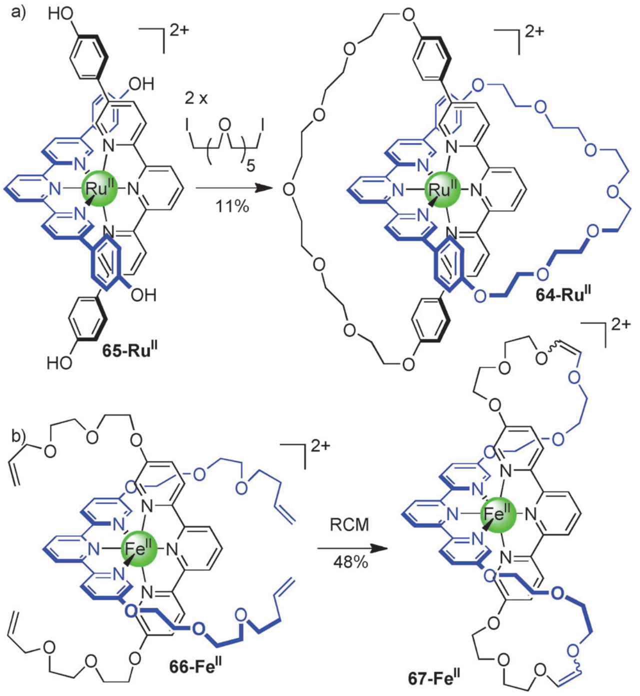
tetrahedral Cu^{I}(dpp)$_2$ motif at a separate site to direct the template synthesis. The resulting structures contain multiple recognition sites in one or more of the components and their differing coordination properties can be used to change the relative positions of the interlocked components (see Figure 10 and 11).[2,151,152]

2.3. Octahedral Geometries

2.3.1. Octahedral "3+3" Donor Ligand Set

Some of the issues that arise in using a "3+3" donor set for octahedral metal ion template catenane and rotaxane synthesis are similar to those that apply when using a "2+2" donor set for tetrahedral coordination template: having the same number of donor atoms on each ligand means that forming the heteroleptic complexes required for heterocircuit catenane or rotaxane assembly is non-trivial (see Section 1.2.1.1). Although the idea of using an octahedral metal ion coordination geometry to direct catenane formation was actually proposed[19] a decade before tetrahedral Cu^{I} was used for this purpose, the first catenane assembled around an octahedral metal ion was reported in 1991 by Sauvage and Ward.[159] They used a tridentate 5,5''-diphenyl-tpy ligand for the synthesis of catenate **64-Ru^{II}** (Scheme 24a). A 5,5''-substitution pattern was employed as it generates a less hindered binding site for the metal ion than a 6,6''-system. Double macrocyclization of **65-Ru^{II}** by Williamson ether synthesis afforded [2]catenate **64-Ru^{II}** in a modest 11% yield. The stability of the ruthenium catenate prevented its demetalation and attempts to make the more labile Fe^{II} analogue from **66-Fe^{II}** by RCM resulted in the formation of the "figure-of-eight" complex **67-Fe^{II}** (Scheme 24b).[160] Yet again (see Schemes 6–9) this illustrates the crucial role that ligand bite-angle, metal size and geometry, and interligand interactions (Section 1.2.1) can play in directing mechanical interlocking in metal ion template syntheses.

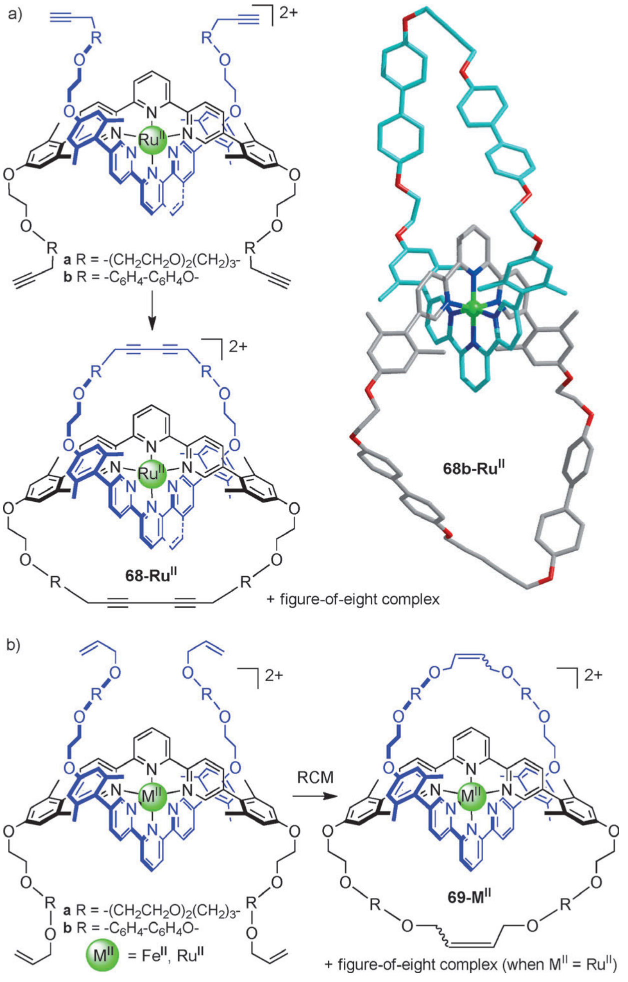
Siegel and co-workers developed an octahedral metal template for catenane synthesis based on 5,5''-manisyl-tpy



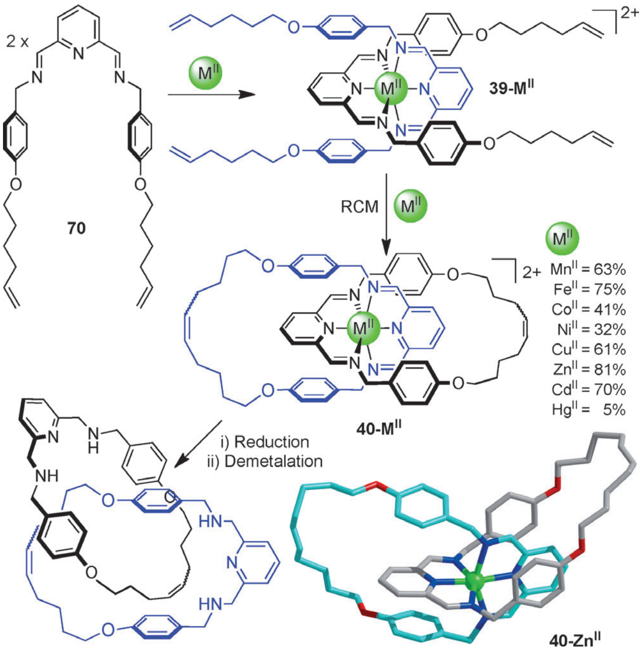
Scheme 24. a) Sauvage's octahedral template synthesis of catenate **64-Ru^{II}** using Ru^{II} and Williamson ether synthesis macrocyclization reactions of pre-catenate **65-Ru^{II}**.[159] b) Attempts to increase the yield using RCM macrocyclization on pre-catenate **66-Fe^{II}** afforded "figure-of-eight" complex **67-Fe^{II}**.[160]

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

and 2-pyridyl-phen-based ligands and Ru^{II} or Fe^{II} templates (Scheme 25).[161] Ru^{II} complexes with terminal olefins or acetylene groups were cyclized using RCM or copper-mediated oxidative acetylene coupling respectively to yield ≈1:2 mixtures of catenanes (**68 a/69 a-Ru^{II}**) and "figure-of-eight" complexes in each case. Incorporating a more rigid biphenyl linker (**68 b/69 b-Ru^{II}**) resulted in an improved ratio (1:1) and, when combined with the use of Fe^{II} as the template ion, resulted in the formation of a [2]catenane **69 b-Fe^{II}** as the exclusive product (Scheme 25 b).



Scheme 25. Siegel's synthesis of catenanes about octahedral metal centers using tpy-based ligands. A Ru^{II} octahedral template in combination with a) oxidative acetylide coupling macrocyclizations or b) RCM led to a ≈1:2 mixture of catenane (**68 a/b-Ru^{II}** or **69 a-Ru^{II}**) and the corresponding figure-of-eight complexes. The use of an Fe^{II} template with more rigid linkers and RCM macrocyclization led exclusively to catenane **69 b-Fe^{II}**.[161] In the X-ray crystal structure of **68 b-Ru^{II}** the Ru^{II} center adopts a distorted octahedral geometry with the tpy groups almost orthogonal (79.1°).

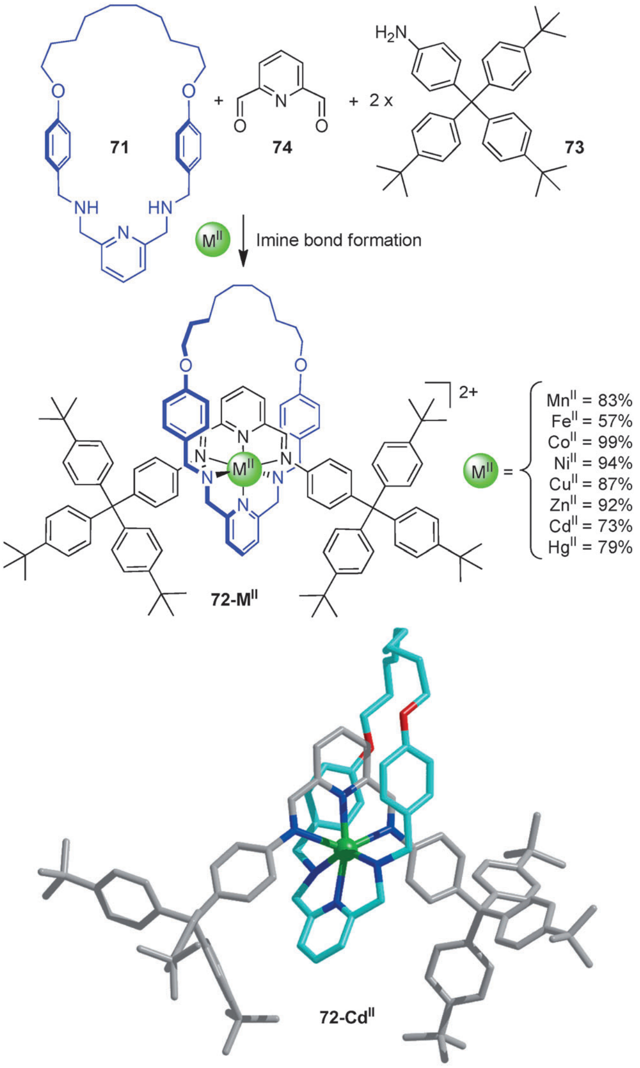


Scheme 26. Octahedral [2]catenates **40-M^{II}** formed around a range of divalent metal ions through double RCM reactions of pre-catenate **39-M^{II}** or imine-bond formation (see Scheme 11).[84] The Zn^{II} center in the X-ray structure of **40-Zn^{II}** is distorted octahedral (*cis*-(N-Zn-N) bond angles 74.7(3)–99.7(3)° due to ligand bite angle) and the least-squares planes of the two pyridine rings are almost perfectly orthogonal (89.8°). Stabilizing π–π interactions between the phenyl and "sandwiched" pyridyl rings (ring-to-ring distances 3.10–3.38 Å) are present in both ligands and likely play an important role in the assembly of the catenanes (see Section 1.2.2.2).

A simple method for preparing [2]catenanes using a variety of divalent octahedral transition metal ions has been developed (Scheme 26).[84] Ligand **70** is based on the structure successfully used to assemble hydrogen bond-assembled benzylic amide catenanes and rotaxanes.[162] It is modified to incorporate a tridentate 2,6-diiminopyridine coordination motif that allows two distinct routes for the preparation of catenates. A kinetic template effect route utilizes formation of pre-catenate complex **39-M^{II}**. Subsequent double macrocyclization by RCM reactions between the terminal alkenes generated the [2]catenane (**40-M^{II}**) in good yields. Alternatively, the thermodynamic template effect can be exploited by forming the catenates through reversible imine bond formation between the bis-benzylamine chain and 2,6-diformylpyridine in the presence of a divalent metal salt (Scheme 11 d, Section 1.2.2). The solid state structures of several of the catenates show interligand aromatic stacking interactions which are a feature of benzylic amide catenanes and rotaxanes and serve to favor assembly of the interlocked structure rather than the macrocyclic "figure-of-eight" isomer (Scheme 10, Section 1.2.1).

Although the same number of donor atoms are present in each building block ligand, [2]rotaxanes could be efficiently formed using this system by exploiting the principle of maximal site occupancy (Section 1.2.2.1).[163] Using a pre-formed bis-amine macrocycle **71**, rotaxanes **72-M^{II}** could be formed in good-to-excellent (57–99 %) yields by imine bond formation between stopper aniline **73** and 2,6-diformylpyridine (**74**) in the presence of an appropriate divalent metal ion (Scheme 27). To demonstrate that the rotaxane was thermodynamically favored, amine-based macrocycle **71** was treated with one equivalent of Zn^{II}. Addition of two equivalents of imine-based thread quickly led to abstraction of the octahedral metal ion from the macrocycle to form a bis-thread metal

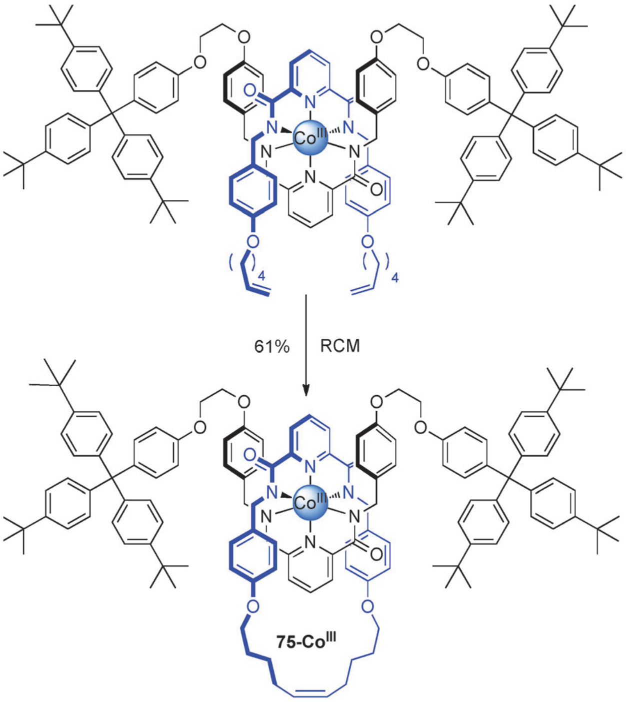
© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 27. Octahedral amine/imine-based [2]rotaxanes **72-M**^{II} formed through reversible imine bond formation, templated around a range of divalent metal ions.[163] As is common for Cd^{II} complexes, in the X-ray crystal structure of rotaxane **72-Cd**^{II} the metal coordination geometry is distorted octahedral with *cis*-(N-Cd-N) bond angles ranging from 68.6(2)–124.6(2)°.

complex. However, over the course of a 24 hour period, the product distribution altered to give [2]rotaxane **72-Zn**^{II} in quantitative yield. π-Stacking between the thread and the macrocycle, which is absent in the bis-thread complex, also contributes to the stability of the rotaxane.

With the same basic scaffold, this ligand system could be modified to work with harder, trivalent, metal ion templates such as Co^{III} by using a 2,6-pyridinedicarboxamide coordinating motif (Scheme 7 and Scheme 28).[76] [2]Catenane **30-Co**^{III} (see Scheme 7) and [2]rotaxane **75-Co**^{III} were assembled using either a preformed macrocycle (in the case of the catenane) or thread (in the case of the rotaxane) bound to Co^{II}. Oxidation of Co^{II} to Co^{III} locked the ligands in place (Co^{III} undergoes very slow ligand exchange) and RCM generated the interlocked structures. (Double RCM of two bis-olefin ligands coordinated to Co^{III} gave the non-interlocked "figure-of-eight" isomer (see Scheme 7 in Section 1.2.2)).



Scheme 28. Co^{III} template synthesis of [2]rotaxane **75-Co**^{III} formed by assembly of the components around a labile Co^{II} center followed by oxidation to kinetically stable Co^{III}.[163] For a related [2]catenate synthesis see Scheme 7.[76]

2.3.2. *Octahedral "4+2" Donor Ligand Set*

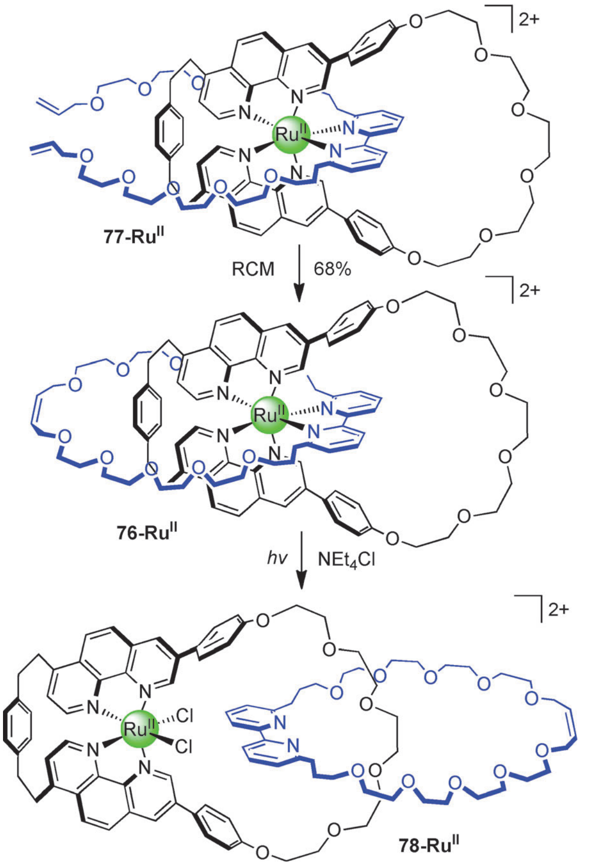
Heteroleptic complexes (necessary for accessing rotaxanes and heterocircuit catenanes) can be conveniently accessed with octahedral metal ions by using a "4+2" set of donor atoms on the ligands. Catenate **76-Ru**^{II} was assembled in 68% yield by RCM of **77-Ru**^{II} (Scheme 29).[164] In the resulting Ru^{II}-catenate the bipyridyl ligand can be selectively decomplexed upon photochemical excitation in the presence of chloride ions or acetonitrile to form **78-Ru**^{II}.[165] A similar system could be assembled through a double macrocyclization approach.[165] Changing to a less hindered 4,4′-substitution pattern for the bipyridyl-ligand allowed the preparation of a [2]catenate in 34% yield with Rh^{III} as the template ion.[166]

A similar octahedral "4+2" donor ligand set has also been used for the template synthesis of rotaxanes (Scheme 30).[167] Ru^{II} complex **79-Ru**^{II} was complexed with a bipy-based macrocycle **80** to afford a pseudorotaxane which was covalently captured by Williamson ether synthesis to form [2]rotaxane **81-Ru**^{II} in 56% yield.[167] As in the catenane system,[164b] decomplexation of the bipy macrocycle from the metal center could be accomplished photochemically.

2.3.3. *Octahedral "2+2+2" Donor Ligand Set*

Entwining three strands about a single metal ion template (see Scheme 3c for triple-stranded helicates) opens up the possibility of assembling doubly-threaded rotaxanes and other complex interlocked architectures. The first investigations of such metal ion template systems have been carried

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

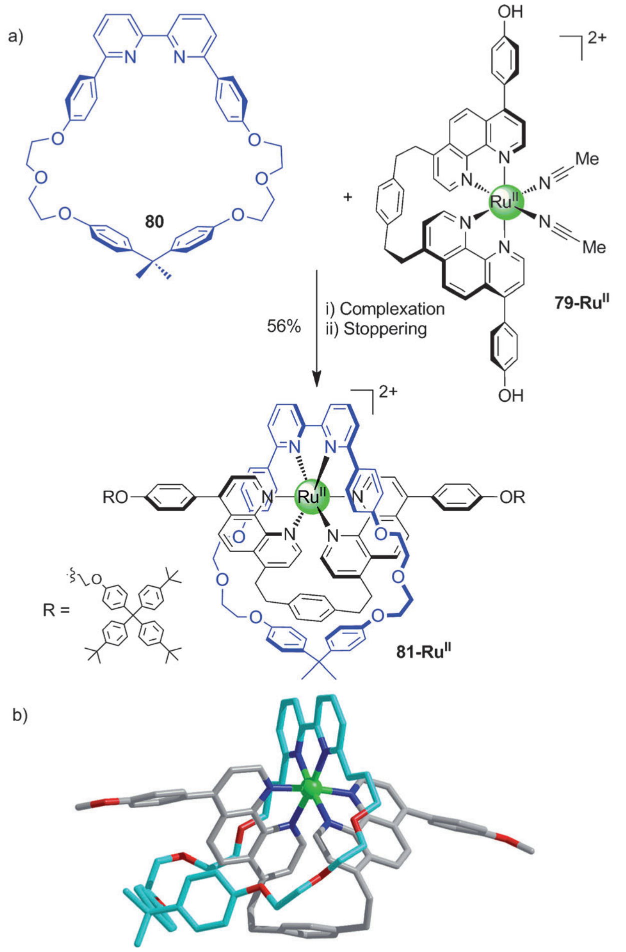


Scheme 29. Sauvage's octahedral "4+2" motif using Ru^{II} as the template ion. RCM of pre-catenate **77-Ru^{II}** affords [2]catenate **76-Ru^{II}** in 68% yield.[164b] Treatment of **76-Ru^{II}** with a chloride source and irradiation affords [2]catenane **78-Ru^{II}**.[165] A related [2]catenane formed by double RCM ring closure was prepared in 46% yield.[165]

out by the Sauvage group (Scheme 31) using biisoquinoline-based ligands.[168] These systems have a similar bite angle to dpp systems but, with an appropriately large macrocycle, their shape results in less steric crowding around the metal center.[152l,m,169] This allows an octahedral metal ion to coordinate three bidentate biisoquinoline ligands, one a macrocycle (**82**) the others acyclic (**83**), to generate the "2+2+2" doubly-threaded complex **84-M^{II}** (where **M^{II}** = Fe^{II} or Co^{II}) (Scheme 31).[168] Derivatizing the azides of the threaded axles with bulky groups through a CuAAC reaction afforded [3]rotaxane **85-M^{II}/M^{III}**. Although the metal complexes **85-Fe^{II}** and **85-Co^{III}** are extremely stable, upon demetalation the components slowly dissociate showing that the bulky groups are insufficiently large to prevent dethreading.

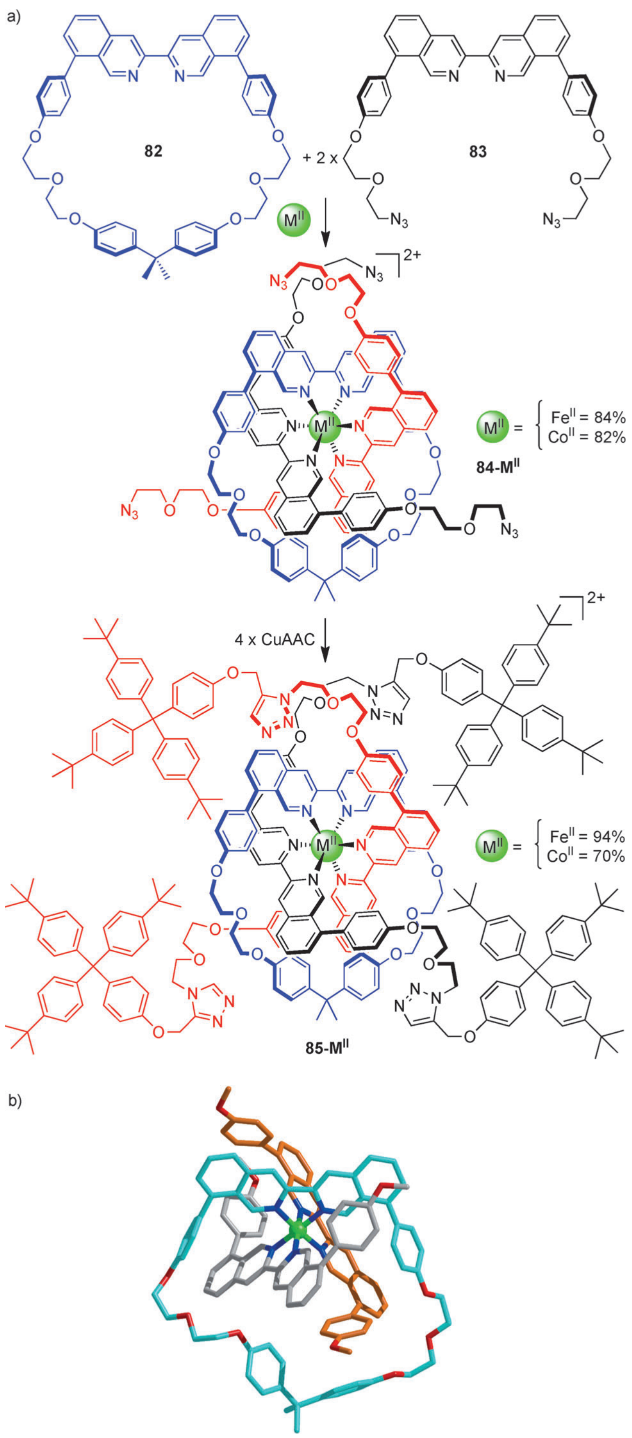
2.4. Square Planar Geometries

A "3+1" donor ligand set[77] necessarily forms a heteroleptic complex and the steric demands of the tridentate ligand can be used to orient the monodentate out of the plane of the donor atoms in a square planar coordination complex to create a crossing point. This, in turn, can be used to generate a three-dimensional interlocked structure from a two-dimensional template. A tridentate pyridine-2,6-dicarboxamide ligand was complexed with Pd^{II} to form **32-Pd^{II}** (Scheme 32). Substitution of the acetonitrile ligand with a 2,6-substituted pyridine-based thread **86** formed a pre-rotaxane which upon RCM and hydrogenation of the resulting olefin yielded [2]rotaxane **87-Pd^{II}** in 77% yield.[170] The crystal structure of **87-Pd^{II}** shows the square planar coordination geometry of the Pd^{II} template and the conformation of the macrocycle reveals the reasons behind some subtleties in the ligand design. The 2,6-substitution pattern of the pyridine unit in the thread is necessary for the formation of the interlocked product, as with a 3,5-substitution pattern macrocyclization preferentially occurs without encircling the thread, forming a non-interlocked ring-on-thread complex. The restrictions on the degrees of freedom of the components of interlocked molecules often force functional groups into unusual positions and the demetallated [2]rotaxane **87**[170] was used to demonstrate binding motifs, such as bifurcated pyridine-amide-pyridine hydrogen bonding, that are either

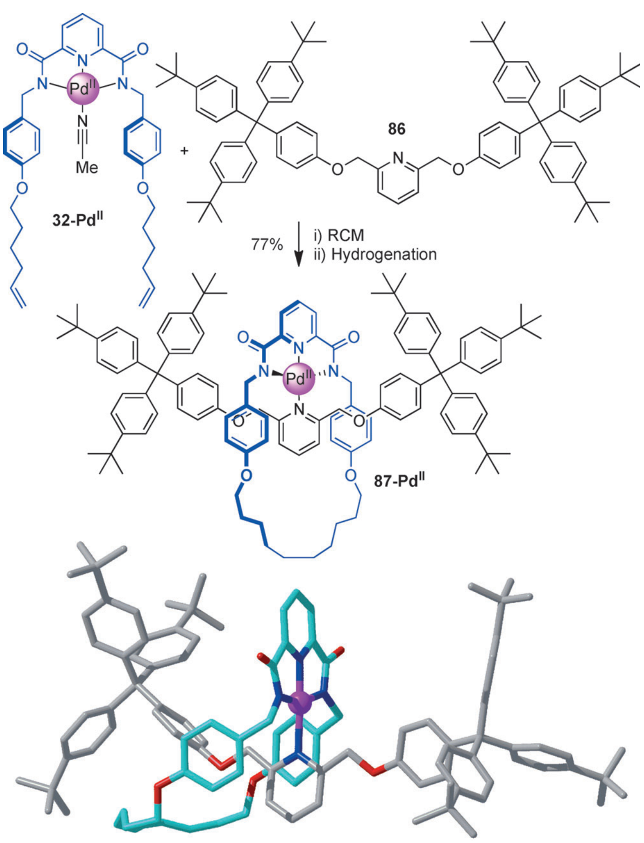


Scheme 30. a) Sauvage's "4+2" octahedral construction of rotaxane **81-Ru^{II}**.Thread **79-Ru^{II}** contains two phen units and macrocycle **80** contains a bipy unit for coordination to an octahedral metal ion. The macrocycle can be displaced photochemically (quantitatively) from the metal center.[167] b) X-Ray crystal structure of a related Ru^{II} pseudorotaxane (R = Me). All the coordination bond angles and lengths are similar to [Ru(phen)$_2$(bpy)](PF$_6$)$_2$ (CSD refcode UCUSIV)—indicating that the threaded structure is relatively strain-free.[167a]

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 31. a) The formation of a triply-entwined complex of biisoquinoline ligand with Fe^{II} or Co^{II} leads to the synthesis of doubly-threaded [3]rotaxane **85-M^{II}**.[168] Where M = Co^{II} the metal is first oxidized to kinetically inert Co^{III} before the subsequent click reaction.[168b] b) X-Ray crystal structure of a related Co^{III}-containing pseudorotaxane in which the coordination bond angles show little deviation from ideal octahedral, indicating the doubly-threaded structure is not particularly sterically crowded (the *cis*-N-Co-N bond angles, 83.8(3)–95.1(3)°, deviate less than 1.3° from the corresponding angles in [Co(bpy)$_3$](ClO$_4$)$_3$·2 H$_2$O (CSD refcode: FIXKUT)).[168]



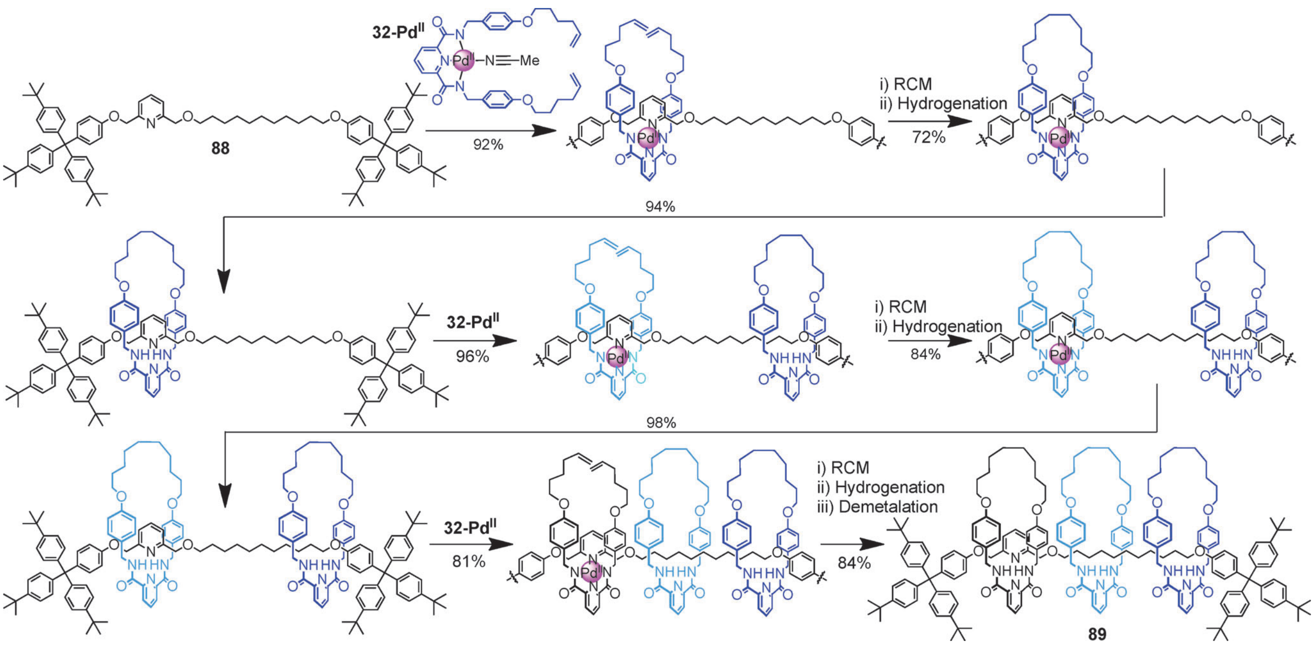
Scheme 32. [2]Rotaxane **87-Pd^{II}** assembled around a square-planar Pd^{II} template by RCM.[170] Note the intercomponent π-stacking interactions in the solid state. The "kinked" conformation of the benzylic macrocycle means that a 2,6-substituted pyridyl thread is necessary for rotaxane formation (a 3,5-substituted thread forms a non-interlocked perch complex). The coordination geometry about the metal center is similar to the structures shown in Scheme 9.

unobserved or unstable in non-interlocked structures.[171] [2]Catenanes could be synthesized using the same basic ligand structure and template, but required pre-forming the monodentate macrocycle (see Scheme 9, Section 1.2.2.1).[78]

Similar [2]rotaxane syntheses based on the same "3+1" approach were later reported by Takata and Hirao[172] and, more recently by Chiu[173] using the same type of Pd^{II}-containing macrocycle. In both cases the precursor pseudorotaxane was stoppered by reaction of bulky isocyanate units with the terminal hydroxyl groups of the thread. A subsequent report demonstrated that the Pd^{II} center was capable of progressively catalyzing isomerization reactions of propargyl- or allyl-urethane groups within the thread, transforming them into oxazolidone and oxazolidinone units respectively.[174]

The exceptional kinetic stability of Pd^{II} complexes makes this template particularly versatile. The heteroleptic precatenate and pseudorotaxane complexes are stable to purification by column chromatography which means that this template motif can be used in ways that dynamic complexes of metal ions cannot.

The robust nature of the square-planar Pd^{II} methodology was used in the synthesis of rotaxanes with multiple rings by the repetitious use of a single template site on axle **88** (Scheme 33).[175] Macrocycles were added in an iterative



Scheme 33. Synthesis of [4]rotaxane **89** by the repetitious use of a single template site on the axle. Assembled by an iterative assembly procedure of 1) complexation, 2) macrocyclization, 3) demetalation, repeated *n* times to build up *n* threaded rings.[175]

fashion through the following steps: 1) complexation of the pyridine group of the thread or rotaxane with **32-Pd^{II}**; 2) RCM macrocyclization to mechanically lock an additional macrocycle onto the thread; 3) demetalation, to regenerate the metal-free pyridine coordination site. Repeating this procedure three times generated [4]rotaxane **89**. In principle, the only limiting factor in the synthesis of higher order rotaxanes is the length of the thread.[176] The concept was extended to produce controlled sequence isomerism in rotaxanes, through constitutionally different macrocycles being sequentially added to the thread in any order (**90a** and **90b**, Figure 12).[177]

Incorporation of a second heterocycle into the thread component, a 2,6-substituted dimethylaminopyridine (DMAP) unit, allowed the synthesis of a proton-driven molecular shuttle (Scheme 34).[178] Under neutral conditions

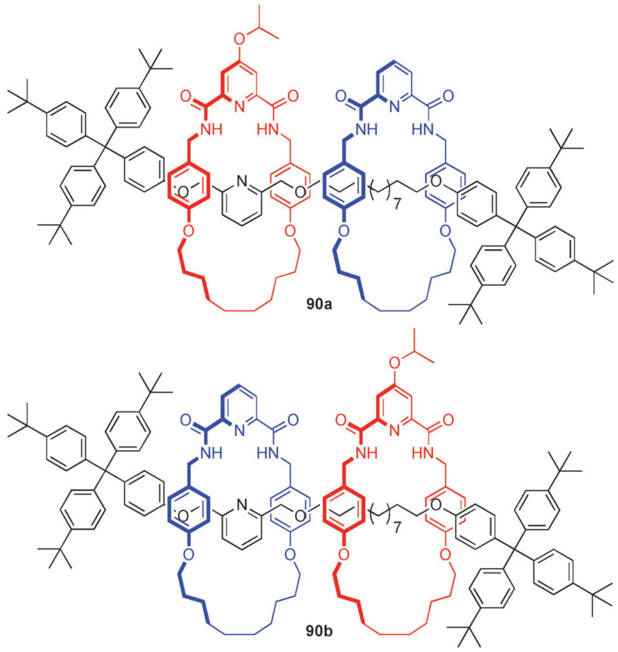
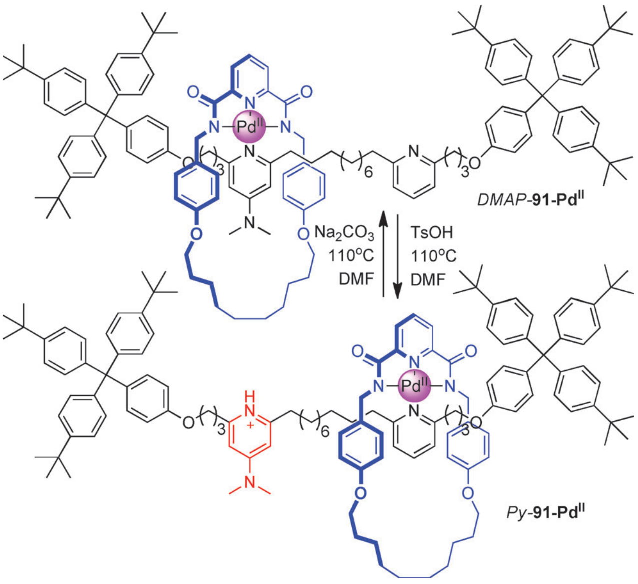


Figure 12. Sequence isomerism in [3]rotaxanes. Diastereomers **90a** and **90b** are constitutionally identical other than for the relative positions of the different macrocycles on the thread, a sequence determined by the order of addition of the rings to the thread.[177]



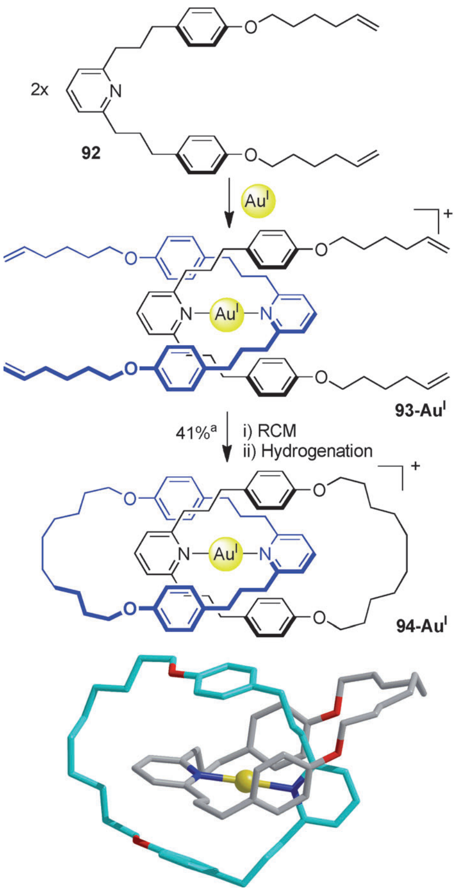
Scheme 34. A bistable acid-base driven molecular shuttle **91-Pd^{II}**.[178] In the absence of acid, the Pd^{II}-center preferentially coordinates to the stronger binding ligand, DMAP. The addition of acid selectively protonates the more basic DMAP site and displaces the macrocycle to the free pyridine site.

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

the Pd^{II}-macrocycle preferentially resides on the more basic heterocycle (*DMAP*-**91**-**Pd^{II}**), but upon protonation and heating to 110°C the macrocycle is translocated to the less basic pyridine unit (*Py*-**91**-**Pd^{II}**). Treatment with base and heating re-establishes the original equilibrium position of the macrocycle coordinated preferentially to the DMAP binding site. A second generation molecular shuttle, using a macrocycle with different steric constraints around the metal center, gave more rapid dynamics and improved positional bias in both the protonated and neutral states of the rotaxane.[179]

2.5. Linear Geometries

The one-dimensional linear coordination geometry of Au^{I} has been used to template the assembly of mechanical interlocked architectures (Scheme 35).[180] A monodentate pyridine ligand (**92**) coordinates to Au^{I} in a 2:1 stoichiometry to form **93**-**Au^{I}**. RCM followed by hydrogenation afforded [2]catenane **94**-**Au^{I}** in 41% yield, the efficiency of catenane formation being aided by intercomponent stacking interactions between the ligands. The X-ray crystal structure of the Au^{I} [2]catenate shows the near-linear pyridine-Au^{I}-pyridine coordination geometry. Rotaxanes could also be made through a statistical heteroleptic Au^{I} complex with **92** and an appropriate thread ligand.



Scheme 35. The linear coordination geometry of Au^{I} allowed the synthesis of catenanes (above) and rotaxanes.[180] The N-Au-N angle in the X-ray crystal structure of the Au^{I}-catenate, **94-Au^{I}** is close to linear (175.3(3)°). Note also the offset intercomponent π-stacking interactions. [a] The yield is from the free ligand **92**.

3. Active Metal Template Synthesis

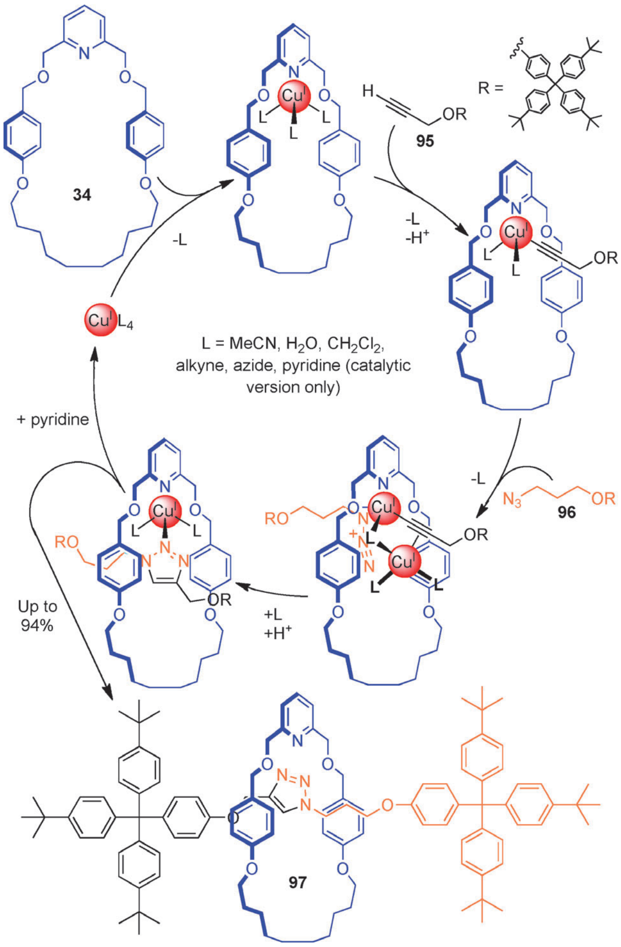
The key feature of active template synthesis[100] is that, unlike the systems detailed in the previous section, the metal plays a dual role during the assembly of the interlocked architecture, acting as both a template for entwining or threading the components and as a catalyst for covalently capturing the interlocked product. Unlike passive metal template methods, permanent recognition motifs are not always required on each of the components to be interlocked (i.e., the assembly can be traceless) and the template can often be used in sub-stoichiometric quantities. A rapidly growing number of different metal-catalyzed reactions have proven suitable for the active metal template synthesis of rotaxanes and catenanes including the copper(I)-catalyzed terminal alkyne–azide cycloaddition (the CuAAC "click" reaction), palladium- and copper-catalyzed alkyne homocouplings and heterocouplings, and palladium-catalyzed oxidative Heck couplings and Michael additions. In addition to simple interlocked structures, the synthetic strategy has been used to construct switchable molecular shuttles with weak intercomponent interactions (a requirement for fast shuttling) and to provide insight into the mechanisms of transition metal-catalyzed reactions.

3.1. Active Template Copper(I)-Catalyzed Azide–Alkyne 1,3-Cycloaddition

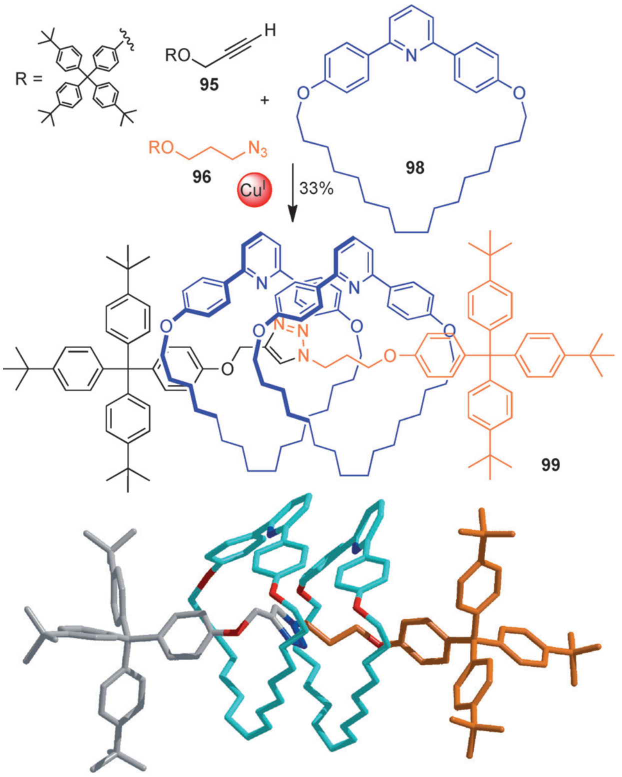
3.1.1. [2]- and [3]Rotaxanes

The first active metal template synthesis reaction was reported in 2006.[101] A copper(I)-catalyzed azide–alkyne 1,3-cycloaddition (CuAAC) was employed to generate rotaxanes (Scheme 36) from macrocycle **34**, featuring a monodentate pyridine unit, alkyne functionalized "stopper" **95** and azide functionalized "stopper" **96**. With a stoichiometric quantity of Cu^{I}, [2]rotaxane **97** was formed in up to 94% yield.[101] Varying the ligating motif in the macrocycle showed that either mono- or bidentate macrocyclic ligands could form [2]rotaxanes in this way,[181] and by adding pyridine the metal could turn over during the reaction (82% yield with only 20 mol% of Cu^{I}) giving a catalytic active metal template assembly process. Both the stoichiometric and catalytic versions of the reaction were used to synthesize more complex two-station molecular shuttles in which the dynamics of the translocation of the macrocycle by ligand exchange could be controlled by coordination to different metal ions (rapid shuttling is observed with Cu^{I}, slow shuttling with Pd^{II}). Under active metal template reaction conditions that feature a high macrocycle (**98**):Cu^{I} ratio, [3]rotaxane **99** (two macrocycles on a thread containing a single triazole ring) was unexpectedly produced during the reaction (Scheme 37). This shows that under these conditions the mechanism of the Cu^{I}-

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 36. Active metal template CuAAC reaction of macrocycle **34**, alkyne **95** and azide **96** to form [2]rotaxane **97** in the presence of stoichiometric (94% yield of **97**) and sub-stoichiometric (20 mol% Cu^I, 82% yield of **97**) quantities of Cu^I.[101]



Scheme 37. Active metal template CuAAC reaction using macrocycle **98**. At high macrocycle:copper ratios [3]rotaxane **99** is formed (33% yield). The X-ray crystal structure confirmed two pyridine macrocycles threaded onto an axle featuring only one triazole unit.[181]

catalyzed terminal alkyne-azide cycloaddition involves a reactive intermediate that features at least two metal ions.

3.1.2. [2]Catenanes

Active template synthesis of [2]catenanes through the CuAAC reaction can be achieved either through macrocyclization about one preformed macrocycle (Scheme 38a) or by forming both rings during the reaction (Scheme 38b).[182] The latter approach is particularly demanding, with the metal ion having to catalyze two covalent bond forming reactions as well as templating the assembly of the interlocked product. Although the reaction is highly concentration dependent, [2]catenane **102** can be formed in up to 46% yield from open chain precursor **103**.[182]

3.1.3. Macrobicyclic [3]Rotaxanes: Forming Threads Through Two Rings with One Template Site

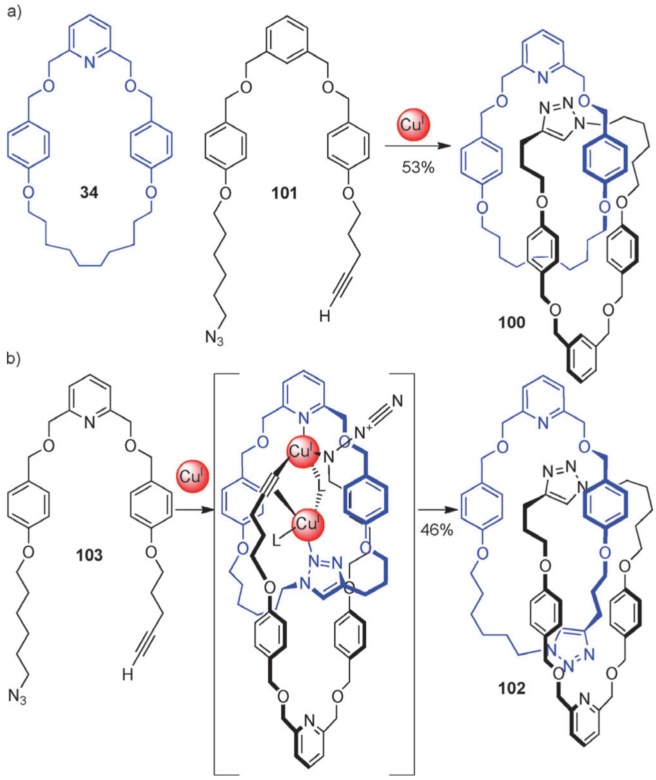
Active metal template synthesis allows access to types of mechanically interlocked structures that are not accessible through traditional passive template methods. By incorporating the metal-ion-ligating group at the junction of two rings, it is possible to use one template site to direct the formation of mechanical bonds through *both* rings, forming two threads that are either constitutionally identical or different depending on the reaction protocol (Scheme 39). [2]- and [3]rotaxanes (**104** and **105**, respectively) were prepared from macrobicycle **106** by two successive active template CuAAC reactions with alkyne **95** and azide **96**.[183] Two diastereomers of [3]rotaxane **105** were formed, differing in the relative orientations of the two threads (*syn–syn* and *syn–anti*) in the [3]rotaxane.

It is even possible to use two different chemical reactions, catalyzed by different metal ions, to form the two threads in a macrobicyclic [3]rotaxane by successively using two different active template reactions (Scheme 39). Active template Pd^{II}–alkyne homocoupling (see Section 3.3.2) of alkyne **107** and bicyclic macrocycle **106** afforded [2]rotaxane **108** in 10% yield. Subsequent treatment of **108** with alkyne **95** and azide **96** formed [3]rotaxane **109** (40%) through a CuAAC active template threading reaction.

3.2. Active Template Alkyne–Alkyne Couplings

Metal-catalyzed alkyne–alkyne homo- and heterocouplings are often high yielding, structurally tolerant, reactions that produce a bis-alkyne group in the product. This is a rigid structural unit for the rotaxane thread, potentially useful for

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

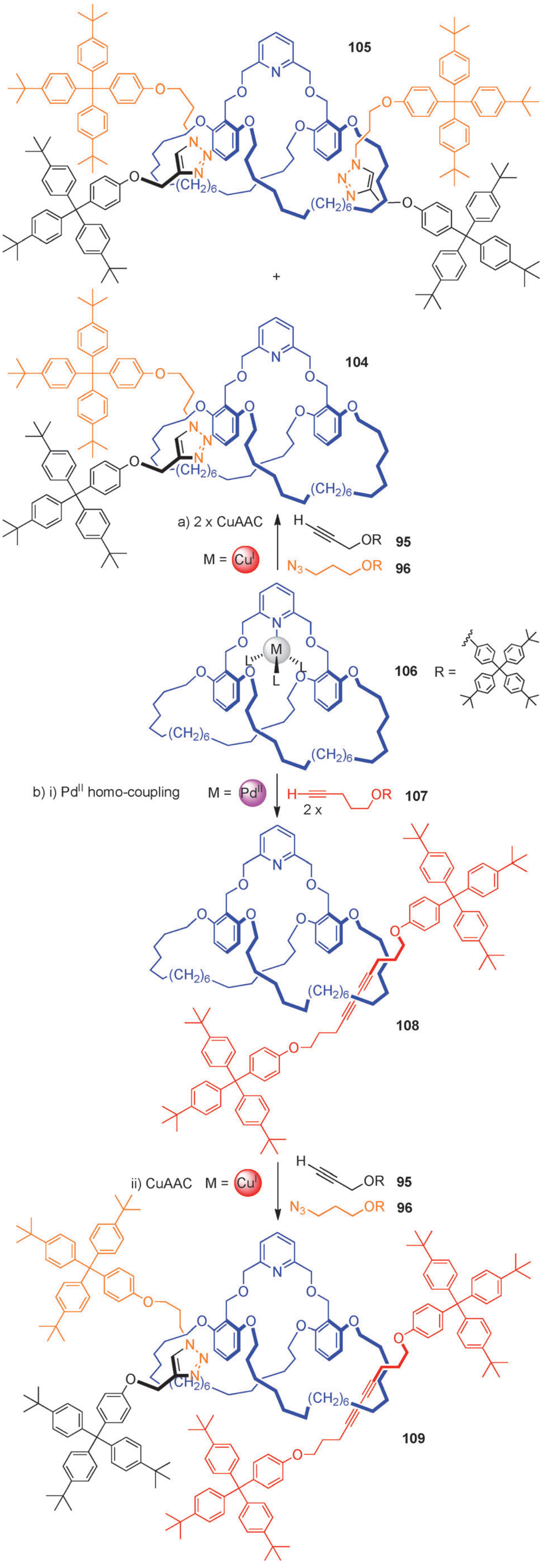


Scheme 38. Active metal template catenane synthesis through the CuAAC reaction. a) Heterocircuit [2]catenane **100** formed from macrocycle **34** and **101** in 53 % yield. b) Homocircuit [2]catenane **102** produced in 46 % yield by successive CuAAC reactions with two equivalents of **103**.[182]

materials applications (insulated molecular wires) and in molecular machines (rigid, nonfolding axles). Accordingly, several different active template alkyne–alkyne coupling reactions have been developed employing a range of different metal ions.

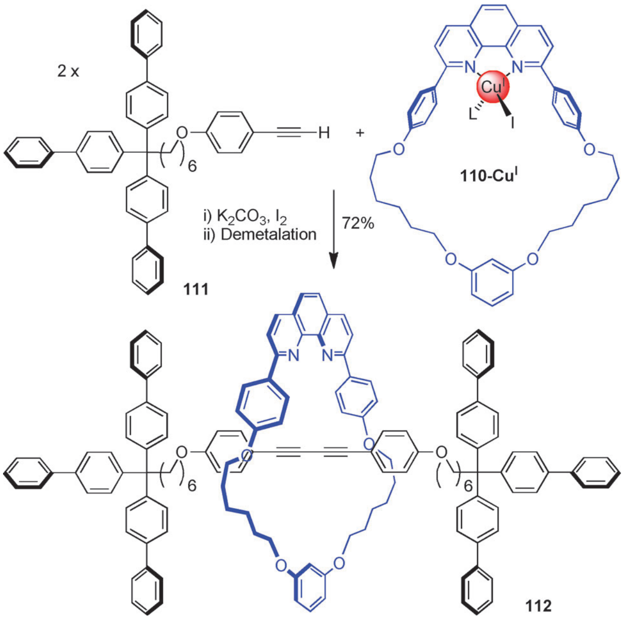
3.2.1. Cu^I-Mediated (Glaser) Alkyne Homocoupling

Saito and co-workers reported active metal template rotaxane formation using a dpp-based macrocycle **110** and the Cu^I-catalyzed Glaser oxidative homocoupling of arylalkyne stopper **111** (Scheme 40).[102] The active template Glaser reaction generated [2]rotaxane **112** in 72 % yield (Scheme 40). [2]Catenanes could also be prepared using this method in 64 % yield.[184] In all cases the reactions employed at least stoichiometric quantities of metal (i.e. the catalyst/template does not turn over during the reaction).



Scheme 39. Active template synthesis of two threaded axles by one ligating site of a macrobicycle. a) [3]Rotaxane **105** in which both threads are formed by CuAAC reactions (of the two diastereomers formed, only the *syn,syn*-[3]rotaxane is shown). b) [3]Rotaxane **109** in which the different threads are formed by successive active metal template reactions: the first by a Pd^{II}-catalyzed alkynyl homo-coupling (forming **108**) and, secondly, a CuAAC active metal template reaction.[183]

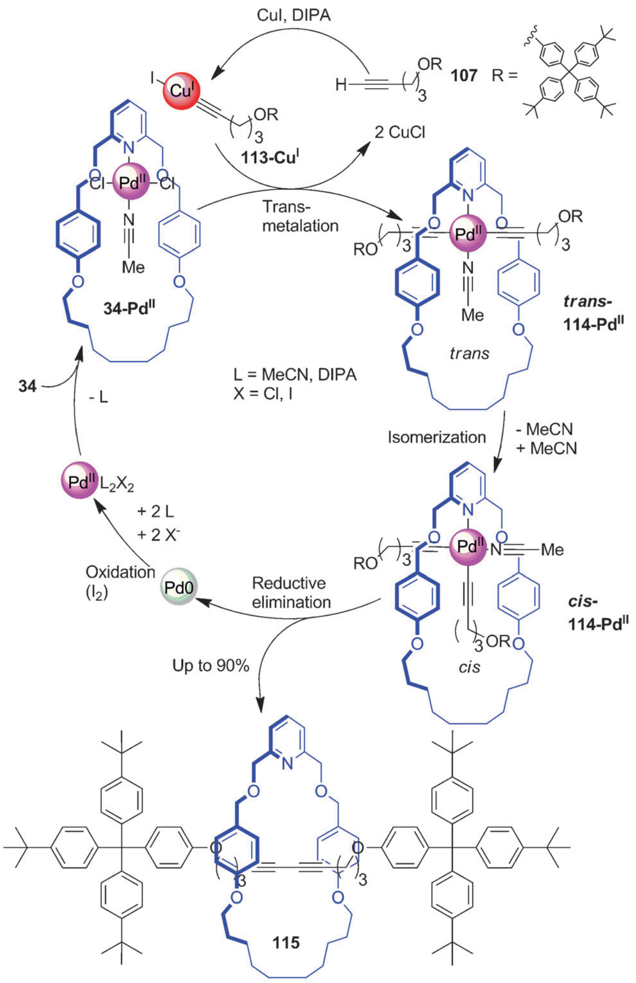
© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 40. Saito's active template Cu^I oxidative (Glaser) homo-coupling of aryl–alkyne stopper **111** to generate rotaxane **112** in 72% yield.[102]

3.2.2. *Pd^{II}-Mediated Alkyne Homocoupling*

The use of Pd^{II} as the catalyst for alkyne–alkyne bond formation allows for substoichiometric amounts of the active template metal ion to be employed (Scheme 41).[104] During the reaction the alkyne groups add to opposite faces of macrocycle-Pd^{II} complex **34-Pd^{II}** through transmetalation of the copper-acetylide **113-Cu^I**. A concerted *trans–cis* isomerization of **114-Pd^{II}** in which the ligands do not detach from the Pd^{II} center ensuring the threaded geometry is maintained, allows for C−C bond formation by reductive elimination of *cis*-**114-Pd^{II}** to form [2]rotaxane **115**. In fact, both stoichiometric and sub-stoichiometric quantities of Pd^{II} resulted in good conversions of alkyne-functionalized stopper **107** to [2]rotaxane **115** However, conditions which employ 5-10 mol% of Pd^{II} and iodine to oxidize Pd^0 back to Pd^{II}, resulted in higher yields of [2]rotaxane (90%) compared to the stoichiometric reaction (61%).[104] This reaction was used in conjunction with the Cu^I-catalyzed active template CuAAC reaction to form a [3]rotaxane of a bicyclic macrocycle with two different axles formed by successive different active template reactions (Scheme 39).[183]

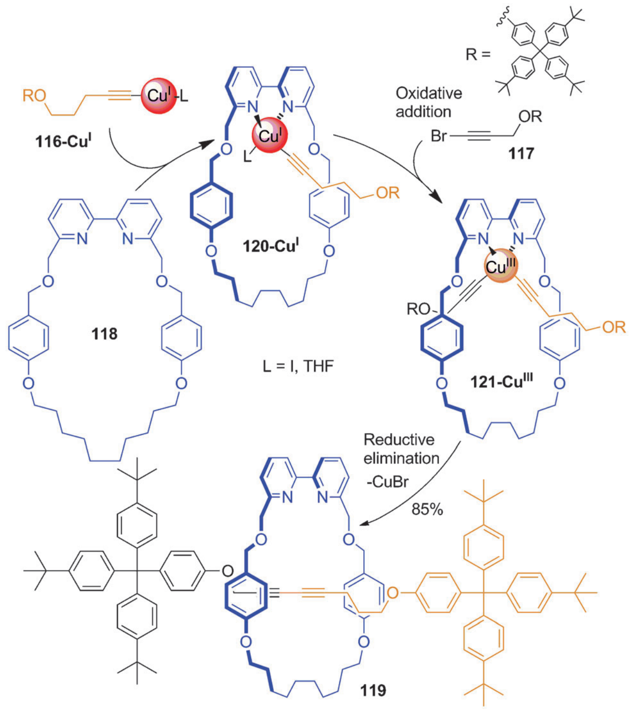


Scheme 41. Active template Pd^{II}-catalyzed homo-coupling of alkyne **107** in the presence of pyridine-based macrocycle **34** to form [2]rotaxane **115**. The reaction proceeds with either stoichiometric (61% yield) or sub-stoichiometric (90% yield with 5 mol% of Pd^{II}) quantities of metal.[104] DIPA = diisopropylamine.

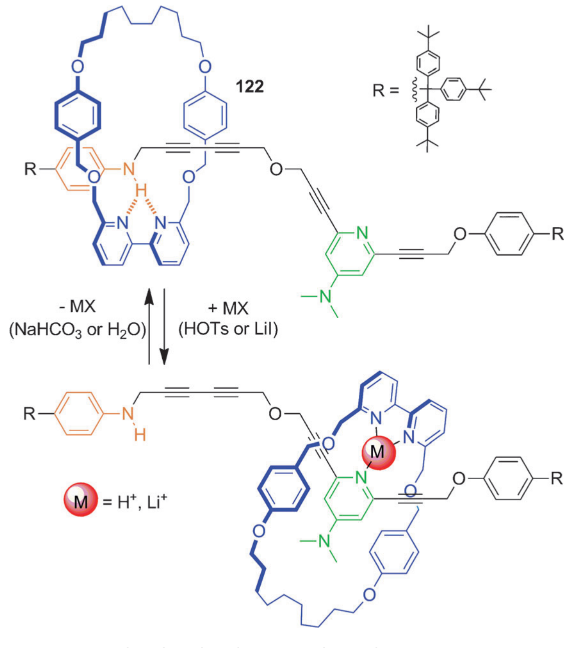
3.2.3. *Cu^I-Mediated (Cadiot–Chodkiewicz) Alkyne–Alkyne Heterocoupling*

Homocoupling active template reactions can only be used to form rotaxanes with symmetrical axles. The active template cross-couplings of alkynes to form rotaxanes with unsymmetrical axles has been demonstrated using the Cadiot–Chodkiewicz Cu^I-catalyzed reaction of copper acetylide and bromoalkynes (Scheme 42).[103] Reaction of **116-Cu^I** with **117** in the presence of a bipy-based macrocycle **118** led to [2]rotaxane **119** in 85% yield, with > 98% selectivity for the hetero- *vs* homo-coupled product. The reaction is proposed to proceed through coordination of **116-Cu^I** to the bidentate macrocycle **118** (Scheme 42) forming **120-Cu^I**. Oxidative addition of **117** forms the presumed intermediate **121-Cu^{III}**, in which both acetylides are coordinated to the macrocycle through coordination to Cu^{III}. Subsequent reductive elimination forms [2]rotaxane **119**.

This reaction was used to illustrate the potential utility of a feature of most active template reactions: the interactions used to assemble the interlocked structure do not persist in the products. A switchable rotaxane-based molecular shuttle **122** was assembled by active template Cadiot-Chodkiewicz reaction of alkyne-derivatized aniline and dimethylaminopyridine (DMAP) units in the presence of bipy-macrocycle **118** (Scheme 43). The position of the ring in **122** is determined by the hydrogen bond interactions between the bipyridyl macrocycle and the aniline group of the thread. Protonation of the DMAP group, or coordination to Li^I, means that the most favorable intercomponent interactions then occur when the macrocycle is translocated to the DMAP group. The position



Scheme 42. Cadiot–Chodkiewicz active template synthesis of [2]rotaxane **119** (with an unsymmetrical bisalkyne thread) in 85 % yield.[103]

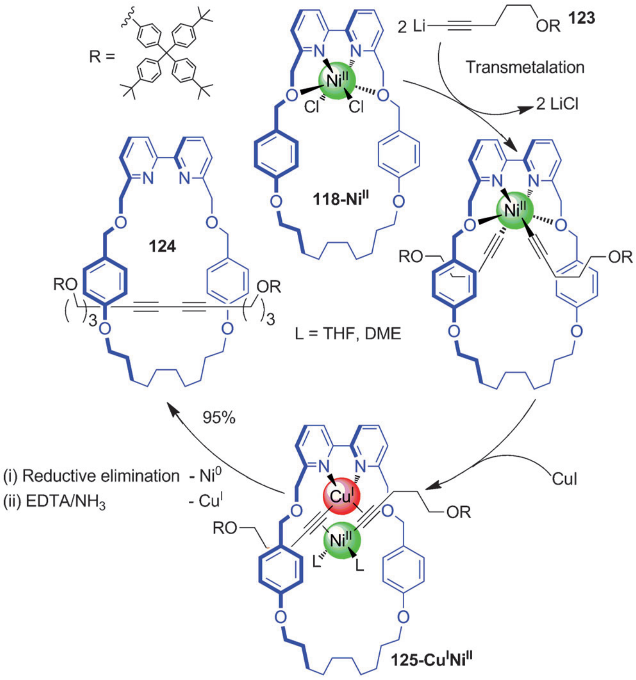


Scheme 43. A molecular shuttle **122** with weak intercomponent interactions (fast shuttling dynamics) synthesized by an active template Cadiot–Chodkiewicz reaction. The position of the macrocycle on the axle is switched by addition of *p*-toluenesulfonic acid (or lithium iodide); addition of base (or water) drives the macrocycle back to the starting position.[103]

of the ring in the rotaxane is thus determined by much weaker intercomponent forces than are usually introduced into molecular shuttle systems through passive template methods. Strong attractive intercomponent interactions necessarily dampen rotaxane dynamics.[103]

3.2.4. Ni^{II}-Cu^{I}-Mediated Alkyne Homocoupling

Whilst attempting to develop a Ni^{II}-mediated active template system, an unusual Ni^{II}–Cu^{I} bimetallic alkyne homocoupling reaction was discovered and applied to the active template synthesis of rotaxanes (Scheme 44).[108] Treatment of the Ni^{II}-complexed macrocycle **118-Ni^{II}** with a lithium acetylide (**123**) affords a threaded Ni^{II}-bis-acetylide complex. Addition of copper iodide results in formation of [2]rotaxane **124** in 95 % yield, the highest yield for any active template alkyne-alkyne coupling reaction developed to date. The effectiveness of having both nickel and copper present can be rationalized by the nature of a π-activated, σ-bonded, bimetallic intermediate **125-Cu^{I}Ni^{II}** in which the substitution of Ni^{II} for one Cu^{I} ion in the classic bimetallic Glaser reaction intermediate aids reductive elimination of the acetylide ligands (Scheme 44). The system may prove useful for the development of general mixed-metal protocols for catalytic alkyne coupling reactions as well as being a highly effective route to rotaxanes with bis-alkyne threads.



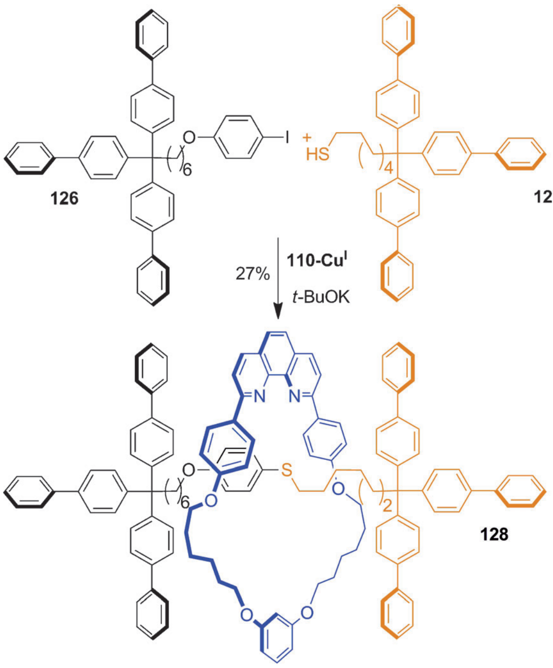
Scheme 44. Active template synthesis of [2]rotaxane **124** by Ni^{II}-Cu^{I} mediated alkyne homo-coupling of **123**. [2]Rotaxane **124** was formed in up to 95 % yield.[108] DME = dimethyoxyethane; EDTA = ethylenediaminetetraacetic acid.

3.3. Active Template Ullmann C–S Bond Formation

Saito and co-workers have employed dpp-based macrocycle **110** (see Scheme 40) in an active template Cu^{I}-catalyzed

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Ullmann C–S bond forming reaction.[102] Aryl iodide **126** and thiol-functionalized stopper **127** gave a modest 27 % yield of [2]rotaxane **128** (Scheme 45).[102]

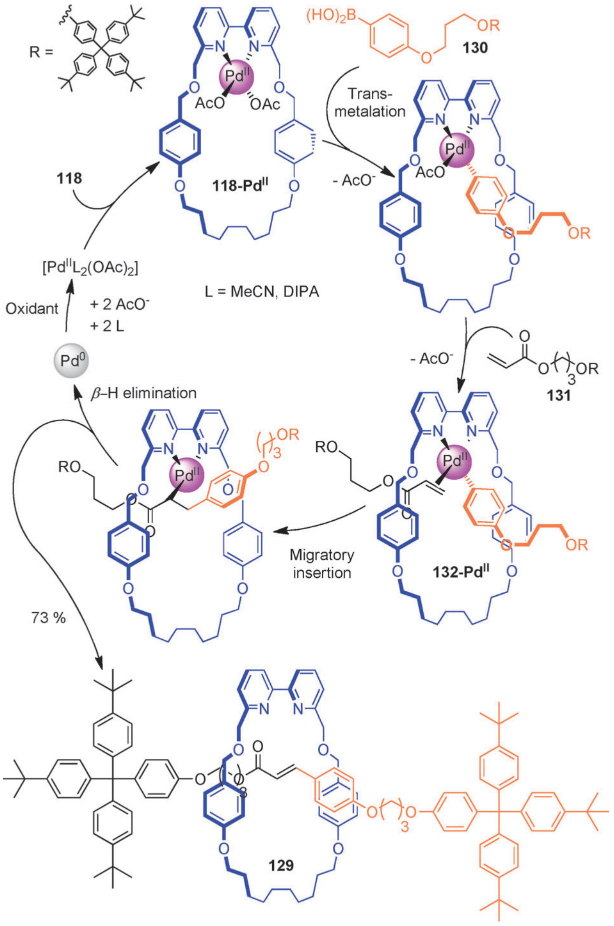


Scheme 45. Saito's active template Cu^I-catalyzed Ullmann C–S bond forming reaction which generates [2]rotaxane **128** in 27 % yield.[102]

3.4. Active Template Pd^{II}-Catalyzed Oxidative Heck Coupling

Efforts to utilize the plethora of available Pd^0-mediated coupling reactions[185] in active template synthesis have thus far proved unsuccessful because of the difficulty of coordinating Pd^0 to the macrocycle and ligands (required to achieve and maintain threading) throughout key stages of the catalytic cycle. However, the oxidative Heck reaction is a Pd^{II}-catalyzed variant that couples aryl boronic acids with activated olefins, and this reaction has proved applicable to active template rotaxane synthesis (Scheme 46).[105]

Using just 10 mol % of Pd(OAc)$_2$, [2]rotaxane **129** was prepared in 73 % yield from bipy-based macrocycle **118**, aryl boronic acid **130** and vinylic ester **131** in the presence of benzophenone and atmospheric oxygen. Reducing the amount of Pd to 1 mol % still produced [2]rotaxane in 66 % yield (i.e. the metal template/catalyst turns over 65 times during the reaction). The proposed mechanism for rotaxane formation is shown in Scheme 46. Transmetalation of boronic acid **130** with macrocyclic Pd^{II} complex **118-Pd^{II}**, followed by π-coordination to alkene **131**, leads to complex **132-Pd^{II}** that features the groups coordinated through opposite faces of the macrocycle. Migratory insertion and subsequent β-hydride elimination forms the covalent bond through the cavity of **118** to generate [2]rotaxane **129**. Re-oxidation of Pd^0 to Pd^{II} with O$_2$-benzophenone regenerates the catalytically-active complex **118-Pd^{II}** and enables the reaction to be conducted using substoichiometric amounts of palladium.



Scheme 46. Active template oxidative Heck reaction between alkene functionalized stopper **131** and boronic acid functionalized stopper **130** in the presence of bipy-based macrocycle **118** generates [2]rotaxane **129** in good yield with sub-stoichiometric quantities of Pd^{II} (72 % yield using 10 mol %, 66 % yield using 1 mol %).[105]

The active template reaction works well with vinyl esters, vinyl ketones and styrenes and proved tolerant to both electron-rich and electron-poor aryl boronic acids and alkene boronic acids.[105]

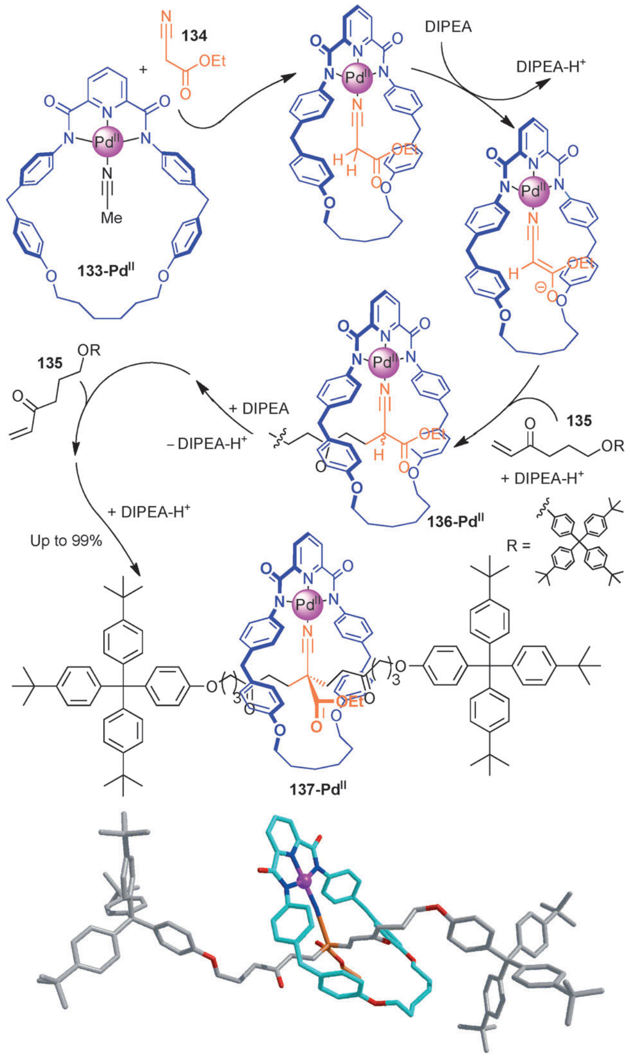
3.5. Active Template Lewis Acid Catalysis

Most active template syntheses involve metal-ligation to the functional groups directly involved in covalent bond formation, sites that are chemically changed in the interlocked product. An exception is active template reactions in which metal ion coordination is used to promote a chemical reaction at an adjacent site. In such cases the original coordination group is retained in the final product in a similar manner to traditional passive template synthesis.

3.5.1. Coordination-Promoted Michael Addition

Double Pd^{II}-mediated Michael addition has been used to assemble rotaxanes with exceptional efficiency (Scheme 47).[106] Upon coordination to Pd^{II}–macrocycle com-

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

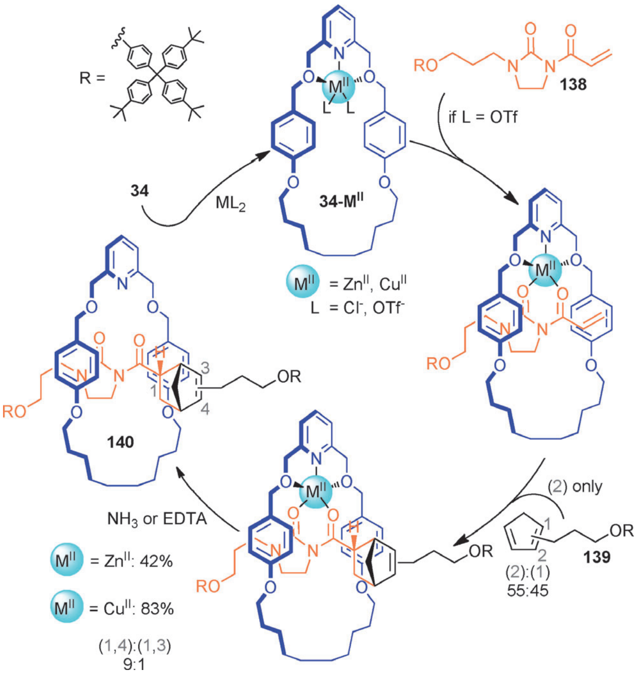


Scheme 47. Four component active template Michael addition synthesis of [2]rotaxane **137-Pd**$^{\mathbf{II}}$ in up to 99% yield. The X-ray crystal structure of the [2]rotaxane shows the Pd^{II} center coordinated to both macrocycle and thread.[106] DIPEA = diisopropylethylamine.

plex **133-Pd**$^{\mathbf{II}}$, ethyl cyanoacetate **134** becomes activated to deprotonation by *N,N*-diisopropylethylamine (DIPEA) (Scheme 47). The resulting enolate, still bound within the cavity of the macrocycle, undergoes 1,4-conjugate addition to vinyl ketone **135** generating "mono-stoppered" Pd^{II}–macrocycle complex **136-Pd**$^{\mathbf{II}}$. A second Michael addition forms [2]rotaxane complex **137-Pd**$^{\mathbf{II}}$ in yields of up to 99%. The X-ray crystal structure (Scheme 47) shows that the coordination motif is fully maintained in the rotaxane product. In the demetallated [2]rotaxane, the amide macrocycle shuttles between the two ketone groups of the thread.

3.5.2. *Coordination-Promoted Diels–Alder Cycloaddition*

Functional group activation by coordination to a metal ion has also been exploited in Diels–Alder active template rotaxane formation.[107] Coordination of Zn^{II} or Cu^{II} to tridentate macrocycle **34** generates a complex in which the acryloyl imidazolidinone unit **138** (see Scheme 48) is activated to reaction with a diene. The steric congestion of the macrocycle means that the dieneophile reacts with a 2-substituted cyclopentadiene (**139**) in preference to the 1-substituted cyclopentadiene it is in equilibrium with, generating one of four possible rotaxane isomers with 90–99% selectivity (**140**, Scheme 48). Here, the original metal binding site remains essentially unchanged in the rotaxane, a feature that was exploited to construct a molecular shuttle in which the position of the macrocycle could be controlled according to the coordination requirements of different metal ions.[107]

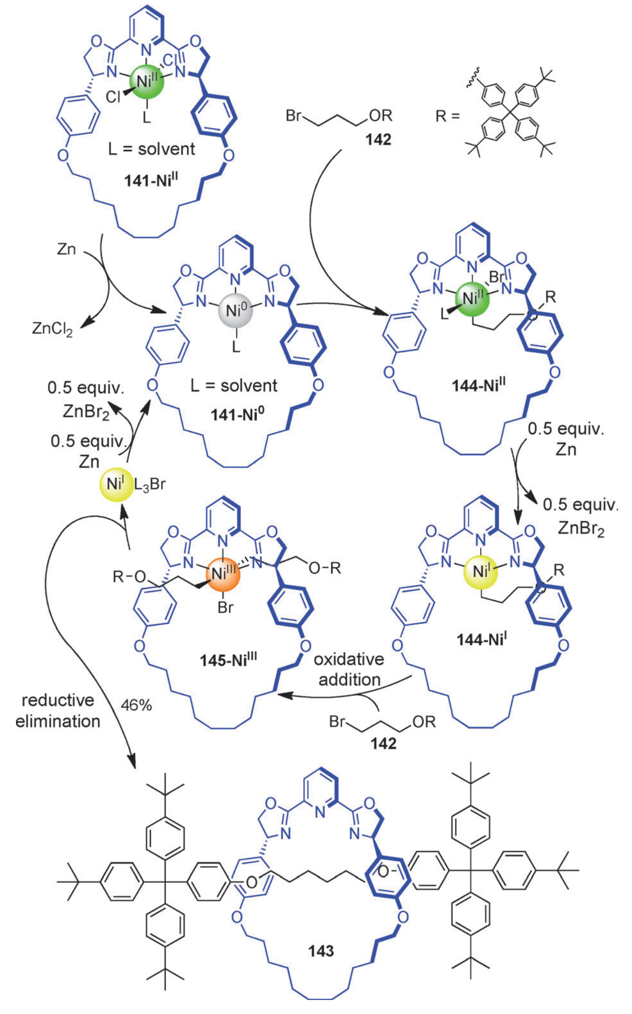


Scheme 48. Lewis-acid-mediated active template Diels–Alder synthesis of [2]rotaxane **140** from imidazolidinone-dienophile **138** and diene **139**. The active template reaction selects 2-substituted cyclopentadienes over 1-substituted cyclopentadienes to react with the dienophile in the generation of **140**.[107]

3.6. *Active Template Alkyl–Alkyl Coupling*

3.6.1. *Ni^{II}-Mediated C(sp^3)–C(sp^3) Homocoupling*

The rigorous coordination requirements during the covalent bond forming steps means that active template synthesis can serve as a useful probe of reaction mechanism and even as a source of reaction discovery. Whilst investigating the possibility of using the Ni^{II}-mediated cross-coupling of alkyl halides with alkyl zincates for active template rotaxane synthesis, a high yielding Ni^{II}-catalyzed C(sp^3)–C(sp^3) homocoupling of unactivated alkyl bromides was discovered.[109,186] The active template rotaxane-forming reaction that achieves this unusual transformation employs a pybox-based macrocycle **141**, inspired by studies on the enantioselective cross-coupling of racemic alkyl bromides with alkyl nucleophiles by Fu and co-workers.[187] Reaction of **141** with alkyl bromide **142** in the presence of Ni^{II} and Zn^0 afforded [2]rotaxane **143** in up to 46% yield (Scheme 49). The mechanism probably involves



Scheme 49. A novel Ni-mediated active template C(sp^3)–C(sp^3) coupling reaction used for the synthesis of [2]rotaxane **143**. Two equivalents of unactivated alkyl bromide **142** is coupled through the macrocyclic cavity to generate the rotaxane. The reaction pathway led to the development of a general method for alkyl bromide homocoupling.[109]

reduction of **141-Ni^{II}** to **141-Ni^0** by Zn^0. Oxidative addition of **142** to **141-Ni^0** forms intermediate **144-Ni^{II}**, which is reduced by Zn^0 to **144-Ni^I**. A second oxidative addition of **142** forms **145-Ni^{III}**, which reductively eliminates to form the [2]rotaxane (**143**).

4. Metal–Organic Interlocked Architectures

As well as being used as templates based on their coordination chemistry and catalytic properties, metal ions have also been incorporated into catenanes, rotaxanes and knots as integral parts of one or more of the components. Advances in this area have led to effective synthetic routes to both rudimentary and higher order interlocked molecular architectures. The presence of metal ions brings about the possibility of combining the electrochemical, magnetic or catalytic properties of the metal centers with the dynamic behavior often associated with mechanically bonded molecules.

4.1. Metal–Organic Rotaxanes

Coordination complexes can be incorporated into rotaxanes either through the macrocycle or the thread, where they can connect various parts of the axle or can act as bulky terminal groups that prevent dethreading.

4.1.1. Metal-Ion Coordination within the Axle

A 1987 report[93] from Richey provided evidence that diarylmagnesium compounds could form rotaxane-like complexes with crown ethers (e.g. **146-Mg^{II}**, Figure 13 a). This was later corroborated by Bickelhaupt and co-workers who determined the X-ray crystal structure of the related (1,3-xylyl-[18]crown-5)diphenyl magnesium compound **147-Mg^{II}** (Figure 13 b).[188] The Bickelhaupt group also prepared an organomagnesium [2]catenane[189] **148-Mg^{II}** and a bicyclic [3]rotaxane.[190] In these systems the primary driving force for threading is electrostatic interactions between the Mg^{II} ion and the electron-rich crown ether, with the aryl groups protruding from opposite sides of the crown ether ring.

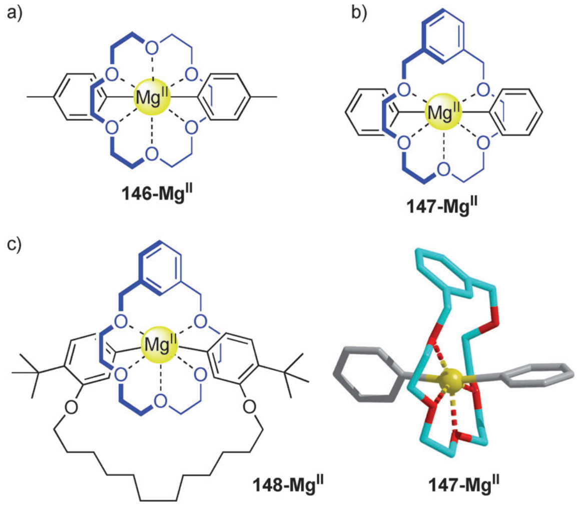
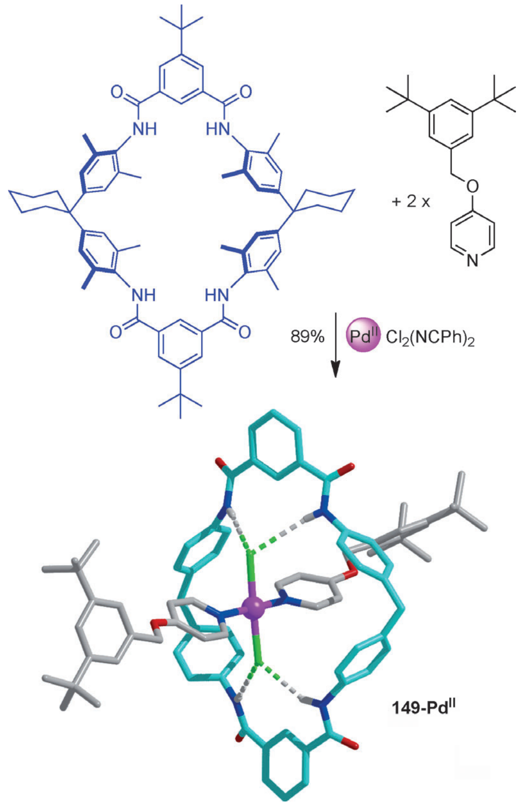


Figure 13. a) Richey's Mg^{II} rotaxane-like complex **146-Mg^{II}**.[93] b) Bickelhaupt's related compound **147-Mg^{II}**[188] (including X-ray structure) and c) [2]catenane **148-Mg^{II}**.[189]

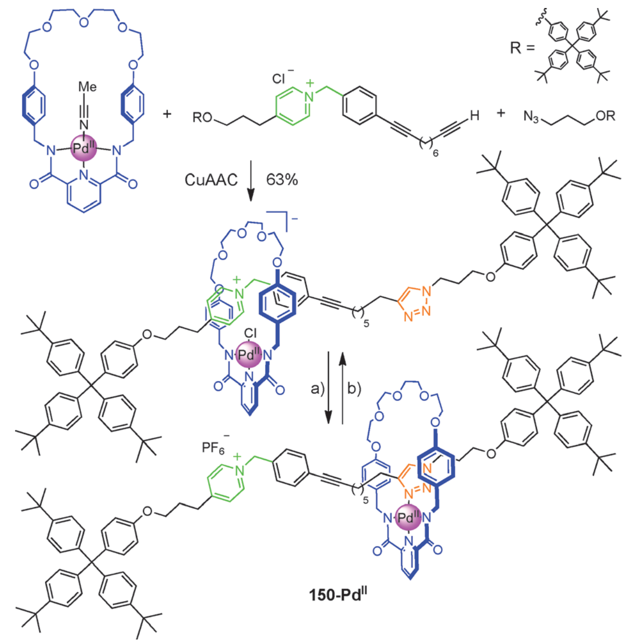
Second-sphere coordination of metal ions has been introduced as a method for forming interlocked structures, with the metal centers acting both as templates to form crossing-points and as connecting units.[191] Wisner described the formation of [2]rotaxanes (e.g. **149-Pd^{II}**) with metal-containing axles through reversible second-sphere coordination.[191] Interlocking is driven by intercomponent hydrogen bonding between *trans*-palladium(II)-dichloride complexes and isophthalamide units (Scheme 50).[192] Bromide[193] and thiocyanate ligands[194] also give interlocked structures. The use of second-sphere coordination through ion-pairing

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



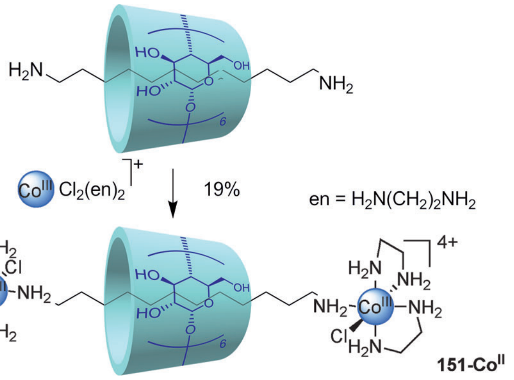
149-Pd^{II}

Scheme 50. Wisner's rotaxane **149-Pd^{II}**[191] assembled around both primary and secondary coordination spheres. With no bond angle restrictions imposed by the ligands, the Pd^{II} center adopts a close-to-ideal square planar geometry. NH⋯Cl distances 2.54–2.86 Å, N-H-Cl angles 152–162°. Cyclohexyl and macrocycle *tert*-butyl groups removed for clarity.



150-Pd^{II}

Scheme 51. Second-sphere coordination of a Pd^{II} complex in the assembly of an ion-pair [2]rotaxane shuttle **150-Pd^{II}**.[9c] Covalent capture of the threaded complex was achieved using the CuAAC reaction. The position of the macrocycle could be controlled by a) addition of AgPF$_6$ (removing Cl$^-$, enabling the triazole unit to bind to the Pd^{II} center) and b) addition of Bu$_4$NCl (replacing PF$_6^-$ for Cl$^-$, which coordinates to Pd^{II}).



151-Co^{II}

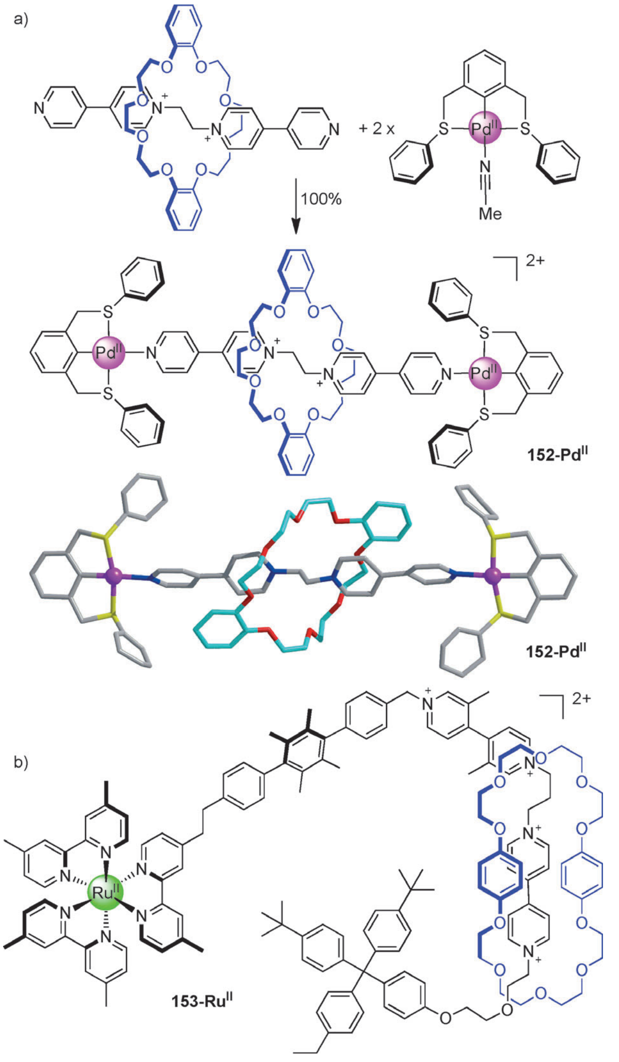
Scheme 52. Ogino's α-CD [2]rotaxane (**151-Co^{III}**) stoppered with Co^{III}en$_2$Cl units.[20]

between an anionic macrocycle metal complex and a cationic thread has been used to assemble a [2]rotaxane molecular shuttle, **150-Pd^{II}** (Scheme 51).[9c]

4.1.2. *Coordination Complexes as Stoppers*

The first example of a metal-containing interlocked structure was Ogino's 1981 trapping of a threaded 1,2-diaminododecane-α-cyclodextrin (CD) inclusion complex with [CoCl$_2$(en)$_2$]Cl, (en = 1,2-diaminoethane) affording [2]rotaxane **151-Co^{III}** in 19% yield (Scheme 52).[20] Related CD-containing rotaxanes were later prepared using stoppers incorporating Co^{III},[195] Fe^{II},[196] Pt^{II},[197] Ru^{II},[198] or mixed valence heteronuclear metal (Fe^{II} and Ru^{III}) complexes.[199] In a similar fashion Kim et al. synthesized a Mn^{III}-stoppered [2]rotaxane employing cucurbituril as the macrocycle.[200]

Loeb and co-workers modified the classic Stoddart alkyl viologen-crown ether system to assemble pseudorotaxanes[201] comprising of electron-rich dibenzo-[24]crown-8 (DB24C8) and electron-poor bis(4,4′-bipyridinium)ethane units through CH⋯O hydrogen bonding and π-stacking interactions. Coordination capture of the threaded host–guest complex with a Pd^{II} complex formed [2]rotaxane **152-Pd^{II}** in quantitative yield (Scheme 53a).[98] The same approach was used for the assembly of Ru^{II}- and Fe^{II}-bis-terpyridine [2]rotaxanes that exhibited interesting photoelectron transfer properties.[202] CoBr$_3^-$ and MnBr$_3^-$ groups have also been incorporated as stoppering groups in related systems.[99] Balzani, Stoddart and co-workers have used a Ru^{II} complex as both a stopper and photosensitzer in a molecular shuttle in which the favored position of the ring can be transiently switched by visible light (Scheme 53b, **153-Ru^{II}**).[203] Other metal ion complexes (including Co^{II}[204] and Ru^{II}[205] complexes) have also been employed as stoppering groups in rotaxanes.

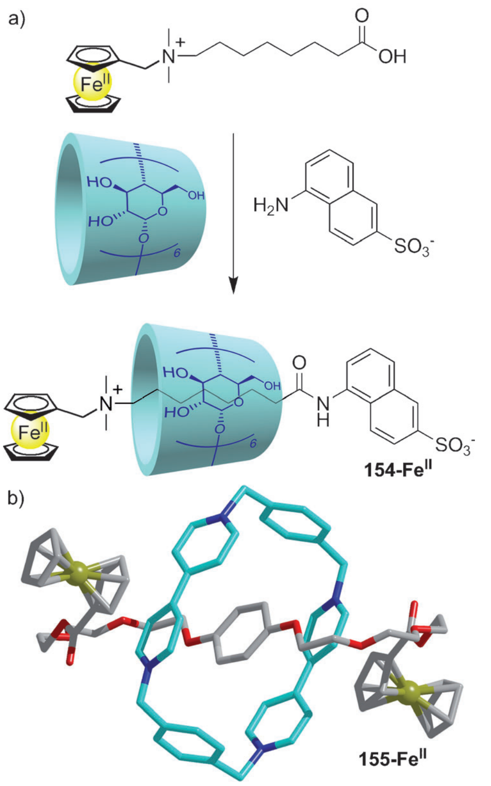


Scheme 53. a) Loeb and co-workers' [2]rotaxane **152-Pd^{II}** formed by coordinating Pd^{II} stoppers to terminal pyridyl groups of a bis-pyridinium ethane-based [2]pseudorotaxane,[98] b) Stoddart, Balzani and co-workers' Ru^{II}-tris-bipyridine-stoppered photoswitchable molecular shuttle (**153-Ru^{II}**).[203]

4.1.3. Ferrocene and Porphyrin Units as Stoppers

In view of their interesting electrochemical, photochemical and catalytic properties, both ferrocene and porphyrin derivatives have been incorporated into a range of rotaxane structures.[127,135,207] The most common synthetic approach to such systems is to use the organometallic unit to covalently capture a pseudorotaxane complex (e.g. Scheme 54).

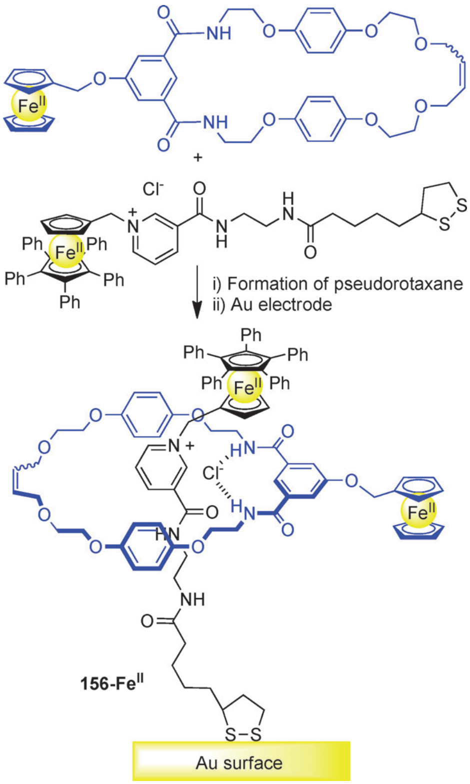
Building on a 1991 report describing inclusion complexes of α/β-CDs with alkylammonium-ferrocene derivatives,[208] Kaifer and co-workers used an amide-coupling reaction to stopper a threaded α-CD-alkylammonium complex with ferrocenoyl chloride to afford [2]rotaxane **154-Fe^{II}** in a modest 15% yield.[209] Their investigation inspired the development of a number of ferrocenyl-stoppered rotaxanes,[135,207] such as **155-Fe^{II}**.[210] Takata and co-workers have shown that 1-ferrocene carboxylate is an excellent moiety for assembling [2]rotaxanes comprised of a crown ether macrocycle and alkylammonium threads.[211] Osakada et al. have prepared related [2]- and [3]rotaxanes making use of cross-alkene metathesis to install the stopper groups[206,212] and Beer et al. have used bulky ferrocence derivatives to prepare surface-assembled rotaxane sensors, such as **156-Fe^{II}** (Scheme 55).[213]



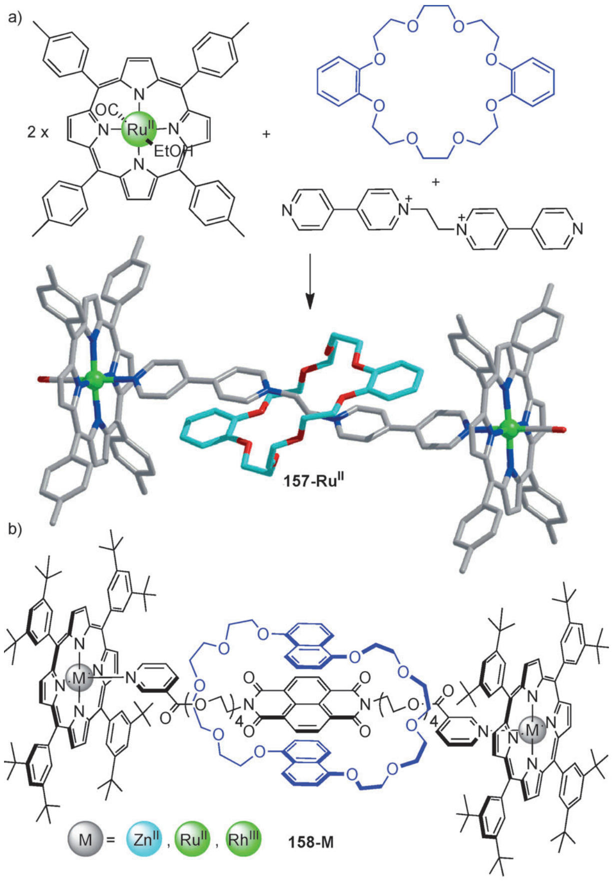
Scheme 54. a) Ferrocene groups were introduced as stopper units for rotaxanes in 1991 by Kaifer, forming **154-Fe^{II}**.[208] b) X-ray crystal structure of a ferrocene stoppered rotaxane **155-Fe^{II}** reported by Harriman and co-workers.[210]

Axially-coordinated porphyrin-like (e.g. vitamin B12, cobalamine) stoppers have been introduced into rotaxane systems by Kräutler et al.[214] Synthesized electrochemically (50% yield), the displacement reaction results in the formation of stable Co–C bonds from 1,12-dibromododecane and preformed cobalamine. Branda et al. employed axial coordination of a substituted pyridine thread to an octahedral Ru^{II} metallo-porphyrin complex to form [2]rotaxane **157-Ru^{II}** with the aim of studying photochemical charge-transfer processes between the chromophores (Scheme 56a).[215] The groups of Gunter and Sanders stoppered a [2]pseudorotaxane comprising a pyridyl-terminated naphthodiimide thread encircled by a crown-ether based macrocycle with various metallo-porphyrins to form [2]rotaxanes **158-M** (M = Zn^{II}, Ru^{II}, and Rh^{III}) (Scheme 56b).[216] The lability of the metal–ligand coordinate bonds allowed the rotaxanes to be formed under thermodynamic control at room temperature. The same system was used to prepare rotaxanes bonded to polymer supports.[217] This methodology has also been exploited with pyridyl-terminated dialkylammonium-crown ether pseudorotaxanes, using Rh^{III} metallo-porphyrin complexes as the stoppering groups.[218] Porphyrin groups have

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 55. Using an anion template, Beer et al. prepared [2]rotaxane **156-Fe**^{II} stoppered with a pentaphenylferrocene unit at one end and a gold surface at the other. The molecule can act as a redox-active chloride sensor.[213]



Scheme 56. Porphyrin-stoppered [2]rotaxanes from a) Branda (**157-Ru**^{II})[215] and b) Sanders and Gunter (**158-M**^{II})[216].

also been used as stoppering groups for [2]rotaxanes templated by amide-based hydrogen-bonding interactions.[219] Porphyrin-containing rotaxanes and catenanes have been recently reviewed.[127]

4.1.4. Rotaxanes Incorporating Metal–Organic Macrocycles

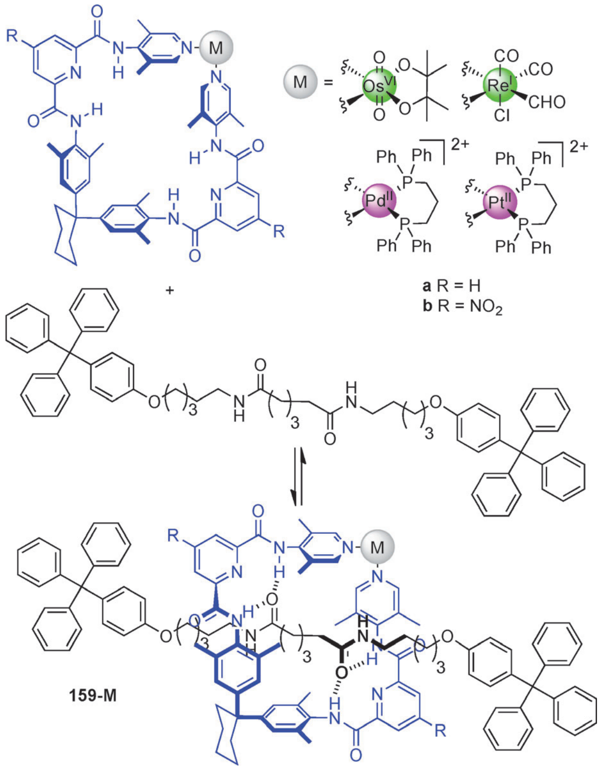
Labile metal–pyridine bonds in metal–organic macrocycles have been exploited to assemble metal–organic rotaxanes using reversible bond forming/breaking conditions. Jeong et al. employed Os^{VI}-corner units for the formation of rotaxanes **159a-Os**^{VI} and **159b-Os**^{VI} through a clipping mechanism driven by the formation of inter-component NH···O hydrogen bonds (Scheme 57).[97] Later examples incorporated Pd^{II} and Pt^{II} corner units to form [2]rotaxanes[220] and homo-bimetallic Os^{VI} macrocycles to assemble [2]- and [3]rotaxanes.[221] All of these examples exist in equilibrium with their non-interlocked components. A Re^{I}-coordinated metallo-macrocycle proved to be kinetically stable at room temperature enabling [2]rotaxane **159-Re**^{I} to be isolated in 62 % yield.[220] A related [2]rotaxane molecular shuttle was also prepared.[222]

Hunter et al. have utilized axial coordination between pyridine and zinc(II)-porphyrins to assemble macrocycles suitable for rotaxane formation.[90] The assembly of rotaxane **160-Zn**^{II} is driven by amide–amide hydrogen bonding between macrocycle **161-Zn**^{II} and the terephthalamide thread **162** (Scheme 58). Osakada and co-workers described the synthesis of [2]rotaxanes (through a crown ether–ammonium ion template) in which ferrocene groups form part of the macrocycle and impart interesting photochemical and electrochemical properties on the resulting structures.[223]

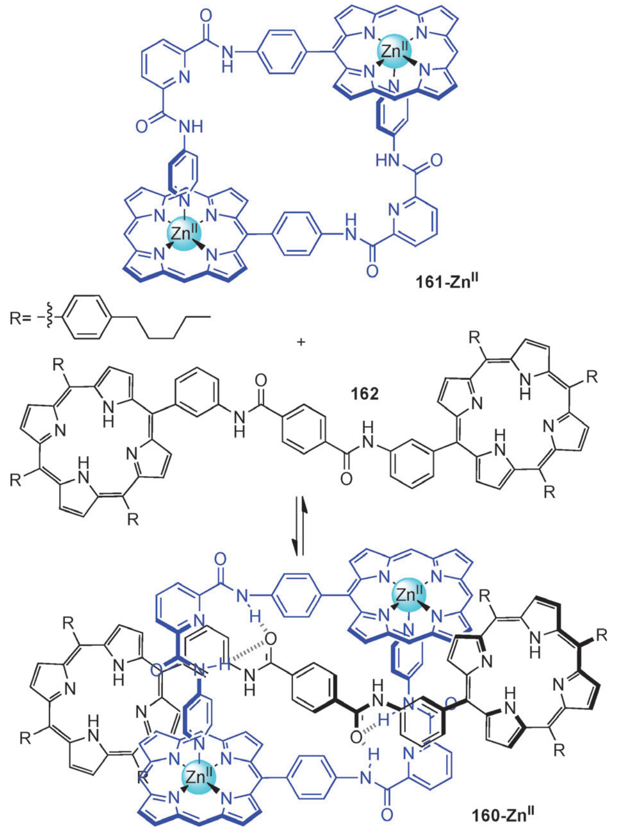
One of the largest synthetic pseudorotaxanes reported to date (**163-M**^{II}) was recently described by Shionoya and Clever (Scheme 59).[224] Using a cage held together by Pd^{II} or Pt^{II} coordination bonds the pseudorotaxane **163-M**^{II} assembles through distortion of the portals of the pre-formed cage or, in the case of Pd^{II}, by reversible breaking/formation of labile Pd–N bonds.

Rotaxanes such as **164-Pd**^{II} have also been prepared in which metal coordination is used to reduce the size of the macrocycle cavity so that it may no longer pass over the bulky stoppers. Asakawa and co-workers introduced this "threading-followed-by-shrinking" concept by utilizing a macrocycle that incorporated both crown ether and salophen moieties (Scheme 60).[225] The strategy was extended to porphyrin-stoppered [2]rotaxanes and macrobicyclic [3]rotaxanes.[226] Using larger stoppers and Ni^{II} centers the group demonstrated that [2]rotaxanes could be formed under thermodynamic control through the reversible ring-opening-ring-closing[227] of the salen macrocycle.[228]

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 57. [2]Rotaxanes from Jeong et al. in which dynamic metal–ligand bonds in the macrocycle provide a pathway for interlocking.[97,221] [2]Rotaxanes **159a/b-Os^{VI}** **159a-Pd^{II}**, and **159a-Pt^{II}**[220] exist in equilibrium with their non-interlocked components. [2]Rotaxane **159a-Re^{I}** proved to be kinetically stable at room temperature.[220]



Scheme 58. Hunter's [2]rotaxane **160-Zn^{II}** assembled through dynamic formation of Zn^{II}-porphyrin-based macrocycle **161-Zn^{II}**.[90]

4.1.5. Hybrid Organic–Inorganic Rotaxanes

In addition to using coordination bonds to link together organic ligands to form interlocked molecules, hybrid organic-inorganic rotaxanes have been assembled from organic threads and heterometallic rings consisting of eight or more metal ions bridged by alkylcarboxylate and fluoride anions (Scheme 61).[229,230] In a 33 component assembly process, macrocycle **165-Cr$^{III}_7$Co^{II}** forms around axle **166** to generate [2]rotaxane **167-Cr$^{III}_7$Co^{II}**.[229]

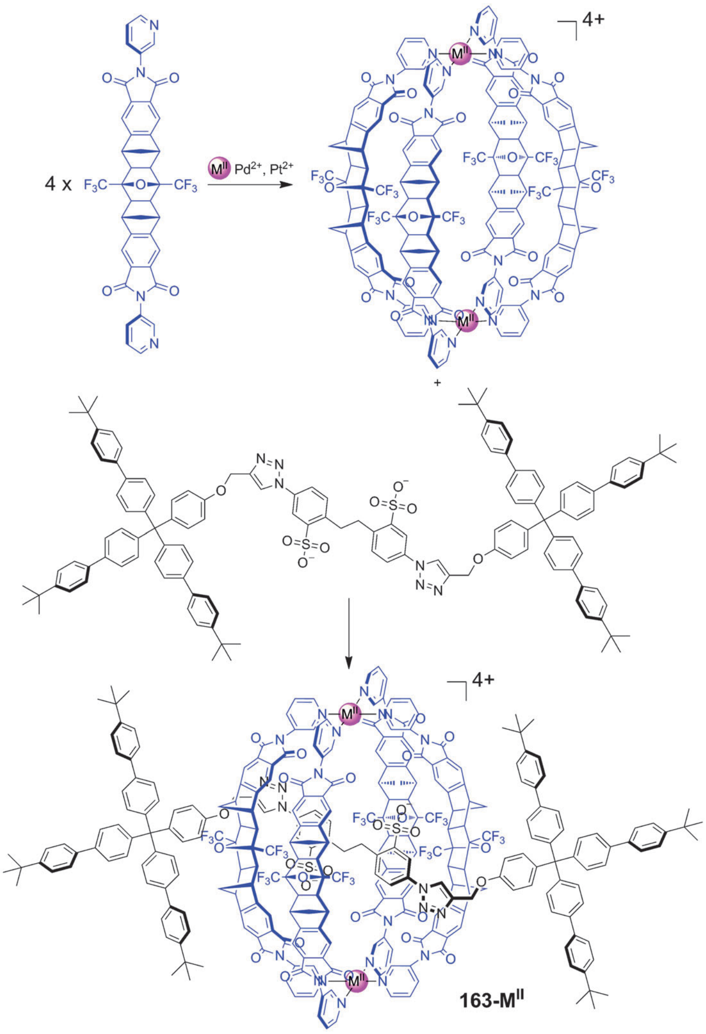
Rotaxane **167-Cr$^{III}_7$Co^{II}** is a neutral molecule; the positive charge on the secondary ammonium thread is balanced by the single charge remaining on the heterometallic macrocycle consisting of 24 anionic ligands (8 fluorides and 16 pivalate groups) bound to seven trivalent Cr^{III} cations and a single divalent Co^{II} cation. Ion pairing and hydrogen bonding between the secondary ammonium group and the fluoride ligands of the heterometallic wheel direct the assembly of the interlocked structure. Changing the divalent ion from Co^{II} to Ni^{II}, Fe^{II}, Mn^{II}, Zn^{II}, Cu^{II} or Cd^{II} also led to [2]rotaxane formation (Scheme 61).[231] By using more stable stopper groups and additives to template the heterometallic ring assembly, [2]rotaxanes (**168-Cr$^{III}_7$M^{II}**) could be formed in up to 92 % yield.[231] Using two appropriately spaced secondary ammonium sites on the thread a [3]rotaxane (**169-Cr$^{III}_{14}$Co$^{II}_2$**, Figure 14a) and [2]rotaxane molecular shuttle were synthesized with the Cr$^{III}_7$–Co^{II} macrocycle.[229] With the two ammonium site thread and Cu^{II} as the divalent metal ion, a remarkable [4]rotaxane (**170-Cr$^{III}_{20}$Cu$^{II}_4$**) featuring two dodecametallic rings each encircling two threads was assembled in 37 % yield from 98 components (Figure 14b).[229]

4.1.6. Metal Centers as Connectors in Higher Order Rotaxanes

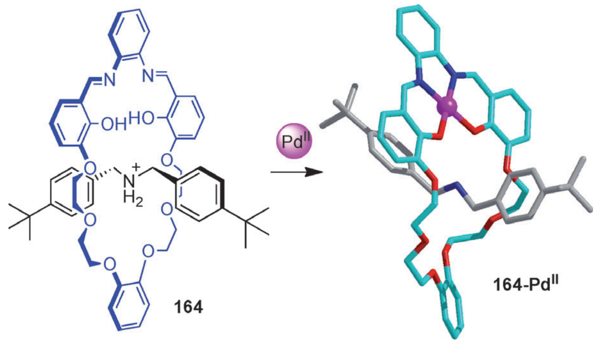
The reversible formation of metal–ligand coordination bonds to link pseudorotaxanes has proved useful for the assembly of higher order [*n*]rotaxane structures in both solution and the solid state.

Metal ions have been used to assemble threaded cyclodextrin or cucurbituril complexes into rotaxanes. For example, Anderson and co-workers have described an α-cyclodextrin-based [3]rotaxane (**171-Co^{III}**) prepared by coordinating two pseudo[2]rotaxanes to Co^{III} (Scheme 62).[232] A cyclodextrin-based [5]rotaxane has been reported by Osakada and co-workers, using Pd^{II} or Pt^{II} coordination to bridge two pseudo[3]rotaxanes.[233] Kim demonstrated the construction of 1D polyrotaxanes such as **172-Ag^{I}**, by employing Co^{II},[95] Ni^{II},[95] Cd^{II},[95] Cu^{II} [95,200] or Ag^{I} [95,234–236] as "connectors" to form a linear network of pseudorotaxane cucurbituril-bispyridyl-bis(dialkylammonium) units, threaded by intercomponent hydrogen bonding (Scheme 63). Lui and co-workers[237] prepared related 1D-polyrotaxanes based on 4,4′-bipyridine and cyclodextrins linked by Ni^{II}[237a] or Cu^{II} ions[237b] or Ru^{II}(bpy)$_2$ groups.[238] A number of 1D-,[95,234–236] 2D-,[95,234,236,239] and 3D-[236,240] polyrotaxane networks have been

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

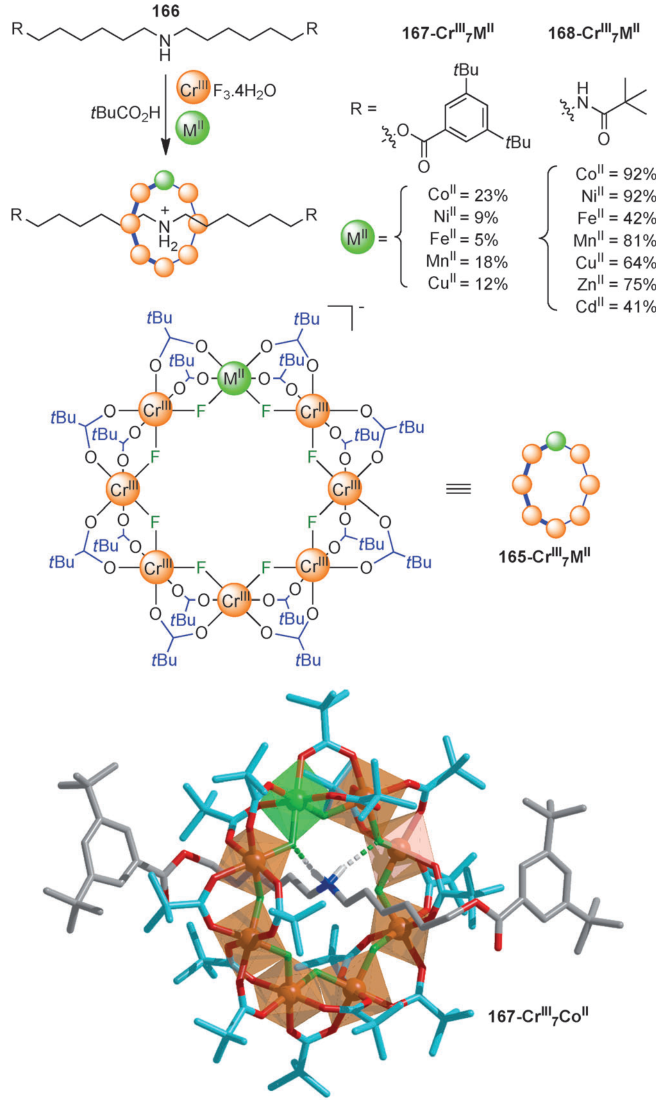


Scheme 59. Clever and Shionoya's large pseudo[2]rotaxanes **163-M^{II}** using cages formed with Pd^{II} and Pt^{II} and threaded with (very) bulky stoppers[224] De-threading occurs on addition of acid.



Scheme 60. Asakawa's "threading-followed-by-shrinking" strategy for preparing rotaxanes. The size of the cavity of pseudorotaxane **164** is contracted by Pd^{II} coordination within the macrocycle so that the macrocycle can no longer pass over the stoppers, forming rotaxane **164-Pd^{II}**.[225] Yield 30%, from free macrocycle and thread.

assembled using a variety of metal centers, making use of different coordination geometries and coordinating counterions to govern the structural geometries of the networks.[236]



Scheme 61. Hybrid organic-inorganic rotaxane **167-Cr^{III}$_7$Co^{II}** assembled in pivalic acid at 140 °C. The polyhedra in the X-ray crystal structure represent the octahedral coordination geometry of the metal ions.[229,231] The Co^{II} ion is disordered over the eight metal sites in each heterometallic wheel. N-H⋯F hydrogen bonds template the assembly with H⋯F lengths of 2.03 and 2.01 Å, and N-H-F angles of 168.9 and 168.2°. In addition, the fluoride anion between the two metal centers is close enough to both ammonium protons to provide some electrostatic stabilization of the intercomponent binding motif (that is, it participates in what can be considered long and poorly directional NH⋯F hydrogen bonds, not depicted in the figure): NH⋯F = 2.38 and 2.56 Å, N-H-F angles of 114.2 and 101.7°.

The DB24C8-crown-ether–1,2-bis(pyridinium)ethane cation pseudorotaxane motif introduced by Loeb[5c] (see Scheme 53 a) was used to generate [2]rotaxanes **173-Co^{II}** and **173-Mn^{II}** through reaction of the pseudo[2]rotaxane with anionic metal complexes $[CoBr_3]^-$ or $[MnBr_3]^-$ in a 2:1 ratio (Figure 15 a).[99] Treatment of the pseudorotaxane with a 1:1 stoichiometry of Co^{II} or Zn^{II} tetrafluoroborate in a coordinating solvent gave solid state 1D polyrotaxanes, termed "metal–organic rotaxane frameworks" (MORFs),[241] while reaction in non-coordinating solvents led to 2D-networks

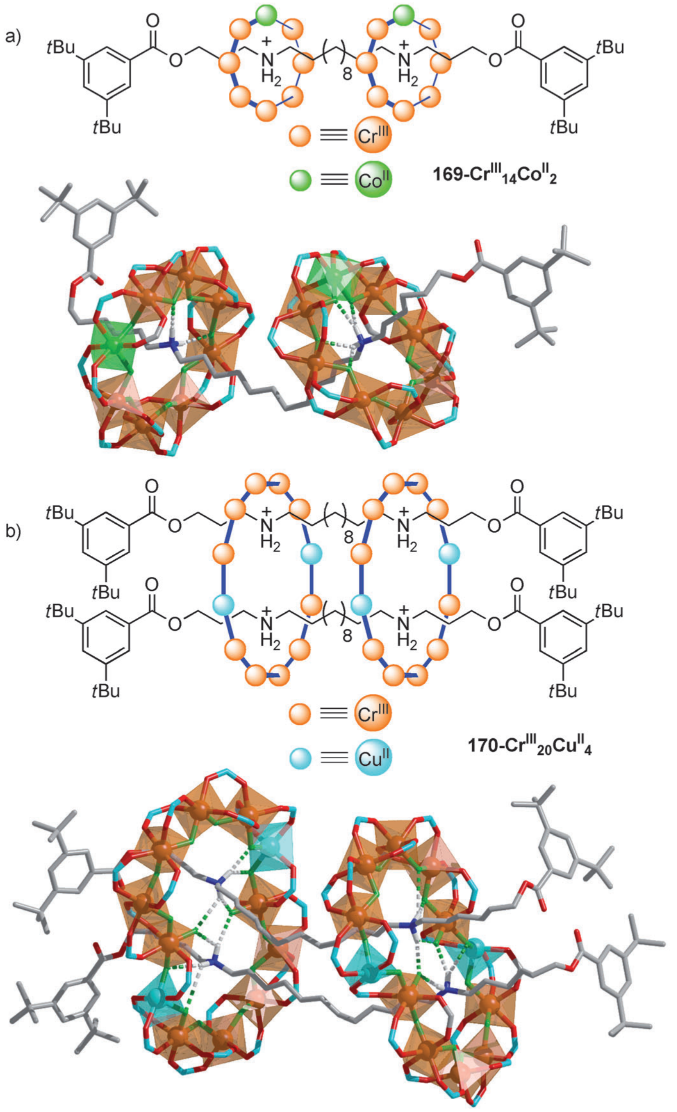


Figure 14. Hybrid organic–inorganic a) [3]rotaxane **169-Cr$^{III}_{14}$Co$^{II}_{2}$** and b) [4]rotaxane **170-Cr$^{III}_{20}$Cu$^{II}_{4}$** assembled in pivalic acid at 140 °C. The polyhedra in the X-ray crystal structure indicate the coordination geometries of the metal ions (pivalate *t*Bu-groups removed for clarity).[229] In **169-Cr$^{III}_{14}$Co$^{II}_{2}$** the divalent metal ion, Co^{II} is disordered over the eight metal sites on each heterometallic wheel (as for [2]rotaxane **167-Cr$^{III}_{7}$Co^{II}**); in **170-Cr$^{III}_{20}$Cu$^{II}_{4}$** the divalent Cu^{II} ions are localized at the positions shown. Intercomponent hydrogen bonding motifs responsible for templating the interlocked structure are indicated in the X-ray structures. Hydrogen bond length and angles: **169-Cr$^{III}_{14}$Co$^{II}_{2}$** NH···F 2.03–2.31 Å, N-H-F 138.6–159.1°; **170-Cr$^{III}_{20}$Cu$^{II}_{4}$** NH···F 1.84–2.85 Å, N-H-F 109.8–170.4°.

(**174-Cd^{II}**, Figure 15 b).[241] The assembly of 3D arrays was realized by employing lanthanide ions (Sm^{III}, Eu^{III}, Gd^{III}, Tb^{III}, and Yb^{III}) with N-oxide derivatives of the DB24C8-bis-bipyridinium ethane ligands.[242] Recently, 1D polyrotaxanes were assembled with non-coordinating counterions incorporated into the macrocycle, balancing the charges of the metal center and removing the need for additional anionic ligands.[243]

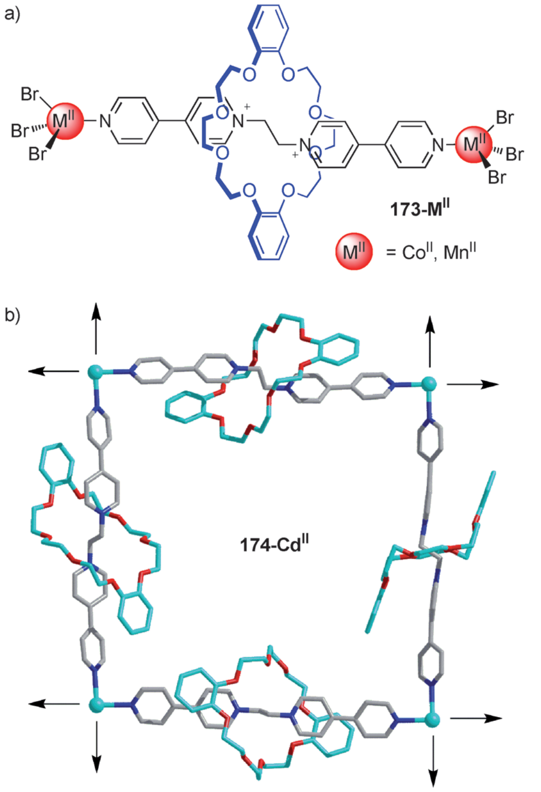
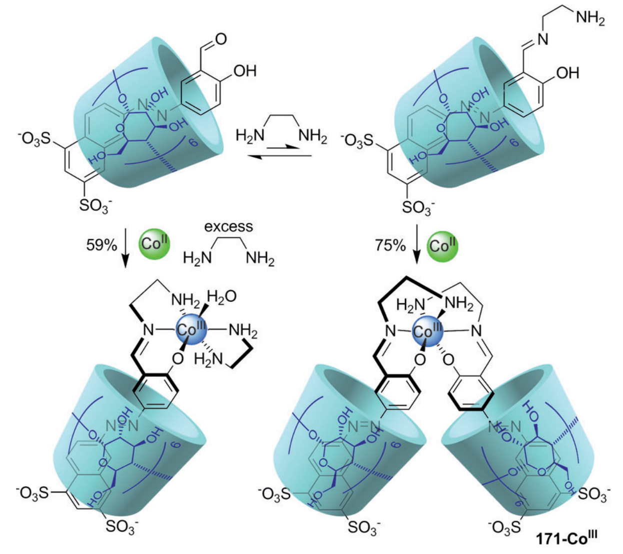
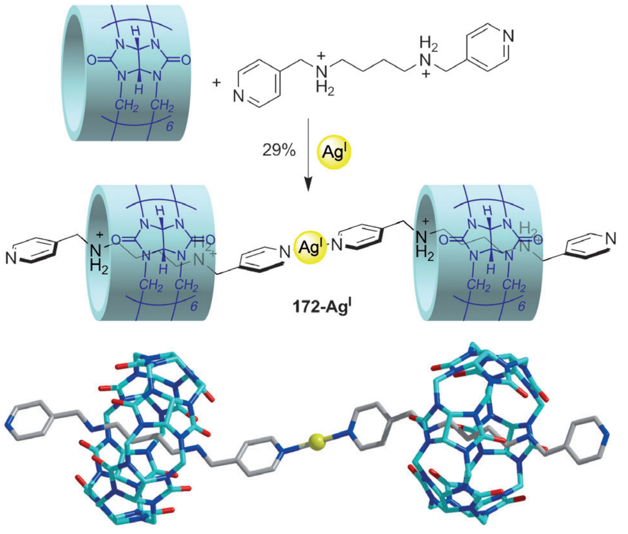


Figure 15. Progression in the development of higher order rotaxane structures, from a) discrete [2]rotaxanes (**173-Co^{II}** and **173-Mn^{II}**)[99] to b) 2D-polyrotaxane arrays (**174-Cd^{II}**).[241] Black arrows indicate direction of repeat units. 3D-Polyrotaxanes, termed "MORFs", have also been assembled.[242] The Cd^{II} ions in **174-Cd^{II}** are close to ideal octahedral (*cis*-N-Cd-N angles 88.4(2)–92.7(2)°) with a BF$_4^-$ ion and a water molecule completing the coordination sphere.



Scheme 62. Anderson's [3]rotaxane **171-Co^{III}** assembled from α-cyclodextrin and Co^{II}. Under the reaction conditions, Co^{II} is oxidized to kinetically stable Co^{III} generating the [3]rotaxane. Using an excess of the diamine to compete for the coordinating sites on the metal ion, [2]rotaxanes could also be formed.[232]

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 63. Silver(I)-assembled 1D polyrotaxane (**172-Ag^I**) prepared by Kim and co-workers.[234] The N-Ag-N angle is close to linear (170.0(5)°) in the solid state. Linear bis-pyridyl ligands with a variety of transition metals have been used to assemble 1D-, 2D- and 3D-polyrotaxanes.[95,236] The host–guest [2]pseudorotaxane complex is pre-assembled in water, followed by addition of the metal ion in methanol.

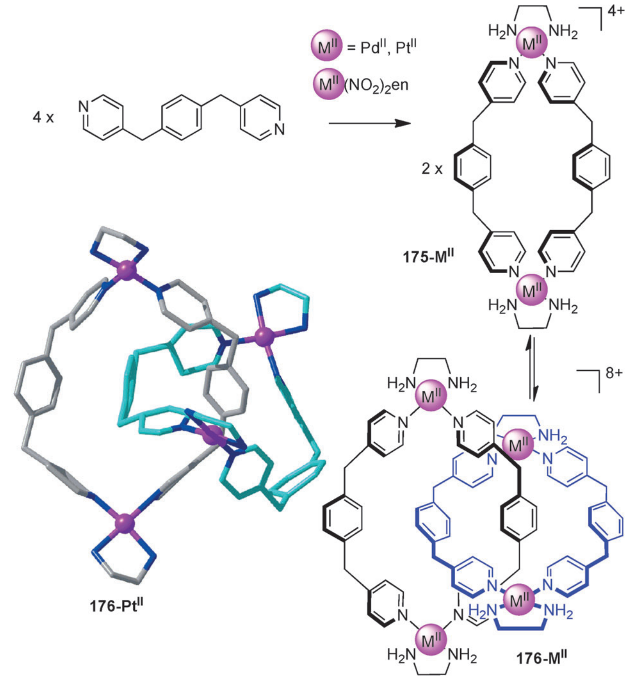
4.2. Metal–Organic Catenanes

Coordination complexes can be incorporated into catenanes with the lability of some metal–ligand bonds allowing their formation to be carried out under thermodynamic control.

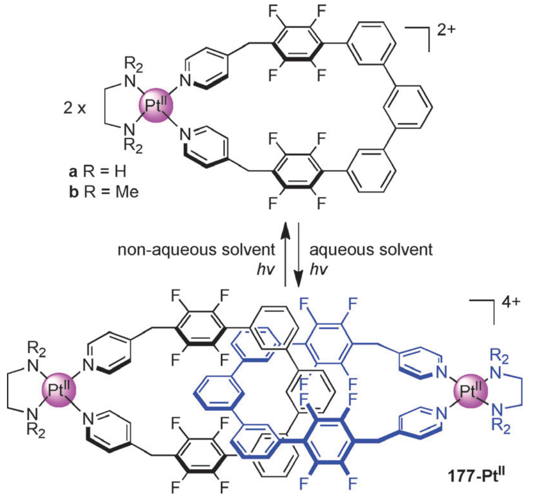
4.2.1. Self-Assembled Metal–Organic Catenanes

The use of dynamic metal–ligand coordination in the assembly of interlocked molecules was pioneered by Fujita, following his group's discovery that Pd^{II}-macrocycles form [2]catenanes in aqueous solution driven by hydrophobic binding (Scheme 64).[91,244,245] In basic aqueous solution macrocycle **175-Pd^{II}** spontaneously interlocks (a feat memorably likened by the authors to a conjuror's linking of "magic" rings[91]) to form [2]catenane **176-Pd^{II}**. At low concentrations the equilibrium lies towards the macrocycle, however at high concentrations (or at high salt concentrations to increase the hydrophobic effect) the [2]catenane is formed almost quantitatively.[246] Using Pt^{II} instead of Pd^{II}, the slower dynamics of ligand exchange require elevated temperatures to form [2]catenane **176-Pt^{II}**.[247] The strategy was extended to the formation of chiral,[150c] mixed (complementary) ligand,[248] mixed-metal (Pd^{II} and Pt^{II})[249] and higher order cyclic[250] and linear[251] catenanes.

The photochemical lability of some types of Pt^{II}–pyridine bonds enabled the preparation of [2]catenane **177-Pt^{II}** that could be assembled and disassembled in response to light (Scheme 65).[252] As in the previous examples, catenane formation is driven by hydrophobic effects which enables changes of solvent and/or concentration to alter the position of equilibrium in favor of either the catenane or discrete macrocycles.

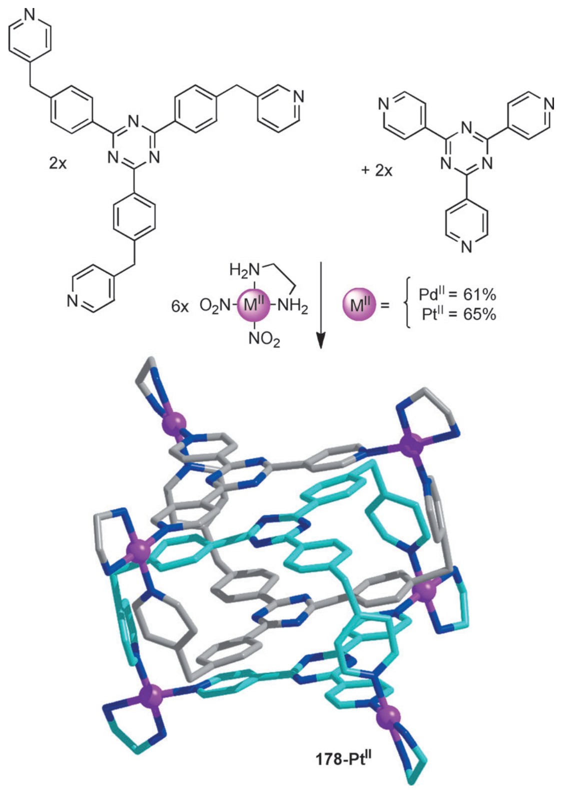


Scheme 64. Fujita's "magic ring" [2]catenane synthesis, exploiting dynamic metal–ligand interactions and driven by hydrophobic binding. The equilibrium between macrocycle **175-M^{II}** and [2]catenane **176-M^{II}** is influenced by the use of high salt concentration ($NaNO_3$ in D_2O) to strongly favor catenane formation and the introduction of guest molecules or less polar solvent (D_2O/glycerol mixtures) to favor discrete macrocycles.[91,245]

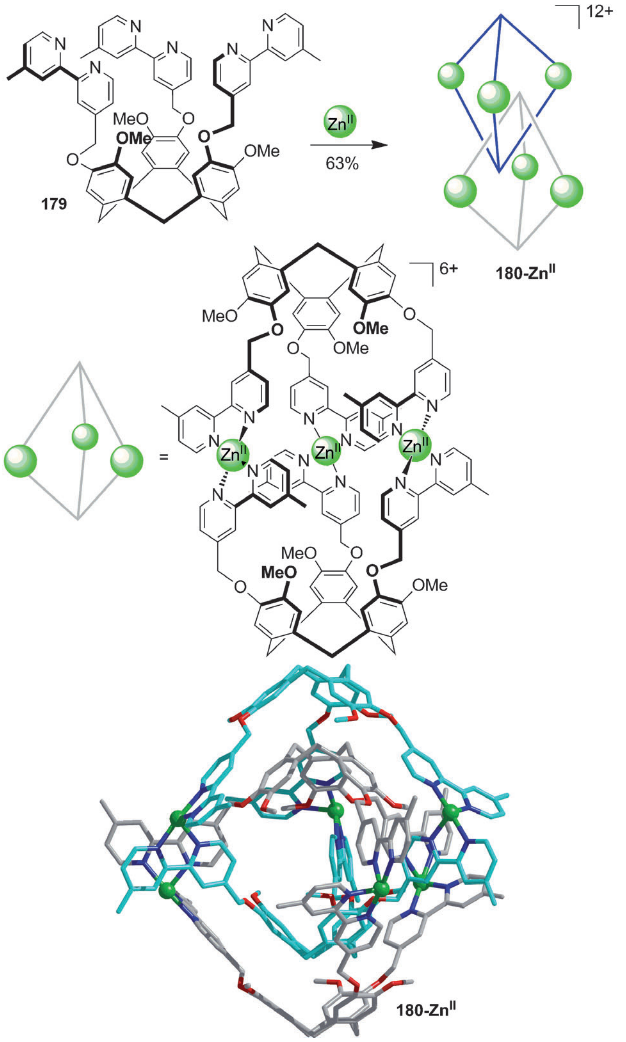


Scheme 65. Fujita's photoswitchable molecular lock **177-Pt^{II}**.[252] UV-light labilizes the Pt^{II}—N bonds allowing rearrangement to the most thermodynamically stable assembly. Catenane formation is driven by hydrophobic effects in polar solvents, which can be reversed by "unlocking" in non-aqueous solvents.

The Fujita group extended these assembly principles to create a triply interlocked molecular cage in a one-pot ten-component self-assembly reaction.[253] Two equivalents of two different tripodal monodentate pyridyl-based ligands with six equivalents of a square planar metal, Pd^{II} or Pt^{II}, in D_2O



Scheme 66. Fujita's triply-interlocked cages **178-Pt^{II}**, formed spontaneously on mixing the ten components.[253] The Pt^{II} ions are in close-to-ideal square planar geometries (*cis* N-Pt-N bond angles 86.6(1)–93.4(1)°) and extensive intercomponent π-stacking is a major feature of the solid state structure.



Scheme 67. Hardie's triply interlocked cages **180-Zn^{II}** constructed from two bipy-derivatized cyclotriveratrylene units and three octahedral metal ions. In the solid state structure two coordination sites of each Zn^{II} ion are taken up by the two oxygen atoms of a nitrate anion (omitted for clarity).[254]

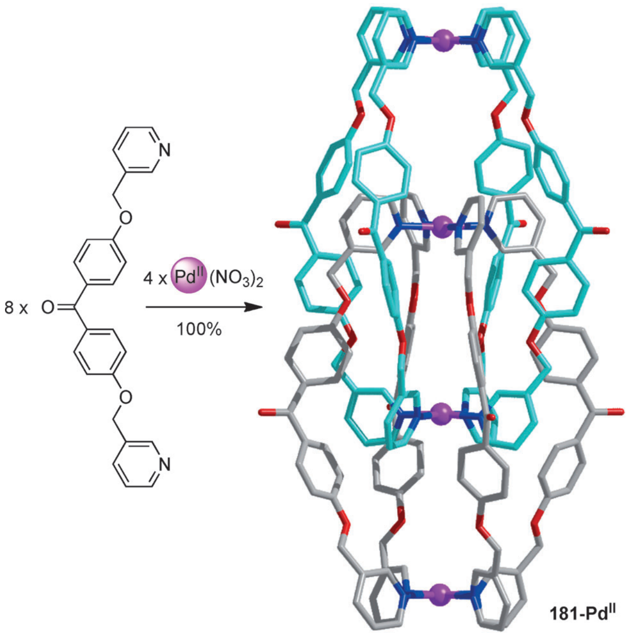
resulted in spontaneous formation of the interlocked molecular cage **178-M^{II}** in 61–65 % yield (Scheme 66).

A topologically related interlocked cage structure has been reported by Hardie and co-workers, using Zn^{II} or Co^{II} ions to connect bipy-derivatized cyclotriveratrylene units (Scheme 67).[254] Reaction of two equivalents of **179** in the presence of three equivalents of Zn^{II} in DMSO generated interlocked cage **180-Zn^{II}** in 63 % yield.[255] Similiarly, Kuroda and co-workers have used a pyridine-functionalized benzophenone ligand and Pd^{II} ions to form quadruply interlocked cages **181-Pd^{II}** (Scheme 68).[256] Remarkably, single cages form rapidly in DMSO solution and upon heating assemble into the interlocked form, which is thermodynamically stable. The driving force for interlocking in both these systems is probably a combination of solvophobic forces (expulsion of poorly solvated DMSO molecules from the cage cavities) and intercomponent aromatic stacking interactions.[257]

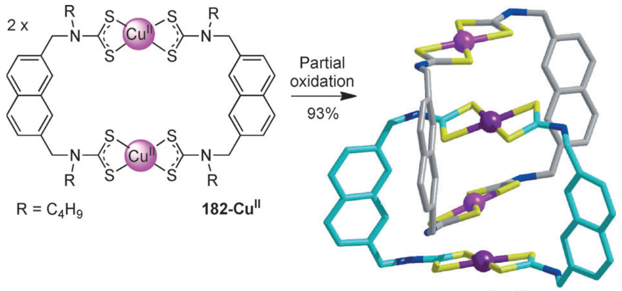
A novel type of metal–organic catenane was serendipitously discovered by Beer and co-workers when bis-Cu^{II}-dithiocarbamate macrocycle **182-Cu^{II}** was partially chemically oxidized by iron(III) chloride (Scheme 69).[96] The resulting mixed-valency [2]catenane, **183-Cu^{II}Cu^{III}** was obtained in 93 % yield and the solid state structure revealed each metal ion to be in a four coordinate square planar environment. It is thought that charge transfer interactions between the Cu^{II} and Cu^{III} centers, in conjunction with weak intermolecular S···Cu contacts, drive the formation of the catenane. This reasoning was later applied to a "magic ring" synthesis of mixed-metal Cu^{II}–Au^{III} catenanes.[258] Various spacer groups between the dithiocarbamate moieties were investigated but the original naphthyl spacer afforded catenanes in the highest yields.

Korybut-Daszkiewicz and co-workers have prepared catenanes featuring a crown ether threaded onto a large macrocycle containing two cyclen rings bearing the same,[259] or different,[260] metals ions (Scheme 70). Catenane formation is driven by the affinity of the electron-rich crown ether aromatic rings for the electron-poor metal-cyclen units. In solution and the solid state, the crown ether sits over the Ni^{II} center (see crystal structure of **184-Cu^{II}Ni^{II}**, Scheme 70). However, Cu^{II} is more easily oxidized than Ni^{II} and the resulting Cu^{III} center provides an effective electron-poor station for the π-donor macrocycle. Subsequent oxidation of the nickel moves the crown ether back to its original site.

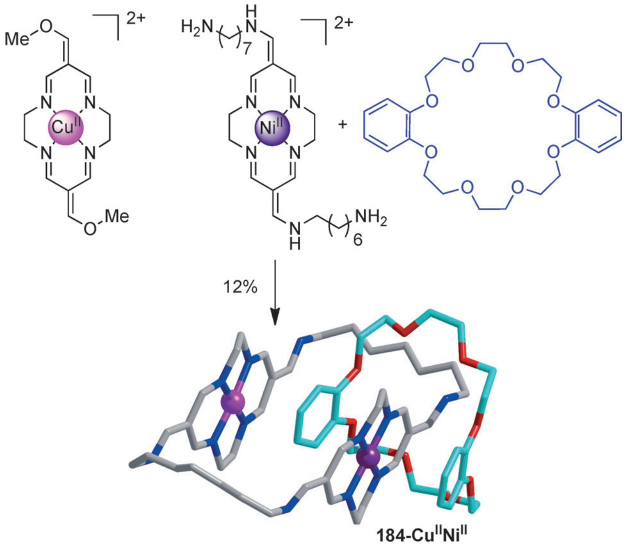
© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



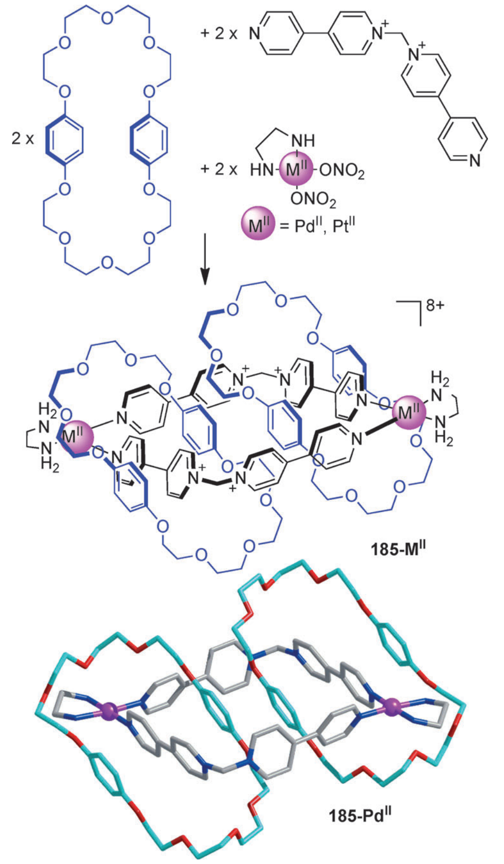
Scheme 68. Kuroda's quadruply interlocked cages **181-Pd**^{II}. With no ligand imposed bite angle restrictions, the Pd^{II} centers are near-idealized square planar (*cis*-N-Pd-N angles 89.9(2)–90.0(5)°). The solid state structure is highly symmetric, with all four Pd atoms laying on a 4-fold rotation axis.[256]



Scheme 69. Beer's mixed valence Cu^{II}–Cu^{III} catenane **183-Cu**^{II}**Cu**^{III} formed from a partial oxidation and re-arrangement of Cu^{II} macrocycle **182-Cu**^{II} (*n*butyl groups omitted for clarity).[96] The X-ray structure contains four non-equivalent copper centers which adopt distorted square planar geometries restricted by the bite angle of the ligands (*cis*-S–Cu–S angles: 76.3(4)–79.6(4)° and 101.2(4)–104.3(4)°). The different oxidation state copper ions, Cu^{II} and Cu^{III}, have average Cu–S bond lengths of 2.29(1) and 2.25(1) Å, respectively. Cu–Cu distances range from 3.87–3.92 Å.



Scheme 70. Korybut-Daszkiewicz's crown ether–mixed-metal cyclen [2]catenanes in which the position of the crown ether can be switched electrochemically.[259–261] The crystal structure of **184-Cu**^{II}**Ni**^{II} shows intercomponent π-stacking between the electron-rich aromatics of the crown ether and the electron-poor metal cyclen units.



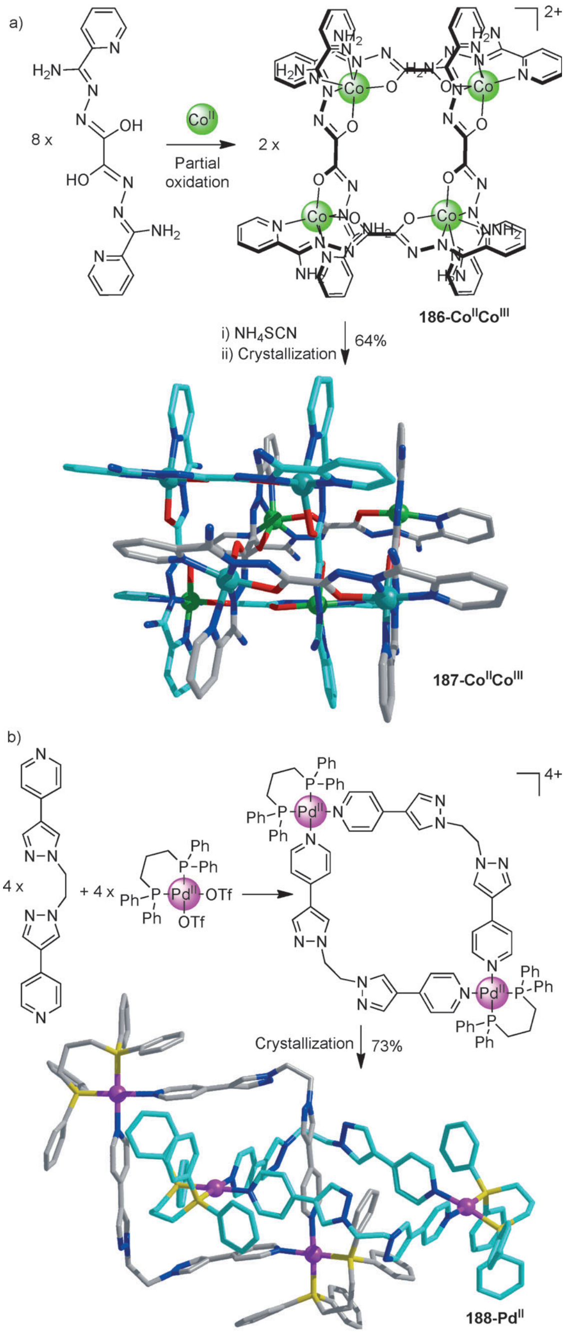
Scheme 71. Quintela's [3]catenane **185-Pd**^{II} employing two Pd^{II}en corner units.[264a] These types of metallomacrocycles have since been studied for their inclusion complexes.[264c] As in Fujita's systems, the Pd^{II} centers are almost perfect square planar in the solid state (*cis*-N-Pd-N bond angles range 84.0(1)–95.4(1)°). An NH proton is engaged in a hydrogen-bonding interaction with an oxygen of the glycol chain (N···O distance 3.023(4) Å), which is attributed as assisting formation of the interlocked structure. See Scheme 89 for a related system.

Quintela's group have modified the viologen unit introduced for catenane and rotaxane synthesis by Stoddart,[262] so that catenanes can be assembled using metal ion connectors in one of the rings.[263] Pd^{II} or Pt^{II} complexes were used to form [2]-[263] and [3]catenanes[264] from crown ethers and the viologen-like ligands in good yields (e.g. 70% for **185-Pt**^{II}, Scheme 71).[265] Favorable aromatic interactions and hydrogen bonds between the crown ether macrocycle and the bisamine ligands of the metal corner units (see crystal structure, Scheme 71) drive [3]catenane formation. Upon masking the hydrogen bond donor abilities of the corner units

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

by methylation of the biamine ligand, Stoddart and coworkers were able to form a ring-in-ring complex in preference to the [3]catenane.[266]

Crystal packing forces have been found to drive the formation of catenanes.[257] Tetranuclear [$Co^{II}_2Co^{III}_2$(2-picolylamine oxalic dihydrazide)$_4$] units that form squares (**186-$Co^{II}Co^{III}$**) in solution crystallize as discrete [2]catenanes (**187-$Co^{II}Co^{III}$**) in the presence of NH_4SCN (Scheme 72 a).[267] Similarly, a Pd^{II}-coordinated ligand set which exists largely as a metallomacrocycle in solution forms [2]catenane **188-Pd^{II}** in the solid state (Scheme 72 b). Extensive π–π stacking interactions are a feature of its X-ray structure (Scheme 72 b).[268]

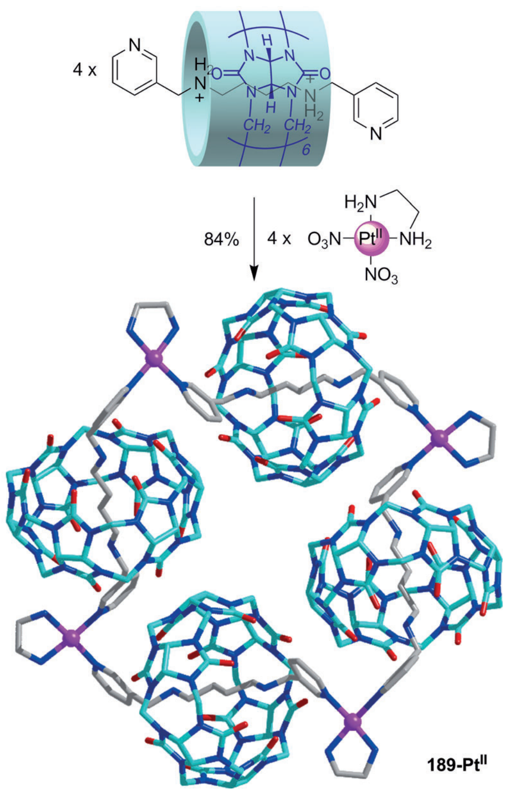


Scheme 72. Crystallization-driven formation of a) Thompson's Co^{II}–Co^{III} [2]catenane **187-$Co^{II}Co^{III}$**.[267] The solid state structure shows two types of distorted octahedral metal centers (Co^{III} centers *cis*-N-Co-N bond angles 81.0(3)-103.0(3)°; Co^{II} centers *cis*-(N-Co-N) bond angles 73.7(3)-120.0(3)°). b) Batten's Pd^{II}-coordinated [2]catenane **188-Pd^{II}**.[268]

4.2.2. *Metal Centers as Connectors of Pseudorotaxanes to Form Catenanes*

Metal ions have also been used to form catenanes by acting to ring-close pseudorotaxane structures (see Scheme 12 d and Figure 6). Yu and co-workers used Zn^{II}-porphyrin tweezers to cap the ends of a bispyridyl thread bearing an ammonium crown ether pseudorotaxane to generate a [2]catenane.[269] Sanders and co-workers formed [2]catenanes using Zn^{II}–bpy coordination to interlock electron-rich dinaphthocrown ether and electron-poor naphthodiimide units.[270]

By switching from a polyrotaxane-forming linear Ag^{I} coordination mode (see Scheme 64) to a 90° (en)Pt^{II} connector unit, Kim connected three cucurbituril–bis-ammoniumbutane pseudorotaxanes into a ring to form a "molecular necklace" [4]catenane in 90 % yield (Scheme 73).[92,236] Using the same procedure but altering the substitution pattern of the pyridyl group from 4- to 3-substitution gave [5]catenane **189-Pt^{II}** in 84 % yield.[271] A phen-containing thread was also used to prepare a related Cu^{II}-containing [5]catenane by joining two pseudo[3]rotaxanes through five- and six-coordinate Cu^{II} ions.[272]

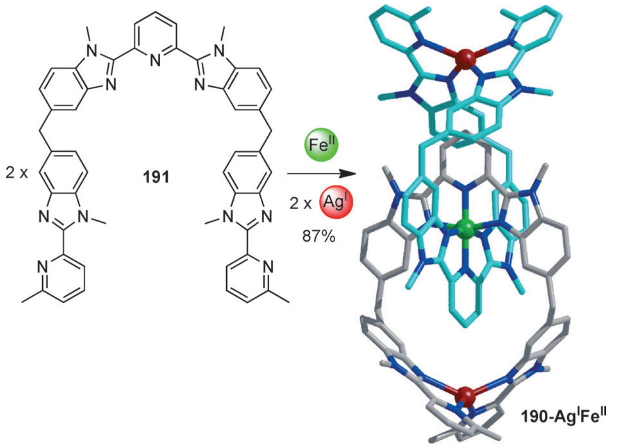


Scheme 73. Kim's synthesis of [5]catenane "molecular necklace" **189-Pt^{II}**, assembled from threaded cucurbituril macrocycles and Pt^{II}(en) connecting units.[92,271]

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

4.2.3. *Coordination-Capture of Metal Template Catenanes*

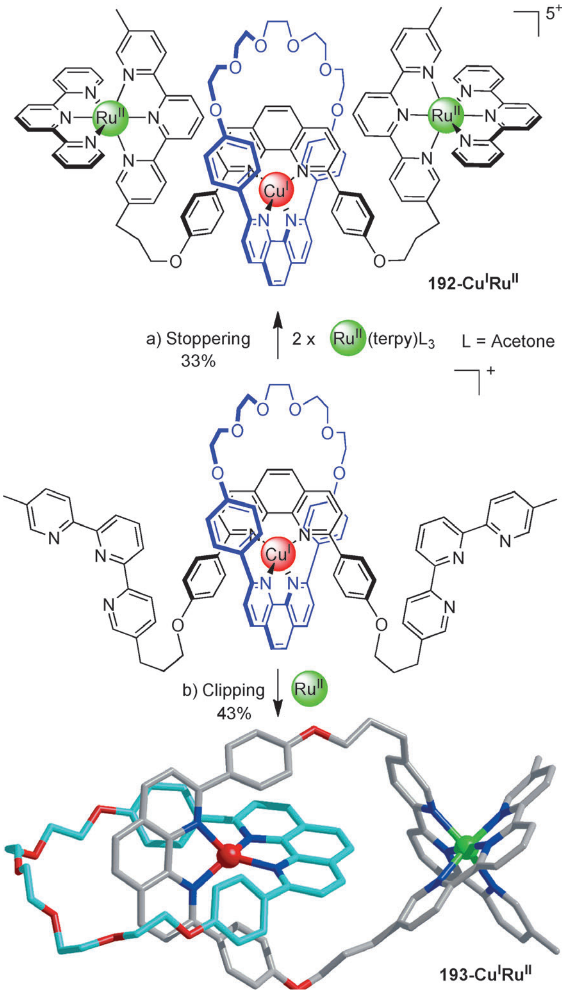
Metal ion coordination has been used to ring-close catenanes assembled around traditional metal ion templates (see Section 2). Piguet et al. prepared catenane **190-Ag^{I}Fe^{II}** by assembling two units of **191**, which possess a tridentate coordinating motif, about an octahedral Fe^{II} center followed by coordination of the bidentate end-groups to Ag^{I} ions (Scheme 74).[273] A similar type of [2]catenane was unexpectedly obtained by Ward and co-workers whilst investigating helicates formed between Ag^{I}, Hg^{I} and Hg^{II} and multidentate pyrazolyl–pyridine ligands.[274] The crystal structure revealed that a Hg^{II} ion acted as a distorted octahedral template organizing the central tridentate unit of each ligand, while two additional Hg^{II} ions coordinatively connect the arms of each ligand through N- and C-donors formed by cyclometalation to a pyrazolyl ring.



Scheme 74. Piguet's trinuclear [2]catenane **190-Ag^{I}Fe^{II}** assembled around an octahedral Fe^{II} ion and coordinatively captured with two Ag^{I} ions.[273a] The crystal structure shown is of the *meso*-diastereomer of **190-Ag^{I}Fe^{II}**.[273b] The Ag^{I} geometry is severely distorted tetrahedral (N-Ag-N bond angles 72.6(3)–135.3(3)°).

Sauvage et al. have used Ru^{II}–terpyridine complexes both as the stoppering groups in Cu^{I}(dpp)$_2$ rotaxanes[275] (e.g. **192-Cu^{I}Ru^{II}**) and as connectors to close a ring to form catenanes[276–278] (e.g. **193-Cu^{I}Ru^{II}**), depending upon the source and stoichiometry of Ru^{II} used (Scheme 75).[277] No competition was observed between the dpp and terpy units for complexation to Cu^{I}, demonstrating the advantages of using metal ions with particularly preferred coordination geometries (see Section 1.2.1.1). The different labilities of the metal–ligand coordination bonds meant that the Cu^{I} template could be removed from both the rotaxane and the catenane whilst leaving the Ru^{II} complexes intact. Related catenanes incorporating three different metals have also been prepared using related ligand systems employing Cu^{I} and Ru^{II} with Cu^{II}, Co^{II}, Zn^{II} or Fe^{II}.[278]

Using a second-sphere template strategy previously applied to [2]rotaxane synthesis (Scheme 50), Wisner et al. prepared [2]catenane **194-Pd^{II}** (Scheme 76), where an acyclic ligand **195** spontaneously assembles into [2]catenane **194-Pd^{II}** on addition of [PdCl$_2$(PhCN)$_2$].[279] Puddephatt et al. have used a similar motif and *trans*-pyridine–PdCl$_2$ coordination to generate a [2]catenane.[280]

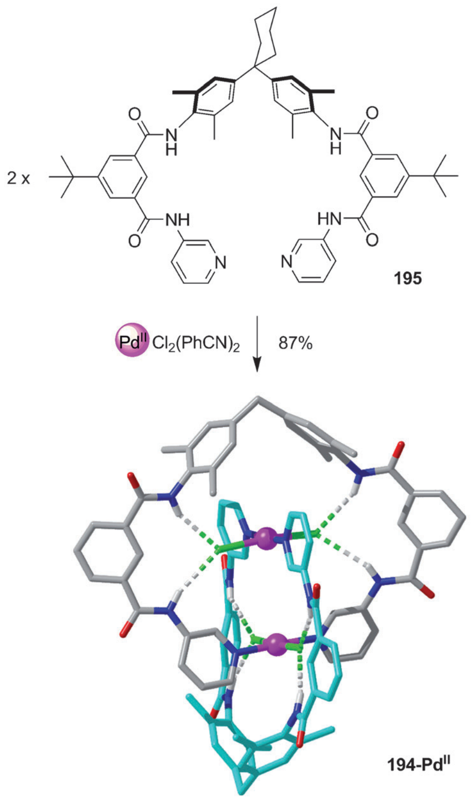


Scheme 75. Sauvage's use of octahedral Ru^{II} ions to coordinatively capture a) [2]rotaxane **192-Cu^{I}Ru^{II}**,[275] in which the metal ion acts a stoppering unit, and b) [2]catenane **193-Cu^{I}Ru^{II}**, where the metal ion is an integral part of one macrocycle.[276–278]

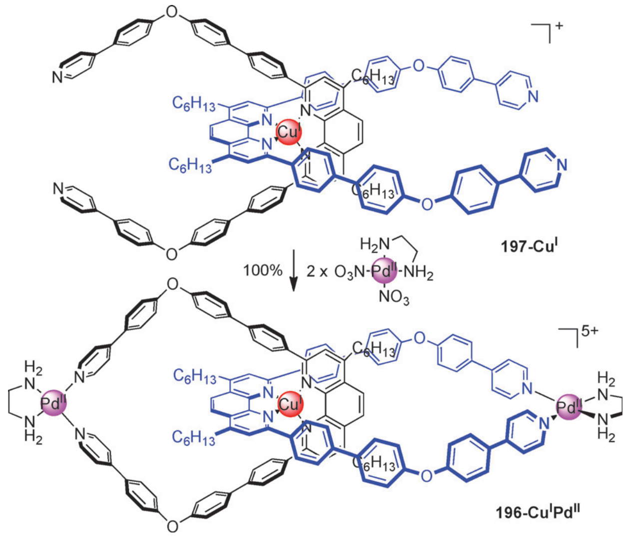
Pd^{II}-coordination has been used to quantitatively ring-close ligands entwined using the Cu^{I}(dpp)$_2$ template motif to form [2]catenane **196-Cu^{I}Pd^{II}** (Scheme 77).[281] The same ligand system, **197-Cu^{I}**, was cyclized with Ru^{II}–bis-phen complexes to form a [2]catenane.[282]

Using a related strategy, Sauvage et al. used bispyridyl ligands to bridge metal centers of Zn^{II}-[283] or Rh^{III}- containing[274] porphyrins appended to a Cu^{I}(dpp)$_2$ core to generate [2]catenanes. Other examples of metal–organic catenanes where metal ions act as both templates and bridging centers include Rees and co-workers[285] use of nine-coordinate Ba^{II} to form [2]catenane **198-Ba^{II}** (Figure 16).

The use of metal ion coordination to form rings within a catenane was taken a step further by the Bäuerle group in the synthesis of a remarkable [2]catenane made from fully π-conjugated oligothiophene-based rings (Scheme 78).[286] Using a Cu^{I}(phen)$_2$ motif, [2]catenane **199-Cu^{I}Pt^{II}** was synthesized by insertion of Pt^{II} to bridge the terminal alkynes.



Scheme 76. Wisner's use of Pd^{II} ions to assemble metal–organic [2]catenane **194-Pd^{II}** through first and second sphere coordination.[279] (For a related [2]rotaxane see Scheme 50.) NH···Cl distances and angles: 2.46–2.74 Å; N-H-Cl 151–163°. Cyclohexane and macrocycle *tert*-butyl groups removed for clarity.



Scheme 77. Sauvage's Cu^{I}(dpp)$_2$ motif is combined with Fujita's Pd^{II}–pyridyl "clipping" strategy to form catenate **196-Cu^{I}Pd^{II}**.[281]

Iodine-mediated reductive elimination of platinum gave [2]catenane **200-Cu^{I}**. The template Cu^{I} ion could be removed by treatment with potassium cyanide to form a [2]catenane in which each macrocycle consists of an unbroken sequence of unsaturated centers.[286b]

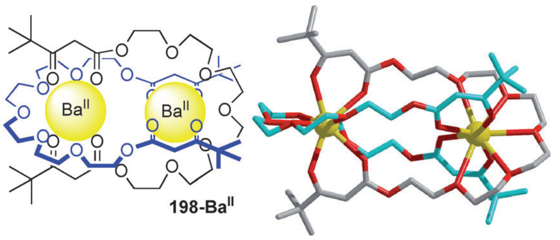
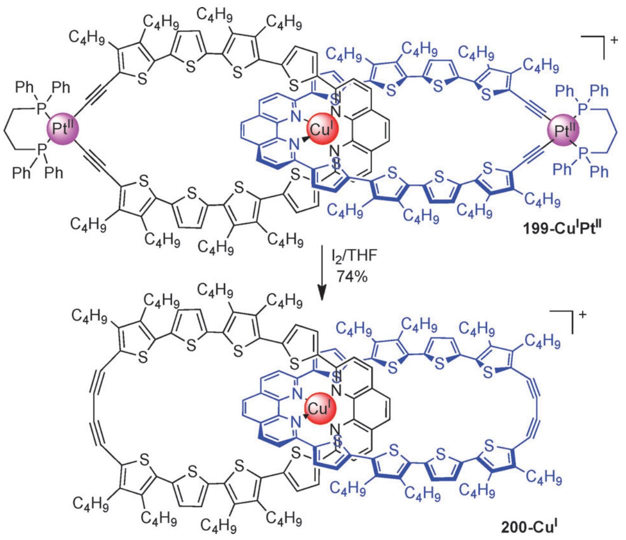


Figure 16. Rees' catenane **198-Ba^{II}** assembled around the coordination spheres of two barium ions. Each Ba^{II} ion is coordinated to nine oxygen atoms in the X-ray crystal structure.[285]



Scheme 78. Bäuerle's π-conjugated catenate assembled around a Cu^{I}–phen motif. Pt^{II} coordination is used to close the macrocyclic rings prior to reductive elimination to generate catenate **200-Cu^{I}**.[286b]

4.2.4. *Catenanes Formed Through Metal–Metal Interactions*

Gold(I) has been used to prepare a range of simple inorganic catenanes in which aurophilic interactions are the driving force for catenane formation. Mingos et al. reported a Au^{I} organometallic catenane, **201-Au$^{I}_{12}$** (Figure 17a),[287] in which each macrocycle contains six Au^{I} ions connected through a mixture of coordination modes. Catenanes have also been accessed through Au^{I}-thiolate interactions.[288] Che and co-workers have described a mechanically interlocked precursor (**202-Au$^{I}_{11}$**) of the Au^{I} anti-rheumatic drug Auranofin (Figure 17b).[289]

A family of organometallic catenanes assembled from Au^{I} ions and bis-alkynyl and bis-phosphine ligands has been reported by Puddephatt and co-workers.[290] Reaction of Au^{I}-acetylenes, such as **203-Au^{I}**, with bis-phosphine ligands with various spacers (such as **204**) afforded a range of macrocycles (e.g. **205-Au^{I}**), [2]catenanes (e.g. **206-Au^{I}**) and higher-order interlocked structures, depending on the components employed (Scheme 79). For example, for the system containing **206-Au^{I}**, catenanes were isolated by crystallization, but when re-dissolved in dichloromethane the system reverted to the non-interlocked macrocycle and other higher-order oligomers over the course of several days.[291] Other structural

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

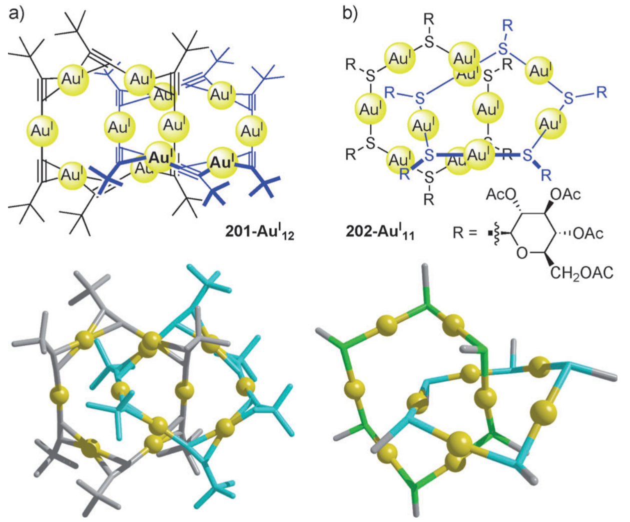
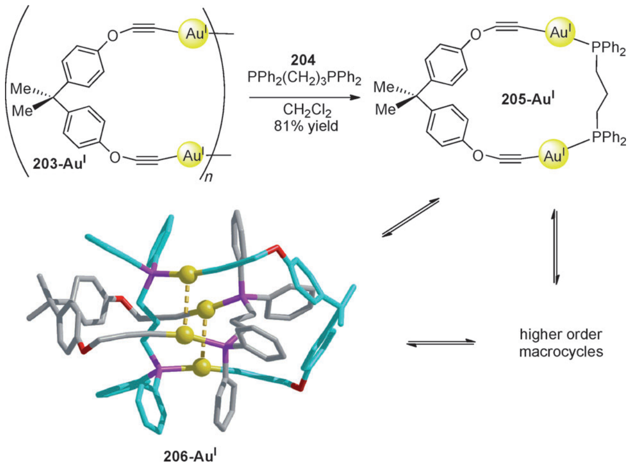


Figure 17. Gold(I) catenanes from a) Mingos et al.[287] (**201-Au$^I_{12}$**) and b) Che et al.[289] (**202-Au$^I_{11}$**). Sulfur atoms are shown in green and carbon atoms light blue with the peripheral glycosylate units omitted for clarity. The structure of **201-Au$^I_{12}$** contains six crystallographic independent Au^I atoms of which only two have linear coordination geometries (C-Au-C bond angles 176.3(1) and 177.8(1)°); the remaining Au^I ions are dihapto (η^2) to one or two acetylene groups. The inner core of the structure of **202-Au$^I_{11}$** is made up of eleven crystallographically non-equivalent linear Au^I ions bridged by thiolate anions (S-Au-S angles 165.5(4)–179.8(4)°). The distance between the two "non-bonded" Au^I atoms is 3.149(2) Å.



206-Au^I

Scheme 79. Puddephatt and co-workers control of the topological outcome of cyclization reactions by careful ligand design, generating catenane **206-Au^I** through aurophillic interactions.[291,294] P-Au-C angles for the two crystallographically non-equivalent **206-Au^I** catenanes 166.3(1)–174.9(8)°; inter-component Au-Au distances 3.216(2)–3.686(2) Å. With a *n*-propyl bis-phosphine linker *n* = 3, a mixture of macrocycle, [2]catenane and higher order macrocycles is formed, from which the catenane was isolated in 68% yield on crystallization.[291] Shorter spacers (ethyl) gave exclusively macrocycle formation and *n*-butyl gave exclusive [2]catenanes. Different substituents on the central methylene group of the bis-alkyne bridging unit could be used to selectively generate macrocycles, catenanes[293,295] or a Solomon link[297] (see Scheme 88).

permutations were studied[292–294] which led to controlled topological outcomes depending on linker length[289,292] and substituents on the bridging unit (**204-Au^I**).[293,295] This type of aurophilic assembly was extended to rotaxane structures by Raubenheimer and Barbour, incorporating N-heterocyclic carbenes into a tris-Au^I macrocyclic species while using an Au^I-diphosphine thread.[296]

4.3. Polycatenanes and Interpenetrated Networks

Interpenetrated and polycatenated architectures are common in the solid state for coordination complexes that feature weak or reversibly formed bonds.[298,299] They arise not because of particular recognition motifs between building blocks, like in solution, but rather because "nature abhors a vacuum". In the solid state this manifests itself in the tendency for filled cavities that maximize van der Waals interactions and reduce the energy of the resulting structure.

An example of a linear poly[*n*]catenane system is **207-Ag^I**, formed in the solid state from the self-assembly of Ag^I and bis(2-methylimidazolyl)methane ligands (Figure 18).[300] Geerts and Sauvage have covalently linked Cu^I(dpp)$_2$ catenanes to form short mechanically linked polymers.[299a] Interpenetrated networks and polycatenanes structures, some of which possess interesting properties that are potentially useful for gas storage, sensing or catalysis, have been reviewed elsewhere.[298]

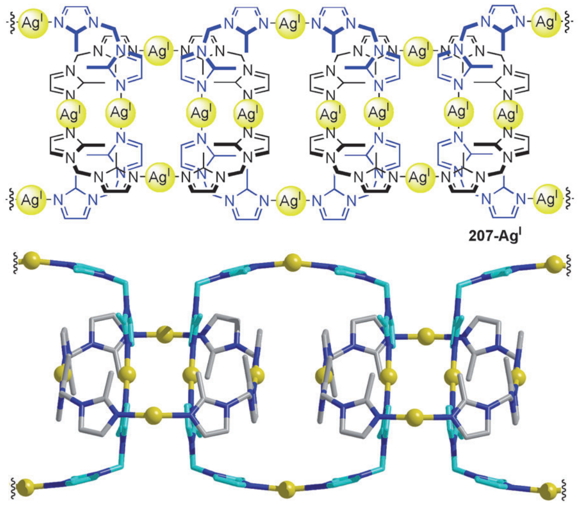


Figure 18. Jin's solid state [*n*]catenane **207-Ag^I** formed from bis(2-methylimidazolyl)methane ligands connected by Ag^I ions.[300] Carbon atoms of one ring are shown in light blue and those of the other in grey. The four different Ag^I centers have N-Ag-N angles 164.7(4)–177.9(2)° with inter-component Ag···Ag distances 3.656(2) and 3.875(1) Å.

5. Knots and Higher Order Links

Knots[301] are mathematically defined as an entwined closed loop and can be characterized by their "crossing number" (the number of crossing points needed to represent the knot in two dimensions) and a second identifier (the "order" of the knot), often indicated by a numerical subscript

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

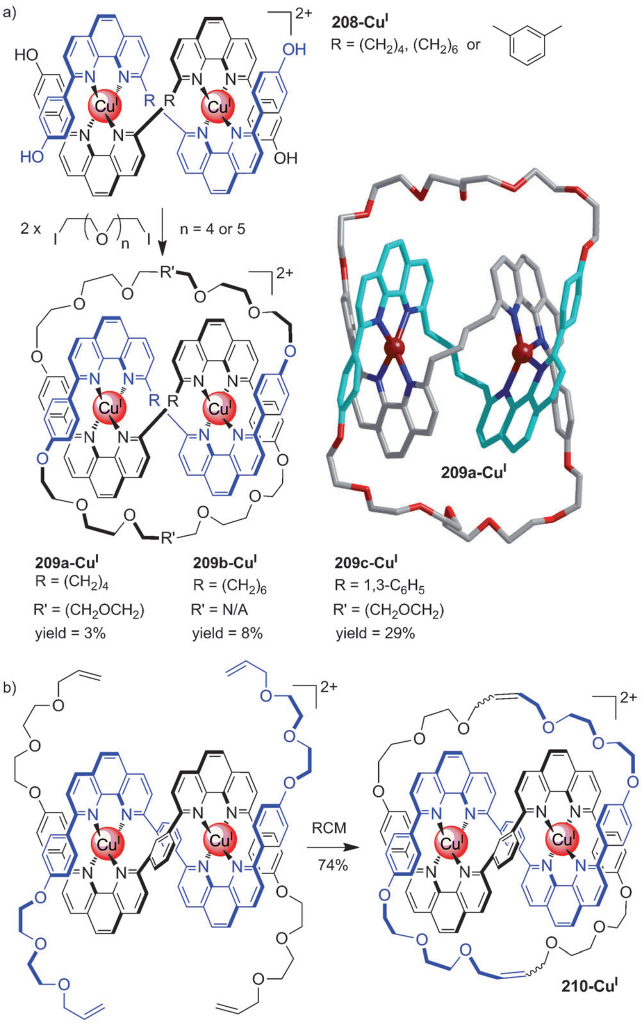
in modern knot tables, to unambiguously assign their topology.[302] The trefoil knot, with only three cross-over points, is the simplest non-trivial knot (3A in Tait's original knot tables; 3_1 in most modern knot tables[302]), and complexity increases rapidly with increasing crossing number. Unlike knots, which are single component species, links consist of two or more components that cannot be separated without breaking the connectivity of at least one of them. Links can be mathematically characterized by their crossing number, the number of components and, as with knots, additional identifiers to uniquely identify the topology of the link. The simplest non-trivial link is the Hopf link, consisting of two loops with two crossover points (i.e. the topology of a simple [2]catenane). Brunnian links are higher order link systems in which the components cannot be separated without breaking a loop, but in which no two loops are directly linked. The simplest example of a Brunnian link is the Borromean rings (see Section 5.5).

Molecular knots and entanglements are important structural elements in some types of DNA and proteins and can contribute significantly to the properties of synthetic polymers.[1g] The synthesis of specific molecular knots and higher order links offers a significant challenge to the synthetic strategies and abilities of chemists. Remarkably, of the 249 different prime knots with three to ten crossing points, just one type—the trefoil knot—has succumbed to total synthesis to date.[303] Sauvage extended the Strasbourg strategy of linking helicates with multiple turns (Figure 5) used for catenane formation to the synthesis of the first molecular trefoil knot[304] and attempted unsuccessfully to use it to make higher prime knots. Other metal template strategies to knots and links have evolved over the past 20 years. Knotted molecular architectures have also been obtained using hydrogen bonding templates or DNA, approaches that have been reviewed elsewhere.[305]

5.1. Molecular Trefoil Knots

5.1.1. Trefoil Knots using Two Tetrahedral Metal Templates

The synthesis of molecular trefoil knots by linking Cu(dpp)$_2$ template motifs to form double helices such as **208-Cu$^{\mathrm{I}}$** is shown in Scheme 80. Covalent capture of the three crossing points in **208-Cu$^{\mathrm{I}}$** through Williamson ether bond formation gave the molecular trefoil knot **209-Cu$^{\mathrm{I}}$** in 3% yield.[304] The molecular topology was indicated by a variety of analytical techniques and later conclusively demonstrated by X-ray crystallography (structure shown in Scheme 80).[306] ^{1}H NMR analysis of the bis-Cu$^{\mathrm{I}}$ helicate **208-Cu$^{\mathrm{I}}$** showed that a significant amount of the mononuclear Cu$^{\mathrm{I}}$ complex was present; that is, the ligand had folded to act as a tetradentate ligand for one Cu$^{\mathrm{I}}$ center. Accordingly, different spacers were tried to help induce tighter entwinement in the helicate leading to improved yields (up to 29%) of trefoil knot **209-Cu$^{\mathrm{I}}$** (Scheme 80a).[307] The use of mild, high yielding, covalent capture reactions such as ring closing olefin metathesis (see Section 1.2.2.3), as with the synthesis of [2]catenanes (Scheme 11c), resulted in significantly higher yields of knotted products, with **210-Cu$^{\mathrm{I}}$** being synthesized in 74% yield.[308] A number of studies on this series of molecular trefoil knots ensued, examining chirality,[309] introduction of other metal ions,[310] the kinetics of demetalation,[311] and electrochemical treatments of the entwined structures.[312]



Scheme 80. Sauvage's synthesis of trefoil knots **209-Cu$^{\mathrm{I}}$**[304,306,307] and **210-Cu$^{\mathrm{I}}$**.[308] The yields of knots of type **209-Cu$^{\mathrm{I}}$** were improved by adjustment of the spacer groups R and R′. The introduction of a longer R spacer (**209b**) allowed the formation of a more stable helicate precursor giving a modest increase in yield (3% to 8%). The use of a rigid phenylene R spacer (**209c**) further stabilized the precursor helicate and resulted in a more significant yield increase (to 29%). The X-ray crystal structure of **209a-Cu$^{\mathrm{I}}$** is shown. Bond angles are distorted in comparision with non-interlocked Cu(dpp)$_2$ complexes (ligand bite angles 78.8(9)–83.5(10)°; other N-Cu-N angles 112.7(9)–143.1(11)°). Note the short inter-dpp spacer still allows for extensive dpp–dpp π-stacking. For other crystal structures see refs [309b] and [310].

5.1.2. Stereoselective Synthesis of a Trefoil Knot using Two Tetrahedral Metal Templates

A trefoil knot is intrinsically topologically chiral, the structure cannot be deformed into its mirror image. The use of achiral ligands produces trefoil knots as racemic mixtures.

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

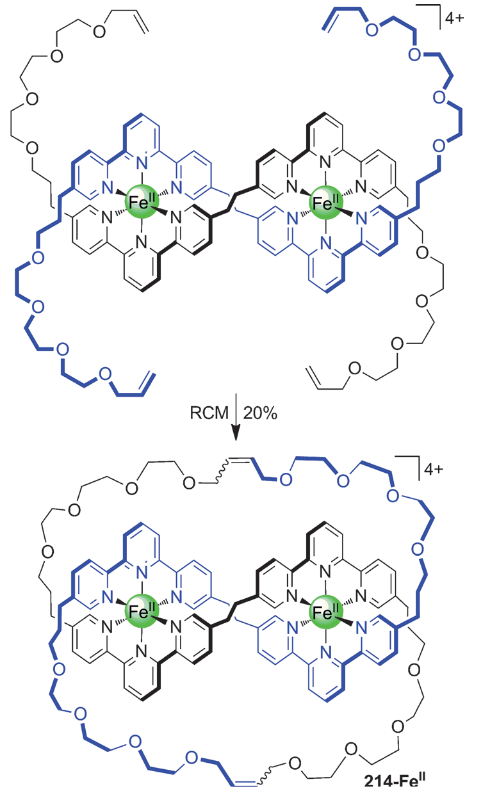
Using the chiral ligand **211**, von Zelewsky, Sauvage and co-workers were able to form double helicate **212-Cu^I** with a single helical twist sense. When cyclized under RCM conditions this generated a homochiral trefoil knot, **213-Cu^I**, in 74 % yield (Scheme 81).[313] The single handedness of the knot was established by the presence of a strong signal in the circular dichromism spectrum of **213-Cu^I**. Demetalation gave the metal-free homochiral knot.

5.1.3. Trefoil Knots using Two Octahedral Metal Templates

The linking of extended helicates has also been used to construct a trefoil knot around octahedral metal centers (Scheme 82). Terpyridine-derived ligands and Fe^{II} ions were employed to form a precursor helicate, and RCM successfully generated trefoil knot **214-Fe^{II}** in 20 % yield.[308b] (For an attempt to form a [2]catenane using a related terpyridine motif, see Section 2.3.1, Scheme 24.[160])

5.1.4. Trefoil Knots using One Octahedral Metal Template

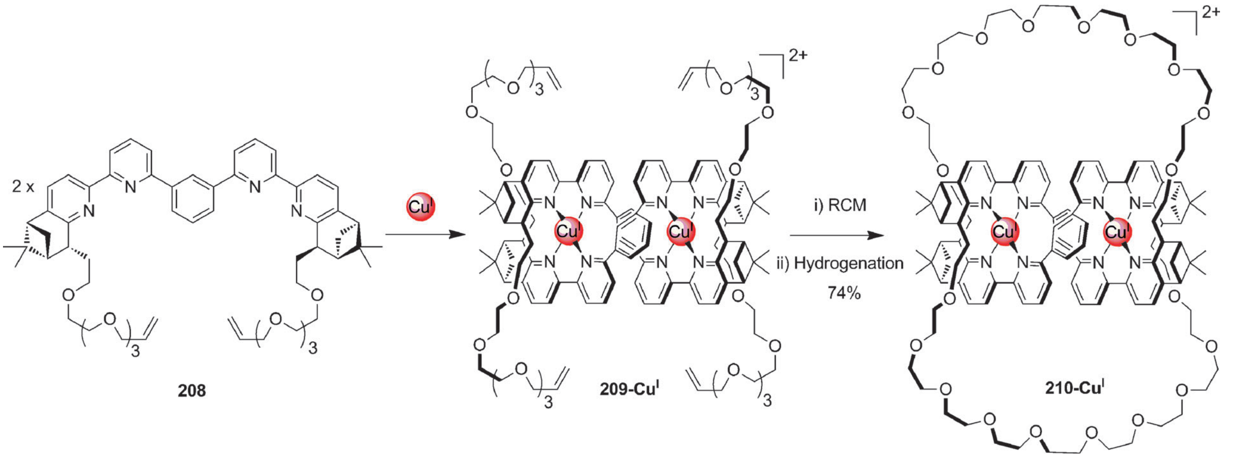
An interesting example of an open-knotted structure assembled about an octahedral metal center was described by Hunter and co-workers in 2001 (Scheme 83).[314] An octahedral Zn^{II} template was used to entwine a multidentate ligand containing three bipyridyl units into an open knot conformation **215-Zn^{II}**. The structure was confirmed by X-ray crystallography. The folding process is fully reversible. Addition of chloride ion regenerated the free ligand, and subsequent addition of silver salts (precipitating the chloride ion as AgCl) reassembles the open knot complex. In a recent report, it was demonstrated that the open knot could be closed to a trefoil knot through either a bis-esterification reaction of the two terminal alcohols in **215-Zn^{II}**, or by ring closing metathesis from **216/217-Zn^{II}** to form **218/219-Zn^{II}**.[315] Successful removal of the Zn^{II} template from **219-Zn^{II}** was achieved with Li_2S.



Scheme 82. Sauvage's molecular knot, **214-Fe^{II}** synthesized using helicates based on octahedral metal ions.[308b]

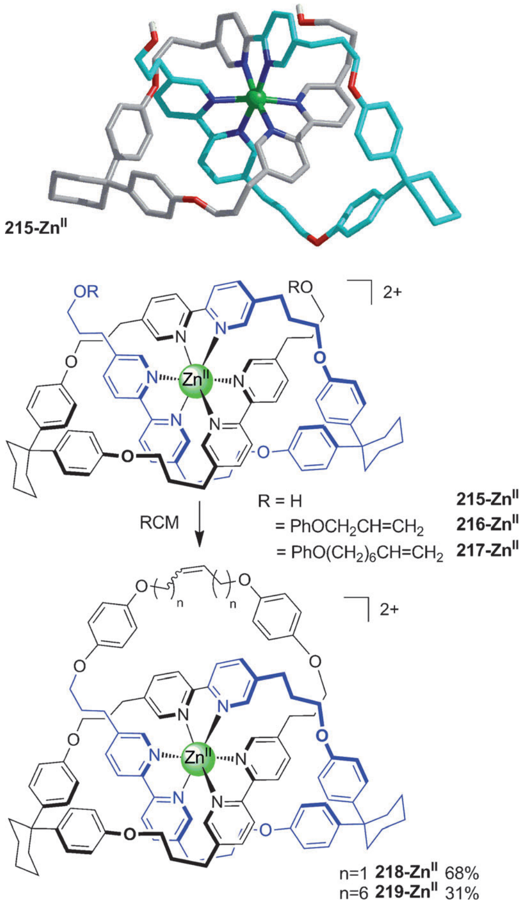
5.2. Molecular Composite Knots

Composite knots are entwined closed loops that can be expressed as the connected sum of two or more prime knots. The simplest composite knots are derived from the sum of two trefoil knots. This addition can take place in one of two ways: If two trefoil knots of the same handedness are combined a granny knot is formed, which is topologically chiral, whereas if two trefoil knots of opposite handedness are combined a *meso* species, a square knot, is produced. Composite knots can be formed from the addition of any two prime knots meaning



Scheme 81. von Zelewsky and Sauvage's stereoselective synthesis of homochiral trefoil knot **213-Cu^I** through chiral bisbipyridine ligand **211**.[313]

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

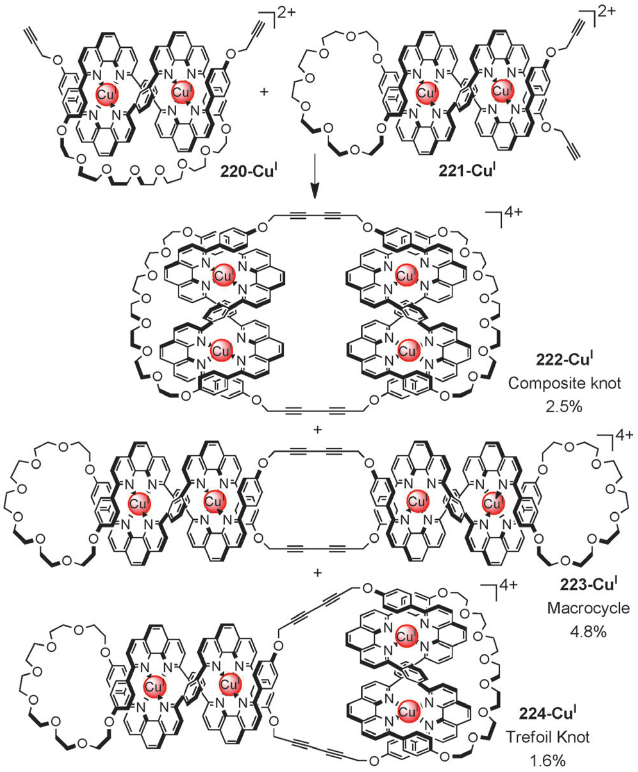


Scheme 83. Hunter's open-knot **215/216/217-Zn$^{\mathrm{II}}$**[314] derivatives of which could be cyclized to produce trefoil knot **218/219-Zn$^{\mathrm{II}}$**.[315] In the solid state structure of the open knot the Zn$^{\mathrm{II}}$ ion adopts a slightly distorted octahedral geometry (N···Zn bond lengths 2.110(8)–2.176(7) Å, *cis*-(N-Zn-N) angles 76.8(3)–99.5(3)°).

that even with a relatively small number of crossing points, the number of possible composite knots rapidly becomes enormous.

5.2.1. Square and Granny Knots using Four Tetrahedral Metal Templates

Sauvage and co-workers synthesized molecular composite knots by employing their strategy of linking linear helicates (Figure 5).[316] The isomers **220-Cu$^{\mathrm{I}}$** and **221-Cu$^{\mathrm{I}}$** form in a 3:7 ratio upon Cu$^{\mathrm{I}}$ complexation with the precursor open chain ligand (Scheme 84). When this mixture was cyclodimerized through Glaser–Eglinton alkyne coupling, three reactions were observed to take place: homocoupling of **220-Cu$^{\mathrm{I}}$** generates the desired composite square and granny knots **222-Cu$^{\mathrm{I}}$**; homocoupling of **221-Cu$^{\mathrm{I}}$** gives the large macrocycle **223-Cu$^{\mathrm{I}}$**; and heterocoupling of the two isomers produces trefoil knot **224-Cu$^{\mathrm{I}}$**. The square/granny composite knots were isolated from the crude reaction mixture by column chromatography in 2.5% yield and were fully characterized in their metallated and demetallated form.



Scheme 84. Sauvage's synthesis of a molecular composite knot through acetylenic oxidative coupling of two trefoil knot precursors.[316]

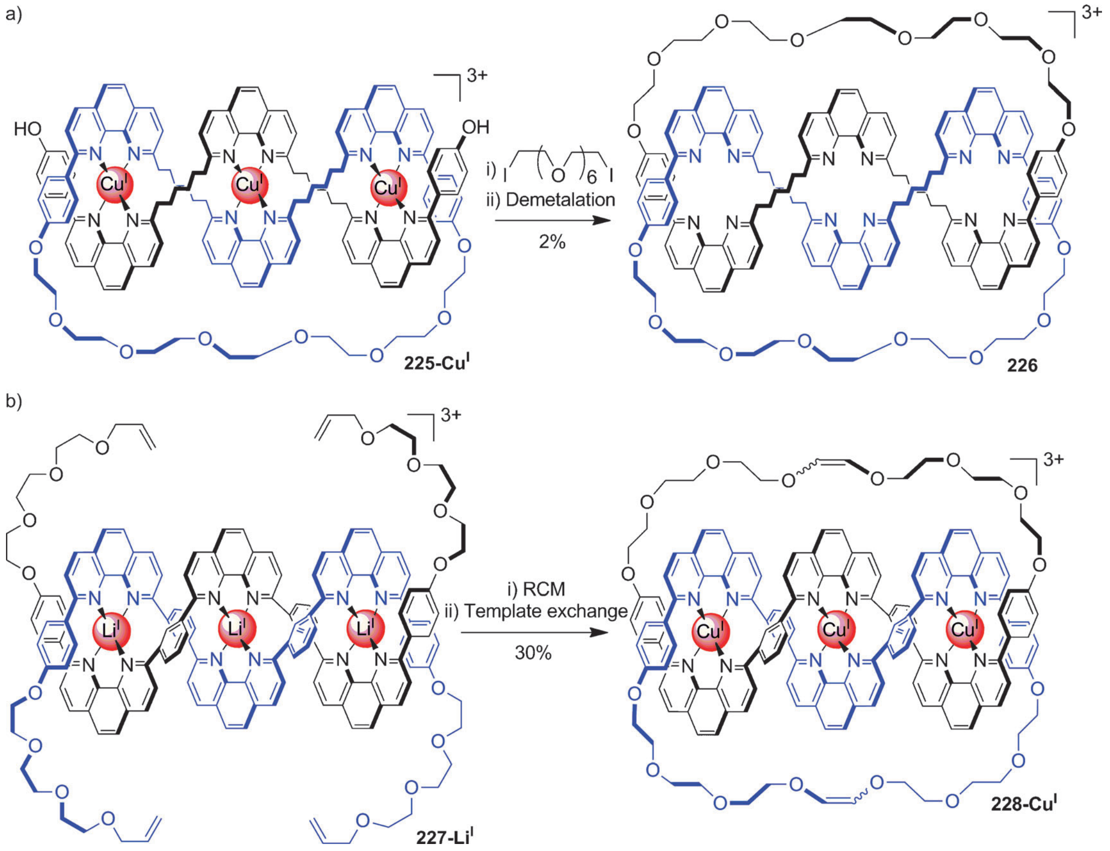
5.3. Molecular Solomon Links

A Solomon link (the topology is actually that traditionally known as a "Solomon knot", but as it is a link rather than a knot, chemists have renamed it for molecular structural purposes)[317] is composed of two components that are interlocked with four crossing points (Figure 5). The structure is that of a [2]catenane possessing an additional two crossing points—a "doubly interlocked" [2]catenane. Like trefoil knots, Solomon links are intrinsically chiral.

5.3.1. Solomon Links using Three Tetrahedral Metal Templates

Sauvage's group prepared molecular Solomon links by cyclizing the end groups of helicates derived from three dpp-coordination units (Figure 5).[318] Cyclization of **225-Cu$^{\mathrm{I}}$** was achieved through William ether synthesis. The interlinked complex **226-Cu$^{\mathrm{I}}$**, (Scheme 85) proved to be unstable, thus purification was attempted after demetalation to yield metal-free **226** in 2% yield.[318] An improved synthesis was achieved with the more stable double-stranded tri-Li$^{\mathrm{I}}$ helix **227-Li$^{\mathrm{I}}$** combined with RCM cyclization reactions to give the doubly-entwined catenane **228-Li$^{\mathrm{I}}$**.[319] Purification difficulties prevented isolation of catenane **228-Li$^{\mathrm{I}}$**. Instead it was converted to the copper analogue **228-Cu$^{\mathrm{I}}$**, which was more amenable to purification and was isolated in 30% yield. Catalytic hydrogenation followed by demetalation gave the metal-free Solomon link.

This strategy of using multiple crossing points from linear helicates (Figure 5) for the synthesis of knots and links could

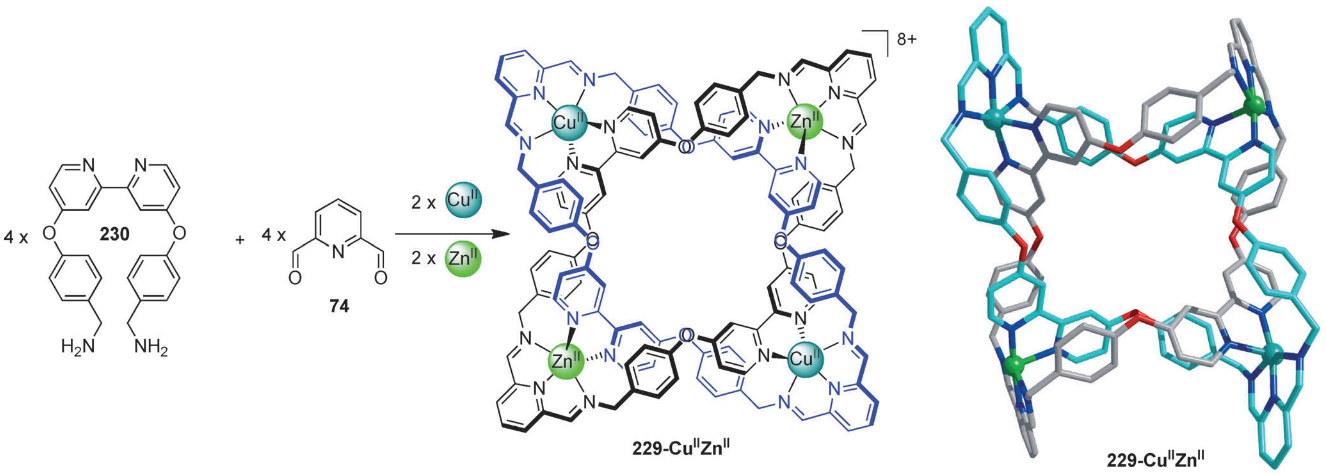


Scheme 85. Sauvage's original (**226-Cu^I**)[318] and improved (**228-Li^I/Cu^I**)[319] synthesis of Solomon links.

theoretically be extended to the synthesis of a pentafoil knot and a "Star of David" link and higher order topologies. However, to date, the Solomon links are the most complex topology synthesized by this approach.[115]

5.3.2. *Solomon Links using Four 5-Coordinate Metal Templates*

Stoddart and co-workers have employed dynamic bond-forming reactions with multiple metal template sites in the assembly of topologically complex structures such as Solomon links and Borromean rings (see Section 5.5.4). Solomon link **229-Cu^IIZn^II** was an unexpected product from the reaction of four equivalents of ligands **74** and **230** and two equivalents of each of Zn^II and Cu^II ions, with the link isolated by crystallization (Scheme 86).[317] An all-Zn^II Solomon link was recently isolated as a side product from a reaction that also produces Borromean rings (see Section 5.5.4).[320] The factors influencing the formation of Solomon links in preference to the Borromean rings remain unclear.[320]

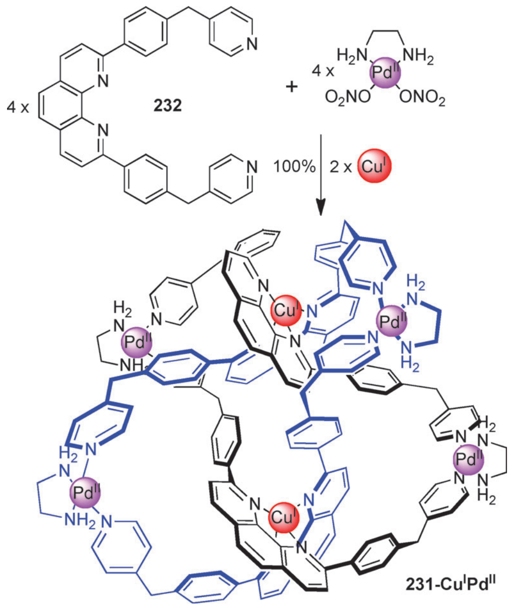


Scheme 86. Stoddart's Solomon link **229-Cu^IIZn^II**, assembled by imine bond formation around a multi Cu^II and Zn^II ion template.[317] The structure contains one crystallographically independent octahedral metal center (for both Cu^II and Zn^II) with a coordinated trifluoroacetate anion (not shown for clarity). Extensive intercomponent π-stacking is a feature of the crystal structure.

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

5.3.3. Metal–Organic Solomon Links

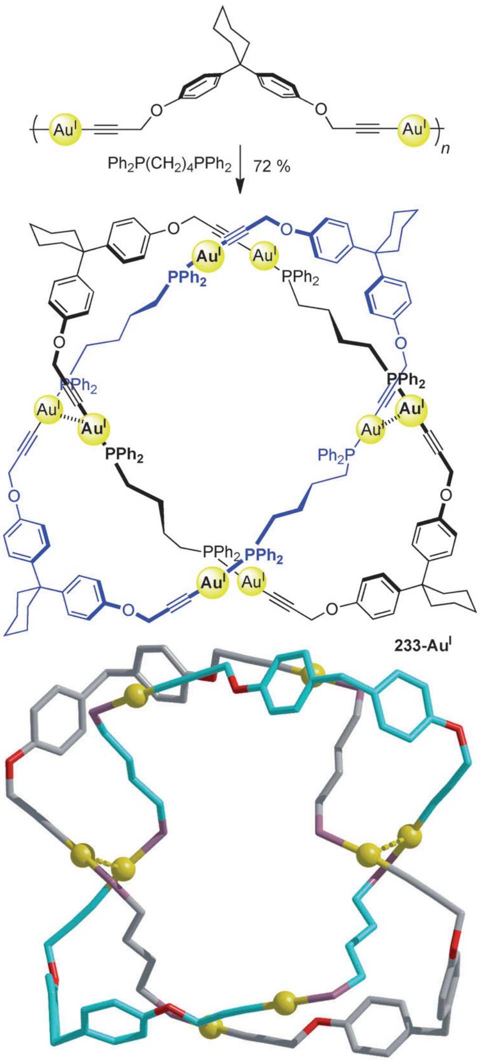
Sauvage and Fujita combined metal–template and metal–connector approaches (see also Scheme 77, Section 4.2.3) to produce both singly (**196-Cu^{I}Pd^{II}**) and doubly (**231-Cu^{I}Pd^{II}**) interlocked [2]catenanes. Early attempts resulted in the serendipitous formation of the topologically more complex Solomon link (**231-Cu^{I}Pd^{II}**, Scheme 87).[321] The bidentate ligand **232** is too small to form a simple singly entwined [2]catenane from one Cu^I ion, two Pd^{II} ions and two dpp-based ligands. Instead, two Cu^I ions, four Pd^{II} ions and four equivalents of **232** assembled to generate a larger [2]catenane with four crossing-points, **231-Cu^{I}Pd^{II}**. The Solomon link was the preferred product irrespective of the order of addition of the metal ions. Use of a larger macro-bidentate ligand resulted in the formation of the simple Hopf link [2]catenane **196-Cu^{I}Pd^{II}** (Scheme 77).[281]



Scheme 87. Fujita and Sauvage's Solomon link **231-Cu^{I}Pd^{II}**.[321]

Building on their Au-catenane systems[294] (Scheme 79), Puddephatt and co-workers reported the formation of a "doubly braided" [2]catenane (Solomon link **233-Au^I**) assembled through aurophilic interactions.[295,297] Incorporating a diphenylcyclohexyl unit as the spacer changes the topology of the product from the catenane-forming reactions shown in Scheme 79 to the Solomon link **233-Au^I** (Scheme 88). The topology was determined by X-ray crystallography.

Recently, Quintela and co-workers reported the synthesis (Scheme 89) of a Solomon link (**234-Pd^{II}**)[322] using π-donor–acceptor interactions to template the molecular link and pyridyl–Pd^{II} or Pt^{II} coordinate bonds (see also the assembly of [3]catenane **185-Pd^{II}**,[264] Scheme 71). The palladium Solomon link is in exchange with its non-interlocked components at room temperature, however, the platinum-containing molecular link was isolated in 61 % yield. A diazopyrene derivative (**234-Pd^{II}**) was crystallized and the doubly entwined nature of the molecular link confirmed by X-ray crystallography (Scheme 89).

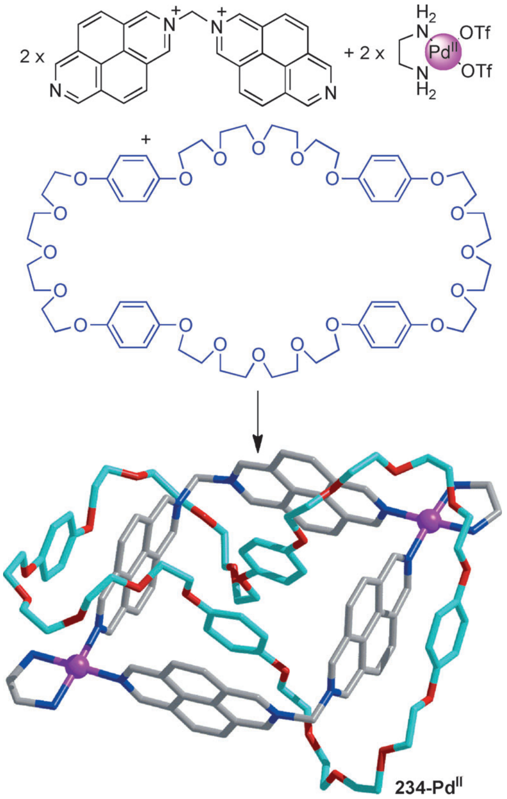


Scheme 88. Puddephatt and co-workers' synthesis of Solomon link **233-Au^I** through aurophillic interactions.[297] In the solid state the P-Au-C angles are near-linear (170.9(12)–177.9(9)°) with intercomponent Au-Au distances 3.130(2) and 3.239(2) Å. In the crystal structure the phospho-phenyl and cyclohexyl groups are omitted for clarity.

5.4. Other Metal–Organic "Metallaknots"

5.4.1. Silver(I) "Metallaknots"

Two examples of metal–organic knots based on Ag^I coordination to quinoline ligands come from Hosseini's group (Scheme 90).[323] Subtle changes in the spacer of the ligand used, penta-ethyleneoxy **235** or tetra-ethyleneoxy **236**, have a significant impact on the constitution of the final knots. The larger ligand **235** led to a trinuclear entwined complex **237-Ag^I**, whereas the smaller ligand **236** led to the tetranuclear entwined complex **238-Ag^I**.



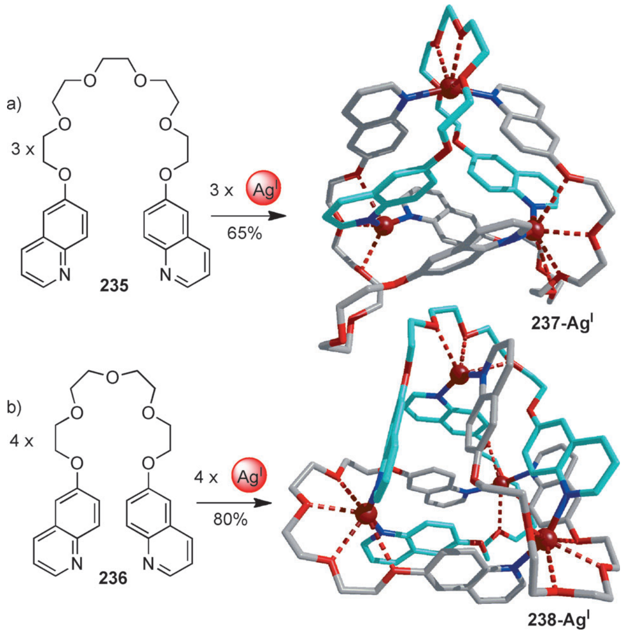
Scheme 89. Quintela's Solomon link **234-Pd^{II}**.[322] In the solid state the amino protons of the ethylenene diamine ligand are involved in hydrogen bonding interactions with the glycol chain (NH···O 2.18 Å) and a triflate counterion. Extensive π-stacking is observed between the pyrene and hydroquinol units (3.39 and 3.51 Å), with a large spacing between the internal hydroquinol groups (3.72 Å). See Scheme 71 for a related structure.

5.4.2. Metal–Organic "Solomon Cube"

Hardie and co-workers have described the assembly of a "Solomon cube" (**239-Pd^{II}**), a cage structure related to a Solomon link (Scheme 91).[324] Inter-ring Pd^{II}–ligand bridging creates eight triple-connecting centers, like a cube, as part of the Pd$^{II}_4$L$_4$ system's doubly-braided topology. The remarkable structure was assembled in DMSO from ligand **240** and Pd^{II}(NO$_3$)$_2$. The product, **239-Pd^{II}**, was isolated in 80% yield by crystallization, which may provide much of the driving force for its formation[257] (see Scheme 72 for other examples of crystallization-driven catenane formation).

5.5. Molecular Borromean Rings

Borromean rings[325] are a Brunnian link consisting of three rings, each threaded (not interlocked) through one of the other rings and threaded by the other one. Although each ring is not interlocked with any other individual ring the ensemble cannot be dissociated without breaking any one ring. Synthetic molecular Borromean rings were first constructed using DNA by Seeman and co-workers,[326] and molecular strategies[111] to them have ranged from multistep "rack"[327] and "ring-in-ring" attempts[328–330] to metal–organic self-assembly[331] and a remarkable one-pot 18 component multiple metal ion template assembly.[332]



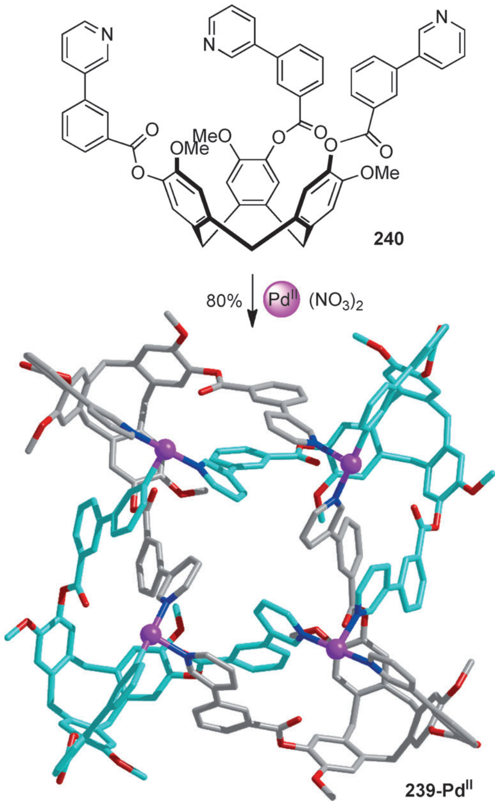
Scheme 90. Hosseini's metal–organic knots. Depending on the size of the polyether unit either a) the trinuclear knot **237-Ag^{I}** or b) the tetranuclear knot **238-Ag^{I}** are produced.[323] In the solid state structures each Ag^{I} center can be considered primarily N-coordinated with N-Ag-N angles 146.5(6)–157.3(3)° and Ag–N bond distances 2.18(2)–2.24(2) Å. For **237-Ag^{I}** each Ag^{I} atom is weakly coordinated to two oxygen atoms (Ag–O distances 2.60(1)–2.62(3) Å). In **238-Ag^{I}** each Ag^{I} center is involved in interactions with four oxygens of the glycol chains (Ag–O distances 2.60(2)–3.09(2) Å).

5.5.1. Metal–Organic Borromean Rings

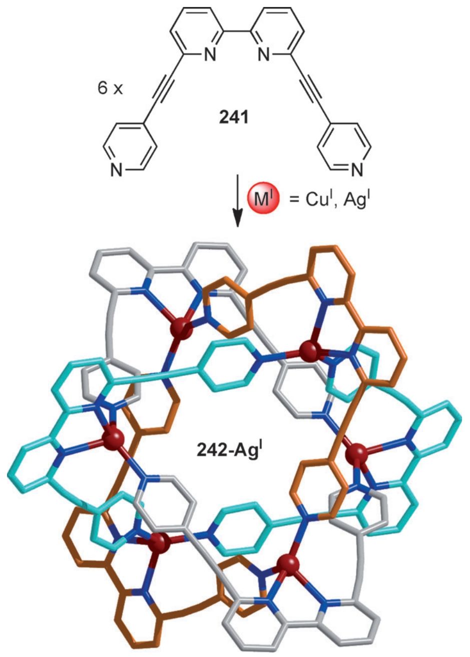
The first molecular Borromean ring structure featuring metal ions was serendipitously discovered by Champness, Schröder and co-workers.[331] In the presence of tetrahedral metal templates Cu^{I} and Ag^{I}, ligand **241** spontaneously assembles into a structure with a Borromean ring-like topology, albeit with metal–ligand bonds between the macrocycles (Scheme 92). The Cu^{I} structure (**242-Cu^{I}**) proved to be stable in both solid and solution phases whereas **242-Ag^{I}** could only be isolated in the solid state and was unstable in acetonitrile because of the lability of the Ag–pyridine bond. Encapsulation of a single counter anion was observed in the central cavity of the Borromean rings, suggesting the anion may also template the assembly. A closely related structure was reported by Schmittel using a phen ligand with similarly positioned pendant pyridyl groups.[331b]

5.5.2. Rack Approach using Two Octahedral Metal Templates

A strategy that has been pursued towards molecular Borromean ring involves a "rack approach" (see Scheme 14eii, Section 1.3). Siegel and co-workers constructed a basic rack assembly **243-Ru^{II}** based on orthogonal positioning



Scheme 91. Hardie's "Solomon cube" **239-Pd^{II}**.[324] In the solid state all of the Pd^{II} centers are crystallographically equivalent and are 5-coordinate, with a weakly coordinated nitrate anion (here omitted for clarity) completing the coordination sphere. Bond angles: N-Pd-N: 89.0(3), 90.8(3), 178.1(5); N-Pd-O$_{\text{in-plane}}$: 163.3(4), 92.0(3), 88.7(4); N-Pd-O$_{\text{out-of-plane}}$: 152.6(5), 96.5(5), 82.9(5); O-Pd-O: 43.7(5)°. Pd–N bond lengths 2.01(1)–2.03(1) Å; Pd–O bond lengths 2.31(1)–2.50(2) Å.



Scheme 92. Champness and Schröder's metal–organic Borromean ring-like complex **242-Cu^{I}/Ag^{I}**.[331] All Ag^{I} centers are equivalent and adopt a distorted tetrahedral geometry (ligand-bite angle 69.6(2)° with the remainder N-Ag^{I}-N angles 102.6(2)-131.7(2)°).

of tridentate molecular fragments by octahedral Ru^{II} ions that could possibly be developed towards a Borromean ring synthesis (Figure 19).[327]

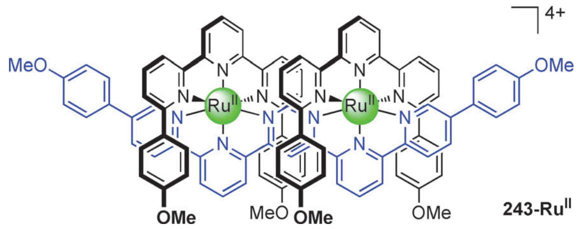


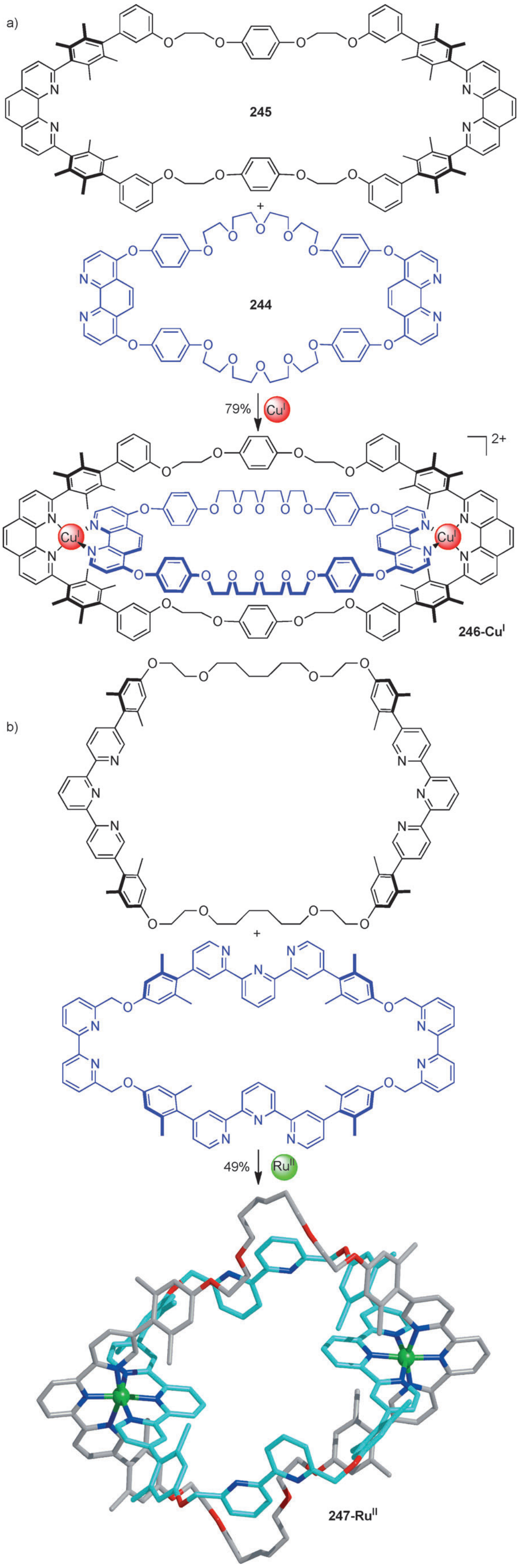
Figure 19. Siegel's rack complex **243-Ru^{II}**, part of a strategy towards Borromean rings (Scheme 14eii, Section 1.3).[327]

5.5.3. Ring-in-Ring Approaches using Two Tetrahedral or Two Octahedral Metal Templates

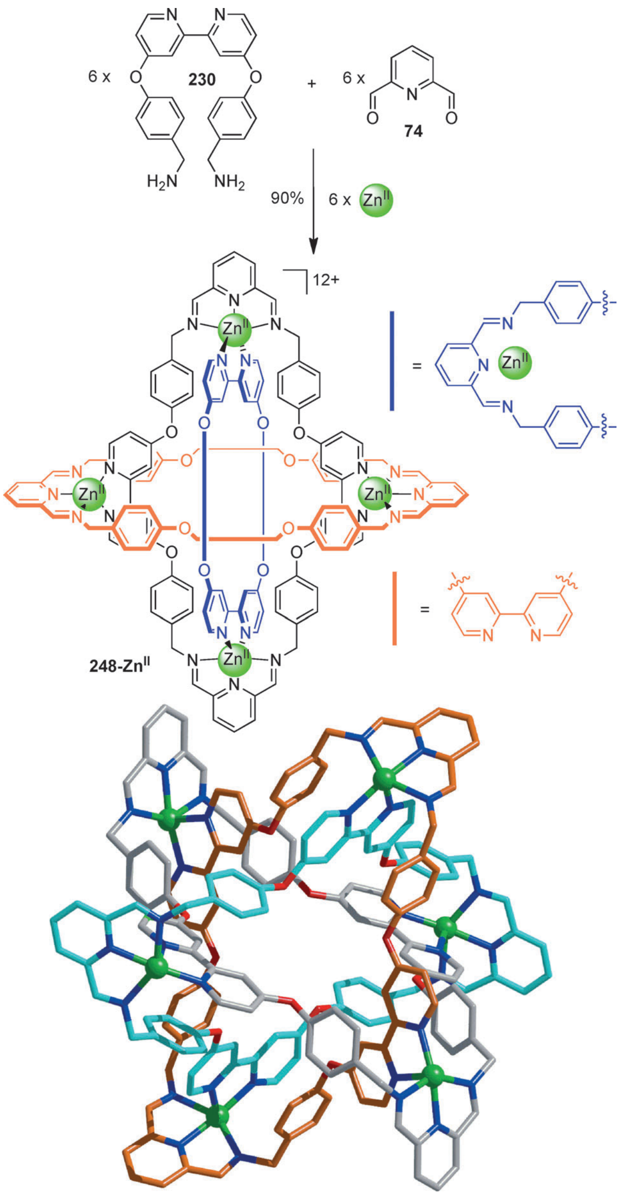
A "ring-in-ring" approach (Scheme 14ei) to Borromean rings has been investigated which involves threading one preformed macrocycle through the cavity of a second. A third ring would then need to be inserted such that it was threaded through one ring whilst encircling the other. Stoddart's group reported a ring-in-ring assembly based on ammonium–crown ether interactions,[328] which was followed by reports from two other groups on using metal–ligand coordination to generate ring-in-ring complexes. Schmittel's group made use of the tetrahedral Cu^{I}(phen)$_2$ motif, one macrocycle (**244**) featuring two exotopic phen units while the other (**245**) had two complementary endotopic dpp-sites (Scheme 93a). Treatment with Cu^{I} generated ring-in-ring complex **246-Cu^{I}** in 79% yield.[329] Siegel's group utilized an octahedral metal–terpyridine motif with two vacant bipy units built into one ring to assemble ring-in-ring complex **247-Ru^{II}** in 49% yield. (Scheme 93b).[330] As yet there have been no reports on elaborating any of these ring-in-ring strategies further towards either Borromean rings or other higher order links.

5.5.4. Molecular Borromean Rings using Six 5-Coordinate Metal Templates

A one-pot metal template synthesis of molecular Borromean rings was reported by Stoddart and co-workers.[332,333] Six Zn^{II} metal ions direct the assembly of six bipy-based ligands **230** featuring terminal primary amines groups and six 2,6-diformylpyridine ligands **74** to form **248-Zn^{II}** (Scheme 94). The homocircuit Borromean ring structure was confirmed by X-ray crystallography, which also reveals non-covalent interactions that presumably aid the assembly process. Each bipy unit is flanked by a pair of phenolic rings at a distance well-suited for π-stacking. Reduction of the imine bonds with NaBH$_4$ to form secondary amines, followed by demetalation with ethylenediaminetetraacetic acid (EDTA, 22°C, 5 days) resulted in metal-free Borromean rings.[334] Other Borromean rings have been self-assembled with differing substitution on the pyridine ring,[335,336] and the resulting assemblies demonstrated to be in dynamic exchange.[335] The introduction of appended alkene groups allowed simple functionalization by cross metathesis,[337] the use of appended thiol groups allowed attachment to gold surfaces,[338] and the inclusion of chiral groups in the components generated chiral Borromean rings.[339] Synthesis of Borromean rings using the same or related ligands and employing other transition metals (Cu^{II}, Co^{II}, Mn^{II} and Cd^{II}) as templates has also been achieved.[320]



Scheme 93. a) Schmittel's **246-Cu**^{I}[329] and b) Siegel's **247-Ru**^{II}[330] ring-in-ring complexes, model routes for positioning two of the three macrocycles of Borromean rings.



Scheme 94. Stoddart's Borromean rings **248-Zn**^{II}.[332] The carbon atoms of each macrocycle are shown in different colors—grey, light blue and orange. The anions occupying the sixth coordination site in the solid state structure have been omitted for clarity. The Zn^{II} centers are all crystallographically equivalent with distorted octahedral geometries (*cis*-N-Zn^{II}-N bond angles 72.5(2)–109.5(3)°). Extensive π-stacking occurs between the phenyl rings and bipyridine groups (distances of 3.51 and 3.72 Å).

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

6. Conclusions and Outlook

The kinetic and thermodynamic metal template effects introduced for preparing macrocycles in the 1960s have proved key to the development of increasingly effective synthetic routes to ever more complex molecular topologies (Section 1). The tetrahedral Cu^I-template system introduced by Sauvage in the 1980s has been joined in recent years by template systems based on every common metal coordination geometry (octahedral, trigonal bipyramidal, square planar and linear; Section 2), with tactics based on maximal site occupancy, the shape of ligands, stereoelectronic effects, and non-covalent interactions between the components helping to create turn angles and favor ring closure or threading. The kinetic stability of some metal–ligand bonds enable metal-organized ligand systems (e.g. square planar template Pd^{II} complexes) to be isolated, purified, and used as stable building blocks in their own right, while the lability of other metal–ligand coordination bonds allows for the dynamic assembly of structures around multiple metal ions under thermodynamic control. The development of highly effective methods for the covalent capture of supramolecular intermediates (especially RCM and CuAAC) has dramatically improved the yields of many types of mechanical interlocking strategies (Section 1.2.2). Metal ions have been extensively used themselves to "coordinatively capture" threaded or entwined organic building blocks, becoming an intrinsic part of the interlocked structure itself (Section 4). Systems have been developed where template sites can be used repetitively to direct the assembly of multiple ligands, meaning that the number of interlocked components in an assembly is no longer limited to the number of template sites available. In addition to using the coordinating properties (geometries and binding) of metal ions, the catalytic properties of metals are have been used to actively promote covalent bond reactions in the precise region of space required to form mechanically interlocked structures (Section 3).

Moving beyond catenanes and rotaxanes, metal template routes have allowed synthetic chemists to access the simplest classes of knots and higher links (Section 5). Whilst only the most basic types of such architectures have been prepared to date, synthetic strategies and techniques are rapidly developing that will enable far more elaborate structures to be tackled rationally. The challenge that such structures represent—for example, as yet unachieved molecular architectures such as a pentafoil knot, Star of David (a triply interlocked [2]catenane), Whitehead link or a 12-crossing Brunnian link—can be comparable in complexity to the most demanding natural products.

One reason for tackling such problems is that they extend the limit of what it is possible to achieve in synthesis, serving to continually improve the quality of the tools (in terms of both chemistry and strategy) available for molecular construction. However, as biology exemplifies, the organization of matter with topological complexity at the molecular level also offers tremendous potential for achieving novel material properties, for controlling the dynamics of components in molecular machine systems and, in general, for the development of functional molecular/supramolecular/macromolecular systems. Metal-directed synthesis provides powerful, diverse and increasingly sophisticated ways of accessing such structures.

7. Addendum (August 2011)

Since this Review was accepted for publication the field has continued to progress rapidly, with many new and exciting developments. Focused reviews covering topics such as the linking of heterometallic rings (Winpenny),[340] biisoquinoline shuttles (Sauvage)[341] and novel and efficient templates for the assembly of rotaxanes and catenanes (Tian)[342] have all appeared.

The Sauvage group have further developed their "molecular press" [4]rotaxane **51-Cu^I^** (Figure 8), reporting the binding of tetrathiafulvalene between the porphyrin "plates".[343] Using the dpp-containing macrocycle **19** (Scheme 5) and an axle with both bi- and tridentate domains allowed the preparation of a linear [5]rotaxane by a modular assembly strategy.[156] The related [2]-, [3]- and [4]rotaxanes formed from the same axle but with differing numbers of threaded macrocycles were also reported, which have the potential to act as multiple-ring shuttles.[344] The Beer group has used a pyridyl *N*-oxide motif to coordinate alkali metals ($M = Ba^{II}$ or Na^I) to template the formation of [2]rotaxanes.[345] A safer method of demetalation of the classic Sauvage $Cu^I(dpp)_2$ motif—using NH_4OH rather than highly toxic KCN—was reported by Schuster,[346] which could prove a very useful and general procedure. The Schuster group has also reported on the photoexcited state properties of previously reported porphyrin- and fullerene-containing rotaxanes (see Scheme 20 for related structures).[347]

The active metal template strategy has been further refined and its uses elaborated. The use of smaller macrocycle sizes has delivered up to quantitative yields using the CuAAC reaction (with a stoichiometric amount of half-threads), and allowed the use of smaller, commercially available stoppering units, establishing this as amongst the highest yielding and readily accessible routes to stable interlocked structures.[348] Using the Ni^{II}-catalyzed alkyl–alkyl homocoupling active-metal template protocol (Scheme 49), multiple axles have been threaded through a single large macrocycle cavity to form [3]rotaxanes in up to 51 % yield.[349] These were found to be stable to dethreading despite the large macrocycle ring size (unlike previous examples, see Scheme 31). In principle, this approach may allow a rotaxane to be assembled with as many axles in the cavity as the size of the ring and the stoppers will allow. The Anderson group has used an active-metal template directed copper-mediated Glaser coupling[102] to form [2]rotaxanes consisting of butadiyne-linked porphyrin dimers threaded through a phen-based macrocycle (in yields of up to 61 %).[350] The process was used to prepare a spectacular [4]catenane cyclic porphyrin hexamer in 62 % yield, using palladium-catalyzed alkyne homocoupling; a minor by-product shown to be a [7]catenane was also isolated in 6 % yield. Active template synthesis has recently been extended as a strategy to include the synthesis of molecular trefoil knots.[351]

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

A number of new rotaxanes that use metal coordination as stoppering groups or as axle components have been reported. Crown-ether containing pseudorotaxanes with pendant pyridyl groups were capped with Ru^{II} porphyrins or Pd^{II} pybox (pybox = 2,6-bis(4-phenyl-2-oxazolinyl)pyridine) complexes.[352] The Stoddart and Sauvage groups have reported a new $Ru^{II}(bpy)_3$-stoppered rotaxane where the Ru^{II} center acts as a photosensitizer (in the presence of the sacrificial electron donor) to reduce the viologen units to their radical cations and induce switching.[353] A cucurbituril–viologen rotaxane was also stoppered with $Ru^{II}(bpy)_3$ groups in 21% yield by Sun,[354] and its photoinduced electron-transfer properties studied. Ferrocene groups were used by Osakada to stopper rotaxanes in which the rings with pendant Pd^{II} centers were shown to catalyze the ring-closure Mizoroki–Heck reaction more effectively than palladium(II) acetate alone.[355] A rotaxane containing an axle with ferrocene in the center was reported by Beer, which proved capable of electrochemically sensing chloride and sulfate anions.[356] A related system with a ferrocene appended to the macrocycle has also been described.[357] "Branched" [3]rotaxane molecular shuttles with Pd^{II} or Pt^{II} ions in the center that could be operated by photoisomerization of an azobenzene unit,[358] and rotaxane-like structures with axially coordinated Fe^{III}(cyclam) complexes (topologically related to the Mg^{II} containing species shown in Figure 13) have also recently been reported.[359] A $Cu^{I}(dpp)_2$ core with pendant pyridyl groups was coordinated to the Zn^{II} centers of a porphyrin dimer to form a 43-membered ring metal–organic catenane in quantitative yield.[360] The assembly has a high association constant due to the high degree of preorganization and matched spatial orientation of the components. Building on their previous strategy (**180-Zn^{II}**, Scheme 67) the Hardie group has incorporated Ag^{I} ions into new triply interlocked cages;[361] minor modifications of the ligands allowed control over the formation of either interlocked or non-interlocked assemblies.

New metal–organic rotaxane frameworks (MORFs) have been developed by Sessler and co-workers (see Figure 15 for related concepts introduced by Loeb) from a macrocyclic tetraimidazolium "molecular box", a naphthalene dicarboxylate bridging ligand and Zn^{II} cations.[362] Loeb has prepared new [2]rotaxanes with aromatic nitrogen donors appended to the crown-ether macrocycle which act as ligands to coordinate Cd^{II} ions to form extended polyrotaxane systems.[363] Examples in the more traditional sense of polycatenated networks include those by Yang, Ma and co-workers which incorporate rotaxane-like elements[364] and a remarkable 54-fold interpenetrated coordination network[365] that demonstrates the complexity which can be achieved using metal-directed assembly.

A topologically interesting triskelion knotted cyclophane has been prepared by Siegel[366] based on a diphenylbipyridine-containing ligand and Cu^{I} ions, following a previously synthetic strategy to open analogues;[367] the removal of the central template would lead to a trefoil knot. The first molecular example of a new class of interwoven molecules—"ravels"[368]—has been reported by Lindoy.[369] Unlike the other structures in this Review, ravels are not links or knots but have nodes that join multiple connectors making them a type of "branched knot". The beautiful 20-component "universal 3-ravel" was assembled with Fe^{III} ions and bis-β-diketone ligands to generate the $[Fe_8L_{12}]$ structure in 97% yield (on crystallization over a 3 month period).

The $Cu^{I}(dpp)_2$ template has also found new applications. Functionalized with terminal thiol groups, the $Cu^{I}(dpp)_2$ template has been used to form catenated species by coordination to silver or gold nanoparticles.[370] The interlocked nanoparticles were shown to exhibit intense Raman spectra, which may have future sensing applications.[370] When functionalized with suitable groups, a $Cu^{I}(dpp)_2$ template motif acts as an initiator for atom-transfer radical polymerization (ATRP) reaction which can generate interlocking polymer rings.[371] This may also prove an effective route to higher order knotted polymeric structures with useful physico-mechanical properties.

The CuAAC "click" reaction continues to increase in popularity as a method for covalent capture,[88] with many of the above recent examples exploiting this versatile reaction.[344,345,348,353,372]

Finally, inspired by Sauvage's strategy for generating complex molecular topologies by linking the end groups of entwined metal complexes (Figure 5),[115] the seminal work of Lehn in the development of circular helicates (Scheme 4),[59] and by employing many of the strategies and tactics discussed in this Review (Sections 1.1, 1.2 and 1.3), the first synthetic pentafoil knot has been prepared through metal- and anion-directed self-assembly in combination with reversible imine bond formation.[373] More than six billion prime knots are known to mathematics.[301d,374] The number[303] that have succumbed to small molecule chemical synthesis now stands at three.

We thank Dr. A. M. Fuller and Dr. D. B. Walker for their assistance with early versions of this review and Prof. Len Lindoy for useful discussions. We are grateful for financial support from the EPSRC and ERC and for postdoctoral fellowships to J.E.B. (Swiss National Science Foundation) and B.A.B. (EU Marie Curie International Incoming Fellowship program).

Received: December 16, 2010

---

[1] a) "Interlacing Molecular Threads on Transition Metals: Catenands, Catenates, and Knots": (J.-P. Sauvage, *Acc. Chem. Res.* **1990**, *23*, 319–327) is a wonderful account of the thinking behind the Strasbourg group's work on catenane and knot synthesis in the years before other types of template approaches to interlocked molecules were invented. For other reviews of the Sauvage group's early work, see: b) C. O. Dietrich-Buchecker, J.-P. Sauvage, *Chem. Rev.* **1987**, *87*, 795–810; c) J.-C. Chambron, C. Dietrich-Buchecker, C. Hemmert, A. K. Khemiss, D. Mitchell, J.-P. Sauvage, J. Weiss, *Pure Appl. Chem.* **1990**, *62*, 1027–1034; d) C. Dietrich-Buchecker, J.-P. Sauvage, *Tetrahedron* **1990**, *46*, 503–512; e) J.-C. Chambron, C. O. Dietrich-Buchecker, J.-F. Nierengarten, J.-P. Sauvage, *Pure Appl. Chem.* **1994**, *66*, 1543–1550; f) J.-C. Chambron, C. Dietrich-Buchecker, J.-P. Sauvage in *Comprehensive Supramolecular Chemistry*, *Vol. 9* (Eds.: J.-P. Sauvage, M. W. Hos-

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

seini), Elsevier, Oxford, **1996**, pp. 43 – 83; g) *Molecular Catenanes, Rotaxanes and Knots* (Eds.: J.-P. Sauvage, C. O. Dietrich-Buchecker), Wiley-VCH, Weinheim, **1999**.

[2] For reviews on metal template interlocked systems as molecular machine prototypes, see: a) J.-P. Sauvage, *Acc. Chem. Res.* **1998**, *31*, 611 – 619; b) J.-P. Collin, C. Dietrich-Buchecker, P. Gaviña, M. C. Jiménez-Molero, J.-P. Sauvage, *Acc. Chem. Res.* **2001**, *34*, 477 – 487; c) C. Dietrich-Buchecker, M. C. Jiménez-Molero, V. Sartor, J.-P. Sauvage, *Pure Appl. Chem.* **2003**, *75*, 1383 – 1393; d) J.-P. Collin, V. Heitz, S. Bonnet, J.-P. Sauvage, *Inorg. Chem. Commun.* **2005**, *8*, 1063 – 1074; e) J.-P. Collin, V. Heitz, J.-P. Sauvage, *Top. Curr. Chem.* **2005**, *262*, 29 – 62; f) S. Bonnet, J.-P. Collin, M. Koizumi, P. Mobian, J.-P. Sauvage, *Adv. Mater.* **2006**, *18*, 1239 – 1250; g) B. Champin, P. Mobian, J.-P. Sauvage, *Chem. Soc. Rev.* **2007**, *36*, 358 – 366; h) E. R. Kay, D. A. Leigh, F. Zerbetto, *Angew. Chem.* **2007**, *119*, 72 – 196; *Angew. Chem. Int. Ed.* **2007**, *46*, 72 – 191; i) S. Durot, F. Reviriego, J.-P. Sauvage, *Dalton Trans.* **2010**, *39*, 10557 – 10570.

[3] For statistical and directed methods to interlocked structures, see: a) G. Schill, *Catenanes, Rotaxanes and Knots*, Academic Press, New York, **1971**; b) G. Schill, C. Zürcher, *Naturwissenschaften* **1971**, *58*, 40 – 45; for recent examples, see: c) A. Godt, *Eur. J. Org. Chem.* **2004**, 1639 – 1654; d) T. Umehara, H. Kawai, K. Fujiwara, T. Suzuki, *J. Am. Chem. Soc.* **2008**, *130*, 13981 – 13988.

[4] For general reviews on the use of templates to form interlocked structures, see: a) R. Hoss, F. Vögtle, *Angew. Chem.* **1994**, *106*, 389 – 398; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 375 – 384; b) D. B. Amabilino, J. F. Stoddart, *Chem. Rev.* **1995**, *95*, 2725 – 2829; c) M. Fujita in *Comprehensive Supramolecular Chemistry, Vol. 9* (Eds.: J.-P. Sauvage, M. W. Hosseini), Elsevier, Oxford, **1996**, pp. 253 – 282; d) M.-J. Blanco, M. Consuelo Jimenez, J.-C. Chambron, V. Heitz, M. Linke, J.-P. Sauvage, *Chem. Soc. Rev.* **1999**, *28*, 293 – 305; e) D. A. Leigh, A. Murphy, *Chem. Ind.* **1999**, 178 – 183; f) T. J. Hubin, D. H. Busch, *Coord. Chem. Rev.* **2000**, *200–202*, 5 – 52; g) J.-P. Collin, C. Dietrich-Buchecker, C. Hamann, D. Jouvenot, J.-M. Kern, P. Mobian, J.-P. Sauvage in *Comprehensive Coordination Chemistry II, Vol. 7*, **2004**, pp. 303 – 326; h) F. Aricó, J. D. Badjic, S. J. Cantrill, A. H. Flood, K. C. F. Leung, Y. Liu, J. F. Stoddart, *Top. Curr. Chem.* **2005**, *249*, 203 – 259; i) P. Gaviña, S. Tatay, *Curr. Org. Synth.* **2010**, *7*, 24 – 43.

[5] For reviews of the use of π-electron-rich/π-electron-poor interactions to form interlocked structures, see: a) J. F. Stoddart, H.-R. Tseng, *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 4797 – 4800; b) K. E. Griffiths, J. F. Stoddart, *Pure Appl. Chem.* **2008**, *80*, 485 – 506; c) S. J. Loeb, *Chem. Soc. Rev.* **2007**, *36*, 226 – 235; for other examples, see: d) D. G. Hamilton, J. K. M. Sanders, J. E. Davies, W. Clegg, S. J. Teat, *Chem. Commun.* **1997**, 897 – 898; e) H. Y. Au-Yeung, G. D. Pantos, J. K. M. Sanders, *Proc. Natl. Acad. Sci. USA* **2009**, *106*, 10466 – 10470.

[6] For examples of the use of amide-based templates to form interlocked structures, see: a) C. A. Hunter, *J. Am. Chem. Soc.* **1992**, *114*, 5303 – 5311; b) F. Vögtle, S. Meier, R. Hoss, *Angew. Chem.* **1992**, *104*, 1628 – 1631; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1619 – 1622; c) A. G. Johnston, D. A. Leigh, R. J. Pritchard, M. D. Deegan, *Angew. Chem.* **1995**, *107*, 1324 – 1327; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1209 – 1212; d) A. G. Johnston, D. A. Leigh, L. Nezhat, J. P. Smart, M. D. Deegan, *Angew. Chem.* **1995**, *107*, 1327 – 1331; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1212 – 1216; e) A. G. Johnston, D. A. Leigh, A. Murphy, J. P. Smart, M. D. Deegan, *J. Am. Chem. Soc.* **1996**, *118*, 10662 – 10663; f) D. A. Leigh, A. Murphy, J. P. Smart, A. M. Z. Slawin, *Angew. Chem.* **1997**, *109*, 752 – 756; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 728 – 732; g) F. G. Gatti, D. A. Leigh, S. A. Nepogodiev, A. M. Z. Slawin, S. J. Teat, J. K. Y. Wong, *J. Am. Chem. Soc.* **2001**, *123*, 5983 – 5989; h) M. Asakawa, G. Brancato, M. Fanti, D. A. Leigh, T. Shimizu, A. M. Z. Slawin, J. K. Y. Wong, F. Zerbetto, S. Zhang, *J. Am. Chem. Soc.* **2002**, *124*, 2939 – 2950; i) T. Da Ros, D. M. Guldi, A. Farran Morales, D. A. Leigh, M. Prato, R. Turco, *Org. Lett.* **2003**, *5*, 689 – 691; j) G. Bottari, D. A. Leigh, E. M. Pérez, *J. Am. Chem. Soc.* **2003**, *125*, 13360 – 13361; k) J. S. Hannam, S. M. Lacy, D. A. Leigh, C. G. Saiz, A. M. Z. Slawin, S. G. Stitchell, *Angew. Chem.* **2004**, *116*, 3322 – 3326; *Angew. Chem. Int. Ed.* **2004**, *43*, 3260 – 3264; l) D. A. Leigh, M. Á. F. Morales, E. M. Pérez, J. K. Y. Wong, C. G. Saiz, A. M. Z. Slawin, A. J. Carmichael, D. M. Haddleton, A. M. Brouwer, W. J. Buma, G. W. H. Wurpel, S. León, F. Zerbetto, *Angew. Chem.* **2005**, *117*, 3122 – 3127; *Angew. Chem. Int. Ed.* **2005**, *44*, 3062 – 3067; m) "Molecular Machines" (Ed.: T. R. Kelly): E. R. Kay, D. A. Leigh, *Top. Curr. Chem.* **2005**, *262*, 133 – 177.

[7] For examples of the use of ammonium-crown ether templates to form interlocked structures, see: a) S. J. Cantrill, A. R. Pease, J. F. Stoddart, *Dalton* **2000**, 3715 – 3734; b) J. D. Badjic, V. Balzani, A. Credi, J. F. Stoddart, *Science* **2004**, *303*, 1845 – 1849; c) V. Serreli, C.-F. Lee, E. R. Kay, D. A. Leigh, *Nature* **2007**, *445*, 523 – 527; d) D. A. Leigh, A. R. Thomson, *Tetrahedron* **2008**, *64*, 8411 – 8416.

[8] For examples of the use of DNA, RNA or proteins to form artificial interlocked structures, see: a) N. C. Seeman, *Acc. Chem. Res.* **1997**, *30*, 357 – 363; b) N. C. Seeman, H. Wang, X. Yang, F. Liu, C. Mao, W. Sun, L. Wenzler, Z. Shen, R. Sha, H. Yan, M. H. Wong, P. Sa-Ardyen, B. Liu, H. Qiu, X. Li, J. Qi, S. M. Du, Y. Zhang, J. E. Mueller, T.-J. Fu, Y. Wang, J. Chen, *Nanotechnology* **1998**, *9*, 257 – 273; c) L. Z. Yan, P. E. Dawson, *Angew. Chem.* **2001**, *113*, 3737 – 3739; *Angew. Chem. Int. Ed.* **2001**, *40*, 3625 – 3627; d) D. Ackermann, T. L. Schmidt, J. S. Hannam, C. S. Purohit, A. Heckel, M. Famulok, *Nat. Nanotechnol.* **2010**, *5*, 436 – 442.

[9] For examples of the use of ion-pairing to form interlocked structures, see: a) D. J. Hoffart, J. Tiburcio, A. de La Torre, L. K. Knight, S. J. Loeb, *Angew. Chem.* **2008**, *120*, 103 – 107; *Angew. Chem. Int. Ed.* **2008**, *47*, 97 – 101; b) E. Lestini, K. Nikitin, H. Müller-Bunz, D. Fitzmaurice, *Chem. Eur. J.* **2008**, *14*, 1095 – 1106; c) M. J. Barrell, D. A. Leigh, P. J. Lusby, A. M. Z. Slawin, *Angew. Chem.* **2008**, *120*, 8156 – 8159; *. Chem. Int. Ed.* **2008**, *47*, 8036 – 8039; d) Y. Nakatani, Y. Furusho, E. Yashima, *Angew. Chem.* **2010**, *122*, 5595 – 5599; *Angew. Chem. Int. Ed.* **2010**, *49*, 5463 – 5467.

[10] For examples of the use of hydrophobic interactions to form interlocked stuctures, see: a) M. Fujita, K. Ogura, *Coord. Chem. Rev.* **1996**, *148*, 249 – 264; b) M. Fujita, *Chem. Soc. Rev.* **1998**, *27*, 417 – 425; c) S. A. Nepogodiev J. F. Stoddart, *Chem. Rev.* **1998**, *98*, 1959 – 1976; e) M. Fujita, *Acc. Chem. Res.* **1999**, *32*, 53 – 61; f) M. Fujita, M. Tominaga, A. Hori, B. Therrien, *Acc. Chem. Res.* **2005**, *38*, 369 – 378; d) M. J. Frampton, H. L. Anderson, *Angew. Chem.* **2007**, *119*, 1046 – 1083; *Angew. Chem. Int. Ed.* **2007**, *46*, 1028 – 1064.

[11] For reviews on the use of anion templates to form interlocked structures, see: a) M. S. Vickers, P. D. Beer, *Chem. Soc. Rev.* **2007**, *36*, 211 – 225; b) K. M. Mullen, P. D. Beer, *Chem. Soc. Rev.* **2009**, *38*, 1701 – 1713; other examples: c) C. Reuter, W. Wienand, G. M. Hübner, C. Seel, F. Vögtle, *Chem. Eur. J.* **1999**, *5*, 2692 – 2697; d) J. M. Mahoney, R. Shukla, R. A. Marshall, A. M. Beatty, J. Zajicek, B. D. Smith, *J. Org. Chem.* **2002**, *67*, 1436 – 1440; e) P. Ghosh, O. Mermagen, C. A. Schalley, *Chem. Commun.* **2002**, 2628 – 2629.

[12] For the use of radical templates to form interlocked structures, see: H. Li, A. C. Fahrenbach, S. K. Dey, S. Basu, A. Trabolsi, Z. Zhu, Y. Y. Botros, J. F. Stoddart, *Angew. Chem.* **2010**, *122*, 8436 – 8441; *Angew. Chem. Int. Ed.* **2010**, *49*, 8260 – 8265.

[13] For reviews on synthesizing interlocked molecules using reversible reactions, see: a) C. D. Meyer, C. S. Joiner, J. F.

Stoddart, *Chem. Soc. Rev.* **2007**, *36*, 1705 – 1723; b) P. C. Haussmann, J. F. Stoddart, *Chem. Rec.* **2009**, *9*, 136 – 154.

[14] For details concerning CSD searches of coordination complexes, see: a) A. G. Orpen, *Acta Crystallogr. Sect. B* **2002**, *58*, 398 – 406. For the structure search software program Conquest, see: b) I. J. Bruno, J. C. Cole, P. R. Edgington, M. Kessler, C. F. Macrae, P. McCabe, J. Pearson, R. Taylor, *Acta Crystallogr. Sect. B* **2002**, *58*, 389 – 397.

[15] H. L. Frisch, E. Wasserman, *J. Am. Chem. Soc.* **1961**, *83*, 3789 – 3795.

[16] D. M. Lemal, personal communication to D.A.L., 21 December 2010.

[17] a) Wasserman credits L. Friedman, an Ohio State graduate student, with a proposal for a many-step catenane synthesis in 1956 (E. Wasserman in *Molecular Catenanes, Rotaxanes and Knots* (Eds.: J.-P. Sauvage, C. O. Dietrich-Buchecker), Wiley-VCH, Weinheim, **1999**, chap. 1). In addition to Lemal and Wasserman, at least four other groups were independently tackling the problem of catenane synthesis in the middle-to-late 1950s: Lüttringhaus (Freiburg), Cramer (Heidelberg), Köhler and Dietrich (Tübingen), and von Gulick (Oregon), see: b) D. M. Walba, *Tetrahedron* **1985**, *41*, 3161 – 3212. For the earliest attempts at catenane synthesis reported in the scientific literature, see: c) A. Lüttringhaus, F. Cramer, H. Prinzbach, F. M. Henglein, *Justus Liebigs Ann. Chem.* **1958**, *613*, 185 – 198; d) A. Lüttringhaus, F. Cramer, H. Prinzbach, *Angew. Chem.* **1957**, *60*, 137.

[18] G. Schill, A. Lüttringhaus, *Angew. Chem.* **1964**, *76*, 567 – 568; *Angew. Chem. Int. Ed. Engl.* **1964**, *3*, 546 – 547.

[19] Sokolov suggested that "Coordination compounds of metals can be used as scaffolding for building up catenoid structures", see: V. I. Sokolov, *Usp. Khim.* **1973**, *42*, 1037 – 1059. (English translation: *Russ. Chem. Rev.* **1973**, *42*, 452 – 463).

[20] a) H. Ogino, *J. Am. Chem. Soc.* **1981**, *103*, 1303 – 1304; b) H. Ogino, K. Ohata, *Inorg. Chem.* **1984**, *23*, 3312 – 3316.

[21] C. O. Dietrich-Buchecker, J.-P. Sauvage, J.-P. Kintzinger, *Tetrahedron Lett.* **1983**, *24*, 5095 – 5098.

[22] C. O. Dietrich-Buchecker, J.-P. Sauvage, J.-M. Kern, *J. Am. Chem. Soc.* **1984**, *106*, 3043 – 3045.

[23] There are several early examples of macrocycle synthesis by metal template effects, although the cyclic nature of the products was not always appreciated at the time: In 1898 Posner (accidentally) condensed 2-aminobenzaldehyde in the presence of Zn^{II}, see a) T. Posner, *Ber. Dtsch. Chem. Ges.* **1898**, *31*, 656 – 660. Twenty-eight years later the reaction was repeated by Seidel, see b) F. Seidel, *Ber. Dtsch. Chem. Ges. B* **1926**, *59*, 1894 – 1908, and the elemental composition determined and later shown to be macrocycle **4**, see Ref. [28a]. For a review of these systems, see c) A. G. Kolchinski, *Coord. Chem. Rev.* **1998**, *174*, 207 – 239. Another very early example is Cu^{II}-phthalocyanine, prepared in 1927 (d) H. de Diesbach, E. von der Weid, *Helv. Chem. Acta* **1927**, *10*, 886 – 888) but correctly identified (and named) by Linstead in 1934, see: e) R. P. Linstead, *J. Chem. Soc.* **1934**, 1016 – 1017; f) C. E. Dent, R. P. Linstead, *J. Chem. Soc.* **1934**, 1027 – 1031; g) C. E. Dent, R. P. Linstead, A. R. Lowe, *J. Chem. Soc.* **1934**, 1033 – 1039; h) G. T. Byrne, R. P. Linstead, A. R. Lowe, *J. Chem. Soc.* **1934**, 1017 – 1022; i) R. P. Linstead, A. R. Lowe, *J. Chem. Soc.* **1934**, 1022 – 1027. Almost contemporaneously a metallophthalocyanine complex was also synthesized by chance in 1928 in Grangemouth (25 miles north of Edinburgh) at Scottish Dyes Ltd (later to become part of ICI), see Ref. [23e].

[24] Around the same time as Busch's reports, Curtis extensively investigated condensation reactions of aldehydes and amines in the presence of metal salts, preparing (a) N. F. Curtis, *J. Chem. Soc.* **1960**, 4409 – 4413) and recognizing (b) N. F. Curtis, D. A. House, *Chem. Ind.* **1961**, 1708 – 1709) the first non-aromatic tetraazamacrocycles, see: c) D. A. House, N. F. Curtis, *J. Am. Chem. Soc.* **1962**, *84*, 3248 – 3250; d) N. F. Curtis, *Coord. Chem. Rev.* **1968**, *3*, 3 – 47. These cyclization reactions, where the mode of action of the metal was not identified, were also later suggested (see ref. [31]) to have been the result of successive thermodynamic template and kinetic template reactions.

[25] For reviews on the template effect, see: a) D. H. Busch, *Science* **1971**, *171*, 241 – 248; b) D. H. Busch, N. A. Stephenson, *Coord. Chem. Rev.* **1990**, *100*, 119 – 154. For historical views, principles and perspectives on template effects, see c) D. H. Busch, A. L. Vance, A. G. Kolchinski in *Comprehensive Supramolecular Chemistry*, *Vol. 9* (Eds.: J.-P. Sauvage, M. W. Hosseini), Elsevier, Oxford, **1996**, pp. 1 – 42; d) "Templates in Organic Synthesis: Definitions and Roles": S. Anderson, H. L. Anderson in *Templated Organic Synthesis* (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, Weinheim, **2000**, chap. 1, pp. 1 – 38; e) D. H. Busch, *Top. Curr. Chem.* **2005**, *249*, 1 – 65; f) for a recent interview with D. H. Busch, see: D. H. Busch, J. A. Heppert, *Coord. Chem. Rev.* **2010**, 1593 – 1606.

[26] A prescient suggestion that synthetic chemists might try to mimic the selectivity observed with biological templates was put forward by Todd, see: A. R. Todd in *Perspectives in Organic Chemistry* (Ed.: A. R. Todd), Interscience, London, **1956**, p. 263.

[27] For the first discussions of the template effect, see: a) M. C. Thompson, D. H. Busch, *Chem. Eng. News* **1962**, *17*, 57; b) M. C. Thompson, D. H. Busch, *J. Am. Chem. Soc.* **1962**, *84*, 1762 – 1763.

[28] For Busch's first investigation of **4-Ni^{II}**, see: a) G. A. Melson, D. H. Busch, *Proc. Chem. Soc.* **1963**, 223 – 224; b) G. A. Melson, D. H. Busch, *J. Am. Chem. Soc.* **1964**, *86*, 4830 – 4833.

[29] For later studies of **4-M^{II}**, see: a) G. A. Melson, D. H. Busch, *J. Am. Chem. Soc.* **1964**, *86*, 4834 – 4837; b) G. A. Melson, D. H. Busch, *J. Am. Chem. Soc.* **1965**, *87*, 1706 – 1710; c) D. H. Busch, S. C. Cummings, *Inorg. Chem.* **1971**, *10*, 1220 – 1224; d) V. Katovic, S. C. Vergez, D. H. Busch, *Inorg. Chem.* **1977**, *16*, 1716 – 1720; e) A. M. Tait, D. H. Busch, *Inorg. Synth.* **1978**, *18*, 30 – 36.

[30] For the first deliberate use of the kinetic template effect, see a) M. C. Thompson, D. H. Busch, *J. Am. Chem. Soc.* **1964**, *86*, 3651 – 3656; b) E. L. Blinn, D. H. Busch, *Inorg. Chem.* **1968**, *7*, 820 – 824.

[31] For explanations of the thermodynamic and kinetic template effects, see: M. C. Thompson, D. H. Busch, *J. Am. Chem. Soc.* **1964**, *86*, 213 – 217.

[32] For the first example of a template effect where a ligand completely encapsulated a metal ion, see: a) J. D. Curry, D. H. Busch, *J. Am. Chem. Soc.* **1964**, *86*, 592 – 594; b) for a related square planar Ni^{II} complex, see: J. L. Karn, D. H. Busch, *Nature* **1966**, *211*, 160 – 162; c) for a related 7-coordinate Fe^{III} complex, see: S. M. Nelson, P. Bryan, D. H. Busch, *Chem. Commun.* **1966**, 641 – 642.

[33] Busch defined a chemical template in the following way: "A chemical template organizes an assembly of atoms with respect to one or more geometric loci, in order to achieve a particular linking of atoms." D. H. Busch, *J. Inclusion Phenom. Mol. Recognit. Chem.* **1992**, *12*, 389 – 395.

[34] The term "thermodynamic template" effect can refer to the formation of species that are kinetically trapped and thereby removed from dynamic exchange with other components: there is no requirement that these are thermodynamically preferred products. See also ref. [54].

[35] Proximity effects are common in enzyme catalysis: "Because enzyme-catalyzed reactions are contained within an active site of a protein, proximity effects caused by the high effective concentrations of reactive groups are important for enzyme-catalyzed reactions." (a) "Enzyme catalysis: chemical strat-

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

egies": T. D. H. Bugg, *Wiley Encycl. Chem. Biol.* **2009**, *1*, 653–663); b) for a discussion of the template synthesis of benzo-[18]crown-6 in terms of proximity effects, see: G. Illuminati, L. Mandolini, B. Masci, *J. Am. Chem. Soc.* **1983**, *105*, 555–563; c) G. Ercolani, L. Mandolini, B. Masci, *J. Am. Chem. Soc.* **1983**, *105*, 6146–6149.

[36] E. Bamberger, *Ber. Dtsch. Chem. Ges. B* **1927**, *60*, 314–319.

[37] When $\mathrm{Ni^{II}}$ is used both tetramer **4-$\mathrm{Ni^{II}}$** and a trimer complex were obtained (in almost equal amounts), see Ref. [29a] and [29b], as the latter can assemble in a *fac*-coordination mode around octahedral $\mathrm{Ni^{II}}$, see Ref. [25e] and [27].

[38] The kinetic template effect often relies on "substitution-inert" complexes. However, the coordinated ligand may be required to be detached from the metal in order to react or, alternatively, the metal may activate the ligand for further reaction (as occurs in metal catalysis). The only requirement is that the metal center assists in bringing the two reactive groups close together in space.

[39] In this example the coordinated sulfur atoms will be deactivated by coordination and although they may react when coordinated, it is more likely that the reaction proceeds primarily through de-coordinated sulfide. See Ref. [38].

[40] The metal template approach was first extended to three dimensions by Boston and Rose who reported a clathrochelate complex in 1968, see a) D. R. Boston, N. J. Rose, *J. Am. Chem. Soc.* **1968**, *90*, 6859–6860; for other early metal template cage compounds, see: b) J. E. Parks, B. E. Wagner, R. H. Holm, *Inorg. Chem.* **1971**, *10*, 2472–2478; c) J. E. Parks, B. E. Wagner, R. H. Holm, *J. Am. Chem. Soc.* **1970**, *92*, 3500–3502.

[41] a) I. I. Creaser, J. M. Harrowfield, A. J. Herlt, A. M. Sargeson, J. Springborg, R. J. Geue, M. R. Snow, *J. Am. Chem. Soc.* **1977**, *99*, 3181–3182. Sargeson prepared other cage complexes, see for example: b) R. J. Geue, T. W. Hambley, J. M. Harrowfield, A. M. Sargeson, M. R. Snow, *J. Am. Chem. Soc.* **1984**, *106*, 5478–5488. These and their derivatives continue to be studied as supramolecular synthons, see for example: c) J. Clark, A. Crispini, P. S. Donnelly, L. M. Engelhardt, J. M. Harrowfield, S.-H. Jeong, Y. Kim, G. A. Koutsantonis, Y. H. Lee, N. A. Lengkeek, M. Mocerino, G. L. Nealon, M. I. Ogden, Y. C. Park, C. Pettinari, L. Polanzan, E. Rukmini, A. M. Sargeson, B. W. Skelton, A. N. Sobolev, P. Thuery, A. H. White, *Aust. J. Chem.* **2009**, *62*, 1246–1260.

[42] For the discovery of the template synthesis of crown ethers, see: a) C. J. Pedersen, *J. Am. Chem. Soc.* **1967**, *89*, 2495–2496; b) C. J. Pedersen, *Aldrichimica Acta* **1971**, *4*, 1–4; c) C. J. Pedersen, *Science* **1988**, *241*, 536–540. For the development of host-guest chemistry of crown ethers by Cram, see: d) D. J. Cram, J. M. Cram, *Science* **1974**, *183*, 803–809; e) D. J. Cram, *Science* **1983**, *219*, 1177–1183; f) D. J. Cram, *Angew. Chem.* **1988**, *100*, 1041–1052; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1009–1020; g) D. J. Cram, *Science* **1988**, *240*, 760–767. For the development and study of cryptates by Lehn, see: h) B. Dietrich, J.-M. Lehn, J.-P. Sauvage, *Tetrahedron Lett.* **1969**, *10*, 2889–2892; i) J. M. Lehn, *Pure Appl. Chem.* **1978**, *50*, 871–892; j) J. M. Lehn, *Acc. Chem. Res.* **1978**, *11*, 49–57.

[43] For a detailed discussion of macrocycle complexes, see: a) L. F. Lindoy, *The Chemistry of Macrocyclic Ligand Complexes*, Cambridge University Press, Cambridge, **1989**. For the metal template synthesis of cyclam, see: b) E. K. Barefield, F. Wagner, A. W. Herlinger, A. R. Dahl, *Inorg. Synth.* **1976**, *16*, 220–225; and for important early dibenzotetraaza[14]annulenes macrocycle derivatives, see: c) E. G. Jaeger, *Z. Anorg. Allg. Chem.* **1969**, *364*, 177–191.

[44] For other examples of cages formed by metal template methods, see: a) T. J. McMurry, S. J. Rodgers, K. N. Raymond, *J. Am. Chem. Soc.* **1987**, *109*, 3451–3453; b) D. F. Perkins, L. F. Lindoy, A. McAuley, G. V. Meehan, P. Turner, *Proc. Natl. Acad. Sci. USA* **2006**, *103*, 532–537.

[45] For other recent examples of the use of metal templates in synthesis, see: a) F. E. Hahn, V. Langenhahn, T. Lügger, T. Pape, D. Le Van, *Angew. Chem.* **2005**, *117*, 3825–3829; *Angew. Chem. Int. Ed.* **2005**, *44*, 3759–3763; b) P. G. Edwards, R. Haigh, D. Li, P. D. Newman, *J. Am. Chem. Soc.* **2006**, *128*, 3818–3830; c) O. Kaufhold, A. Stasch, T. Pape, A. Hepp, P. G. Edwards, P. D. Newman, F. E. Hahn, *J. Am. Chem. Soc.* **2009**, *131*, 306–317; d) P. O. Lagaditis, A. A. Mikhailine, A. J. Lough, R. H. Morris, *Inorg. Chem.* **2010**, *49*, 1094–1102; e) for a review of template-directed macrocycle synthesis, see: f) Z. R. Laughrey, B. C. Gibb, *Top. Curr. Chem.* **2005**, *249*, 67–125; g) L. Fabbrizzi, M. Licchelli, L. Mosca, A. Poggi, *Coord. Chem. Rev.* **2010**, *254*, 1628–1636.

[46] C. M. Harris, E. D. McKenzie, *J. Chem. Soc. A* **1969**, *5*, 746–753.

[47] C. J. Carrano, K. N. Raymond, *J. Am. Chem. Soc.* **1978**, *100*, 5371–5374.

[48] a) D. Wester, G. J. Palenik, *J. Chem. Soc. Chem. Commun.* **1975**, 74–75; b) D. Wester, G. J. Palenik, *Inorg. Chem.* **1976**, *15*, 755–761; c) G. Struckmeier, U. Thewalt, J. H. Fuhrhop, *J. Am. Chem. Soc.* **1976**, *98*, 278–279; for a related structure reported later, see: d) W. S. Sheldrick, J. Engel, *J. Chem. Soc. Chem. Commun.* **1980**, 5–6.

[49] G. C. van Stein, H. van der Poel, G. van Koten, A. L. Spek, A. J. M. Duisenberg, P. S. Pregosin, *J. Chem. Soc. Chem. Commun.* **1980**, 1016–1018.

[50] For the first entwinned complex from Lehn's lab, see: a) J.-M. Lehn, J.-P. Sauvage, J. Simon, R. Ziessel, C. Piccinni-Leopardi, G. Germain, J.-P. Declercq, M. van Meerssche, *Nouv. J. Chim.* **1983**, *7*, 413–420; Lehn later coined the term "helicate" to describe this class of architecture, see: b) J. M. Lehn, A. Rigault, J. Siegel, J. Harrowfield, B. Chevrier, D. Moras, *Proc. Natl. Acad. Sci. USA* **1987**, *84*, 2565–2569.

[51] For reviews of self-assembled helicates, see: a) E. C. Constable, *Tetrahedron* **1992**, *48*, 10013–10059; b) M. Albrecht, *Chem. Rev.* **2001**, *101*, 3457–3497; c) C. Piguet, G. Bernardinelli, G. Hopfgartner, *Chem. Rev.* **1997**, *97*, 2005–2062.

[52] Lehn introduced the "self-assembly" and "self-recognition" principles using helicates, see: a) J.-M. Lehn, A. Rigault, *Angew. Chem.* **1988**, *100*, 1121–1122; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1095–1097; b) R. Kramer, J. M. Lehn, A. Marquis-Rigault, *Proc. Natl. Acad. Sci. USA* **1993**, *90*, 5394–5398.

[53] For reviews on the thermodynamics of self-assembly of multinuclear systems (including helicates), see: a) C. Piguet, M. Borkovec, J. Hamacek, K. Zeckert, *Coord. Chem. Rev.* **2005**, *249*, 705–726; b) J. Hamacek, M. Borkovec, C. Piguet, *Chem. Eur. J.* **2005**, *11*, 5217–5226; c) J. Hamacek, M. Borkovec, C. Piguet, *Chem. Eur. J.* **2005**, *11*, 5227–5237.

[54] Whilst the terms "thermodynamic template" and "thermodynamic control" are sometimes used interchangeably in the literature they actually mean two quite different things: In the sense introduced by Busch, see Ref. [27], "thermodynamic template" (also called an "equilibrium template") refers to a reaction in which the composition of a dynamic mixture is altered by the formation of a complex between one or more of the components and a template. Through Le Châtelier's principle the reactants are converted to a product favored by the template. This product may be the most thermodynamically stable, or its formation may be a kinetic trap (through crystallization, for example) in which case its formation is not (fully) reversible. Systems under "thermodynamic control" neccessarily involve reversible reactions between the reacting species and, by definition, the major product formed is always the most thermodynamically stable.

[55] For early examples of helicates formed from oligopyridine ligands, see: a) E. C. Constable, M. G. B. Drew, M. D. Ward, *J. Chem. Soc. Chem. Commun.* **1987**, 1600 – 1601; b) M. Barley, E. C. Constable, S. A. Corr, R. C. S. McQueen, J. C. Nutkins, M. D. Ward, M. G. B. Drew, *J. Chem. Soc. Dalton Trans.* **1988**, 2655 – 2662.

[56] a) A. F. Williams, C. Piguet, G. Bernardinelli, *Angew. Chem.* **1991**, *103*, 1530 – 1532; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1490 – 1492; b) the first triple helicate formed with two metal ions was reported by Harris and McKenzie, see Ref. [46].

[57] R. Krämer, J. M. Lehn, A. De Cian, J. Fischer, *Angew. Chem.* **1993**, *105*, 764 – 767; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 703 – 706.

[58] For an example of a helicate formed from two different strands (one with bpy groups, the other with tpy groups) and Cu^{II}, see: B. Hasenknopf, J.-M. Lehn, G. Baum, D. Fenske, *Proc. Natl. Acad. Sci. USA* **1996**, *93*, 1397 – 1400.

[59] For early circular helicates, see: a) B. Hasenknopf, J.-M. Lehn, B. O. Kneisel, G. Baum, D. Fenske, *Angew. Chem.* **1996**, *108*, 1987 – 1990; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1838 – 1840; b) B. Hasenknopf, J.-M. Lehn, N. Boumediene, A. Dupont-Gervais, A. van Dorsselaer, B. Kneisel, D. Fenske, *J. Am. Chem. Soc.* **1997**, *119*, 10956 – 10962; c) for a discussion on the role of the anion in templating the assembly of these systems, see: B. Hasenknopf, J.-M. Lehn, N. Boumediene, E. Leize, A. van Dorsselaer, *Angew. Chem.* **1998**, *110*, 3458 – 3460; *Angew. Chem. Int. Ed.* **1998**, *37*, 3265 – 3268.

[60] C. O. Dietrich-Buchecker, P. A. Marnot, J.-P. Sauvage, *Tetrahedron Lett.* **1982**, *23*, 5291 – 5294.

[61] a) C. O. Dietrich-Buchecker, P. A. Marnot, J.-P. Sauvage, J. R. Kirchoff, D. R. McMillin, *J. Chem. Soc. Chem. Commun.* **1983**, 513 – 515; b) C. O. Dietrich-Buchecker, J.-P. Sauvage, *Tetrahedron Lett.* **1983**, *24*, 5091 – 5094.

[62] M. Cesario, C. O. Dietrich-Buchecker, J. Guilhem, C. Pascard, J.-P. Sauvage, *J. Chem. Soc. Chem. Commun.* **1985**, 244 – 247.

[63] Sauvage introduced the name "catenates" to refer to metal complexes of catenanes. The free interlocked ligands are termed "catenands", see Ref. [22].

[64] Covalent capture refers to a process that stabilizes a supramolecular structure by the introduction of covalent bonds, the formation of which does not significantly change the overall structure of the captured assembly. For a reviews, see: a) J. D. Hartgerink, *Curr. Opin. Chem. Biol.* **2004**, *8*, 604 – 609; b) L. J. Prins, P. Scrimin, *Angew. Chem.* **2009**, *121*, 2324 – 2343; *Angew. Chem. Int. Ed.* **2009**, *48*, 2288 – 2306.

[65] For a review covering atomic orbitals, symmetry, and coordination geometries of metal complexes, see R. B. King, *Coord. Chem. Rev.* **2000**, *197*, 141 – 168.

[66] Ideal tetrahedral centers orientate two bidentate ligands orthogonally in a "2+2" arrangement. Octahedral centers have been used in three distinct coordination modes, shown in Figure 2c: a "3+3" coordination motif, whereby two tridentate ligands bind in a *mer* configuration to the metal center placing the two ligands in an orthogonal arrangement, and "4+2" and "2+2+2" coordination motifs that employ tetradentate and/or *cis*-bidentate ligands. Trigonal bipyramidal (Figure 2b) enables a "3+2" approach in which the ligands can also be organized orthogonally.

[67] In the simplest cases, where no ligand field effects are present (as is the case with main group metals or transition metal ions with d^{0}, d^{5} and d^{10} configurations; see a) R. J. Deeth in *Comprehensive Coordination Chemistry II*, *Vol. 2* (Eds.: J. A. McCleverty, T. J. Meyer), Elsevier, Oxford, **2004**, pp. 439 – 442) the arrangement of the ligands around the metal ion should be in accord with VPSER rules, see Ref. [51a] and b) R. J. Gillespie, *Coord. Chem. Rev.* **2008**, *252*, 1315 – 1327. That is, with no ligand field stabilization, the coordination geometry is determined only by size, electrostatic and covalent bonding factors. Other commonly used metal ions: Ru^{II} and Fe^{II} (both d^{6}) which commonly form low-spin pseudo-octahedral complexes; Pd^{II} (d^{8}) which is almost exclusively square planar and Zn^{II} (d^{10}) is typically 5-coordinate. Co^{II}, Co^{III}, Fe^{III} all commonly form octahedral complexes. Ag^{I} and Au^{I} although also d^{10} ions, are significantly larger in size than Cu^{I} and there are few chemical similarities with these adopting a wide range of coordination numbers (2- to 6-coordinate) with linear arrangements as the most common geometry, see c) F. A. Cotton, G. Wilkinson, *Advanced Inorganic Chemistry*, 5 ed., Wiley, New York, **1988**.

[68] The thermodynamic stability of a metal – ligand complex is related to both ligand preorganization and metal – ligand complementarity, see: P. Comba, W. Schiek, *Coord. Chem. Rev.* **2003**, *238*, 21 – 29. It is for this reason that matching the coordination preferences of the metal with the donor environment provided by the ligand(s) is of critical importance for the desired structure to be thermodynamically preferred.

[69] The use of a limited collection of metal ions has been in part influenced by the desire to use diamagnetic metal ions (e.g. Cu^{I}, Ag^{I}, Zn^{II}, Cd^{II}, Pd^{II}, low spin Fe^{II} and Ru^{II}) to allow standard NMR techniques to be used to study the resulting complexes.

[70] For a detailed study of the kinetics of formation of **20-Cu**$^{\mathbf{I}}$ and the stability delivered by the catenand effect, see: a) A. M. Albrecht-Gary, Z. Saad, C. O. Dietrich-Buchecker, J.-P. Sauvage, *J. Am. Chem. Soc.* **1985**, *107*, 3205 – 3209. For studies on the kinetics and stability of the complexation of Cu^{I}, Ag^{I}, Li^{I}, Co^{II}, Zn^{II} and Cd^{II} ions by catenand **20**, see: b) A. M. Albrecht-Gary, C. Dietrich-Buchecker, Z. Saad, J.-P. Sauvage, *J. Am. Chem. Soc.* **1988**, *110*, 1467 – 1472; c) F. Arnaud-Neu, E. Marques, M. J. Schwing-Weill, C. Dietrich-Buchecker, J.-P. Sauvage, J. Weiss, *New J. Chem.* **1988**, *12*, 15 – 20.

[71] A number of other catenates [Li^{I}, Ni^{II}, Zn^{II}, and Cd^{II}] have been prepared while the non-interlocked analogues proved too unstable to be isolated, highlighting the stability of interlocked assemblies, see: a) C. Dietrich-Buchecker, J. P. Sauvage, J. M. Kern, *J. Am. Chem. Soc.* **1989**, *111*, 7791 – 7800. In the most impressive example, an air stable tetrahedral Ni^{I} complex was prepared, see: b) C. O. Dietrich-Buchecker, J. Guilhem, J.-M. Kern, C. Pascard, J.-P. Sauvage, *Inorg. Chem.* **1994**, *33*, 3498 – 3502. However, although Pd^{II} was found to coordinate to catenand **20**, this d^{8} metal fulfilled its desire to form a square planar coordination geometry by undergoing orthometalation to a phenyl group to avoid the imposed tetrahedral geometry of the catenand, see: c) A. J. Blake, C. O. Dietrich-Buchecker, T. I. Hyde, J. P. Sauvage, M. Schröder, *J. Chem. Soc. Chem. Commun.* **1989**, 1663 – 1665.

[72] An anionic copper complex was formed by a two electron reduction of the **20-Cu**$^{\mathbf{I}}$ catenane, demonstrating the ability of the catenane to stabilize lower oxidation states, see: Ref. [71a].

[73] The destabilizing effect of the catenand on high oxidation states was demonstrated, with attempts to form catenates with Fe^{III} or Co^{III} with catenand **20** proving unsuccessful (oxidation of the ligand resulted instead), see: Ref. [71a].

[74] Piguet and co-workers have discussed in detail the thermodynamics of self-assembly in the context of polynuclear complexes, see: a) Ref. [53b–d]; b) J. Hamacek, M. Borkovec, C. Piguet, *Dalton Trans.* **2006**, 1473 – 1490; c) T. Riis-Johannessen, N. Dalla Favera, T. K. Todorova, S. M. Huber, L. Gagliardi, C. Piguet, *Chem. Eur. J.* **2009**, *15*, 12702 – 12718; d) C. Piguet, *Chem. Commun.* **2010**, *46*, 6209 – 6231.

[75] Intermolecular reactions (that is, between complexes) will result in the formation of oligomers and historically this is a major contributing factor to the low yields found in the preparation of interlocked structures. This problem can be minimized by employing high dilution conditions.

[76] D. A. Leigh, P. J. Lusby, R. T. McBurney, A. Morelli, A. M. Z. Slawin, A. R. Thomson, D. B. Walker, *J. Am. Chem. Soc.* **2009**, *131*, 3762–3771.

[77] C. Hamann, J.-M. Kern, J.-P. Sauvage, *Dalton Trans.* **2003**, 3770–3775.

[78] a) A.-M. L. Fuller, D. A. Leigh, P. J. Lusby, A. M. Z. Slawin, D. B. Walker, *J. Am. Chem. Soc.* **2005**, *127*, 12612–12619; b) D. A. Leigh, P. J. Lusby, A. M. Z. Slawin, D. B. Walker, *Chem. Commun.* **2005**, 4919–4921.

[79] N. S. Zefirov, *Tetrahedron* **1977**, *33*, 3193–3202.

[80] S. Wolfe, *Acc. Chem. Res.* **1972**, *5*, 102–111.

[81] G. R. Desiraju, *Angew. Chem.* **1995**, *107*, 2541–2558; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2311–2327.

[82] The increased yield of cyclization of the complex compared to the cyclization of the free ligand provides evidence for the stabilizing interactions, see a) B. Mohr, M. Weck, J.-P. Sauvage, R. H. Grubbs, *Angew. Chem.* **1997**, *109*, 1365–1367; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1308–1310; b) M. Weck, B. Mohr, J.-P. Sauvage, R. H. Grubbs, *J. Org. Chem.* **1999**, *64*, 5463–5471.

[83] a) P. Schwab, M. B. France, J. W. Ziller, R. H. Grubbs, *Angew. Chem.* **1995**, *107*, 2179–2181; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2039–2041; b) P. Schwab, R. H. Grubbs, J. W. Ziller, *J. Am. Chem. Soc.* **1996**, *118*, 100–110.

[84] D. A. Leigh, P. J. Lusby, S. J. Teat, A. J. Wilson, J. K. Y. Wong, *Angew. Chem.* **2001**, *113*, 1586–1591; *Angew. Chem. Int. Ed.* **2001**, *40*, 1538–1543.

[85] C. O. Dietrich-Buchecker, A. Khemiss, J.-P. Sauvage, *J. Chem. Soc. Chem. Commun.* **1986**, 1376–1378.

[86] a) V. V. Rostovtsev, L. G. Green, V. V. Fokin, K. B. Sharpless, *Angew. Chem.* **2002**, *114*, 2708–2711; *Angew. Chem. Int. Ed.* **2002**, *41*, 2596–2599. For a metal-complex-tolerant CuAAC protocol applied to mixed metal complex rotaxanes, see: b) D. González Cabrera, B. D. Koivisto, D. A. Leigh, *Chem. Commun.* **2007**, 4218–4220.

[87] P. Mobian, J.-P. Collin, J.-P. Sauvage, *Tetrahedron Lett.* **2006**, *47*, 4907–4909. A later study saw the replacement of the bpy unit with a phen-based group although the more inert $[\mathrm{Cu^I(phen)_2}]$ motif resulted in only a modest increase in the yield of rotaxane (67%), see: S. Durot, P. Mobian, J.-P. Collin, J.-P. Sauvage, *Tetrahedron* **2008**, *64*, 8496–8503.

[88] K. D. Hänni, D. A. Leigh, *Chem. Soc. Rev.* **2010**, *39*, 1240–1251.

[89] C. Dietrich-Buchecker, G. Rapenne, J.-P. Sauvage, *Coord. Chem. Rev.* **1999**, *185–186*, 167–176.

[90] C. A. Hunter, C. M. R. Low, M. J. Packer, S. E. Spey, J. G. Vinter, M. O. Vysotsky, C. Zonta, *Angew. Chem.* **2001**, *113*, 2750–2754; *Angew. Chem. Int. Ed.* **2001**, *40*, 2678–2682.

[91] M. Fujita, F. Ibukuro, H. Hagihara, K. Ogura, *Nature* **1994**, *367*, 720–723.

[92] D. M. Whang, K. M. Park, J. Heo, P. Ashton, K. Kim, *J. Am. Chem. Soc.* **1998**, *120*, 4899–4900.

[93] H. G. Richey, D. M. Kushlan, *J. Am. Chem. Soc.* **1987**, *109*, 2510–2512.

[94] Other template interactions, such as hydrogen-bonding, π-donor/π-acceptor, hydrophobic interactions, and anion template are usually responsible for directing formation of the crossing point before the metal ion connects the subcomponents together.

[95] K. M. Park, D. Whang, E. Lee, J. Heo, K. Kim, *Chem. Eur. J.* **2002**, *8*, 498–508.

[96] M. E. Padilla-Tosta, O. D. Fox, M. G. B. Drew, P. D. Beer, *Angew. Chem.* **2001**, *113*, 4365–4369; *Angew. Chem. Int. Ed.* **2001**, *40*, 4235–4239.

[97] K.-S. Jeong, J. S. Choi, S.-Y. Chang, H.-Y. Chang, *Angew. Chem.* **2000**, *112*, 1758–1761; *Angew. Chem. Int. Ed.* **2000**, *39*, 1692–1695.

[98] S. J. Loeb, J. A. Wisner, *Chem. Commun.* **1998**, 2757–2758.

[99] G. J. E. Davidson, S. J. Loeb, N. A. Parekh, J. A. Wisner, *J. Chem. Soc. Dalton Trans.* **2001**, 3135–3136.

[100] J. D. Crowley, S. M. Goldup, A.-L. Lee, D. A. Leigh, R. T. McBurney, *Chem. Soc. Rev.* **2009**, *38*, 1530–1541.

[101] V. Aucagne, K. D. Hänni, D. A. Leigh, P. J. Lusby, D. B. Walker, *J. Am. Chem. Soc.* **2006**, *128*, 2186–2187.

[102] S. Saito, E. Takahashi, K. Nakazono, *Org. Lett.* **2006**, *8*, 5133–5136.

[103] J. Berná, S. M. Goldup, A.-L. Lee, D. A. Leigh, M. D. Symes, G. Teobaldi, F. Zerbetto, *Angew. Chem.* **2008**, *120*, 4464–4468; *Angew. Chem. Int. Ed.* **2008**, *47*, 4392–4396.

[104] J. Berná, J. D. Crowley, S. M. Goldup, K. D. Hänni, A.-L. Lee, D. A. Leigh, *Angew. Chem.* **2007**, *119*, 5811–5815; *Angew. Chem. Int. Ed.* **2007**, *46*, 5709–5713.

[105] J. D. Crowley, K. D. Hänni, A.-L. Lee, D. A. Leigh, *J. Am. Chem. Soc.* **2007**, *129*, 12092–12093.

[106] S. M. Goldup, D. A. Leigh, P. J. Lusby, R. T. McBurney, A. M. Z. Slawin, *Angew. Chem.* **2008**, *120*, 3429–3432; *Angew. Chem. Int. Ed.* **2008**, *47*, 3381–3384.

[107] J. D. Crowley, K. D. Hänni, D. A. Leigh, A. M. Z. Slawin, *J. Am. Chem. Soc.* **2010**, *132*, 5309–5314.

[108] J. D. Crowley, S. M. Goldup, N. D. Gowans, D. A. Leigh, V. E. Ronaldson, A. M. Z. Slawin, *J. Am. Chem. Soc.* **2010**, *132*, 6243–6248.

[109] S. M. Goldup, D. A. Leigh, R. T. McBurney, P. R. McGonigal, A. Plant, *Chem. Sci.* **2010**, *1*, 383–386.

[110] Intramolecular cyclizations between "A + Y" and "B + X" termini lead to a trefoil knot whereas intermolecular cyclizations between "A + B" and "X + Y" lead to the doubly-entwined rings (a Solomon link).

[111] Borromean rings (Scheme 14ei) can, in principle, be built up by a "ring-in-ring" approach. Starting from one macrocycle (orange), a second macrocycle (blue) can be orientated within the cavity of the orange ring by the use of two metal ions as anchors. A third pre-macrocycle (green) can then be positioned outside the orange ring but through the cavity of the blue ring. Cyclization of the termini of the green ring captures the interlocked molecule. Alternatively, in principle, a "rack" strategy could be followed (Scheme 14e,ii). See Sections 5.5.2 and 5.5.3.

[112] Incorporation of phenyl groups in the 4 and 7 positions of the phen unit of one macrocycle reduces the conformational freedom of the system (no macrocycle ring rotation is possible) reducing the rate of demetalation by two orders of magnitude compared to catenate **20-Cu**$^{\mathrm{I}}$, see: a) A. M. Albrecht-Gary, C. Dietrich-Buchecker, Z. Saad, J.-P. Sauvage, J. Weiss, *J. Chem. Soc. Chem. Commun.* **1986**, 1325–1327.

[113] Electrochemical studies showed that the formation of $\mathrm{Li^I}$ and $\mathrm{Cd^{II}}$-catenates involved two kinetically observable steps and a negative enthalpy of activation, see A. M. Albrecht-Gary, C. Dietrich-Buchecker, Z. Saad, J. P. Sauvage, *J. Chem. Soc. Chem. Commun.* **1992**, 280–282.

[114] For photophysical and electrochemical properties of catenane **20-M** with a range of metal ions, see: a) N. Armaroli, L. De Cola, V. Balzani, J.-P. Sauvage, C. O. Dietrich-Buchecker, J.-M. Kern, A. Bailal, *J. Chem. Soc. Dalton Trans.* **1993**, 3241–3247; b) N. Armaroli, M. A. J. Rodgers, P. Ceroni, V. Balzani, C. O. Dietrich-Buchecker, J.-M. Kern, A. Bailal, J.-P. Sauvage, *Chem. Phys. Lett.* **1995**, *241*, 555–558.

[115] C. Dietrich-Buchecker, B. Colasson, D. Jouvenot, J.-P. Sauvage, *Chem. Eur. J.* **2005**, *11*, 4374–4386.

[116] J.-P. Sauvage, J. Weiss, *J. Am. Chem. Soc.* **1985**, *107*, 6108–6110.

[117] J. Guilhem, C. Pascard, J.-P. Sauvage, J. Weiss, *J. Am. Chem. Soc.* **1988**, *110*, 8711–8713.

[118] In order to selectively generate [3]catenates, Sauvage and co-workers opted to use a single-cyclization approach. In order to selectively generate [3]catenates, Sauvage and co-workers used

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

a single-cyclization approach. Two dpp-based macrocycles (related to macrocycle **19**) were threaded on a ligand containing two dpp units and terminal alkynes. Glaser coupling was used to close the [3]pseudorotaxane to generate the [3]catenate in 48% yield, see: J.-M. Kern, J.-P. Sauvage, J.-L. Weidmann, *Tetrahedron* **1996**, *52*, 10921 – 10934.

[119] For photophysical studies of homo- and heterometallic complexes of catenand **43**, see: a) C. O. Dietrich-Buchecker, C. Hemmert, A. K. Khemiss, J.-P. Sauvage, *J. Am. Chem. Soc.* **1990**, *112*, 8002 – 8008; b) N. Armaroli, V. Balzani, F. Barigelletti, L. De Cola, J.-P. Sauvage, C. Hemmert, *J. Am. Chem. Soc.* **1991**, *113*, 4033 – 4035; c) N. Armaroli, V. Balzani, F. Barigelletti, L. De Cola, L. Flamigni, J.-P. Sauvage, C. Hemmert, *J. Am. Chem. Soc.* **1994**, *116*, 5211 – 5217.

[120] For the X-ray crystal structure of **43-Cu**$^{\text{I}}$, see: C. O. Dietrich-Buchecker, J. Guilhem, A. K. Khemiss, J.-P. Kintzinger, C. Pascard, J.-P. Sauvage, *Angew. Chem.* **1987**, *99*, 711 – 714; *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 661 – 663.

[121] F. Bitsch, C. O. Dietrich-Buchecker, A. K. Khemiss, J.-P. Sauvage, A. van Dorsselaer, *J. Am. Chem. Soc.* **1991**, *113*, 4023 – 4025.

[122] C. Dietrich-Buchecker, B. Frommberger, I. Lüer, J.-P. Sauvage, F. Vögtle, *Angew. Chem.* **1993**, *105*, 1526 – 1529; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1434 – 1437.

[123] C. Wu, P. R. Lecavalier, Y. X. Shen, H. W. Gibson, *Chem. Mater.* **1991**, *3*, 569 – 572.

[124] J.-C. Chambron, V. Heitz, J.-P. Sauvage, *J. Chem. Soc. Chem. Commun.* **1992**, 1131 – 1133.

[125] J.-C. Chambron, V. Heitz, J.-P. Sauvage, *J. Am. Chem. Soc.* **1993**, *115*, 12378 – 12384.

[126] a) N. Solladié, J.-C. Chambron, C. O. Dietrich-Buchecker, J.-P. Sauvage, *Angew. Chem.* **1996**, *108*, 957 – 960; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 906 – 909; b) N. Solladié, J.-C. Chambron, J.-P. Sauvage, *J. Am. Chem. Soc.* **1999**, *121*, 3684 – 3692.

[127] For a review of porphyrin-containing catenanes and rotaxanes, see: J. A. Faiz, V. Heitz, J.-P. Sauvage, *Chem. Soc. Rev.* **2009**, *38*, 422 – 442.

[128] J.-C. Chambron, A. Harriman, V. Heitz, J.-P. Sauvage, *J. Am. Chem. Soc.* **1993**, *115*, 6109 – 6114.

[129] The resulting [2]catenane is the first prepared with a $\text{Cu}^{\text{I}}(\text{bpy})_2$ core, see: J. R. Price, J. K. Clegg, R. R. Fenton, L. F. Lindoy, J. C. McMurtrie, G. V. Meehan, A. Parkin, D. Perkins, P. Turner, *Aust. J. Chem.* **2009**, *62*, 1014 – 1019.

[130] The use of olefin metathesis to form catenanes was attempted in the early 1970s, see: a) R. Wolovsky, *J. Am. Chem. Soc.* **1970**, *92*, 2132 – 2133; b) D. A. Ben-Efraim, C. Batich, E. Wasserman, *J. Am. Chem. Soc.* **1970**, *92*, 2133 – 2135.

[131] a) J. Frey, T. Kraus, V. Heitz, J.-P. Sauvage, *Chem. Commun.* **2005**, 5310 – 5312; b) J. Frey, T. Kraus, V. Heitz, J.-P. Sauvage, *Chem. Eur. J.* **2007**, *13*, 7584 – 7594.

[132] M. Gupta, S. Kang, M. F. Mayer, *Tetrahedron Lett.* **2008**, *49*, 2946 – 2950.

[133] Z. Xue, M. F. Mayer, *J. Am. Chem. Soc.* **2010**, *132*, 3274 – 3276.

[134] a) J. Frey, C. Tock, J.-P. Collin, V. Heitz, J.-P. Sauvage, *J. Am. Chem. Soc.* **2008**, *130*, 4592 – 4593; b) J.-P. Collin, J.-P. Sauvage, Y. Trolez, K. Rissanen, *New J. Chem.* **2009**, *33*, 2148 – 2154; c) J.-P. Collin, J. Frey, V. Heitz, J.-P. Sauvage, C. Tock, L. Allouche, *J. Am. Chem. Soc.* **2009**, *131*, 5609 – 5620.

[135] a) D. I. Schuster, K. Li, D. M. Guldi, *C. R. Chim.* **2006**, *9*, 892 – 908; b) J. D. Megiatto, Jr., R. Spencer, D. I. Schuster, *Org. Lett.* **2009**, *11*, 4152 – 4155; c) J. D. Megiatto, Jr., K. Li, D. I. Schuster, A. Palkar, M. A. Herranz, L. Echegoyen, S. Abwandner, G. de Miguel, D. M. Guldi, *J. Phys. Chem. B* **2010**, *114*, 14408 – 14419.

[136] Photoinduced electron transfer was also studied in a related [2]rotaxane prepared without CuAAC chemistry, see: M. Jakob, A. Berg, R. Rubin, H. Levanon, K. Li, D. I. Schuster, *J. Phys. Chem. A* **2009**, *113*, 5846 – 5854.

[137] a) J. D. Megiatto, Jr., D. I. Schuster, *J. Am. Chem. Soc.* **2008**, *130*, 12872 – 12873; b) J. D. Megiatto, Jr., D. I. Schuster, *New J. Chem.* **2010**, *34*, 276 – 286.

[138] J. D. Megiatto, Jr., D. I. Schuster, S. Abwandner, G. de Miguel, D. M. Guldi, *J. Am. Chem. Soc.* **2010**, *132*, 3847 – 3861.

[139] J. D. Megiatto, Jr., D. I. Schuster, *Chem. Eur. J.* **2009**, *15*, 5444 – 5448.

[140] a) J.-P. Collin, F. Durola, J. Frey, V. Heitz, F. Reviriego, J.-P. Sauvage, Y. Trolez, K. Rissanen, *J. Am. Chem. Soc.* **2010**, *132*, 6840 – 6850; b) Removal of the Cu^{I} template from the cyclic [4]rotaxane led to collapse of the structure. The metal-free species no longer acts as a molecular receptor with the triazole unit of the thread coordinating to the Zn^{II} in the porphyrin: J.-P. Collin, F. Durola, V. Heitz, F. Reviriego, J.-P. Sauvage, Y. Trolez, *Angew. Chem.* **2010**, *122*, 10370 – 10373; *Angew. Chem. Int. Ed.* **2010**, *49*, 10172 – 10175.

[141] M. Yamamoto, M. Takeuchi, S. Shinkai, *Tetrahedron* **2002**, *58*, 7251 – 7258.

[142] D. B. Amabilino, C. O. Dietrich-Buchecker, A. Livoreil, L. Pérez-García, J.-P. Sauvage, J. F. Stoddart, *J. Am. Chem. Soc.* **1996**, *118*, 3905 – 3913.

[143] a) M. J. MacLachlan, A. Rose, T. M. Swager, *J. Am. Chem. Soc.* **2001**, *123*, 9180 – 9181; b) P. H. Kwan, T. M. Swager, *J. Am. Chem. Soc.* **2005**, *127*, 5902 – 5909; c) P. H. Kwan, T. M. Swager, *Chem. Commun.* **2005**, 5211 – 5213.

[144] S. Saito, K. Nakazono, E. Takahashi, *J. Org. Chem.* **2006**, *71*, 7477 – 7480.

[145] a) F. Diederich, C. Dietrich-Buchecker, J.-F. Nierengarten, J.-P. Sauvage, *J. Chem. Soc. Chem. Commun.* **1995**, 781 – 782; b) N. Armaroli, F. Diederich, C. O. Dietrich-Buchecker, L. Flamigni, G. Marconi, J.-F. Nierengarten, J.-P. Sauvage, *Chem. Eur. J.* **1998**, *4*, 406 – 416.

[146] For a review of topological chirality, see: J.-C. Chambron, C. Dietrich-Buchecker, J.-P. Sauvage, *Top. Curr. Chem.* **1993**, *165*, 131 – 162.

[147] C. O. Dietrich-Buchecker, A. Edel, J. P. Kintzinger, J.-P. Sauvage, *Tetrahedron* **1987**, *43*, 333 – 344.

[148] For an interesting example of an achiral catenane that is chiral in *every* conformation, see: J.-C. Chambron, J.-P. Sauvage, K. Mislow, A. De Cian, J. Fischer, *Chem. Eur. J.* **2001**, *7*, 4085 – 4096.

[149] For examples of topologically chiral catenanes formed from achiral macrocycles, see: a) D. K. Mitchell, J.-P. Sauvage, *Angew. Chem.* **1988**, *100*, 985 – 987; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 930 – 931; b) J.-C. Chambron, D. K. Mitchell, J.-P. Sauvage, *J. Am. Chem. Soc.* **1992**, *114*, 4625 – 4631; c) although originally isolated as a racemate, separation of the enantiomers was later achieved through the use of chiral HPLC, see: Y. Kaida, Y. Okamoto, J.-C. Chambron, D. K. Mitchell, J.-P. Sauvage, *Tetrahedron Lett.* **1993**, *34*, 1019 – 1022.

[150] For examples of metal template catenanes containing chiral groups, see: a) M. Koizumi, C. Dietrich-Buchecker, J.-P. Sauvage, *Eur. J. Org. Chem.* **2004**, 770 – 775; b) A. Theil, C. Mauve, M.-T. Adeline, A. Marinetti, J.-P. Sauvage, *Angew. Chem.* **2006**, *118*, 2158 – 2161; *Angew. Chem. Int. Ed.* **2006**, *45*, 2104 – 2107. c) For an example of a chiral metal–organic catenane formed using Pd^{II} ions, see: A. Hori, A. Akasaka, K. Biradha, S. Sakamoto, K. Yamaguchi, M. Fujita, *Angew. Chem.* **2002**, *114*, 3403 – 3406.

[151] For systems with two binding sites on the macrocyclic ring, see: a) A. Livoreil, C. O. Dietrich-Buchecker, J.-P. Sauvage, *J. Am. Chem. Soc.* **1994**, *116*, 9399 – 9400; b) D. J. Cárdenas, A. Livoreil, J.-P. Sauvage, *J. Am. Chem. Soc.* **1996**, *118*, 11980 – 11981; c) A. Livoreil, J.-P. Sauvage, N. Armaroli, V. Balzani, L. Flamigni, B. Ventura, *J. Am. Chem. Soc.* **1997**, *119*, 12114 –

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

12124; d) F. Baumann, A. Livoreil, W. Kaim, J.-P. Sauvage, *Chem. Commun.* **1997**, 35 – 36; e) G. Periyasamy, A. Sour, J.-P. Collin, J.-P. Sauvage, F. Remacle, *J. Phys. Chem. B* **2009**, *113*, 6219 – 6229.

[152] For molecular shuttles based on Cu^{I}/Cu^{II} electrochemical switching, see: a) P. Gaviña, J.-P. Sauvage, *Tetrahedron Lett.* **1997**, *38*, 3521 – 3524; b) L. Raehm, J.-M. Kern, J.-P. Sauvage, *Chem. Eur. J.* **1999**, *5*, 3310 – 3317; c) N. Armaroli, V. Balzani, J.-P. Collin, P. Gaviña, J.-P. Sauvage, B. Ventura, *J. Am. Chem. Soc.* **1999**, *121*, 4397 – 4408; d) J.-M. Kern, L. Raehm, J.-P. Sauvage, B. Divisia-Blohorn, P.-L. Vidal, *Inorg. Chem.* **2000**, *39*, 1555 – 1560; e) N. Weber, C. Hamann, J.-M. Kern, J.-P. Sauvage, *Inorg. Chem.* **2003**, *42*, 6780 – 6792; f) I. Poleschak, J.-M. Kern, J.-P. Sauvage, *Chem. Commun.* **2004**, 474 – 476; g) U. Létinois-Halbes, D. Hanss, J. M. Beierle, J.-P. Collin, J.-P. Sauvage, *Org. Lett.* **2005**, *7*, 5753 – 5756; h) F. Durola, J.-P. Sauvage, *Angew. Chem.* **2007**, *119*, 3607 – 3610; *Angew. Chem. Int. Ed.* **2007**, *46*, 3537 – 3540; i) G. Periyasamy, J.-P. Collin, J.-P. Sauvage, R. D. Levine, F. Remacle, *Chem. Eur. J.* **2009**, *15*, 1310 – 1313; j) J.-P. Collin, F. Durola, J. Lux, J.-P. Sauvage, *Angew. Chem.* **2009**, *121*, 8684 – 8687; *Angew. Chem. Int. Ed.* **2009**, *48*, 8532 – 8535; k) F. Durola, J. Lux, J.-P. Sauvage, *Chem. Eur. J.* **2009**, *15*, 4124 – 4134; for shuttle **56** and related systems see: l) J.-P. Collin, F. Durola, J. Lux, J.-P. Sauvage, *New J. Chem.* **2010**, *34*, 34 – 43; m) F. Durola, J.-P. Sauvage, O. S. Wenger, *Coord. Chem. Rev.* **2010**, *254*, 1748 – 1759.

[153] For metal complex “molecular muscles”, see: a) M. C. Jiménez, C. Dietrich-Buchecker, J.-P. Sauvage, *Angew. Chem.* **2000**, *112*, 3422 – 3425; *Angew. Chem. Int. Ed.* **2000**, *39*, 3284 – 3287; b) M. C. Jiménez-Molero, C. Dietrich-Buchecker, J.-P. Sauvage, *Chem. Eur. J.* **2002**, *8*, 1456 – 1466; c) for reviews of these and related systems see: Ref. [2a].

[154] M. Hutin, C. A. Schalley, G. Bernardinelli, J. R. Nitschke, *Chem. Eur. J.* **2006**, *12*, 4069 – 4076.

[155] C. Hamann, J.-M. Kern, J.-P. Sauvage, *Inorg. Chem.* **2003**, *42*, 1877 – 1883.

[156] J.-P. Collin, S. Durot, M. Keller, J.-P. Sauvage, Y. Trolez, M. Cetina, K. Rissanen, *Chem. Eur. J.* **2011**, *17*, 947 – 957.

[157] G. Kaiser, T. Jarrosson, S. Otto, Y.-F. Ng, A. D. Bond, J. K. M. Sanders, *Angew. Chem.* **2004**, *116*, 1993 – 1996; *Angew. Chem. Int. Ed.* **2004**, *43*, 1959 – 1962.

[158] a) S. A. Vignon, T. Jarrosson, T. Iijima, H.-R. Tseng, J. K. M. Sanders, J. F. Stoddart, *J. Am. Chem. Soc.* **2004**, *126*, 9884 – 9885; b) T. Iijima, S. A. Vignon, H.-R. Tseng, T. Jarrosson, J. K. M. Sanders, F. Marchioni, M. Venturi, E. Apostoli, V. Balzani, J. F. Stoddart, *Chem. Eur. J.* **2004**, *10*, 6375 – 6392.

[159] J.-P. Sauvage, M. Ward, *Inorg. Chem.* **1991**, *30*, 3869 – 3874.

[160] N. Belfrekh, C. Dietrich-Buchecker, J.-P. Sauvage, *Inorg. Chem.* **2000**, *39*, 5169 – 5172.

[161] J. C. Loren, P. Gantzel, A. Linden, J. S. Siegel, *Org. Biomol. Chem.* **2005**, *3*, 3105 – 3116.

[162] a) T. D. Kidd, D. A. Leigh, A. J. Wilson, *J. Am. Chem. Soc.* **1999**, *121*, 1599 – 1600; b) E. M. Pérez, D. T. F. Dryden, D. A. Leigh, G. Teobaldi, F. Zerbetto, *J. Am. Chem. Soc.* **2004**, *126*, 12210 – 12211; c) D. A. Leigh, E. M. Pérez, *Chem. Commun.* **2004**, 2262 – 2263; d) J. V. Hernández, E. R. Kay, D. A. Leigh, *Science* **2004**, *306*, 1532 – 1537; e) J. Berná, D. A. Leigh, M. Lubomska, S. M. Mendoza, E. M. Pérez, P. Rudolf, G. Teobaldi, F. Zerbetto, *Nat. Mater.* **2005**, *4*, 704 – 710; f) D. S. Marlin, D. González Cabrera, D. A. Leigh, A. M. Z. Slawin, *Angew. Chem.* **2006**, *118*, 83 – 89; *Angew. Chem. Int. Ed.* **2006**, *45*, 77 – 83; g) D. S. Marlin, D. González Cabrera, D. A. Leigh, A. M. Z. Slawin, *Angew. Chem.* **2006**, *118*, 1413 – 1418; *Angew. Chem. Int. Ed.* **2006**, *45*, 1385 – 1390; h) M. Alvarez-Pérez, S. M. Goldup, D. A. Leigh, A. M. Z. Slawin, *J. Am. Chem. Soc.* **2008**, *130*, 1836 – 1838; i) G. Fioravanti, N. Haraszkiewicz, E. R. Kay, S. M. Mendoza, C. Bruno, M. Marcaccio, P. G. Wiering, F. Paolucci, P. Rudolf, A. M. Brouwer, D. A. Leigh, *J. Am. Chem. Soc.* **2008**, *130*, 2593 – 2601; j) A. Fernandes, A. Viterisi, F. Coutrot, S. Potok, D. A. Leigh, V. Aucagne, S. Papot, *Angew. Chem.* **2009**, *121*, 6565 – 6569; *Angew. Chem. Int. Ed.* **2009**, *48*, 6443 – 6447; k) S. Smolarek, A. M. Rijs, J. S. Hannam, D. A. Leigh, M. Drabbels, W. J. Buma, *J. Am. Chem. Soc.* **2009**, *131*, 12902 – 12903; l) M. R. Panman, P. Bodis, D. J. Shaw, B. H. Bakker, A. C. Newton, E. R. Kay, A. M. Brouwer, W. J. Buma, D. A. Leigh, S. Woutersen, *Science* **2010**, *328*, 1255 – 1258; m) D. M. D’Souza, D. A. Leigh, L. Mottier, K. M. Mullen, F. Paolucci, S. J. Teat, S. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 9465 – 9470.

[163] L. Hogg, D. A. Leigh, P. J. Lusby, A. Morelli, S. Parsons, J. K. Y. Wong, *Angew. Chem.* **2004**, *116*, 1238 – 1241; *Angew. Chem. Int. Ed.* **2004**, *43*, 1218 – 1221.

[164] a) P. Mobian, J.-M. Kern, J.-P. Sauvage, *J. Am. Chem. Soc.* **2003**, *125*, 2016 – 2017; b) J.-C. Chambron, J.-P. Collin, V. Heitz, D. Jouvenot, J.-M. Kern, P. Mobian, D. Pomeranc, J.-P. Sauvage, *Eur. J. Org. Chem.* **2004**, 1627 – 1638.

[165] F. Aricó, P. Mobian, J.-M. Kern, J.-P. Sauvage, *Org. Lett.* **2003**, *5*, 1887 – 1890.

[166] P. Mobian, J.-M. Kern, J.-P. Sauvage, *Inorg. Chem.* **2003**, *42*, 8633 – 8637.

[167] a) D. Pomeranc, D. Jouvenot, J.-C. Chambron, J.-P. Collin, V. Heitz, J.-P. Sauvage, *Chem. Eur. J.* **2003**, *9*, 4247 – 4254; b) J.-P. Collin, D. Jouvenot, M. Koizumi, J.-P. Sauvage, *Eur. J. Inorg. Chem.* **2005**, 1850 – 1855.

[168] a) A. I. Prikhod’ko, F. Durola, J.-P. Sauvage, *J. Am. Chem. Soc.* **2008**, *130*, 448 – 449; b) A. I. Prikhod’ko, J.-P. Sauvage, *J. Am. Chem. Soc.* **2009**, *131*, 6794 – 6807.

[169] a) F. Durola, L. Russo, J.-P. Sauvage, K. Rissanen, O. S. Wenger, *Chem. Eur. J.* **2007**, *13*, 8749 – 8753; b) F. Durola, J.-P. Sauvage, O. S. Wenger, *Chem. Commun.* **2006**, 171 – 173.

[170] A.-M. Fuller, D. A. Leigh, P. J. Lusby, I. D. H. Oswald, S. Parsons, D. B. Walker, *Angew. Chem.* **2004**, *116*, 4004 – 4008; *Angew. Chem. Int. Ed.* **2004**, *43*, 3914 – 3918.

[171] D. A. Leigh, P. J. Lusby, A. M. Z. Slawin, D. B. Walker, *Angew. Chem.* **2005**, *117*, 4633 – 4640; *Angew. Chem. Int. Ed.* **2005**, *44*, 4557 – 4564.

[172] Y. Furusho, T. Matsuyama, T. Takata, T. Moriuchi, T. Hirao, *Tetrahedron Lett.* **2004**, *45*, 9593 – 9597.

[173] W.-C. Hung, L.-Y. Wang, C.-C. Lai, Y.-H. Liu, S.-M. Peng, S.-H. Chiu, *Tetrahedron Lett.* **2009**, *50*, 267 – 270.

[174] Significantly, these reactions were shown to operate only where the axle was threaded through the macrocyclic ring. The combination of a stoppered thread with a closed macrocycle gave no product, whereas other combinations (unstoppered thread with closed Pd-macrocycle or stoppered thread with acyclic Pd-complex) were also found to give the isomerization products. For details, see: N. Miyagawa, M. Watanabe, T. Matsuyama, Y. Koyama, T. Moriuchi, T. Hirao, Y. Furusho, T. Takata, *Chem. Commun.* **2010**, *46*, 1920 – 1922.

[175] A.-M. L. Fuller, D. A. Leigh, P. J. Lusby, *Angew. Chem.* **2007**, *119*, 5103 – 5107; *Angew. Chem. Int. Ed.* **2007**, *46*, 5015 – 5019.

[176] In contrast, another [*n*]rotaxane synthesis requires that $n-1$ binding sites have to be built into the thread, see: J. Wu, K. C.-F. Leung, J. F. Stoddart, *Proc. Natl. Acad. Sci. USA* **2007**, *104*, 17266 – 17271.

[177] A.-M. L. Fuller, D. A. Leigh, P. J. Lusby, *J. Am. Chem. Soc.* **2010**, *132*, 4954 – 4959.

[178] J. D. Crowley, D. A. Leigh, P. J. Lusby, R. T. McBurney, L.-E. Perret-Aebi, C. Petzold, A. M. Z. Slawin, M. D. Symes, *J. Am. Chem. Soc.* **2007**, *129*, 15085 – 15090.

[179] D. A. Leigh, P. J. Lusby, R. T. McBurney, M. D. Symes, *Chem. Commun.* **2010**, *46*, 2382 – 2384.

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

[180] S. M. Goldup, D. A. Leigh, P. J. Lusby, R. T. McBurney, A. M. Z. Slawin, *Angew. Chem.* **2008**, *120*, 7107 – 7111; *Angew. Chem. Int. Ed.* **2008**, *47*, 6999 – 7003.

[181] V. Aucagne, J. Berná, J. D. Crowley, S. M. Goldup, K. D. Hänni, D. A. Leigh, P. J. Lusby, V. E. Ronaldson, A. M. Z. Slawin, A. Viterisi, D. B. Walker, *J. Am. Chem. Soc.* **2007**, *129*, 11950 – 11963.

[182] S. M. Goldup, D. A. Leigh, T. Long, P. R. McGonigal, M. D. Symes, J. Wu, *J. Am. Chem. Soc.* **2009**, *131*, 15924 – 15929.

[183] S. M. Goldup, D. A. Leigh, P. R. McGonigal, V. E. Ronaldson, A. M. Z. Slawin, *J. Am. Chem. Soc.* **2010**, *132*, 315 – 320.

[184] Y. Sato, R. Yamasaki, S. Saito, *Angew. Chem.* **2009**, *121*, 512 – 515; *Angew. Chem. Int. Ed.* **2009**, *48*, 504 – 507.

[185] a) J. Tsuji, *Palladium Reagents and Catalysis: New Perspectives for the 21st Century*, 2nd ed., Wiley, Chichester, **2004**; b) *Metal-Catalyzed Cross-Coupling Reactions*, *Vol. 1*, 2nd ed. (Eds.: A. de Meijere, F. Diederich), Wiley-VCH, Weinheim, **2004**.

[186] The reaction was independently discovered by the Weix group at around the same time: M. R. Prinsell, D. A. Everson, D. J. Weix, *Chem. Commun.* **2010**, *46*, 5743 – 5745.

[187] a) C. Fischer, G. C. Fu, *J. Am. Chem. Soc.* **2005**, *127*, 4594 – 4595; b) F. O. Arp, G. C. Fu, *J. Am. Chem. Soc.* **2005**, *127*, 10482 – 10483; c) B. Saito, G. C. Fu, *J. Am. Chem. Soc.* **2007**, *129*, 9602 – 9603; d) S. W. Smith, G. C. Fu, *J. Am. Chem. Soc.* **2008**, *130*, 12645 – 12647.

[188] P. R. Markies, T. Nomoto, O. S. Akkerman, F. Bickelhaupt, W. J. J. Smeets, A. L. Spek, *J. Am. Chem. Soc.* **1988**, *110*, 4845 – 4846.

[189] G.-J. M. Gruter, F. J. J. de Kanter, P. R. Markies, T. Nomoto, O. S. Akkerman, F. Bickelhaupt, *J. Am. Chem. Soc.* **1993**, *115*, 12179 – 12180.

[190] G. P. M. van Klink, T. Nomoto, M. Lutz, A. L. Spek, O. S. Akkerman, F. Bickelhaupt, *Eur. J. Inorg. Chem.* **2004**, 154 – 159.

[191] B. A. Blight, J. A. Wisner, M. C. Jennings, *Chem. Commun.* **2006**, 4593 – 4595.

[192] a) B. A. Blight, K. A. Van Noortwyk, J. A. Wisner, M. C. Jennings, *Angew. Chem.* **2005**, *117*, 1523 – 1528; *Angew. Chem. Int. Ed.* **2005**, *44*, 1499 – 1504; b) B. A. Blight, J. A. Wisner, M. C. Jennings, *Inorg. Chem.* **2009**, *48*, 1920 – 1927.

[193] B. A. Blight, J. A. Wisner, M. C. Jennings, *Can. J. Chem.* **2009**, *87*, 205 – 211.

[194] B. A. Blight, X. Wei, J. A. Wisner, M. C. Jennings, *Inorg. Chem.* **2007**, *46*, 8445 – 8447.

[195] a) K. Yamanari, Y. Shimura, *Chem. Lett.* **1982**, 1959 – 1962; b) K. Yamanari, Y. Shimura, *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2283 – 2289; c) K. Yamanari, Y. Shimura, *Bull. Chem. Soc. Jpn.* **1984**, *57*, 1596 – 1603.

[196] a) R. S. Wylie, D. H. Macartney, *J. Am. Chem. Soc.* **1992**, *114*, 3136 – 3138; b) D. H. Macartney, C. A. Waddling, *Inorg. Chem.* **1994**, *33*, 5912 – 5919; c) A. P. Lyon, D. H. Macartney, *Inorg. Chem.* **1997**, *36*, 729 – 736; d) V. X. Jin, D. H. Macartney, E. Buncel, *Can. J. Chem.* **2005**, *83*, 195 – 201.

[197] V. X. Jin, D. H. Macartney, E. Buncel, *Can. J. Chem.* **2005**, *83*, 2091 – 2097.

[198] Suzuki-coupling was used to form the rotaxane from a diboronic ester included within the β-CD macrocycle: G. Chen, J. Xia, Z. Li, G.-A. Yu, S. Jin, S. H. Liu, *J. Organomet. Chem.* **2010**, *695*, 323 – 326.

[199] A. D. Shukla, H. C. Bajaj, A. Das, *Angew. Chem.* **2001**, *113*, 460 – 462; *Angew. Chem. Int. Ed.* **2001**, *40*, 446 – 448.

[200] D. Whang, Y.-M. Jeon, J. Heo, K. Kim, *J. Am. Chem. Soc.* **1996**, *118*, 11333 – 11334.

[201] S. J. Loeb, J. A. Wisner, *Angew. Chem.* **1998**, *110*, 3010 – 3013; *Angew. Chem. Int. Ed.* **1998**, *37*, 2838 – 2840.

[202] a) Ref. [5c]; b) G. J. E. Davidson, S. J. Loeb, *Dalton Trans.* **2003**, 4319 – 4323; c) G. J. E. Davidson, S. J. Loeb, P. Passaniti, S. Silvi, A. Credi, *Chem. Eur. J.* **2006**, *12*, 3233 – 3242.

[203] a) P. R. Ashton, R. Ballardini, V. Balzani, A. Credi, K. R. Dress, E. Ishow, C. J. Kleverlaan, O. Kocian, J. A. Preece, N. Spencer, J. F. Stoddart, M. Venturi, S. Wenger, *Chem. Eur. J.* **2000**, *6*, 3558 – 3574; b) V. Balzani, M. Clemente-Léon, A. Credi, B. Ferrer, M. Venturi, A. H. Flood, J. F. Stoddart, *Proc. Natl. Acad. Sci. USA* **2006**, *103*, 1178 – 1183; c) E. R. Kay, D. A. Leigh, *Nature* **2006**, *440*, 286 – 287; d) V. Balzani, G. Bergamini, P. Ceroni, *Coord. Chem. Rev.* **2008**, *252*, 2456 – 2469.

[204] Y. Tokunaga, N. Ohiwa, G. Ohta, Y. Yamauchi, T. Goda, N. Kawai, T. Sugihara, Y. Shimomura, T. Hoshi, *Heterocycles* **2009**, *77*, 1045 – 1056.

[205] For alkynyl-terminated pseudorotaxanes stoppered through hydrometalation with $[\mathrm{RuHCl(CO)(PPh_3)_3}]$ to form [2]rotaxanes, see: H. Sasabe, N. Kihara, K. Mizuno, A. Ogawa, T. Takata, *Chem. Lett.* **2006**, *35*, 212 – 213.

[206] For a recent review of rotaxanes with $\mathrm{Fe^{II}}$- $\mathrm{Pd^{II}}$- and $\mathrm{Pt^{II}}$-containing axles, see: Y. Suzaki, T. Taira, K. Osakada, M. Horie, *Dalton Trans.* **2008**, 4823 – 4833.

[207] For other ferrocene containing rotaxanes, see: a) A. C. Benniston, A. Harriman, *Angew. Chem.* **1993**, *105*, 1553 – 1555; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1459 – 1461; b) J.-S. Marois, J.-F. Morin, *Langmuir* **2008**, *24*, 10865 – 10873.

[208] R. Isnin, C. Salam, A. E. Kaifer, *J. Org. Chem.* **1991**, *56*, 35 – 41.

[209] R. Isnin, A. E. Kaifer, *J. Am. Chem. Soc.* **1991**, *113*, 8188 – 8190.

[210] A. C. Benniston, A. Harriman, V. M Lynch, *J. Am. Chem. Soc.* **1995**, *117*, 5275 – 5291.

[211] a) N. Kihara, M. Hashimoto, T. Takata, *Org. Lett.* **2004**, *6*, 1693 – 1696; b) G. A. Rajkumar, A. S. D. Sandanayaka, K.-I. Ikeshita, Y. Araki, Y. Furusho, T. Takata, O. Ito, *J. Phys. Chem. B* **2006**, *110*, 6516 – 6525; c) A. S. D. Sandanayaka, H. Sasabe, Y. Araki, N. Kihara, Y. Furusho, T. Takata, O. Ito, *Aust. J. Chem.* **2006**, *59*, 186 – 192.

[212] a) Y. Suzaki, K. Osakada, *Chem. Lett.* **2006**, *35*, 374 – 375; b) Y. Suzaki, K. Osakada, *Dalton Trans.* **2007**, 2376 – 2383.

[213] S. R. Bayly, T. M. Gray, M. J. Chmielewski, J. J. Davis, P. D. Beer, *Chem. Commun.* **2007**, 2234 – 2236.

[214] B. Hannak, G. Farber, R. Konrat, B. Krautler, *J. Am. Chem. Soc.* **1997**, *119*, 2313 – 2314.

[215] K. Chichak, M. C. Walsh, N. R. Branda, *Chem. Commun.* **2000**, 847 – 848.

[216] M. J. Gunter, N. Bampos, K. D. Johnstone, J. K. M. Sanders, *New J. Chem.* **2001**, *25*, 166 – 173.

[217] a) K. D. Johnstone, N. Bampos, J. K. M. Sanders, M. J. Gunter, *Chem. Commun.* **2003**, 1396 – 1397; b) K. M. Mullen, K. D. Johnstone, M. Webb, N. Bampos, J. K. M. Sanders, M. J. Gunter, *Org. Biomol. Chem.* **2008**, *6*, 278 – 286; c) K. M. Mullen, K. D. Johnstone, D. Nath, N. Bampos, J. K. M. Sanders, M. J. Gunter, *Org. Biomol. Chem.* **2009**, *7*, 293 – 303.

[218] a) M. Asakawa, T. Ikeda, N. Yui, T. Shimizu, *Chem. Lett.* **2002**, 174 – 175; b) T. Ikeda, M. Asakawa, M. Goto, Y. Nagawa, T. Shimizu, *Eur. J. Org. Chem.* **2003**, 3744 – 3751; c) T. Ikeda, M. Asakawa, T. Shimizu, *New J. Chem.* **2004**, *28*, 870 – 873.

[219] M. J. Gunter, S. M. Farquhar, K. M. Mullen, *New J. Chem.* **2004**, *28*, 1443 – 1449.

[220] S.-Y. Chang, H.-Y. Jang, K.-S. Jeong, *Chem. Eur. J.* **2003**, *9*, 1535 – 1541.

[221] S.-Y. Chang, J. S. Choi, K.-S. Jeong, *Chem. Eur. J.* **2001**, *7*, 2687 – 2697.

[222] S. Y. Chang, K. S. Jeong, *J. Org. Chem.* **2003**, *68*, 4014 – 4019.

[223] Y. Suzaki, E. Chihara, A. Takagi, K. Osakada, *Dalton Trans.* **2009**, 9881 – 9891.

[224] G. H. Clever, M. Shionoya, *Chem. Eur. J.* **2010**, *16*, 11792 – 11796.

[225] a) I. Yoon, M. Narita, T. Shimizu, M. Asakawa, *J. Am. Chem. Soc.* **2004**, *126*, 16740 – 16741; b) for a related synthetic strategy using purely organic synthesis in which a macrocycle is first threaded on to a mono-stoppered axle, then a thermal

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

cyclization reaction generates the second stopper and thus forms the [2]rotaxane, see: C.-W. Chiu, C.-C. Lai, S.-H. Chiu, *J. Am. Chem. Soc.* **2007**, *129*, 3500 – 3501.

[226] M. Narita, I. Yoon, M. Aoyagi, M. Goto, T. Shimizu, M. Asakawa, *Eur. J. Inorg. Chem.* **2007**, 4229 – 4237.

[227] For other examples of dynamic "ring-opening-ring-closing" in catenane and rotaxane synthesis, see: a) Ref. [162]; b) J. S. Hannam, T. J. Kidd, D. A. Leigh, A. J. Wilson, *Org. Lett.* **2003**, *5*, 1907 – 1910; c) R. L. E. Furlan, S. Otto, J. K. M. Sanders, *Proc. Natl. Acad. Sci. USA* **2002**, *99*, 4801 – 4804.

[228] I. Yoon, M. Narita, M. Goto, T. Shimizu, M. Asakawa, *Org. Lett.* **2006**, *8*, 2341 – 2344.

[229] a) C.-F. Lee, D. A. Leigh, R. G. Pritchard, D. Schultz, S. J. Teat, G. A. Timco, R. E. Winpenny, *Nature* **2009**, *458*, 314 – 318; b) E. K. Brechin, L. Cronin, *Angew. Chem.* **2009**, *121*, 7082 – 7083; *Angew. Chem. Int. Ed.* **2009**, *48*, 6948 – 6949.

[230] For organic-inorganic polypseudorotaxanes formed by assembling large ring polyoxomolybdates about rigid organic polymers, see: M. A. Alam, Y. S. Kim, S. Ogawa, A. Tsuda, N. Ishii, T. Aida, *Angew. Chem.* **2008**, *120*, 2100 – 2103; *Angew. Chem. Int. Ed.* **2008**, *47*, 2070 – 2073.

[231] B. Ballesteros, T. B. Faust, C.-F. Lee, D. A. Leigh, C. A. Muryn, R. G. Pritchard, D. Schultz, S. J. Teat, G. A. Timco, R. E. P. Winpenny, *J. Am. Chem. Soc.* **2010**, *132*, 15435 – 15444.

[232] A. G. Cheetham, T. D. W. Claridge, H. L. Anderson, *Org. Biomol. Chem.* **2007**, *5*, 457 – 462.

[233] a) T. Taira, Y. Suzaki, K. Osakada, *Chem. Lett.* **2008**, *37*, 182 – 183; b) T. Taira, Y. Suzaki, K. Osakada, *Chem. Asian J.* **2008**, *3*, 895 – 902.

[234] D. Whang, K. Kim, *J. Am. Chem. Soc.* **1997**, *119*, 451 – 452.

[235] D. Whang, J. Heo, C.-A. Kim, K. Kim, *Chem. Commun.* **1997**, 2361 – 2362.

[236] a) For a review of cucurbituril rotaxane and catenane systems, see: K. Kim, *Chem. Soc. Rev.* **2002**, *31*, 96 – 107; b) for a review of polymeric rotaxanes focused on cyclodextrin-containing systems, see: A. Harada, A. Hashidzume, H. Yamaguchi, Y. Takashima, *Chem. Rev.* **2009**, *109*, 5974 – 6023.

[237] a) Y. Liu, Y.-L. Zhao, H.-Y. Zhang, H.-B. Song, *Angew. Chem.* **2003**, *115*, 3382 – 3385; *Angew. Chem. Int. Ed.* **2003**, *42*, 3260 – 3263. In a related example when Cu^{II} was used with γ-CD a doubly-threaded structure was obtained, see: b) Y. W. Yang, Y. Chen, Y. Liu, *Inorg. Chem.* **2006**, *45*, 3014 – 3022.

[238] Y. Liu, S.-H. Song, Y. Chen, Y.-L. Zhao, Y.-W. Yang, *Chem. Commun.* **2005**, 1702 – 1704.

[239] E. Lee, J. Kim, J. Heo, D. Whang, K. Kim, *Angew. Chem.* **2001**, *113*, 413 – 416; *Angew. Chem. Int. Ed.* **2001**, *40*, 399 – 402.

[240] In this example Tb^{3+} is used as the metal ion: E. Lee, J. Heo, K. Kim, *Angew. Chem.* **2000**, *112*, 2811 – 2813; *Angew. Chem. Int. Ed.* **2000**, *39*, 2699 – 2701.

[241] G. J. E. Davidson, S. J. Loeb, *Angew. Chem.* **2003**, *115*, 78 – 81; *Angew. Chem. Int. Ed.* **2003**, *42*, 74 – 77.

[242] a) D. J. Hoffart, S. J. Loeb, *Angew. Chem.* **2005**, *117*, 923 – 926; *Angew. Chem. Int. Ed.* **2005**, *44*, 901 – 904; b) S. J. Loeb, *Chem. Commun.* **2005**, 1511 – 1518.

[243] L. K. Knight, V. N. Vucotic, E. Viljoen, C. B. Caputo, S. J. Loeb, *Chem. Commun.* **2009**, 5585 – 5587.

[244] For reviews, see: Ref. [10a,b,e,f].

[245] For a discussion on the mechanism of catenane formation in these systems, see: M. Fujita, F. Ibukuro, H. Seki, O. Kamo, M. Imanari, K. Ogura, *J. Am. Chem. Soc.* **1996**, *118*, 899 – 900.

[246] A later paper reported DOSY evidence for the formation of higher order catenanes using this method, see: A. Hori, K. Kumazawa, T. Kusukawa, D. K. Chand, M. Fujita, S. Sakamoto, K. Yamaguchi, *Chem. Eur. J.* **2001**, *7*, 4142 – 4149.

[247] M. Fujita, F. Ibukuro, K. Yamaguchi, K. Ogura, *J. Am. Chem. Soc.* **1995**, *117*, 4175 – 4176.

[248] M. Fujita, M. Aoyagi, F. Ibukuro, K. Ogura, K. Yamaguchi, *J. Am. Chem. Soc.* **1998**, *120*, 611 – 612.

[249] A. Hori, H. Kataoka, T. Okano, S. Sakamoto, K. Yamaguchi, M. Fujita, *Chem. Commun.* **2003**, 182 – 183.

[250] a) A. Hori, K. Yamashita, T. Kusukawa, A. Akasaka, K. Biradha, M. Fujita, *Chem. Commun.* **2004**, 1798 – 1799; b) A. Hori, T. Sawada, K. Yamashita, M. Fujita, *Angew. Chem.* **2005**, *117*, 4974 – 4977; *Angew. Chem. Int. Ed.* **2005**, *44*, 4896 – 4899.

[251] K. Yamashita, A. Hori, M. Fujita, *Tetrahedron* **2007**, *63*, 8435 – 8439.

[252] a) K. Yamashita, M. Kawano, M. Fujita, *J. Am. Chem. Soc.* **2007**, *129*, 1850 – 1851; b) K. Yamashita, K. Sato, M. Kawano, M. Fujita, *New J. Chem.* **2009**, *33*, 264 – 270.

[253] M. Fujita, N. Fujita, K. Ogura, K. Yamaguchi, *Nature* **1999**, *400*, 52 – 55.

[254] A. Westcott, J. Fisher, L. P. Harding, P. Rizkallah, M. J. Hardie, *J. Am. Chem. Soc.* **2008**, *130*, 2950 – 2951.

[255] Hardie was able to assemble the cage complex (**179-Zn^{II}**) using Co^{II} as a substitute for Zn^{II}. In the Co^{II} system ES-MS evidence found only the [2]catenane with "*no indication of a single cage species*", suggesting it is preferentially formed in solution.

[256] M. Fukuda, R. Sekiya, R. Kuroda, *Angew. Chem.* **2008**, *120*, 718 – 722; *Angew. Chem. Int. Ed.* **2008**, *47*, 706 – 710.

[257] For a related all-organic example of triply-interlocked cages, the assembly of which appears to be driven by crystallization, see: a) T. Hasell, X. Wu, J. T. A. Jones, J. Bacsa, A. Steiner, T. Mitra, A. Trewin, D. J. Adams, A. I. Cooper, *Nat. Chem.* **2010**, *2*, 750 – 755; b) J. E. Beves, D. A. Leigh, *Nat. Chem.* **2010**, *2*, 708 – 710.

[258] W. W. H. Wong, J. Cookson, E. A. L. Evans, E. J. L. McInnes, J. Wolowska, J. P. Maher, P. Bishop, P. D. Beer, *Chem. Commun.* **2005**, 2214 – 2216.

[259] a) B. Korybut-Daszkiewicz, A. Więckowska, R. Bilewicz, S. Domagała, K. Woźniak, *J. Am. Chem. Soc.* **2001**, *123*, 9356 – 9366; b) A. Więckowska, R. Bilewicz, S. Domagała, K. Woźniak, B. Korybut-Daszkiewicz, A. Tomkiewicz, J. Mroziński, *Inorg. Chem.* **2003**, *42*, 5513 – 5522.

[260] a) B. Korybut-Daszkiewicz, A. Więckowska, R. Bilewicz, S. Domagała, K. Woźniak, *Angew. Chem.* **2004**, *116*, 1700 – 1704; *Angew. Chem. Int. Ed.* **2004**, *43*, 1668 – 1672; b) R. Bilewicz, B. Korybut-Daszkiewicz, A. Rogowska, J. Szydlowska, A. Więckowska, S. Domagała, K. Woźniak, *Electroanalysis* **2005**, *17*, 1463 – 1470.

[261] B. Korybut-Daszkiewicz, R. Bilewicz, K. Woźniak, *Coord. Chem. Rev.* **2010**, *254*, 1637 – 1660.

[262] a) P. R. Ashton, B. Odell, M. V. Reddington, A. M. Z. Slawin, J. F. Stoddart, D. J. Williams, *Angew. Chem.* **1988**, *100*, 1608 – 1611; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1550 – 1553; b) P. R. Ashton, T. T. Goodnow, A. E. Kaifer, M. V. Reddington, A. M. Z. Slawin, N. Spencer, J. F. Stoddart, C. Vicent, D. J. Williams, *Angew. Chem.* **1989**, *101*, 1404 – 1408; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 1396 – 1399.

[263] M. Chas, E. Pia, R. Toba, C. Peinador, J. M. Quintela, *Inorg. Chem.* **2006**, *45*, 6117 – 6119.

[264] a) V. Blanco, M. Chas, D. Abella, C. Peinador, J. M. Quintela, *J. Am. Chem. Soc.* **2007**, *129*, 13978 – 13986; b) M. Chas, V. Blanco, C. Peinador, J. M. Quintela, *Org. Lett.* **2007**, *9*, 675 – 678; c) V. Blanco, D. Abella, E. Pía, C. Platas-Iglesias, C. Peinador, J. M. Quintela, *Inorg. Chem.* **2009**, *48*, 4098 – 4107; d) V. Blanco, A. Guitérrez, C. Platas-Iglesias, C. Peinador, J. M. Quintela, *J. Org. Chem.* **2009**, *74*, 6577 – 6583.

[265] For a structurally similar approach, see: a) Y. Liu, A. Bruneau, J. He, Z. Abliz, *Org. Lett.* **2008**, *10*, 765 – 768; b) G. Koshkakaryan, K. Parimal, J. He, X. Zhang, Z. Abliz, A. H. Flood, Y. Liu, *Chem. Eur. J.* **2008**, *14*, 10211 – 10218.

[266] R. S. Forgan, D. C. Friedman, C. L. Stern C. J. Bruns, J. F. Stoddart, *Chem. Commun.* **2010**, *46*, 5861 – 5863.

[267] T. S. M. Abedin, L. K. Thompson, D. O. Miller, *Chem. Commun.* **2005**, 5512 – 5514.

[268] J. Lu, D. R. Turner, L. P. Harding, L. T. Byrne, M. V. Baker, S. R. Batten, *J. Am. Chem. Soc.* **2009**, *131*, 10372 – 10373.

[269] J. Wu, F. Fang, W.-Y. Lu, J.-L. Hou, C. Li, Z.-Q. Wu, X.-K. Jiang, Z.-T. Li, Y.-H. Yu, *J. Org. Chem.* **2007**, *72*, 2897 – 2905.

[270] A. C. Try, M. M. Harding, D. G. Hamilton, J. K. M. Sanders, *Chem. Commun.* **1998**, 723 – 724.

[271] K.-M. Park, S.-Y. Kim, J. Heo, D. Whang, S. Sakamoto, K. Yamaguchi, K. Kim, *J. Am. Chem. Soc.* **2002**, *124*, 2140 – 2147.

[272] S.-G. Roh, K.-M. Park, G.-J. Park, S. Sakamoto, K. Yamaguchi, K. Kim, *Angew. Chem.* **1999**, *111*, 671 – 675; *Angew. Chem. Int. Ed.* **1999**, *38*, 637 – 641.

[273] a) C. Piguet, G. Hopfgartner, B. Bocquet, O. Schaad, A. F. Williams, *J. Am. Chem. Soc.* **1994**, *116*, 9092 – 9102; b) C. Piguet, G. Bernardinelli, A. F. Williams, B. Bocquet, *Angew. Chem.* **1995**, *107*, 618 – 621; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 582 – 584.

[274] S. P. Argent, H. Adams, T. Riis-Johannessen, J. C. Jeffery, L. P. Harding, W. Clegg, R. W. Harrington, M. D. Ward, *Dalton Trans.* **2006**, 4996 – 5013.

[275] D. J. Cárdenas, P. Gaviña, J.-P. Sauvage, *Chem. Commun.* **1996**, 1915 – 1916.

[276] D. J. Cárdenas, P. Gaviña, J.-P. Sauvage, *J. Am. Chem. Soc.* **1997**, *119*, 2656 – 2664.

[277] D. J. Cárdenas, J.-P. Collin, P. Gaviña, J.-P. Sauvage, A. De Cian, J. Fischer, N. Armaroli, L. Flamigni, V. Vicinelli, V. Balzani, *J. Am. Chem. Soc.* **1999**, *121*, 5481 – 5488.

[278] D. J. Cárdenas, J.-P. Sauvage, *Inorg. Chem.* **1997**, *36*, 2777 – 2783.

[279] B. A. Blight, J. A. Wisner, M. C. Jennings, *Angew. Chem.* **2007**, *119*, 2893 – 2896; *Angew. Chem. Int. Ed.* **2007**, *46*, 2835 – 2838.

[280] T. J. Burchell, D. J. Eisler, R. J. Puddephatt, *Dalton Trans.* **2005**, 268 – 272.

[281] a) C. Dietrich-Buchecker, N. Geum, A. Hori, M. Fujita, S. Sakamoto, K. Yamaguchi, J.-P. Sauvage, *Chem. Commun.* **2001**, 1182 – 1183; b) C. Dietrich-Buchecker, B. Colasson, M. Fujita, A. Hori, N. Geum, S. Sakamoto, K. Yamaguchi, J.-P. Sauvage, *J. Am. Chem. Soc.* **2003**, *125*, 5717 – 5725.

[282] B. X. Colasson, J.-P. Sauvage, *Inorg. Chem.* **2004**, *43*, 1895 – 1901.

[283] a) M. Beyler, V. Heitz, J.-P. Sauvage, *Chem. Commun.* **2008**, 5396 – 5398; b) M. Beyler, V. Heitz, J.-P. Sauvage, *J. Am. Chem. Soc.* **2010**, *132*, 4409 – 4417.

[284] M. Beyler, V. Heitz, J.-P. Sauvage, *New J. Chem.* **2010**, *34*, 1825 – 1829.

[285] S. L. Castro, O. Just, W. S. Rees, Jr., *Angew. Chem.* **2000**, *112*, 963 – 965; *Angew. Chem. Int. Ed.* **2000**, *39*, 933 – 935.

[286] a) M. Ammann, A. Rang, C. A. Schalley, P. Bäuerle, *Eur. J. Org. Chem.* **2006**, 1940 – 1948; b) P. Bäuerle, M. Ammann, M. Wilde, G. Götz, E. Mena-Osteritz, A. Rang, C. A. Schalley, *Angew. Chem.* **2007**, *119*, 367 – 372; *Angew. Chem. Int. Ed.* **2007**, *46*, 363 – 368.

[287] D. M. P. Mingos, J. Yau, S. Menzer, D. J. Williams, *Angew. Chem.* **1995**, *107*, 2045 – 2047; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1894 – 1895.

[288] M. R. Wiseman, P. A. Marsh, P. T. Bishop, B. J. Brisdon, M. F. Mahon, *J. Am. Chem. Soc.* **2000**, *122*, 12598 – 12599.

[289] S. S.-Y. Chui, R. Chen, C.-M. Che, *Angew. Chem.* **2006**, *118*, 1651 – 1654; *Angew. Chem. Int. Ed.* **2006**, *45*, 1621 – 1624.

[290] For reviews focusing on Puddephatt's work, see: a) R. J. Puddephatt, *Coord. Chem. Rev.* **2001**, *216*, 313 – 332; b) N. C. Habermehl, M. C. Jennings, C. P. McArdle, F. Mohr, R. J. Puddephatt, *Organometallics* **2005**, *24*, 5004 – 5014; c) N. C. Habermehl, D. J. Eisler, C. W. Kirby, N. L.-S. Yue, R. J. Puddephatt, *Organometallics* **2006**, *25*, 2921 – 2928; d) R. J. Puddephatt, *Chem. Soc. Rev.* **2008**, *37*, 2012 – 2027.

[291] C. P. McArdle, M. J. Irwin, M. C. Jennings, R. J. Puddephatt, *Angew. Chem.* **1999**, *111*, 3571 – 3573; *Angew. Chem. Int. Ed.* **1999**, *38*, 3376 – 3378.

[292] C. P. McArdle, M. J. Irwin, M. C. Jennings, J. J. Vittal, R. J. Puddephatt, *Chem. Eur. J.* **2002**, *8*, 723 – 734.

[293] a) F. Mohr, M. C. Jennings, R. J. Puddephatt, *Eur. J. Inorg. Chem.* **2003**, 217 – 223; b) C. P. McArdle, S. Van, M. C. Jennings, R. J. Puddephatt, *J. Am. Chem. Soc.* **2002**, *124*, 3959 – 3965; c) F. Mohr, D. J. Eisler, C. P. McArdle, K. Atieh, M. C. Jennings, R. J. Puddephatt, *J. Organomet. Chem.* **2003**, *670*, 27 – 36.

[294] N. C. Habermehl, F. Mohr, D. J. Eisler, M. C. Jennings, R. J. Puddephatt, *Can. J. Chem.* **2006**, *84*, 111 – 123.

[295] C. P. McArdle, M. C. Jennings, J. J. Vittal, R. J. Puddephatt, *Chem. Eur. J.* **2001**, *7*, 3572 – 3583.

[296] U. E. I. Horvath, J. M. McKenzie, S. Cronje, H. G. Raubenheimer, L. J. Barbour, *Chem. Commun.* **2009**, 6598 – 6600.

[297] C. P. McArdle, J. J. Vittal, R. J. Puddephatt, *Angew. Chem.* **2000**, *112*, 3977 – 3980; *Angew. Chem. Int. Ed.* **2000**, *39*, 3819 – 3822.

[298] a) S. R. Batten, R. Robson, *Angew. Chem.* **1998**, *110*, 1558 – 1595; *Angew. Chem. Int. Ed.* **1998**, *37*, 1460 – 1494; b) L. Carlucci, G. Ciani, D. M. Proserpio, *Coord. Chem. Rev.* **2003**, *246*, 247 – 289; c) Z. Niu, H. W. Gibson, *Chem. Rev.* **2009**, *109*, 6024 – 6046.

[299] For examples of polycatenated structures, interpenetrated networks, frameworks, nets and metal-organic frameworks (MOFs), see: a) for an example of a polycatenane formed using Sauvage's Cu^{I}(dpp)$_2$ motif, see: b) J.-L. Weidmann, J.-M. Kern, J.-P. Sauvage, Y. Geerts, D. Muscat, K. Müllen, *Chem. Commun.* **1996**, 1243 – 1244; c) J.-L. Weidmann, J.-M. Kern, J.-P. Sauvage, D. Muscat, S. Mullins, W. Köhler, C. Rosenauer, H. J. Räder, K. Martin, Y. Geerts, *Chem. Eur. J.* **1999**, *5*, 1841 – 1851; d) for frameworks formed from 4,4′-bipyridine, see: A. J. Blake, M. T. Brett, N. R. Champness, A. N. Khlobystov, D.-L. Long, C. Wilson, M. Schröder, *Chem. Commun.* **2001**, 2258 – 2259; e) N. L. Rosi, M. Eddaoudi, J. Kim, M. O'Keeffe, O. M. Yaghi, *CrystEngComm* **2002**, *4*, 401 – 404; f) G. J. Halder, C. J. Kepert, B. Moubaraki, K. S. Murray, J. D. Cashion, *Science* **2002**, *298*, 1762 – 1765; g) for a discussion of the use of dynamic frameworks for the binding of ions and gases, see: O. M. Yaghi, *Nat. Mater.* **2007**, *6*, 92 – 93; h) for an example of an interpenetrated network that displays hysteretic CO_2 uptake, see: K. L. Mulfort, O. K. Farha, C. D. Malliakas, M. G. Kanatzidis, J. T. Hupp, *Chem. Eur. J.* **2010**, *16*, 276 – 281.

[300] a) C.-M. Jin, H. Lu, L.-Y. Wu, J. Huang, *Chem. Commun.* **2006**, 5039 – 5041; b) C.-M. Jin, L.-Y. Wu, H. Lu, Y. Xu, *Cryst. Growth Des.* **2008**, *8*, 215 – 218.

[301] For general knot reviews, see: a) C. Dietrich-Buchecker, J.-P. Sauvage, *New J. Chem.* **1992**, *16*, 277 – 285; b) C. Dietrich-Buchecker, B. X. Colasson, J.-P. Sauvage, *Top. Curr. Chem.* **2005**, *249*, 261 – 283; c) D. Andrae, *New J. Chem.* **2006**, *30*, 873 – 882; d) E. E. Fenlon, *Eur. J. Org. Chem.* **2008**, 5023 – 5035; e) D. B. Amabilino, L. Pérez-García, *Chem. Soc. Rev.* **2009**, *38*, 1562 – 1571.

[302] The use of crossing number to characterize and tabluate knotted topologies was first employed by Edinburgh mathematician Peter Tait. For an example of one of Tait's knot tables see: a) P. G. Tait, *Trans. R. Soc. Edinburgh* **1883 – 1884**, *32*, 327 – 342. http://www.maths.ed.ac.uk/~aar/knots/; The use of crossing number in combination with the order of a knot was introduced by Alexander and Briggs in 1926, see: b) J. W. Alexander, G. B. Briggs, *Ann. Math.* **1926 – 1927**, *28*, 562 – 586; c) D. Rolfsen, *Knots and Links*, Publish or Perish, Berkeley, **1976**.

[303] The topologically trivial unknot (any simple ring or macrocycle) and the trefoil knot are the only prime knots to have been synthesized to date from small molecules,[373] however,

DNA strands with the connectivity of higher order prime knots are known. For the synthesis of a figure-of-eight (4_1) knot see: a) S. M. Du, B. D. Stollar, N. C. Seeman, *J. Am. Chem. Soc.* **1995**, *117*, 1194 – 1200. For a three-twist (5_2) and an endless (7_4) knot see: b) A. Bucka, A. Stasiak, *Nucleic Acids Res.* **2002**, *30*, 24e.

[304] C. O. Dietrich-Buchecker, J.-P. Sauvage, *Angew. Chem.* **1989**, *101*, 192 – 194; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 189 – 192.

[305] a) For a review of synthetic DNA knots, see: N. C. Seeman, *Angew. Chem.* **1998**, *110*, 3408 – 3428; *Angew. Chem. Int. Ed.* **1998**, *37*, 3220 – 3238; b) for a review of hydrogen bond template knots, see: O. Lukin, F. Vögtle, *Angew. Chem.* **2005**, *117*, 1480 – 1501; *Angew. Chem. Int. Ed.* **2005**, *44*, 1456 – 1477; c) for an example of a synthetic knot constructed from amino acid units, see: M. Feigel, R. Ladberg, S. Engels, R. Herbst-Irmer, R. Fröhlich, *Angew. Chem.* **2006**, *118*, 5827 – 5831; *Angew. Chem. Int. Ed.* **2006**, *45*, 5698 – 5702.

[306] C. O. Dietrich-Buchecker, J. Guilhem, C. Pascard, J.-P. Sauvage, *Angew. Chem.* **1990**, *102*, 1202 – 1204; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1154 – 1156.

[307] For detailed studies on these type of knots, see: a) C. O. Dietrich-Buchecker, J.-P. Sauvage, J.-P. Kintzinger, P. Maltèse, C. Pascard, J. Guilhem, *New J. Chem.* **1992**, *16*, 931 – 942; b) C. O. Dietrich-Buchecker, J.-F. Nierengarten, J.-P. Sauvage, *Tetrahedron Lett.* **1992**, *33*, 3625 – 3628; c) C. O. Dietrich-Buchecker, J.-P. Sauvage, A. De Cian, J. Fischer, *J. Chem. Soc. Chem. Commun.* **1994**, 2231 – 2232.

[308] a) C. Dietrich-Buchecker, G. Rapenne, J.-P. Sauvage, *Chem. Commun.* **1997**, 2053 – 2054; b) G. Rapenne, C. Dietrich-Buchecker, J.-P. Sauvage, *J. Am. Chem. Soc.* **1999**, *121*, 994 – 1001.

[309] For the resolution of a single enantiomerically pure isomer, see: a) G. Rapenne, C. Dietrich-Buchecker, J.-P. Sauvage, *J. Am. Chem. Soc.* **1996**, *118*, 10932 – 10933; b) C. O. Dietrich-Buchecker, G. Rapenne, J.-P. Sauvage, A. De Cian, J. Fischer, *Chem. Eur. J.* **1999**, *5*, 1432 – 1439; c) for a chiro-optical study, see: S. C. J. Meskers, H. P. J. Dekkers, G. Rapenne, J.-P. Sauvage, *Chem. Eur. J.* **2000**, *6*, 2129 – 2134.

[310] a) C. O. Dietrich-Buchecker, J.-P. Sauvage, N. Armaroli, P. Ceroni, V. Balzani, *Angew. Chem.* **1996**, *108*, 1190 – 1193; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1119 – 1121; b) C. Dietrich-Buchecker, N. G. Hwang, J.-P. Sauvage, *New J. Chem.* **1999**, *23*, 911 – 914.

[311] M. Meyer, A.-M. Albrecht-Gary, C. O. Dietrich-Buchecker, J.-P. Sauvage, *J. Am. Chem. Soc.* **1997**, *119*, 4599 – 4607.

[312] C. O. Dietrich-Buchecker, J.-F. Nierengarten, J.-P. Sauvage, N. Armaroli, V. Balzani, L. De Cola, *J. Am. Chem. Soc.* **1993**, *115*, 11237 – 11244.

[313] L.-E. Perret-Aebi, A. von Zelewsky, C. Dietrich-Buchecker, J.-P. Sauvage, *Angew. Chem.* **2004**, *116*, 4582 – 4585; *Angew. Chem. Int. Ed.* **2004**, *43*, 4482 – 4485.

[314] H. Adams, E. Ashworth, G. A. Breault, J. Guo, C. A. Hunter, P. C. Mayers, *Nature* **2001**, *411*, 763.

[315] a) J. Guo, P. C. Mayers, G. A. Breault, C. A. Hunter, *Nat. Chem.* **2010**, *2*, 218 – 222; b) E. E. Fenlon, *Nat. Chem.* **2010**, *2*, 156 – 157.

[316] R. F. Carina, C. Dietrich-Buchecker, J.-P. Sauvage, *J. Am. Chem. Soc.* **1996**, *118*, 9110 – 9116.

[317] C. D. Pentecost, K. S. Chichak, A. J. Peters, G. W. V. Cave, S. J. Cantrill, J. F. Stoddart, *Angew. Chem.* **2007**, *119*, 222 – 226; *Angew. Chem. Int. Ed.* **2007**, *46*, 218 – 222.

[318] a) J.-F. Nierengarten, C. O. Dietrich-Buchecker, J.-P. Sauvage, *J. Am. Chem. Soc.* **1994**, *116*, 375 – 376; b) C. Dietrich-Buchecker, E. Leize, J.-F. Nierengarten, J.-P. Sauvage, A. van Dorsselaer, *J. Chem. Soc. Chem. Commun.* **1994**, 2257 – 2258.

[319] C. Dietrich-Buchecker, J.-P. Sauvage, *Chem. Commun.* **1999**, 615 – 616.

[320] C. D. Meyer, R. S. Forgan, K. S. Chichak, A. J. Peters, N. Tangchaivang, G. W. V. Cave, S. I. Khan, S. J. Cantrill, J. F. Stoddart, *Chem. Eur. J.* **2010**, *16*, 12570 – 12581.

[321] F. Ibukuro, M. Fujita, K. Yamaguchi, J.-P. Sauvage, *J. Am. Chem. Soc.* **1999**, *121*, 11014 – 11015.

[322] C. Peinador, V. Blanco, J. M. Quintela, *J. Am. Chem. Soc.* **2009**, *131*, 920 – 921.

[323] J. Bourlier, A. Jouaiti, N. Kyritsakas-Gruber, L. Allouche, J.-M. Planeix, M. W. Hosseini, *Chem. Commun.* **2008**, 6191 – 6193.

[324] T. K. Ronson, J. Fisher, L. P. Harding, P. J. Rizkallah, J. E. Warren, M. J. Hardie, *Nat. Chem.* **2009**, *1*, 212 – 216.

[325] C. Liang, K. Mislow, *J. Math. Chem.* **1994**, *16*, 27 – 35.

[326] C. Mao, W. Sun, N. C. Seeman, *Nature* **1997**, *386*, 137 – 138.

[327] M. Benaglia, F. Ponzini, C. R. Woods, J. S. Siegel, *Org. Lett.* **2001**, *3*, 967 – 969.

[328] S.-H. Chiu, A. R. Pease, J. F. Stoddart, A. J. P. White, D. J. Williams, *Angew. Chem.* **2002**, *114*, 280 – 284; *Angew. Chem. Int. Ed.* **2002**, *41*, 270 – 274.

[329] M. Schmittel, A. Ganz, D. Fenske, *Org. Lett.* **2002**, *4*, 2289 – 2292.

[330] J. C. Loren, M. Yoshizawa, R. F. Haldimann, A. Linden, J. S. Siegel, *Angew. Chem.* **2003**, *115*, 5880 – 5883; *Angew. Chem. Int. Ed.* **2003**, *42*, 5702 – 5705.

[331] a) O. V. Dolomanov, A. J. Blake, N. R. Champness, M. Schröder, C. Wilson, *Chem. Comm.* **2003**, 682 – 683; b) For a related structure, see: M. Schmittel, B. He, J. Fan, J. W. Bats, M. Engeser, M. Schlosser, H.-J. Deiseroth, *Inorg. Chem.* **2009**, *48*, 8192 – 8200.

[332] a) K. S. Chichak, S. J. Cantrill, A. R. Pease, S. H. Chiu, G. W. V. Cave, J. L. Atwood, J. F. Stoddart, *Science* **2004**, *304*, 1308 – 1312; b) C. A. Schalley, *Angew. Chem.* **2004**, *116*, 4499 – 4501; *Angew. Chem. Int. Ed.* **2004**, *43*, 4399 – 4401; c) S. J. Cantrill, K. S. Chichak, A. J. Peters, J. F. Stoddart, *Acc. Chem. Res.* **2005**, *38*, 1 – 9.

[333] C. D. Pentecost, N. Tangchaivang, S. J. Cantrill, K. S. Chichak, A. J. Peters, J. F. Stoddart, *J. Chem. Educ.* **2007**, *84*, 855 – 859.

[334] A. J. Peters, K. S. Chichak, S. J. Cantrill, J. F. Stoddart, *Chem. Commun.* **2005**, 3394 – 3396.

[335] K. S. Chichak, S. J. Cantrill, J. F. Stoddart, *Chem. Commun.* **2005**, 3391 – 3393.

[336] K. S. Chichak, A. J. Peters, S. J. Cantrill, J. F. Stoddart, *J. Org. Chem.* **2005**, *70*, 7956 – 7962.

[337] C. R. Yates, D. Benítez, S. I. Khan, J. F. Stoddart, *Org. Lett.* **2007**, *9*, 2433 – 2436.

[338] G. D. Scott, K. S. Chichak, A. J. Peters, S. J. Cantrill, J. F. Stoddart, H. W. Jiang, *Phys. Rev. B* **2006**, *74*, 113404 – 113407.

[339] C. D. Pentecost, A. J. Peters, K. S. Chichak, G. W. V. Cave, S. J. Cantrill, J. F. Stoddart, *Angew. Chem.* **2006**, *118*, 4205 – 4210; *Angew. Chem. Int. Ed.* **2006**, *45*, 4099 – 4104.

[340] G. A. Timco, T. B. Faust, F. Tuna, R. E. P. Winpenny, *Chem. Soc. Rev.* **2011**, *40*, 3067 – 3075.

[341] F. Durola, J. Lux, J.-P. Sauvage, O. S. Wenger, *Supramol. Chem.* **2010**, *23*, 42 – 52.

[342] D.-H. Qu, H. Tian, *Chem. Sci.* **2011**, *2*, 1011 – 1015.

[343] J.-P. Sauvage, Y. Trolez, D. Canevet, M. Sallé, *Eur. J. Org. Chem.* **2011**, *2011*, 2413 – 2416.

[344] J.-P. Collin, S. Durot, J.-P. Sauvage, Y. Trolez, *New J. Chem.* **2011**, DOI: 10.1039/C1NJ20213H.

[345] L. M. Hancock, P. D. Beer, *Chem. Commun.* **2011**, *47*, 6012 – 6014.

[346] J. D. Megiatto, D. I. Schuster, *Org. Lett.* **2011**, *13*, 1808 – 1811.

[347] M. Jakob, A. Berg, H. Levanon, D. I. Schuster, J. D. Megiatto, *J. Phys. Chem. A* **2011**, *115*, 5044 – 5052.

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

[348] H. Lahlali, K. Jobe, M. Watkinson, S. M. Goldup, *Angew. Chem.* **2011**, *123*, 4237–4241; *Angew. Chem. Int. Ed.* **2011**, *50*, 4151–4155.

[349] H. M. Cheng, D. A. Leigh, F. Maffei, P. R. McGonigal, A. M. Z. Slawin, J. Wu, *J. Am. Chem. Soc.* **2011**, *133*, 12298–12303.

[350] M. J. Langton, J. D. Matichak, A. L. Thompson, H. L. Anderson, *Chem. Sci.* **2011**, DOI: 10.1039/C1SC00358E.

[351] P. E. Barran, H. L. Cole, S. M. Goldup, D. A. Leigh, P. R. McGonigal, M. D. Symes, J. Wu, M. Zengerle, *Angew. Chem.* **2011**, *123*, DOI: 10.1002/ange.201105012; *Angew. Chem. Int. Ed.* **2011**, *50*, DOI: 10.1002/anie.201105012.

[352] S. Shinoda, T. Maeda, H. Miyake, H. Tsukube, *Supramol. Chem.* **2011**, *23*, 244–248.

[353] H. Li, A. C. Fahrenbach, A. Coskun, Z. Zhu, G. Barin, Y.-L. Zhao, Y. Y. Botros, J.-P. Sauvage, J. F. Stoddart, *Angew. Chem.* **2011**, *123*, 6914–6920; *Angew. Chem. Int. Ed.* **2011**, *50*, 6782–6788.

[354] T. K. Monhaphol, S. Andersson, L. Sun, *Chem. Eur. J.* **2011**, DOI: 10.1002/chem.201002618.

[355] Y. Suzaki, K. Shimada, E. Chihara, T. Saito, Y. Tsuchido, K. Osakada, *Org. Lett.* **2011**, *13*, 3774–3777.

[356] N. H. Evans, C. J. Serpell, P. D. Beer, *Chem. Commun.* **2011**, *47*, 8775–8777.

[357] N. H. Evans, P. D. Beer, *Org. Biomol. Chem.* **2011**, *9*, 92–100.

[358] L. Zhu, M. Lu, D. Qu, Q. Wang, H. Tian, *Org. Biomol. Chem.* **2011**, *9*, 4226–4233.

[359] Z. Cao, W. P. Forrest, Y. Gao, P. E. Fanwick, Y. Zhang, T. Ren, *Inorg. Chem.* **2011**, DOI: 10.1021/ic200836v.

[360] M. Beyler, V. Heitz, J.-P. Sauvage, *New J. Chem.* **2011**, *35*, 1751–1757.

[361] J. J. Henkelis, T. K. Ronson, L. P. Harding, M. J. Hardie, *Chem. Commun.* **2011**, *47*, 6560–6562.

[362] H.-Y. Gong, B. M. Rambo, W. Cho, V. M. Lynch, M. Oh, J. L. Sessler, *Chem. Commun.* **2011**, *47*, 5973–5975.

[363] D. J. Mercer, V. N. Vukotic, S. J. Loeb, *Chem. Commun.* **2011**, *47*, 896–898.

[364] H. Wu, H.-Y. Liu, Y.-Y. Liu, J. Yang, B. Liu, J.-F. Ma, *Chem. Commun.* **2011**, *47*, 1818–1820.

[365] H. Wu, J. Yang, Z.-M. Su, S. R. Batten, J.-F. Ma, *J. Am. Chem. Soc.* **2011**, *133*, 11406–11409.

[366] K. I. Arias, E. Zysman-Colman, J. C. Loren, A. Linden, J. S. Siegel, *Chem. Commun.* **2011**, *47*, 9588–9590.

[367] C. R. Woods, M. Benaglia, S. Toyota, K. Hardcastle, J. S. Siegel, *Angew. Chem.* **2001**, *113*, 771–773; *Angew. Chem. Int. Ed.* **2001**, *40*, 749–751.

[368] T. Castle, M. E. Evans, S. T. Hyde, *New J. Chem.* **2008**, *32*, 1484–1492.

[369] F. Li, J. K. Clegg, L. F. Lindoy, R. B. Macquart, G. V. Meehan, *Nat. Commun.* **2011**, *2*, 205.

[370] C. A. Otter, P. J. Patty, M. A. K. Williams, M. R. Waterland, S. G. Telfer, *Nanoscale* **2011**, *3*, 941–944.

[371] A. Bunha, M. C. Tria, R. Advincula, *Chem. Commun.* **2011**, *47*, 9173–9175.

[372] J.-P. Collin, S. Durot, M. Keller, J.-P. Sauvage, Y. Trolez, M. Cetina, K. Rissanen, *Chem. Eur. J.* **2011**, *17*, 947–957.

[373] J.-F. Ayme, J. E. Beves, D. A. Leigh, R. T. McBurney, K. Rissanen, D. Schultz, submitted for publication.

[374] *Handbook of Knot Theory* (Eds.: W. W. Menasco, M. B. Thistlethwaite), Elsevier, Amsterdam, **2005**.

© 2011 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim