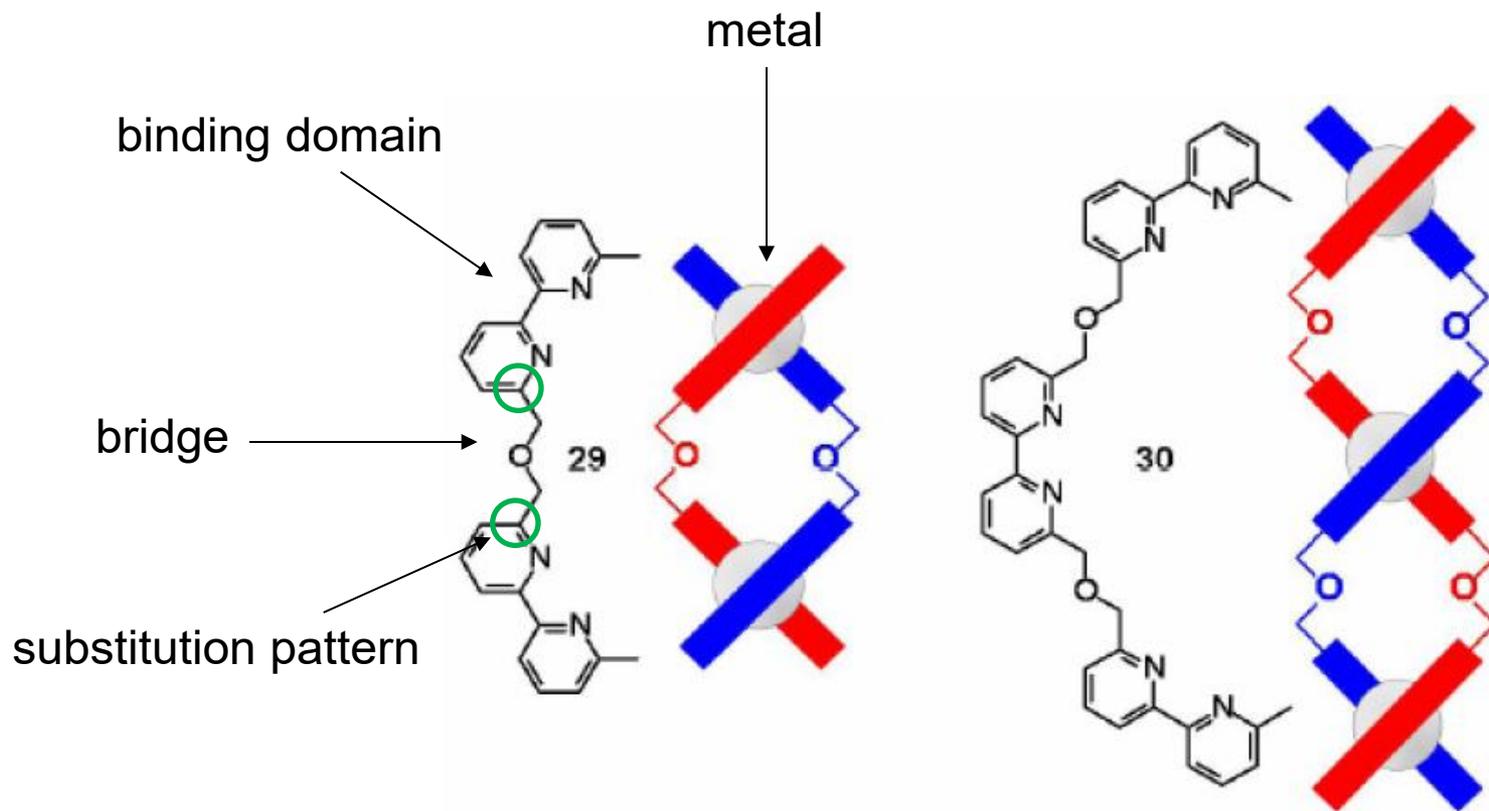
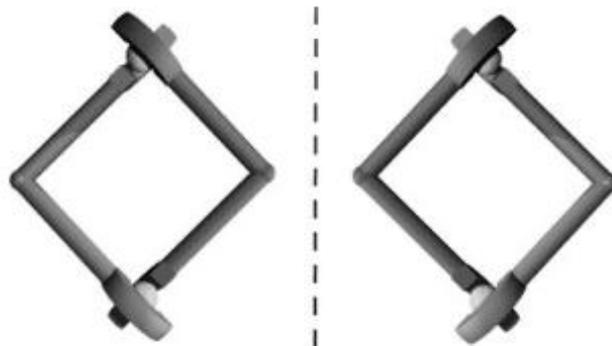


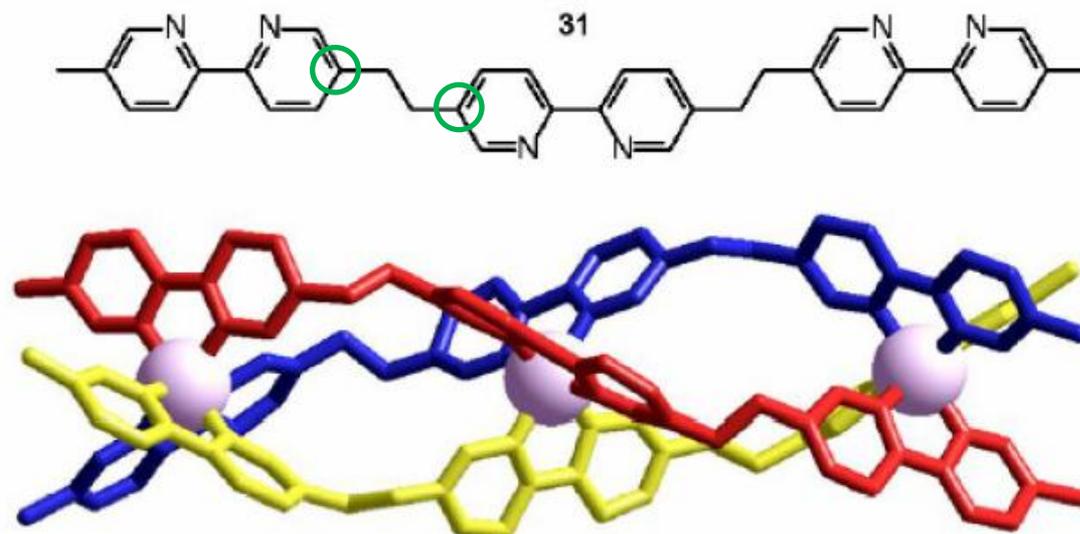
# Double stranded helicates



Chirality

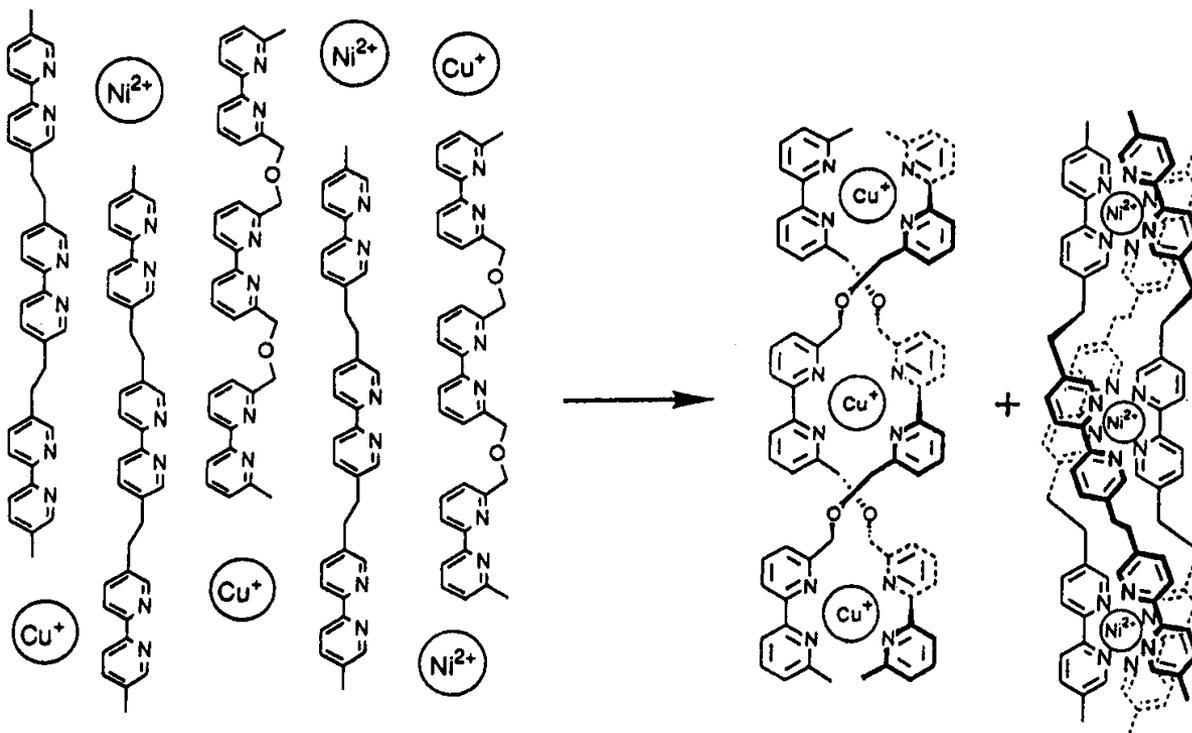


## Triple stranded helicates

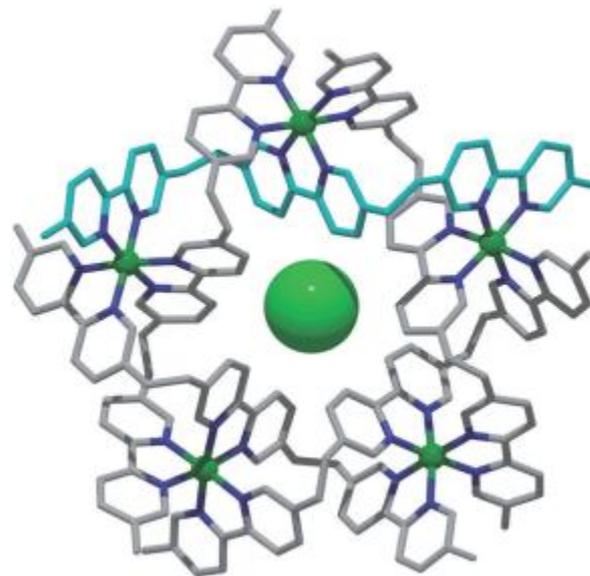
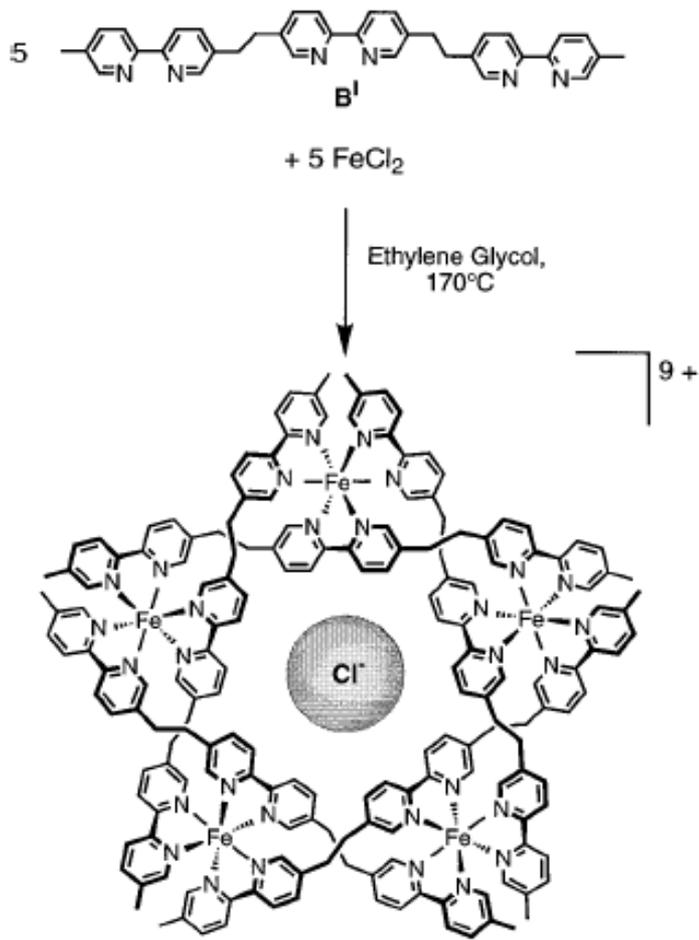


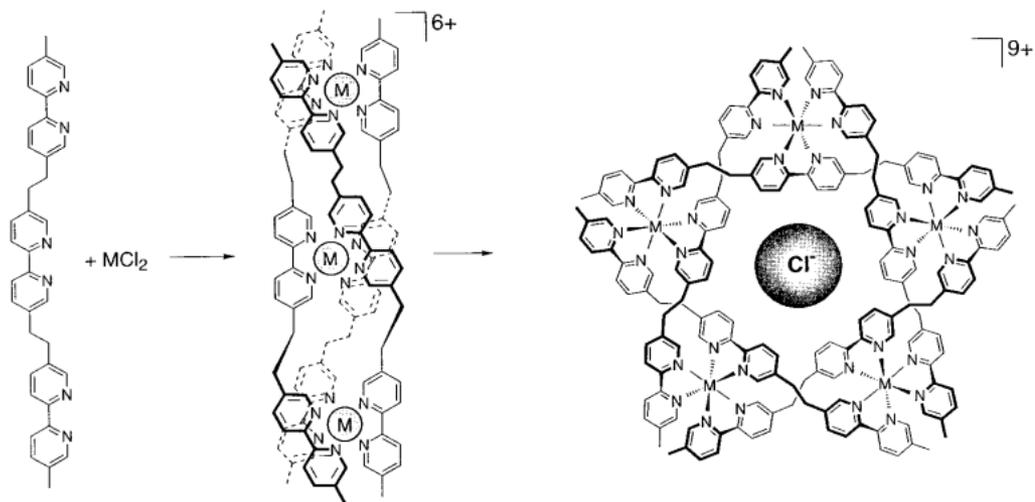
- Ni(II) : octahedral geometry
- one ligand can not wrap around one Ni(II) cation: trimerization
- other metals: Co(II), Fe(II), lanthanides

# Double and Triple Helicates: an example of Self-sorting



# Cyclic Helicates





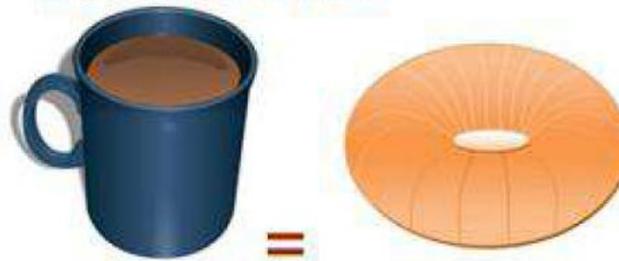
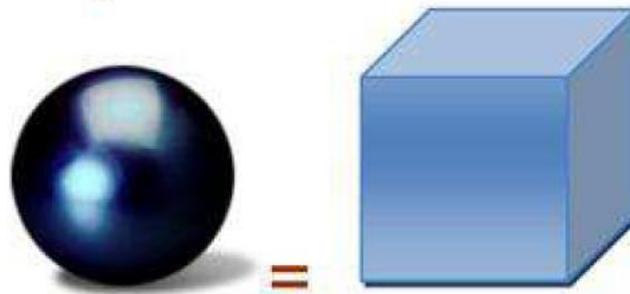
**$^1H$ -NMR**

**ESI-MS**

# Topology

---

In topology, angles, distances or shapes have no meaning  
But the object cannot be cut

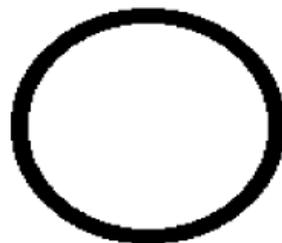


## Molecular graph

---

Representation of the bonds between atoms with no interest in their chemical nature

(a)



→ planar graph

One possible conformation with no crossing in 2D representation

12

## Topological chemistry

---

- If two molecules are different only for their graphs, they are **topological isomers**



**a** is an isomer of **b** and **c**.  
**b** and **c** are topological enantiomers.

Knotted and intertwined patterns have fascinated mankind and artists for centuries, because of the beauty and the symbolism they convey. Therefore it is not surprising if they can be found in the cultural production of virtually all civilizations across time and space.

## Molecular graph

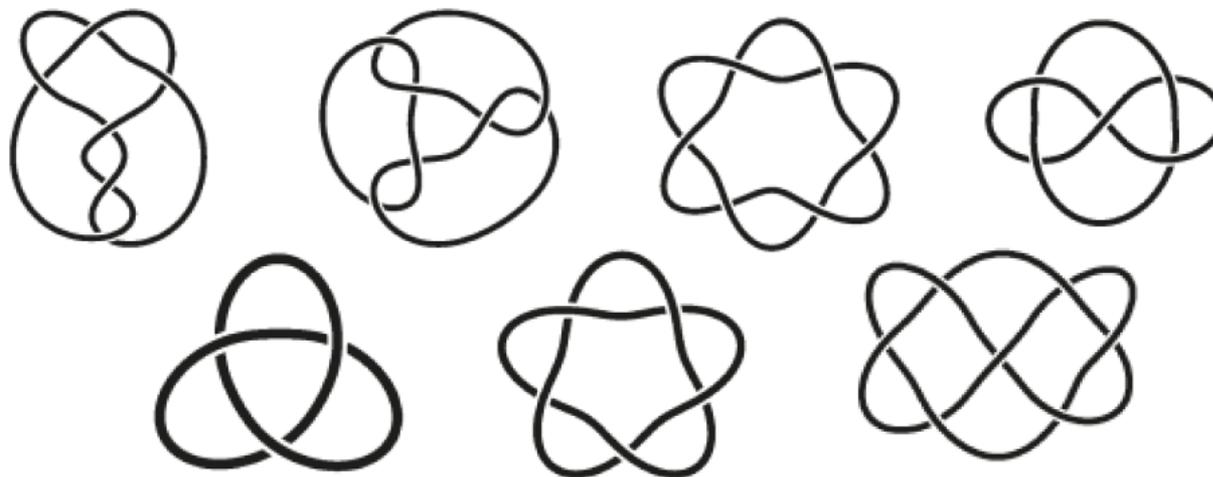
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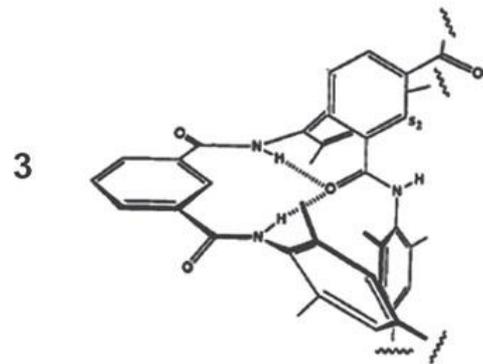
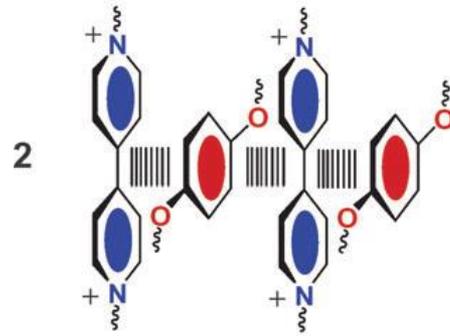
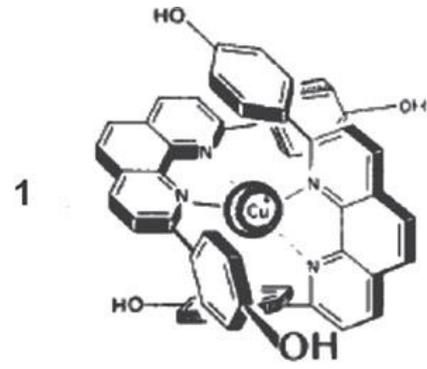


 non-planar graph

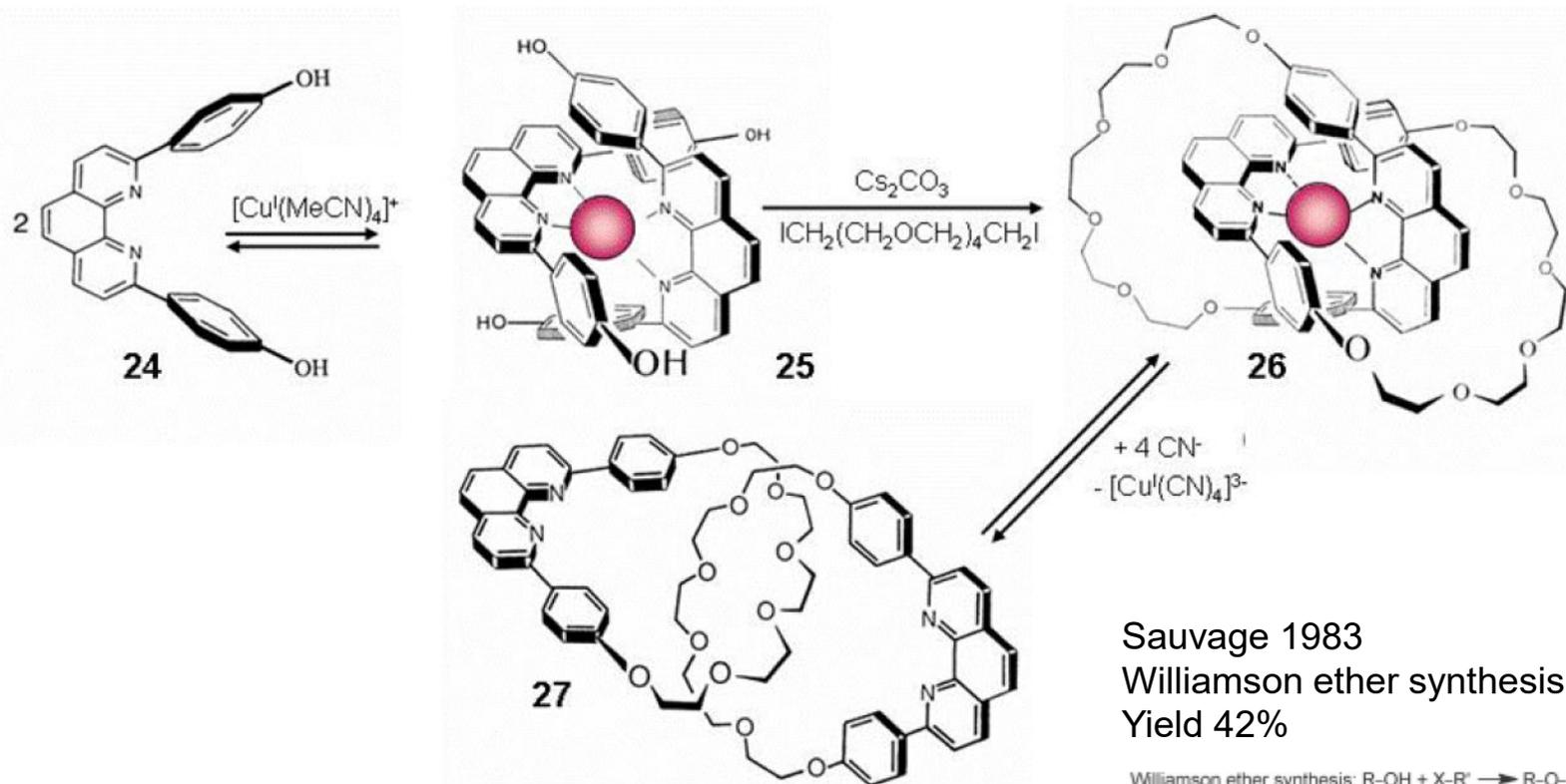
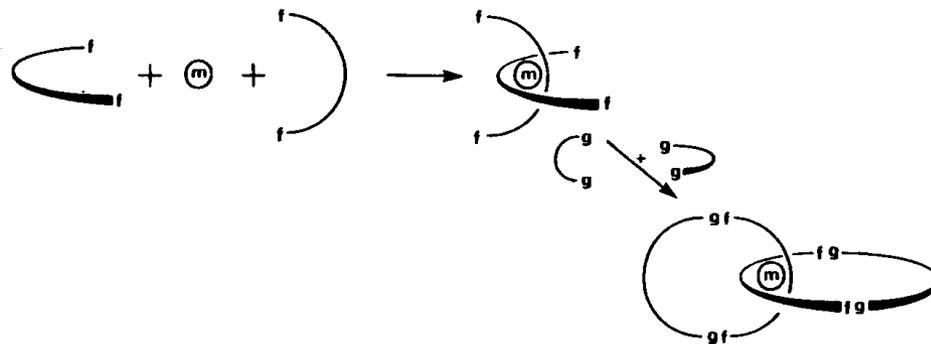
No possible conformation with no crossing in 2D representation

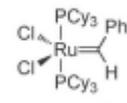
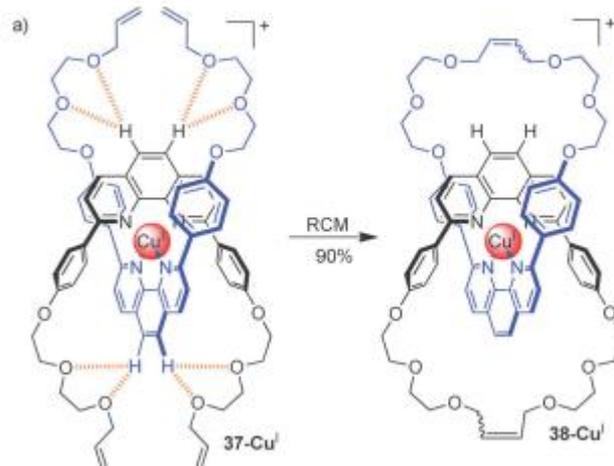
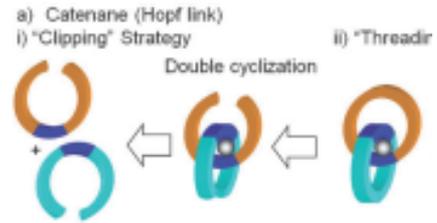
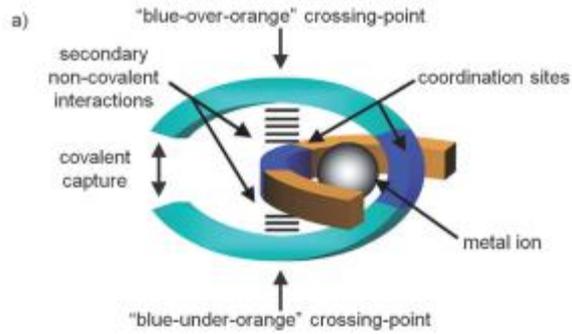
topological chemistry is the chemistry of molecules having a non planar graph

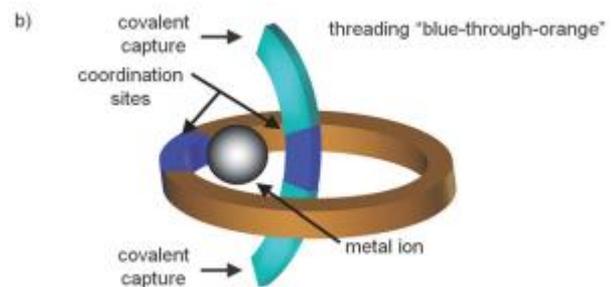




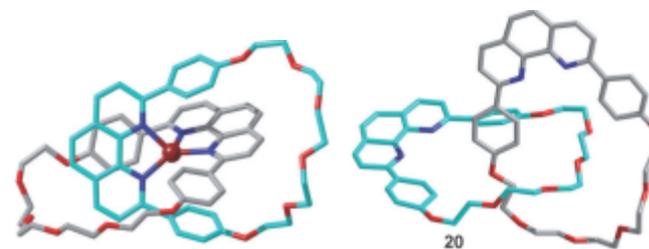
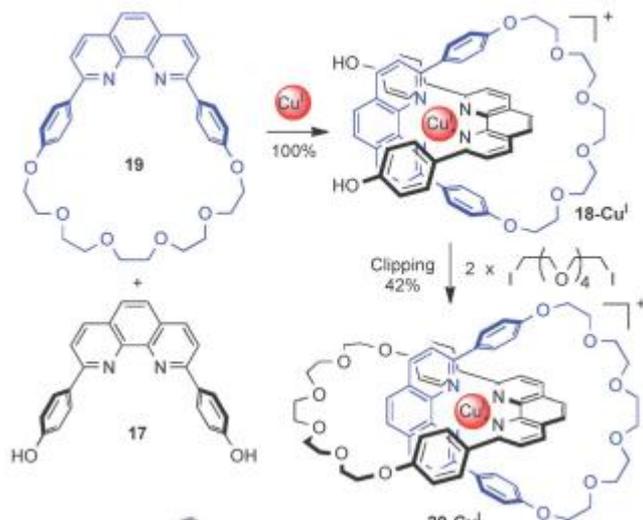
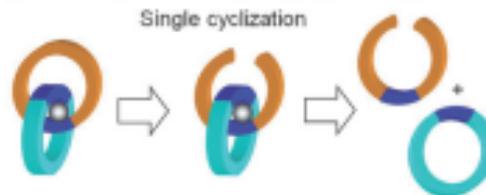
# [n]Catenanes

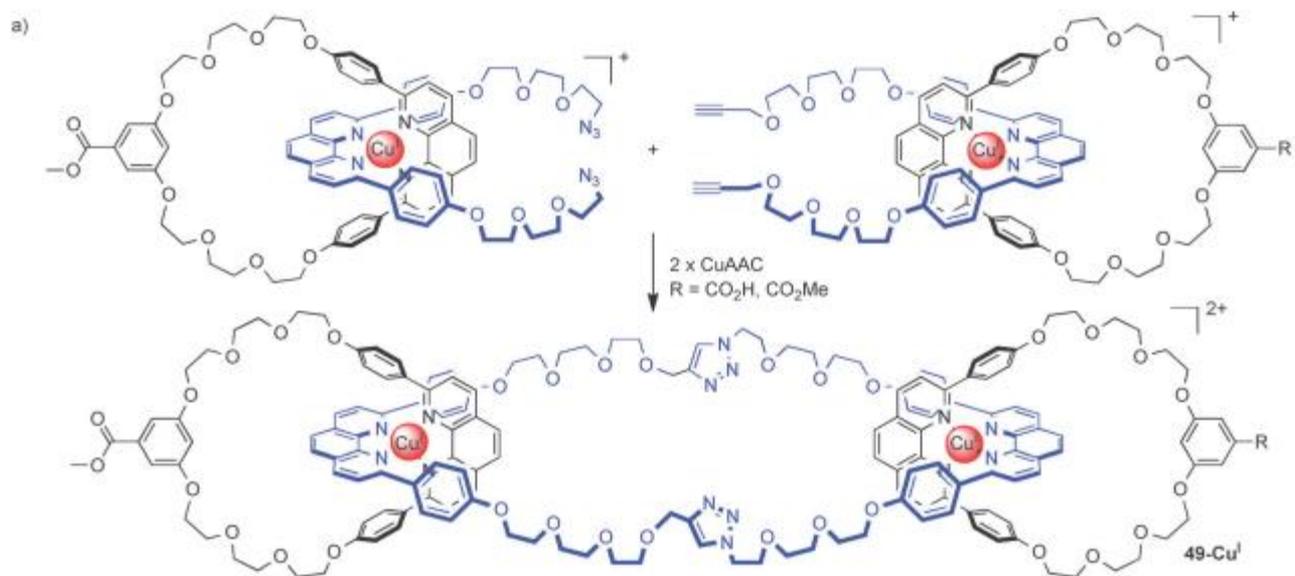


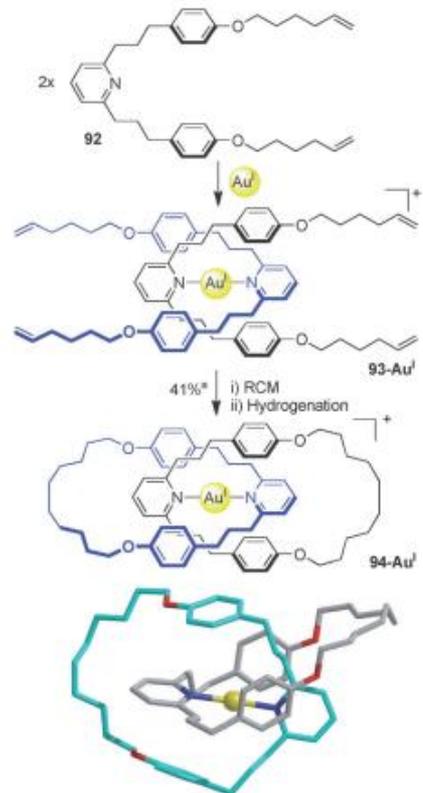
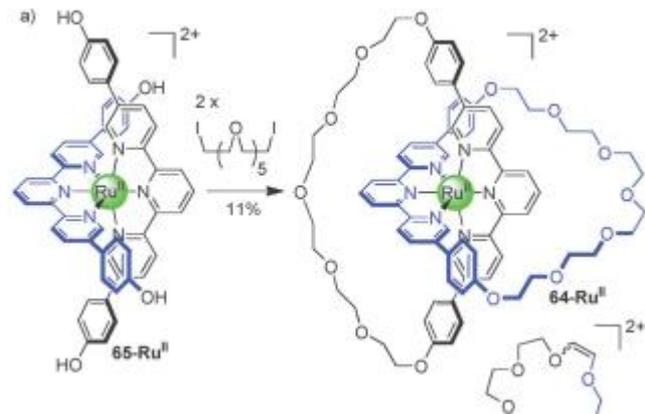


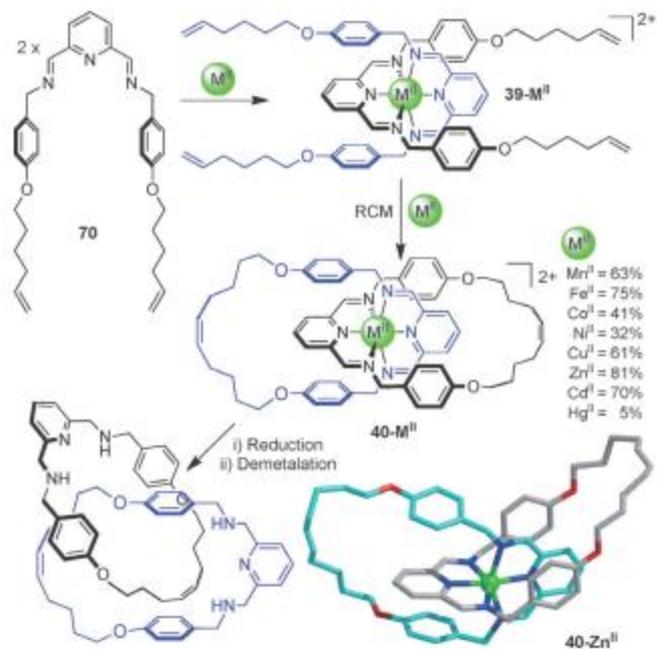


ii) "Threading-followed-by-clipping" strategy

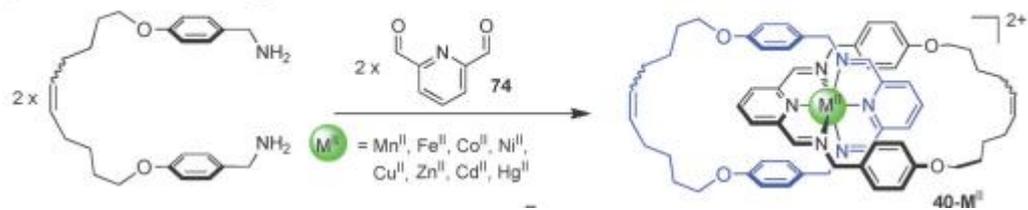




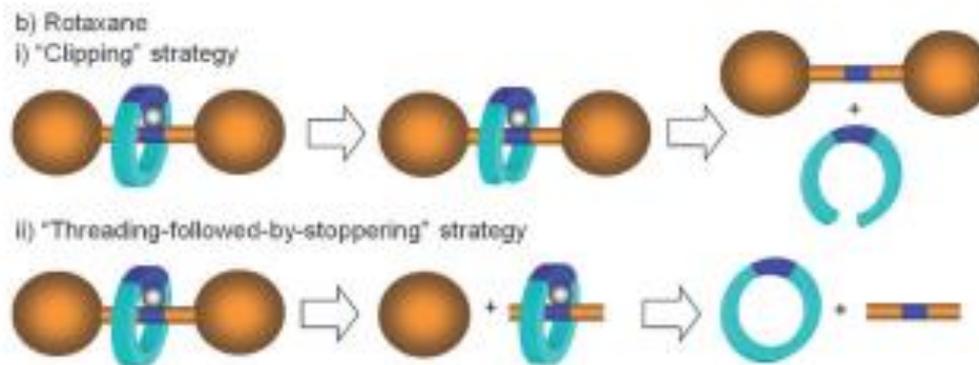


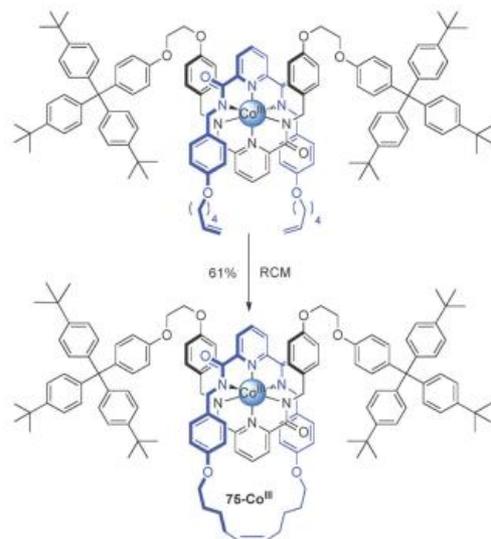
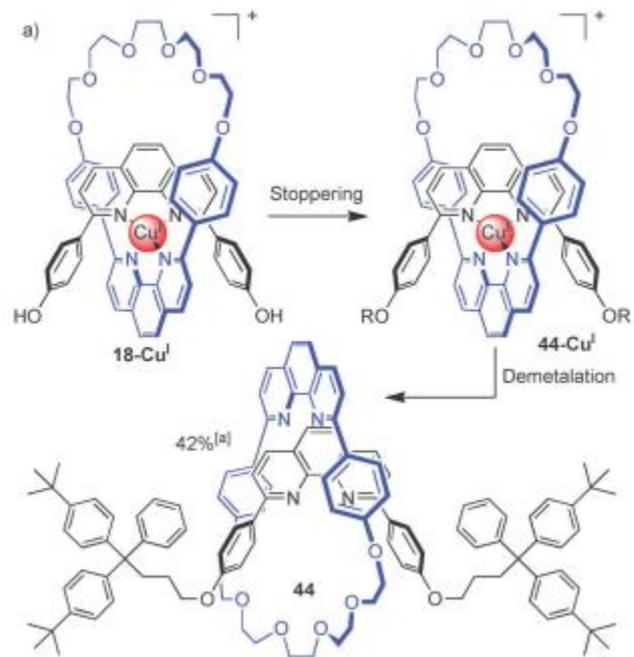


c) Imine bond formation:  $R-NH_2 + R'-CHO \rightarrow R-N=CH-R'$



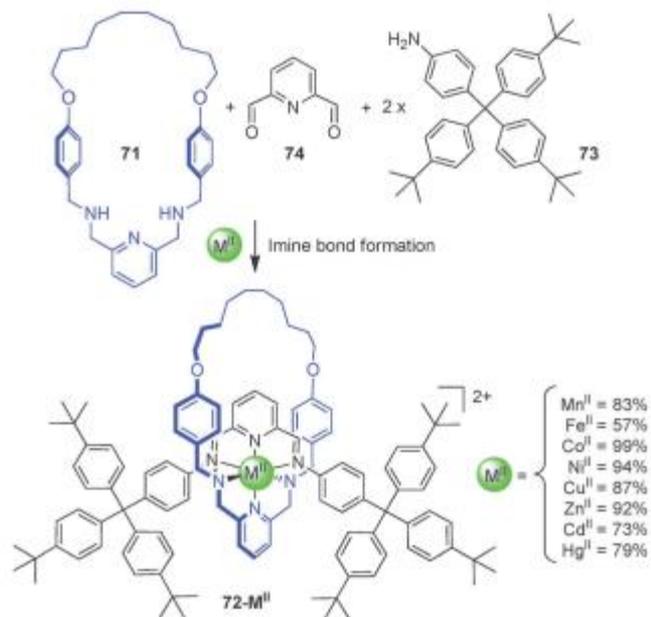
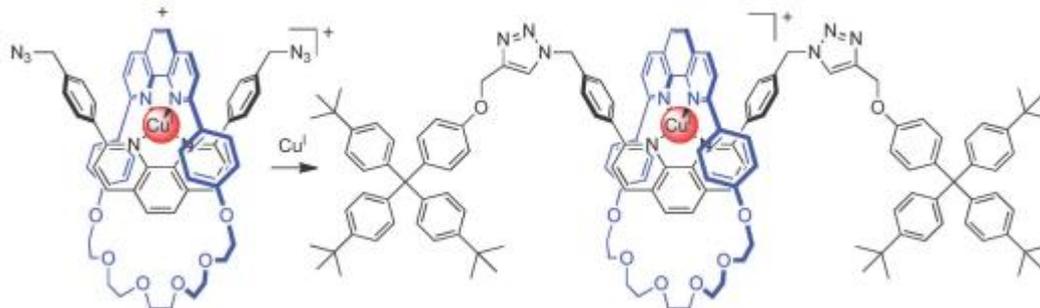
# [2]Rotaxanes

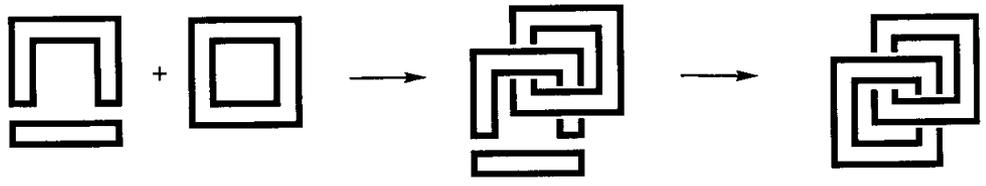




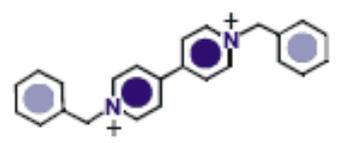


2 x  $(t\text{-BuC}_6\text{H}_4)_3\text{CC}_6\text{H}_4\text{OCH}_2\text{-C}\equiv\text{C-H}$  **95**

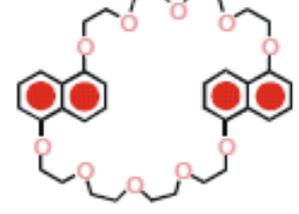




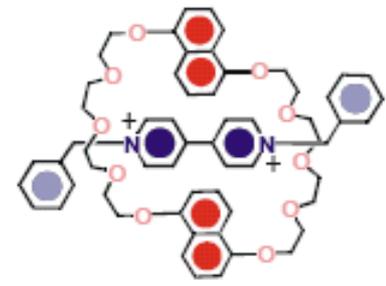
Paraquat cation

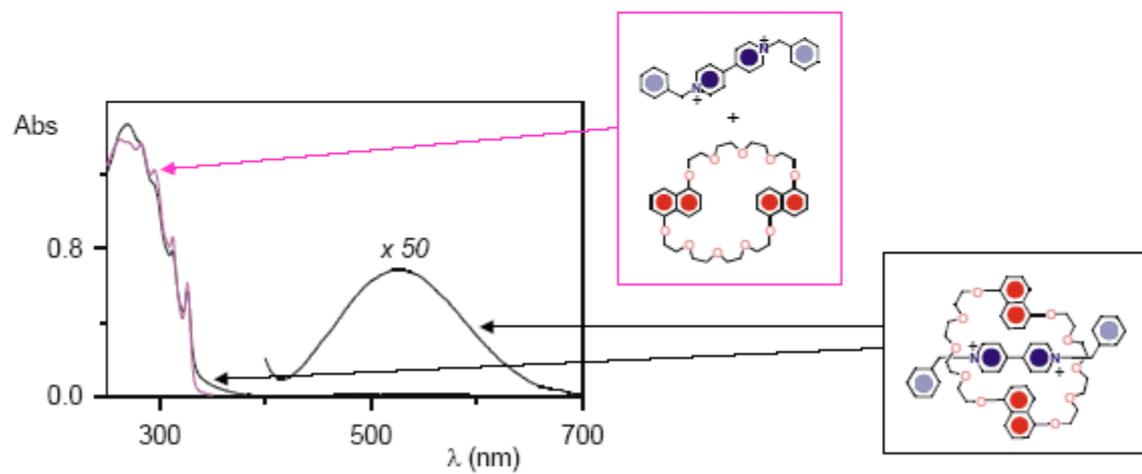
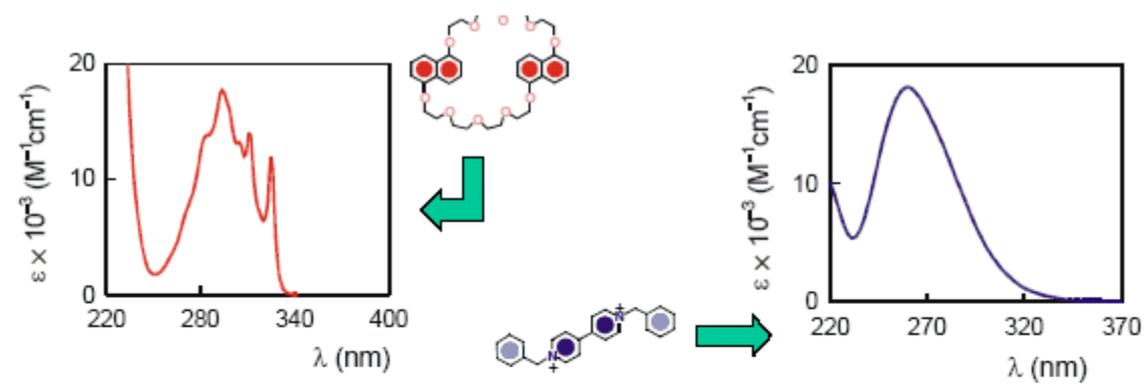


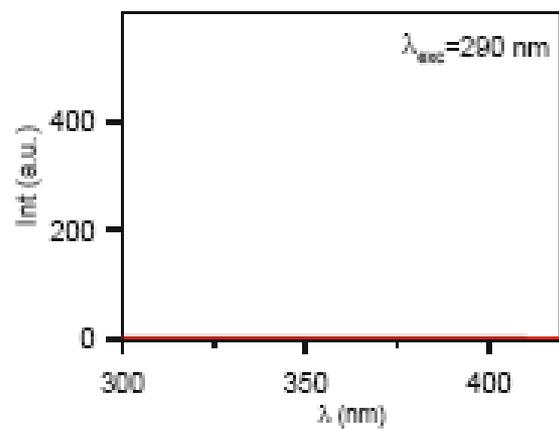
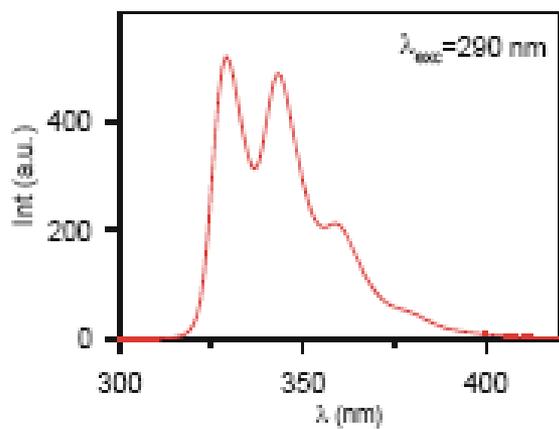
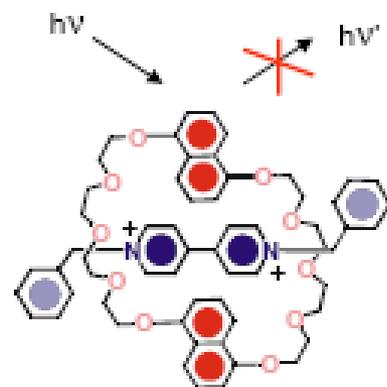
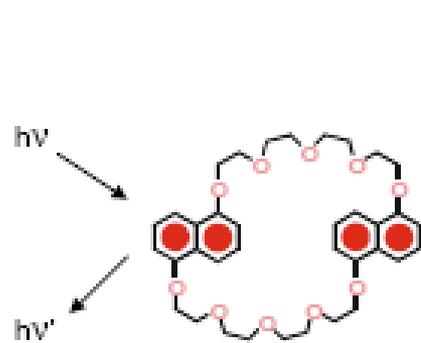
Bis-paraphenyl-[34]-crown-10

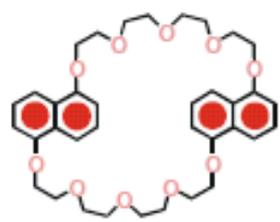
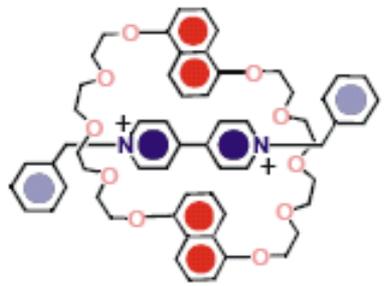
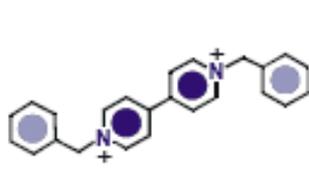
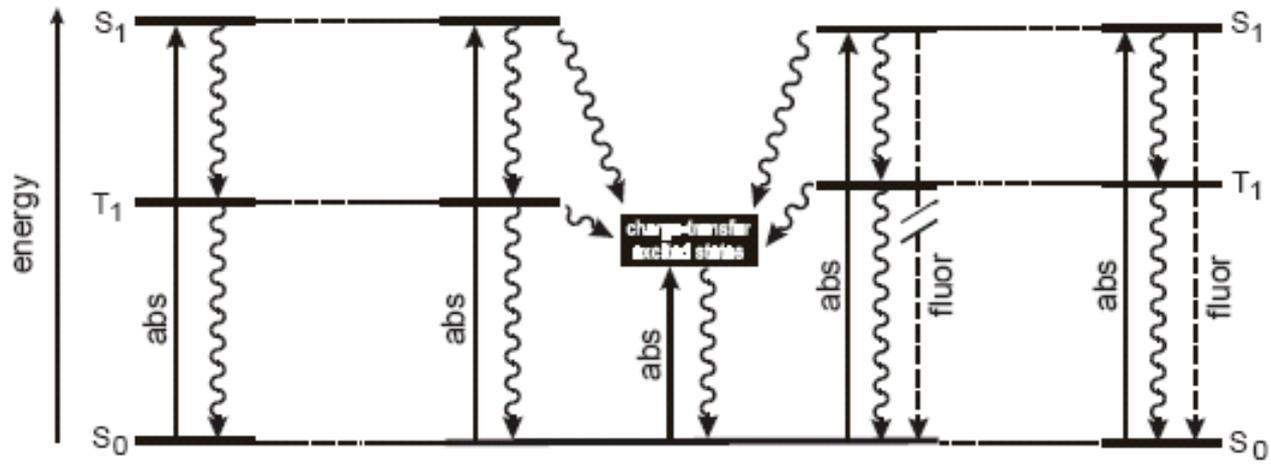


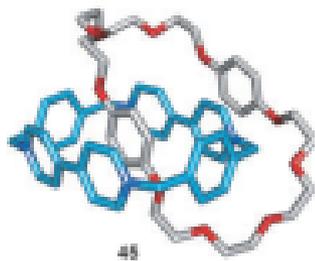
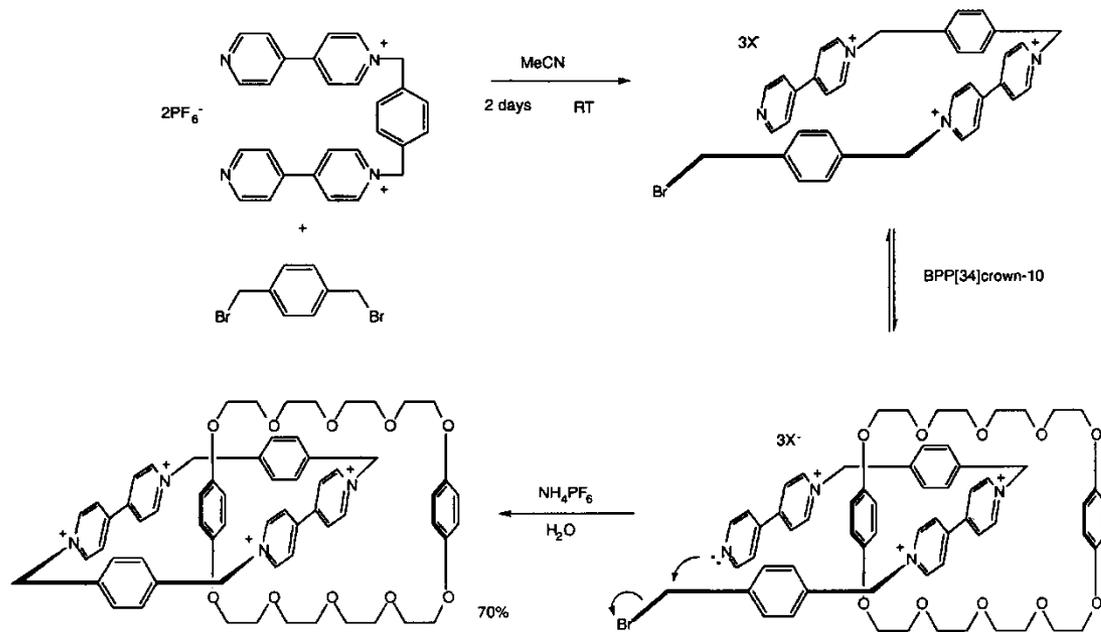
Self-assembly

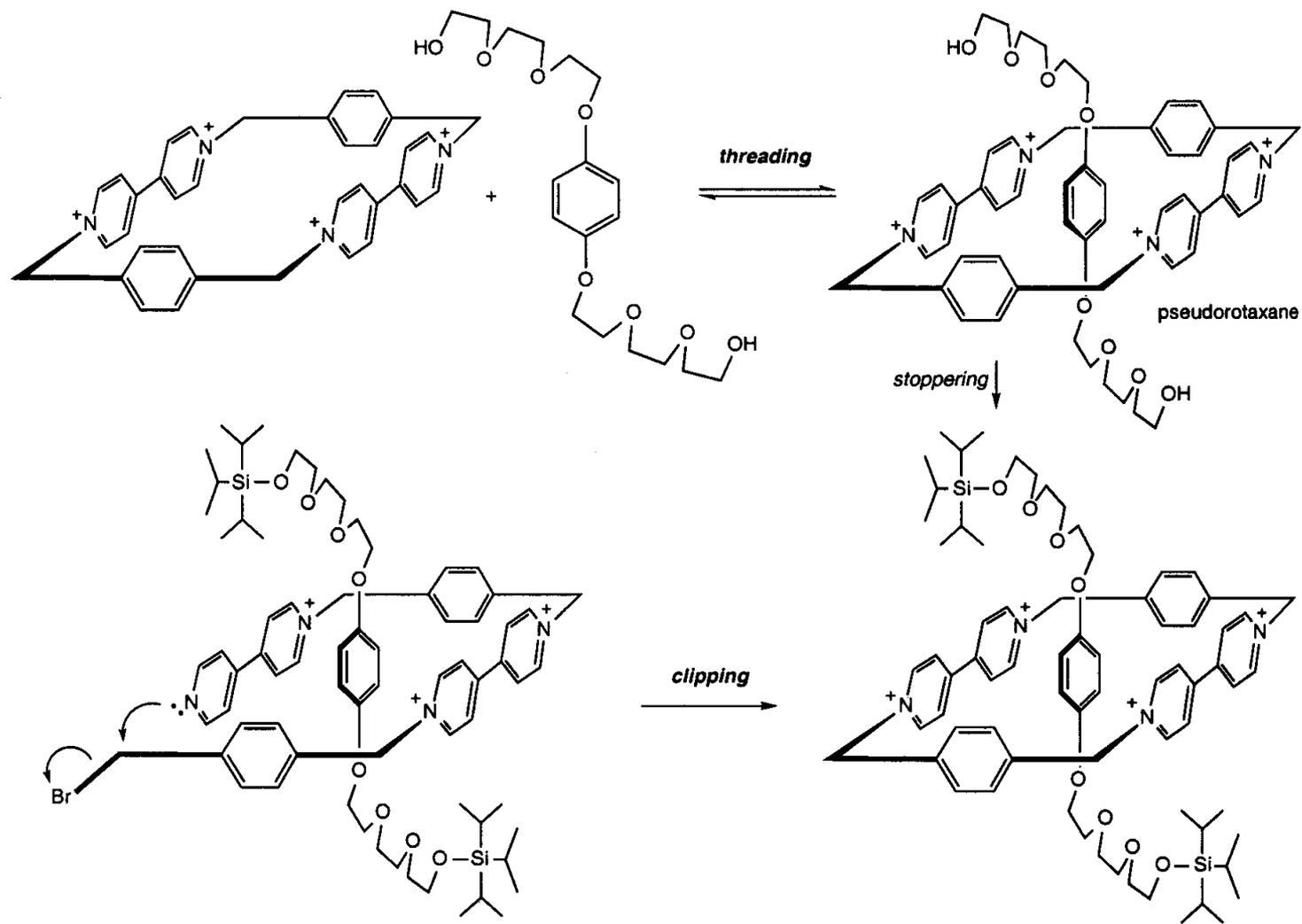






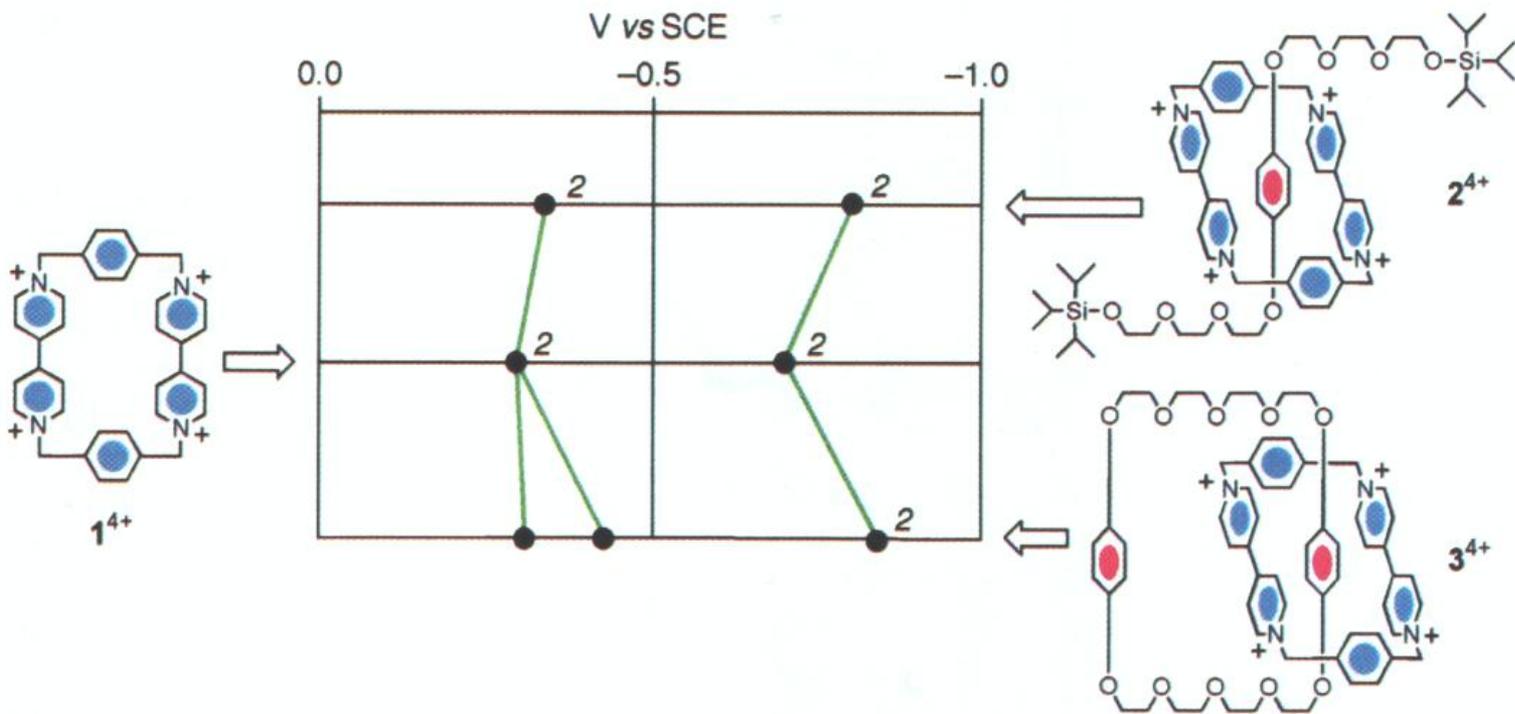


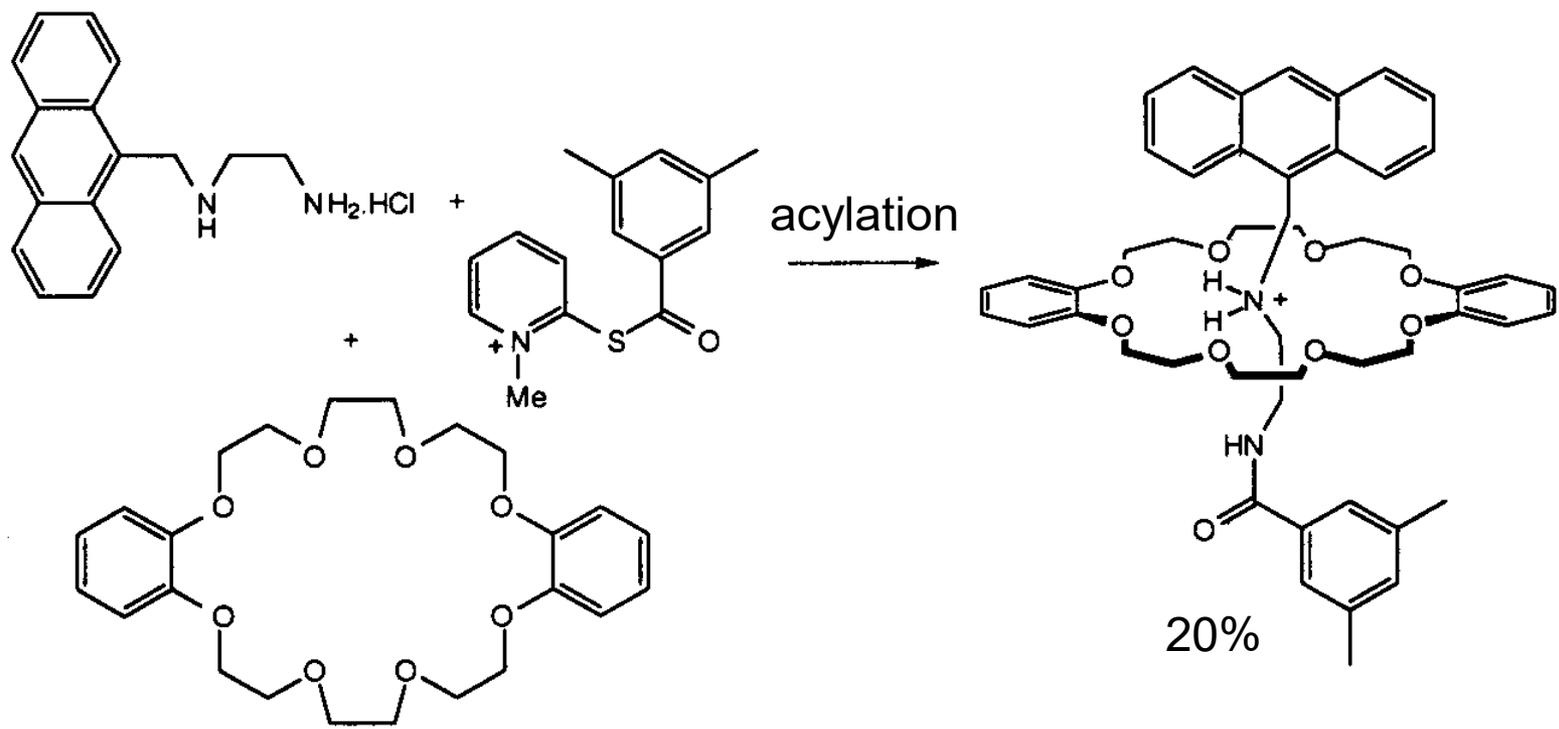


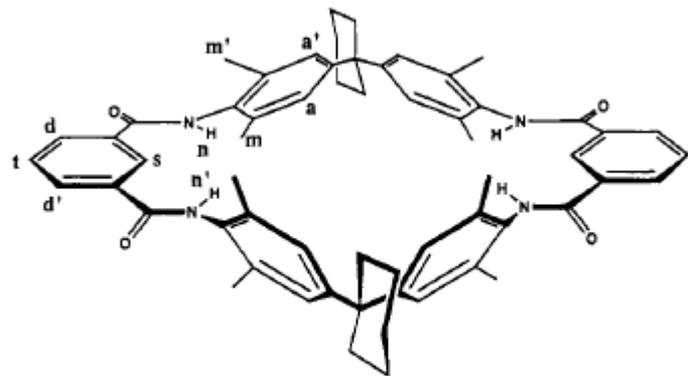


Synthesis of a rotaxane

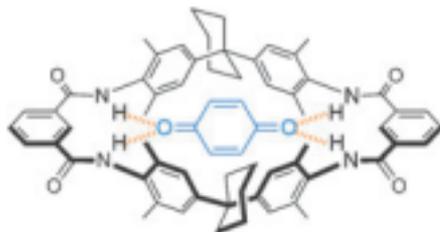
by two different routes: threading and clipping.





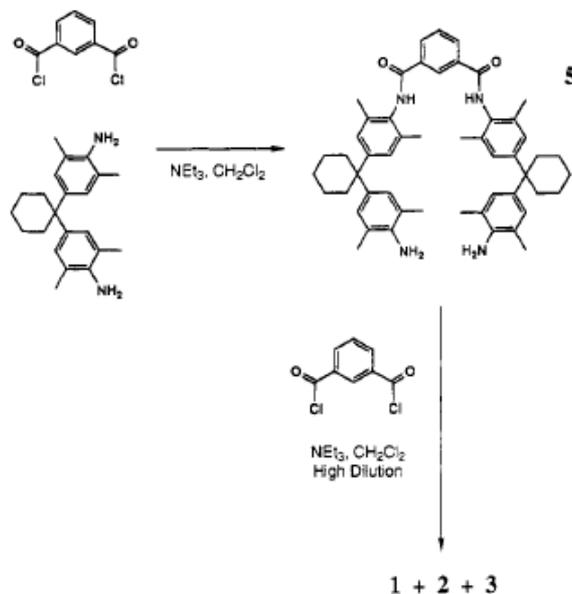


1



**Synthesis.** I recently reported the synthesis of **1**, a receptor for *p*-benzoquinone.<sup>7</sup> This synthesis employed the macrocyclization reaction shown in Scheme I. In an attempt to improve the yield of **1**, I developed the two-step synthesis shown in Scheme II. This reaction yielded three major products, fractions A, B, and C (see Experimental Section). Fraction B was identical with the cyclic dimer, **1**, synthesized via Scheme I. FAB mass spectra of fractions A and C showed molecular ions that corresponded to tetrameric species. Fraction C had a <sup>1</sup>H NMR spectrum that was almost identical with that of **1** in CDCl<sub>3</sub>/CD<sub>3</sub>OD. Thus all four components of the tetramer were equivalent and had retained their symmetry. In contrast, fraction A had a very complex <sup>1</sup>H NMR

Scheme II

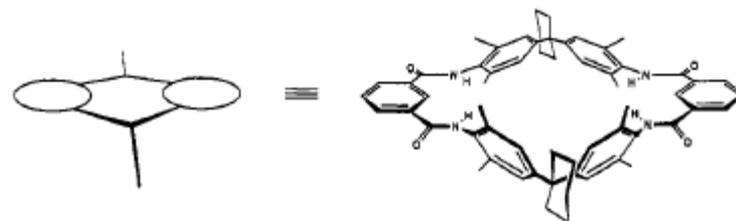
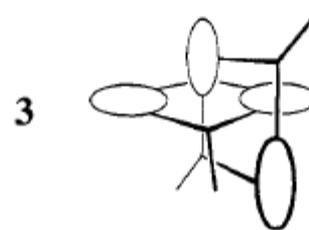
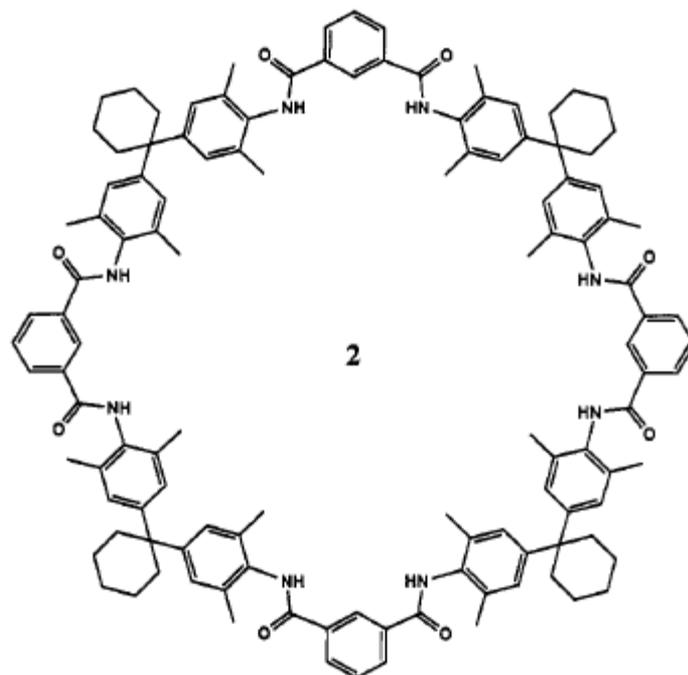


**Cyclic Dimer 1, Cyclic Tetramer 2, and Catenane 3 (Scheme II).** 5, 1 g, and 0.4 mL of triethylamine were dissolved in 250 mL of dry dichloromethane and transferred to a dropping funnel. Isophthaloyl dichloride (0.26 g) was similarly dissolved in 250 mL of dry dichloromethane and transferred to an identical dropping funnel. These two solutions were added dropwise to 1200 mL of dry dichloromethane over a period of 4 h with stirring under nitrogen. The reaction mixture was then stirred for a further 12 h. The precipitate was filtered off and the solvent evaporated under reduced pressure. The products were chromatographed on silica with chloroform-ethanol eluant. Fraction A was eluted with chloroform. Fraction B was eluted with chloroform-ethanol (99:1). Fraction C was eluted with chloroform-ethanol (98:2). All three fractions were recrystallized from chloroform-pentane.

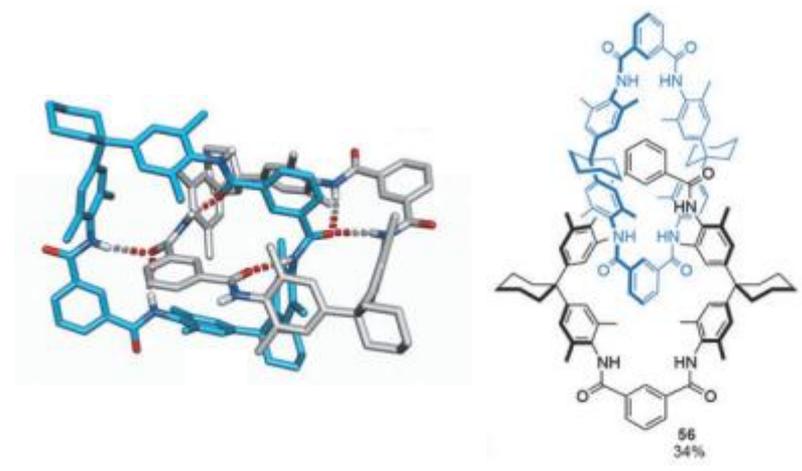
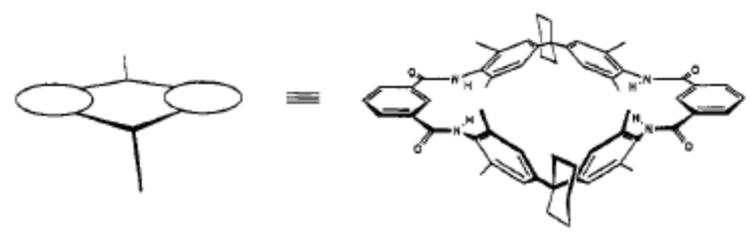
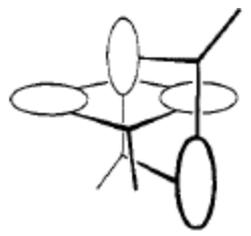
**Fraction A** was obtained as a white crystalline solid (400 mg, 34%). The NMR data are discussed in the main text.  $m/z$  1806 ( $MH^+$ );  $C_{120}H_{128}N_8O_8$  requires  $M^+ = 1808$ .

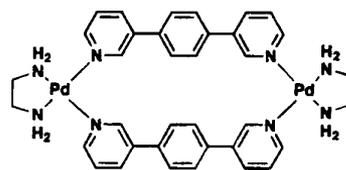
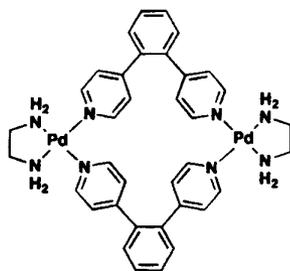
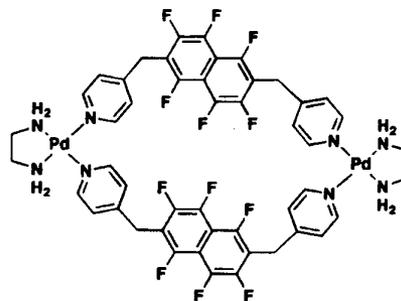
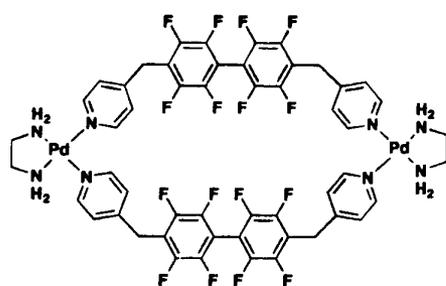
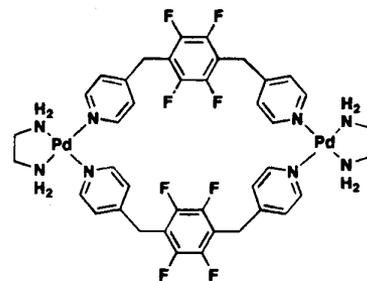
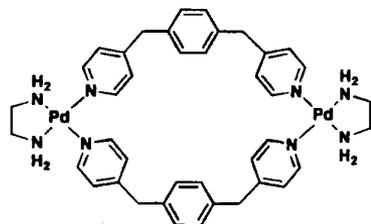
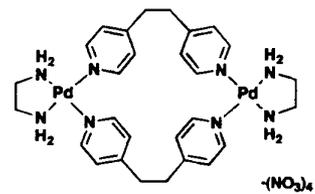
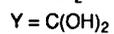
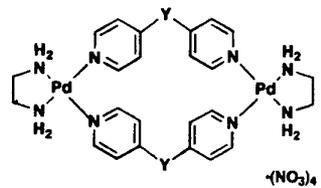
Fraction B was obtained as a white powder (600 mg, 51%). Spectroscopic data were as for the cyclic dimer 1 from Scheme I.

Fraction C was obtained as a white powder (50 mg, 5%). NMR ( $CDCl_3/CD_3OD$ )  $\delta$  8.41 (4 H, s), 7.98 (8 H, d), 7.43 (4 H, t), 6.96 (16 H, s), 2.21 (16 H, br), 2.10 (48 H, s), 1.52 (24 H, br).  $m/z$  1806 ( $MH^+$ );  $C_{120}H_{128}N_8O_8$  requires  $M^+ = 1808$ .

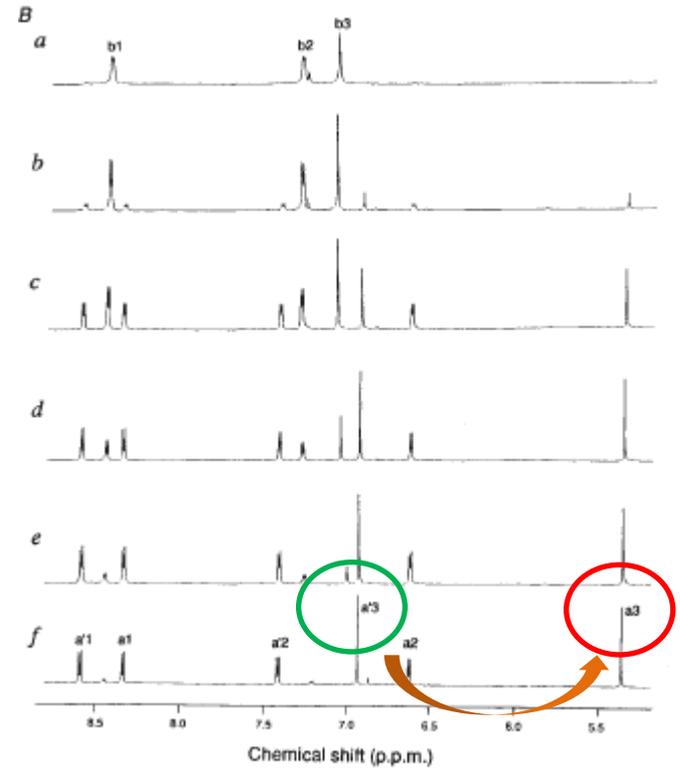
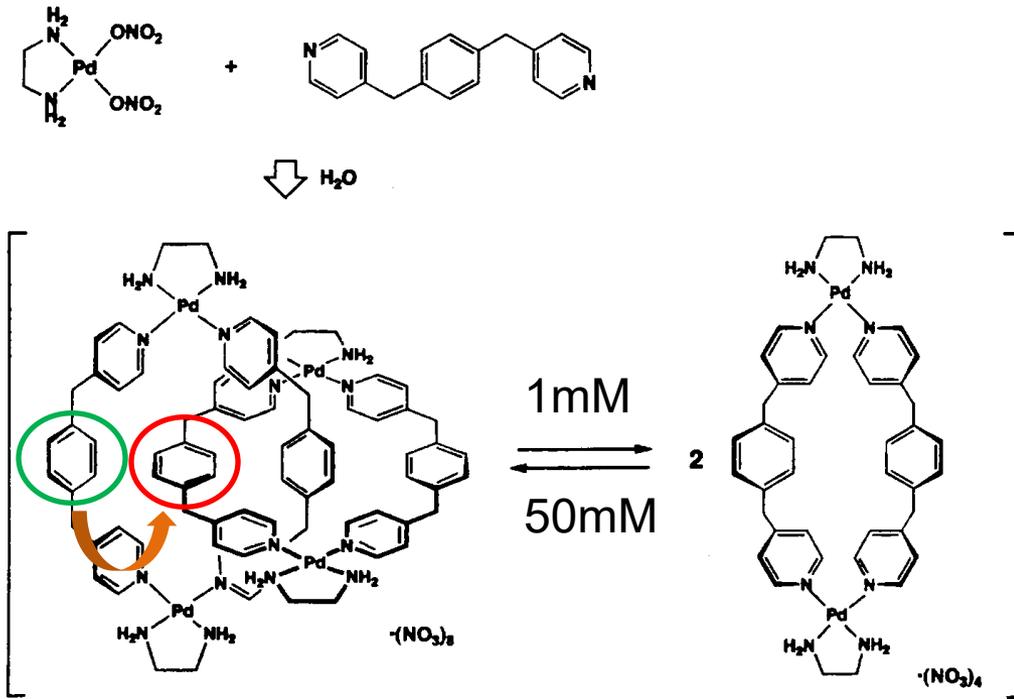


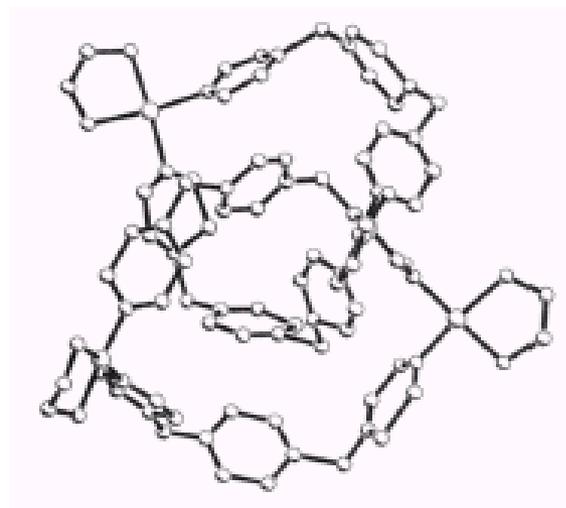
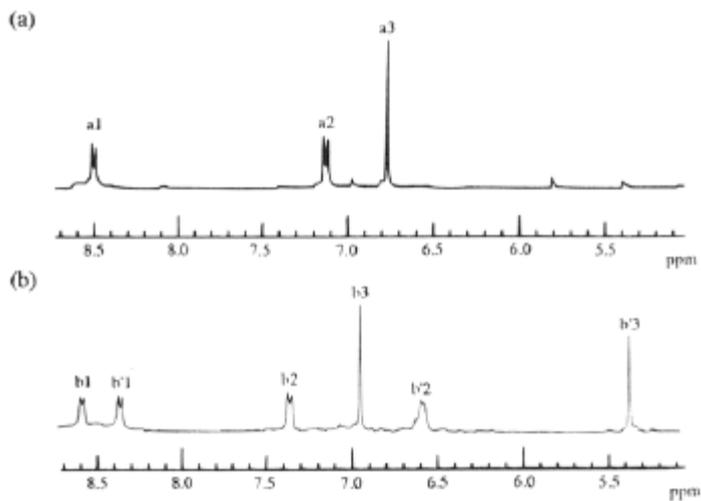
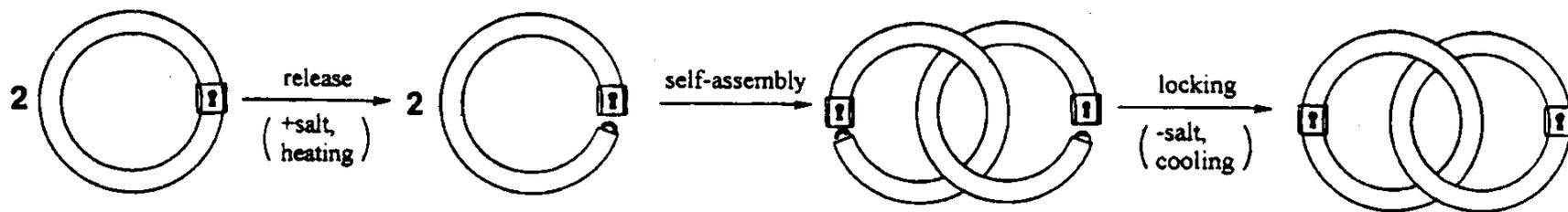
3



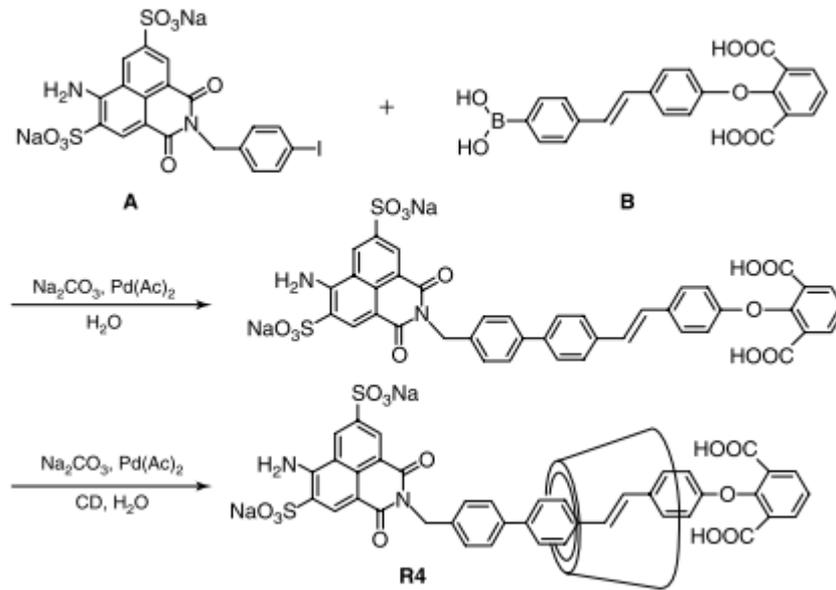


# Catenanes

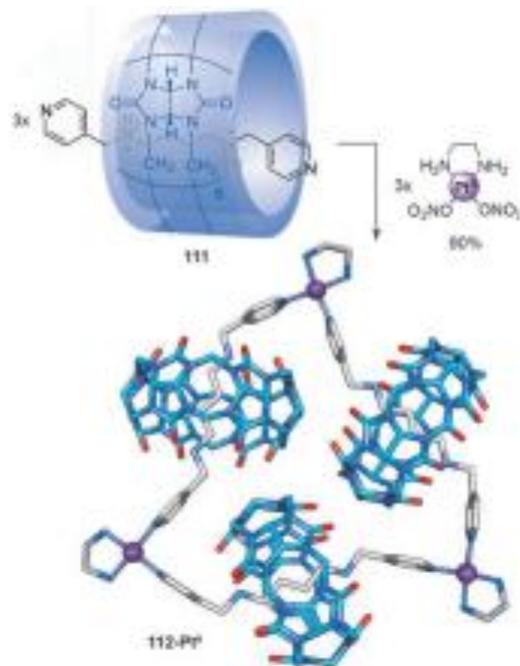




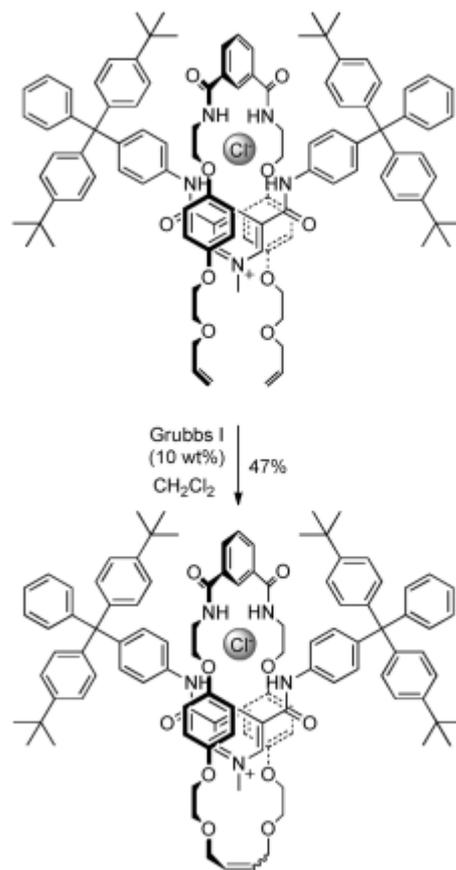
# Hydrophobic effect



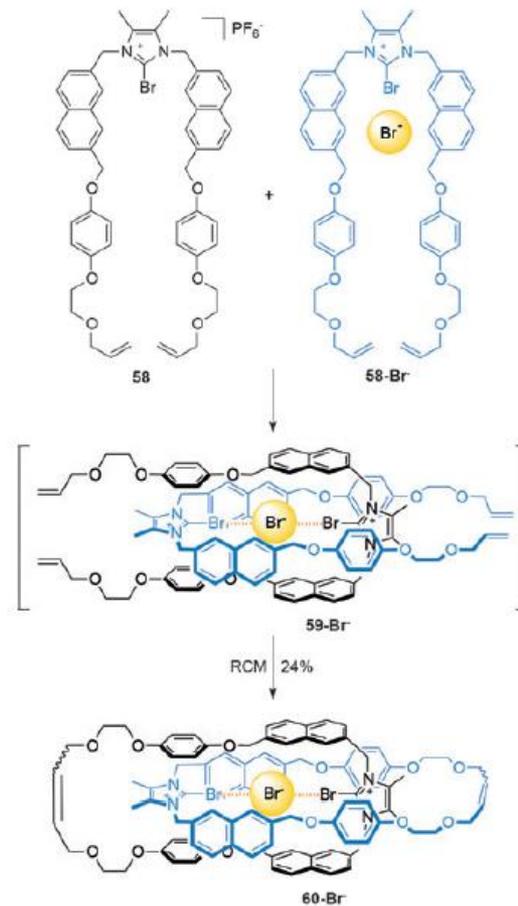
# Hydrophobic effect

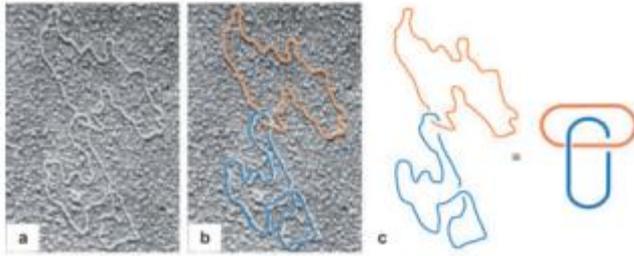


# Anion templating

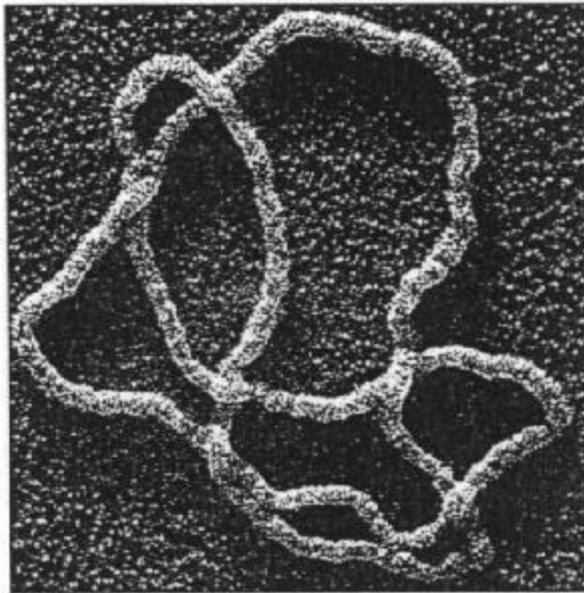


# Halogen bond templating

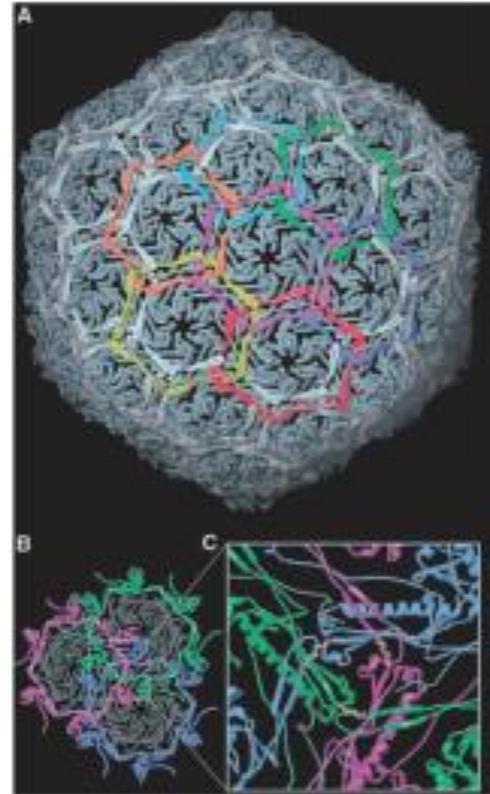




**Figure 4.** a) Electron micrograph of circular DNA revealing a catenane topology. b,c) Highlighting the two component rings of the DNA catenane as a Hopf link. Modified from Ref. [23] with permission.



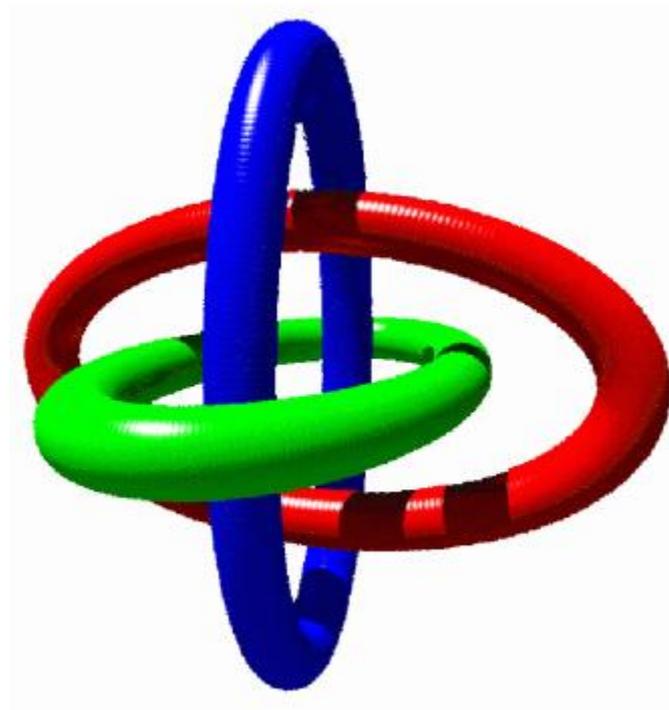
**Figure 5.** The "chainmail" arrangement of proteins found in bacteriophage HK97's capsid (colored sections highlight the individual protein rings). a) The repeating pattern of interlocking proteins which constitute the spherical capsid. b) A cross-section of the capsid in which three protein rings interlock with one another. c) Magnified view of the position at which protein rings overlap [cross-linking isopeptide bonds are highlighted]. Reprinted from Ref. [28] with permission.



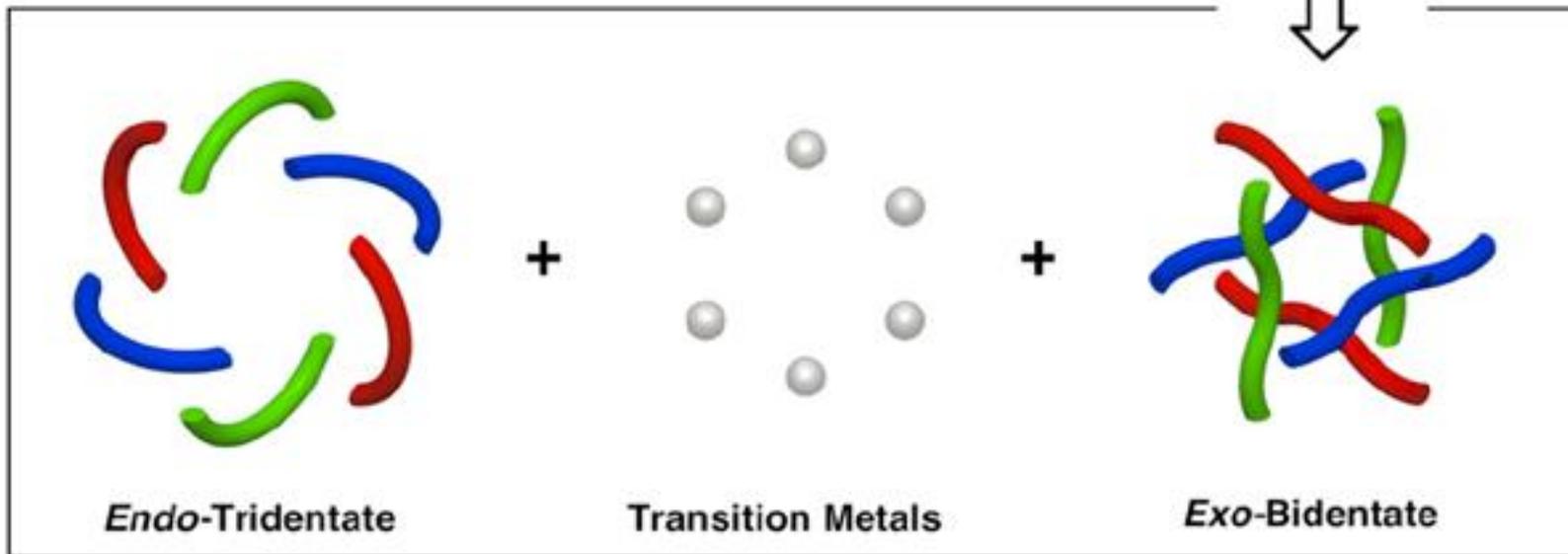
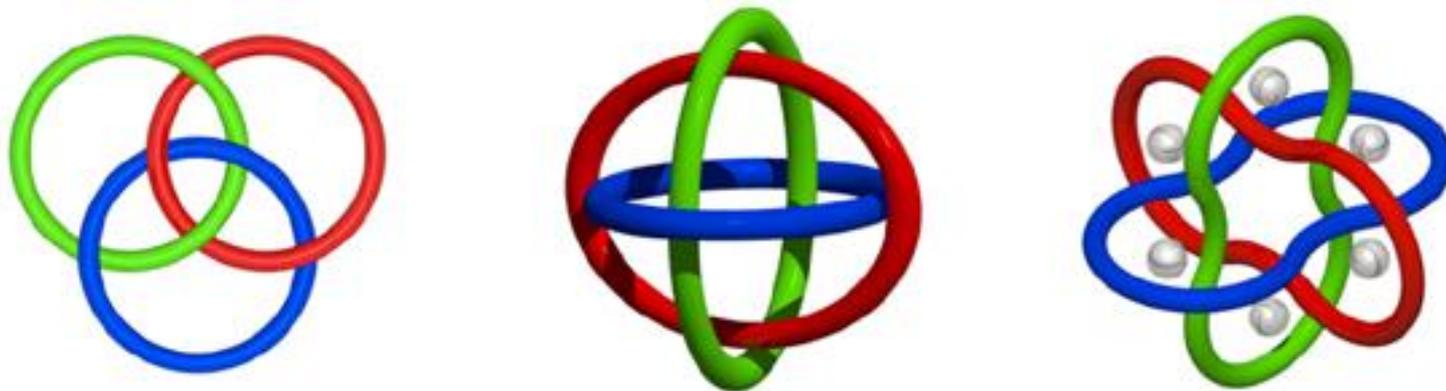
# Molecular Borromean Rings

Kelly S. Chichak,<sup>1</sup> Stuart J. Cantrill,<sup>1</sup> Anthony R. Pease,<sup>1</sup>  
Sheng-Hsien Chiu,<sup>1</sup> Gareth W. V. Cave,<sup>2</sup> Jerry L. Atwood,<sup>2</sup>  
J. Fraser Stoddart<sup>1\*</sup>

28 MAY 2004 VOL 304 SCIENCE [www.sciencemag.org](http://www.sciencemag.org)



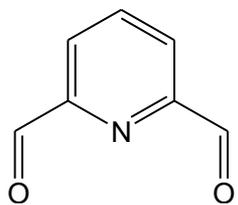
# Borromean Ring



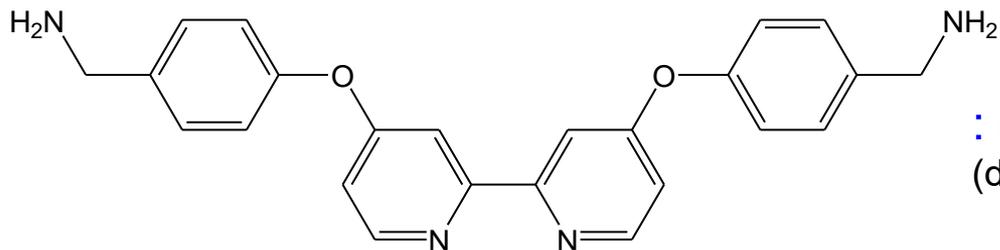
*Endo-Tridentate*

Transition Metals

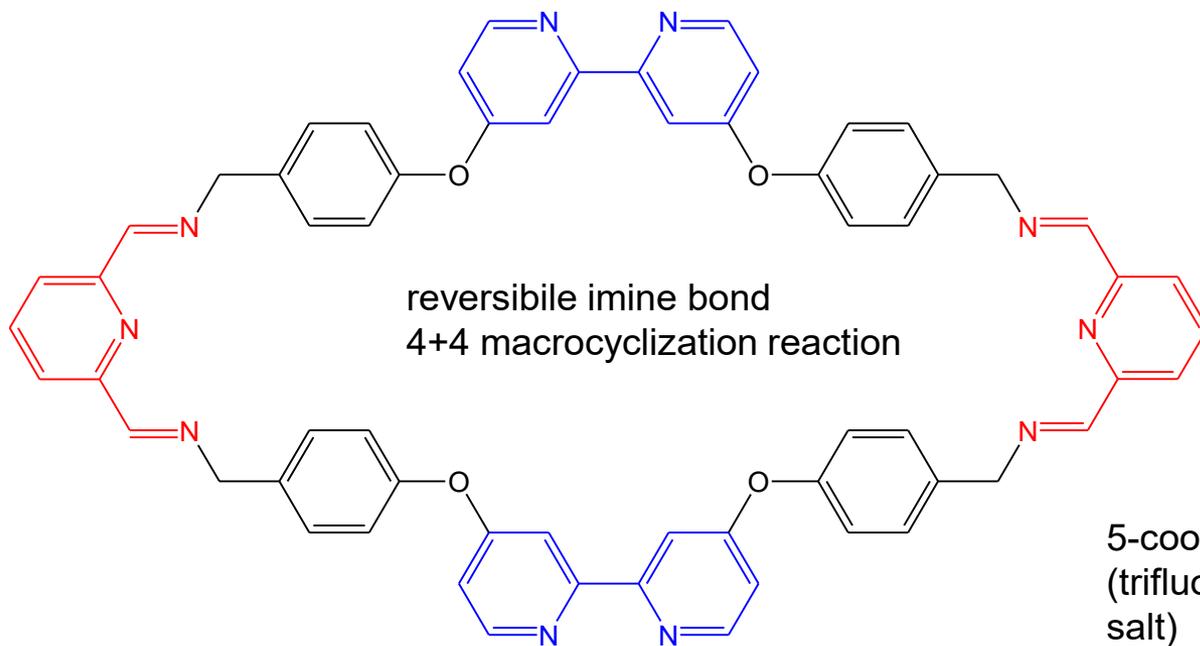
*Exo-Bidentate*



: **endo-tridentate** (2,6 diformilpyridine DFP)

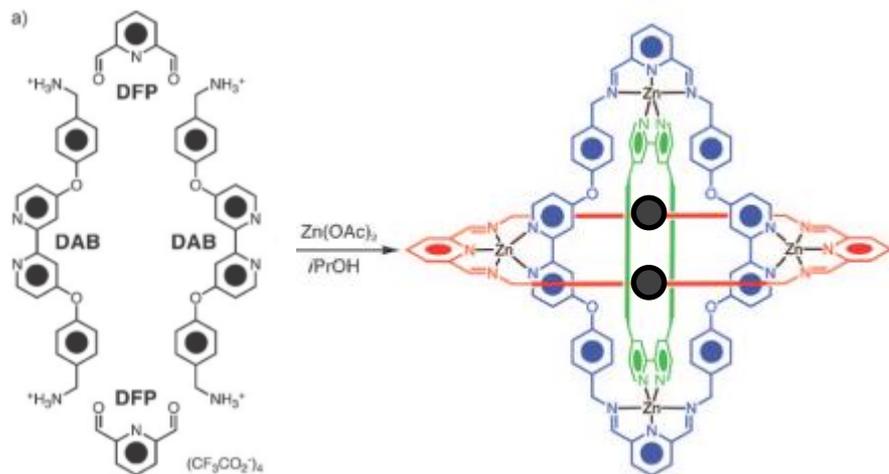


: **exo-bidentate**  
(diamminobipyridiyl ligand DAB)



reversible imine bond  
4+4 macrocyclization reaction

5-coordinated Zn(II)  
(trifluoroacetate  
salt)



After 2 days 90°C, MeOH  
 NMR, mass spectrometry (ESI)

Charge: 12<sup>+</sup>

Counterions: 12TFA<sup>-</sup>

**endo-tridentate**

2,6 diformilpyridine (DFP)

**exo-bidentate**

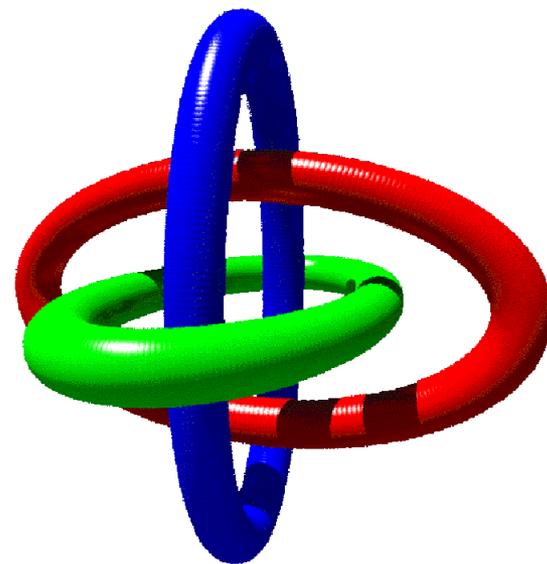
diamminobipyridyl ligand (DAB)

**5-coordinated Zn(II)**

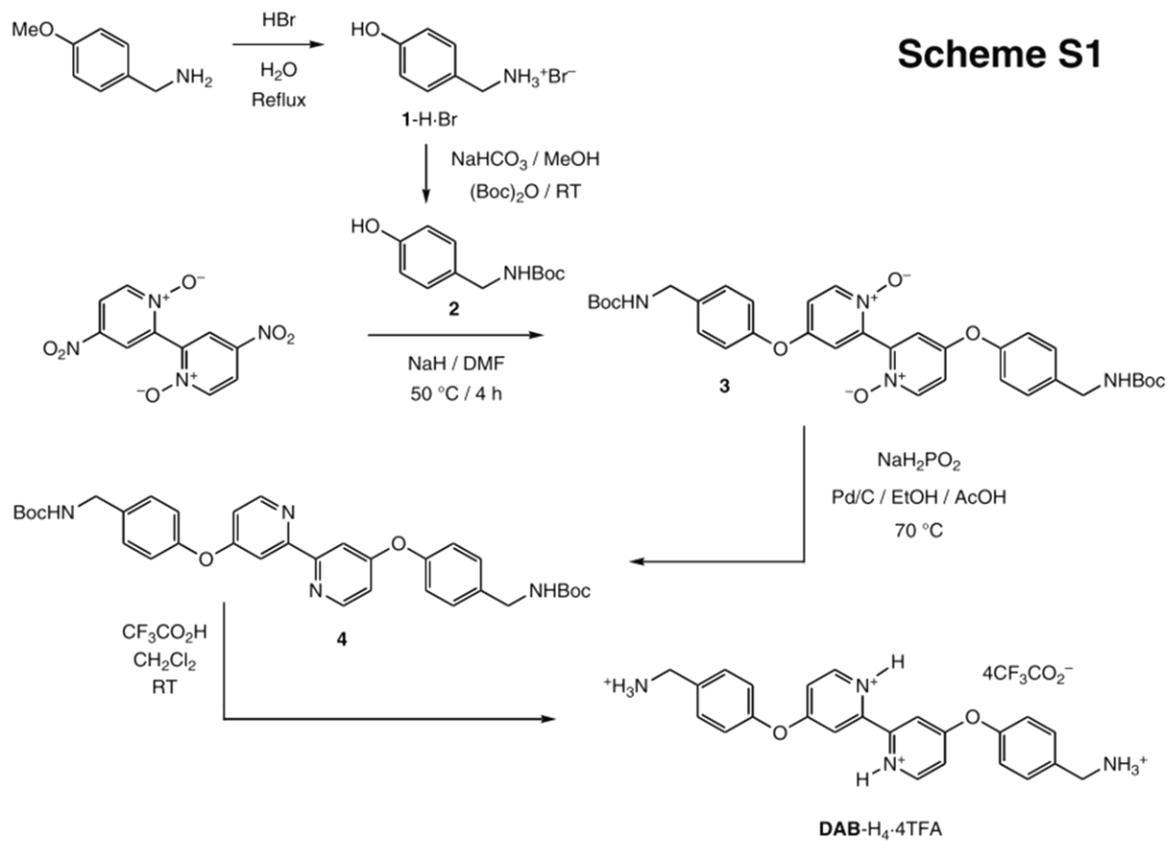
(trifluoroacetate salt)

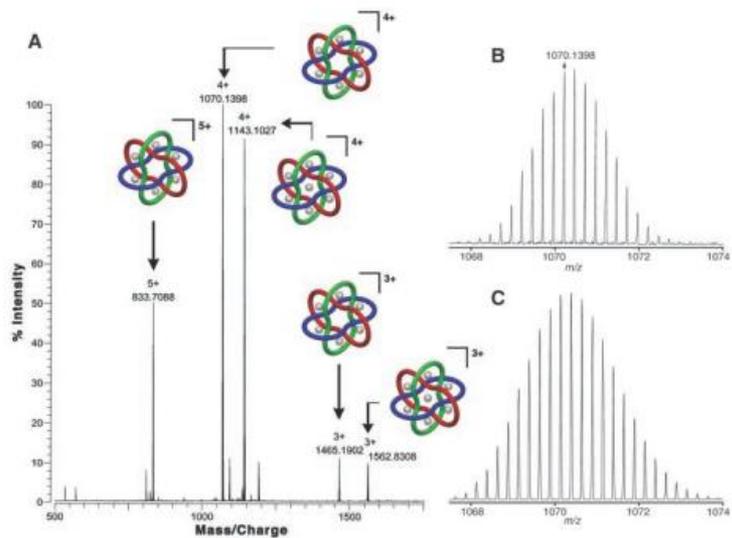
**reversible imine formation**

**reversible coordination**

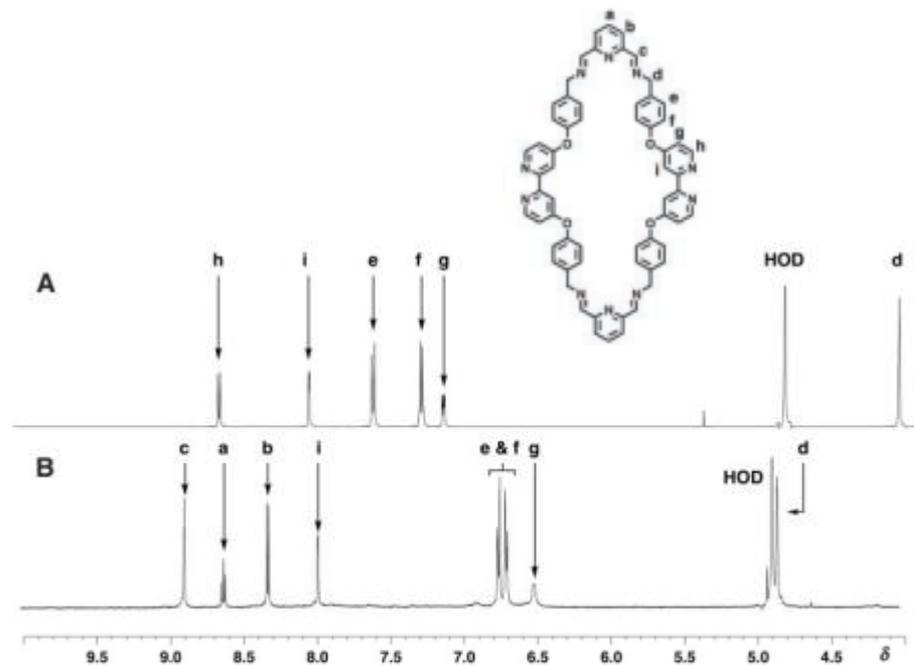


## Scheme S1

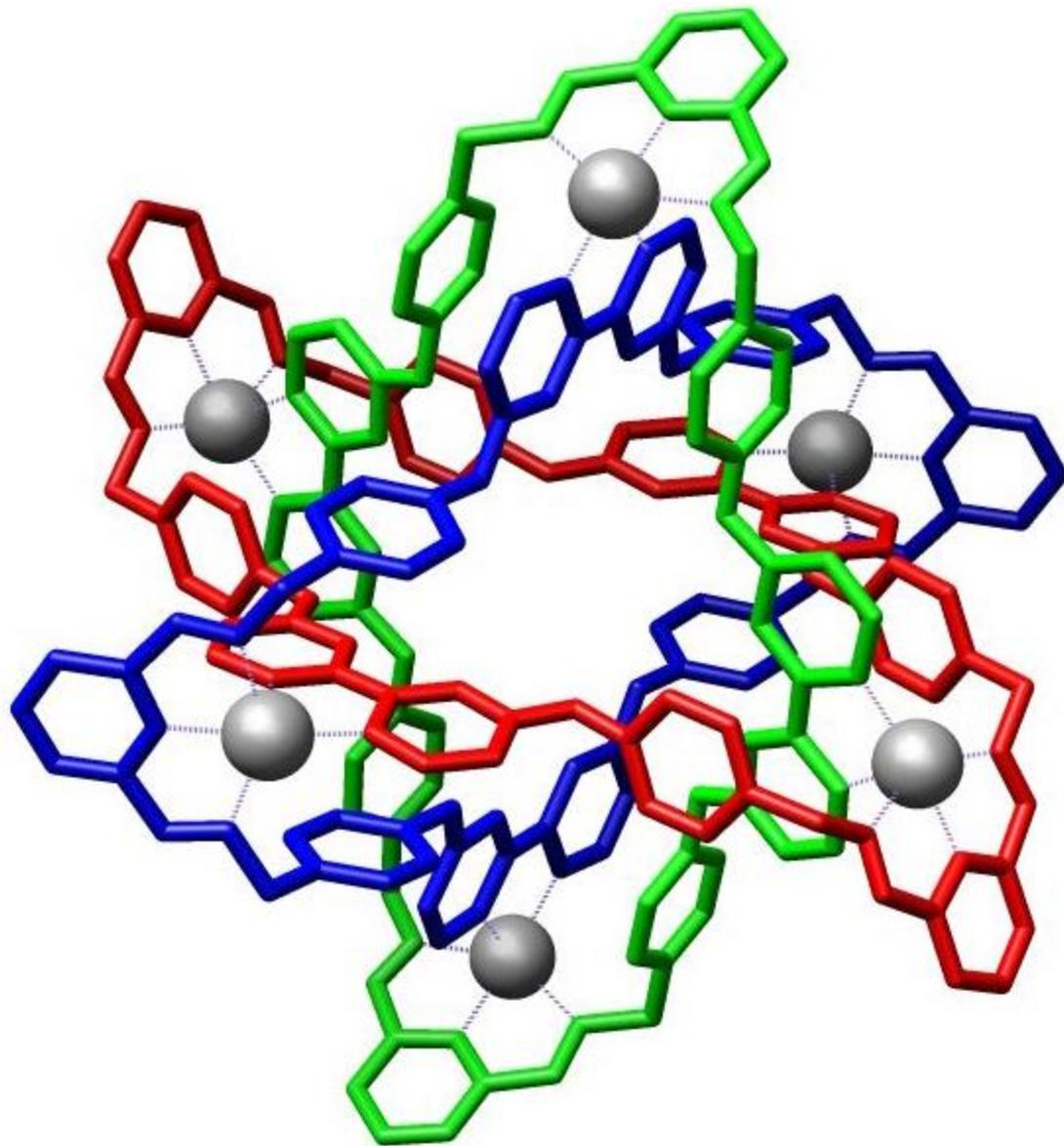


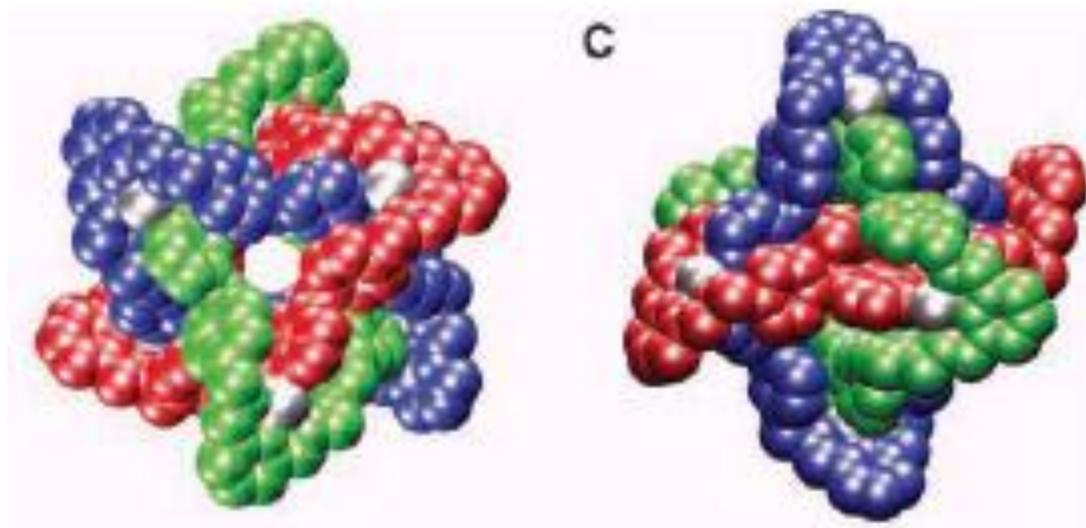


$[M-3TFA]^{3+}$   
 $[M-4TFA]^{4+}$   
 $[M-5TFA]^{5+}$

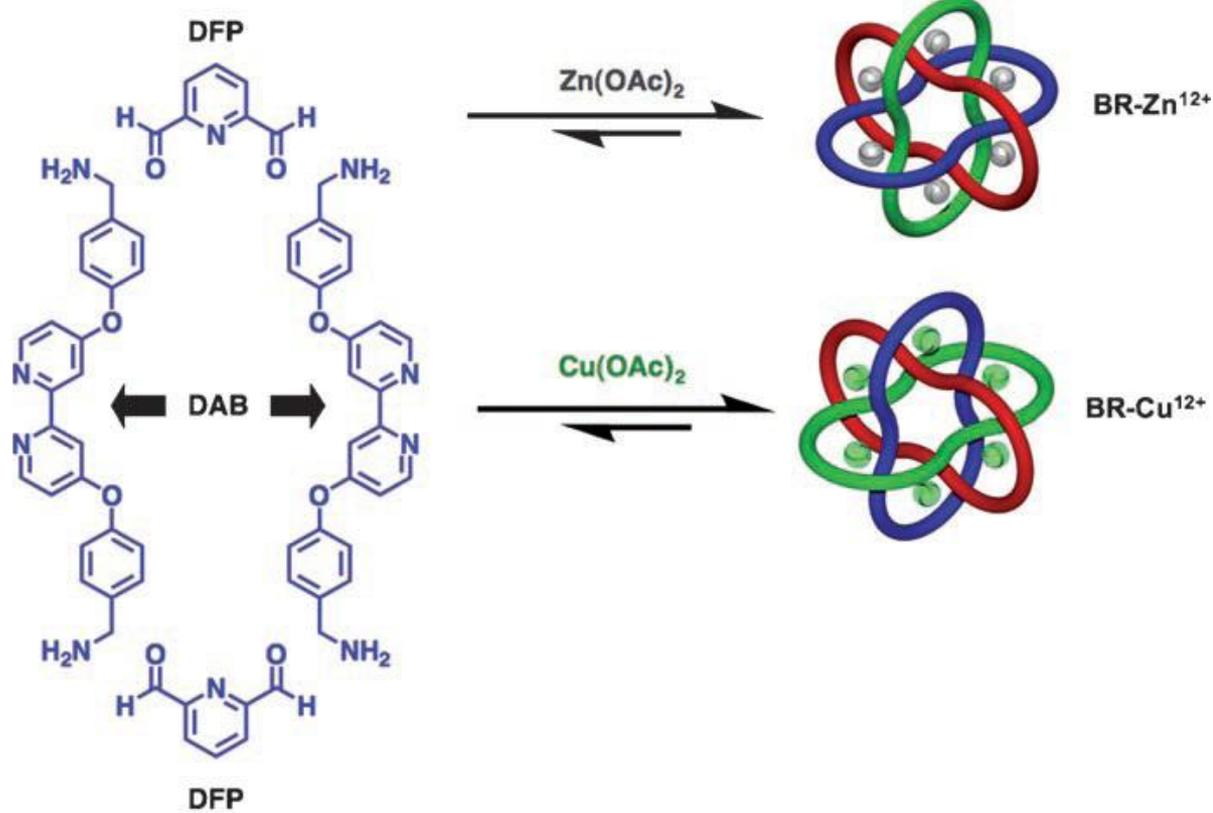
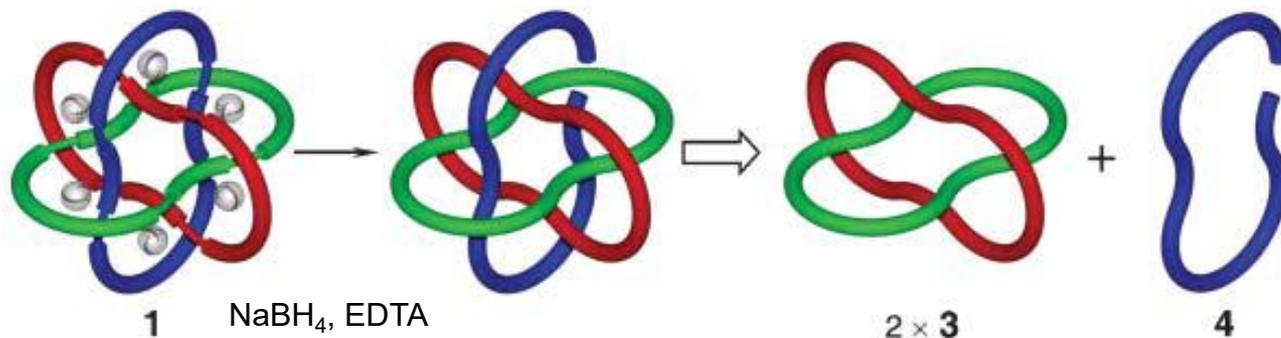


**Fig. 2.** The  $^1\text{H}$  NMR spectra ( $\text{CD}_3\text{OD}$ , 298 K) of (A) the *exo*-bidentate ligand-containing starting material  $\text{DAB}\cdot\text{H}_4\cdot 4\text{TFA}$  (500 MHz), (B) the molecular Borromean rings  $\text{BR}\cdot 12\text{TFA}$  (600 MHz)





6 Zn(II) bound to one bipy and one dimminopyridine (in the solid state 6th position occupied by trifluoroacetate (TFA);  $S_6$  symmetry  $\pi$ - $\pi$  stacking each bipy between 2 phenols 3.61-3.66 Å;  $12^+$



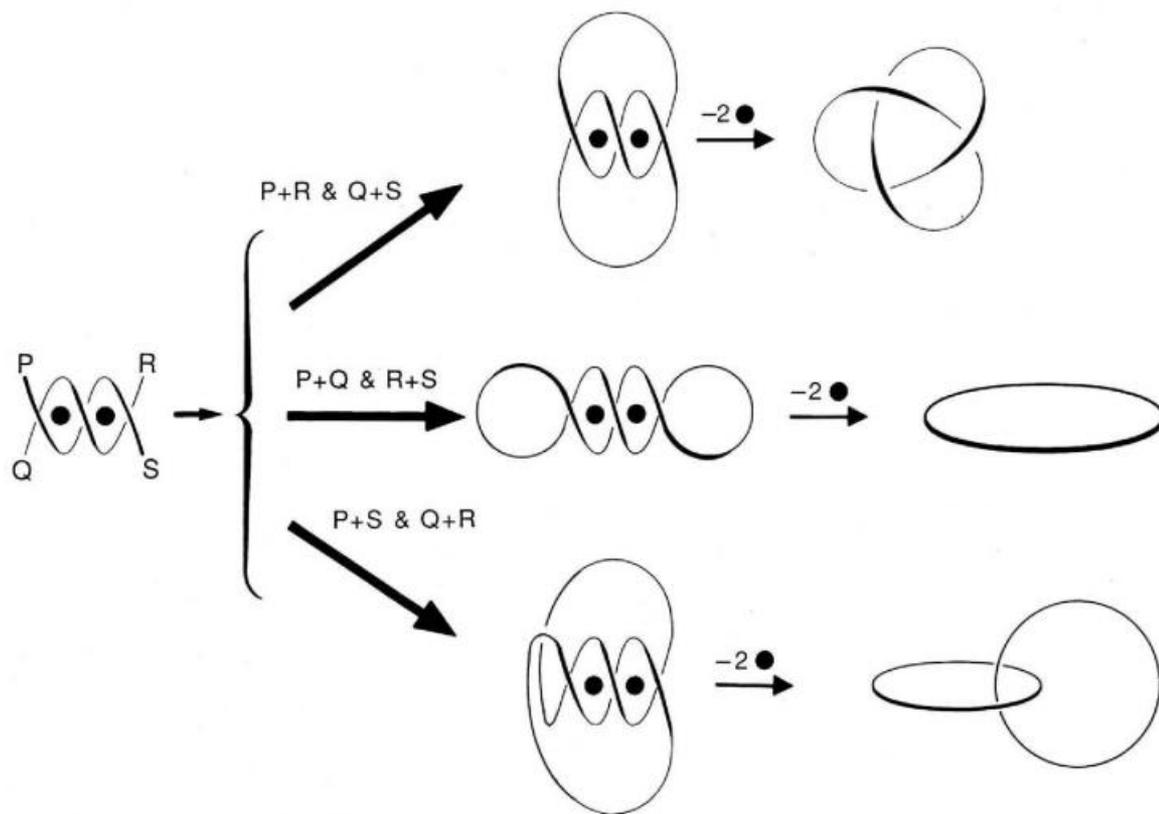
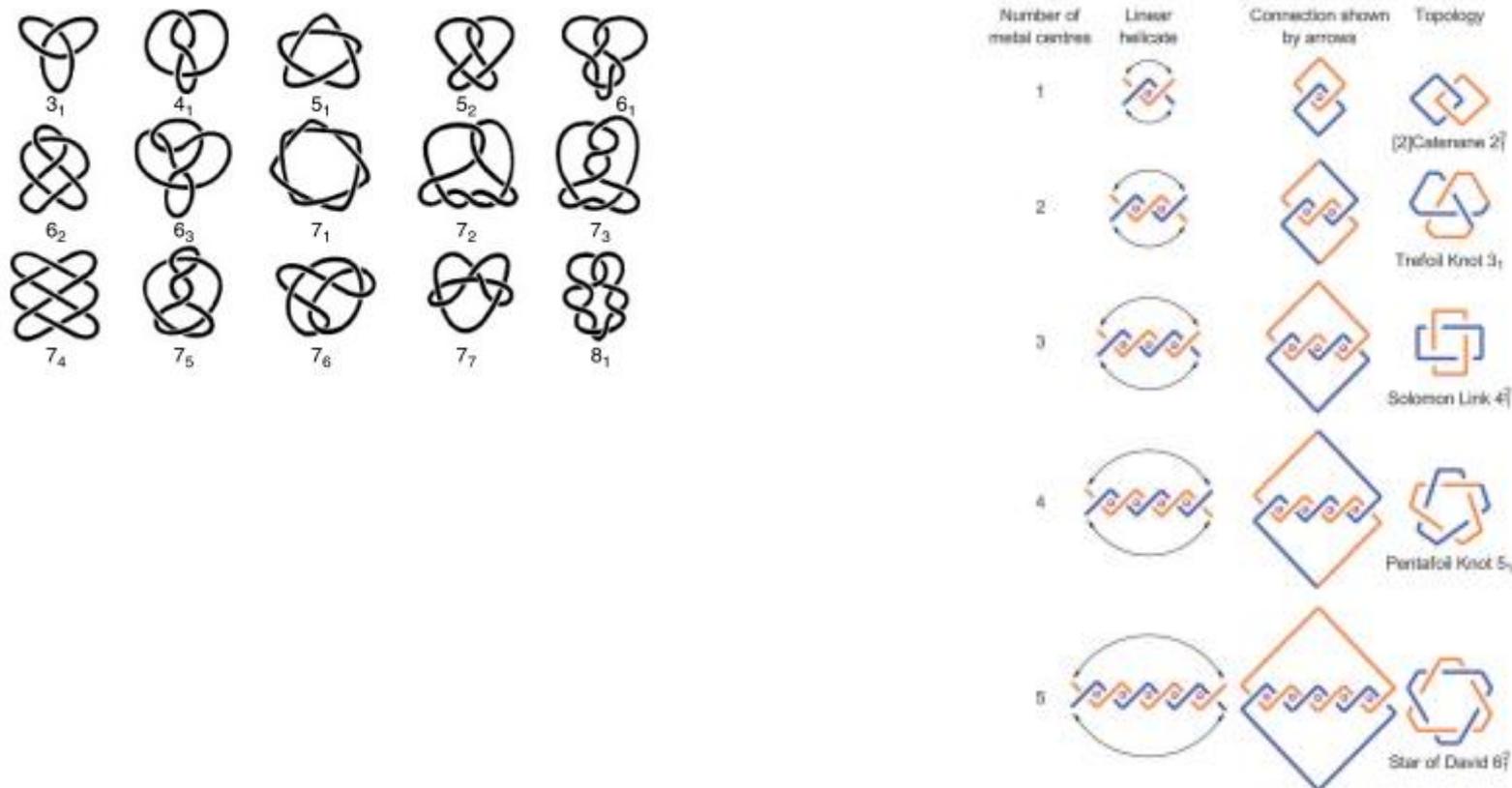


Figure 23. A guide for demonstrating the synthesis of topologically different molecules from the precursor to the trefoil knot.

# Molecular Knots and Links



**Fig. 3** The linear helicate strategy to interlocked molecules introduced by Sauvage.<sup>48</sup> To date the first three entries of this table have been realised experimentally using this strategy, generating catenanes,<sup>4</sup> trefoil knots<sup>38</sup> and doubly-interlocked [2]catenanes (Solomon links)<sup>47</sup> using one, two and three metal centres, respectively. The synthesis of a pentafoil knot or triply-interlocked [2]catenane (the 'Star of David' topology) from a linear helicate has thus far proved unsuccessful.<sup>48</sup>

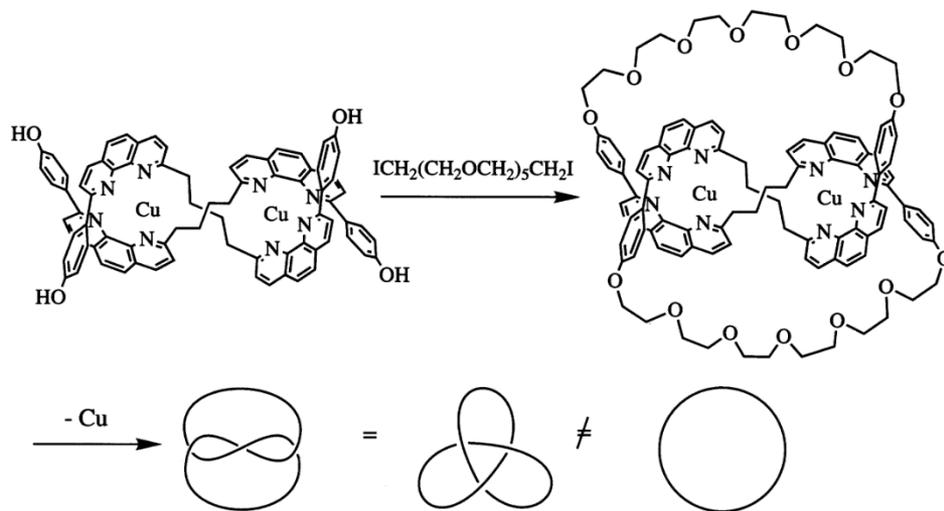
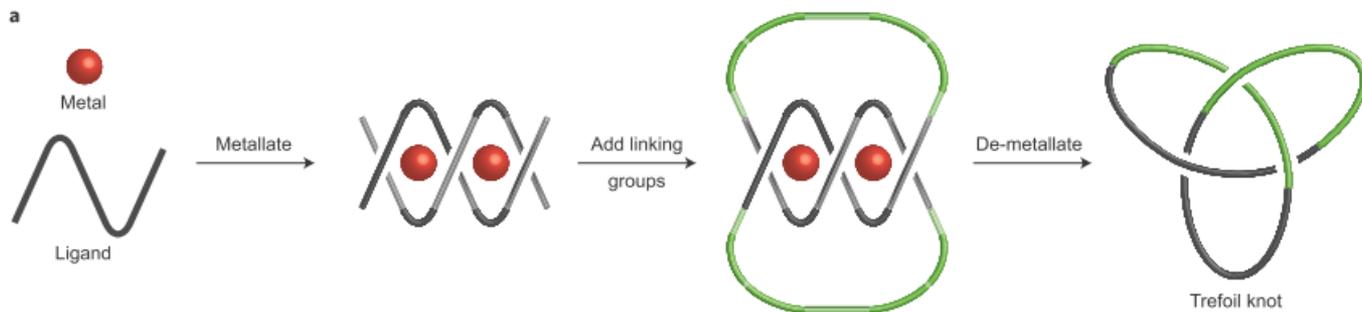
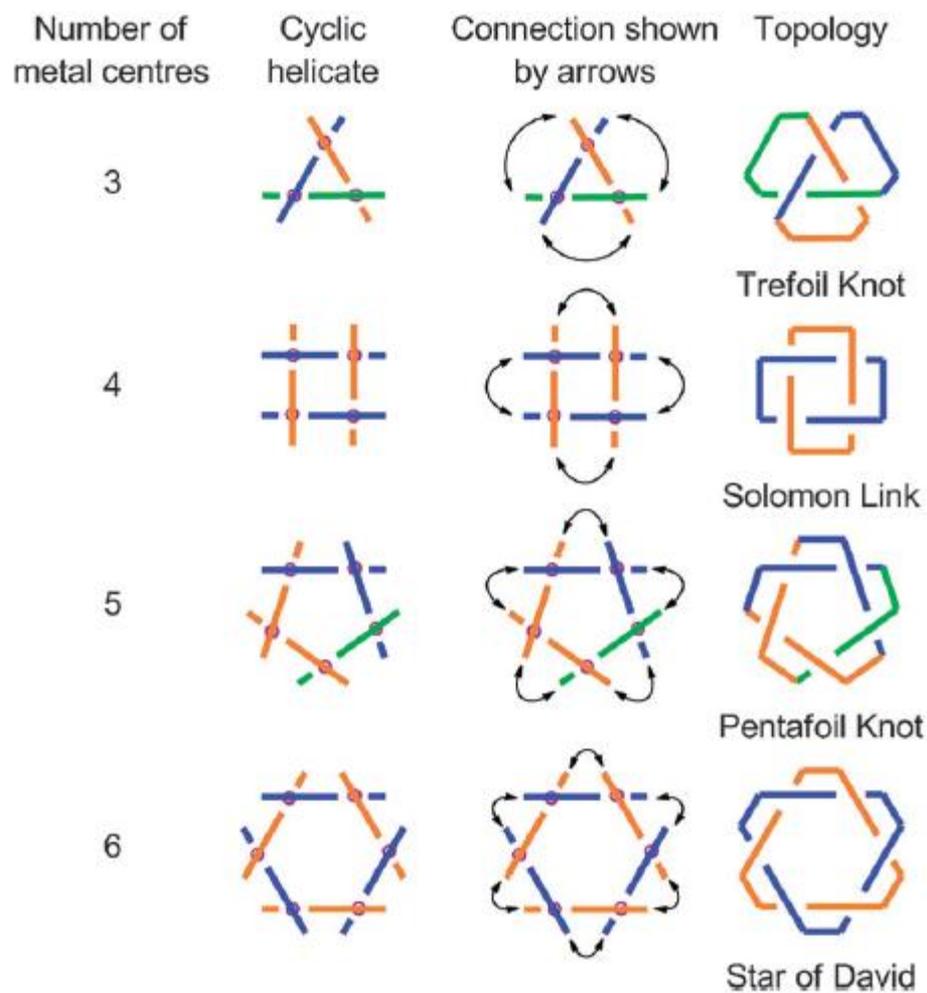


Fig. 8. Synthesis of the first trefoil knot using a two-anchor helical template.



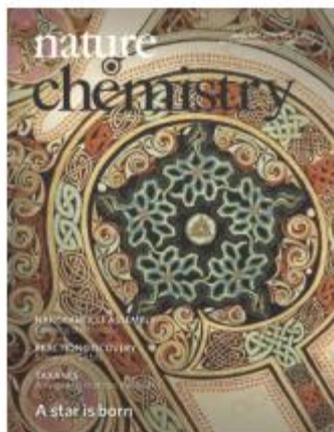
**Fig. 5** The potential of circular metal helicates to form molecular knots and links by connecting adjacent end-groups. To date only a pentafoil knot has been prepared through this strategy.<sup>73</sup>

# A synthetic molecular pentafoil knot

Jean-François Ayme<sup>1</sup>, Jonathon E. Beves<sup>1</sup>, David A. Leigh<sup>1\*</sup>, Roy T. McBurney<sup>1</sup>, Kari Rissanen<sup>2</sup>  
and David Schultz<sup>1</sup>

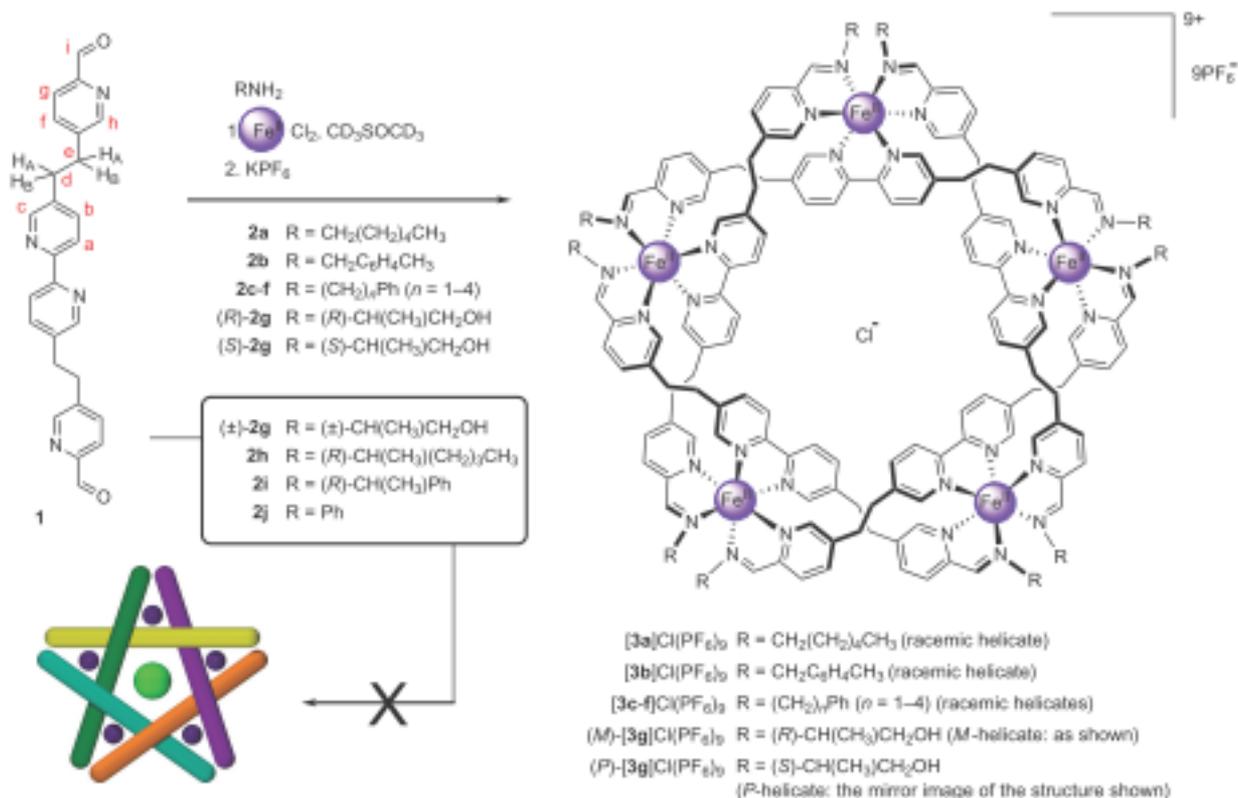
NATURE CHEMISTRY | VOL 4 | JANUARY 2012 | [www.nature.com/naturechemistry](http://www.nature.com/naturechemistry)

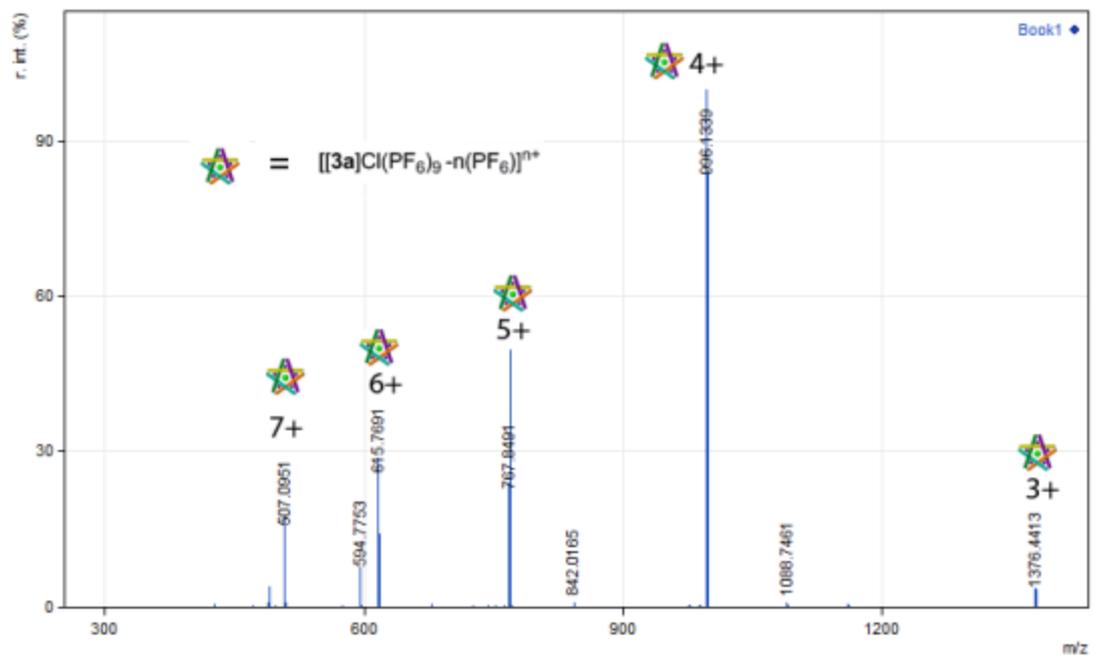


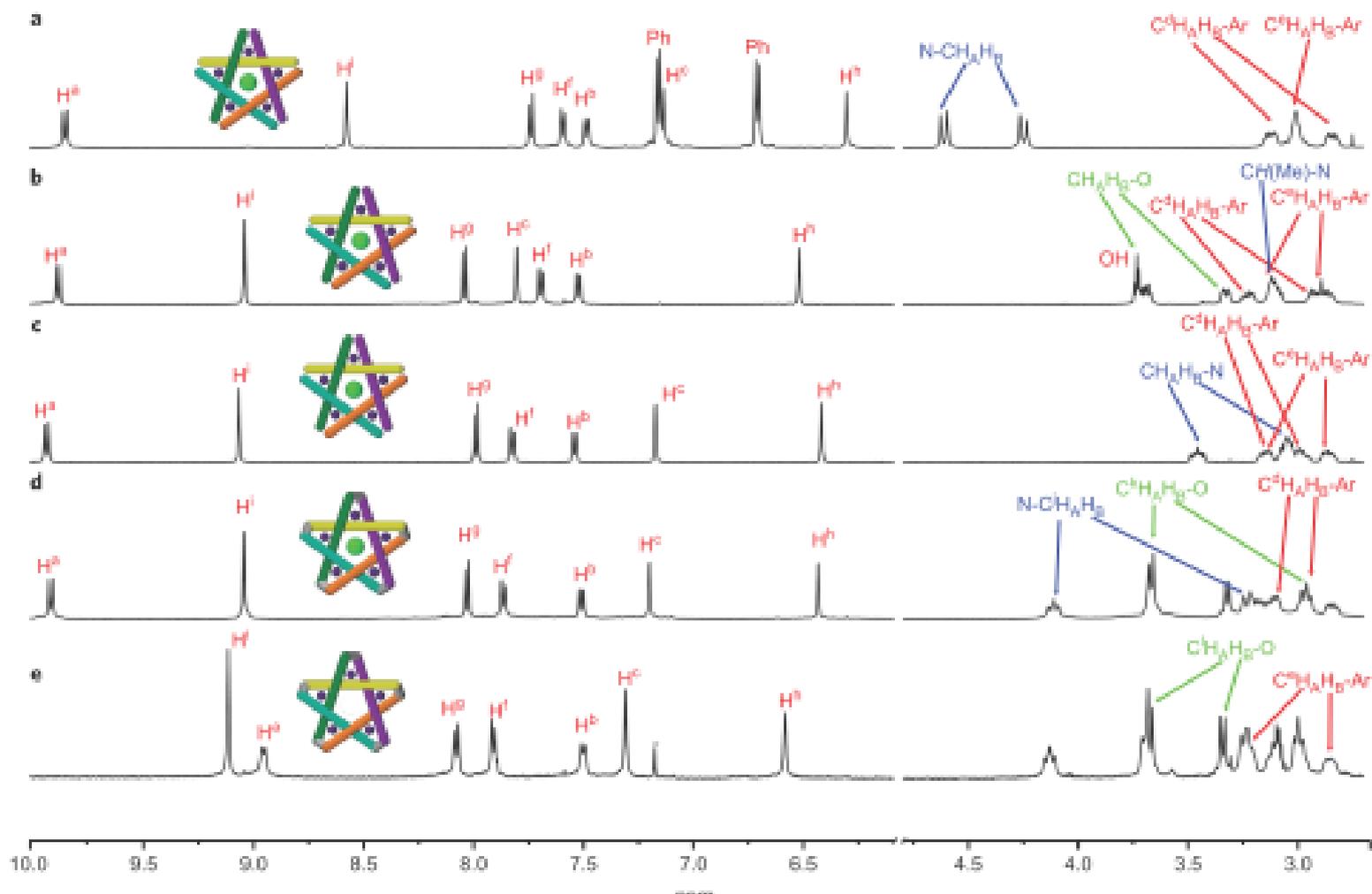
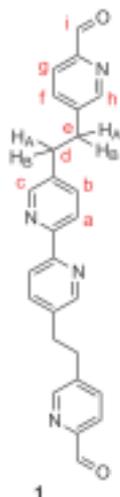


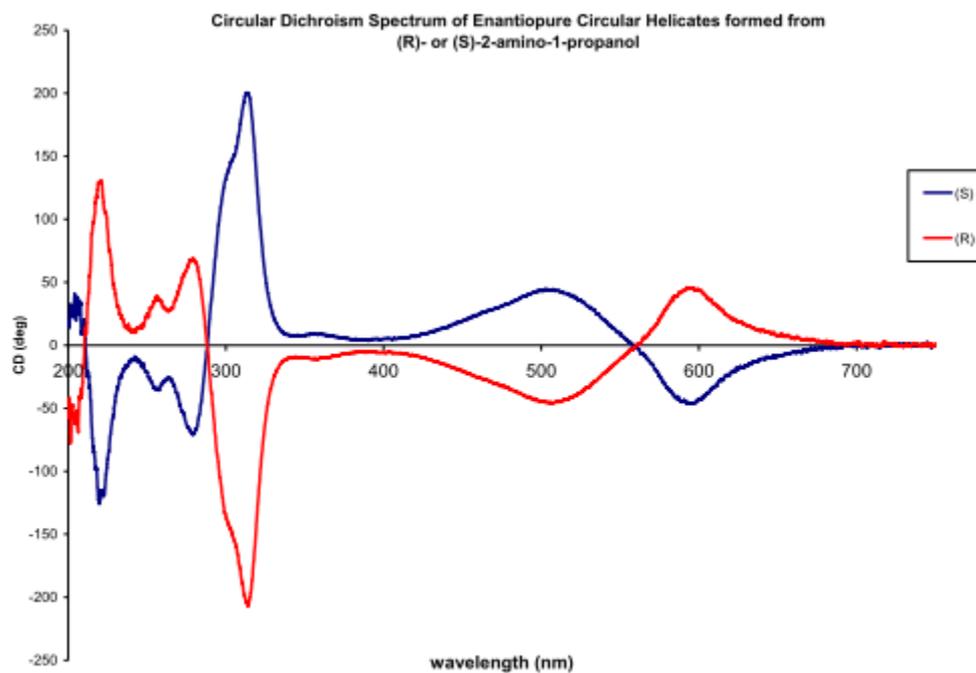
### COVER IMAGE

The cover image features the interlaced 'rho' character from Matthew 1:18 in the Lindisfarne Gospels as a backdrop for the X-ray crystal structure of the most complex non-DNA molecular knot synthesized so far. A team led by David Leigh prepared the 160-atom-long pentafoil knot in a one-step reaction from ten organic building blocks and five iron(II) cations. They use a single chloride anion as a template, which, in the solid-state structure, is located at the centre of the pentafoil knot and exhibits ten  $\text{CH}\cdots\text{Cl}^-$  hydrogen bonds. Article p15; News & Views p7

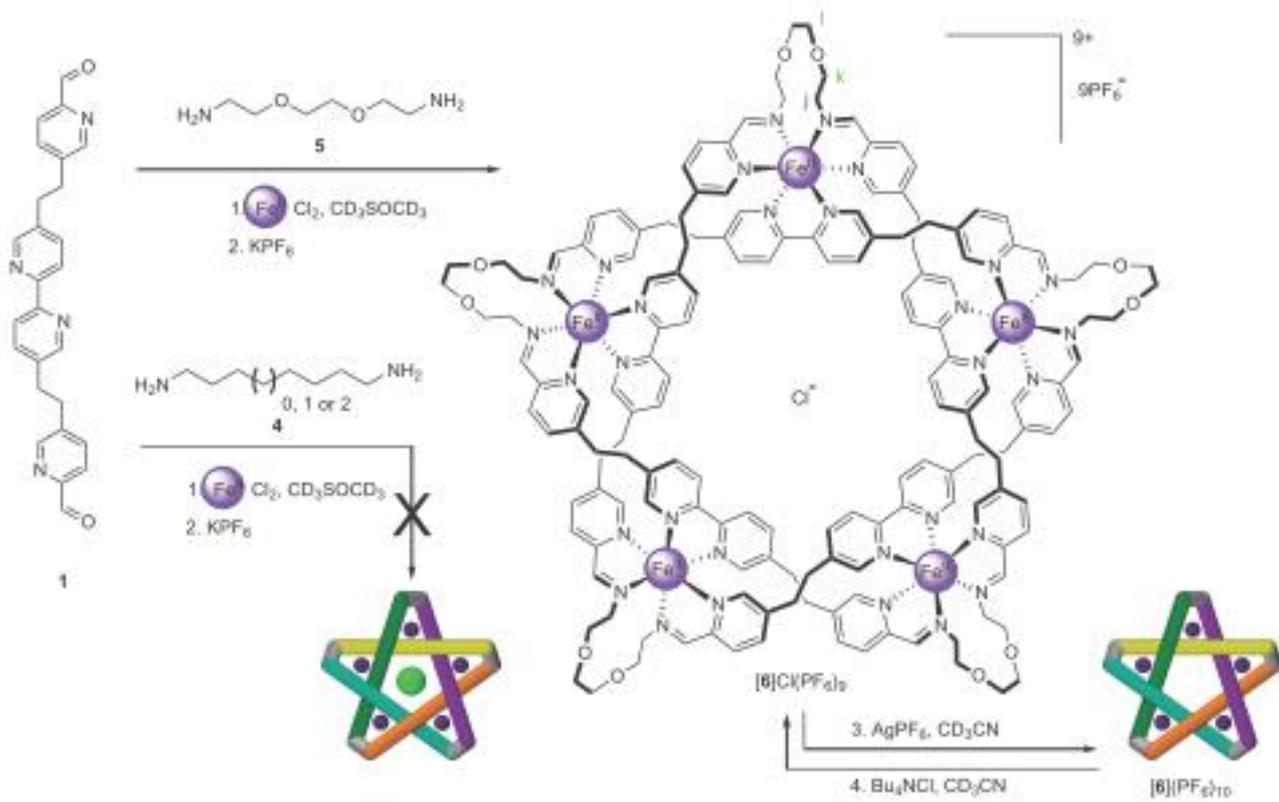


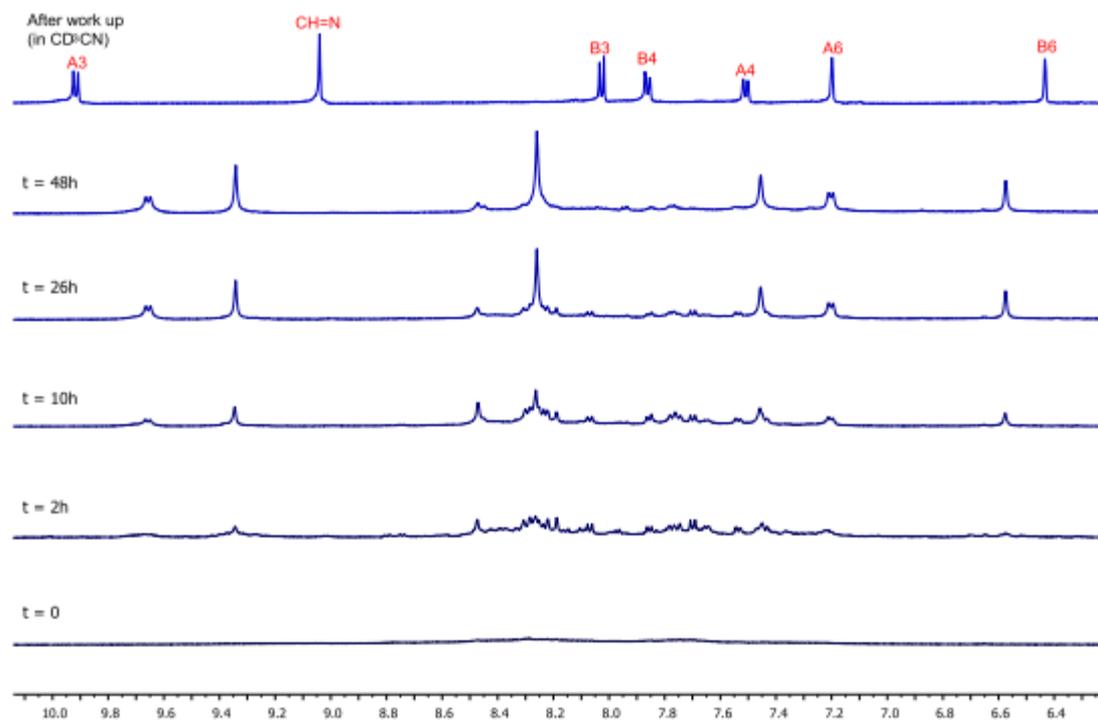




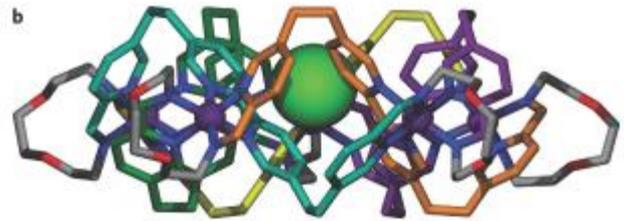
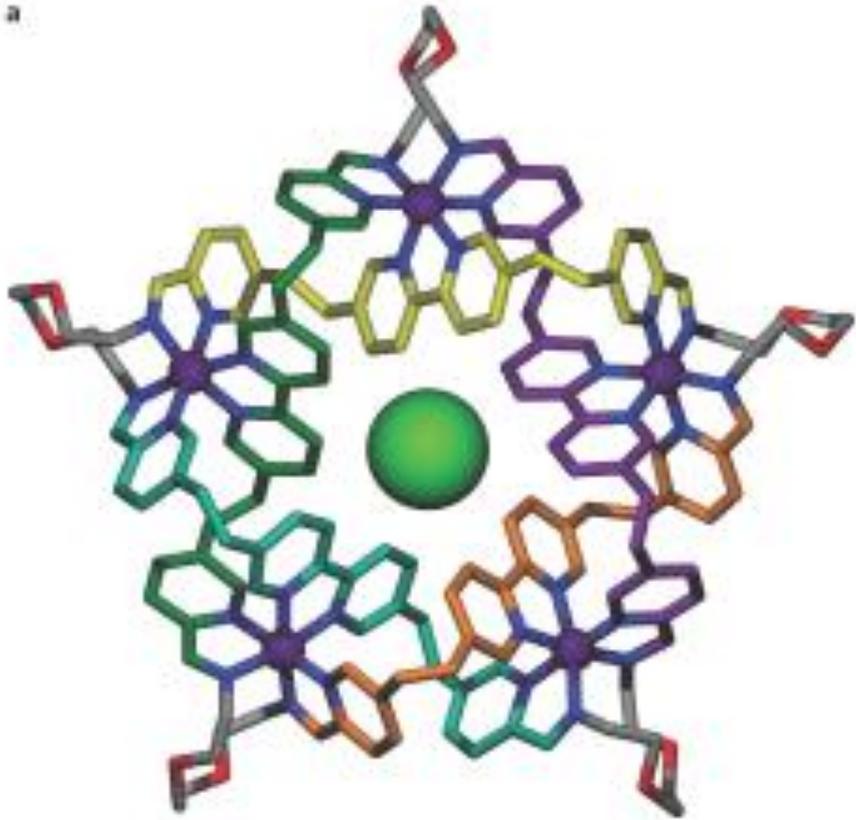


**Figure S8** Circular dichroism spectra of (R)-[3g]Cl(PF<sub>6</sub>)<sub>9</sub> and (S)-[3g]Cl(PF<sub>6</sub>)<sub>9</sub> in MeCN.





**Figure S9** Formation of pentafoil knot  $[6]^{10+}$  monitored by  $^1\text{H}$  NMR (DMSO- $d_6$ , 500 MHz), aromatic region of spectrum shown. Spectra were collected of the crude reaction mixture after  $t = 0$  (bottom), 2h, 10h, 26h and 48h. The top spectra is of the same sample after work-up ( $^1\text{H}$  NMR in  $\text{CD}_3\text{CN}$ ) with  $^1\text{H}$  NMR assignments indicated.



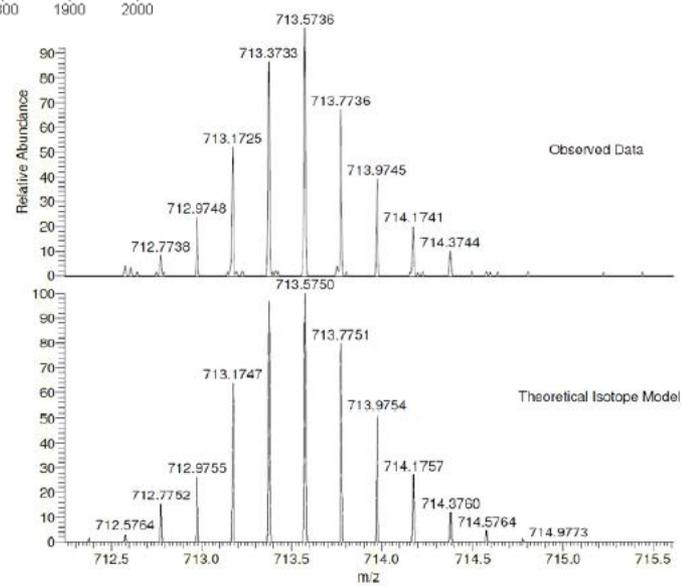
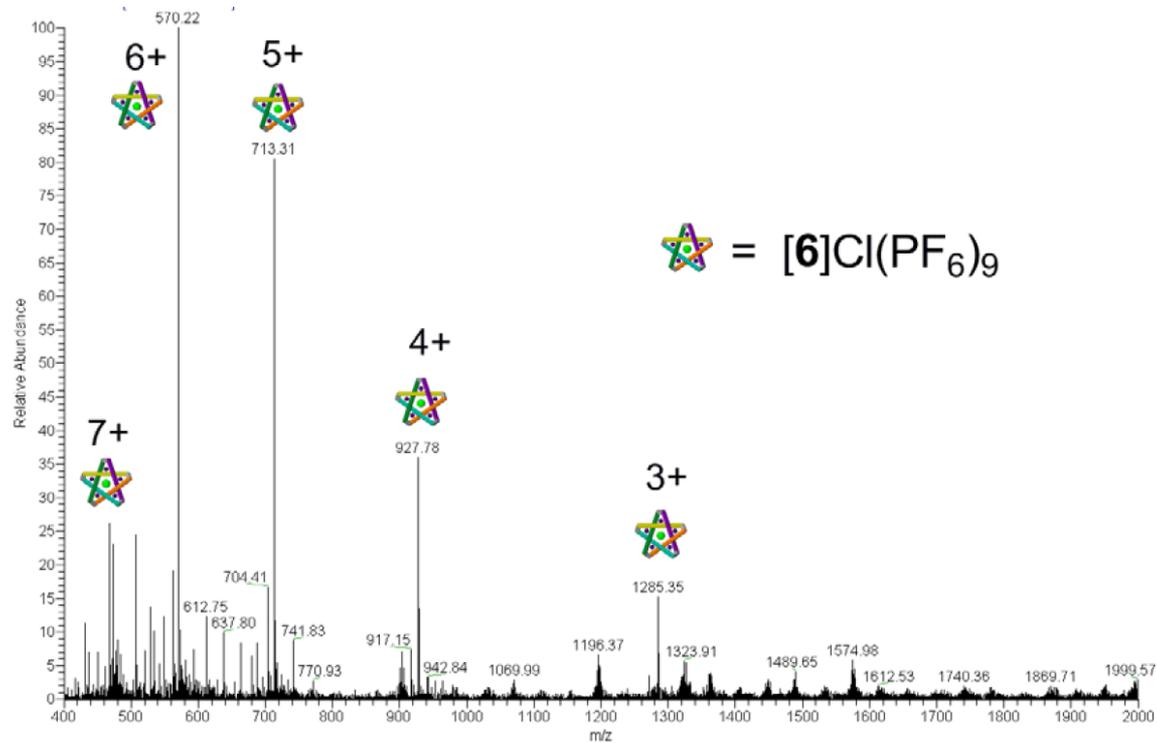
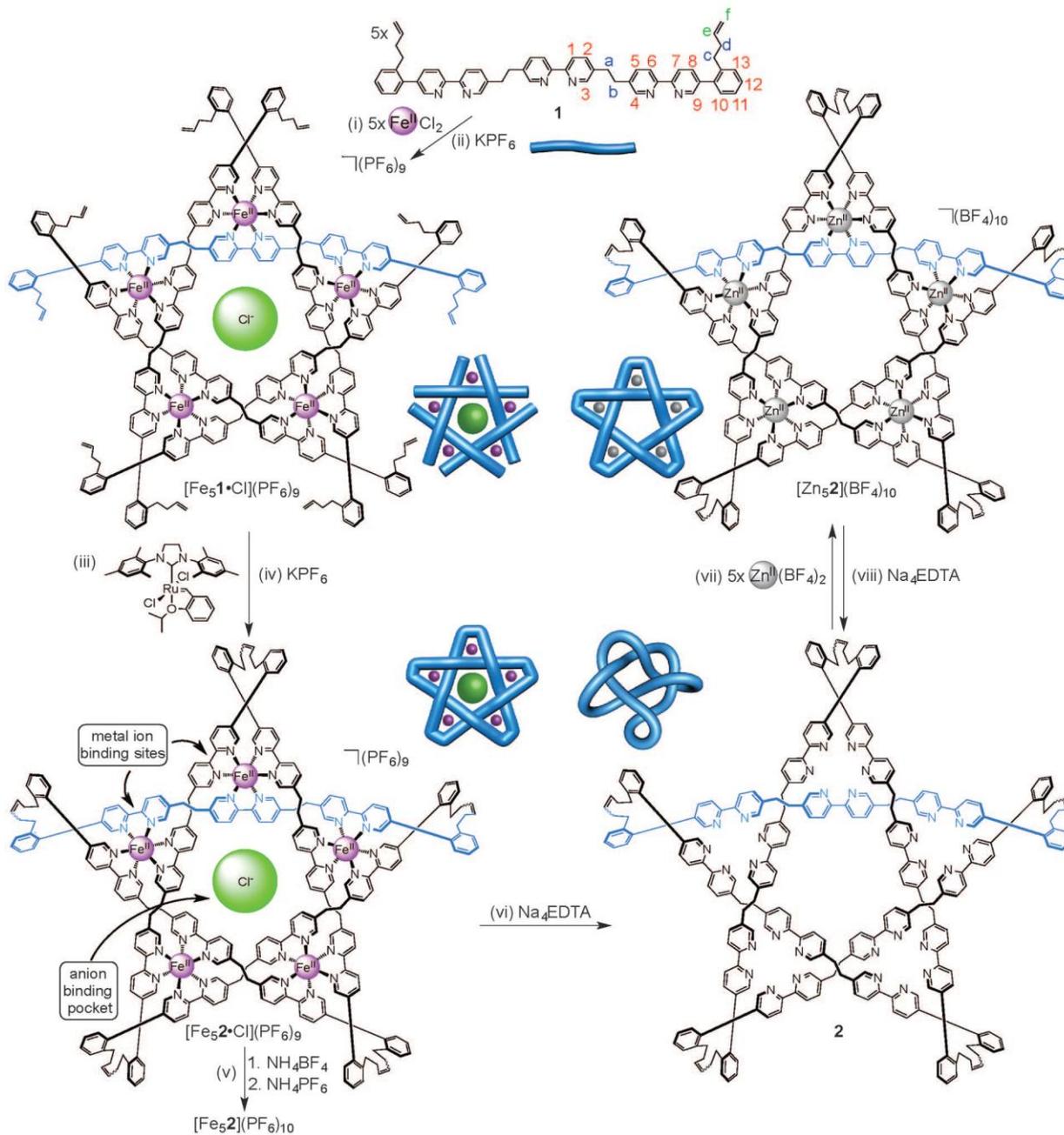


Figure S5 Low-resolution ESI-MS of pentafoil knot  $[6]Cl(PF_6)_9$  (top), and high-resolution isotope pattern (bottom) of  $[M-4PF_6]^{5+}$  peak.



Interlocked Molecules

DOI: 10.1002/anie.201007963

# 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

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## Template synthesis of molecular knots†

Cite this: *Chem. Soc. Rev.*, 2013, 42, 1700

Jean-François Ayme,<sup>ab</sup> Jonathon E. Beves,<sup>a</sup> Christopher J. Campbell<sup>a</sup> and David A. Leigh<sup>\*ab</sup>

Catenanes

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# Catenanes: Fifty Years of Molecular Links

Guzmán Gil-Ramírez, David A. Leigh,\* and Alexander J. Stephens

*Angew. Chem. Int. Ed.* 2015, 54, 6110–6150

Nobel Laureate in Chemistry 2016: Jean-Pierre Sauvage, University of Strasbourg, France.  
The Nobel Committee for Chemistry. From: The Nobel Lectures 2016, 2016-12-08

[https://www.youtube.com/watch?v=voihgqHIU\\_4](https://www.youtube.com/watch?v=voihgqHIU_4)

[http://www.catenane.net/pages/2017\\_819knot.html](http://www.catenane.net/pages/2017_819knot.html)

<https://www.catenane.net/pages/research.html>