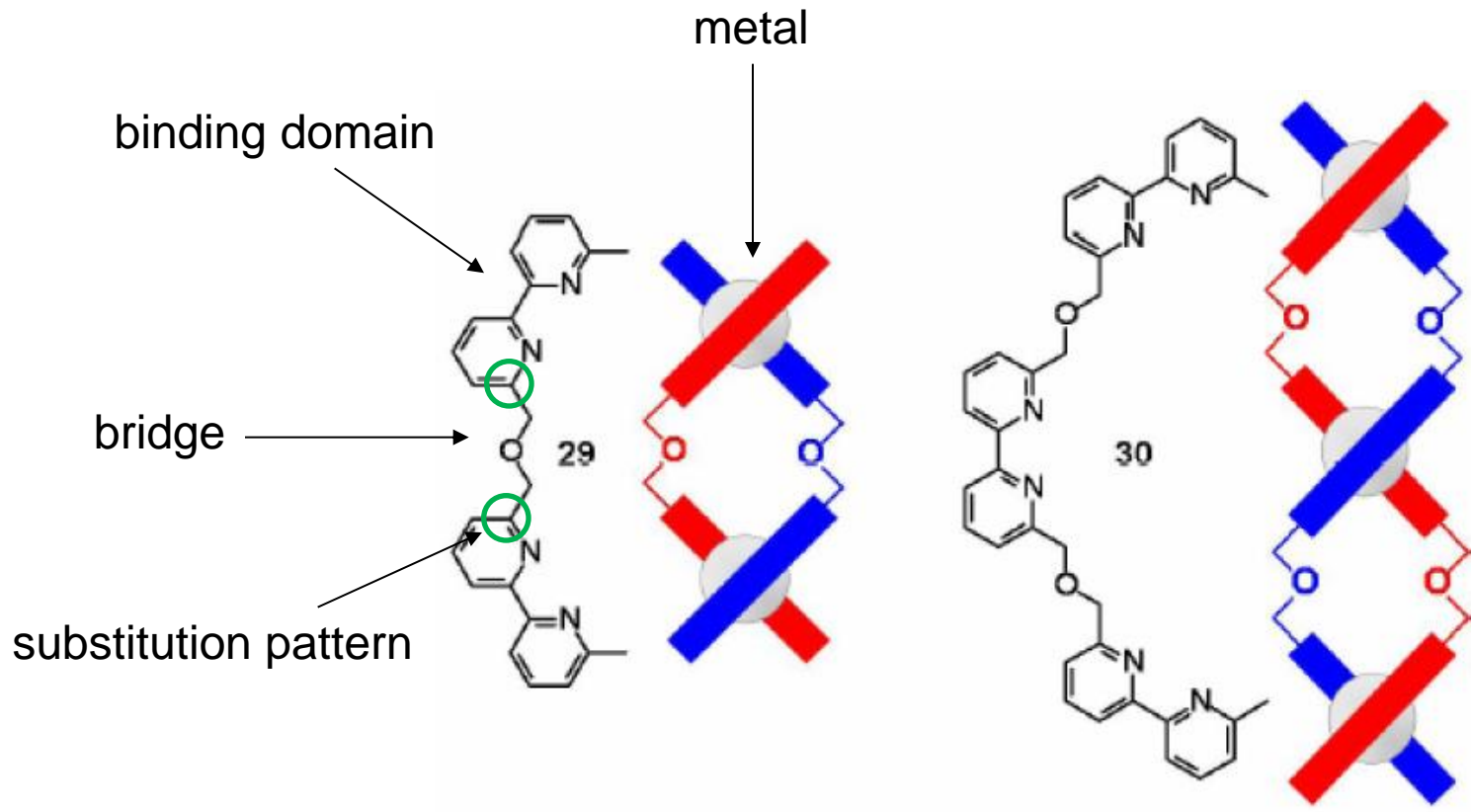
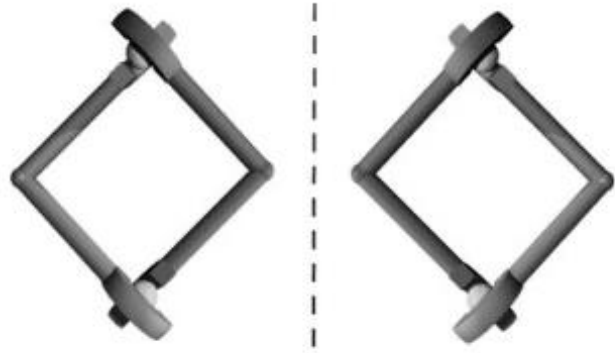
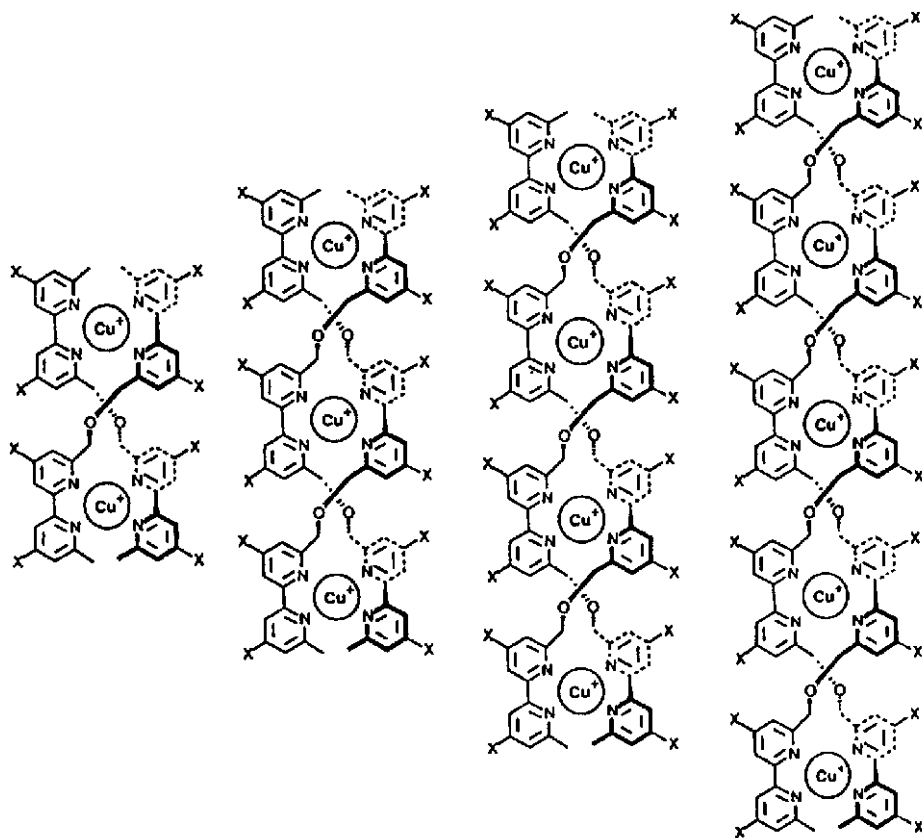


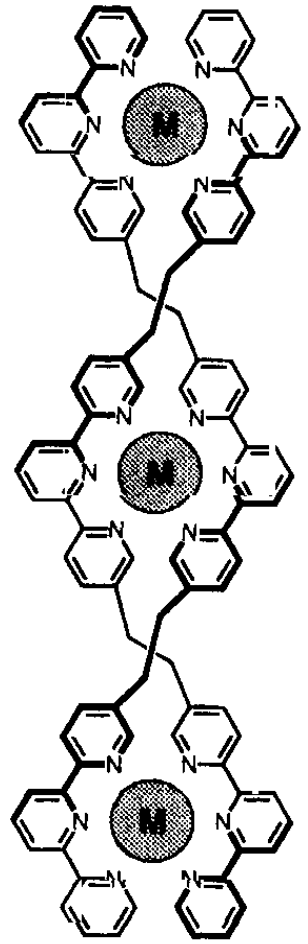
Double stranded helicates



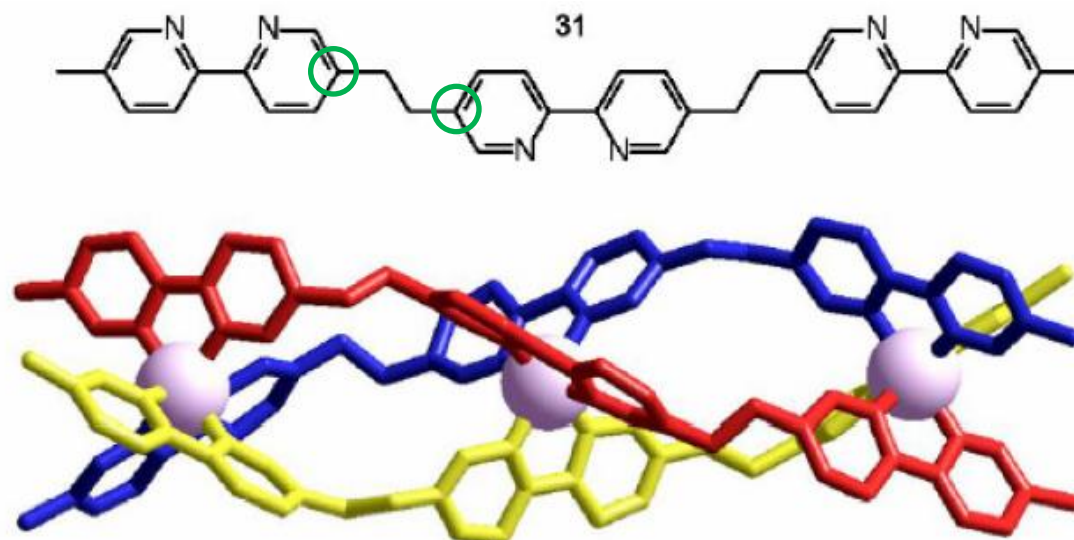


Double helicates



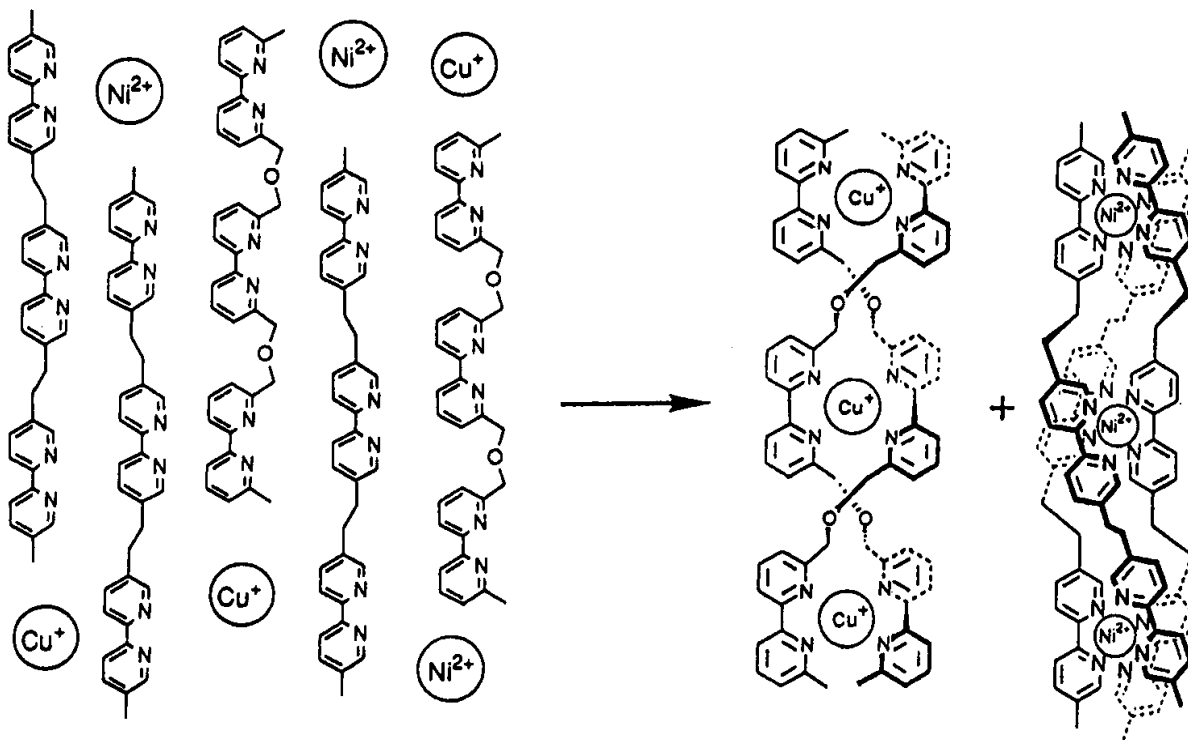


Triple stranded helicates

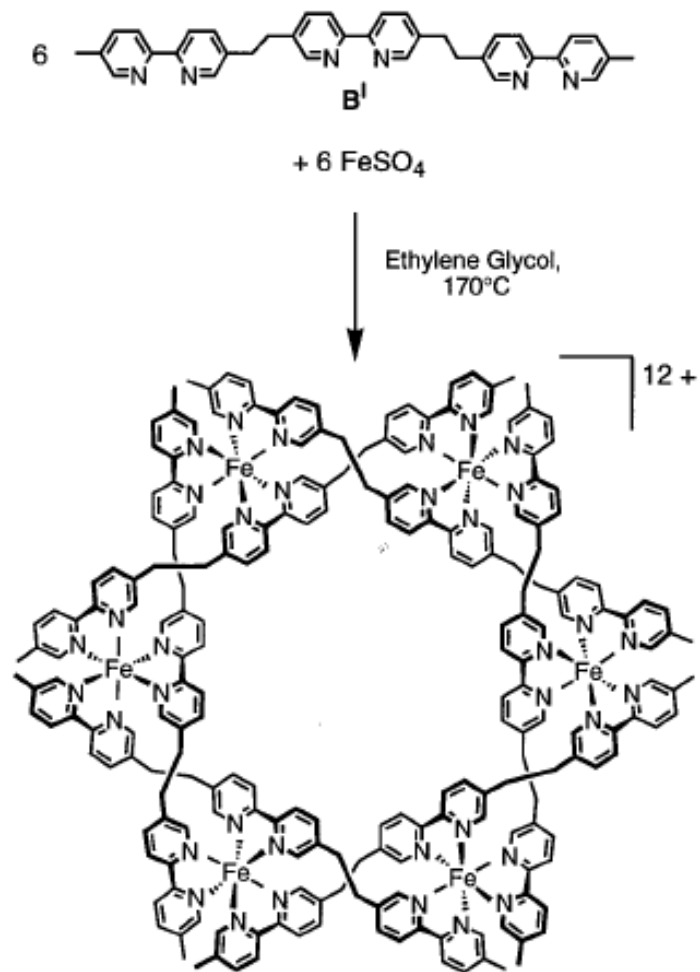
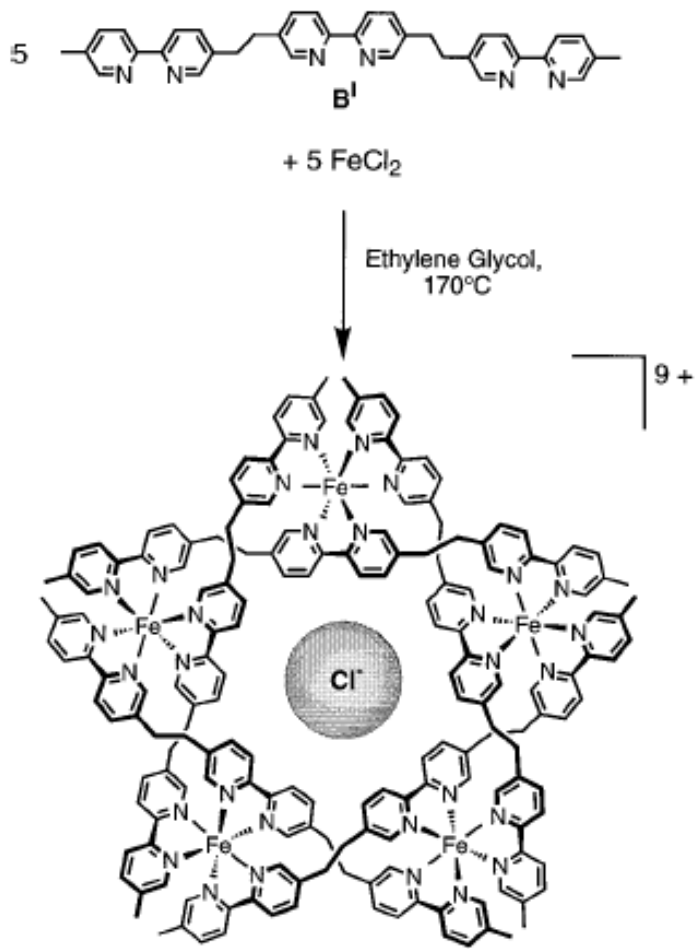


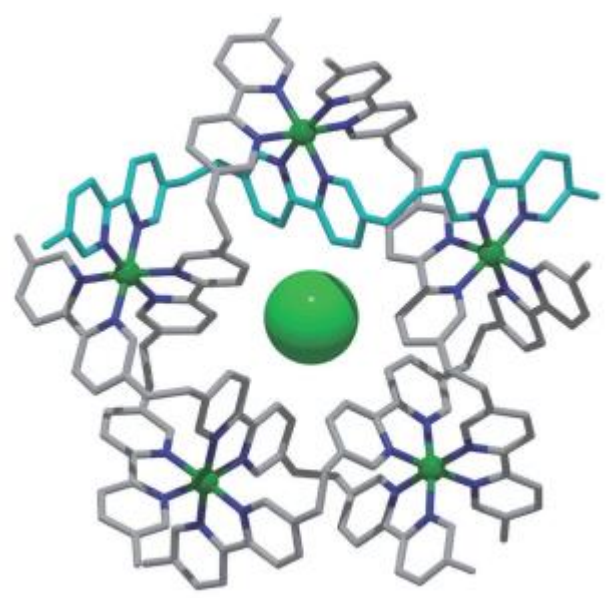
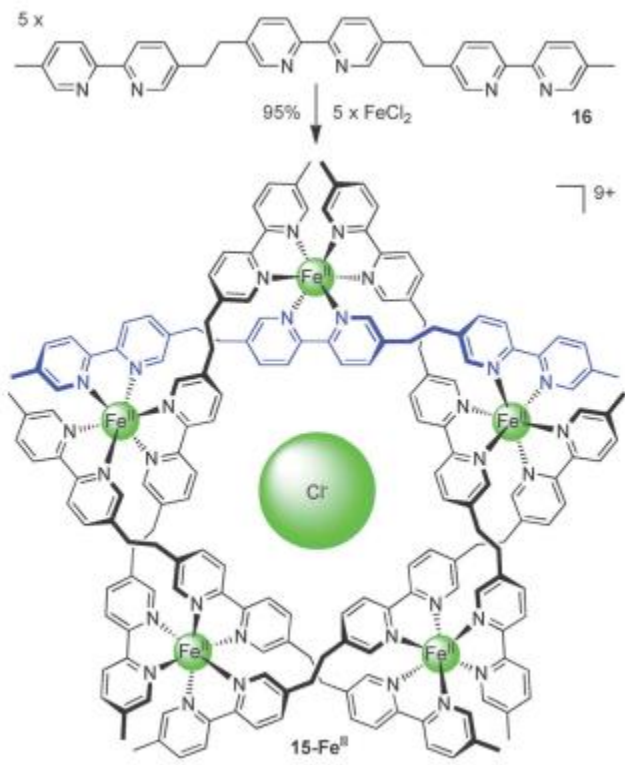
- Ni(II) : octahedral geometry
- one ligand can not wrap around one Ni(II) cation : trimerization
- other metals: Co(II), Fe(II), lanthanides

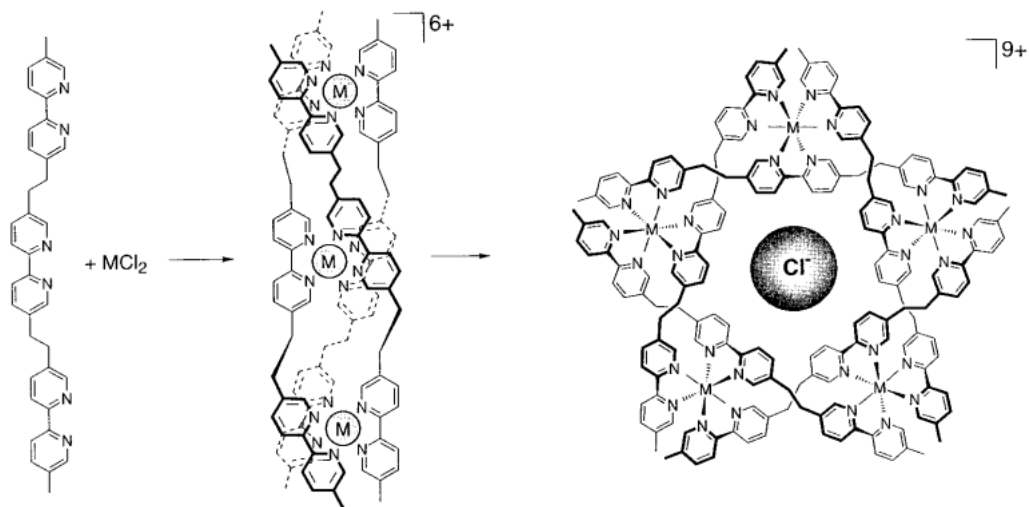
Double and Triple Helicates: an example of Selective-Recognition



Cyclic Helicates



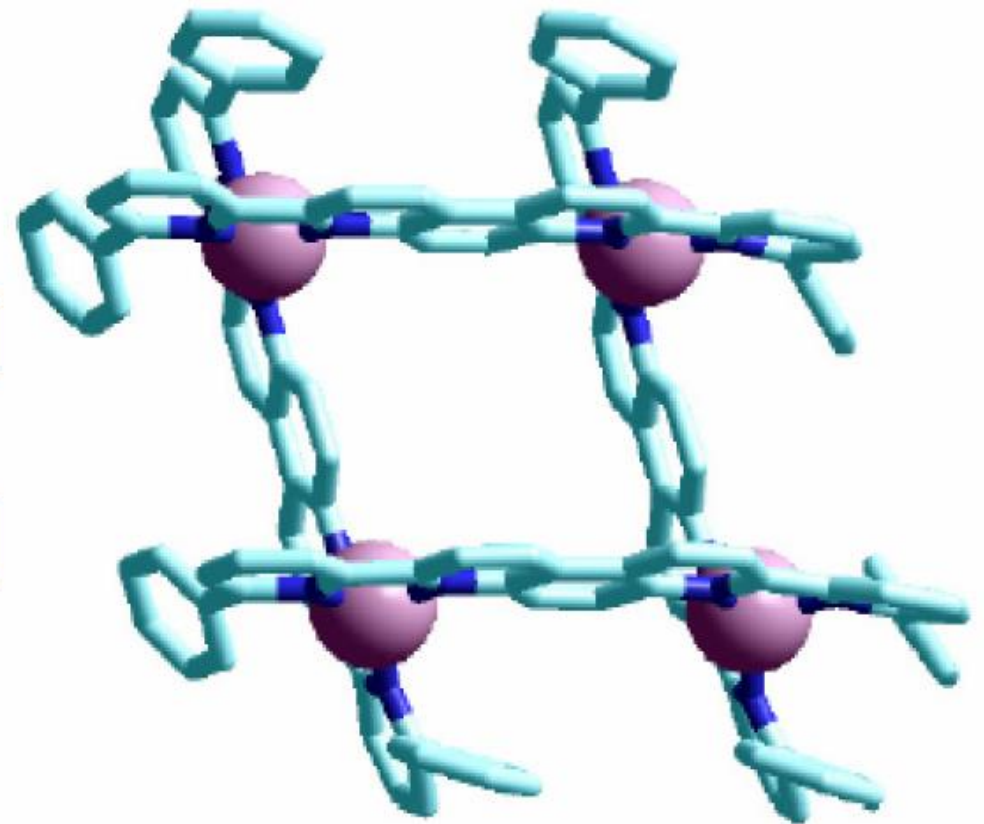
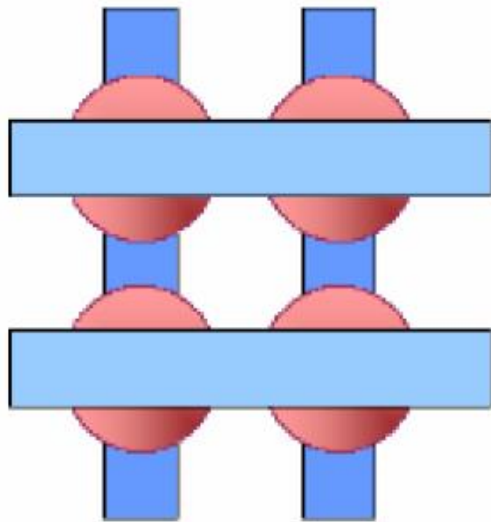
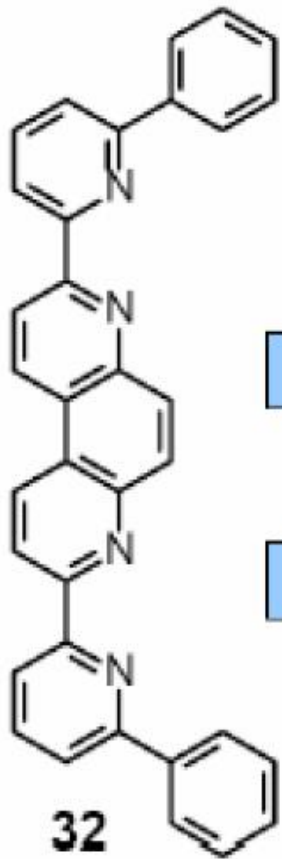




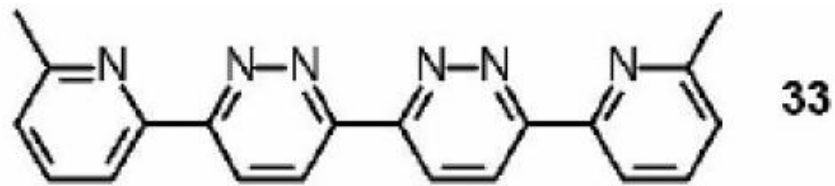
1H -NMR

ESI-MS

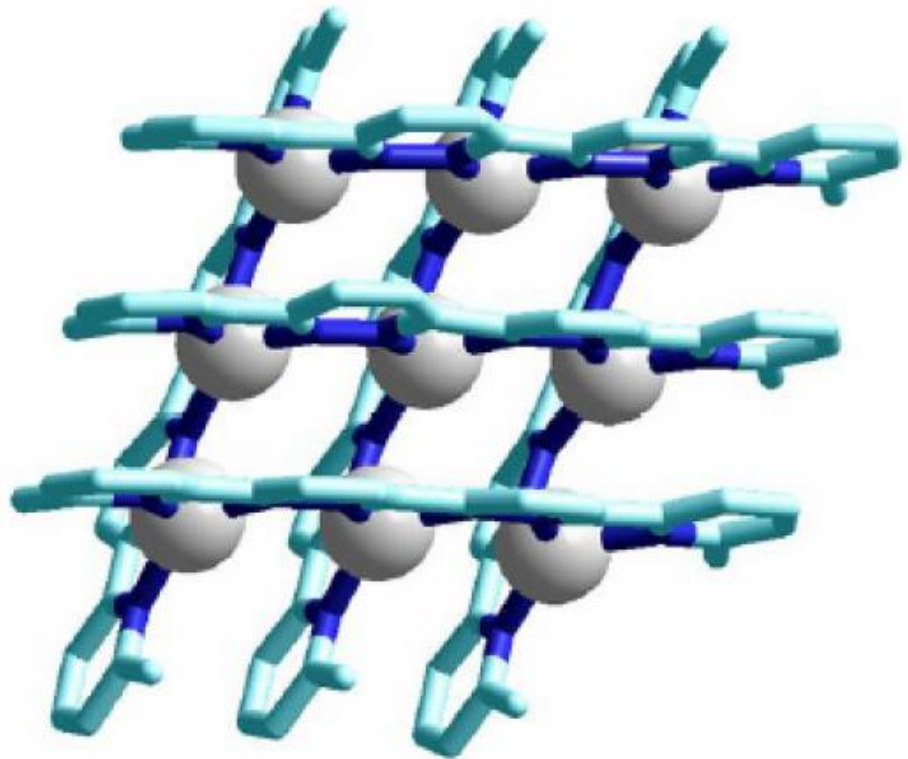
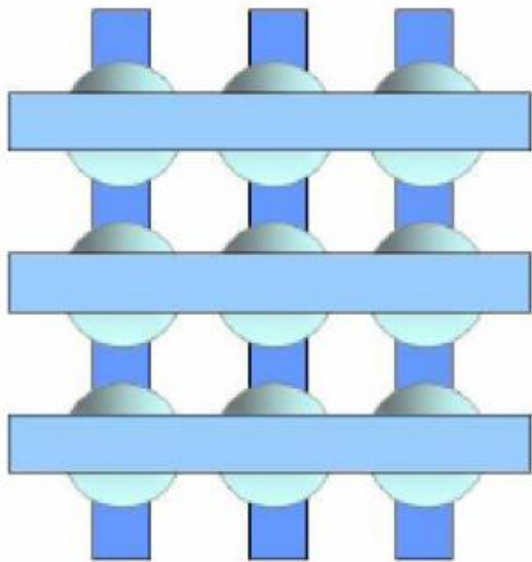
Molecular Grids



Molecular Grids

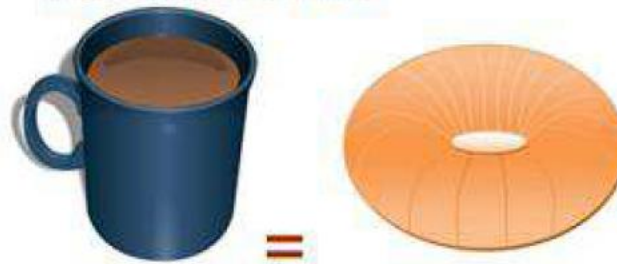
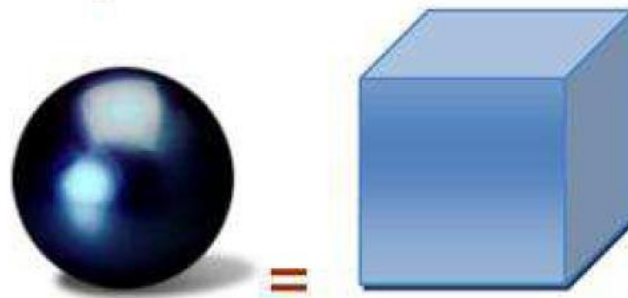


3X3 Ag(I) grid



Topology

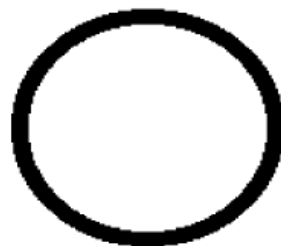
In topology, angles, distances or shapes have no meaning
But the object cannot be cut



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.

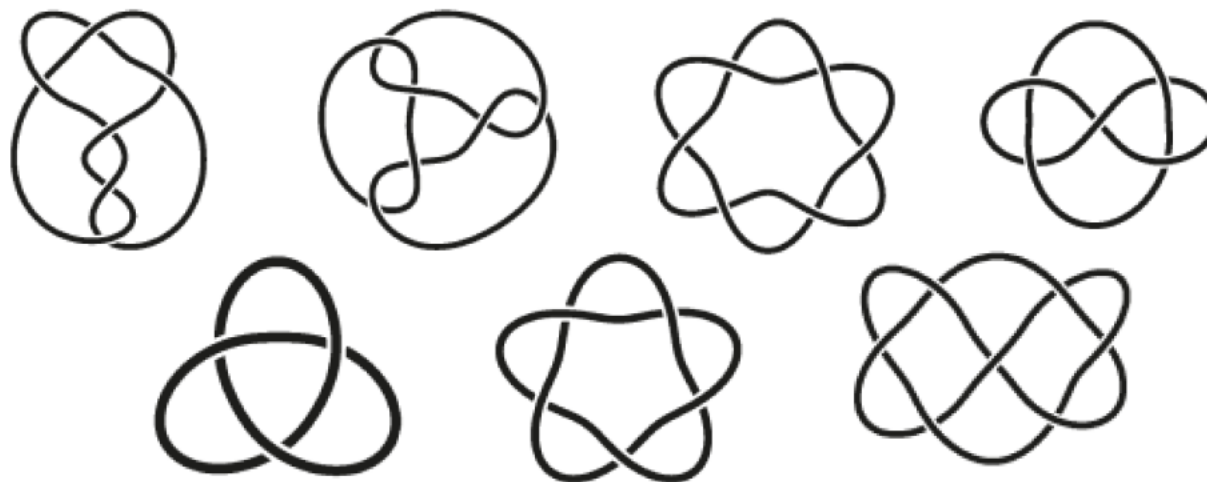
Molecular graph

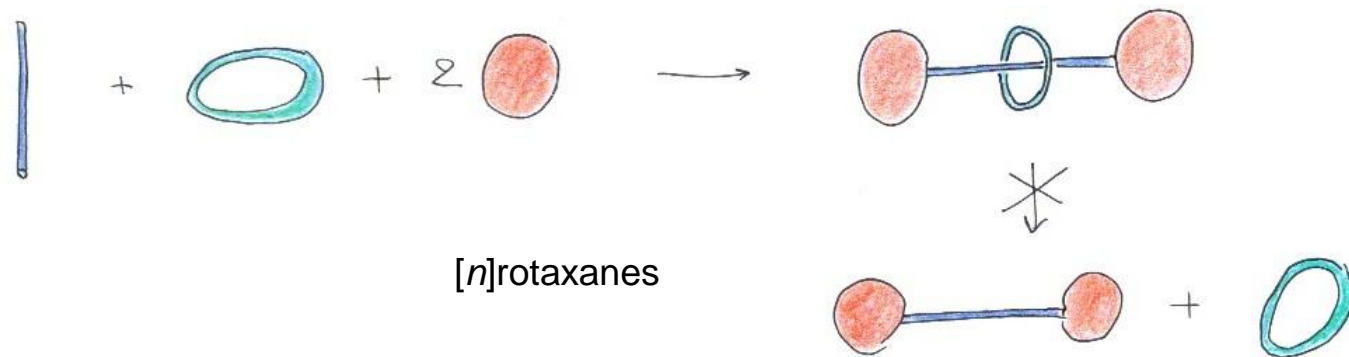
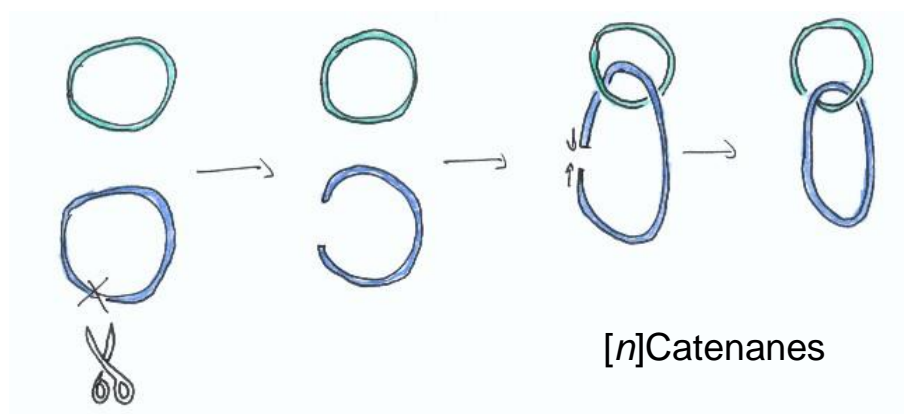


 non-planar graph

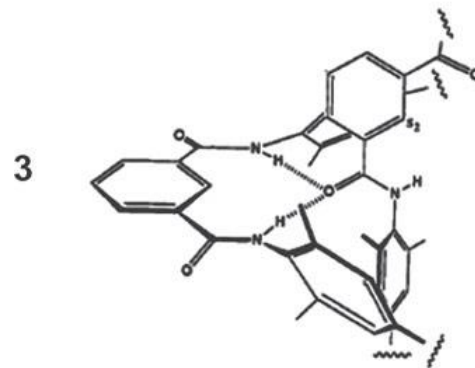
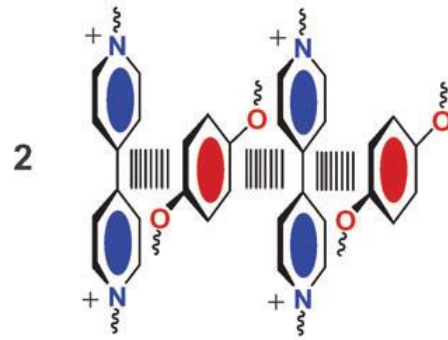
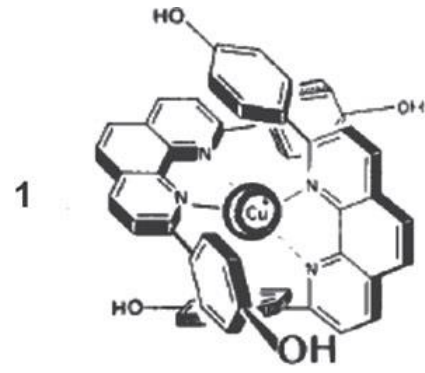
No possible conformation with no crossing in 2D representation

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

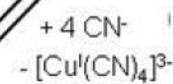
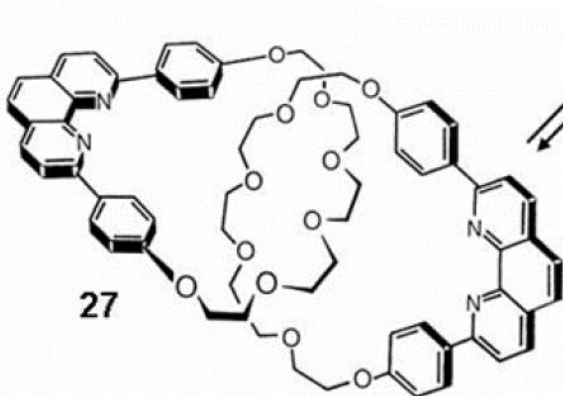
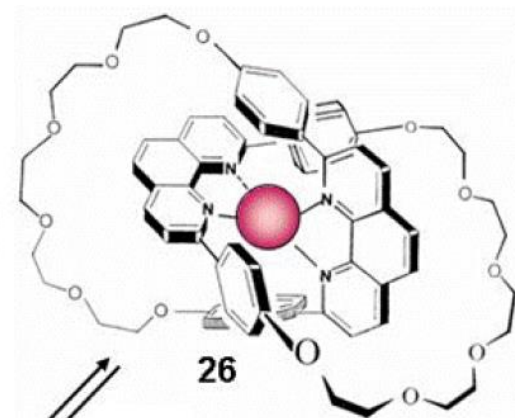
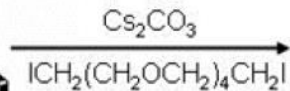
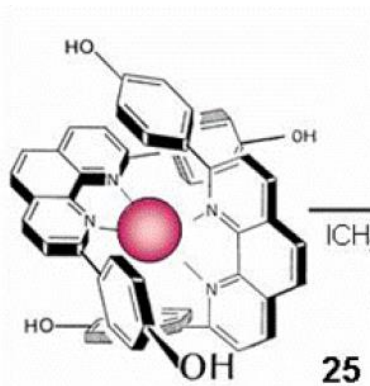
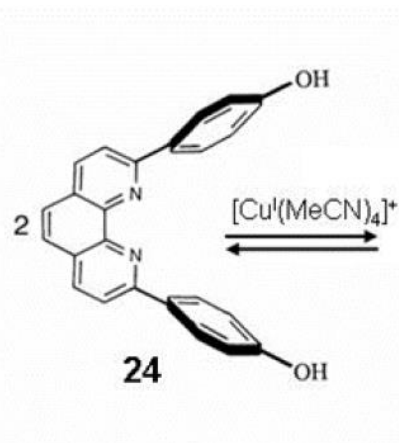
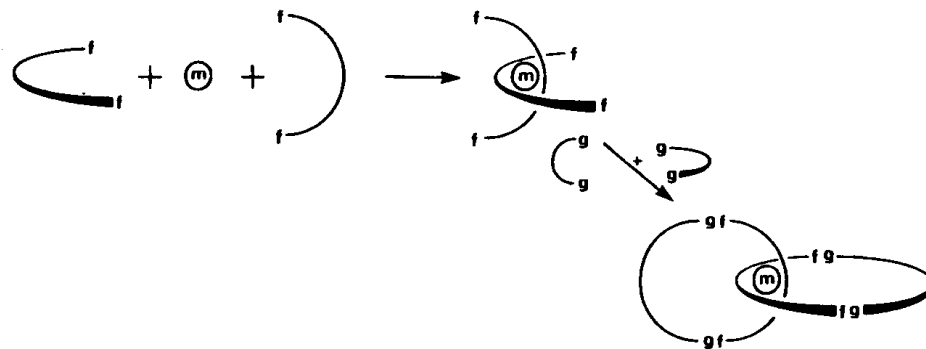






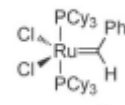
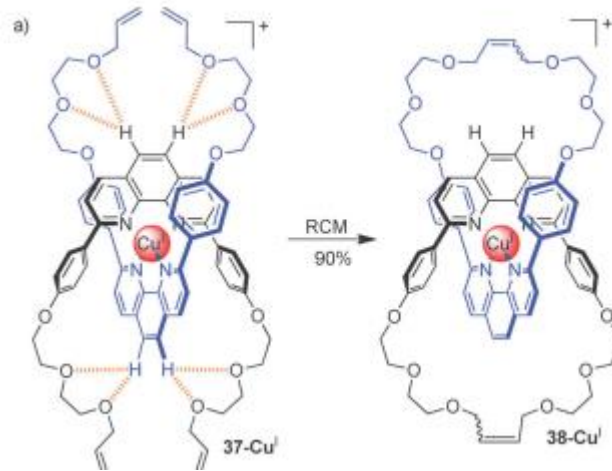
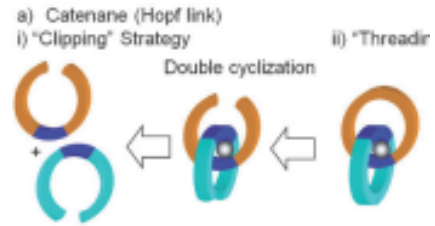
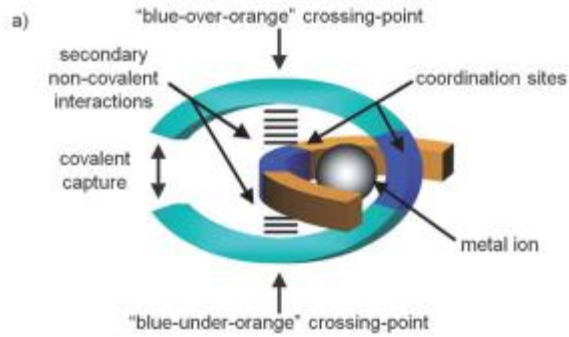


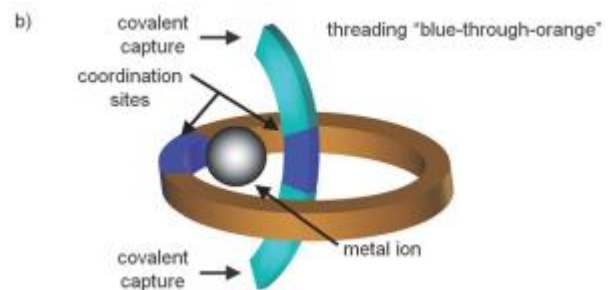
[n]Catenani



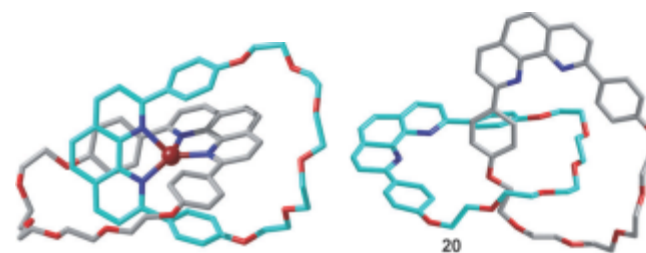
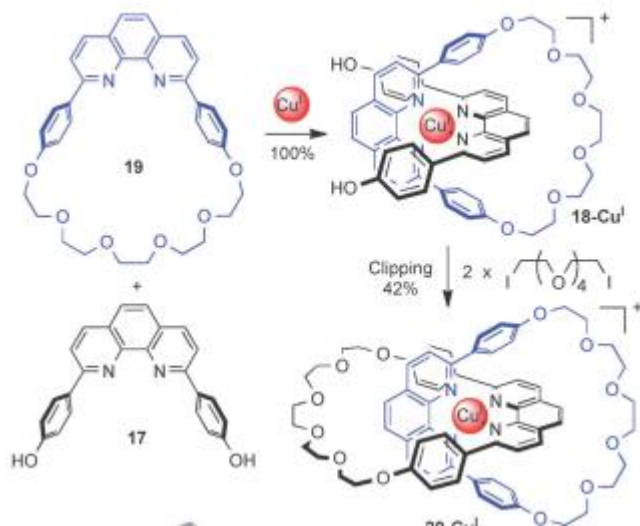
Sauvage 1983
Williamson ether synthesis
Yield 42%

Williamson ether synthesis: $\text{R-OH} + \text{X-R}' \rightarrow \text{R-O-R}'$

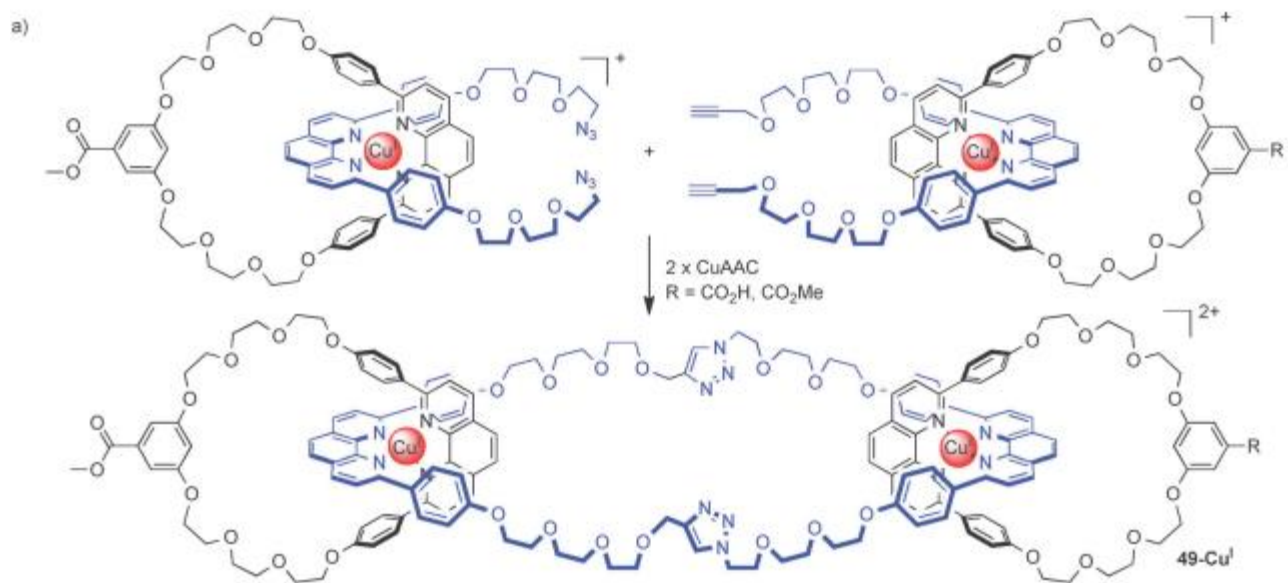
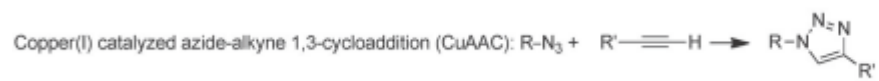




ii) "Threading-followed-by-clipping" strategy



Reaction	year	A		B		h/c	catalyst
Glaser	1869	RC≡CH	sp	RC≡CH	sp	homo	Cu
Ullmann	1901	Ar-X	sp ²	Ar-X	sp ²	homo	Cu
Sonogashira	1975	RC≡CH	sp	R-X	sp ³ sp ²	cross	Pd and Cu
Negishi	1977	R-Zn-X	sp ³ , sp ² , sp	R-X	sp ³ sp ²	cross	Pd or Ni
Stille	1978	R-SnR ₃	sp ³ , sp ² , sp	R-X	sp ³ sp ²	cross	Pd
Suzuki	1979	R-B(OR) ₂	sp ²	R-X	sp ³ sp ²	cross	Pd
Hiyama	1988	R-SiR ₃	sp ²	R-X	sp ³ sp ²	cross	Pd
Buchwald-Hartwig	1994	R ₂ N-R SnR ₃	sp	R-X	sp ²	cross	Pd



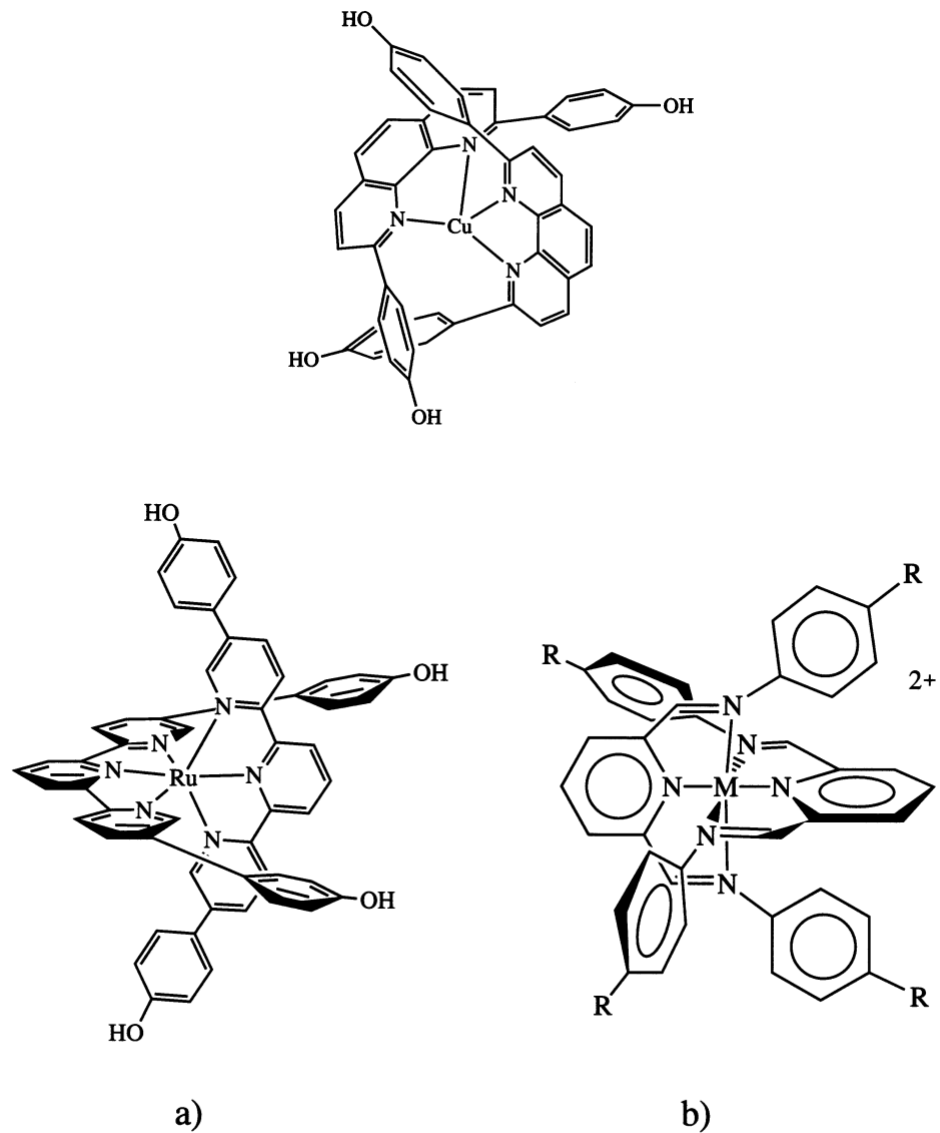
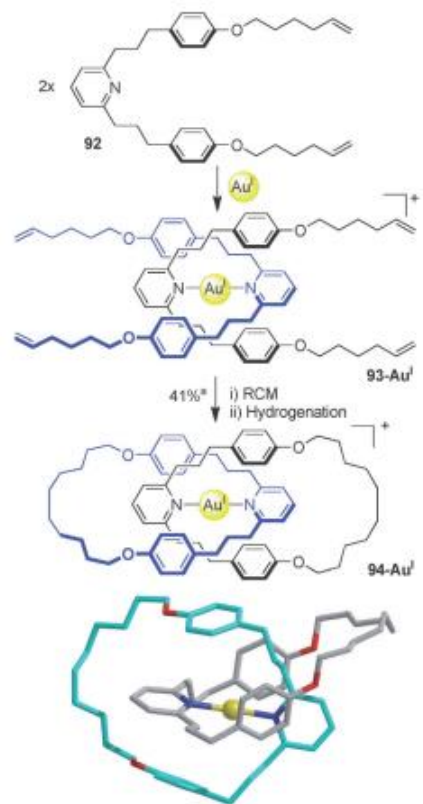
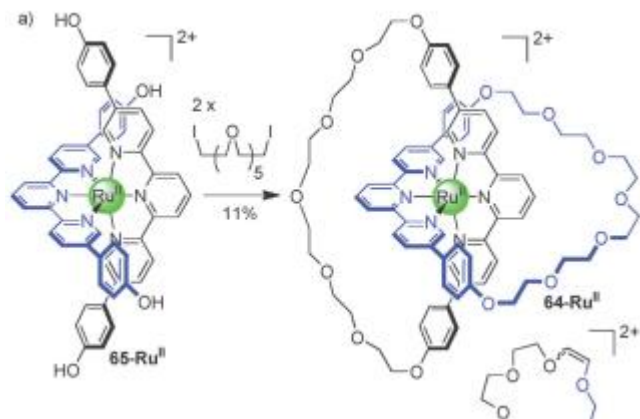
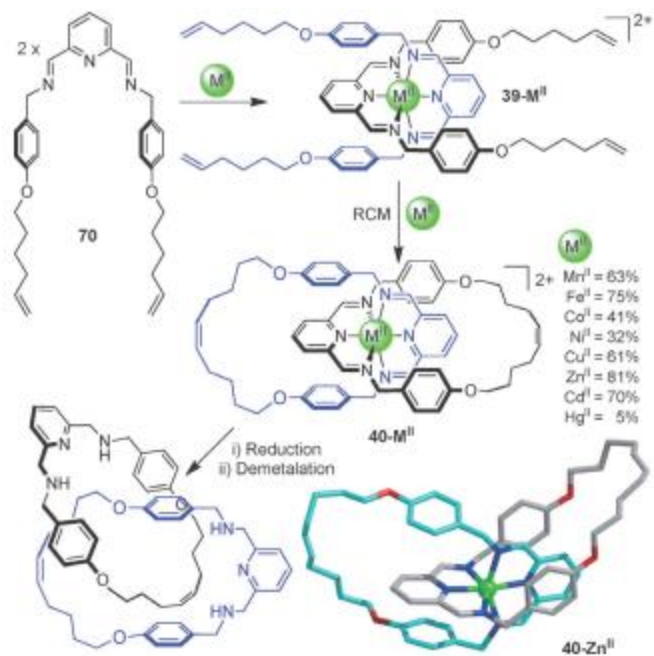
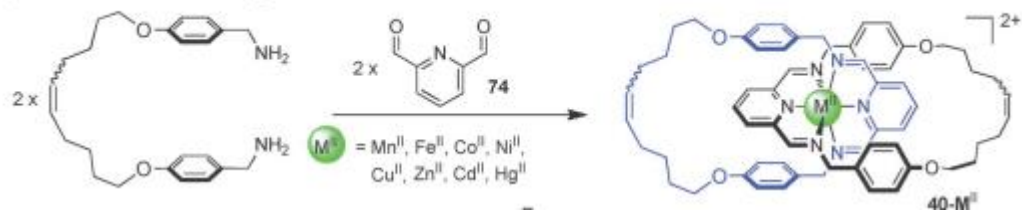


Fig. 13. (a) Sauvage's Ru-terpy octahedral template complex, (b) Vance's Schiff-base octahedral template complex.

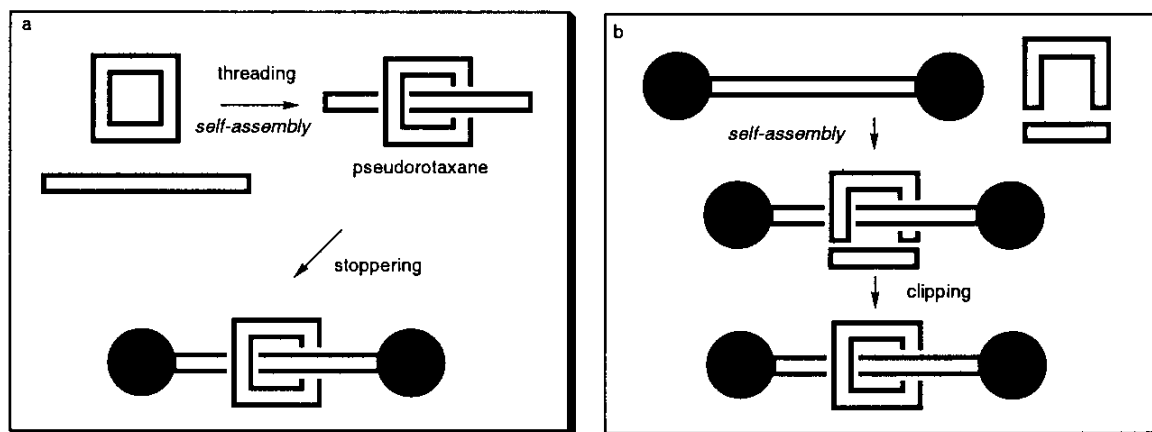




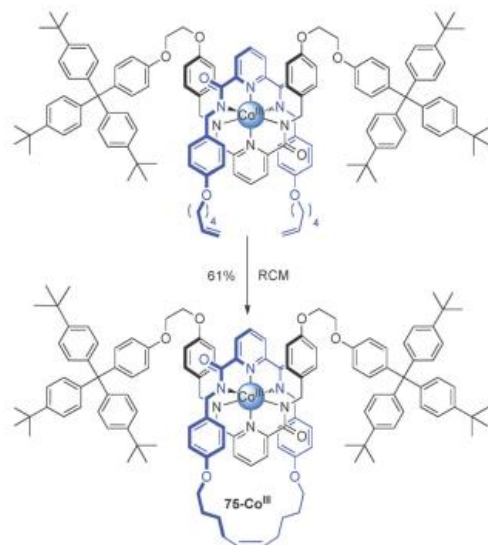
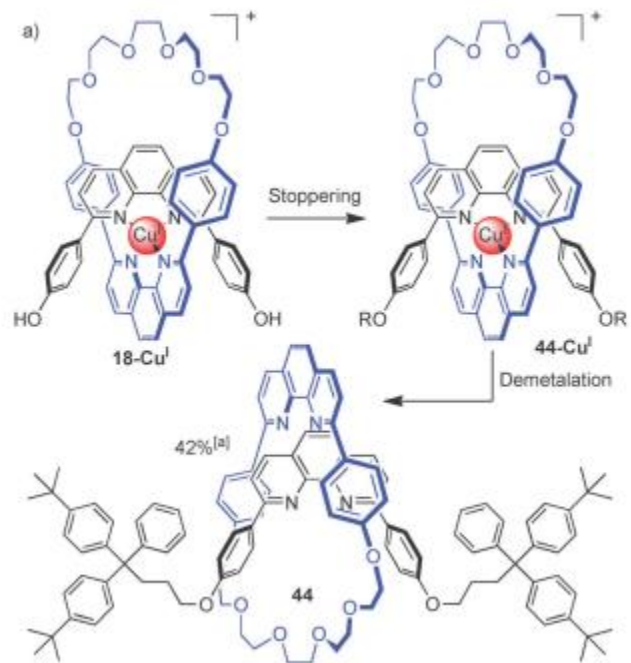
c) Imine bond formation: $R-NH_2 + R'-CHO \rightarrow R-N=CH-R'$

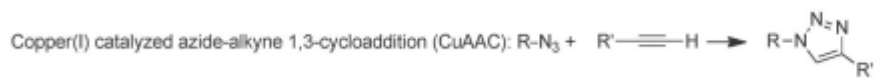


[2]Rotaxani

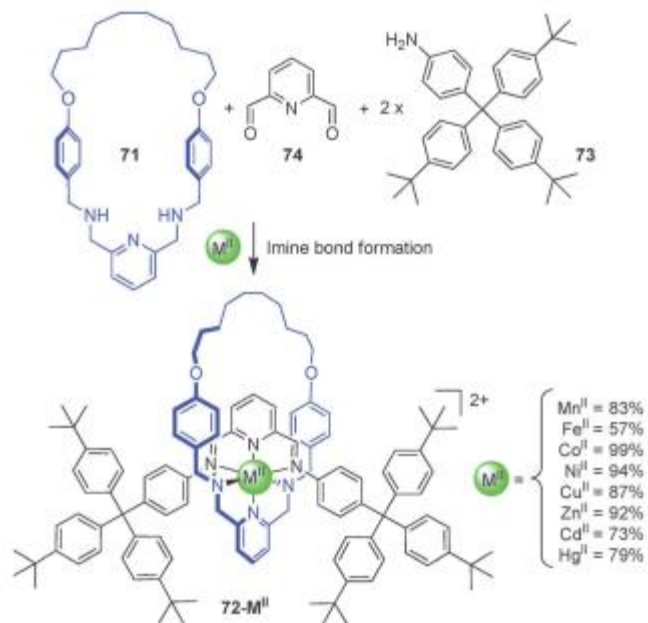
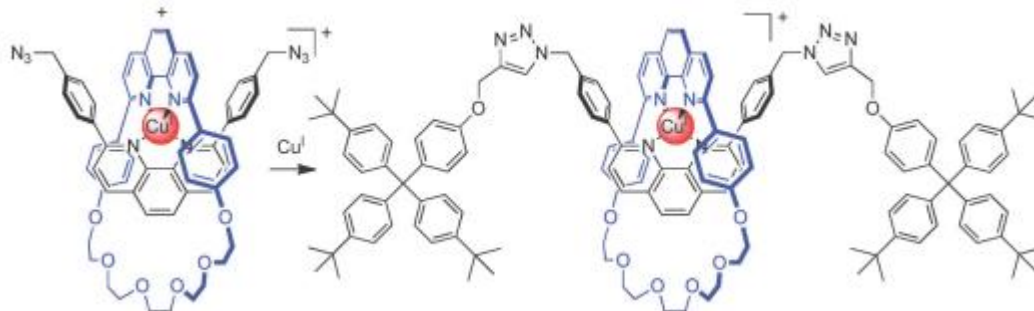


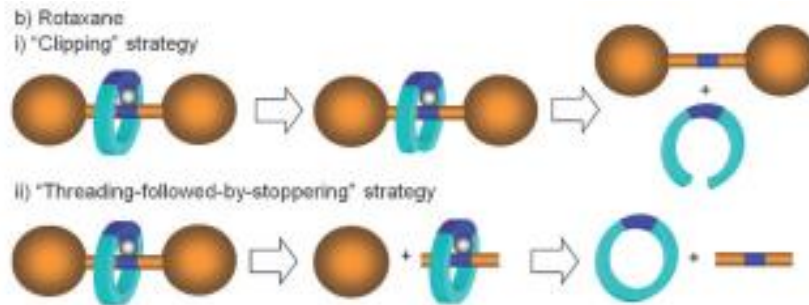
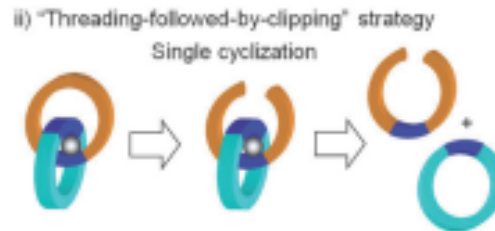
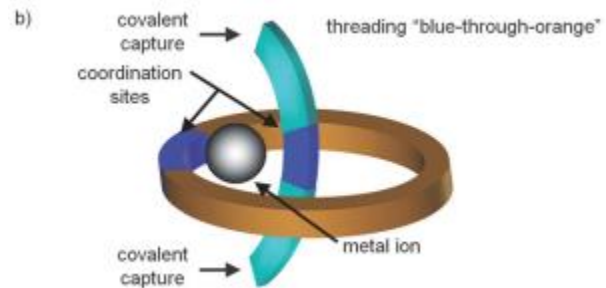
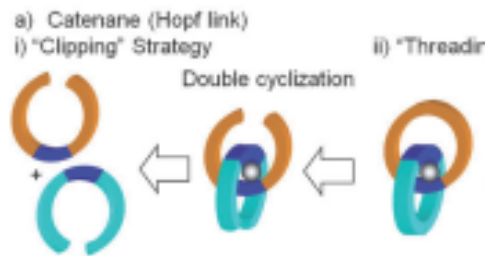
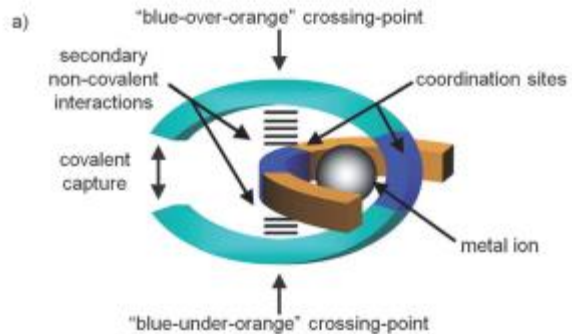
[2] Rotaxane synthesis by a) threading and b) clipping.

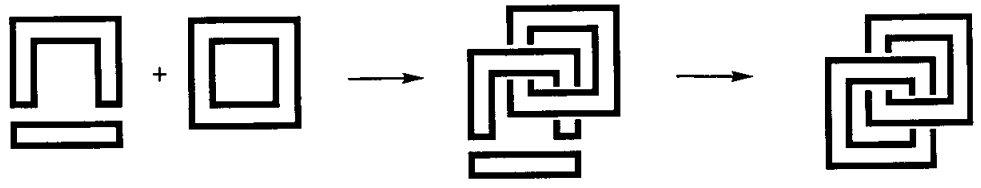




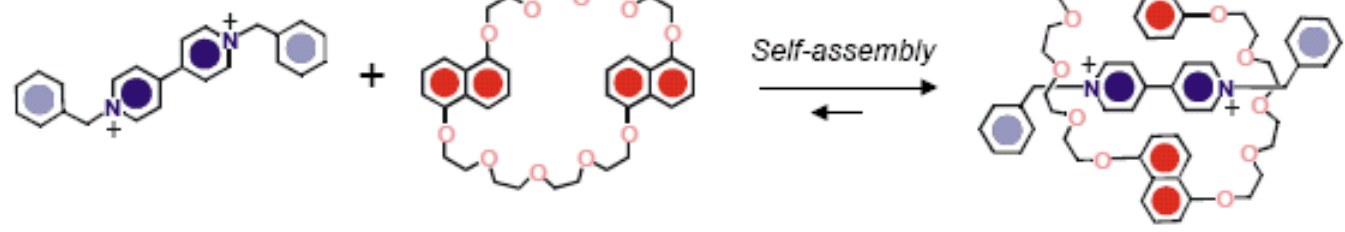
2 x $(t\text{-BuC}_6\text{H}_4)_3\text{CC}_6\text{H}_4\text{OCH}_2\text{-C}\equiv\text{C-H}$ **95**

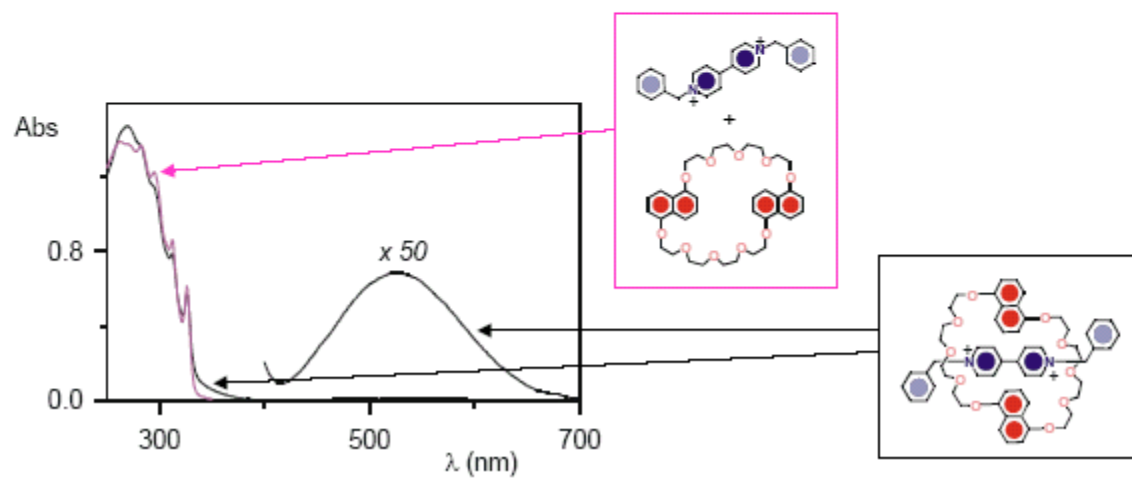
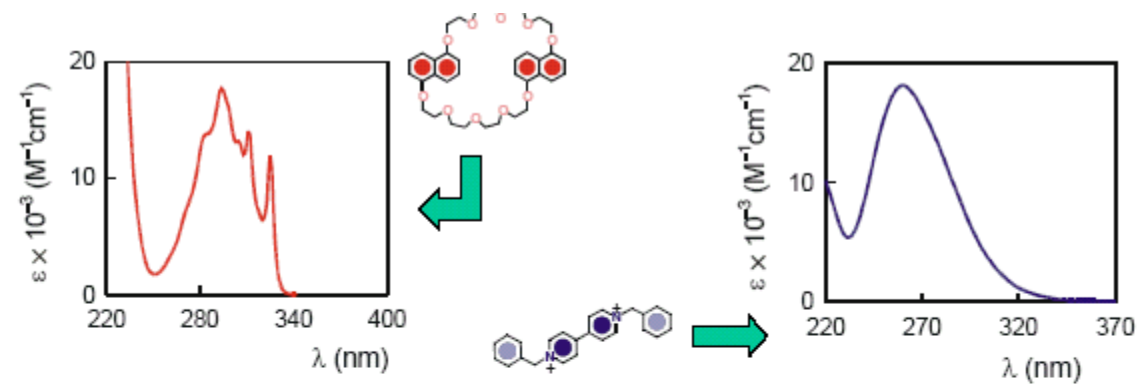


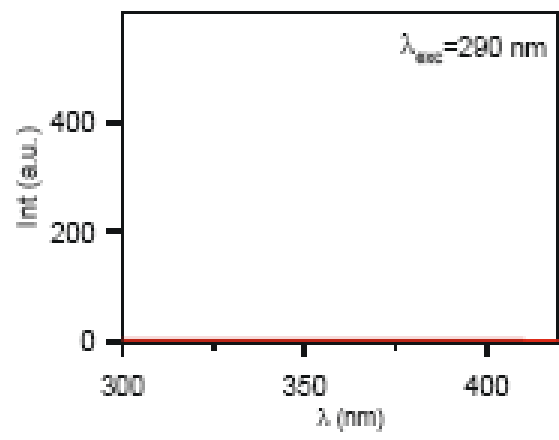
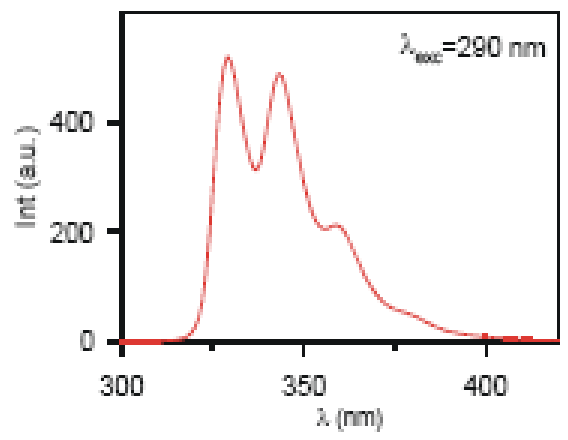
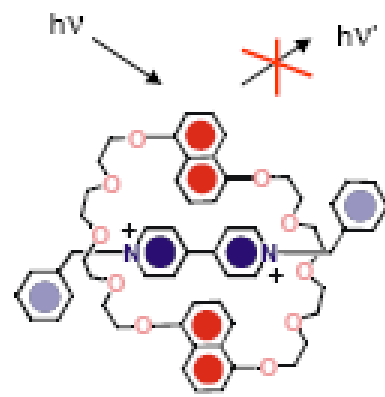
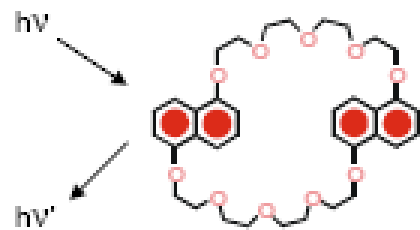


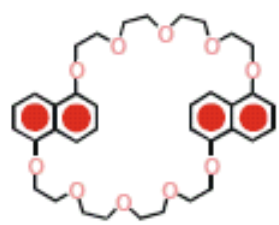
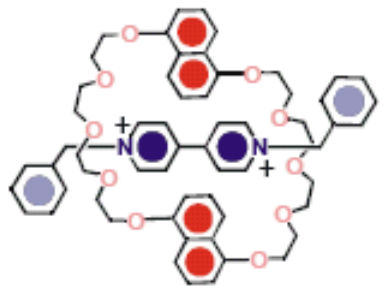
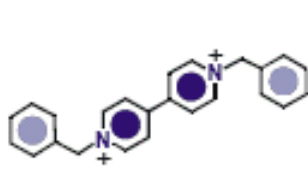
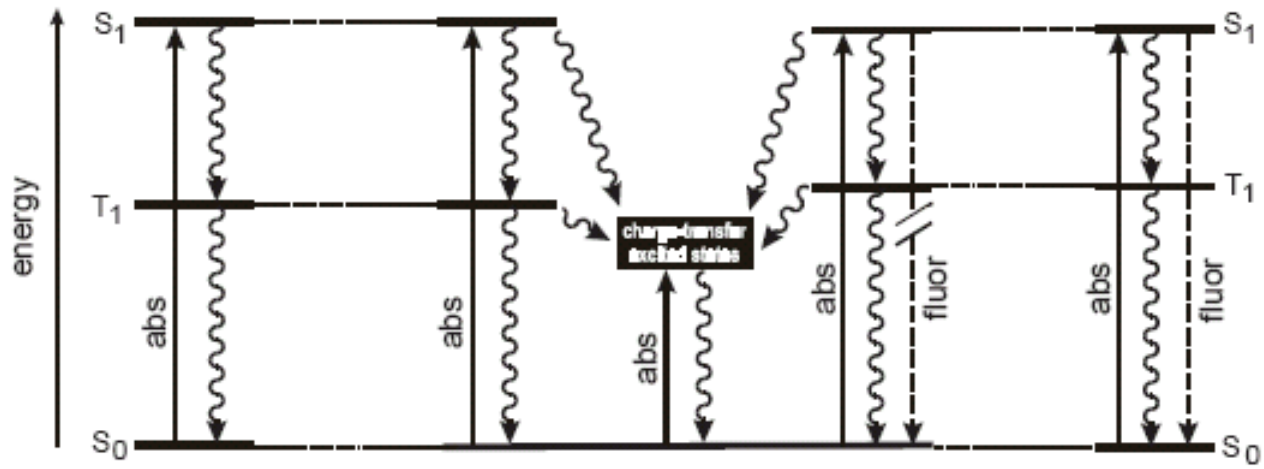


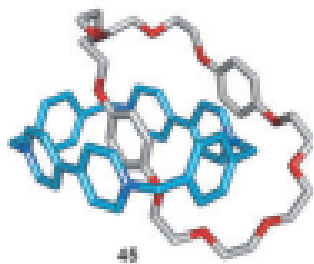
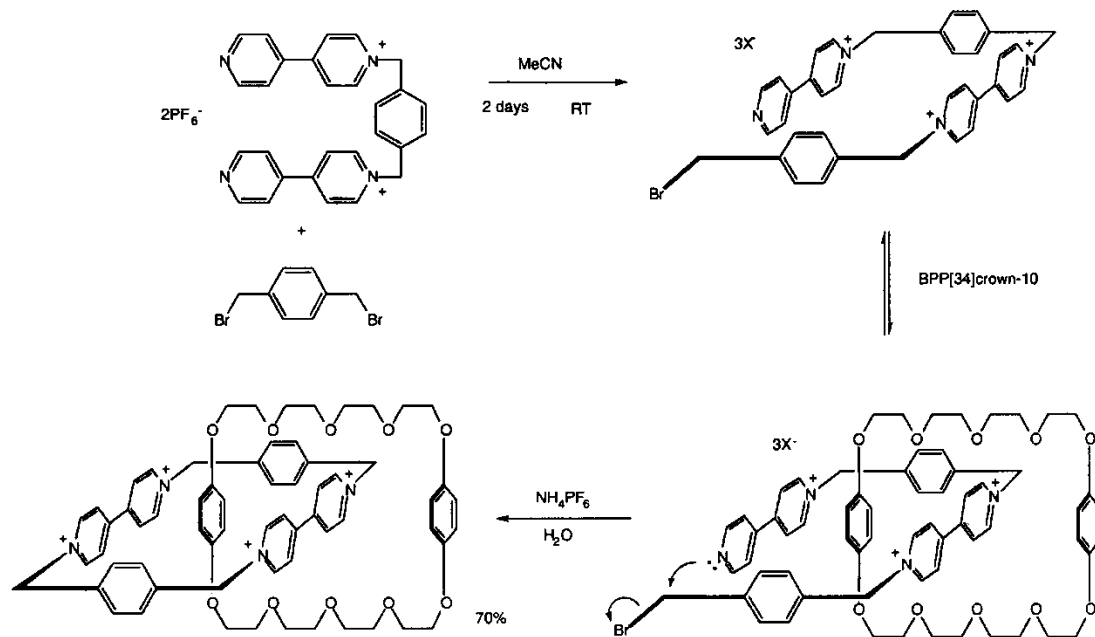
catione paraquat Bis-parafeñilene-[34]-crown-10

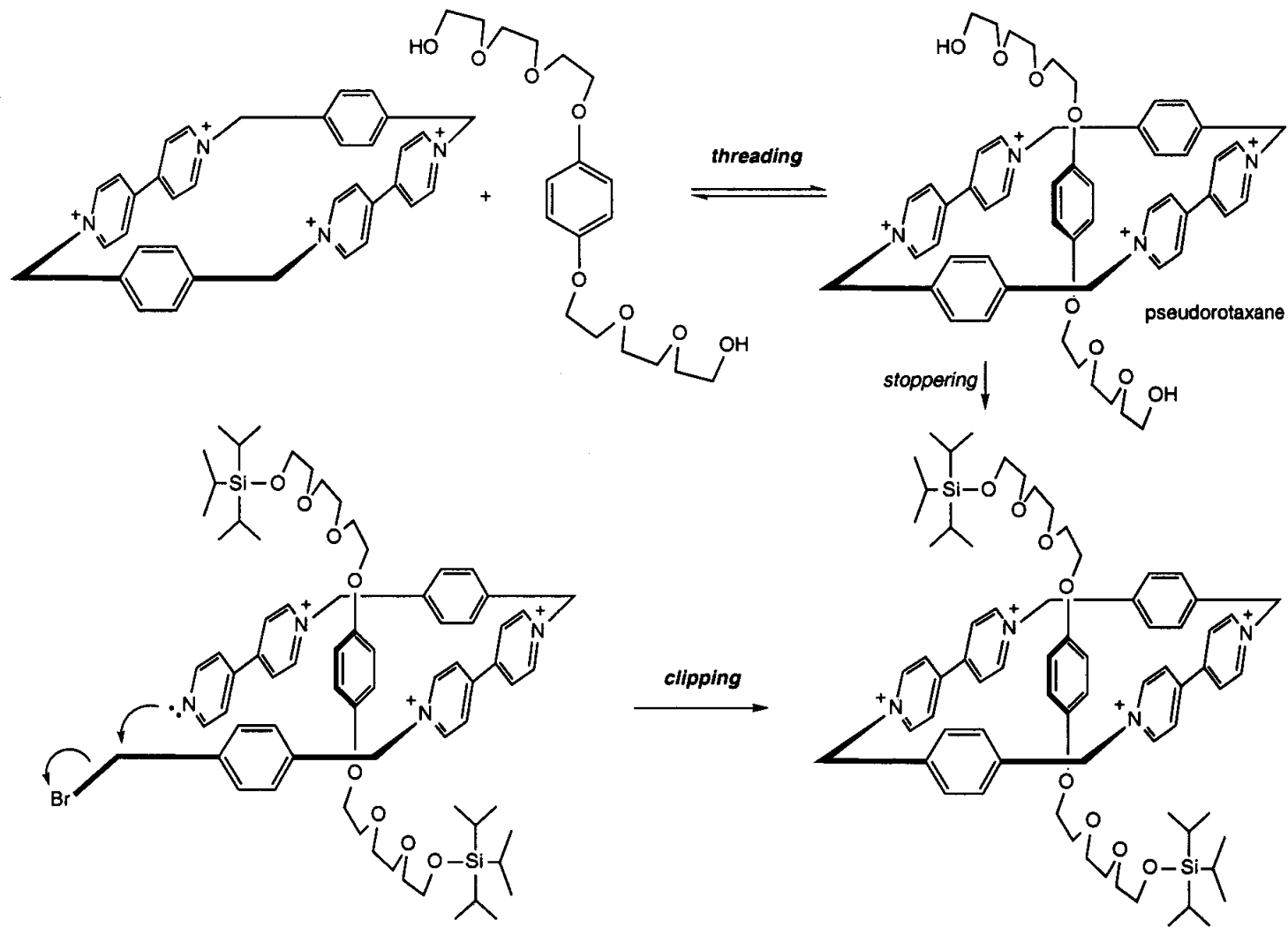






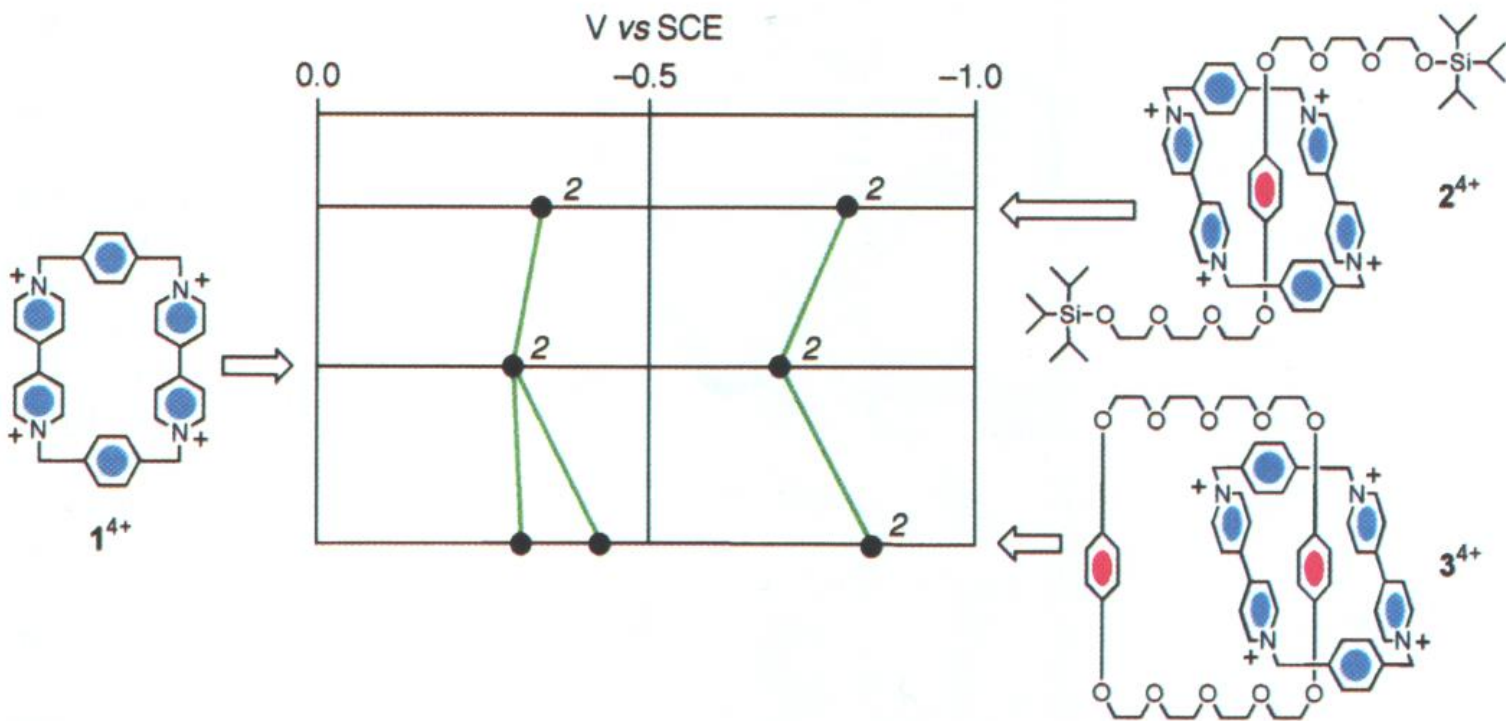


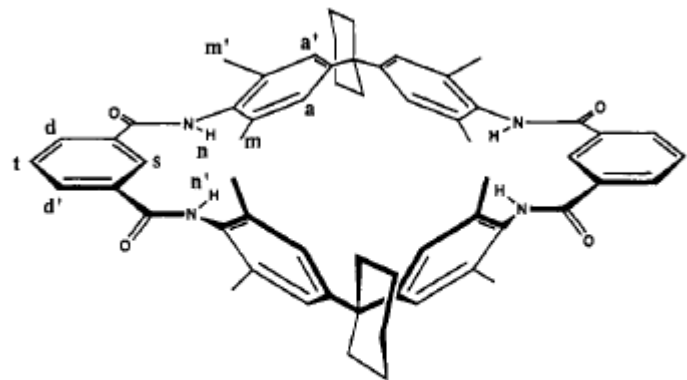




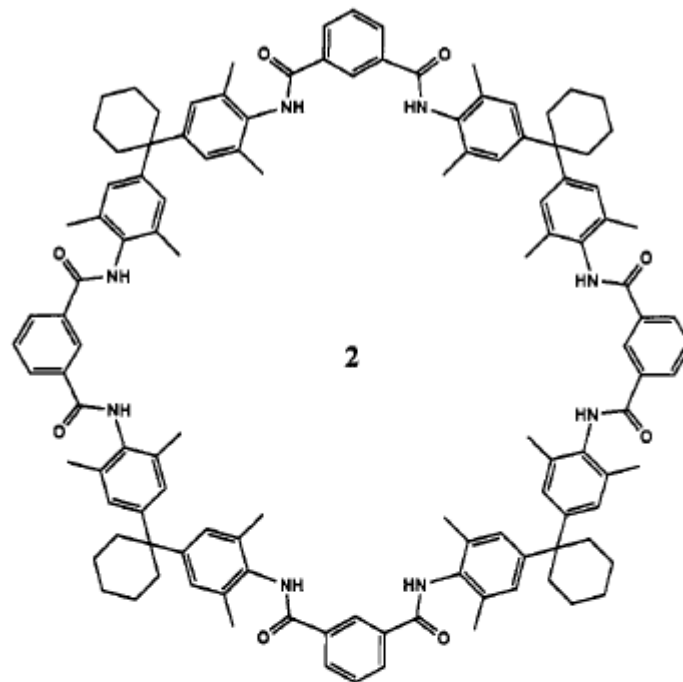
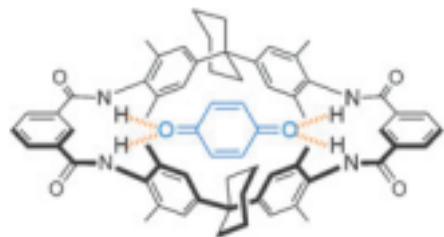
Synthesis of a rotaxane

by two different routes: threading and clipping.



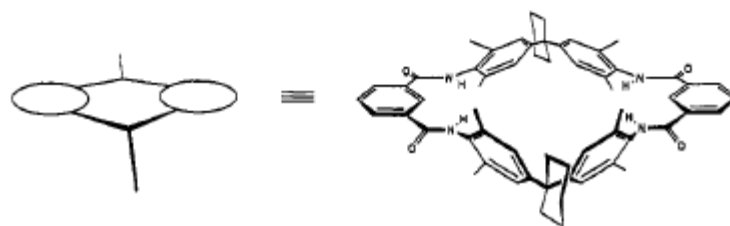
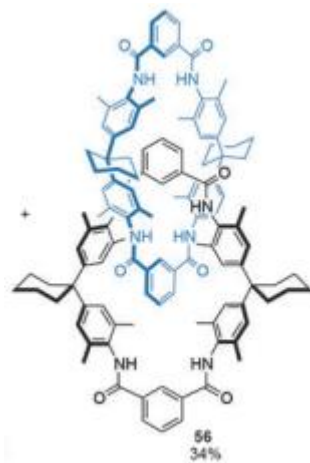
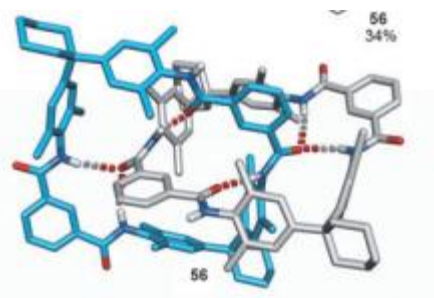
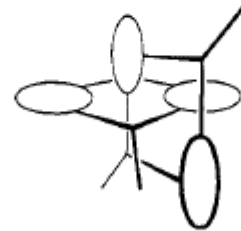


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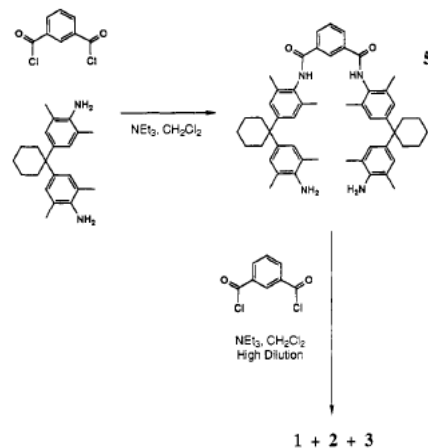


2

3



Scheme II

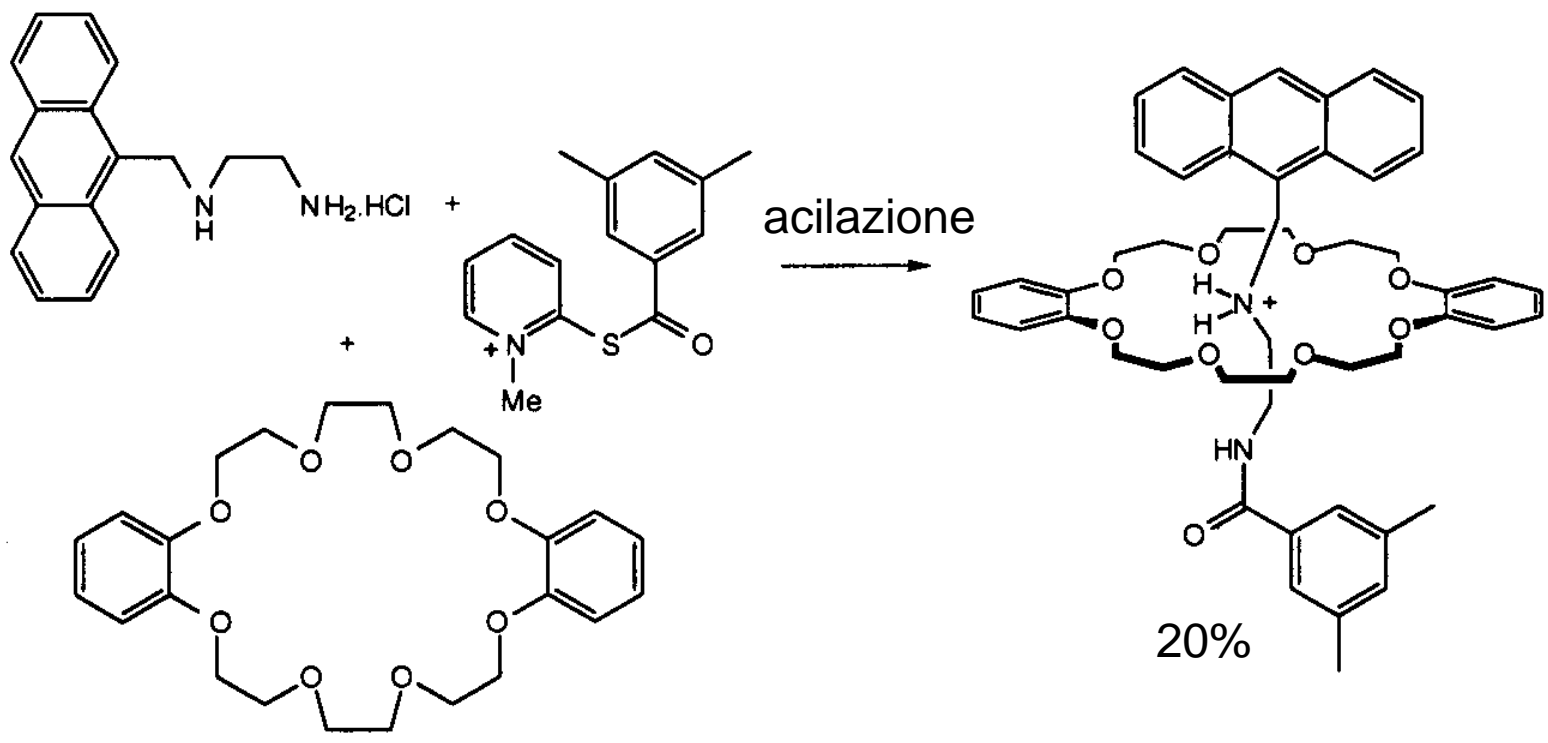


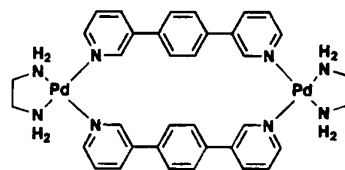
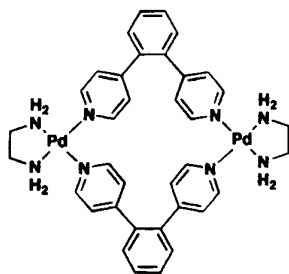
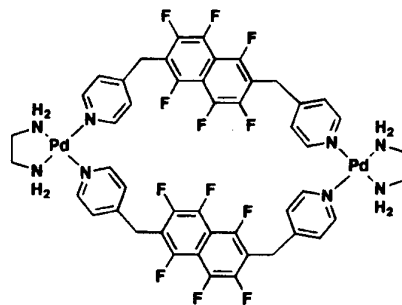
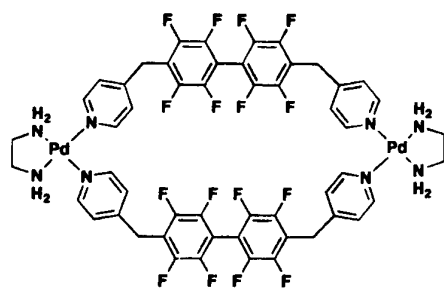
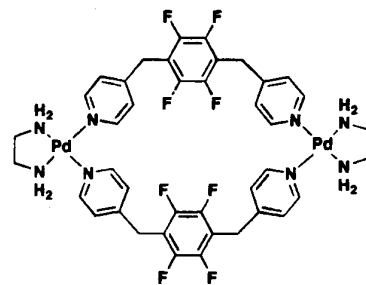
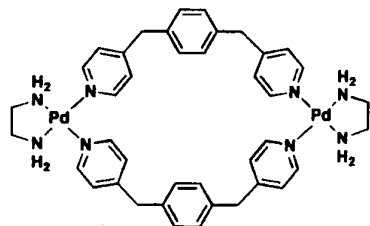
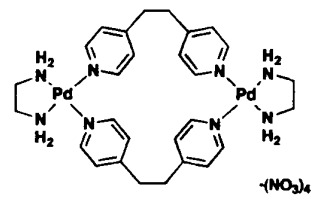
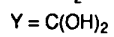
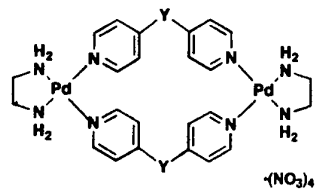
Cyclic Dimer 1, Cyclic Tetramer 2, and Catenane 3 (Scheme II). **5**, 1 g, and 0.4 mL of triethylamine were dissolved in 250 mL of dry dichloromethane and transferred to a dropping funnel. Isophthaloyl dichloride (0.26 g) was similarly dissolved in 250 mL of dry dichloromethane and transferred to an 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^+); $\text{C}_{120}\text{H}_{128}\text{N}_8\text{O}_8$ requires $M^+ = 1808$.

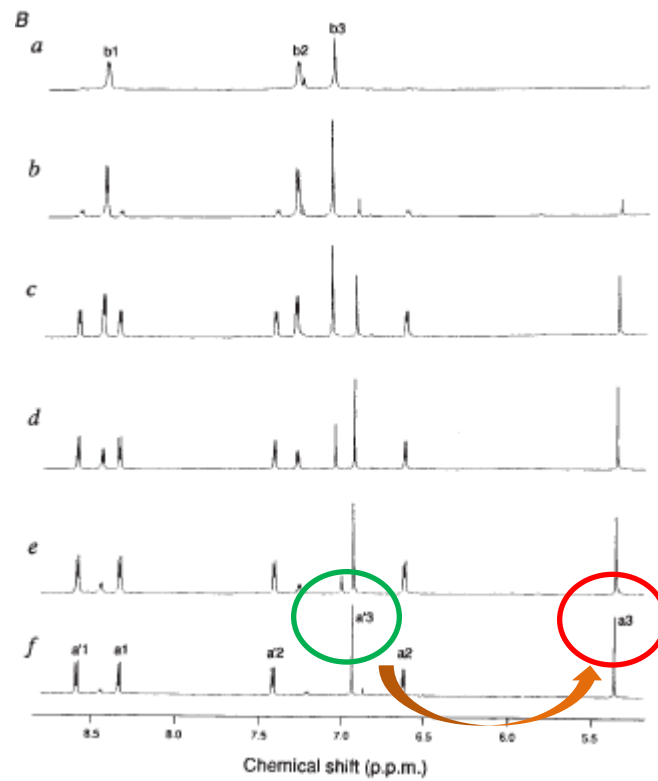
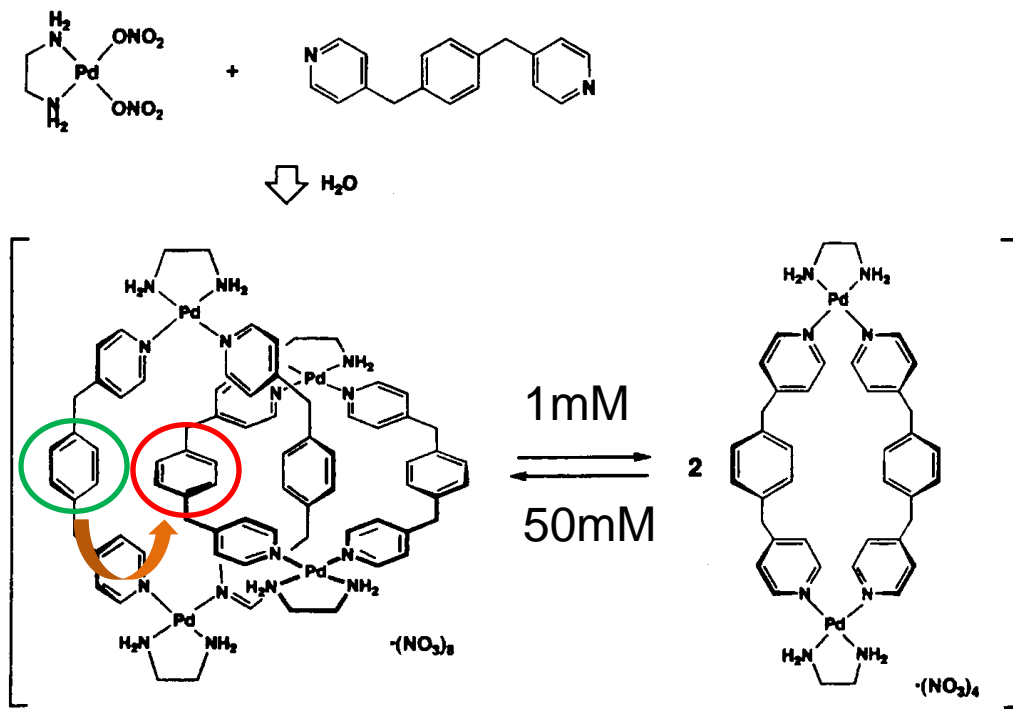
Fraction B was obtained as a white powder (600 mg, 51%). Spectroscopic data were as for the cyclic dimer **1** from Scheme I.

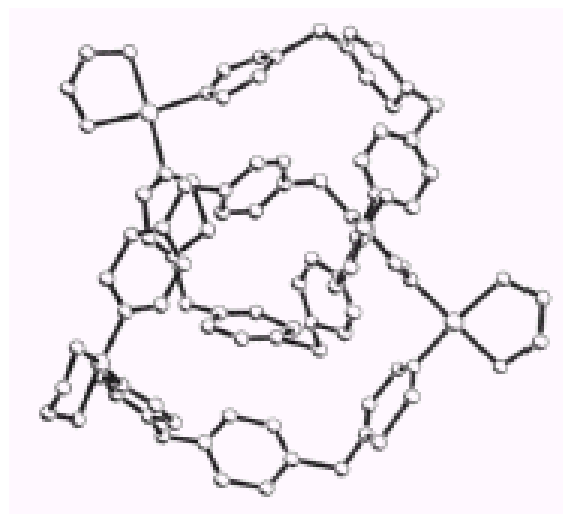
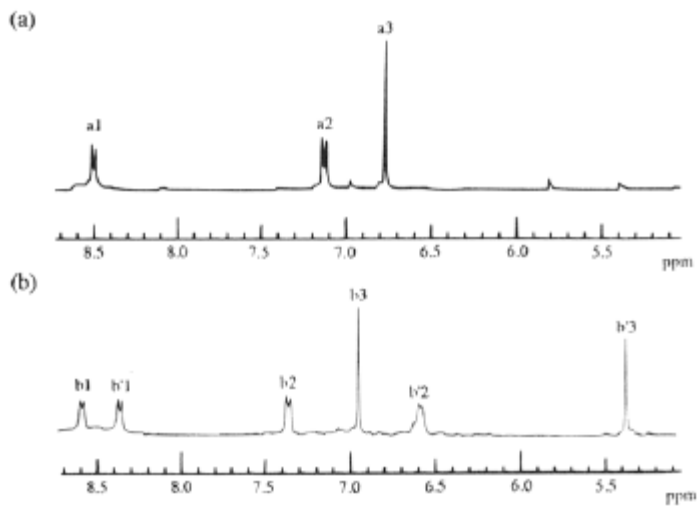
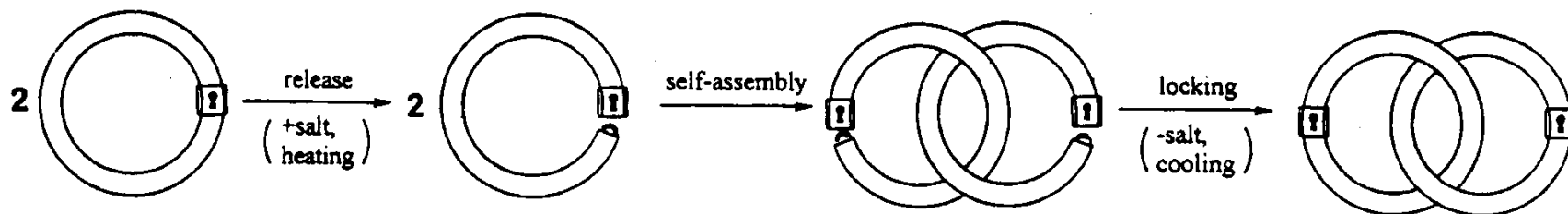
Fraction C was obtained as a white powder (50 mg, 5%). NMR ($\text{CDCl}_3/\text{CD}_3\text{OD}$) δ 8.41 (4 H, s), 7.98 (8 H, d), 7.43 (4 H, t), 6.96 (16 H, s), 2.21 (16 H, br), 2.10 (48 H, s), 1.52 (24 H, br). m/z 1806 (MH^+); $\text{C}_{120}\text{H}_{128}\text{N}_8\text{O}_8$ requires $M^+ = 1808$.



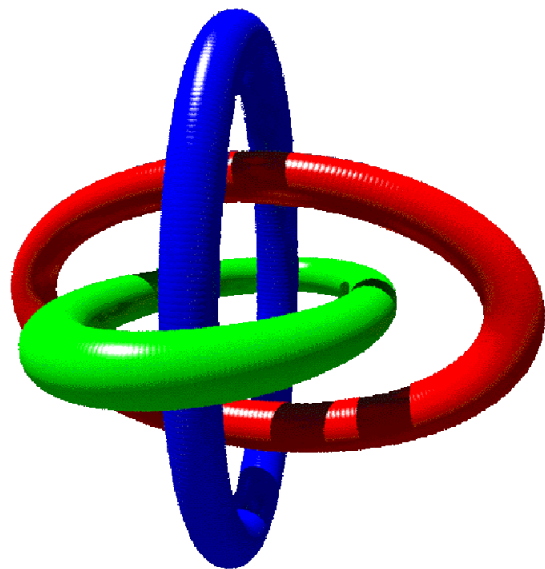


Catenani





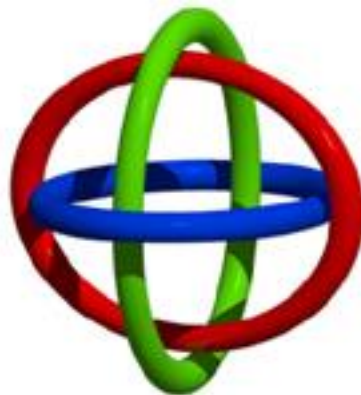
Borromean Rings



three identical rings. Each ring is inside a second one and outside the third one. No catenation.

4 connections: *endo/eso/endo/eso*

Nodo Borromeo



Endo-Tridentate

+

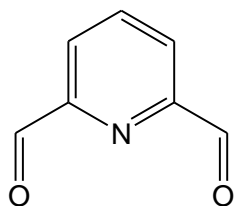


Transition Metals

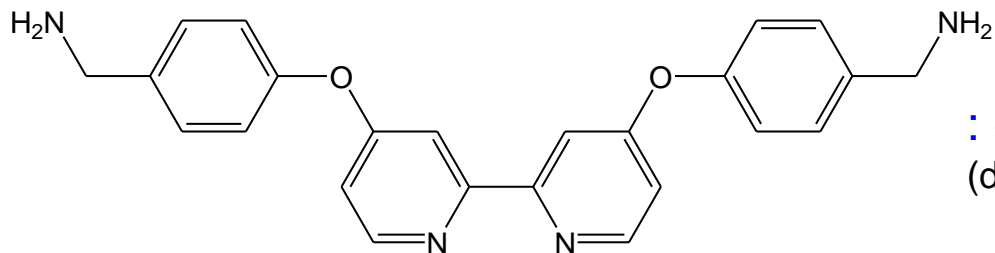
+



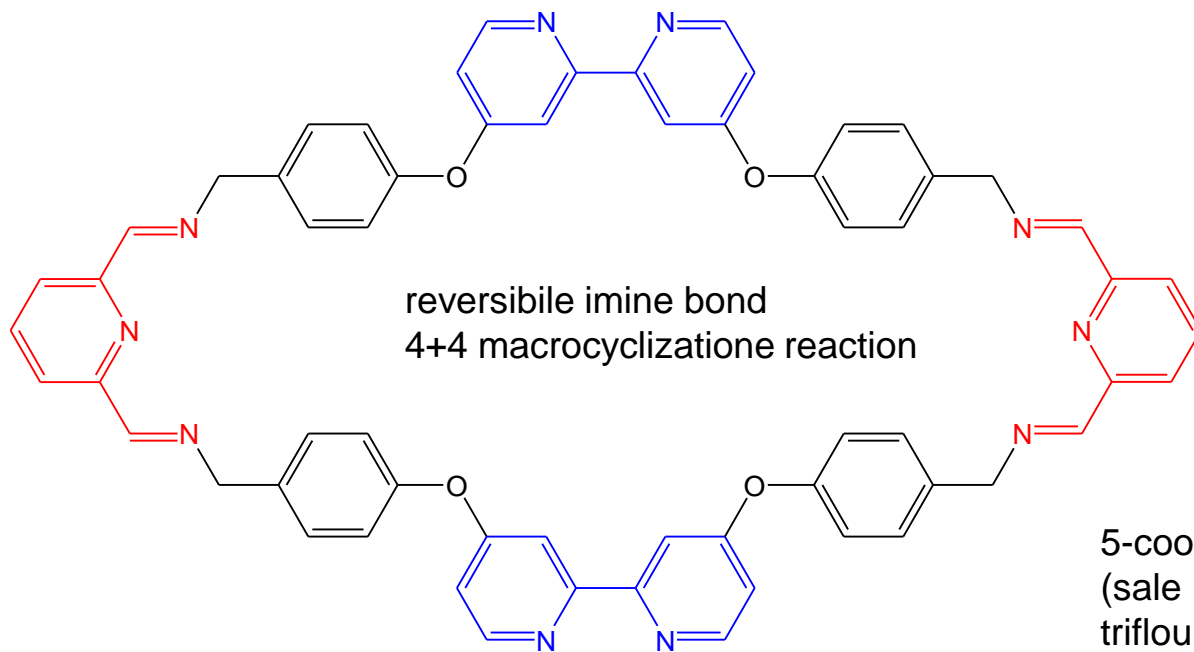
Exo-Bidentate



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

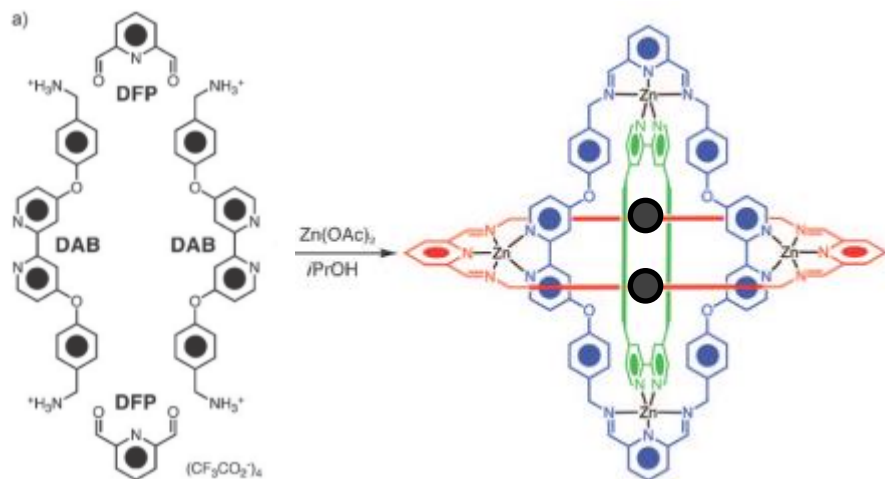


: **exo-bidentate**
(diamminobipyridiyl ligand DAB)



reversible imine bond
4+4 macrocyclization reaction

5-coordinated Zn(II)
(two
trifluoroacetato)



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

Carica: 12⁺

Controioni: 12TFA⁻

endo-tridentate

2,6 diformilpiridine (DFP)

exo-bidentate

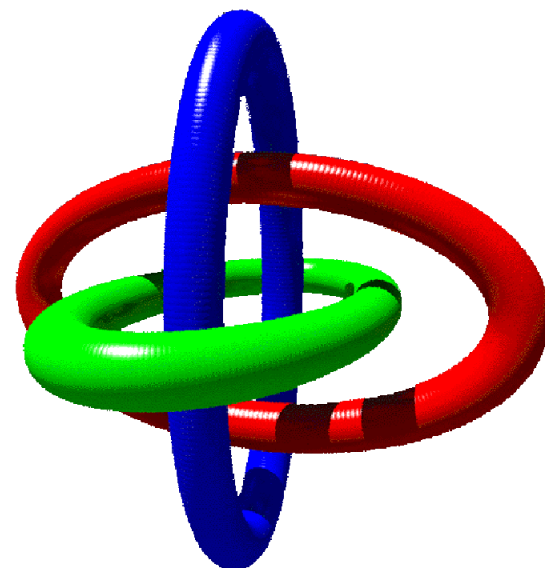
diamminobipiridyl ligand (DAB)

5-coordinated Zn(II)

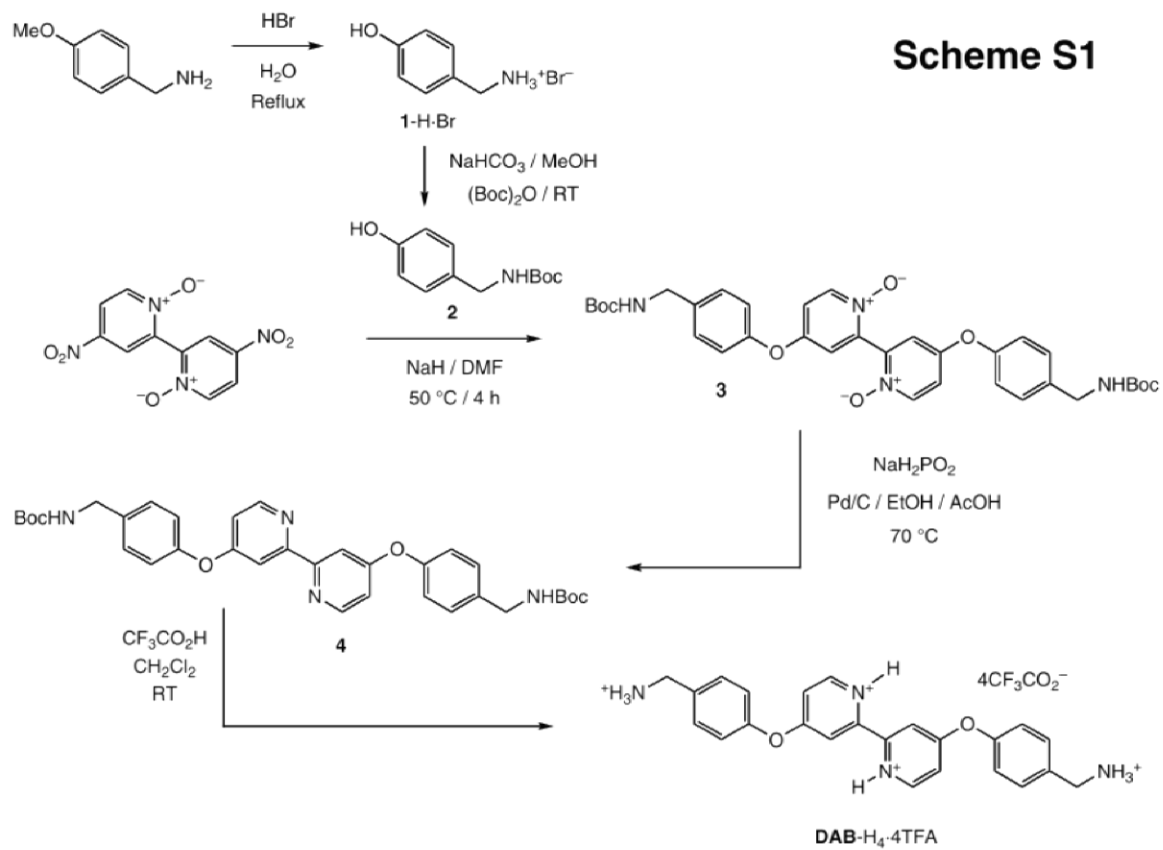
(sale triflouroacetato)

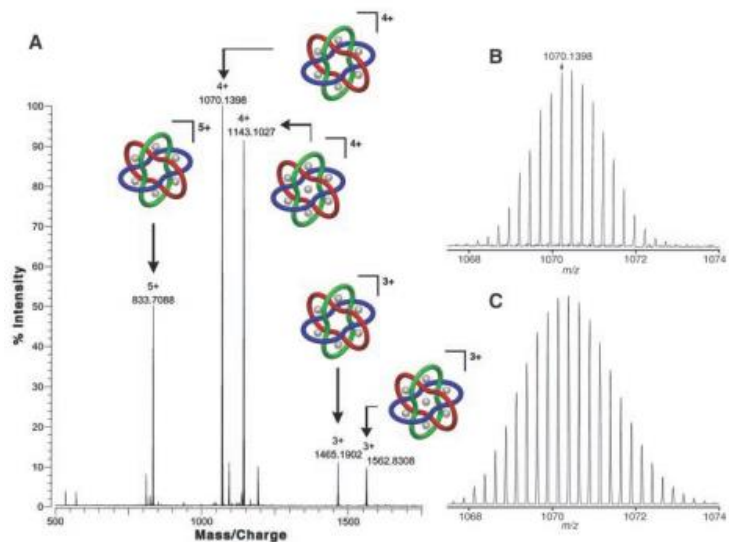
reversibile imine formation

reversibile coordination



Scheme S1





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

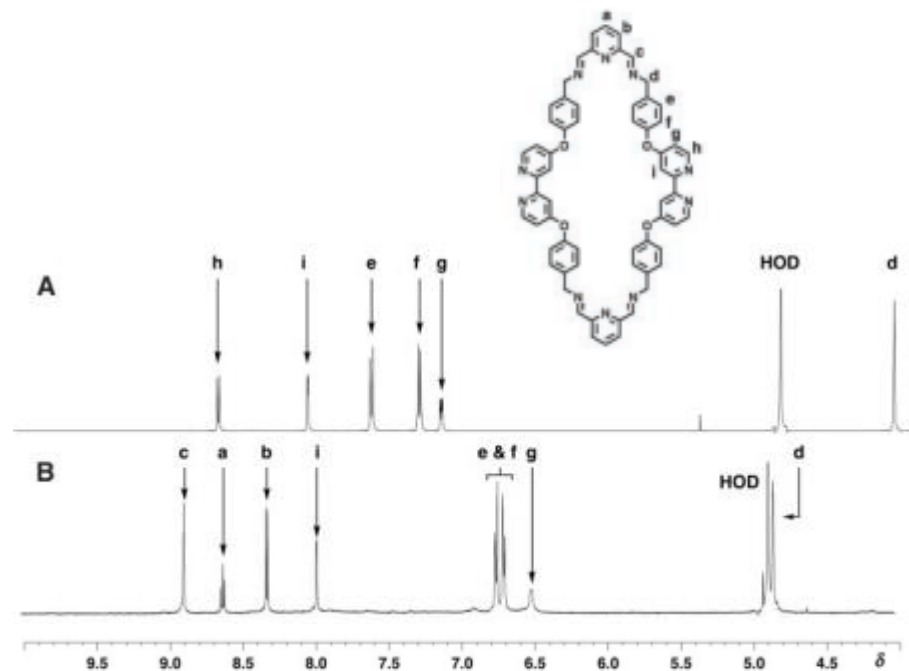
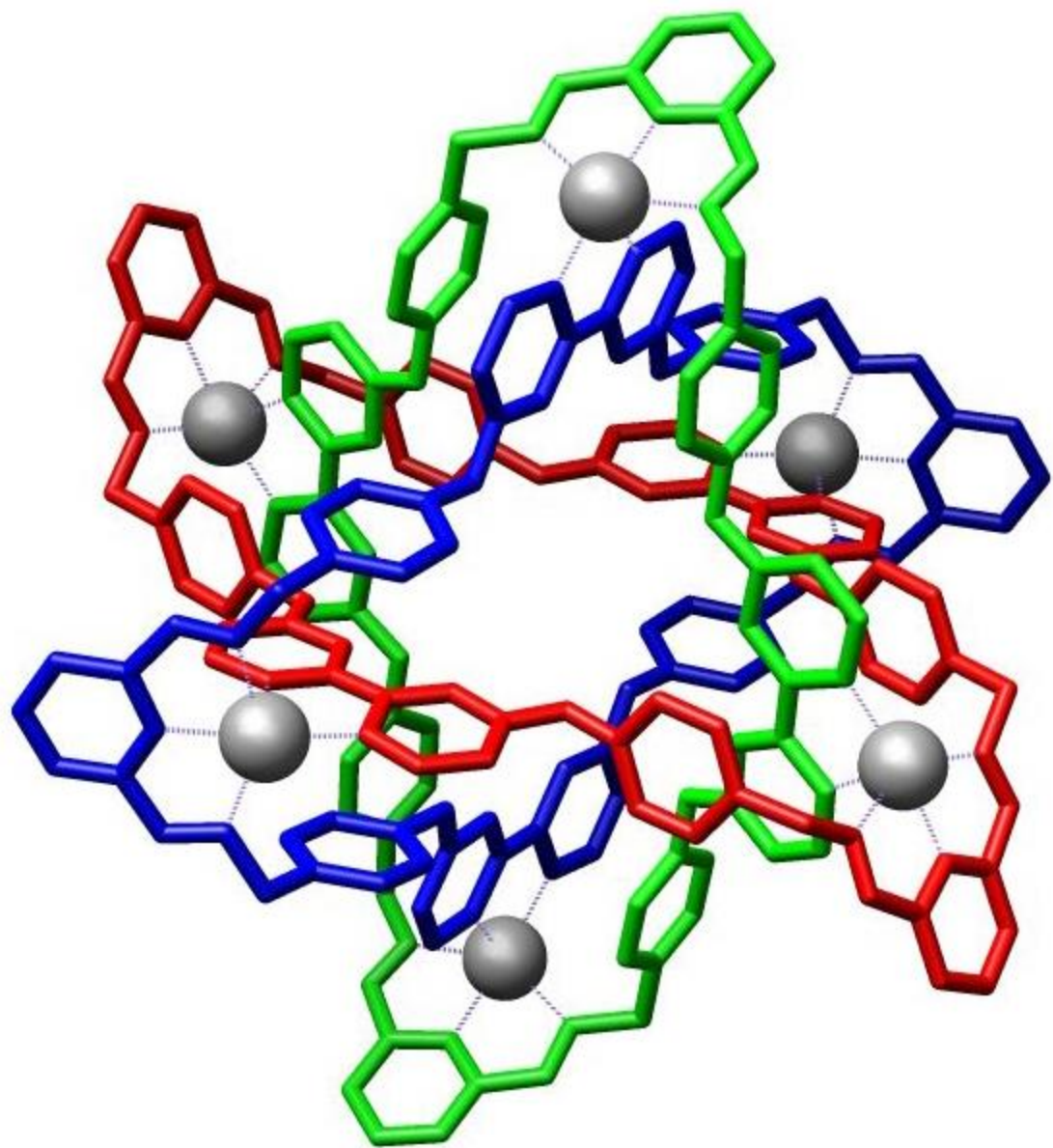
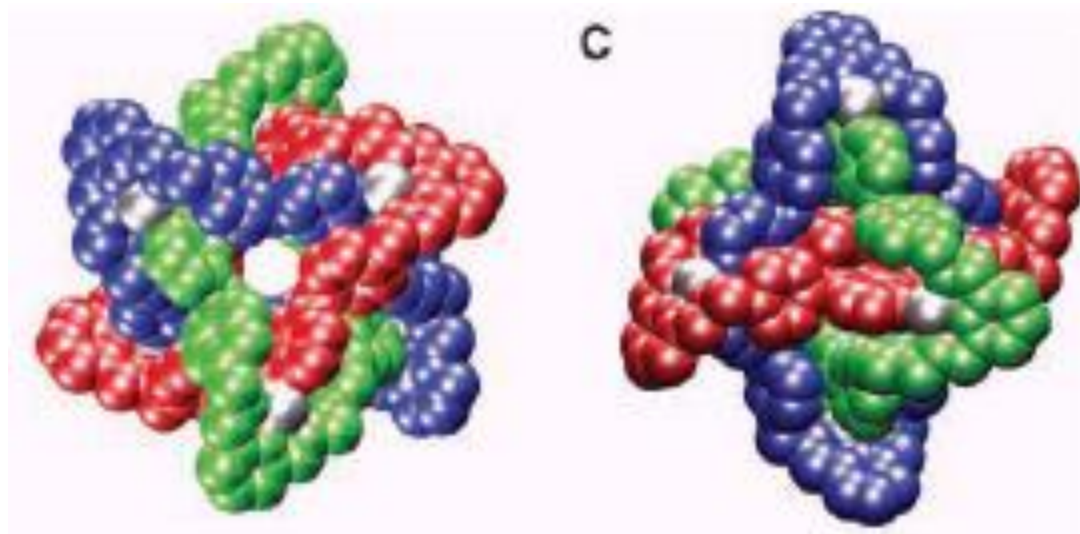
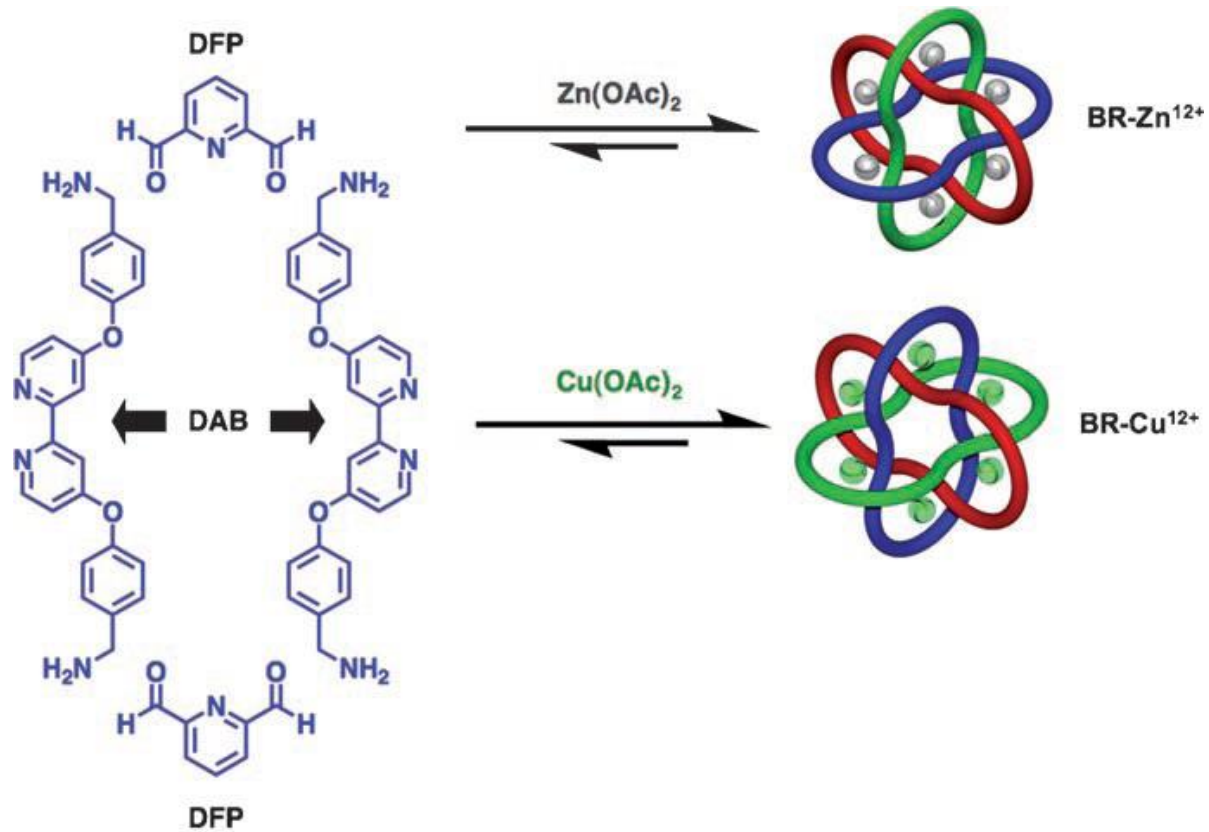
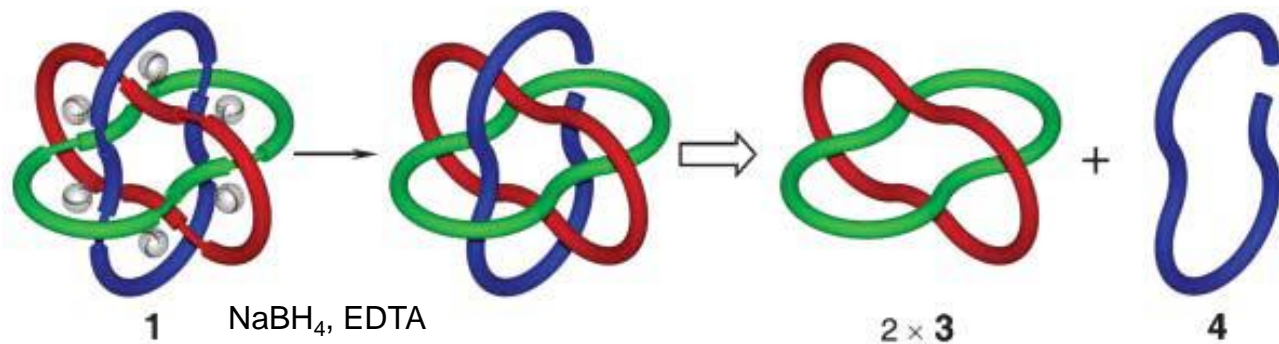


Fig. 2. The ^1H NMR spectra (CD_3OD , 298 K) of (A) the *exo*-bidentate ligand-containing starting material $\text{DAB}\cdot\text{H}_4\cdot 4\text{TFA}$ (500 MHz), (B) the molecular Borromean rings $\text{BR}\cdot 12\text{TFA}$ (600 MHz)

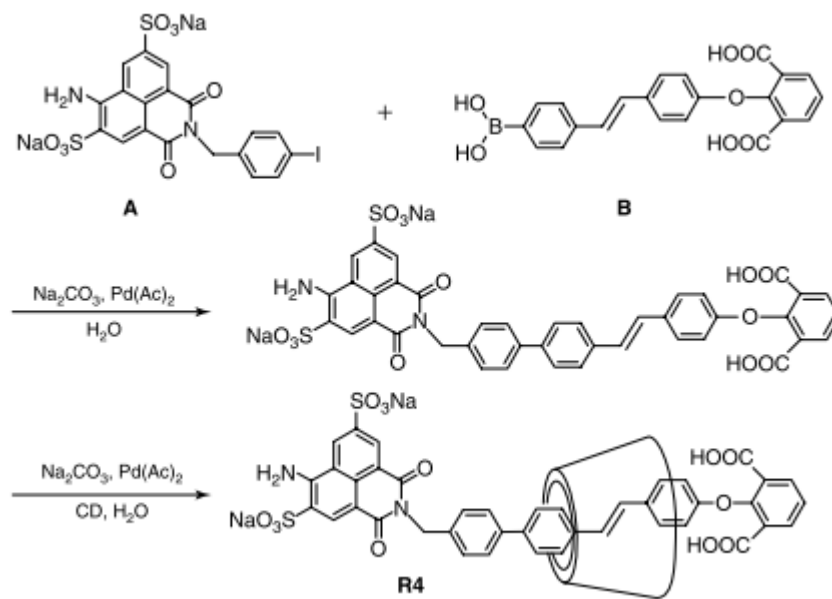




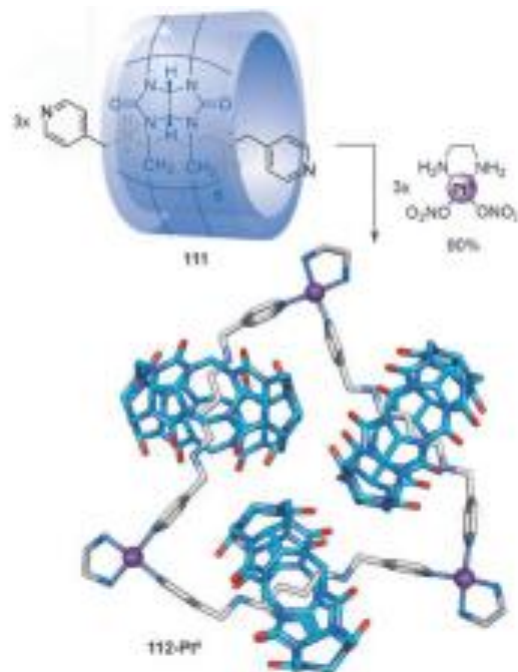
6 Zn(II) bound to one bipy and one dimminopyridine (in the solid state 6th position occupied by trifluoroacetate (TFA); S_6 symmetry π - π stacking each bipy between 2 phenols 3.61-3.66 Å; 12⁺



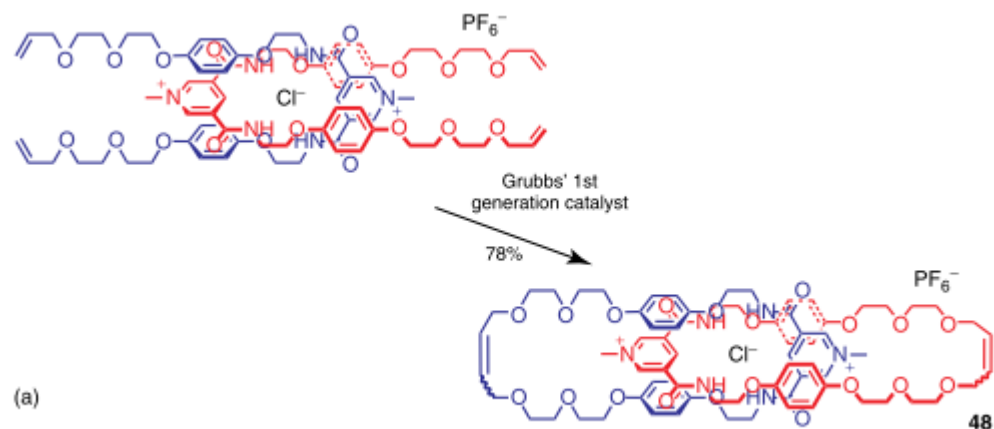
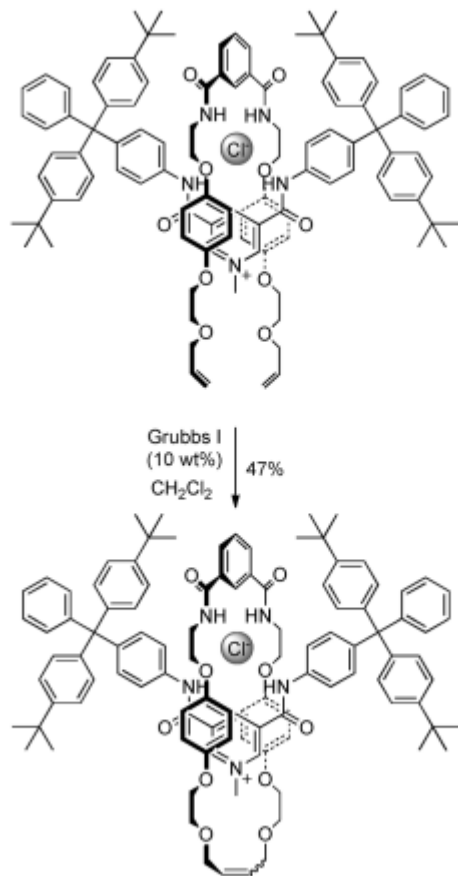
Hydrophobic effect



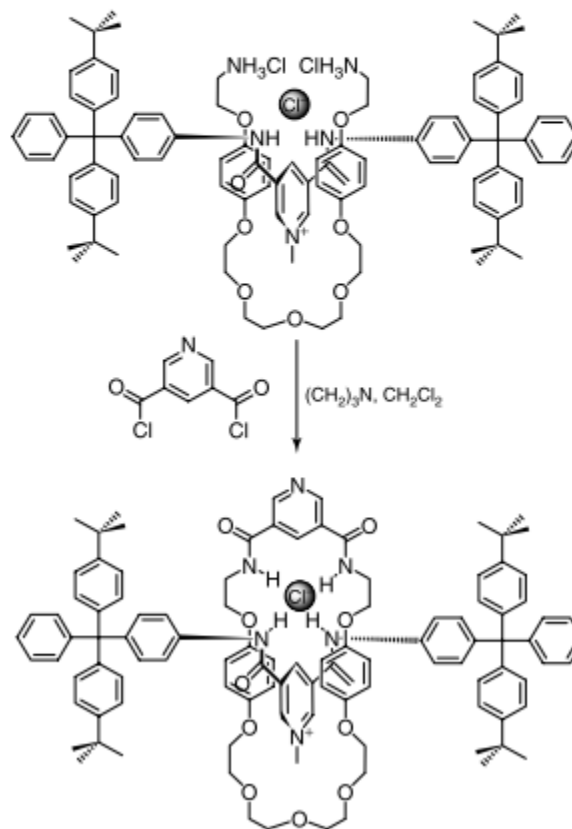
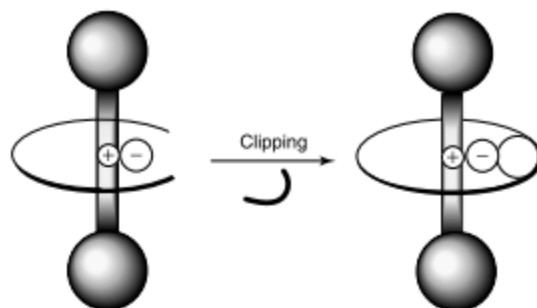
Hydrophobic effect



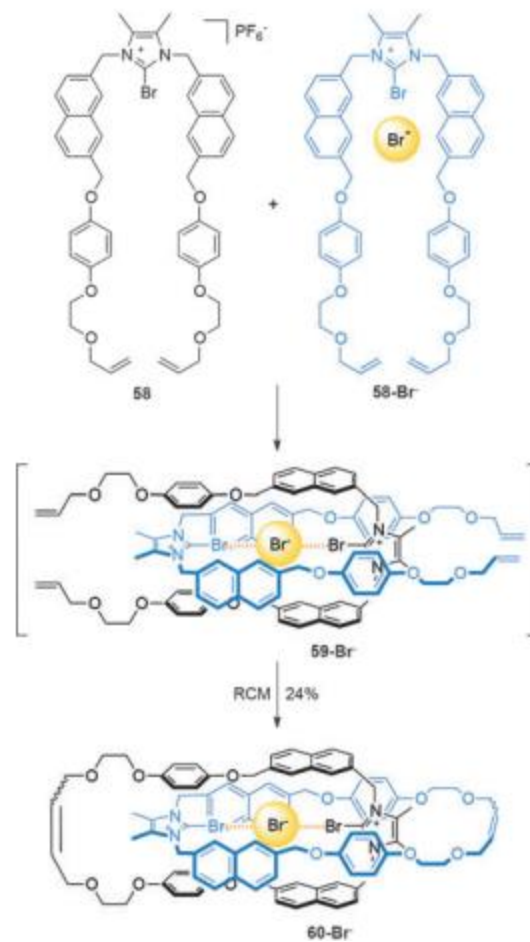
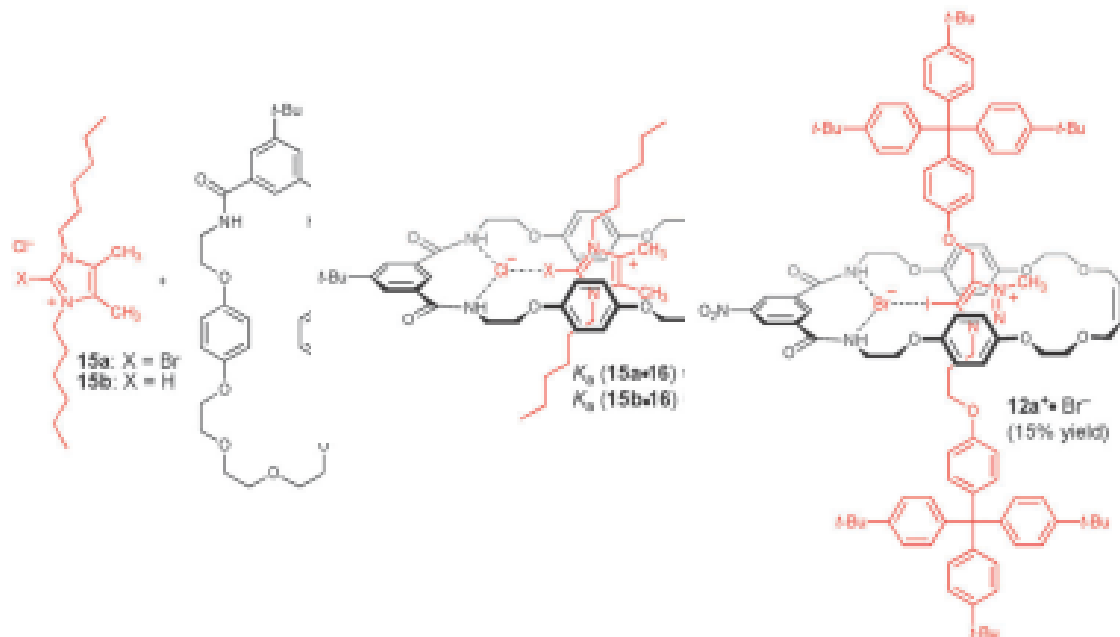
Anion templating

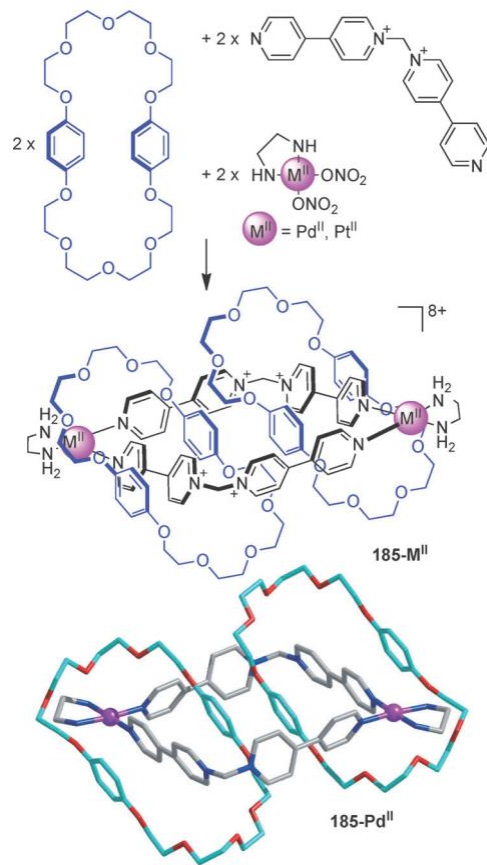


Anion templating



Halogen bond templating





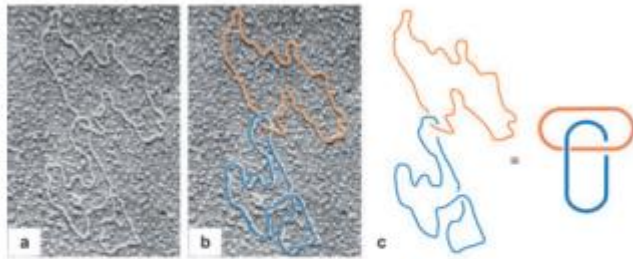


Figure 4. a) Electron micrograph of circular DNA revealing a catenane topology. b,c) Highlighting the two component rings of the DNA catenane as a Hopf link. Modified from Ref. [23] with permission.

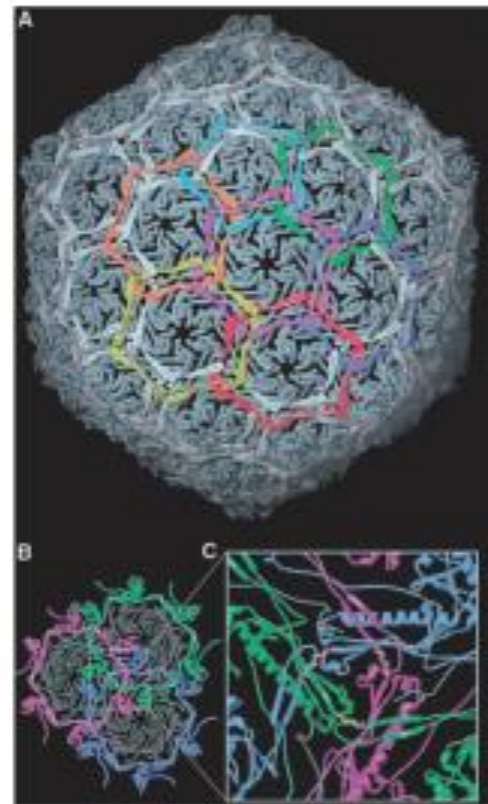


Figure 5. The "chainmail" arrangement of proteins found in bacteriophage HK97's capsid (colored sections highlight the individual protein rings). a) The repeating pattern of interlocking proteins which constitute the spherical capsid. b) A cross-section of the capsid in which three protein rings interlock 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.

Nodi Molecolari e Links

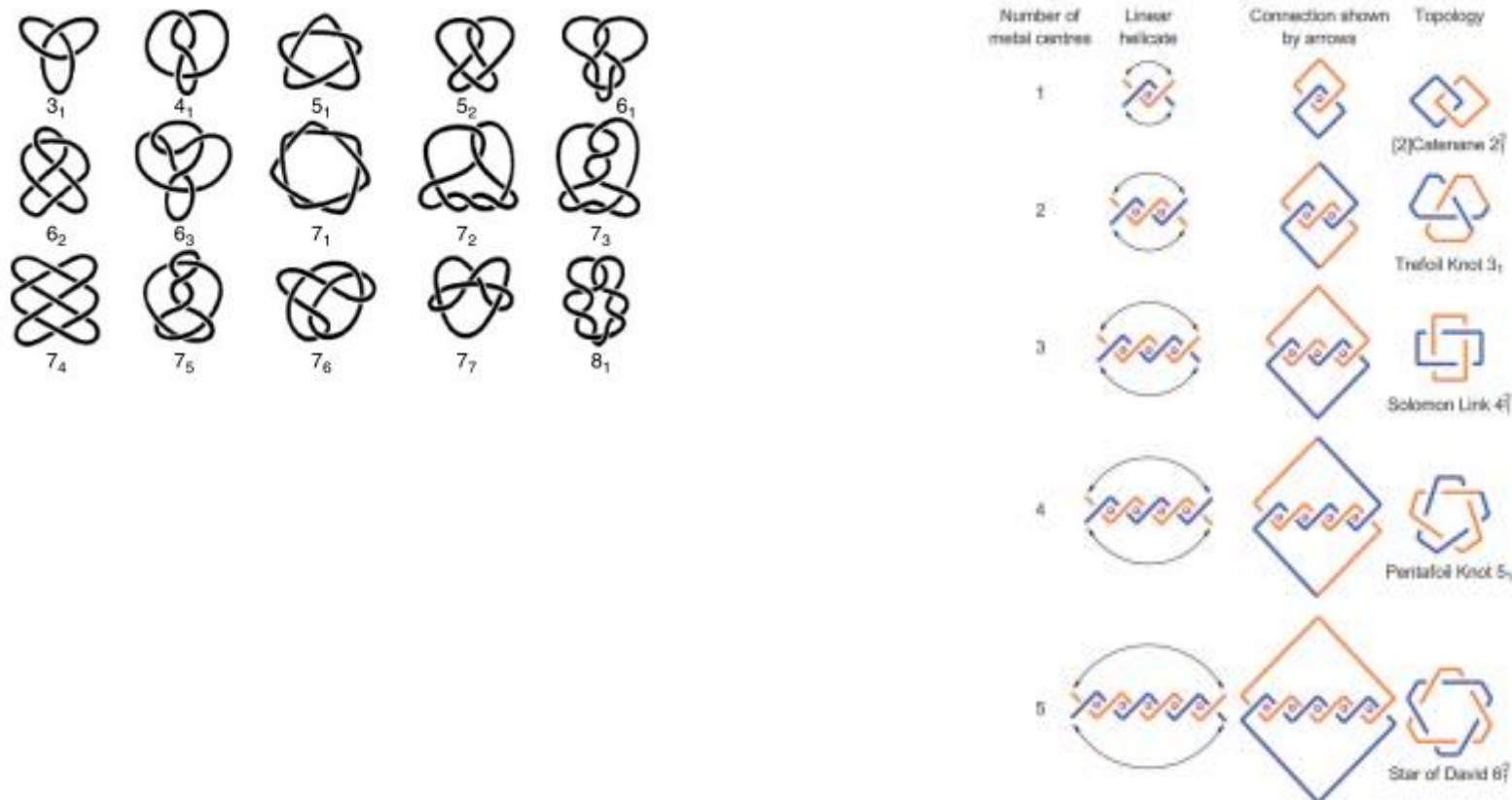


Fig. 3 The linear helicate strategy to interlocked molecules introduced by Sauvage.⁴⁸ To date the first three entries of this table have been realised experimentally using this strategy, generating catenanes,⁴ trefoil knots³⁸ and doubly-interlocked [2]catenanes (Solomon links)⁴⁷ using one, two and three 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.⁴⁸

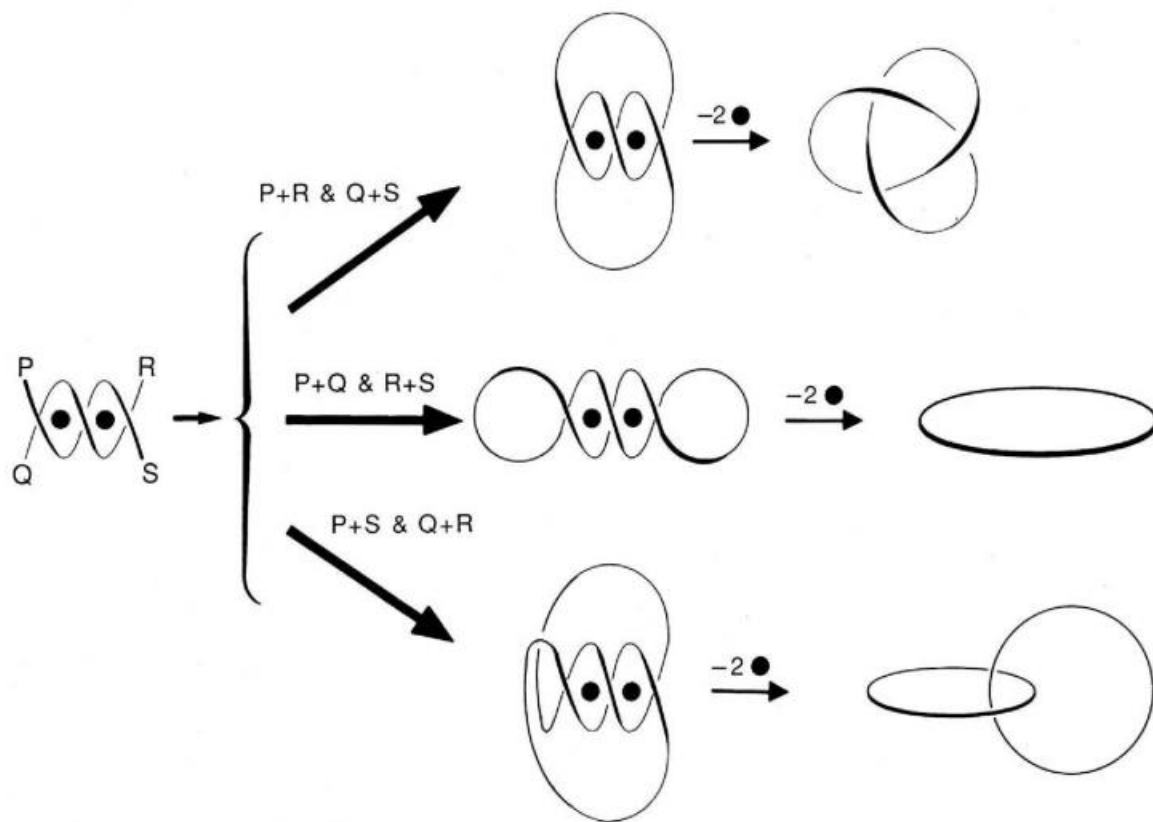


Figure 23. A guide for demonstrating the synthesis of topologically different molecules from the precursor to the trefoil knot.

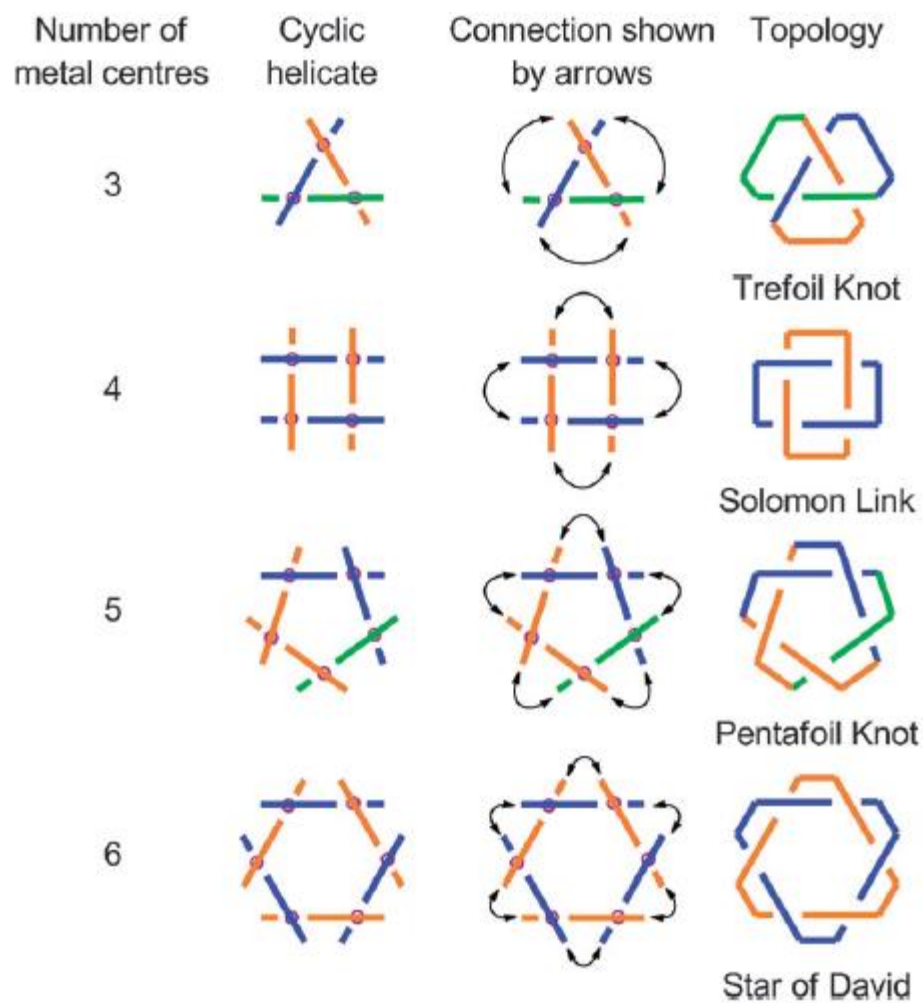


Fig. 5 The potential of circular metal helicates to form molecular knots and links by connecting adjacent end-groups. To date only a pentafoil knot has been prepared through this strategy.⁷³

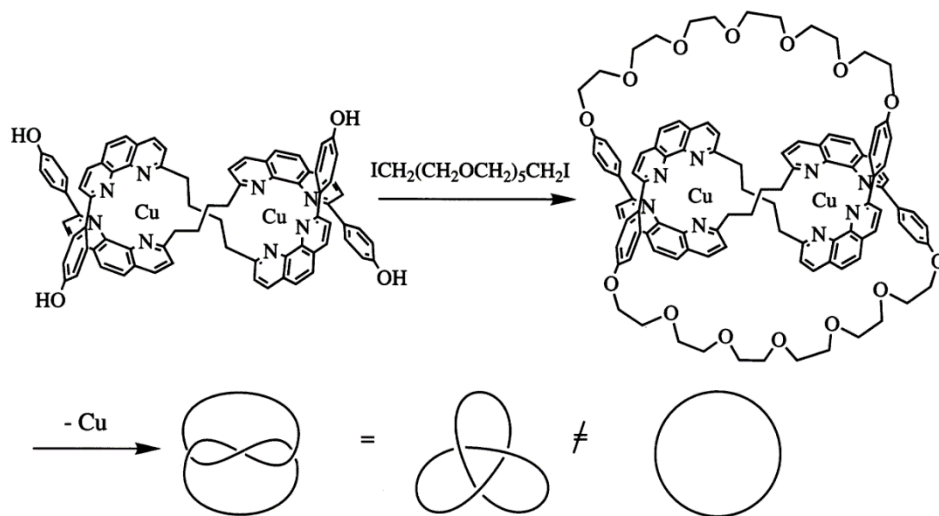
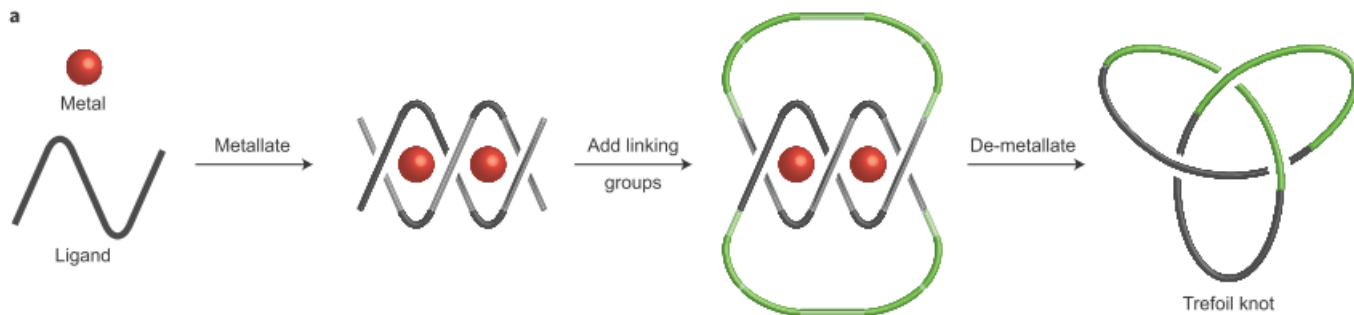
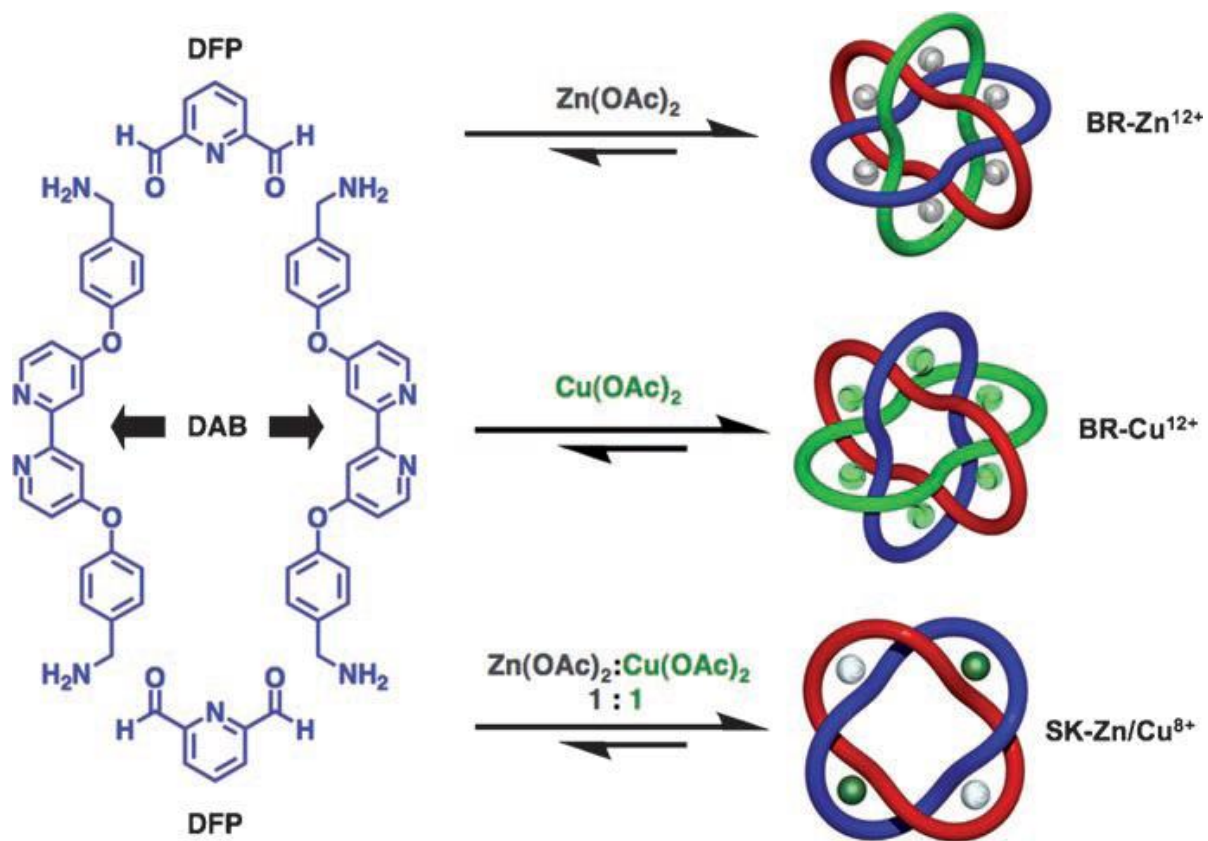
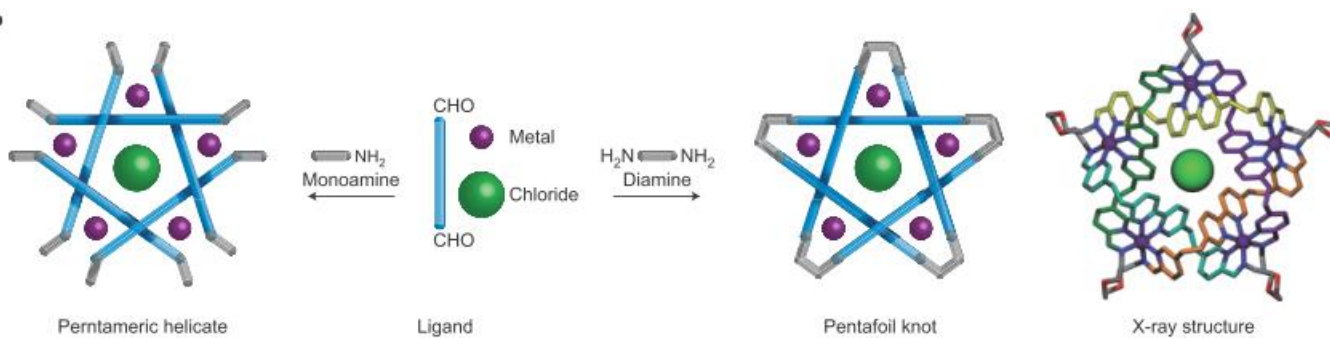
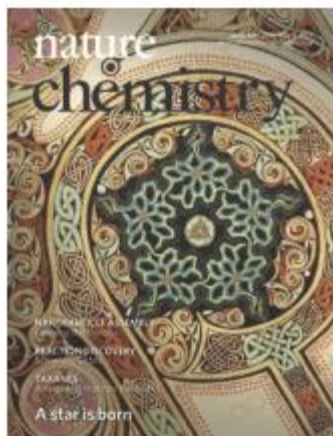


Fig. 8. Synthesis of the first trefoil knot using a two-anchor helical template.



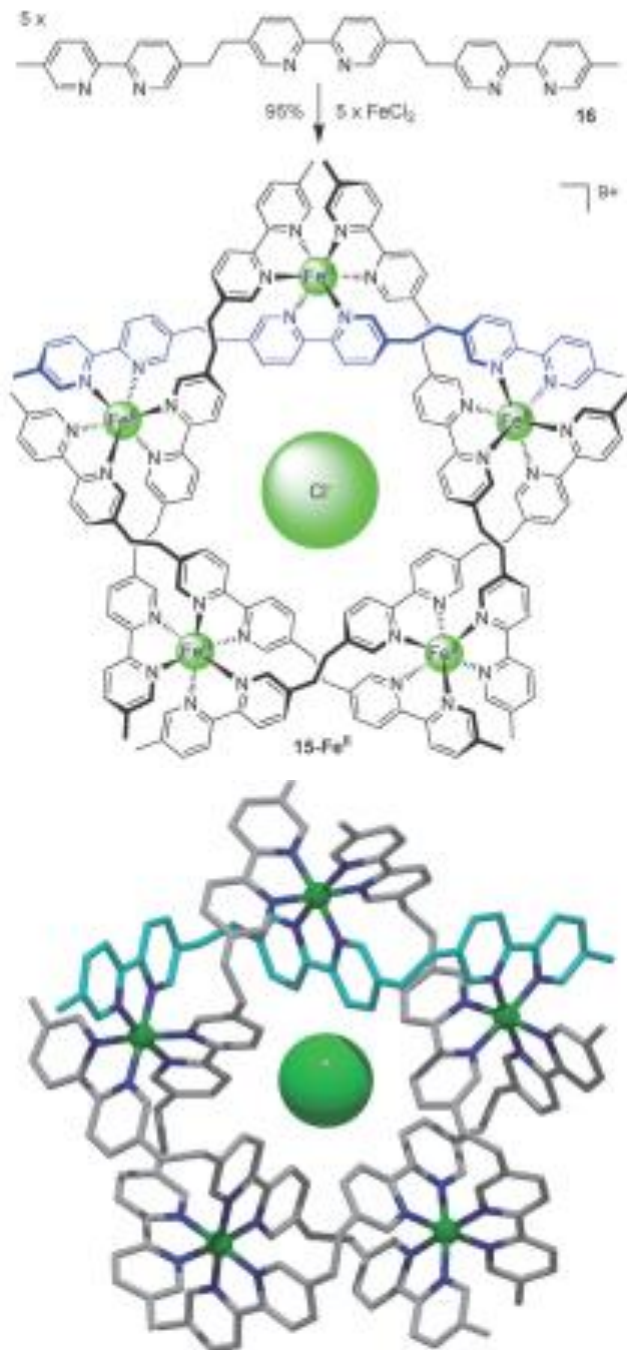
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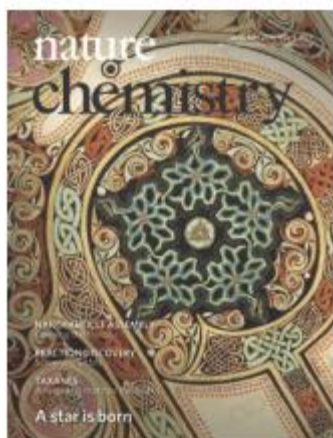




COVER IMAGE

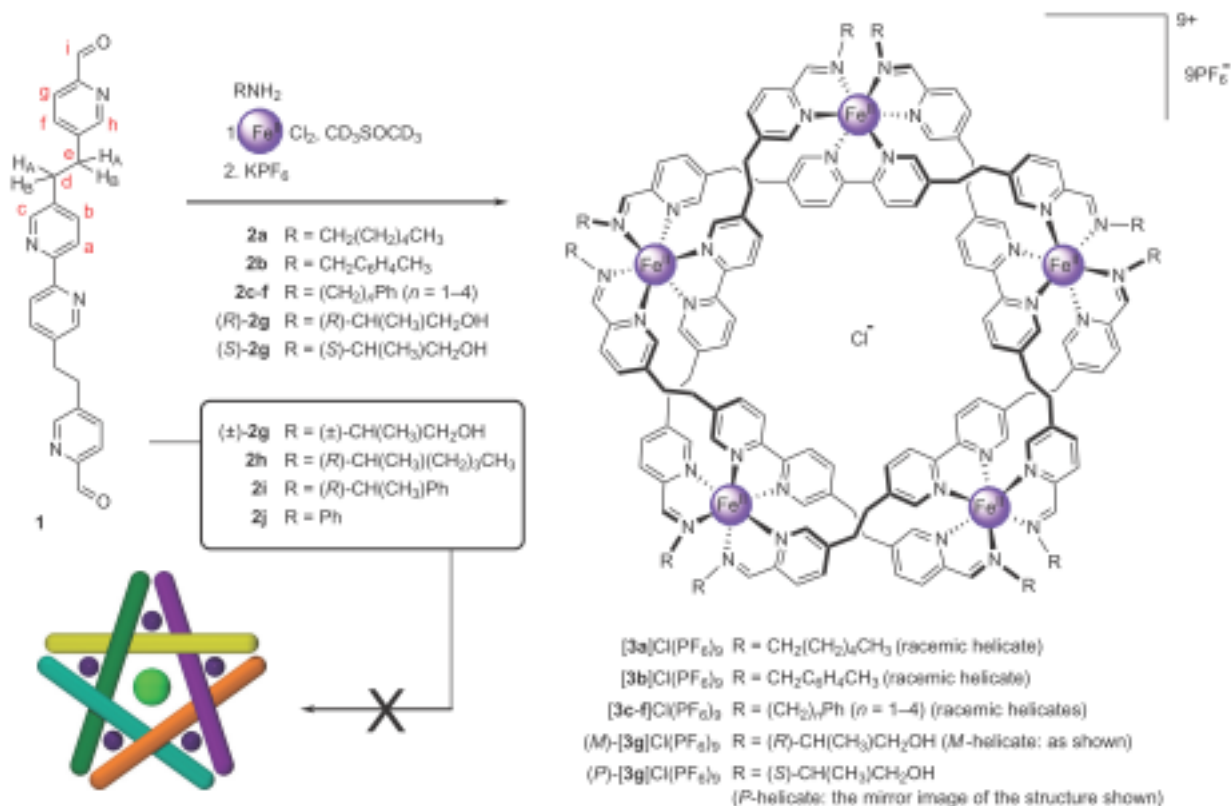
The cover image features the interlaced 'rho' character from Matthew 1:18 in the Lindisfarne Gospels as a backdrop for the X-ray crystal structure of the most complex non-DNA molecular knot synthesized so far. A team led by David Leigh prepared the 160-atom long pentafoil knot in a one-step reaction 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

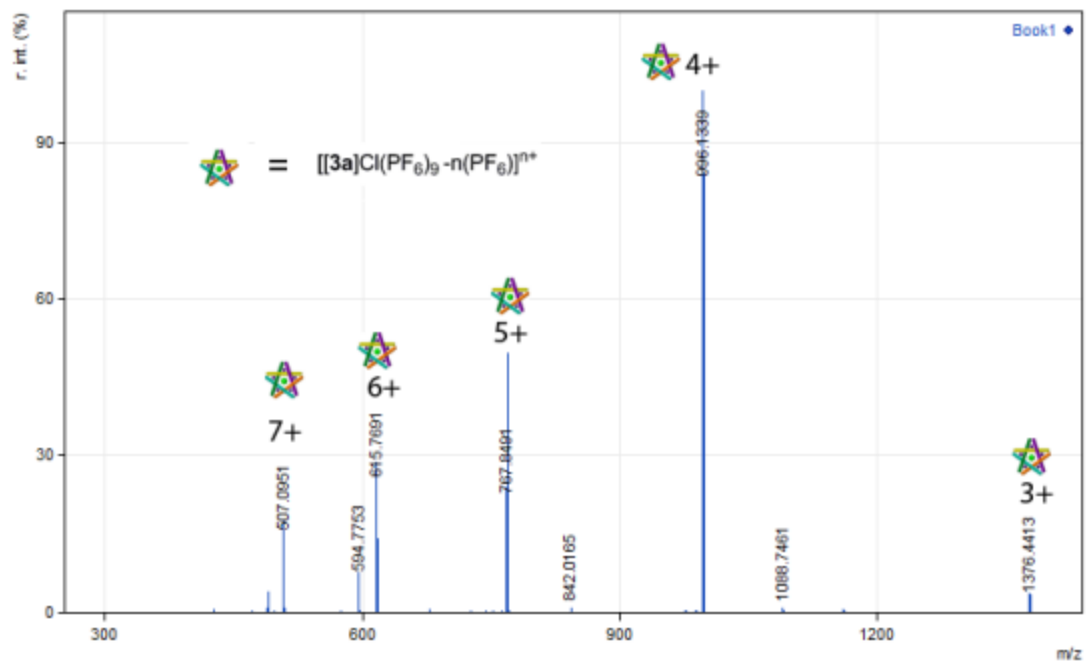


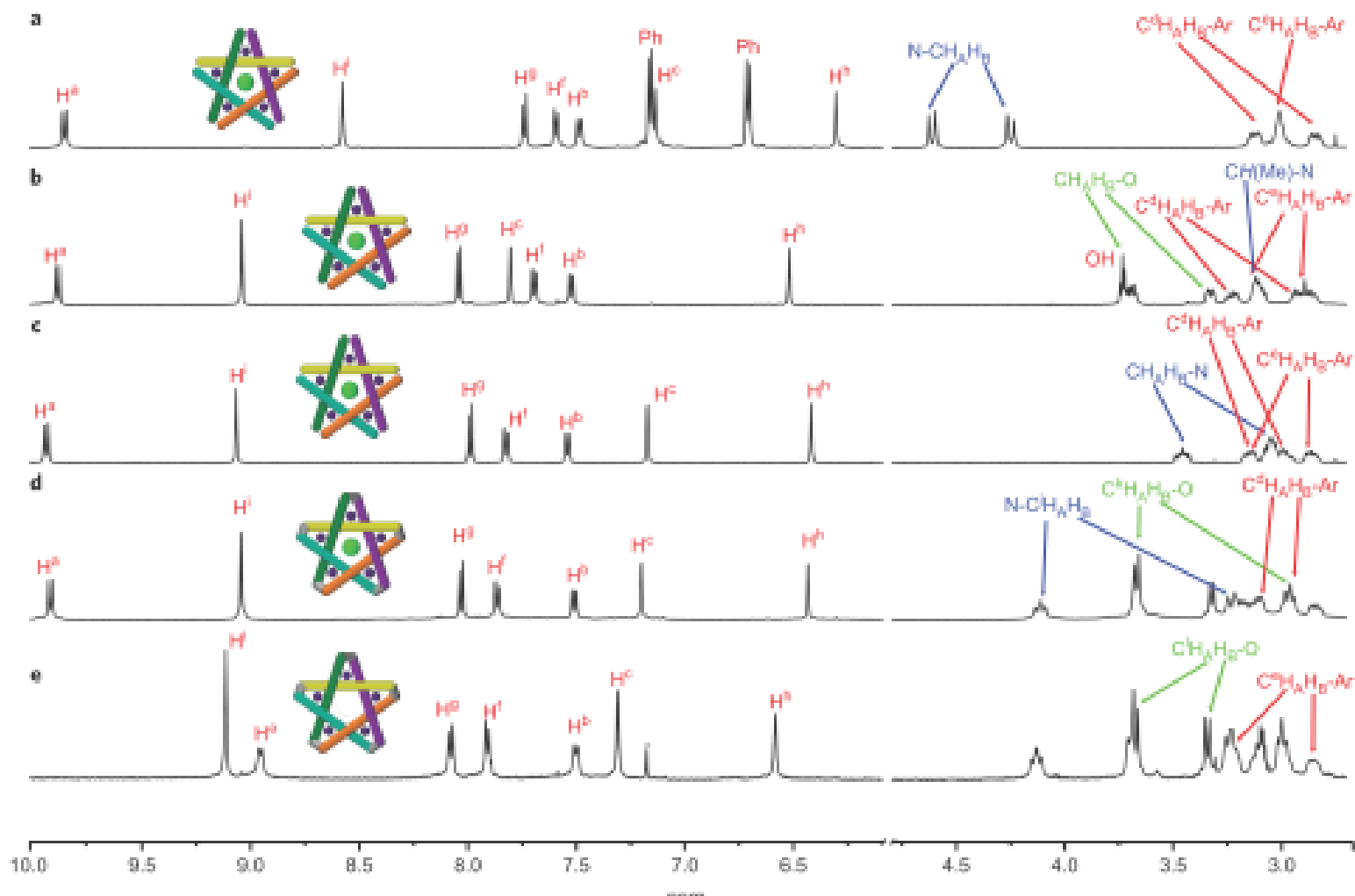
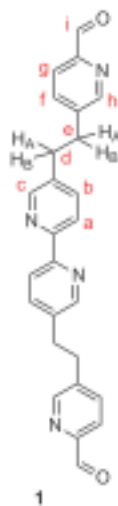


COVER IMAGE

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







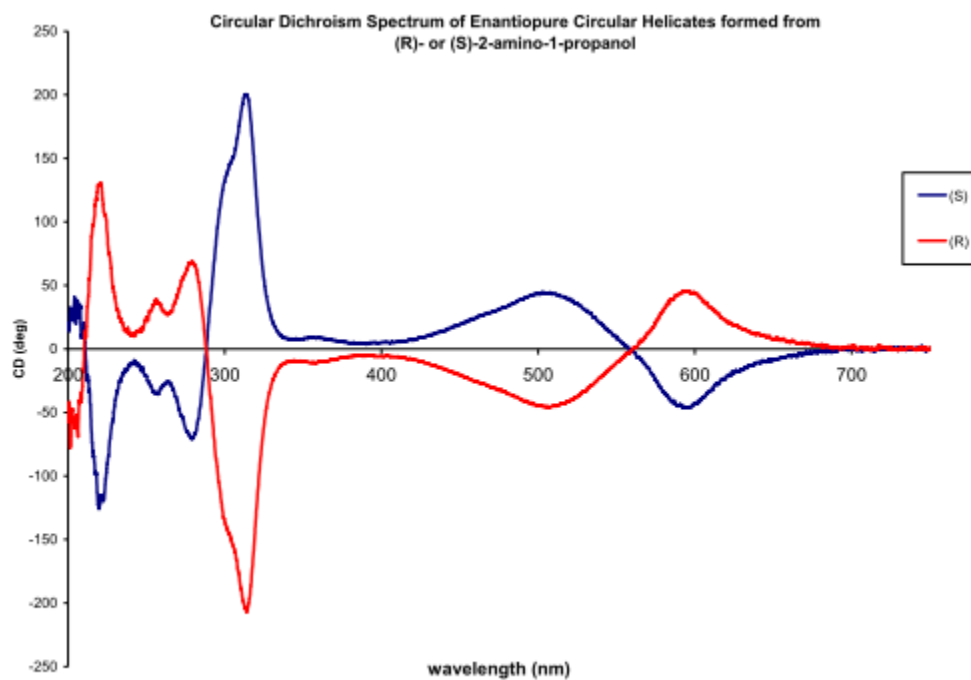
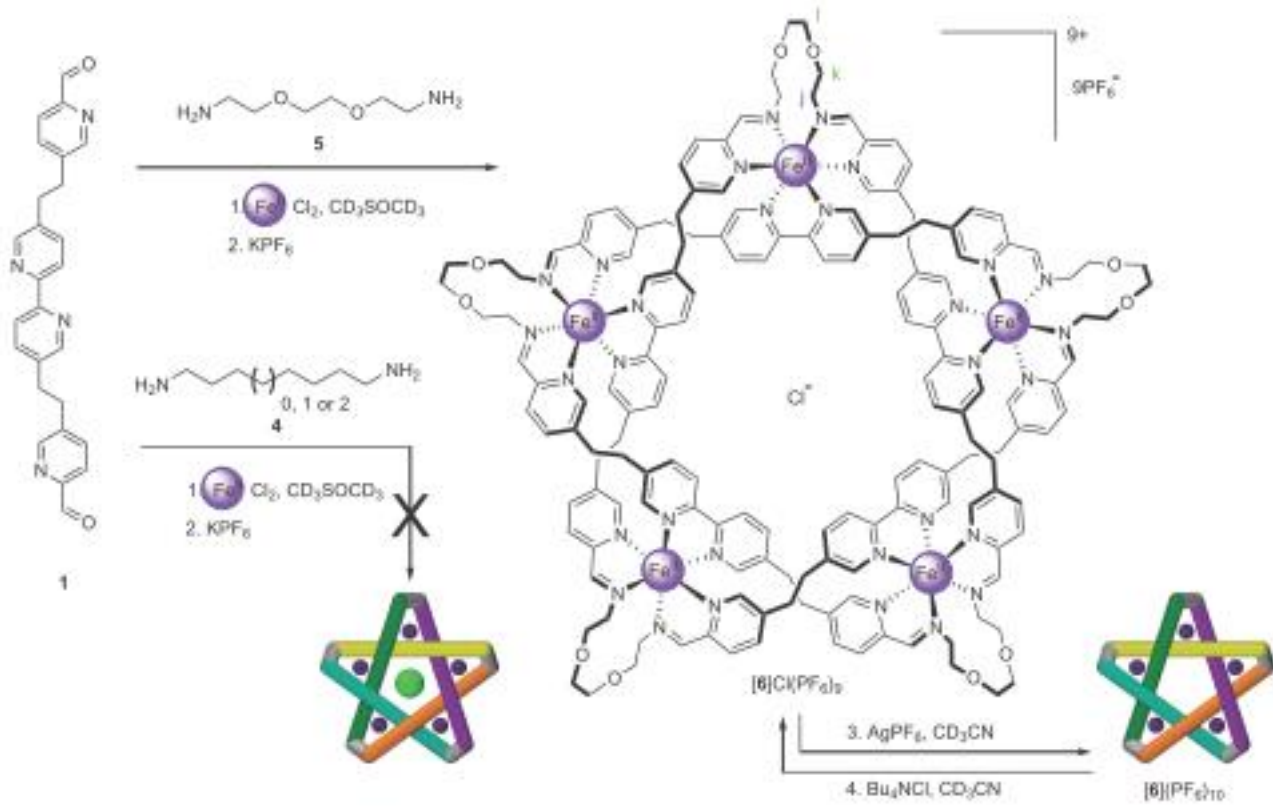


Figure S8 Circular dichroism spectra of (R)-[3g]Cl(PF₆)₉ and (S)-[3g]Cl(PF₆)₉ in MeCN.



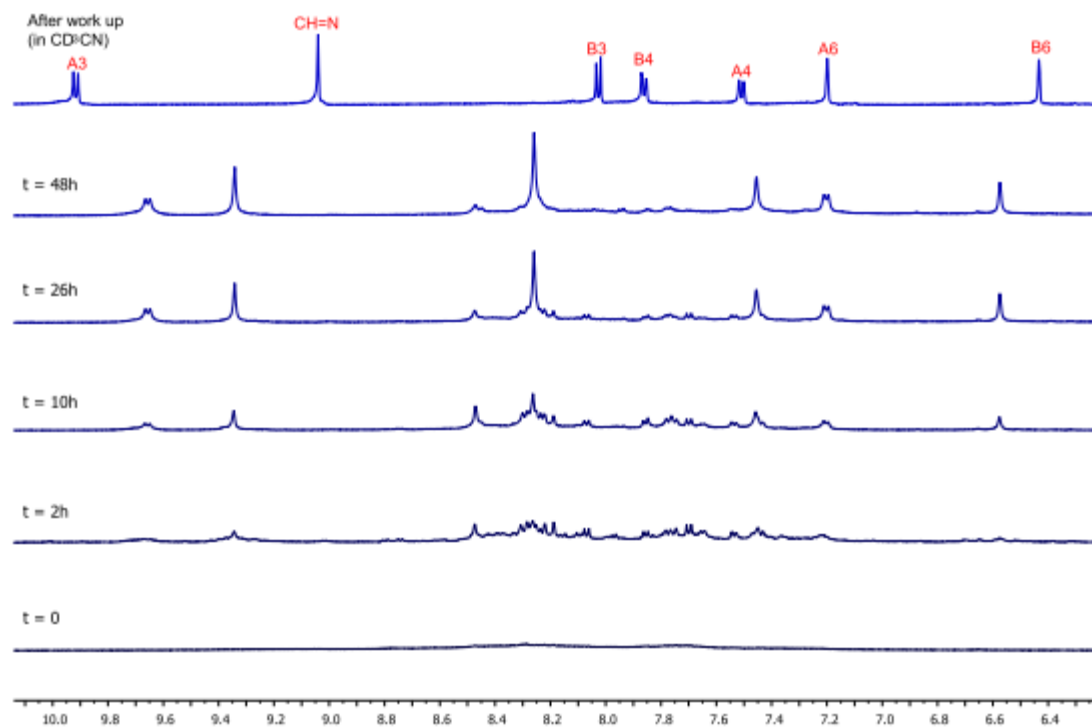
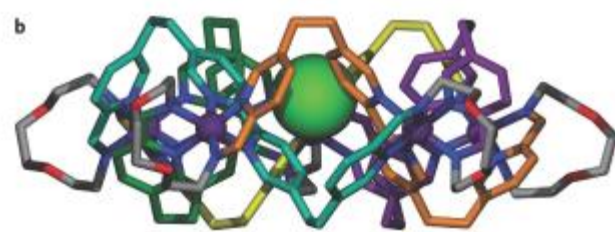
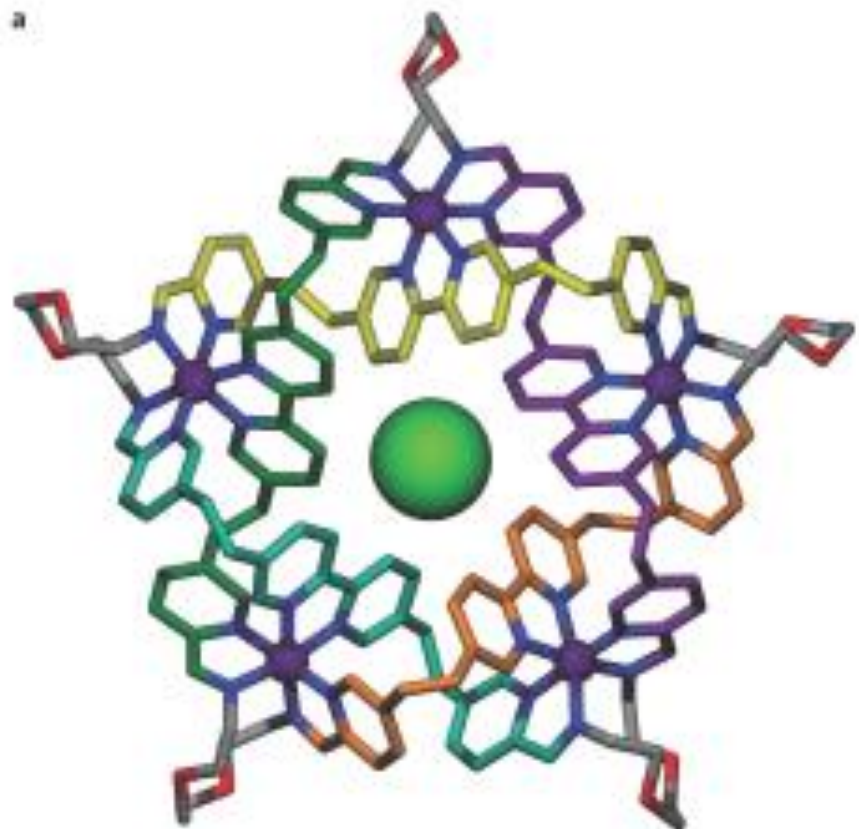


Figure S9 Formation of pentafoil knot $[6]^{10+}$ monitored by ^1H NMR (DMSO- d_6 , 500 MHz), aromatic region of spectrum shown. Spectra were collected of the crude reaction mixture after $t = 0$ (bottom), 2h, 10h, 26h and 48h. The top spectra is of the same sample after work-up (^1H NMR in CD_3CN) with ^1H NMR assignments indicated.



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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Angew. Chem. Int. Ed. 2011, 50, 9260–9327

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Template synthesis of molecular knots†

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Jean-François Ayme,^{ab} Jonathon E. Beves,^a Christopher J. Campbell^a and David A. Leigh^{*ab}

Received 28th June 2012

DOI: 10.1039/c2cs35229j

www.rsc.org/csr

This *tutorial review* outlines the different template strategies that chemists have employed to synthesise knotted molecular topologies. Metal ion coordination, hydrogen bonding and aromatic donor–acceptor interactions have all been used to direct the formation of well-defined crossing points for molecular strands. Advances in the methods used to covalently capture the interwoven structures are highlighted, including the active metal template strategy in which metal ions both organise crossing points and catalyse the bond forming reactions that close the loop to form the topologically complex product. Although most non-trivial knots prepared to date from small-molecule building blocks have been trefoil knots, the first pentafoil knot was recently synthesised. Possible future directions and strategies in this rapidly evolving area of chemistry are discussed.

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=voihggHIU_4

A Synthetic Molecular 8_{19} Knot *'Braiding a molecular knot with eight crossings'*

Jonathan J. Danon, Anneke Krüger, **David A. Leigh**, Jean-François Lemonnier, Alexander J. Stephens, Iñigo J. Vitorica-Yrezabal and Steffen L. Woltering, *Science*, **355**, 159-162 (2017).

http://www.catenane.net/pages/2017_819knot.html

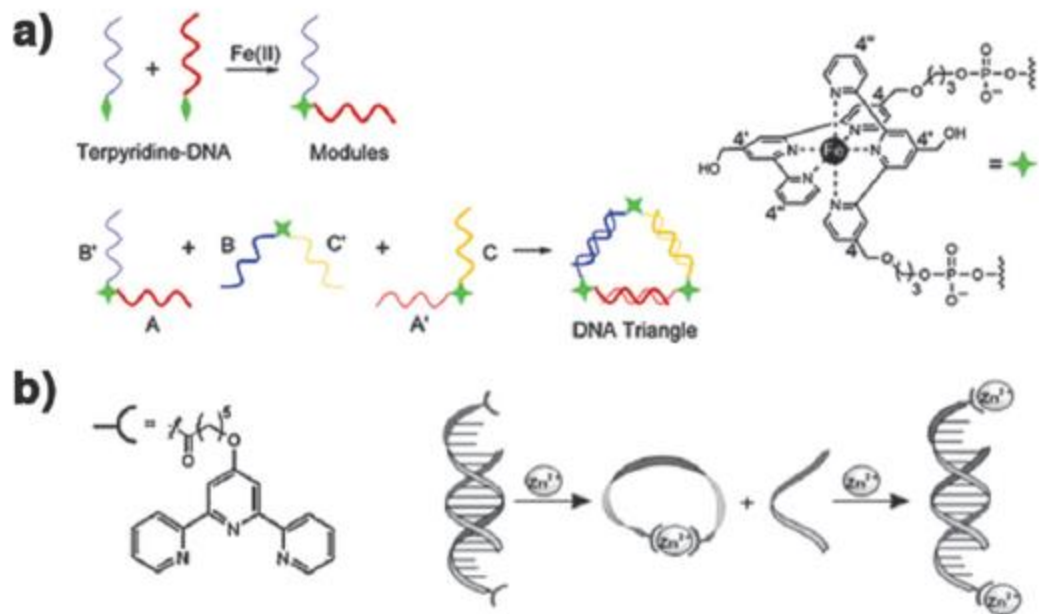


Fig. 8 Ligand modified DNA and nanostructure assemble *via* ligand-metal interactions. (a) Terpyridine modified DNA drives the formation of a DNA triangle using Fe^{2+} coordination. Adapted with permission from ref. 39. Copyright 2004 American Chemical Society. (b) Zn^{2+} drives the opening and closing of DNA cycles. Adapted with permission from ref. 40. Copyright 2005 American Chemical Society.

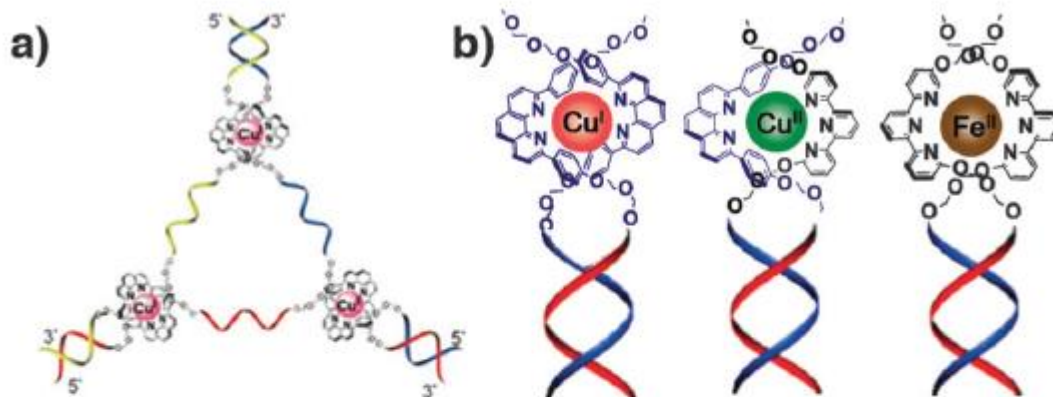


Fig. 9 Metal DNA complexes and structures. (a) Site-specifically incorporating diphenylphenanthroline (dpp) into DNA templates nanostructures with highly stable duplexes. Reproduced from ref. 32 with permission from Wiley-VCH. (b) Using two different ligand insertions, selective coordination environments can be templated with DNA. Reproduced from ref. 43 with permission from Wiley-VCH.

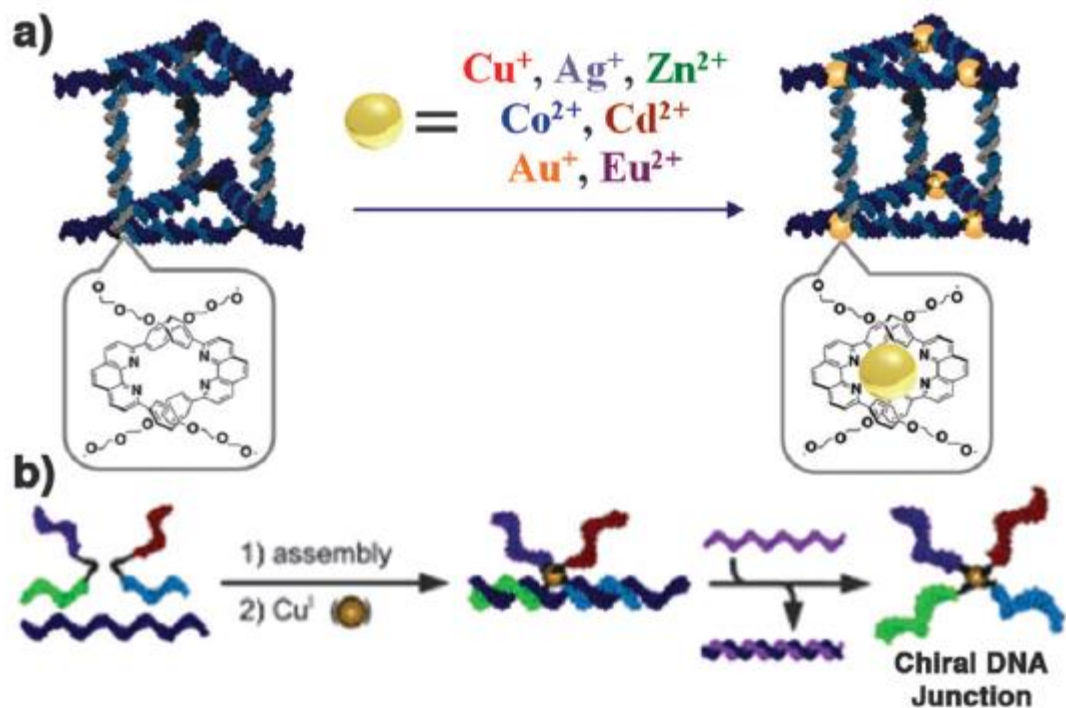


Fig. 10 Metal DNA complexes and structures in 3D. (a) Metal-DNA cage structure with selective coordination environments templated in 3D. (b) Chiral four-way metal-DNA junction formed *via* templated assembly of modified sequences. Reproduced from ref. 45 with permission from Wiley-VCH.