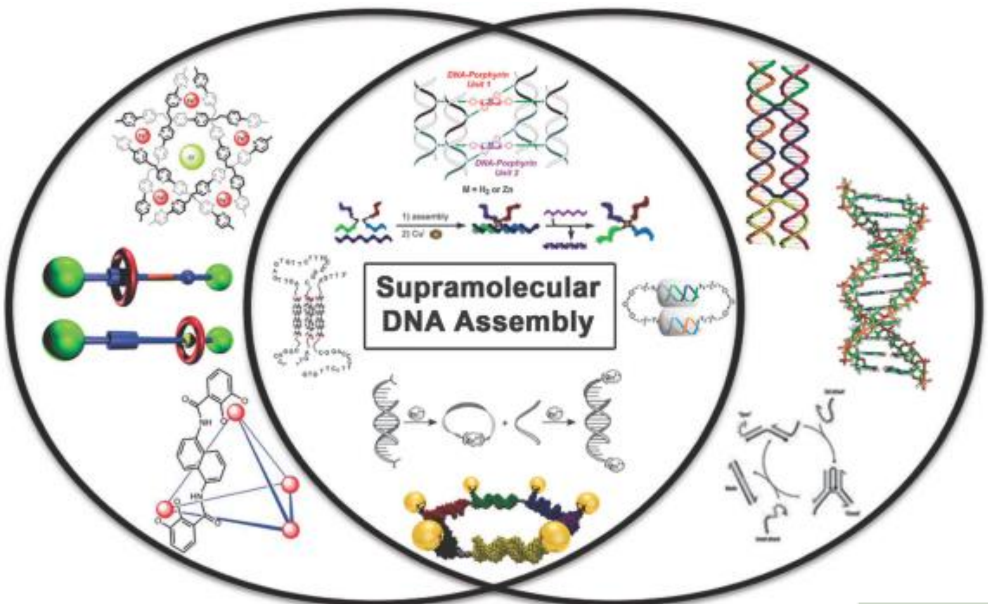
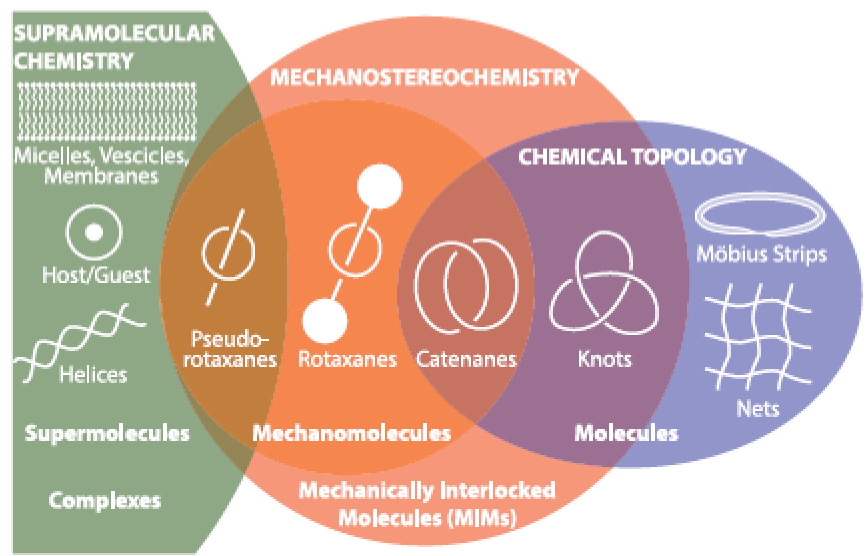
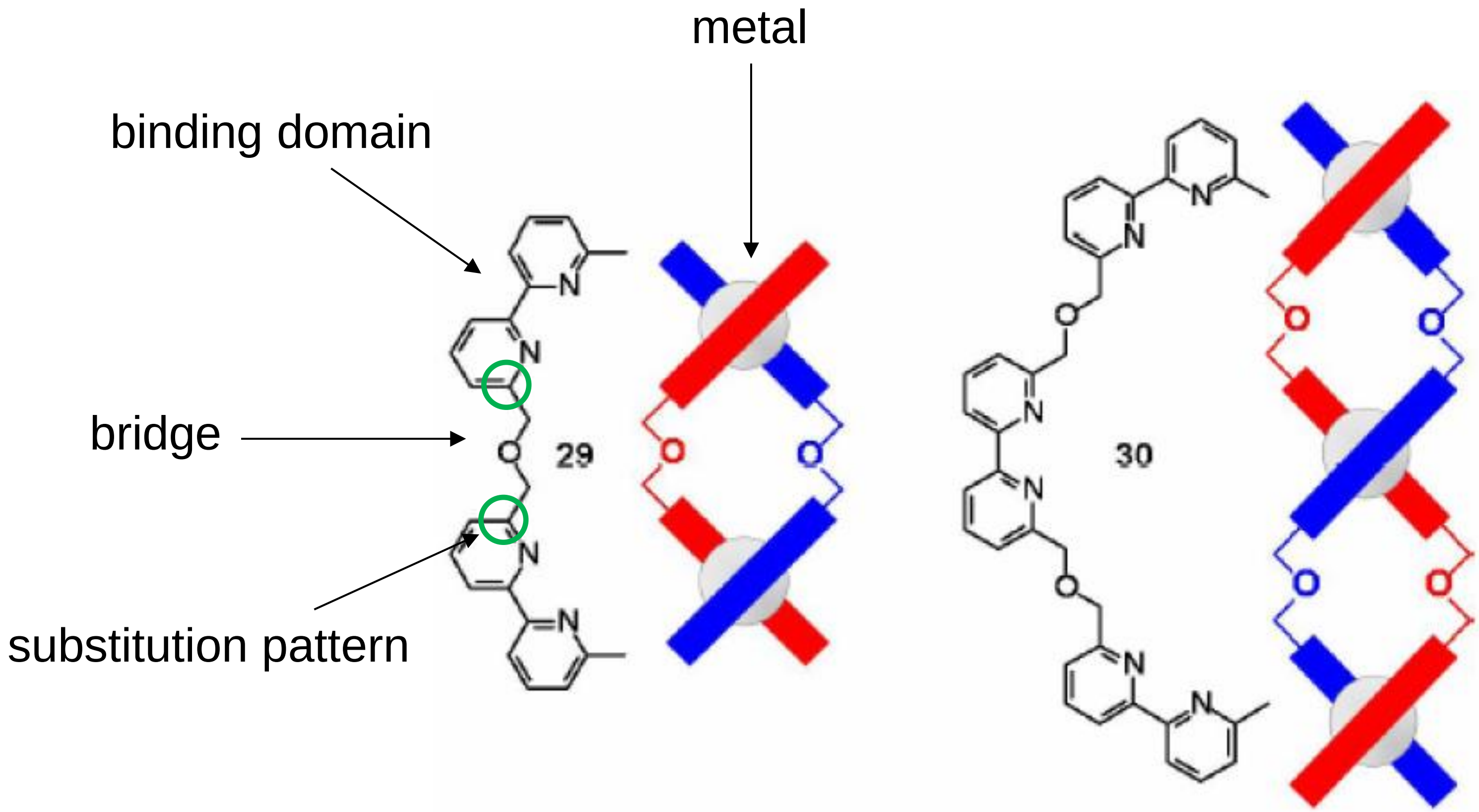
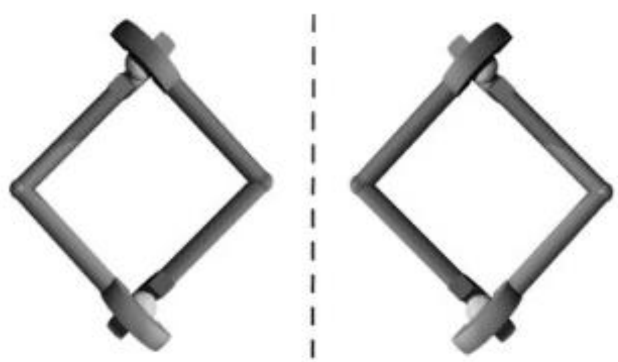

Supramolecular
DNA Assembly


SUPRAMOLECULAR CHEMISTRY
MECHANOSTEREOCHEMISTRY
CHEMICAL TOPOLOGY
Micelles, Vescicles, Membranes
Host/Guest
Helices
Pseudo-rotaxanes
Rotaxanes
Catenanes
Knots
Möbius Strips
Nets
Supermolecules
Mechanomolecules
Molecules
Complexes
Mechanically Interlocked Molecules (MIMs)

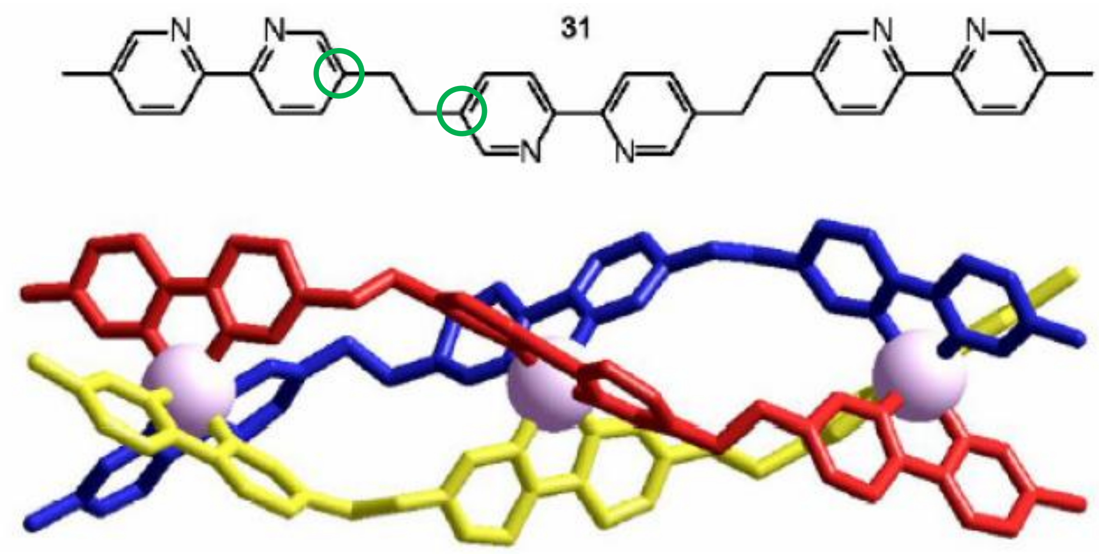
Double stranded helicates



Chirality

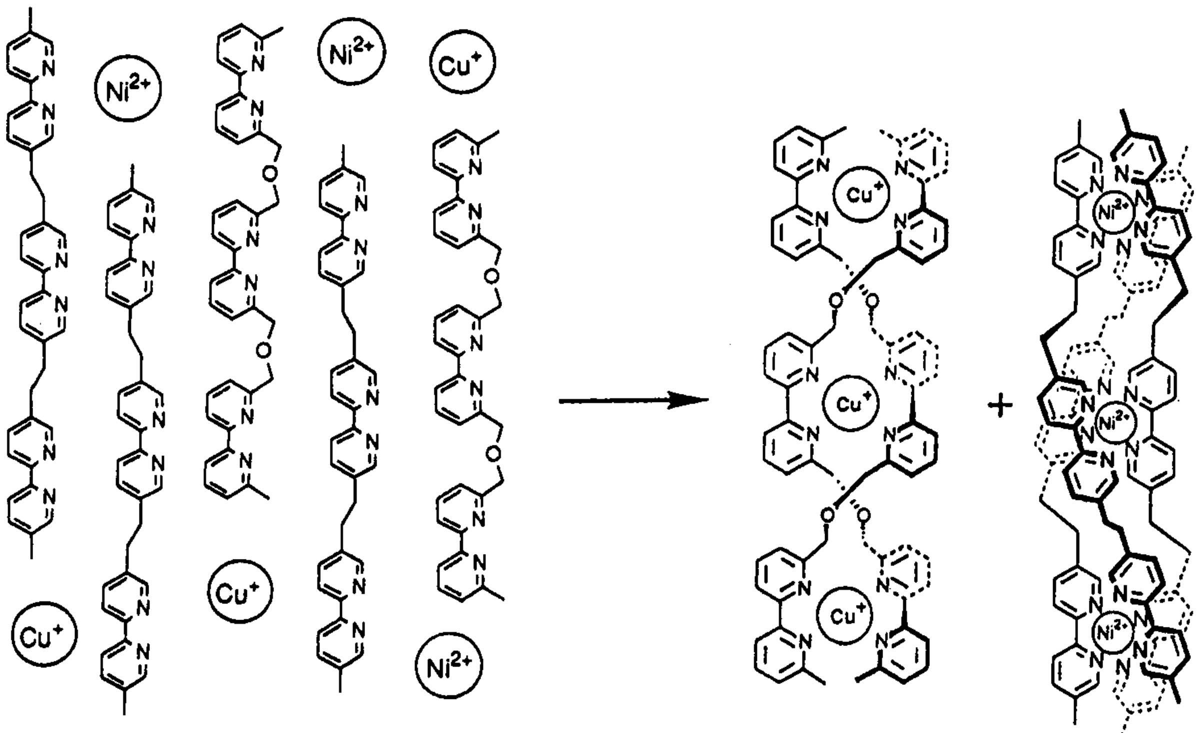


Triple stranded helicates

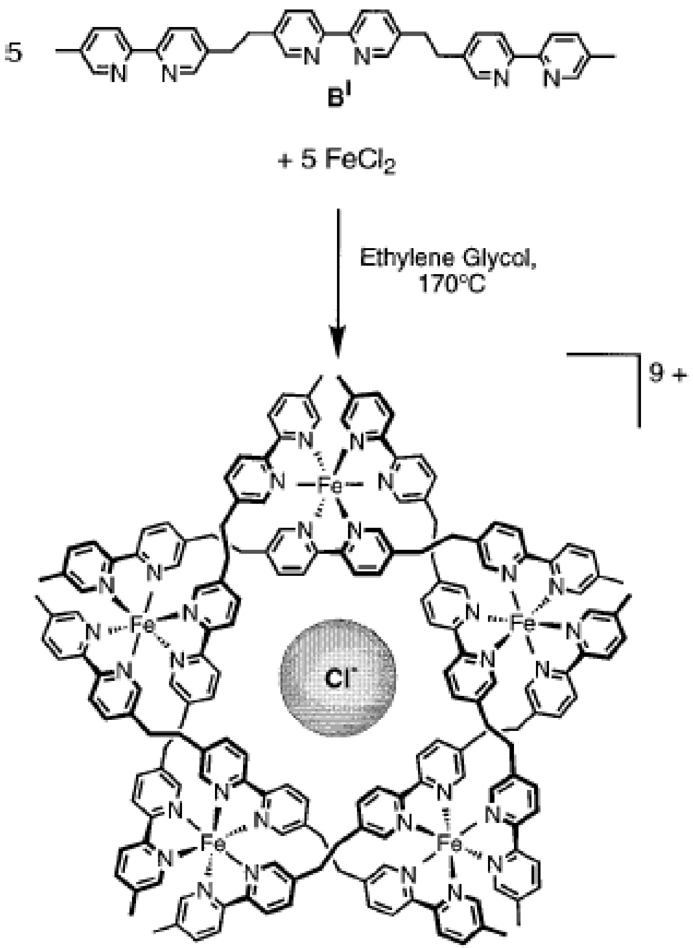


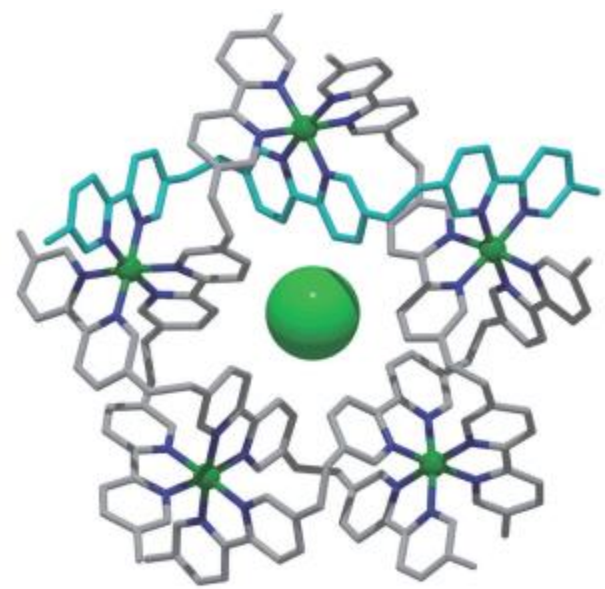
- Ni(II) : octahedral geometry
- one ligand can not wrap around one Ni(II) cation: trimerization
- other metals: Co(II), Fe(II), lanthanides

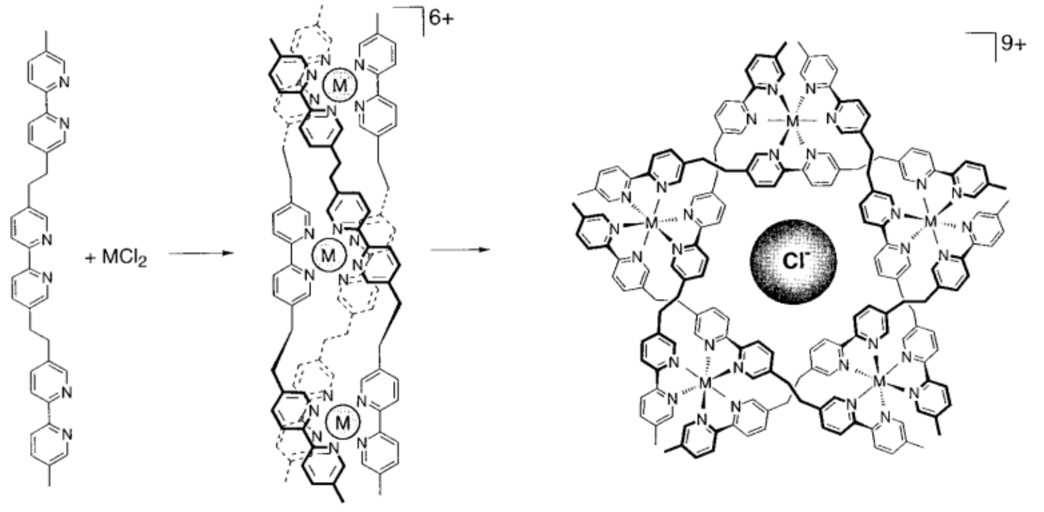
Double and Triple Helicates: an example of Self-sorting



Cyclic Helicates





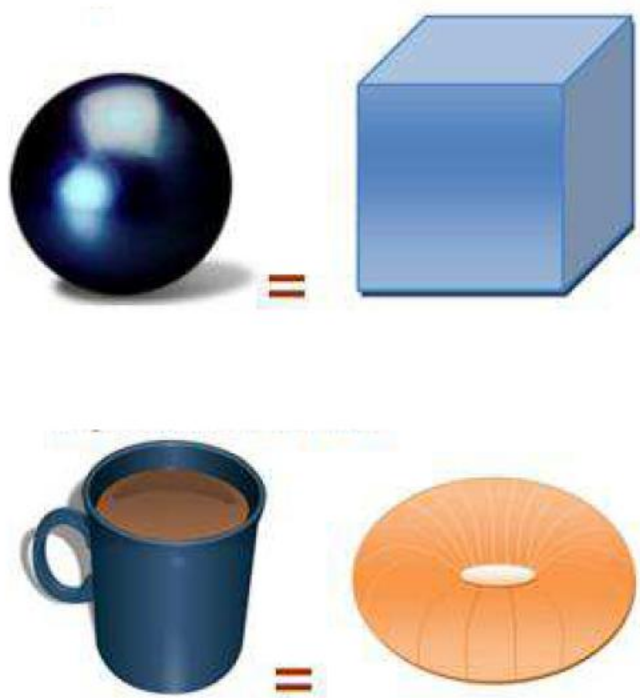


^{1}H-NMR

ESI-MS

Topology

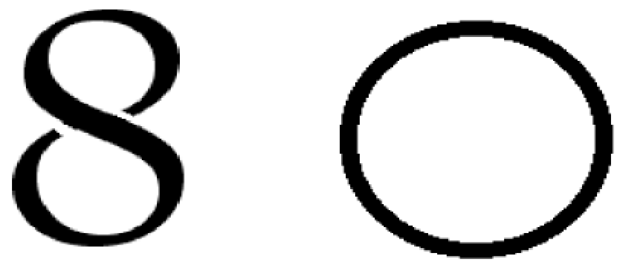
In topology, angles, distances or shapes have no meaning
But the object cannot be cut



Molecular graph

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

(a)

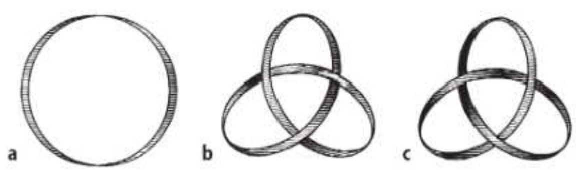


→ planar graph

One possible conformation with no crossing in 2D representation

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.

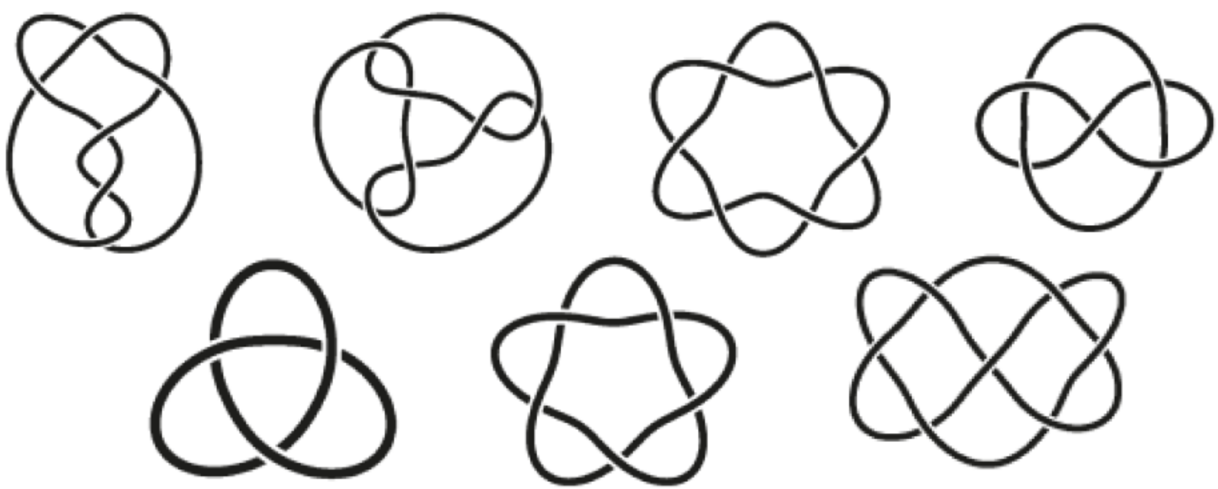
Knotted and intertwined patterns have fascinated mankind and artists for centuries, because of the beauty and the symbolism they convey. Therefore it is not surprising if they can be found in the cultural production of virtually all civilizations across time and space.

Molecular graph

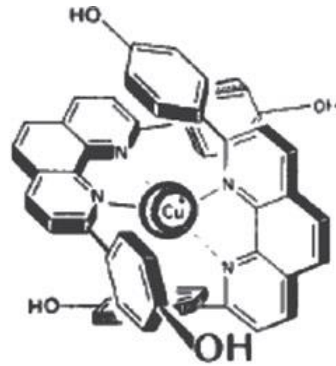
non-planar graph

No possible conformation with no crossing in 2D representation

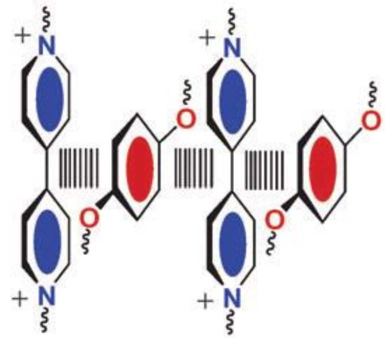
topological chemistry is the chemistry of molecules having a non planar graph



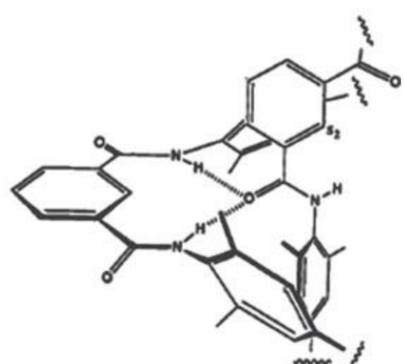
1



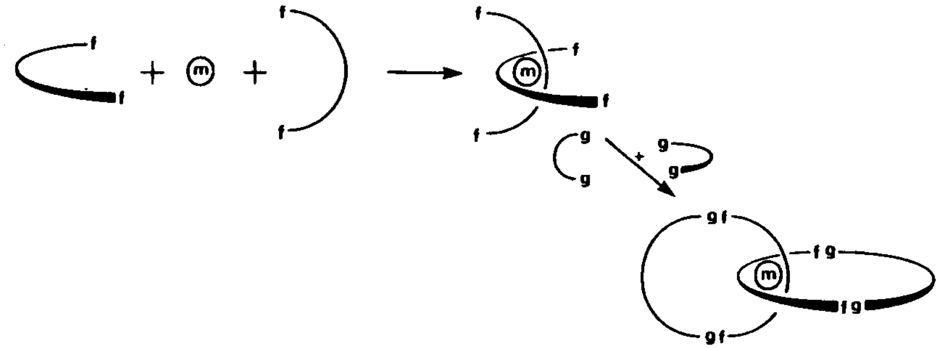
2

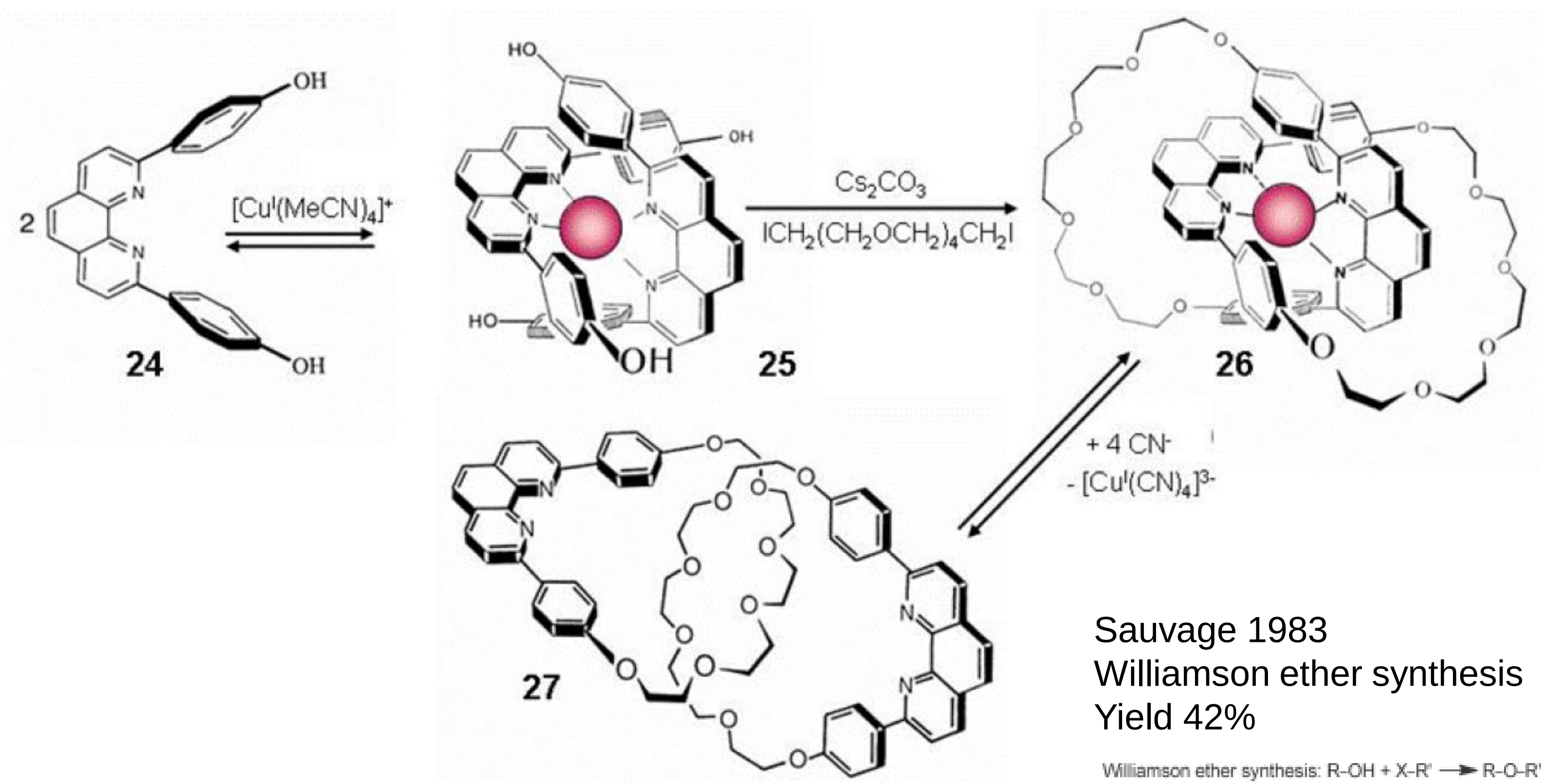


3



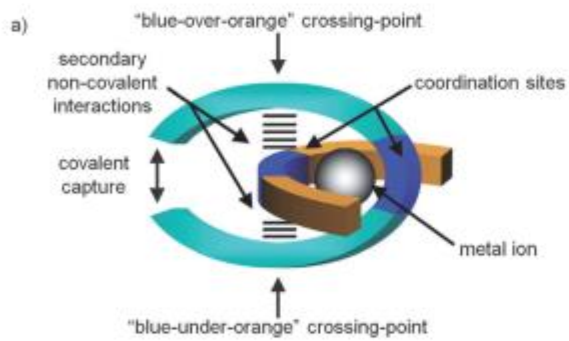
[*n*]Catenanes

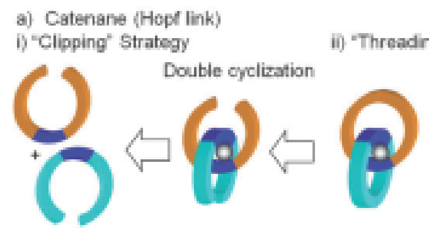


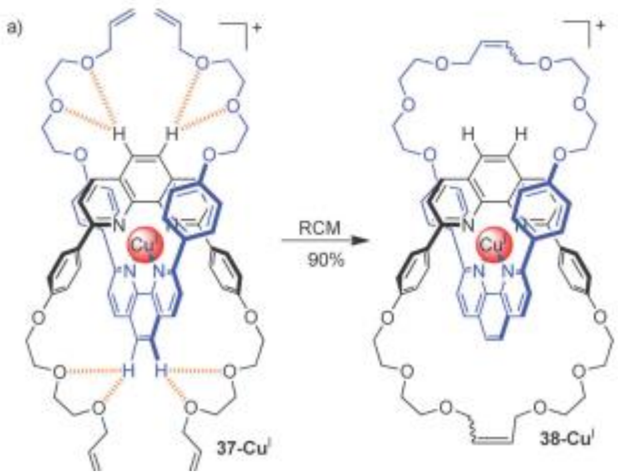


Sauvage 1983
Williamson ether synthesis
Yield 42%

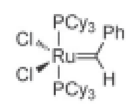
Williamson ether synthesis: R–OH + X–R' ⟶ R–O–R'



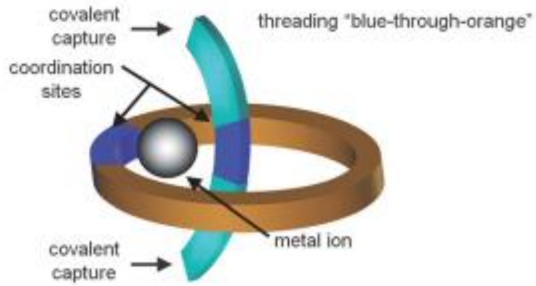


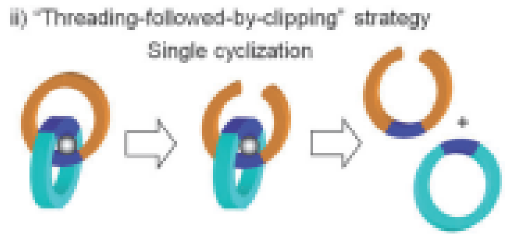


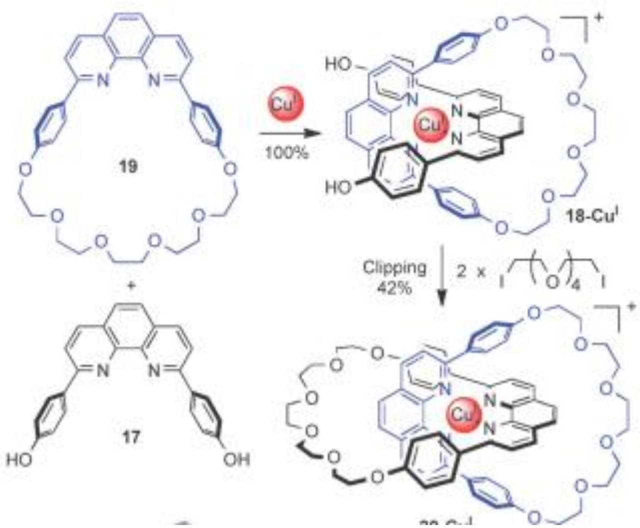
Ring closing metathesis (RCM): 2 x

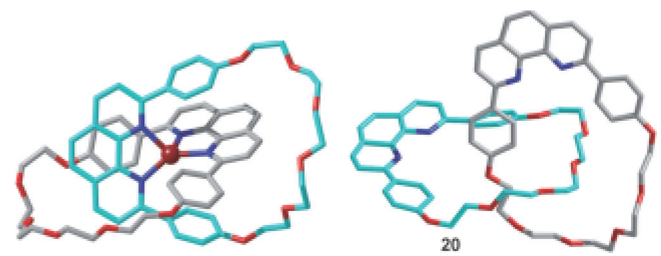


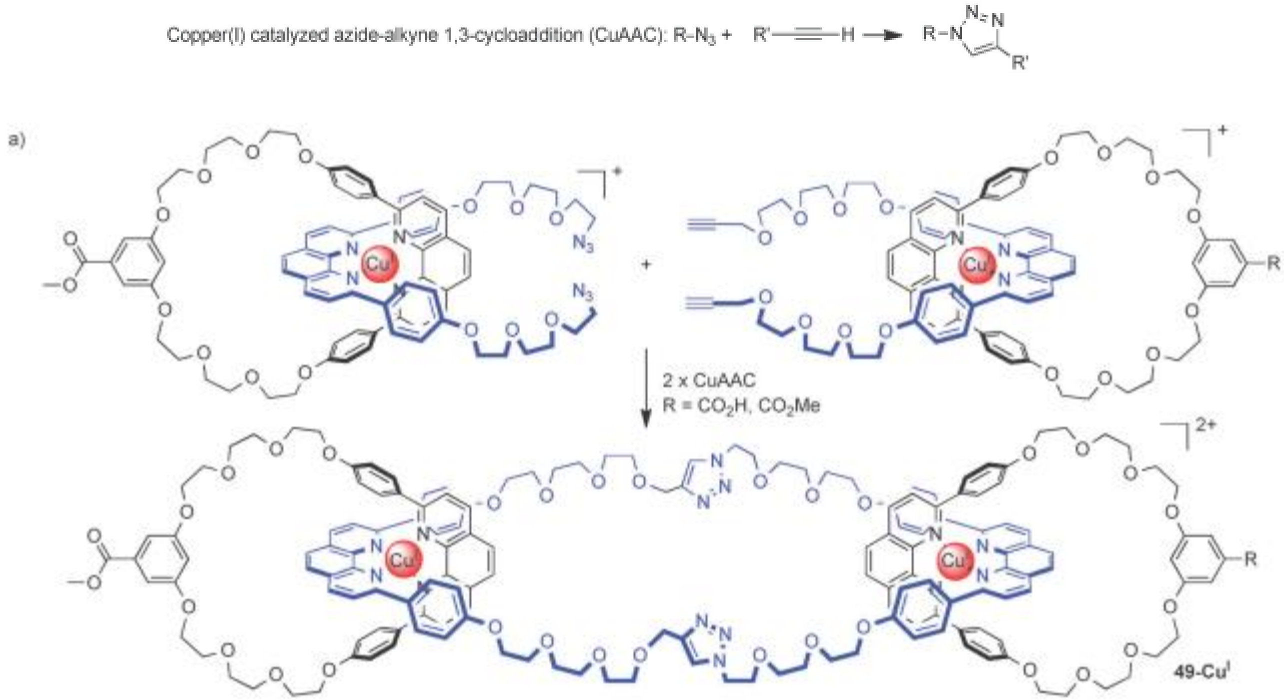
b)

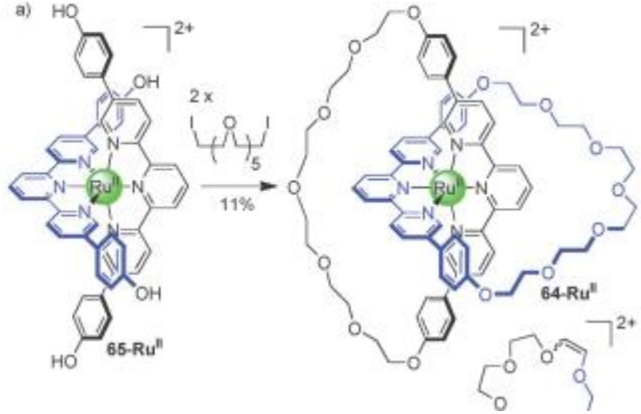

covalent capture
threading "blue-through-orange"
coordination sites
metal ion
covalent capture

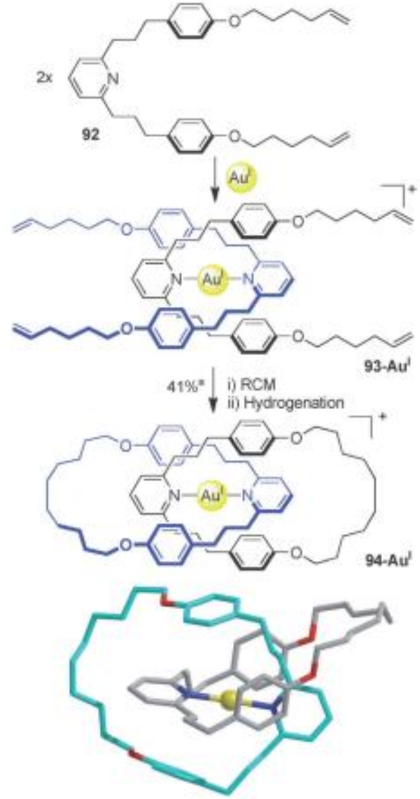

ii) "Threading-followed-by-clipping" strategy
Single cyclization
+

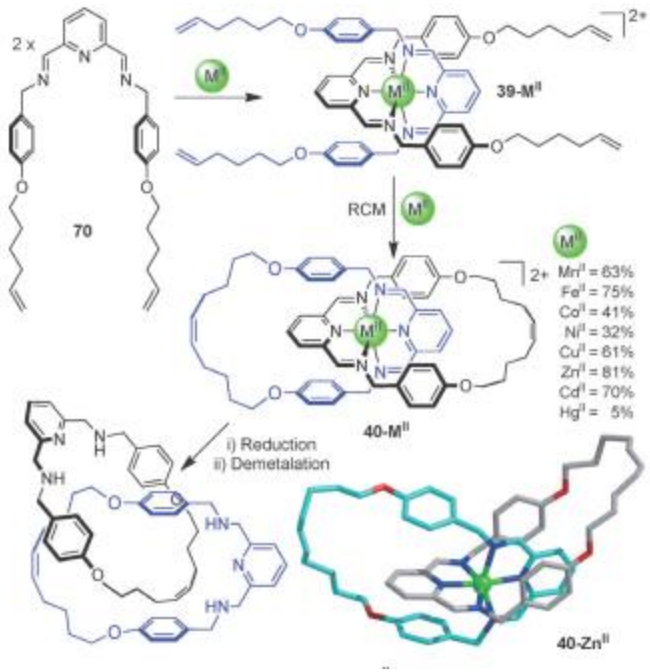

19
+
17
HO
OH
Cu
100%
HO
HO
18-Cu
Clipping
42%
2 ×


20

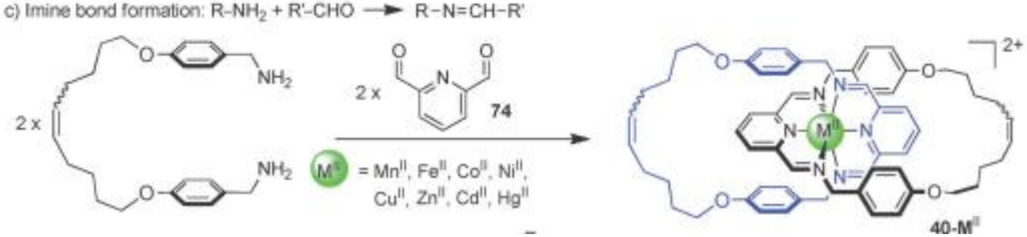

Copper(I) catalyzed azide-alkyne 1,3-cycloaddition (CuAAC): R–N3 + R'—≡—H →
a)
2 x CuAAC
R = CO2H, CO2Me
49-CuI


a)
2 x
11%
65-Ru^II
64-Ru^II

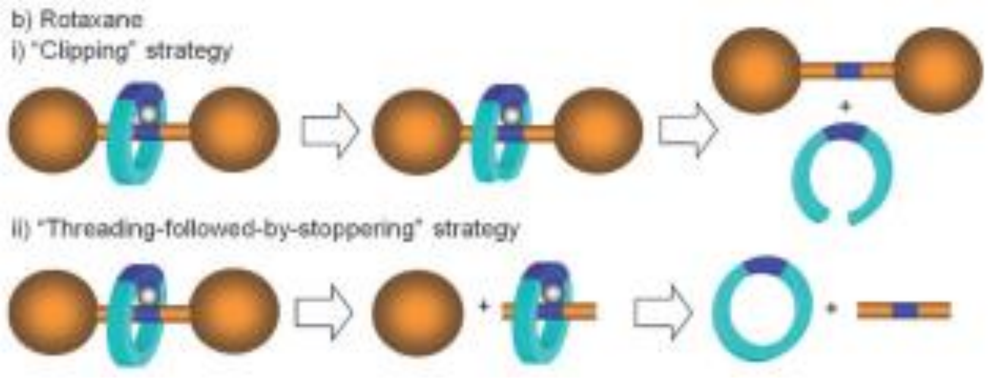

2x
92
Au^I
93-Au^I
41%*
i) RCM
ii) Hydrogenation
94-Au^I

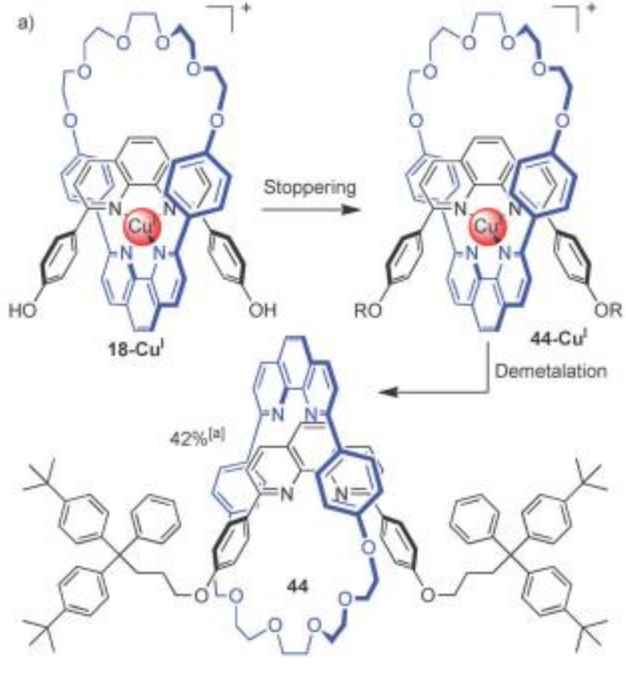


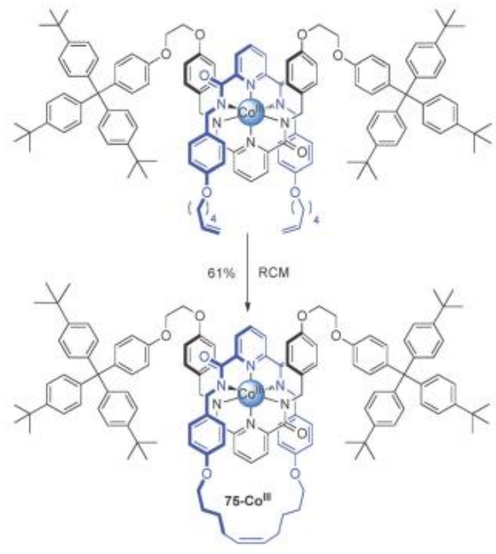
c) Imine bond formation: R-NH$_2$ + R'-CHO ⟶ R−N=CH−R'

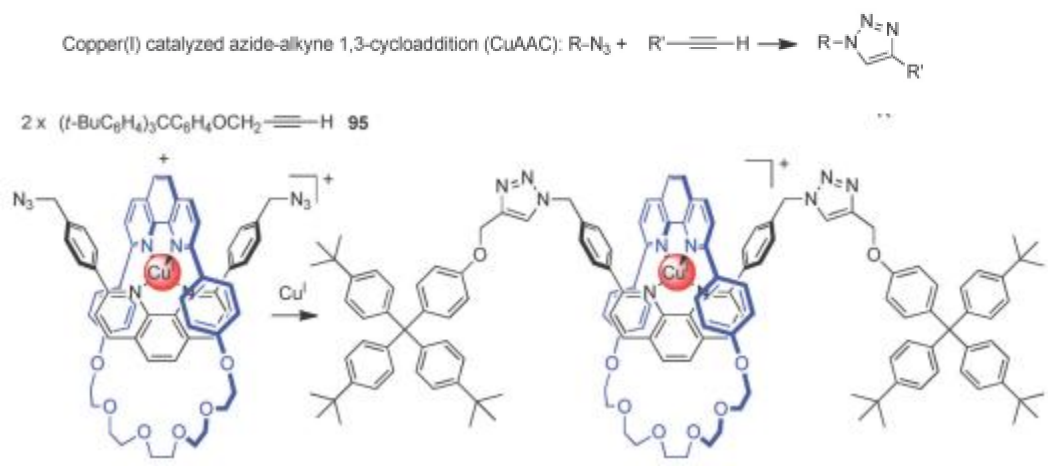


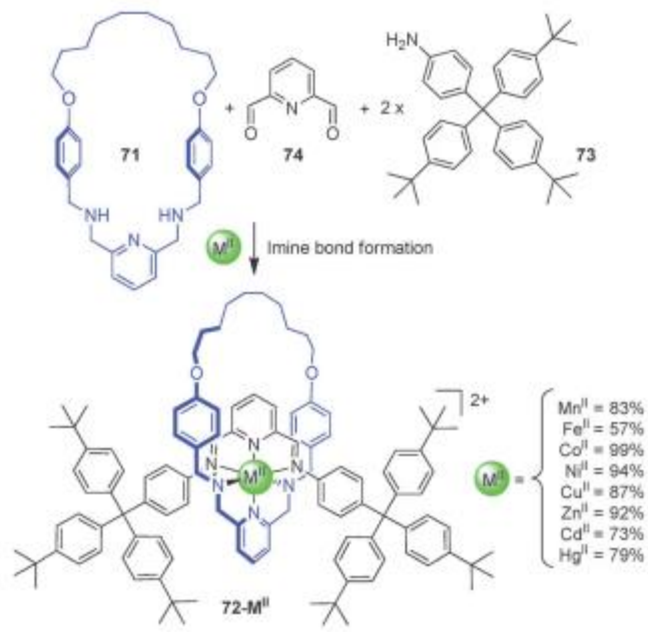
[*2*]Rotaxanes

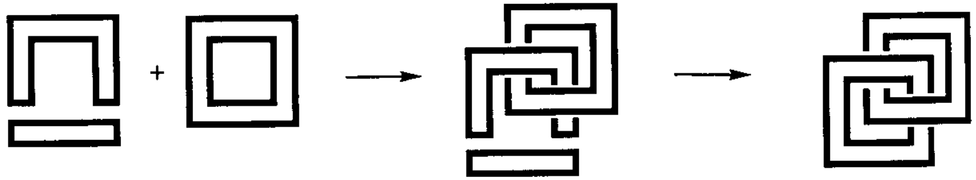

b) Rotaxane
i) "Clipping" strategy
ii) "Threading-followed-by-stoppering" strategy


a)
Stoppering
18-Cu^I
44-Cu^I
Demetalation
42%[a]
44


61%
RCM
75-Co^III

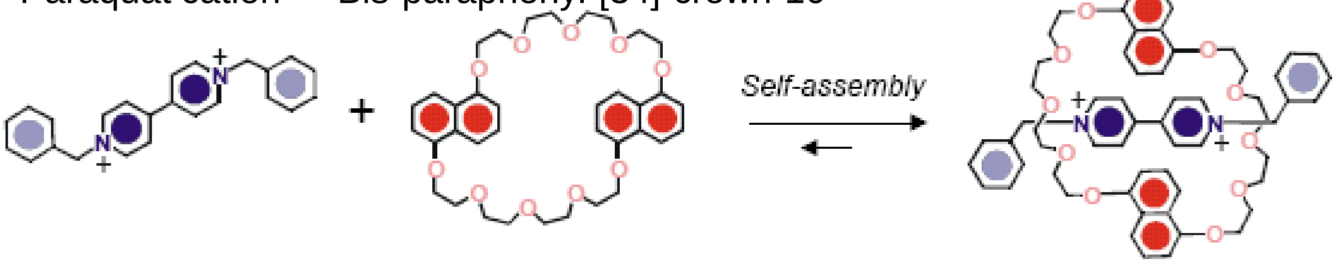

Copper(I) catalyzed azide-alkyne 1,3-cycloaddition (CuAAC): R-N3 + R'—≡—H →
2 x (t-BuC6H4)3CC6H4OCH2—≡—H 95
Cu^I

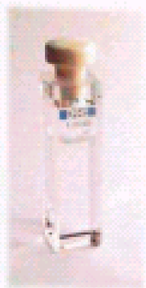

71
74
73
+ 2 x
Imine bond formation
72-M^II
Mn^II = 83%
Fe^II = 57%
Co^II = 99%
Ni^II = 94%
Cu^II = 87%
Zn^II = 92%
Cd^II = 73%
Hg^II = 79%

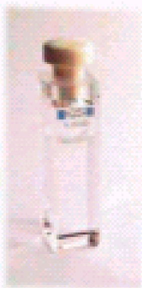


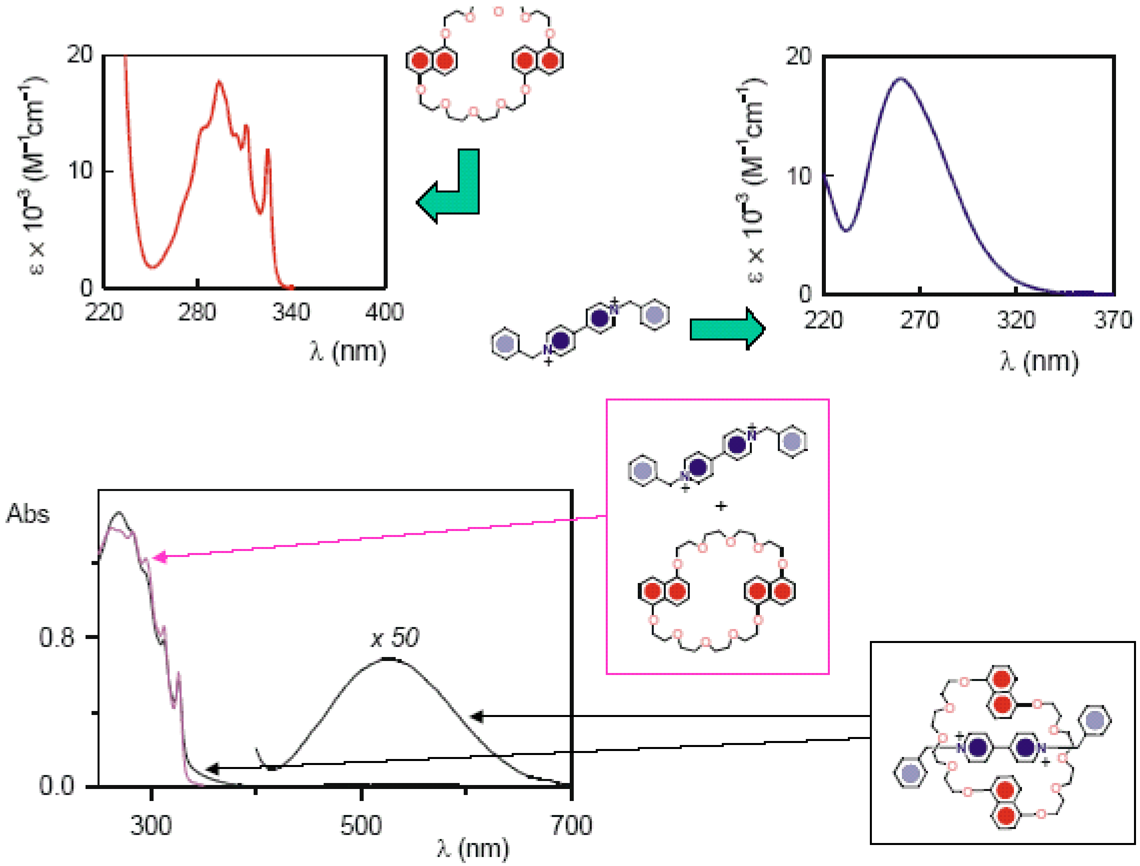
Paraquat cation

Bis-paraphenyl-[34]-crown-10

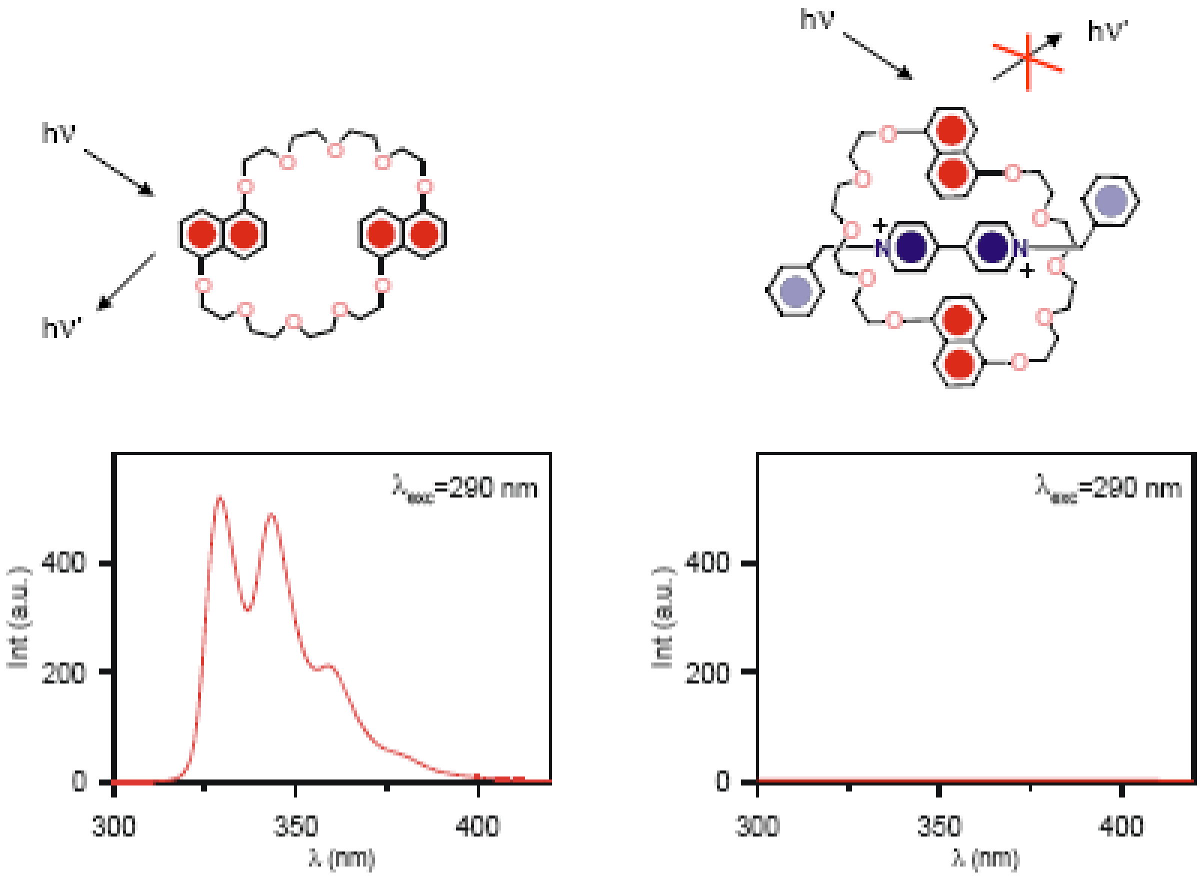


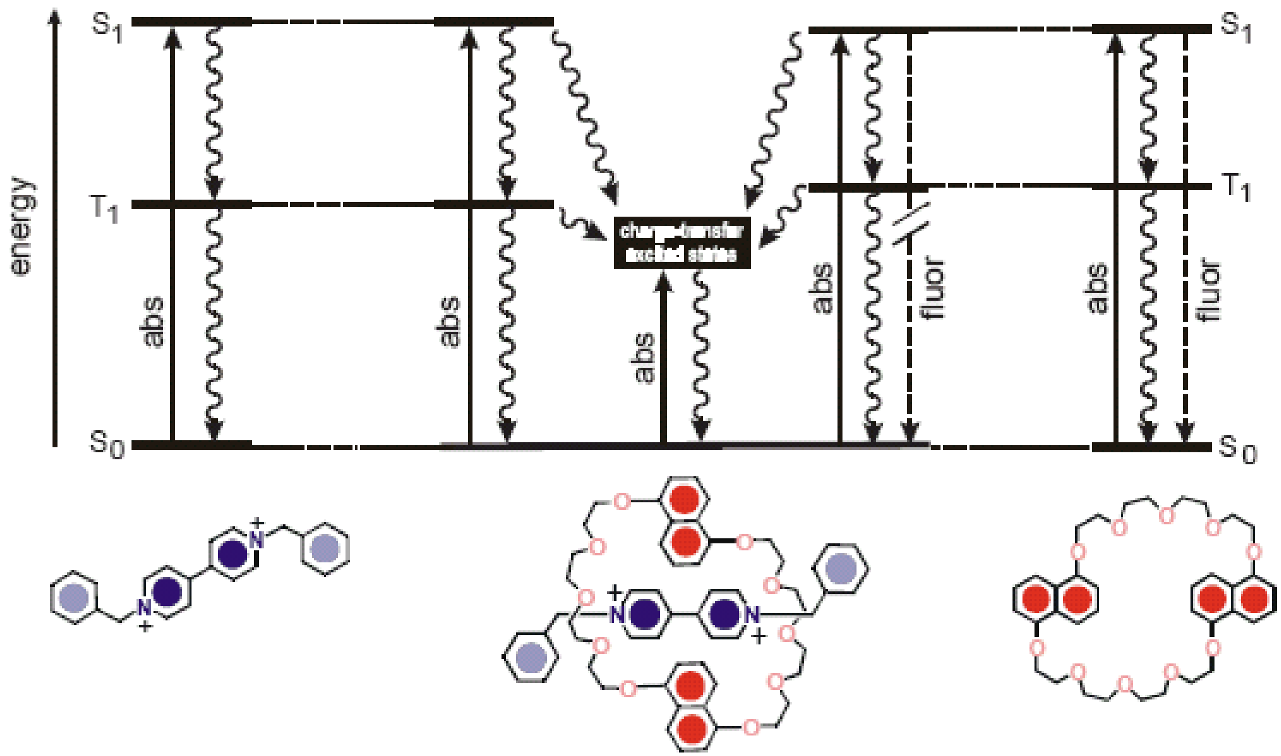


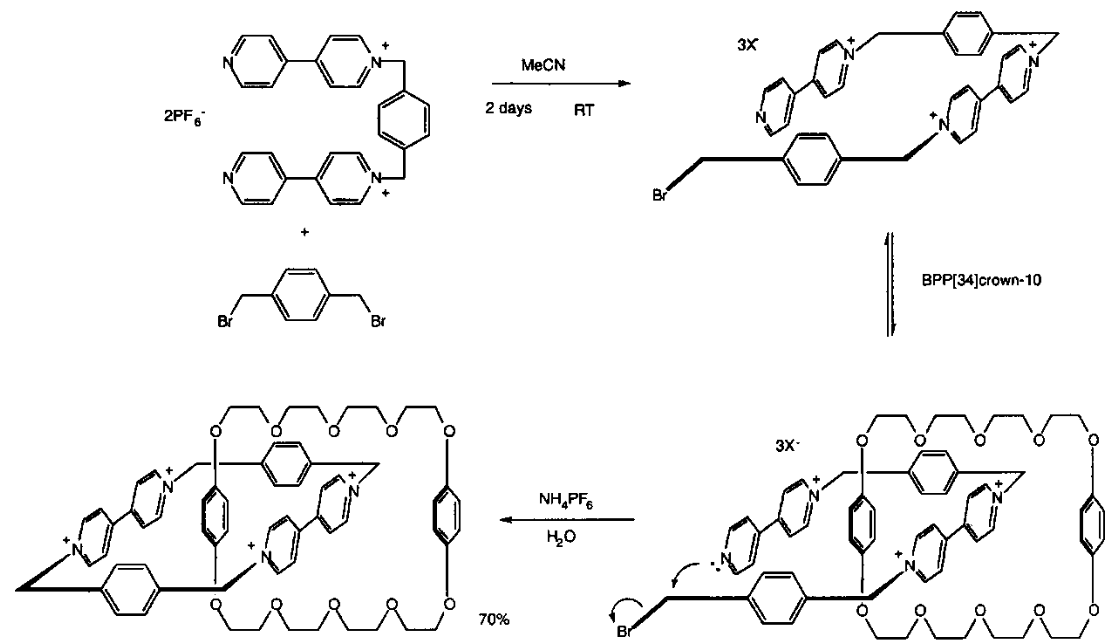


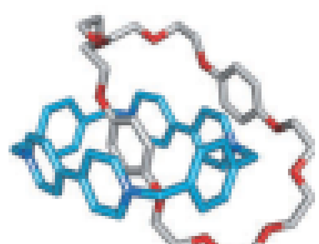


ε × 10⁻³ (M⁻¹cm⁻¹)
20
10
0
220
280
340
400
λ (nm)
ε × 10⁻³ (M⁻¹cm⁻¹)
20
10
0
220
270
320
370
λ (nm)
Abs
0.8
0.0
300
500
700
λ (nm)
x 50
+

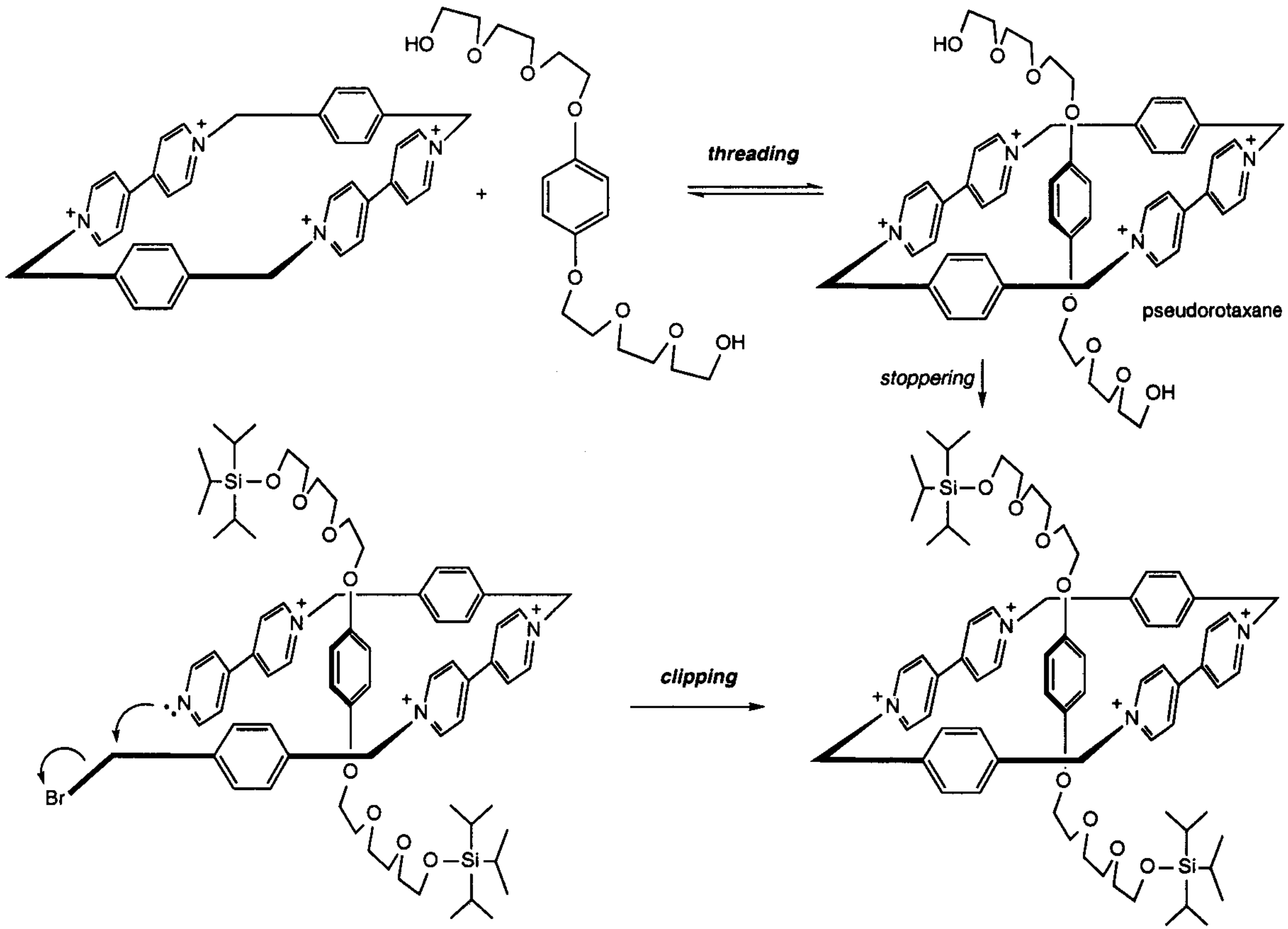

hν
hν'
hν
hν'
λexc=290 nm
λexc=290 nm
Int (a.u.)
Int (a.u.)
400
200
0
400
200
0
300
350
400
300
350
400
λ (nm)
λ (nm)


energy
S1
T1
S0
abs
fluor
charge-transfer
excited states

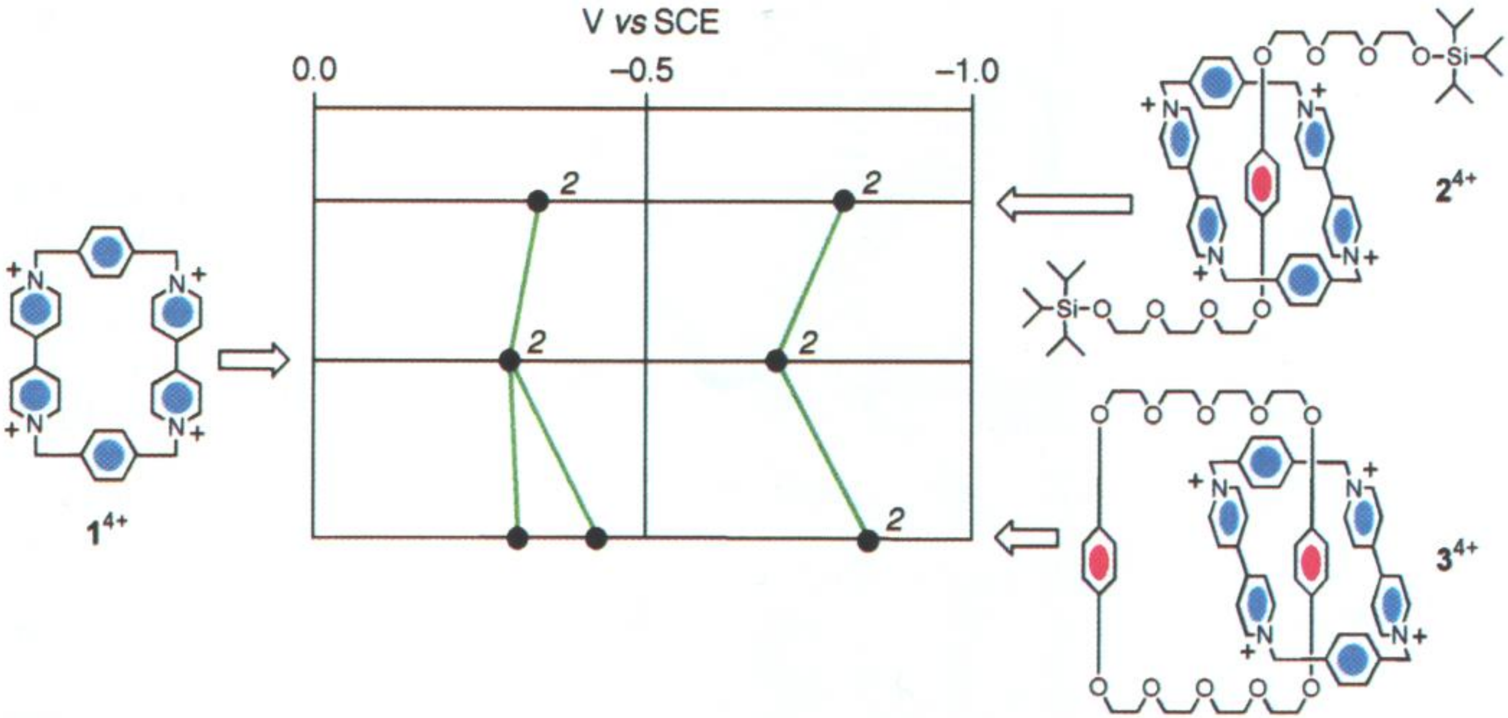


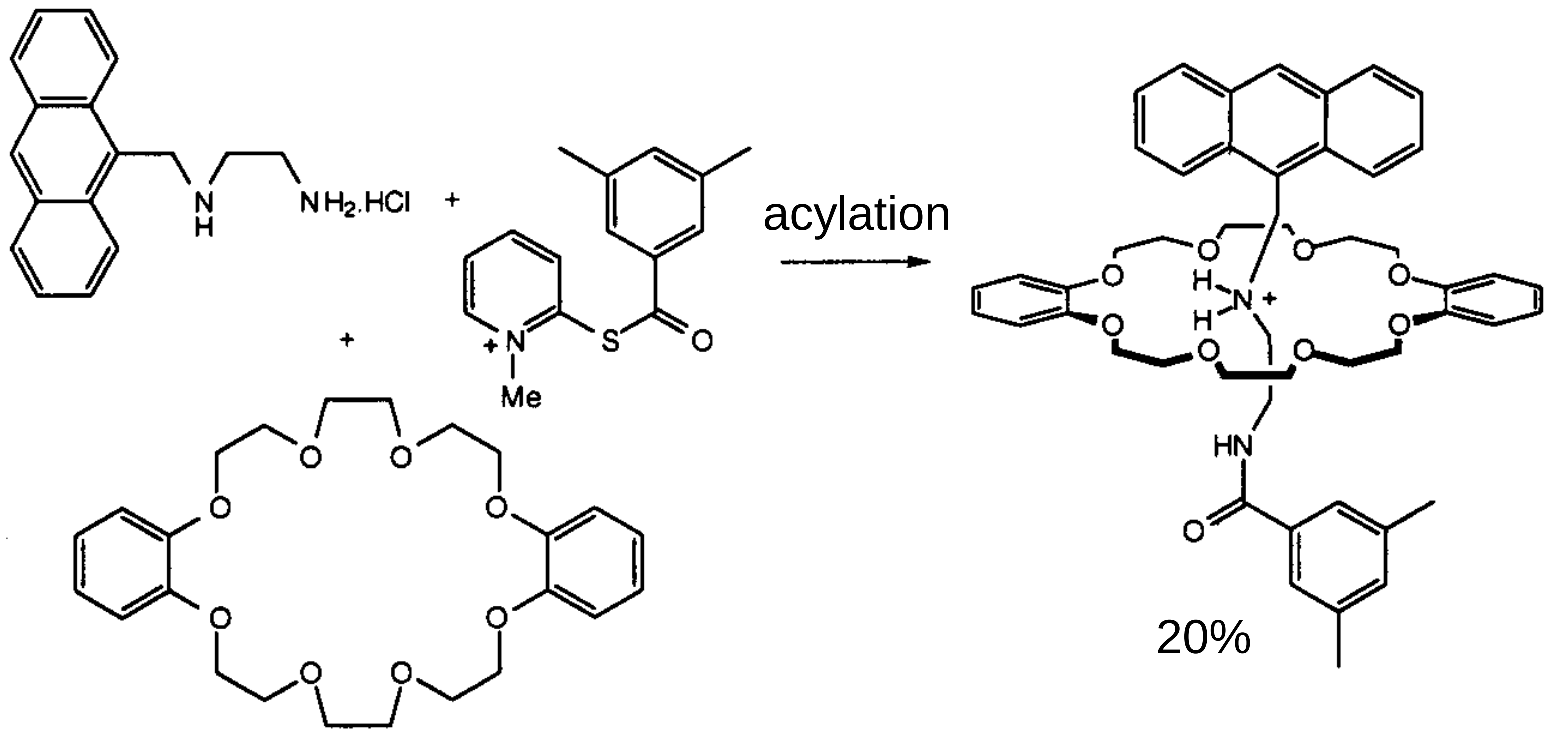


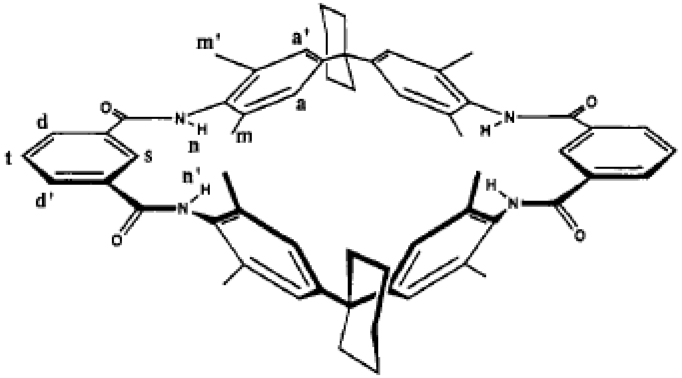
45



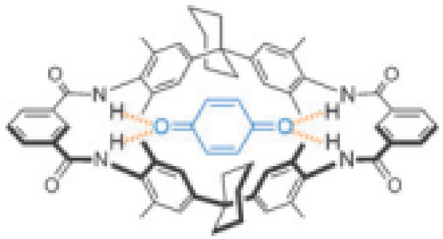
Synthesis of a rotaxane by two different routes: threading and clipping.


V vs SCE
0.0
–0.5
–1.0
2
2
2
2
2
1^{4+}
2^{4+}
3^{4+}
N
Si
O


NH
NH2.HCl
+
+
+N
Me
S
O
acylation
O
H
H
N+
HN
O
20%

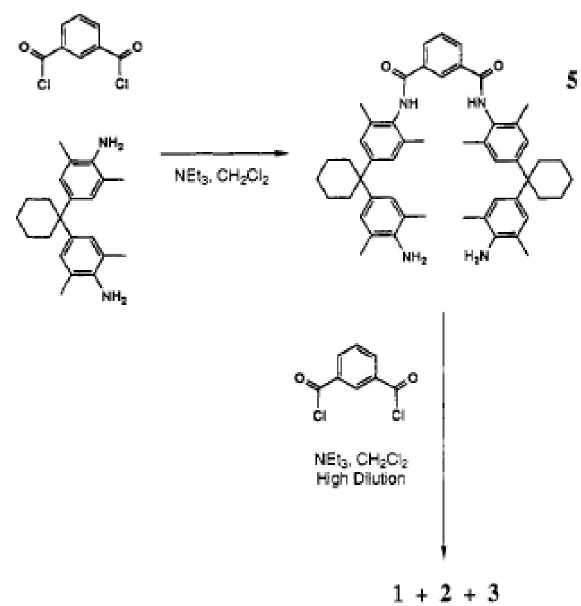


1



Synthesis. I recently reported the synthesis of **1**, a receptor for *p*-benzoquinone.[7] 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 ^{1}H NMR spectrum that was almost identical with that of **1** in $CDCl_3/CD_3OD$. Thus all four components of the tetramer were equivalent and had retained their symmetry. In contrast, fraction A had a very complex ^{1}H NMR

Scheme II

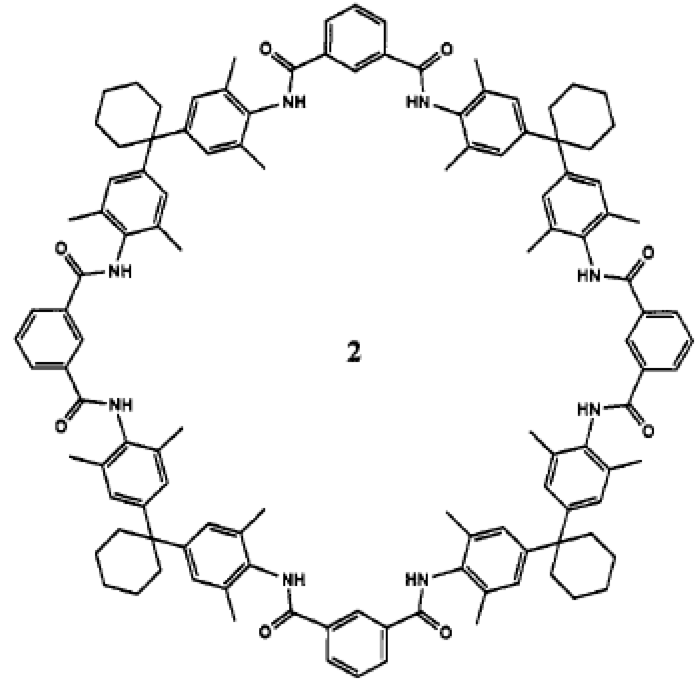


Cyclic Dimer 1, Cyclic Tetramer 2, and Catenane 3 (Scheme II). 5, 1 g, and 0.4 mL of triethylamine were dissolved in 250 mL of dry dichloromethane and transferred to a dropping funnel. Isophthaloyl dichloride (0.26 g) was similarly dissolved in 250 mL of dry dichloromethane and transferred to an identical 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.

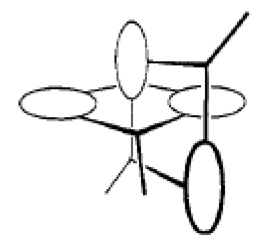
Fraction A was obtained as a white crystalline solid (400 mg, 34%). The NMR data are discussed in the main text. *m/z* 1806 (MH^+); $C_{120}H_{128}N_8O_8$ requires M^+ = 1808.

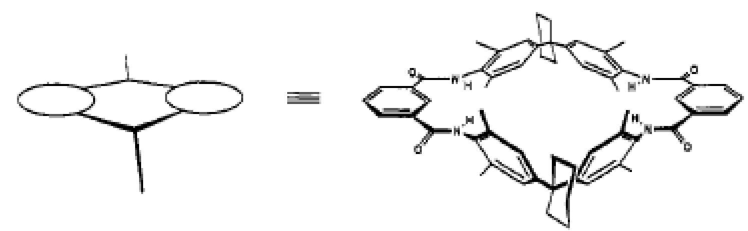
Fraction B was obtained as a white powder (600 mg, 51%). Spectroscopic data were as for the cyclic dimer **1** from Scheme I.

Fraction C was obtained as a white powder (50 mg, 5%). NMR ($CDCl_3/CD_3OD$) 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^+); $C_{120}H_{128}N_8O_8$ requires M^+ = 1808.

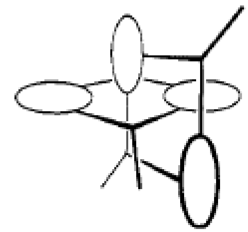


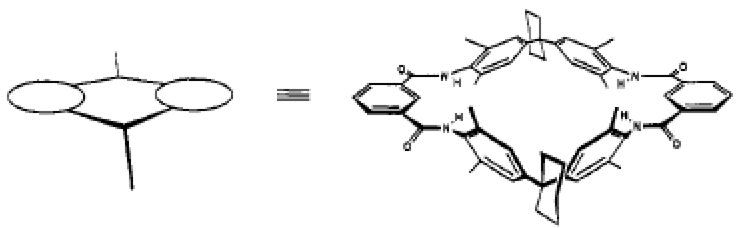
3

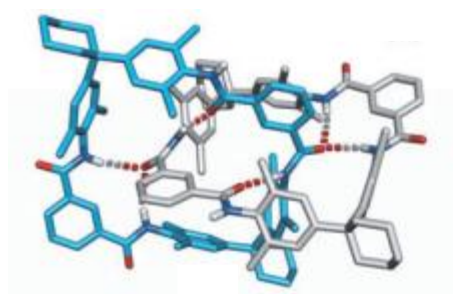


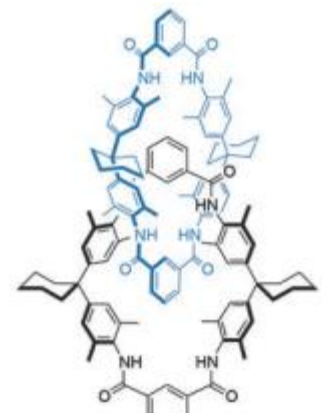


3

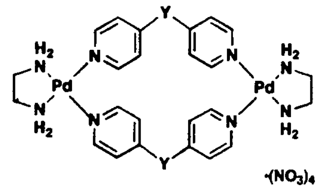




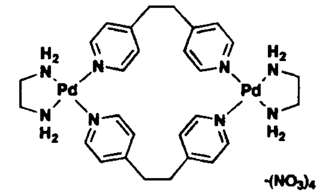


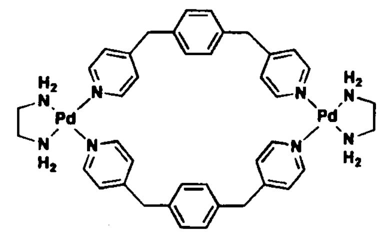


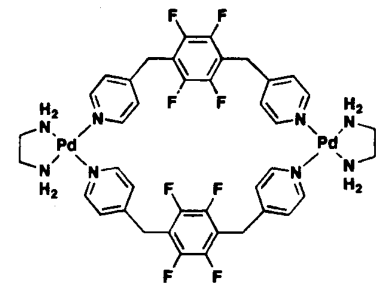
56
34%

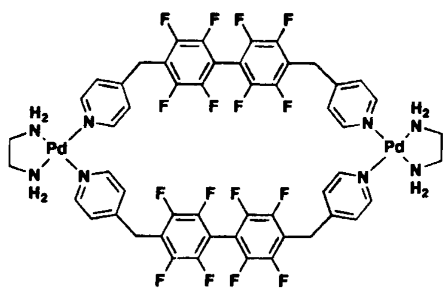


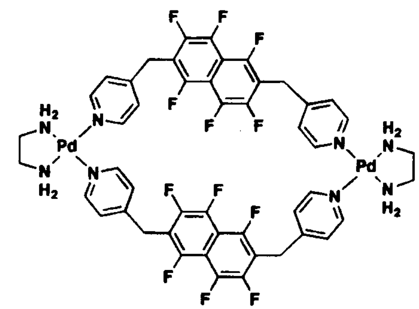
$Y = CH_2$
$Y = C(OH)_2$

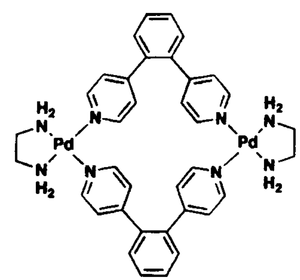


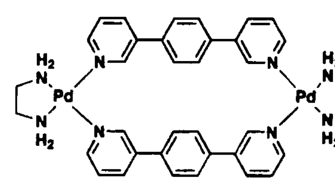




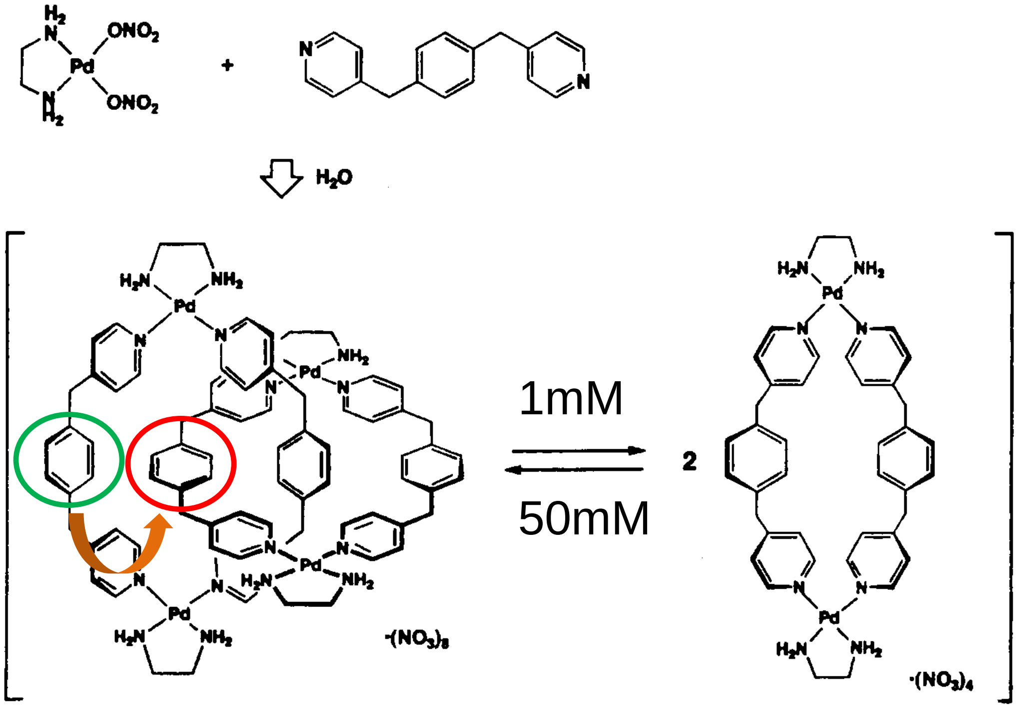




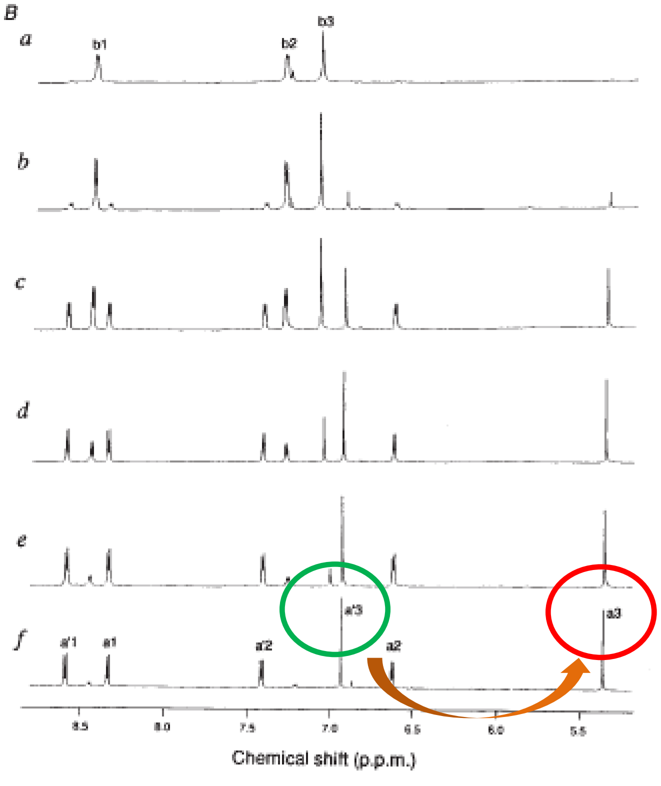




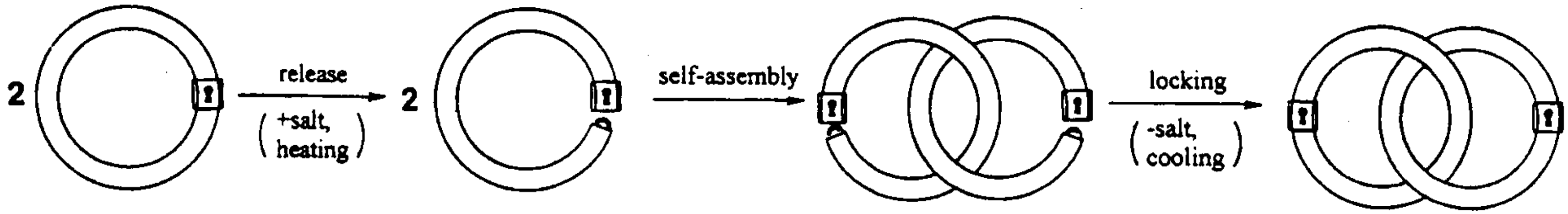
Catenanes

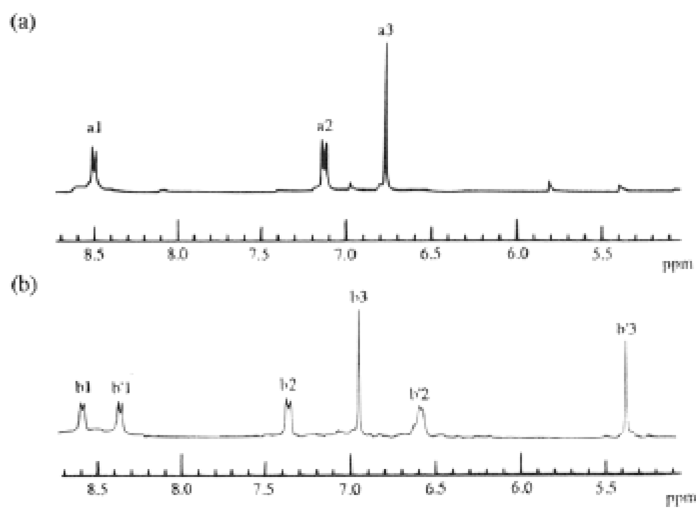


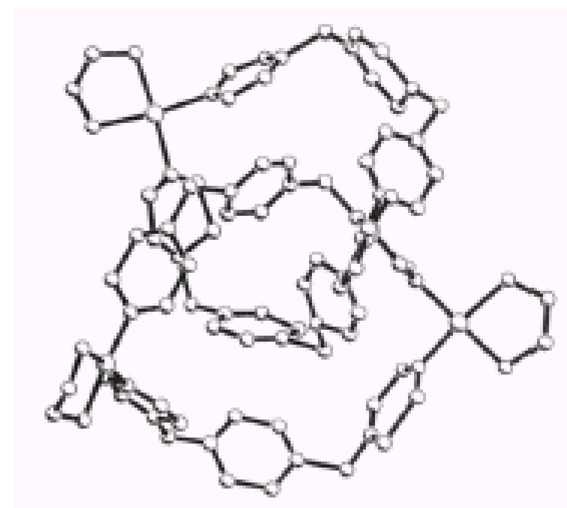
H2O
1mM
50mM
2
·(NO3)8
·(NO3)4



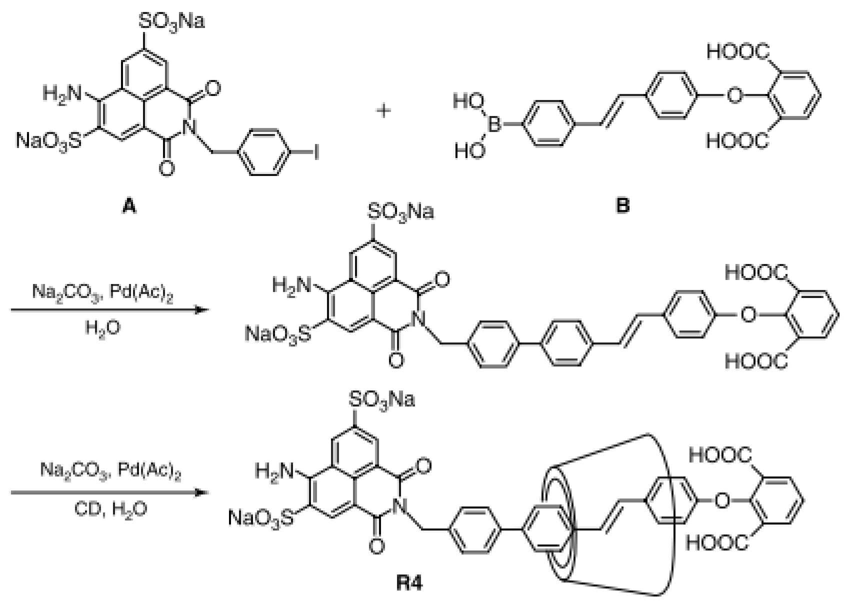
B
a
b
c
d
e
f
b1
b2
b3
a'1
a1
a'2
a'3
a2
a3
Chemical shift (p.p.m.)


2
release
(+salt, heating)
2
self-assembly
locking
(-salt, cooling)

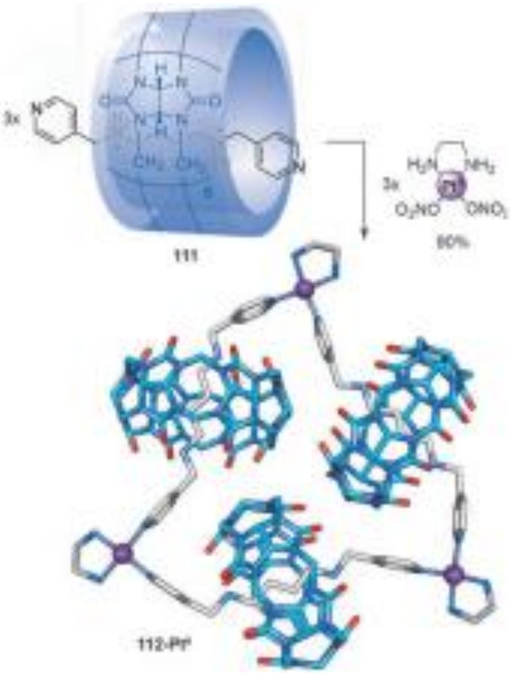

(a)
a1
a2
a3
8.5
8.0
7.5
7.0
6.5
6.0
5.5
ppm
(b)
b1
b'1
b2
b3
b'2
b'3
8.5
8.0
7.5
7.0
6.5
6.0
5.5
ppm



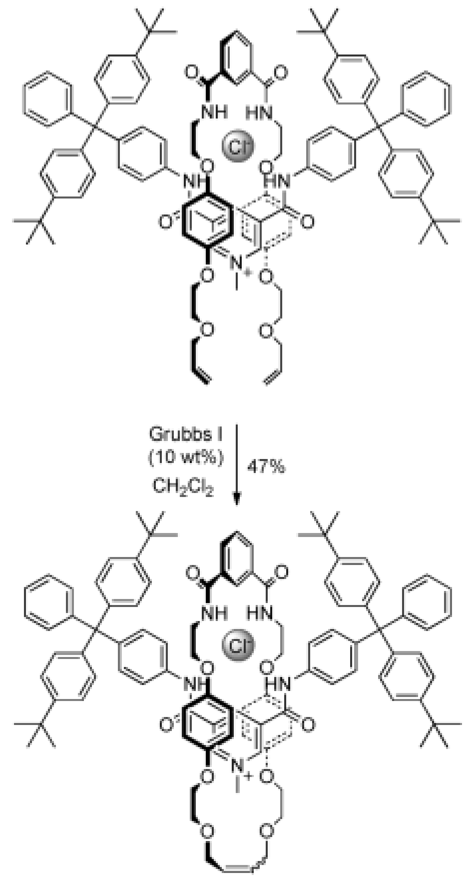
Hydrophobic effect



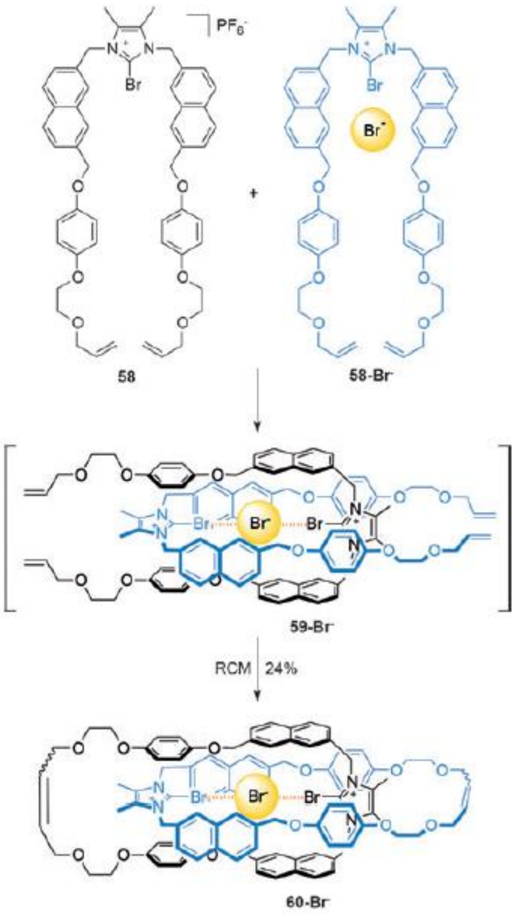
Hydrophobic effect



Anion templating



Halogen bond templating



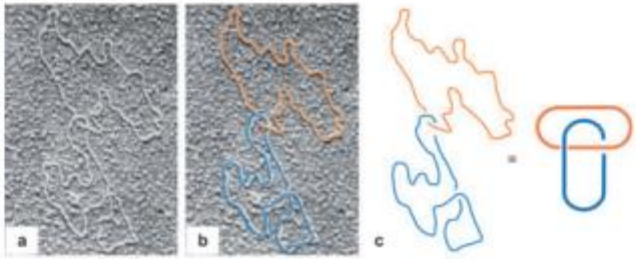
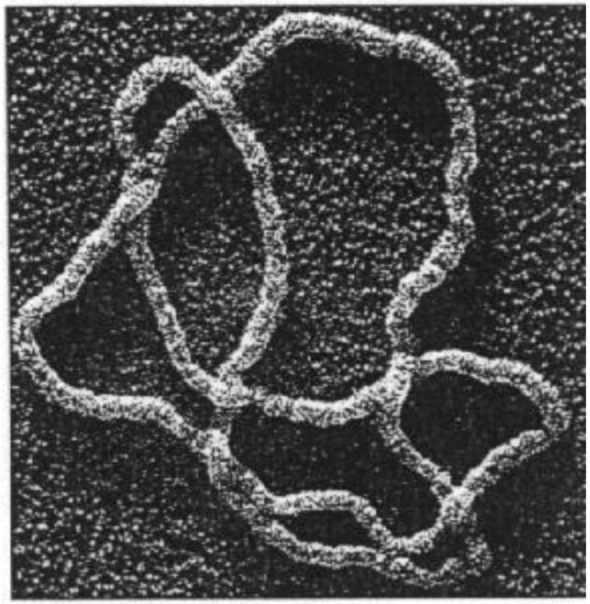


Figure 4. a) Electron micrograph of circular DNA revealing a catenane topology. b,c) Highlighting the two component rings of the DNA catenane as a Hopf link. Modified from Ref. [23] with permission.



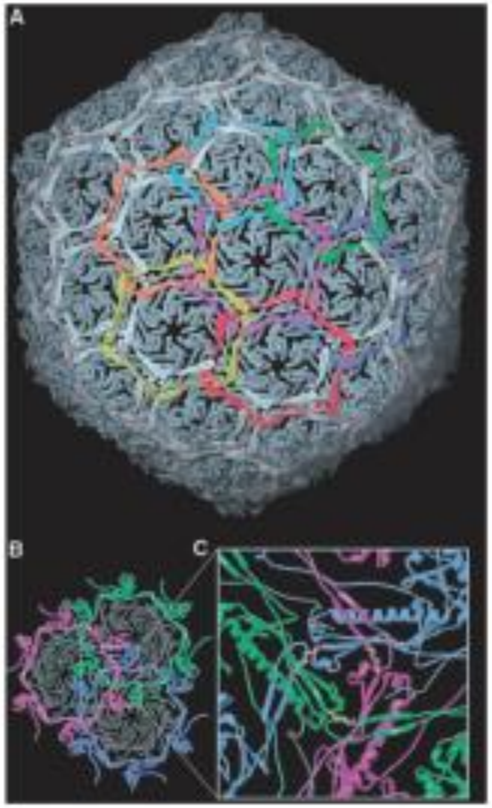
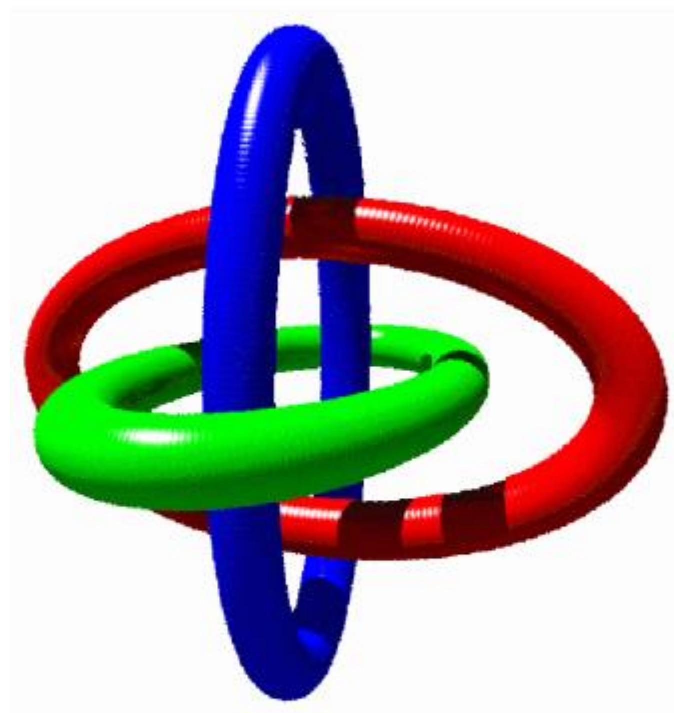


Figure 5. The "chainmail" arrangement of proteins found in bacteriophage HK97s capsid (colored sections highlight the individual protein rings). a) The repeating pattern of interlocking proteins which constitute the spherical capsid. b) A cross-section of the capsid in which three protein rings interlock 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.

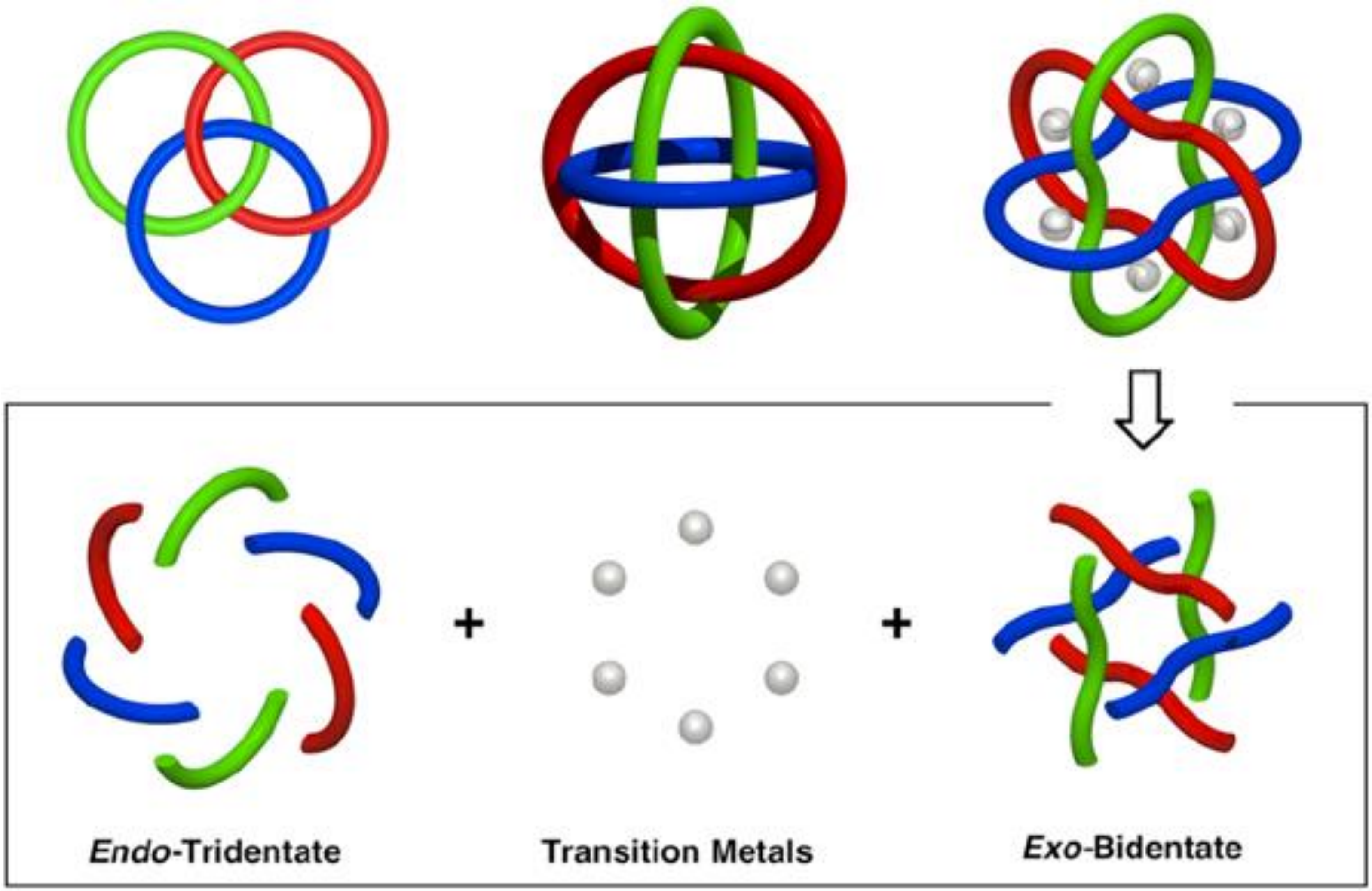
Molecular Borromean Rings

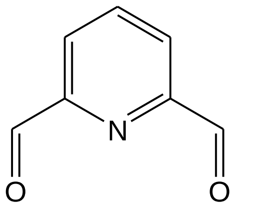
Kelly S. Chichak,[1] Stuart J. Cantrill,[1] Anthony R. Pease,[1]
Sheng-Hsien Chiu,[1] Gareth W. V. Cave,[2] Jerry L. Atwood,[2]
J. Fraser Stoddart[1*]

28 MAY 2004 VOL 304 SCIENCE www.sciencemag.org

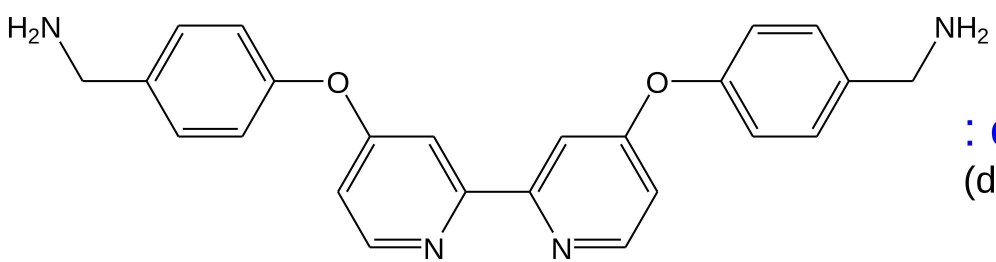


Borromean Ring

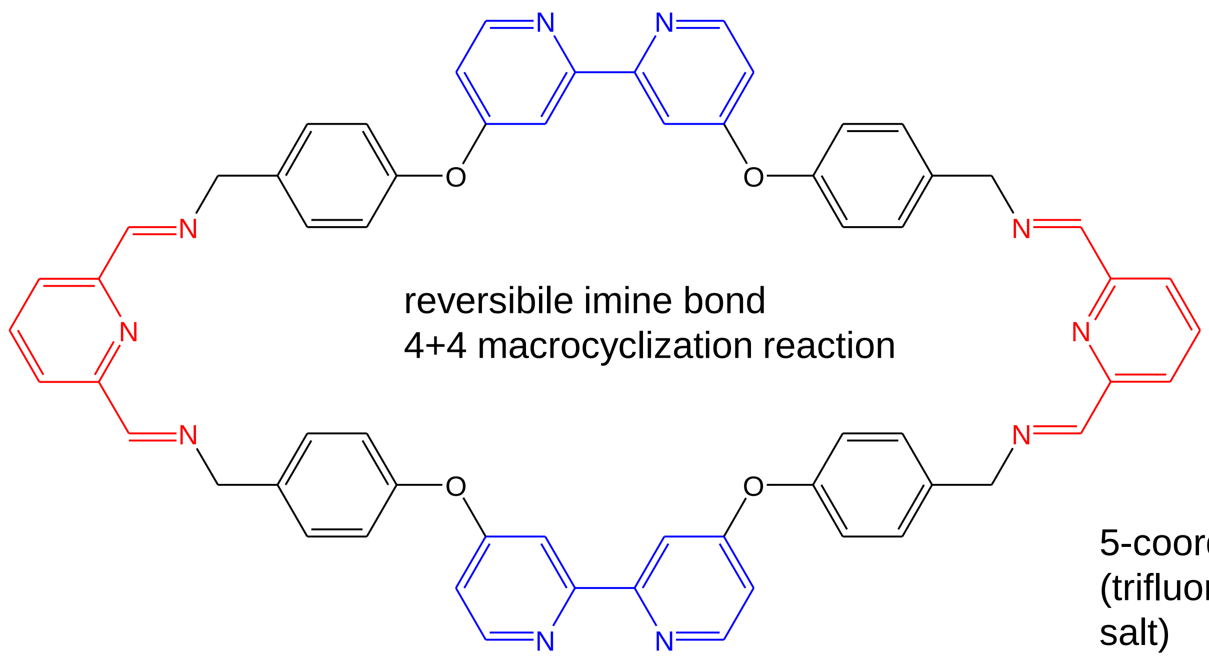




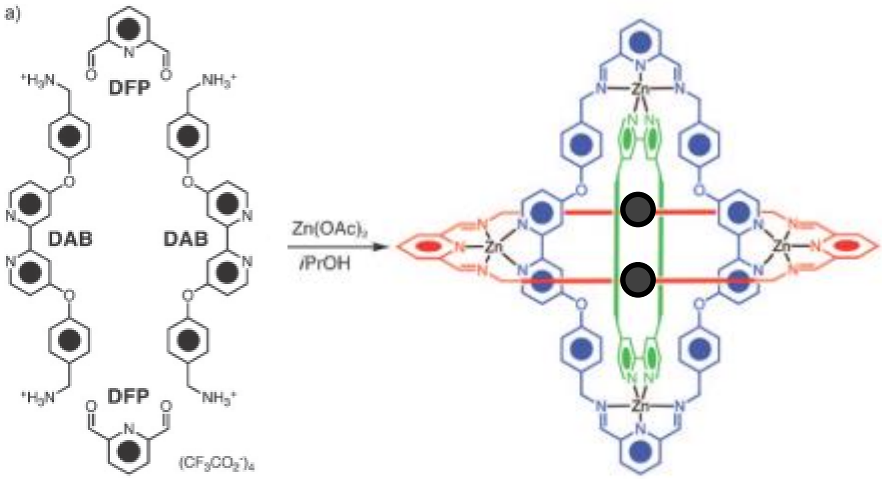
: endo-tridentate (2,6 diformilpyiridine DFP)



: exo-bidentate
(diamminobipyridiyl ligand DAB)



5-coordinated Zn(II)
(trifluoroacetate
salt)



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

Charge: 12^+
Counterions: $12TFA^-$

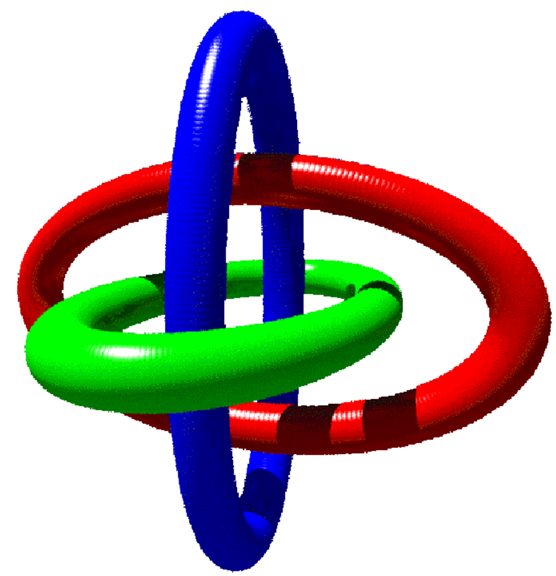
endo-tridentate
2,6 diformilpyiridine (DFP)

exo-bidentate
diamminobipyridiyl ligand (DAB)

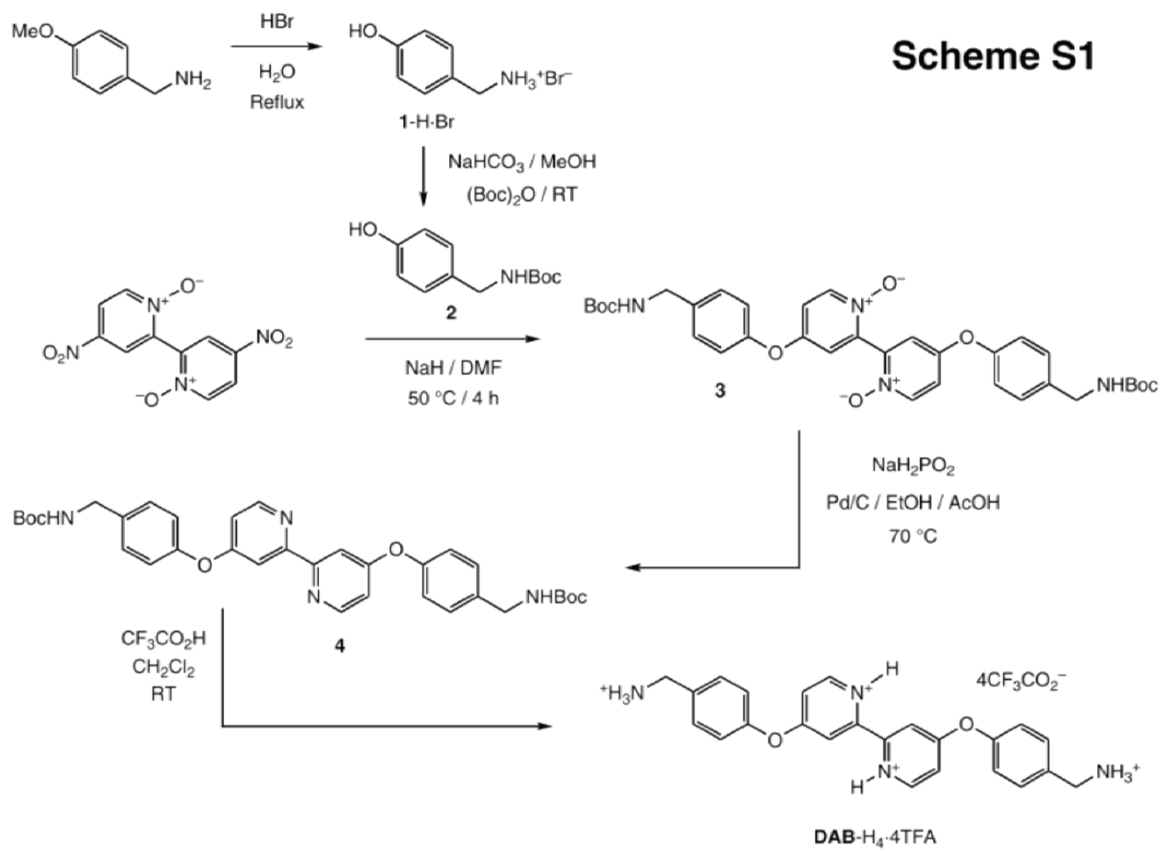
5-coordinated Zn(II)
(triflouroacetatate salt)

reversibile imine formation

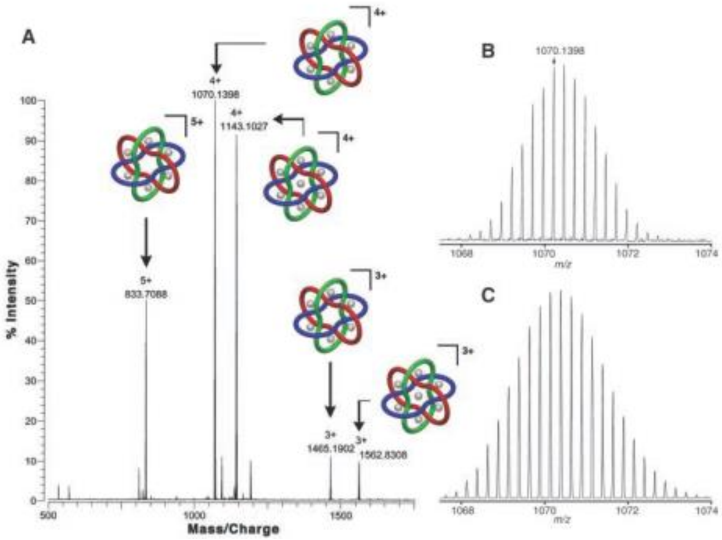
reversible coordination



Scheme S1



MeO
NH2
HBr
H2O
Reflux
HO
NH3+Br−
1-H·Br
NaHCO3 / MeOH
(Boc)2O / RT
HO
NHBoc
2
NaH / DMF
50 °C / 4 h
N+
O−
O2N
NO2
BocHN
O
NHBoc
3
NaH2PO2
Pd/C / EtOH / AcOH
70 °C
BocHN
N
NHBoc
4
CF3CO2H
CH2Cl2
RT
+H3N
H
4CF3CO2−
NH3+
DAB-H4·4TFA



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

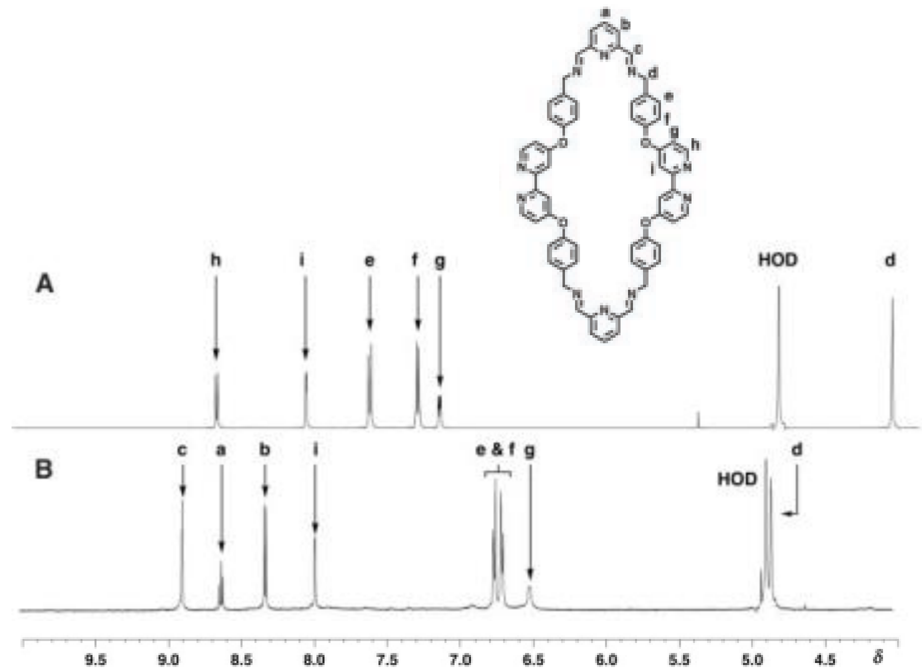
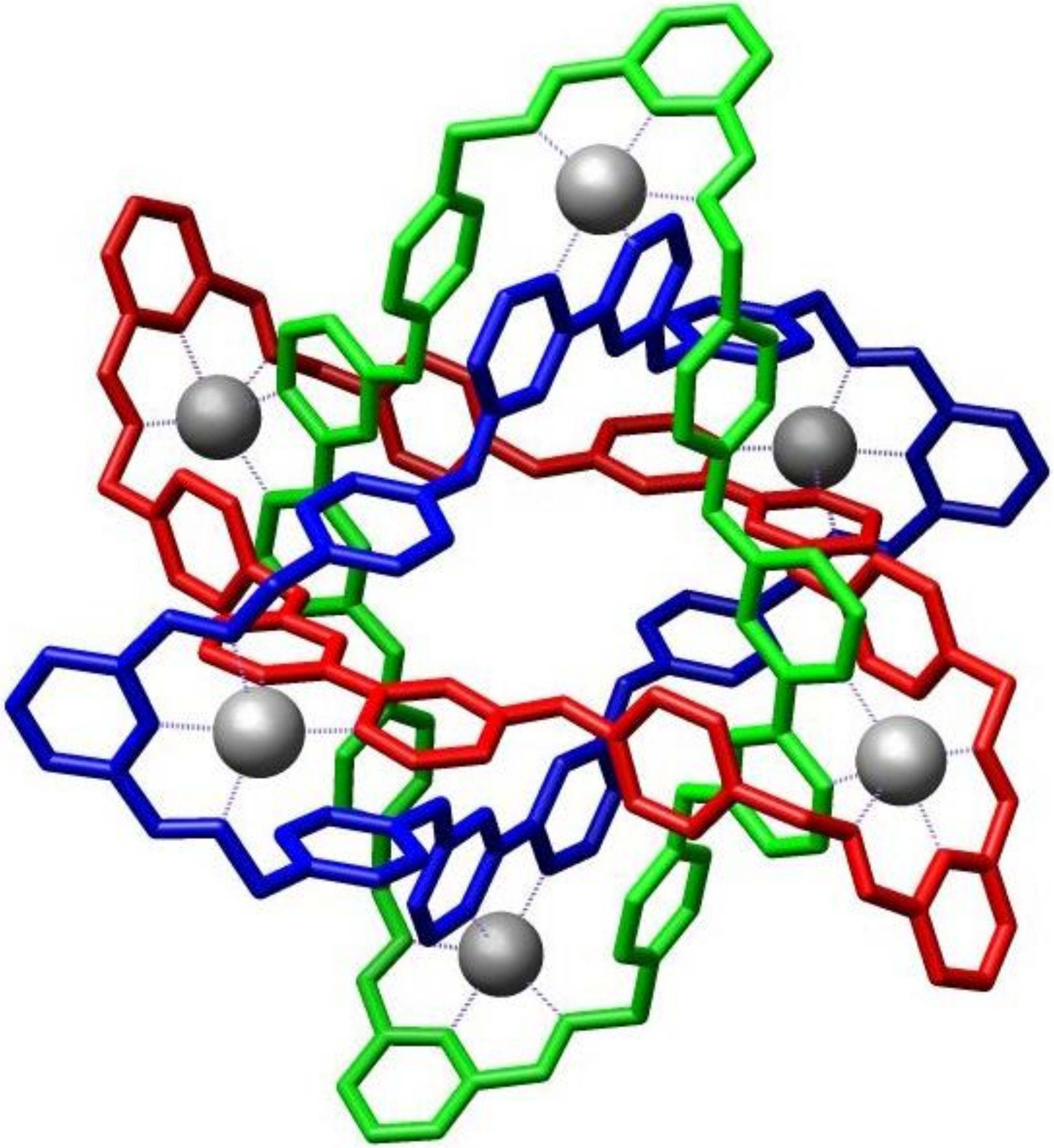
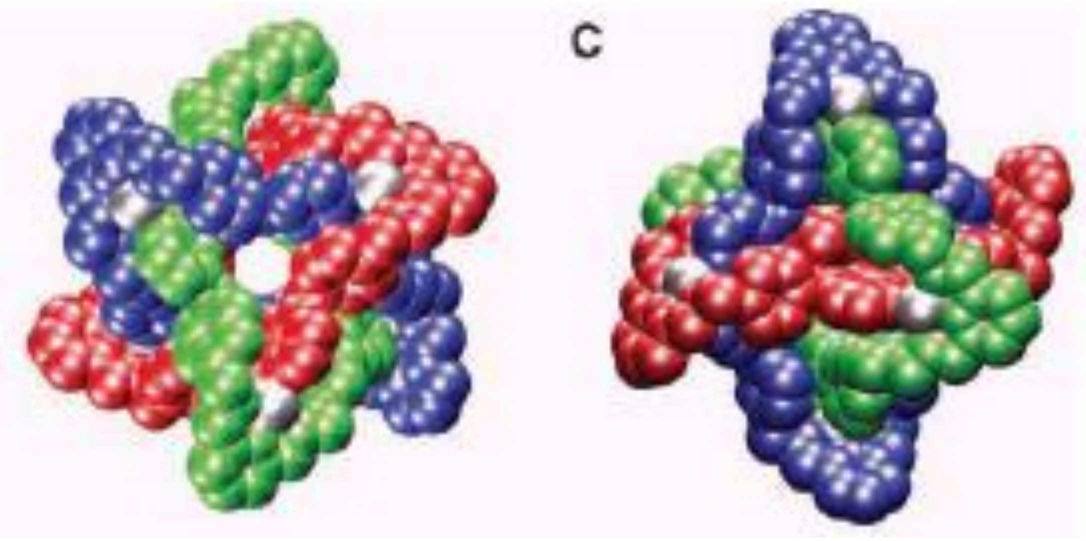
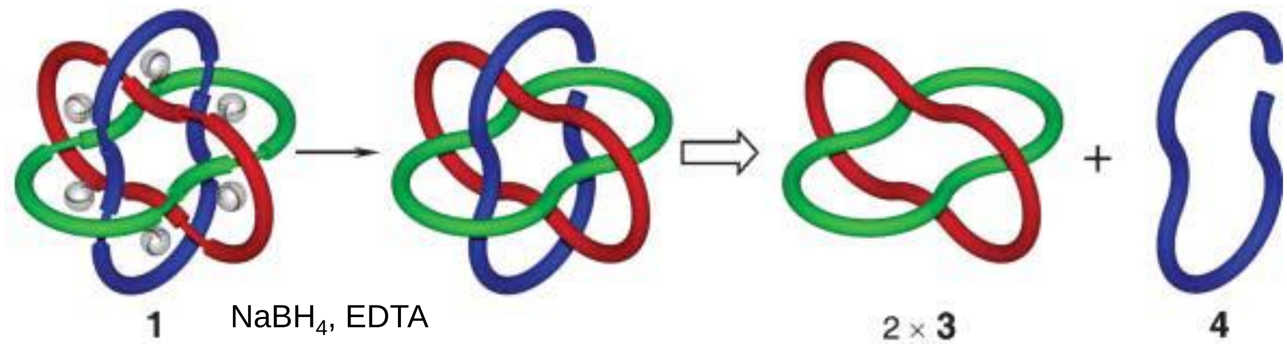


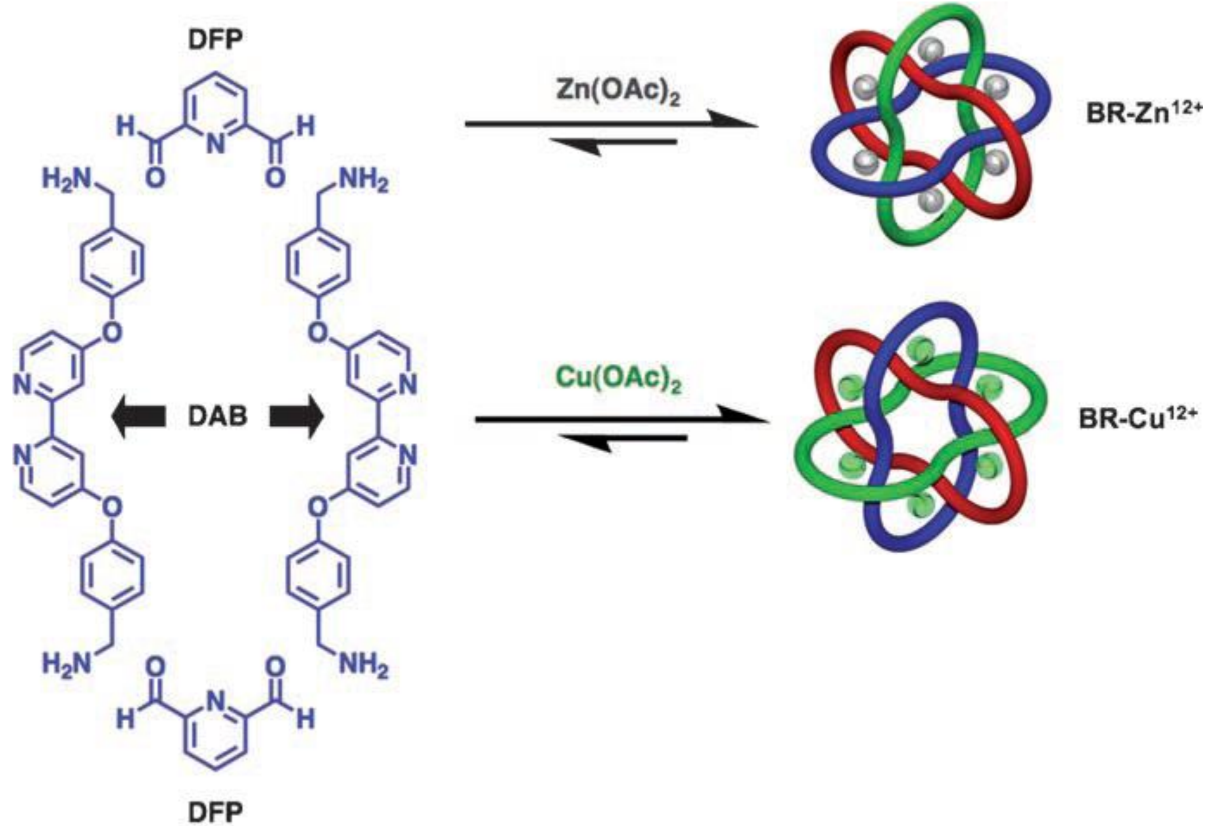
Fig. 2. The ^{1}H NMR spectra (CD_3OD, 298 K) of (**A**) the *exo*-bidentate ligand-containing starting material **DAB**-H_4·4TFA (500 MHz), (**B**) the molecular Borromean rings **BR**·12TFA (600 MHz)





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


1
NaBH$_4$, EDTA
2 × 3
4


DFP
DAB
DFP
Zn(OAc)$_2$
BR-Zn^{12+}
Cu(OAc)$_2$
BR-Cu^{12+}

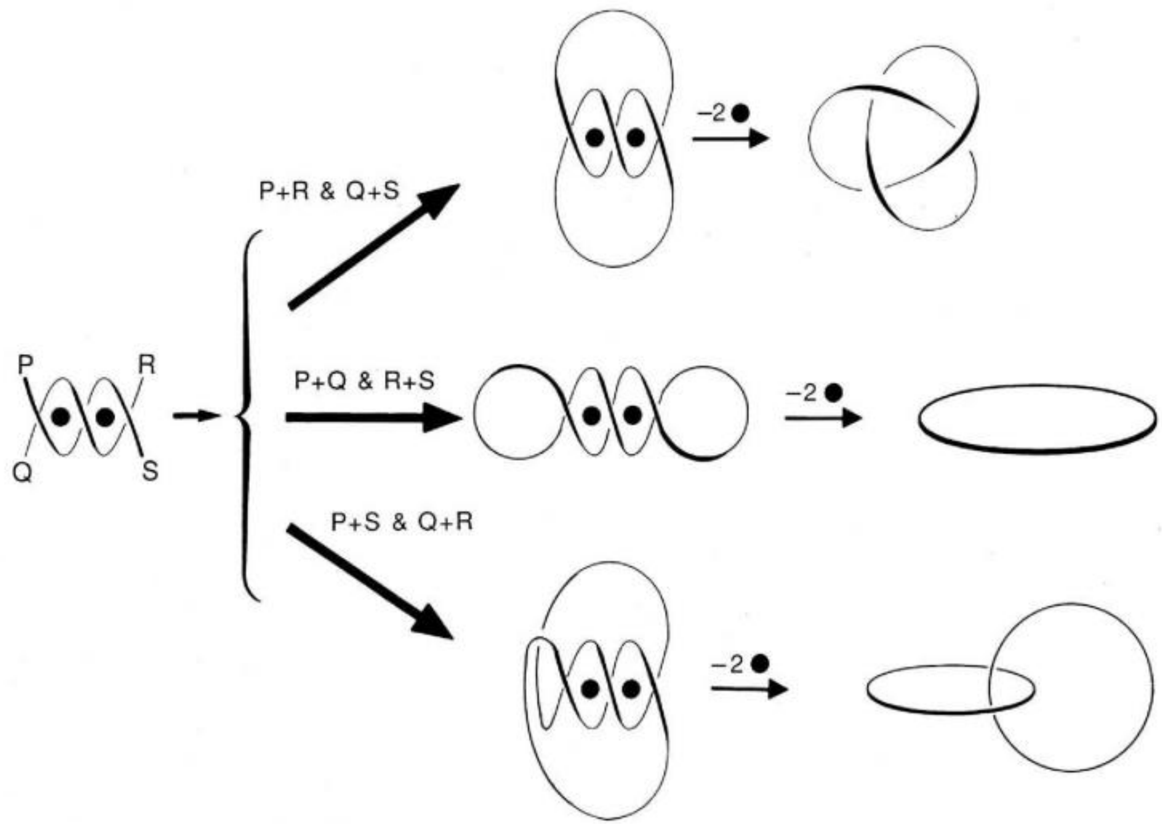
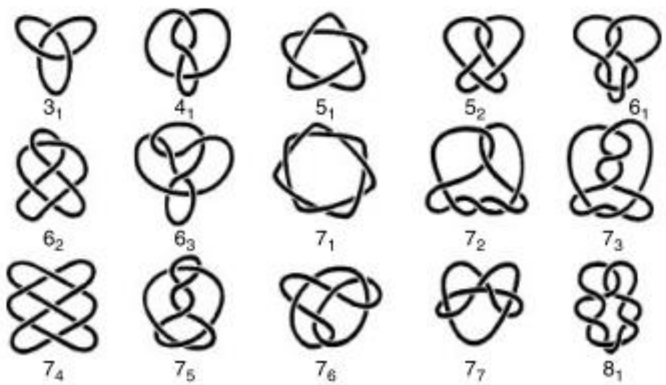


Figure 23. A guide for demonstrating the synthesis of topologically different molecules from the precursor to the trefoil knot.

Molecular Knots and Links



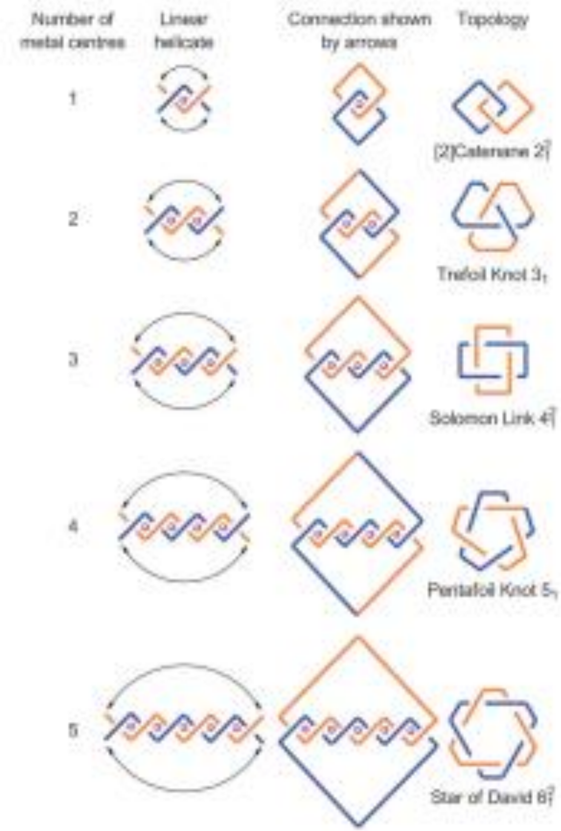
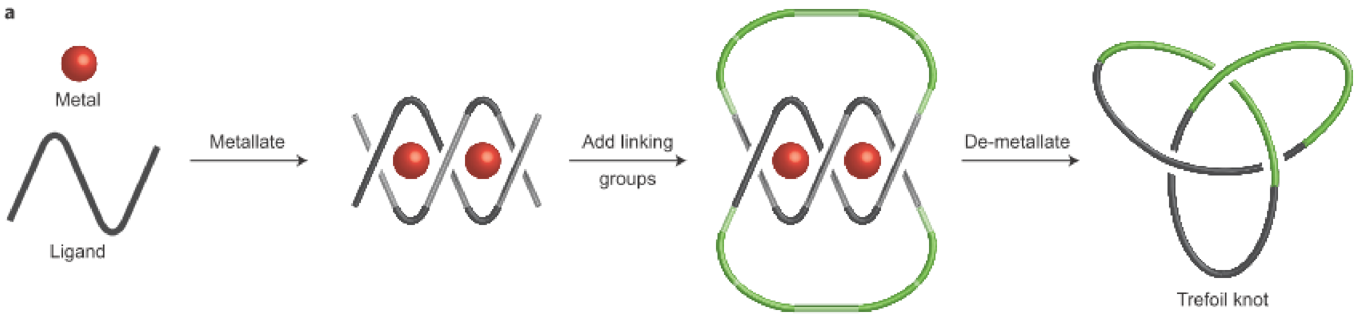


Fig. 3 The linear helicate strategy to interlocked molecules introduced by Sauvage.[48] To date the first three entries of this table have been realised experimentally using this strategy, generating catenanes,[4] trefoil knots[38] and doubly-interlocked [2]catenanes (Solomon links)[47] using one, two 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]

a



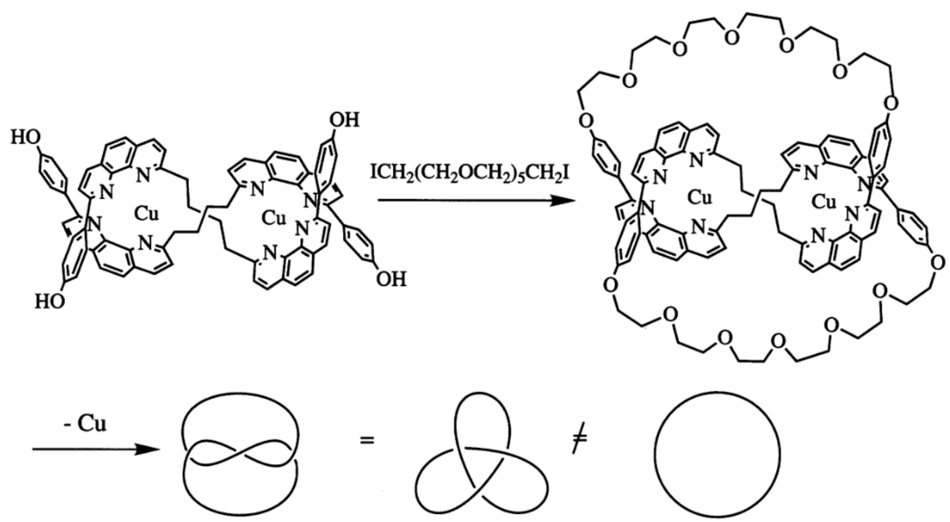


Fig. 8. Synthesis of the first trefoil knot using a two-anchor helical template.

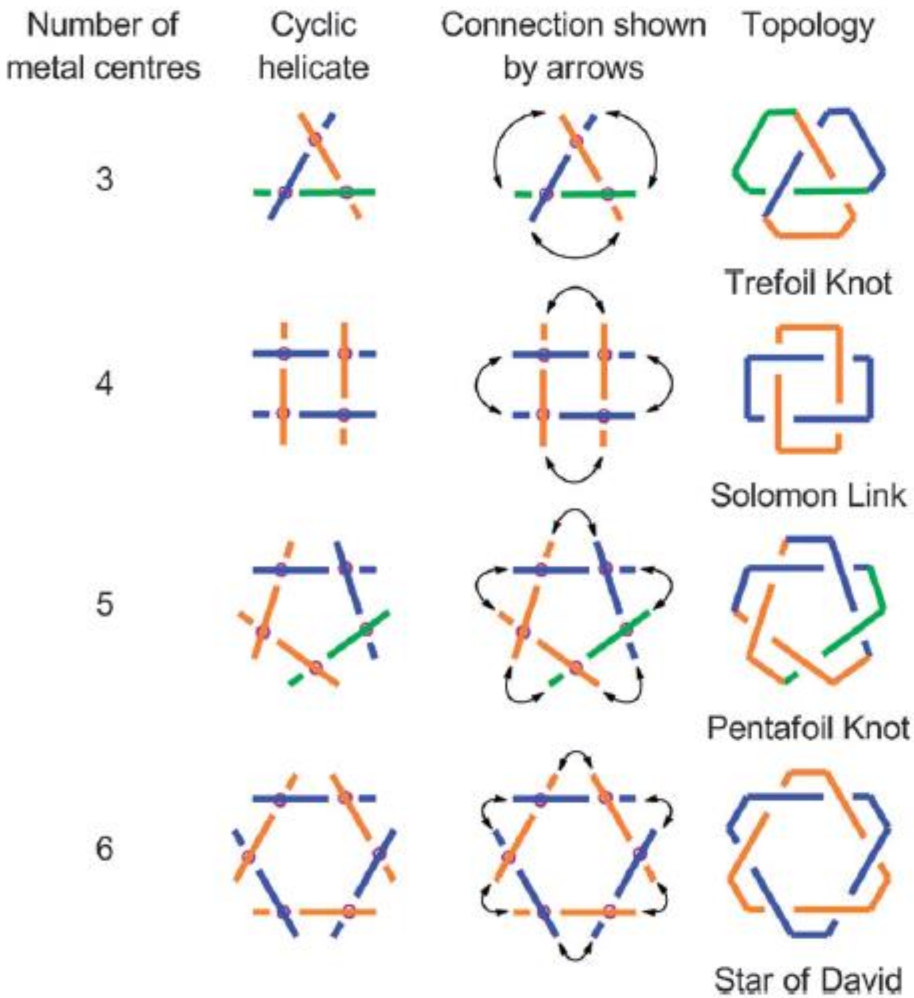


Fig. 5 The potential of circular metal helicates to form molecular knots and links by connecting adjacent end-groups. To date only a pentafoil knot has been prepared through this strategy.[73]

nature chemistry

ARTICLES

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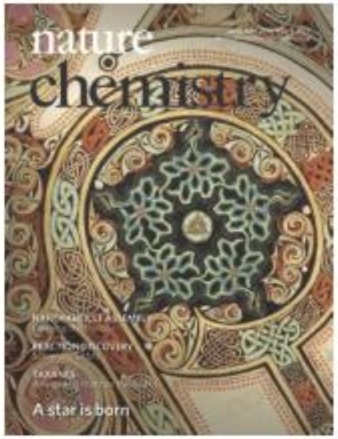
A synthetic molecular pentafoil knot

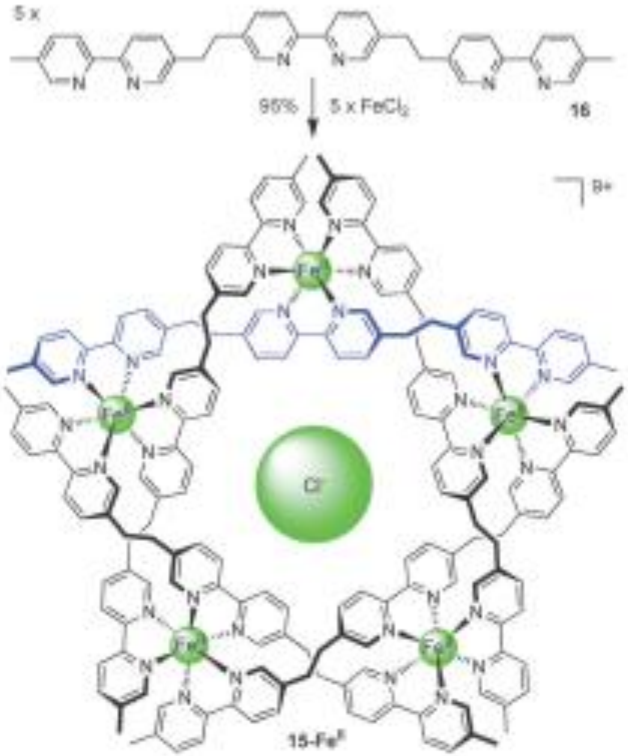
Jean-François Ayme[1], Jonathon E. Beves[1], David A. Leigh[1]*, Roy T. McBurney[1], Kari Rissanen[2] and David Schultz[1]

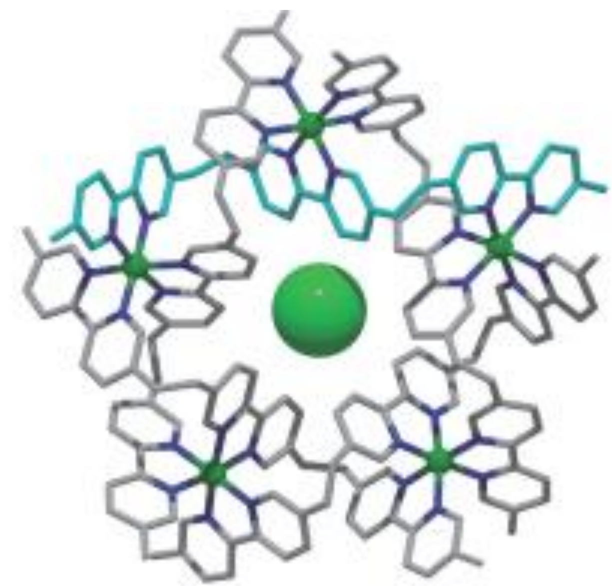


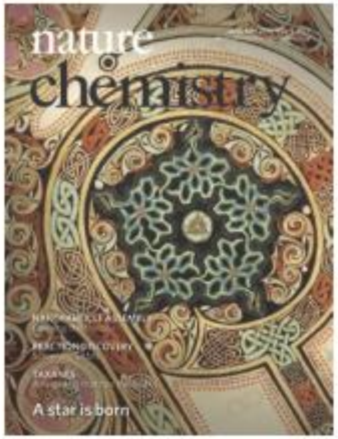
COVER IMAGE

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 **CH···Cl⁻** hydrogen bonds.

Article p15; News & Views p7







COVER IMAGE

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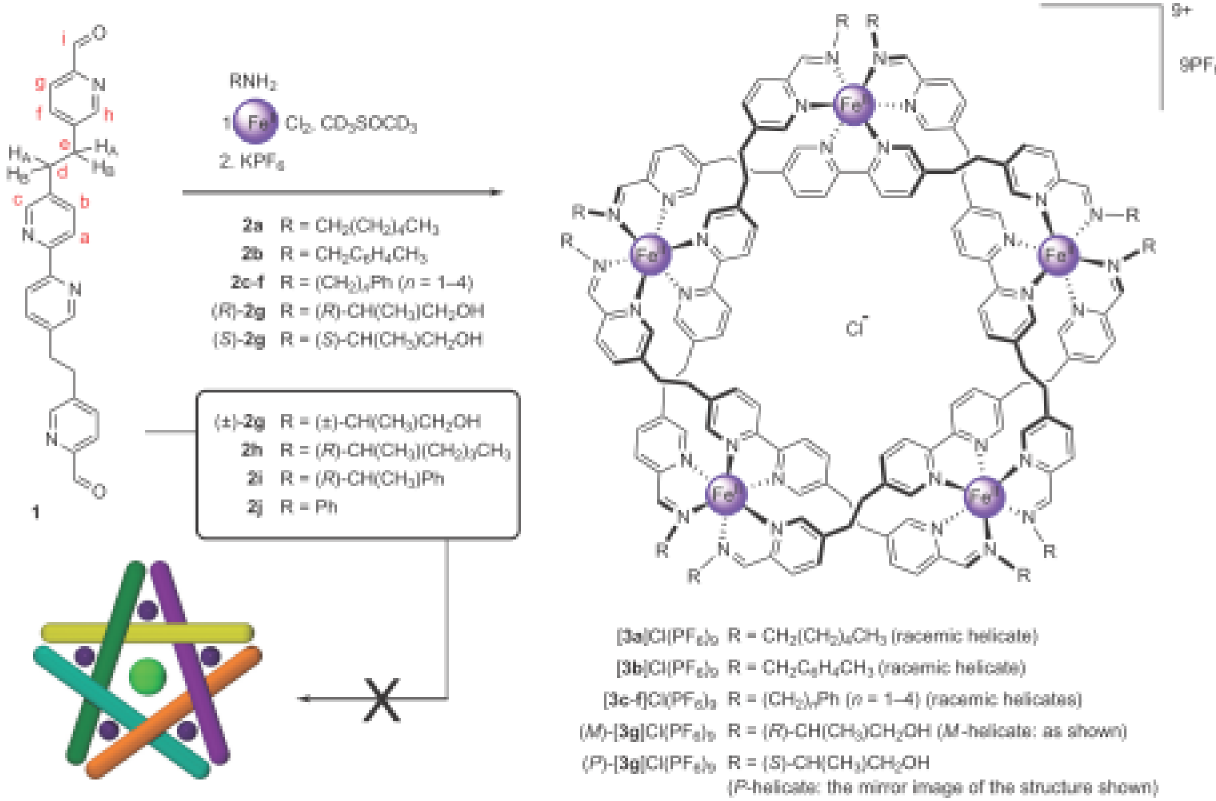
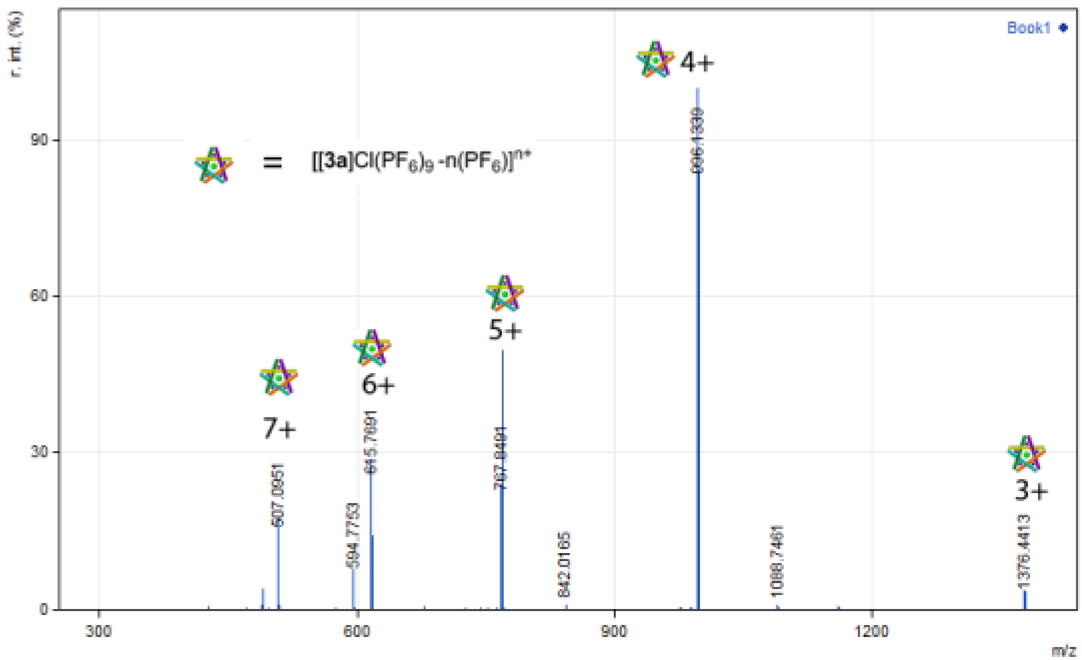
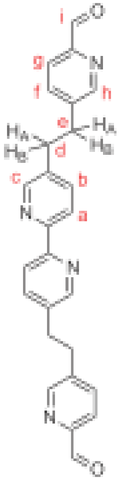
Article p15; News & Views p7

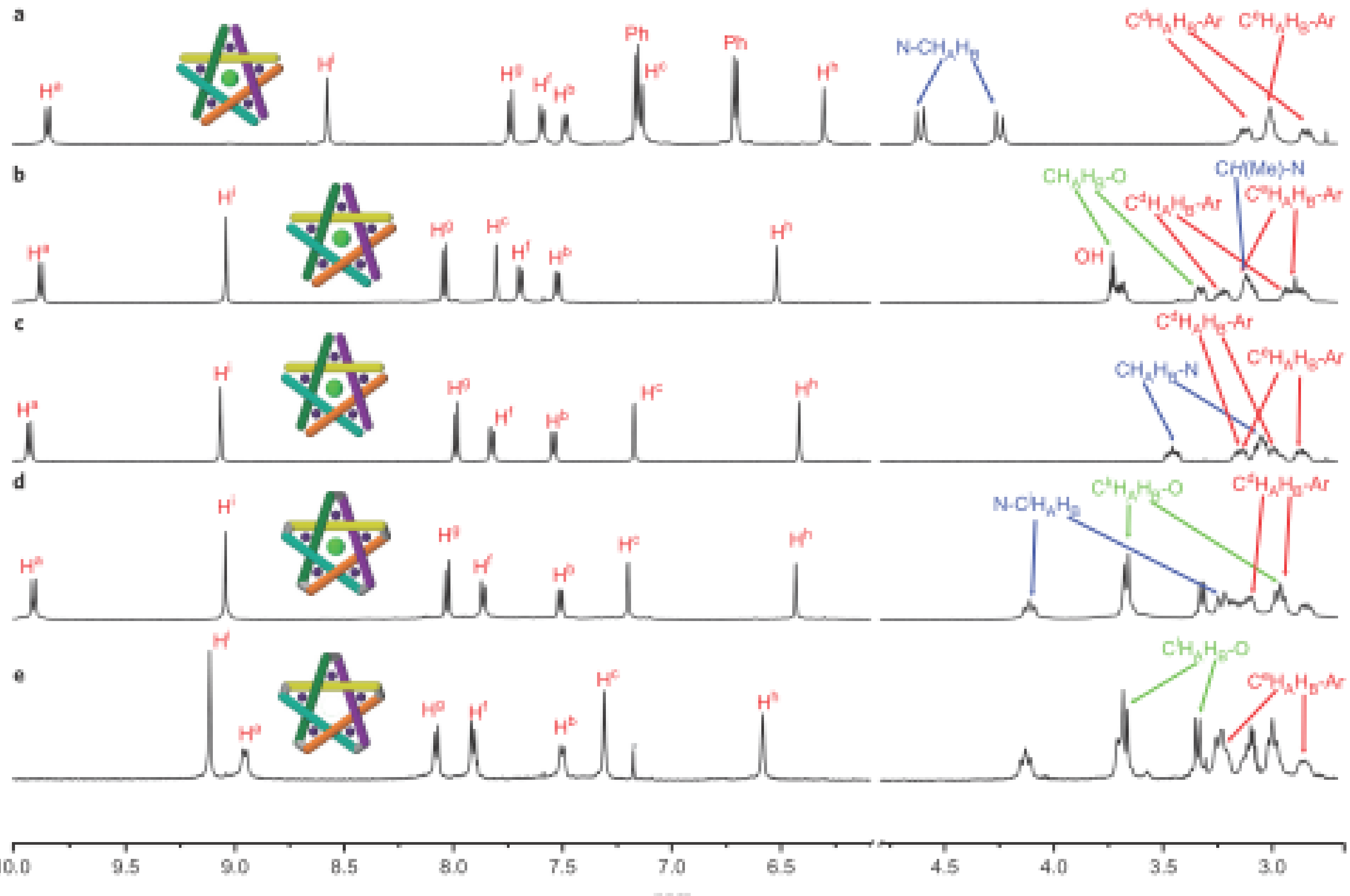




r. int. (%)
Book1
= [[3a]Cl(PF6)9-n(PF6)]n+
4+
5+
6+
7+
3+
996.1339
767.8491
615.7891
607.0951
594.7753
842.0165
1088.7461
1376.4413
0
30
60
90
300
600
900
1200
m/z



1



a
b
c
d
e
Ph
N-CH$_A$H$_B$
CH$_A$H$_B$-O
CH(Me)-N
OH
CH$_A$H$_B$-N
10.0
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8.0
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4.0
3.5
3.0

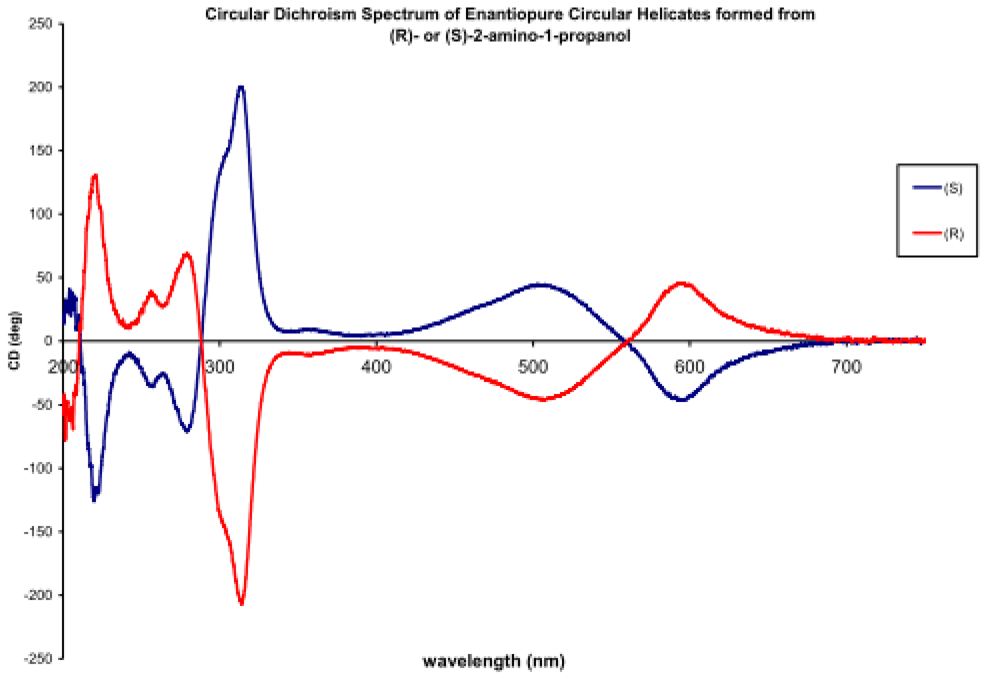
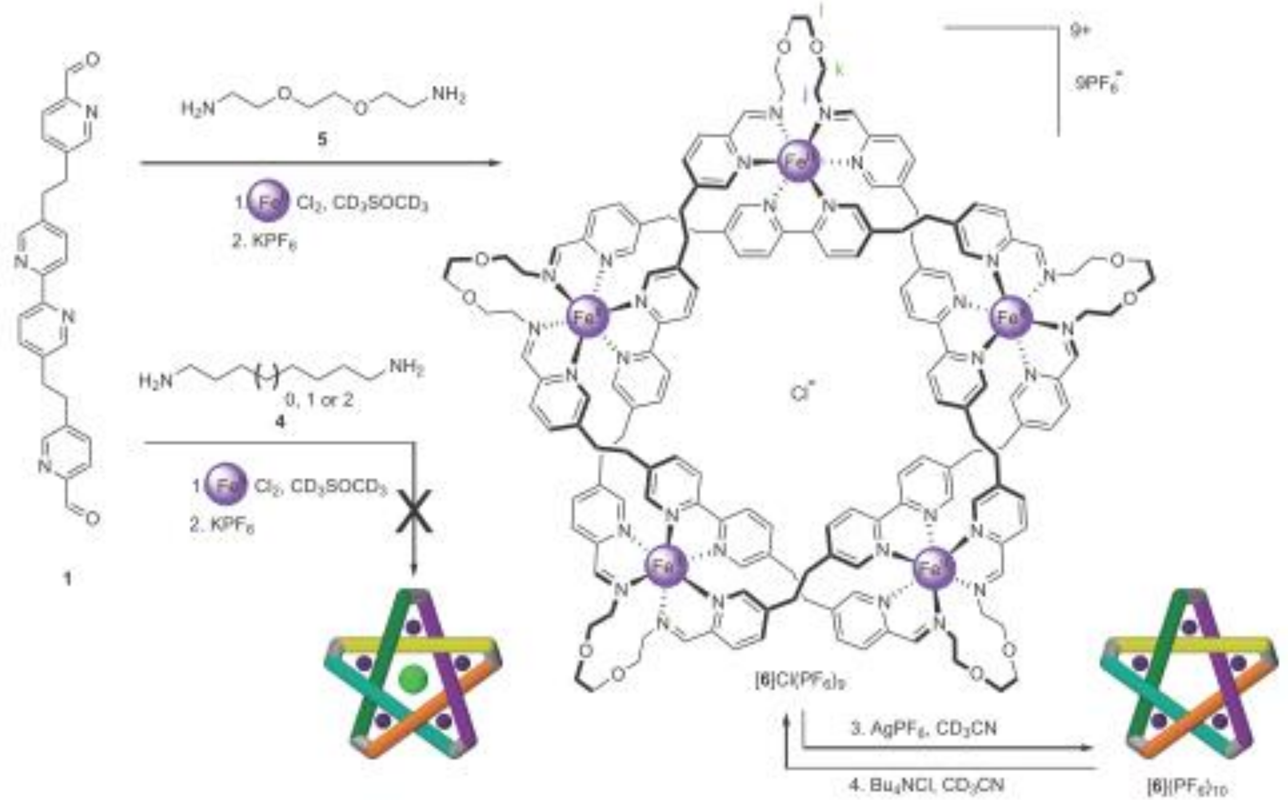


Figure S8 Circular dichroism spectra of (*R*)-[**3g**]Cl$(PF_6)_9$ and (*S*)-[**3g**]Cl$(PF_6)_9$ in MeCN.



5
1. Fe Cl2, CD3SOCD3
2. KPF6
0, 1 or 2
4
1. Fe Cl2, CD3SOCD3
2. KPF6
1
9+
9PF6−
Cl−
[6]Cl(PF6)9
3. AgPF6, CD3CN
4. Bu4NCl, CD3CN
[6](PF6)10

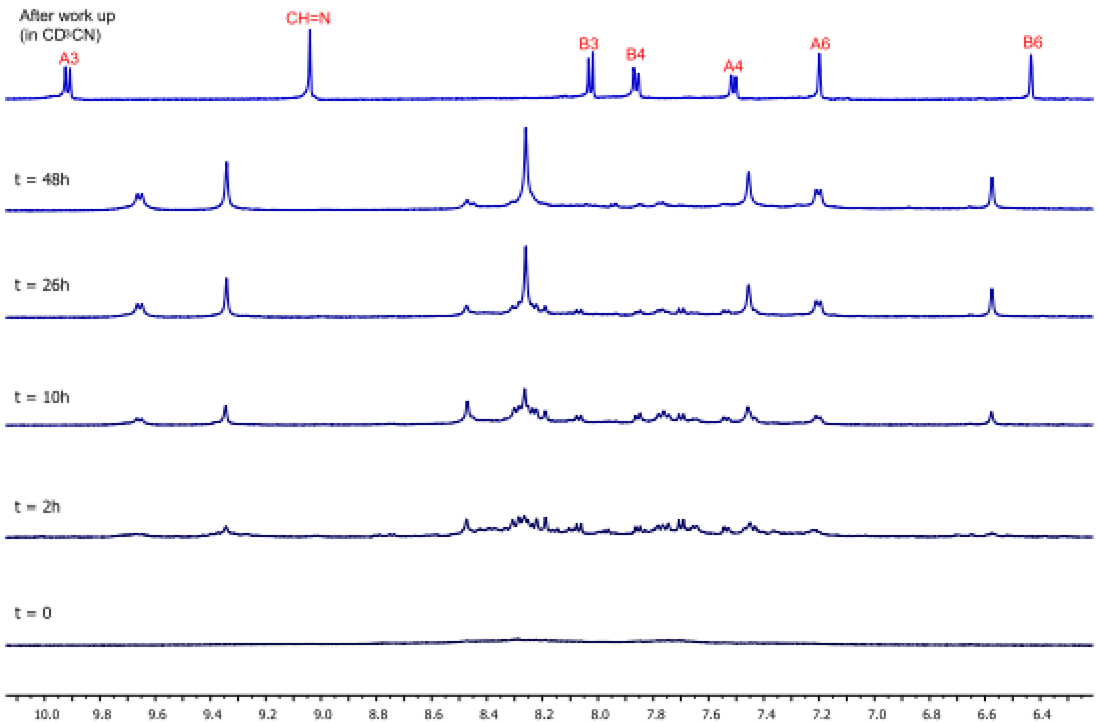
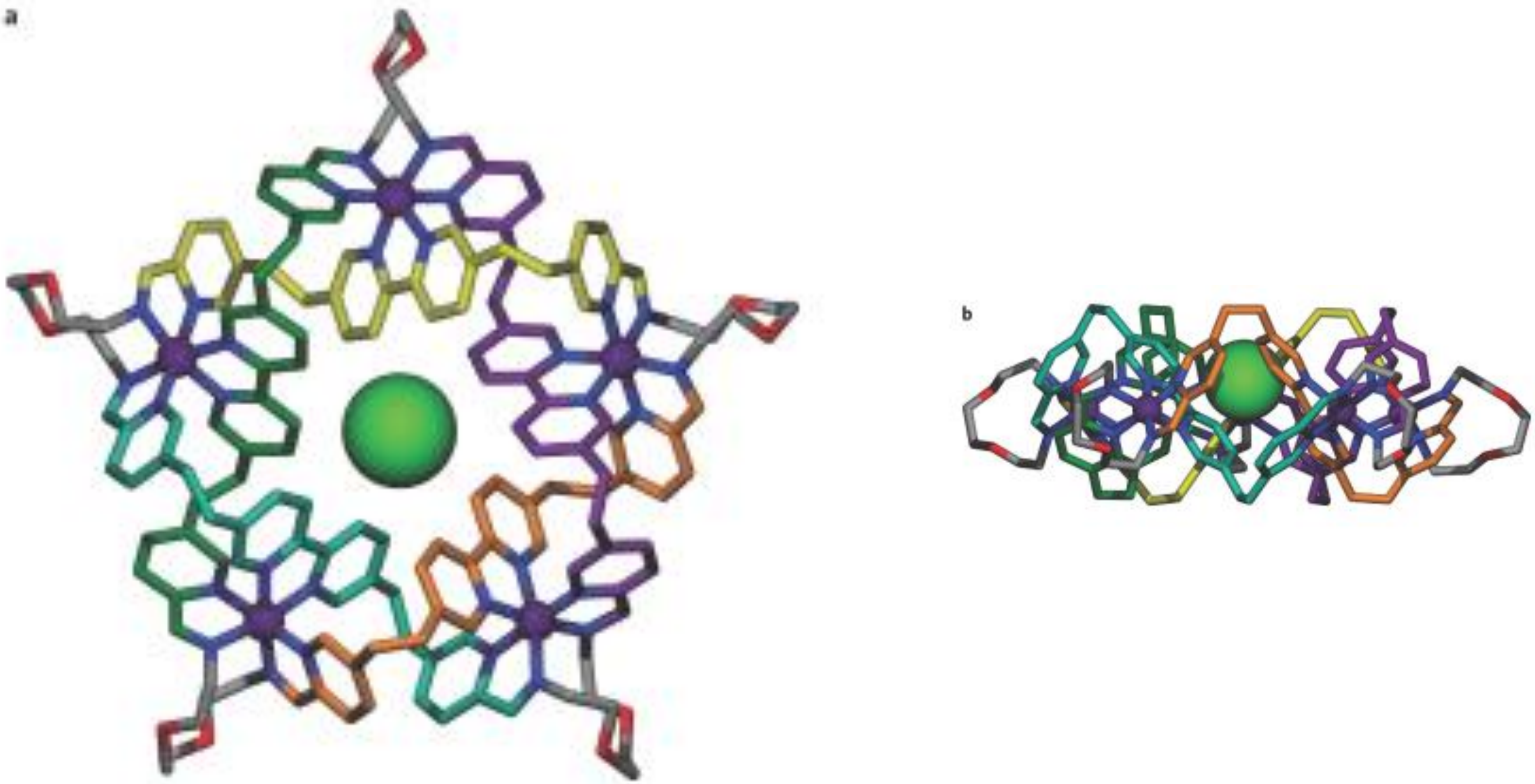


Figure S9 Formation of pentafoil knot [**6**]$^{10+}$ monitored by ^{1}H NMR (DMSO-d$_6$, 500 MHz), aromatic region of spectrum shown. Spectra were collected of the crude reaction mixture after t = 0 (bottom), 2h, 10h, 26h and 48h. The top spectra is of the same sample after work-up (^{1}H NMR in CD_3CN) with ^{1}H NMR assignments indicated.


a
b

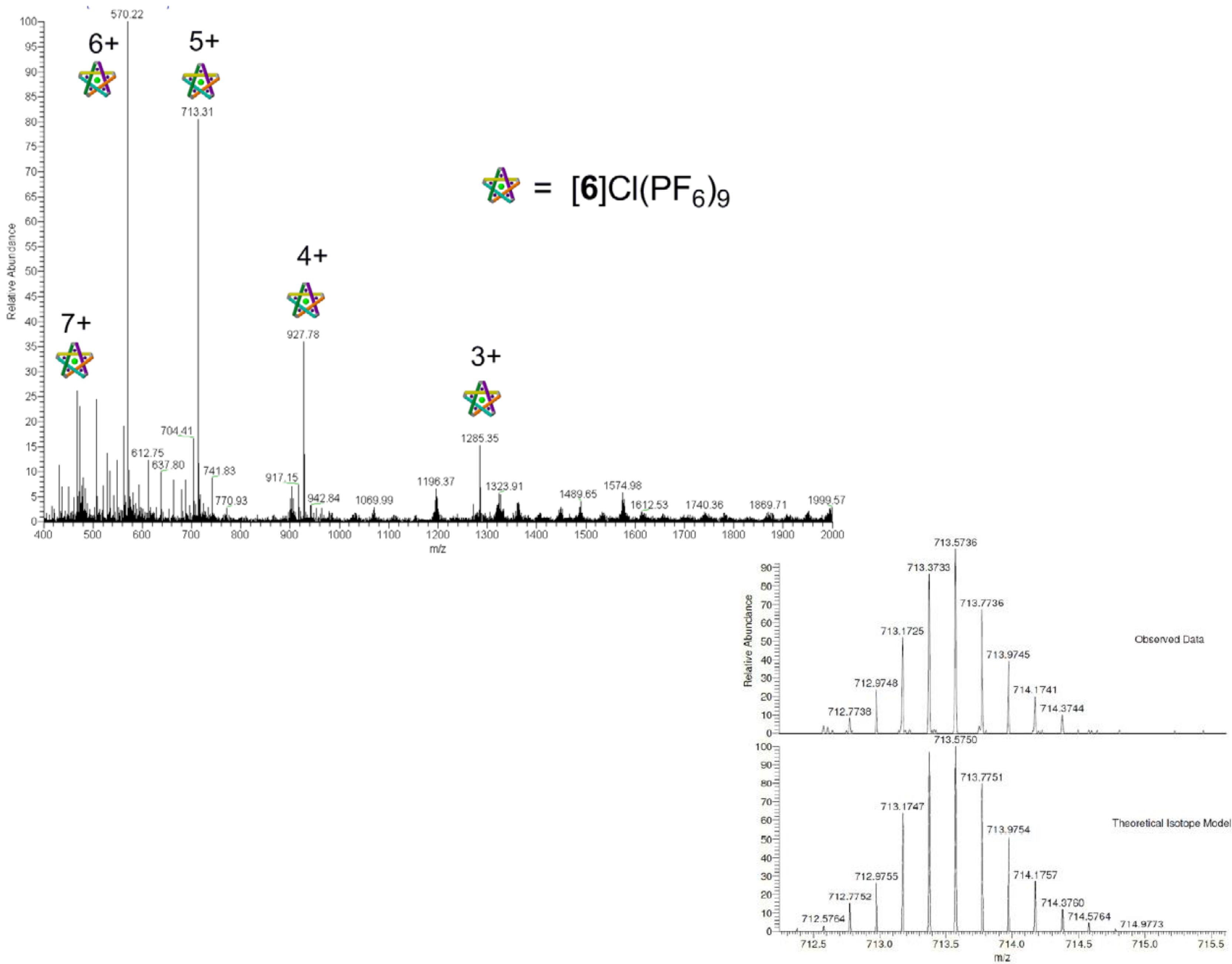


Figure S5 Low-resolution ESI-MS of pentafoil knot [**6**]Cl$(PF_6)_9$ (top), and high-resolution isotope pattern (bottom) of $[M\text{-}4PF_6]^{5+}$ peak.

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*

9260 www.angewandte.org

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

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Template synthesis of molecular knots†

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

Jean-François Ayme,[ab] Jonathon E. Beves,[a] Christopher J. Campbell[a] and David A. Leigh*[ab]

Catenanes
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Catenanes: Fifty Years of Molecular Links

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