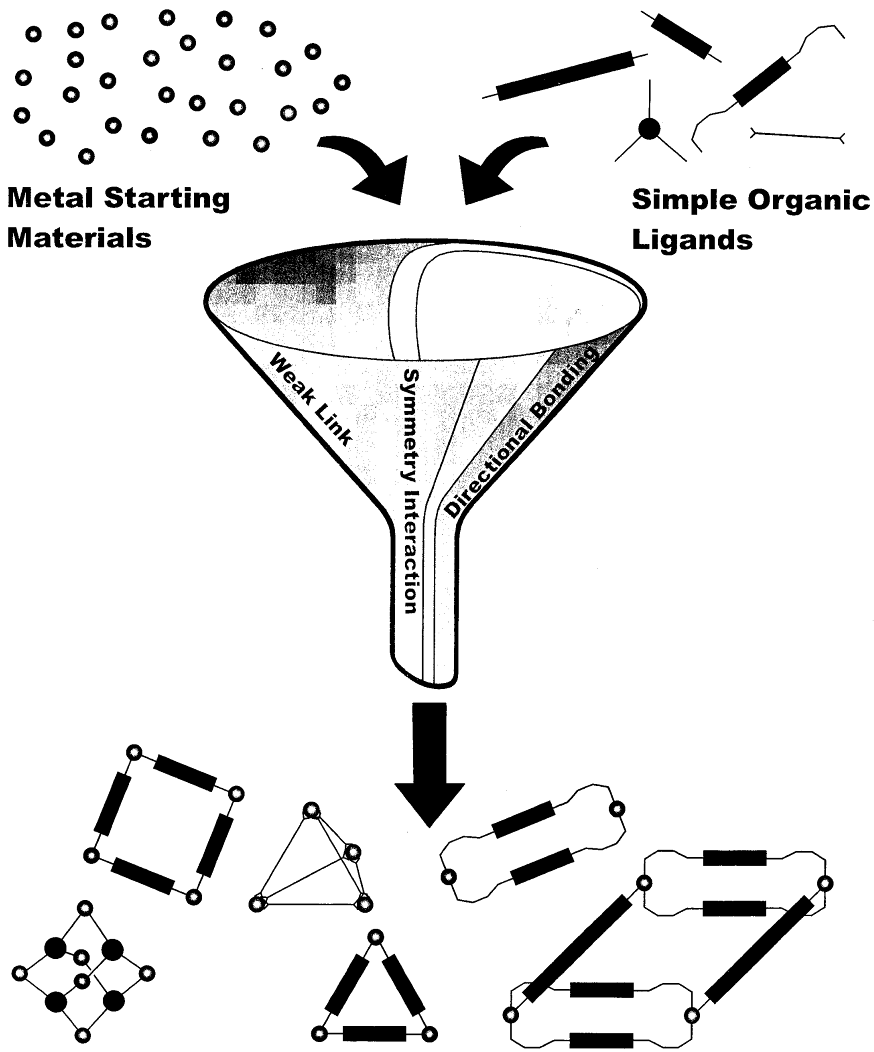
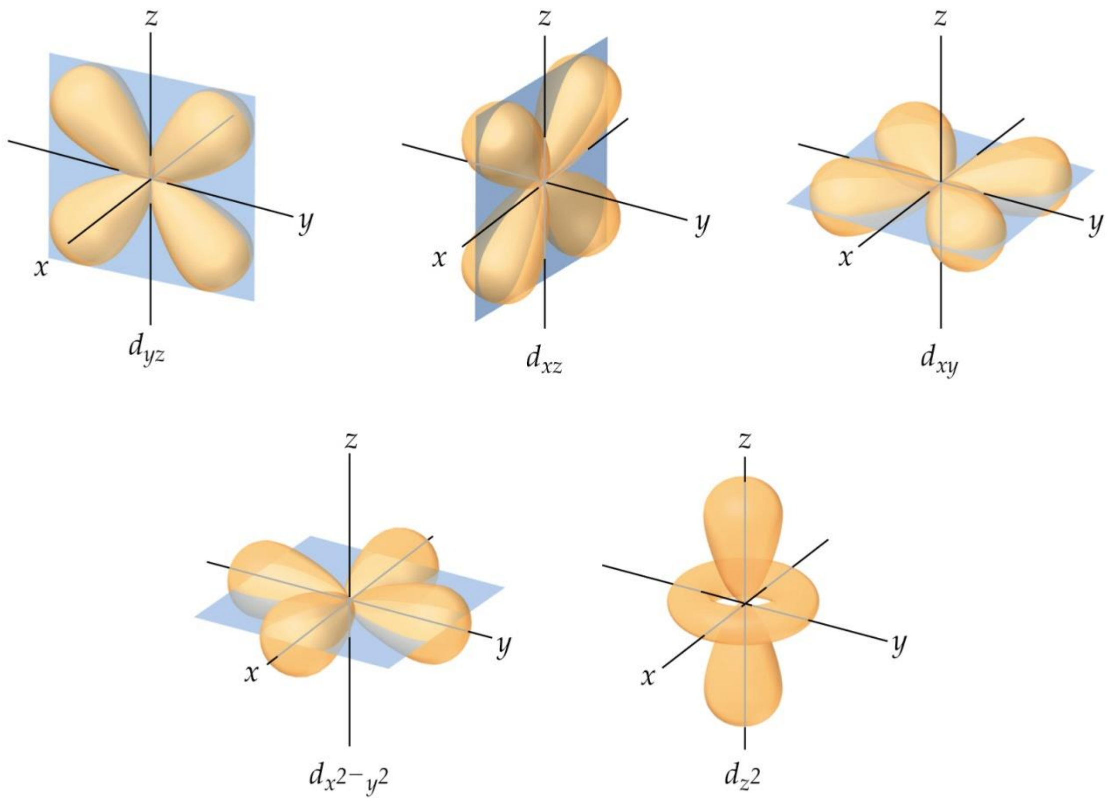
Supramolecular Coordination Chemistry



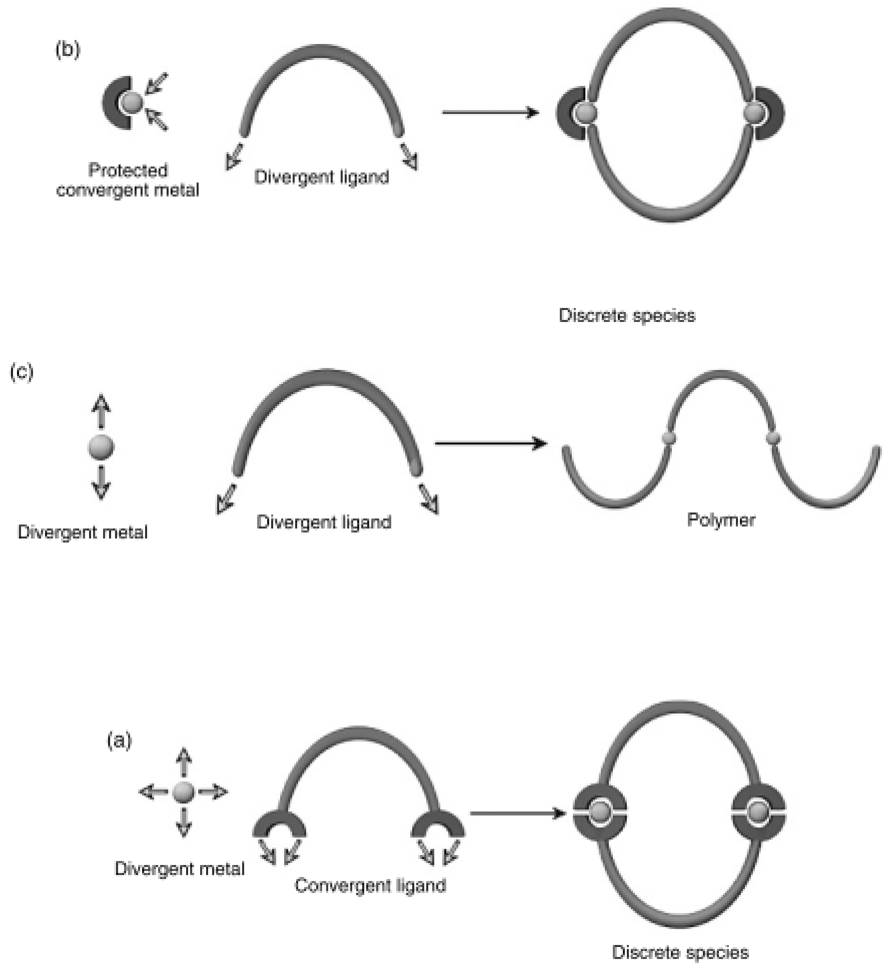
Metal as **connector** :

- labile M-L interaction (kinetic)
- stable compound (thermodynamic)
- highly directional with many geometries available

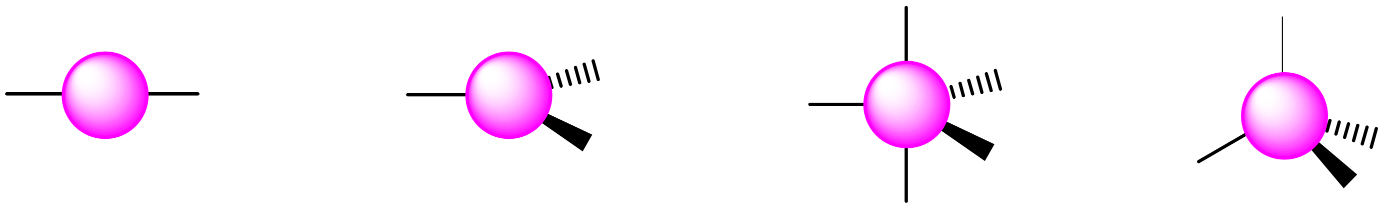


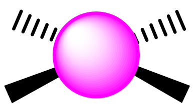
Metal as **functional group** :

- redox active (electron transfer)
- UV-vis active (color)
- photo active (phosphorescence)
- magnetic properties

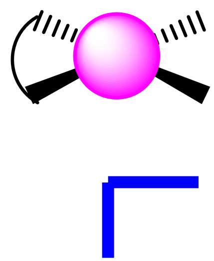


(b)
Protected convergent metal
Divergent ligand
Discrete species
(c)
Divergent metal
Divergent ligand
Polymer
(a)
Divergent metal
Convergent ligand
Discrete species





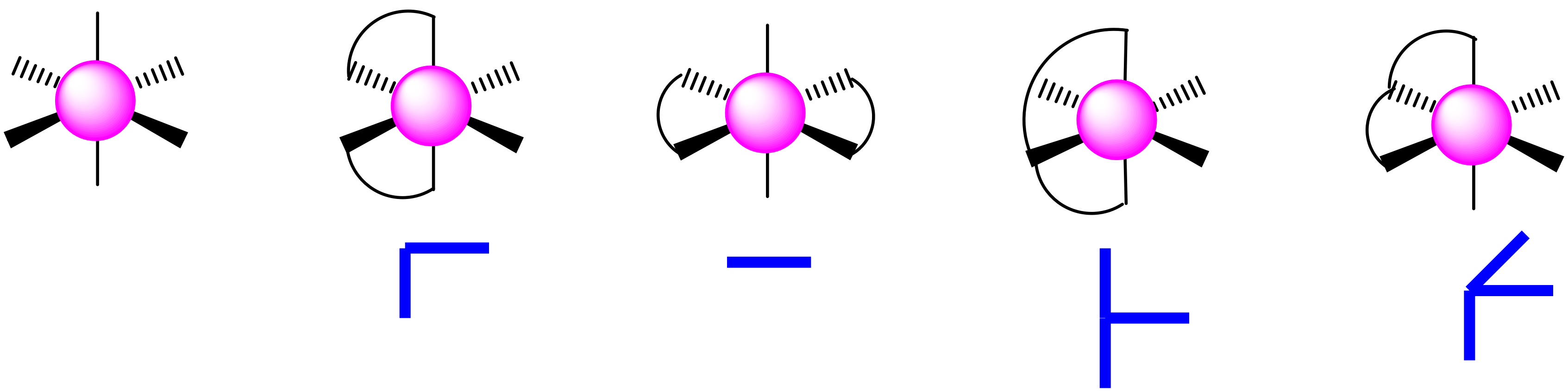
cis



Classical metals used:

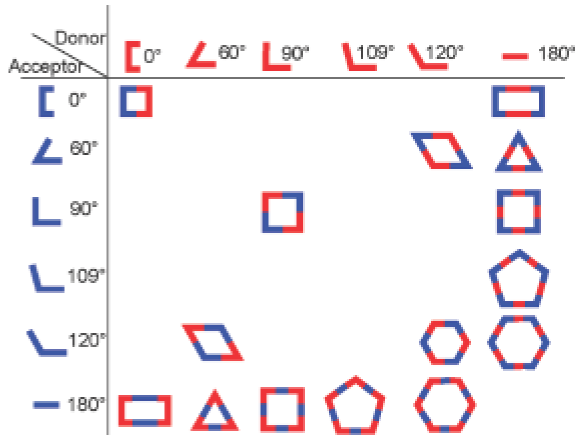
Pd(II), Pt(II), Cu(I), Cu(II), Re(I), Co(II), Fe(II), Ag(I), Zn(II), Ru(II)*…*

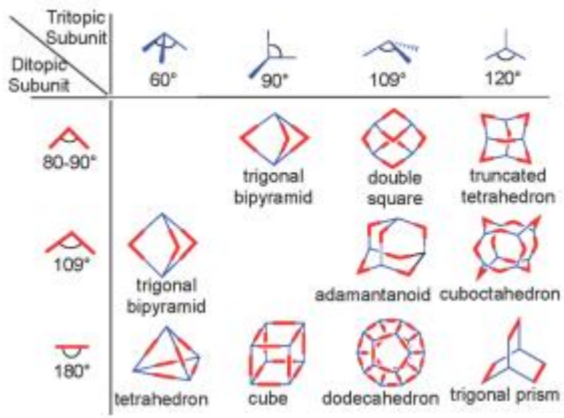
cis *trans* *mer-* *fac-*

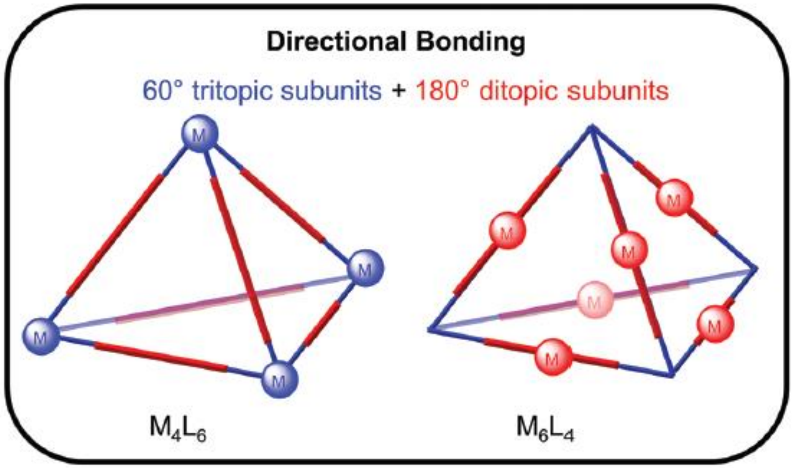


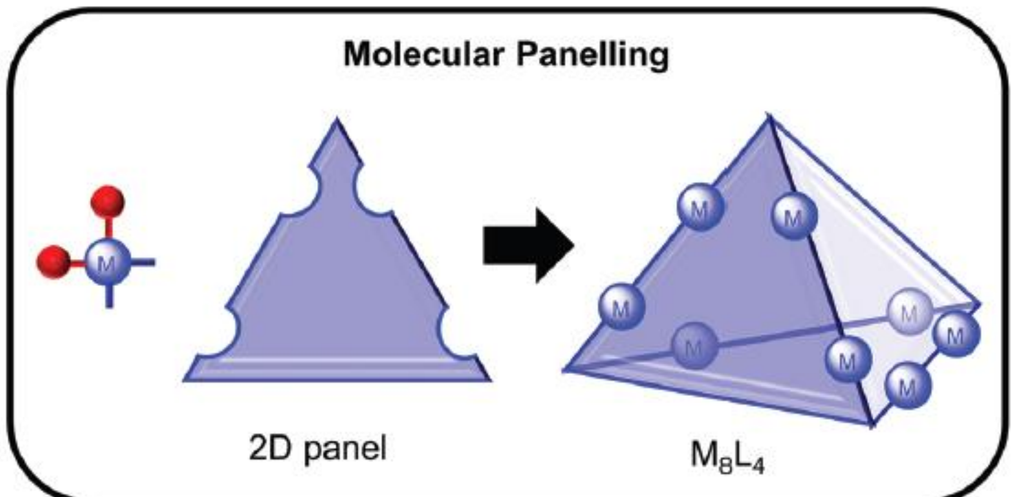
Directonal Bonding Approach

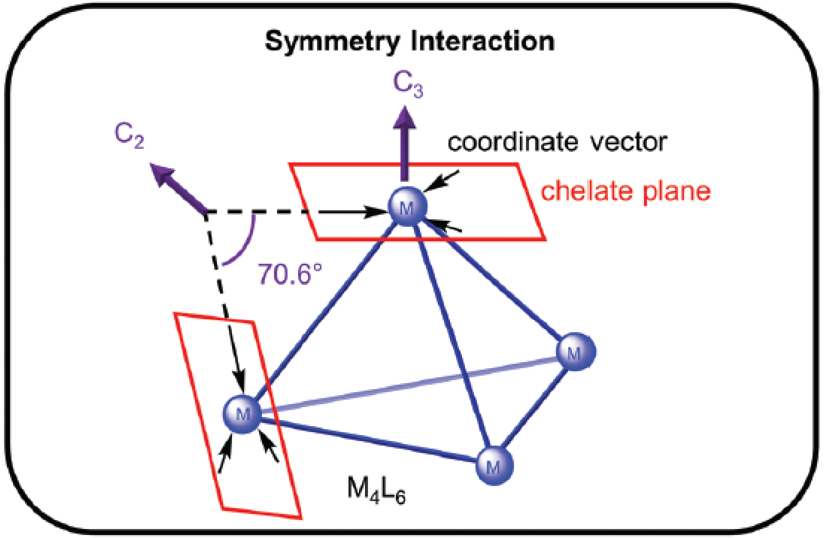
M = bb acido, **L** = bb basico, definiti secondo il numero e geometria relativa dei siti acidi e basici



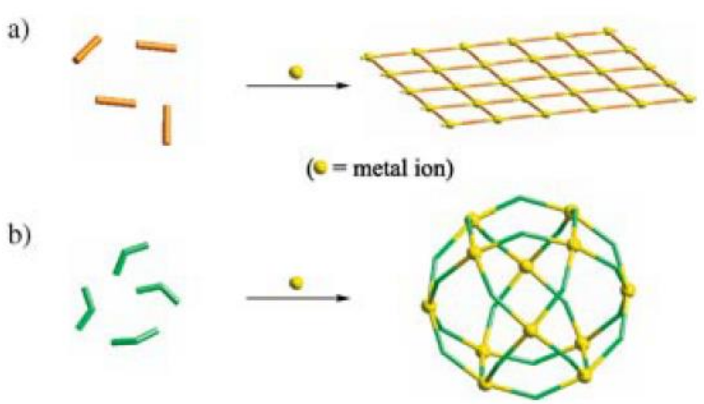



Directional Bonding
60° tritopic subunits + 180° ditopic subunits
M
M_4L_6
M_6L_4

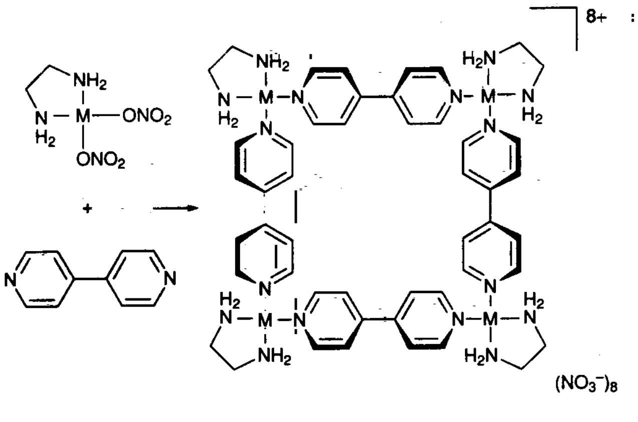

Molecular Panelling
M
2D panel
M_8L_4

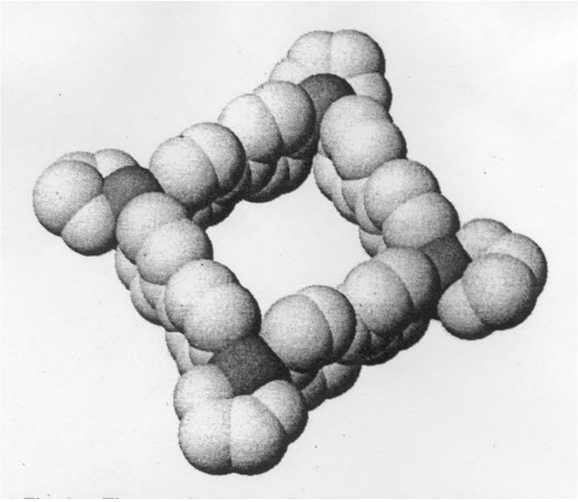


Banana-shaped ligands



Specie poligonali 2D





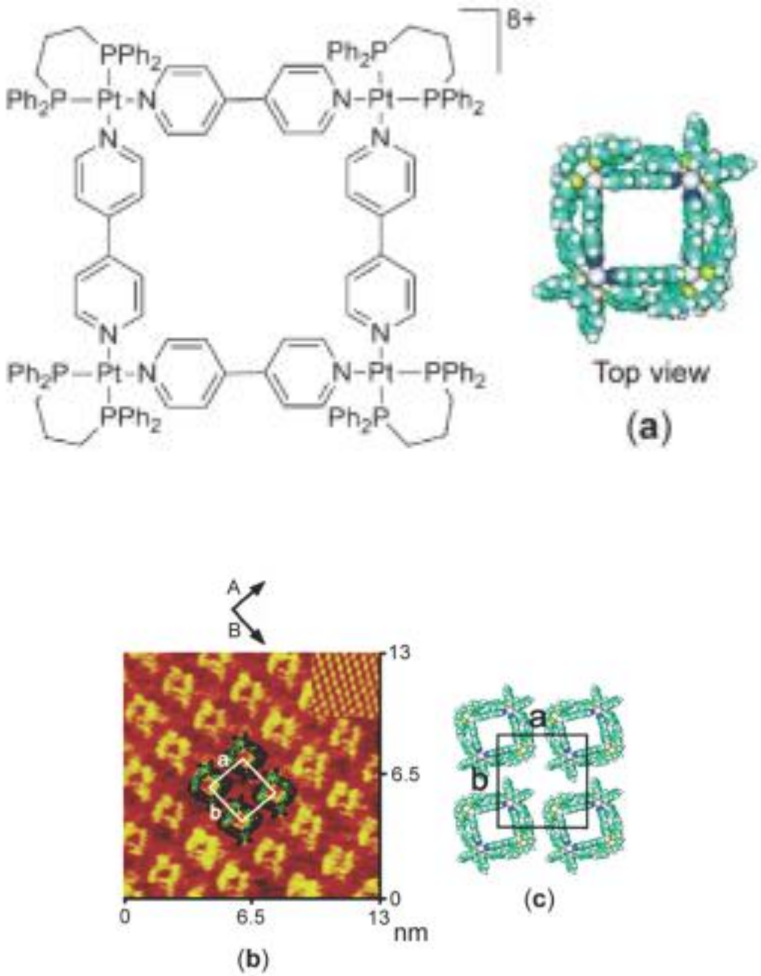
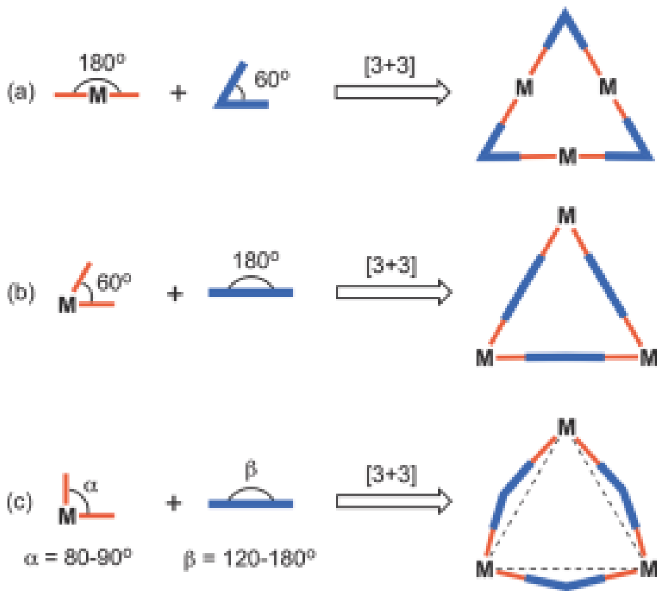
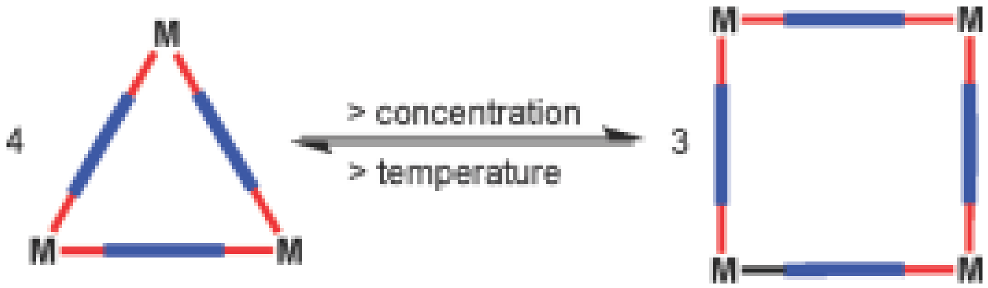


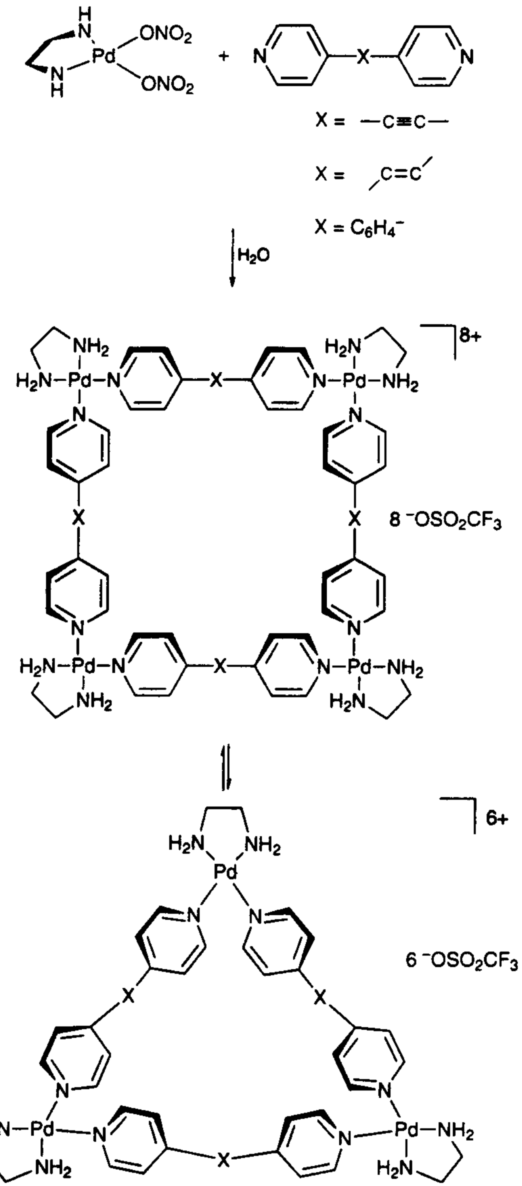
Figure 41. (a) Space-filling model of molecular square [Pt(dppp)(4,4′-bipyridine)]$_4$(PF$_6$)$_8$, (b) high-resolution STM images of the adlayer of square on Au(111), and (c) structural model of the adlayer.

Triangoli Molecolari

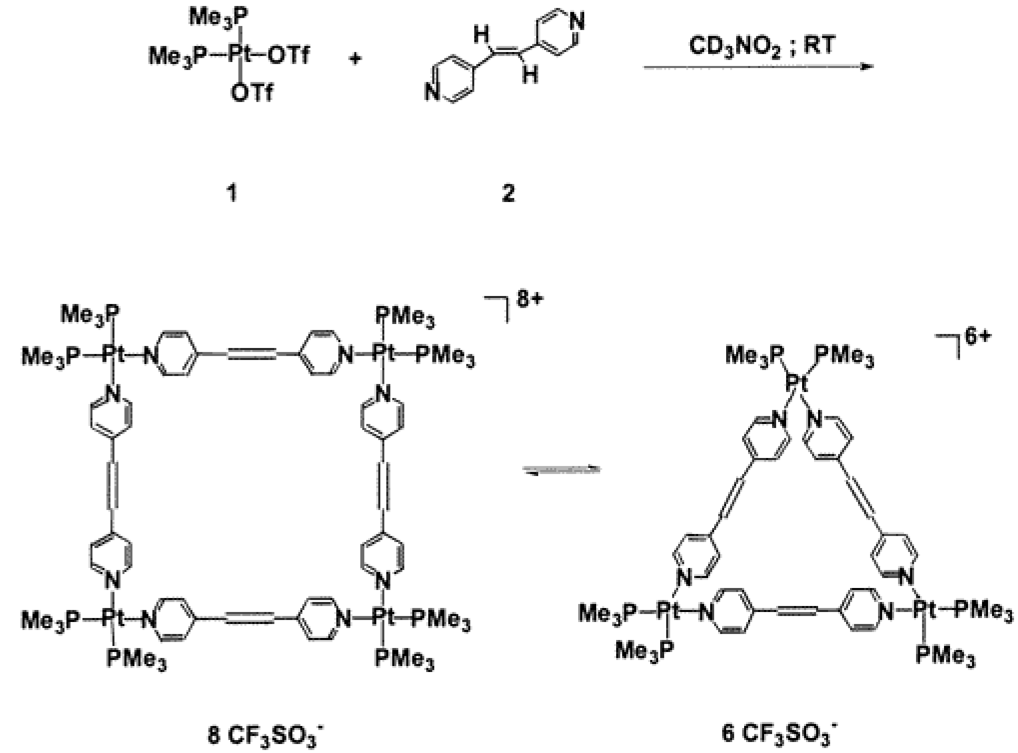




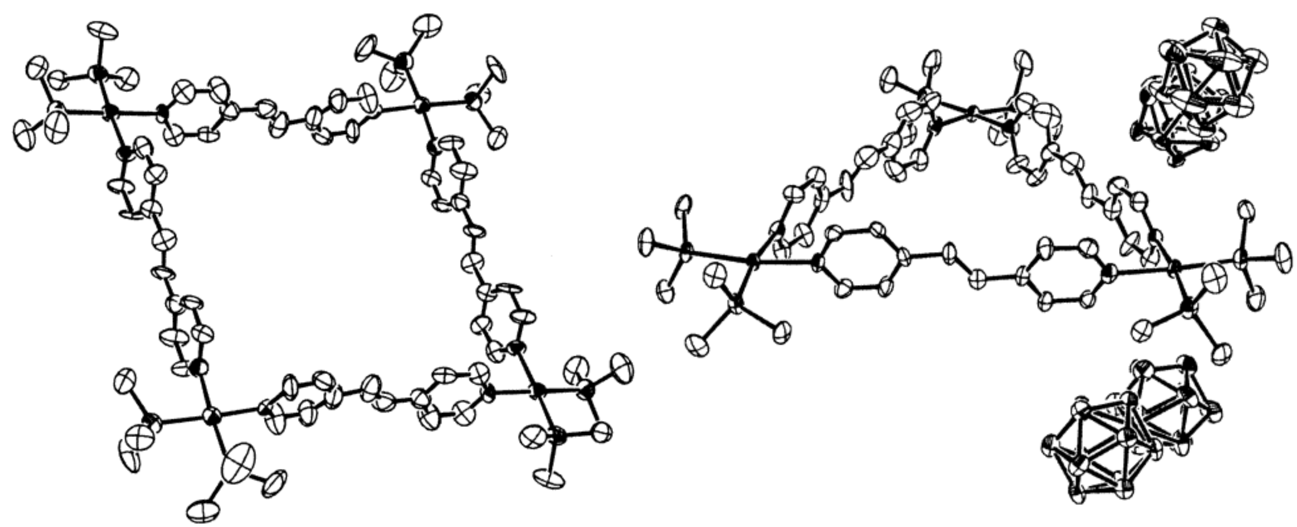
Solvent
Concentration
Temperature

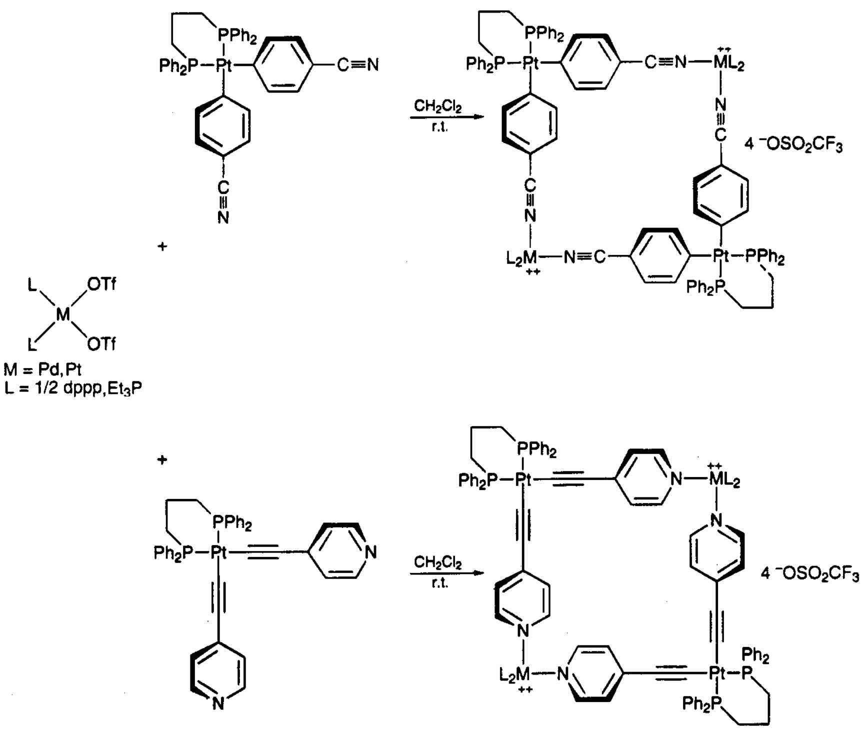


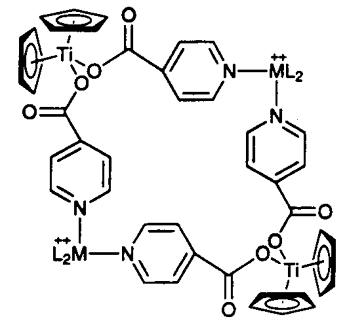
X = —C≡C—
X = C=C
X = C6H4−
H2O
8+
8 −OSO2CF3
6+
6 −OSO2CF3



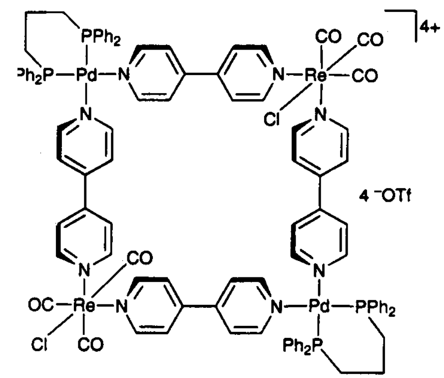
Me3P
Me3P—Pt—OTf
OTf
+
H
N
H
N
CD3NO2 ; RT
1
2
Me3P
Me3P—Pt—N
PMe3
N—Pt—PMe3
8+
Me3P—Pt—N
PMe3
N—Pt—PMe3
PMe3
Me3P
PMe3
Pt
6+
Me3P—Pt—N
Me3P
N—Pt—PMe3
PMe3
8 CF3SO3-
6 CF3SO3-

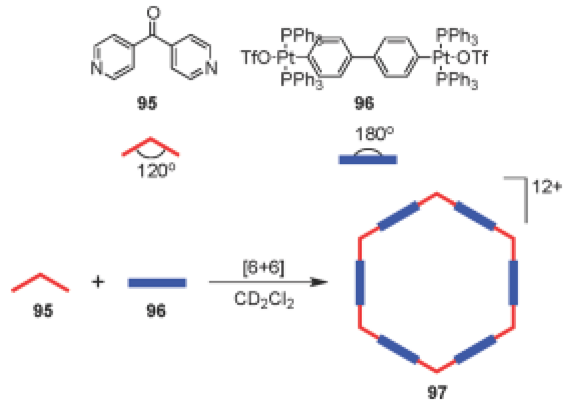




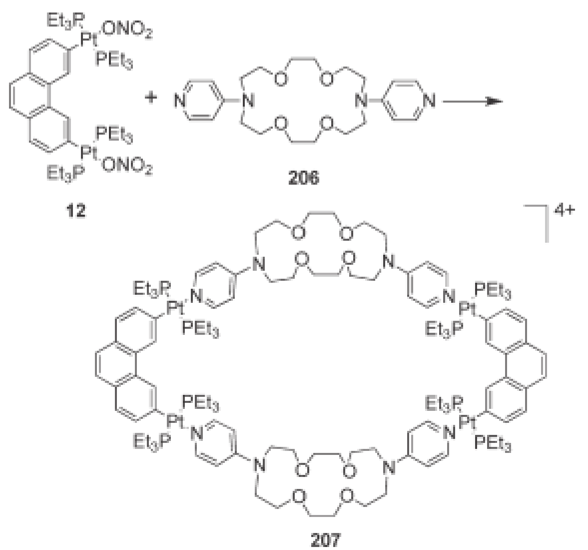


M = Pd, Pt, L = 1/2 dppp, Et_3P

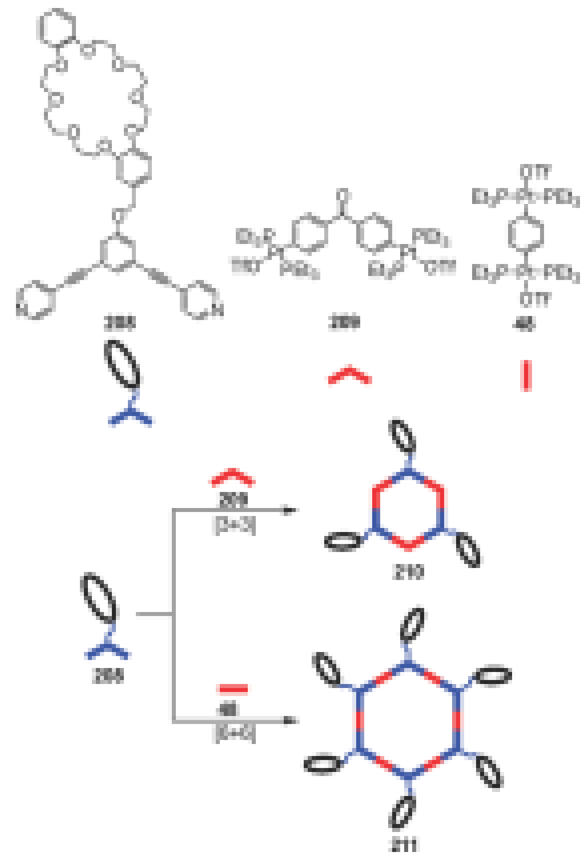




95
96
120°
180°
12+
[6+6]
CD_2Cl_2
97



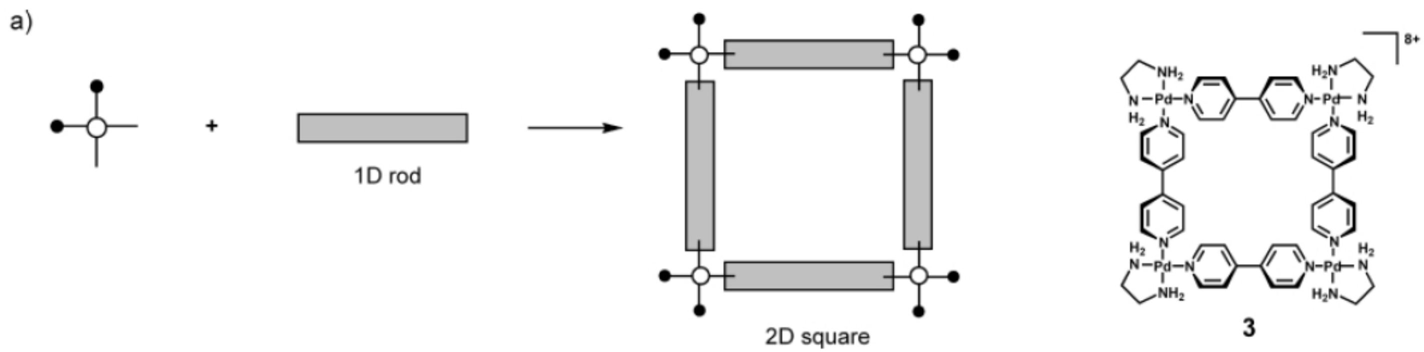
12
206
4+
207

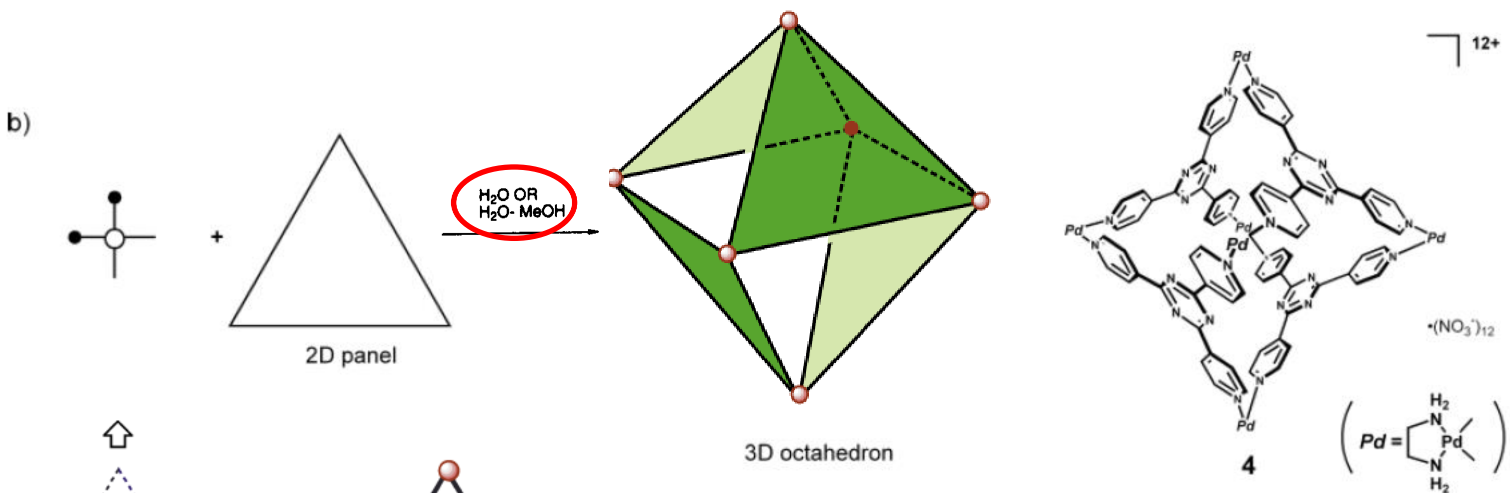


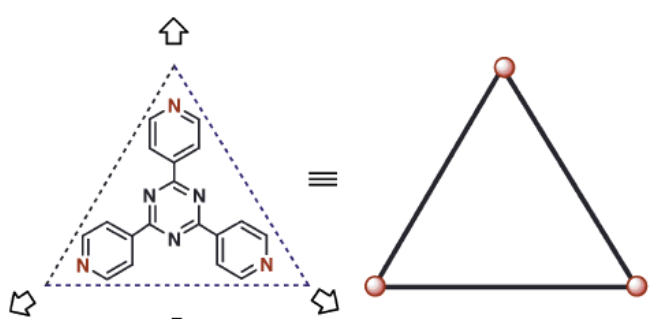
Molecular paneling *via* coordination

Chem. Commun., 2001, 509–518

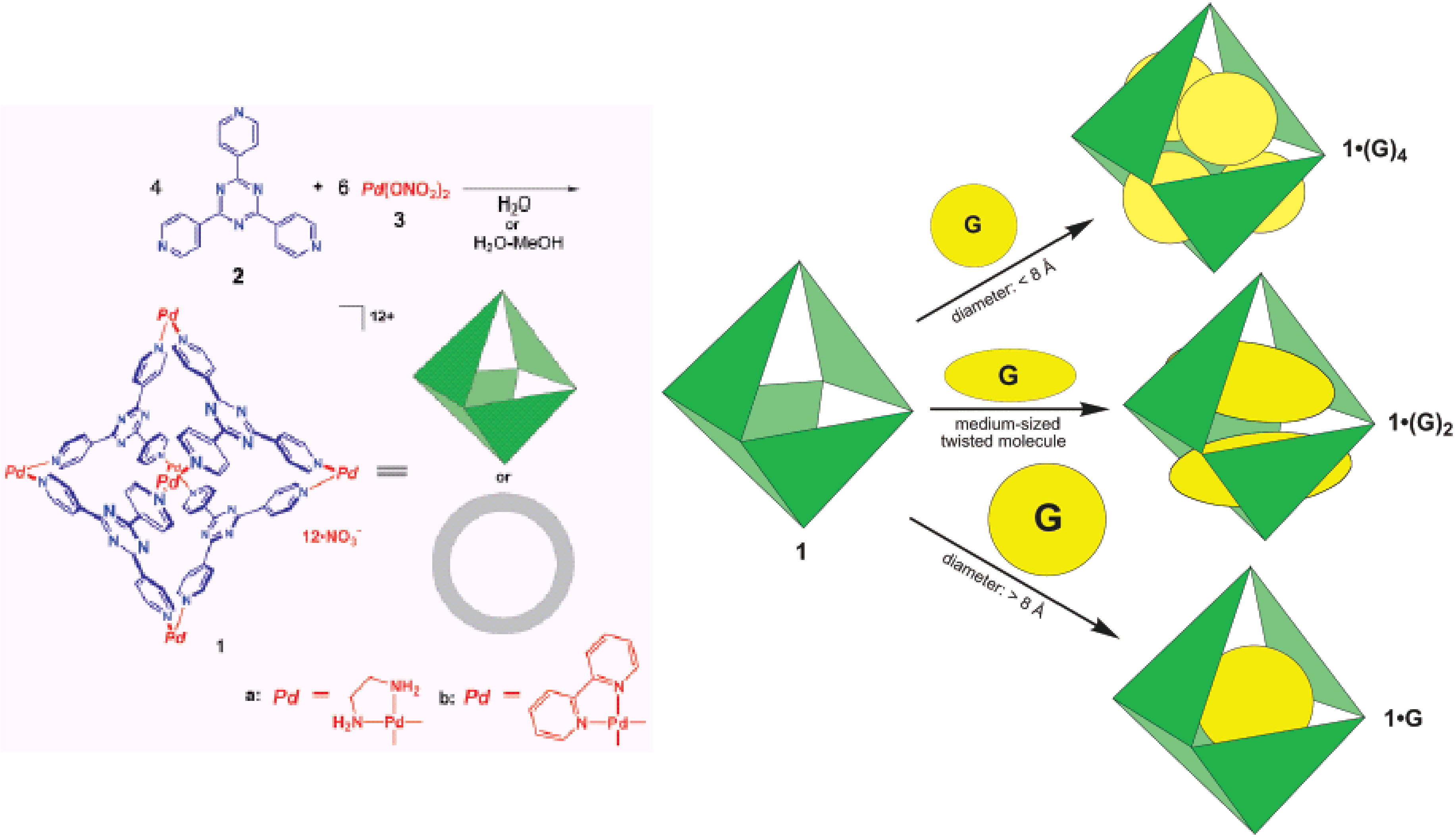
Makoto Fujita,* Kazuhiko Umemoto, Michito Yoshizawa, Norifumi Fujita, Takahiro Kusukawa and Kumar Biradha







$\mathbf{M_6L_4}$
d *ca.* 11 Å
Portali **8 Å**



4
+ 6 Pd(ONO2)2
3
H2O
or
H2O-MeOH
2
12+
Pd
12•NO3−
or
1
a: Pd =
NH2
H2N—Pd—
b: Pd =
N—Pd—
N
G
diameter: < 8 Å
1•(G)4
G
medium-sized
twisted molecule
1•(G)2
G
diameter: > 8 Å
1•G
1

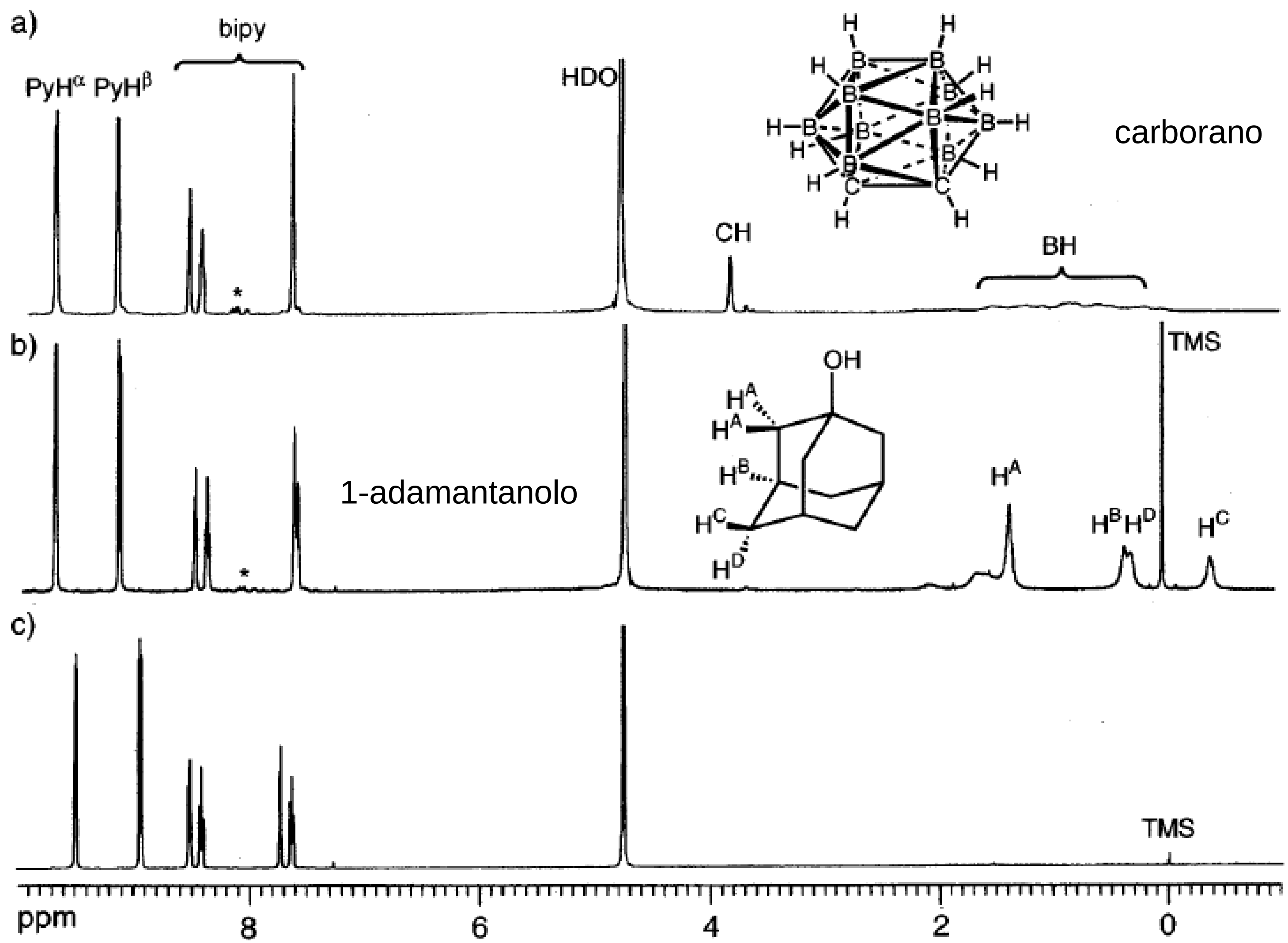
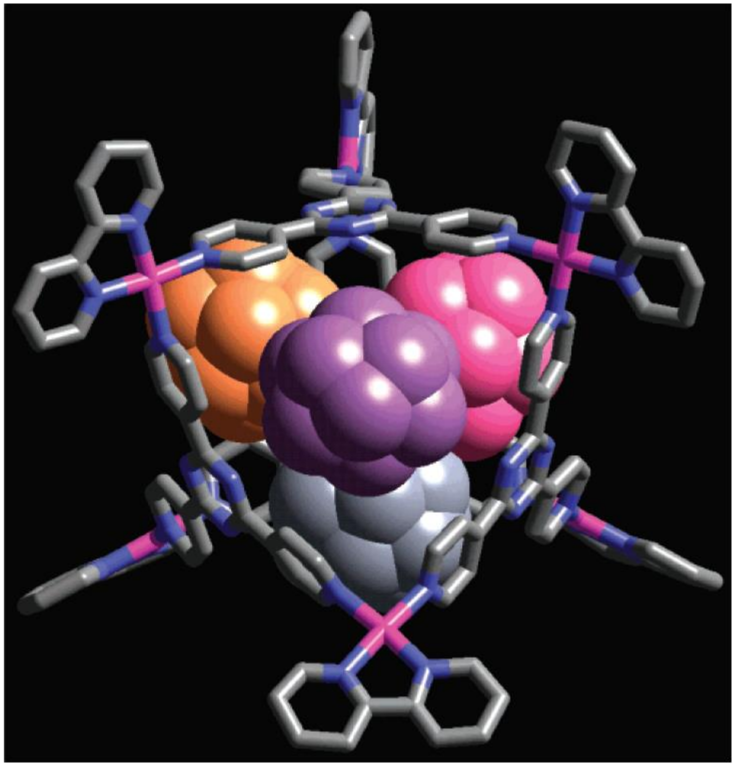
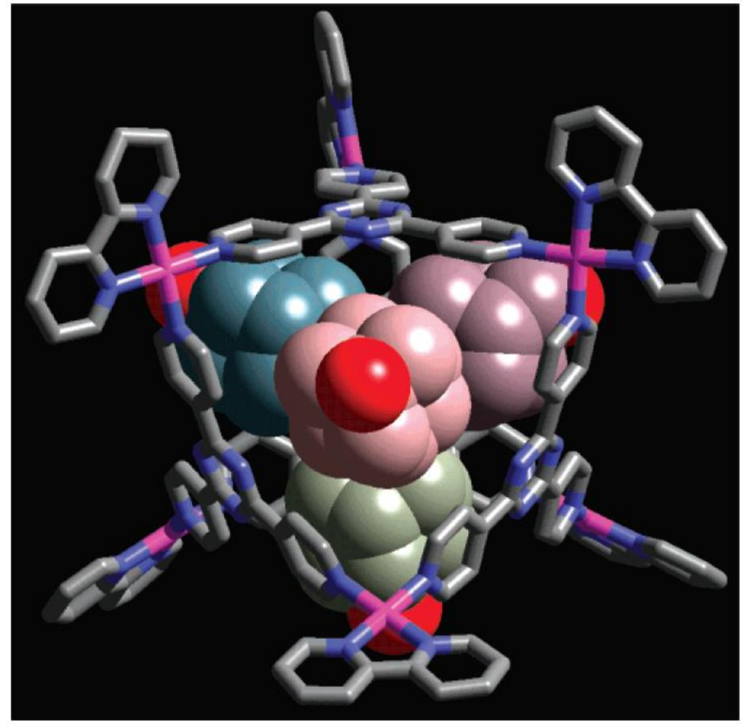
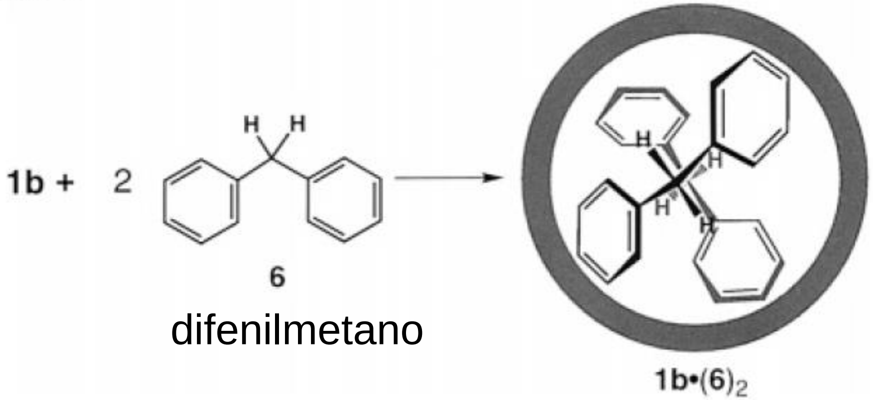


Figure 1. ^{1}H NMR observations of the enclathration of guest molecules in **1b**. (a) **1b**·(**4**)$_4$. (b) **1b**·(**5**)$_4$. (c) Empty **1b** (∗: impurities).

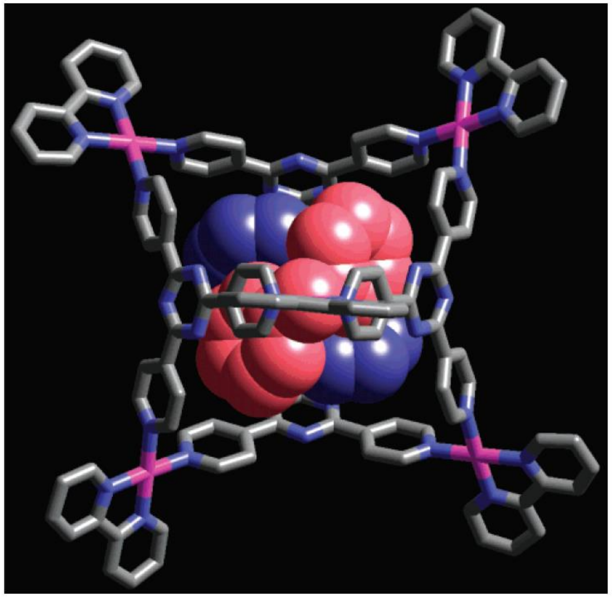




Scheme 2

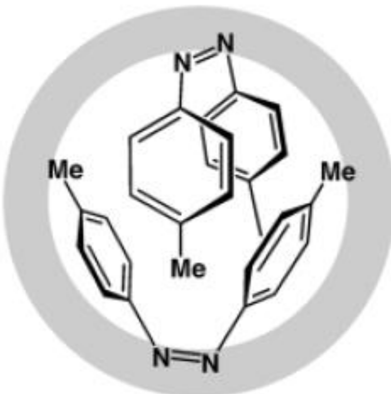


difenilmetano

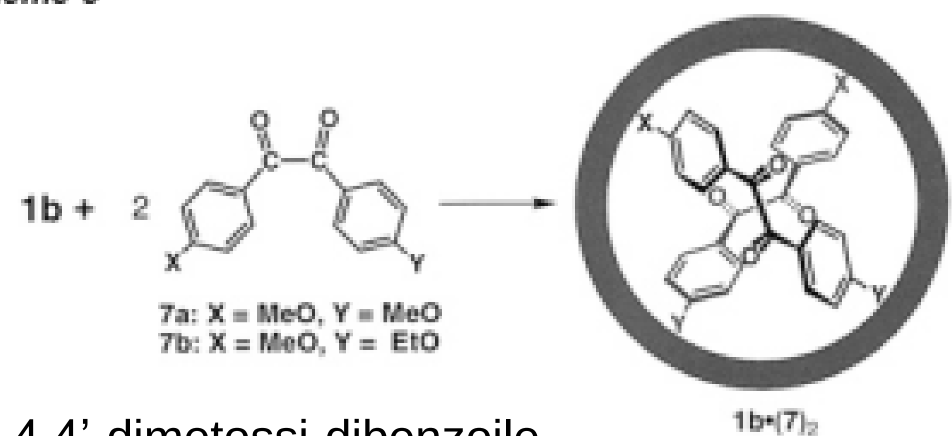


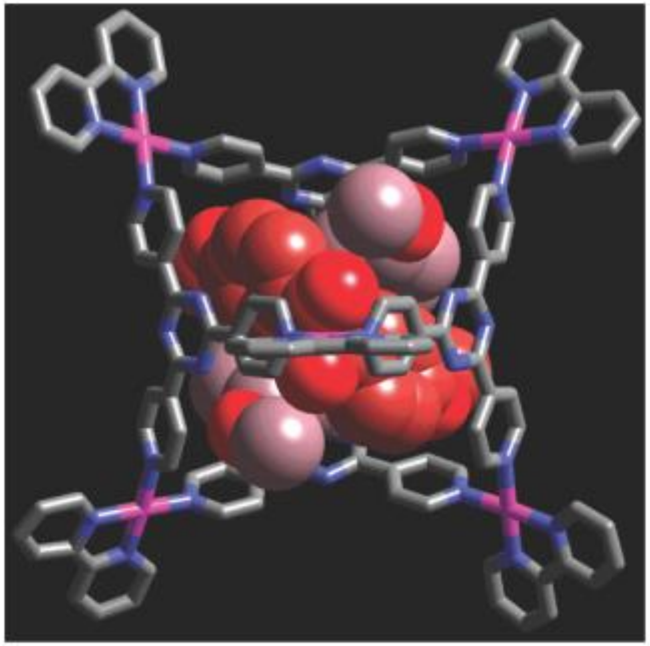
cis-azobenzene

cis-stilbene

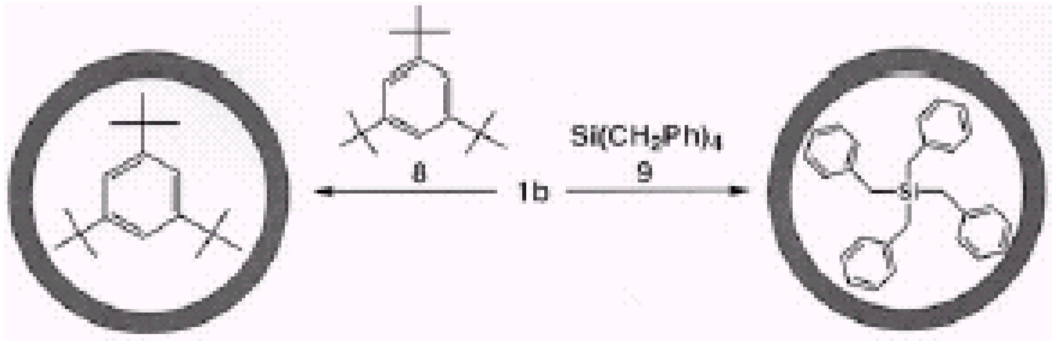


Scheme 3





4,4’-dimetossi-dibenzoile



tri-*tert*-butilbenzene **tetrabenzilsilano**

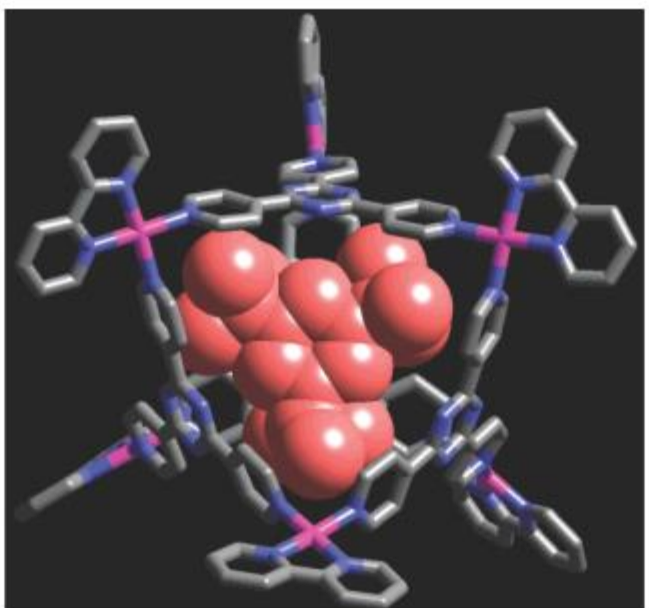
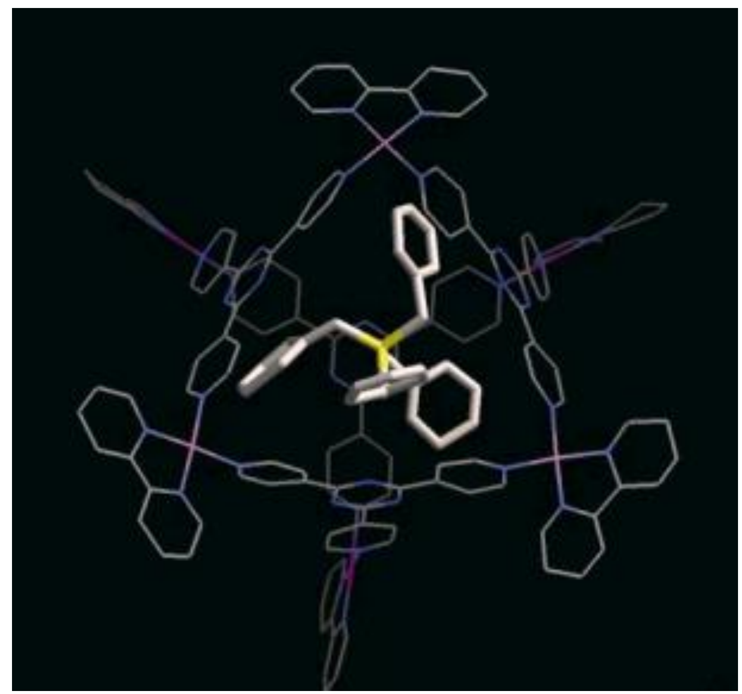
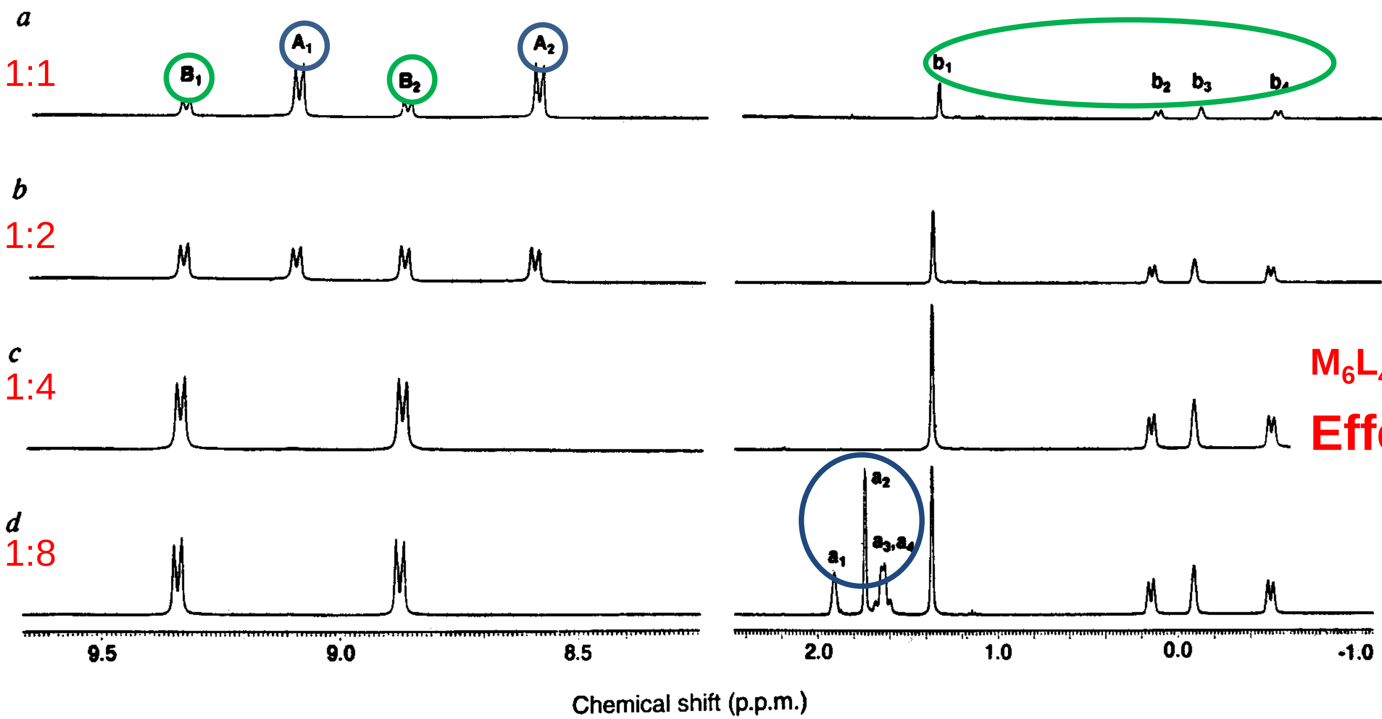


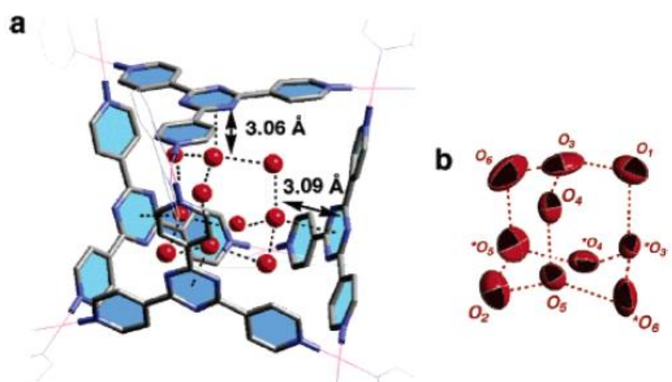
Figure 8. Crystal structure of **1b·8**.

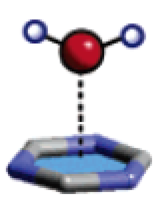




M_6L_4/adamantancarbossilato$_4$

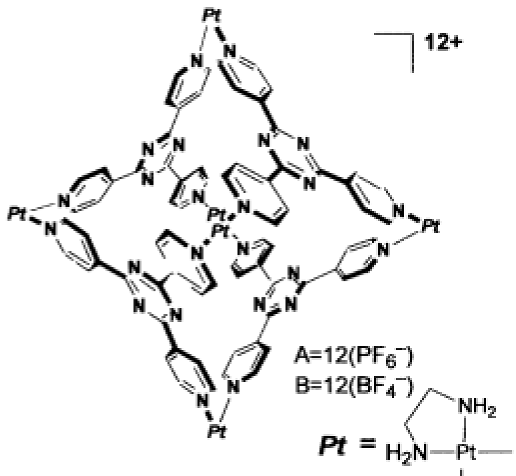
Effetto allosterico!





I_c-type ice.[1,2] The X-ray structural analysis, coupled with neutron diffraction study, reveals that the molecular ice is not simply formed by filling the void space but is a result of specific $H_2O{\cdots}\pi$ interaction within the cage. Whereas there are numerous examples cluster of hypothetical reversed hydrate complexes. Surprisingly, the molecular ice does not "melt" even at room temperature; the adamantanoid framework of 10 water molecules can be located roughly even in a room-temperature diffraction study.

The presence of highly ordered water clusters inside the binding pockets of proteins has been predicted[15] and considered to be crucial in entropy-driven substrate binding.[16] We suggest that the molecular recognition by cage **1** is entropy-driven, in which the binding of guests is compensated by the "melting" of the molecular ice into free water molecules. The endohedral water cluster therefore plays



1

a: $(C_{84}H_{96}N_{36}Pt_6)^{12+}\cdot 12(PF_6^-)$
FW. 4519.98

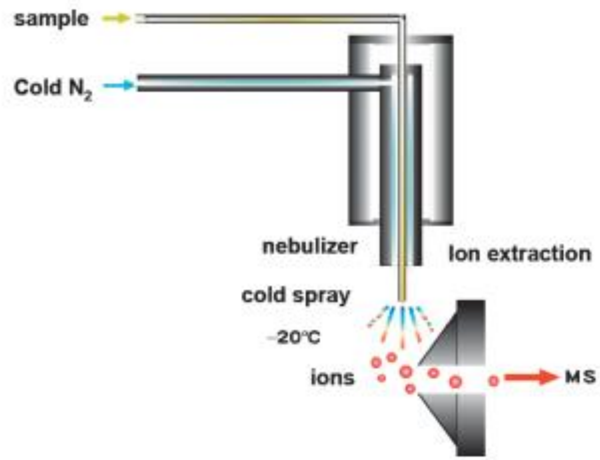


Fig. 1. Schematic illustration of the cold spray.

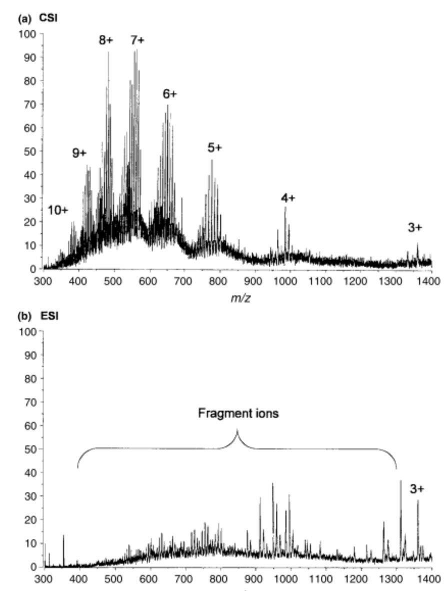
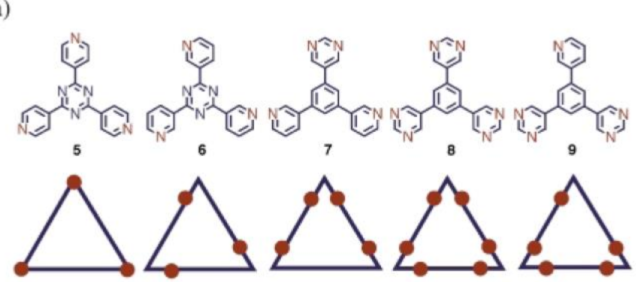
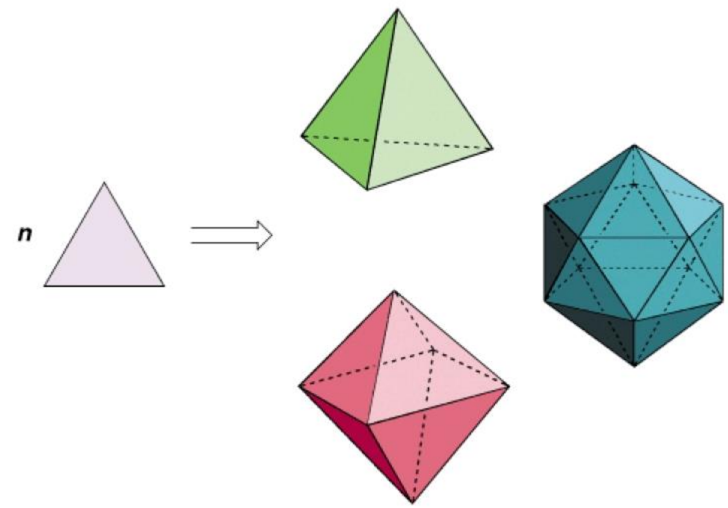


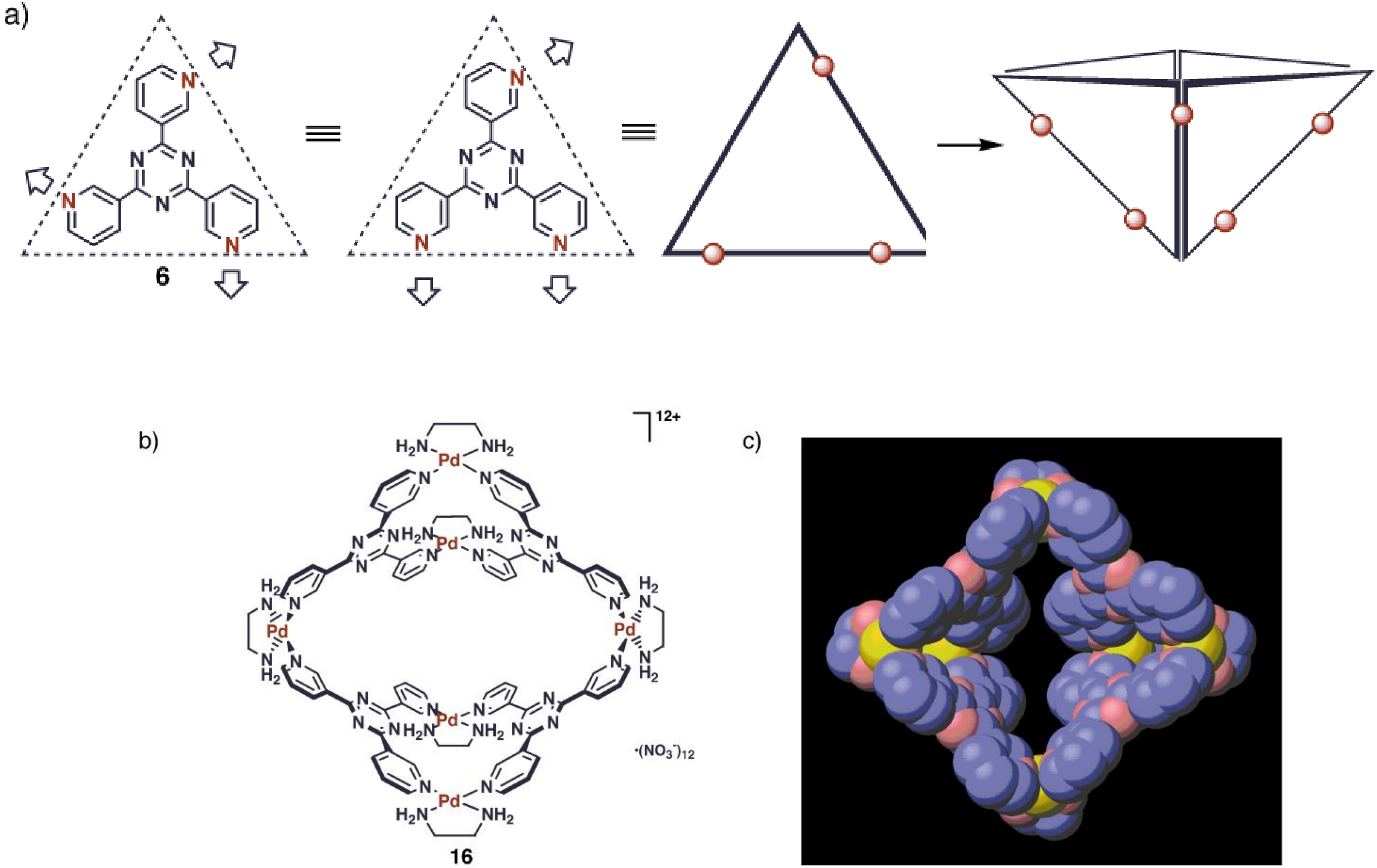
Figure 3. Comparison of (a) CSI and (b) ESI mass spectra of **1a**. Reprinted from Ref. 2 with permission from Elsevier.

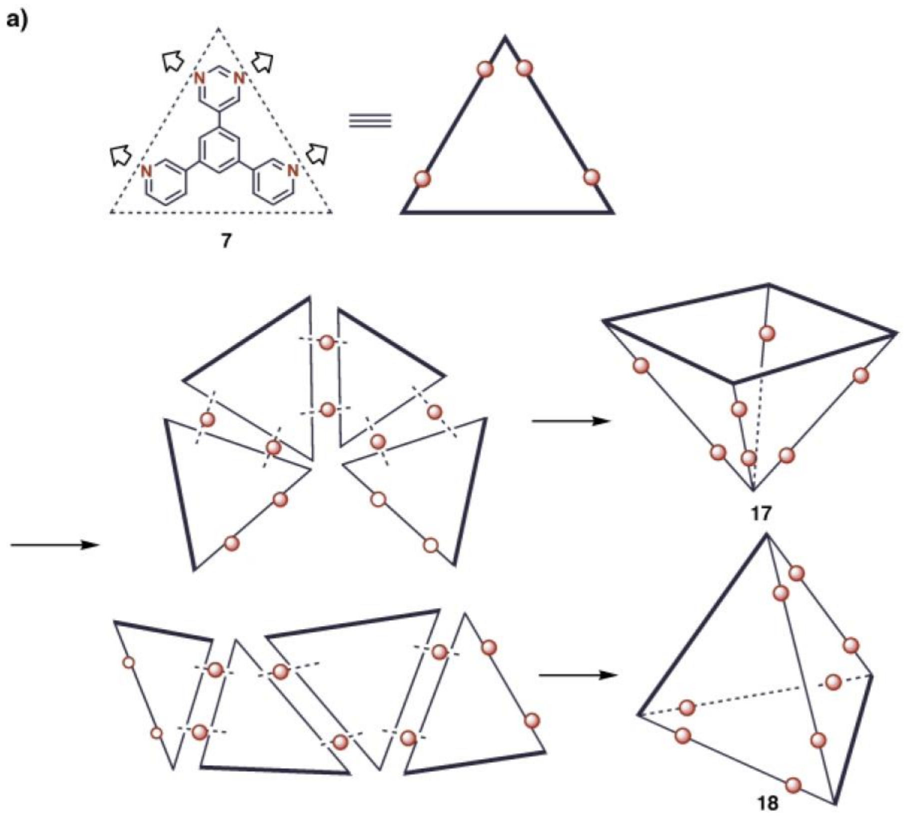
Molecular Paneling

a)

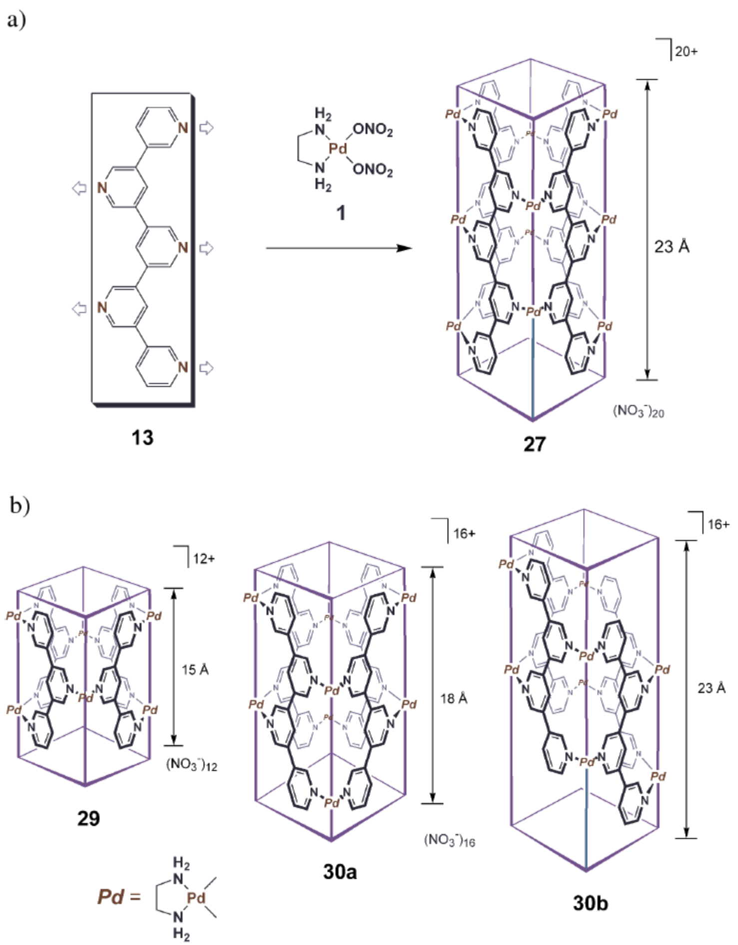


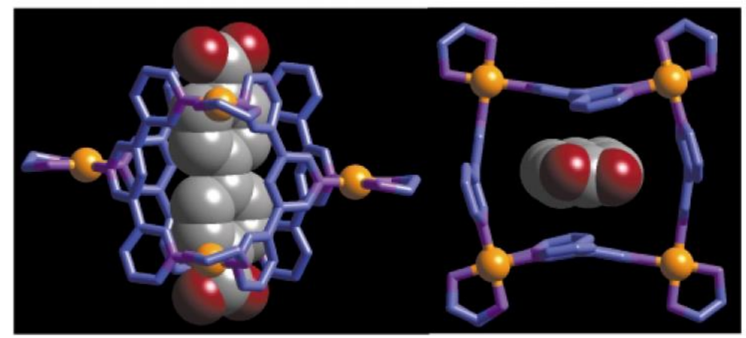


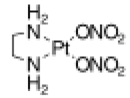

a)
N
N
N
N
N
N
6
≡
≡
b)
12+
H2N
Pd
NH2
N
N
16
•(NO3-)12
c)



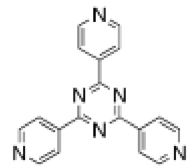
Effetto templato


a)
ONO2
ONO2
1
13
27
20+
23 Å
(NO3-)20
b)
29
12+
15 Å
(NO3-)12
30a
16+
18 Å
(NO3-)16
30b
16+
23 Å
Pd =

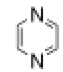




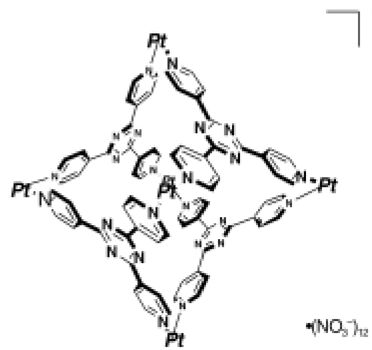
1



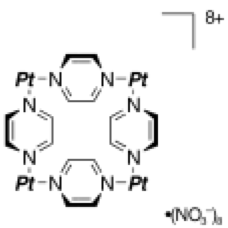
2



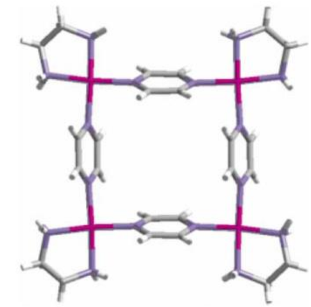
3

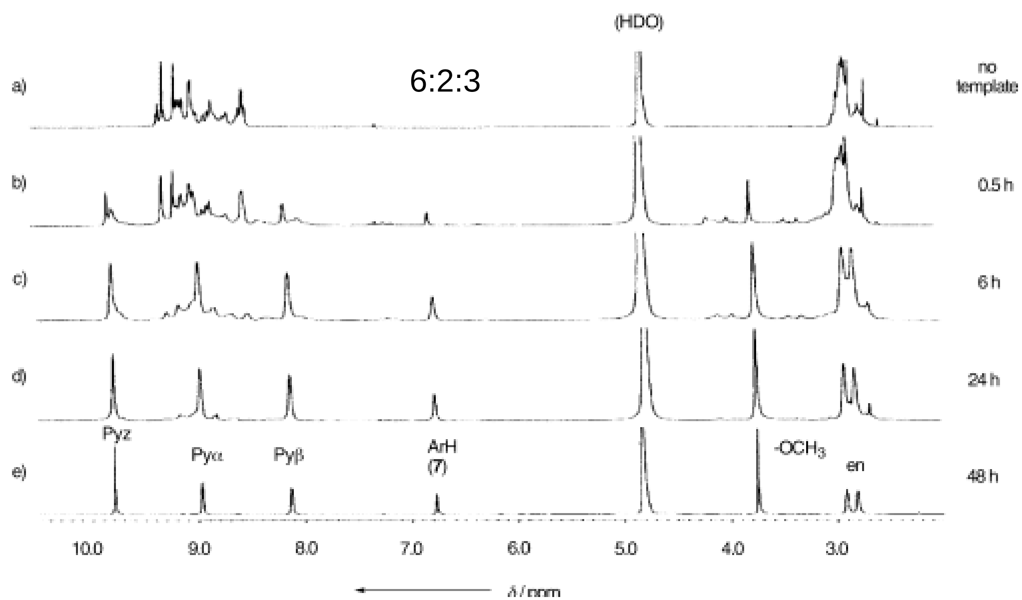


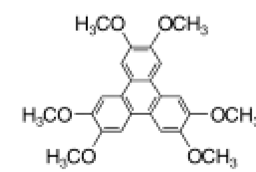
5



6

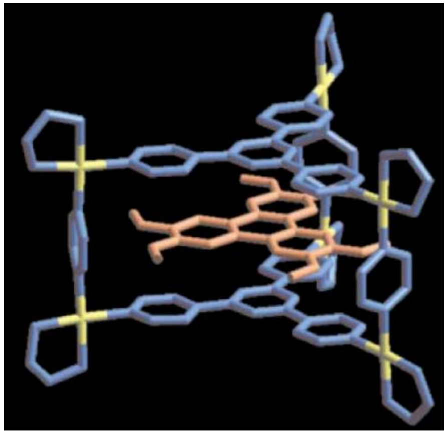


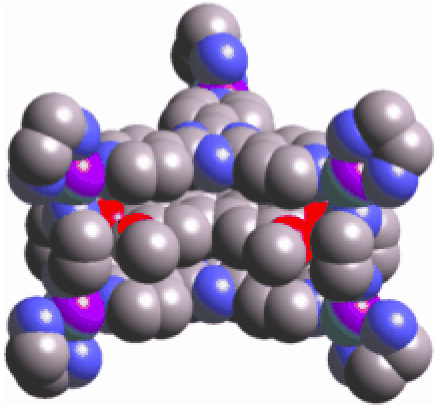


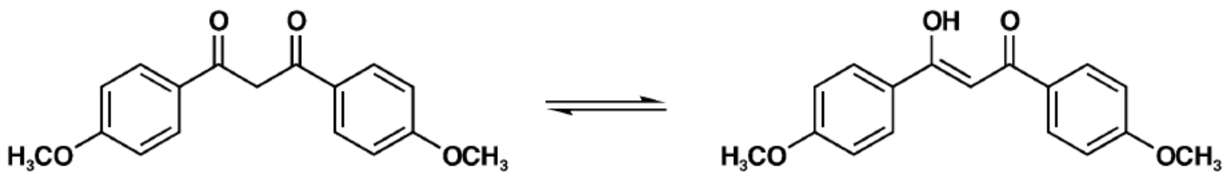


7

Figure 1. ^{1}H NMR spectra showing the guest-templated assembly of **7**⊂**4** complex (500 MHz, D_2O, 25 °C). a) A mixture of **1**, **2**, and **3**. Template **7** was added to this solution and the mixture was heated at 100 °C for b) 0.5 h, c) 6 h, d) 24 h, and e) 48 h. Pyz = pyrazine.





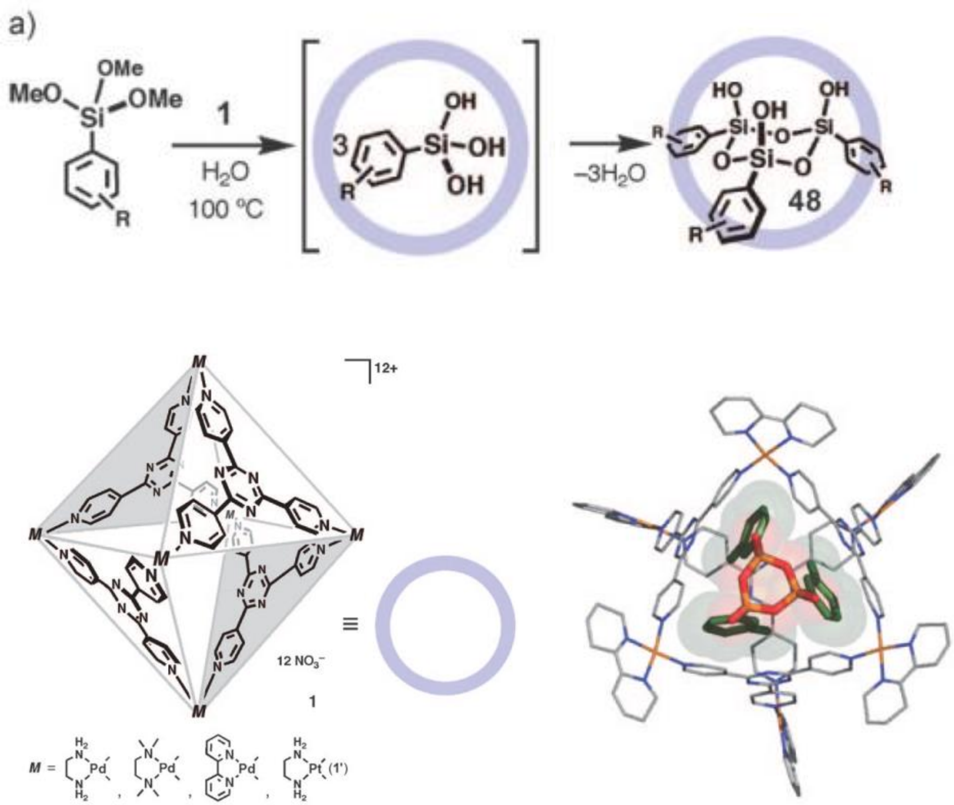


keto **9** enol **9**

The efficient intercalation of planar guest molecules within the cage was applied to the control of the equilibration between planer and nonplanar molecules. Keto and enol tautomers of β-diketone **9**, which exist in a 15:85 ratio in CD_3CN, can never be separated because of rapid tautomerization.

Stabilizzazione di intermedi reattivi: alcossi-silani ciclici

Ship in a Bottle

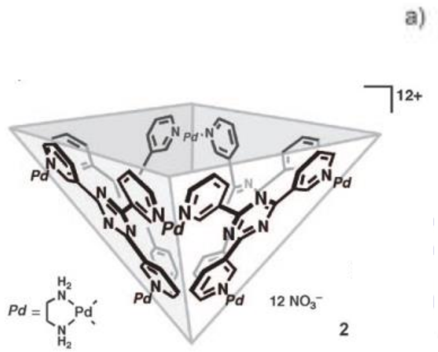


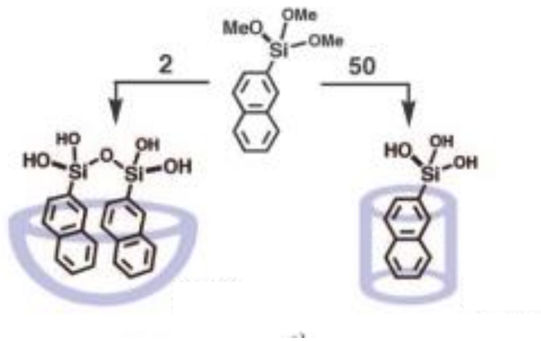
The roughly spherical cage cavity directs the selective formation of the cyclic trimer and prohibits further polycondensation despite the presence of labile Si-OH functional groups.

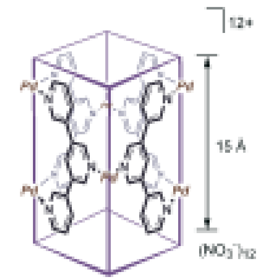
The stereochemistry of the condensation reaction is highly controlled within the cage giving only all-*cis* isomers.

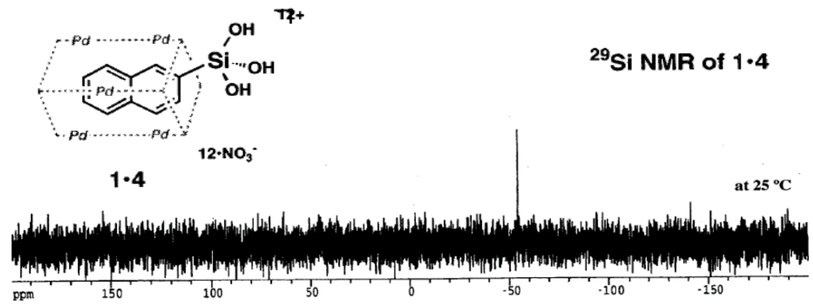
The trimers prepared in situ can no longer escape from the cage because their dimension becomes larger than the portal size.

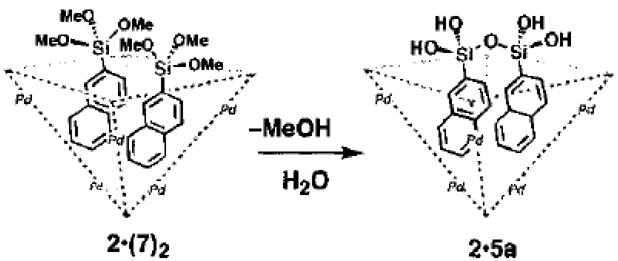
Stabilizzazione di intermedi reattivi: Oligomerizzazione di tri alcossi-silani

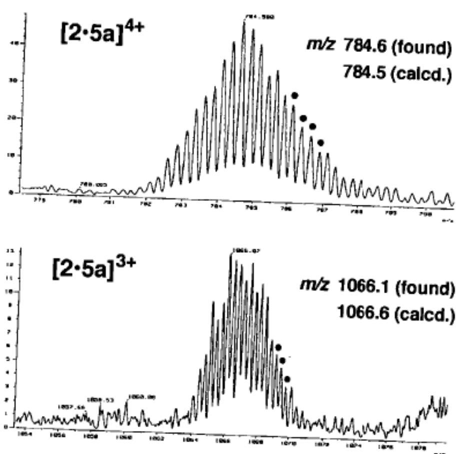


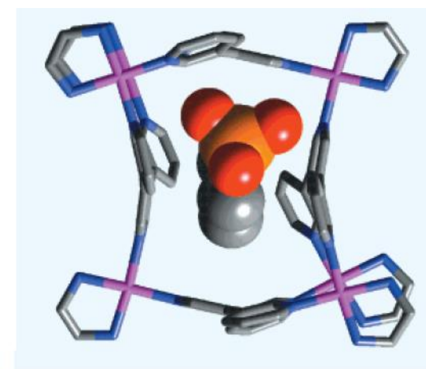










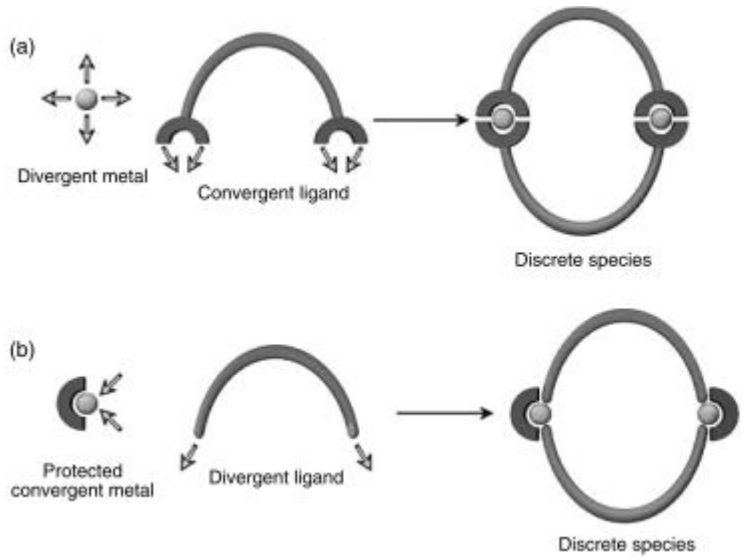


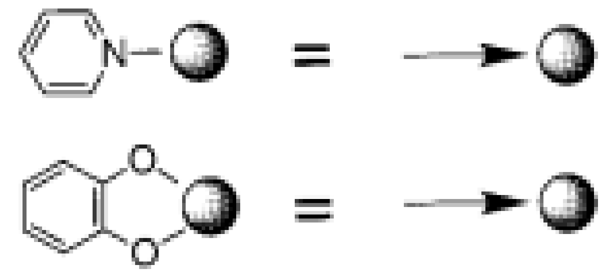
In an aqueous solution at 80 °C, the **1·4** complex remained intact for one week. Furthermore, the complex was tolerant under acidic conditions (pH <1).

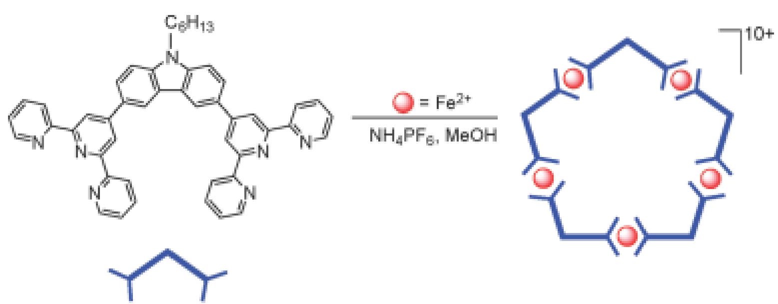
Diels-Alder in Aqueous Molecular Hosts: Unusual Regioselectivity and Efficient Catalysis

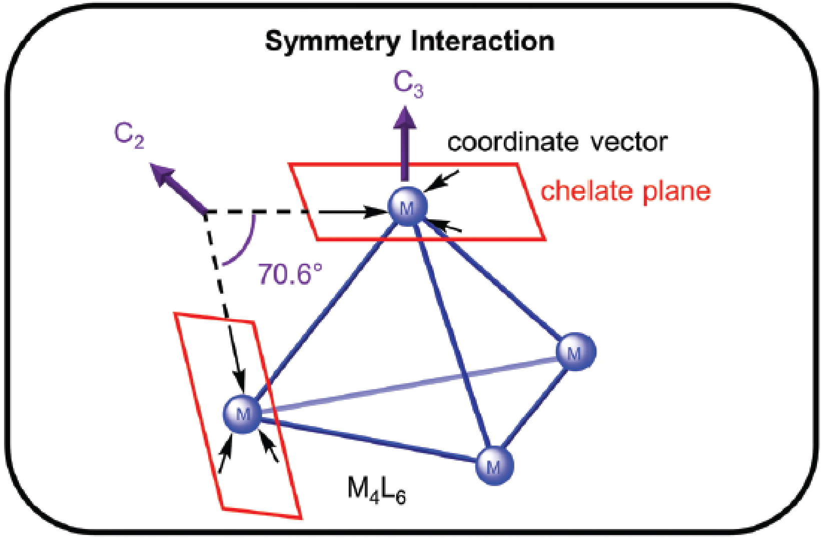
Michito Yoshizawa, Masazumi Tamura, Makoto Fujita*

Science 2006;312:251-254


(a)
Divergent metal
Convergent ligand
Discrete species
(b)
Protected convergent metal
Divergent ligand
Discrete species


N
O
O


C_6H_{13}
N
N
N
N
N
N
N
= Fe^{2+}
NH_4PF_6, MeOH
10+



Supermolecules by Design

DANA L. CAULDER AND
KENNETH N. RAYMOND*

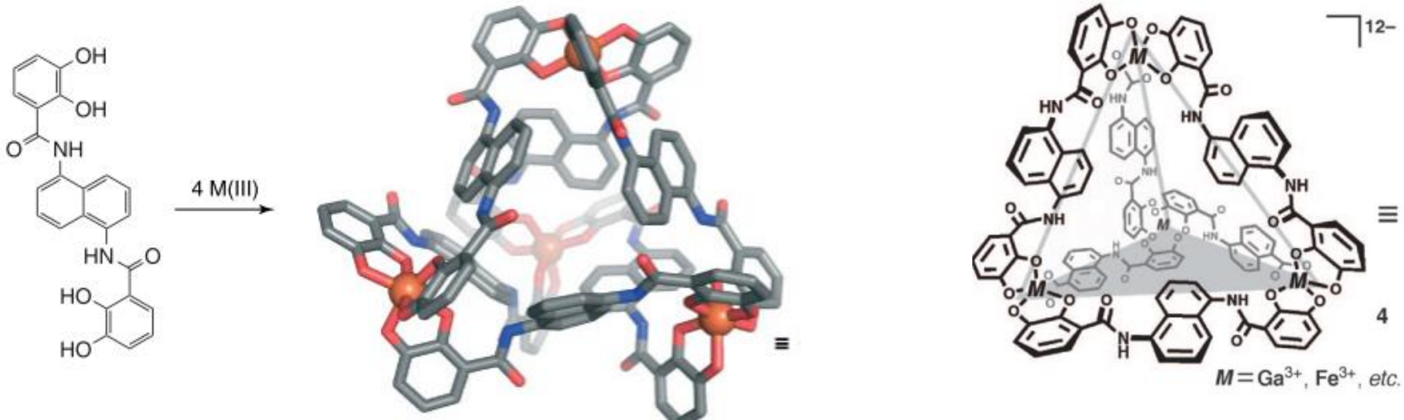
Acc. Chem. Res. **1999,** *32,* 975–982

J. Am. Chem. Soc. **2001,** *123,* 8923–8938

Design, Formation and Properties of Tetrahedral M_4L_4 and M_4L_6 Supramolecular Clusters[1]

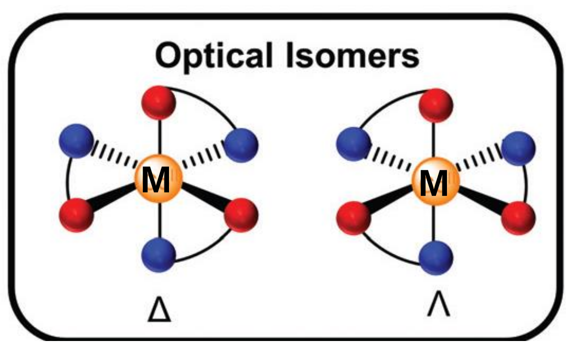
Dana L. Caulder, Christian Brückner, Ryan E. Powers, Stefan König, Tatjana N. Parac, Julie A. Leary, and Kenneth N. Raymond*

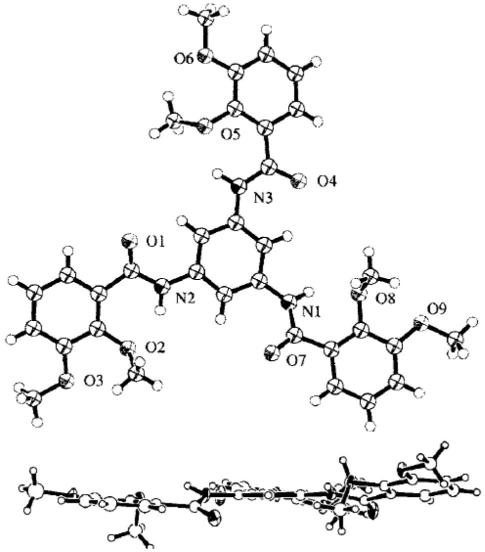
6

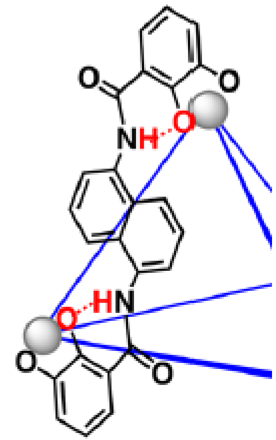


4

M$_4$L$_6$, (Ga^{3+}, Fe^{3+}; biscatecol-amidi) **12**$^{-}$, ΔΔΔΔ, ΛΛΛΛ, 300-350 Å
Stabilizzazione di cationi organici







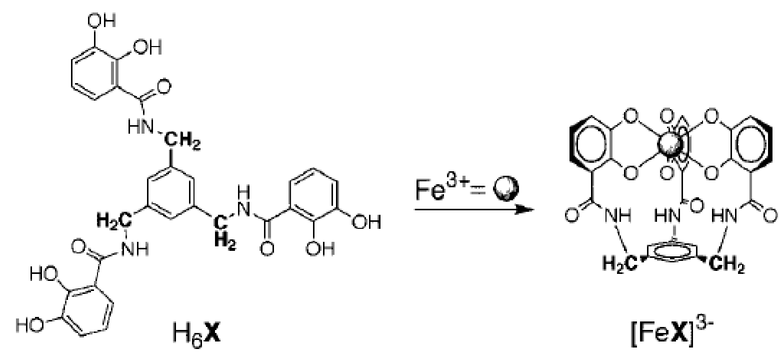


Figure 4. As shown in the enterobactin analogue H_6**X**, simple addition of a methylene group between the three-fold benzene scaffold and the catecholamide binding units gives the ligand enough flexibility to allow each of the arms to coordinate a single metal ion. This type of ligand flexibility must be avoided if multimetal clusters are desired.

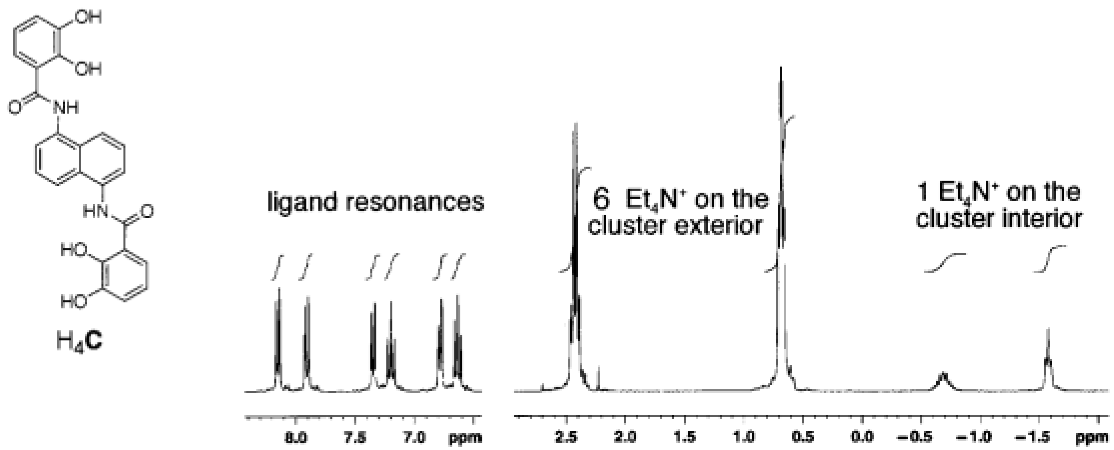


Figure 14. ^1H NMR (D_2O) depicting the two sets of Et_4N^+ resonances characteristic of the exterior and encapsulated cations.

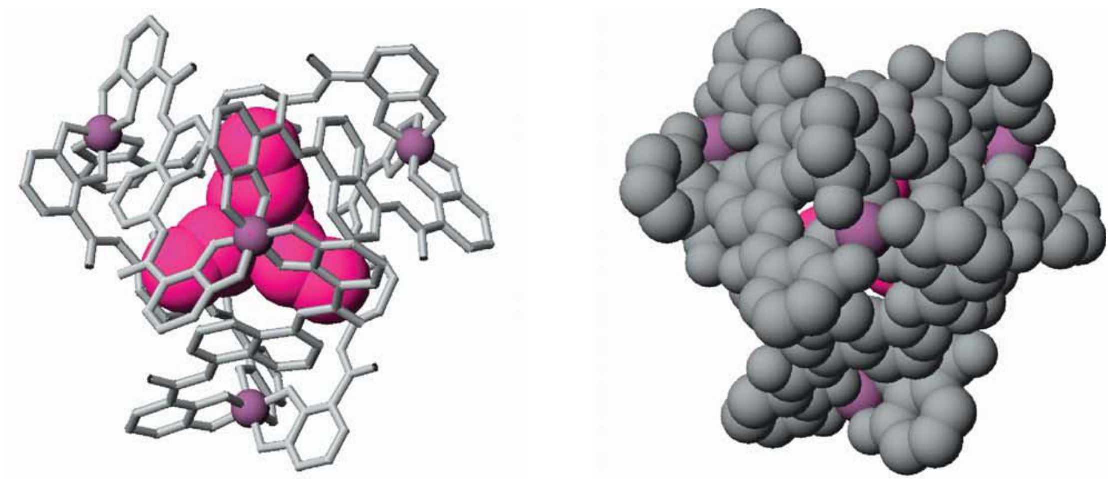
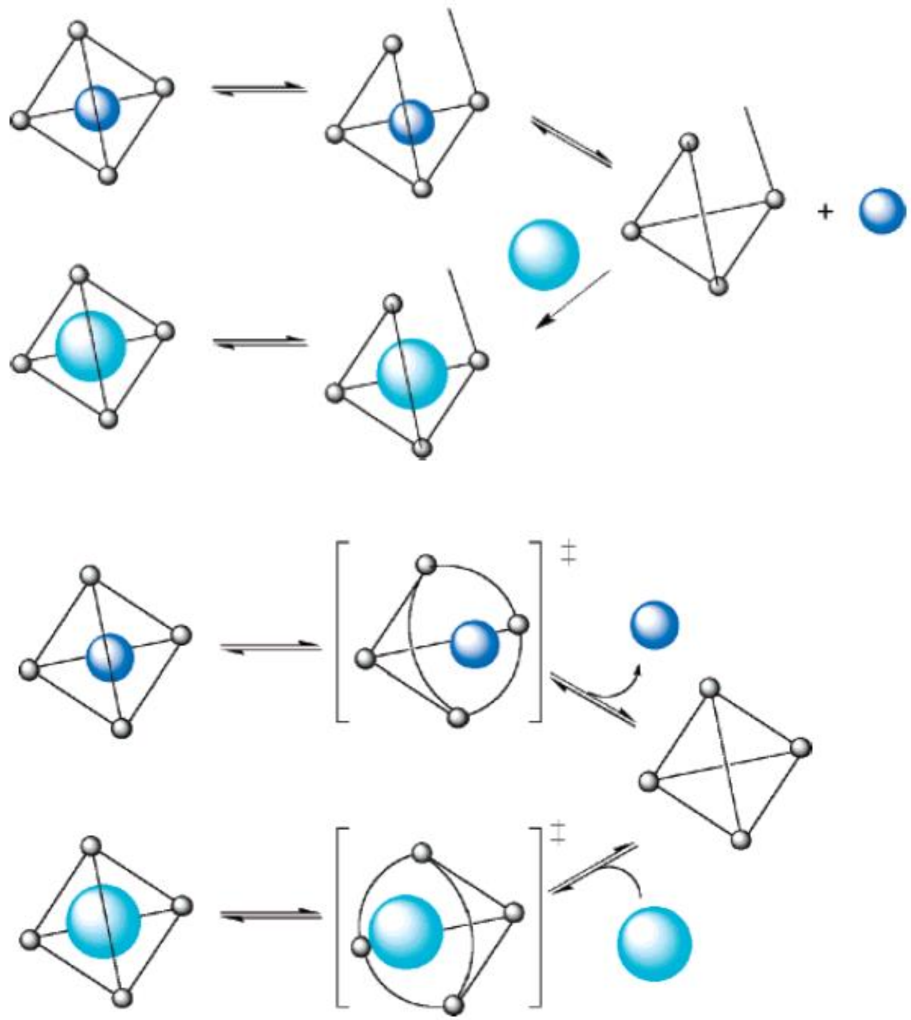
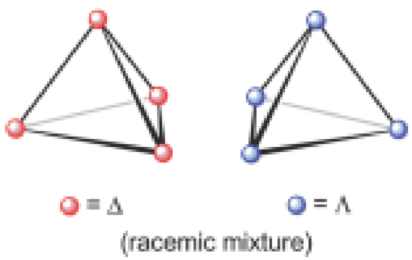


Figure 15. Based on the X-ray structure coordinates, $Et_4N^+ \subset [Fe_4\mathbf{C}_6]^{12-}$ in both (a) wire-frame and (b) space-filling representations.

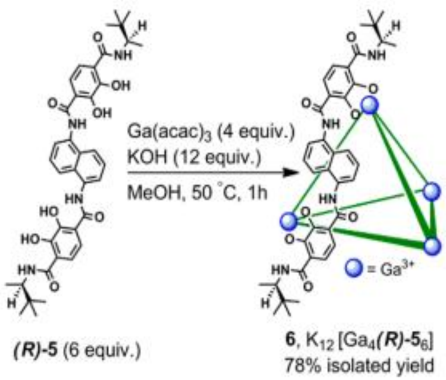
ESI-MS data

Guest exchange in an M_4L_6 supramolecular host has been evaluated to determine whether host rupture is required for guest ingress and egress. Two mechanistic models were evaluated: one requiring partial dissociation of the host structure to create a portal for guest passage and one necessitating deformation of the host structure to create a dilated aperture for guest passage without host rupture.





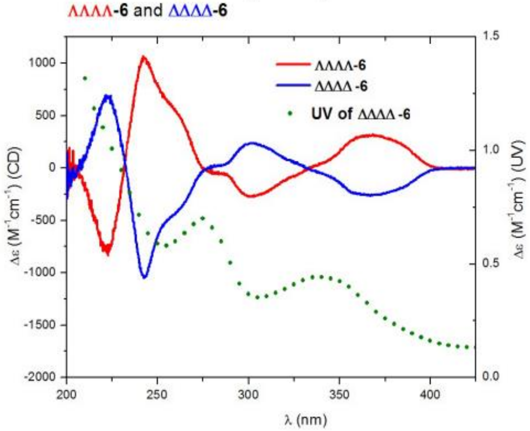
Resolution of the racemate using (−)-N′-methylnicotinium iodide: enantiopure ΛΛΛΛ-(S-nic ⊂ cage) and ΔΔΔΔ-(S-nic ⊂ cage) stereoisomers, after sequential ion exchange chromatography.



Achieving enantiopure M_4L_6 assembly without resolution using an amide-containing chiral directing group at the vertex of ligand - (*R*)-5 OR (*S*)-5.

6-$K_{12}Ga_4$(*R*)-5_6 and **6**-$K_{12}Ga_4$(*S*)-5_6 by CD spectroscopy: similar to those of ΔΔΔΔ-cage and ΛΛΛΛ-cage from racemate resolution.

CD and UV-Vis Absoprtion Spectra of ΛΛΛΛ-6 and ΔΔΔΔ-6



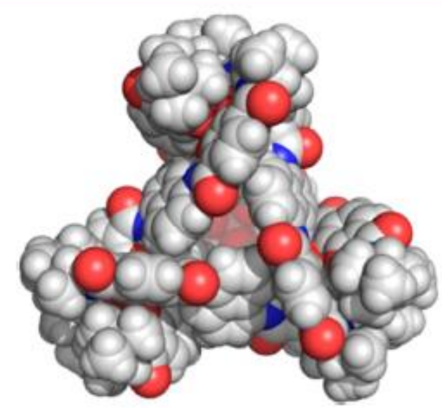
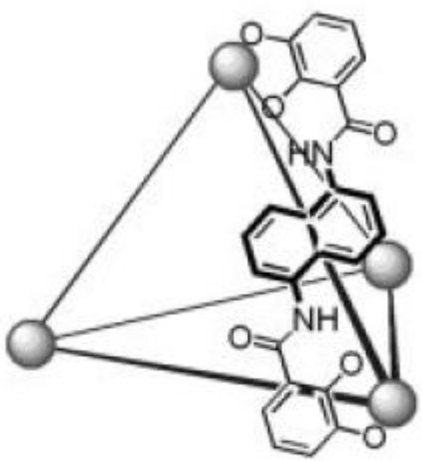
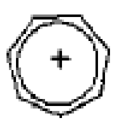


Figure 2. X-ray structure of ΔΔΔΔ-6.





4

Addition of one equivalent of **4** to the $[Ga_4L_6]^{12-}$ assembly in D_2O results in the shift of the tropylium singlet from $\delta = 6.45$ to 2.95 ppm (Figure 4, a). Integration of this upfield-shifted tropylium signal indicates that this cation is encapsulated as a guest inside the tetrahedral assembly with a 1:1 ratio. Addition of a second equivalent of tropylium ion results in a second broad resonance at $\delta = 5.18$ ppm (Figure 4, b). The upfield shift of this resonance, compared to the resonance of free tropylium in D_2O, indicates that the second equivalent of aromatic tropylium cation interacts with the $[Ga_4L_6]^{12-}$ assembly by ion-pair association with the highly-charged assembly, as seen

After 20 h in solution (Figure 4, c), the encapsulated tropylium signal is still sharp, while the signal for the tropylium associated with the assembly was noticeably broadened, and the signal for free tropylium at $\delta = 6.45$ ppm is unobservable. Free tropylium completely decomposes in D_2O after approximately 24 h, so it seems that encapsulation of this cation in the hydrophobic environment of the $[Ga_4L_6]^{12-}$ cavity has significantly increased its stability.[26]

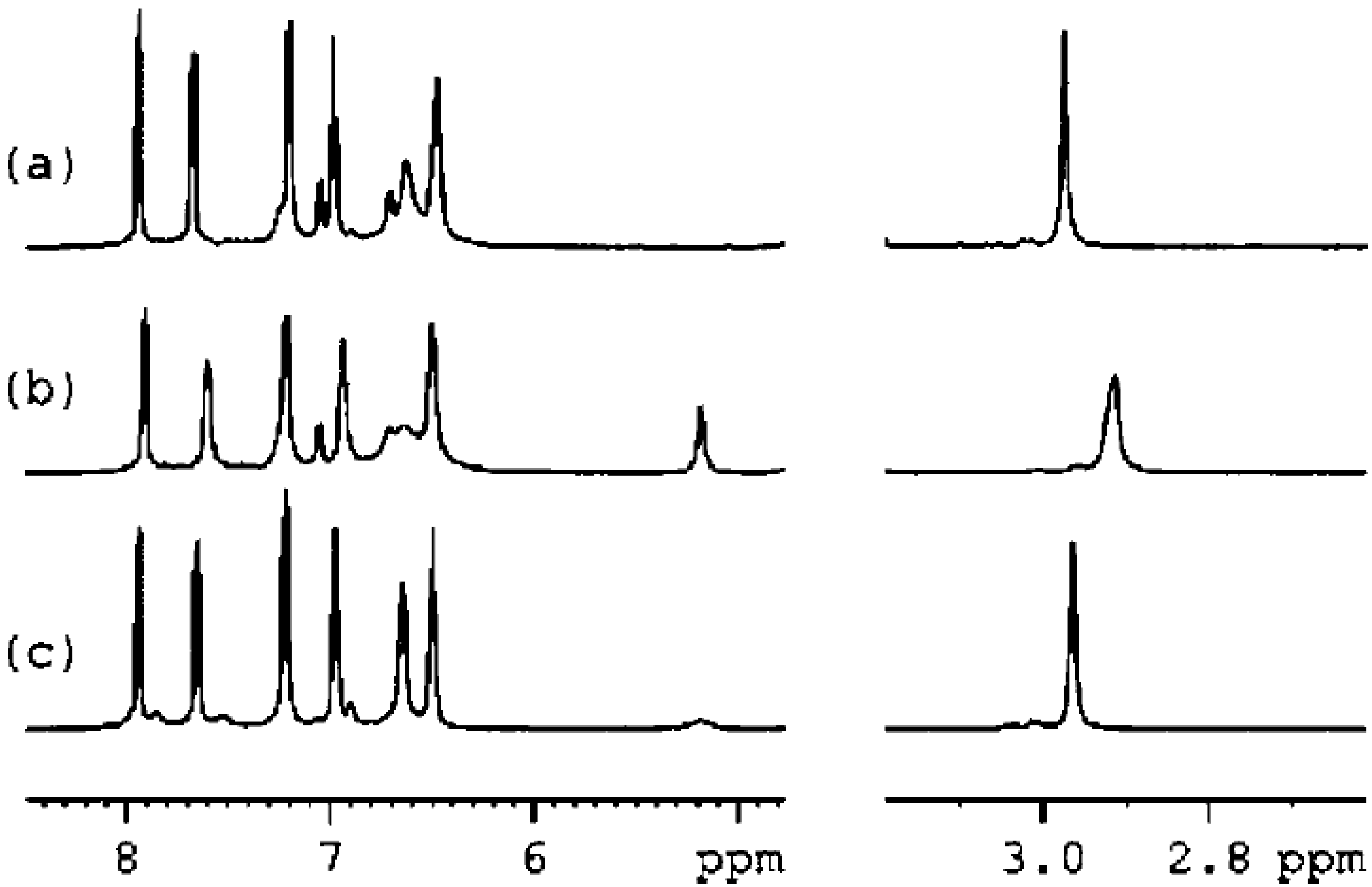
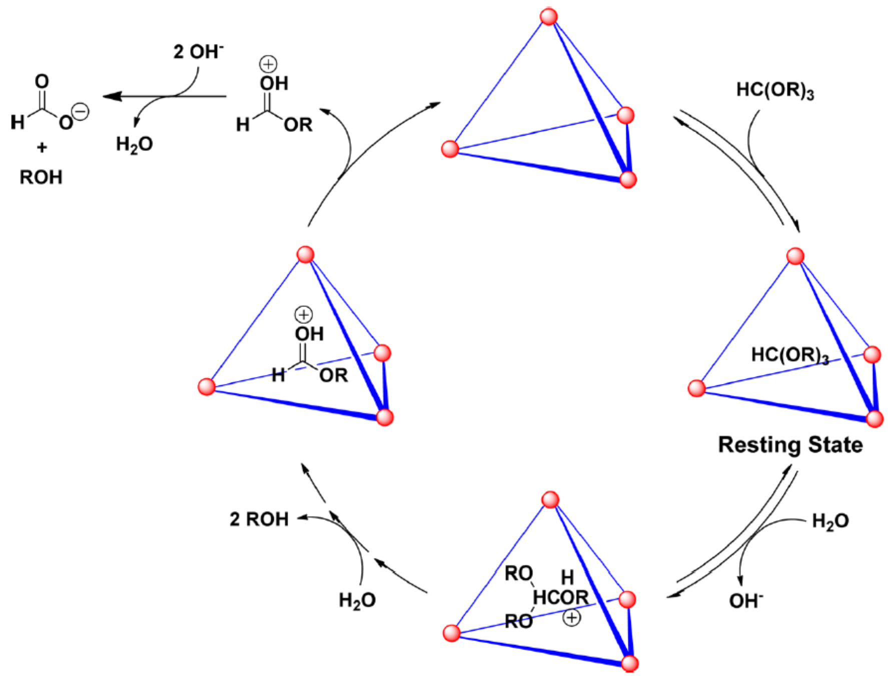


Figure 4. ^{1}H NMR spectra in D_2O of (a) the $[Ga_4L_6]^{12-}$ assembly + 1 equiv. **4**; (b) + 2 equiv. **4**; (c) sample in spectrum b after 20 h

Acid Catalysis in Basic Solution: A Supramolecular Host Promotes Orthoformate Hydrolysis

Michael D. Pluth, Robert G. Bergman,* Kenneth N. Raymond*

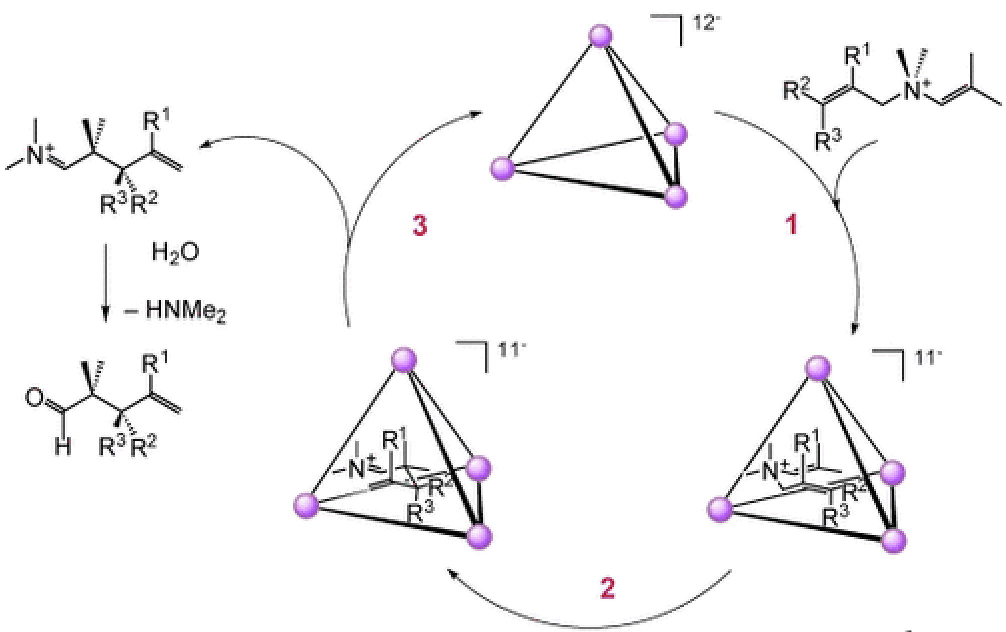


reached. Although the pK_a of **3**-H$^+$ is 10.8 in free solution, stabilization of the protonated form by **1**, which can be calculated as the product of the pK_a and the binding constant of the protonated amine, shifts the effective basicity to 14.3 (*32*). This dramatic shift highlights the substantial stabilization of the protonated species over the neutral species upon encapsulation in the highly charged cavity (*33*).

Supramolecular Catalysis of a Unimolecular Transformation: Aza-Cope Rearrangement within a Self-Assembled Host**

Dorothea Fiedler, Robert G. Bergman, and Kenneth N. Raymond**

These findings highlight the ability of container-like molecules to provide size- and shape-defined nanospaces, highly capable of catalysis of unimolecular organic reactions. By binding the substrates in a reactive conformation, the host assembly accelerates the rates of rearrangement by up to



three orders of magnitude. Release and hydrolysis of the rearranged product generate catalytic turnover. With this, the large potential of supramolecular assemblies as synthetically useful tools in organic chemistry becomes apparent.

ChemComm

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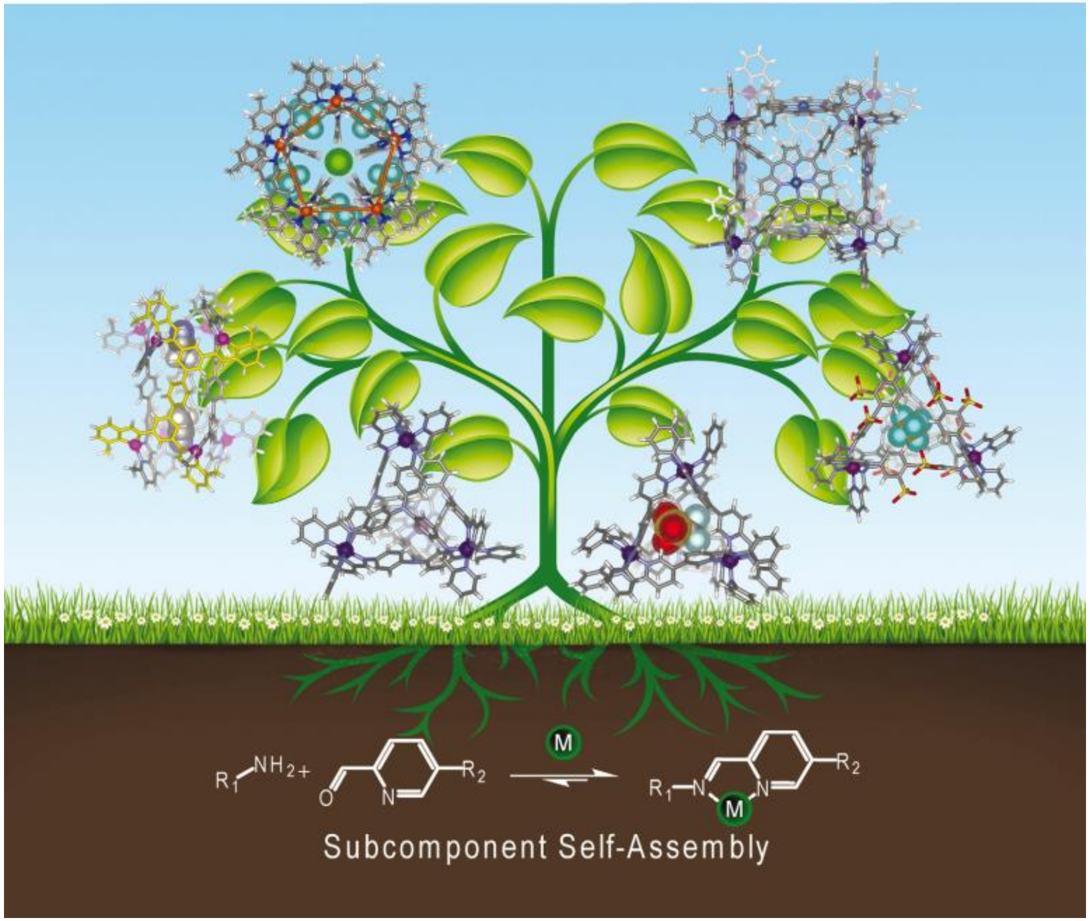
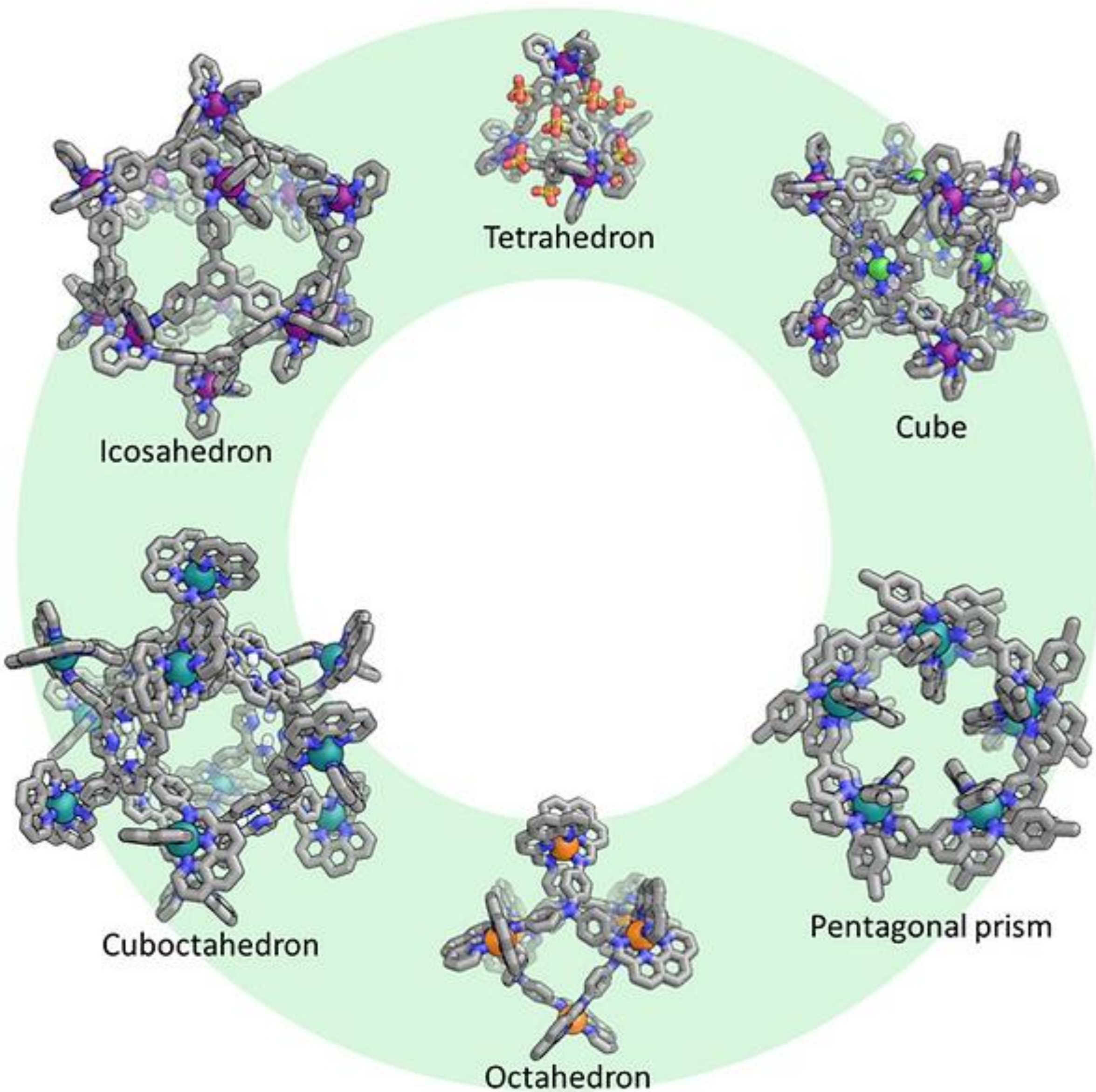
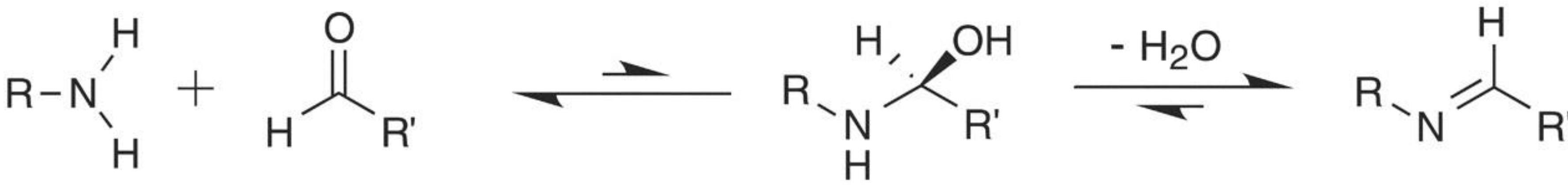
Volume 49 | Number 25 | 28 March 2013 | Pages 2465–2580

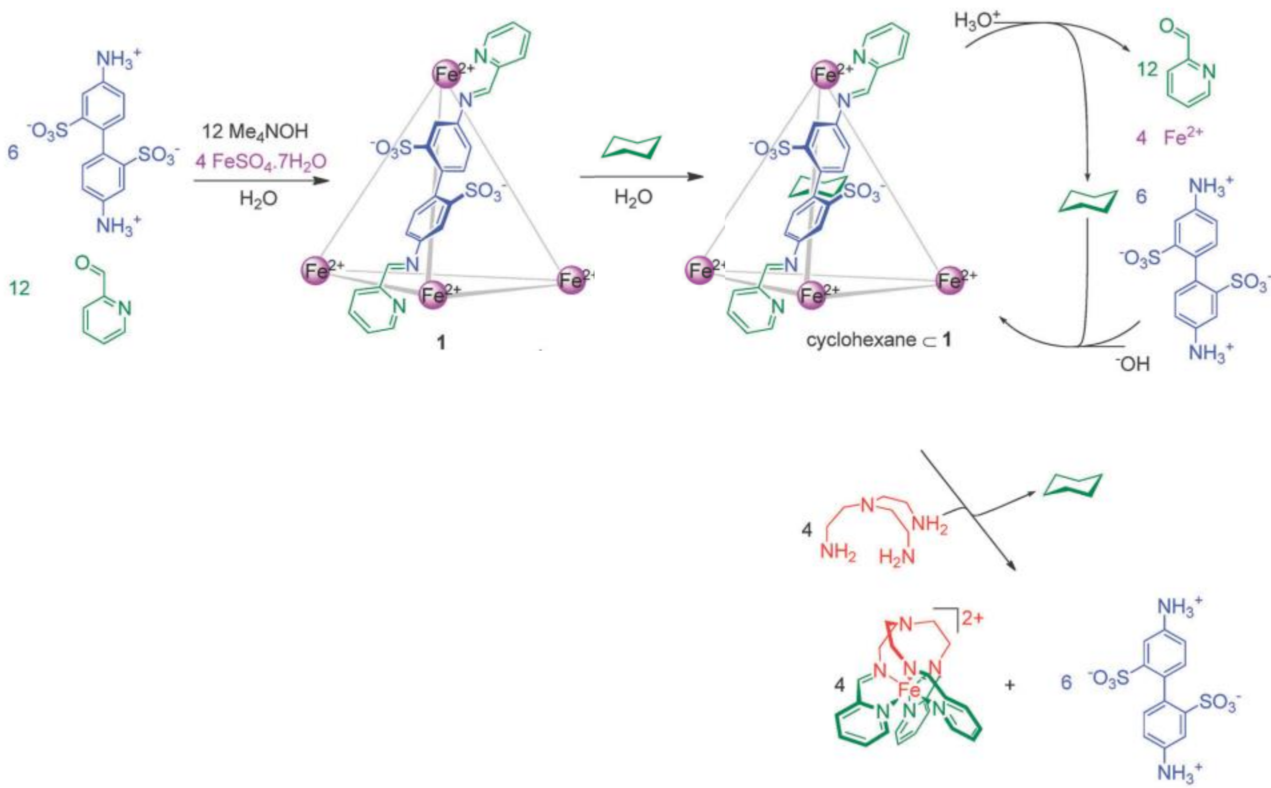


https://www.nitschkegroup-cambridge.com/research-areas

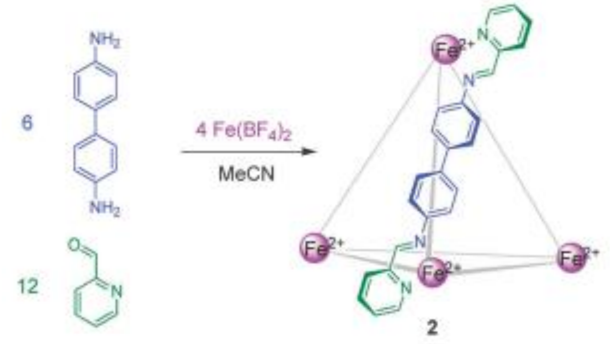


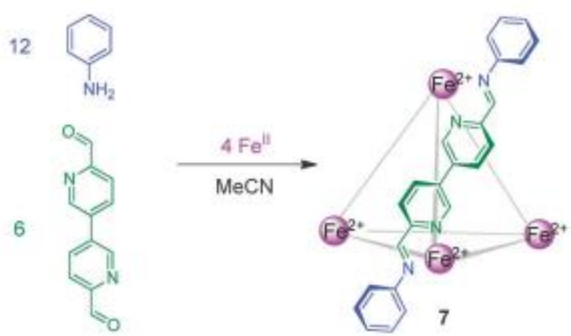


Hemiaminal Imine

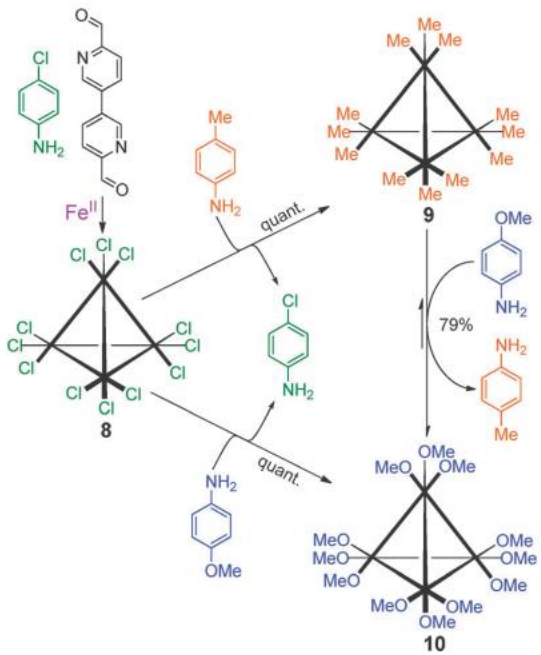


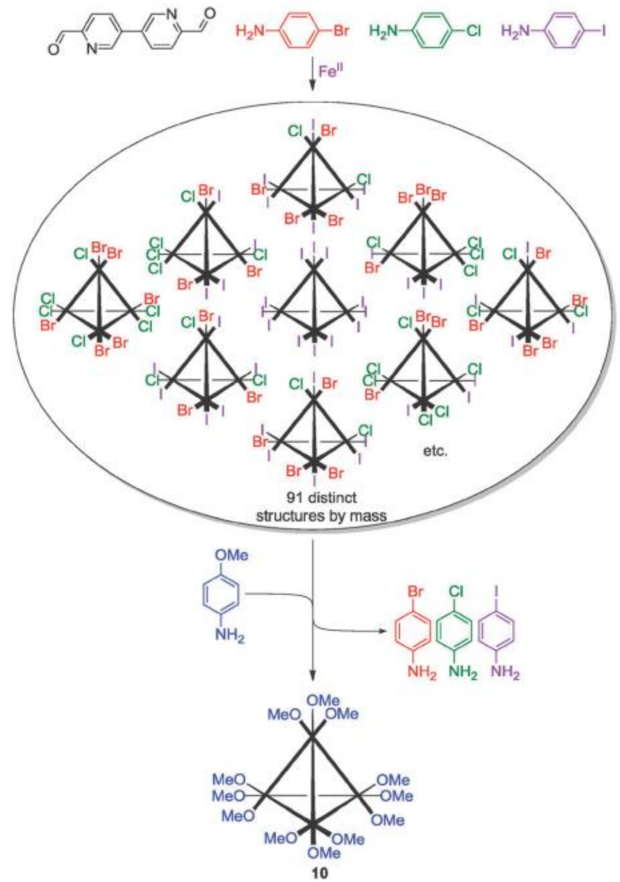
4,4’-diaminobiphenyl/2’-carbossaldeide

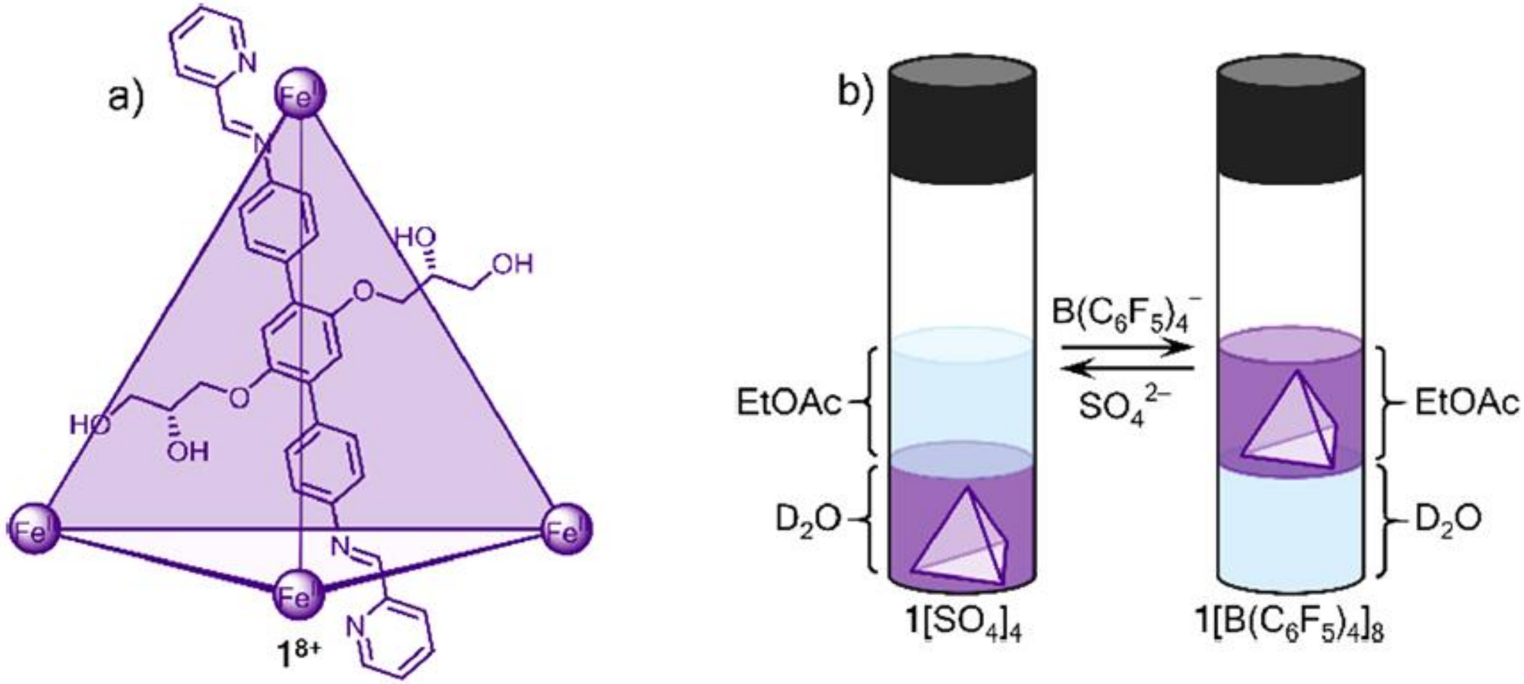


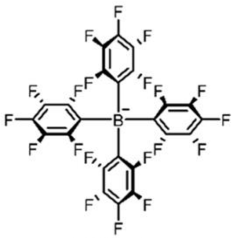


6,6’-diformyl-3,3’-bipyridinel/aniline


Fe^II
quant.
quant.
79%
8
9
10


Fe^II
etc.
91 distinct
structures by mass
10





$B(C_6F_5)_4^-$

$LiB(C_6F_5)_4$ to promote anion metathesis from SO_4^{2-} to $B(C_6F_5)^{4-}$

$(n\mathrm{Bu}_4N)_2SO_4$ to regenerate the solfate cage

White Phosphorus Is Air-Stable Within a Self-Assembled Tetrahedral Capsule

Prasenjit Mal,[1] Boris Breiner,[1] Kari Rissanen,[2] Jonathan R. Nitschke[1*]

SCIENCE VOL 324 26 JUNE 2009 1697

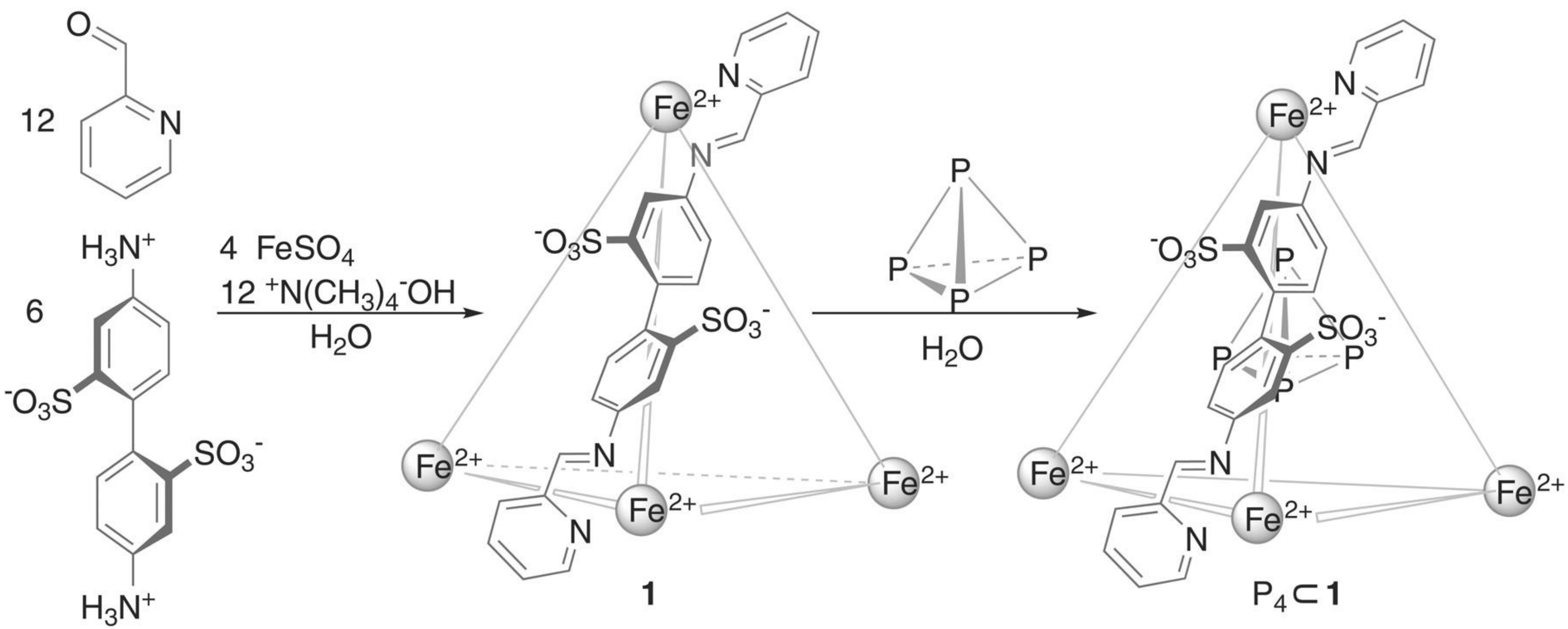


Fig. 1 Synthesis of tetrahedral cage 1 and subsequent incorporation of P4.

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Communication

Light-Powered Reversible Guest Release and Uptake from Zn_4L_4 Capsules

Amit Ghosh, Laura Slappendel, Bao-Nguyen T. Nguyen, Larissa K. S. von Krbek, Tanya K. Ronson, Ana M. Castilla, and Jonathan R. Nitschke*

Cite This: J. Am. Chem. Soc. 2023, 145, 3828–3832

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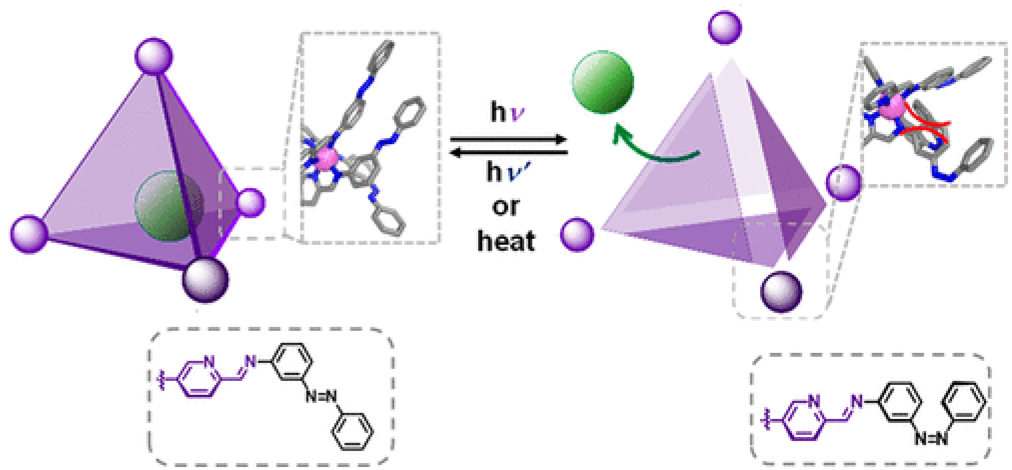


Choice of metal ion - coordination geometry + kinetic lability:

Octahedral - Ga^{III}, Al^{III}, Ti^{IV}, Fe^{II}, Co^{II}, Zn^{II}, Cd^{II}, $Ni^{II;}$
Square planar - Pd^{II} and Pt^{II}
Lanthanide ions kinetically labile BUT variable coordination number and geometry
Kinetically inert metal ions (e.g. Ru^{II} and Ir^{III}): kinetic control unless *trans* effect.

The self-assembly process - interplay between enthalpy and entropy:

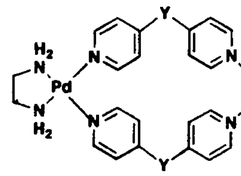
multiple equilibria/variety of factors - metal coordination geometry/kinetic lability/ligand geometry/metal-to-ligand stoichiometry/concentration/solvent/presence of guests.
Therefore, it can be difficult to predict the outcome since there is a delicate balance.

The principle of maximum site occupancy:

species where all the metal coordination sites are occupied with ligands are more stable than those with vacant coordination sites since this maximises the number of metal–ligand bonds and therefore, the enthalpy.

On the other hand, a system containing a larger number of smaller cages with fewer building blocks is favored on entropic grounds over one containing a smaller number of larger cages.

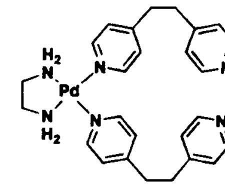
Multiple architectures can be self-assembled from the same building blocks:
(a) a single cage when it is the thermodynamically most stable structure;
(b) a mixture of cages as the thermodynamic products with the distribution reflecting the relative energies of the cages;
(c) a dynamic combinatorial library with a large number of interconverting species in equilibrium.



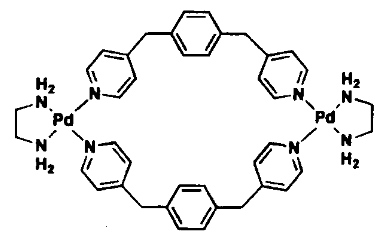
$\cdot(NO_3)_4$

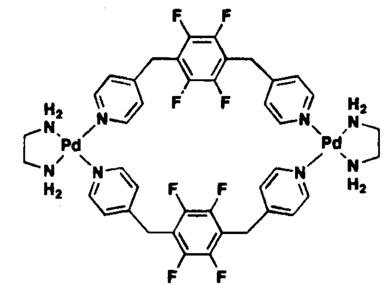
Y = CH_2

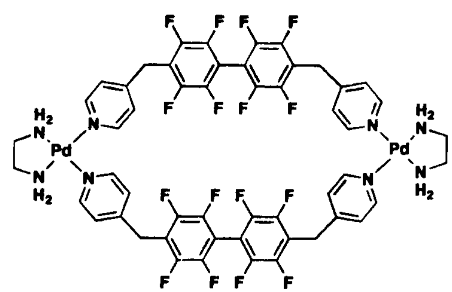
Y = $C(OH)_2$

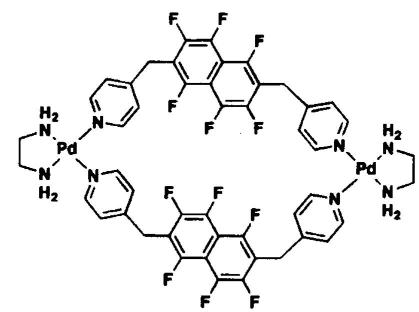


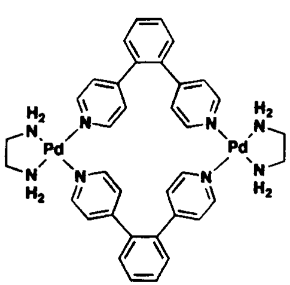
$\cdot(NO_3)_4$

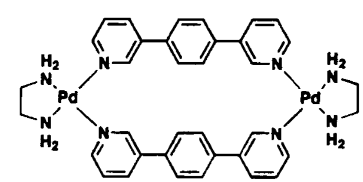


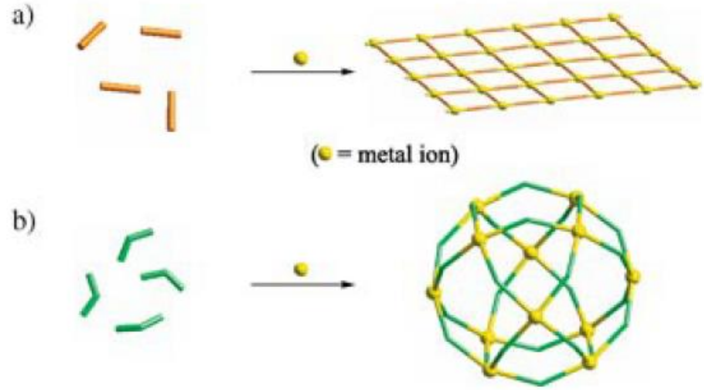


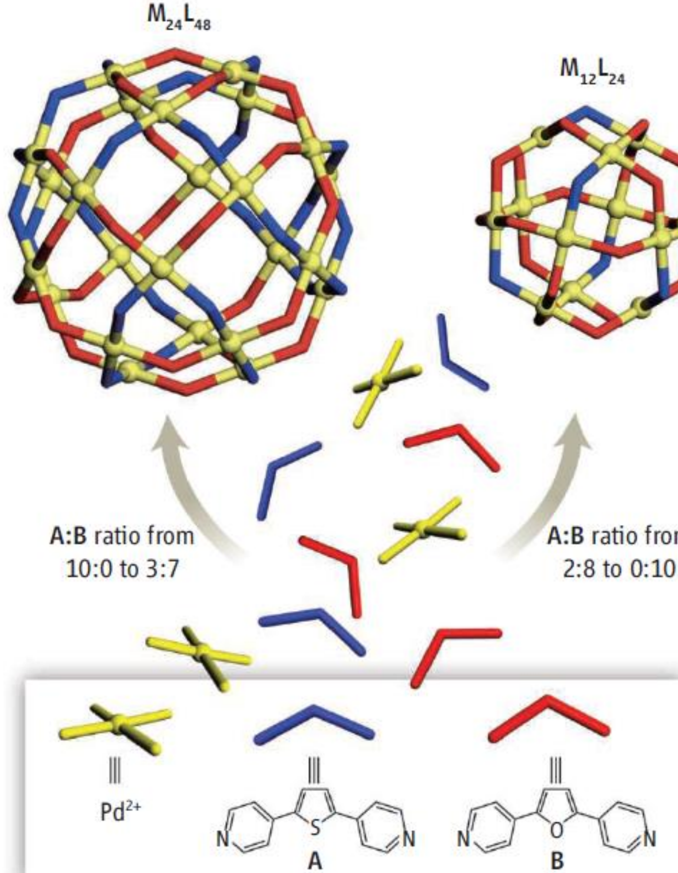









a)
(● = metal ion)
b)

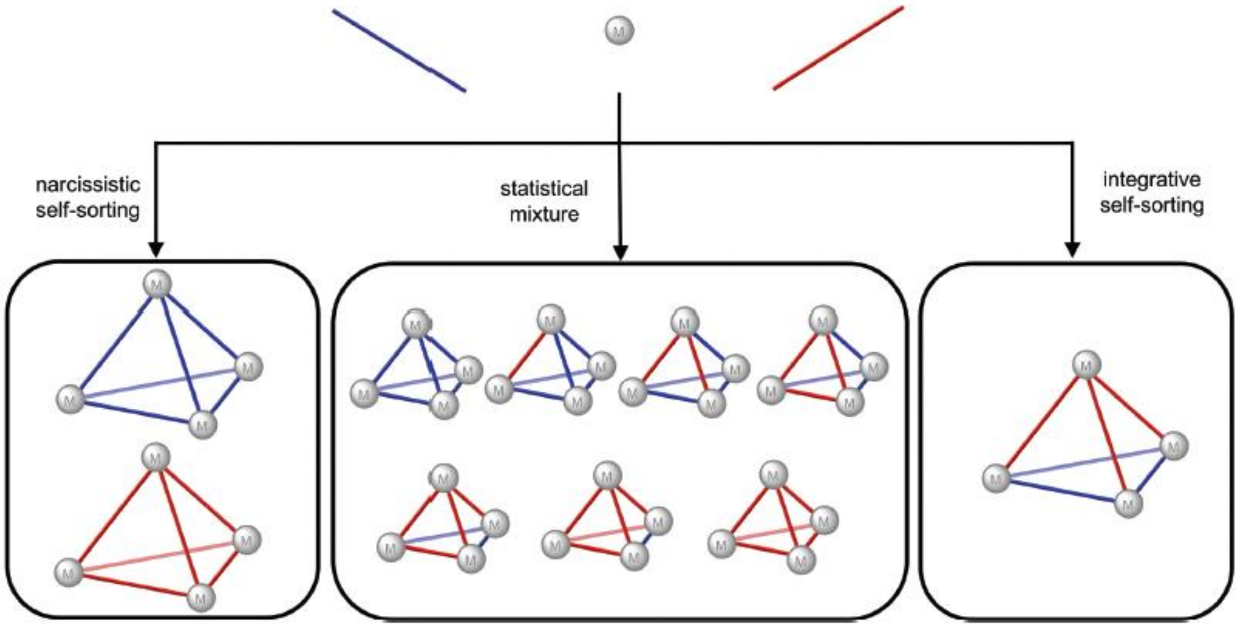

$M_{24}L_{48}$
$M_{12}L_{24}$
A:B ratio from
10:0 to 3:7
A:B ratio from
2:8 to 0:10
Pd^{2+}
N
S
N
A
N
O
N
B

Design of lower symmetry cages

- symmetry breaking of the ligand upon metal coordination
- self-assembly of heteroleptic cages containing multiple ligands
- use of non-symmetric ligands to form homoleptic but lower symmetry cages
- use of multiple metals to form heterometallic cages.

Self-Sorting

narcissistic self-sorting - homoleptic cages with one ligand type in each cage
statistical mixture - both ligands are incorporated into the cages according to their statistical distribution;
integrative self-sorting - a nonstatistical distribution of heteroleptic cages results.



The key challenges to the design of heteroleptic cages via integrative self-assembly are, therefore, stabilisation of the heteroleptic cage/s relative to the homoleptic cages and biasing the system away from the statistical mixture.