Synthetic small molecules as machines: a chemistry perspective

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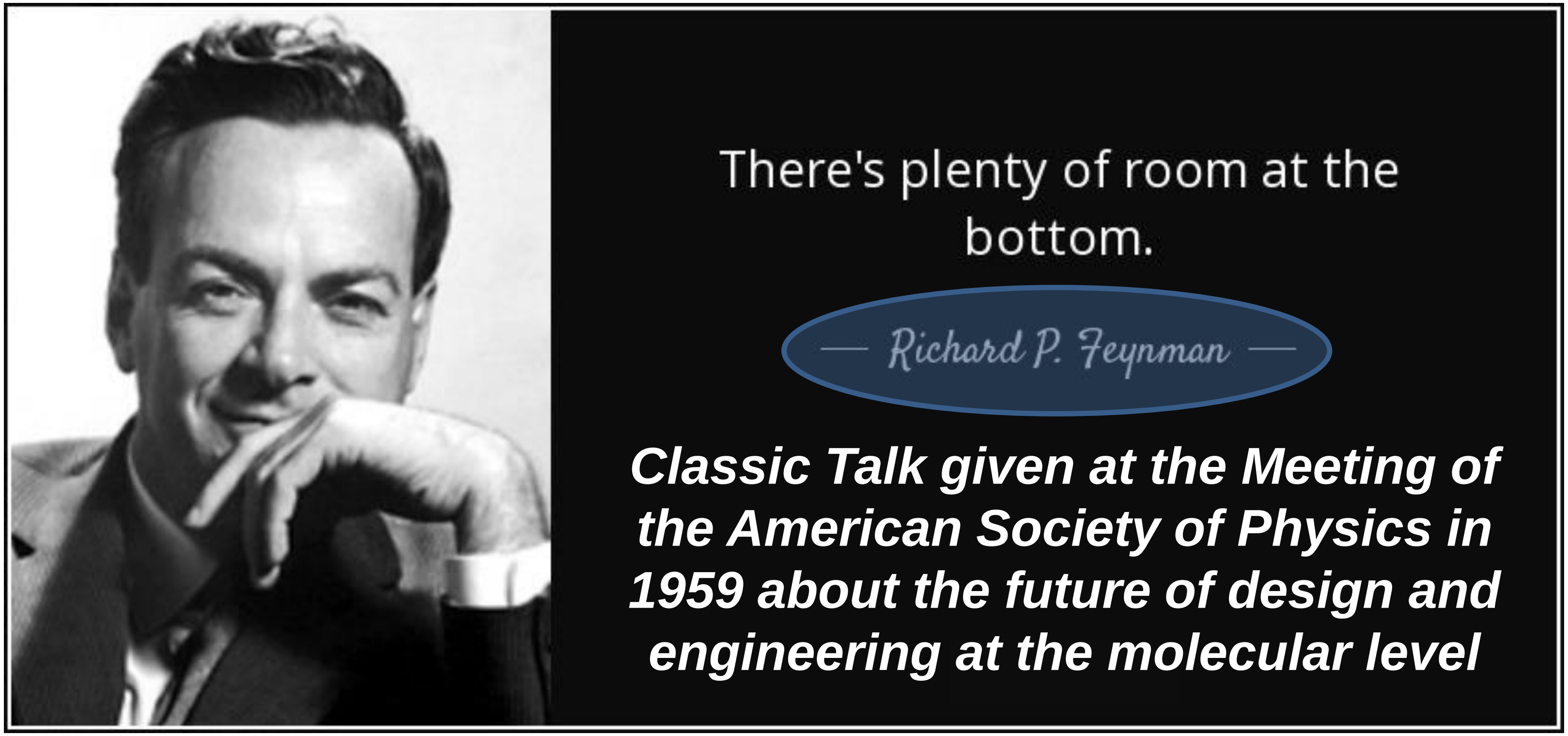
28th Mid-Year Meeting of Indian Academy of Sciences (IASc), Bengaluru, 1st July 2017

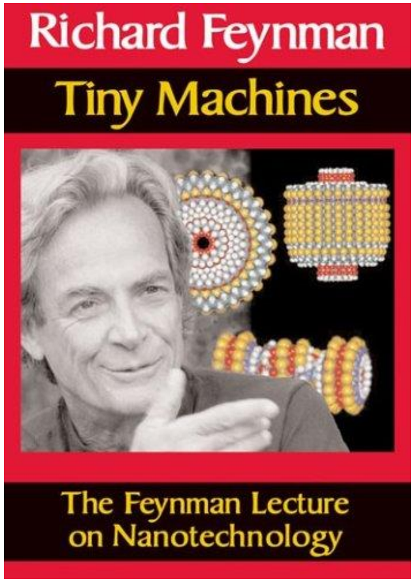
Feynman’s Dream on Molecular Machines



The possibility of building small machines from atoms i.e. machines small enough to manufacture objects with atomic precision.

Transcript of Talk : *Caltech Eng. Sci.* **1960**, *23:5*, 22–36.

Feynman's 1984 Visionary Lecture…….



How small can you make machinery?

Machines with dimensions on the nanometre scale.

These already existed in nature. He gave bacterial flagella, corkscrew-shaped macromolecules as an example.

Future vision – molecular machines will exist within 25–30 years.

The aim of the lecture: To inspire the researchers in the audience, to get them to test the limits of what they believed possible.

What neither Feynman, nor the researchers in the audience, knew at the time was that the first step towards molecular machinery had already been taken, but in a rather different way to that predicted by Feynman.

What is that?

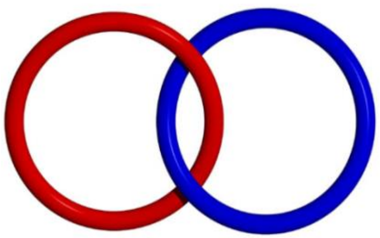
1953: Mechanical Bonds in Molecules

Mid-20th century: Chemists were trying to build molecular chains in which ring-shaped molecules were linked together.

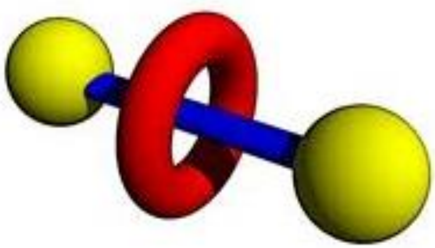
The dream: To create mechanical bonds, where molecules are interlocked without the atoms interacting directly with each other.

Frisch, H. L. *Monatsh. Chem.* **1953**, *84*, 250

Interlocked Molecules:



[2] Catenane

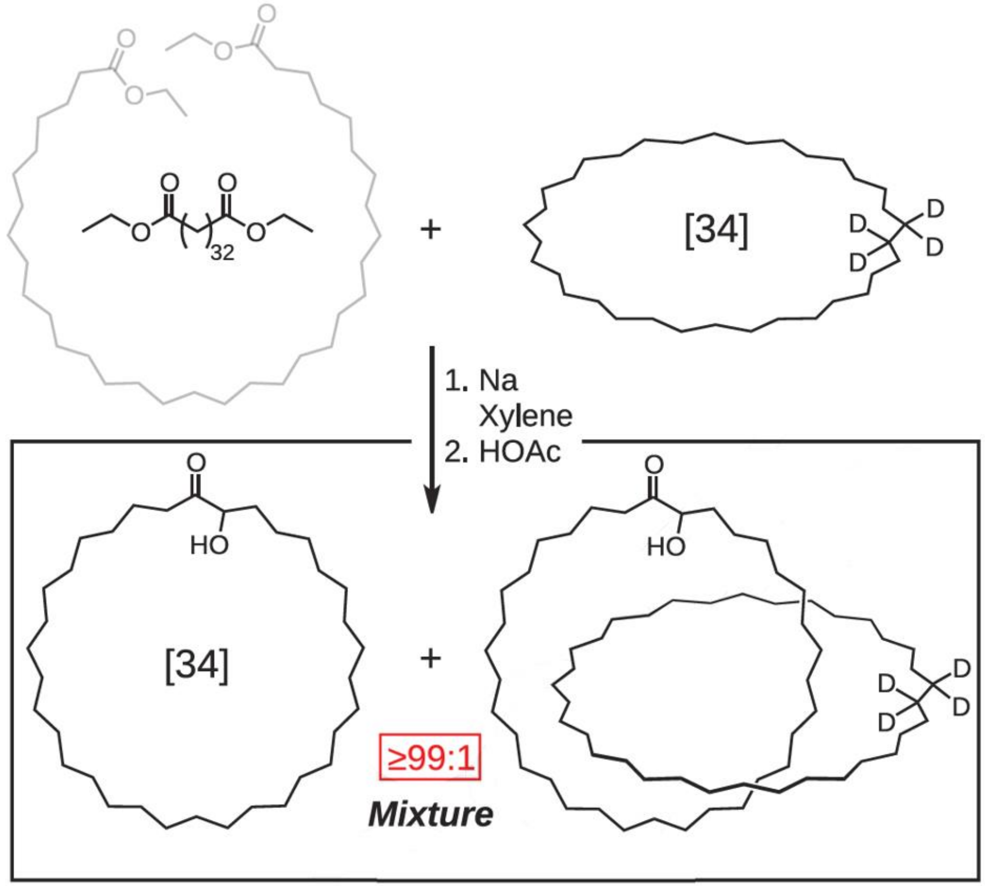


[2] Rotaxane

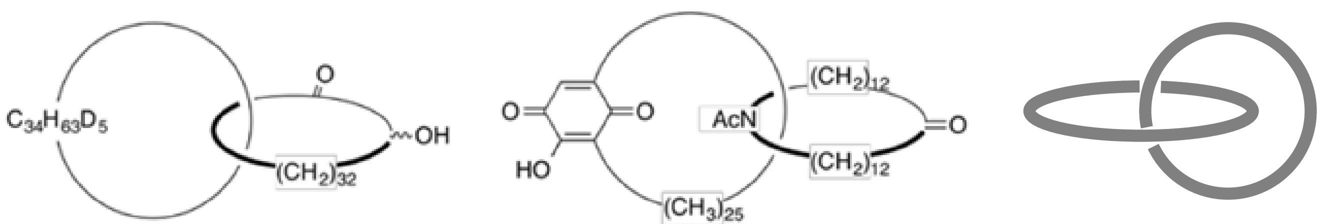
- Many research groups reported in the 1950s and 1960s that their reaction vessels contained molecular chains.
- Yeilds were extremely low and the methods so complex that they were of limited use.
- Progress was regarded more as a curiosity than as functional chemistry.

1960 First Catenane: Statistical Synthesis

Edel Wasserman



1% Yield



Wasserman, E. *J. Am. Chem. Soc.* **1960**, *82*, 4433–4434.

1961: Historical Work on "Chemical Topology

Frisch, H. L. Wasserman, E. J. Am. Chem. Soc. 1961, 3789

ORGANIC AND BIOLOGICAL CHEMISTRY

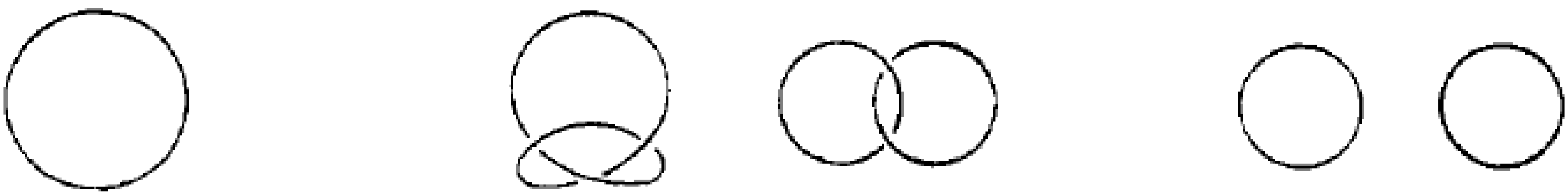
[CONTRIBUTION FROM THE BELL TELEPHONE LABORATORIES, INCORPORATED, MURRAY HILL, NEW JERSEY]

Chemical Topology[1]

BY H. L. FRISCH AND E. WASSERMAN

RECEIVED FEBRUARY 28, 1961

The concept of topological isomerism of cyclic molecules is introduced.



I II III IV

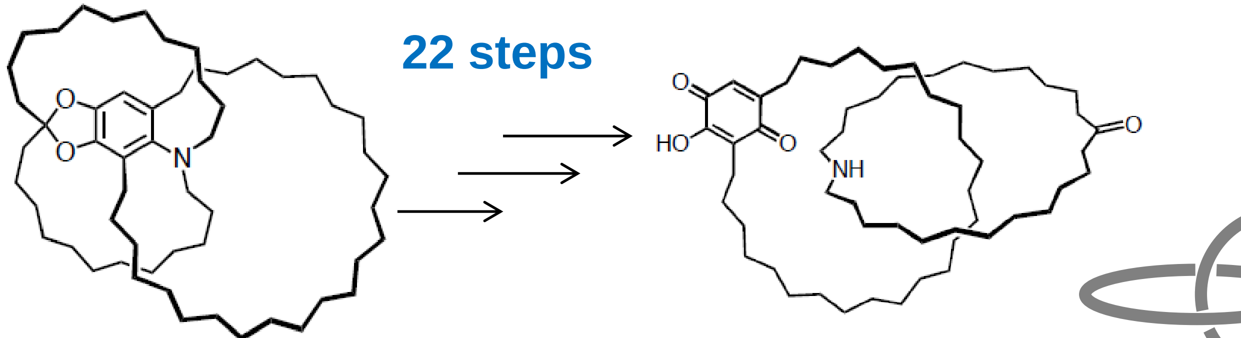
unknotted loop | **Knotted loop** | **Interlocked rings** | **Non-interlocked rings**

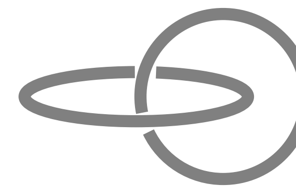
The application to various chemical systems such as knots, Chains and Möbius' strips is discussed.

1964: Early Examples of Mechanical Bonds

Directed Covalent Synthesis by Gottfried Schill

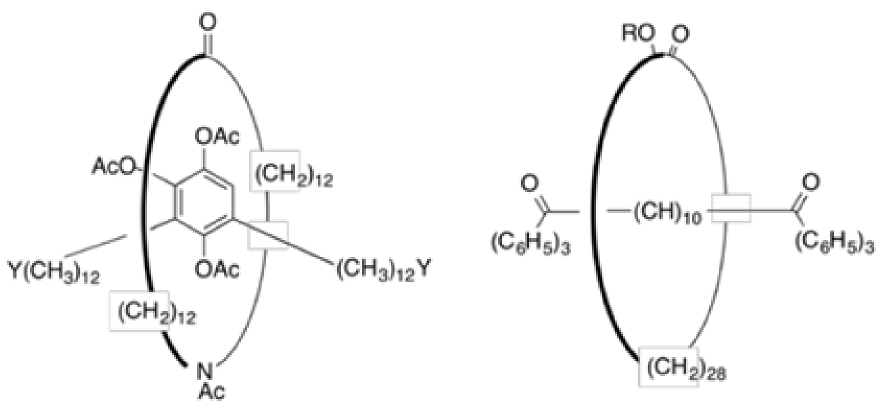
Could prepare small amounts of such compounds *via* elegant but low-yielding and multistep synthetic routes.

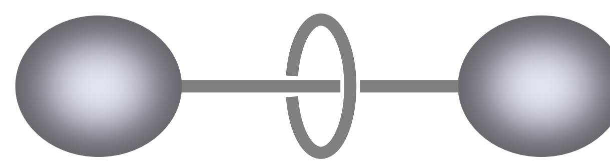




Gottfried Schill
1964

Harrison
1967

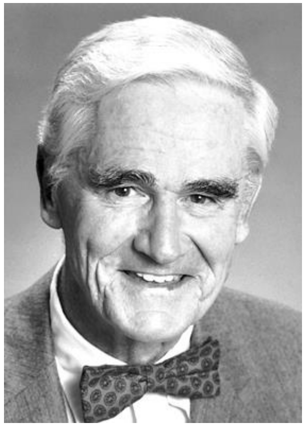




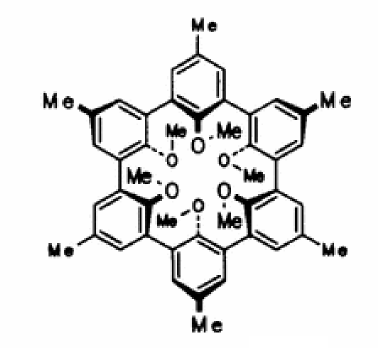
(1) Schill, G.; Lüttringhaus, A. *Angew. Chem. Int. Ed.* **1964**, *3* (8), 546–547.

(2) Harrison, I. T.; Harrison, S. *J. Am. Chem. Soc.* **1967**, *89* (22), 5723–5724.

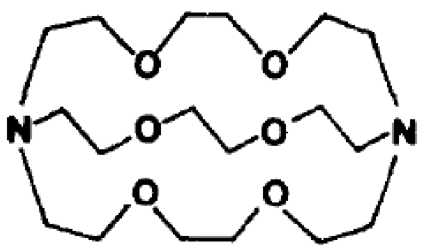
The Nobel Prize in Chemistry 1987



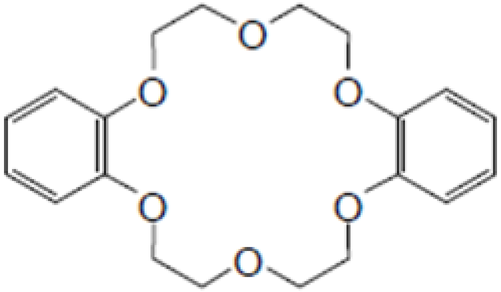
* Donald J. Cram (1919-2001), *UCLA, USA*
* Jean-Marie Lehn (1939-), *U. Louis Pasteur, France*
* Charles J. Pedersen (1904-1989), *Du Pont, USA*



1973



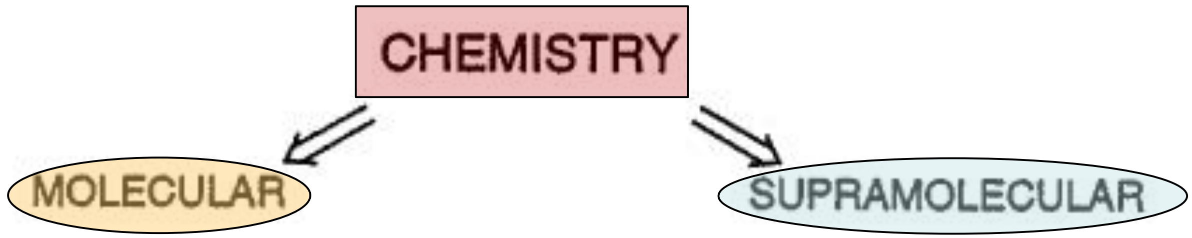
1969

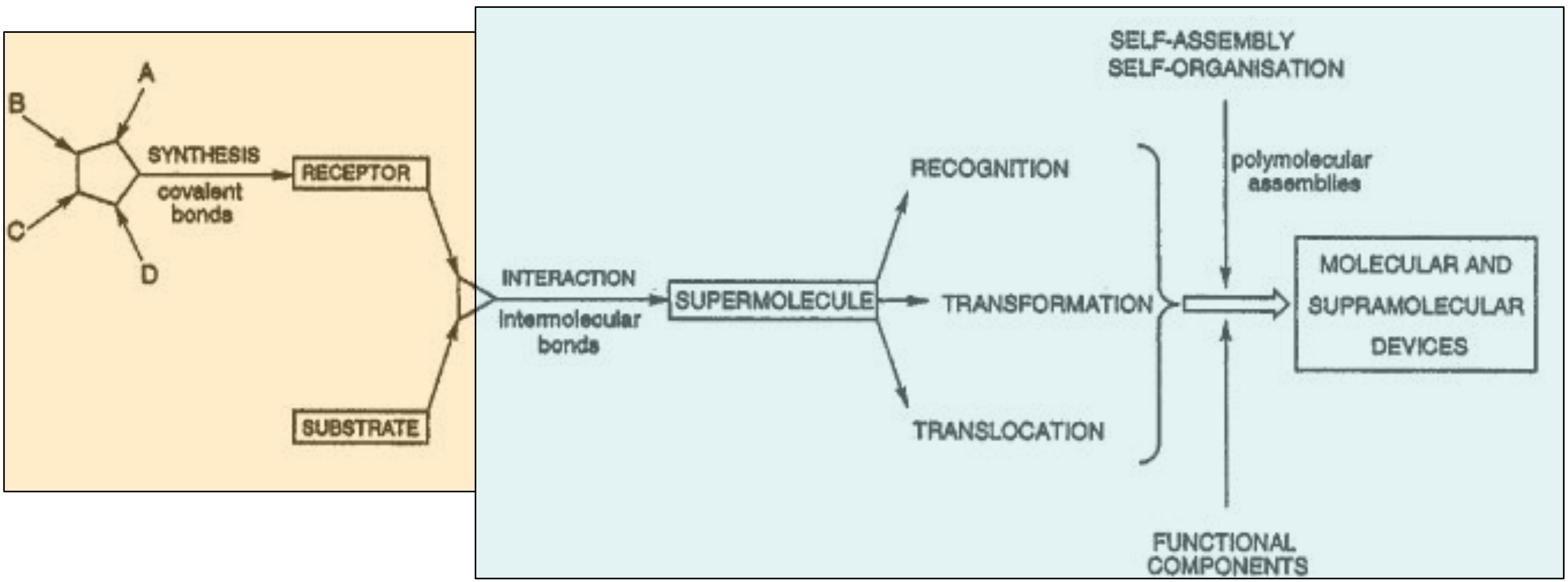


1967

"for their development and use of molecules with structure-specific interactions of high selectivity"

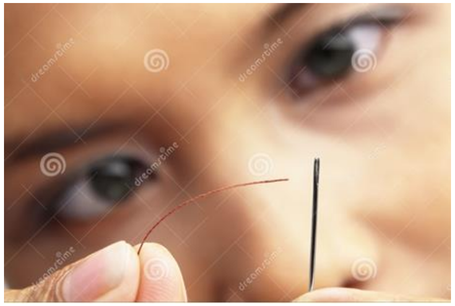
Supramolecular Chemistry by J.-M. Lehn





1987 Nobel Lecture

1983: Cu(I) Templated Threading

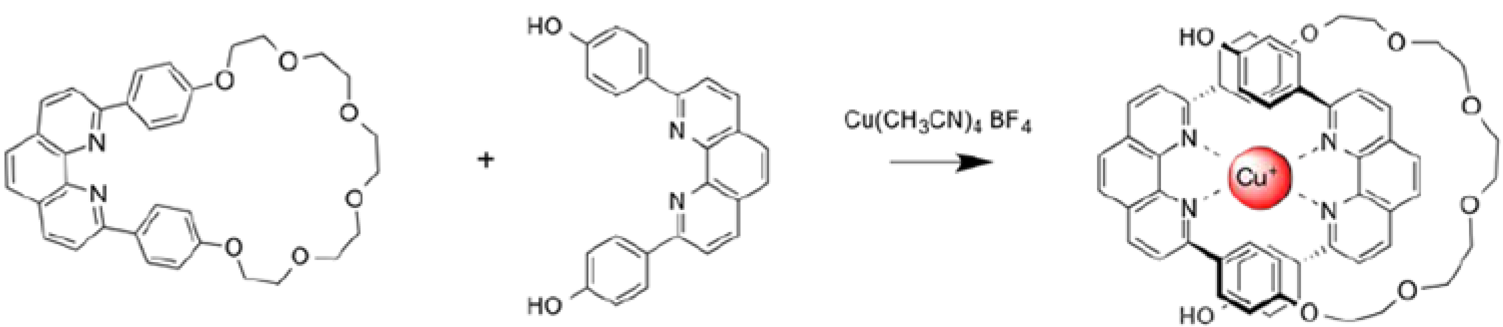


How to thread a string through the eye of a molecular needle?

Jean-Pierre Sauvage (1944-)

(CNRS, Louis Pasteur University, Strasbourg, France)

The major breakthrough came in 1983. Using a copper ion, Jean-Pierre Sauvage research group took control of the molecules.



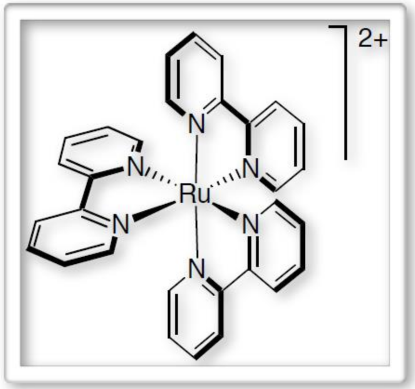
Background of the Discovery

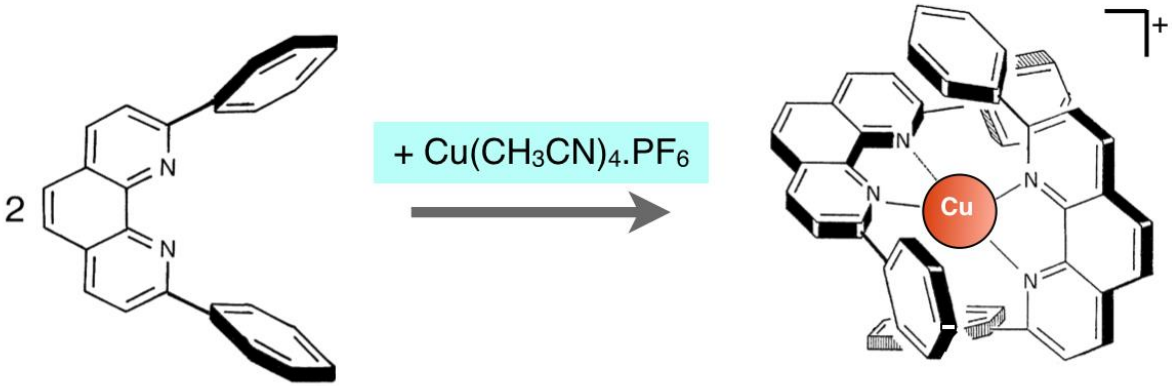
Jean-Pierre Sauvage
(1944-)

C. O. Dietrich-Buchecker
(1942-2008)

David R. McMillin
(1948-)

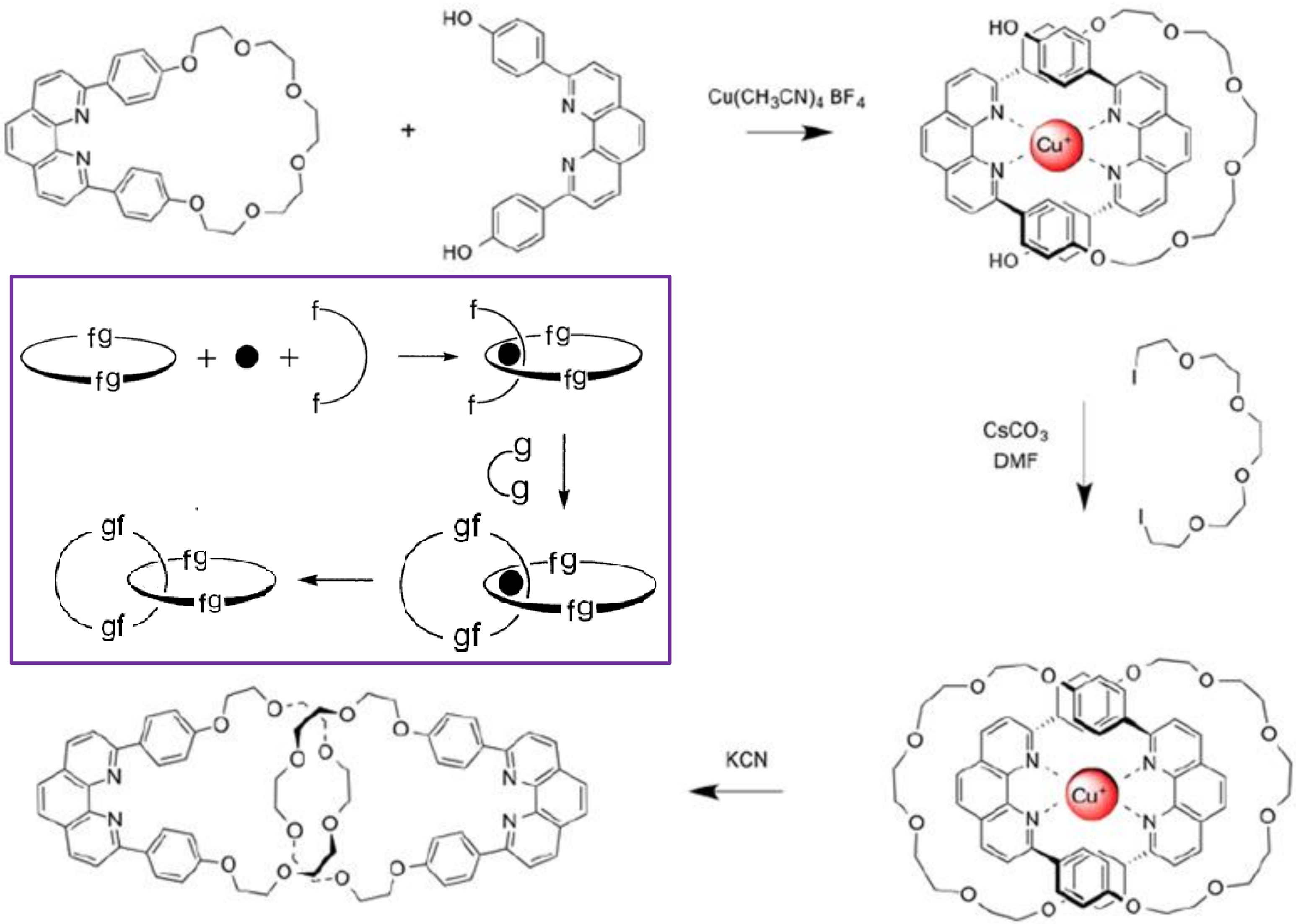
Photochemical cleavage of water to H_2 and O_2 using $[Ru(bpy)_3]^{2+}$ → **Photochemistry of copper(I) complexes with phenanthroline-type ligands with David R. McMillin group at Purdue University**





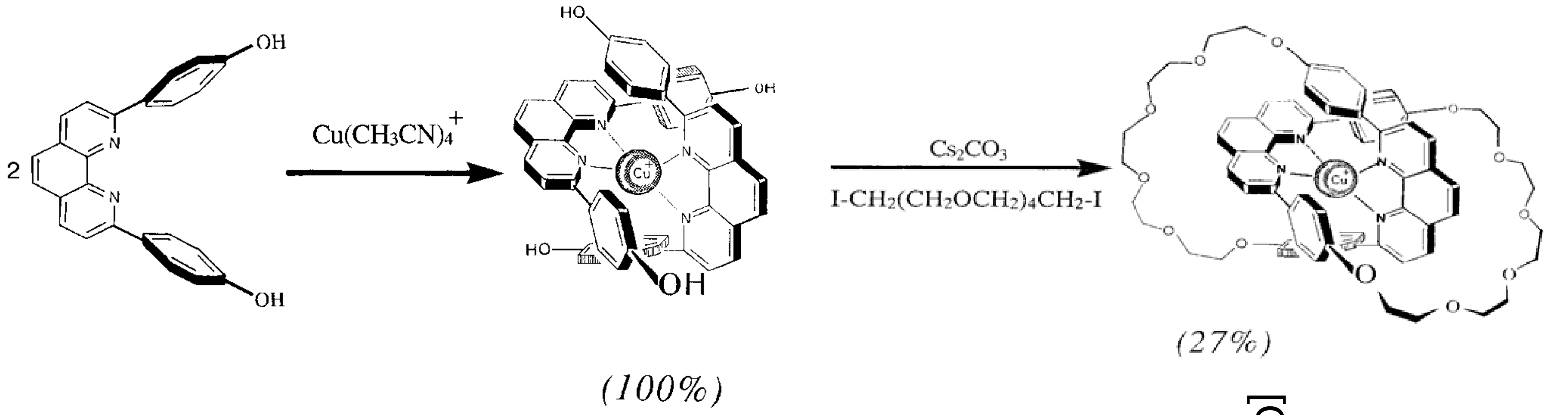
C. O. Dietrich-Buchecker, P. A. Marnot, J. P. Sauvage, J. R. Kirchoff and D. R. McMillin, Chem. Commun. **1983,** 513.

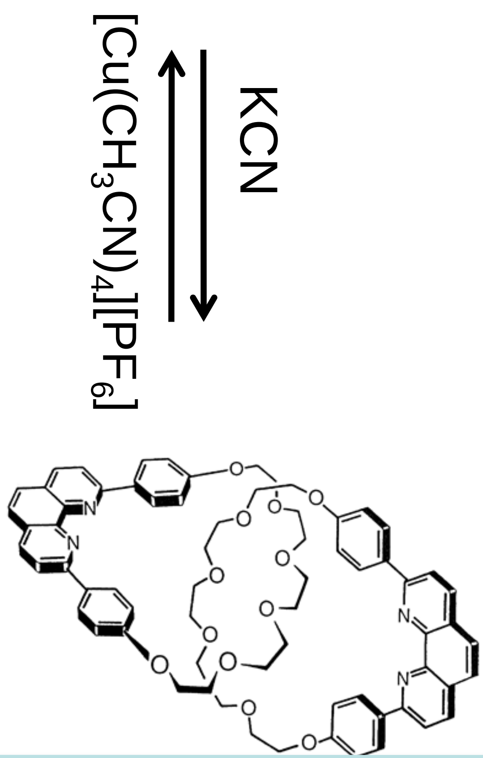
Cu(I) Templated Assembly via threading

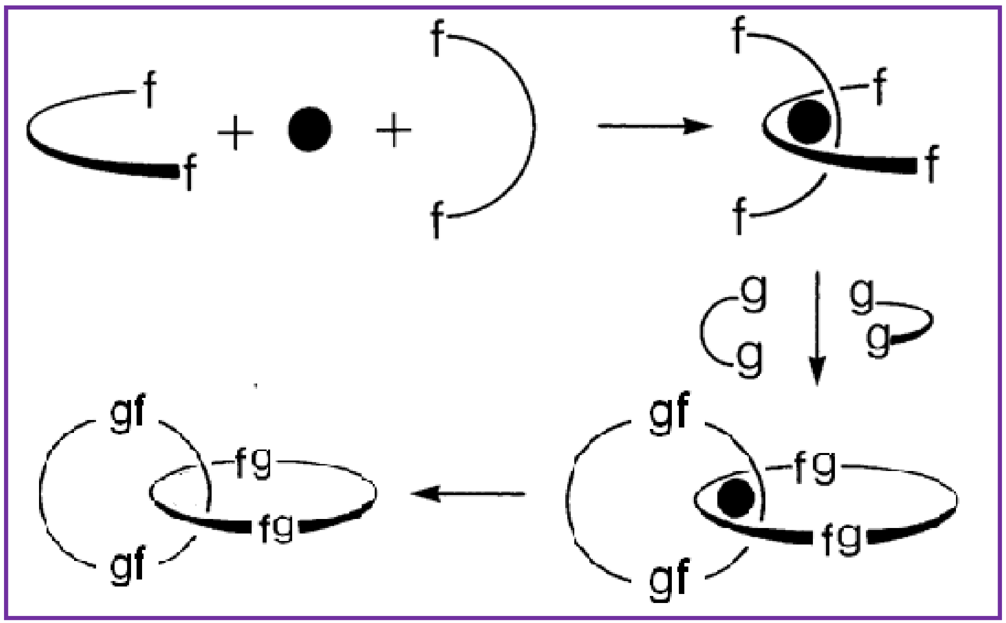


Dietrich-Buchecker, C. O.; Sauvage, J. P.; Kintzinger, J. P. *Tet. Lett.* **1983**, *24* (46), 5095

Cu(I) Templated Entangling and Double Cyclization

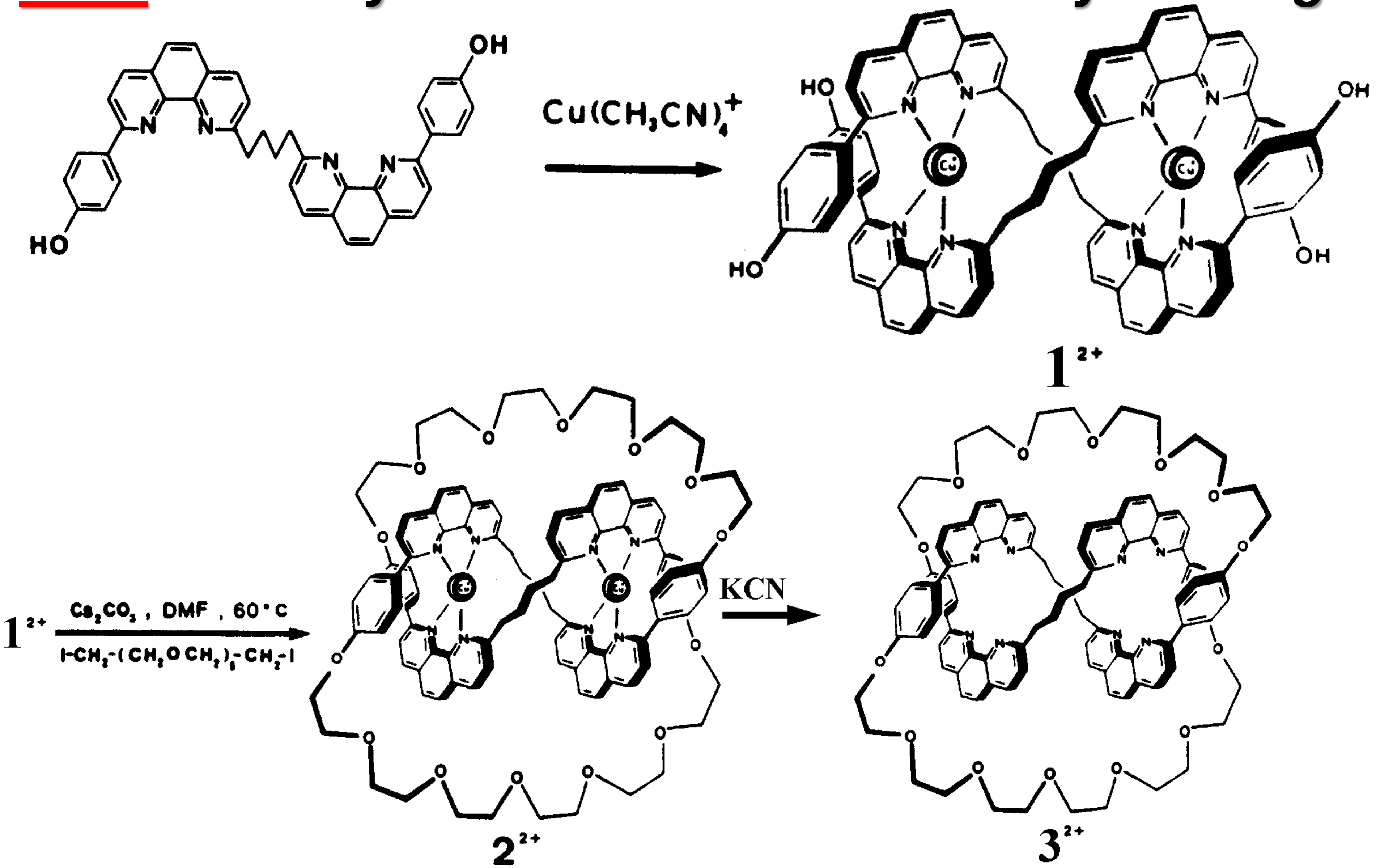






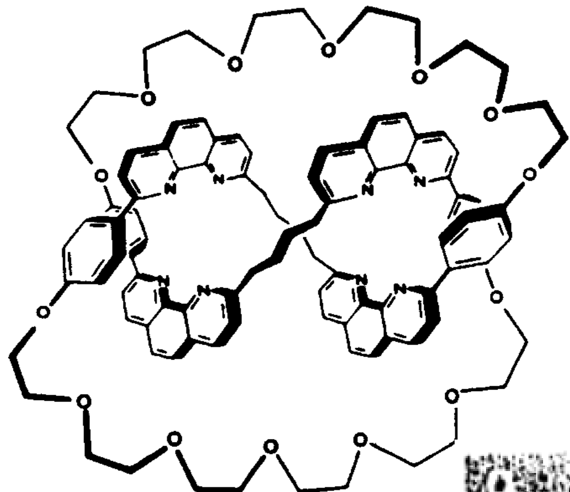
Dietrich-Buchecker et al. (1983-84) and Pascard et al. (1985)

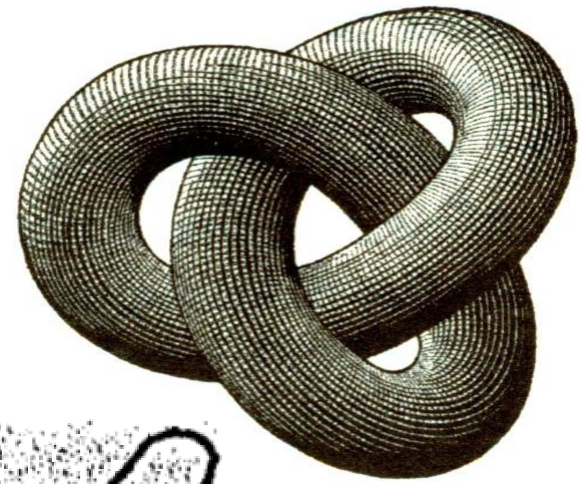
1989: First Synthetic Molecular Knot by Sauvage

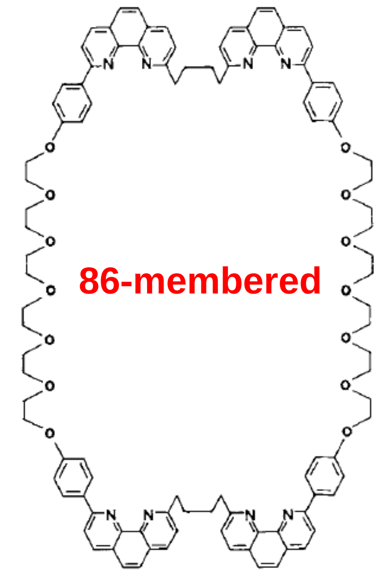


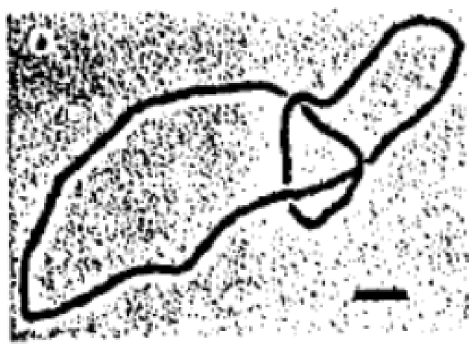
Dietrich-Buchecker, C. O.; Sauvage, J. P. *Angew. Chem. Int. Ed*. **1989**, *28*, 189-192

Topological chemistry: Trefoil Molecular Knot



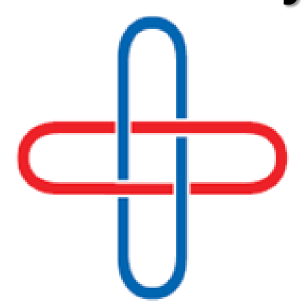






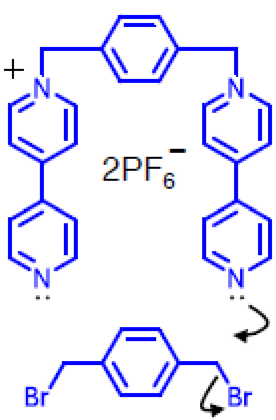
DNA trefoil knot

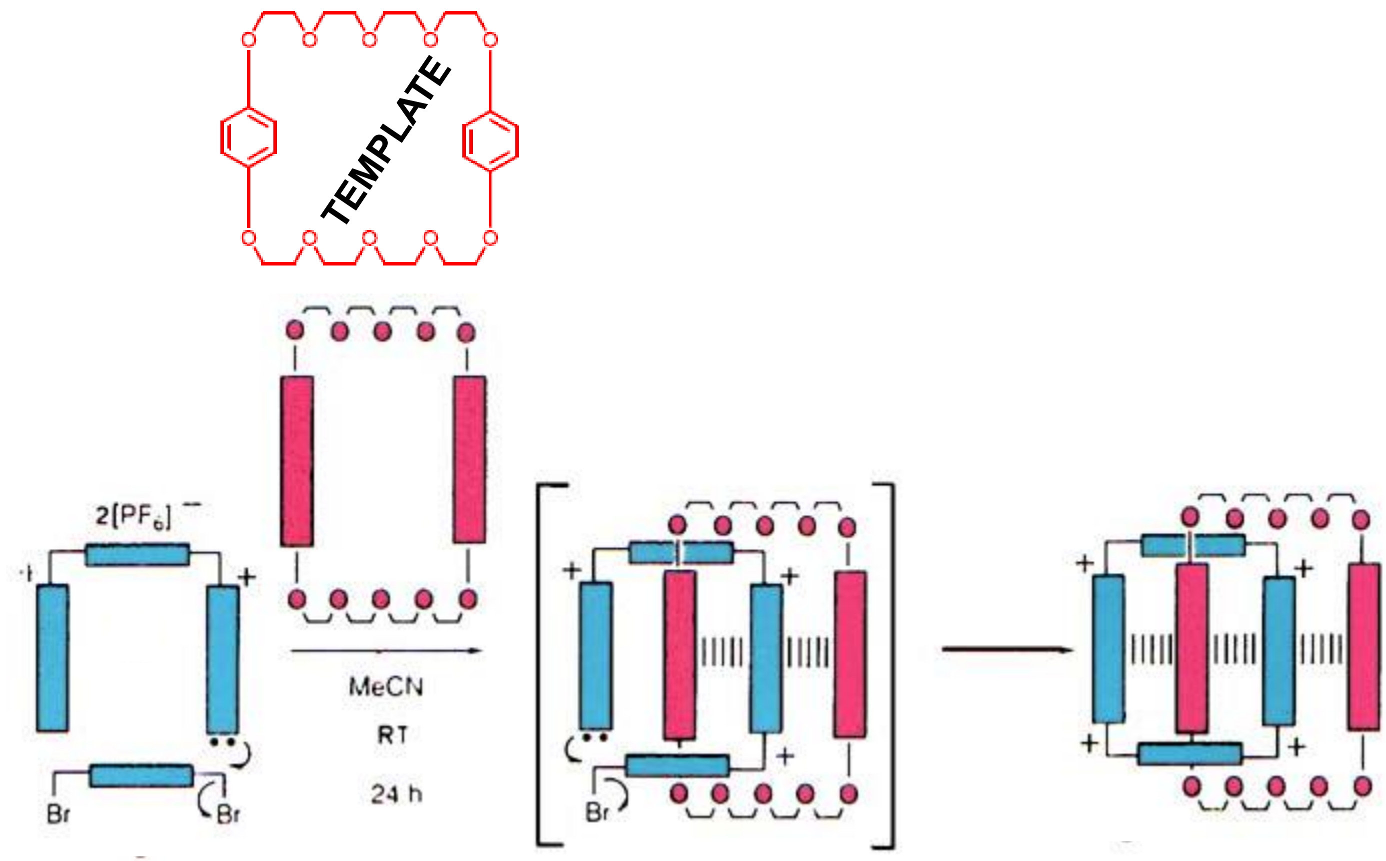
Created molecular versions of cultural symbols such as the trefoil knot, Solomon’s knot and the Borromean rings **(Topological chemistry)**



1989: Fraser Stoddart Introduces Donor-Acceptor Templation

Stoddart



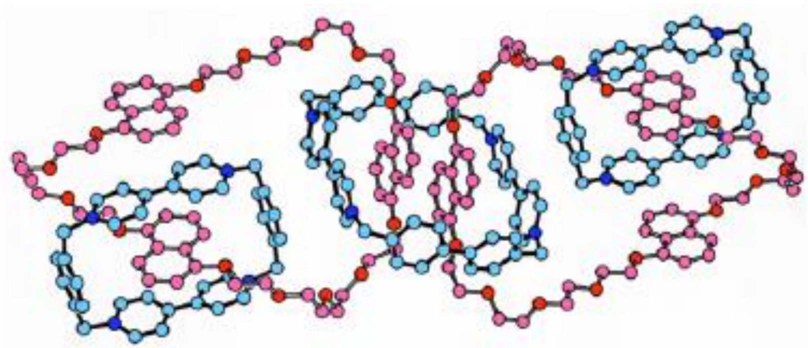


70% Yield

Stoddart et al. Angew. Chem. Int. Ed. Engl. 1989, 28, 1396

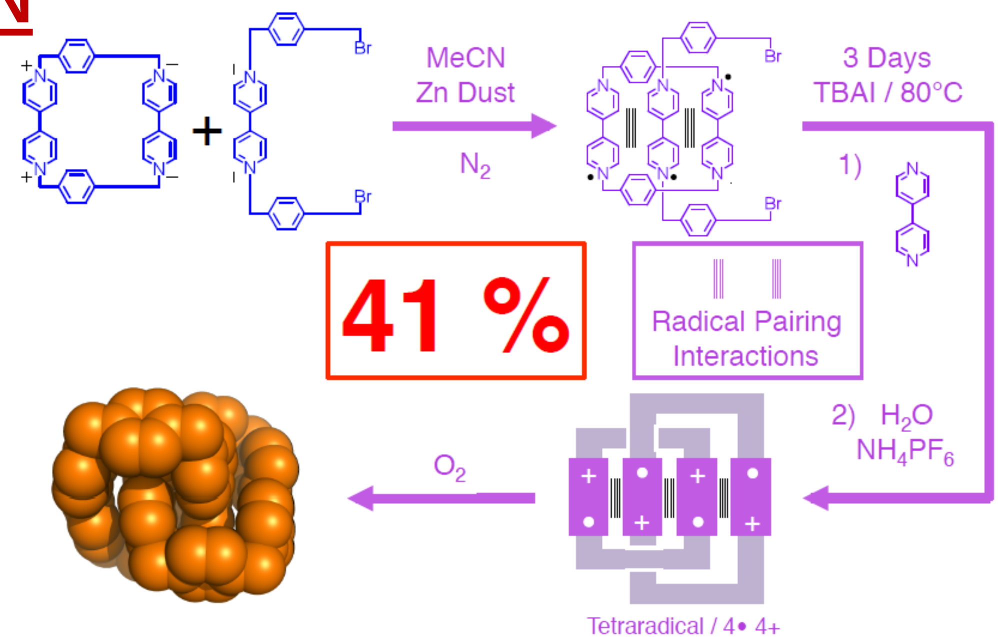
Work of Fraser Stoddart

1994: OLYMPIADANE



Angew. Chem. Int. Ed. Engl. **1994**, *33*, 1286

2013: RADICAL TEMPLATION



Science **2013**, 339, 429

Molecular Machines: Chemists View

The concept of a machine can be extended to the molecular level

A molecular-level machine **can be defined as "an assembly of a distinct number of molecular components that are designed to perform machinelike movements (output) as a result of an appropriate external stimulation (input)".**

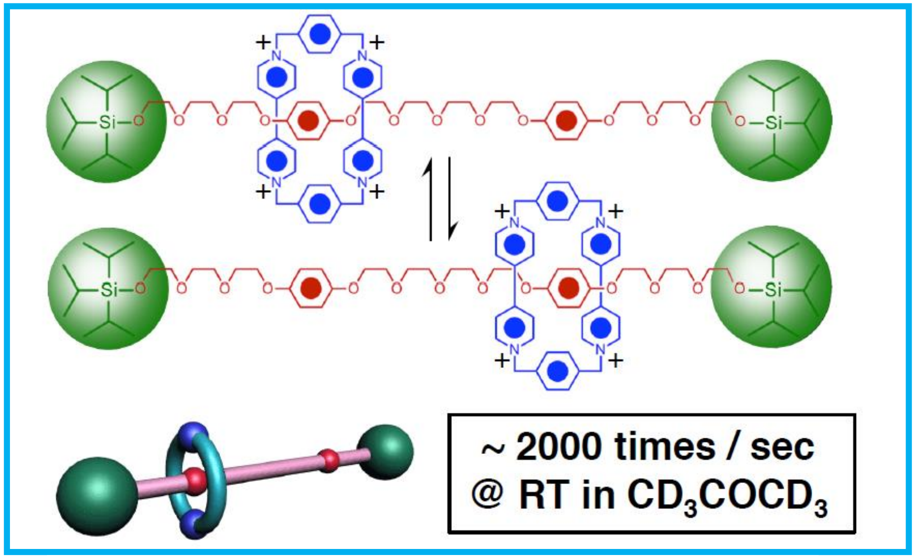
Balzani, V.; Credi, A.; Raymo, F. M.; Stoddart, *J. F. Angew. Chem. Int. Ed.* **2000**, *39*, 3348.

1991: Stoddart Introduces a Molecular "Shuttle"

Bis-paraquat Cyclophane ring

Diphenol

Diphenol

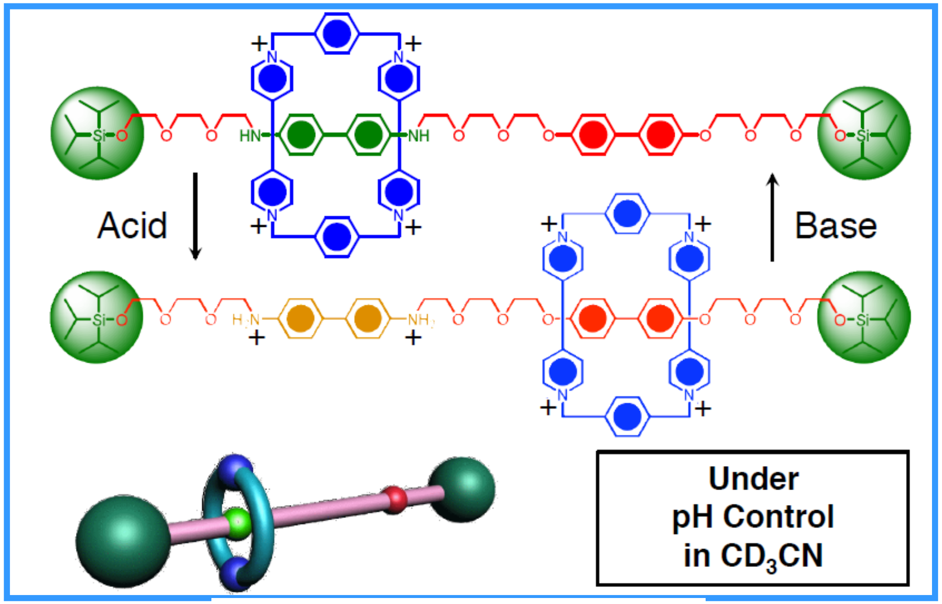


J. Am. Chem. Soc. **1991**, *113*, 5131

Bis-paraquat Cyclophane ring

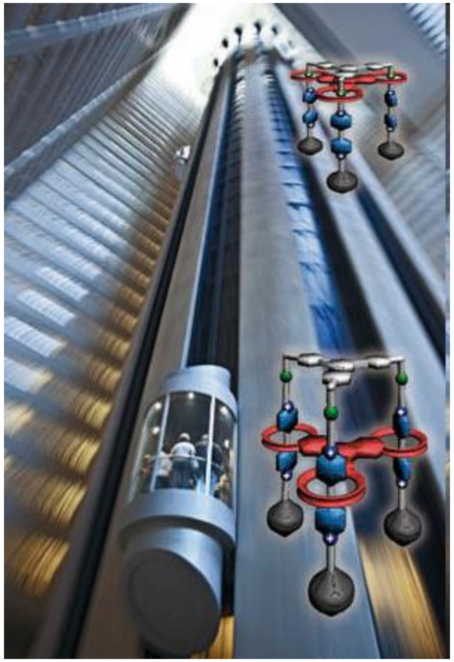
Benzidine

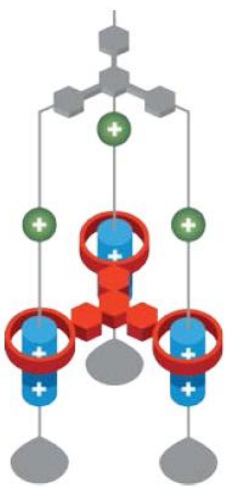
Diphenol

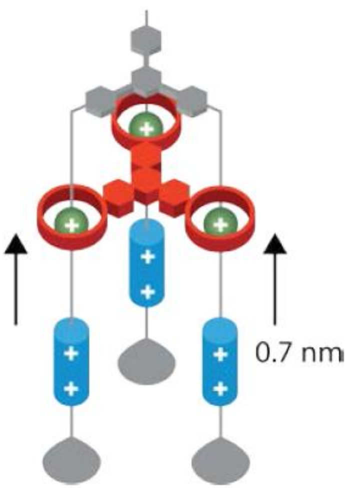


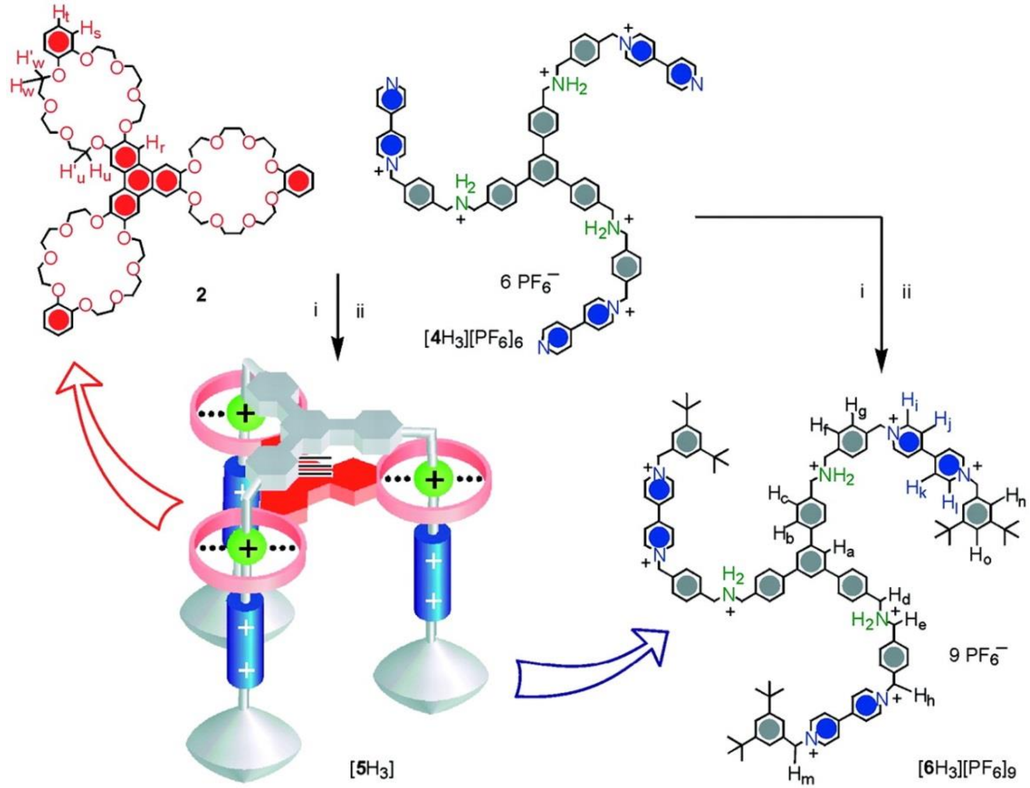
Nature **1994**, *369*, 133

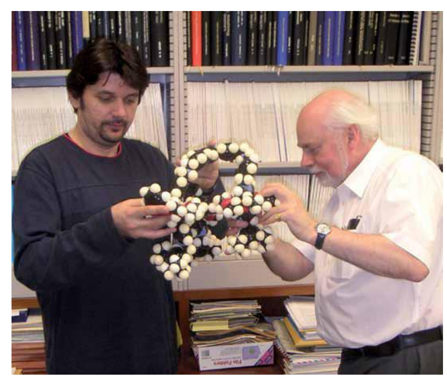
2004: A Molecular Elevator







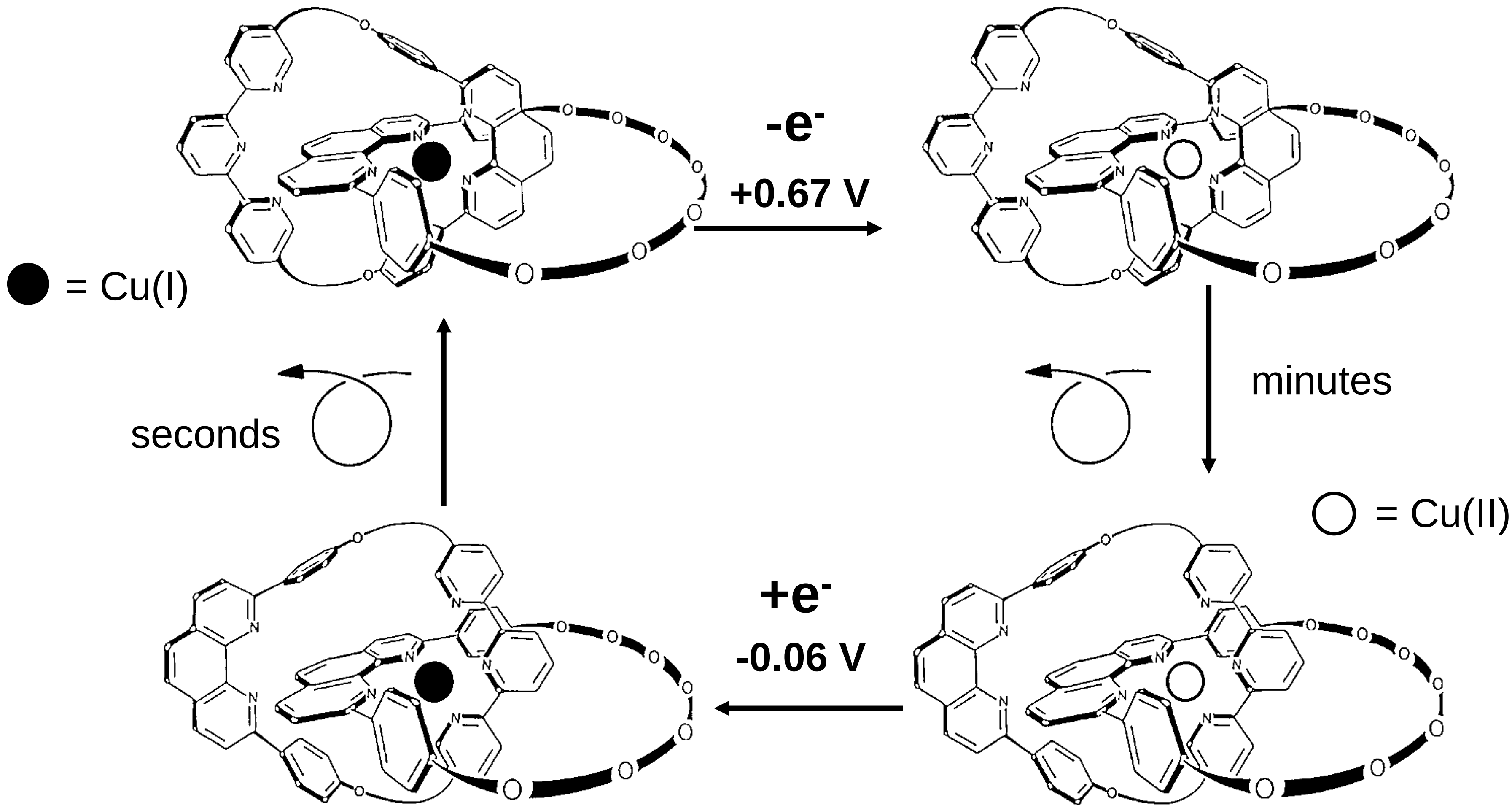




Fraser Stoddart (right) examining his molecular elevator

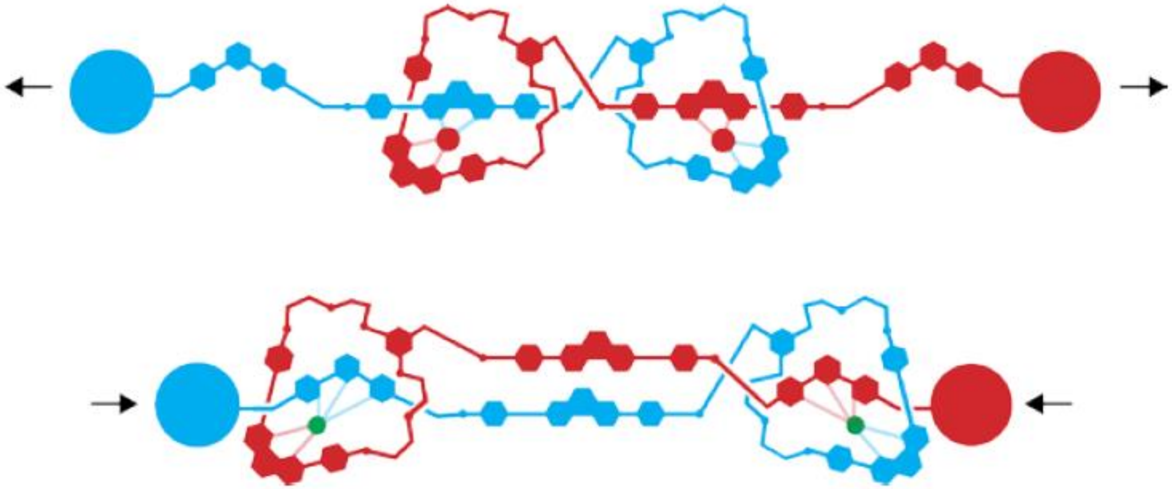
Badjić, J. D.; Balzani, V.; Credi, A.; Silvi, S.; Stoddart, J. F. ***Science*** 2004, *303*, 1845.

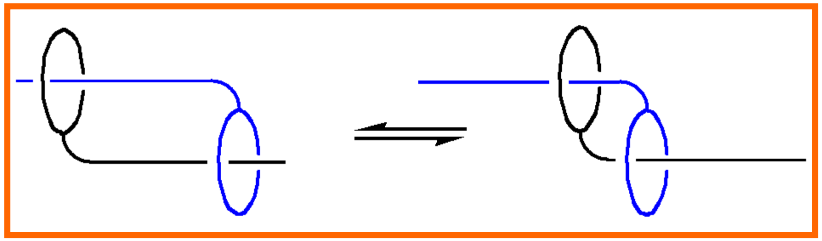
1994: Jean-Pierre Sauvage Showed Rotation of a ring within another ring (no directionality)



Livoreil, A.; Dietrich-Buchecker, C. O.; Sauvage, J. P. *J. Am. Chem. Soc.* **1994**, *116*, 9399–9400.

2000: Extension and Contraction in a Daisy-Chain Rotaxane Structure



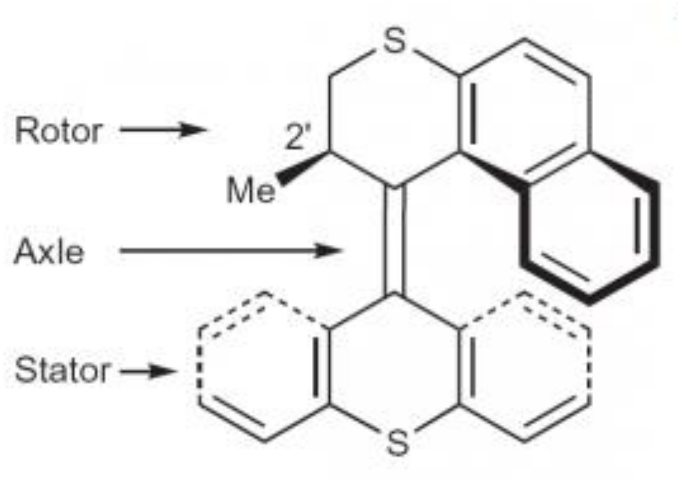


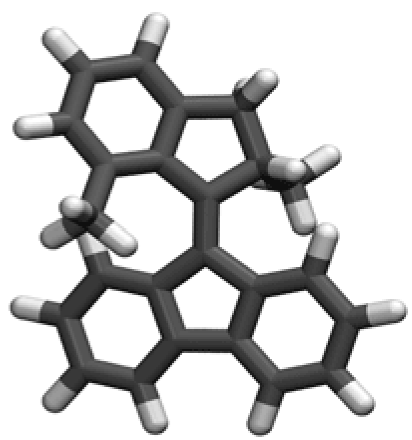
Jiménez, M. C.; Dietrich-Buchecker, C.; Sauvage, J.-P. Towards Synthetic Molecular Muscles: Contraction and Stretching of a Linear Rotaxane Dimer. *Angew. Chem. Int. Ed.* **2000**, *39* (18), 3284.

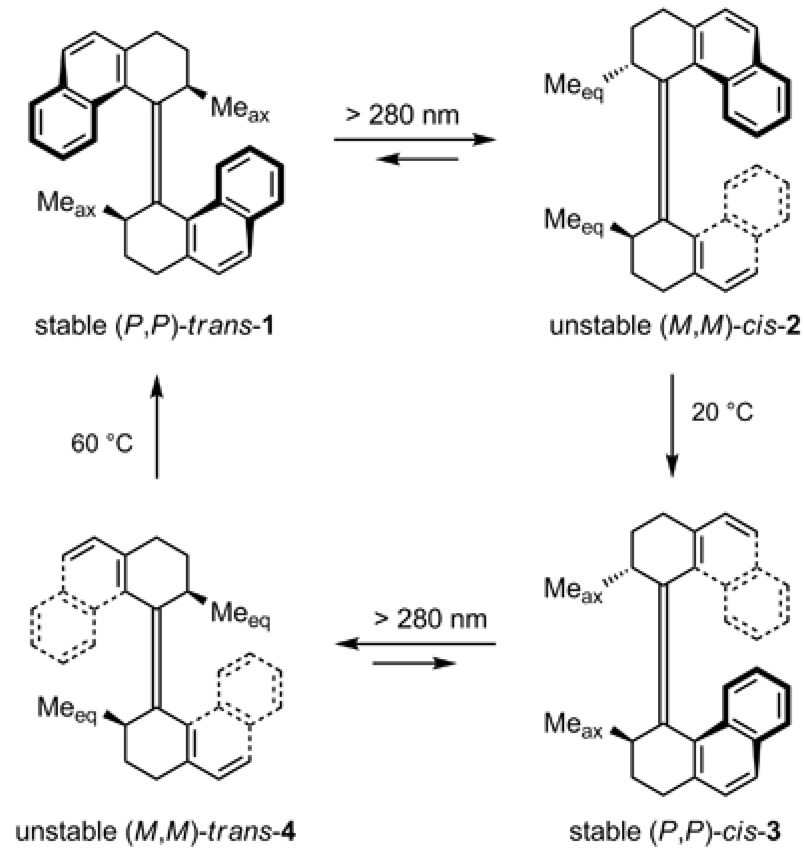
By assimilating two mutually entangled rotaxanes, Sauvage group were able to achieve high control of translational contraction and extension of ca. 2 nm under chemical stimulus. They've also built something that can be likened to a motor, where the rotaxane's ring spins alternately in different directions.

1999: Synthetic Molecular Motor

Motors that continually spin in the same direction has been an important goal for the art of molecular engineering. First across the line was the Dutchman Bernard L. Feringa.



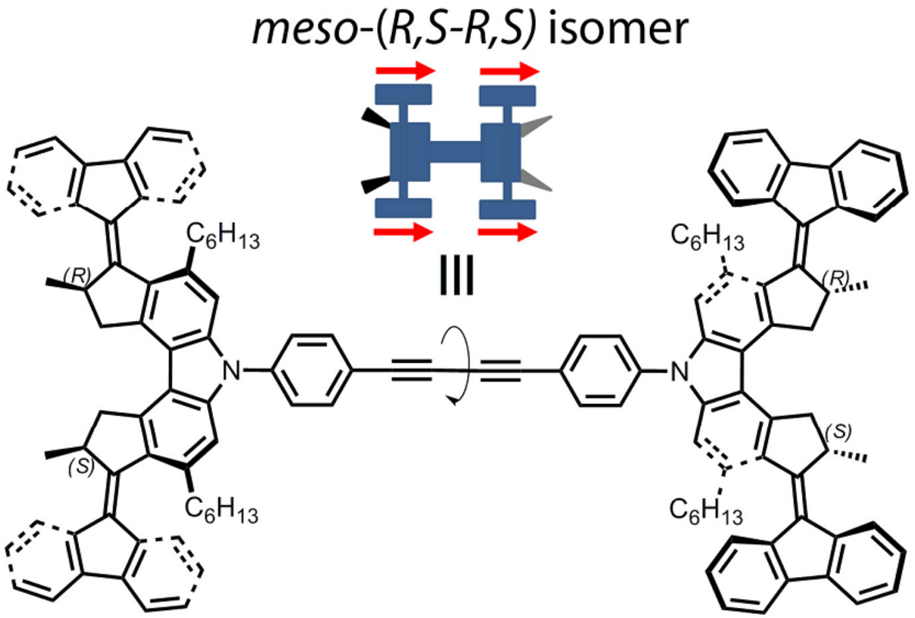


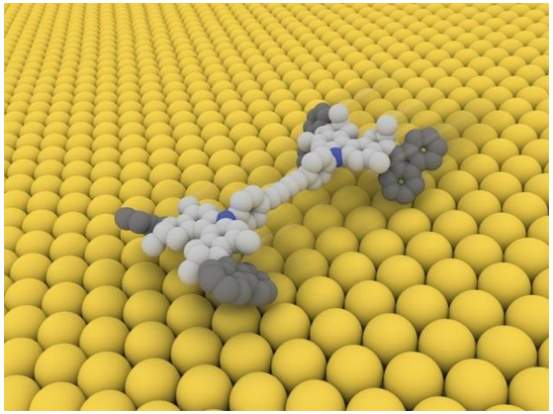


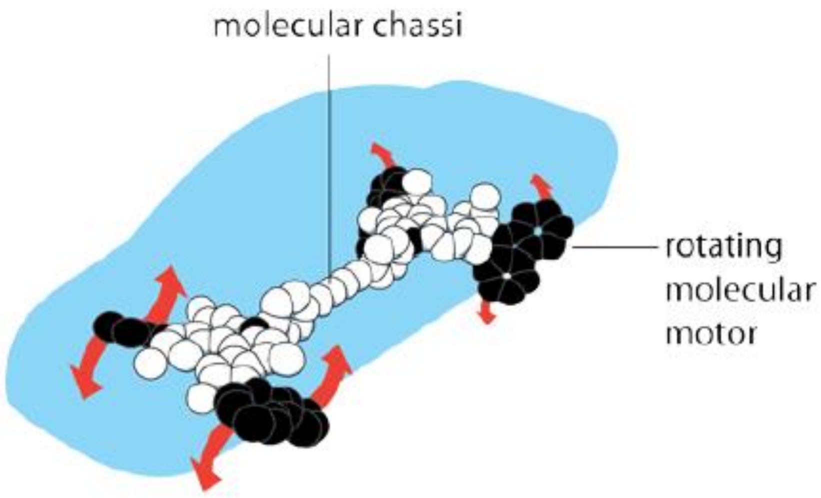
Ben Feringa

Koumura, N.; Zijlstra, R. W. J.; Delden, R. A. van; Harada, N.; Feringa, B. L. *Nature* **1999**, *401*, 152.

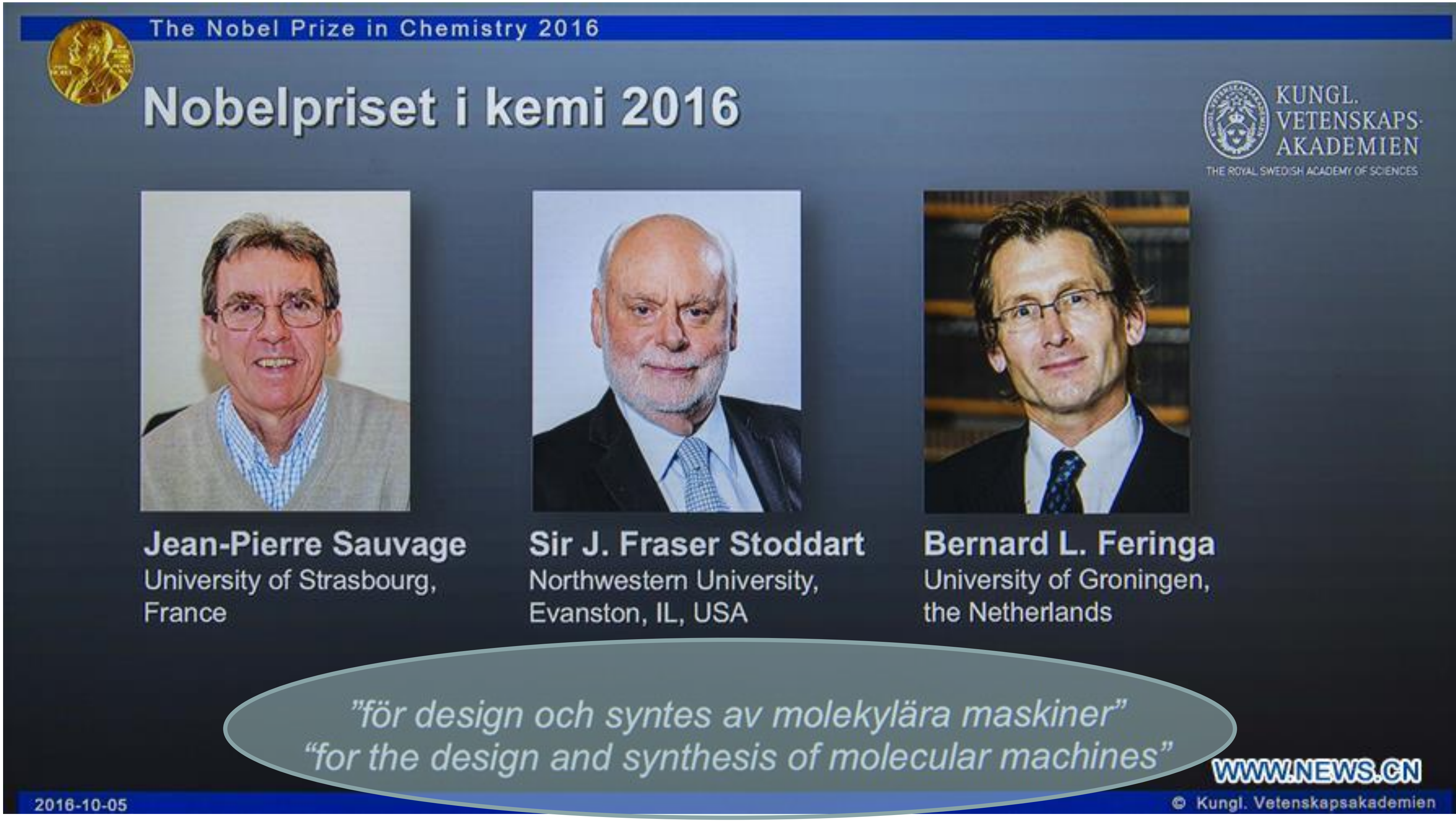
2011: Molecular Nano car







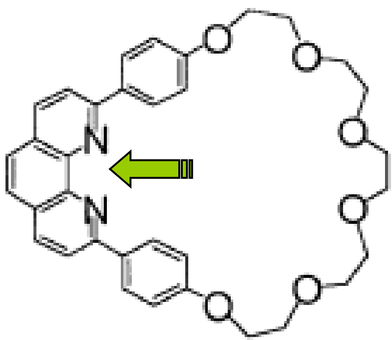
Kudernac, T.; Ruangsupapichat, N.; Parschau, M.; Maci. Electrically Driven Directional Motion of a Four-Wheeled Molecule on a Metal Surface. *Nature* **2011**, *479* , 208–211.



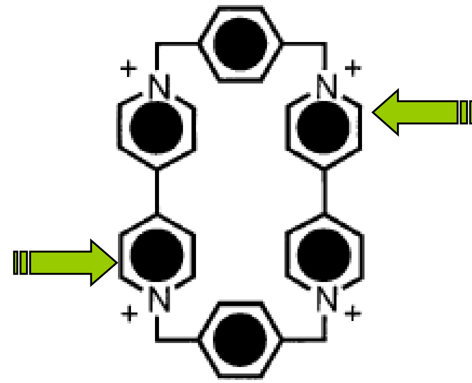
Development of molecular machines that are a thousand times thinner than a hair strand. They succeeded in linking molecules together to design a tiny lift to motors and minuscule muscles.

Branded Wheels

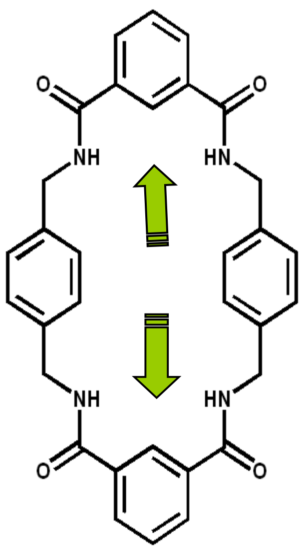
Metal template



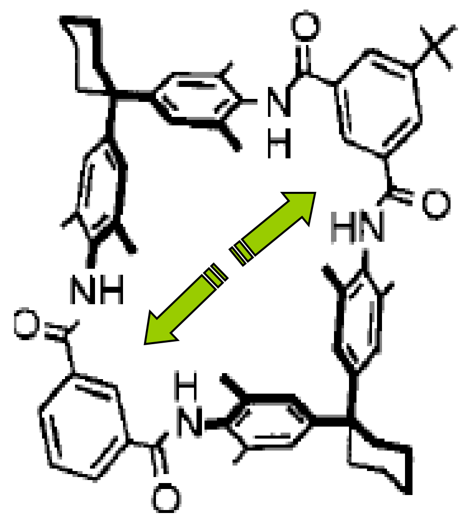
Pi-donor-pi-acceptor



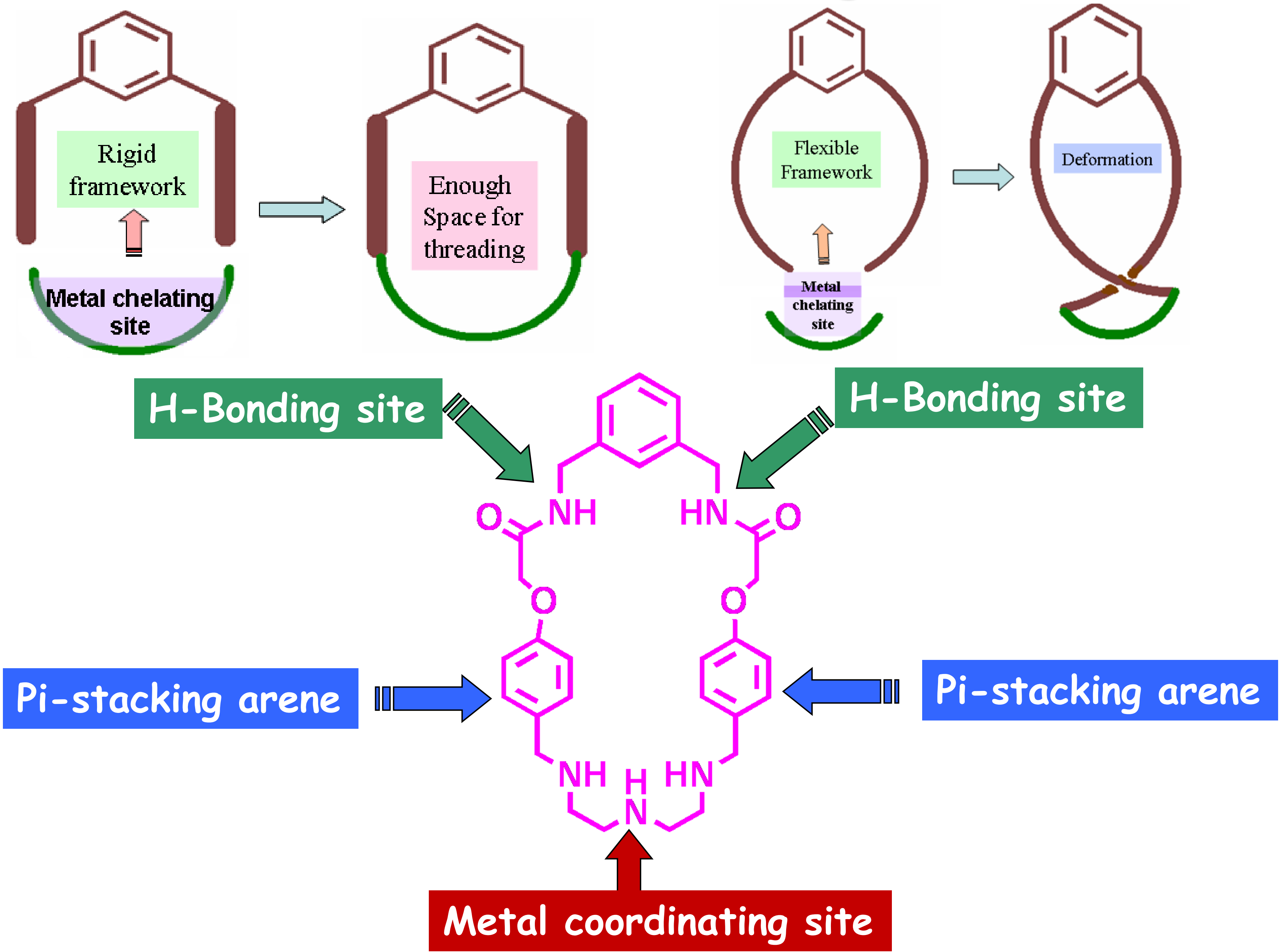
Anionic template



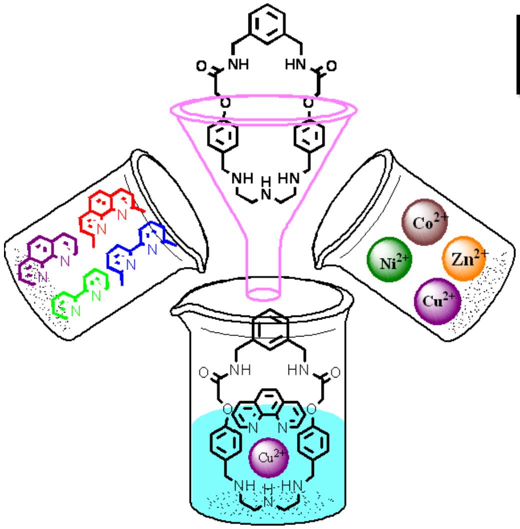
H-bond template

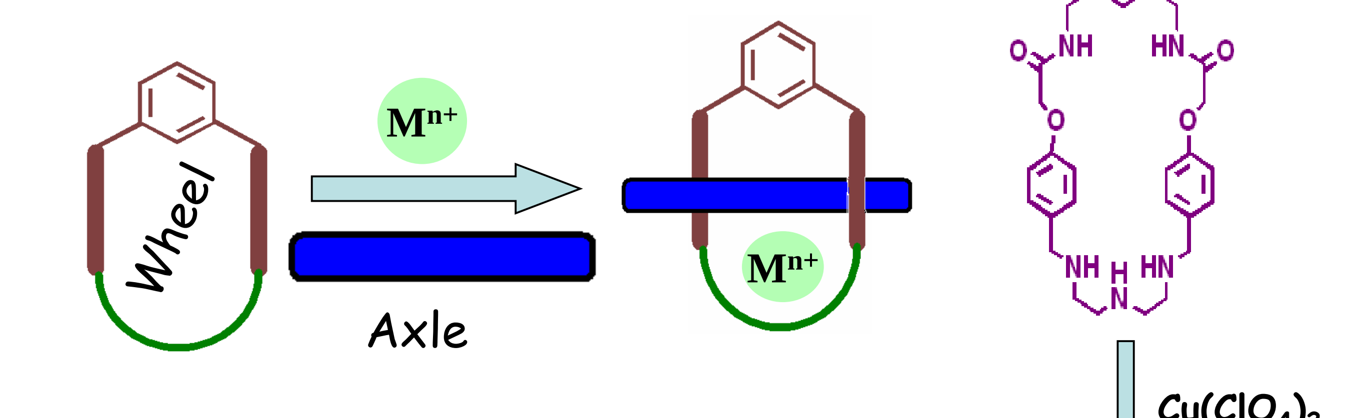


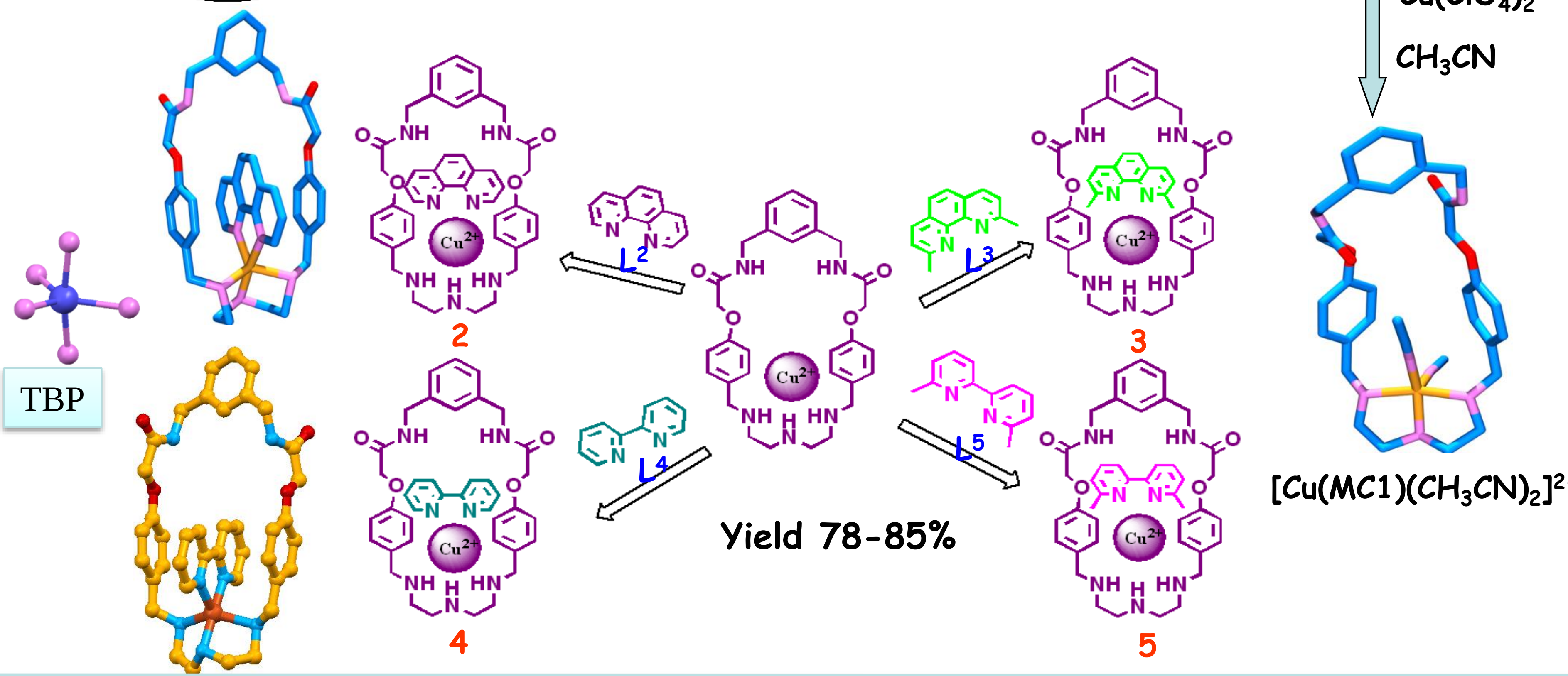
Our Wheel Design



[2]Pseudorotaxanes

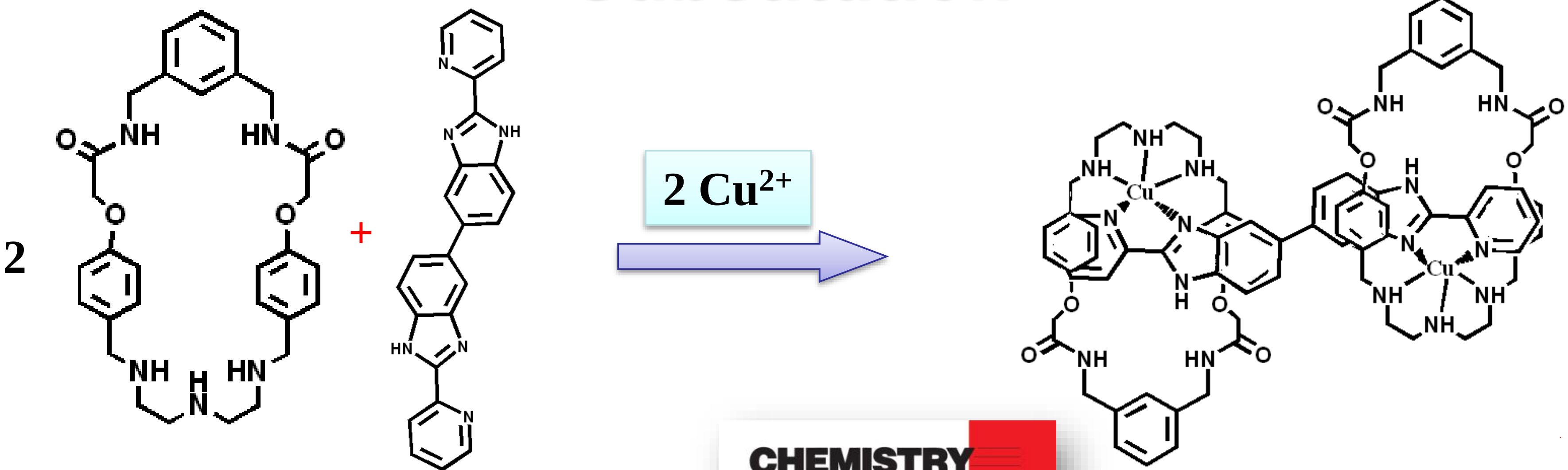


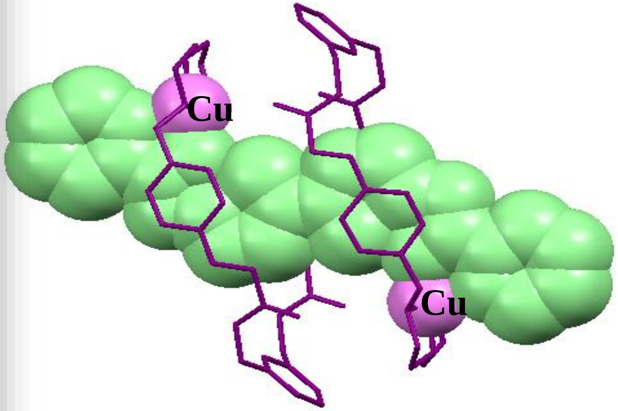




S. Saha, I. Ravikumar, P. Ghosh, ***Chem. Commun.*** 2011, *47*, 6272

Synthesis of [3]Pseudorotaxane and Axle Substitution

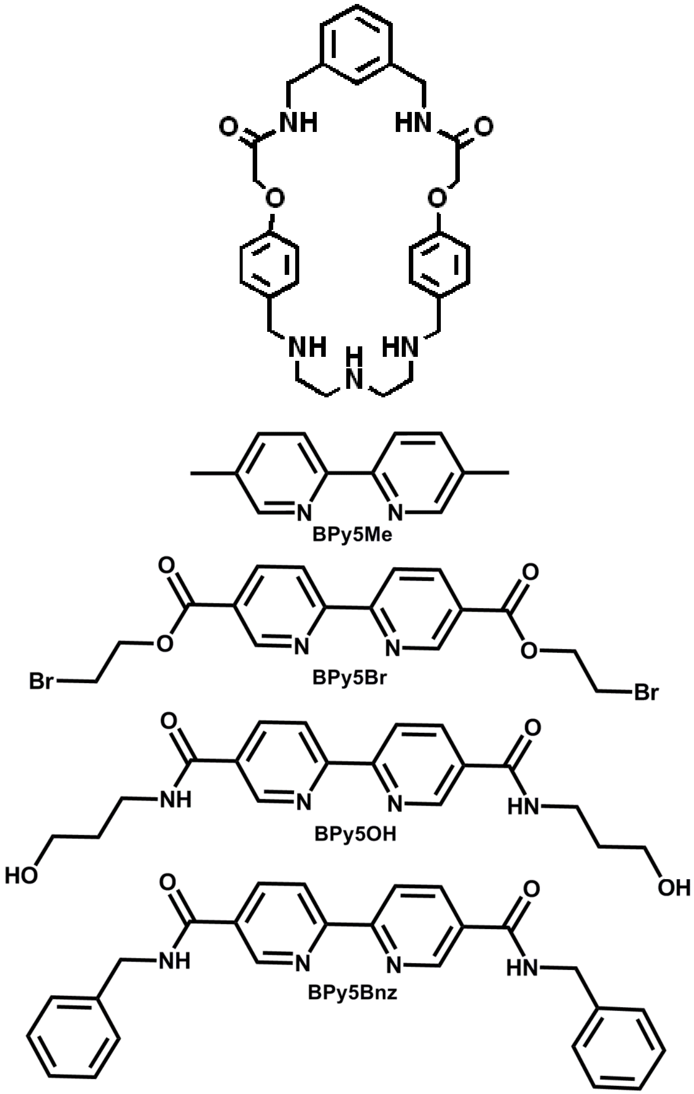


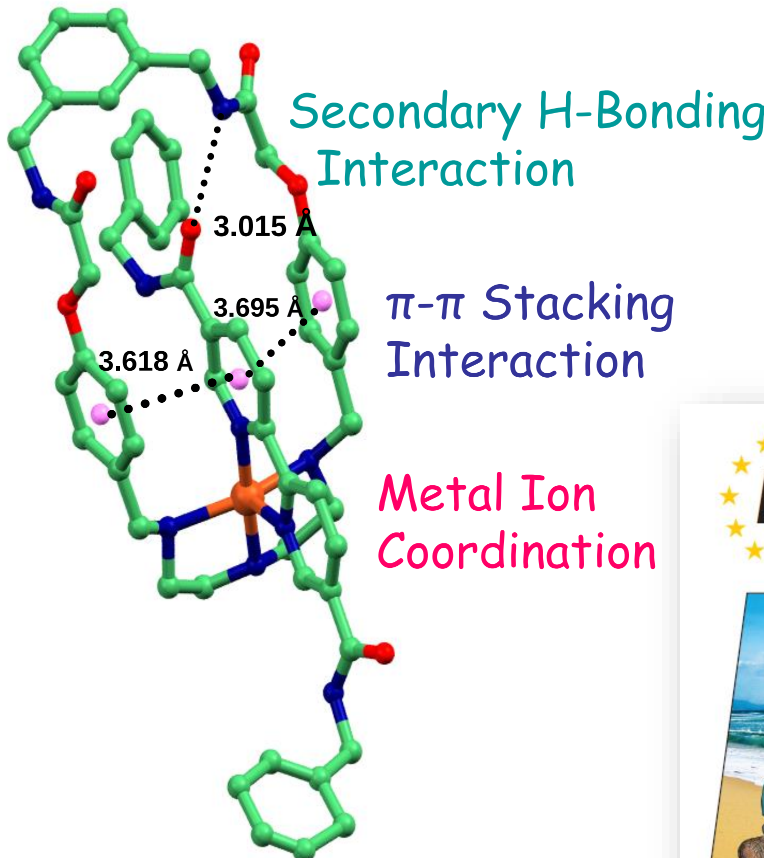


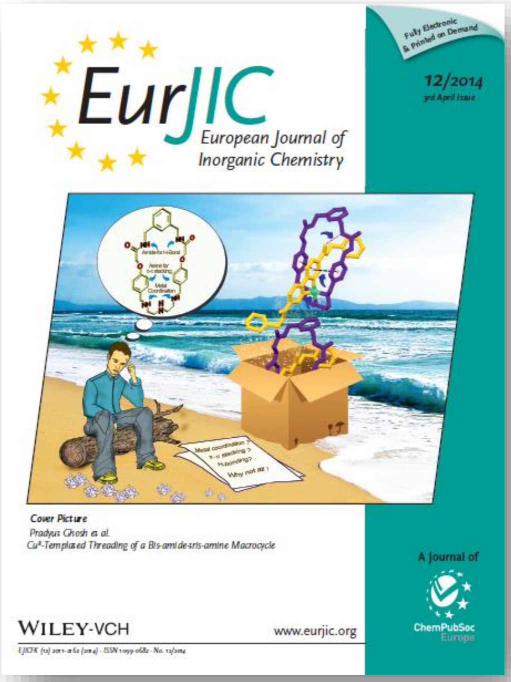
Phenomenon	Association Constant (K_{ass} in M^{-2})		Change in Free Energy (k cal mol^{-1})	
	UV/Vis	Fluorescence	UV/Vis	Fluorescence
Threading	3.38×10^3	2.82×10^3	-4.81	-4.70
De-Threading	2.12×10^4	1.95×10^4	-5.90	-5.85

S. Saha, I. Ravikumar, P. Ghosh, ***Chem. Eur. J.*** 2011, *17*, 13712

Precursor for the Synthesis of [2]Rotaxane



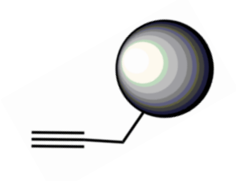


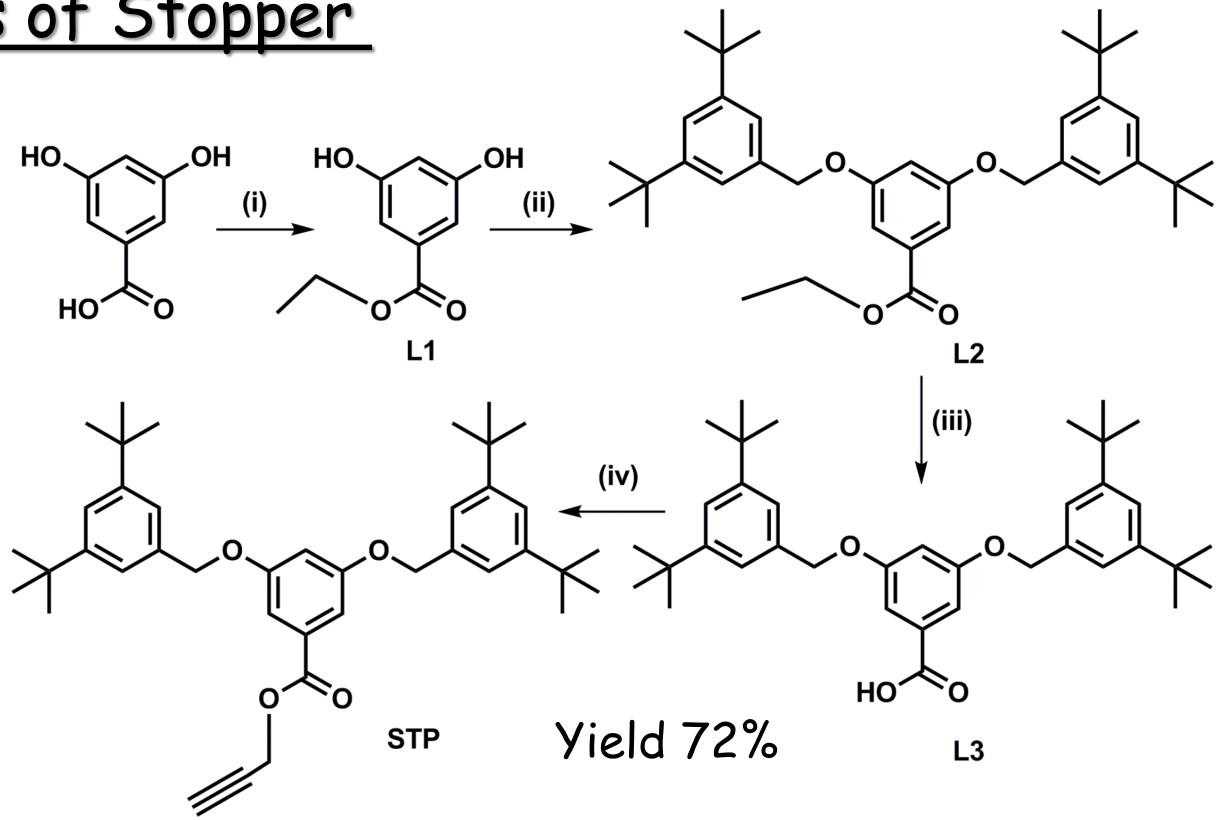


S. Saha, S. Santra, P. Ghosh, ***Eur. J. Inorg. Chem.*** 2014, 2029; S. Santra, S. Mukherjee, S. Bej, S. Saha, P. Ghosh ***Dalton Trans.*** 2015, *44*, 15198; M. Nandi, S. Santra, B. Akhuli, P. Ghosh, ***Dalton Trans.*** 2017, *46*, 7421.

Towards the Synthesis of [2]Rotaxane

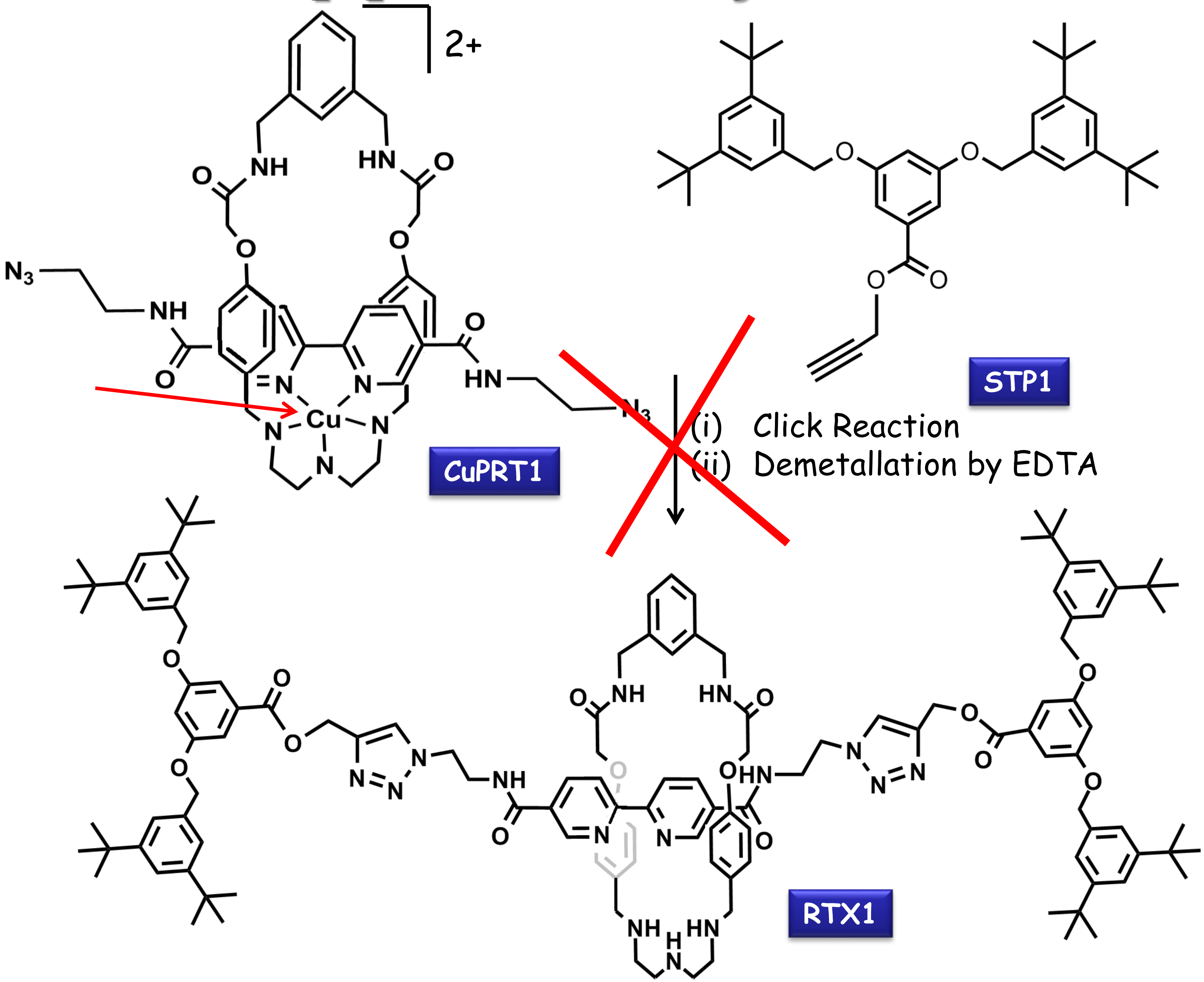
Synthesis of Stopper



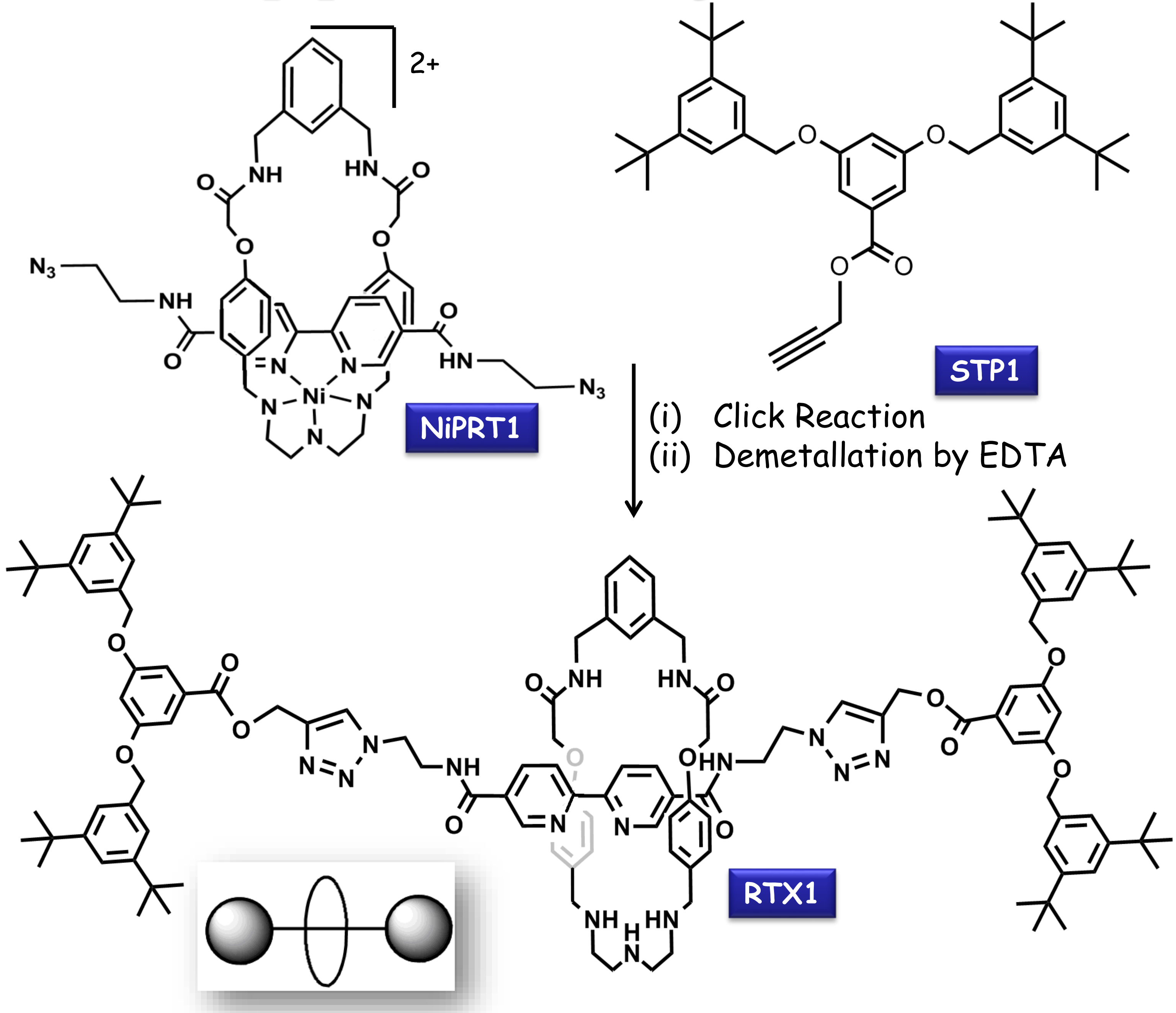


(i) Ethanol , H_2SO_4 , Reflux, 12h; (ii) 3,5- di-*tert*-butyl benzyl bromide, CH_3CN , Reflux, 24h; (iii) LiOH, HCl , THF-H_2O , RT, 24h; (iv) Propargyl bromide , TBAF, THF, RT, 8h .

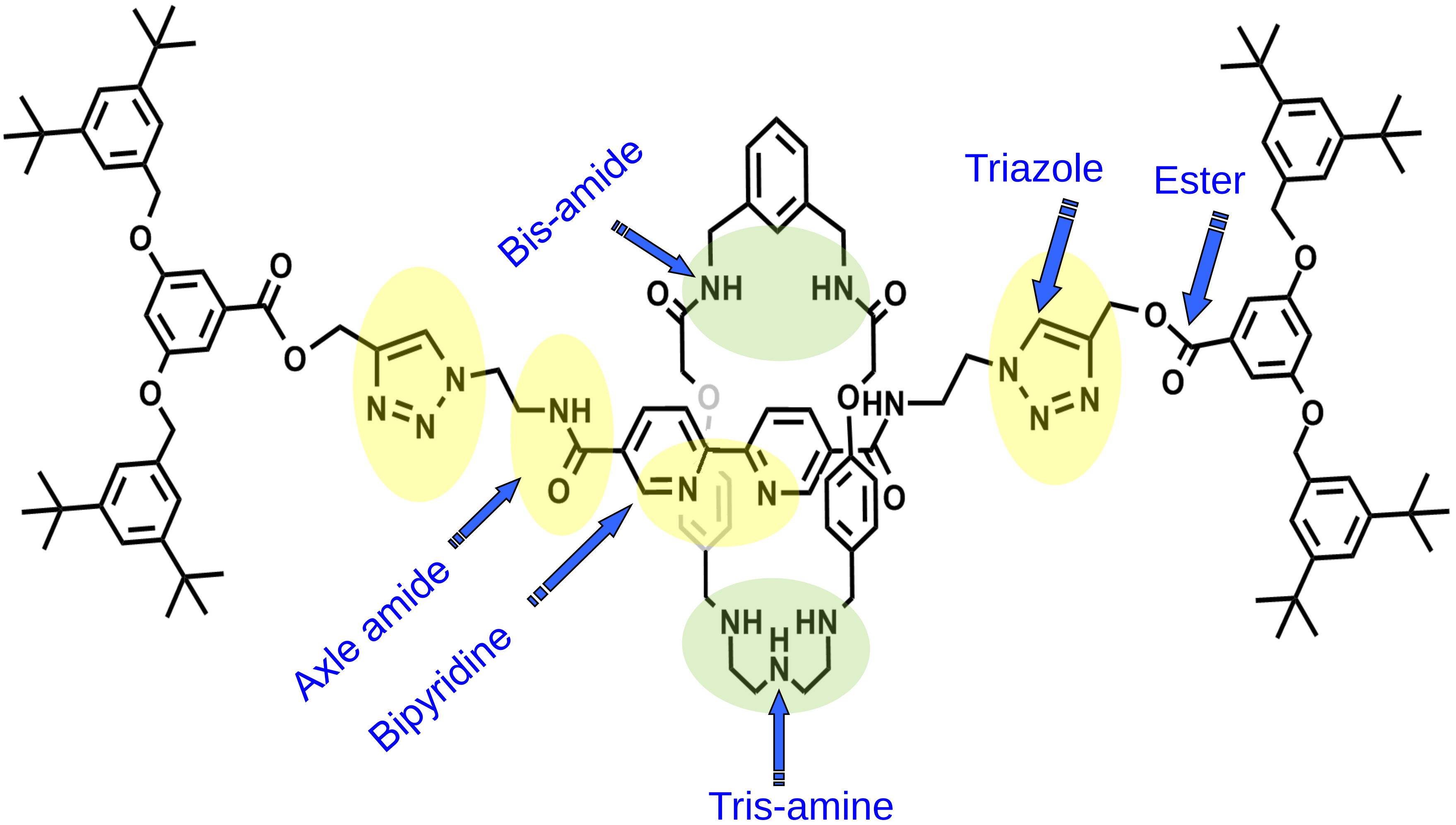
Synthesis of [2]Rotaxane by CuPRT Precursor



Synthesis of [2]Rotaxane by NiPRT Precursor

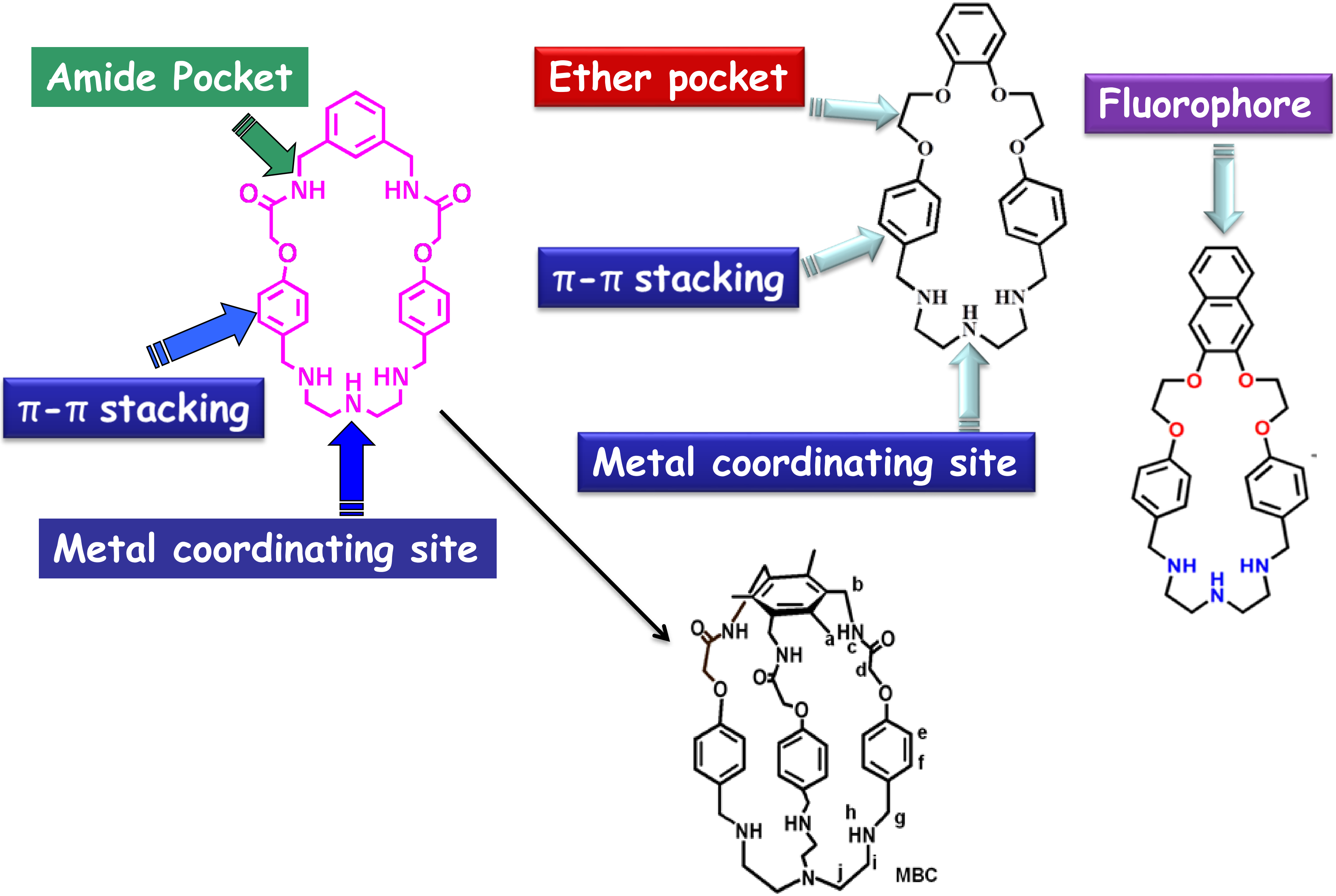


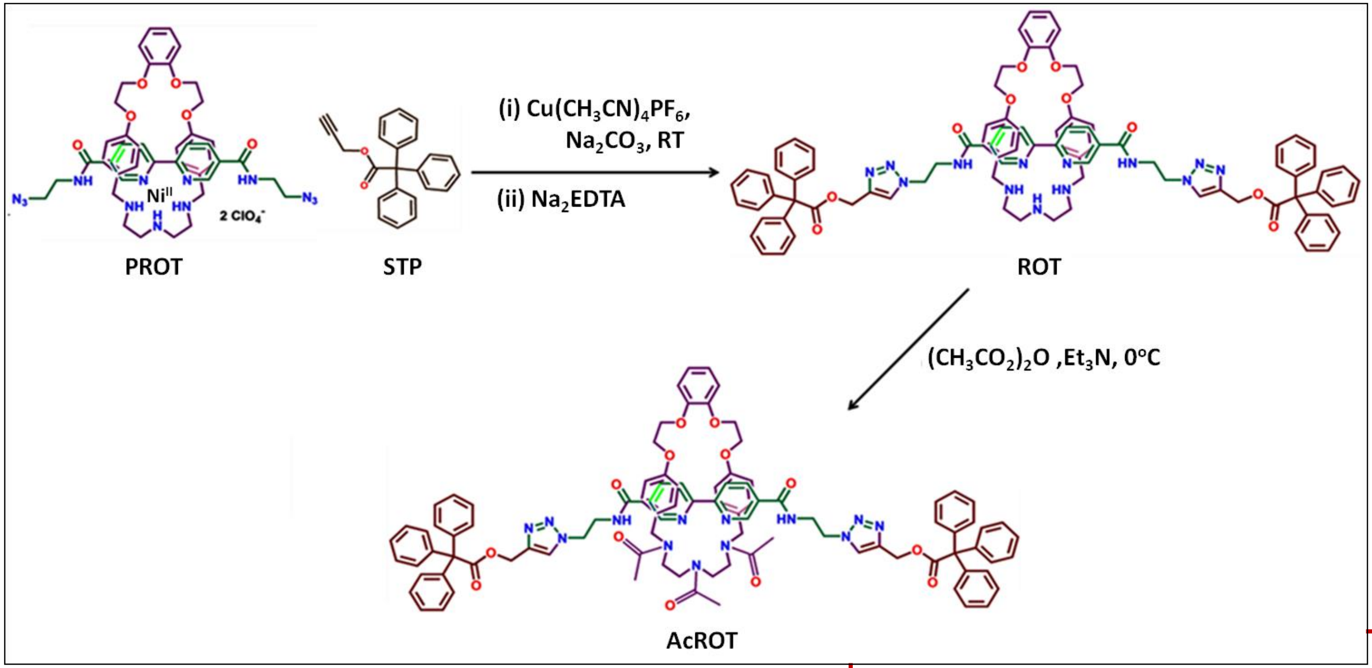
[2]Rotaxane with Multiple Functional Groups



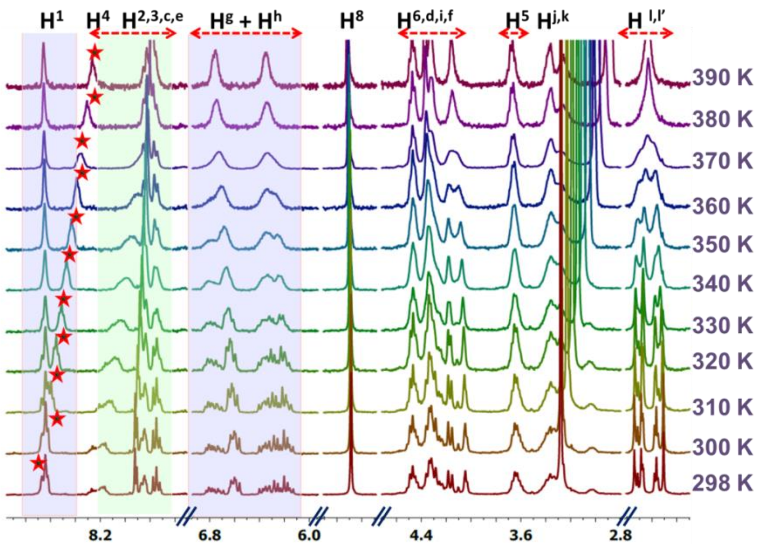
S. Saha, S. Santra, B. Akhuli, P. Ghosh, ***J. Org. Chem.*** 2014, 11170.

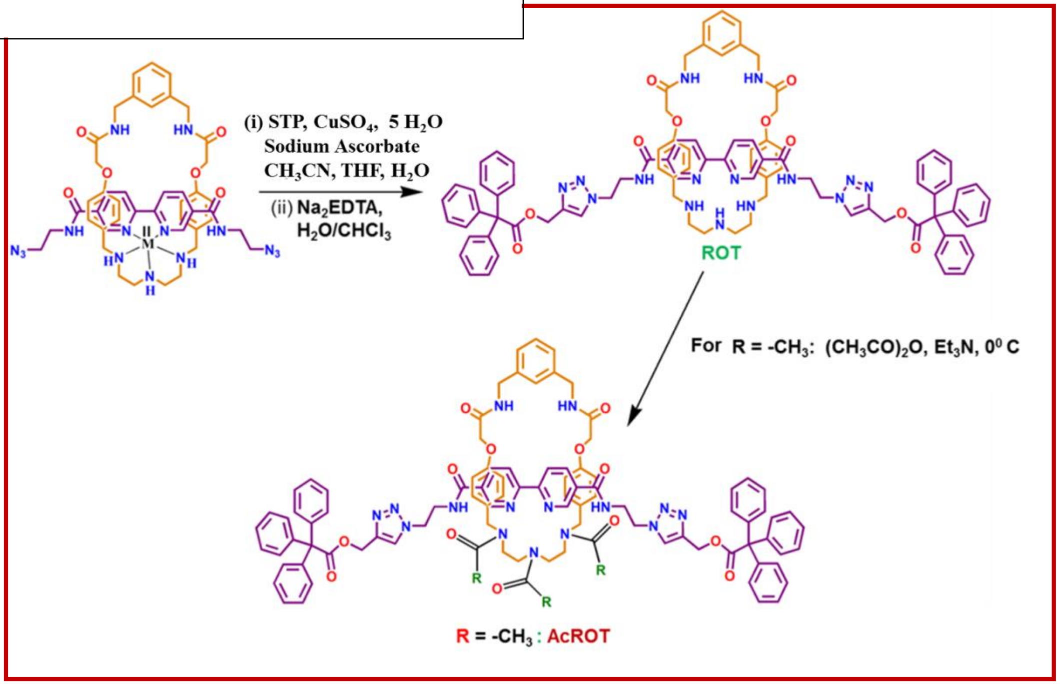
Various Wheels





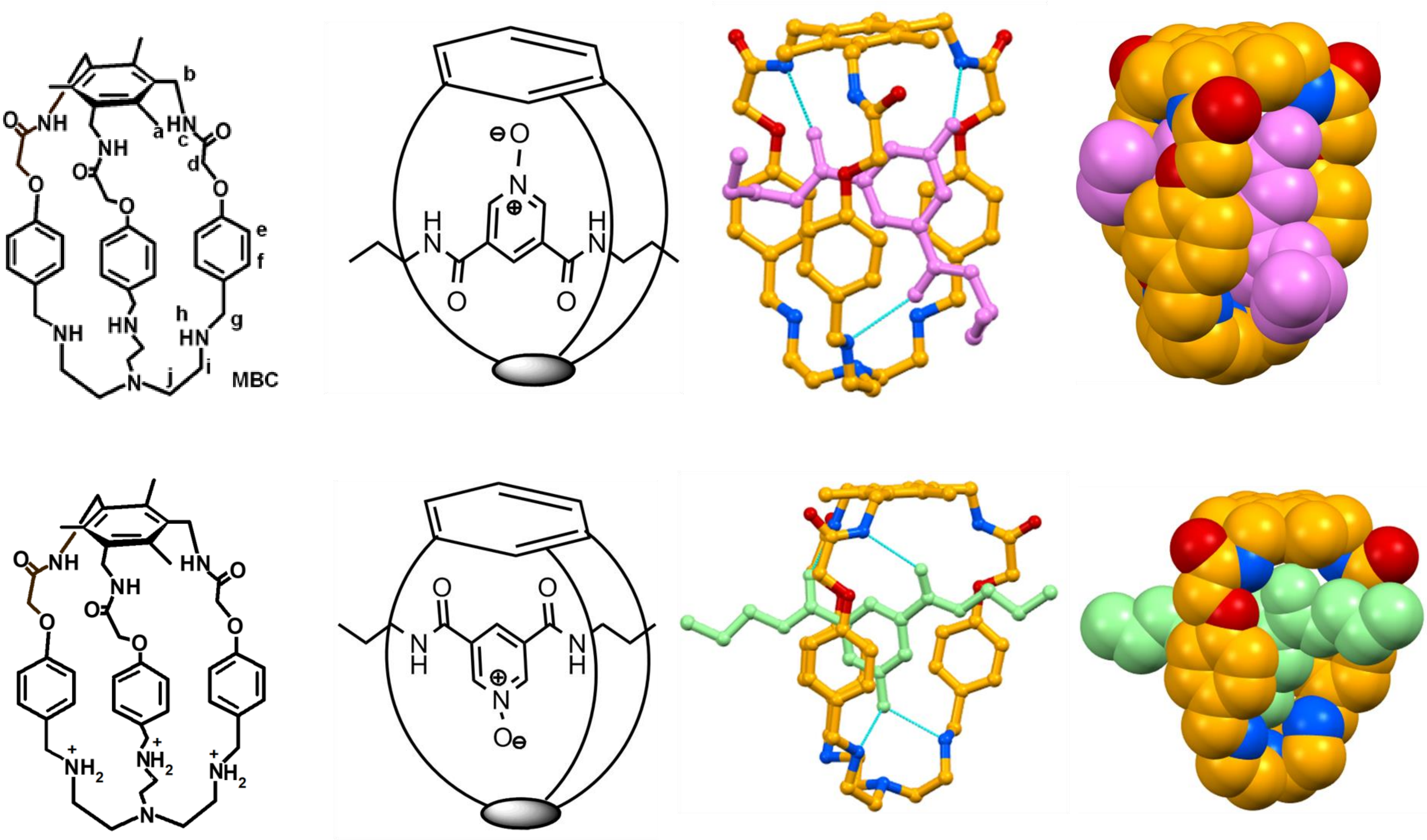
Rotamers Induced Dynamic Property and Stimuli Responsive Control Dynamics





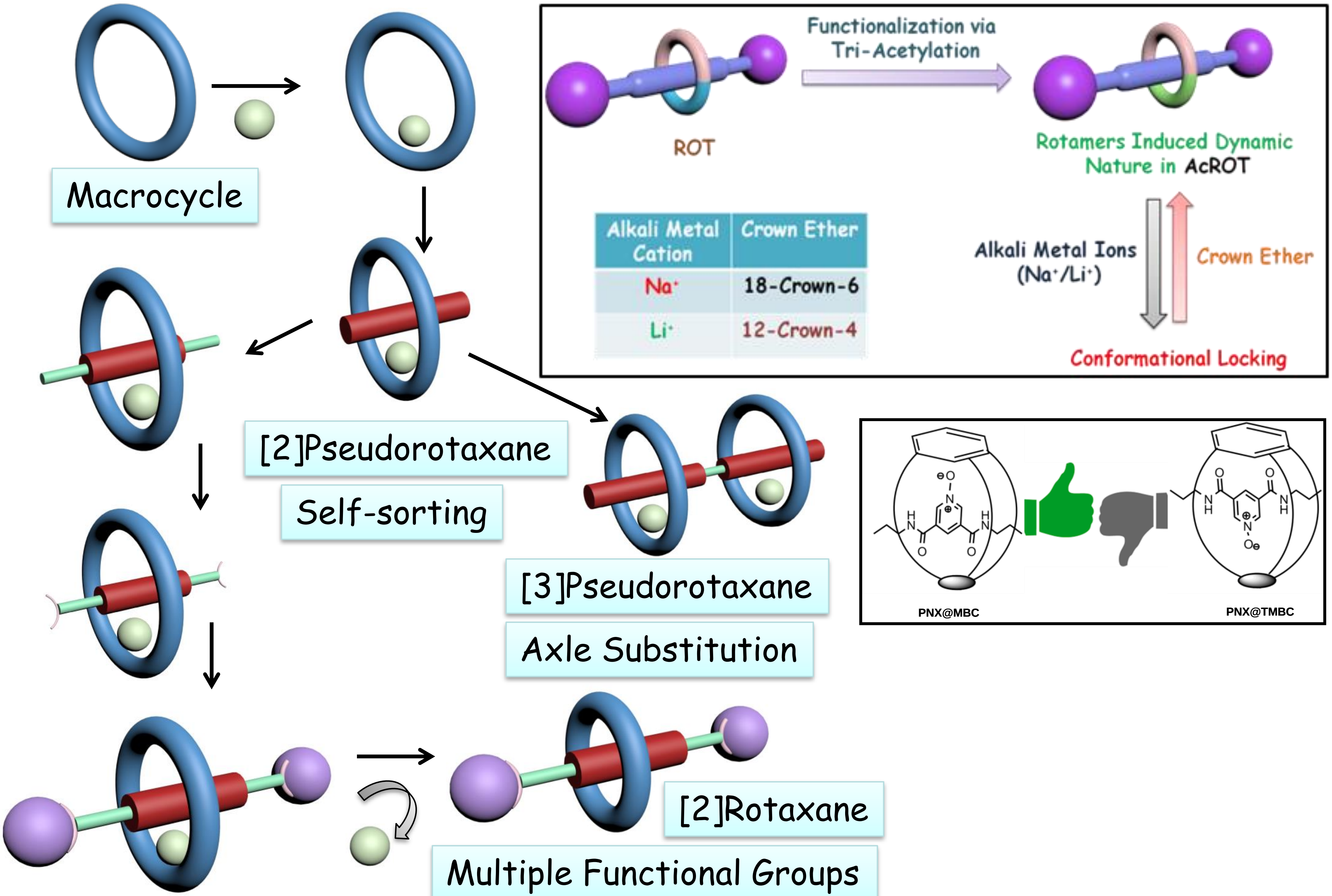
S. Santra, P. Ghosh, ***Eur. J. Org. Chem.*** 2017, 1583; S. Santra, S. Bej, M. Nandi, P. Mondal, P. Ghosh, **Dalton Trans.** 2017, 0000.

Different Binding States of Pyridine N-Oxide Based Axle



S. Saha, S. Santra, P. Ghosh, ***Org Lett.*** 2015, 17, 1854.

Summary of our work



Acknowledgement

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Financial Support……
Swarnajaynti Fellowship
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Science, *339*, **2013**, 189-193.

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