Corso di Chimica Supramolecolare

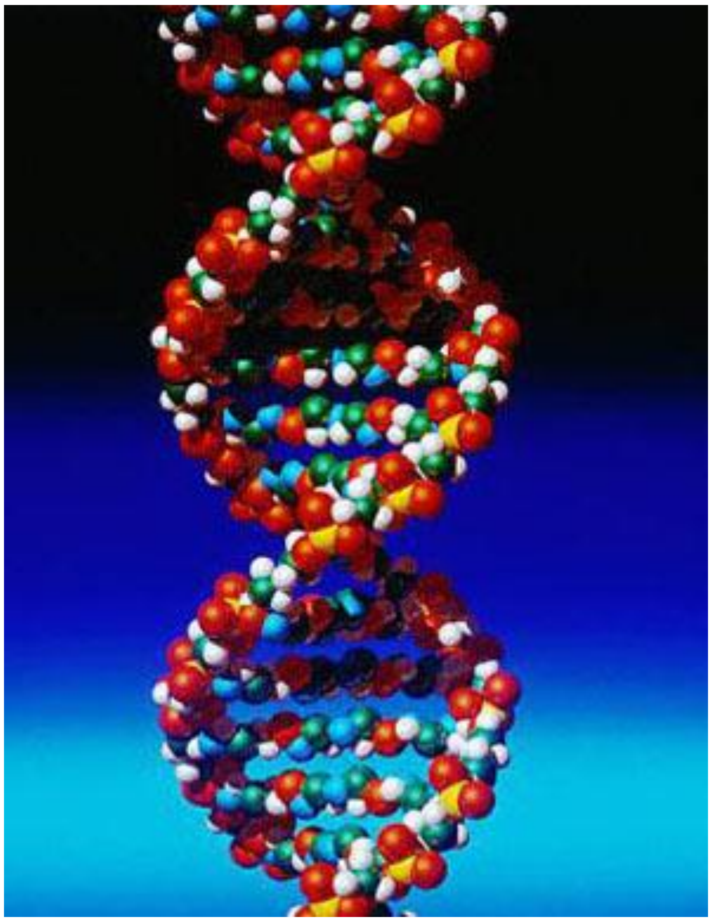
(LM in Chimica @units)

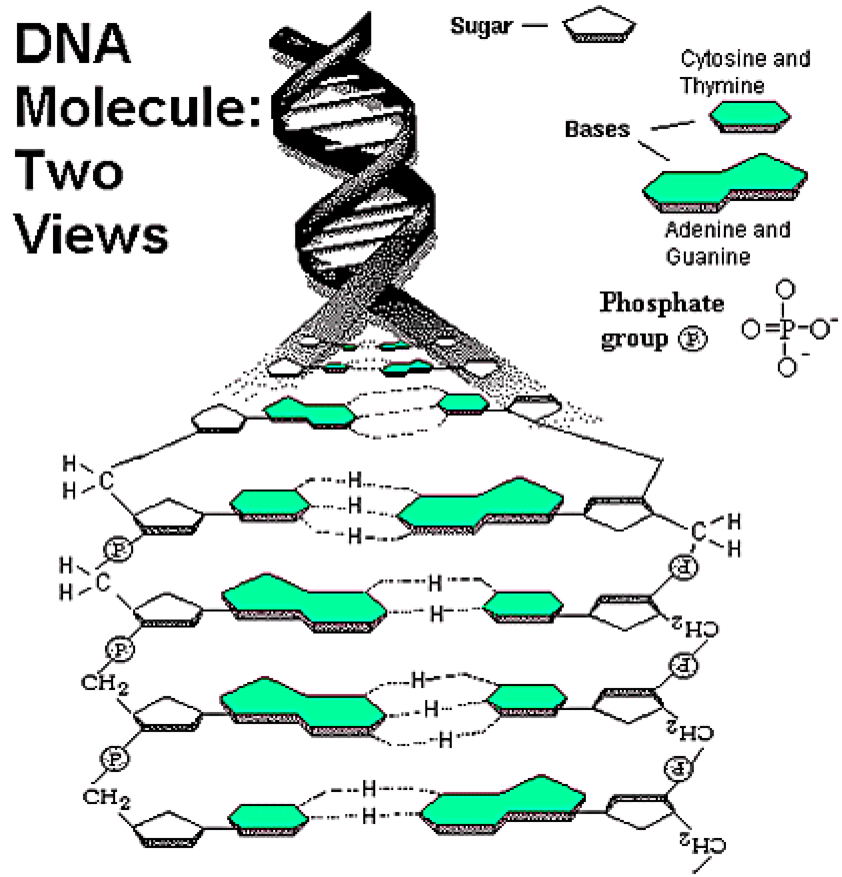
AA 2017/2018

Prof. E. Iengo
eiengo@units.it

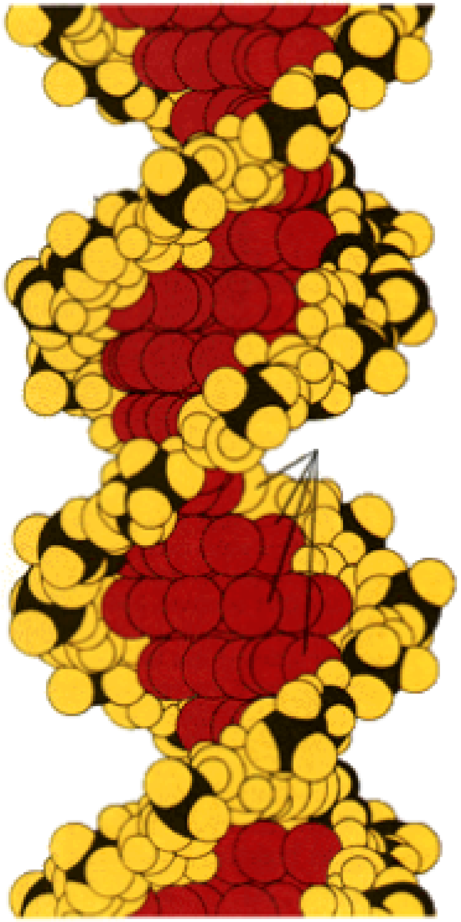
The original inspiration:
Supramolecular systems in Nature

DNA





Information Storage



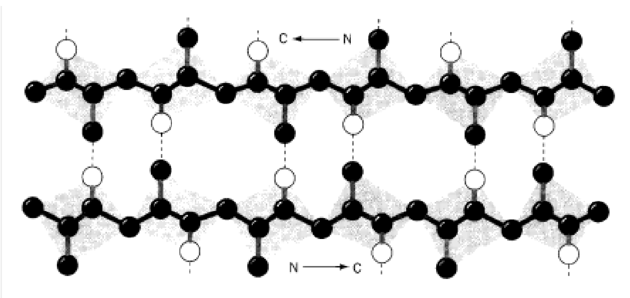
Watson & Crick 1953

The ultimate supramolecular material?

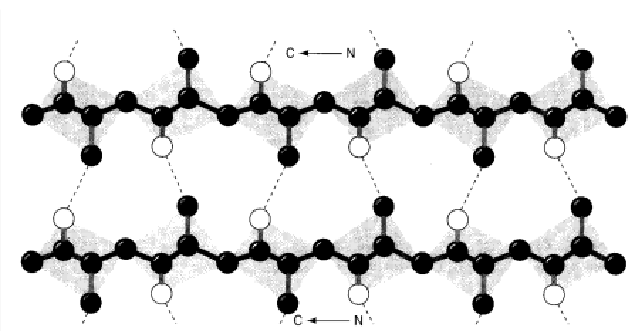
- Encodes gigabytes of data
- Can Self-Replicate
- Built-in Error Correction
- Is the basis of life

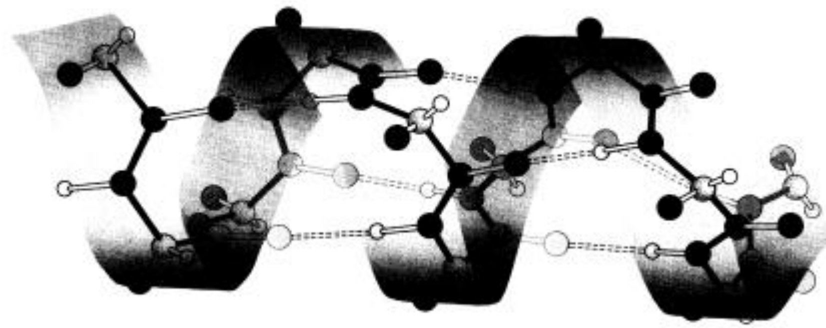
The original inspiration:
Supramolecular systems in Nature

PROTEINS



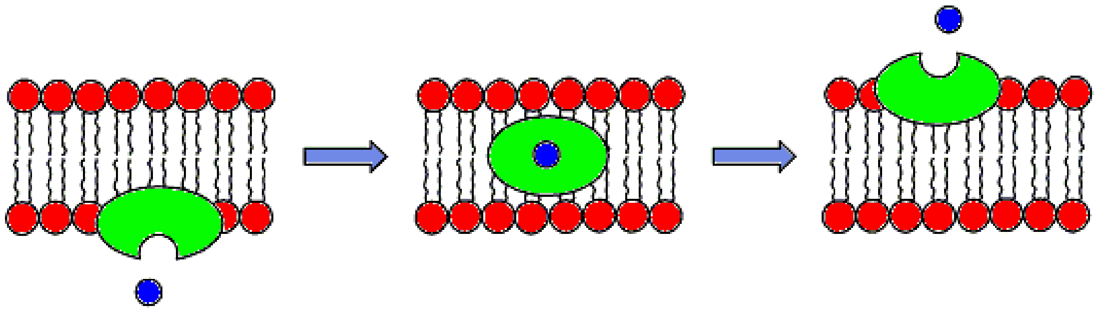
(a)





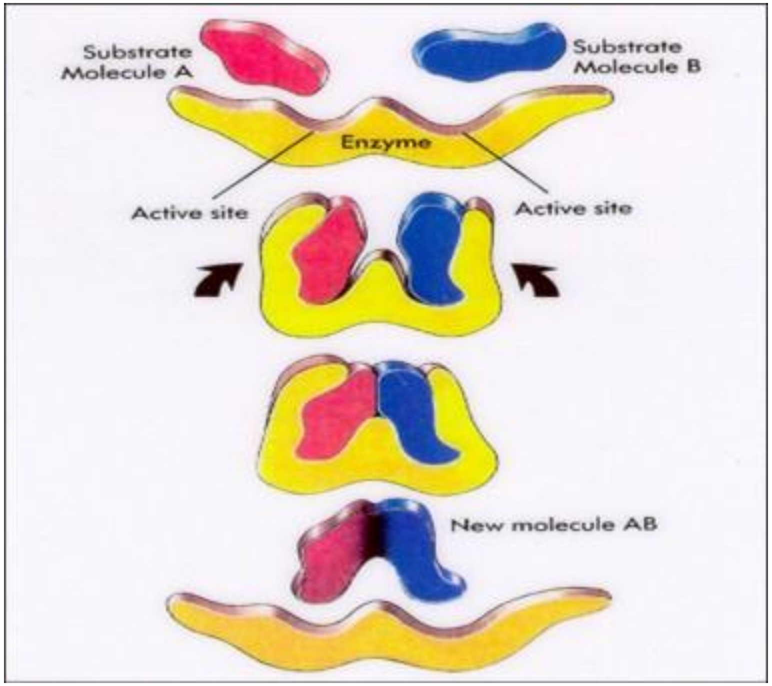
The original inspiration:
Supramolecular systems in Nature

MEMBRANES and TRANSMEMBRANE CARRIERS



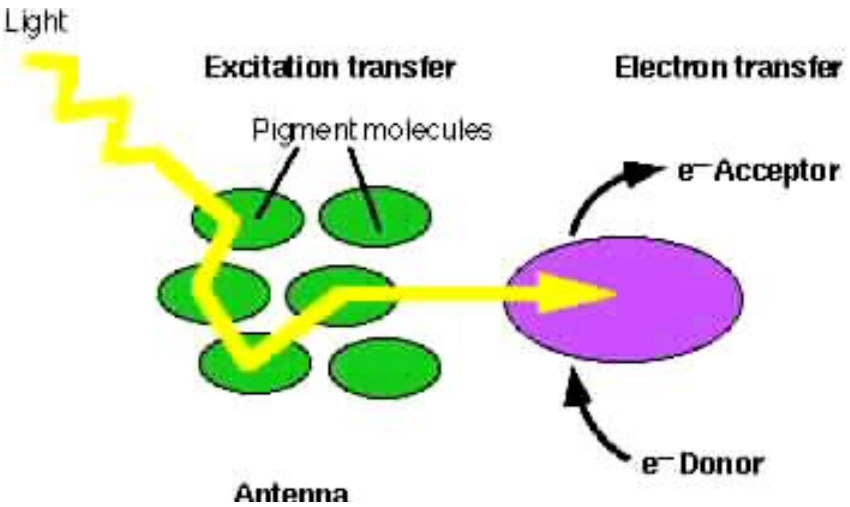
The original inspiration:
Supramolecular systems in Nature

ENZYMES

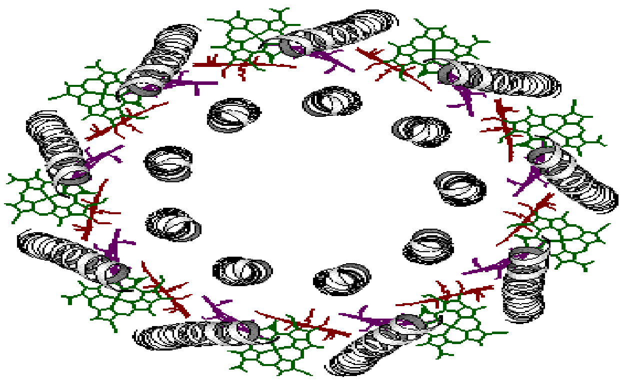


The original inspiration:
Supramolecular systems in Nature

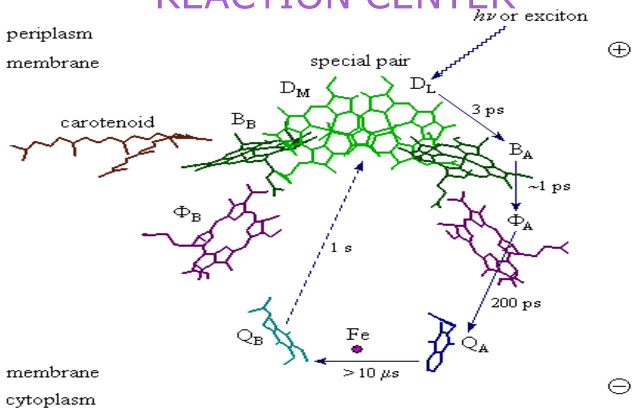
THE PHOTOSYNTHETIC APPARATUS



ANTENNA UNITS

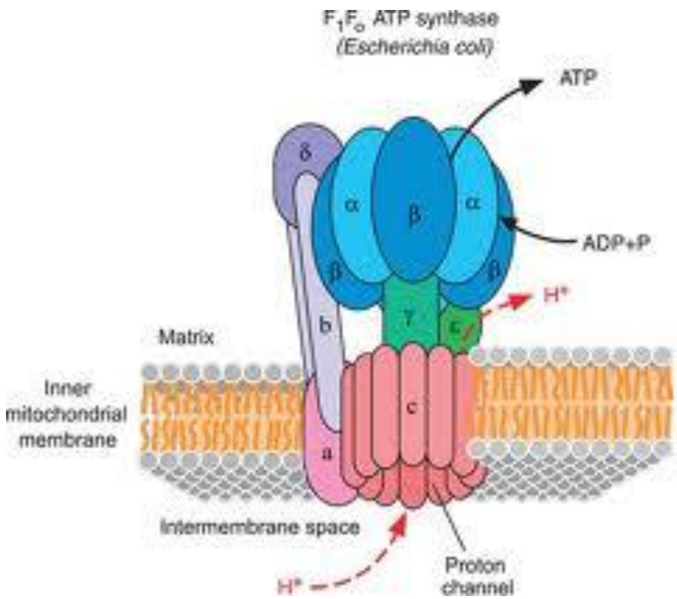


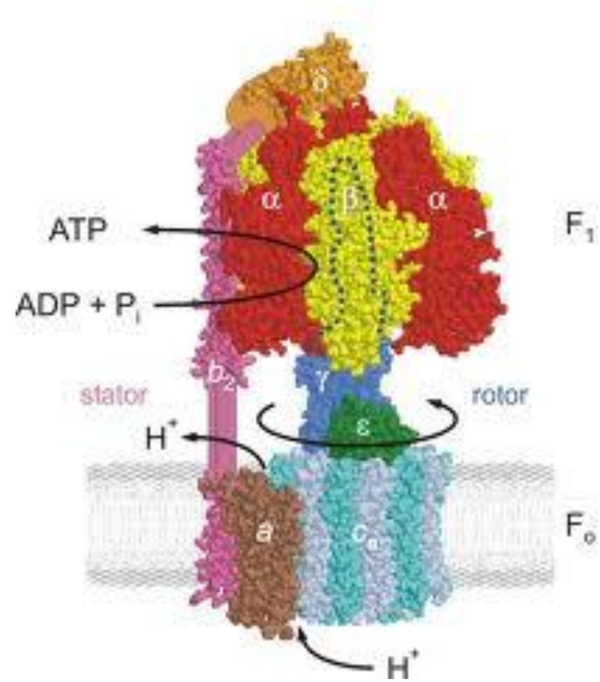
REACTION CENTER

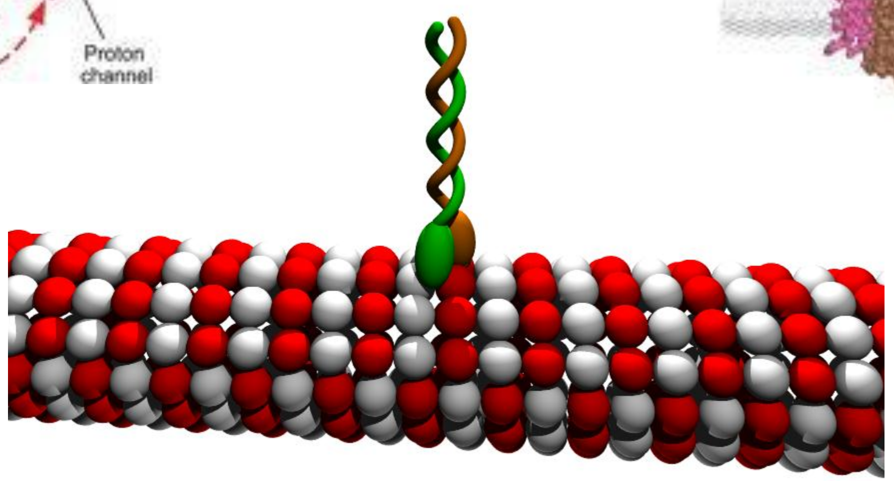


The original inspiration:
Supramolecular systems in Nature

ATP Synthase and KINESIN

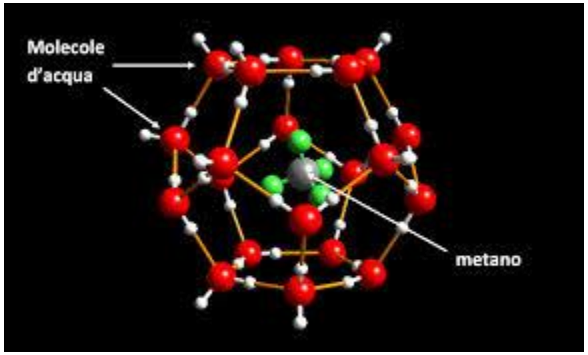






The original inspiration:
Supramolecular systems in Nature

METHANE CLATHRATE (Siberian craters)



Supramolecular Chemistry - definitions

• the chemistry beyond the molecules: molecules are already formed

• the chemistry of molecular assemblies and of the intermolecular bond: association of molecules

• the chemistry of the non covalent bond: weak interactions

Bottom-up approach

Nano objects

Smart and functional materials

Supramolecular Chemistry - vocabulary

Host-Guest, Self-assembly, Supramolecular Assembly, Design, Control, Non covalent Interactions, Electrostatic Int., Anion-Π Int., Solvent effects,…

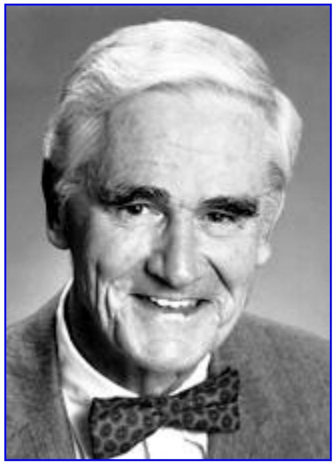
Molecular machines, containers, nanoscale flasks, nanoassemblies, supramolecular architectures, cages, trasporters, molecular magnets, nanoparticles, nanoballs, channels, tubes,…

Macrocycles, Cucubiturils, Helicates, Rotaxanes, Catenanes, Dendrimers..

Functional and complex nanomaterials and devices (smart materials, MOFs, polymers, gels, SAMs..)

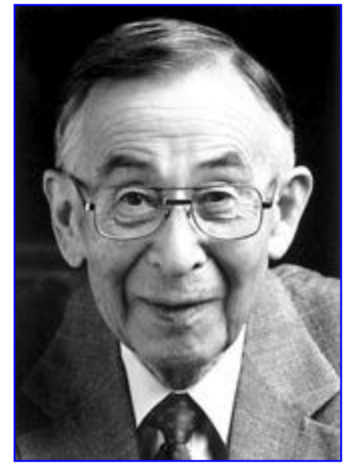
Imaging, Sensing, Recognition, Catalysis, Switching, …

Nobel Prize in Chemistry, 1987



Donald J. Cram

Jean-Marie Lehn



Charles J. Pedersen

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

http://nobelprize.org/nobel_prizes/chemistry/laureates/1987/

The Nobel Prize in Chemistry, 2016

J-P. Sauvage

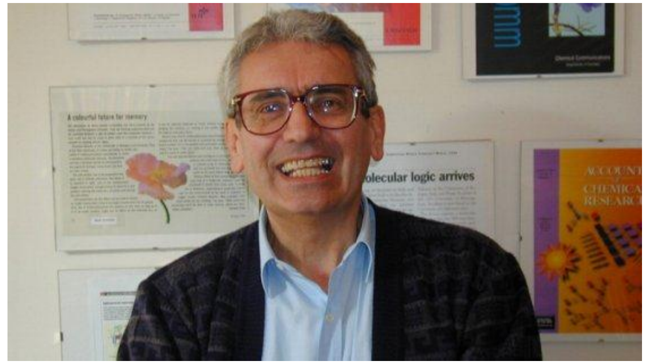
Sir J. F. Stoddart

B. L. Feringa

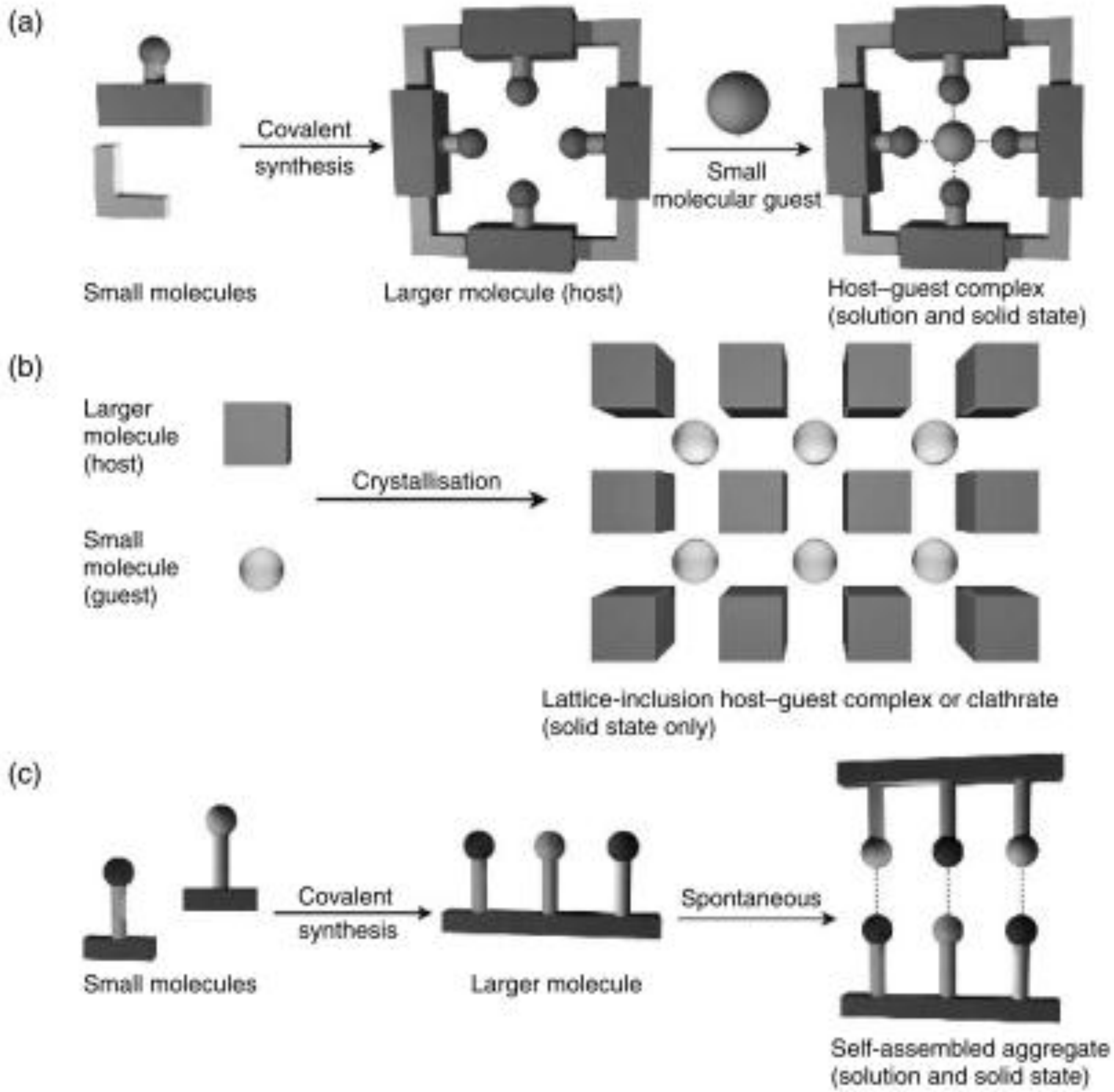
"for the design and synthesis of molecular machines"

https://www.nobelprize.org/nobel_prizes/chemistry/laureates/2016/

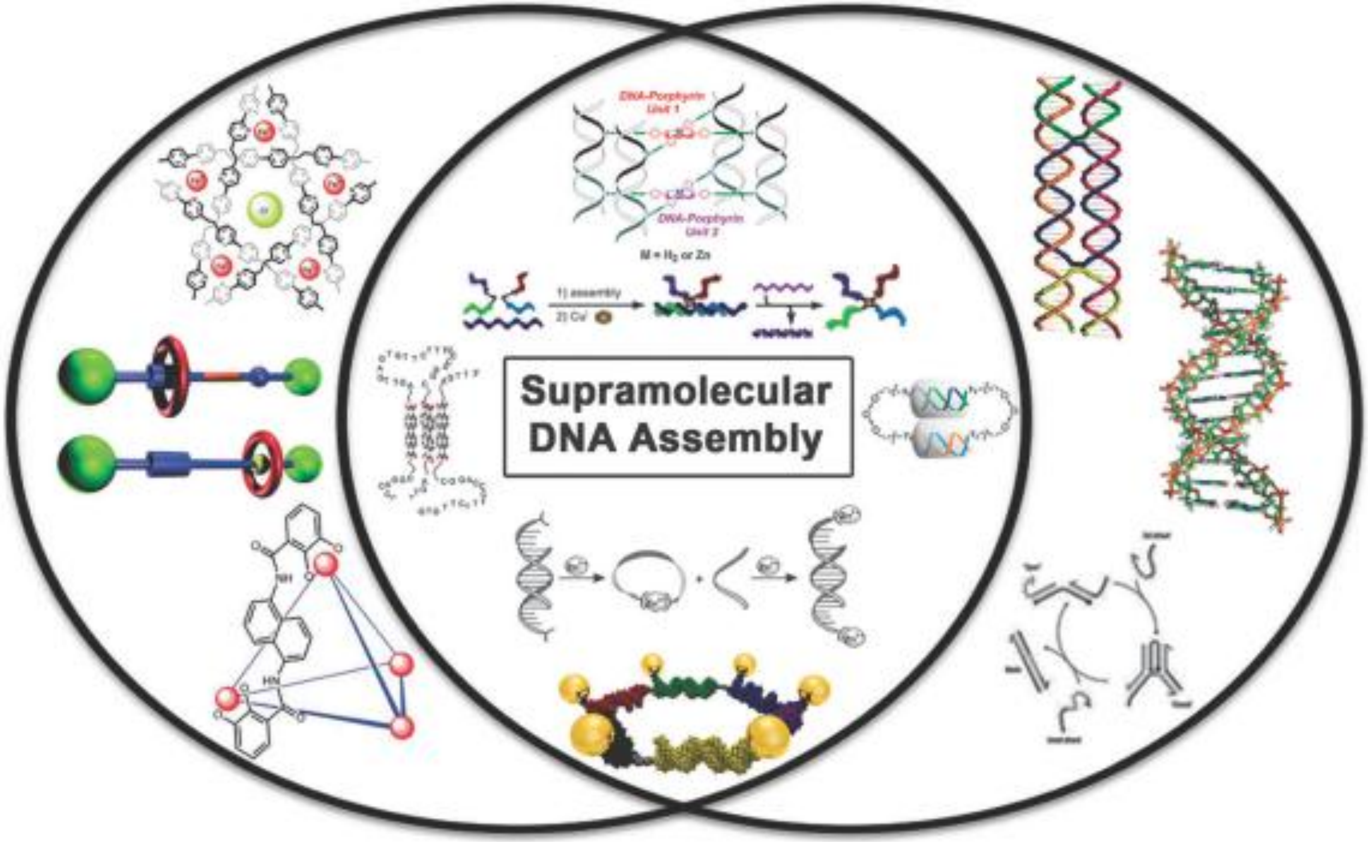
Chimica, il Nobel mancato



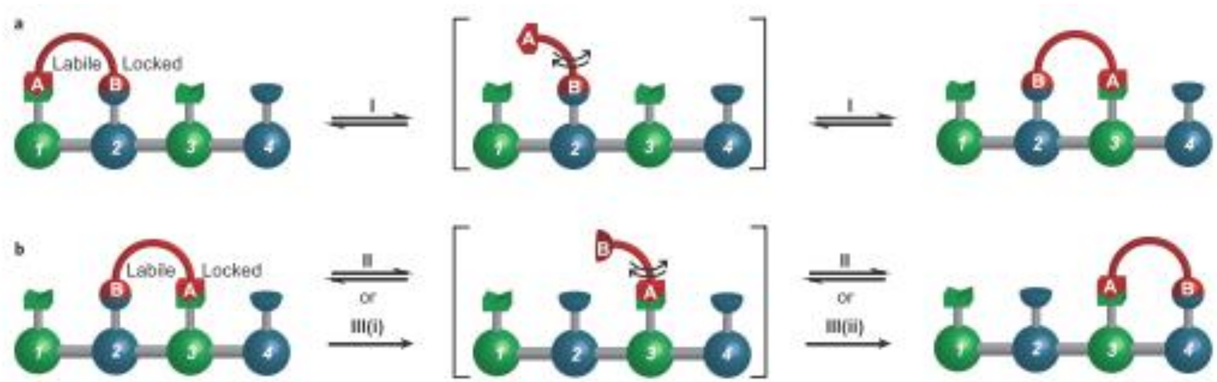
Prof. Vincenzo Balzani, docente emerito dell'Università di Bologna


(a)
Covalent synthesis
Small molecular guest
Small molecules
Larger molecule (host)
Host–guest complex (solution and solid state)
(b)
Larger molecule (host)
Small molecule (guest)
Crystallisation
Lattice-inclusion host–guest complex or clathrate (solid state only)
(c)
Covalent synthesis
Spontaneous
Small molecules
Larger molecule
Self-assembled aggregate (solution and solid state)

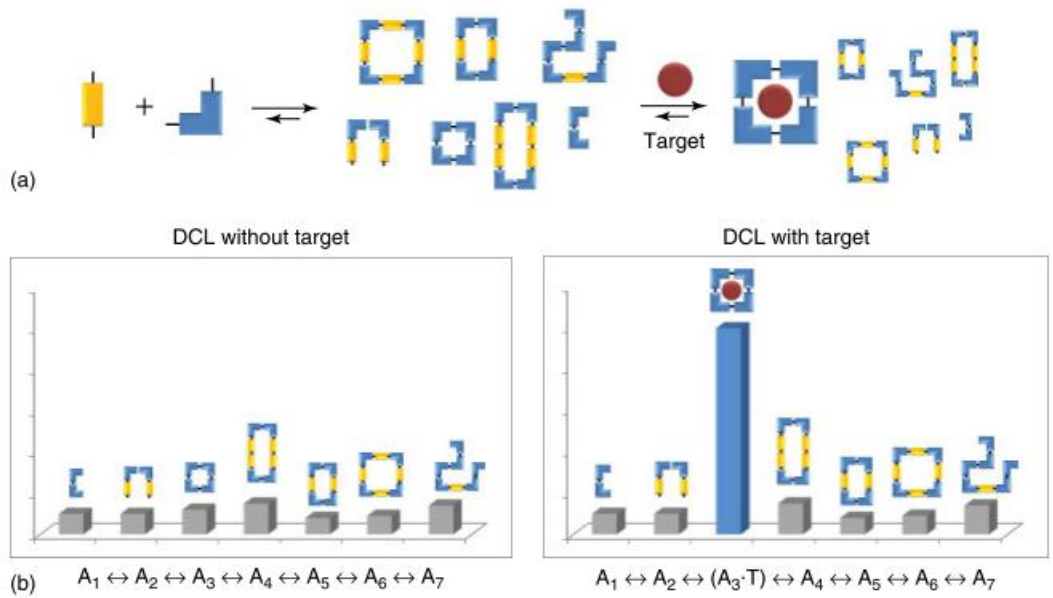
The bridge:
Supramolecular ARTIFICIAL and NATURAL systems



A synthetic molecule that CAN WALK DOWN A TRACK



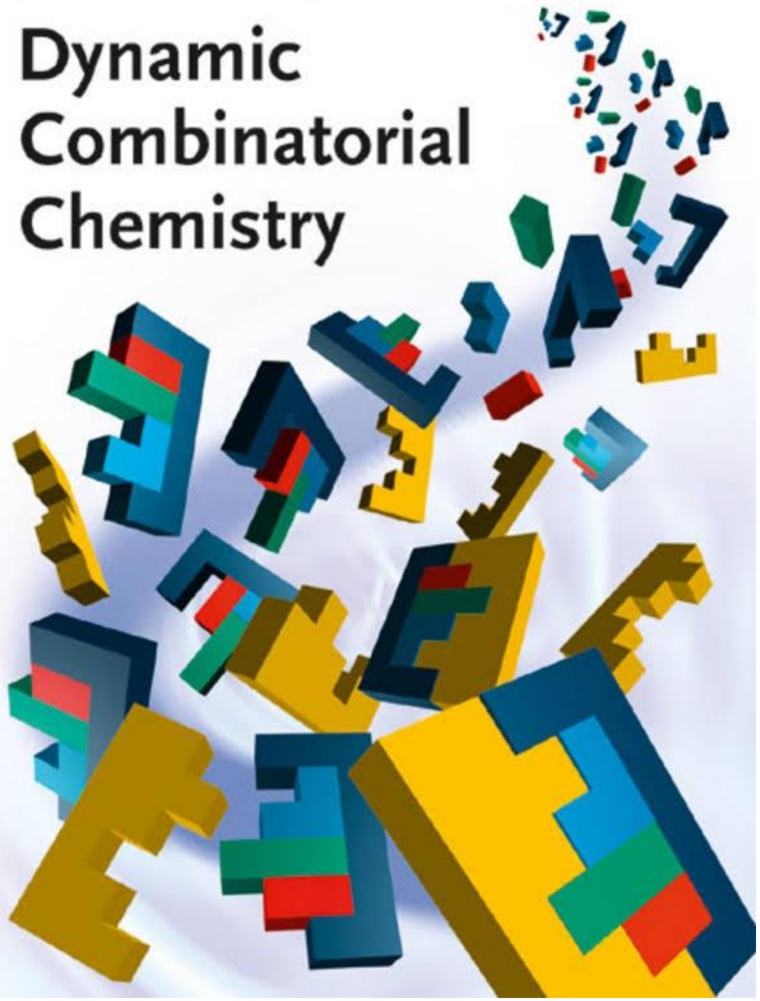
DYNAMIC COMBINATORIAL LIBRARIES



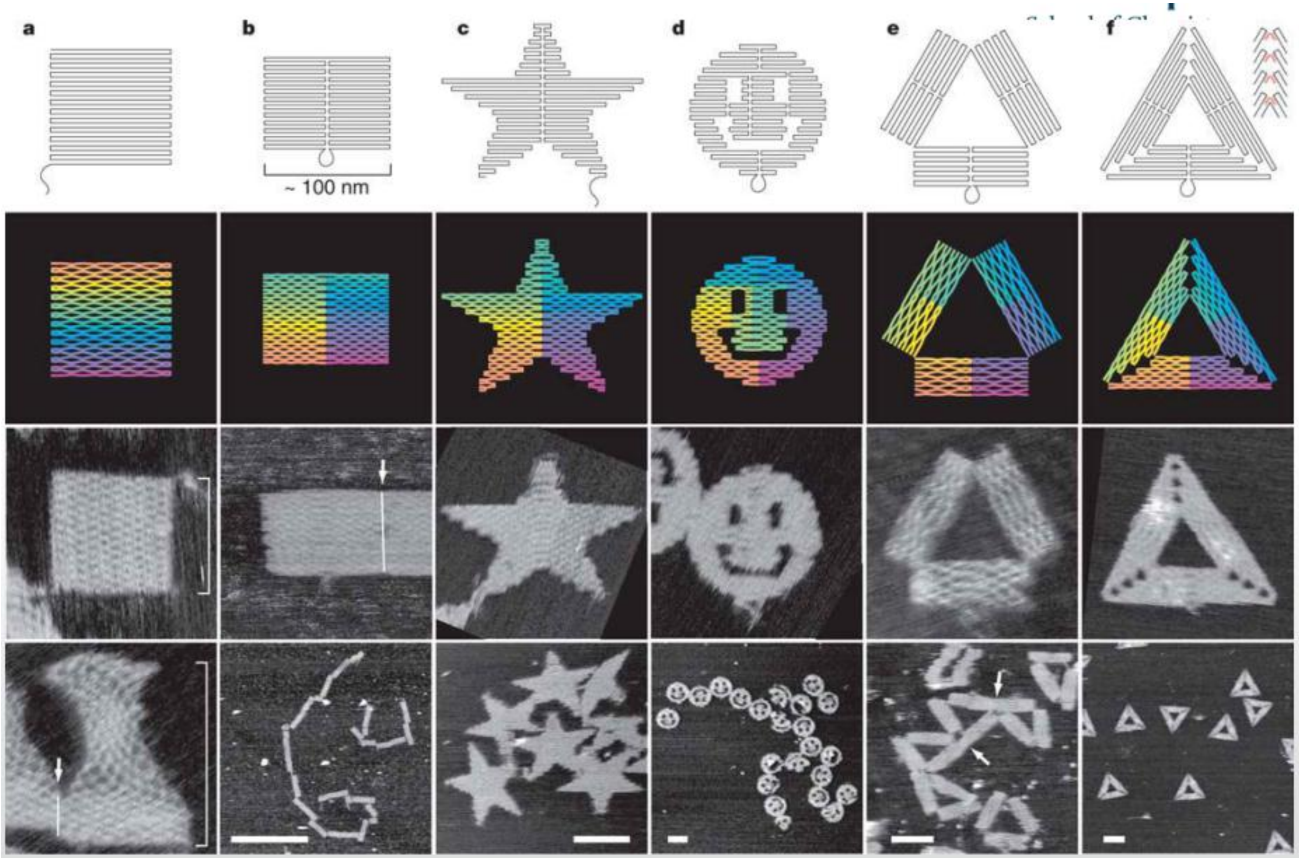
Edited by
Joost N.H. Reek and Sijbren Otto

WILEY-VCH

Dynamic Combinatorial Chemistry



Folding DNA to create NANOSCALE SHAPES AND PATTERNS



P.W. Rothemund, *Nature* 2006

From Supramolecular Chemistry to Nanotechnology

Bibliography

1. J.-M. Lehn *Supramolecular Chemistry: Concepts and Perspectives*, WCH, Weinheim (Germany), **1995**.

2. J. W. Steed, J. L. Atwood *Supramolecular Chemistry*, J. Wiley & Sons, UK, **2000**.

3. J. W. Steed, D. R. Turner, K. J. Wallace *Core Concepts in Chemistry and Nanochemistry*, Wiley, Chichester, **2007**.

4. H.-J. Schneider, A. Yatsimirsky *Principles and Methods in Supramolecular Chemistry*, J. Wiley & Sons, UK, **2000**.

5. L. F. Lindoy, I. M. Atkinson *Self-Assembly in Supramolecular Chemistry*, in *Monograms in Supramolecular Chemistry*, J. F. Stoddart ed., Royal Society of Chemistry, UK, **2000**.

6. V. Balzani, M. Venturi, A. Credi *Molecular Devices and Machines*, Wiley-VCH, Weinheim (Germany), **2003**.

7. P. J. Cragg *A Practical Guide to Supramolecular Chemistry*, J. Wiley & Sons, UK, **2005**.

8. C. A. Schalley (Ed.) *Analytical Methods in Supramolecular Chemistry*, Wiley VHC, Weinheim (Germany), **2007**.

9. P. W. N. M. Van Leeuwen Supramolecular Catalysis, Wiley-VCH, Weinheim (Germany), **2008**.

10. J.-P. Sauvage (Ed.) Perspectives in Supramolecular Chemistry, Wiley-VCH, Weinheim (Germany), **2007**.

Bibliography

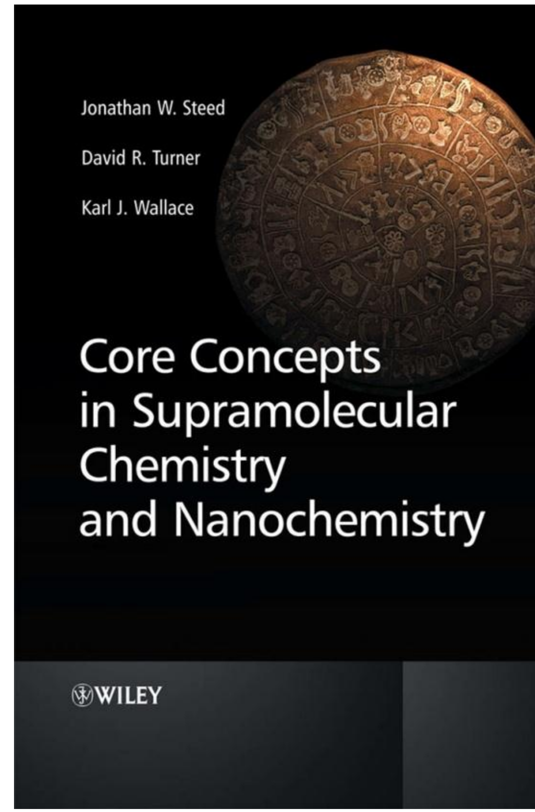
Core Concepts in Supramolecular Chemistry and Nanochemistry

Jonathan W. Steed,
Durham University, UK

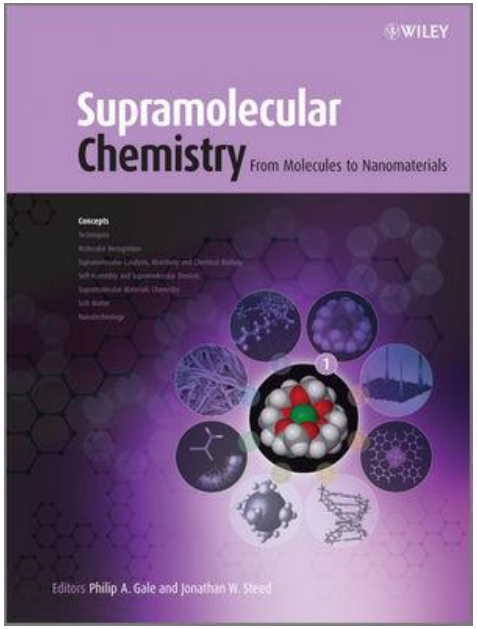
David R. Turner,
Monash University, Australia

Karl J. Wallace,
University of Southern Mississippi, USA

John Wiley & Sons, Ltd



Bibliography



Supramolecular Chemistry: From Molecules to Nanomaterials, 8 Volume Set
Jonathan W. Steed (Editor-in-Chief), Philip A. Gale (Editor-in-Chief), Wiley.

Programma

Interazioni non covalenti

Recettori 1

cationi/anioni/molecole neutre

Metodi Analitici

Recettori 2

Cavitandi/Contenitori molecolari

- Covalenti
-Auto-assemblati (legami H, legami M, legami covalenti dinamici)
-Applicazioni: isolamento di intermedi instabili; reattività nello spazio confinato; catalisi

Programma

Chimica Topologica

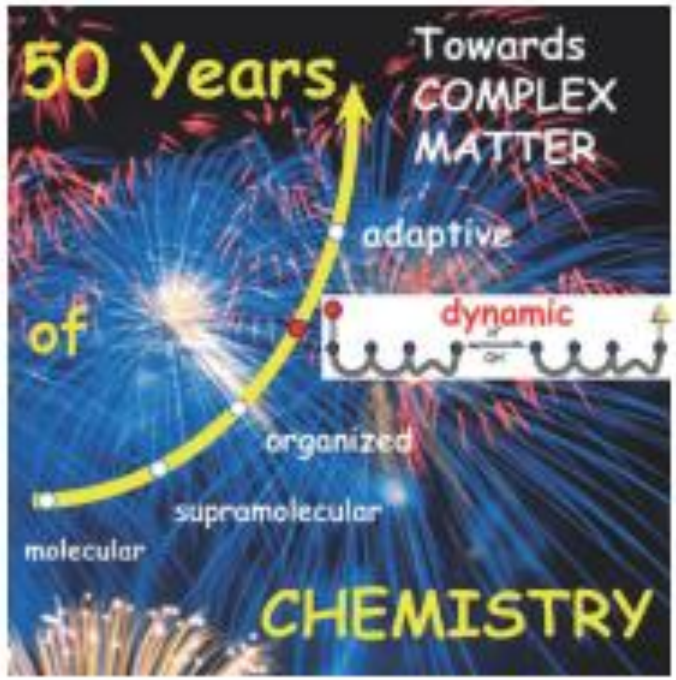
Elicati/Catenani/Rotaxani/Nodi

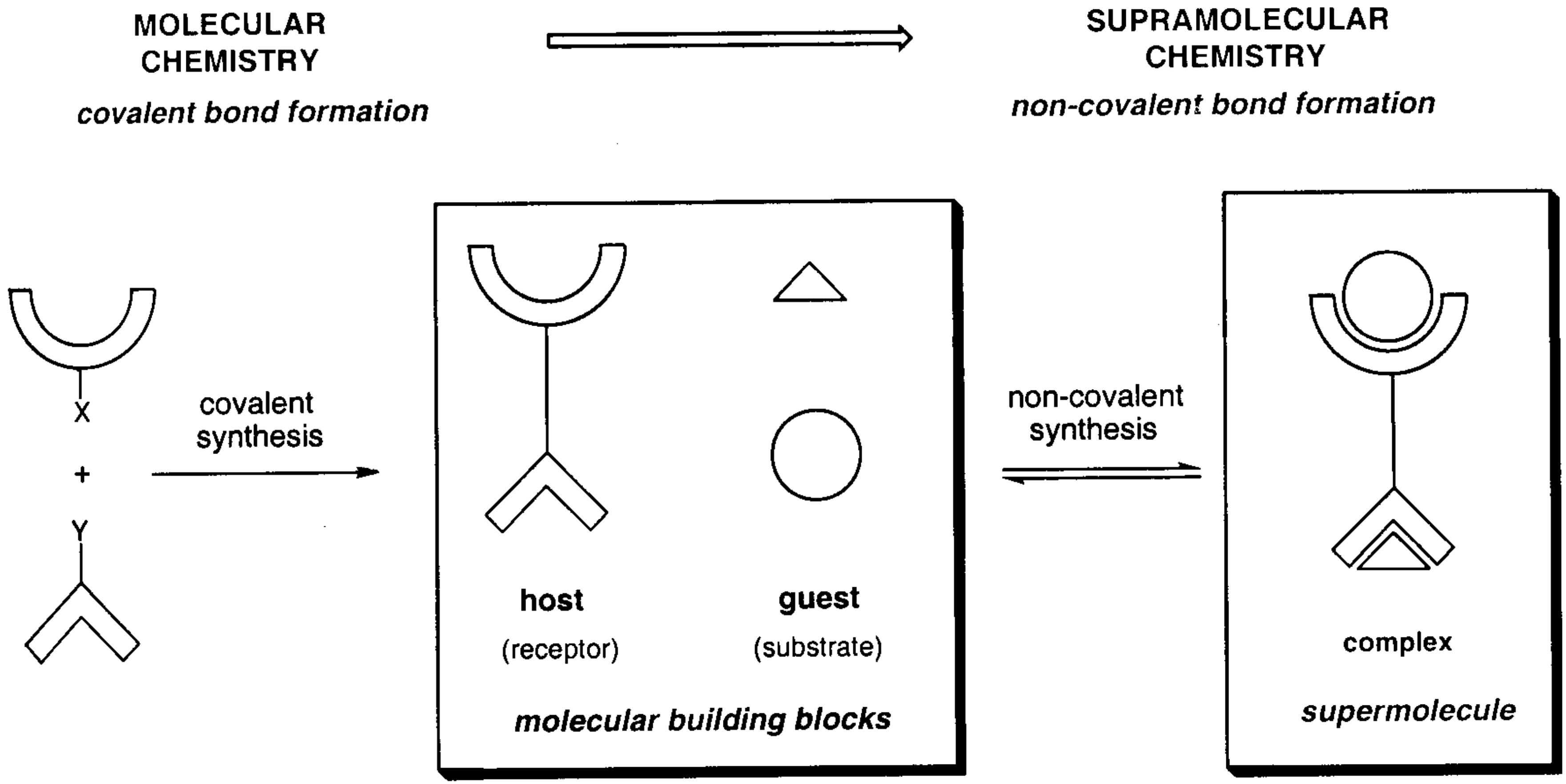
Dispositivi e Macchine molecolari

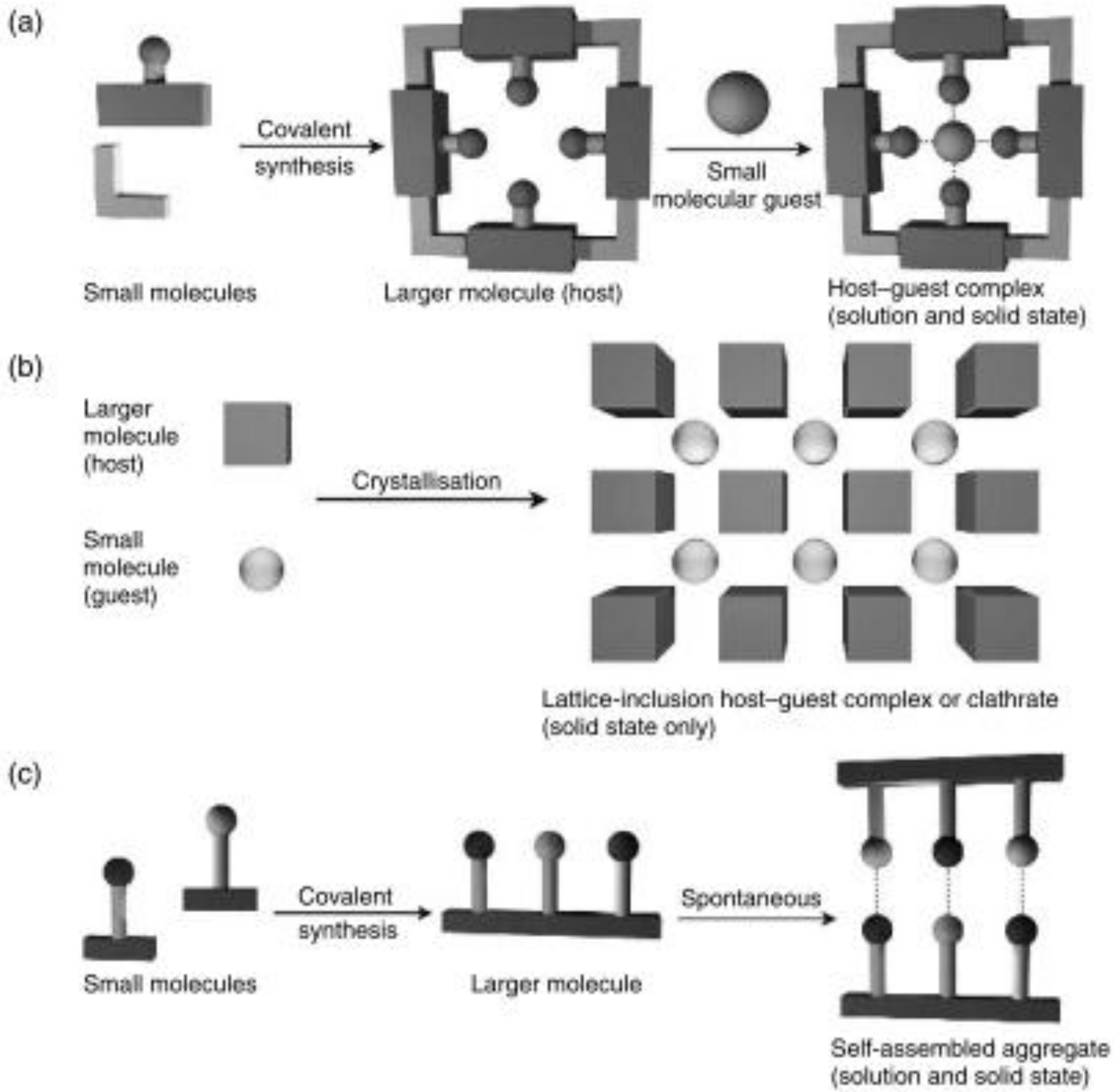
Determinazione delle Costanti di Associazione
(Prof. P. Tecilla 4h)

Sensori **Dynamic Combinatorial Chemistry**

(Prof. P. Pengo 4h)


50 Years
Towards
COMPLEX
MATTER
adaptive
dynamic
of
organized
supramolecular
molecular
CHEMISTRY

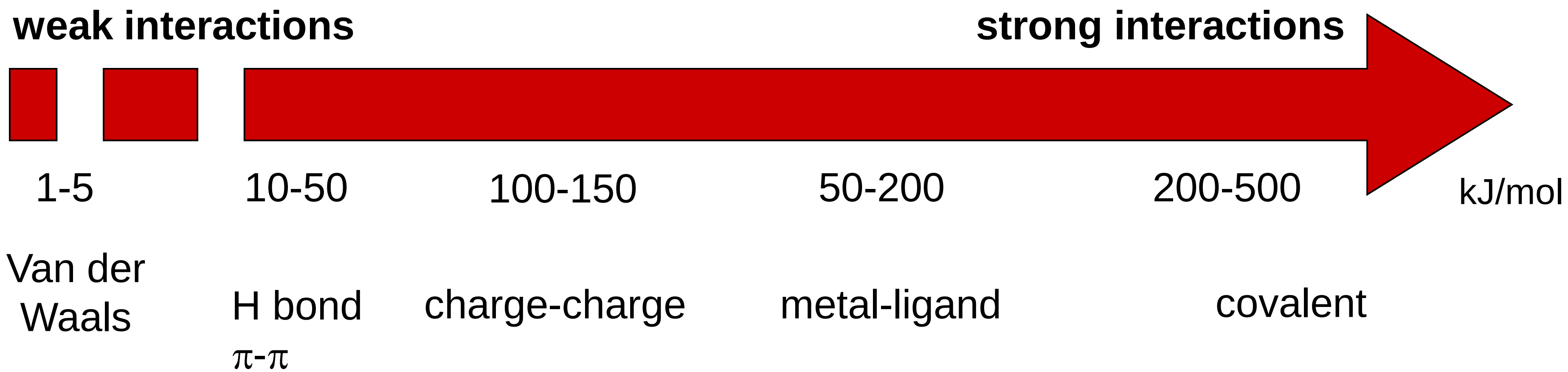

MOLECULAR CHEMISTRY
covalent bond formation
SUPRAMOLECULAR CHEMISTRY
non-covalent bond formation
X
+
Y
covalent synthesis
host
(receptor)
guest
(substrate)
molecular building blocks
non-covalent synthesis
complex
supermolecule


(a)
Covalent synthesis
Small molecular guest
Small molecules
Larger molecule (host)
Host–guest complex (solution and solid state)
(b)
Larger molecule (host)
Small molecule (guest)
Crystallisation
Lattice-inclusion host–guest complex or clathrate (solid state only)
(c)
Covalent synthesis
Spontaneous
Small molecules
Larger molecule
Self-assembled aggregate (solution and solid state)

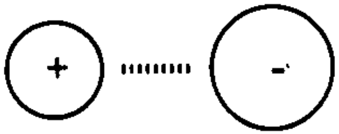
Weak (Reversible) Intermolecular Interactions

- Electrostatic
- π-π
- Cation-π/ Anion-π/CH-π
- H Bonding
- Halogen Bonding
- Metal-Ligand Coordination
- Reversible Covalent Bonding
- Chelate Effect
- Macrocyclic Effect
- Hydrophobic Effect

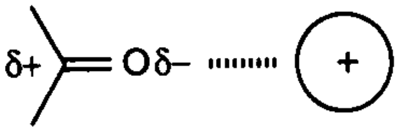
Weak Intermolecular Interactions



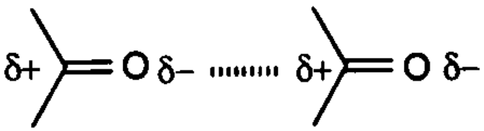
Electrostatic Interactions



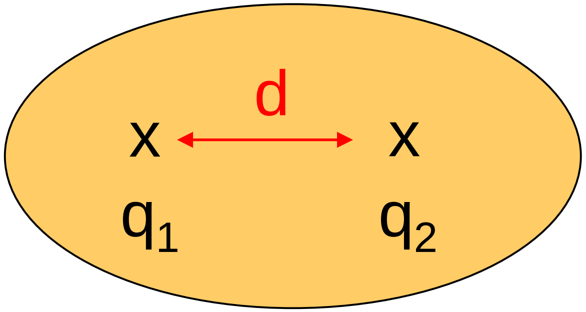
Charge-Charge Interactions 100-350 kJ/mol



Dipole-Charge Interactions 50-200 kJ/mol



Dipole-Dipole Interactions 5-50 kJ/mol



$$W = \frac{1}{4\pi\varepsilon_0} \frac{q_1 q_2}{\varepsilon\, d} \quad (J)$$

vacuum permittivity

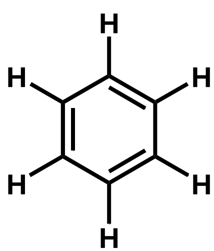
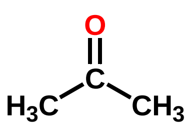
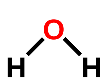
dielectric constant (nature of solvant)

ε(vacuum) = 1

apolar medium ⇔ ε small (~ 2)

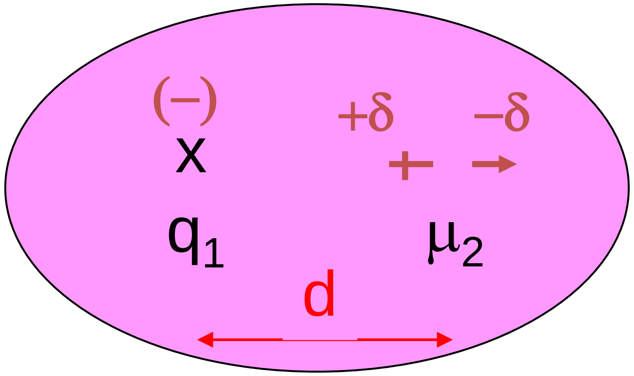
polar medium ⇔ ε big (H_2O ~ 80)

dielectric constant of the solvant

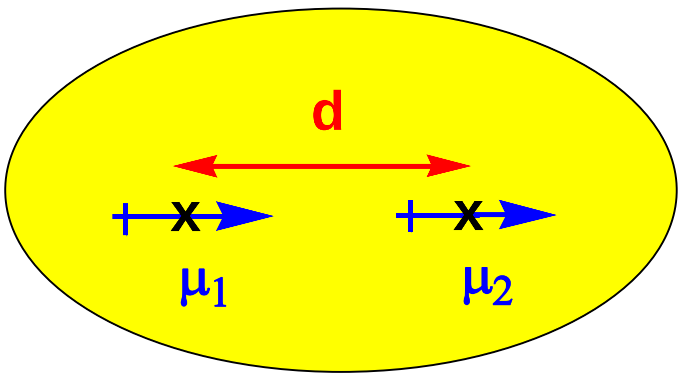
		ε	
Benzene		2,3	apolar
Acetone		20,7	↓
Ethanol	CH_3CH_2OH	24,3	↓
water		78,5	polar

ε = 78.5 d = 0.5 nm => W = 3.75 kJ.mol^{-1}

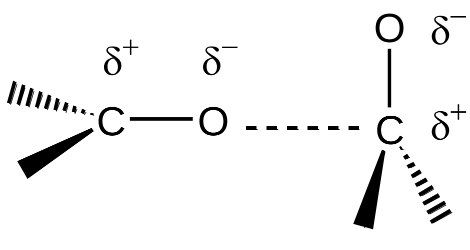
ε = 2 d = 0.5 nm => W = 140 kJ.mol^{-1}

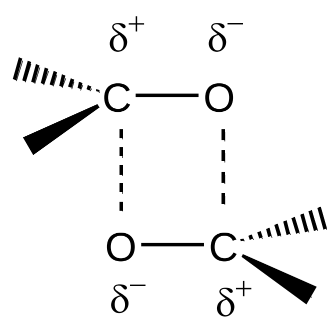


$$W = -\,C^{te} \times \frac{|q|\,\mu_2}{\varepsilon\, d^2}$$

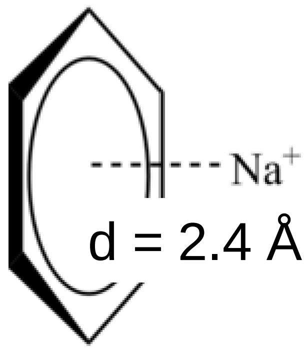


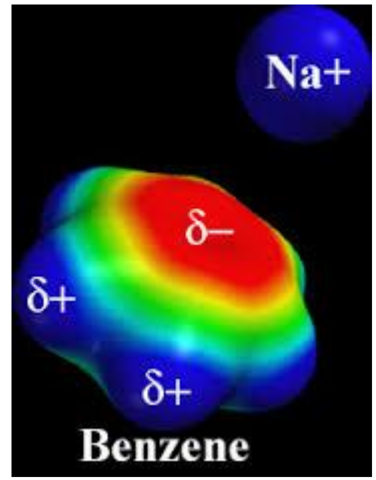
$$W = -\,C^{te}\,\frac{\mu_1\,\mu_2}{\varepsilon\, d^3}$$

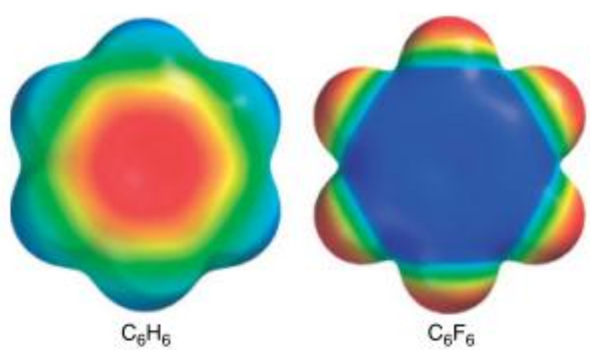




Cation-π Interactions

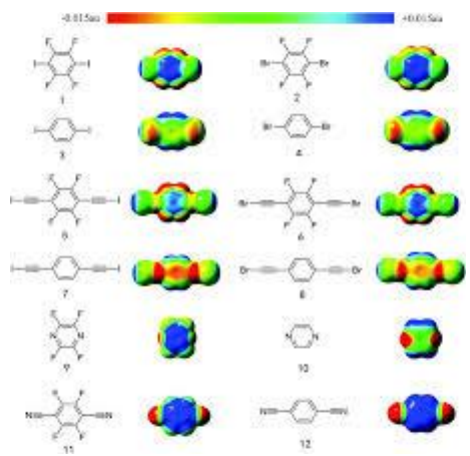




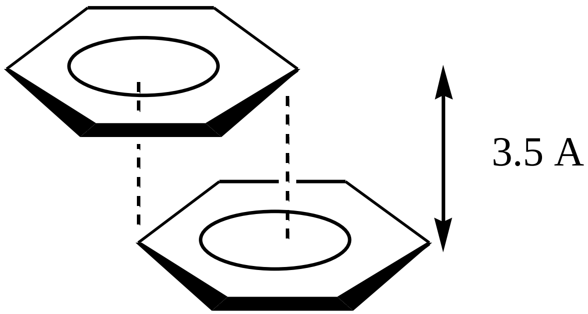


Anion-π Interactions

Proposed by three research groups of theoreticians independently in 2002 based on their theoretical calculations, anion −π interactions are defined as attractive interactions between negatively charged species and electron-deficient aromatic rings.
Typical anion−π interaction indicates the attraction of an anion species to the centroid of an aromatic ring.
In comparison to a plethora of theoretical calculations of anion−π interactions, experimental studies on these intriguing noncovalent bond interactions are limited.

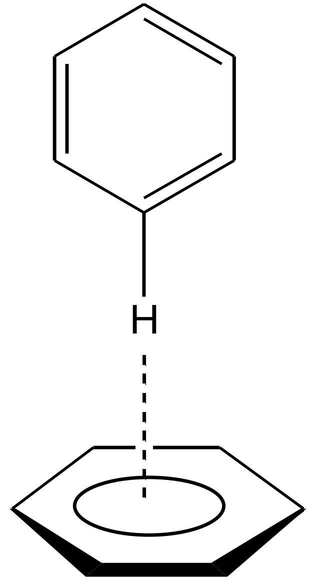


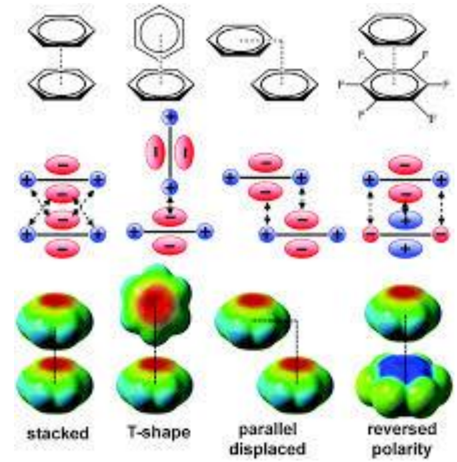
π-π Interactions up to 50 kJ/mol



face to face

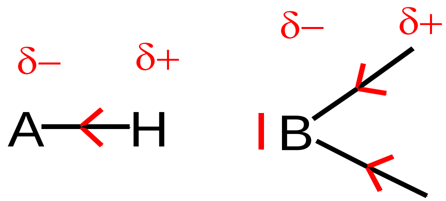
edge to face



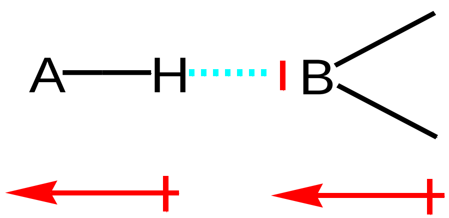


C.A. Hunter and J.K.M. Sanders, ***The Nature of π - π interactions***, *J. Am. Chem. Soc.*, **1990**, *112*, 5525;
E.-I. Kim, S. Paliwal and C.S. Wilcox, ***Measurements of molecular electrostatic field effects in edge-to-face aromatic interactions and CH- π interactions with implications for protein folding and molecular recognition***, *J. Am. Chem. Soc*., **1998**, *120*, 11192.

H Bond 4-120 kJ/mol



A, B electronegative or electrondeficient atoms



permanent dipoles

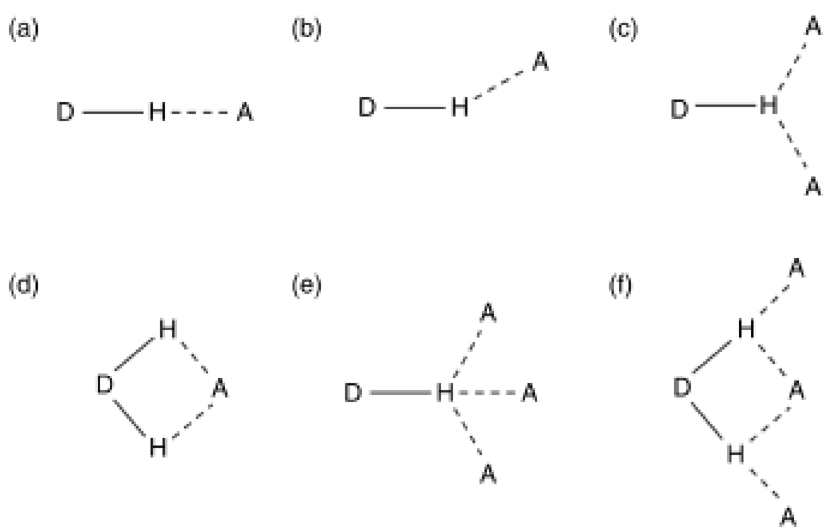


Table 1.5 Properties of hydrogen bonded interactions.

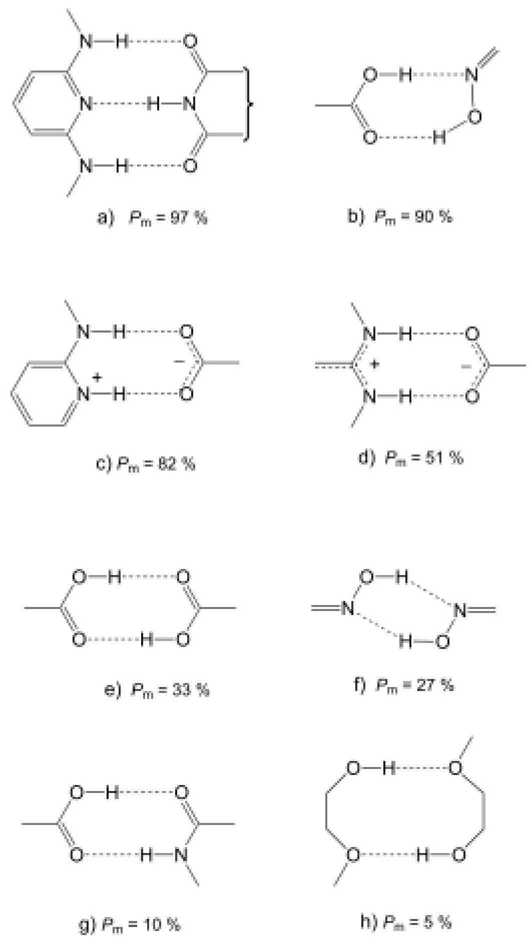
	Strong	Moderate	Weak
A–H···B interaction	Mainly covalent	Mainly electrostatic	Electrostatic
Bond energy (kJ mol^{-1})	60–120	16–60	<12
Bond lengths (Å)			
H···B	1.2–1.5	1.5–2.2	2.2–3.2
A···B	2.2–2.5	2.5–3.2	3.2–4.0
Bond angles (°)	175–180	130–180	90–150
Relative IR vibration shift (stretching symmetrical mode, cm^{-1})	25%	10–25%	<10%
^{1}H NMR chemical shift downfield (ppm)	14–22	<14	?
Examples	Gas phase dimers with strong acids/bases Proton sponge HF complexes	Acids Alcohols Biological molecules	Minor components of bifurcated bonds C–H hydrogen bonds O–H···π hydrogen bonds

G.A. Jeffrey, ***An Introduction to Hydrogen Bonding,*** Oxford University Press: Oxford, **1997**.

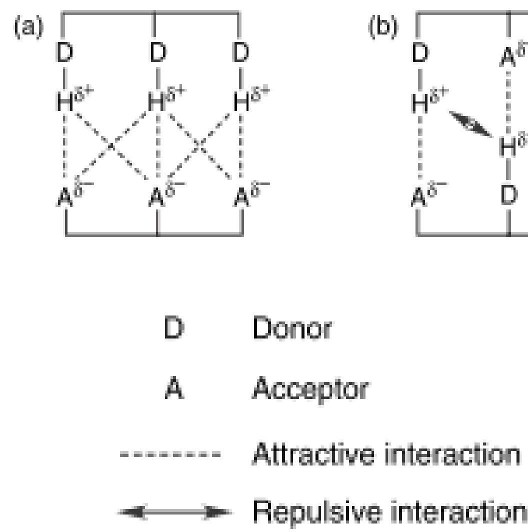
The Hydrogen Bond in the Solid State

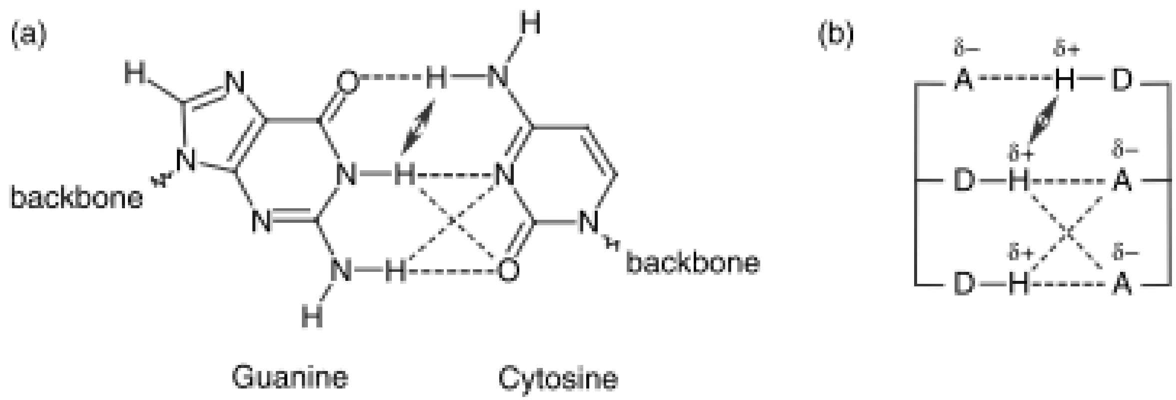
Thomas Steiner*

Angew. Chem. Int. Ed. **2002**, *41*, 48–76



Scheme 17. Eight examples of intermolecular hydrogen bond motifs with their probability of formation (P_m) in crystals.[122] Notice that P_m of the carboxy–oxime heterodimer (b) is much higher than that of the carboxylic acid (e) and oxime homodimers (f).


(a)
D
D
D
H
H
H
A
A
A
(b)
D
A
D
H
H
H
D
A
A
D Donor
A Acceptor
Attractive interaction
Repulsive interaction


(a)
backbone
backbone
Guanine
Cytosine
(b)
δ−
δ+
A
H
D
δ+
δ−
D
H
A
δ+
δ−
D
H
A

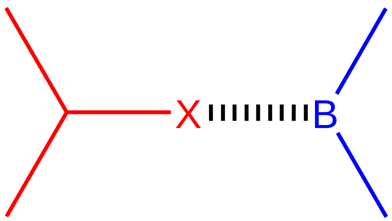
Halogen Bond

In 2009 the International Union of Pure and Applied Chemistry (IUPAC) started a project (project no. 2009-032-1-100) having the aim " to take a comprehensive look at intermolecular interactions involving halogens as electrophilic species and classify them"
http://www.halogenbonding.eu/
http://www.iupac.org/web/ins/2009-032-1-100

An IUPAC recommendation defining these interactions as halogen bonds was issued in 2013 when the project was concluded: This definition states that

" A halogen bond occurs when there is evidence of a net attractive interaction between an electrophilic region associated with a halogen atom in a molecular entity and a nucleophilic region in another, or the same, molecular entity. "

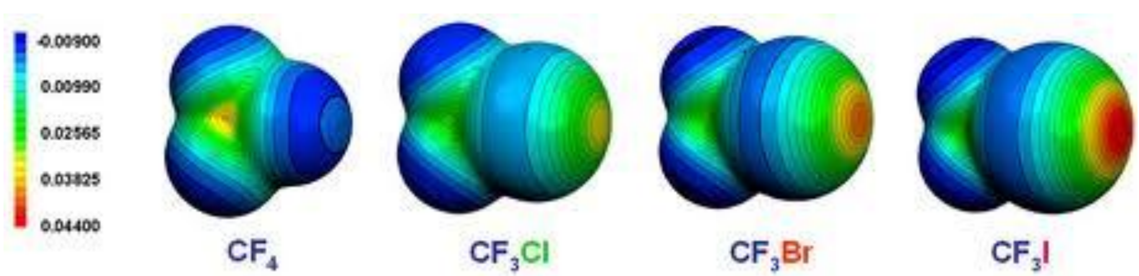
Halogen Bond



B : Lewis base (neutral or anionic)

X : electron-poor halogen atom

- Very directional (180°, but also other geometries)
- As strong as H-bond
- Often encountered in solid state, more rarely in solution



molecule	atom	bond producing a σ-hole
$H_3C{-}F$	F	C−F
$H_3C{-}Cl$	Cl	C−Cl
$H_3C{-}Br$	Br	C−Br
$H_3C{-}I$	I	C−I
$F_3C{-}F$	F	C−F
$F_3C{-}Cl$	Cl	C−Cl
$F_3C{-}Br$	Br	C−Br
$F_3C{-}I$	I	C−I
NC−F	F	C−F
NC−Cl	Cl	C−Cl
NC−Br	Br	C−Br
NC−I	I	C−I
		Dihalogens
F−F	F	F−F
Cl−Cl	Cl	Cl−Cl
Br−Br	Br	Br−Br
		Focus on Bromine
Br—C≡C—Br	Br	C−Br
$H_3Si{-}Br$	Br	C−Br
$F_3Si{-}Br$	Br	Si−Br
$H_3Ge{-}Br$	Br	Ge−Br
$H_2N{-}Br$	Br	N−Br
$F_2N{-}Br$	Br	N−Br
$H_2P{-}Br$	Br	P−Br
$F_2P{-}Br$	Br	P−Br
HO−Br	Br	O−Br
FO−Br	Br	O−Br
HS−Br	Br	S−Br
FS−Br	Br	S−Br
F−Br	Br	F−Br
Cl−Br	Br	Cl−Br

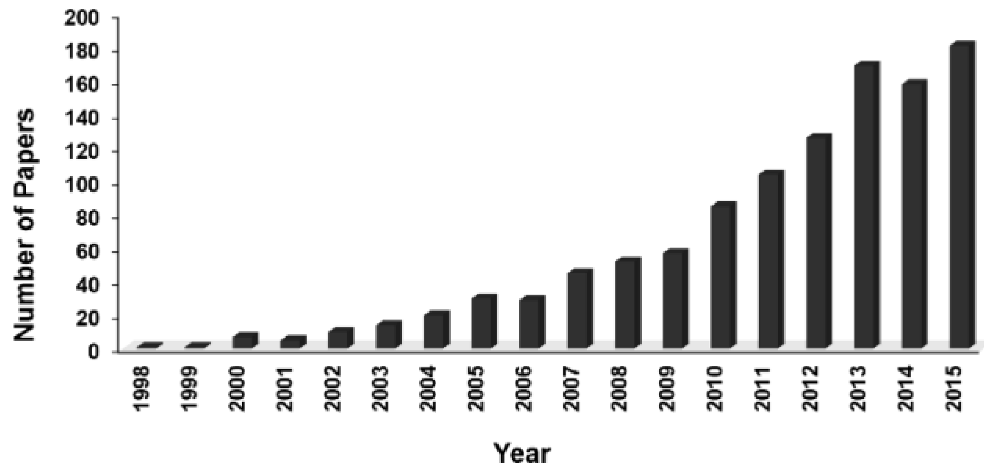


Figure 5. Number of papers per year having "halogen bonding" in the title and/or abstract (source SciFinder, search performed in November 2015).

CHEMICAL REVIEWS

Review

pubs.acs.org/CR

DOI: 10.1021/acs.chemrev.5b00484

The Halogen Bond

Gabriella Cavallo,[†] Pierangelo Metrangolo,[*,†,‡] Roberto Milani,[‡] Tullio Pilati,[†] Arri Priimagi,[§] Giuseppe Resnati,[*,†] and Giancarlo Terraneo[†]

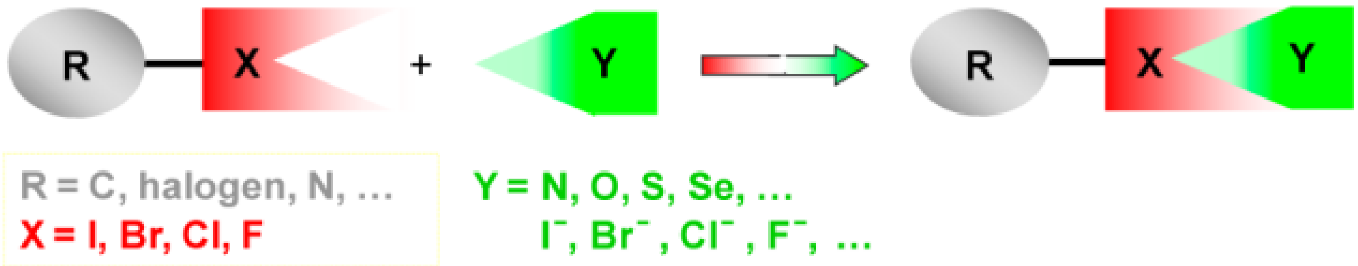


Figure 1. Schematic representation of the halogen bond.

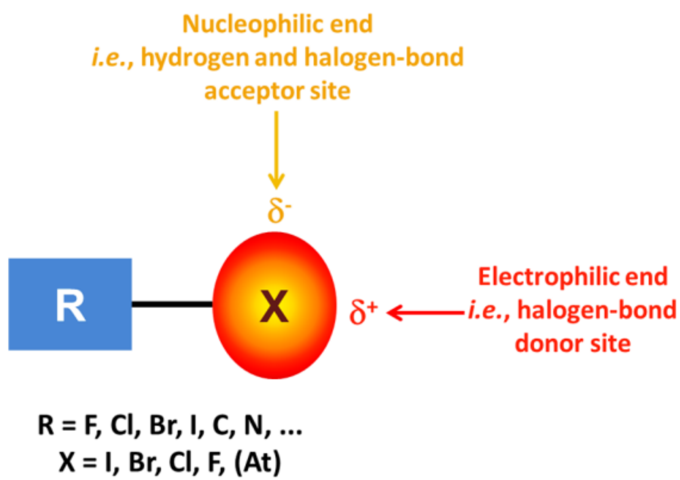
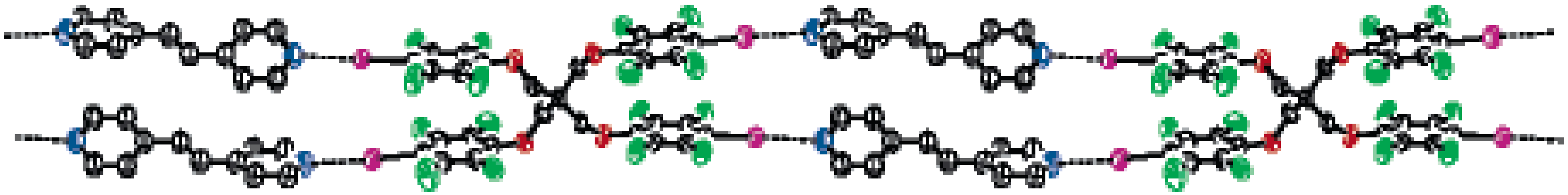
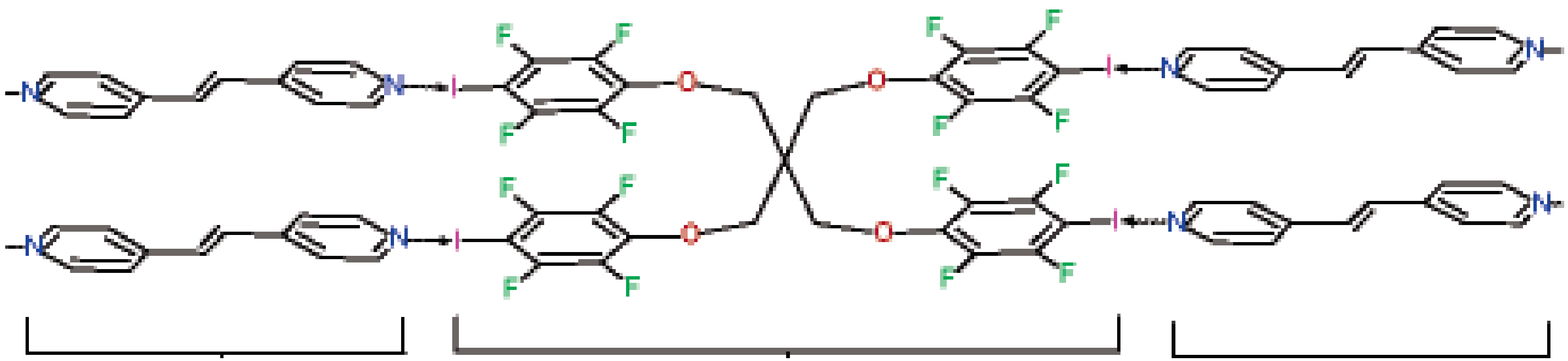
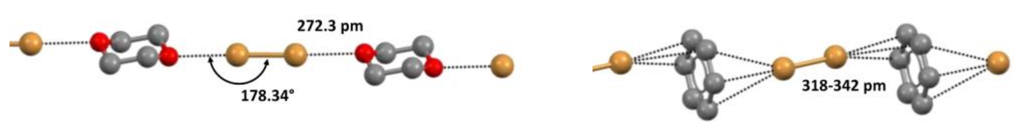


Figure 21. Schematic representation of the anisotropic distribution of the electron density around covalently bound halogen atoms and the pattern of the resulting interactions.

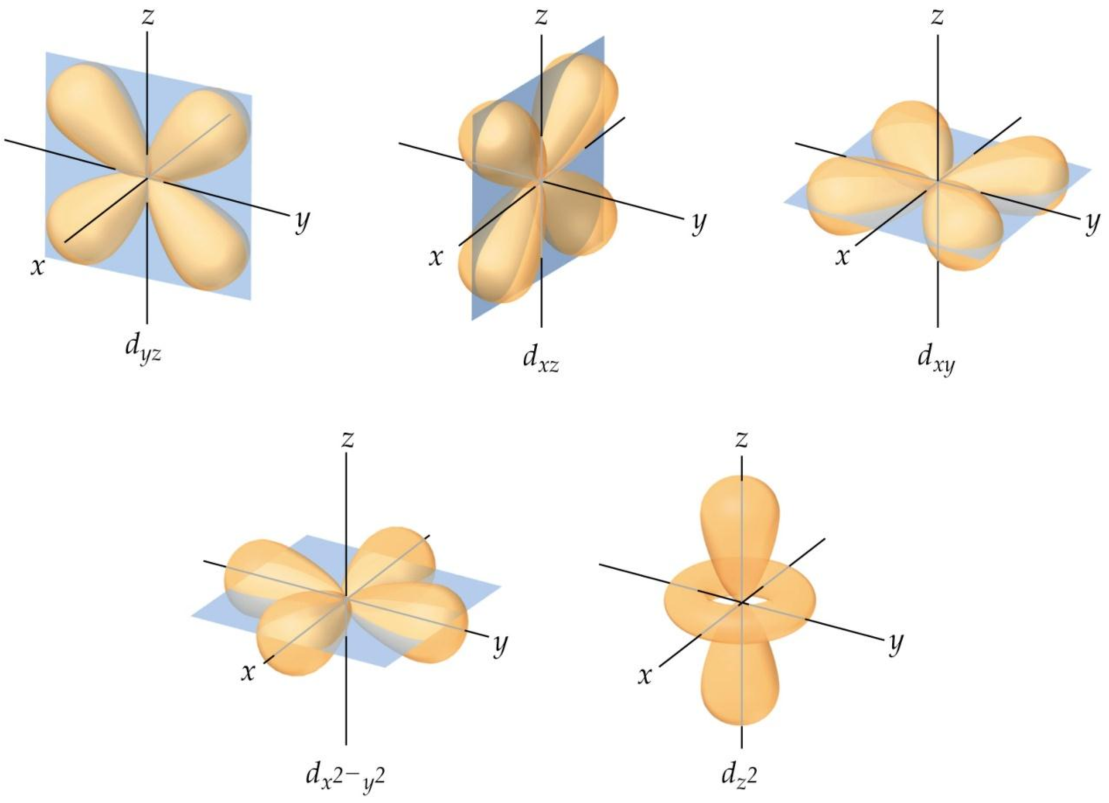


14

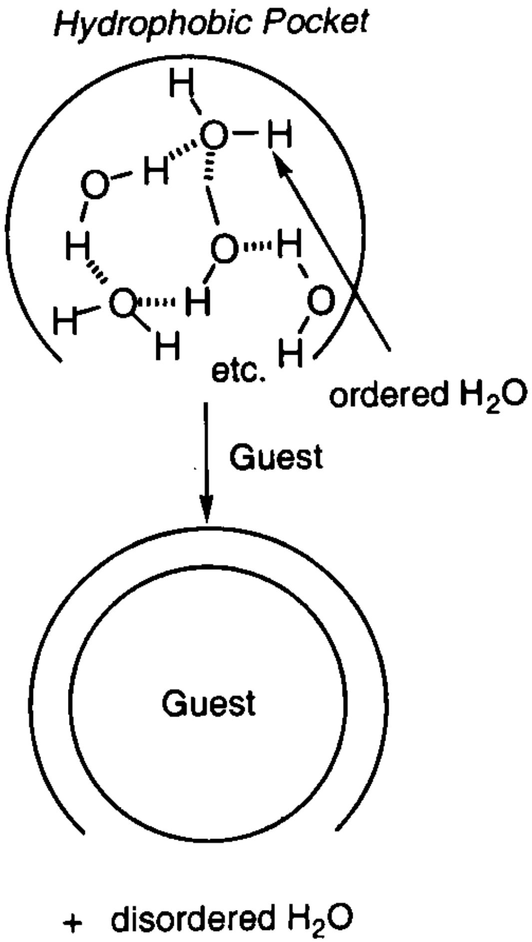


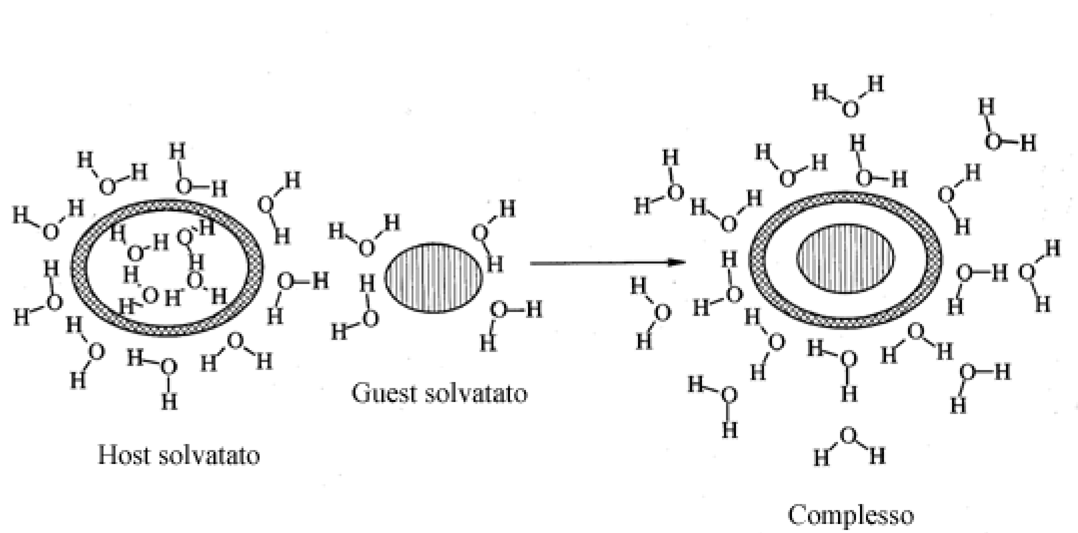


Metal-Ligand Interaction



Hydrophobic Effect



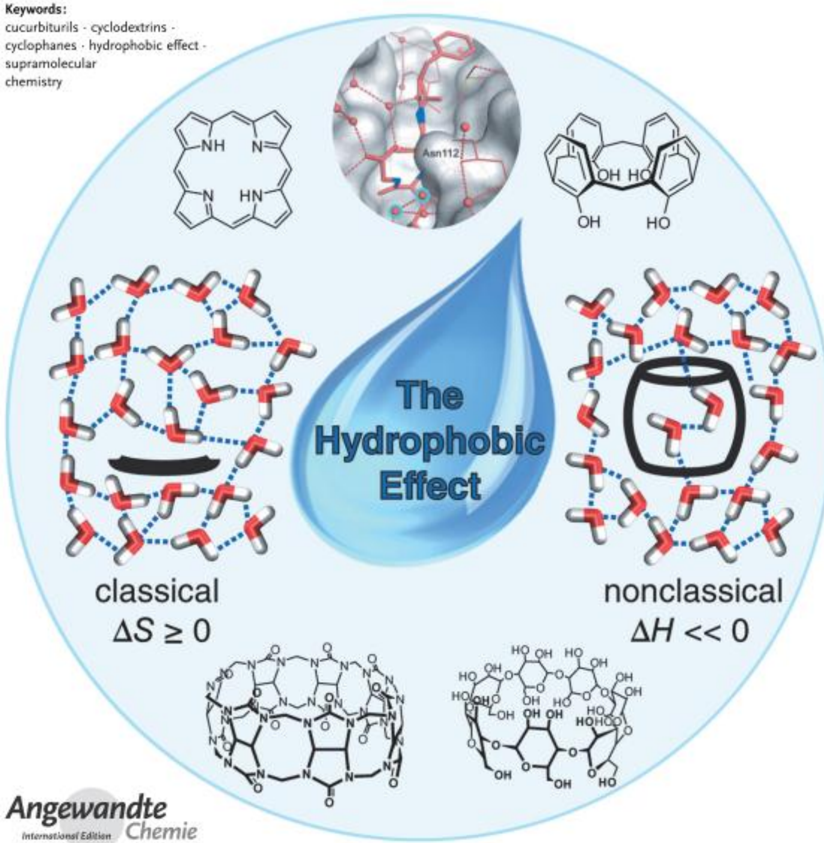


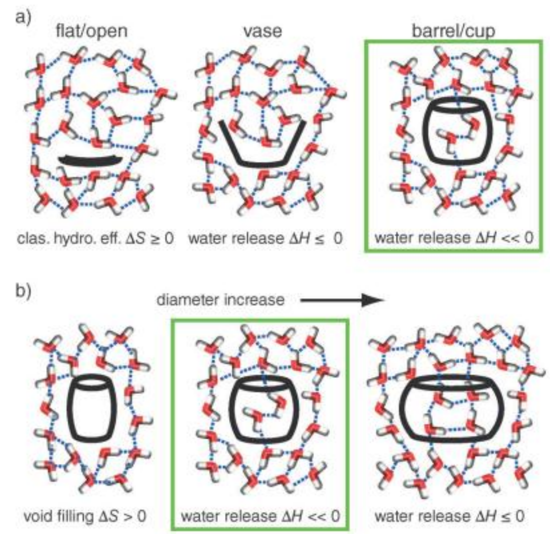
Hydrophobic Effect
DOI: 10.1002/anie.201310958

The Hydrophobic Effect Revisited—Studies with Supramolecular Complexes Imply High-Energy Water as a Noncovalent Driving Force

Frank Biedermann, Werner M. Nau,* and Hans-Jörg Schneider**

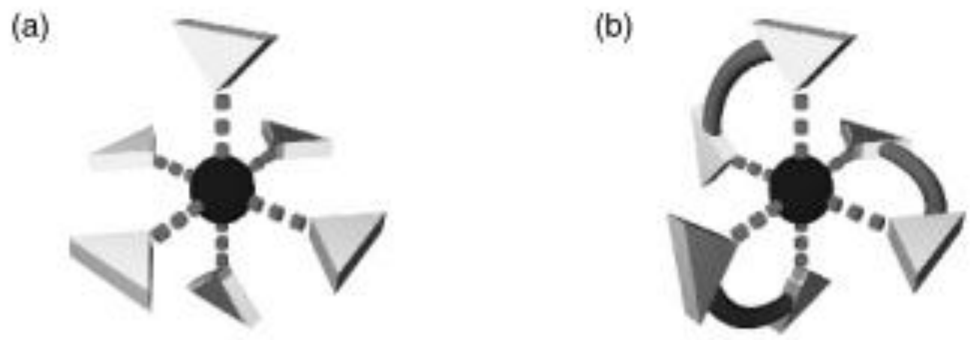
Keywords:
cucurbiturils · cyclodextrins · cyclophanes · hydrophobic effect · supramolecular chemistry



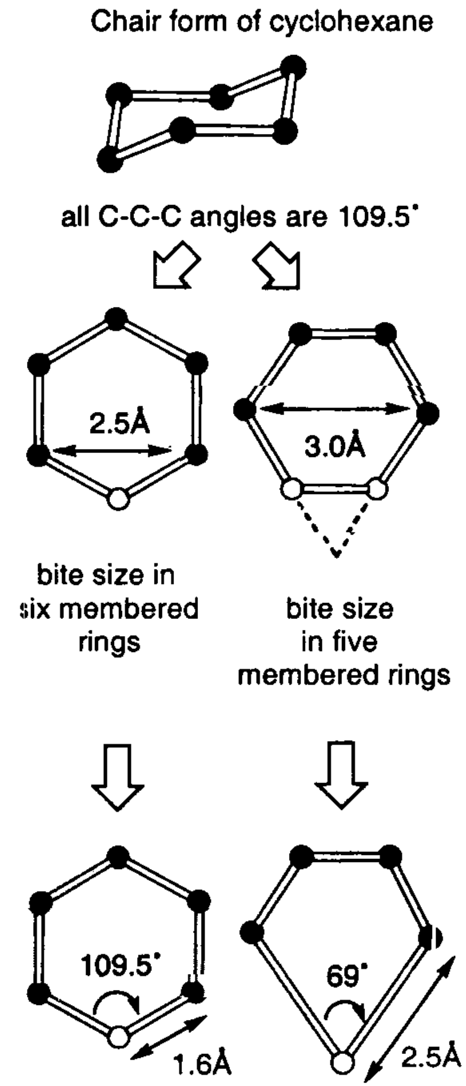


a)
flat/open
vase
barrel/cup
clas. hydro. eff. ΔS ≥ 0
water release ΔH ≤ 0
water release ΔH << 0
b)
diameter increase
void filling ΔS > 0
water release ΔH << 0
water release ΔH ≤ 0

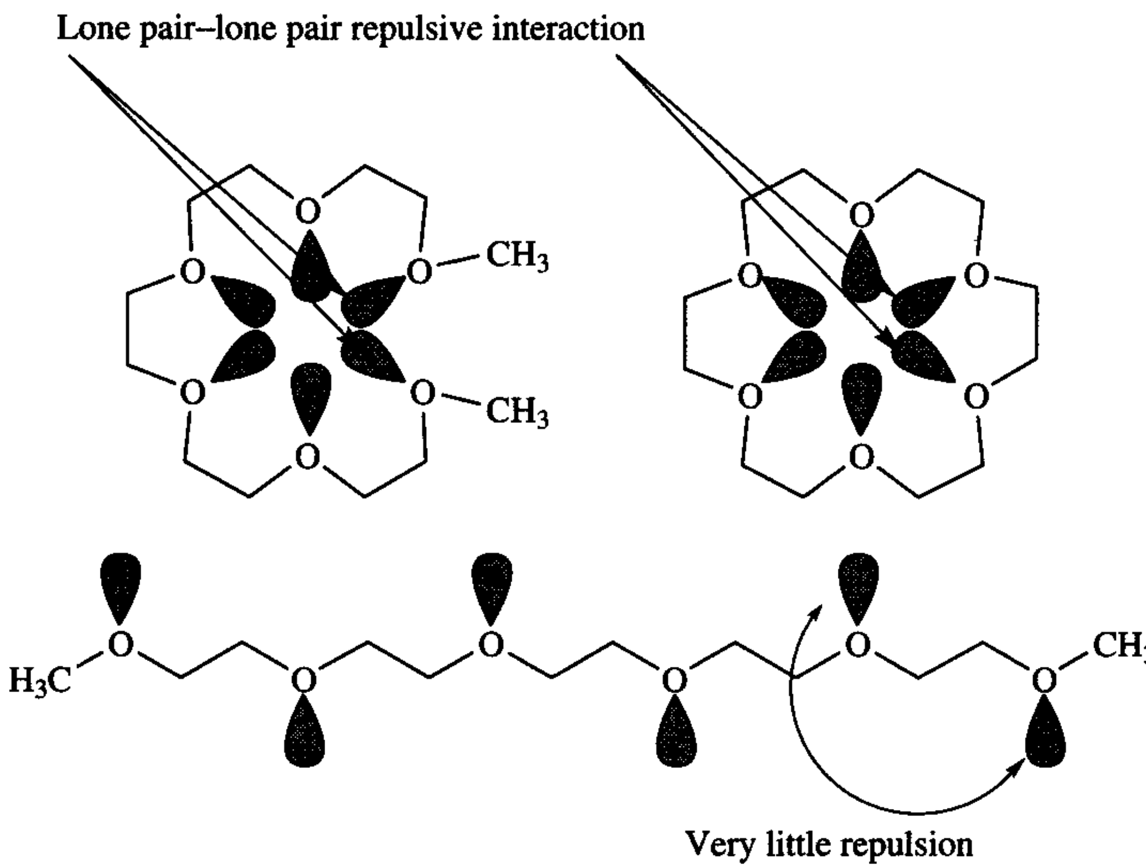
Chelate Effect



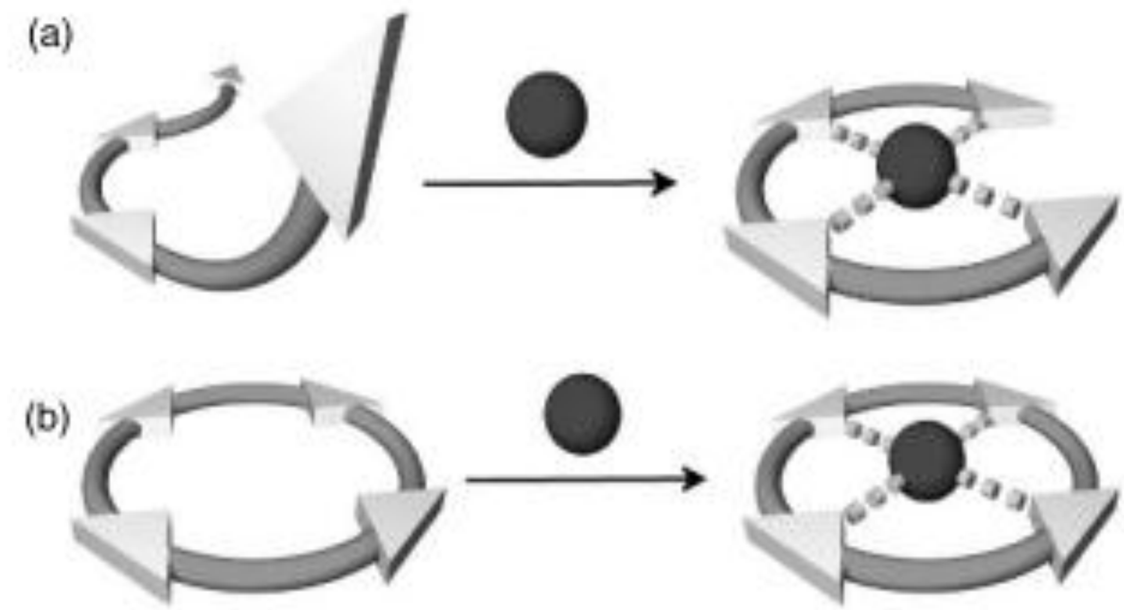
$$[Ni(NH_3)_6]^{2+} + 3NH_2CH_2CH_2NH_2 \underset{}{\overset{\log K = 8.76}{\rightleftharpoons}} [Ni(NH_2CH_2CH_2NH_2)_3]^{2+} + 6NH_3$$

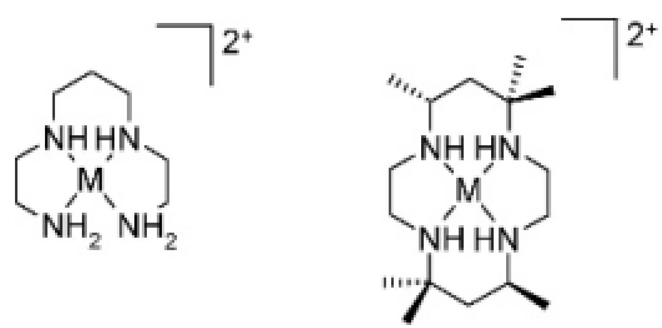


Macrocyclic Effect



Macrocyclic Effect



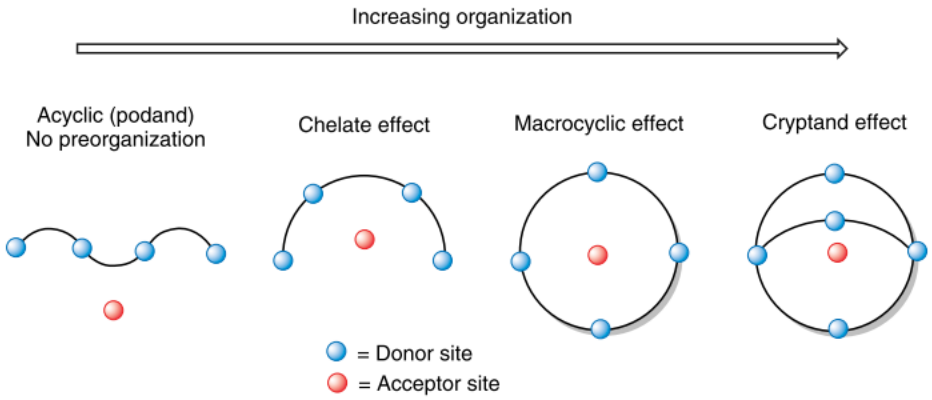


M = Zn, Cu

Stabilià: Sistema Ciclico 10^4 superiore Sistema Aciclico

Chelate and Macrocyclic Effects

$$[Ni(H_2O)_6]^{2+} + 6NH_3 = [Ni(NH_3)_6]^{2+} + 6H_2O$$
$$\beta \sim 10^9,\ \Delta G = -51.8\ \text{kJ mol}^{-1},$$
$$\Delta H = -100\ \text{kJ mol}^{-1},\ \Delta S = -163\ \text{J mol}^{-1}\text{K}^{-1}$$
$$[Ni(H_2O)_6]^{2+} + 3en = [Ni(en)_3]^{2+} + 6H_2O$$
$$\beta \sim 10^{18},\ \Delta G = -101.8\ \text{kJ mol}^{-1},$$
$$\Delta H = -117\ \text{kJ mol}^{-1},\ \Delta S = -42\ \text{J mol}^{-1}\text{K}^{-1}$$



Recettori

cationi

anioni

molecole neutre

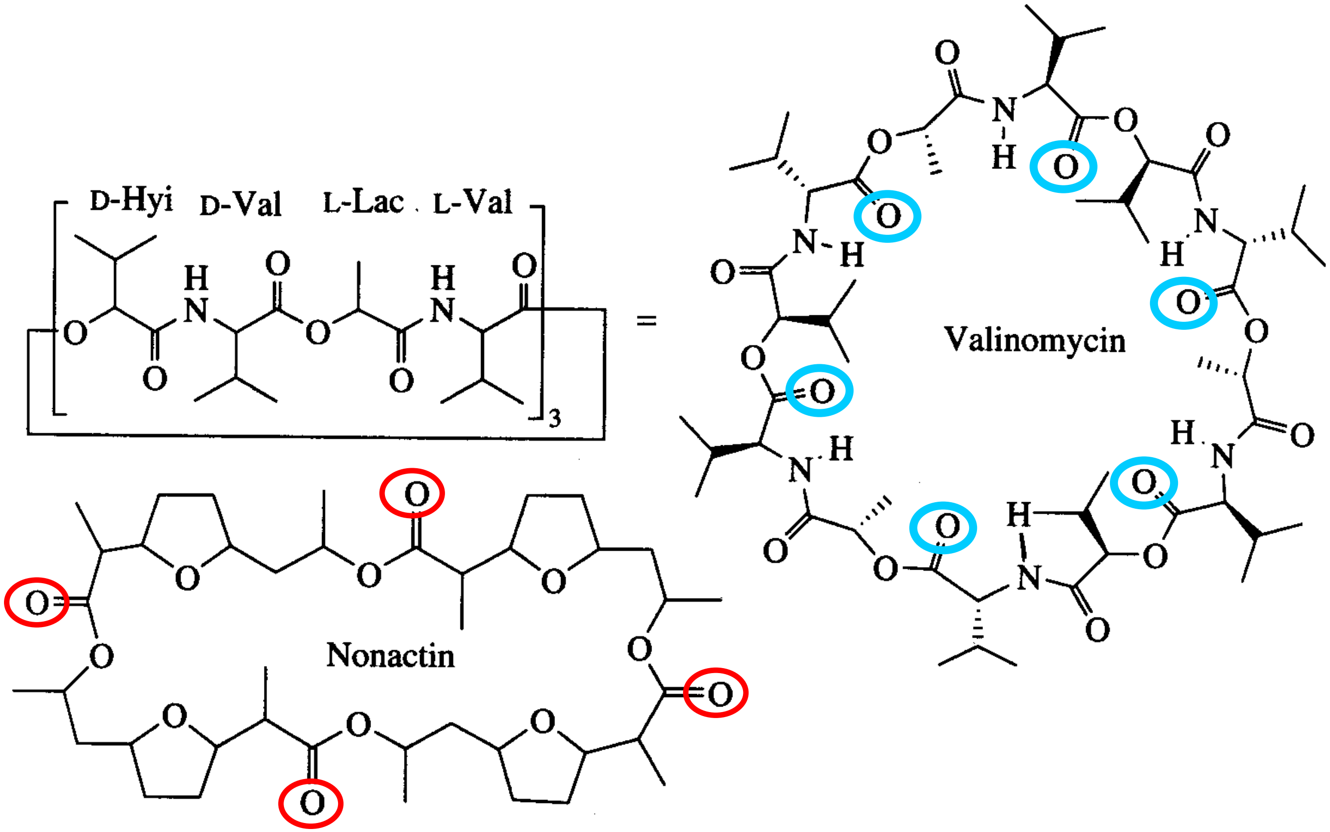
Metodi Analitici

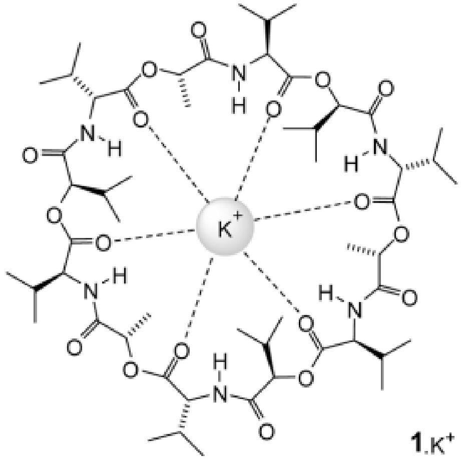
Cavitandi

Contenitori molecolari

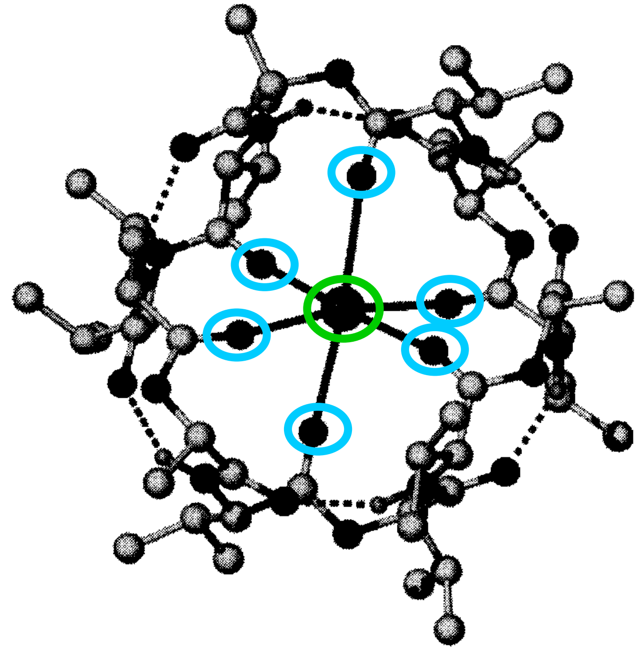
-covalenti
-auto-assemblati (legami idrogeno, legami di coordinazione, legami covalenti dinamici)

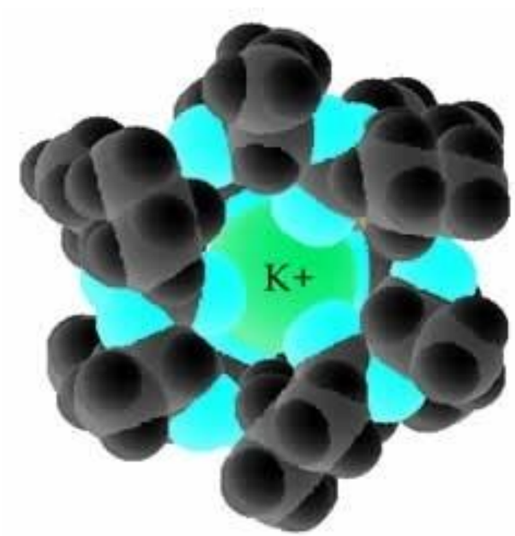
Cations and anions are ubiquitous in biological and chemical systems and their efficient and selective recognition is one of the main goals of Supramolecular Chemistry. As a matter of fact, research in this field started with Pressman's 1964 discovery[1] that valinomycin and other natural antibiotics increase the permeability of lipid bilayer membranes through the selective binding of potassium ion, and with Pedersen's finding[2] that macrocyclic polyethers (crowns) are able to complex salts of alkali metal ions and dissolve them in organic media. Since then, the topic of ion recognition by synthetic receptors has developed tremendously and is still quite fertile as testified to by the recent review articles and books concerning cation[3-7] and anion[8,9] complexation and sensing. More recently, a special role in ion

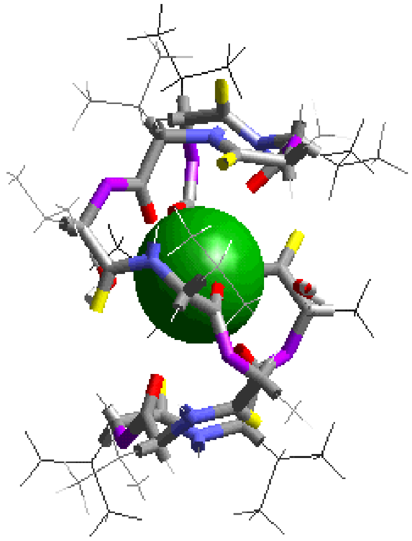

D-Hyi
D-Val
L-Lac
L-Val
Valinomycin
Nonactin



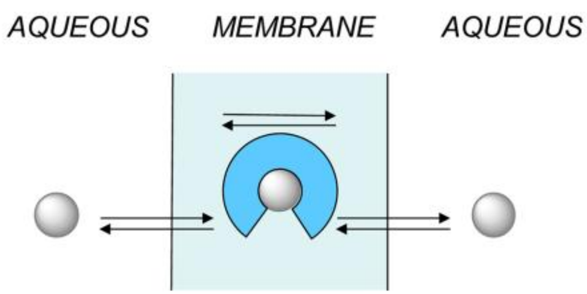
1.K$^+$







$K_{K+}/K_{Na+} = 10^5$

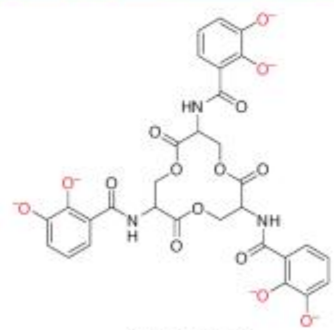


A pH fisiologico 7.4 la concentrazione di $[Fe(H_2O)_6]^{3+}$ - in equilibrio con $Fe(OH)_3$ - è circa 10^{-18}M, mentre per le condizioni ottimali di crescita i micro-organismi richiedono una concentrazione intracellulare di circa 10^{-7}M

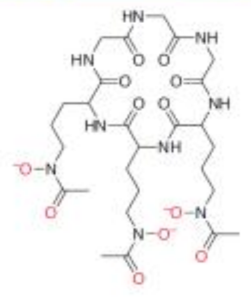
Sideroferi:

I siderofori sono piccoli leganti polidentati con O/N donatori che hanno grande affinità per lo ione hard Fe(III) (e scarsa per Fe(II)) e lo rendono solubile attraverso la formazione di complessi ottaedrici ad alto spin.

Oltre al complesso con citrato, vi sono siderofori basati su fenolati o catecolati come *l'enterobactina* (costante di associazione 10^{52}) e basati su idrossammati come l'esapeptide ciclico *ferricromo* (3 glicine + 3 N-idrossil-l-ornitine).



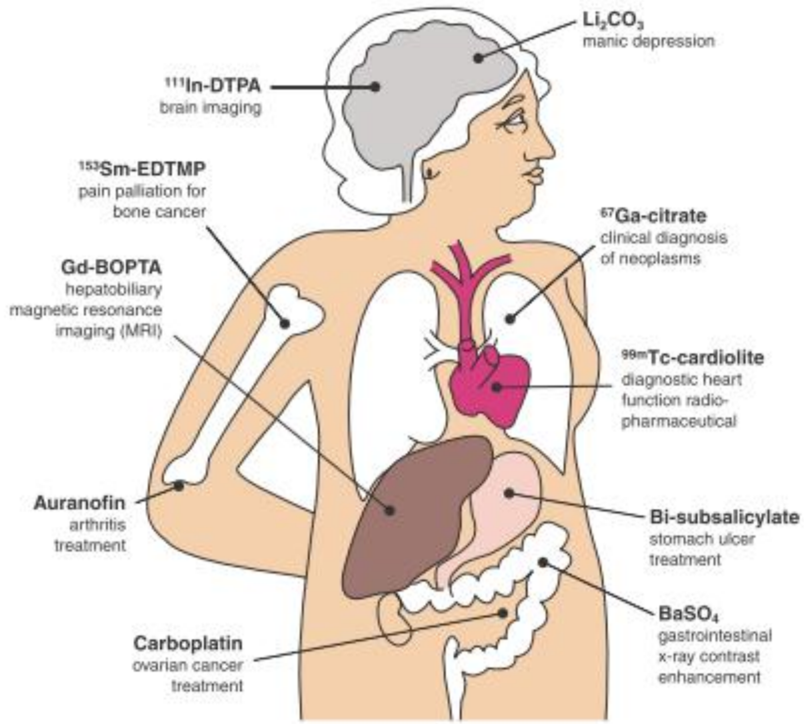
17 Enterobactin



18 Ferrichrome

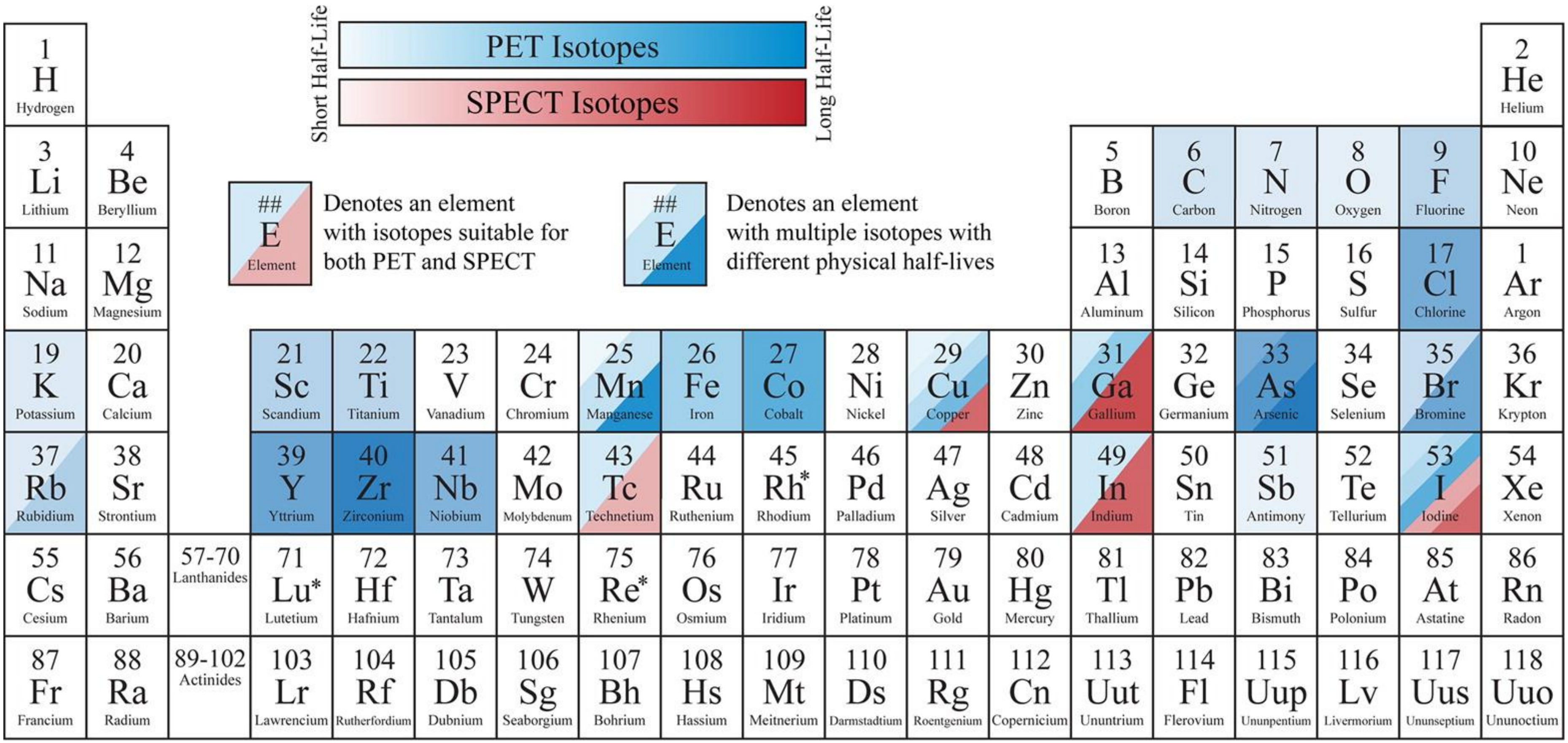
L'enterobactina-Fe^{III} complesso è anche chirale; la struttura del triestere ciclico, che è chirale in quanto ha tre carboni asimmetrici adiacenti agli azoti, impone la configurazione
Δ dei catecolati intorno al Fe(III); il suo enantiomero Λ coordina il ferro, ma non è in grado di rilasciarlo ai batteri perché non è riconosciuto da i recettori dell'enterobactina.

Boon and Bane of Metal Ions in Medicine
Katherine H. Thompson and Chris Orvig
Science **300**, 936 (2003);
DOI: 10.1126/science.1083004



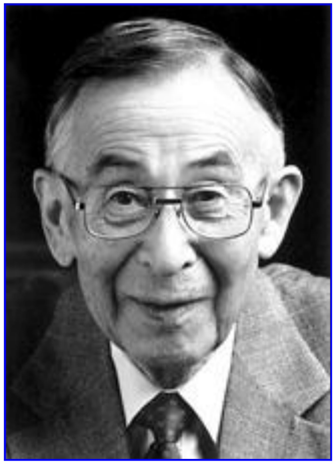
Isotopes suitable for nuclear imaging

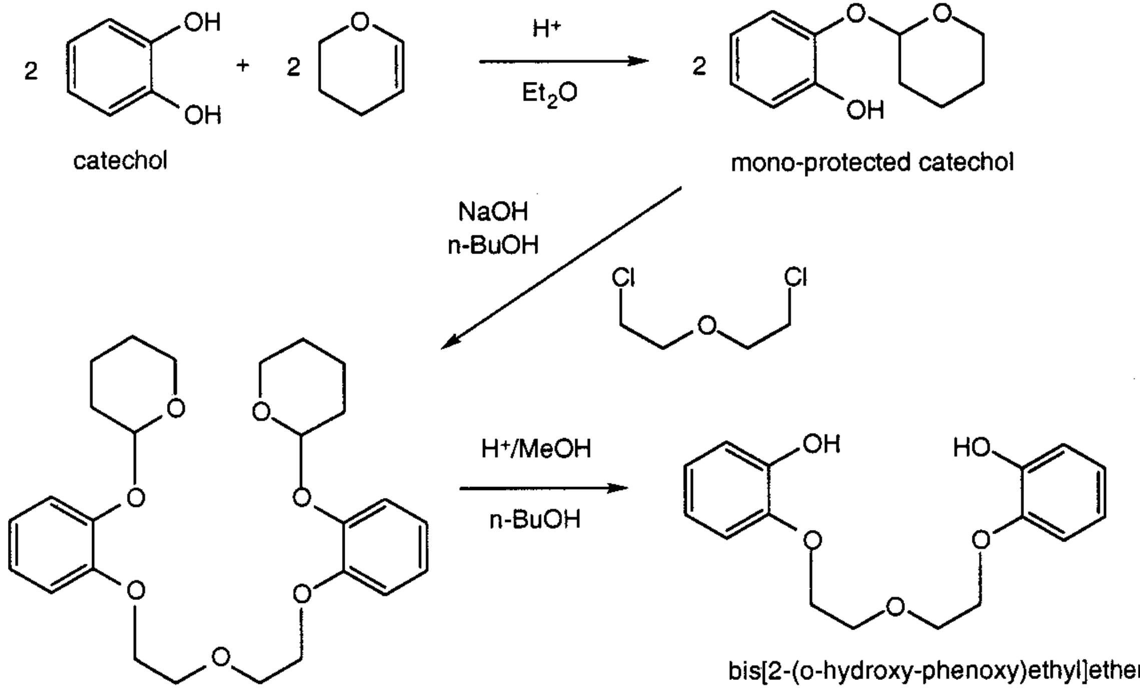
PET Positron Emission Tomography
SPECT Single Photon Emission Counting Tomography



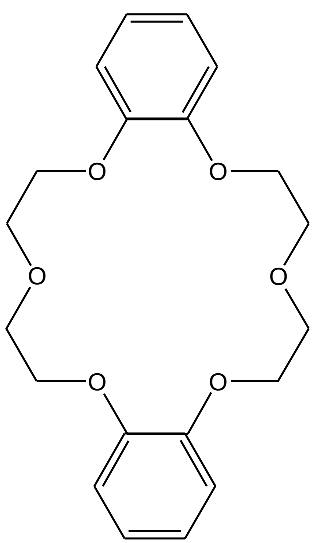
*Isotopes typically used for radiotherapy with which SPECT is also possible but not common — *e.g.*, ^{177}Lu, ^{105}Rh, ^{186}Re, etc. — have been omitted.

PEDERSEN (Nobel 1987), studio di leganti multi dentati per rame e vanadio (Dupont, anni '60)





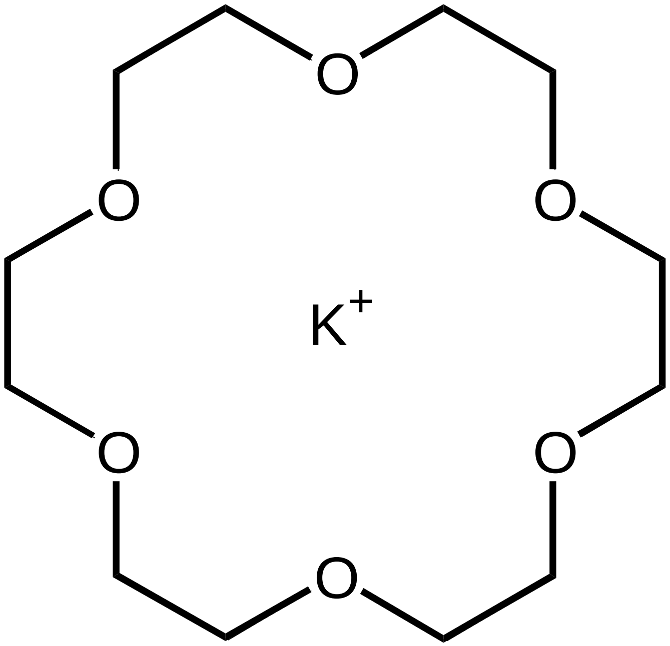
Intended synthesis of Pedersen's ligands



dibenzo[18]crown-6 - sottoprodotto

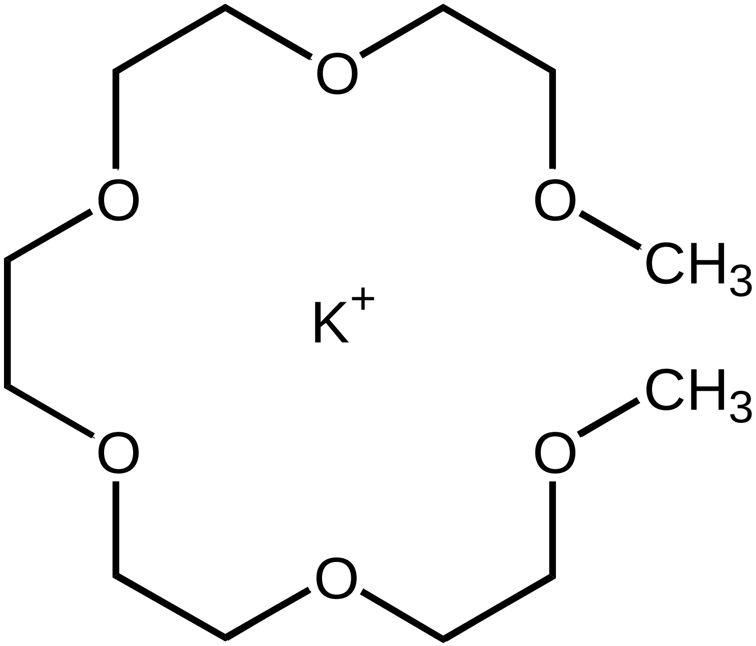
ETERI CORONA (Crown Ethers)
(monocilci = CORANDI)

[18]crown-6

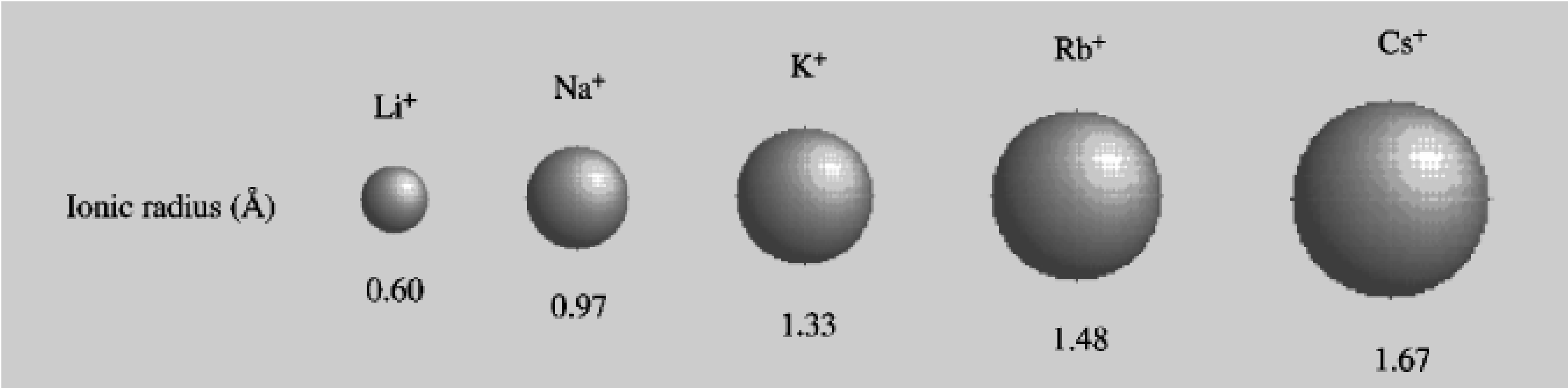


log K = 6.08

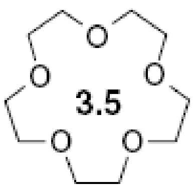
Pentametileneglicol-dietiletere



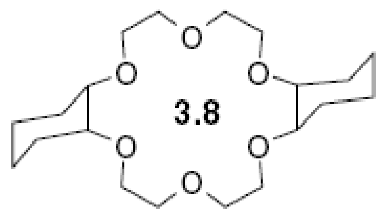
log K = 2.3



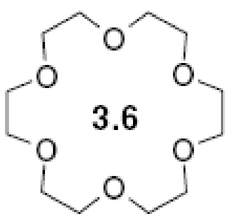
OPTIMAL SPATIAL FIT or SIZE-MATCH



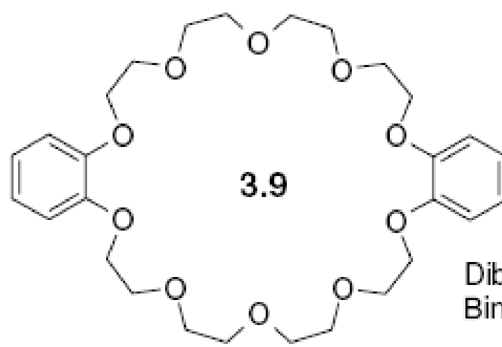
[15]crown-5
Complementary to Na^+



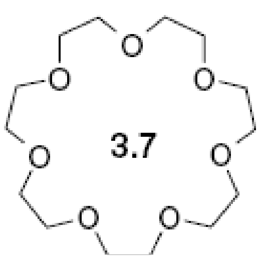
Dicyclohexyl[18]crown-6
More conformationally rigid



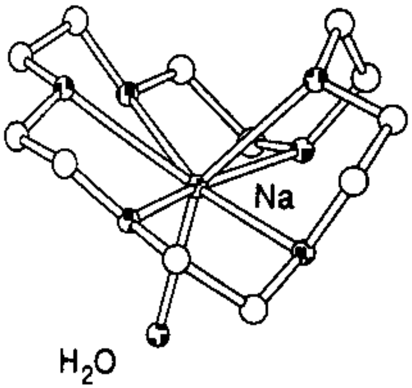
[18]crown-6
Complementary to K^+

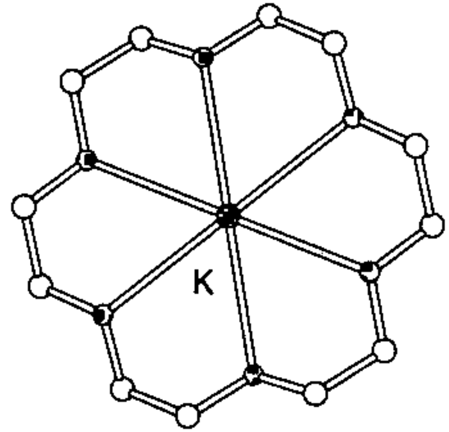


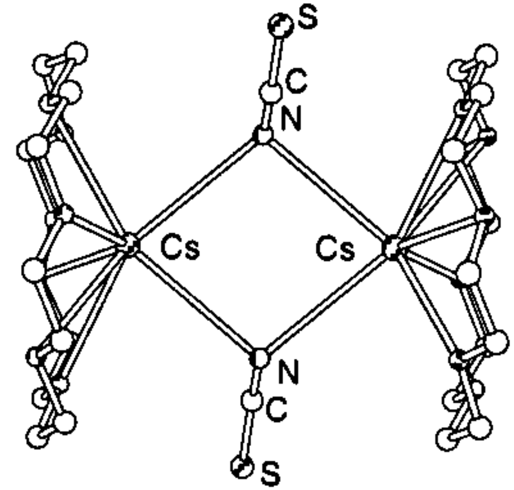
Dibenzo[30]crown-10
Binds two Na^+ ions

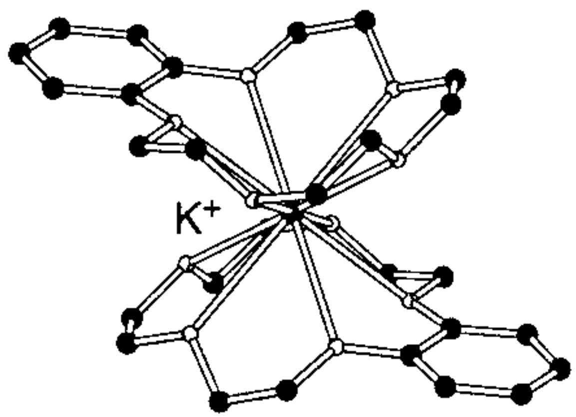


[21]crown-7
Complementary to Cs^+

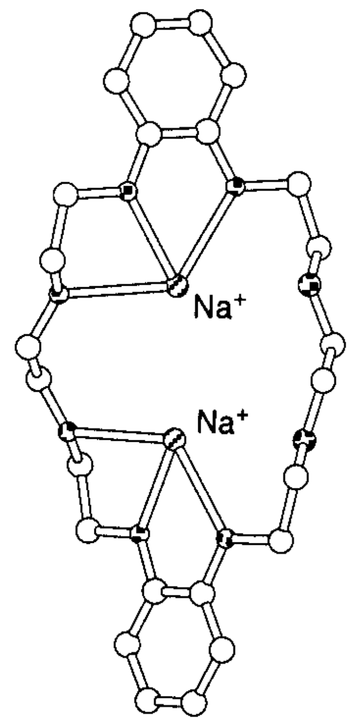








The crystal structure of two benzo-15-crown-5 molecules forming a 'sandwich complex' with a potassium cation



The crystal structure of $2Na^{+}$–[24]crown-8

a Cationi ***hard*** formano complessi in cui le interazioni coulombiane sono dominanti

b Cationi ***soft*** formano complessi in cui è dominante il legame covalente.

Ioni metallici di tipo ***a*** sono principalmente:

- ioni dei metalli alcalini e alcalino-terrosi
- ioni metallici leggeri e con elevata carica: Ti^{4+}, Fe^{3+}, Co^{3+}, Al^{3+}

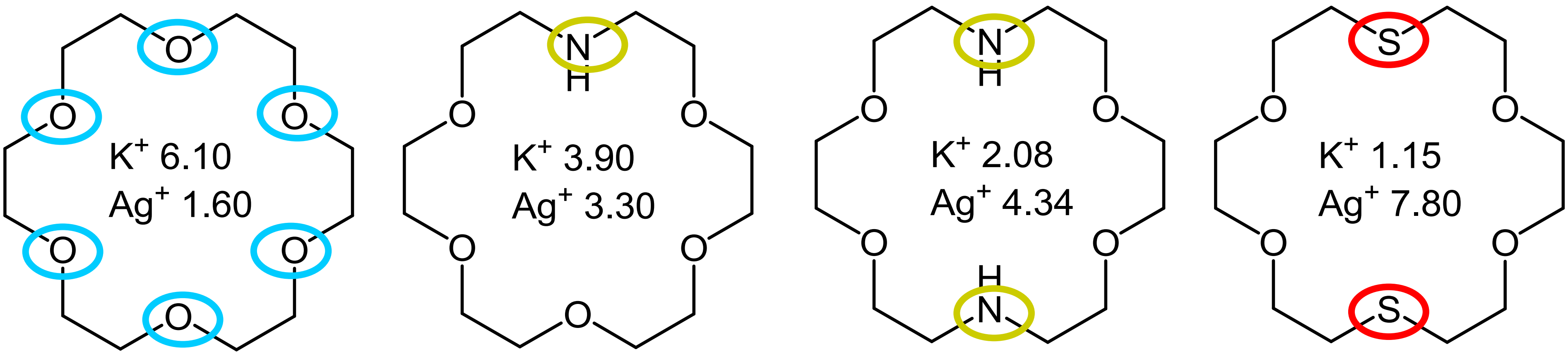
Ioni metallici di tipo ***b*** sono principalmente:

- ioni pesanti di metalli di transizione: Hg_2^{2+}, Hg^{2+}, Pt^{2+}, Pt^{4+}, Ag^{+}, Cu^{+}
- ioni di metalli in bassi stati di ossidazione, ad es. nei metallo carbonili

Alcuni ioni (Fe^{2+}; Co^{2+} ; Ni^{2+}; Cu^{2+} ; Zn^{2+}; Pb^{2+}) formano complessi le cui stabilità non possono essere pronosticate sulla base della classificazione hard/soft: essi formano la classe *border-line*

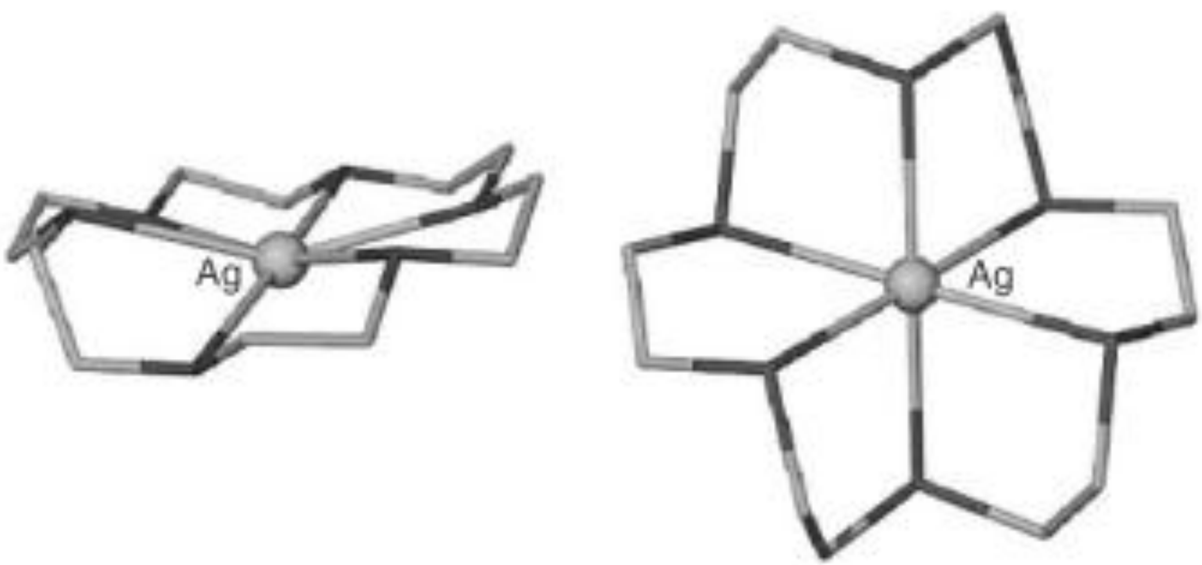
La costante di stabilità dei complessi di questi ioni con un dato legante segue l'ordine, noto come serie di **Irving-Williams**:

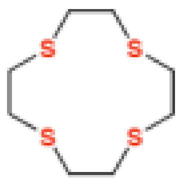
$$Ca^{2+} < Mg^{2+} < Mn^{2+} < Fe^{2+} < Co^{2+} < Ni^{2+} < \mathbf{Cu^{2+}} > Zn^{2+} > Pb^{2+}$$



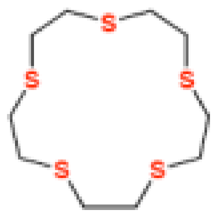
Aza-crown

Tio-crown

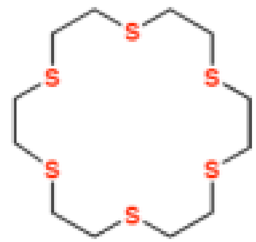




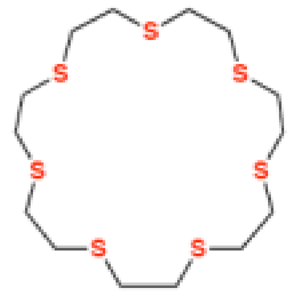
[12]S_4



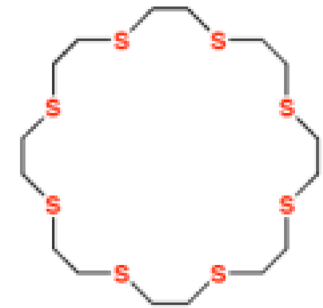
[15]S_5



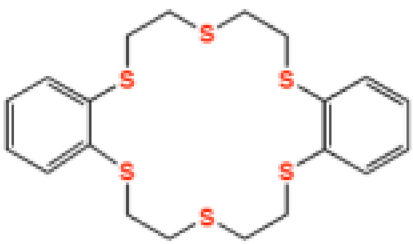
[18]S_6



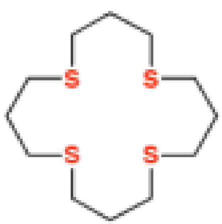
S



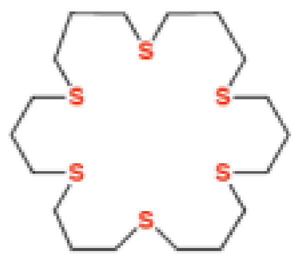
[24]S_8



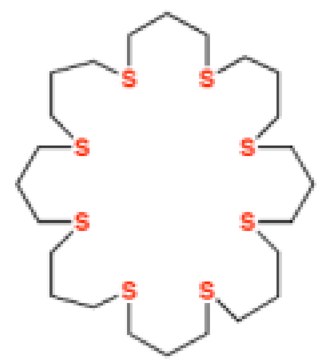
Dibenzo[18]S_6



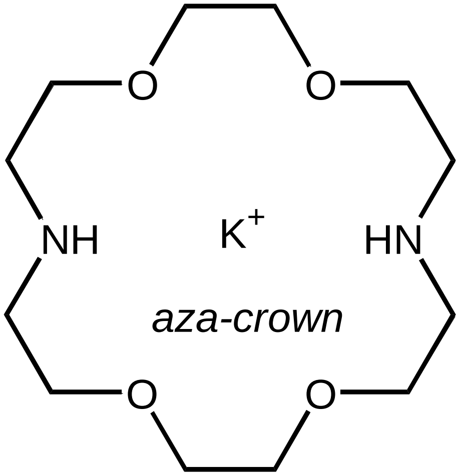
[16]S_4



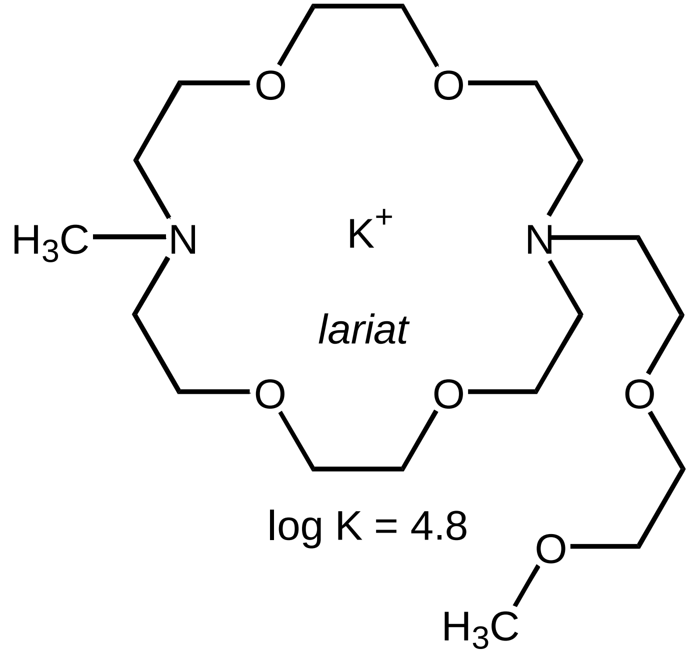
[24]S_6



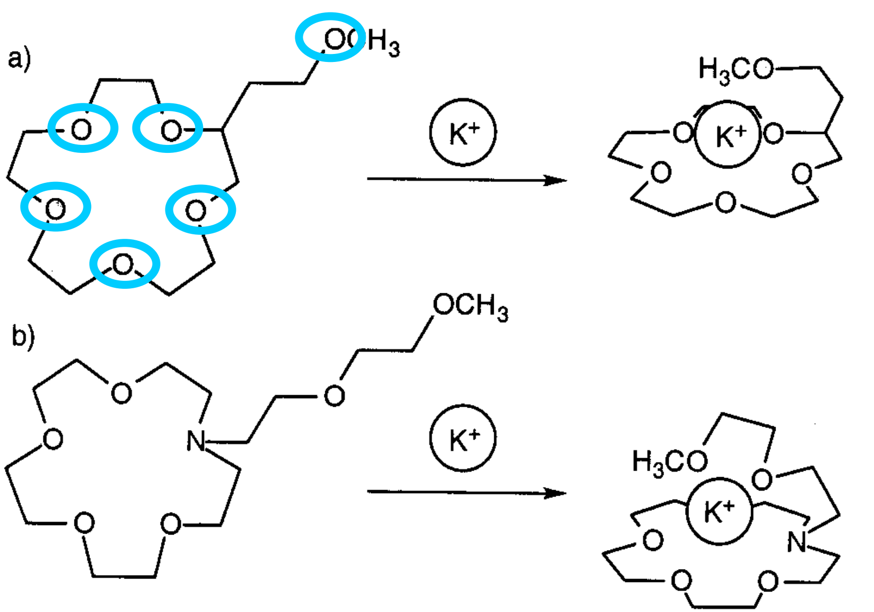
[32]S_8



log K = 2.04



log K = 4.8



(a) Carbon and (b) nitrogen pivot lariat crown ethers binding potassium cations.

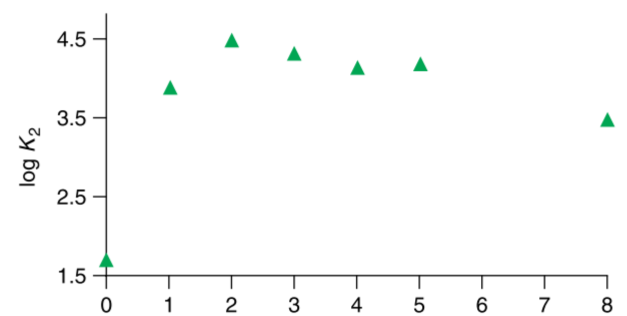
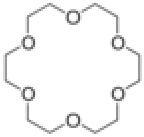
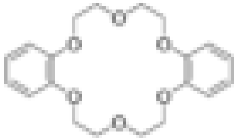


Figure 17 Na^+ complexation by aza-15-crown-5 lariat ethers with *n* oxygen donor atoms in the side arm ($n = 0–8$).[57]



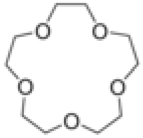
18-crown-6

274984-1G 78.40



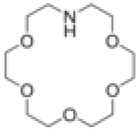
Dibenzo-18-crown-6

158399-2.5G 17.50 euro



15-crown-5

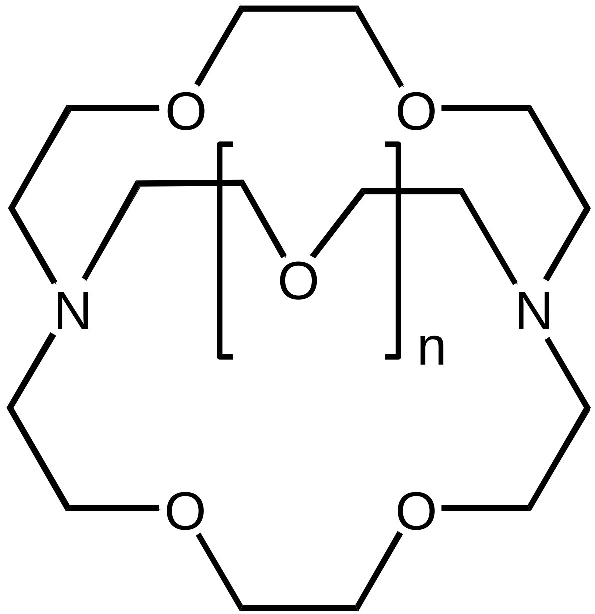
188832-1G 15.30 euro



1-Aza-18-crown-6

11382-1G 212.00 euro

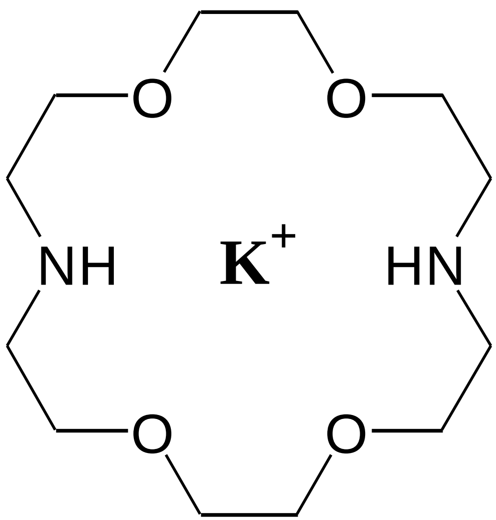
LEHN (Nobel 1987), estensione dei sistemi monociclici a sist. biciclici (CRIPTANDI,anni ‘60)



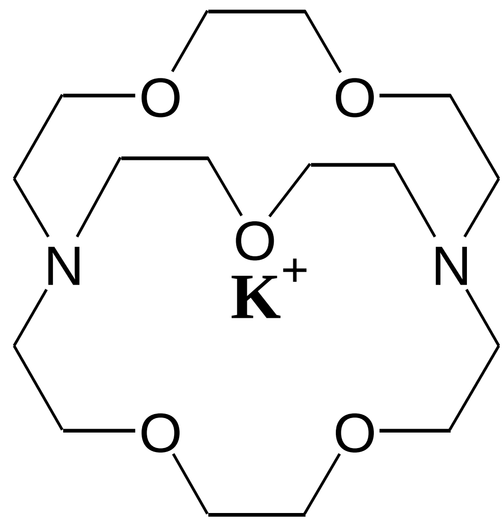
Na^+

n = 1, criptando [2,2,1]
n = 2, criptando [2,2,2]

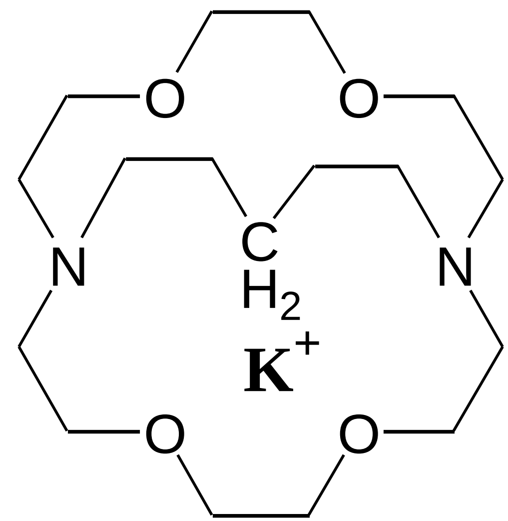
K^+



logK = 2.0

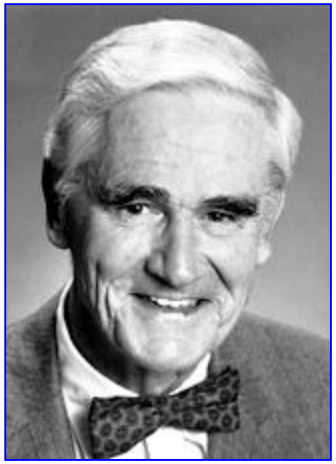


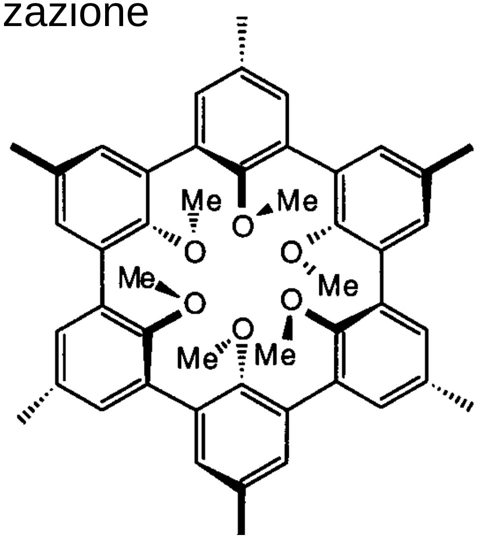
logK = 7.0



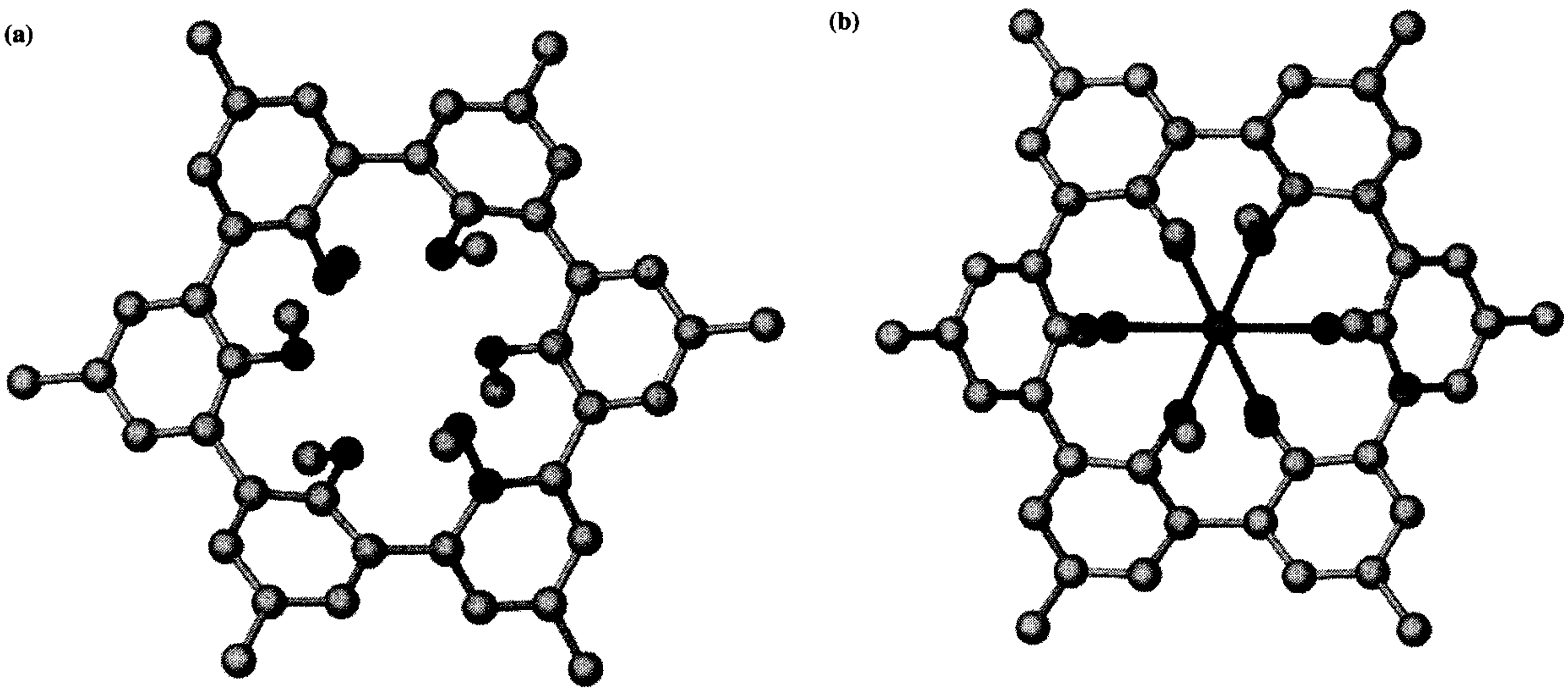
logK = 5.4

CRAM (Nobel 1987) - preorganizzazione

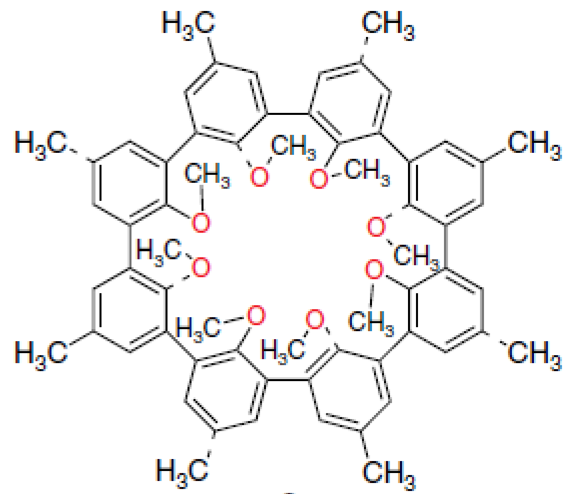




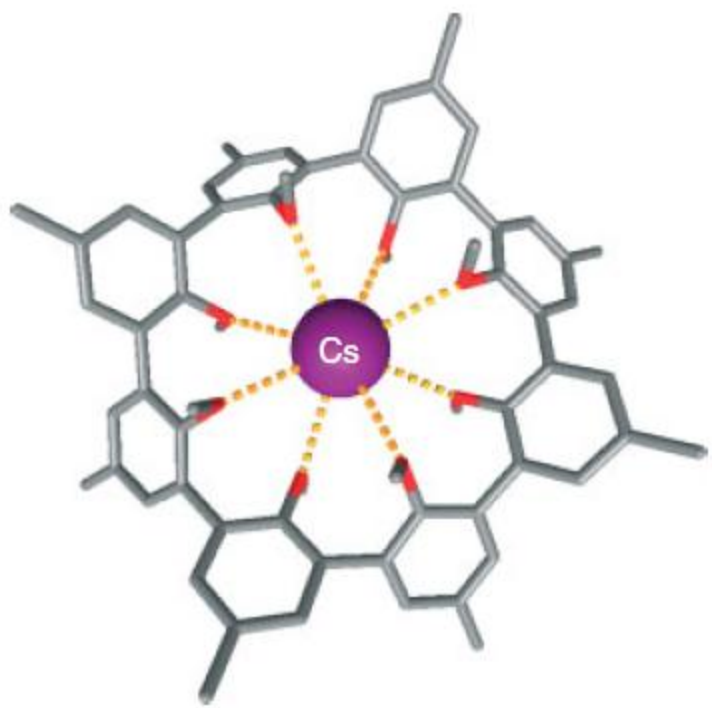
Sferandi
(*p*-metilanisolo)



X-ray crystal structures of **(a)** free spherand (**3.30**) and **(b)** its Li^+ complex (after Trueblood *et al.* 1981).



3



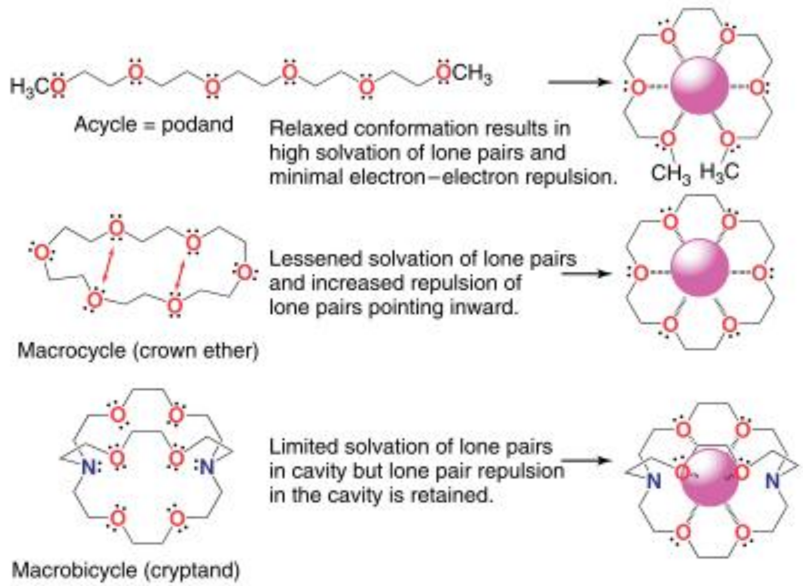
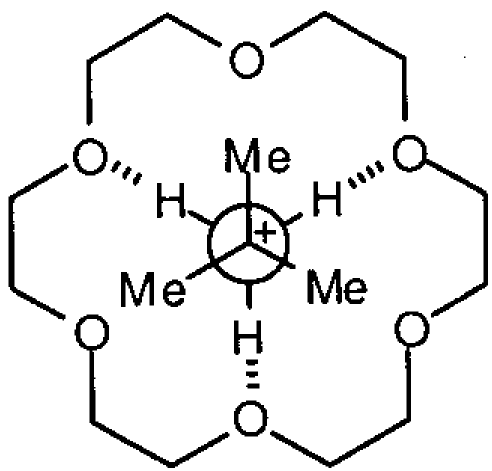


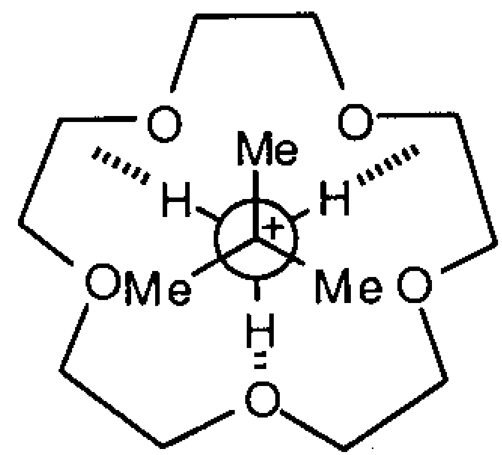
Table 3 Stability constants (log K) in methanol at 25 °C for the binding of alkali metal ions with ionophores that have increasingly complex design and dimension.[33]

Ionophore	Li^+	Na^+	K^+	Rb^+	Cs^+
Pentaglyme	—	1.5	2.2	—	—
Tripod	<2	2.2	2.3	<2	—
Valinomycin	<0.7	0.9	4.7	5.2	4.4
[18]Crown-6	∼0	4.4	6.1	5.4	4.7
[2.2.2]Cryptand	2.6	8.0	10.8	9.0	4.4
Spherand[a]	>16.8	14.1	—	—	—

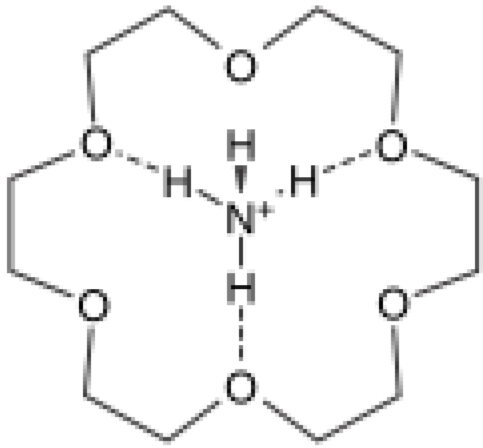
[a] In $CDCl_3$ saturated with H_2O.[35]



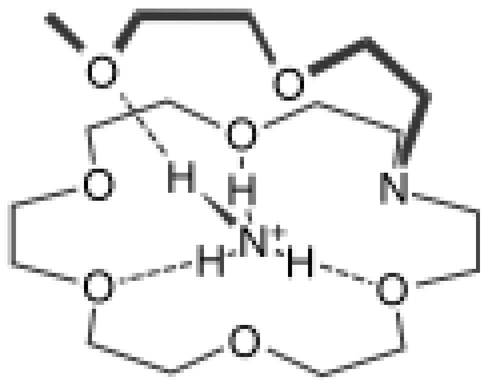
strong complex
ideal arrangement of hydrogen bond
donors and acceptors



weaker complex
mismatch in geometry of hydrogen bond
donors and acceptors



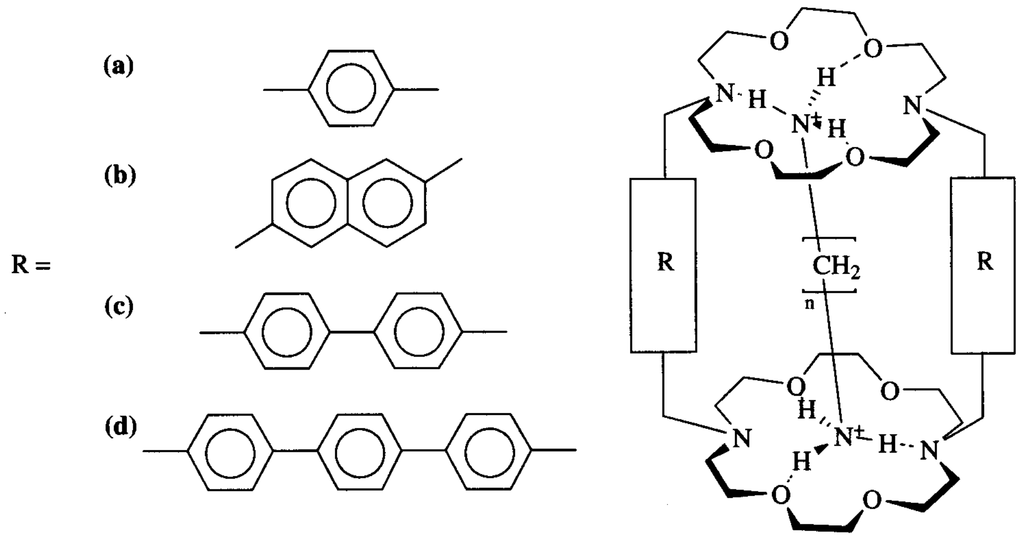
log K = 4.35

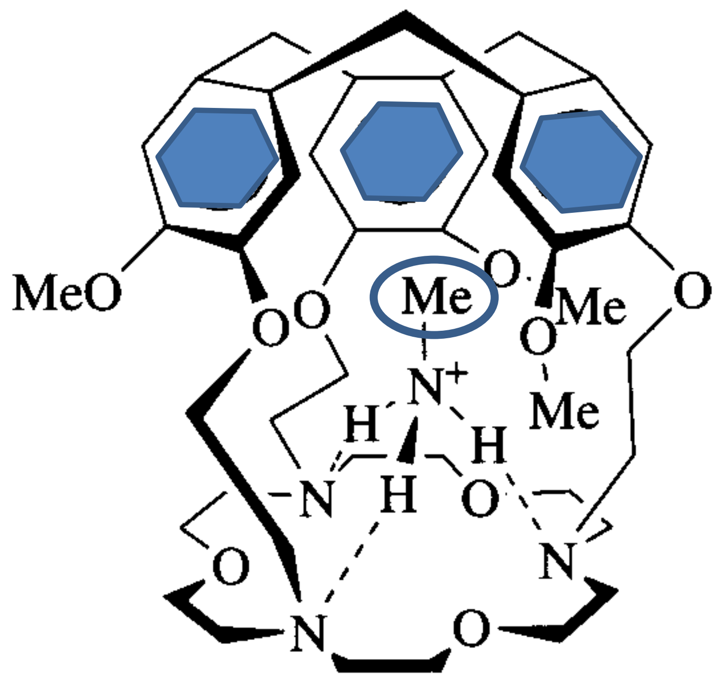


2.23·NH_4^+

log K = 4.75

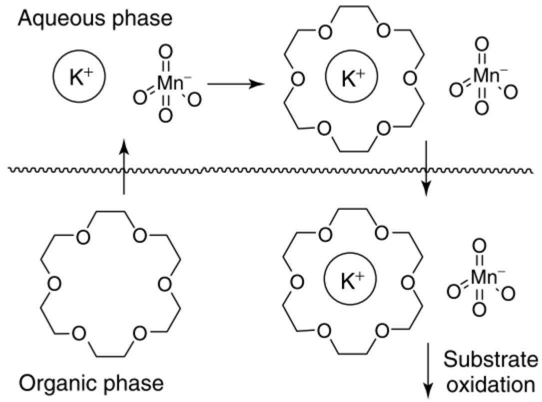
Recettori Politopici

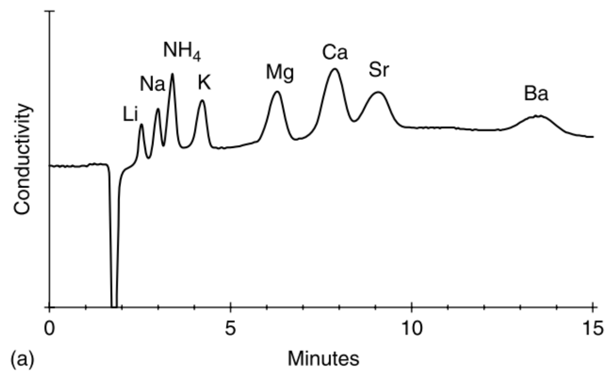


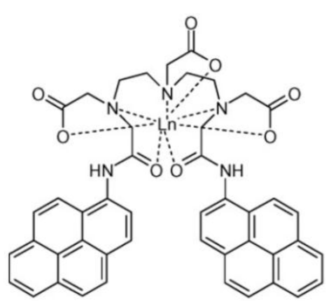


ciclotriveratrilene

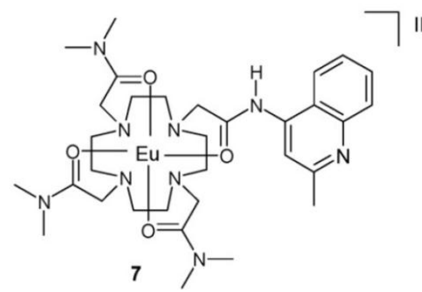
corando







1
Ln = Er(III), Nd(III) and Yb(III)



7

Thermodynamic selectivity : ratio of the binding constant for one guest over another:

$$H + G_1 \rightleftharpoons [HG_1] \qquad K_1$$
$$H + G_2 \rightleftharpoons [HG_2] \qquad K_2$$

$$\text{selectivity} = \frac{K_1}{K_2}$$

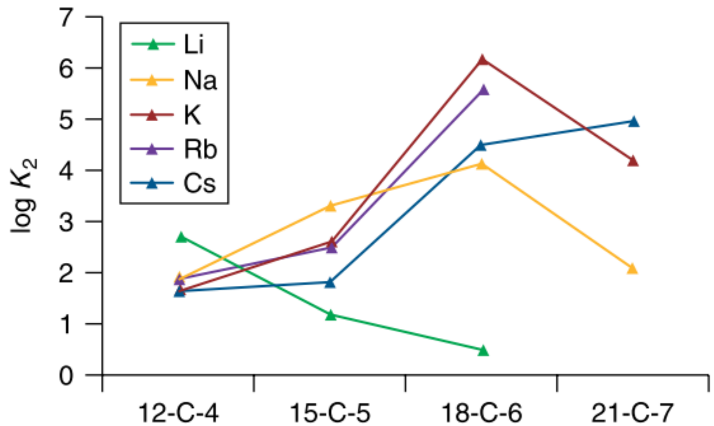
Selectivity is a consequence of preorganization, complementarity…
Needs to be calculated at equilibrium in the same conditions
Temperature! Solvent!

Kinetic selectivity : preference of a host for the fastest transformation of a substrate over another (Michaelis-Menten model)

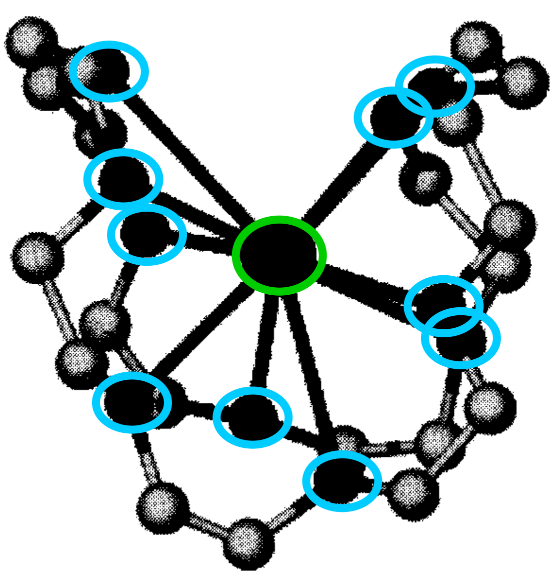
-transport
-catalysis
-sensing and signaling

Selettività

Size-match o optimal-fit (progressivamente più determinante aumentando la rigidità /preorganizzazione dell'Host) – distanza tra i dipoli del macrociclo e la carica ionica



[30]crown-10



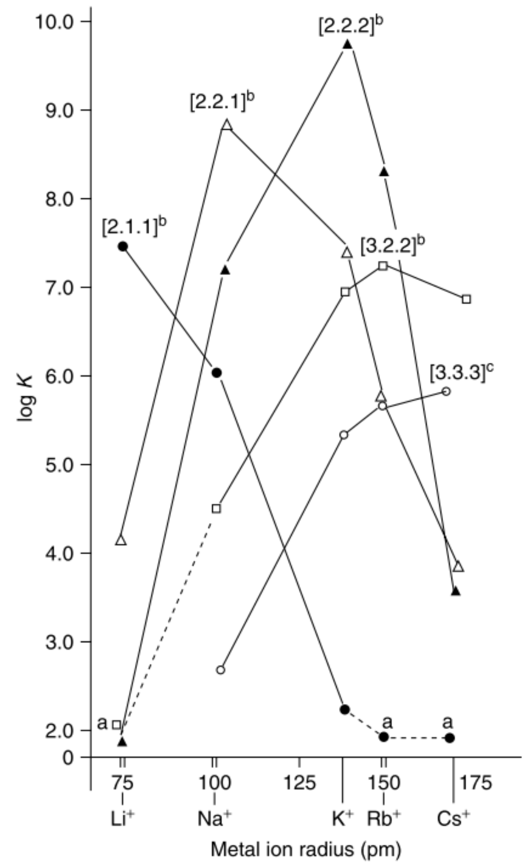


Figure 2 Selectivity of cryptands among alkali metal cations (a, value reported <2.0; b, in 95% CH_3OH; c, in methanol).

Selettività

Natura degli atoni donatori (O vs N VdW radius simile: hard/soft acid-base theory;

Numero e orientazione degli atomi donatori (pesa di più per cationi di M transizione, che per alcalini; alcalinoterrosi e REM).

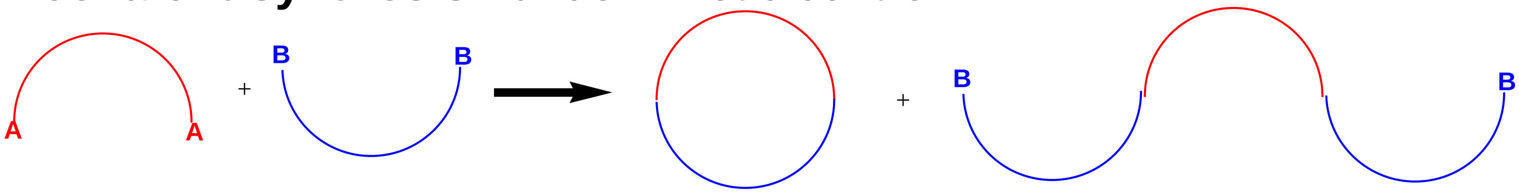
Carica elettrostatica dello ione: a parità di raggio ionico, carica maggiore può corrispondere a maggiore energia di idratazione (*cfr* Ca^{2+} vs Na^{+});

Solvatazione dell'host

Solvente – competitivo per i dipoli/ costante dielettrica

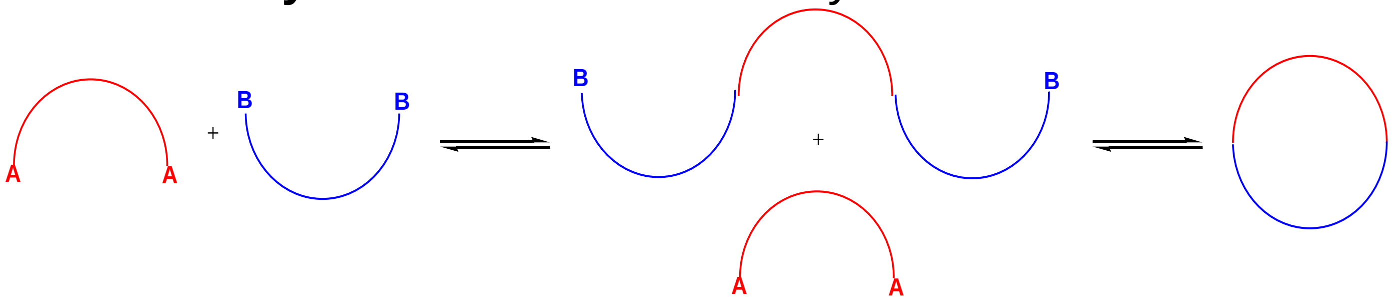
natura del contro-ione

- **covalent synthesis** : under kinetic control



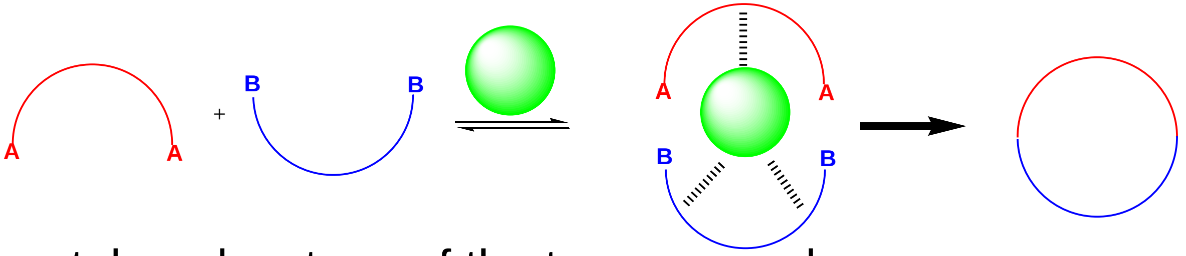
- classical organic chemistry. Irreversible bond formation
- highly stable molecules.
- not adapted to big molecules. low yield

- **non covalent synthesis** : under thermodynamic control



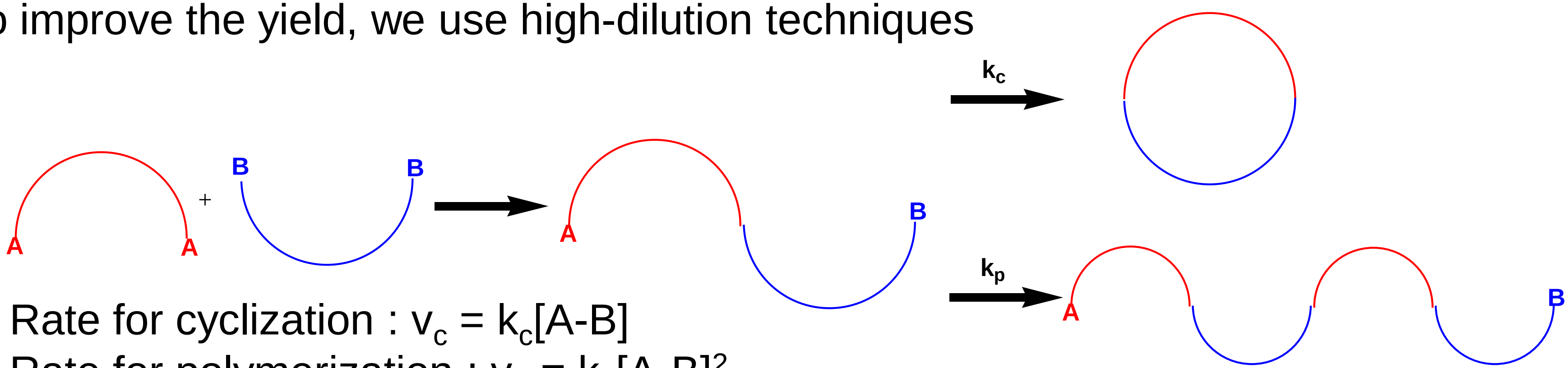
- thermodynamic directed synthesis. Reversible bond formation
- lower stability
- adapted to big molecules. high yield

- a **mix**



- take advantage of the two approaches

To improve the yield, we use high-dilution techniques



Rate for cyclization : $v_c = k_c[A\text{-}B]$

Rate for polymerization : $v_p = k_p[A\text{-}B]^2$

- the more dilute, the more cyclic product is formed
- the reaction has to be fast

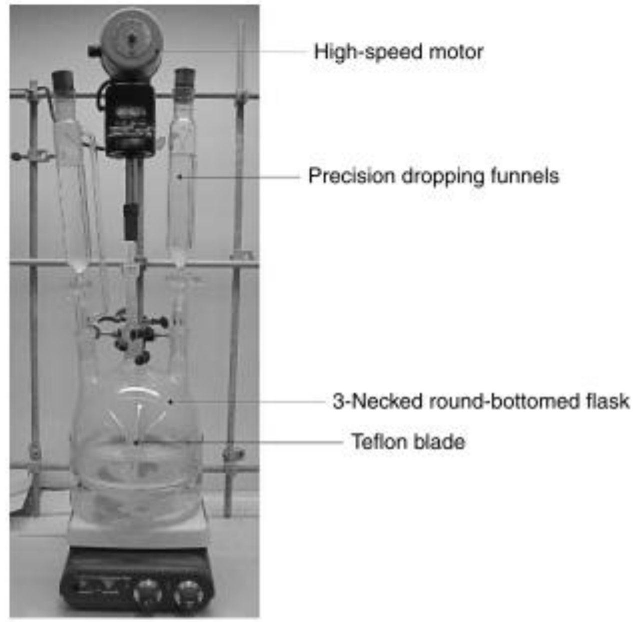
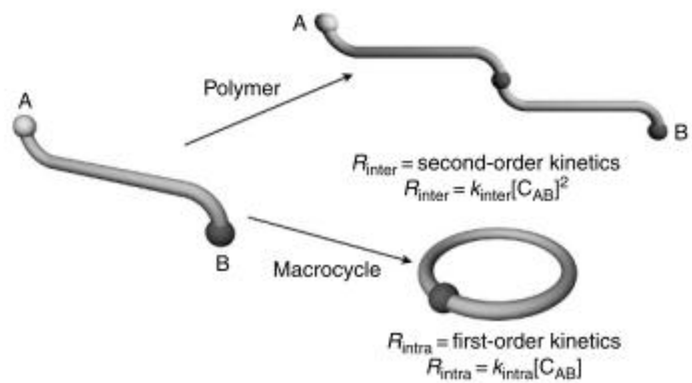
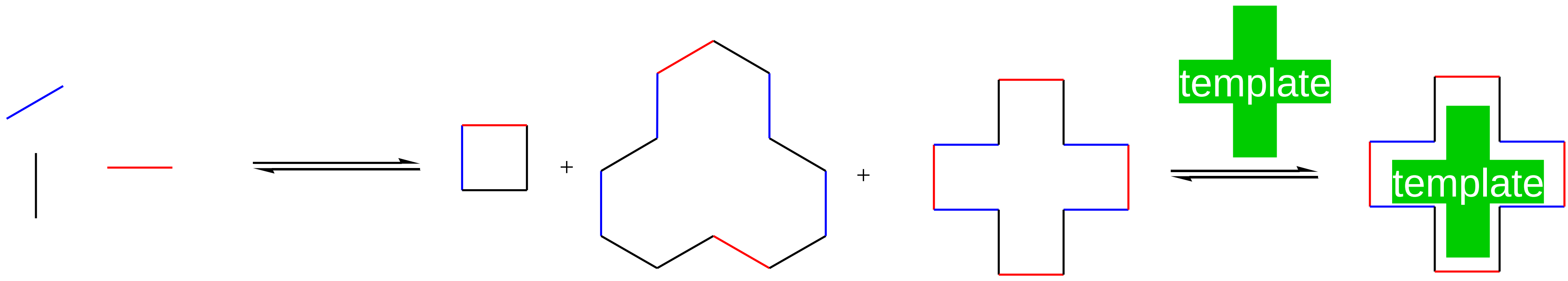
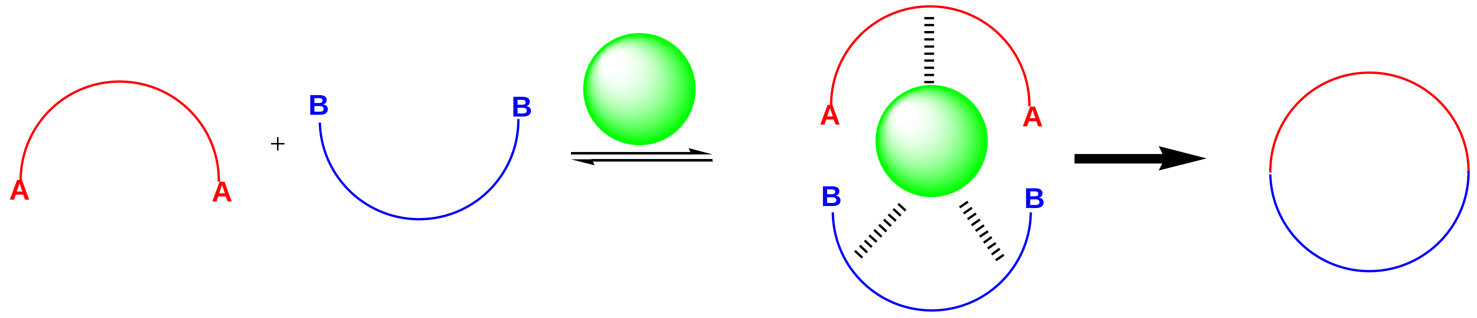


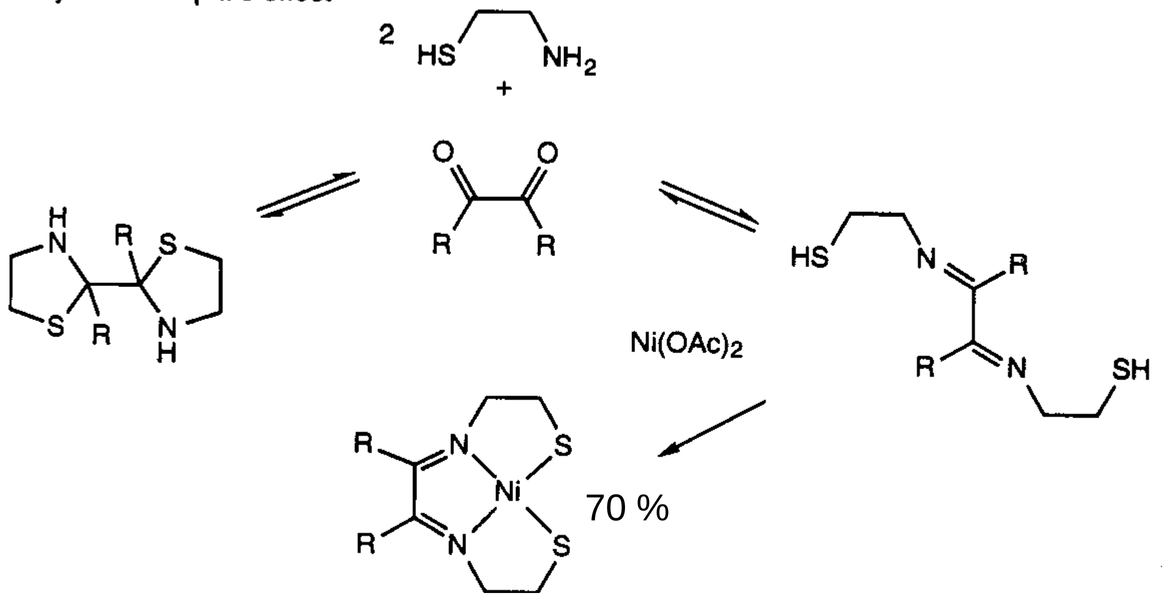
Figure 2.1 Typical apparatus used for high-dilution synthesis.



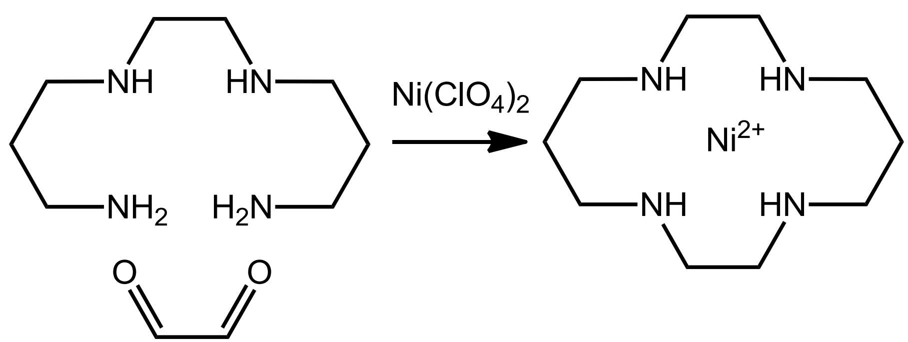

template
template

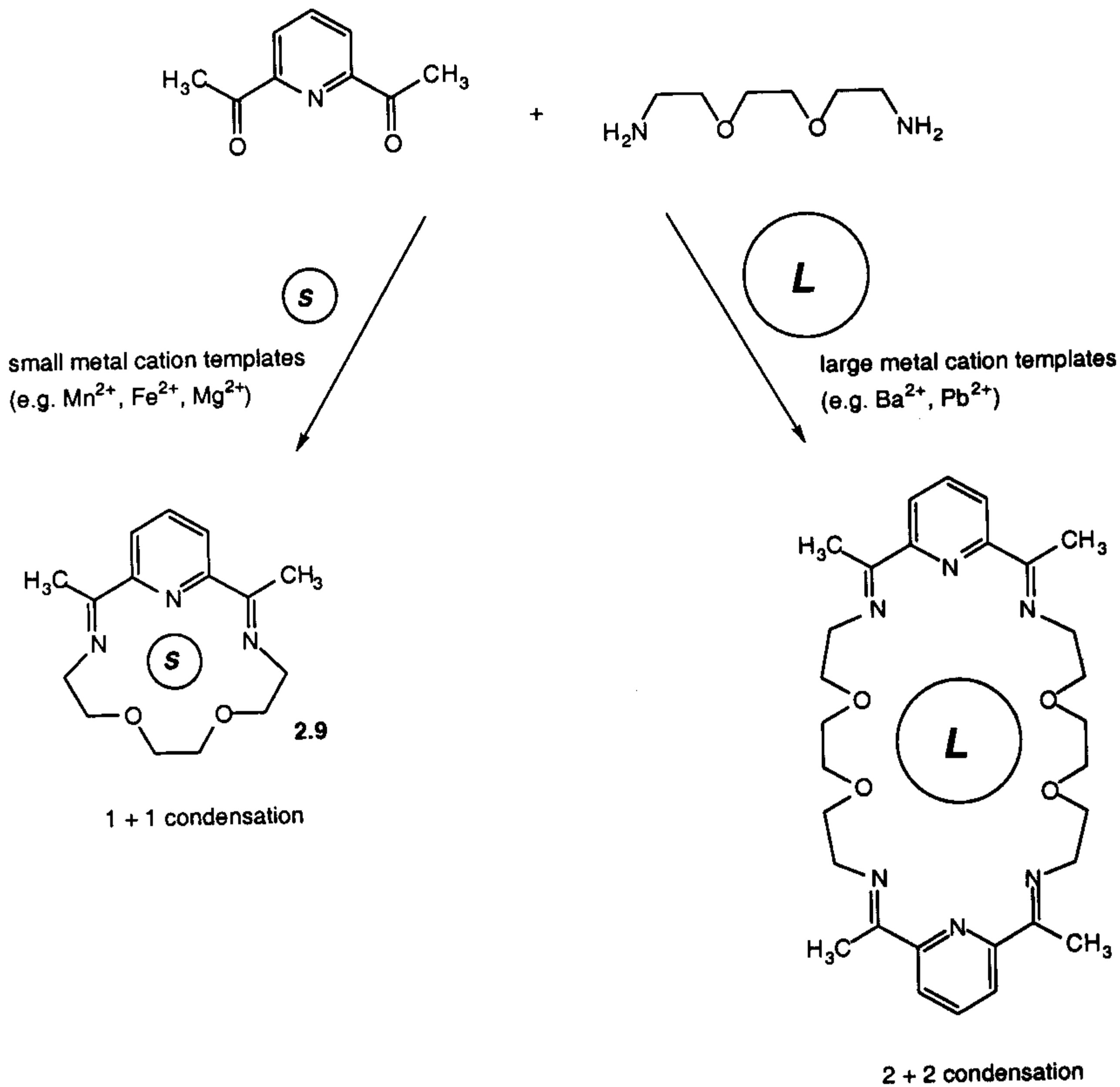

A
A
B
B
A
A
B
B

a) thermodynamic template effect

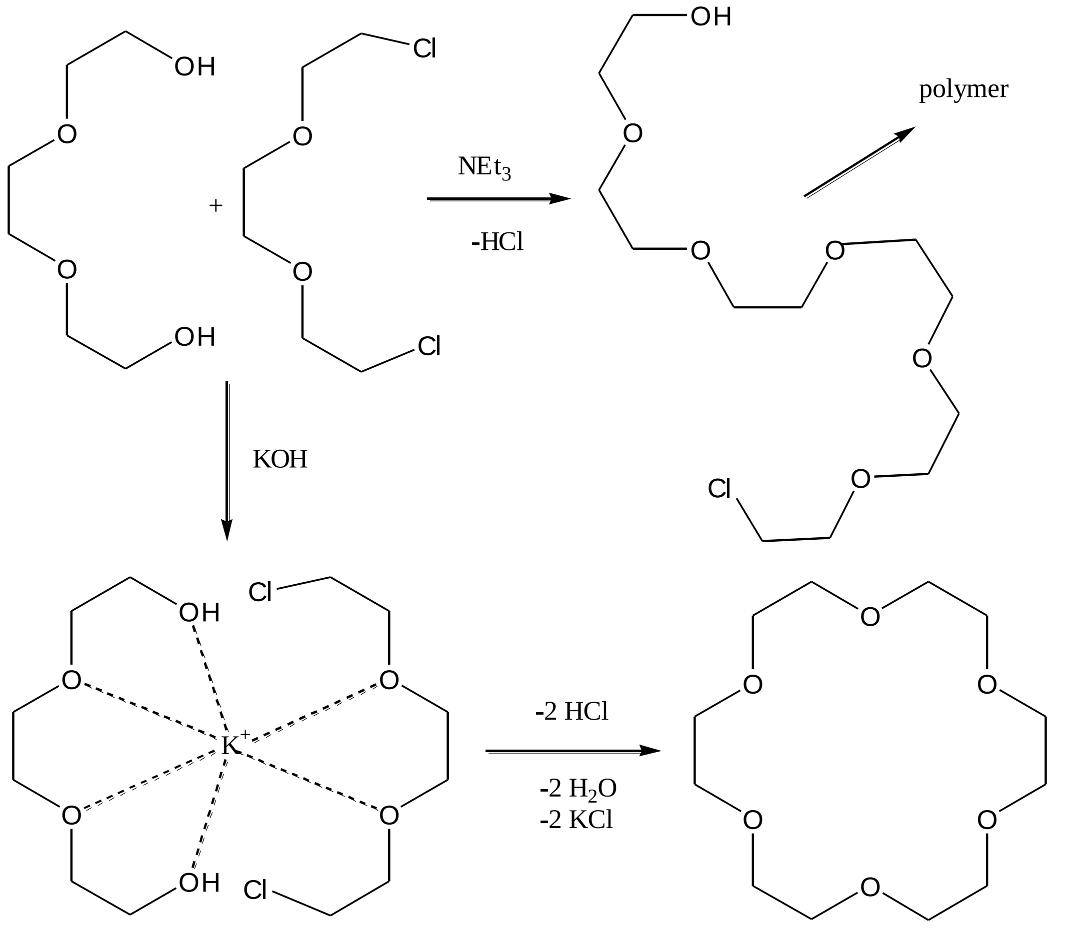


Effetto templato cinetico CYCLAM (base di Schiff)



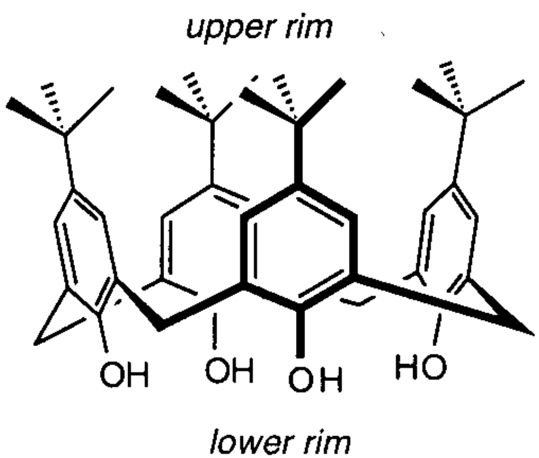


H3C
CH3
N
O
O
+
H2N
O
O
NH2
S
small metal cation templates
(e.g. Mn2+, Fe2+, Mg2+)
L
large metal cation templates
(e.g. Ba2+, Pb2+)
2.9
1 + 1 condensation
2 + 2 condensation



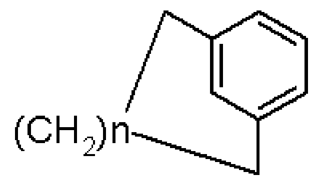
Demetallazione:
gruppi amminici – protonazione
debolm coordinat – estrazione con acqua
complessante più forte
variaz stato ox- inerzia/labilità

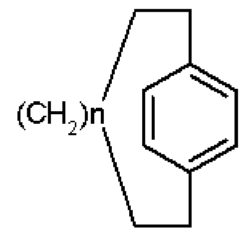
Calix[n]areni

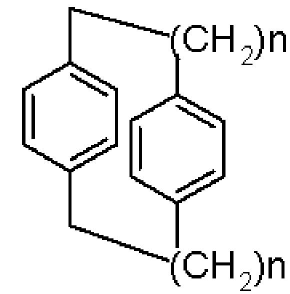


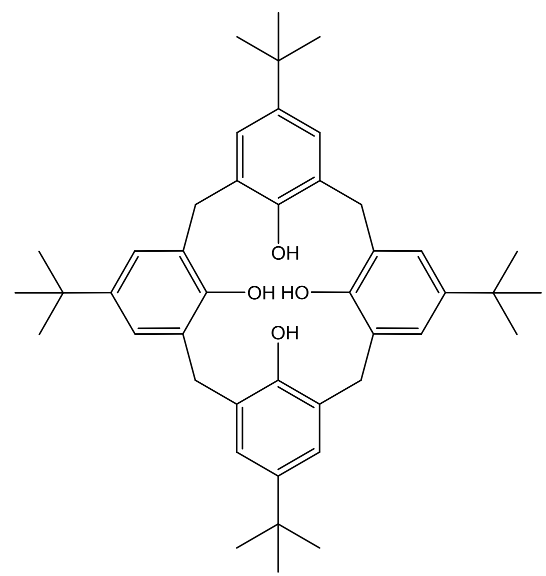
p-tert-Butylcalix[4]arene.

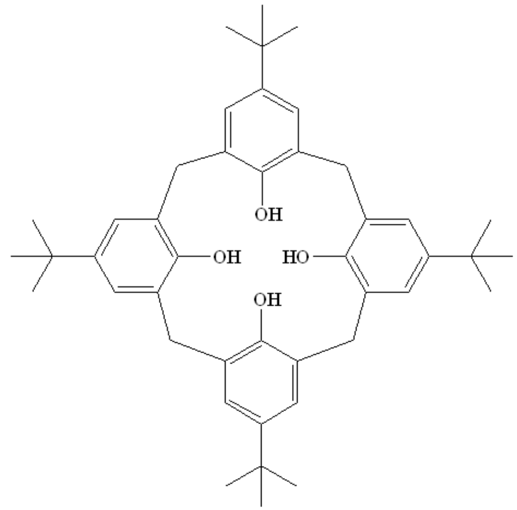
Ciclofani



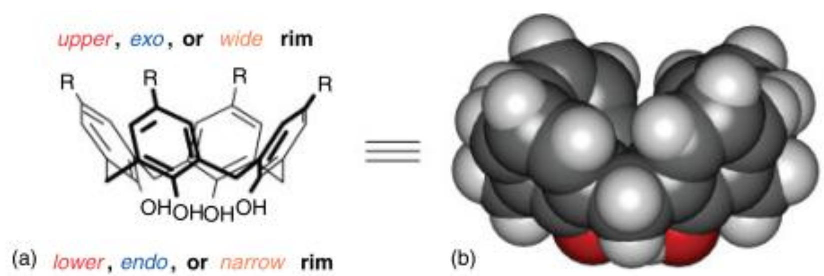




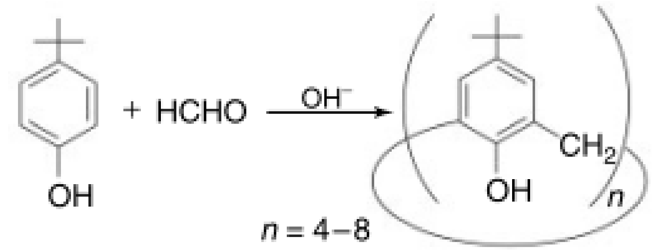




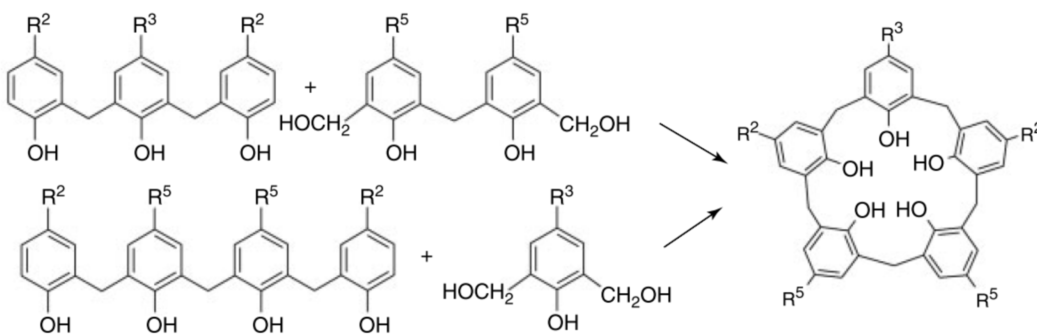
OH
OH
HO
OH



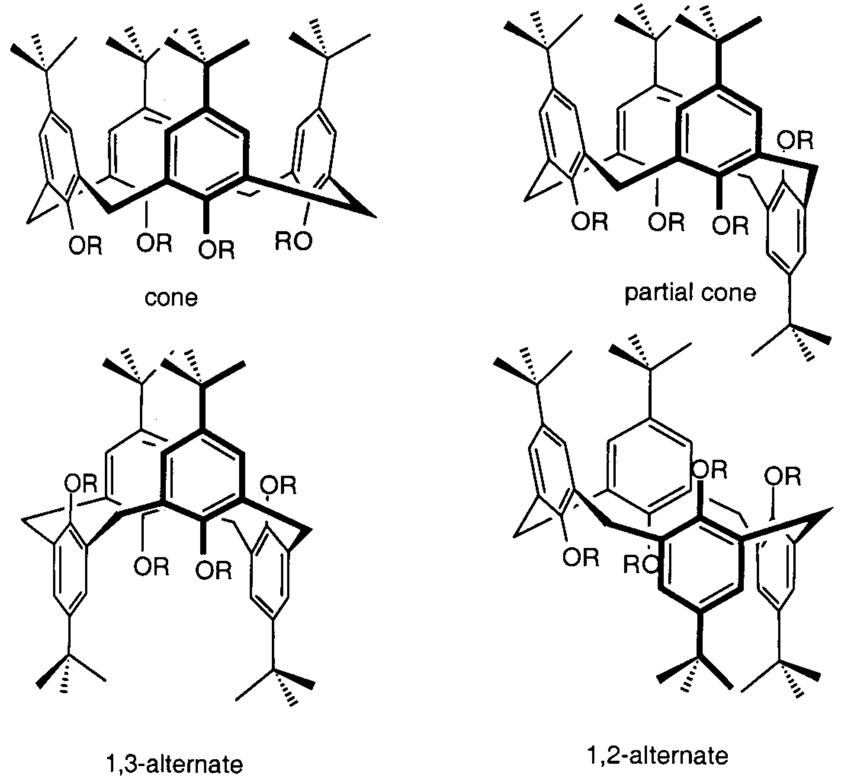
upper, exo, or wide rim
R
R
R
R
OH
OH
OH
OH
(a)
lower, endo, or narrow rim
(b)



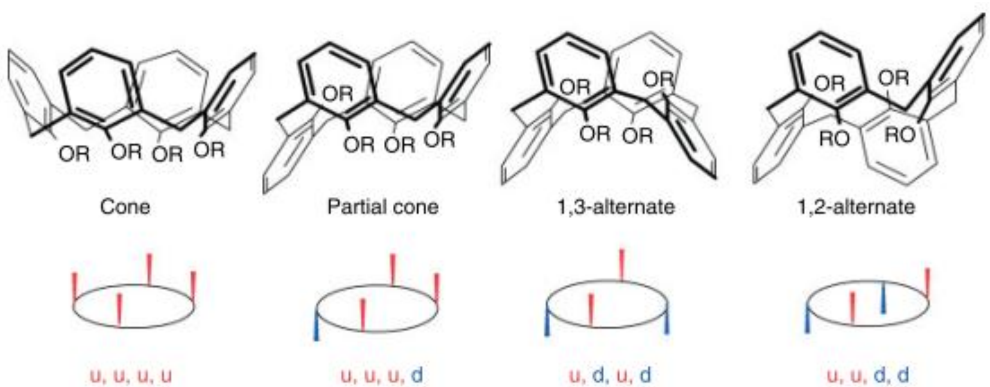
3+2 Fragment condensation

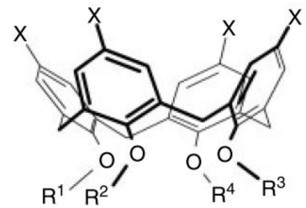


4+1 Fragment condensation

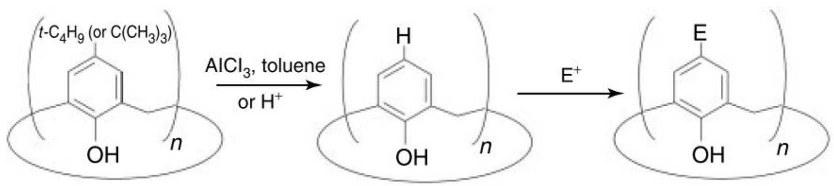


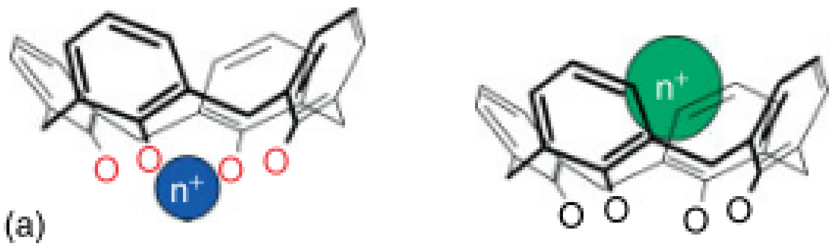
Conformations adopted by calix[4]arenes.



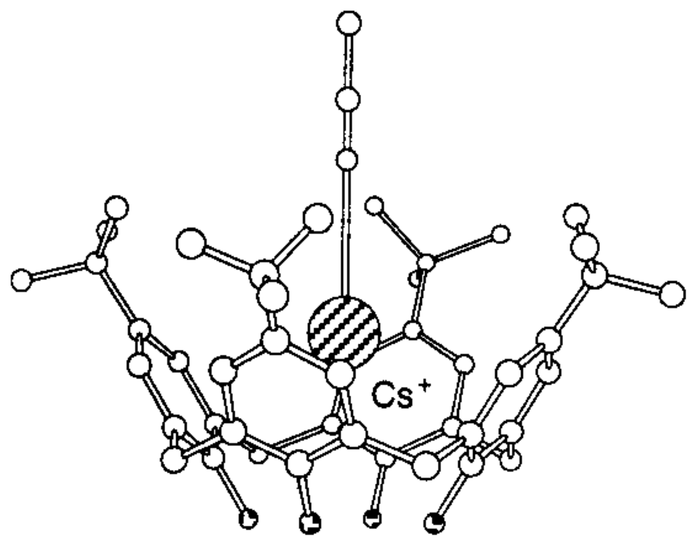


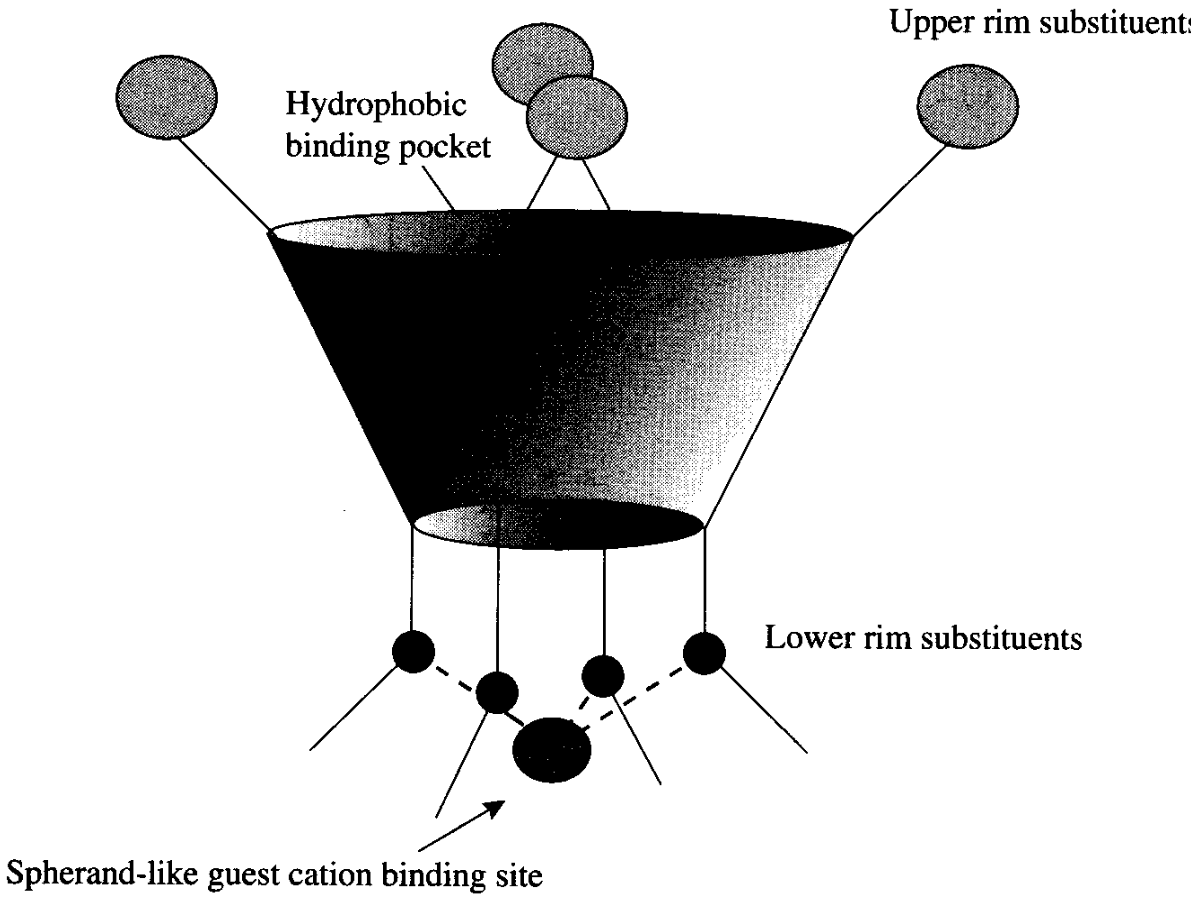
2a: R^1-R^4 = alkyl
2b: R^1, R^2 = alkyl, R^3, R^4 = OH
2c: R^1, R^3 = alkyl, R^2, R^4 = OH
2d: R^1 = alkyl, R^2–R^4 = OH
2e: R^1–R^3 = alkyl, R^4 = OH

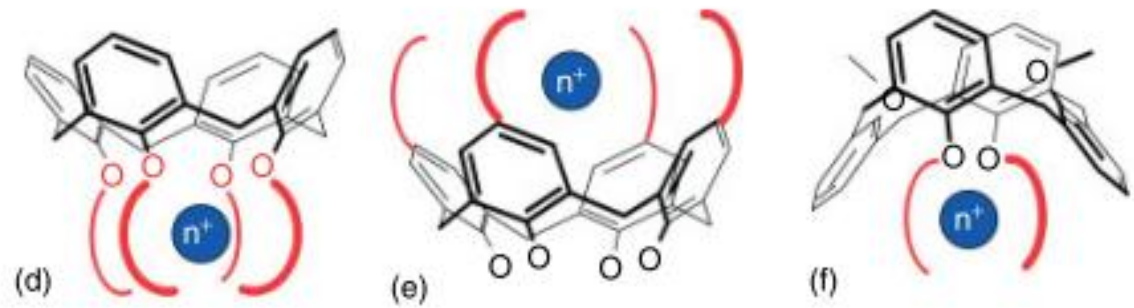


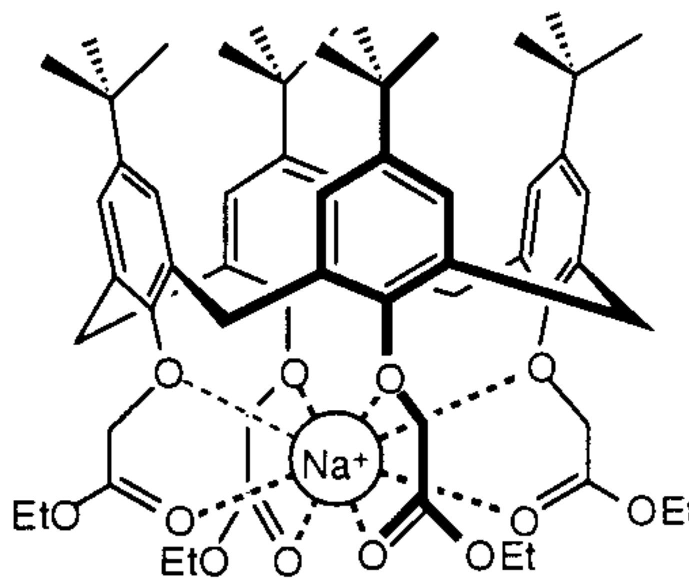


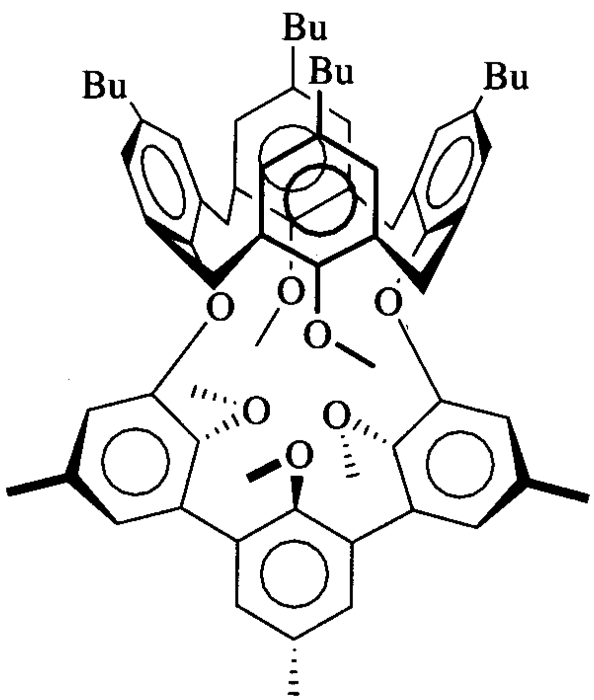
(a)



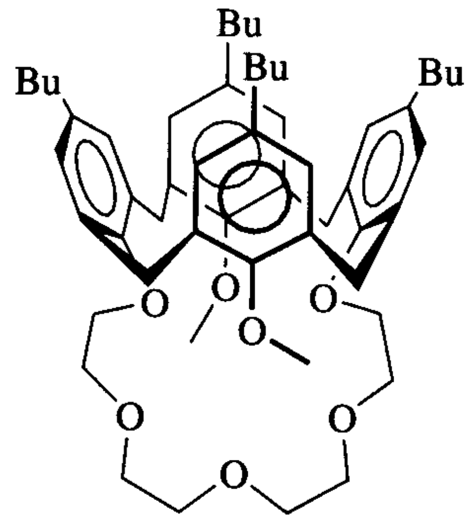

Upper rim substituents
Hydrophobic
binding pocket
Lower rim substituents
Spherand-like guest cation binding site


(d)
(e)
(f)
n+

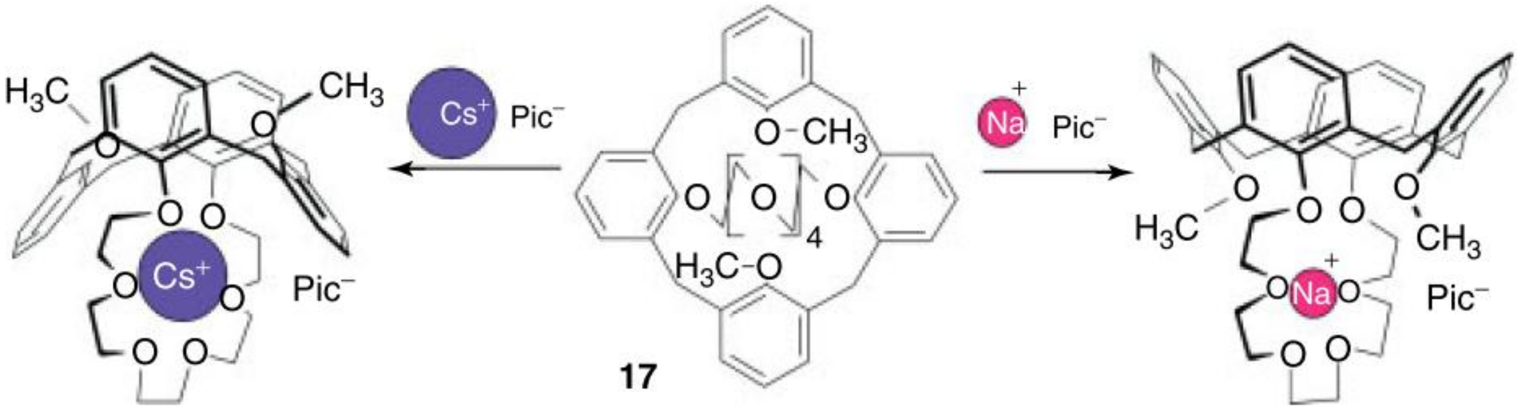

Na+
EtO
OEt



Calix-sferando

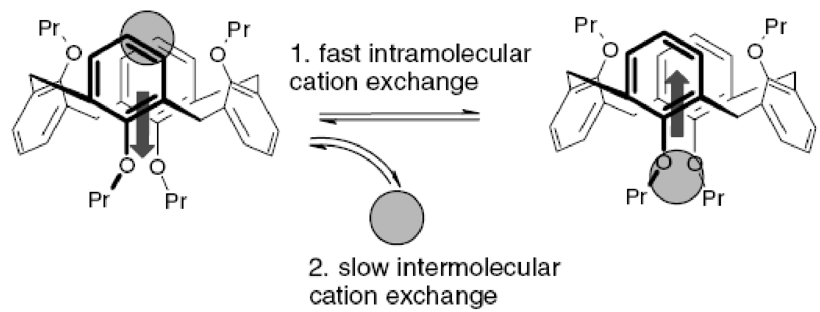


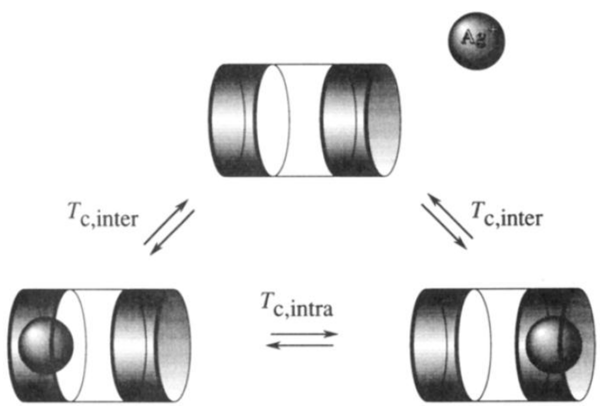
Calix-crown

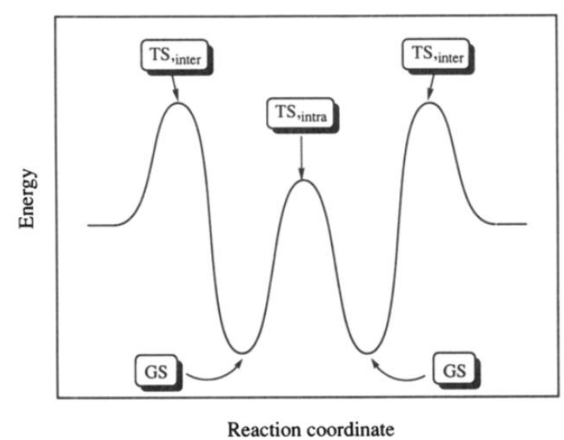


H3C
CH3
Cs+
Pic−
Pic−
O−CH3
O
O
O
4
H3C−O
17
Na+
Pic−
H3C
CH3
Na+
Pic−

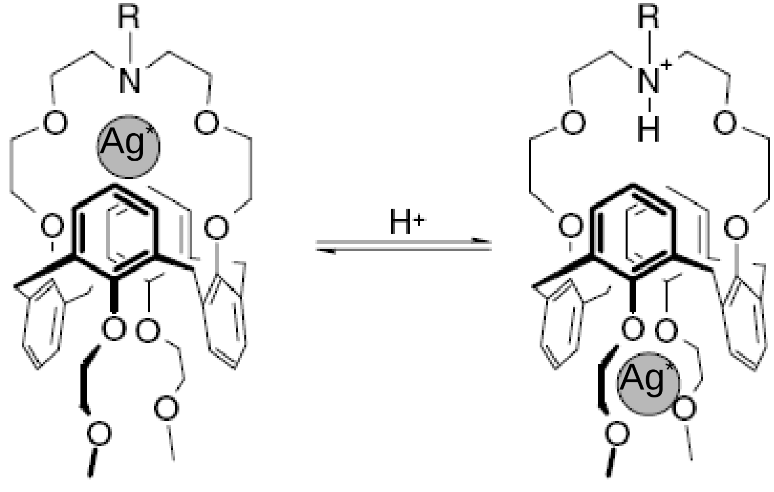
Cation tunnelling





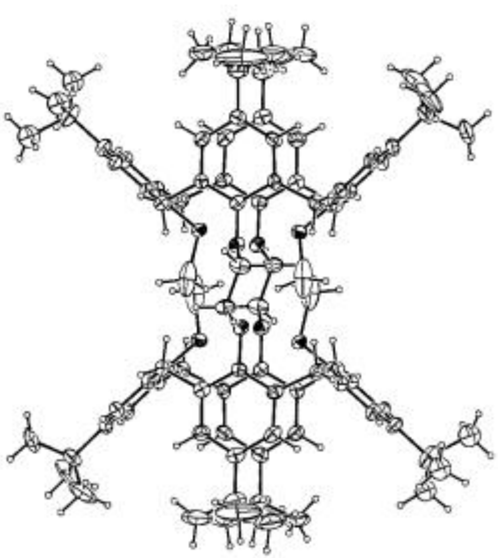


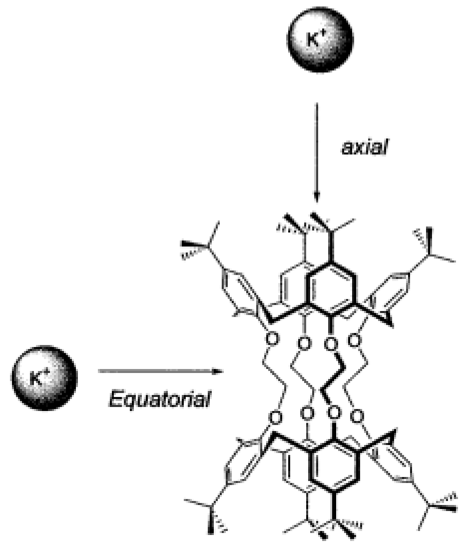
Cation tunnelling: Ag^+ syringe

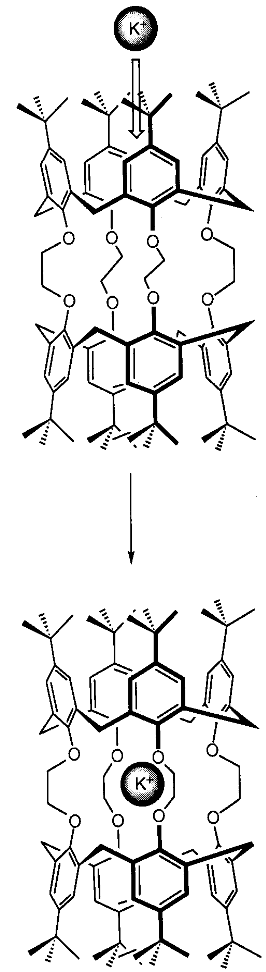


Calix-tubes

J. AM. CHEM. SOC. ■ VOL. 124, NO. 7, 2002 1341

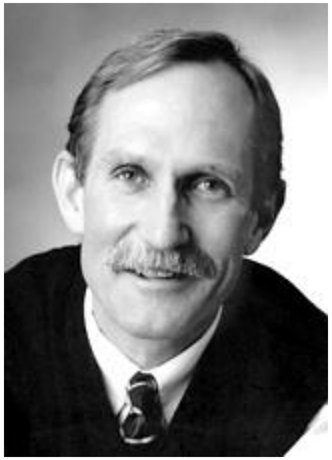






Potassium encapsulation in calix[4]tube

http://www.nobelprize.org/nobel_prizes/chemistry/laureates/2003/



Peter Agre **Roderick MacKinnon**

The Nobel Prize in Chemistry 2003 was awarded *"for discoveries concerning channels in cell membranes"* jointly with one half to Peter Agre *"for the discovery of water channels"* and with one half to Roderick MacKinnon *"for structural and mechanistic studies of ion channels“*.

Science AAAS

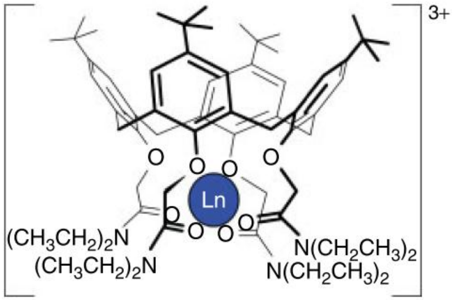
The Structure of the Potassium Channel: Molecular Basis of K^+ Conduction and Selectivity

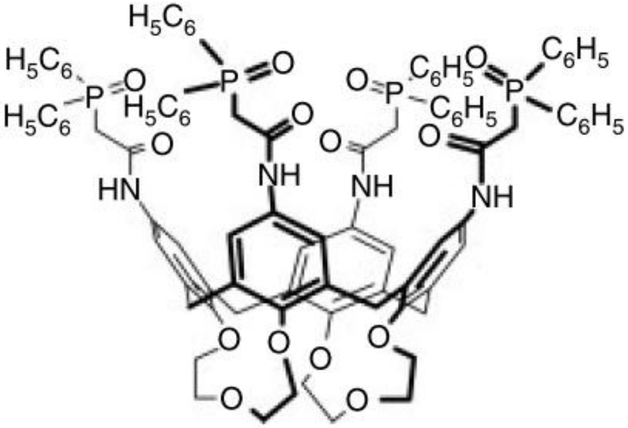
Declan A. Doyle, João Morais Cabral, Richard A. Pfuetzner,
Anling Kuo, Jacqueline M. Gulbis, Steven L. Cohen,
Brian T. Chait, Roderick MacKinnon*

Science **280**, 69 (1998);
DOI: 10.1126/science.280.5360.69

Ln^{3+} recognition

(treatment of radiactive waste/extraction- high distribution coefficiet even from very acidic water solutions)

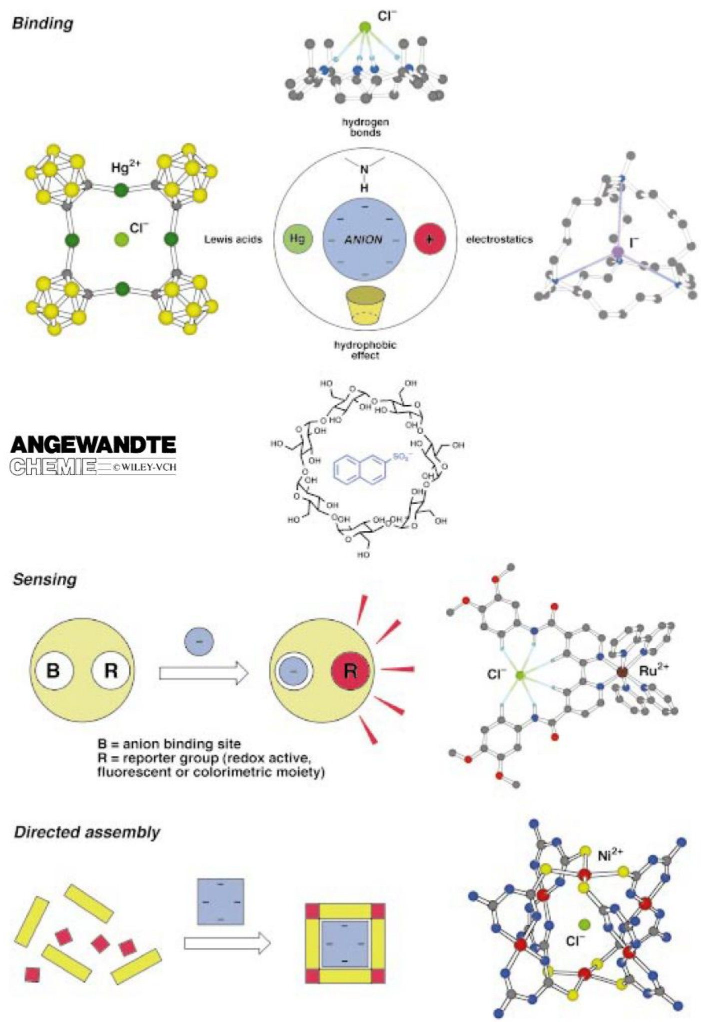




Anion Recognition and Sensing: The State of the Art and Future Perspectives

Paul D. Beer* and Philip A. Gale*

Angew. Chem. Int. Ed. 2011, 50, 1845–1848



N. H. Evans and P. D. Beer

DOI: 10.1002/anie.201309937

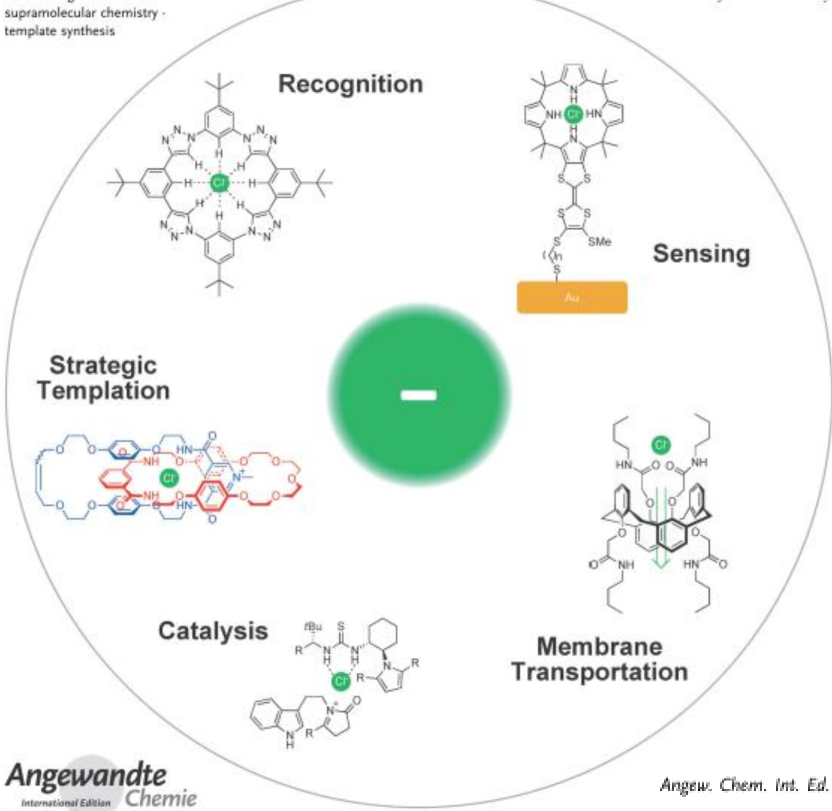
Supramolecular Chemistry of Anions

Advances in Anion Supramolecular Chemistry: From Recognition to Chemical Applications

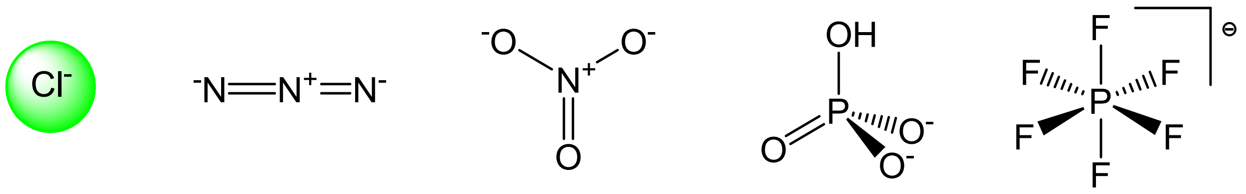
Nicholas H. Evans and Paul D. Beer**

Keywords:
anion recognition · anions · sensors · supramolecular chemistry · template synthesis

Dedicated to Professor Jean-Marie Lehn on the occasion of his 75th birthday



- anions are large and require receptors of bigger size than cations - r(F^-) ≈ rK^+
- large diversity of shapes and geometries (spherical, linear, trigonal, tetrahedral…)



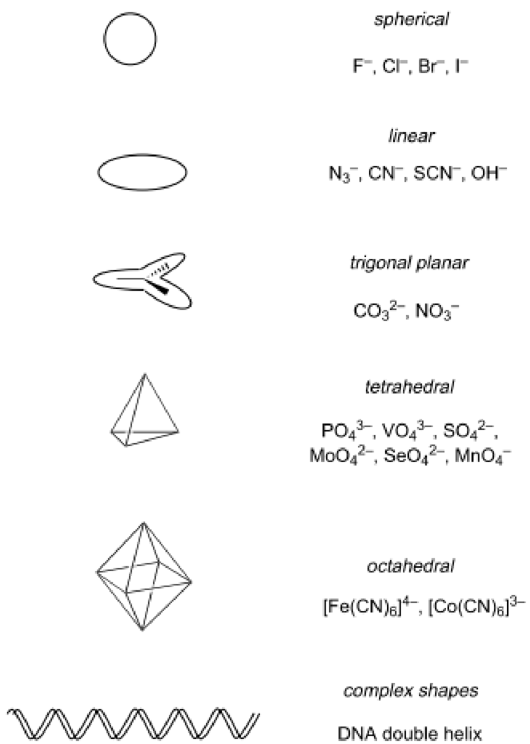
- high free energies of hydration

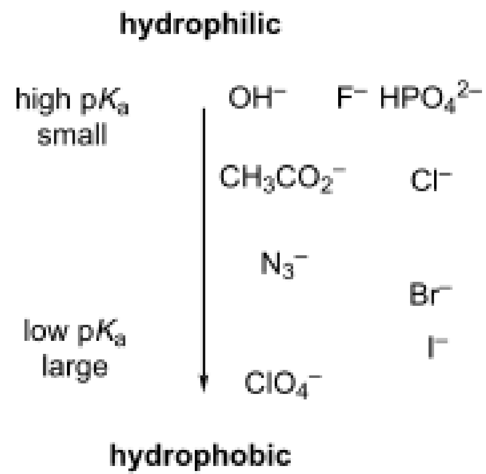
$$\Delta_r G°_{hydr}(F^-) = -465 \text{ kJ.mol}^{-1} \qquad \Delta_r G°_{hydr}(K^+) = -295 \text{ kJ.mol}^{-1}$$

- anions are sensitive to pH (crucial for recognition on water)
- anions are coordinatively saturated : only weak interactions (H bond, electrostatic, Van der Waals), no strict coordination number
- Lewis bases

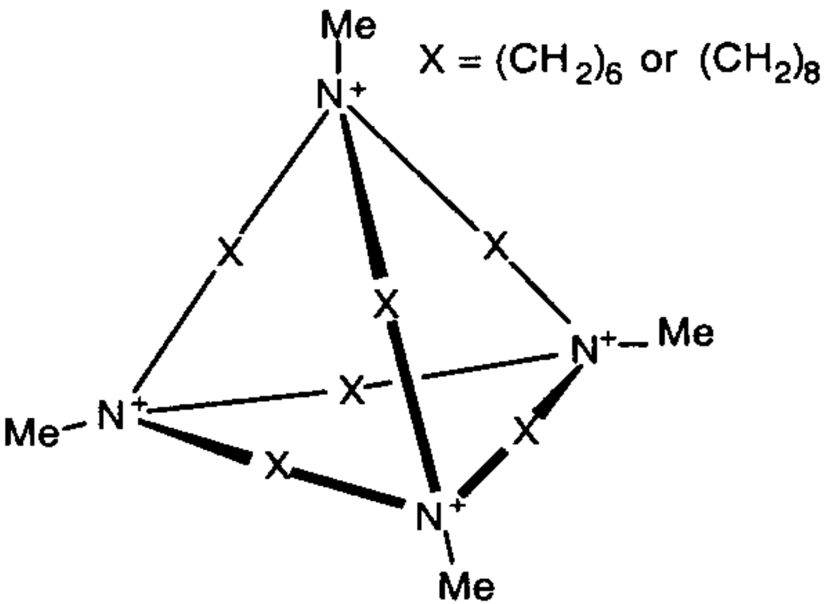
Table 1. A comparison of the radii r of isoelectronic cations and anions in octahedral environments.[7]

Cation	r [Å]	Anion	r [Å]
Na^+	1.16	F^-	1.19
K^+	1.52	Cl^-	1.67
Rb^+	1.66	Br^-	1.82
Cs^+	1.81	I^-	2.06





Host cationici



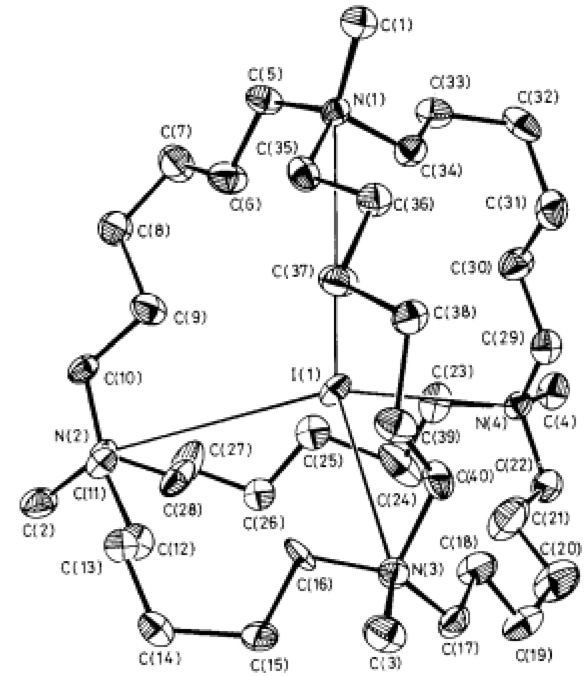
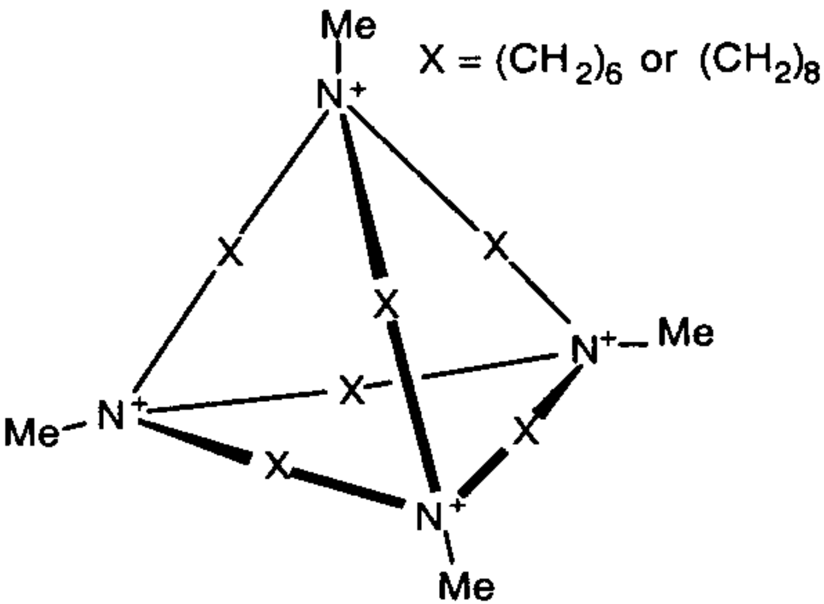


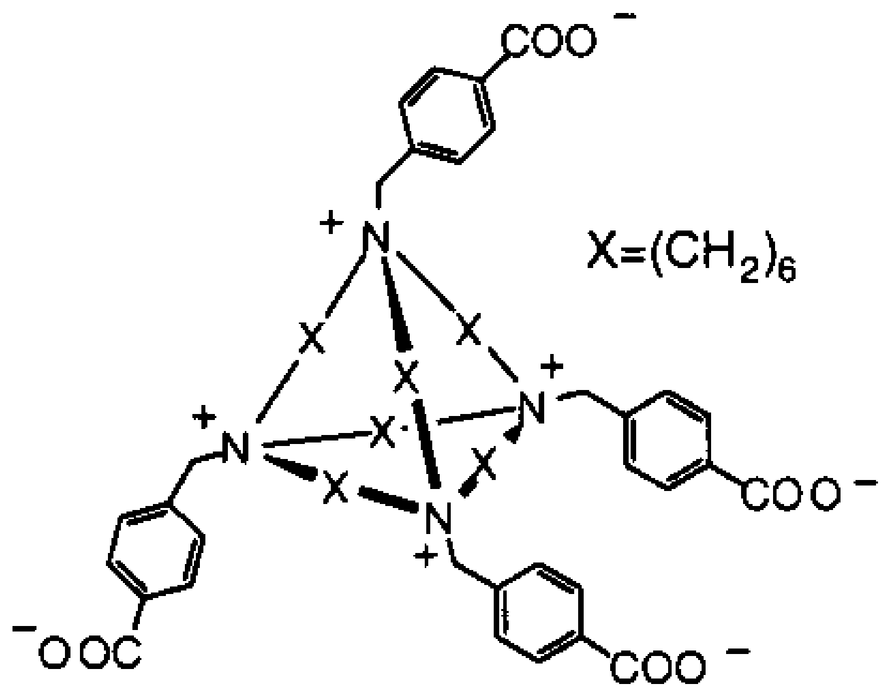
Figure 2. The X-ray crystal structure of the iodide complex of receptor **1**

Schmidtchen

Host cationici



Host zwitter-ionici

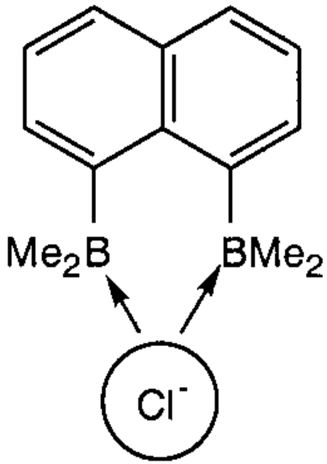


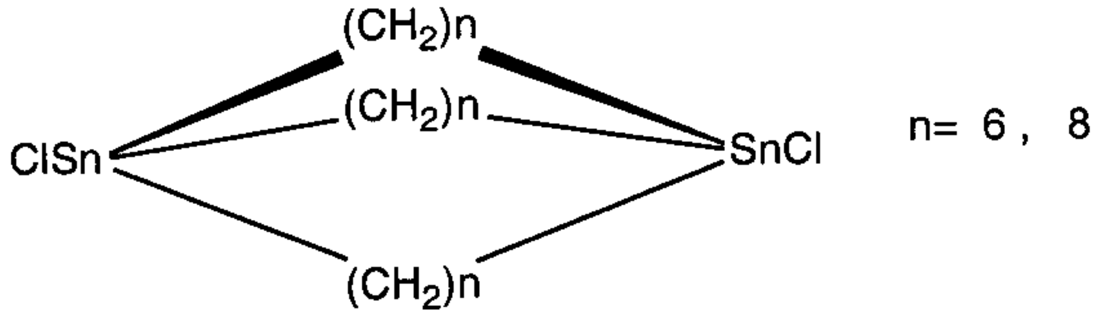
$K(Br^-) = 1020$ (H_2O)

$K(Br^-) = 2150$ (H_2O)

Selettività <<

$K(Br^-) = 1020$ $K(I^-) = 500$ $K(Cl^-) = 50$

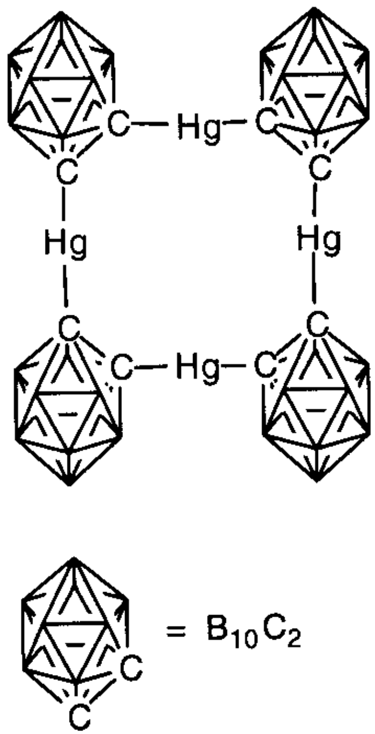




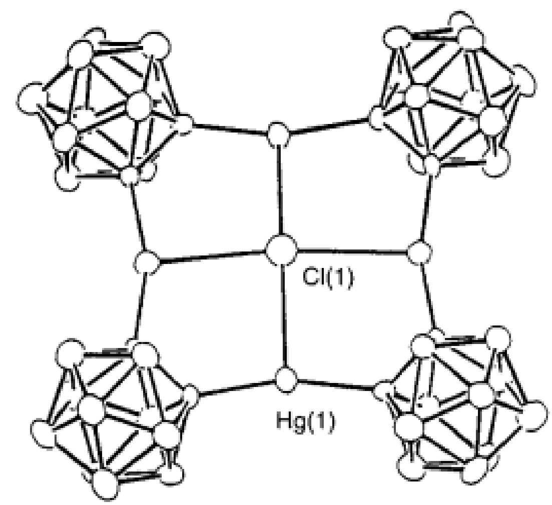
Organotin cryptand encapsulates fluoride anions.

Organo-Boro

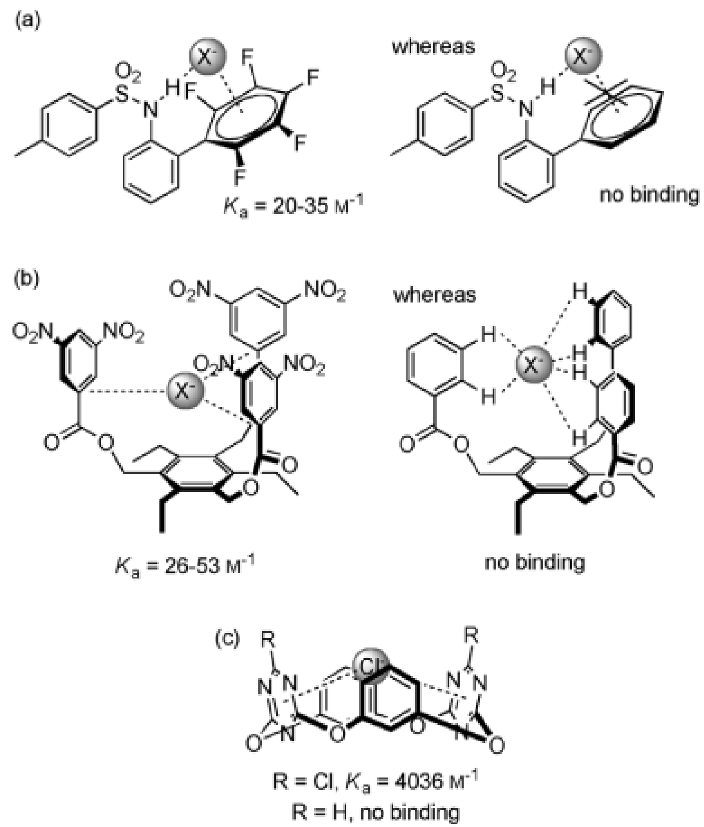
Organo-Sn(IV)



Organo-Hg(II)

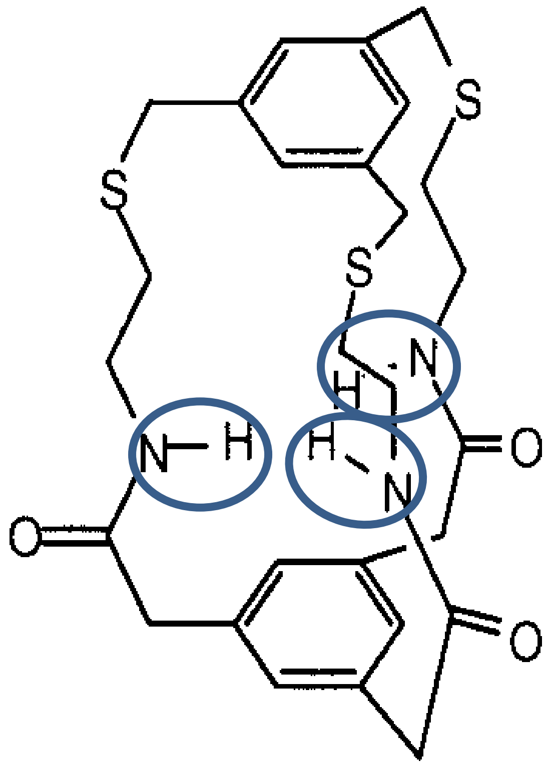


Hawthorne



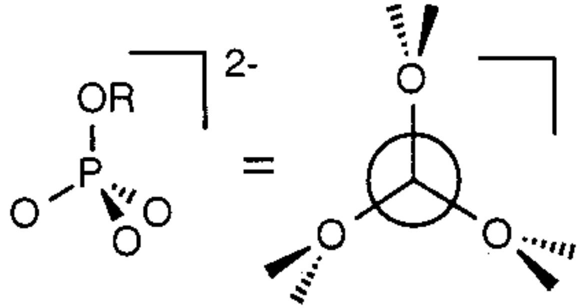
(a)
whereas
K_a = 20-35 M^{-1}
no binding
(b)
whereas
K_a = 26-53 M^{-1}
no binding
(c)
R = Cl, K_a = 4036 M^{-1}
R = H, no binding

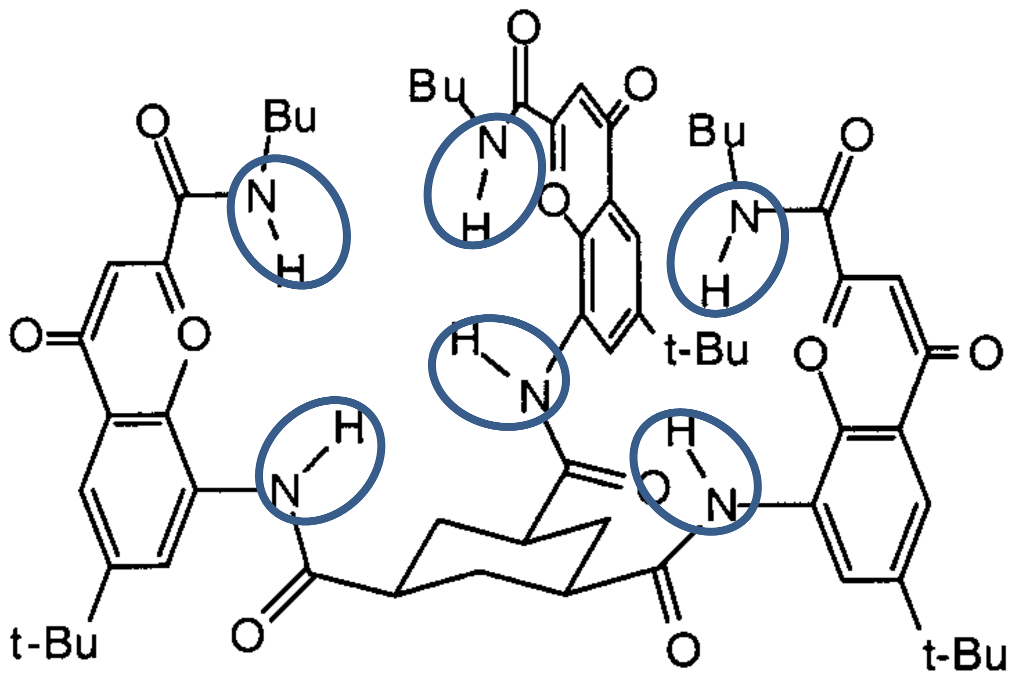
Berryman



Hydrogen bonding receptor for fluoride anions.

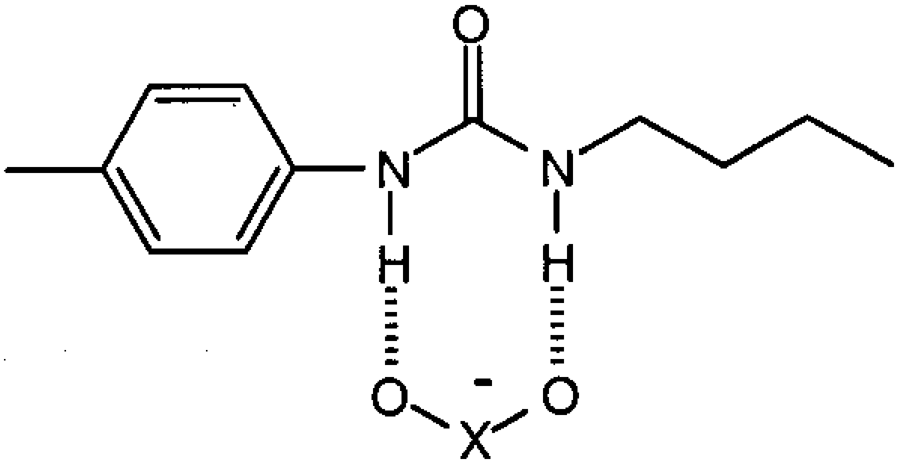
Pascal

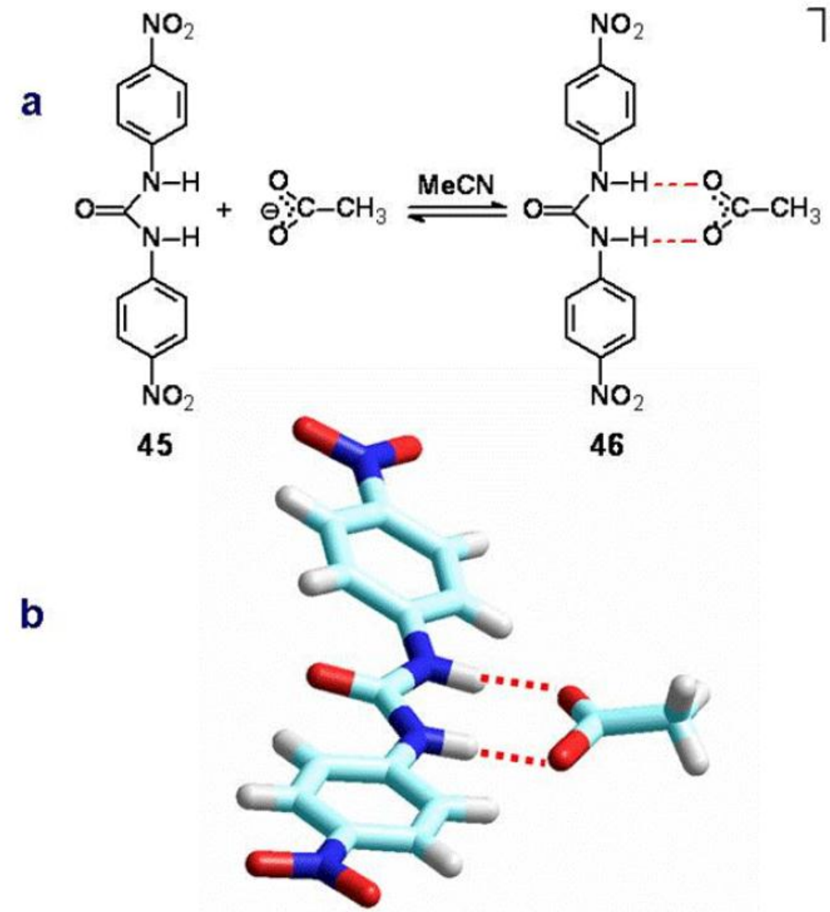




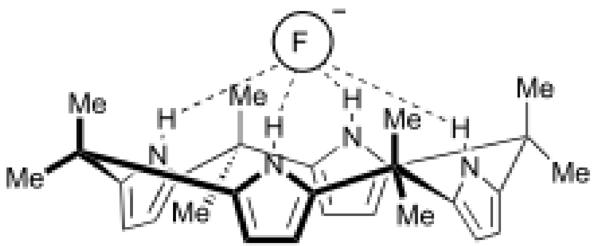
Trigonal receptors can bind phosphate anions strongly in competitive solvents.

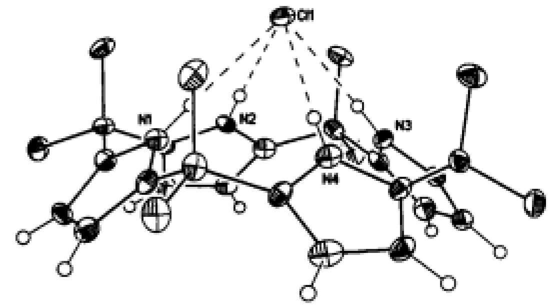
Raposo

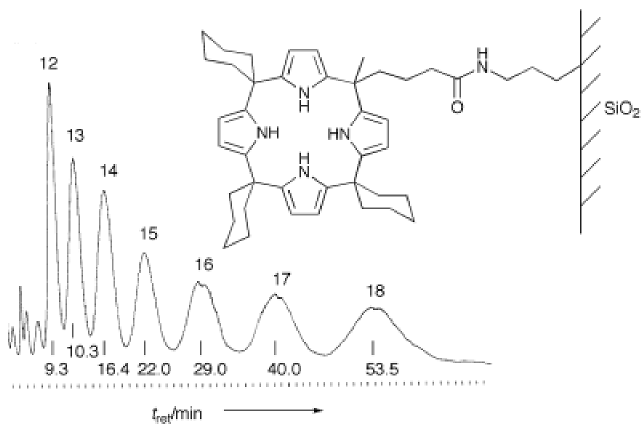

O
N
H
H
N
H
H
O
X
O

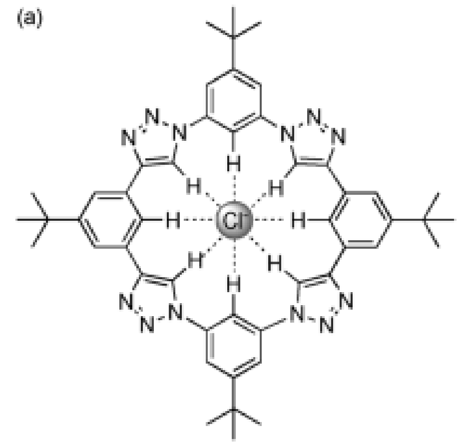

a
NO2
N–H
O=C
N–H
NO2
45
+
C–CH3
MeCN
NO2
N–H
N–H
C–CH3
NO2
46
b

Fabrizzi



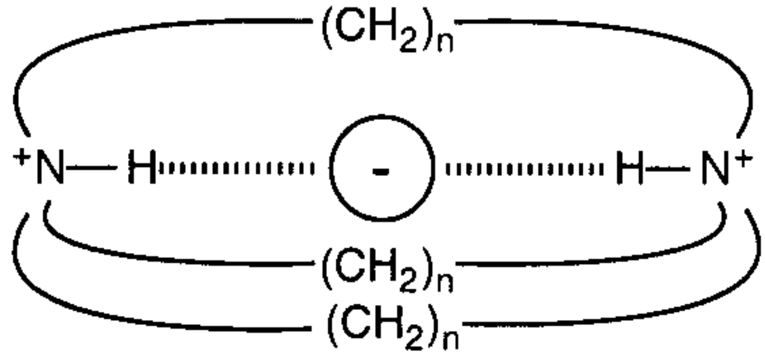




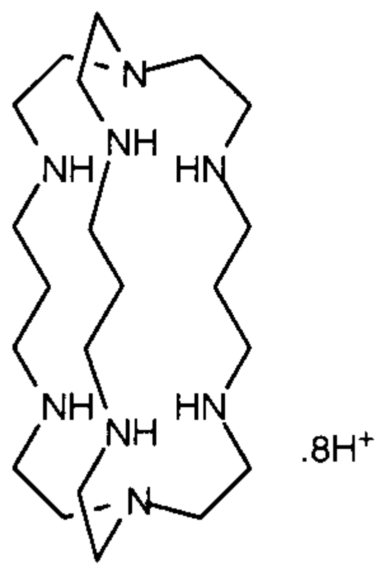


HPLC Separation of oligonuclotides of different lenght

Sessler

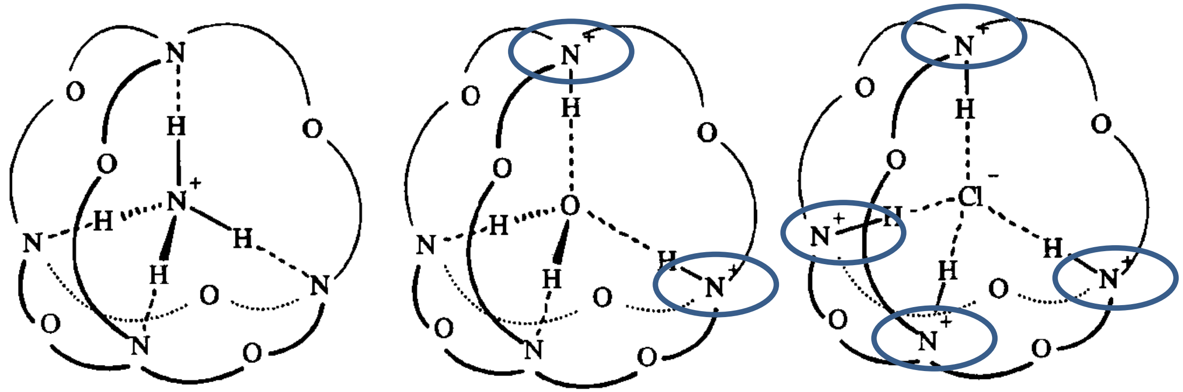


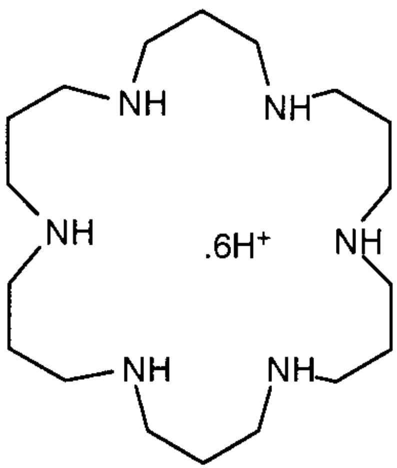
poliazamacrocicli

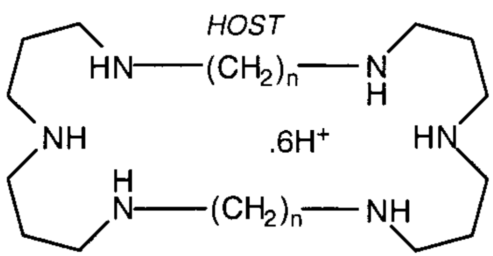


Receptors for anions.

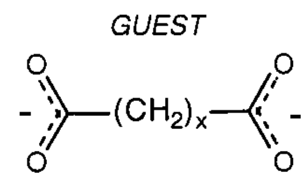
Lehn





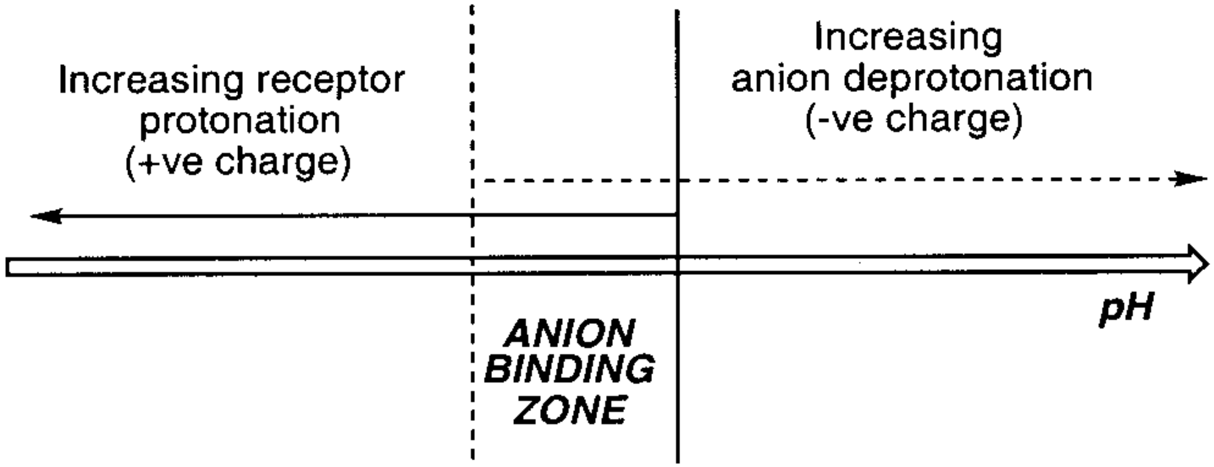


3.18a, n=7
3.18b, n=10

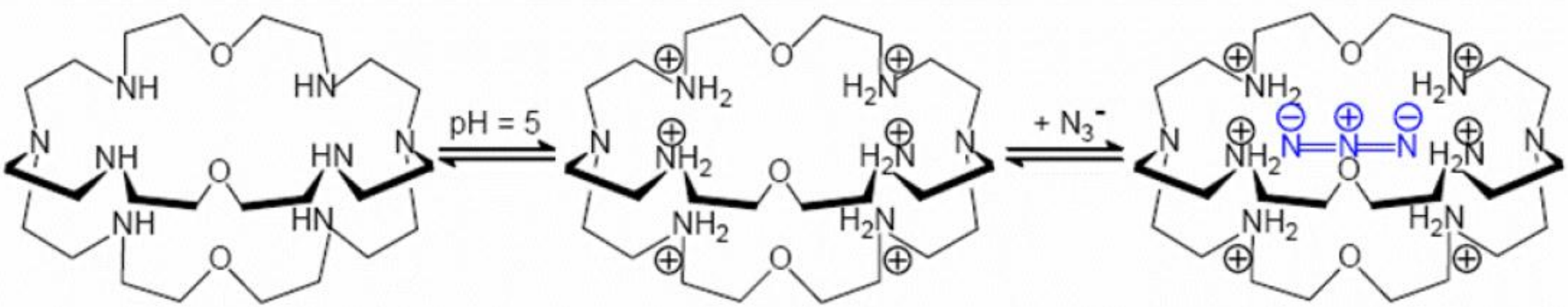


Receptor **3.18** is specific for dicarboxylates of defined chain lengths.

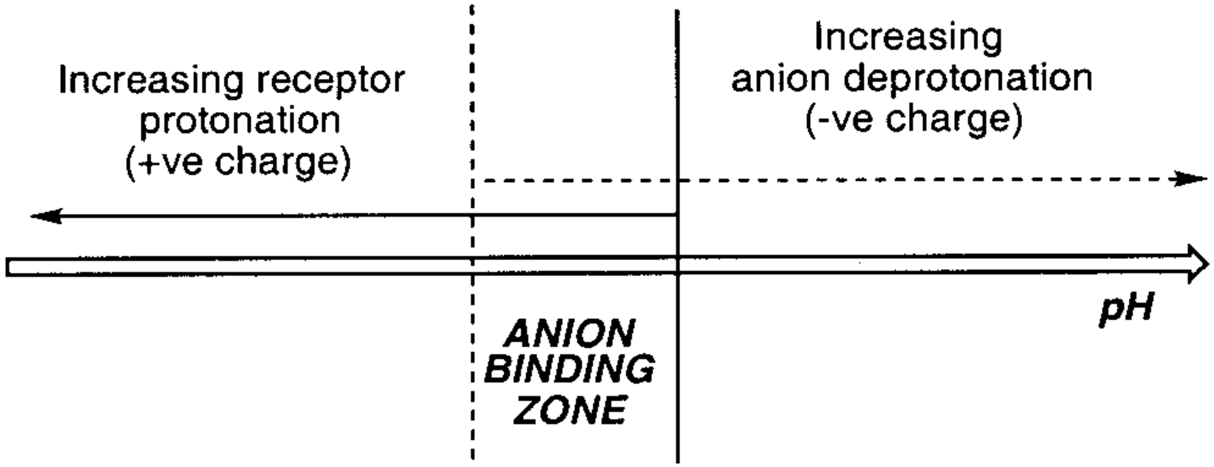
Lehn



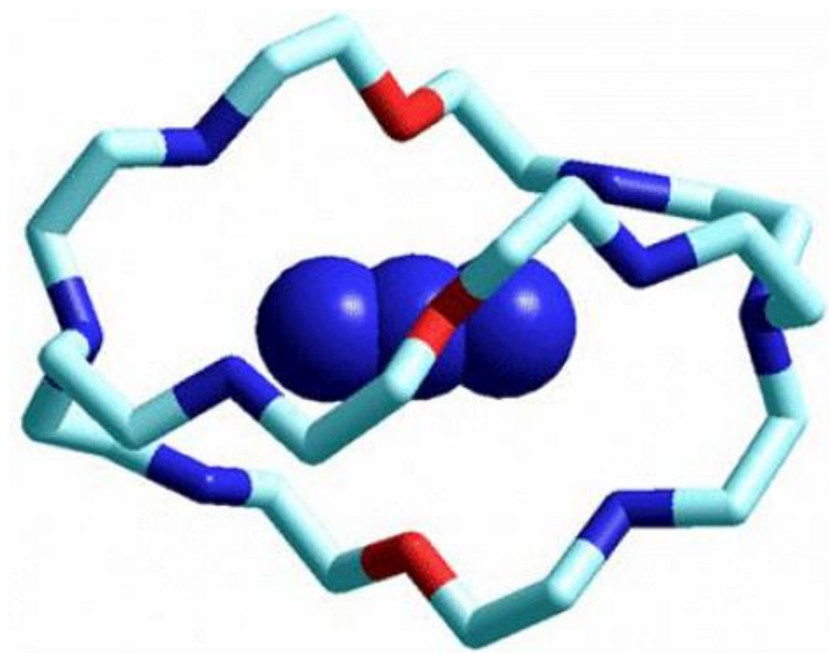
Balance between host protonation and guest deprotonation.

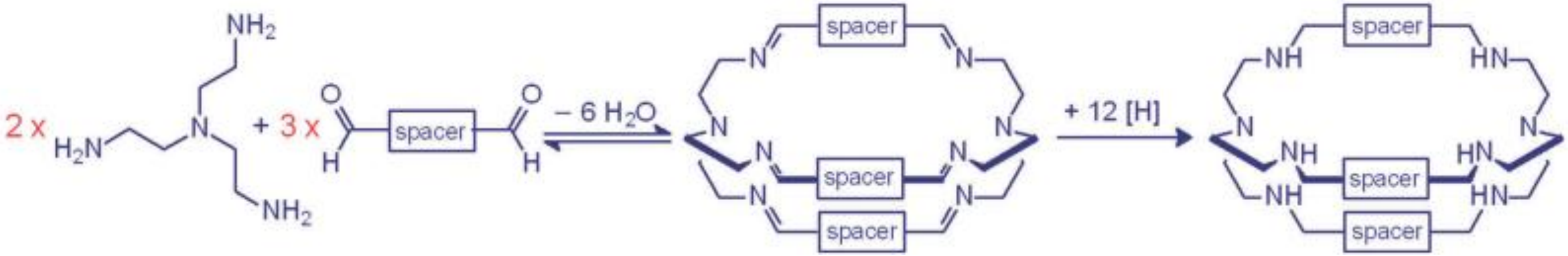


51 52 53

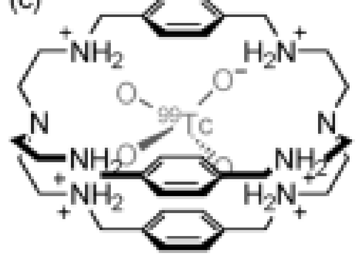


Balance between host protonation and guest deprotonation.

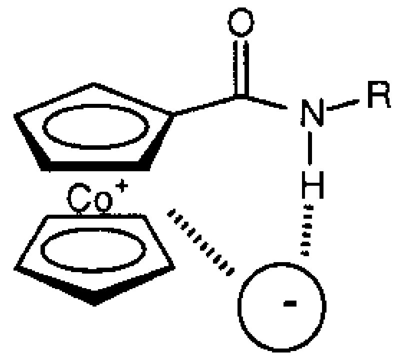




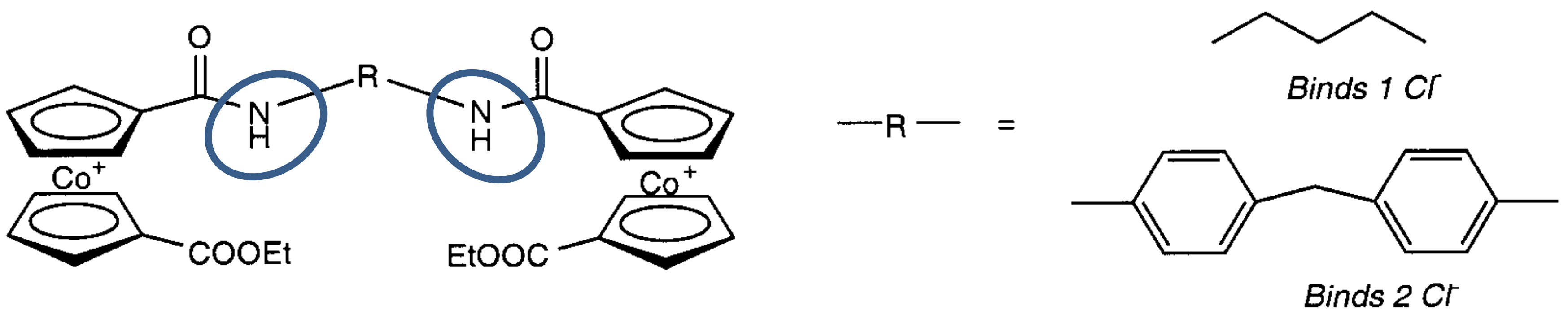
(c)



Fabrizzi

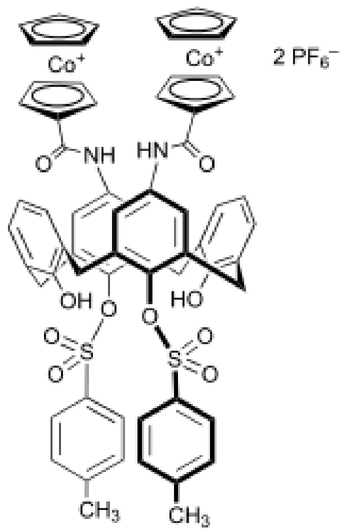


Amide functionalized cobaltocenium binds anions.

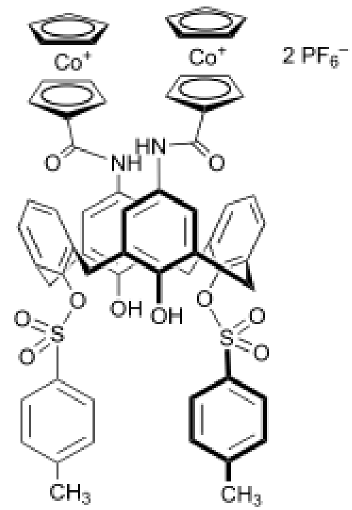


Cobaltocenium based anion receptors have easily tunable binding sites.

Beer



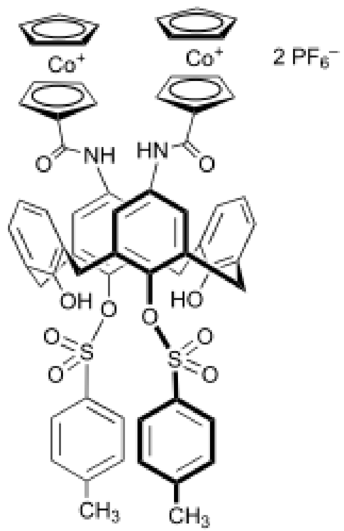
50



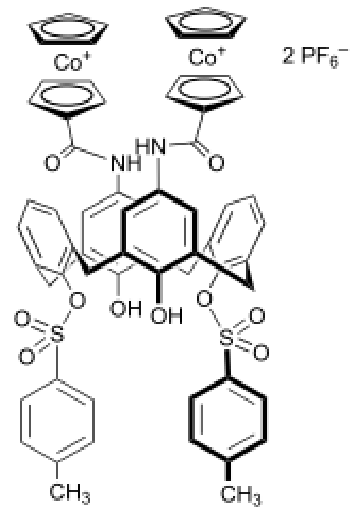
51

50: $CH_3CO_2^{-} \gg H_2PO_4^{-}$

51: $CH_3CO_2^{-} \gg HPO_4^{-}$



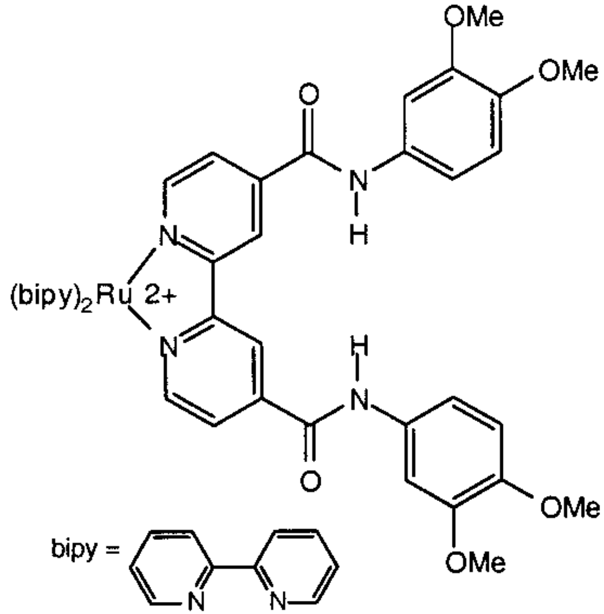
50

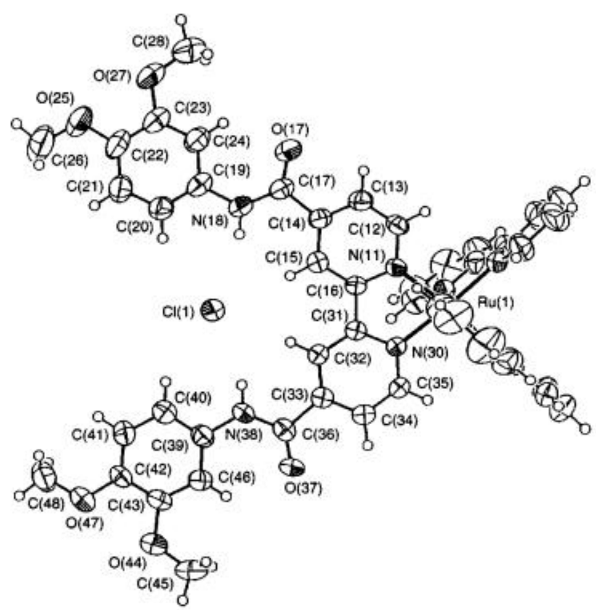


51

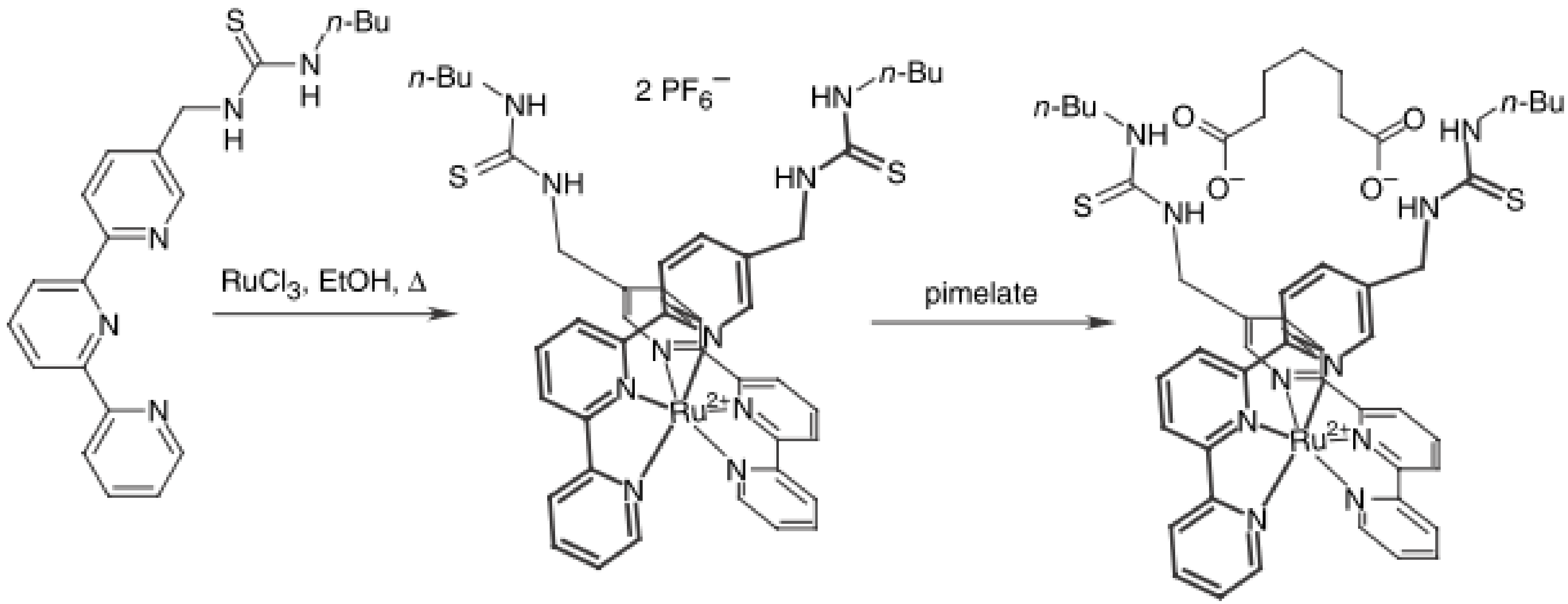
50: $CH_3CO_2^- \gg H_2PO_4^-$

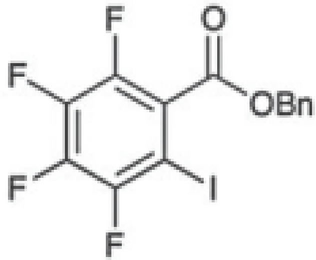
51: $CH_3CO_2^- \gg HPO_4^-$

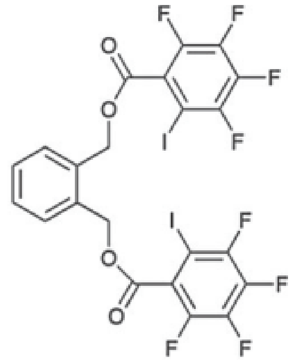


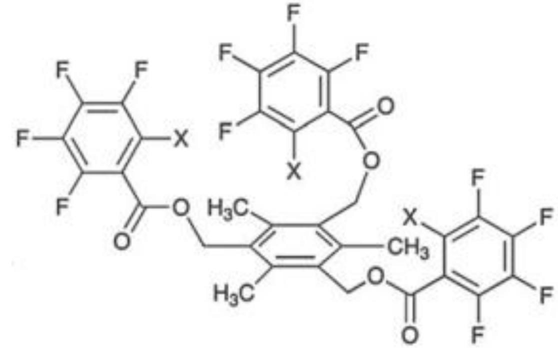


Beer


S
n-Bu
N
H
N
H
N
N
N
RuCl3, EtOH, Δ
n-Bu
NH
2 PF6−
HN
n-Bu
S
NH
HN
S
N
N
N
Ru2+
N
N
N
pimelate
n-Bu
NH
O
O
HN
n-Bu
S
NH
O−
O−
HN
S
N
N
N
Ru2+
N
N
N

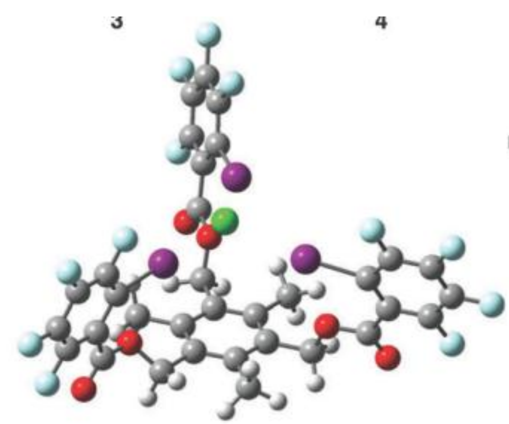




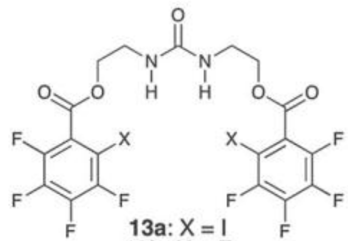


ortho-substituted iodotetrafluroroarenes on to trimethylbenzene scaffold

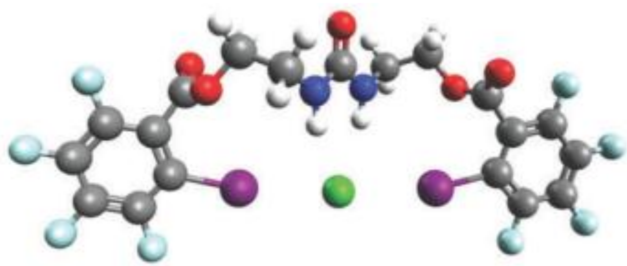
In acetone: $Cl^{-} > Br^{-} > I^{-}$



Taylor



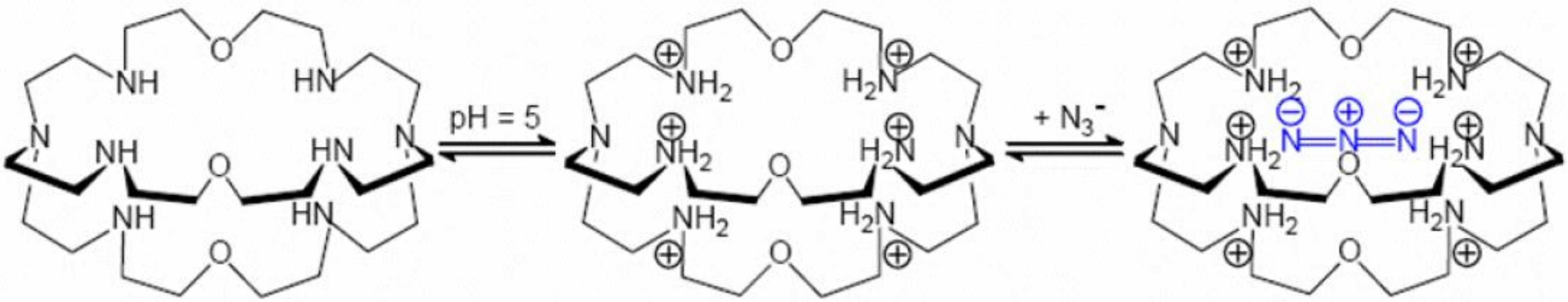
13a: X = I
13b: X = F



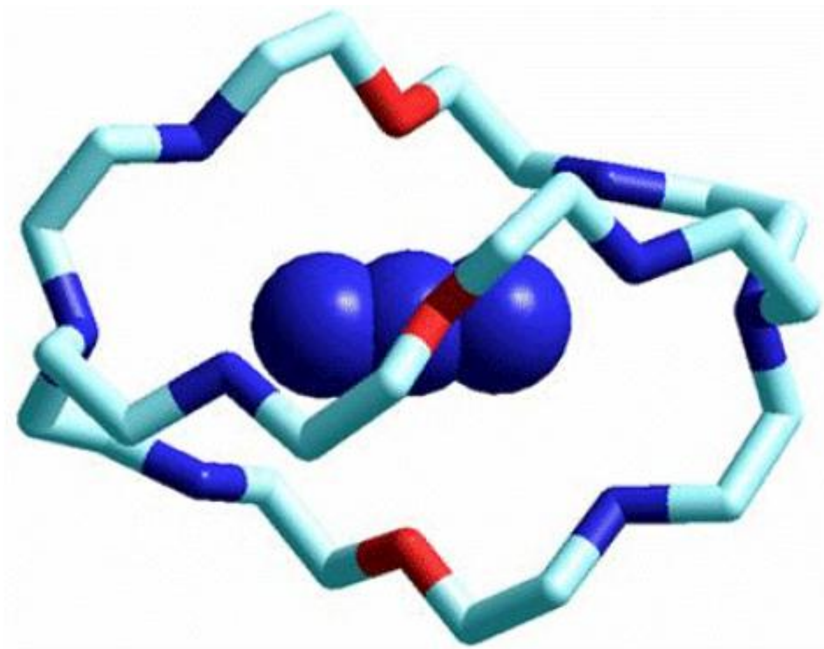
(a) A cascade complex.

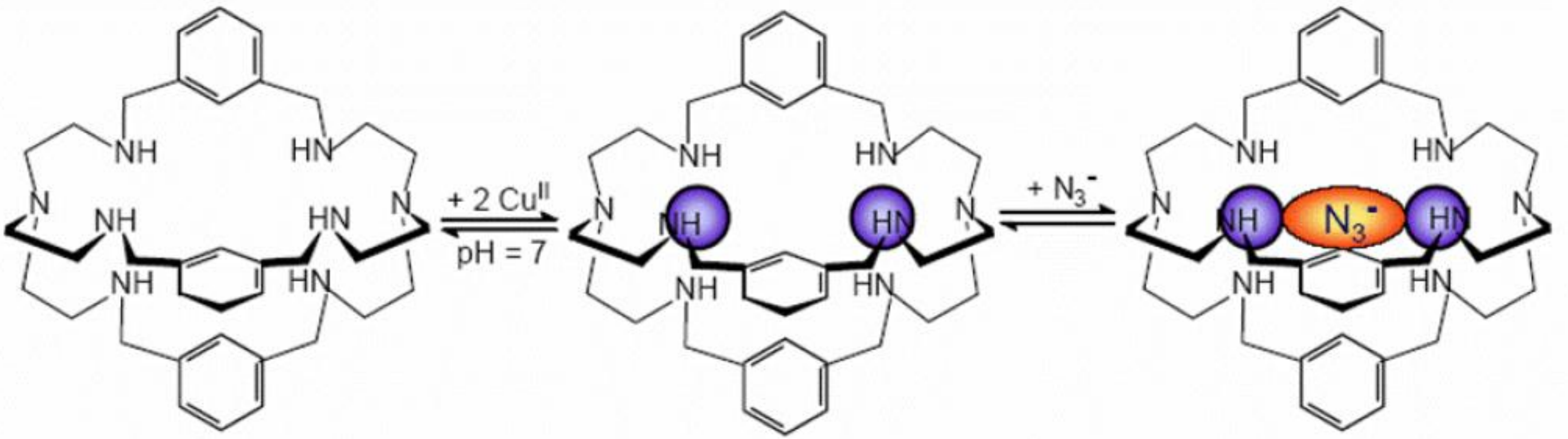
(b) Receptor with individual cation and anion recognition sites.

(c) Receptor for zwitterionic guests.

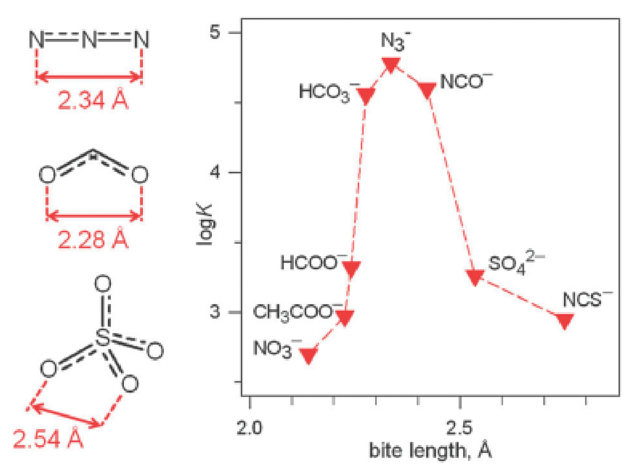


51 **52** **53**

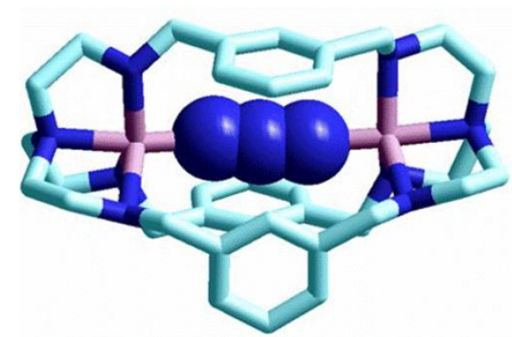


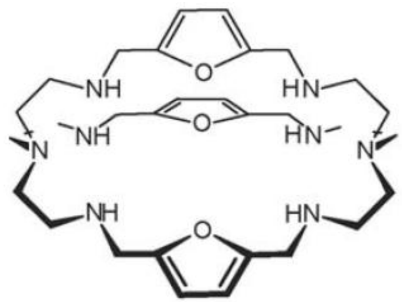


NH
HN
N
+ 2 Cu^II
pH = 7
+ N3-
N3-



2.34 Å
2.28 Å
2.54 Å
log K
bite length, Å
N3-
HCO3−
NCO−
HCOO−
SO4 2−
CH3COO−
NCS−
NO3−
2.0
2.5
3
4
5





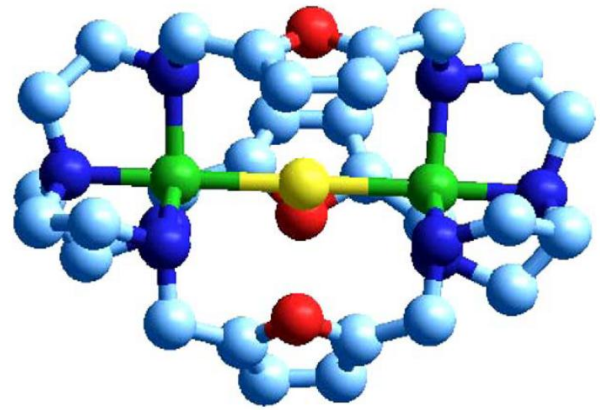


Fig. 3. The structure of the $[Cu_2^{II}(\mathbf{6})(Br)]^{3+}$ supercryptate. The bromide ion bridges the two Cu^{II} centres. Each Cu^{II} ion experiences an axially compressed trigonal bipyramidal geometry, typically observed in tren and bistren complexes.

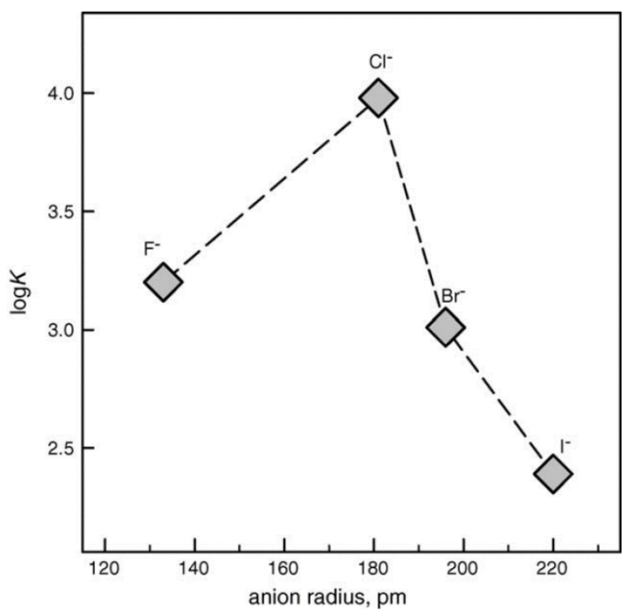


Fig. 6. Selectivity pattern for the inclusion equilibrium: $[Cu_2^{II}(\mathbf{6})]^{4+} + X^- = [Cu_2^{II}(\mathbf{6})(X)]^{3+}$ equilibrium (X^- = halide anion, aqueous solution, buffered at pH 5.2).

If log K values are plotted versus halide ion radius, a defined selectivity pattern in favour of chloride is observed (see Fig. 6). Notice that the anion size effect is rather moderate, ranging within an interval of 1.2 log units. It is possible that it is not determined by steric factors, but simply reflects the coordinating tendencies of halide ions towards transition metals (i.e. their position in the spectrochemical series: $Cl^- > F^- > Br^- > I^-$).

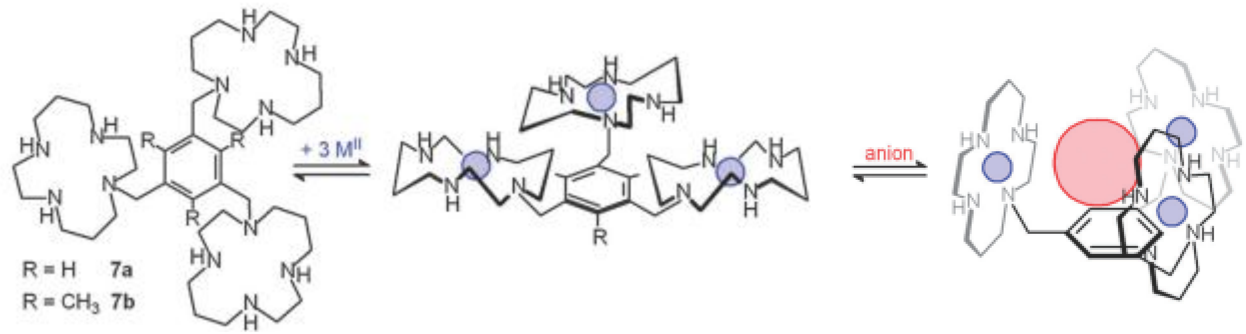
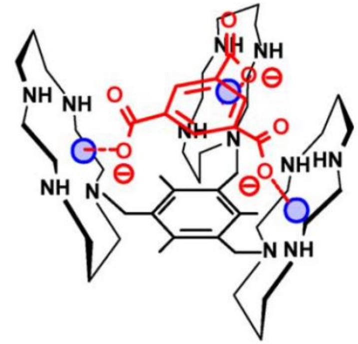
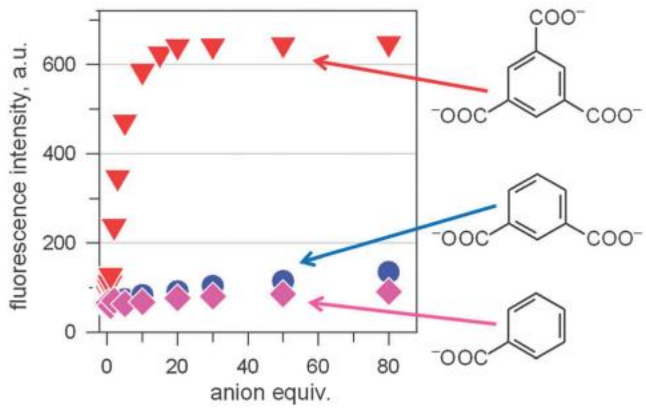
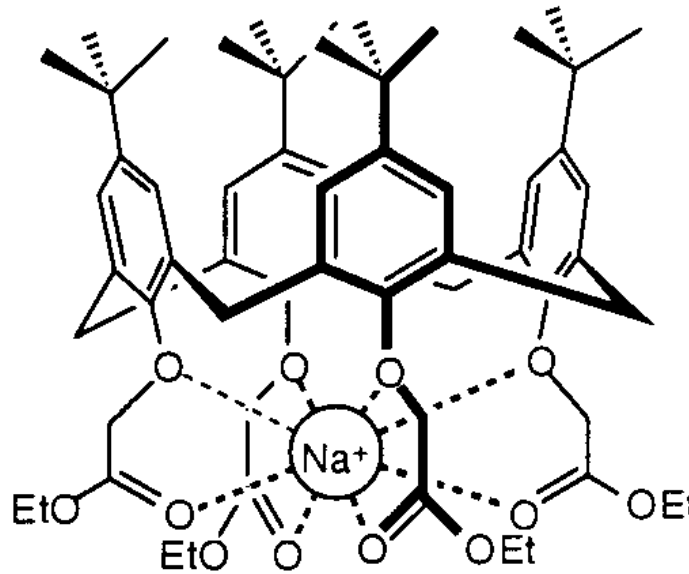


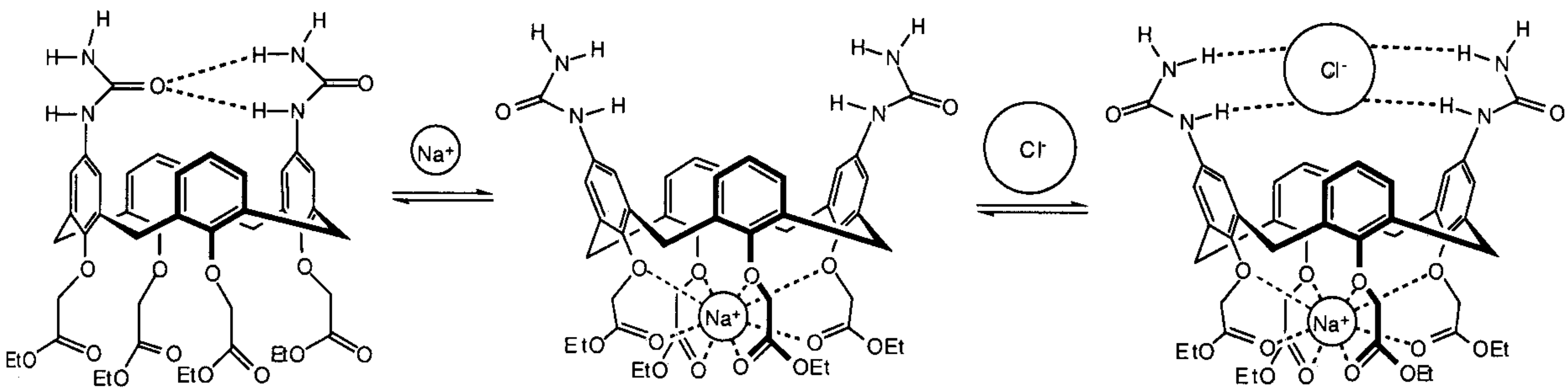
Fig. 25 The crystal structure of the complex salt $[Ni^{II}_3(\mathbf{7a})](ClO_4)_6 \cdot H_2O$.[58] Non-coordinating ClO_4^- ions and water molecule have been omitted for clarity, as well as hydrogen atoms. Each low-spin Ni^{II} centre shows a square coordination geometry.

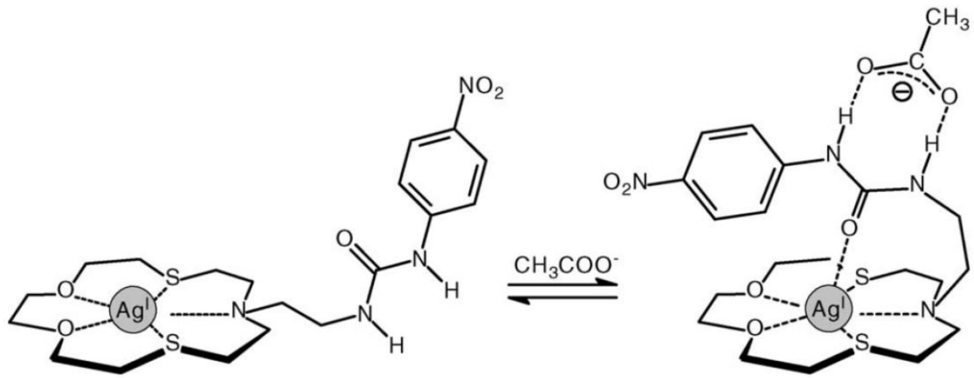




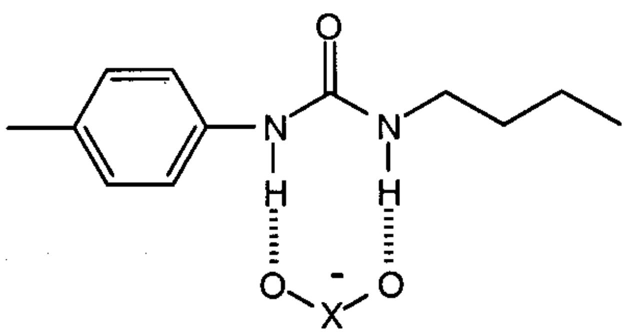
fluorescence intensity, a.u.
600
400
200
0
0
20
40
60
80
anion equiv.
COO⁻
⁻OOC
COO⁻
⁻OOC
COO⁻
⁻OOC

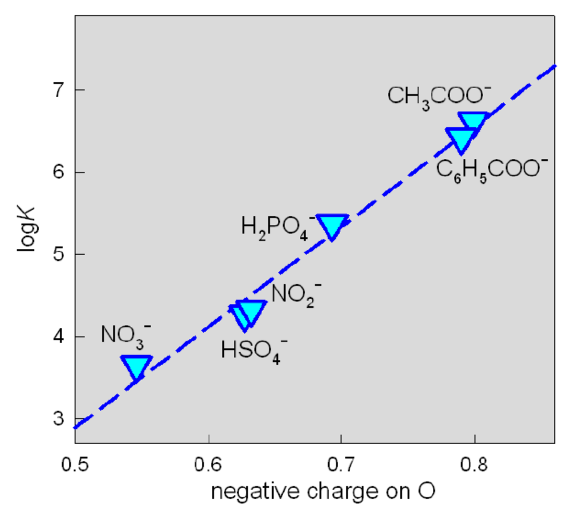

Na+
EtO
O
EtO
O
O
OEt
O
OEt

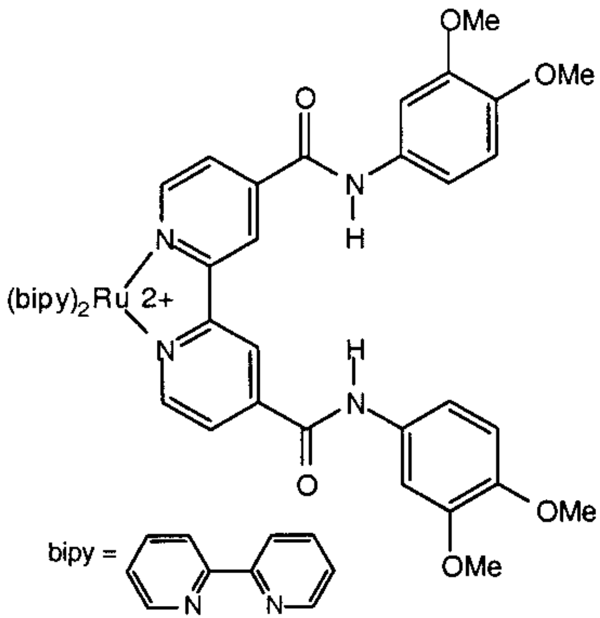

Na+
Cl-
Na+
Na+
EtO
OEt

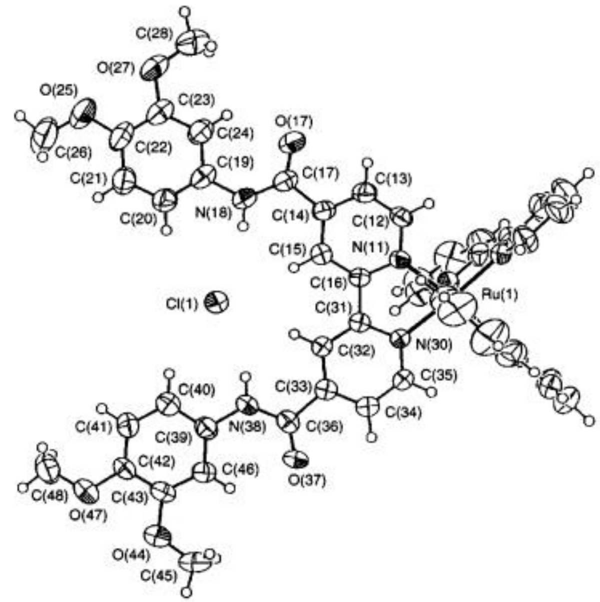


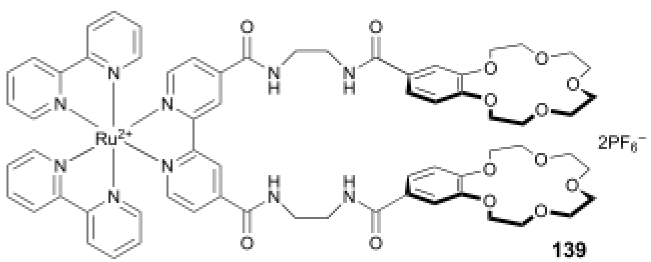
Scheme 4. Enhanced affinity of the urea subunit toward acetate, through coordination of the carbonyl oxygen atom to the proximate Ag^{I} centre.



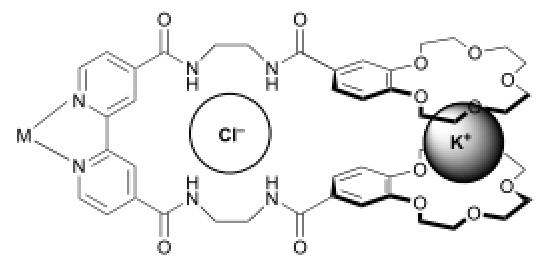



OMe
OMe
O
N
H
N
(bipy)$_2$Ru 2+
N
H
N
O
OMe
OMe
bipy =
N
N

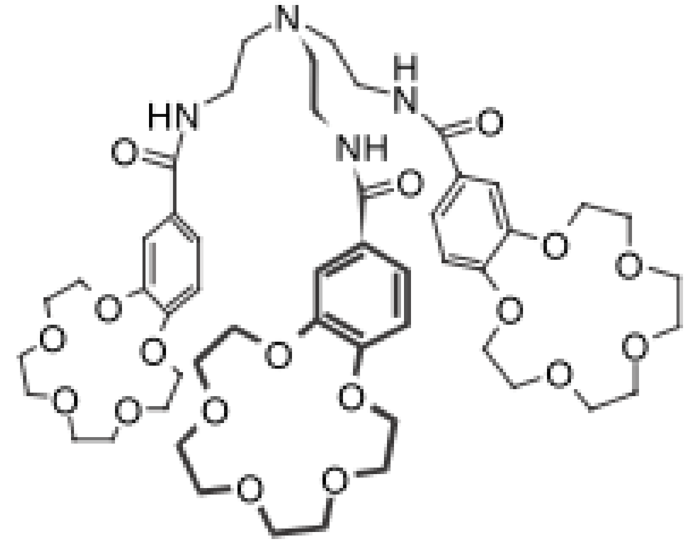

C(28)
O(27)
O(25)
C(23)
C(24)
O(17)
C(26)
C(22)
C(19)
C(17)
C(13)
C(21)
C(12)
C(20)
N(18)
C(14)
N(11)
C(15)
C(16)
Ru(1)
Cl(1)
C(31)
C(32)
N(30)
C(33)
C(35)
C(40)
C(34)
C(41)
C(39)
N(38)
C(36)
C(42)
C(46)
C(48)
C(43)
O(37)
O(47)
O(44)
C(45)

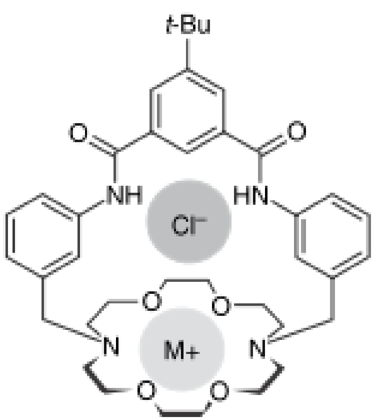

2PF$_6^-$

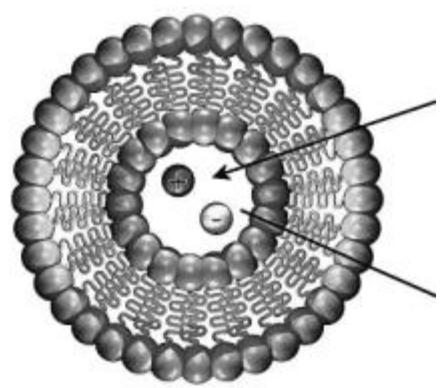
139

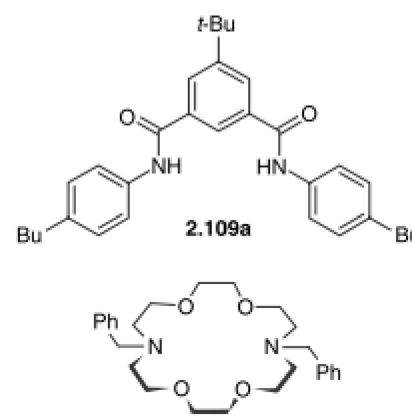

M
Cl$^-$
K$^+$

ReO_4^-, Na^+

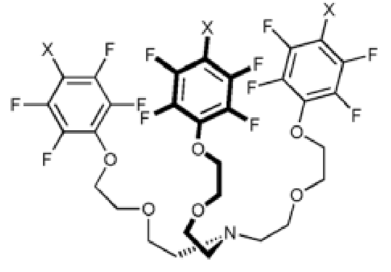




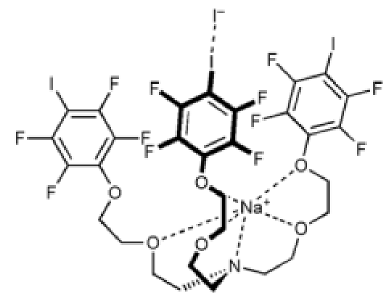




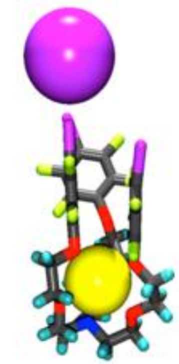
2.109a



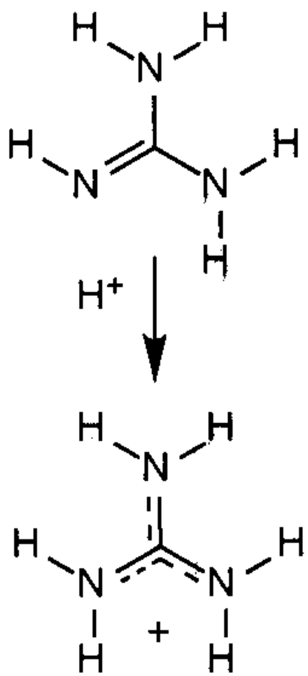
2a: X = I
2b: X = F

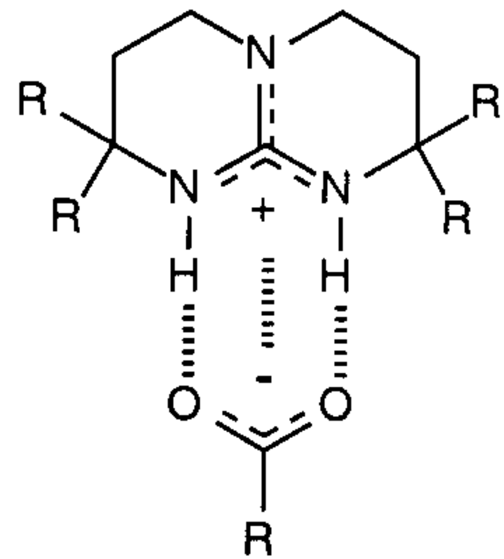


2a---NaI



K_a (**2a**---NaI) = 2.6×10^5 M^{-1}
K_a (**2b**---NaI) = 1.3×10^4 M^{-1}
$\Delta\Delta G_{XB}$ = 7 kJ/mol

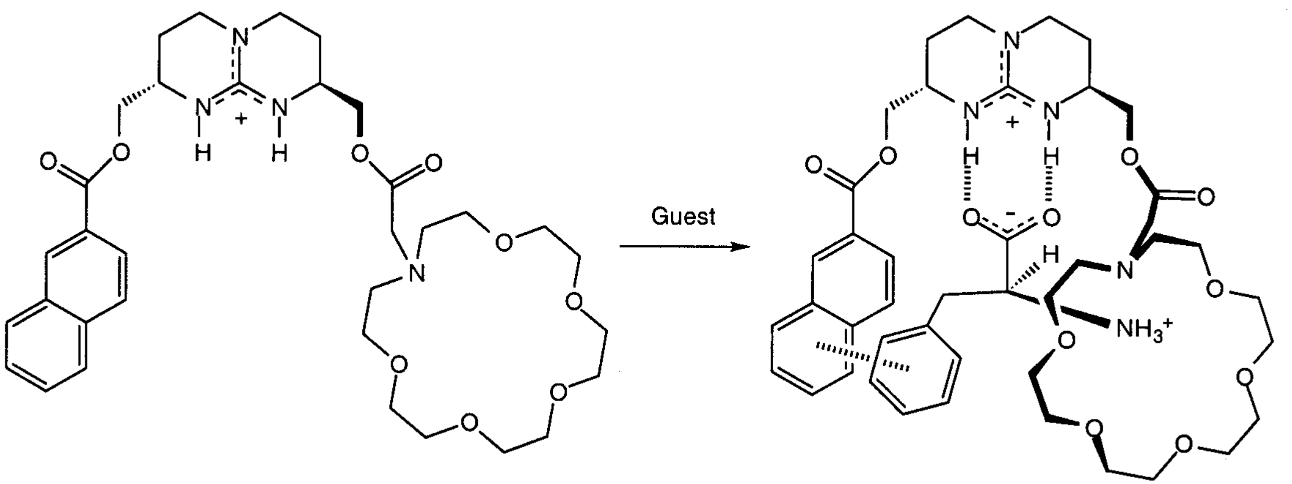


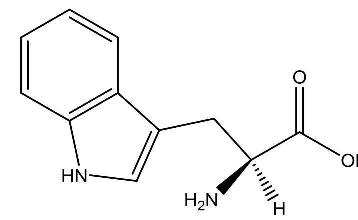


Bicyclic guanidinium is preorganized and complementary for binding bidentate anions.

pKa = 13.6

Estrazione di aa con catene laterali aromatiche (Phe, Trp) in CH_2Cl_2





Three point receptor for the selective recognition and extraction of zwitterionic amino acids.