Corso di Chimica Supramolecolare

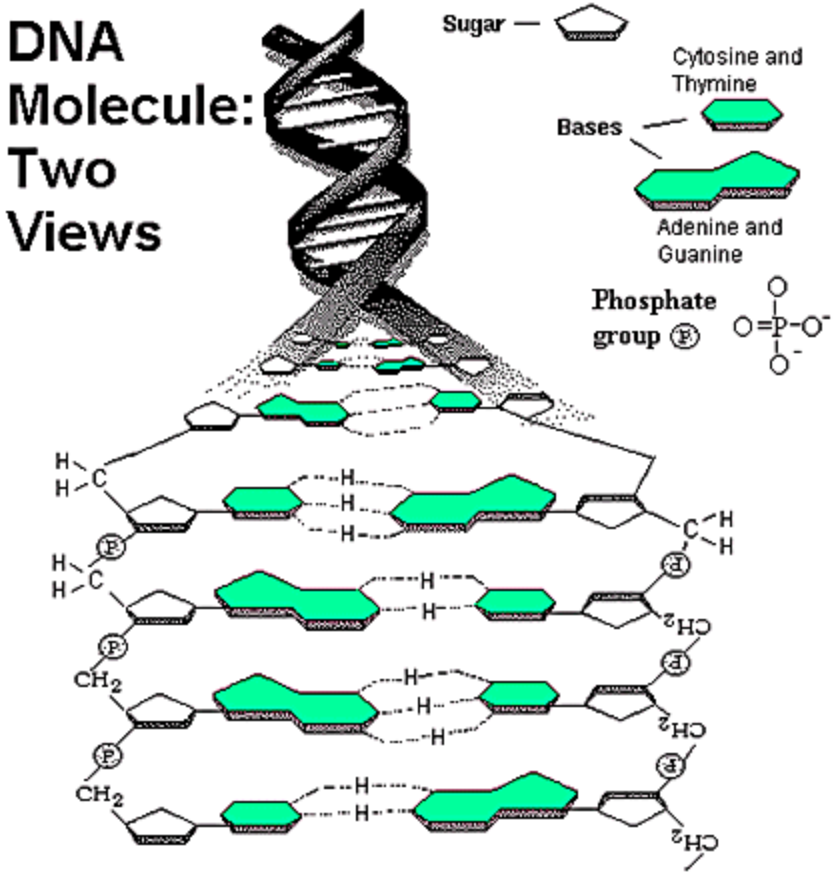
(LM in Chimica @units)

AA 2022/2023

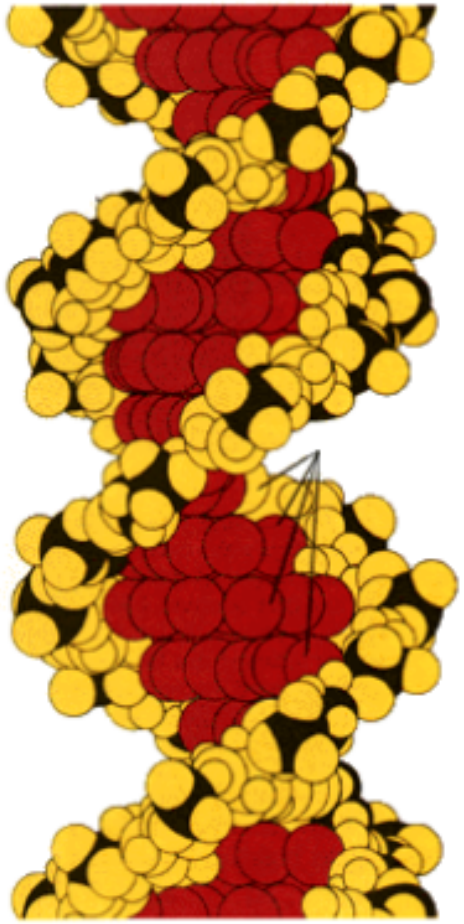
Prof. E. Iengo
eiengo@units.it

The original inspiration: Supramolecular systems in Nature

DNA



Information Storage



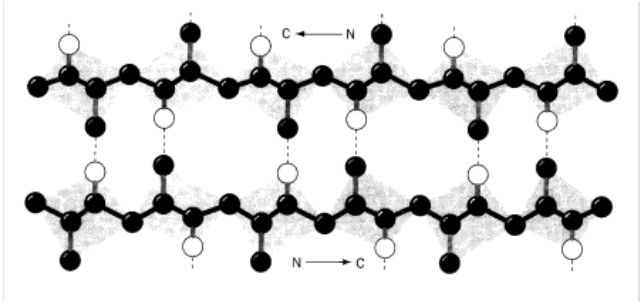
Watson & Crick 1953

The ultimate supramolecular material?

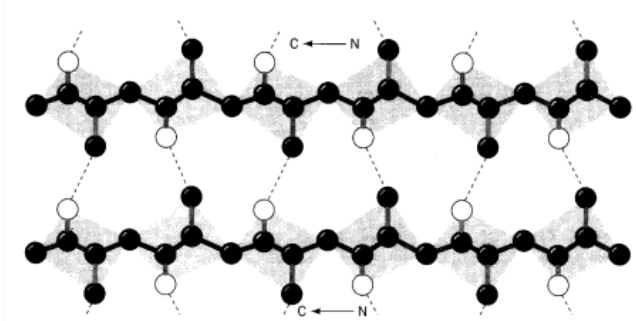
- Encodes gigabytes of data
- Can Self-Replicate
- Built-in Error Correction
- Is the basis of life

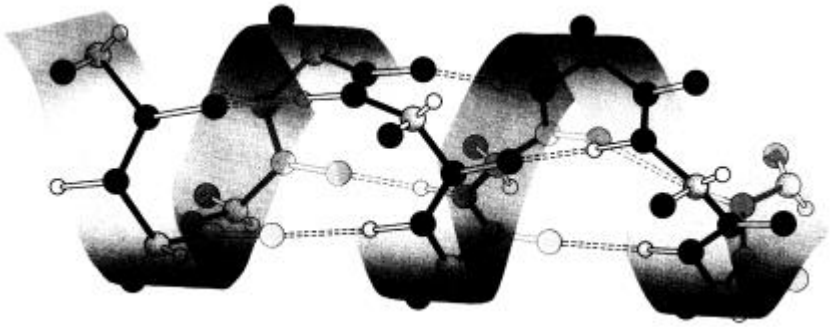
The original inspiration:
Supramolecular systems in Nature

PROTEINS



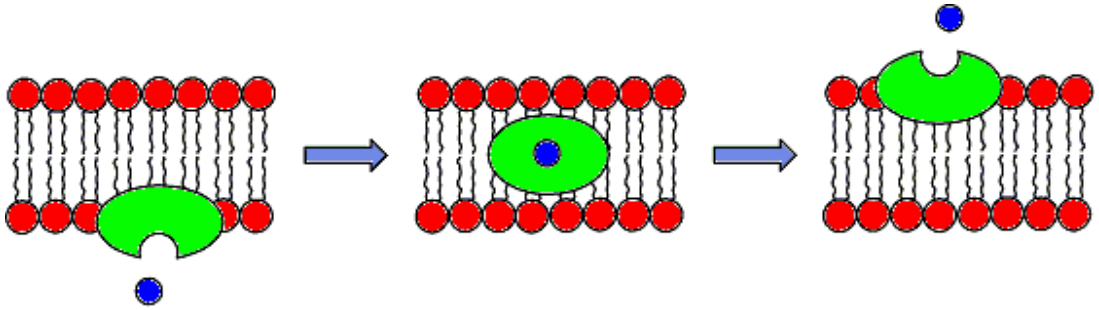
(a)

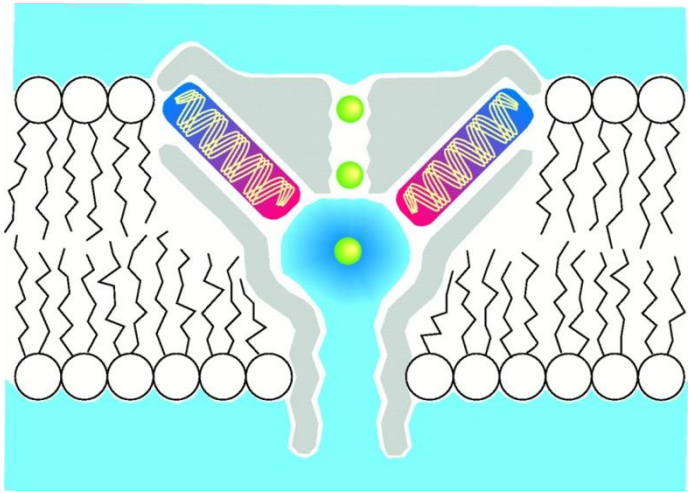




The original inspiration: Supramolecular systems in Nature

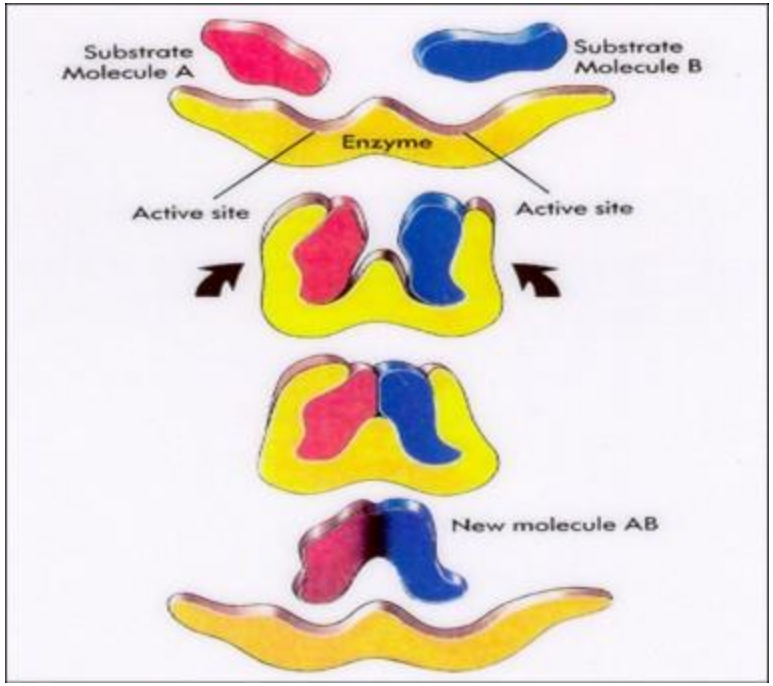
MEMBRANES and TRANSMEMBRANE CARRIERS





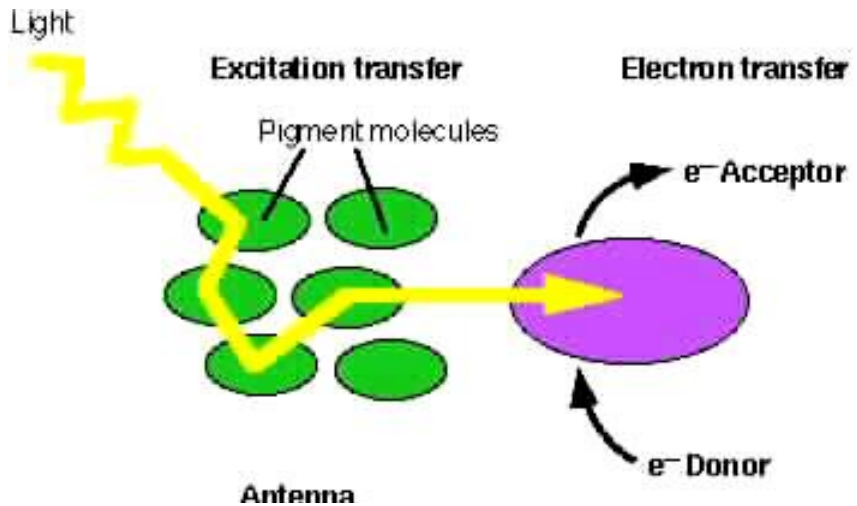
The original inspiration: Supramolecular systems in Nature

ENZYMES

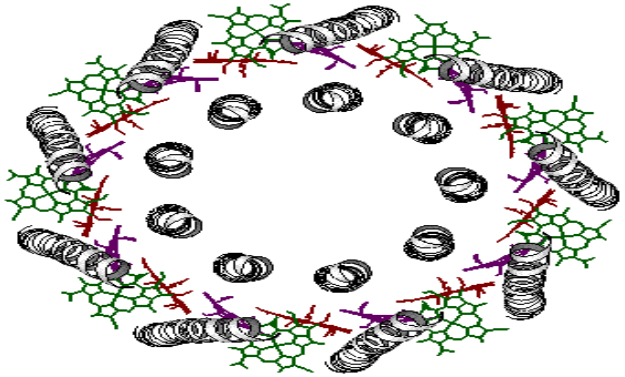


The original inspiration: Supramolecular systems in Nature

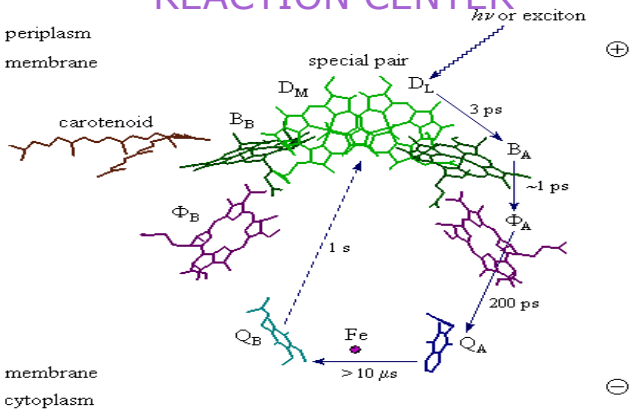
THE PHOTOSYNTHETIC APPARATUS



ANTENNA UNITS

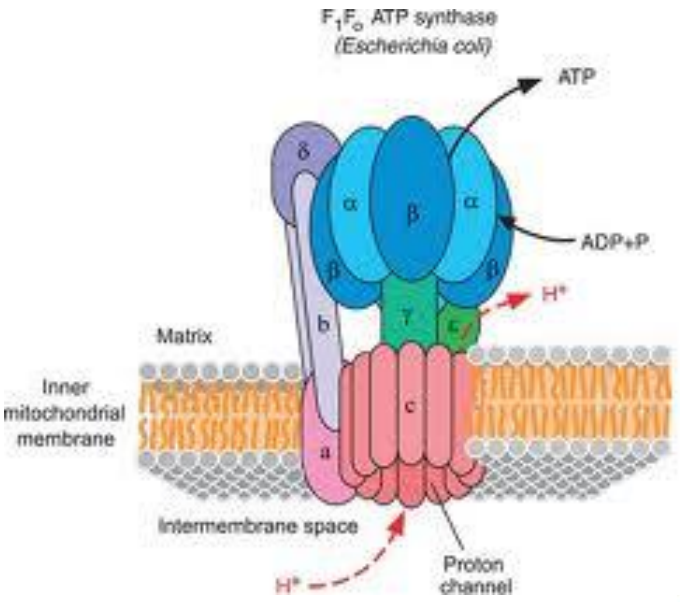


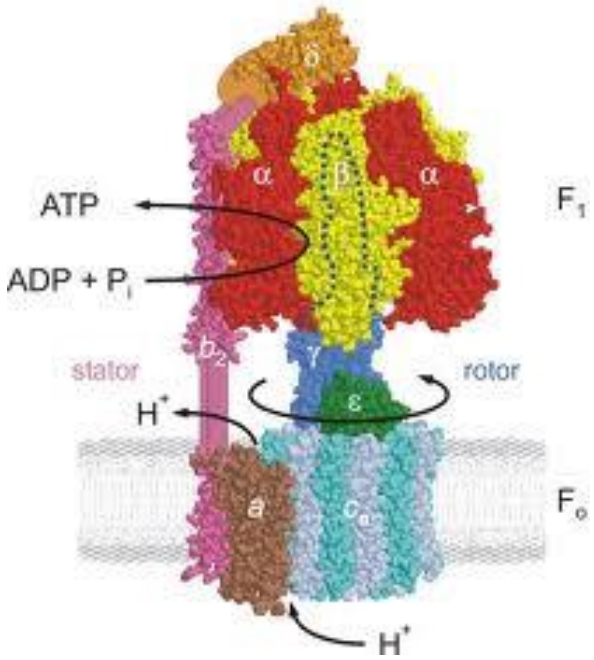
REACTION CENTER



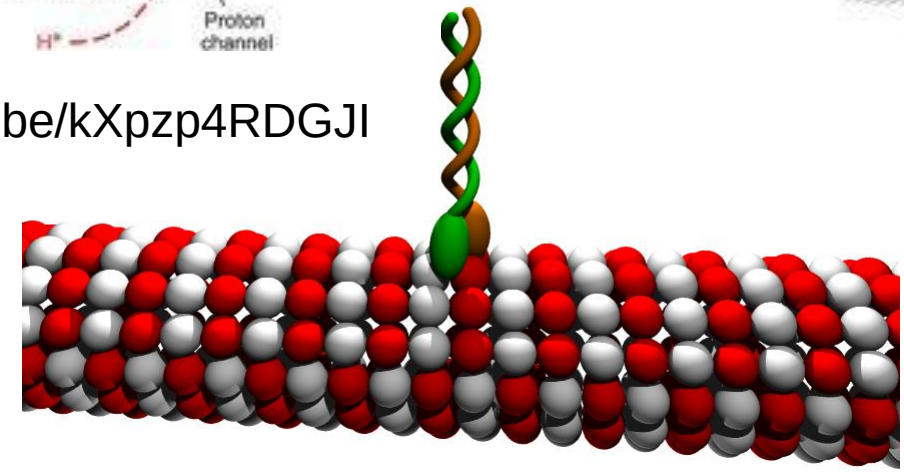
The original inspiration: Supramolecular systems in Nature

ATP Synthase and KINESIN





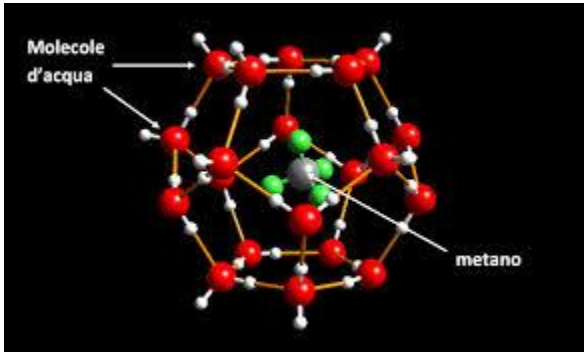
https://youtu.be/kXpzp4RDGJI



https://youtu.be/y-uuk4Pr2i8

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,…

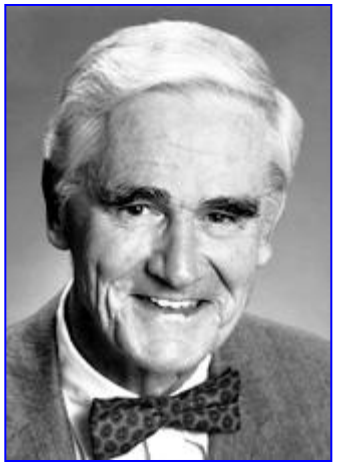
Molecular machines, containers, nanoscale flasks, nanoassemblies, supramolecular architectures, cages, trasporters, molecular magnets, nanoparticles, nanoballs, channels, tubes,…

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

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

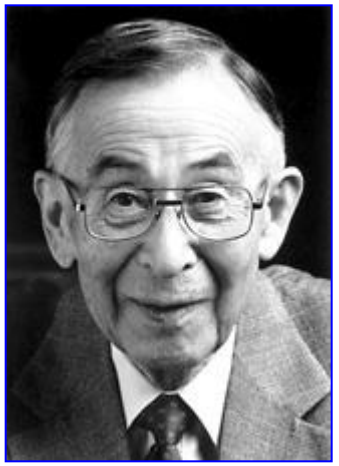
Imaging, Sensing, Recognition, Catalysis, Switching, …

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

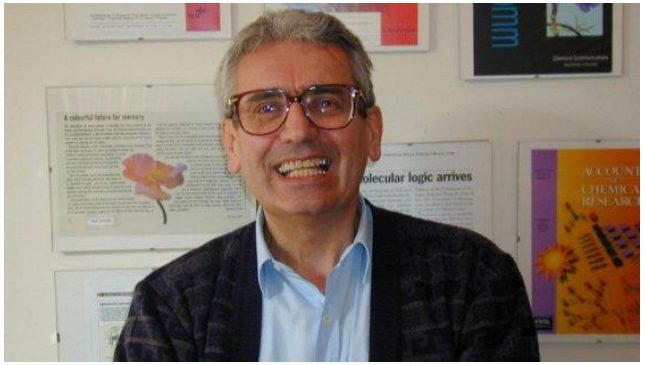
Sir J. F. Stoddart

B. L. Feringa

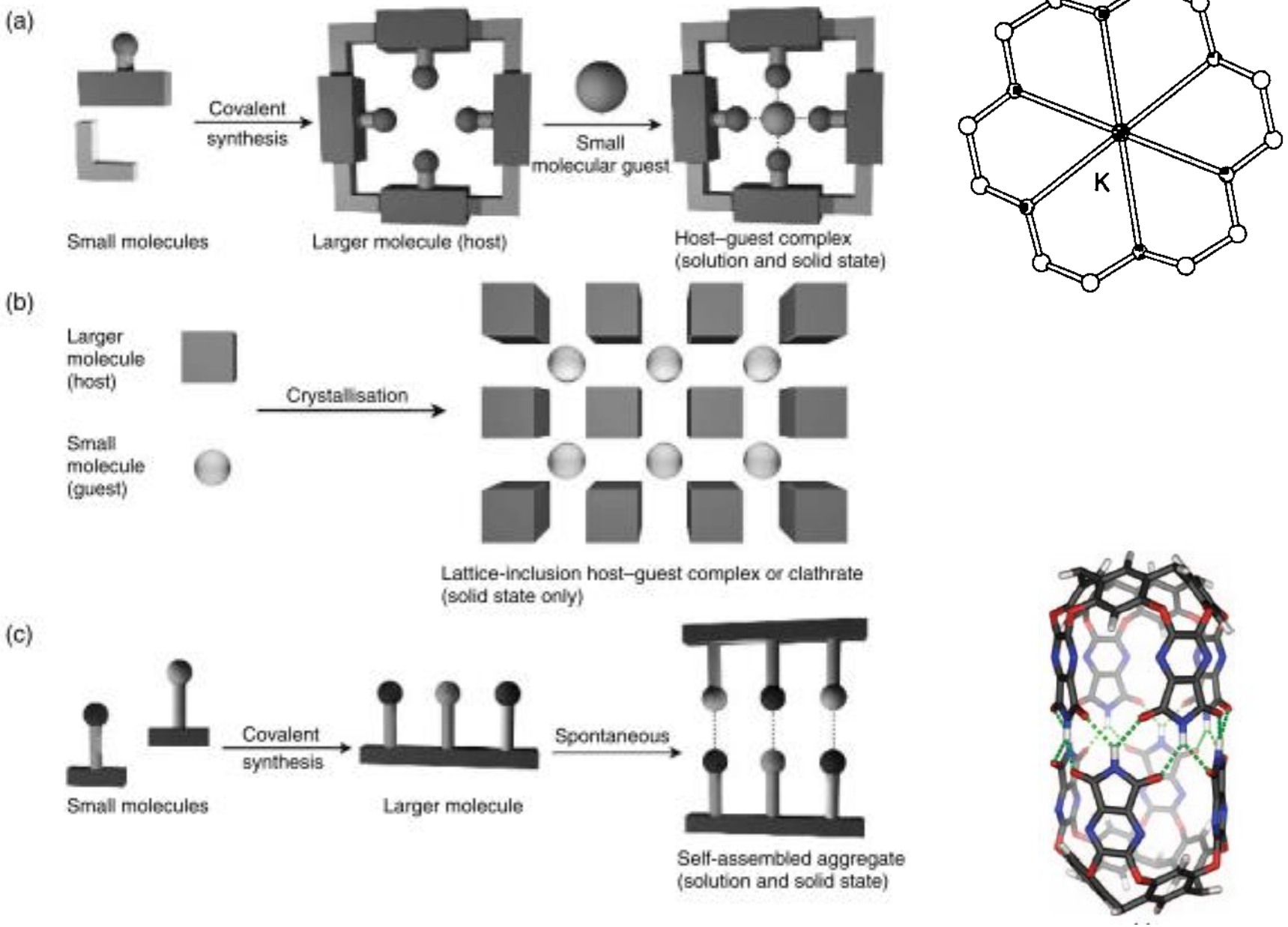
"for the design and synthesis of molecular machines"

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

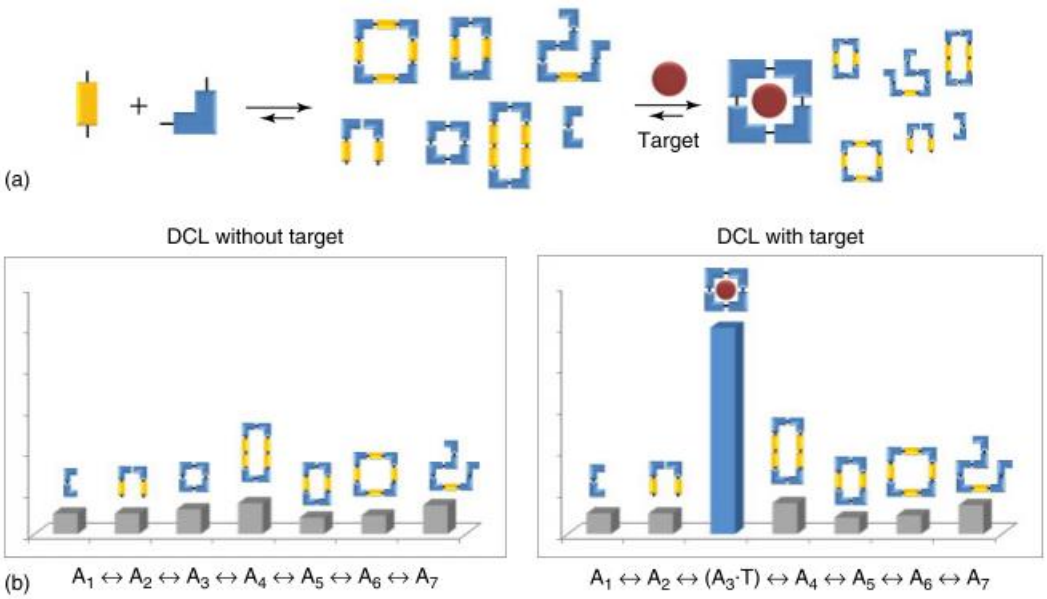
Chimica, il Nobel mancato

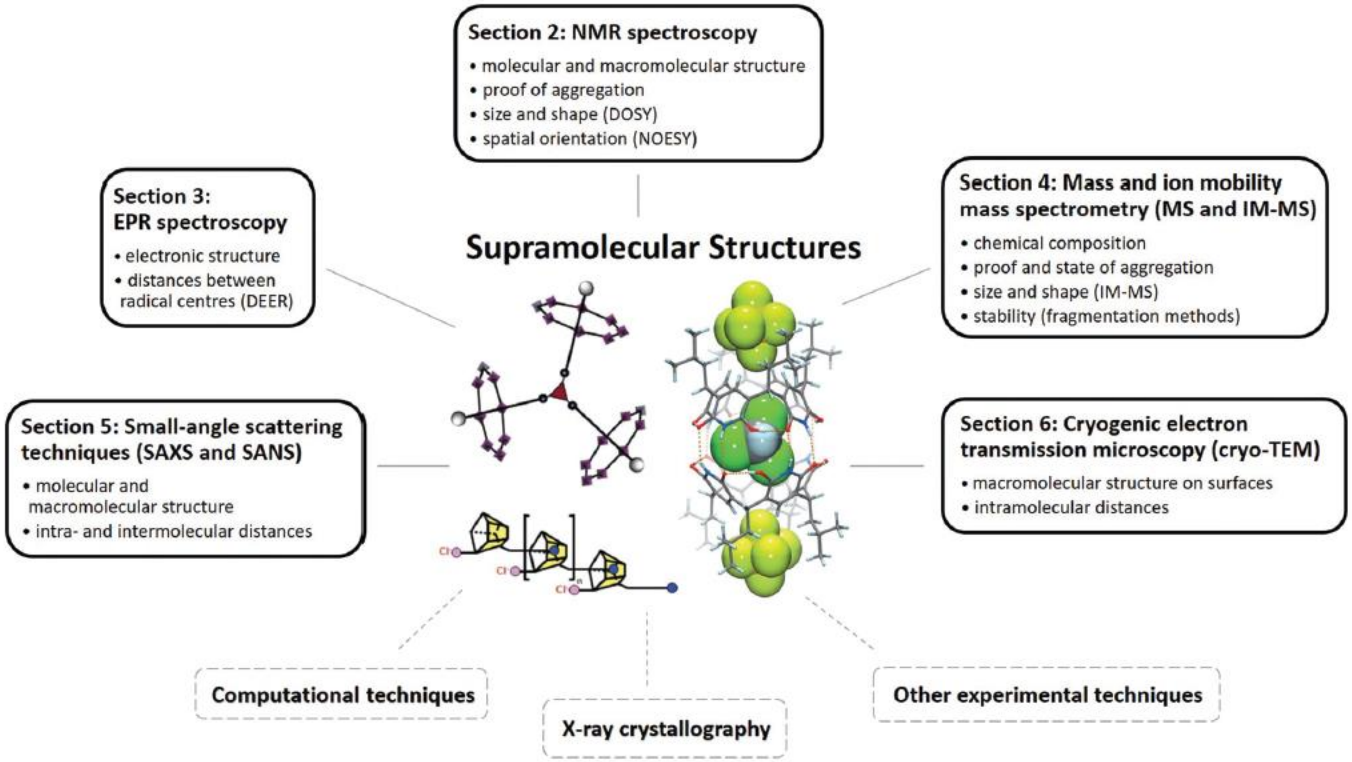


Prof. Vincenzo Balzani, docente emerito dell‘Università di Bologna

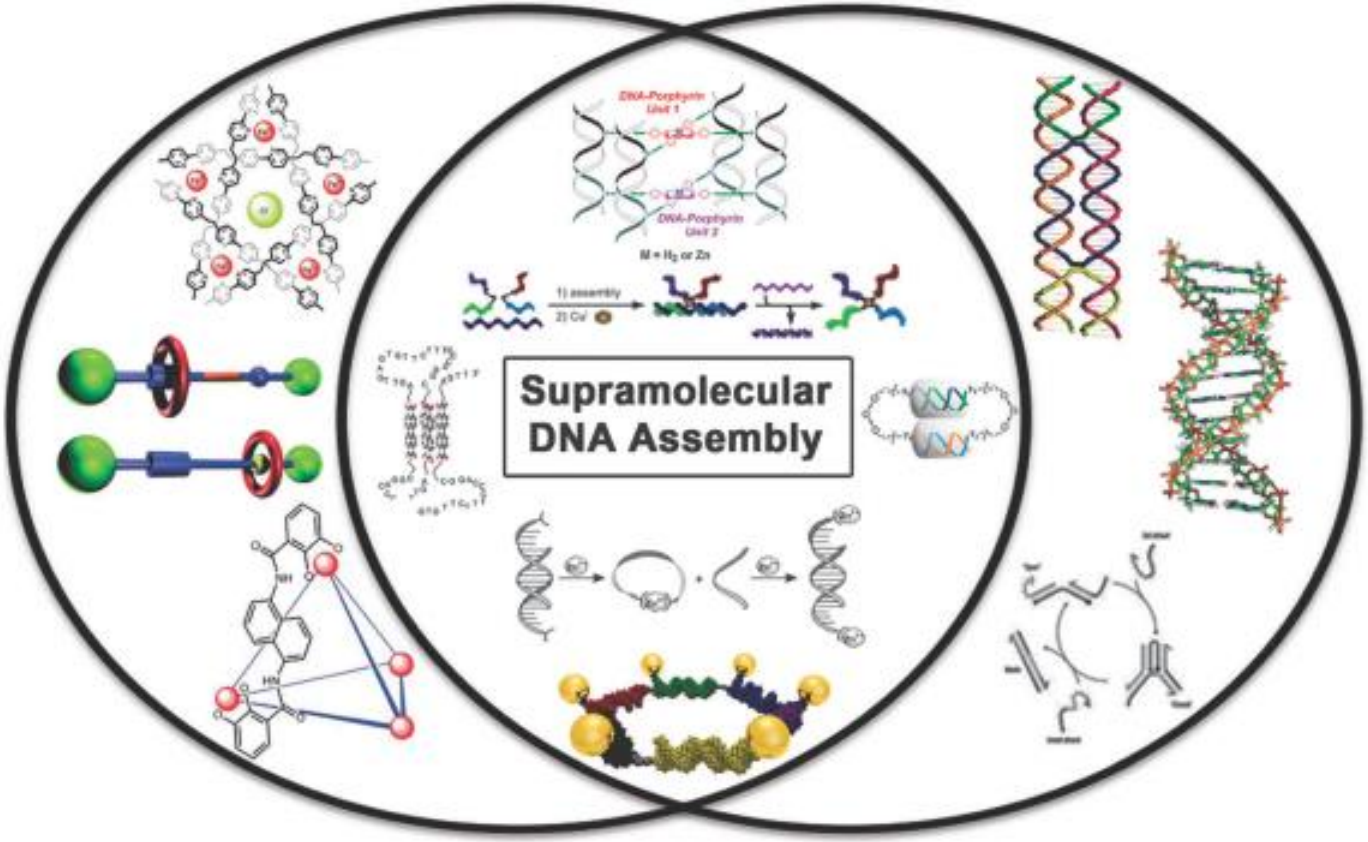

(a)
Covalent
synthesis
Small
molecular guest
Small molecules
Larger molecule (host)
Host–guest complex
(solution and solid state)
(b)
Larger
molecule
(host)
Small
molecule
(guest)
Crystallisation
Lattice-inclusion host–guest complex or clathrate
(solid state only)
(c)
Covalent
synthesis
Spontaneous
Small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

DYNAMIC COMBINATORIAL LIBRARIES

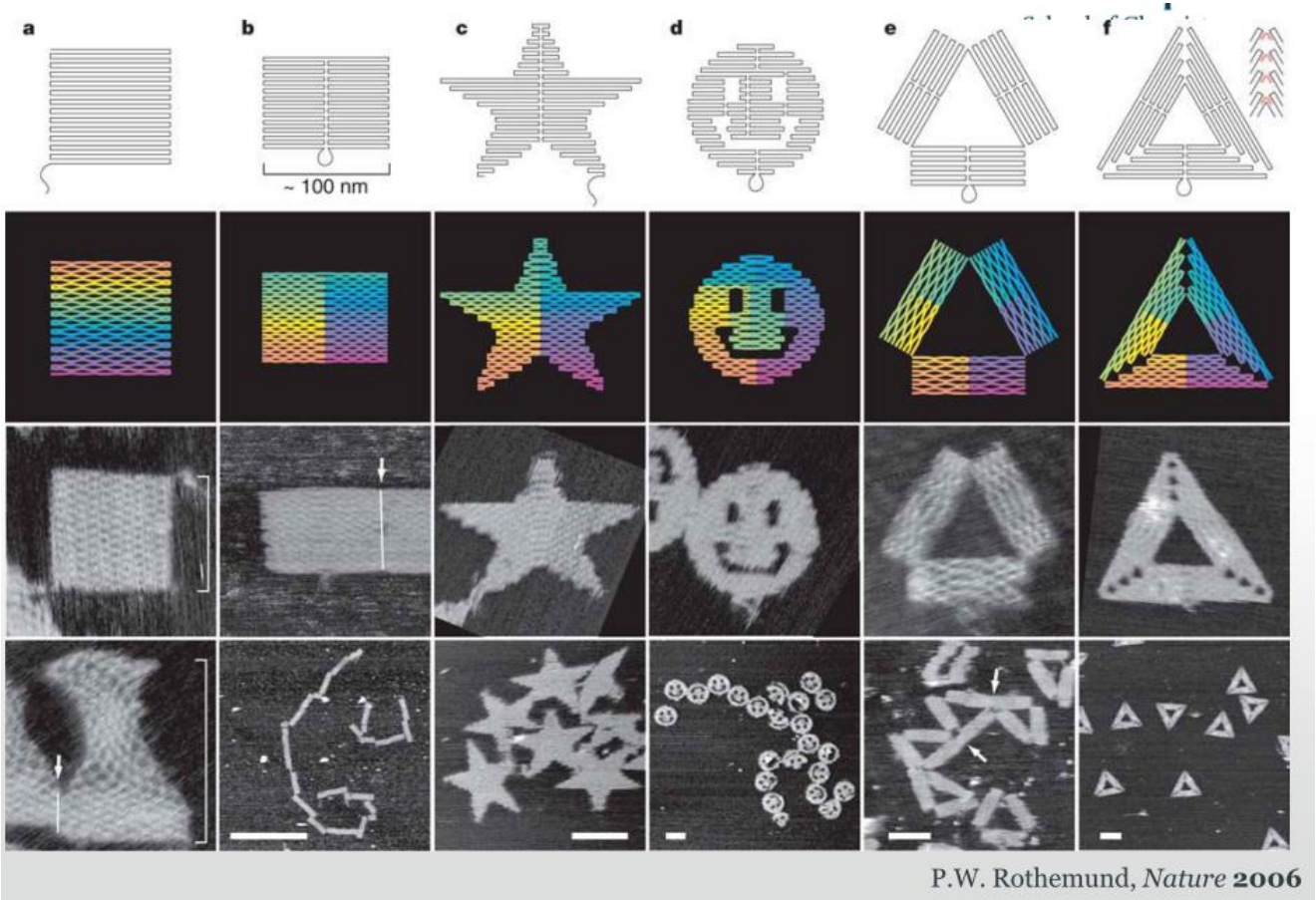



Section 2: NMR spectroscopy
• molecular and macromolecular structure
• proof of aggregation
• size and shape (DOSY)
• spatial orientation (NOESY)
Section 3:
EPR spectroscopy
• electronic structure
• distances between radical centres (DEER)
Supramolecular Structures
Section 4: Mass and ion mobility mass spectrometry (MS and IM-MS)
• chemical composition
• proof and state of aggregation
• size and shape (IM-MS)
• stability (fragmentation methods)
Section 5: Small-angle scattering techniques (SAXS and SANS)
• molecular and macromolecular structure
• intra- and intermolecular distances
Section 6: Cryogenic electron transmission microscopy (cryo-TEM)
• macromolecular structure on surfaces
• intramolecular distances
Computational techniques
X-ray crystallography
Other experimental techniques

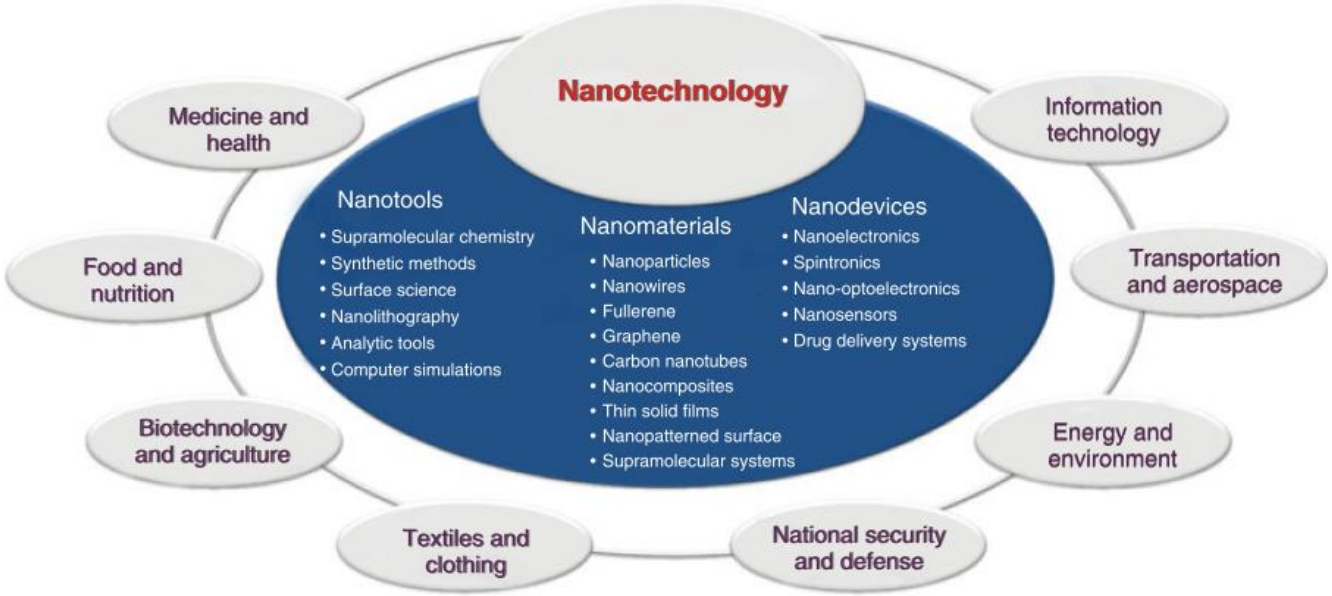
The bridge:
Supramolecular ARTIFICIAL and NATURAL systems

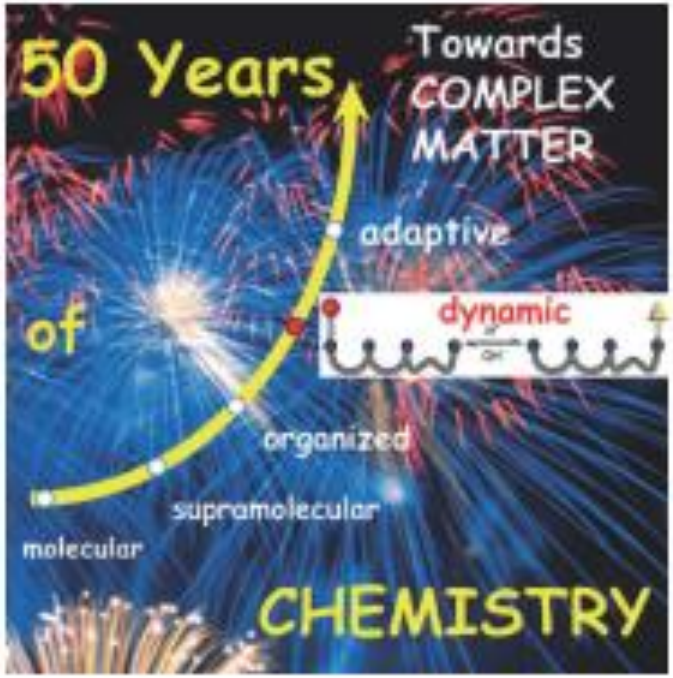


Folding DNA to create NANOSCALE SHAPES AND PATTERNS



From Supramolecular Chemistry to Nanotechnology




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

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**.

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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

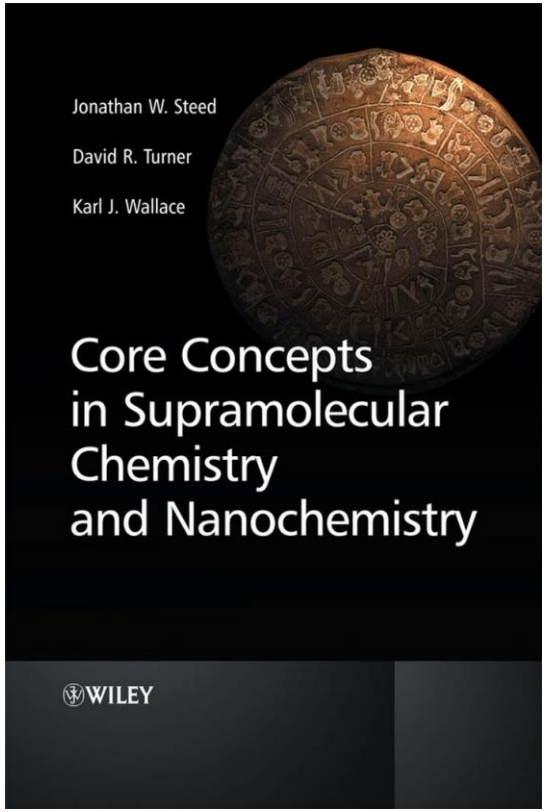
Jonathan W. Steed,
Durham University, UK

David R. Turner,
Monash University, Australia

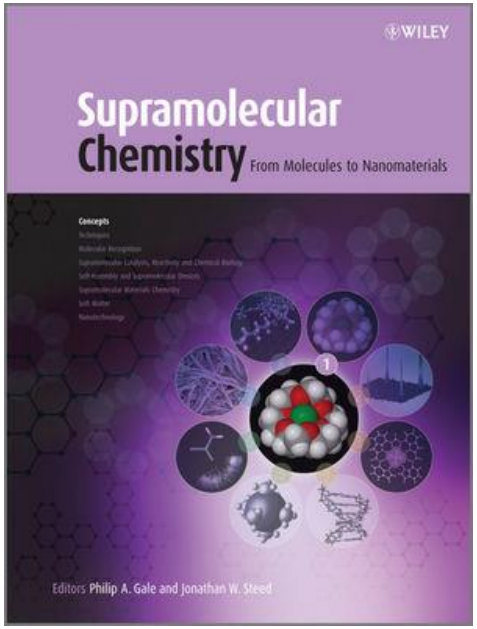
Karl J. Wallace,
University of Southern Mississippi, USA

BICENTENNIAL 1807 WILEY 2007 BICENTENNIAL

John Wiley & Sons, Ltd

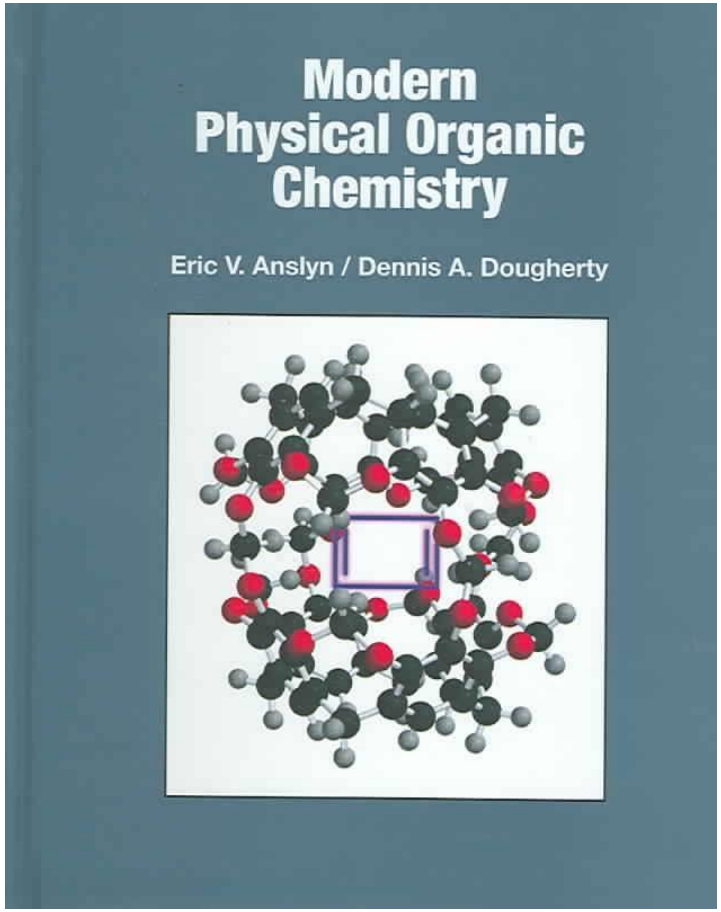


Bibliography



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

Bibliography



Eric V. Anslyn, Dennis A. Dougherty
University Science Books, 2006

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

Autoassemblaggio di gabbie con ioni nudi (Dr. I. Regeni 2h**)**

Programma

Chimica Topologica

Elicati/Catenani/Rotaxani/Nodi

Dispositivi e Macchine molecolari

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

Dynamic Combinatorial Chemistry (Prof. P. Pengo 3h)

Registrazione delle lezioni su MsTeams

Esame orale (discussione articolo)

Dispense e Capitolo su Metodi Analitici

- Dispense
- Capitolo Tecniche Analitiche

Diapositive Parte 1-2

- Prima Parte documento PDF
- Seconda Parte documento PDF

Diapositive Parte 3-4

- Terza Parte documento PDF
- Quarta Parte documento PDF

Diapositive Parte 5-7

- Quinta Parte documento PDF
- Sesta Parte documento PDF
- Parte 7 documento PDF

Articoli Ottobre

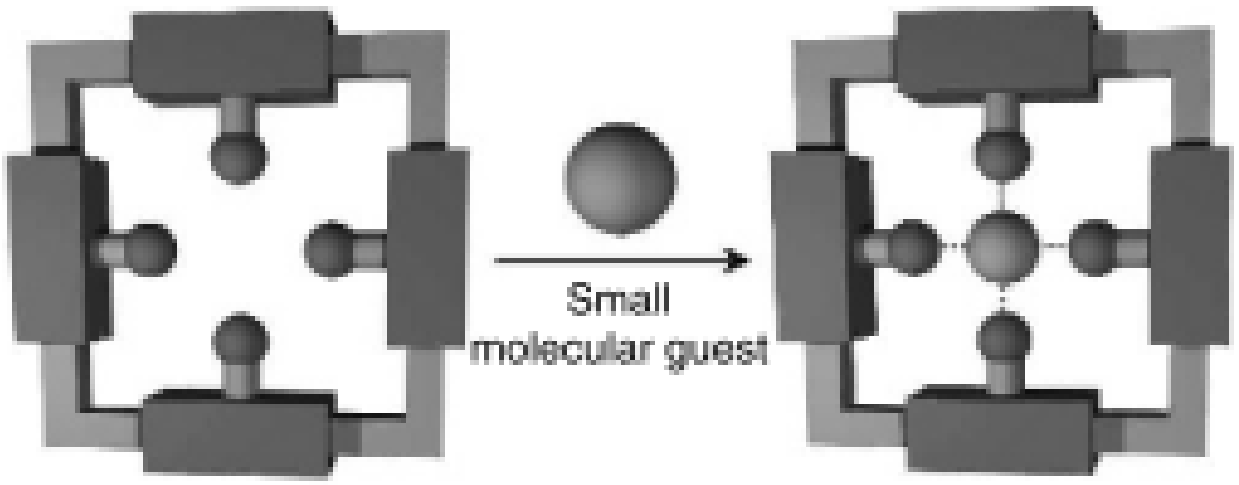
- Approfondimenti
- Discussione

Articoli Novembre

- Approfondimenti
- Discussione

Articoli Dicembre

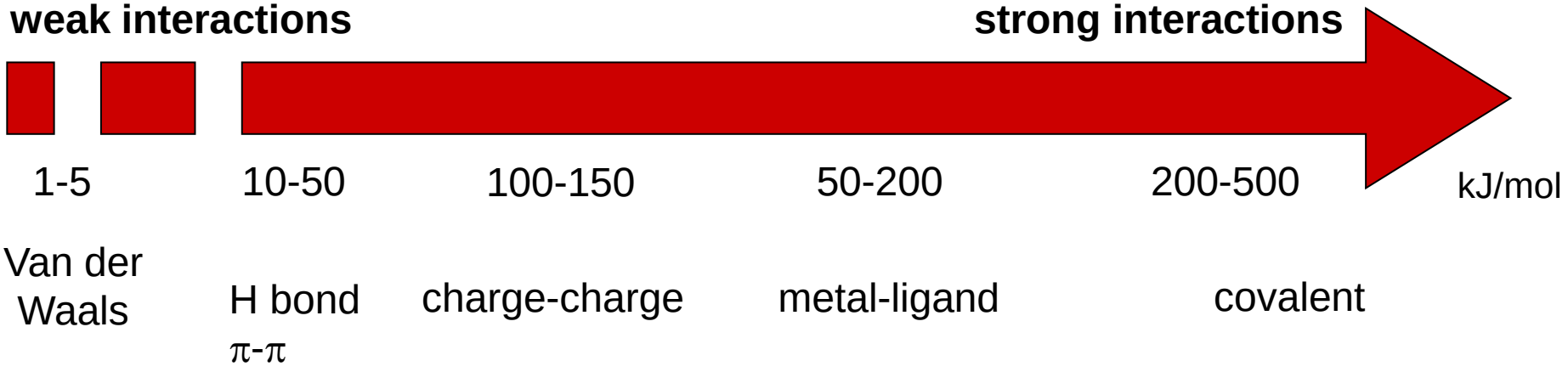
- Approfondimenti
- Discussione


Small
molecular guest

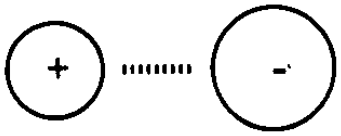
Weak (Reversible) Intermolecular Interactions

- 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

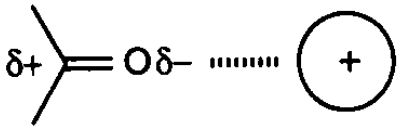
Weak Intermolecular Interactions



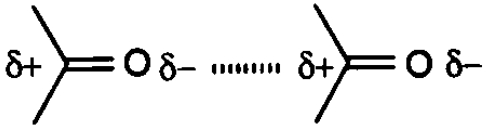
Electrostatic Interactions



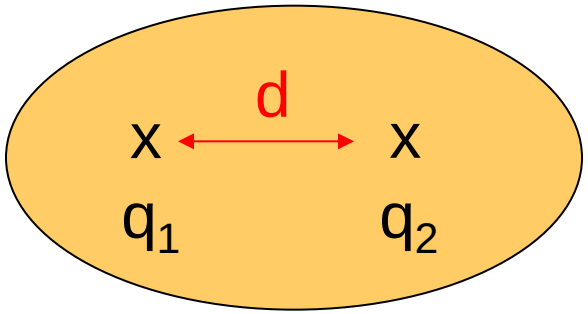
Charge-Charge Interactions 100-350 kJ/mol



Dipole-Charge Interactions 50-200 kJ/mol



Dipole-Dipole Interactions 5-50 kJ/mol



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

vacuum permittivity

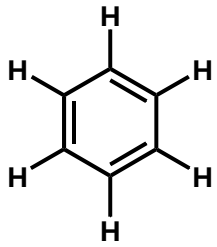
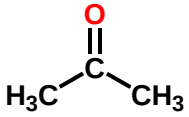
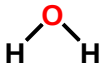
dielectric constant (nature of solvant)

ε(vacuum) = 1

apolar medium ⇔ ε small (~ 2)

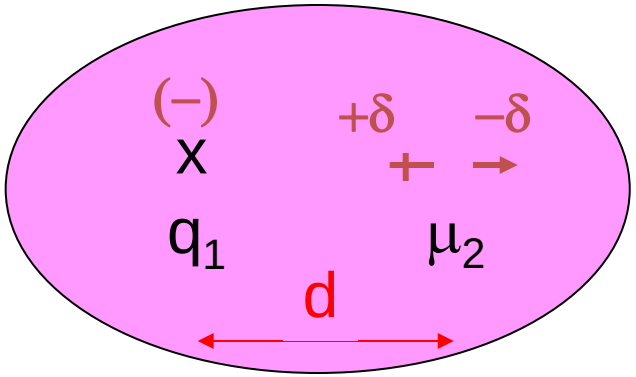
polar medium ⇔ ε big (H_2O ~ 80)

dielectric constant of the solvant

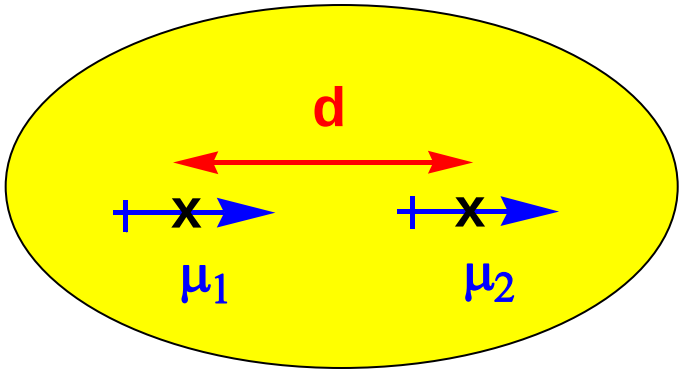
		ε	
Benzene		2,3	apolar
Acetone		20,7	
Ethanol	CH_3CH_2OH	24,3	
water		78,5	polar

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

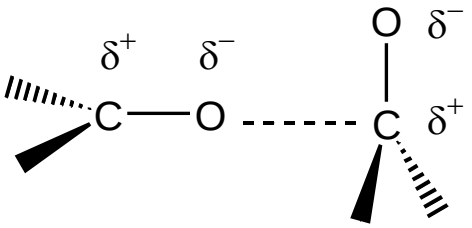
ε = 2 d = 0.5 nm => W = 140 kJ.mol^{-1}

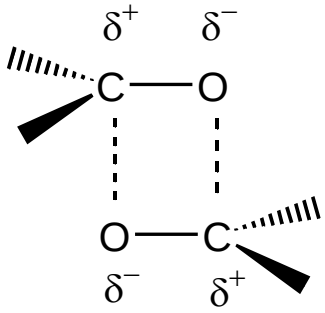


$$W = - C^{te} \times \frac{|q|\mu_2}{\varepsilon d^2}$$

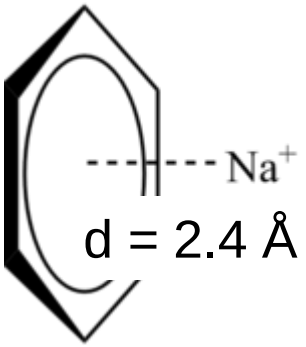


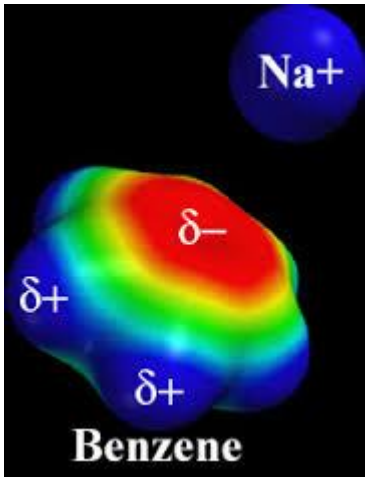
$$W = - C^{te} \frac{\mu_1 \mu_2}{\varepsilon d^3}$$

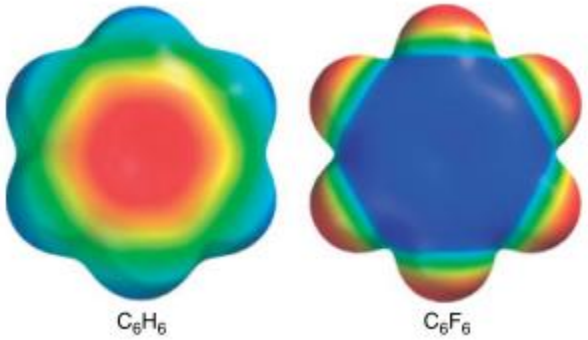




Cation-π Interactions







CHEMICAL REVIEWS

Review

pubs.acs.org/CR

dx.doi.org/10.1021/cr300222d | *Chem. Rev.* 2013, 113, 2100–2138

Cation–π Interaction: Its Role and Relevance in Chemistry, Biology, and Material Science

A. Subha Mahadevi and G. Narahari Sastry*

ACCOUNTS of chemical research

Vol. 46, No. 4 ■ 2013 ■ 885–893 ■ ACCOUNTS OF CHEMICAL RESEARCH

The Cation–π Interaction

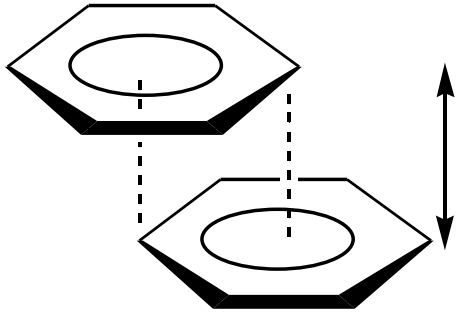
DENNIS A. DOUGHERTY

Chem. Rev. **1997,** *97,* 1303–1324

The Cation–π Interaction

Jennifer C. Ma and Dennis A. Dougherty*

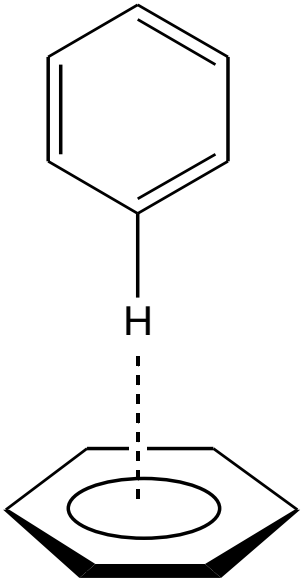
π-π Interactions up to 50 kJ/mol

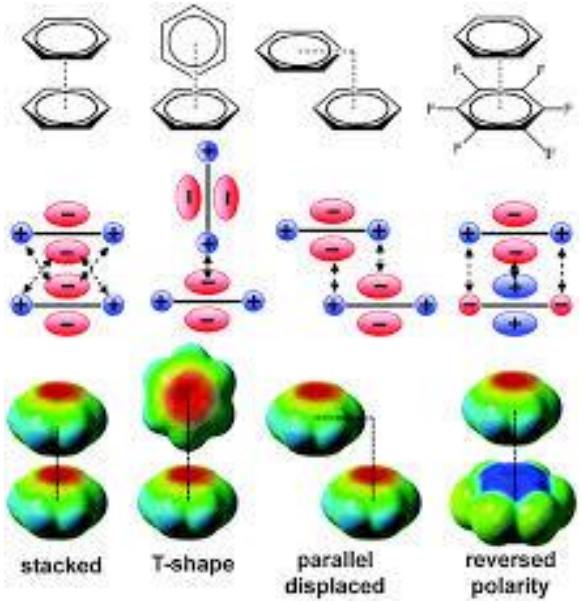


face to face

3.5 A

edge to face

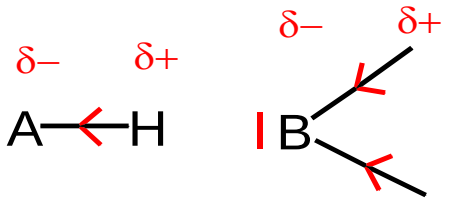




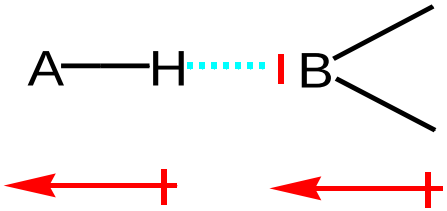
C.A. Hunter and J.K.M. Sanders, ***The Nature of π - π interactions***, *J. Am. Chem. Soc.,* **1990**, *112*, 5525;

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.

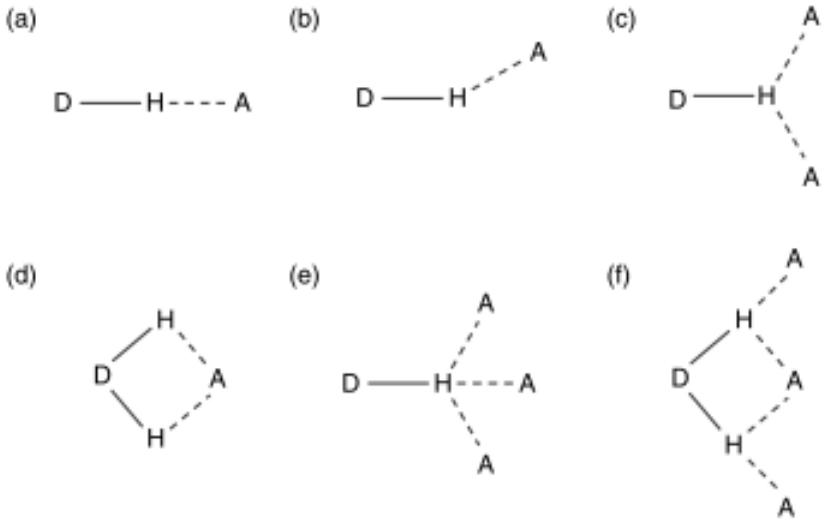
H Bond 4-120 kJ/mol



A, B electronegative or electrondeficient atoms



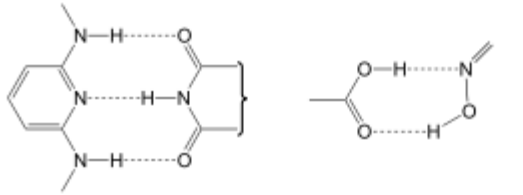
permanent dipoles



The Hydrogen Bond in the Solid State

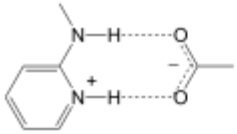
Thomas Steiner*

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



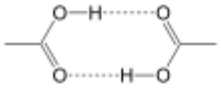
a) P_m = 97 %

b) P_m = 90 %

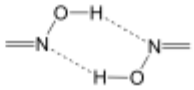


c) P_m = 82 %

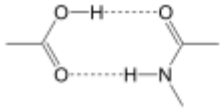
d) P_m = 51 %



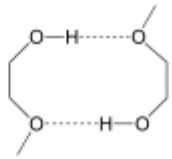
e) P_m = 33 %



f) P_m = 27 %

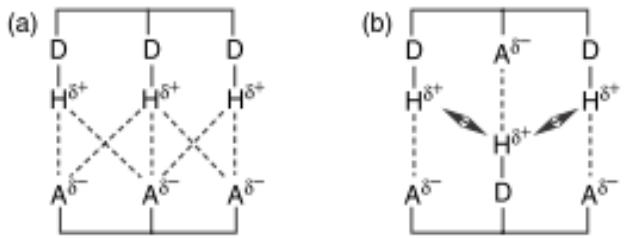


g) P_m = 10 %



h) P_m = 5 %

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).

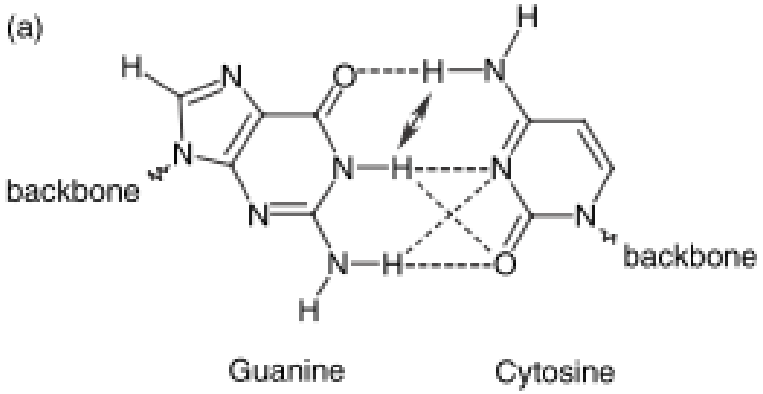


D Donor

A Acceptor

Attractive interaction

Repulsive interaction



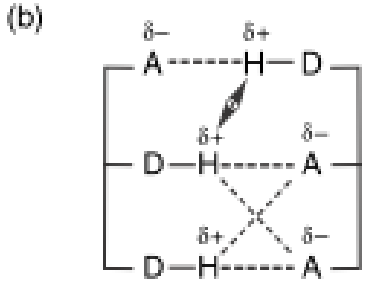


Table 1.5 Properties of hydrogen bonded interactions.

	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%
^1H 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**.

	Strong	Moderate	Weak
interaction type	strongly covalent	mostly electrostatic	electrostat./ dispers.
bond lengths [Å]			
H ··· A	1.2 – 1.5	1.5 – 2.2	> 2.2
lengthening of X–H [Å]	0.08 – 0.25	0.02 – 0.08	< 0.02
X–H versus H ··· A	X–H ≈ H ··· A	X–H < H ··· A	X–H ≪ H ··· A
X ··· A [Å]	2.2 – 2.5	2.5 – 3.2	> 3.2
directionality	strong	moderate	weak
bond angles [°]	170 – 180	> 130	> 90
bond energy [kcal mol^{-1}]	15 – 40	4 – 15	< 4
relat. IR shift $\Delta\tilde{\nu}_{XH}$ [cm^{-1}]	25 %	10 – 25 %	< 10 %
^{1}H downfield shift	14 – 22	< 14	

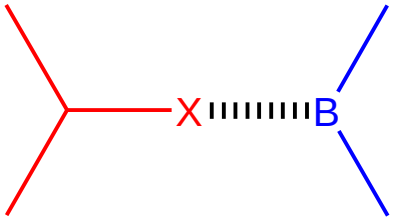
Halogen Bond

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. ”

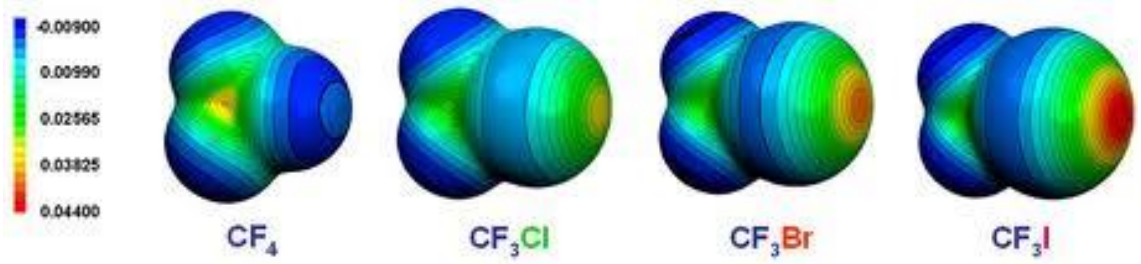
Halogen Bond



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



CHEMICAL REVIEWS

Review

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DOI: 10.1021/acs.chemrev.5b00484

The Halogen Bond

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

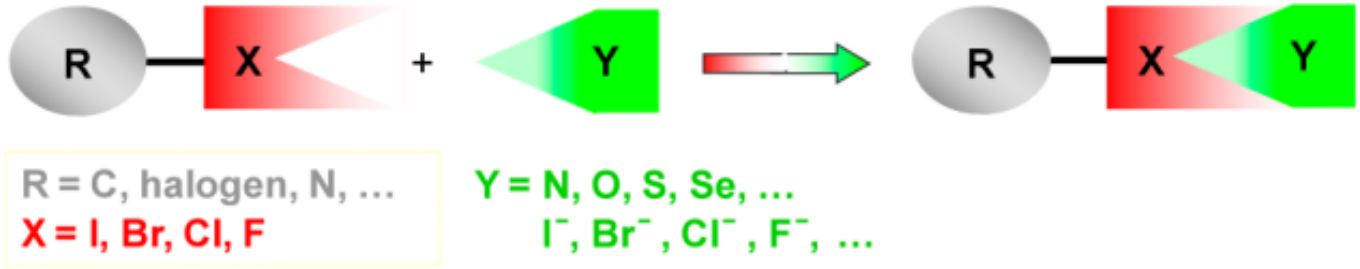


Figure 1. Schematic representation of the halogen bond.

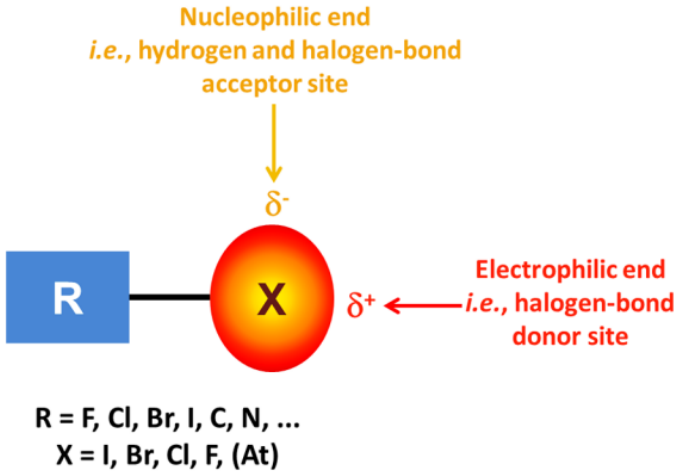


Figure 21. Schematic representation of the anisotropic distribution of the electron density around covalently bound halogen atoms and the pattern of the resulting interactions.

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

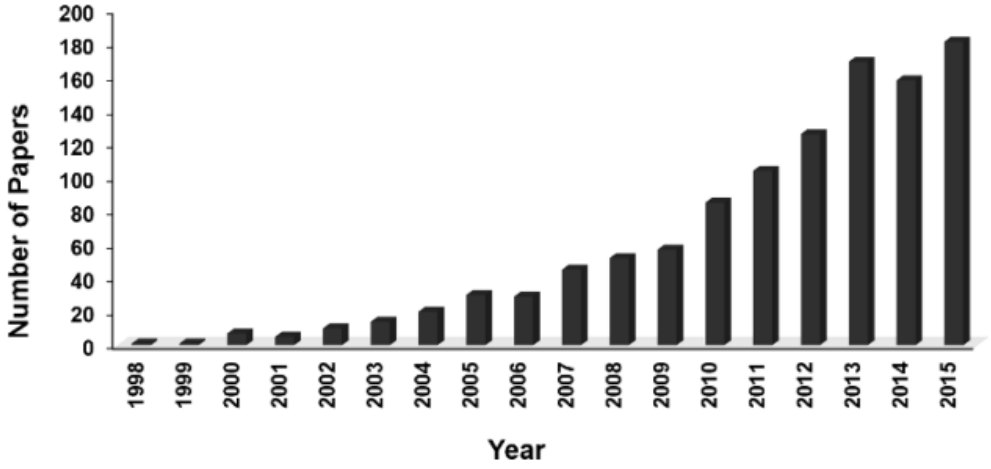
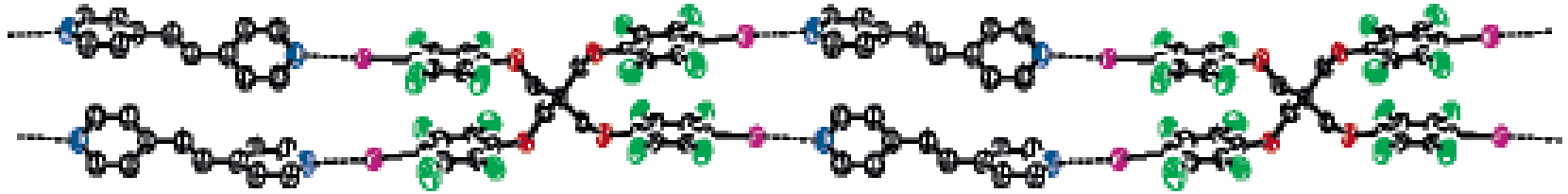
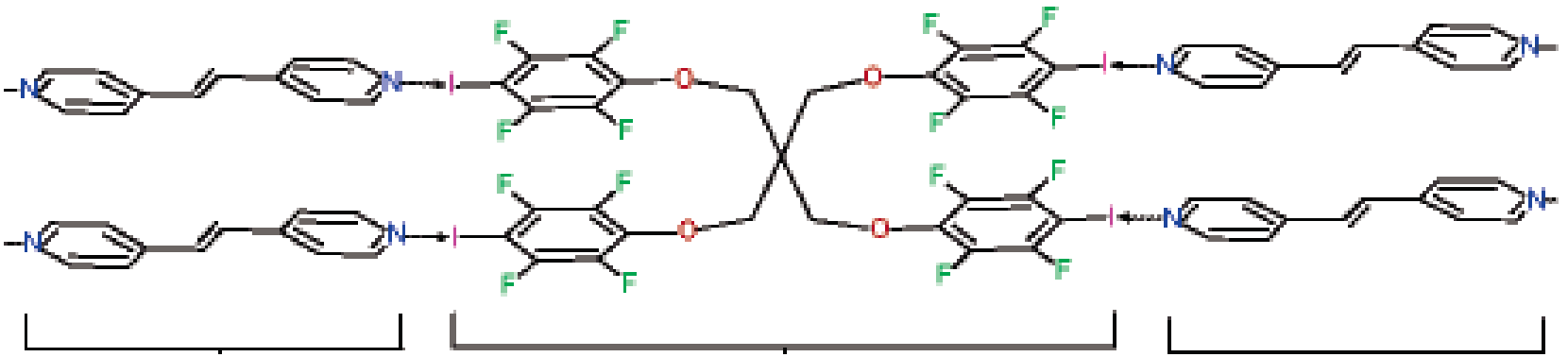
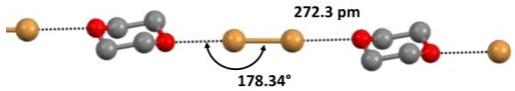


Figure 5. Number of papers per year having "halogen bonding" in the title and/or abstract (source SciFinder, search performed in November 2015).



14





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.

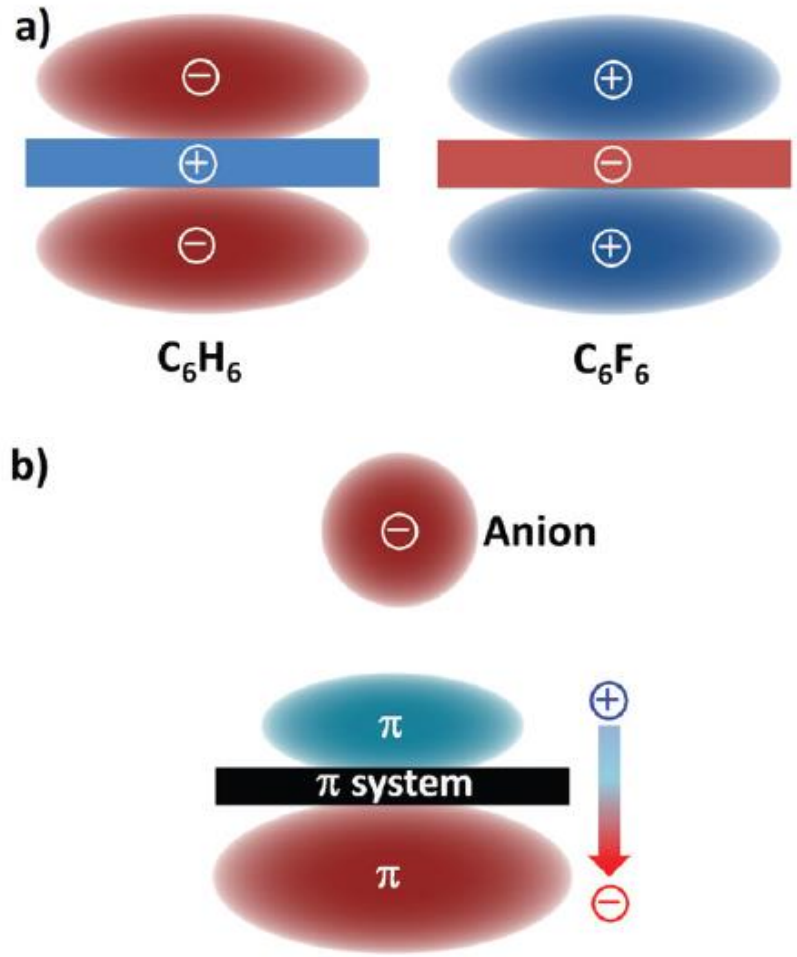


Fig. 1 (a) Schematic representation of the quadrupole moments of benzene (C_6H_6; Q_{zz} = −8.45 B) and hexafluorobenzene (C_6F_6; Q_{zz} = +9.50 B)[21] and (b) the ion-induced dipole[22] (the molecular polarizabilities parallel to the main symmetry axis are $\alpha_{\|}$ = 41.5 and 37.7 a.u (a.u. stands for atomic units), for benzene and hexafluorobenzene respectively).

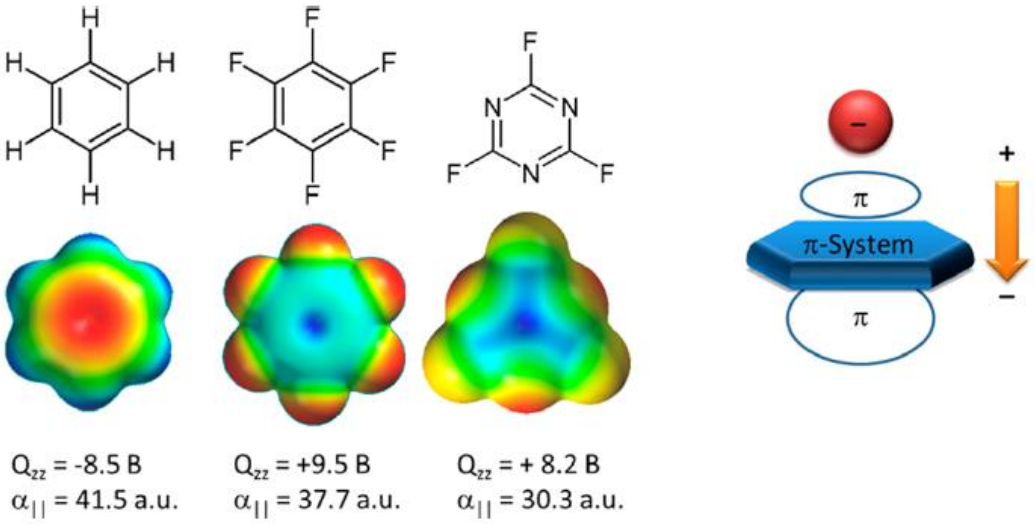


Figure 5. Structures and electron-density surfaces of selected arenes showing low electron density (blue region) in the aromatic core of C_6F_6 and $C_3N_3F_3$ (left). In addition the concept of "anion-induced dipole moment" is illustrated (right).[88]

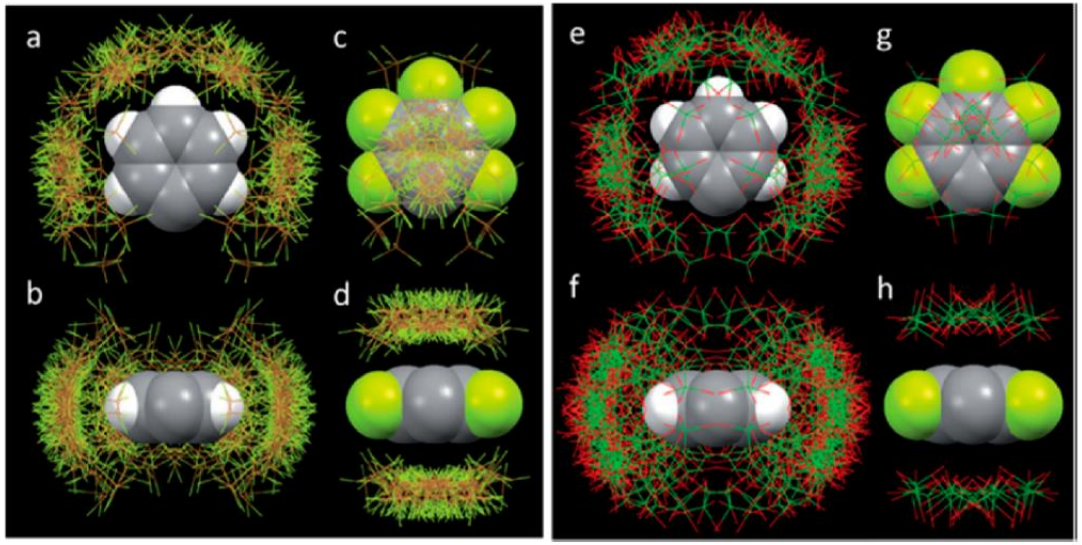


Figure 20. IsoStar plots showing anion contacts between C_6H_5 and BF_4^- (a and b) and ClO_4^- (e and f) as well as anion−π interactions between C_6F_5 and BF_4^- (c and d) and ClO_4^- (g and h). Reproduced and adapted with permission from ref 22. Copyright 2011 John Wiley and Sons.

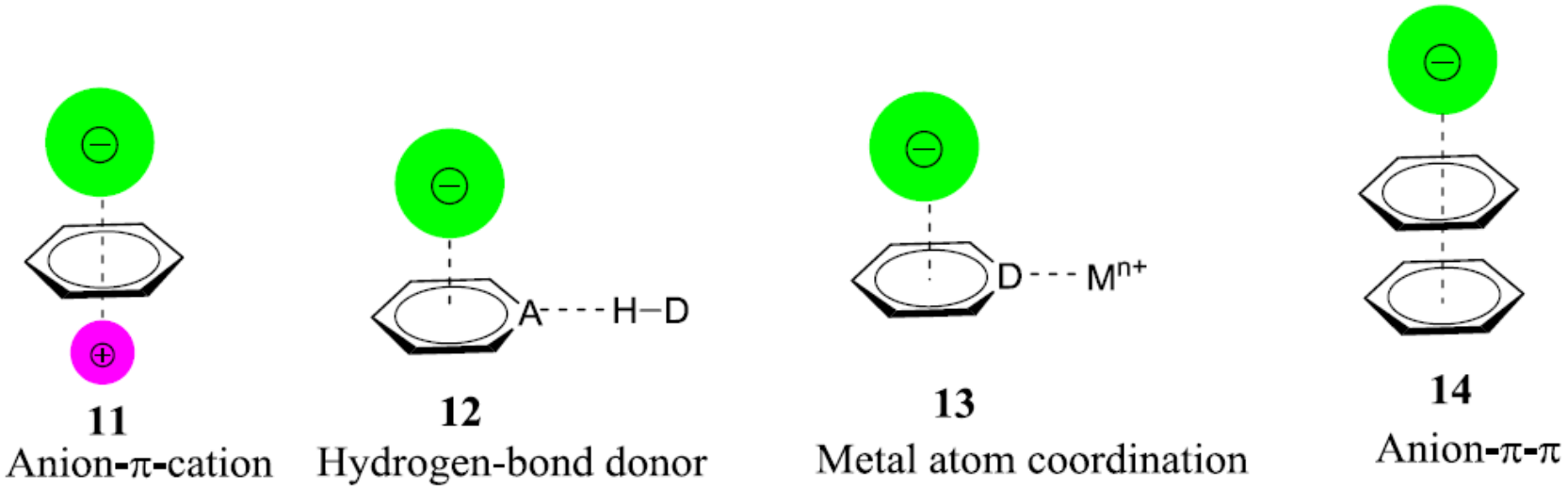


Fig. 4. Illustration of diverse factors affecting the strength of anion-π interactions.

Review Coordination Chemistry Reviews 415 (2020) 213327

Emergence of anion-π interactions: The land of opportunity in supramolecular chemistry and beyond

Ishfaq Ahmad Rather, Shafieq Ahmad Wagay, Rashid Ali *

Anion–π Interactions with Fluoroarenes

Michael Giese,*,† Markus Albrecht,*,‡ and Kari Rissanen*,§

DOI: 10.1021/acs.chemrev.5b00156
Chem. Rev. 2015, 115, 8867–8895

The anion–π interaction: naissance and establishment of a peculiar supramolecular bond

Patrick Gamez[a,b]

Cite this: *Inorg. Chem. Front.*, 2014, **1**, 35

Supramolecular Chemistry

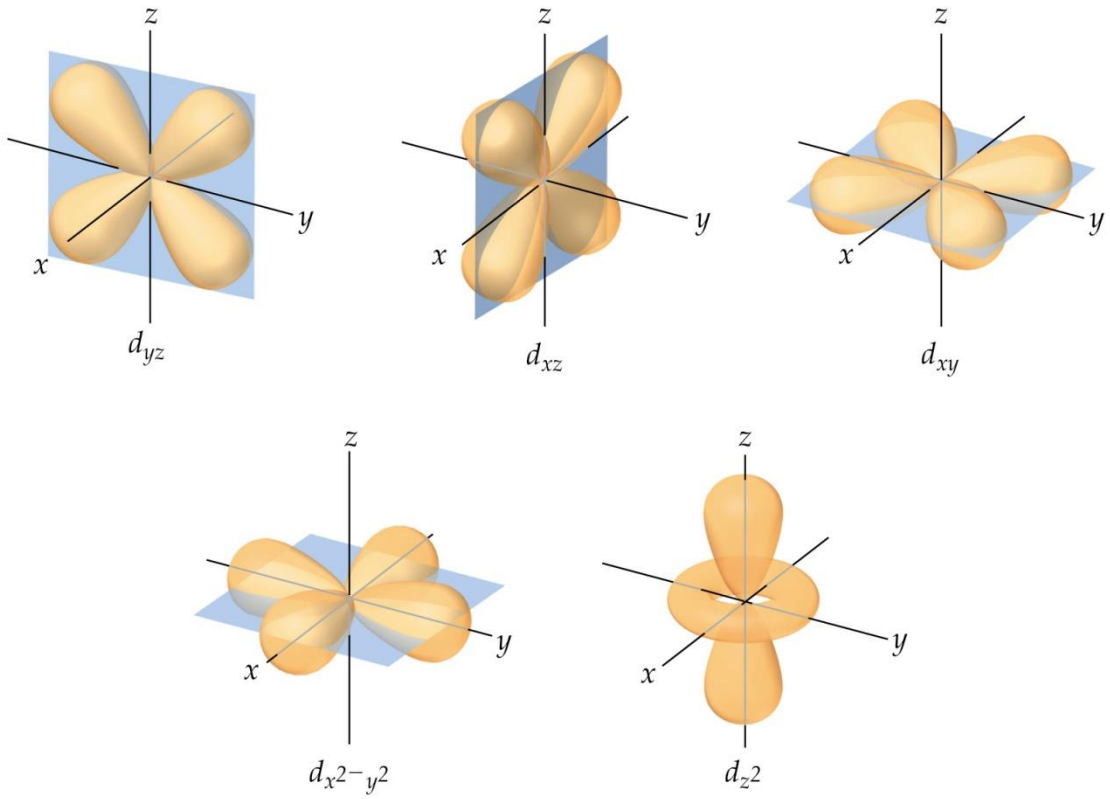
DOI: 10.1002/anie.201100208

Putting Anion–π Interactions Into Perspective

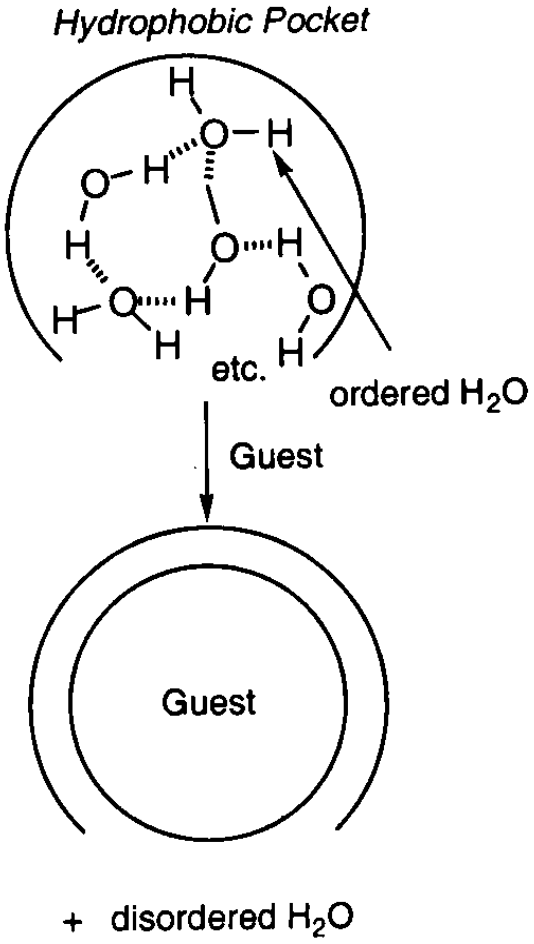
Antonio Frontera, Patrick Gamez,* Mark Mascal,* Tiddo J. Mooibroek,* and Jan Reedijk**

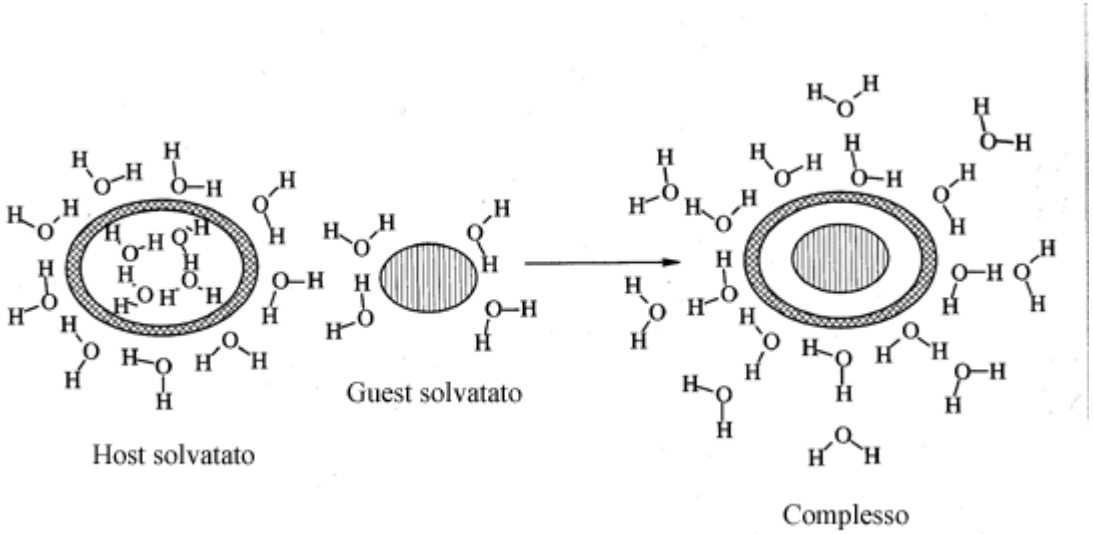
Angew. Chem. Int. Ed. **2011**, 50, 9564 – 9583

Metal-Ligand Interaction



Hydrophobic Effect





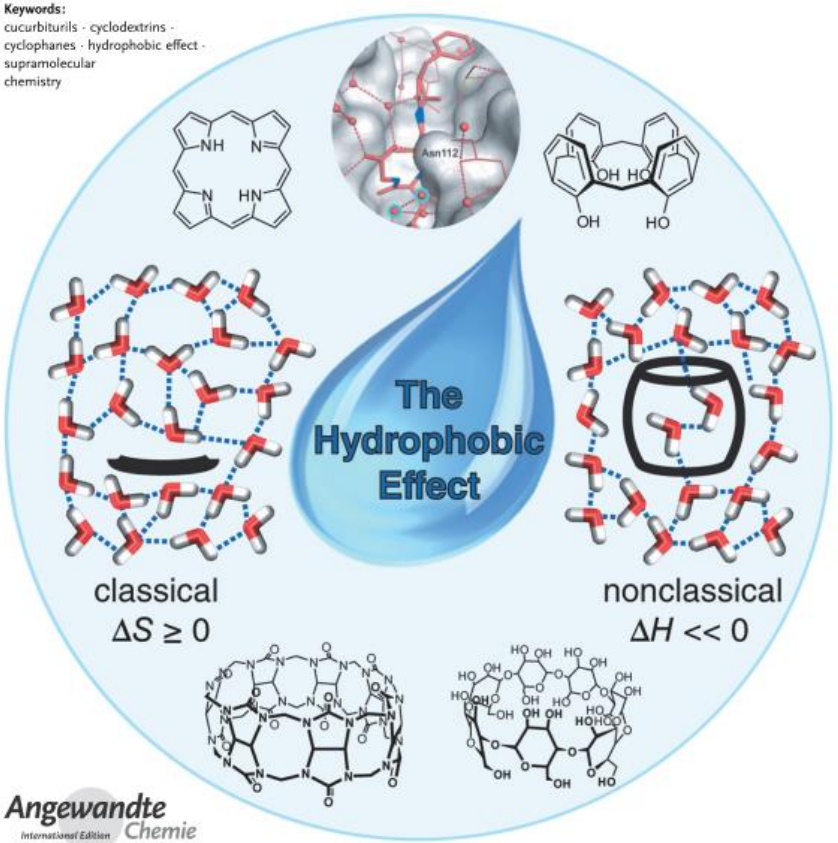
Hydrophobic Effect

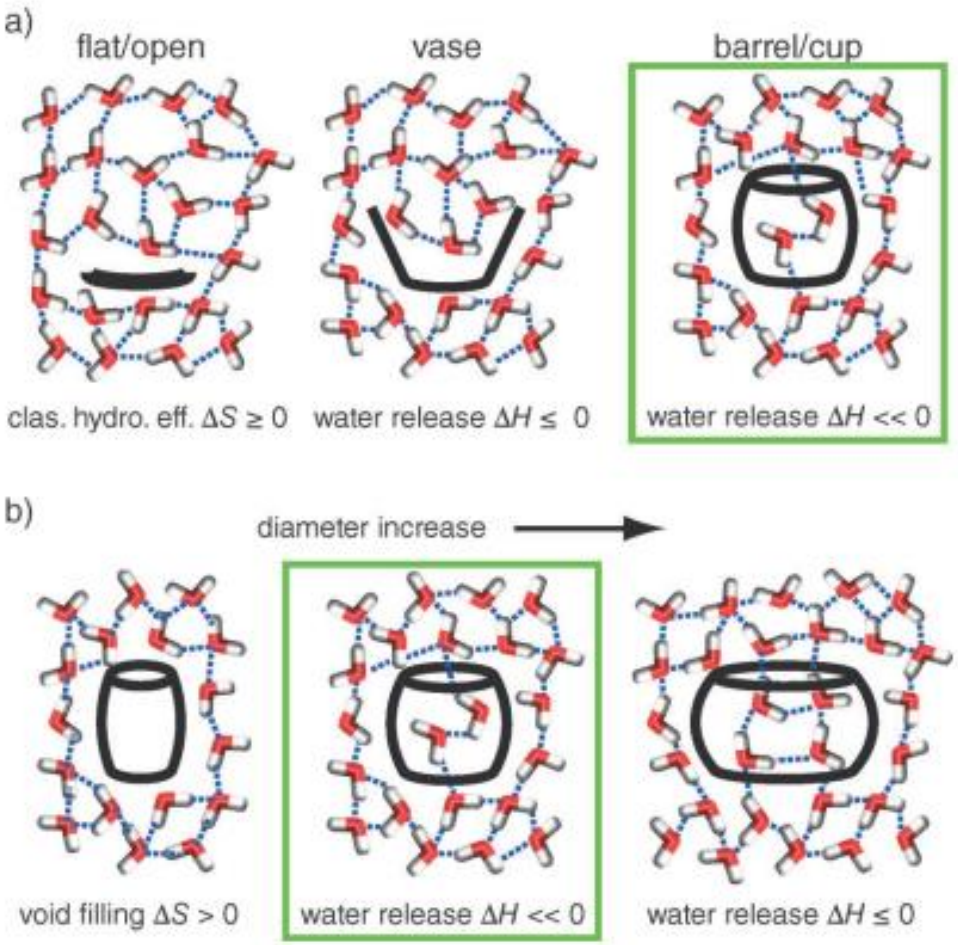
DOI: 10.1002/anie.201310958

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

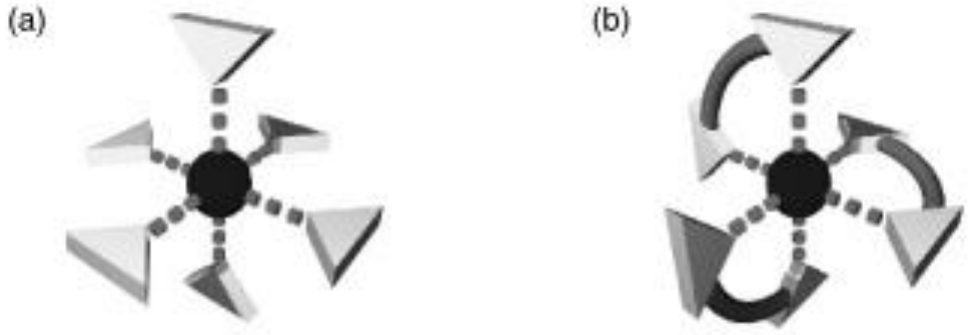
Frank Biedermann, Werner M. Nau,* and Hans-Jörg Schneider**

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



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

$$[Ni(H_2O)_6]^{2+} + 6NH_3 = [Ni(NH_3)_6]^{2+} + 6H_2O$$

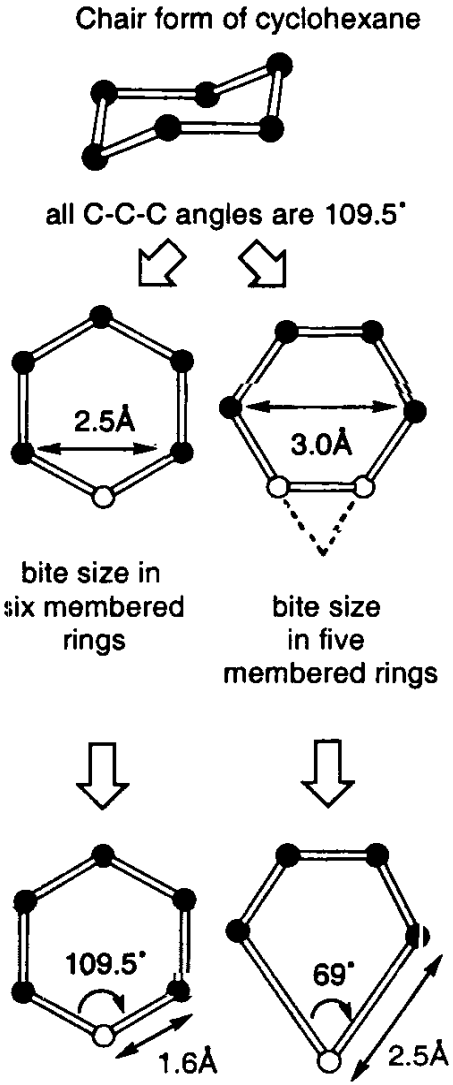
$$\beta \sim 10^9,\ \Delta G = -51.8\ \text{kJ mol}^{-1},$$

$$\Delta H = -100\ \text{kJ mol}^{-1},\ \Delta S = -163\ \text{J mol}^{-1}\text{K}^{-1}$$

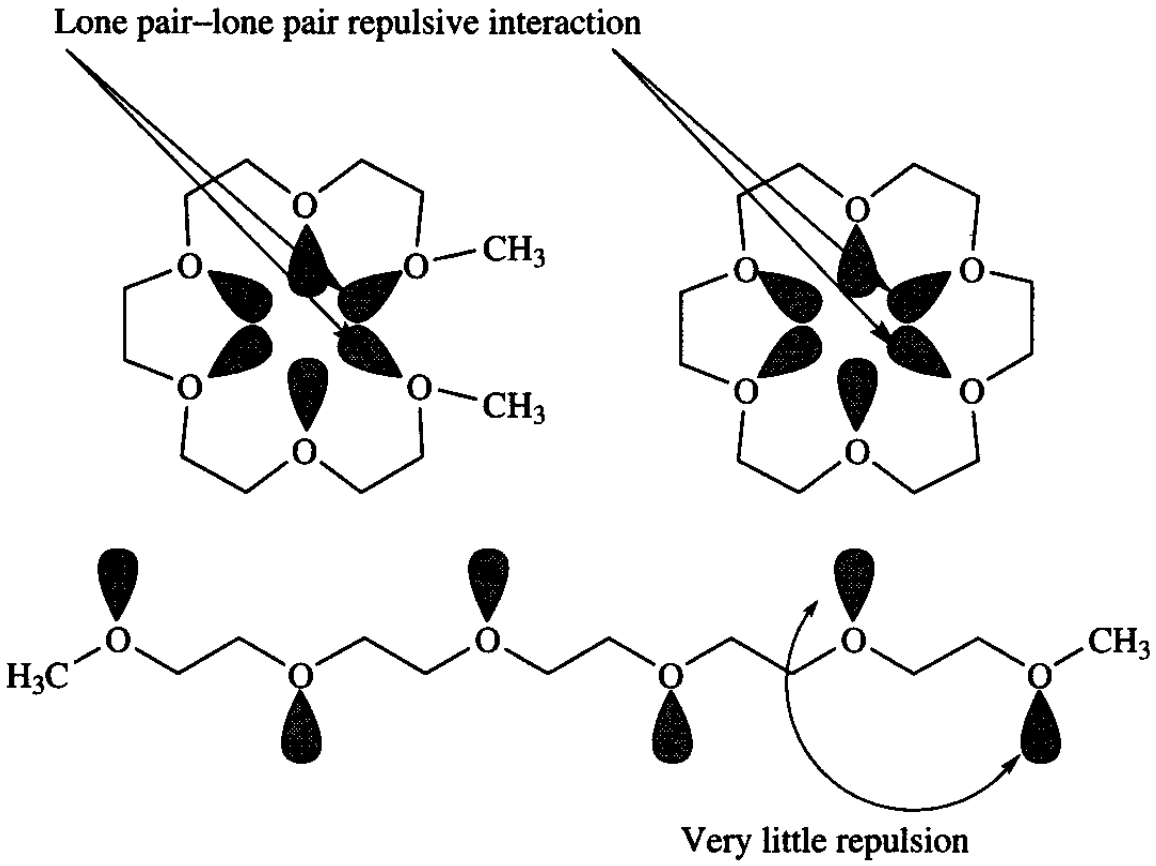
$$[Ni(H_2O)_6]^{2+} + 3en = [Ni(en)_3]^{2+} + 6H_2O$$

$$\beta \sim 10^{18},\ \Delta G = -101.8\ \text{kJ mol}^{-1},$$

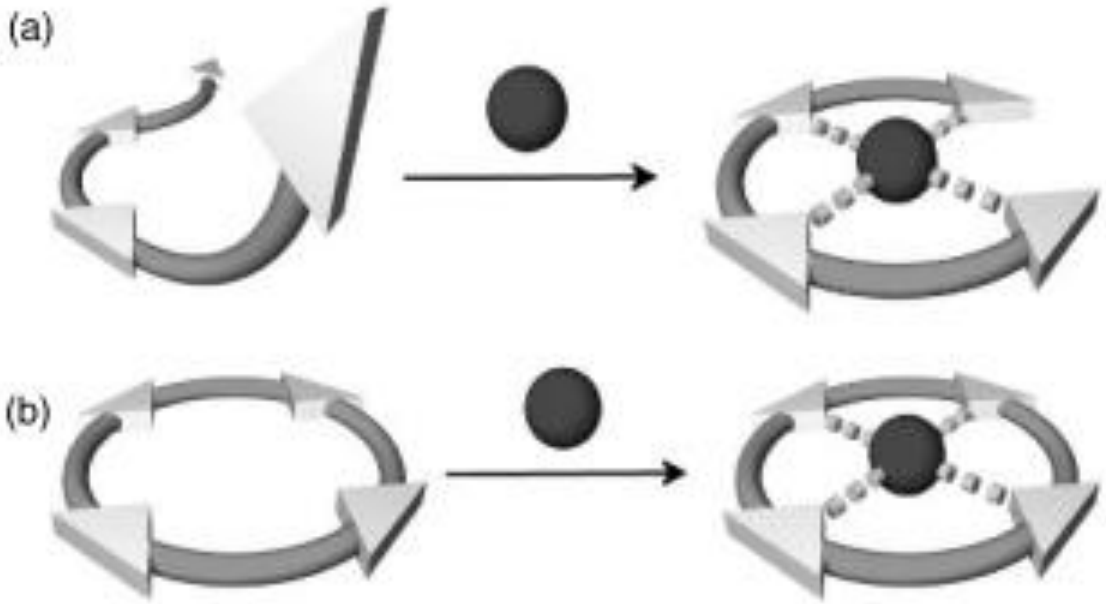
$$\Delta H = -117\ \text{kJ mol}^{-1},\ \Delta S = -42\ \text{J mol}^{-1}\text{K}^{-1}$$

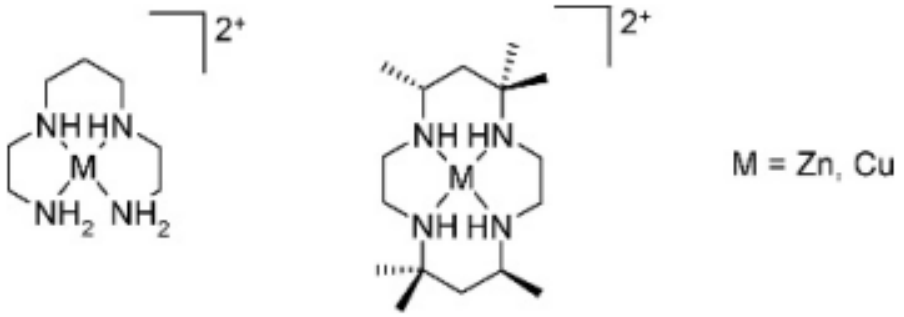


Macrocyclic Effect



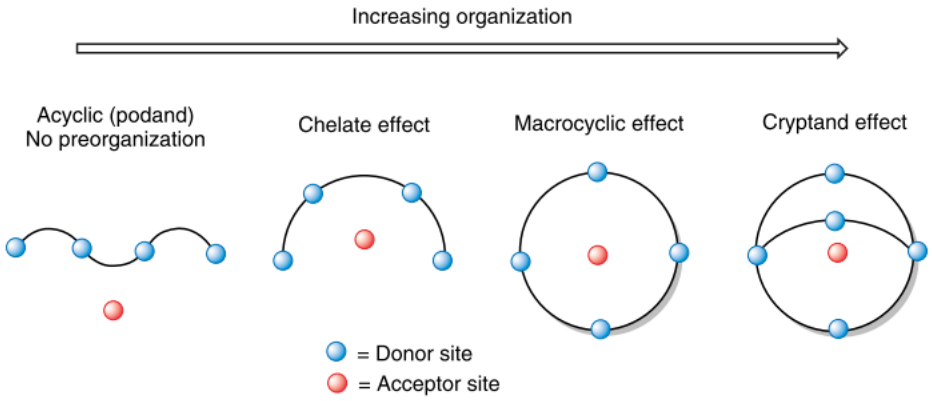
Macrocyclic Effect





Stabilià: Sistema Ciclico 10^4 superiore Sistema Aciclico

Chelate and Macrocyclic Effects



Chem Soc Rev

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Cite this: *Chem. Soc. Rev.*, 2017, **46**, 2622

Assessing cooperativity in supramolecular systems†

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Recettori

cationi

anioni

molecole neutre

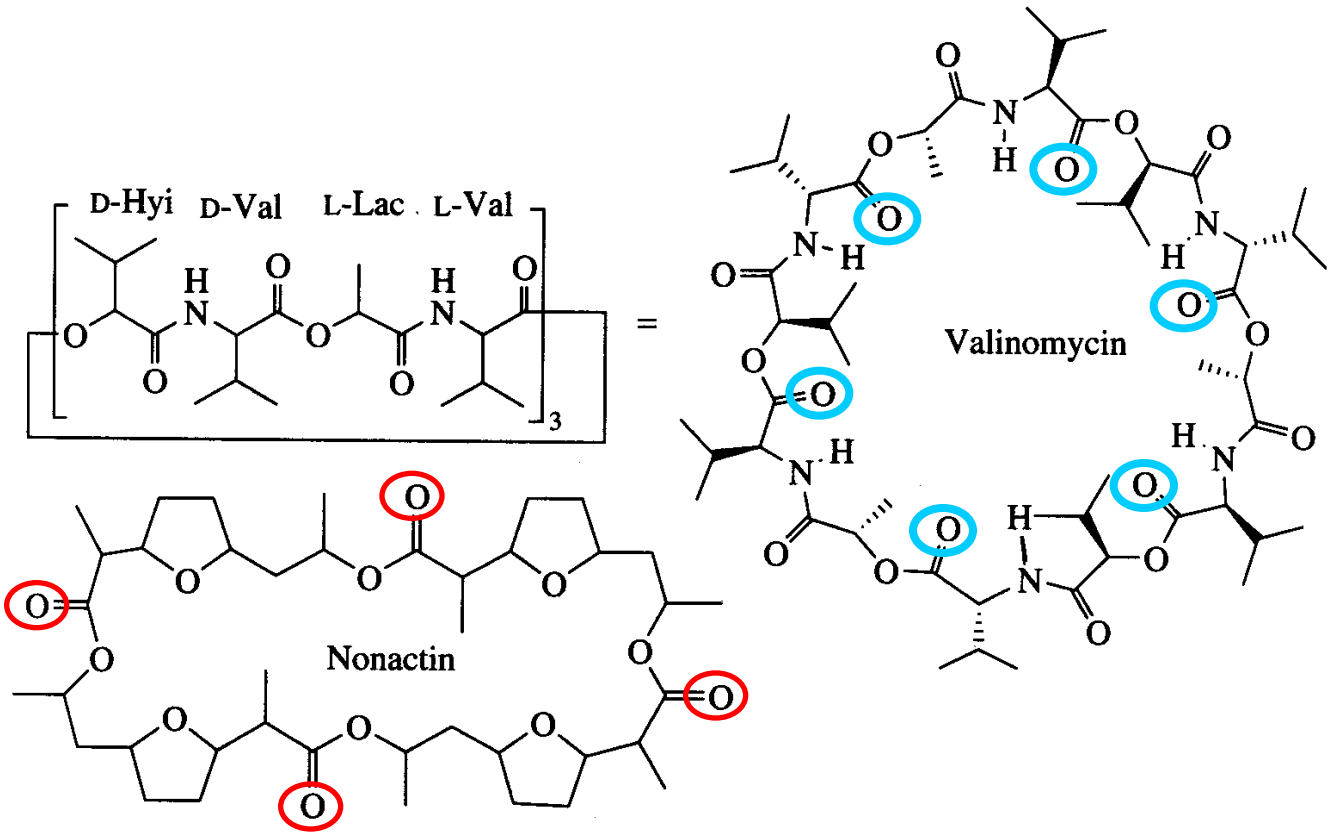
Metodi Analitici

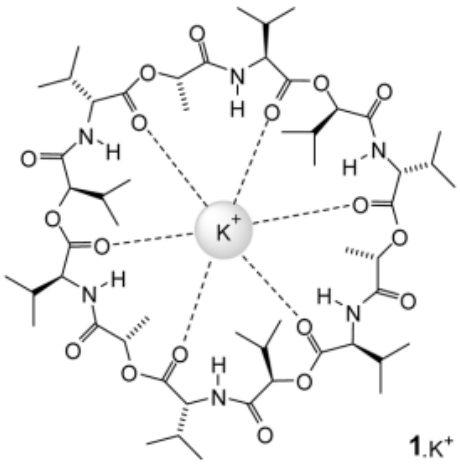
Cavitandi

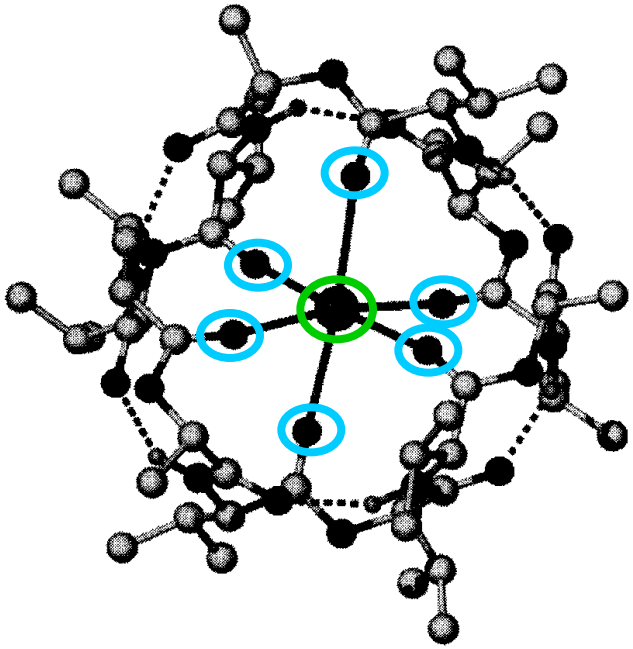
Contenitori molecolari

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

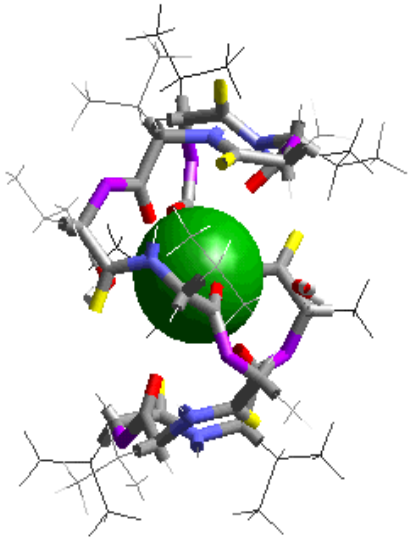
Cations and anions are ubiquitous in biological and chemical systems and their efficient and selective recognition is one of the main goals of Supramolecular Chemistry. As a matter of fact, research in this field started with Pressman's 1964 discovery[1] that valinomycin and other natural antibiotics 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
3
=
Valinomycin
Nonactin

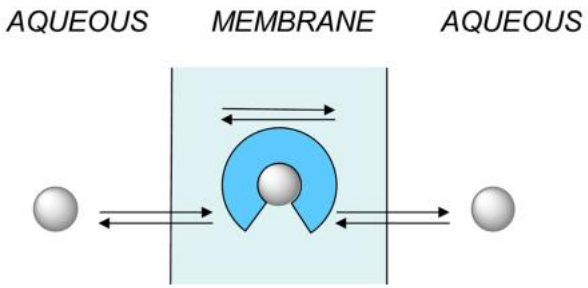

K+
1.K+




K+



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

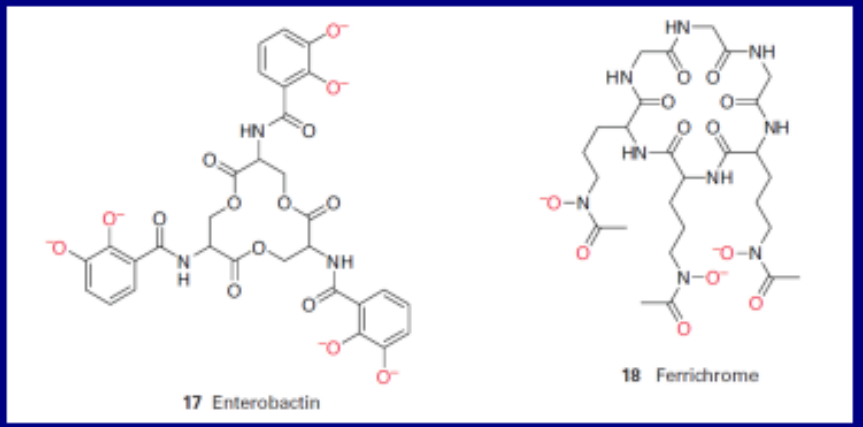


A pH fisiologico 7.4 la concentrazione di $[Fe(H_2O)_6]^{3+}$ - in equilibrio con $Fe(OH)_3$ - è circa 10^{-18}M, mentre per le condizioni ottimali di crescita i micro-organismi richiedono una concentrazione intracellulare di circa 10^{-7}M

Siderofori:

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).

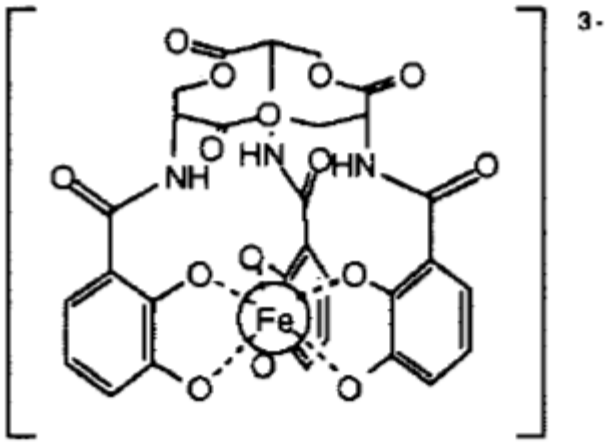


17 Enterobactin

18 Ferrichrome

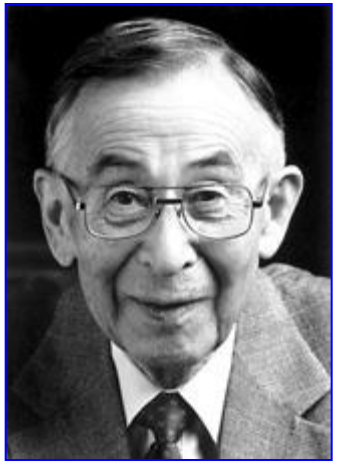
L'enterobactina-Fe^{III} complesso è anche chirale; la struttura del triestere ciclico, che è chirale in quanto ha tre carboni asimmetrici adiacenti agli azoti, impone la configurazione

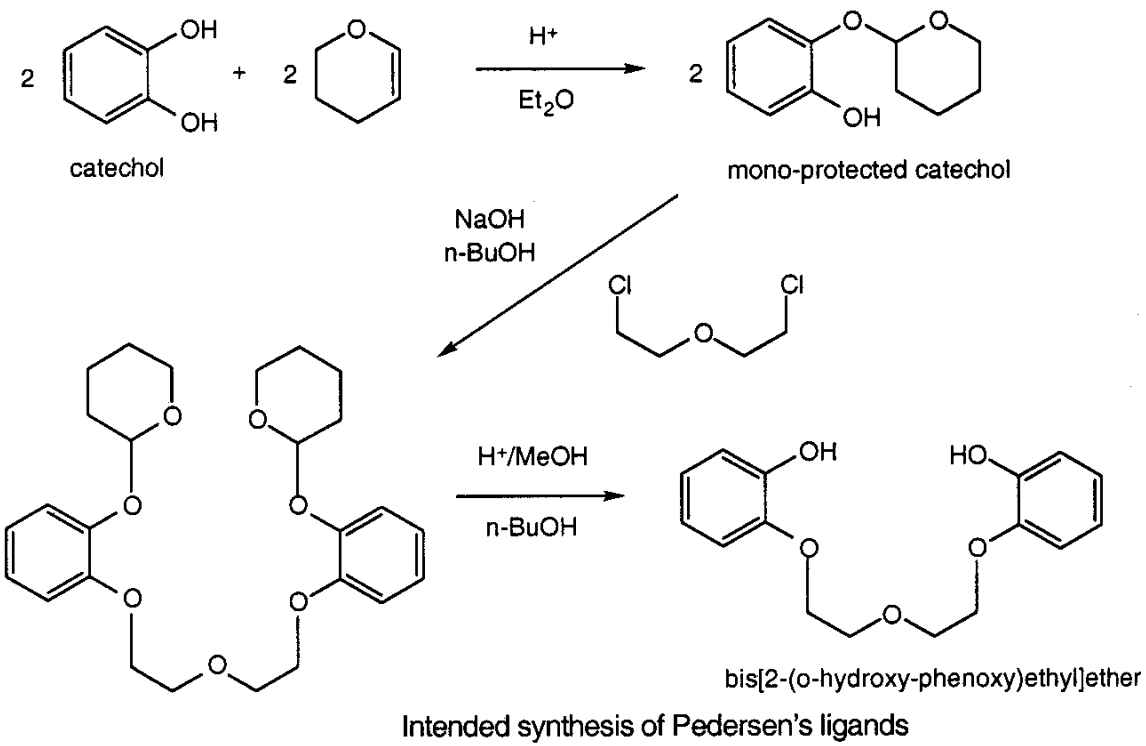
Δ dei catecolati intorno al Fe(III); il suo enantiomero Λ coordina il ferro, ma non è in grado di rilasciarlo ai batteri perché non è riconosciuto da i recettori dell'enterobactina.



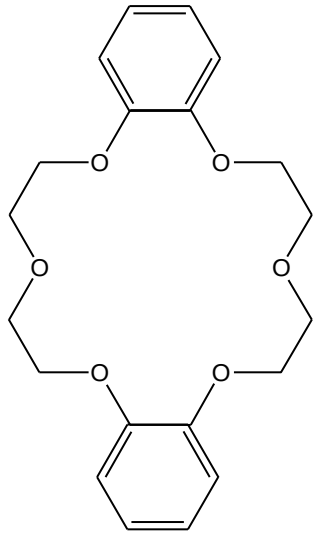
[enterobactin-Fe(III)]$^{3-}$ complex

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

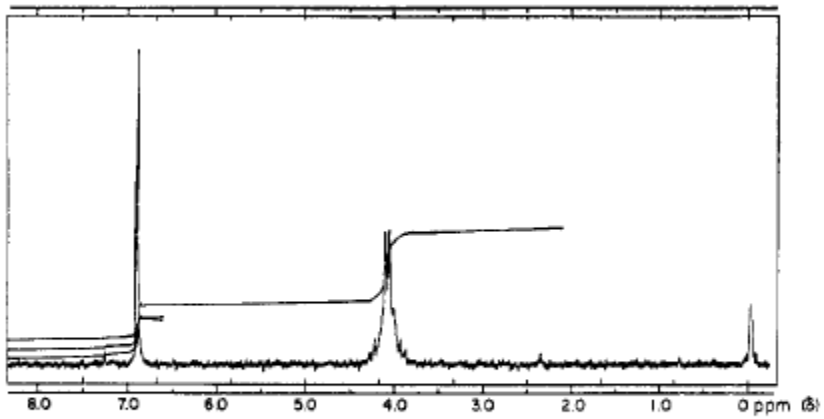


Figure 2. Nmr spectrum of dibenzo-18-crown-6 (XXVII): (upper) multiplet, 4.11 ppm downfield from TMS, area ratio 2.2; (lower) singlet, 6.92 ppm downfield from TMS, area ratio 1.0.

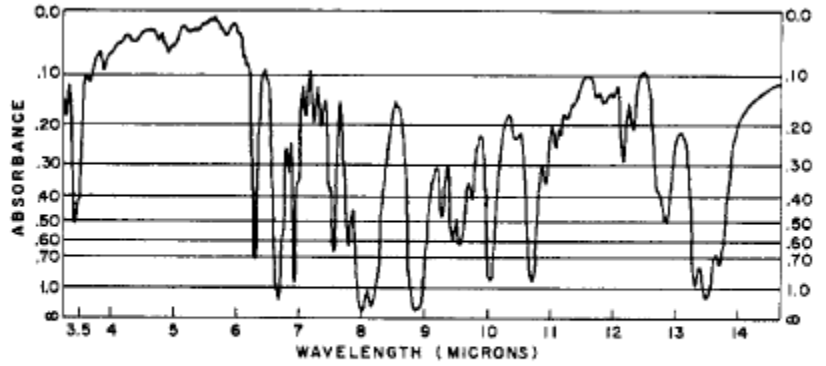


Figure 4. Infrared spectrum of dibenzo-18-crown-6 (XXVIII), KBr pellet.

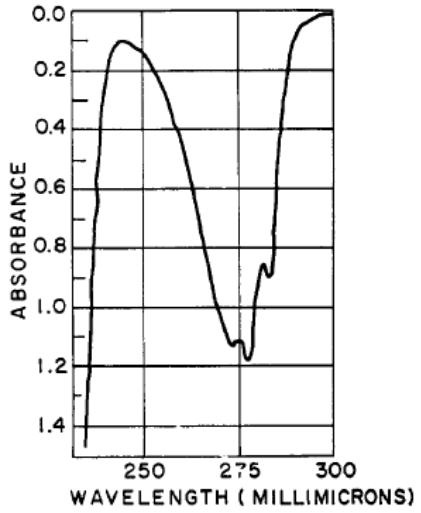


Figure 7. Ultraviolet spectrum of dibenzo-18-crown-6 (XXVIII) in cyclohexane, concentration 0.000255 mole/l., cell path 1 cm; λ_{max} 274 (ϵ 4400), 278 (ϵ 4700), and 283 (ϵ 3600).

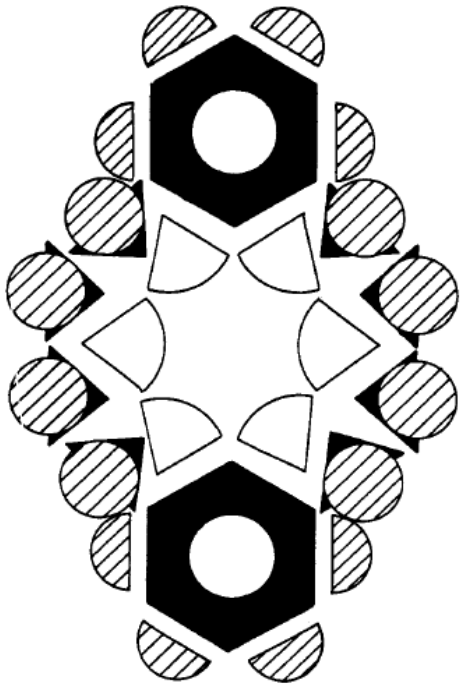
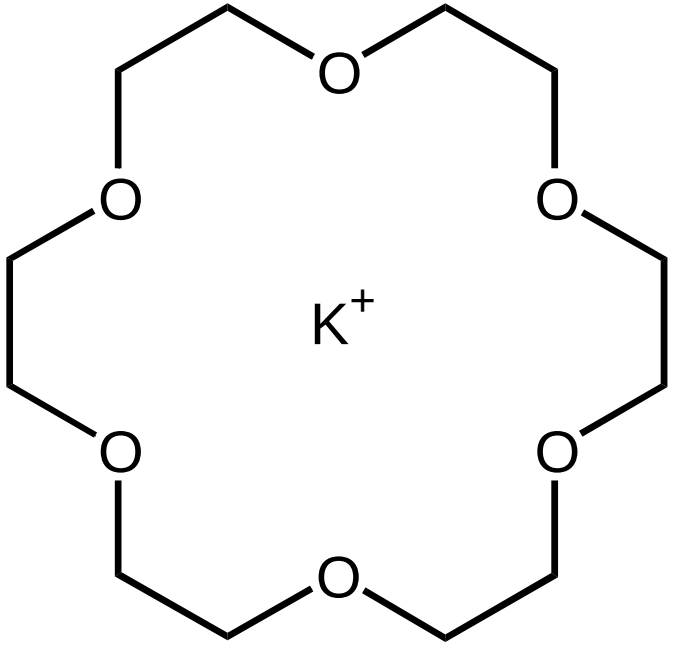


Figure 9. Courtauld model of dibenzo-18-crown-6 (XXVIII).

ETERI CORONA (Crown Ethers)

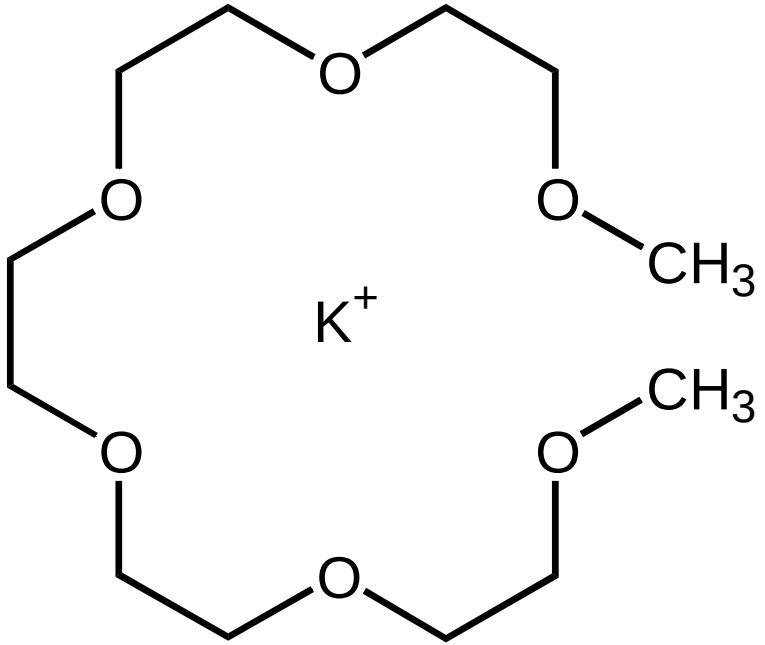
(monocilci = CORANDI)

[18]crown-6

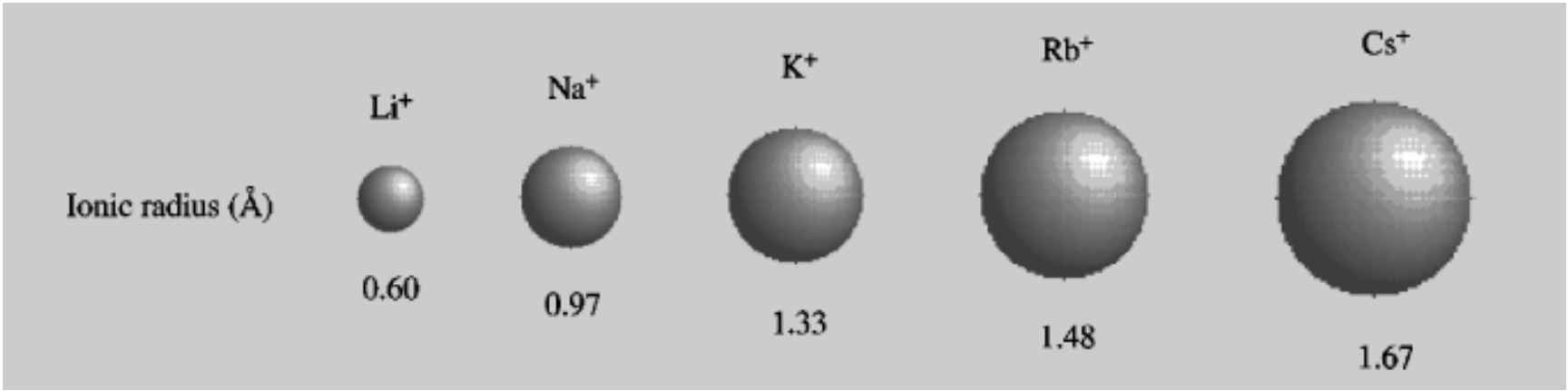


log K = 6.08

Pentametileneglicol-dietiletere

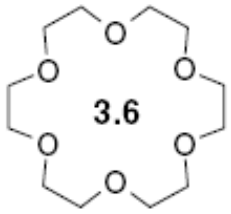


log K = 2.3

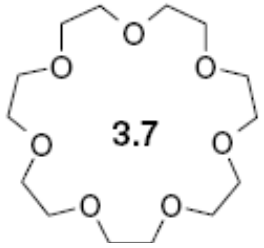


OPTIMAL SPATIAL FIT or SIZE-MATCH

[15]crown-5
Complementary to Na^+

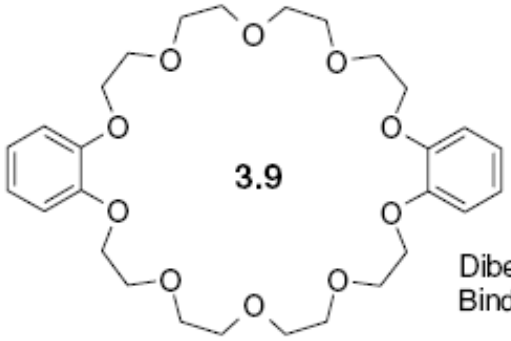


[18]crown-6
Complementary to K^+

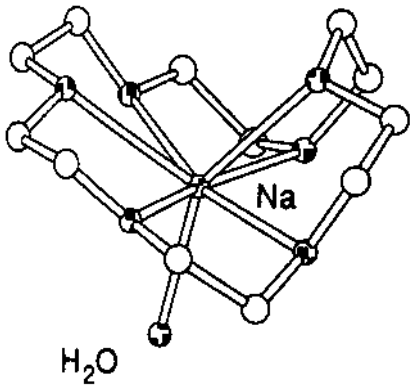


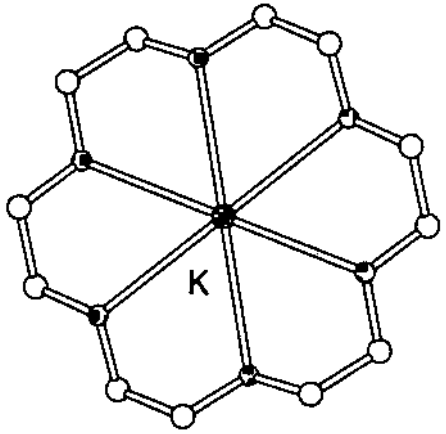
[21]crown-7
Complementary to Cs^+

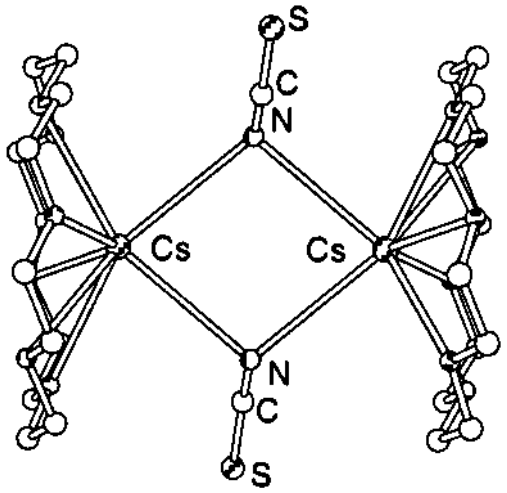
Dicyclohexyl[18]crown-6
More conformationally rigid

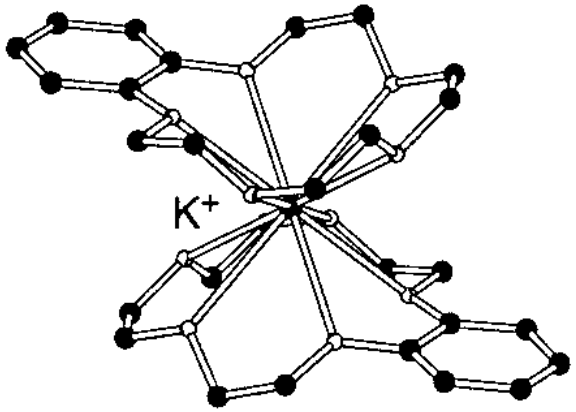


Dibenzo[30]crown-10
Binds two Na^+ ions

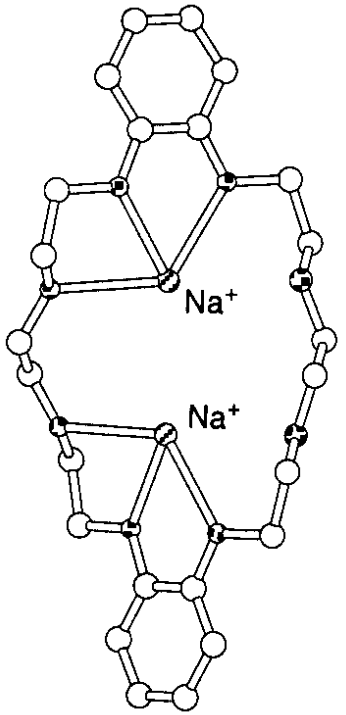








The crystal structure of two benzo-15-crown-5 molecules forming a 'sandwich complex' with a potassium cation



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+}

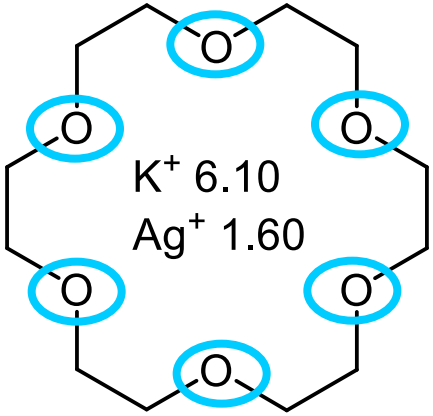
Ioni metallici di tipo ***b*** sono principalmente:

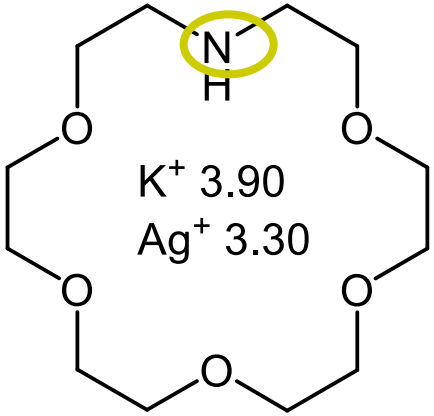
- ioni pesanti di metalli di transizione: Hg_2^{2+}, Hg^{2+}, Pt^{2+}, Pt^{4+}, Ag^{+}, Cu^{+}
- ioni di metalli in bassi stati di ossidazione, ad es. nei metallo carbonili

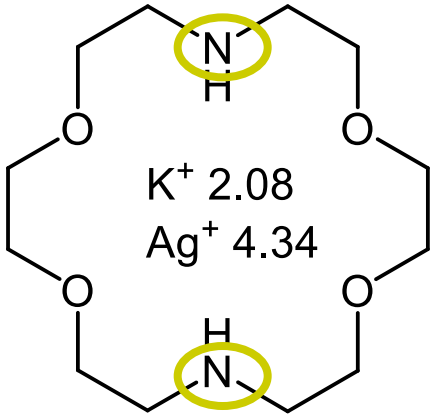
Alcuni ioni (Fe^{2+}; Co^{2+} ; Ni^{2+}; Cu^{2+} ; Zn^{2+}; Pb^{2+}) formano complessi le cui stabilità non possono essere pronosticate sulla base della classificazione hard/soft: essi formano la classe *border-line*

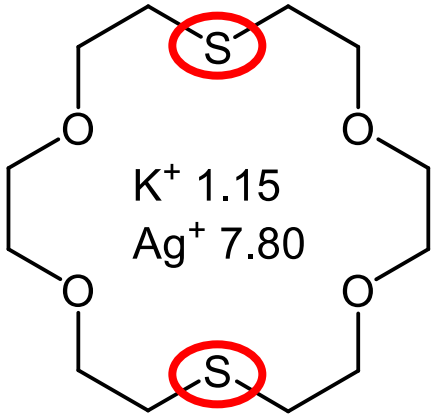
La costante di stabilità dei complessi di questi ioni con un dato legante segue l'ordine, noto come serie di **Irving-Williams**:

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



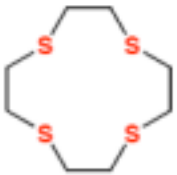




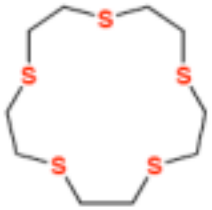


Aza-crown

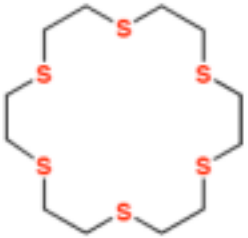
Tio-crown



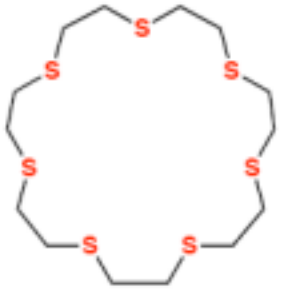
[12]S_4



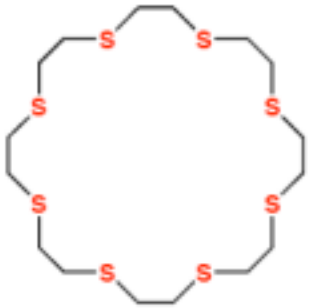
[15]S_5



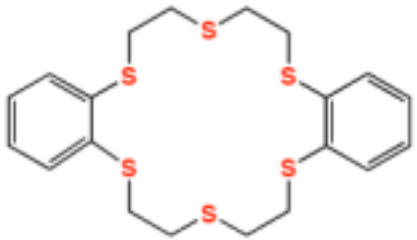
[18]S_6



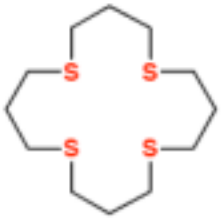
S



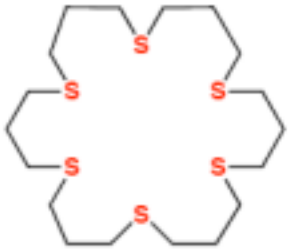
[24]S_8



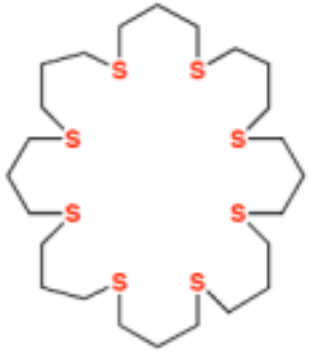
Dibenzo[18]S_6



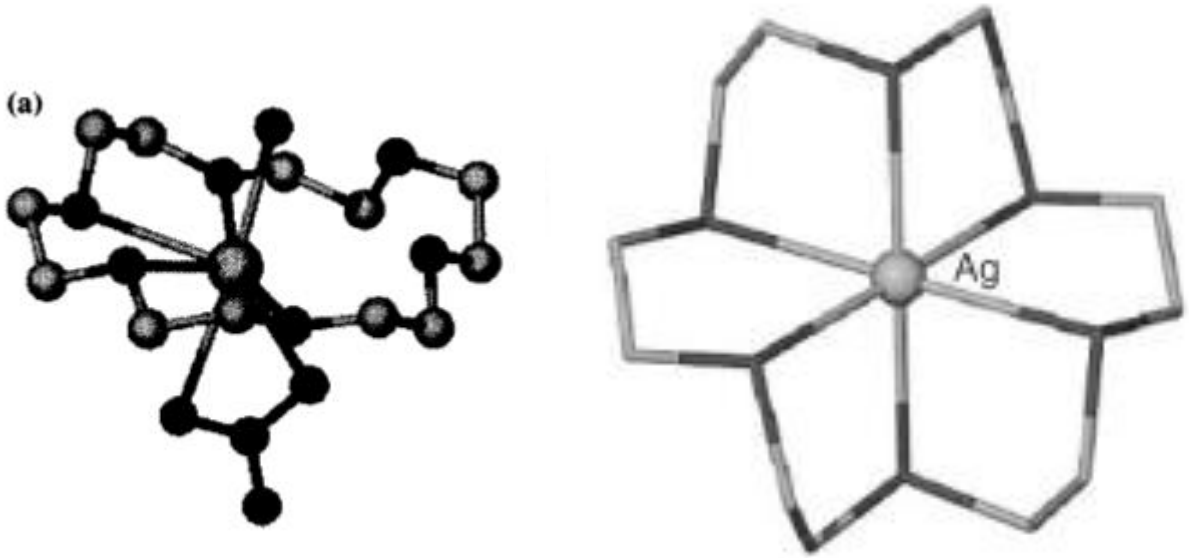
[16]S_4

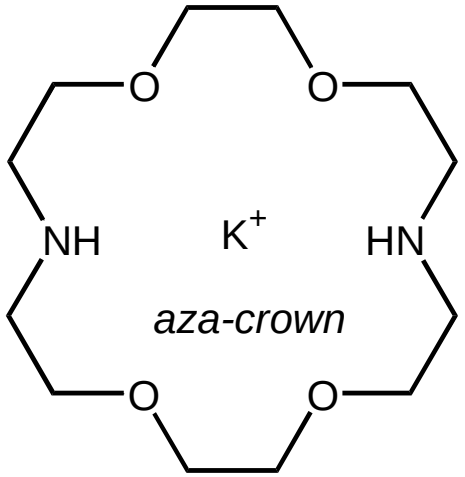


[24]S_6

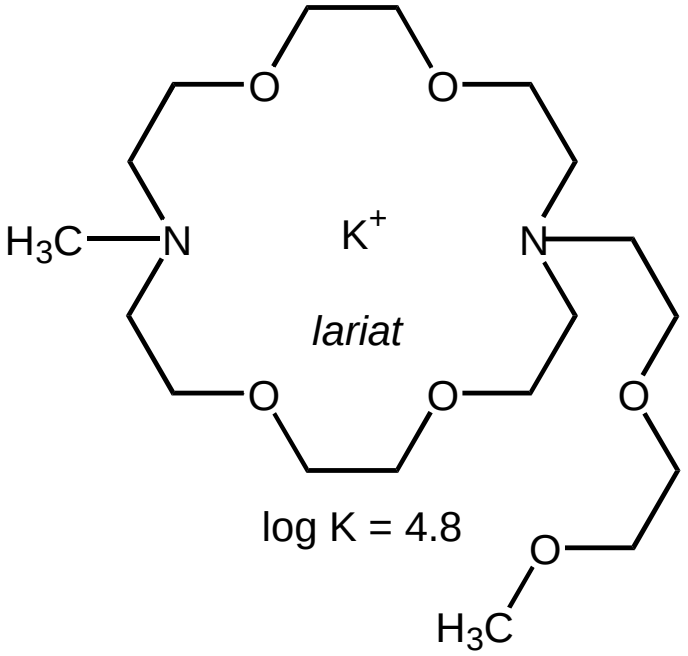


[32]S_8

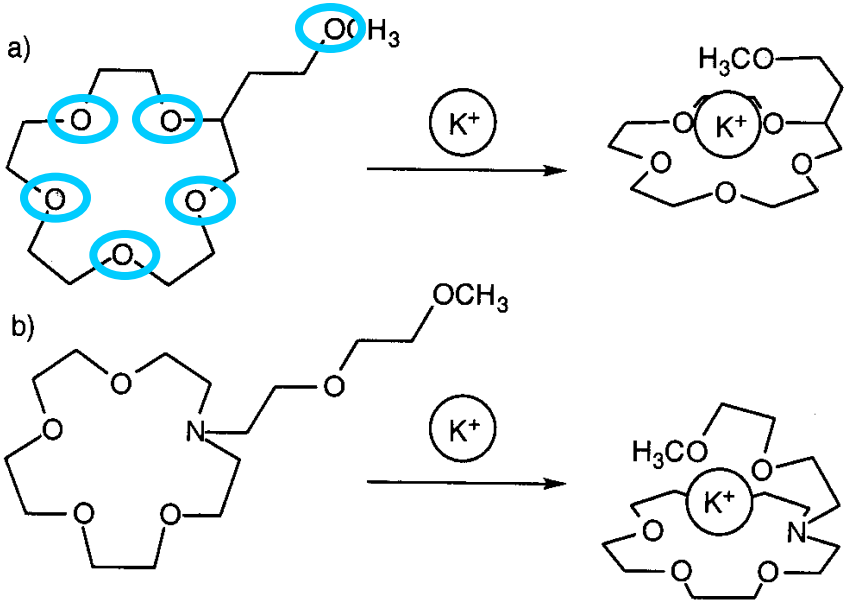

(a)
Ag



log K = 2.04



log K = 4.8



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

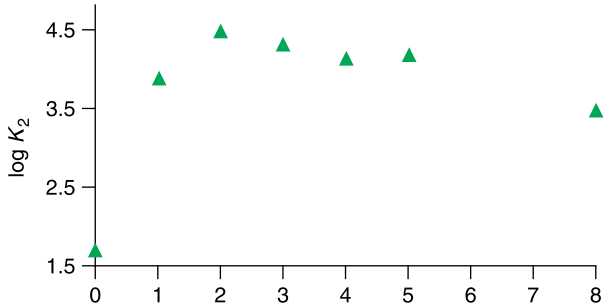
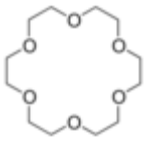
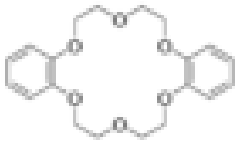


Figure 17 Na^+ complexation by aza-15-crown-5 lariat ethers with n oxygen donor atoms in the side arm ($n = 0–8$).[57]



18-crown-6

274984-1G 78.40 euro



Dibenzo-18-crown-6

158399-2.5G 17.50 euro

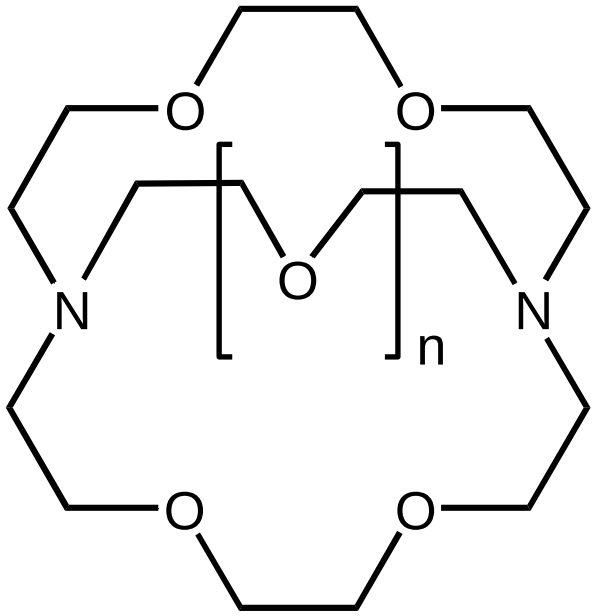
15-crown-5

188832-1G 15.30 euro

1-Aza-18-crown-6

11382-1G 212.00 euro

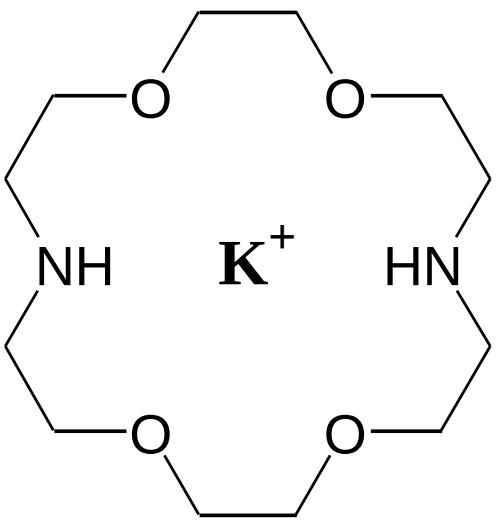
LEHN (Nobel 1987), estensione dei sistemi monociclici a sist. biciclici (CRIPTANDI,anni ‘60)



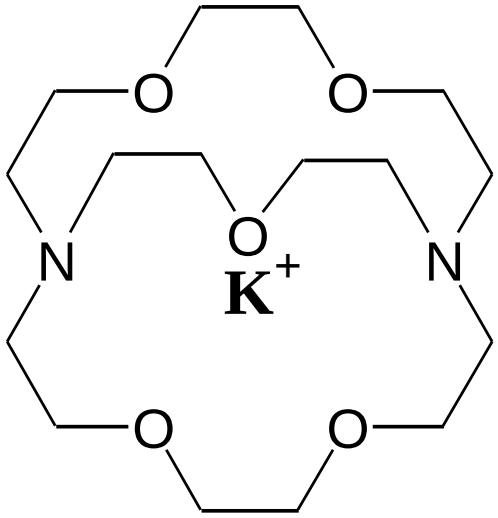
Na^+

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

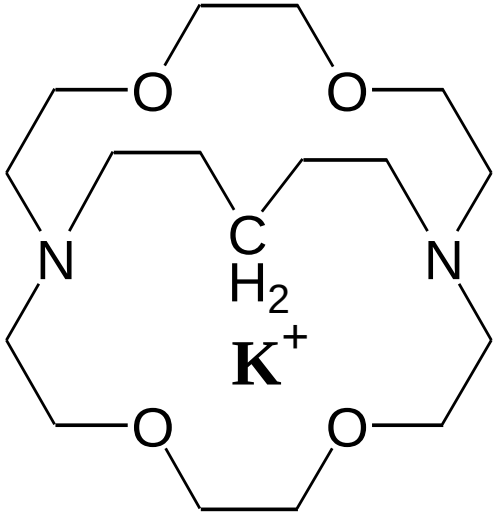
K^+



logK = 2.0

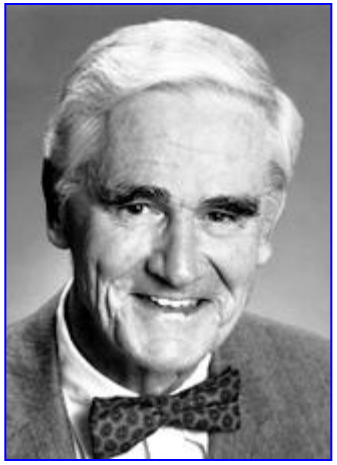


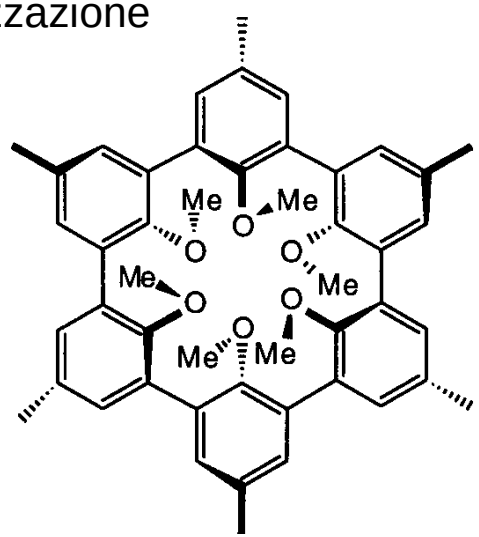
logK = 7.0



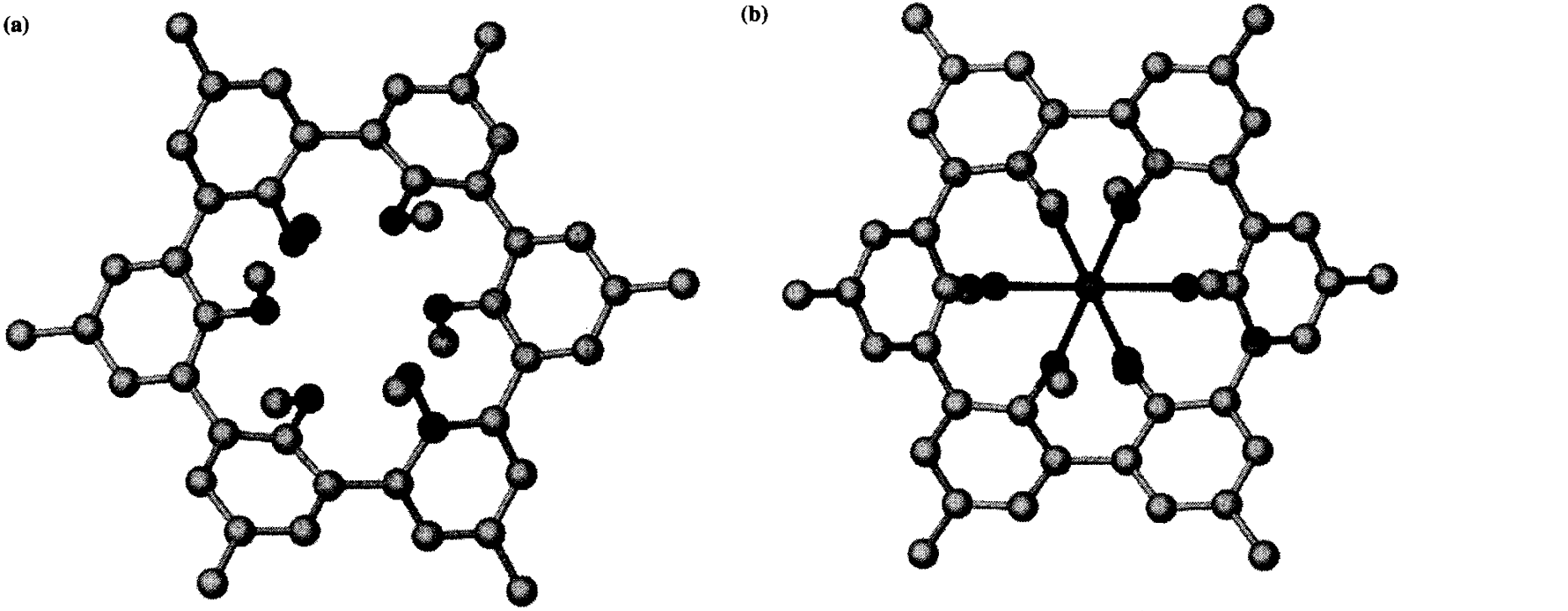
logK = 5.4

CRAM (Nobel 1987) - preorganizzazione

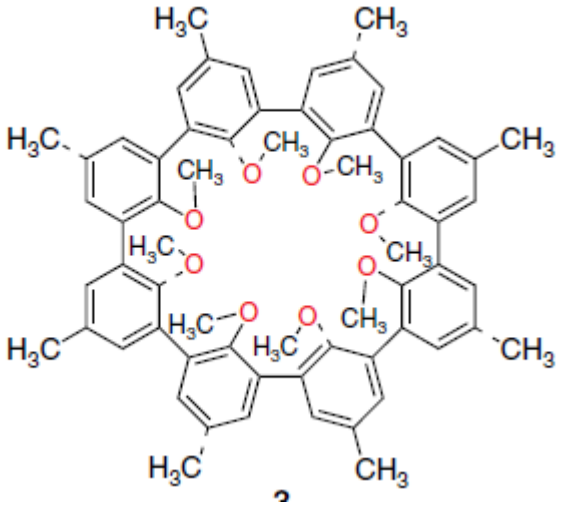




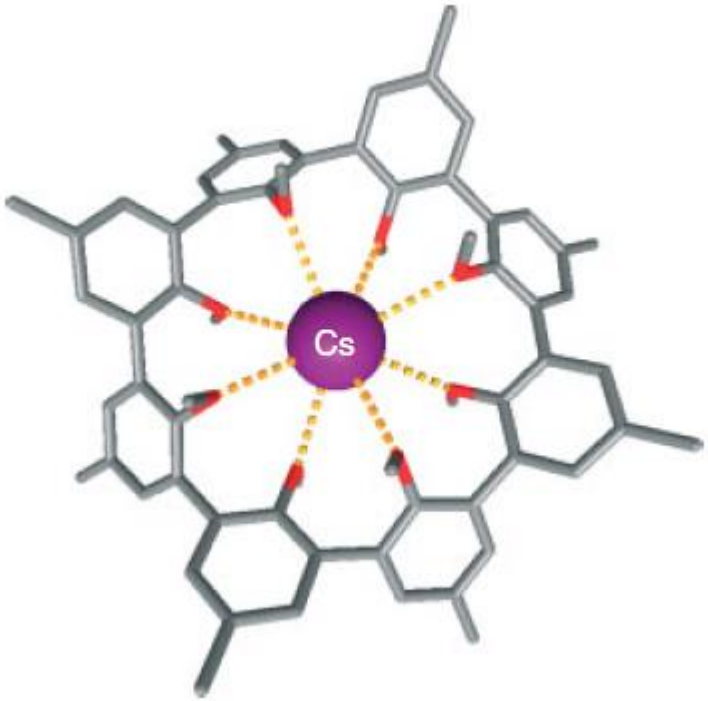
Sferandi
(*p*-metilanisolo)

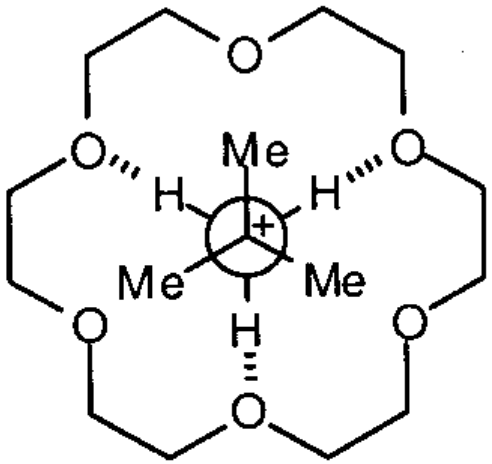


X-ray crystal structures of **(a)** free spherand (**3.30**) and **(b)** its Li^+ complex (after Trueblood *et al.* 1981).

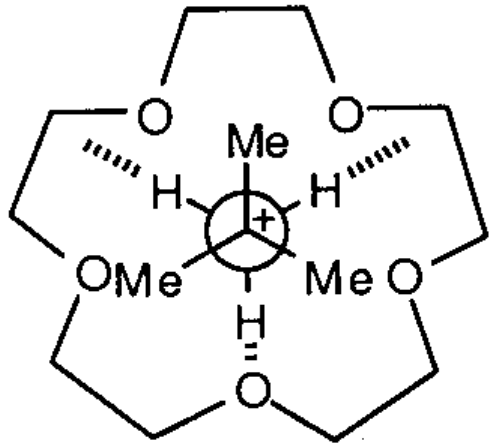

H3C
CH3
H3C
CH3
CH3
O
CH3
O
CH3
O
H3C
O
O
CH3
O
H3C
O
O
CH3
H3C
O
H3C
O
CH3
H3C
CH3
H3C
CH3

2

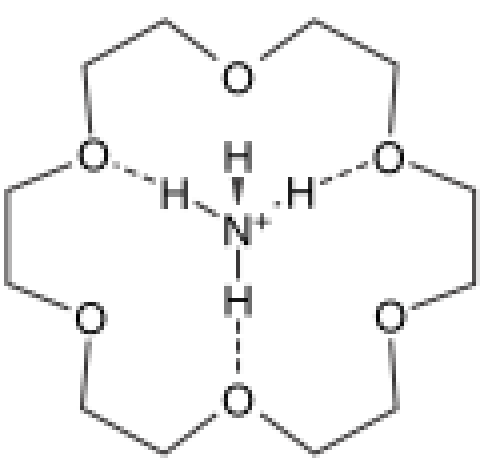

Cs



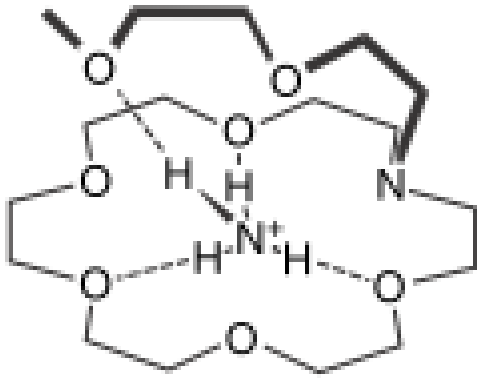
strong complex
ideal arrangement of hydrogen bond
donors and acceptors



weaker complex
mismatch in geometry of hydrogen bond
donors and acceptors

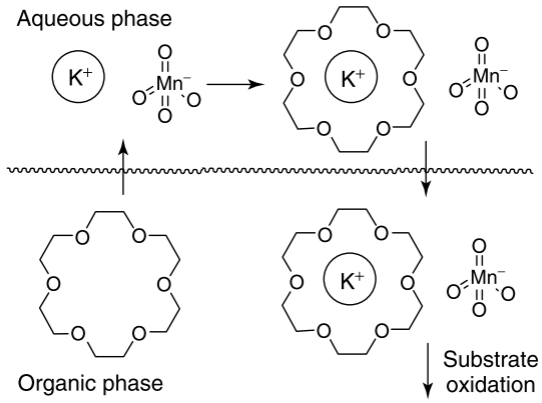


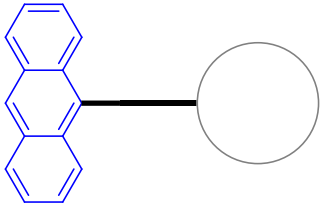
log K = 4.35

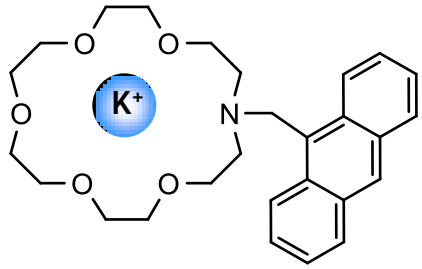


2.23·NH_4^+

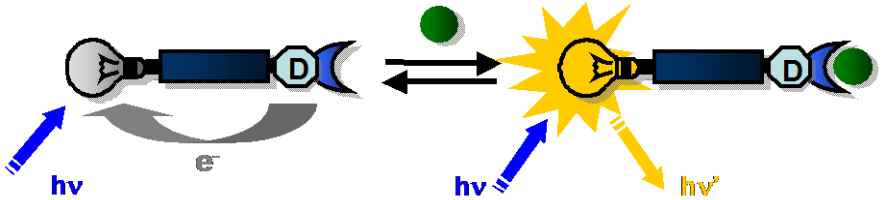
log K = 4.75

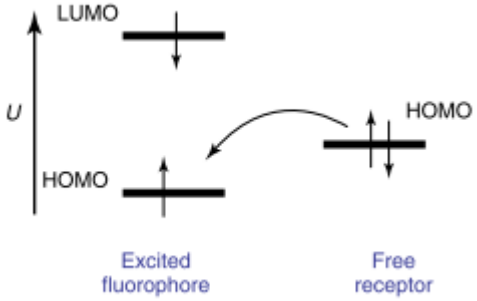

Aqueous phase
K+
Mn
O
Organic phase
Substrate
oxidation

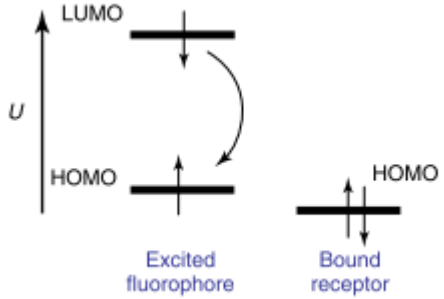




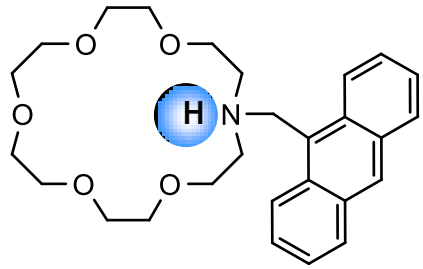
Meccanismo ON/OFF (PET) intrinseco al sensore attivato dall'analita (ammina terziaria)
OFF in ASSENZA di analita
ON in presenza di analita



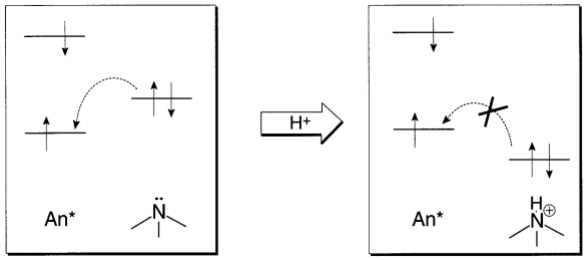




In soluzione acquosa attenzione al pH!



Fluorescenza accesa anche in assenza di catione se ammina protonata;
in presenza di catione l'ammina deve essere deprotonata perché il sensore si accenda!



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

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^{+});

Energie libere di solvatazione dell'host e del catione

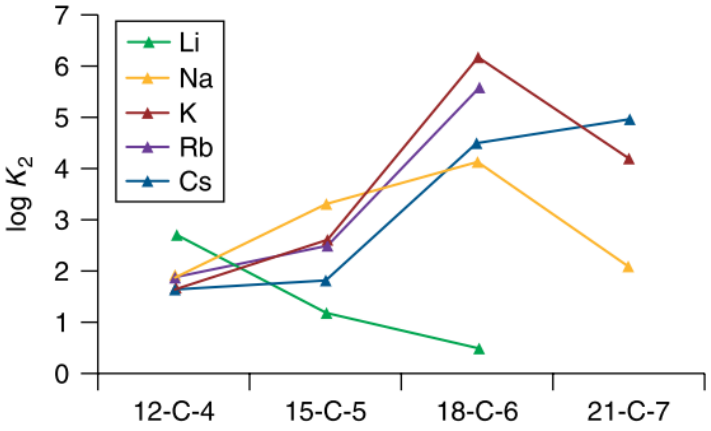
Solvente – competitivo per i dipoli/ costante dielettrica/ legami idrogeno/capacità coordinanti

Natura del contro-ione (interaz con solvente/catione/solvatazione)

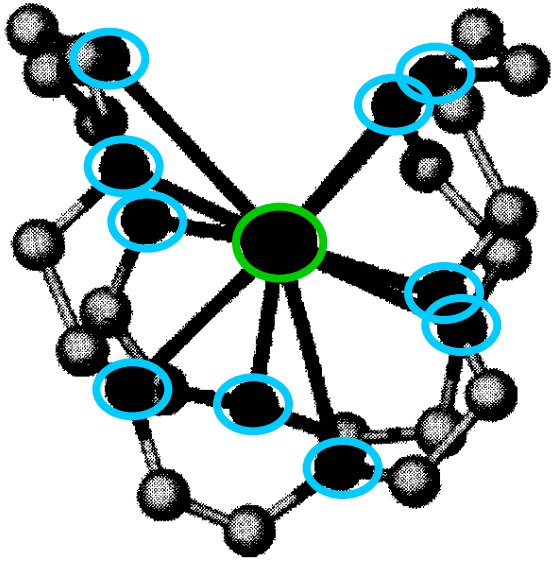
Cinetica di complessazione

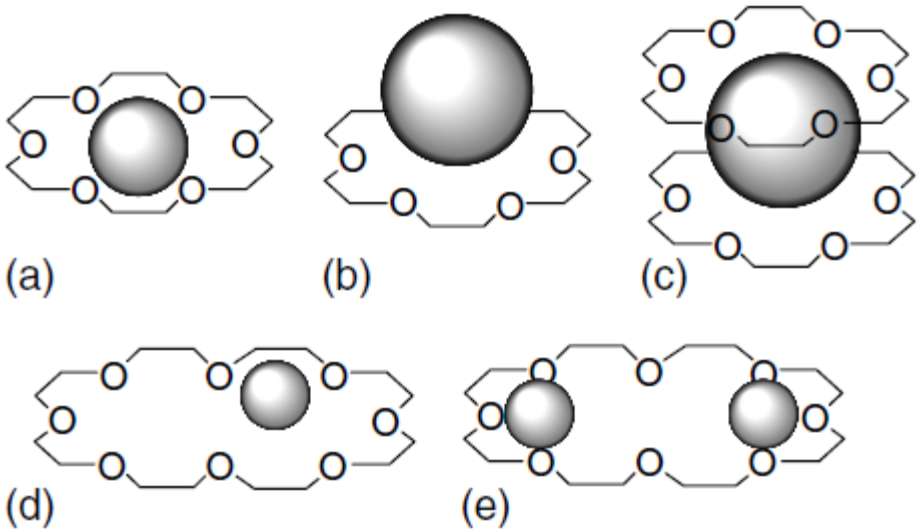
Selettività

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



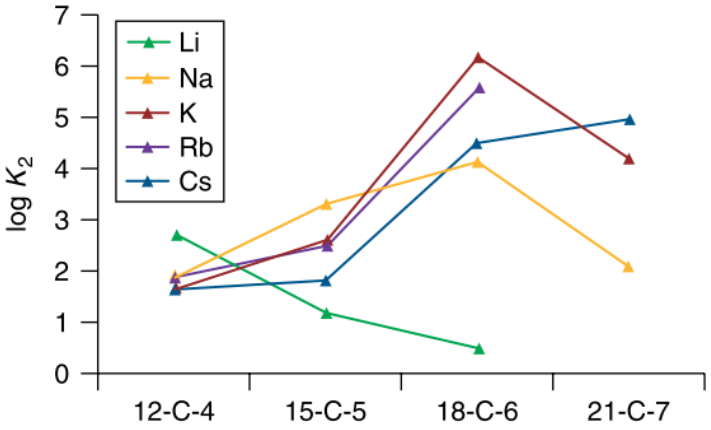
[30]crown-10





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



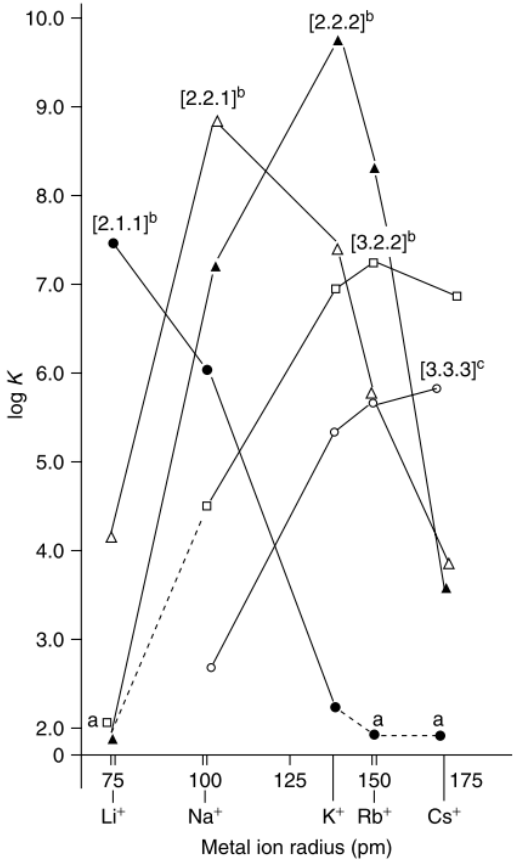
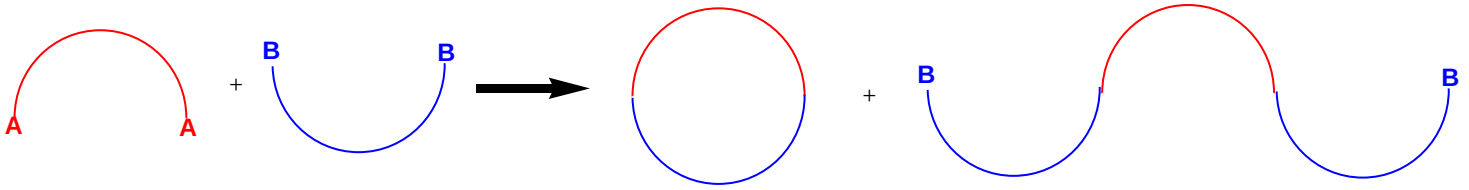


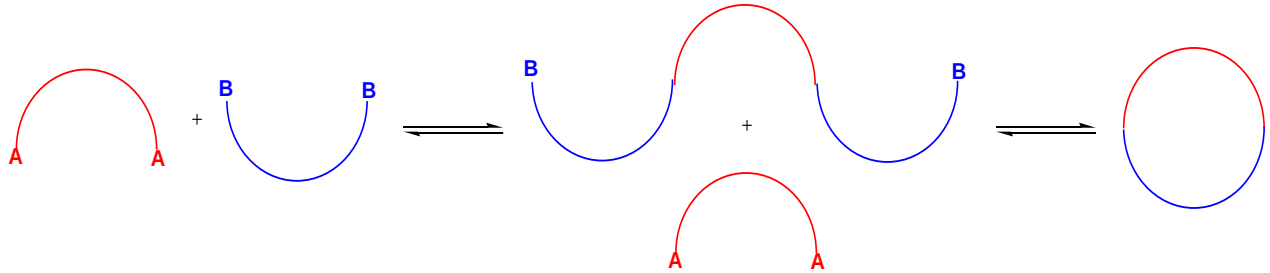
Figure 2 Selectivity of cryptands among alkali metal cations (a, value reported <2.0; b, in 95% CH_3OH; c, in methanol).

- **covalent synthesis** : under kinetic control



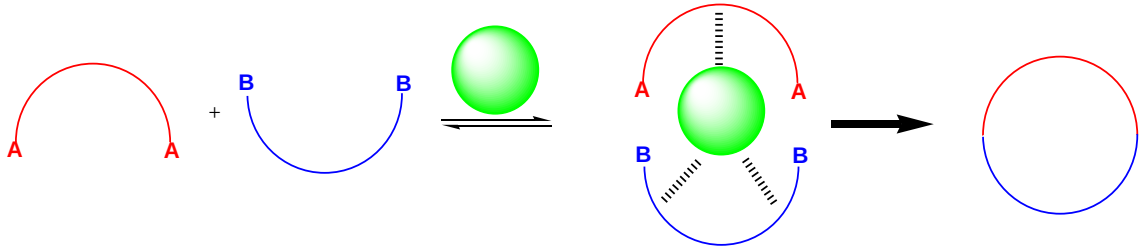
classical organic chemistry. Irreversible bond formation
highly stable molecules
not adapted to big molecules.
low yield

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



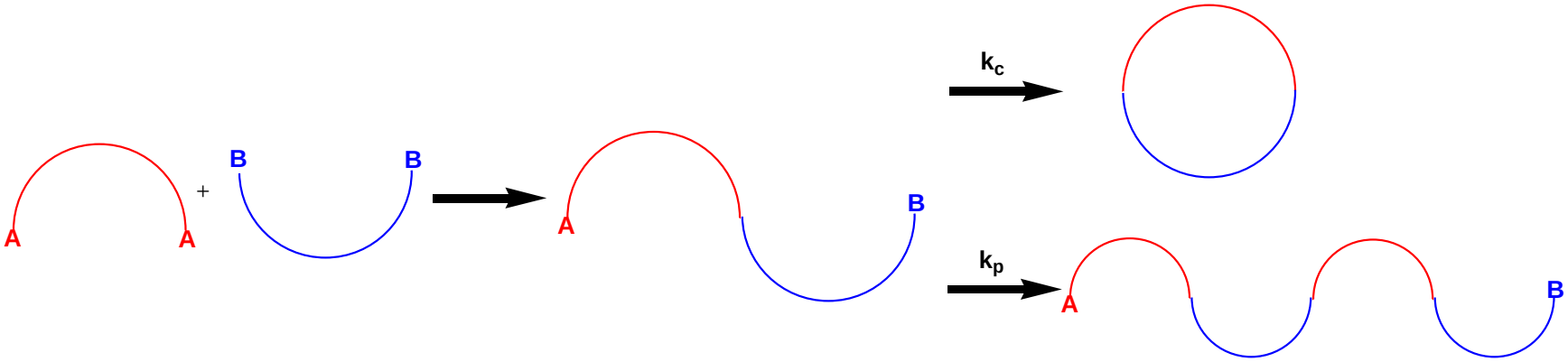
thermodynamic directed synthesis. Reversible bond formation
lower stability
adapted to big molecules.
high yield

- 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

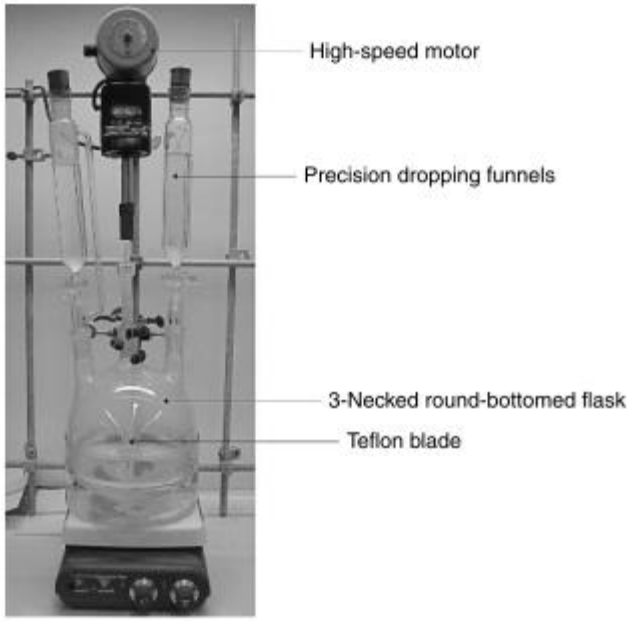
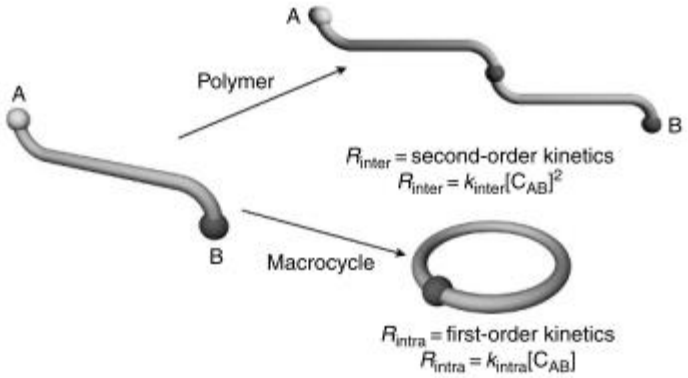
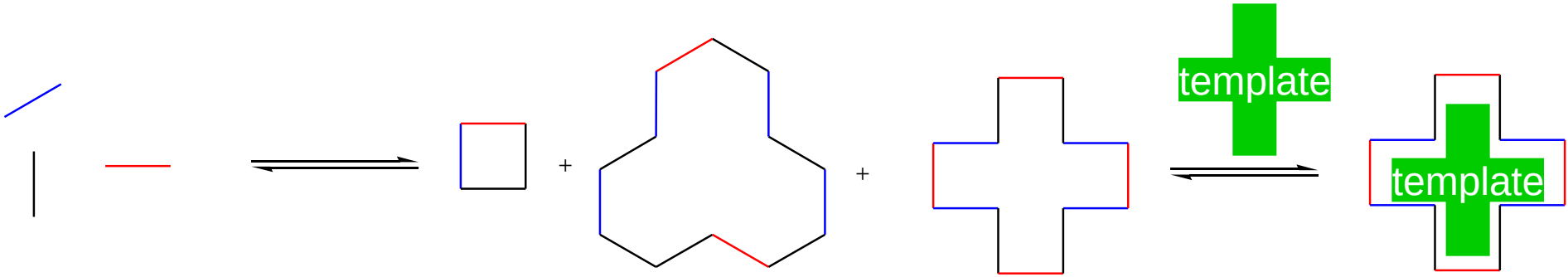
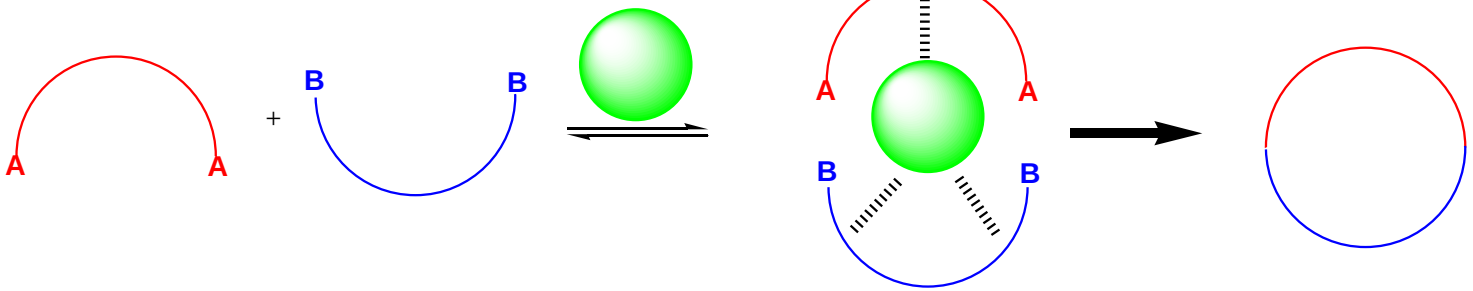


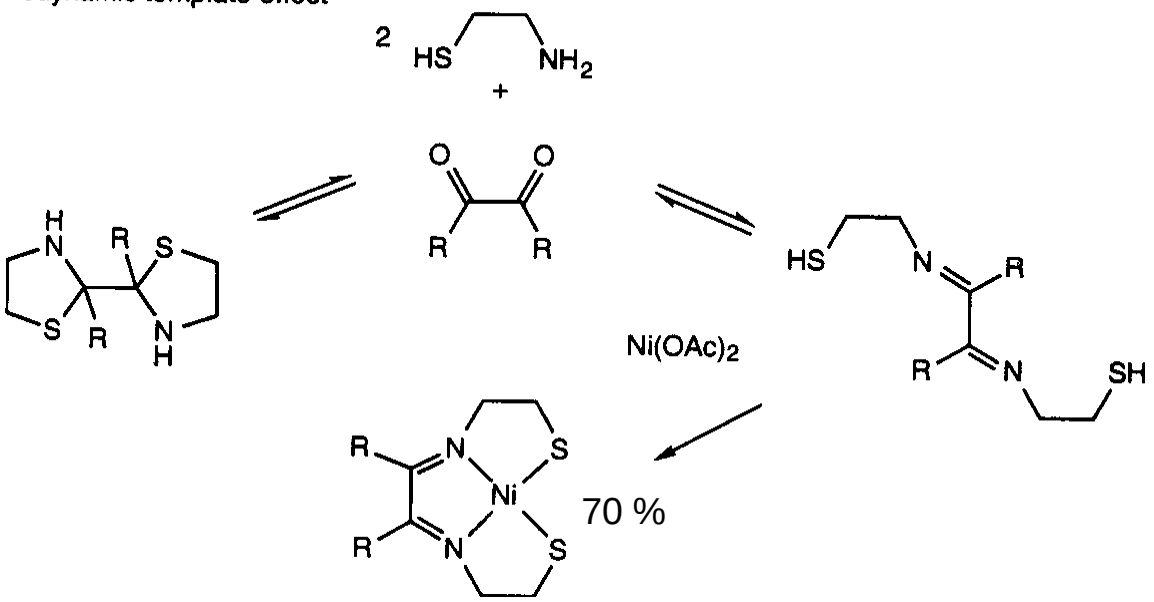
Figure 2.1 Typical apparatus used for high-dilution synthesis.



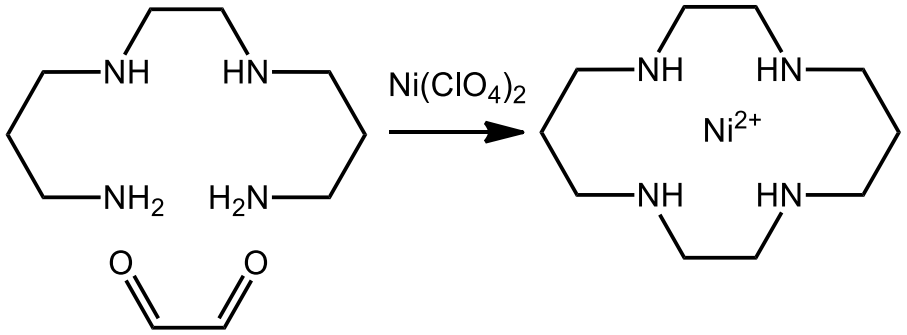

template
template


A
A
B
B
A
A
B
B

a) thermodynamic template effect



Effetto templato cinetico CYCLAM (base di Schiff)



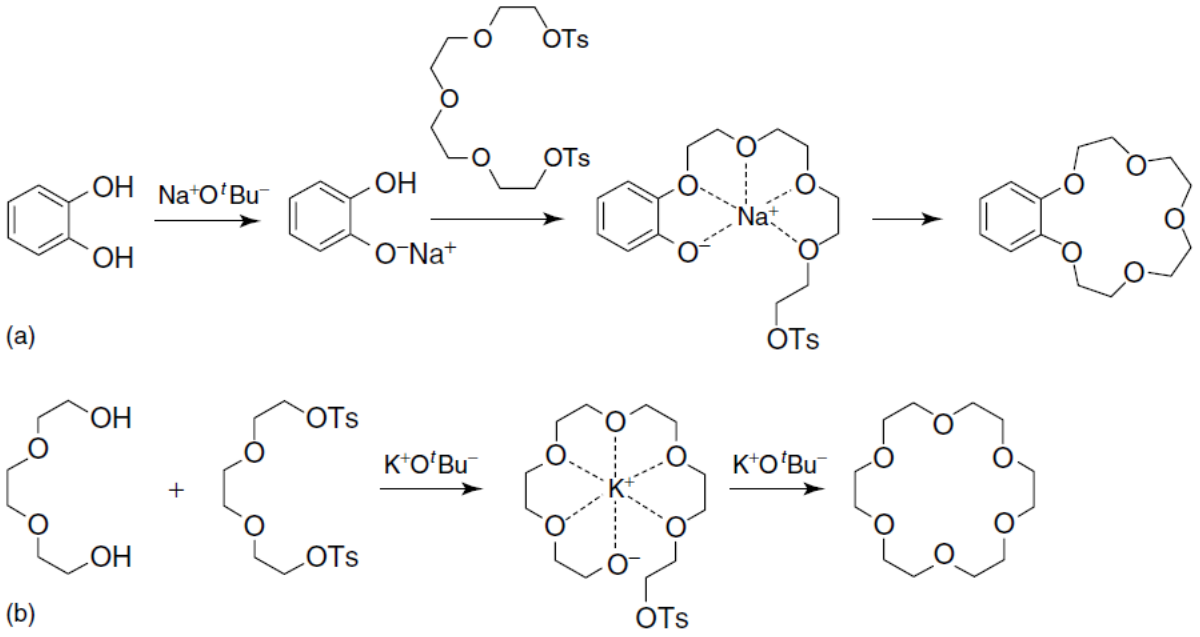
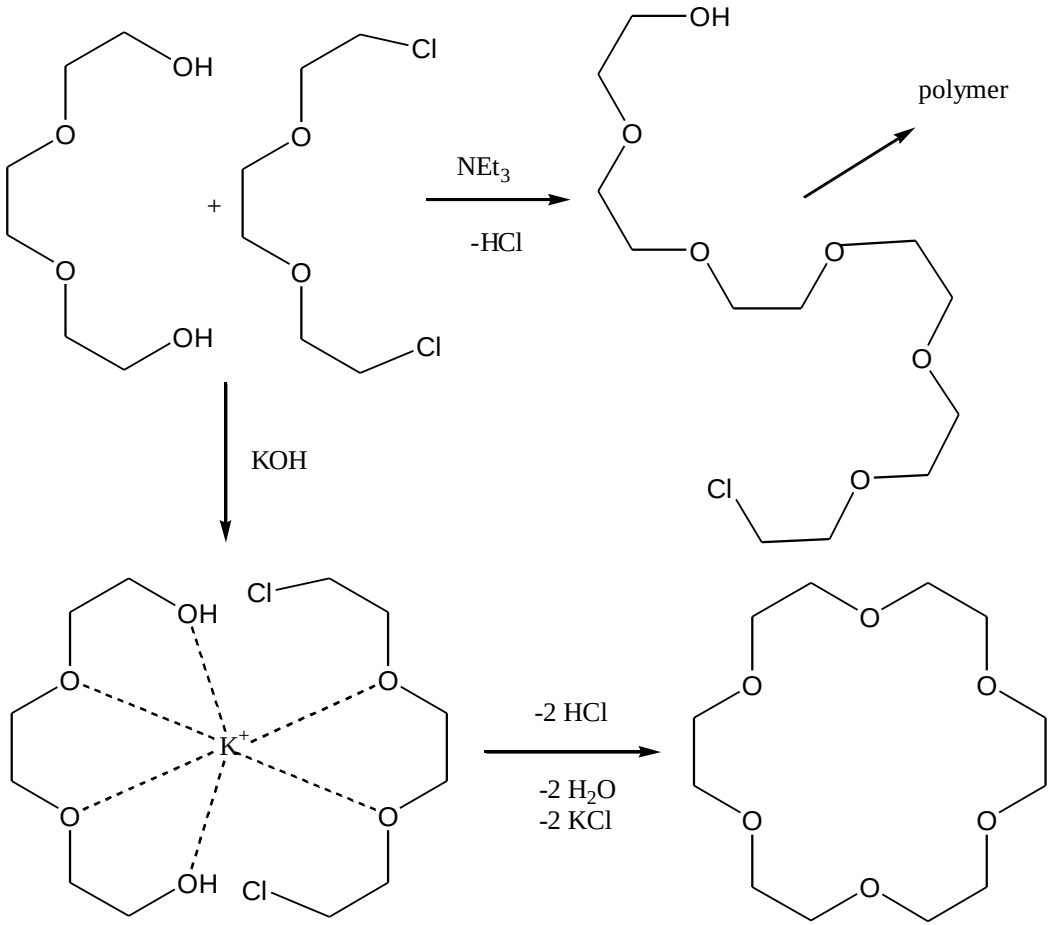
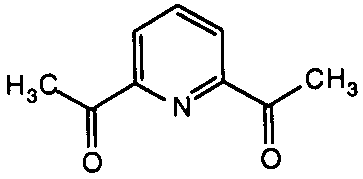


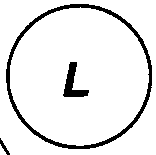
Figure 3 Template synthesis: (a) benzo-15-crown-5; (b) 18-crown-6.


OH
O
O
OH
+
Cl
O
O
Cl
NEt3
-HCl
OH
O
O
O
O
O
Cl
O
polymer
KOH
OH
Cl
O
O
K+
O
O
OH
Cl
-2 HCl
-2 H2O
-2 KCl
O
O
O
O
O
O

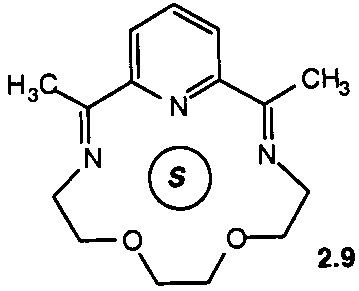


+

small metal cation templates
(e.g. Mn^{2+}, Fe^{2+}, Mg^{2+})

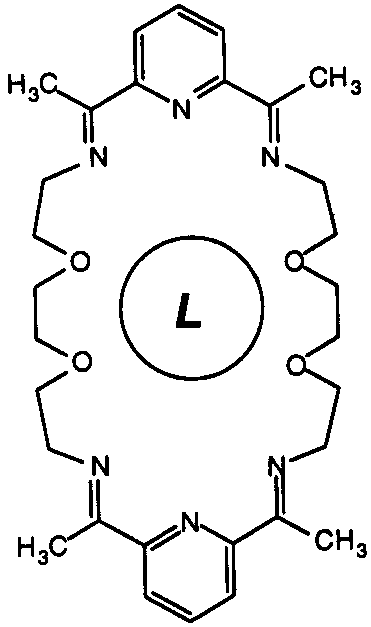


large metal cation templates
(e.g. Ba^{2+}, Pb^{2+})

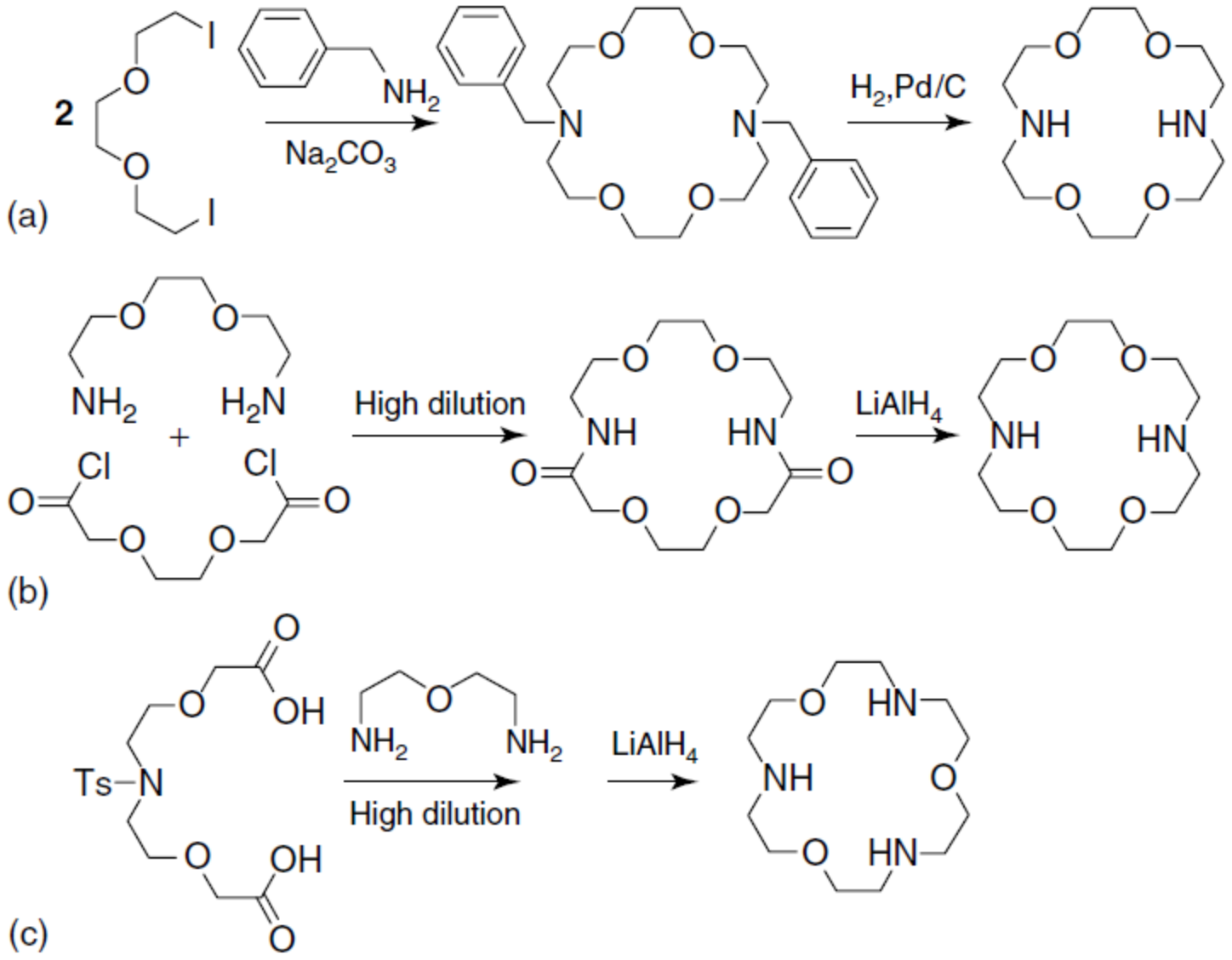


2.9

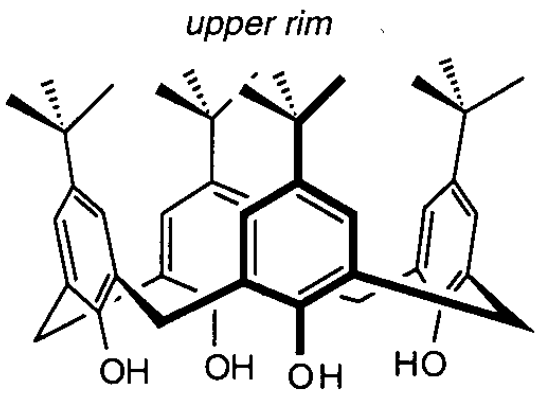
1 + 1 condensation



2 + 2 condensation

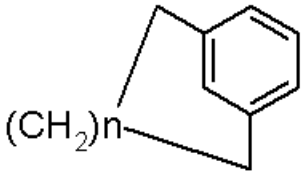

(a)
2
I
O
O
I
NH2
Na2CO3
N
N
O
O
O
O
H2,Pd/C
NH
HN
O
O
O
O
(b)
NH2
H2N
+
Cl
Cl
O
O
O
O
O
O
High dilution
NH
HN
O
O
O
O
O
O
LiAlH4
NH
HN
O
O
O
O
(c)
Ts
N
O
OH
O
OH
O
O
NH2
O
NH2
High dilution
LiAlH4
O
HN
NH
O
O
HN

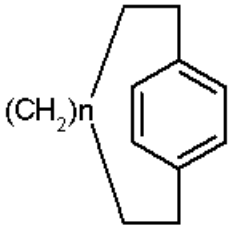
Calix[n]areni

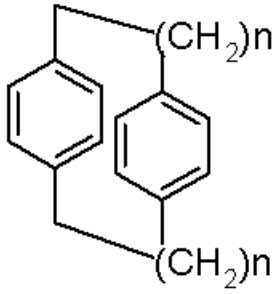


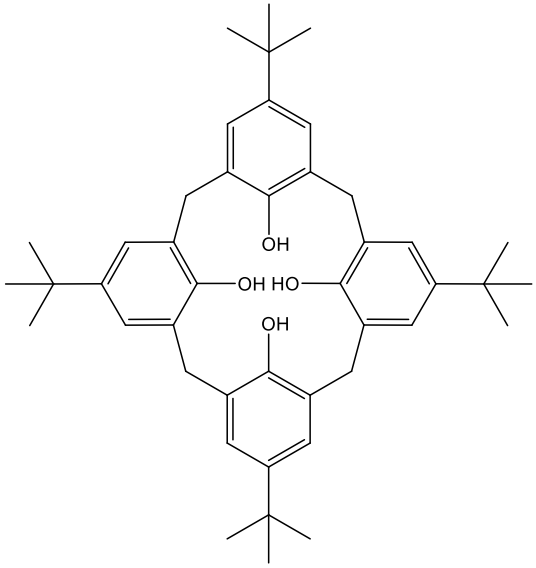
p-tert-Butylcalix[4]arene.

Ciclofani

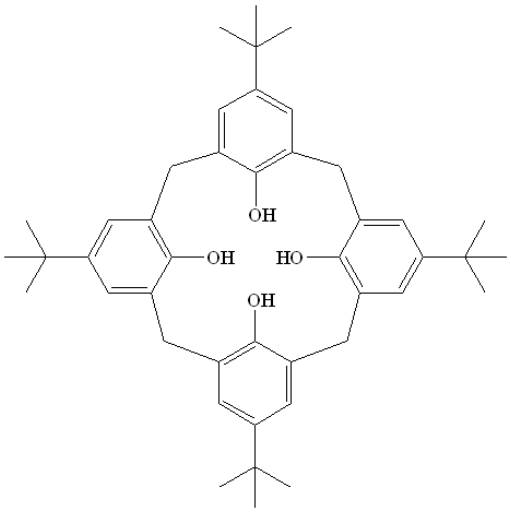


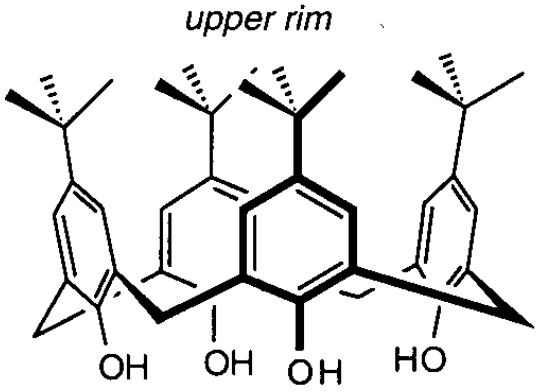




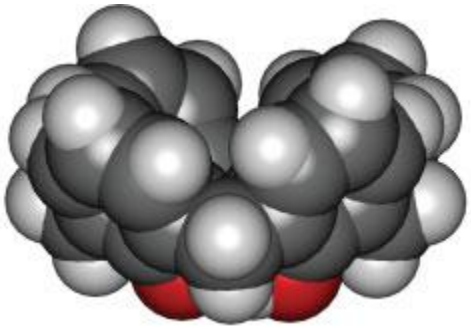


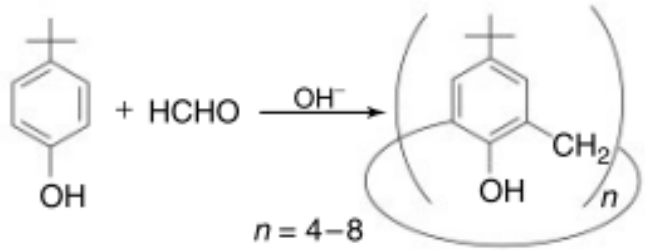
Calix[n]areni



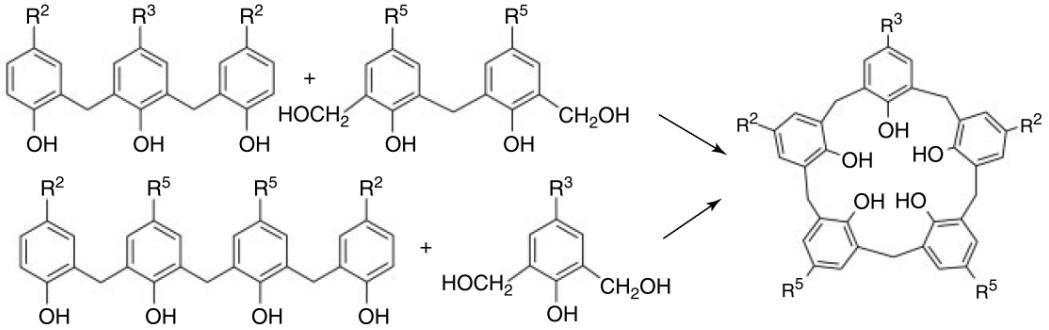


p-tert-Butylcalix[4]arene.

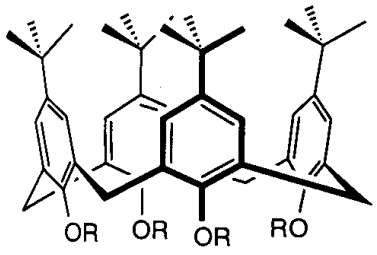




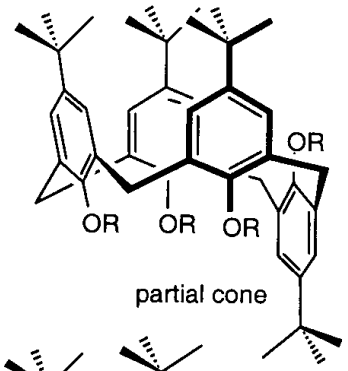
3+2 Fragment condensation



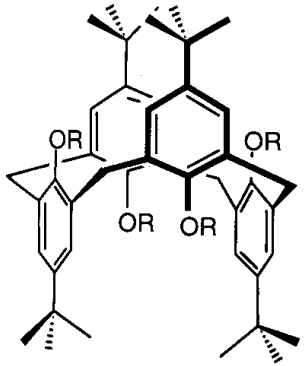
4+1 Fragment condensation



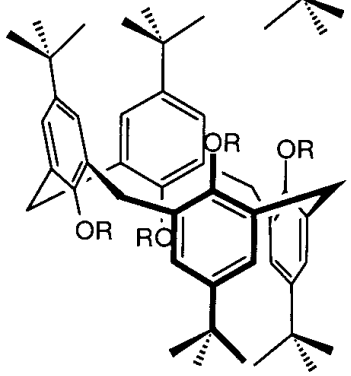
cone



partial cone

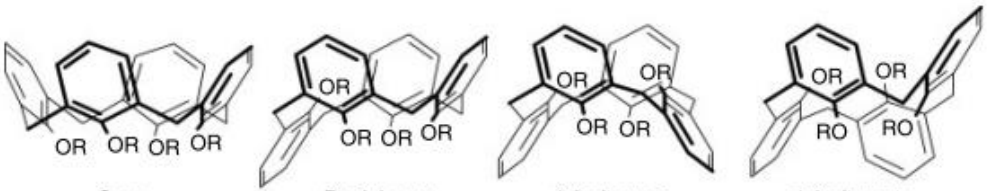


1,3-alternate



1,2-alternate

Conformations adopted by calix[4]arenes.



Cone | Partial cone | 1,3-alternate | 1,2-alternate

u, u, u, u | u, u, u, d | u, d, u, d | u, u, d, d

Calixarenes, which are [1$_n$]metacyclophanes comprising phenolic and methylene units,[1] are conformationally flexible compounds. The smallest of the known calixarenes are the cyclic tetramers, designated as calix[4]arenes (**1**), for which four "up-down" conformations can be specified, *viz* cone (all "up"), partial cone (three "up" and one "down"), 1,2-alternate (two "up" and two "down"), and 1,3-alternate (two "up" and two "down"), as illustrated in Fig. 1. Dynamic ^{1}H NMR measurements of several calix[4]arenes[2–4] have shown that they exist preferentially in the cone conformation but are conformationally mobile at room temperature, interconverting at a rate of *ca* 100 sec^{-1}. The con-

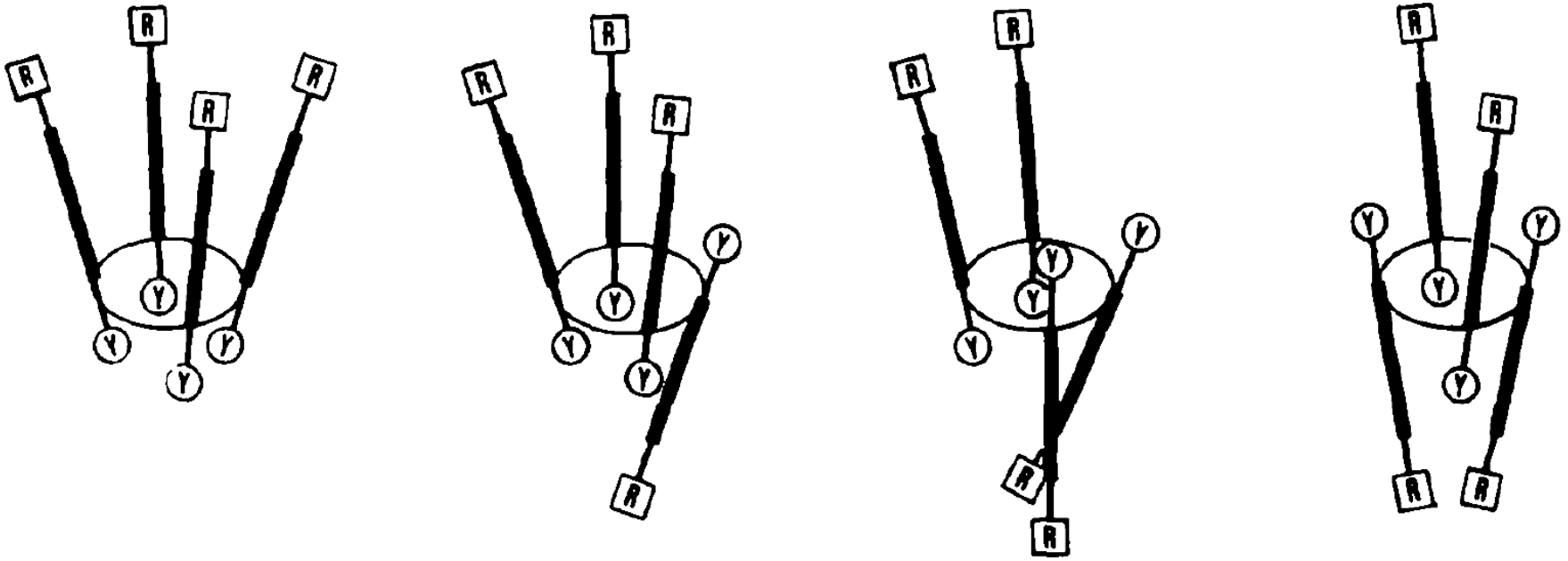
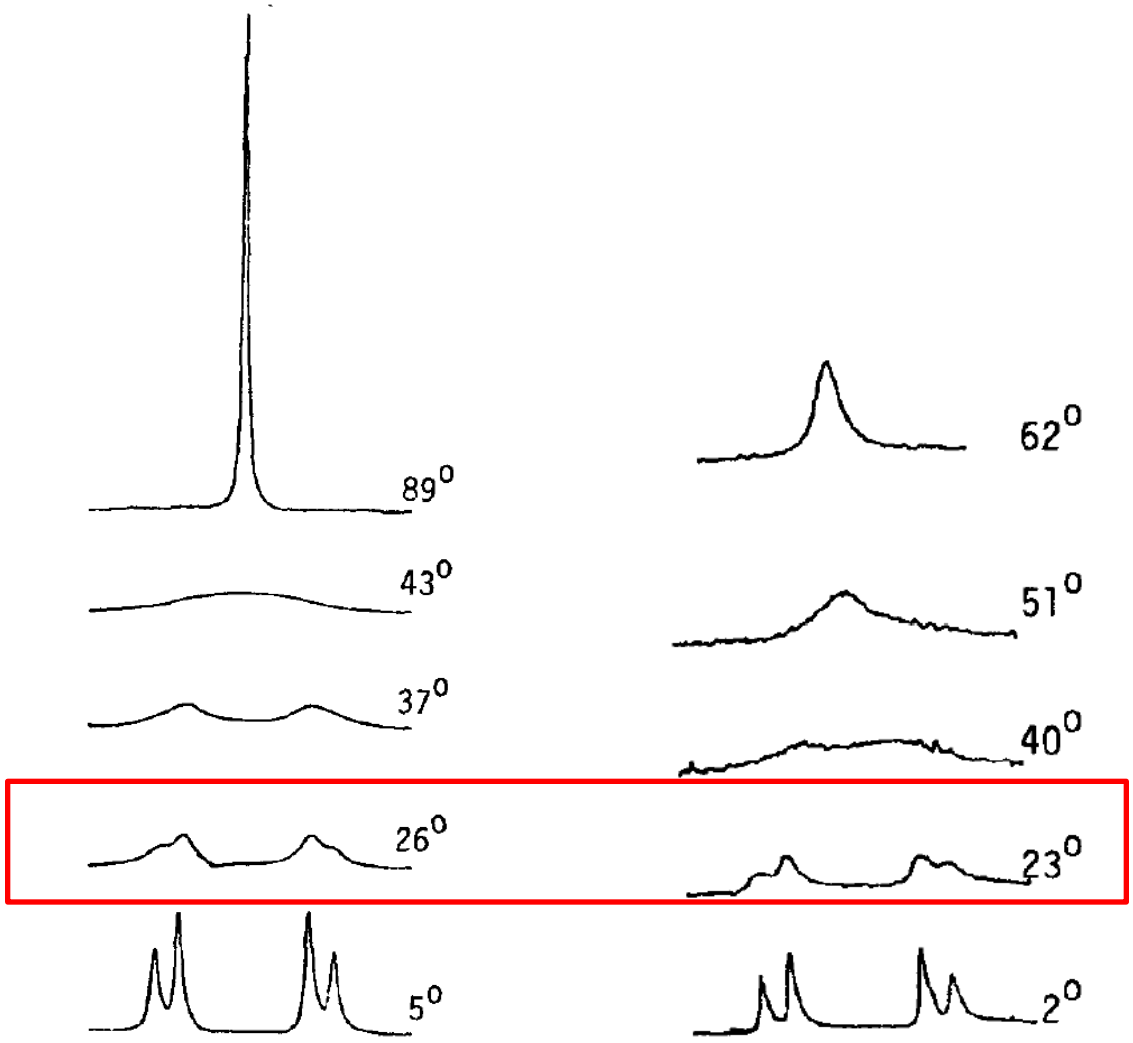
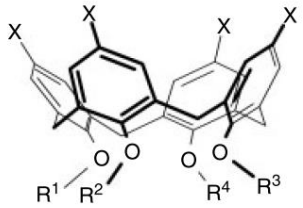


Fig. 1. Conformations of the calix[4]arenes.

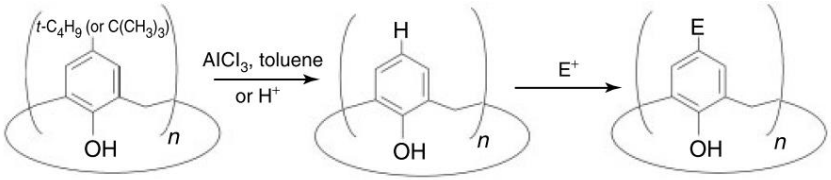


1-A. *p-tert*-butylcalix[4]-arene in bromobenzene-d_5

1-C. *p-tert*-butylcalix[4]-arene in $CDCl_3$

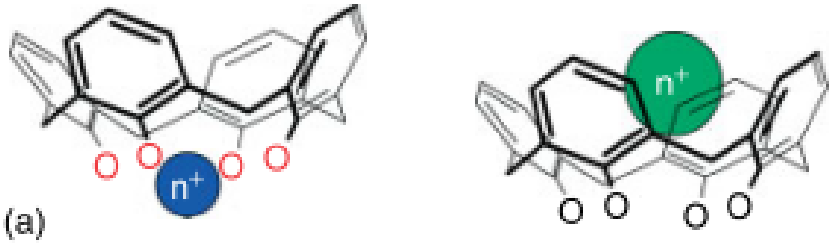


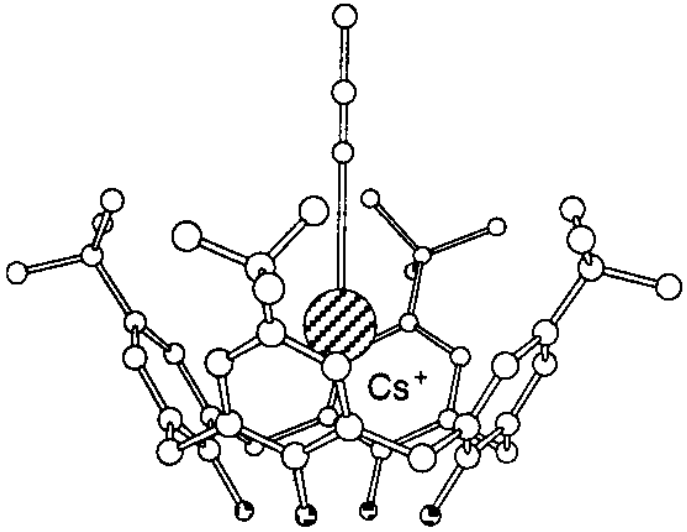
2a: R^1-R^4 = alkyl
2b: R^1, R^2 = alkyl, R^3, R^4 = OH
2c: R^1, R^3 = alkyl, R^2, R^4 = OH
2d: R^1 = alkyl, R^2–R^4 = OH
2e: R^1–R^3 = alkyl, R^4 = OH

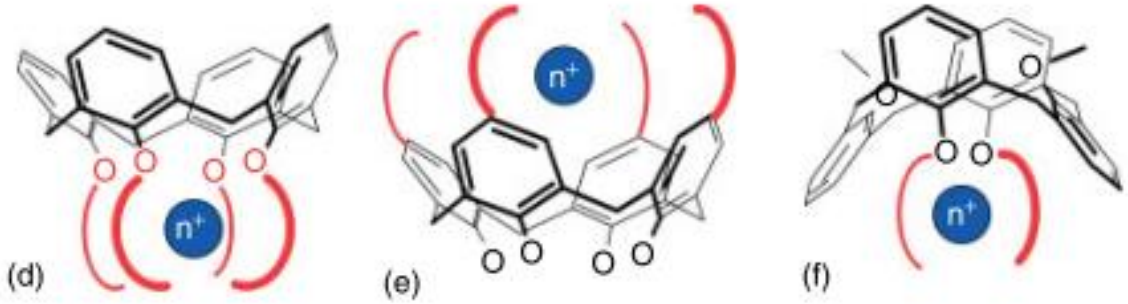


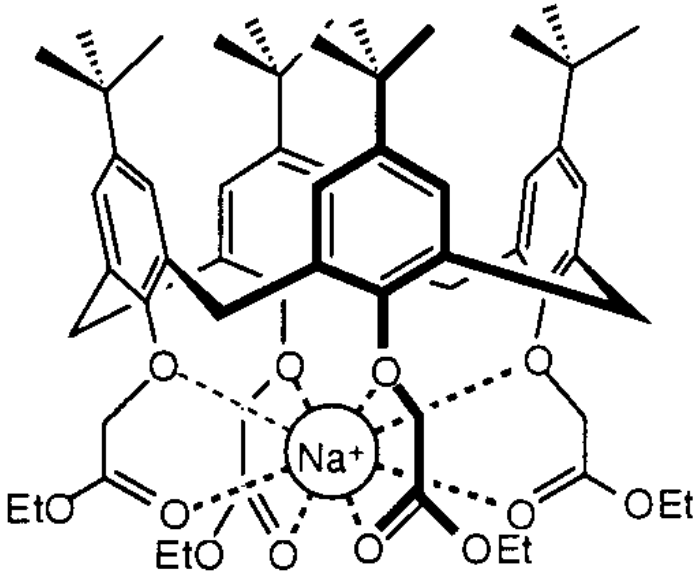
sons. Selective lower-rim (i.e., hydroxy) modification is increasingly important in modifying calixarene function,[4] and this usually involves initial deprotonation; however, much current design is empirical. Comprehensive pK_a data would allow improved rationalization of modification methodology. In calixarene host−guest interactions,[5] many guests are potential bases toward the calixarene; pK_a data would allow better assessment of the extent of ionic (e.g., ion-pair) vs dipolar (e.g., hydrogen-bonded) complexation. Calixarenes are increasingly being used as selective hosts for neutral and cationic guests, and the strength of binding is dependent on the protonation of the calixarene;[6] reliable pK_a data will allow better design of such systems. Calixarenes show a complex and varied conformational chemistry;[7] examination of pK_a data can provide information about conformational effects. Calixarene salts have been proposed as novel surfactants, and

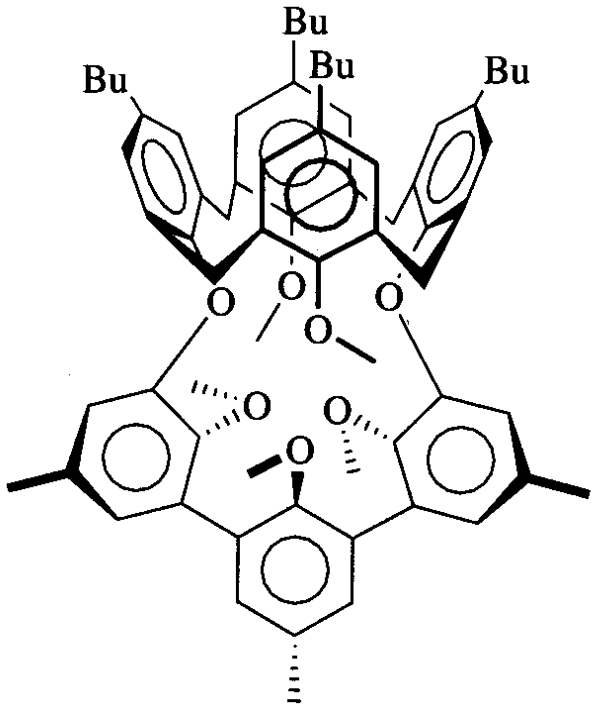
In conclusion, the recently established consistent scale of amine basicity in MeCN has been put to use to determine all accessible pK_a values for calix[4]arene, calix[6]arene, and calix[8]arene in MeCN. For mono-deprotonation, the dominant factor in calixarene acidity is the anion's ability to form internal hydrogen bonds that are not only numerous but also strong. For di-deprotonation, the ability to spatially separate the anions becomes important.


(a)
O
O
n+
O
O
n+
O
O
O
O

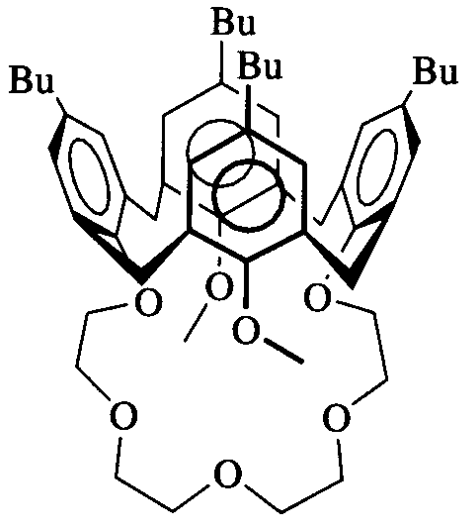

Cs+


(d)
n+
(e)
n+
(f)
n+

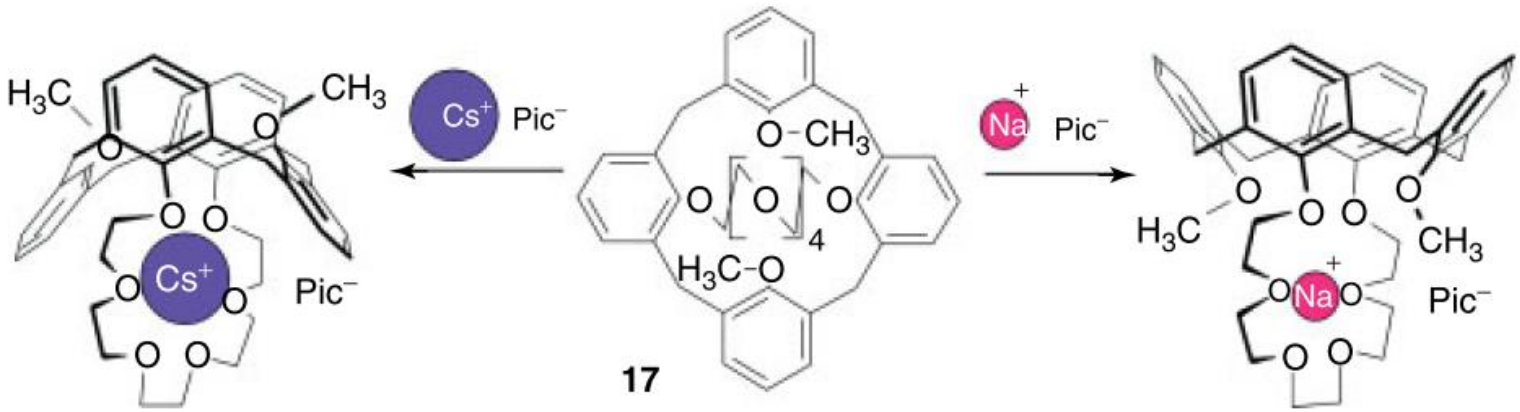

Na+
EtO
EtO
OEt
OEt



Calix-sferando



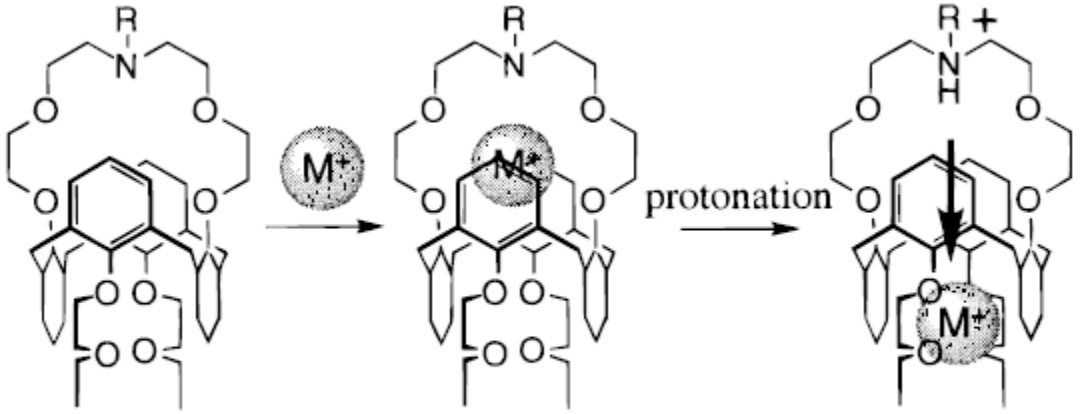
Calix-crown

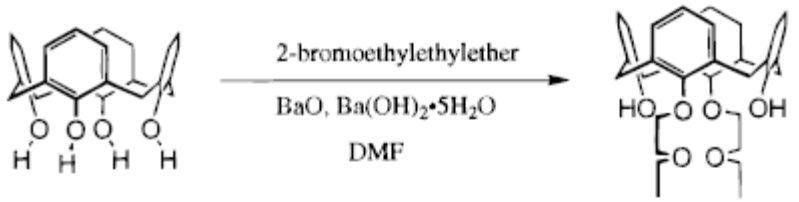

H3C
CH3
O
O
O
O
O
O
O
O
Cs+
Pic−
Cs+
Pic−
O−CH3
O
O
O
4
H3C−O
17
Na+
Pic−
O
O
O
O
H3C
CH3
O
Na+
O
O
O
Pic−

J. Org. Chem. **1997**, *62*, 3568−3574

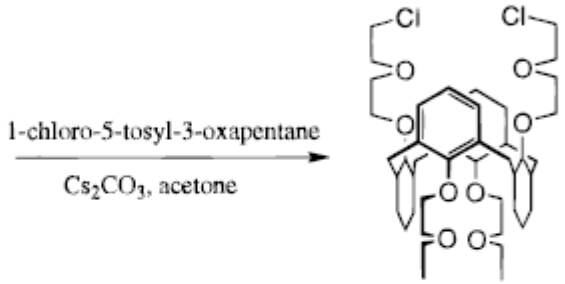
Molecular Design of a "Molecular Syringe" Mimic for Metal Cations Using a 1,3-Alternate Calix[4]arene Cavity

Atsushi Ikeda, Takanobu Tsudera, and Seiji Shinkai*

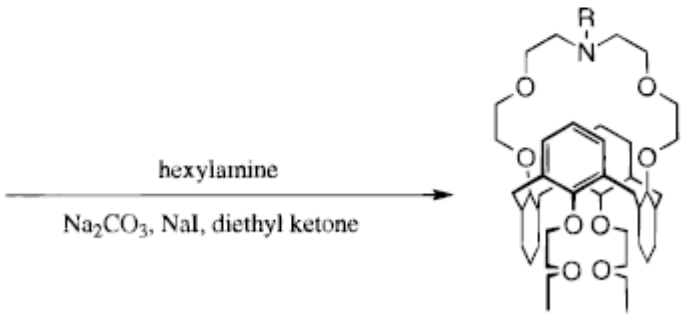




2



1,3-alternate **3**



$R=CH_2(CH_2)_4CH_3$

1

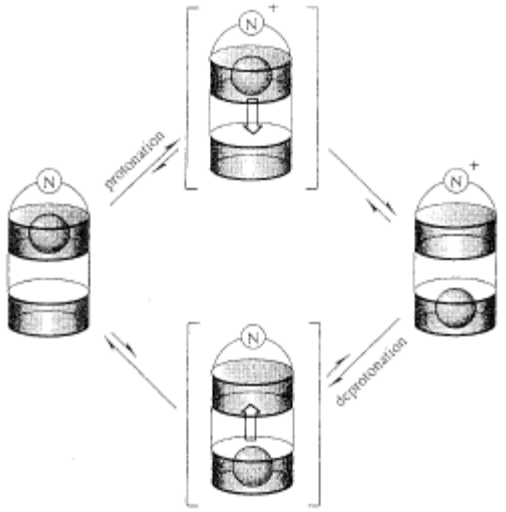
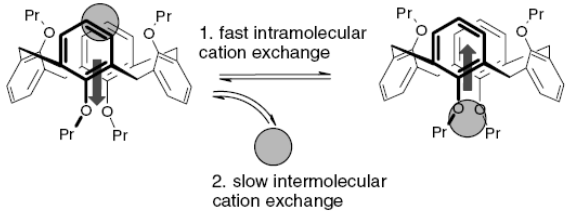


Figure 8. Schematic representation of a reversible metal pumping in a microscopic "molecular syringe" **1** designed from 1,3-alternate calix[4]arene.



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

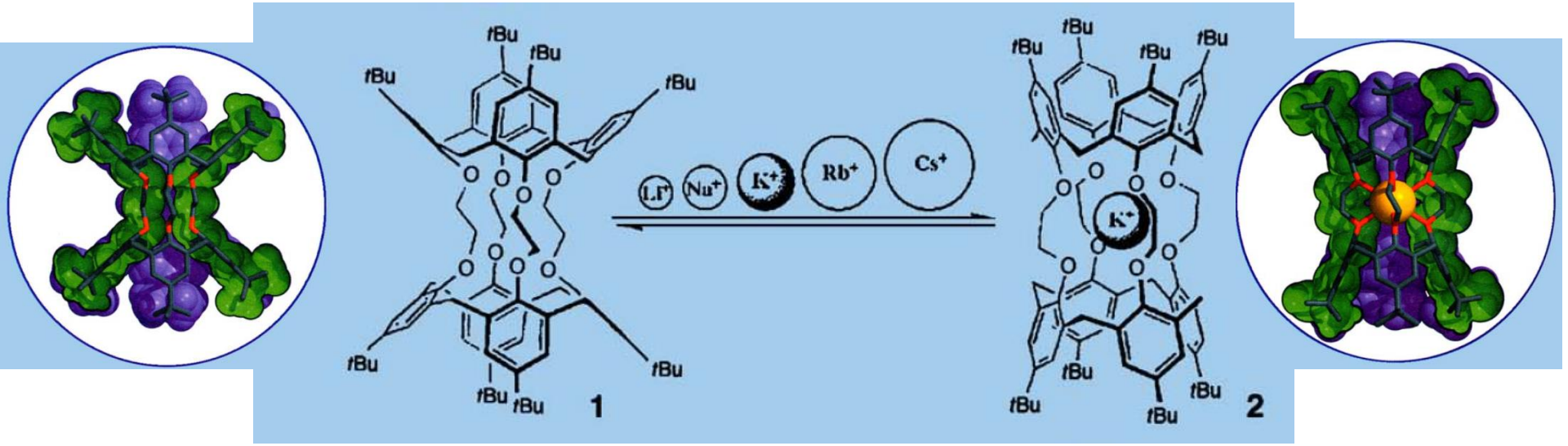
Declan A. Doyle, João Morais Cabral, Richard A. Pfuetzner, Anling Kuo, Jacqueline M. Gulbis, Steven L. Cohen, Brian T. Chait, Roderick MacKinnon*

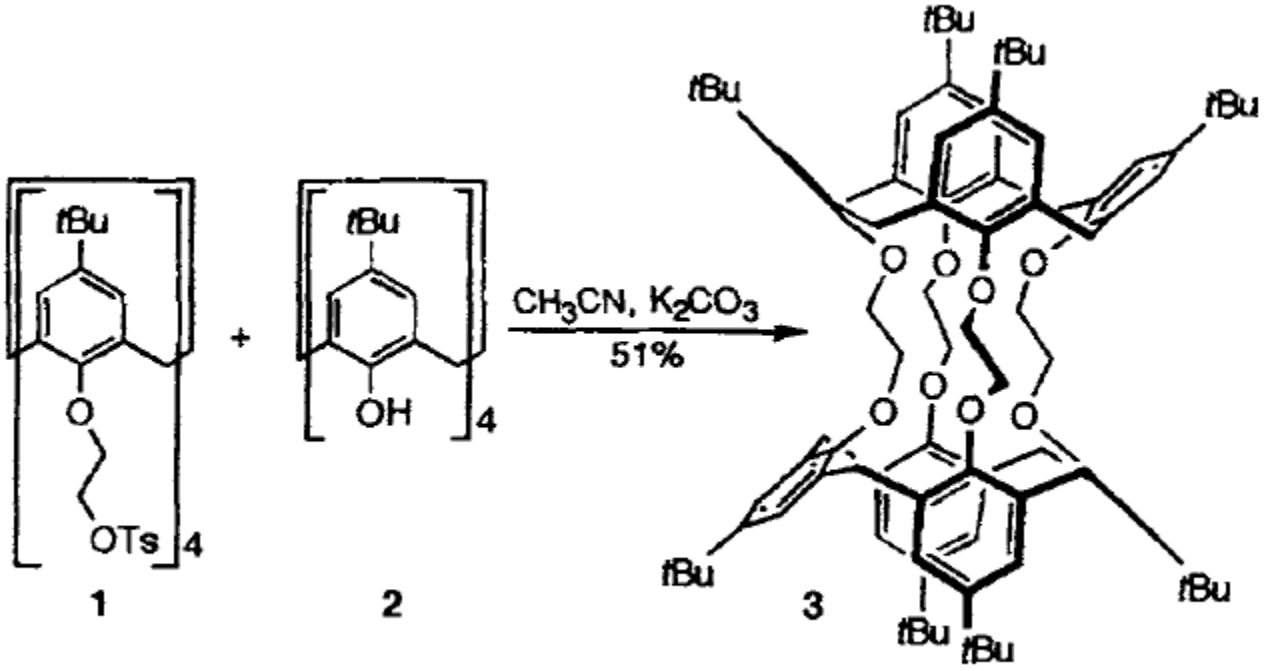
Science **280**, 69 (1998);
DOI: 10.1126/science.280.5360.69

Calix[4]tube: A Tubular Receptor with Remarkable Potassium Ion Selectivity**

Philippe Schmitt, Paul D. Beer,* Michael G. B. Drew, and Paul D. Sheen

Angew. Chem. Int. Ed. Engl. **1997**, *36*, 1840





Scheme 1. Synthesis of the calix[4]tube **3**.

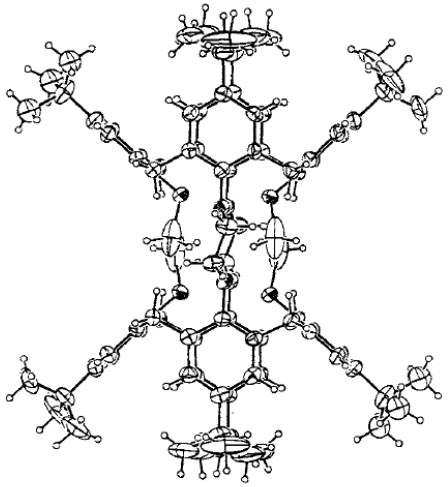


Figure 1. Crystal structure of the centrosymmetric calix[4]tube **3** in $3 \cdot 2.5\,C_6H_6$, with ellipsoids at 30% probability. Hydrogen atoms are included with small arbitrary radii. The benzene solvent molecules are not shown.

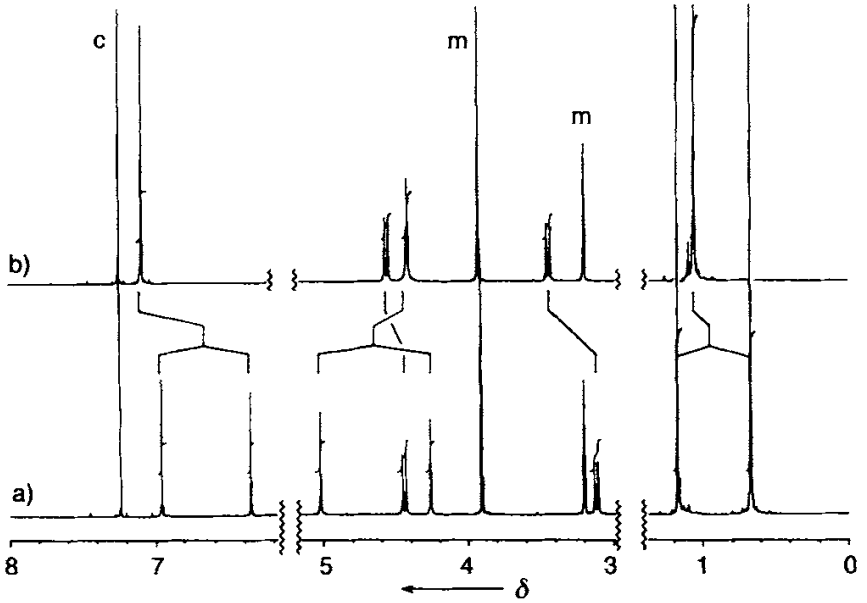


Figure 2. ^1H NMR spectrum of **3** [500 MHz, $CDCl_3/CD_3OD$ 4/1 (v/v)]: a) pure, b) with 10 equivalents of solid potassium iodide (c, m: solvent peaks corresponding to chloroform and methanol, respectively).

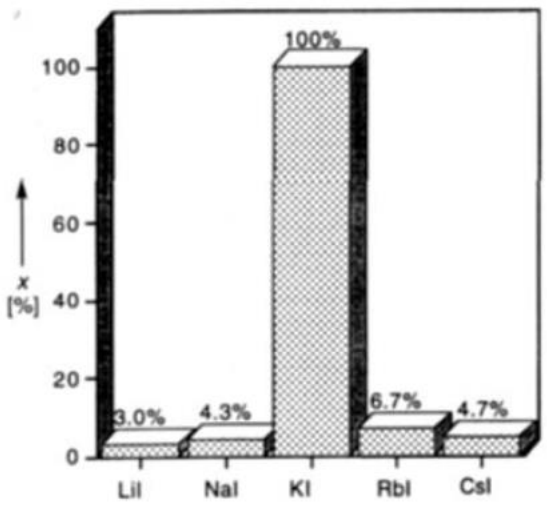


Figure 3. Uptake of alkali metal ions by **3** after treating its chloroform-methanol solution (4/1, [**3**] = 1 mM) with 10 equivalents of alkali metal iodide. The complexation ratio x was determined by integration of the ^{1}H NMR spectra after the samples had been left to stand for 90 h. In the case of KI, equilibrium was reached within an hour.

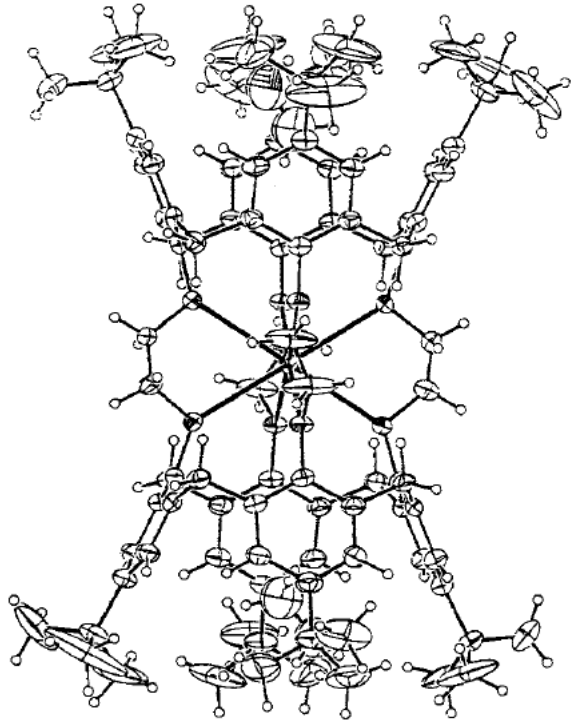
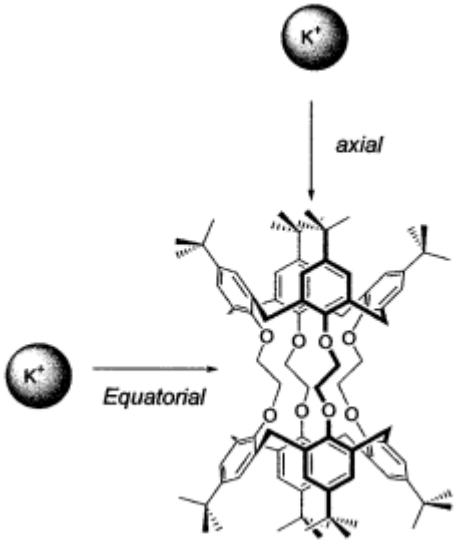
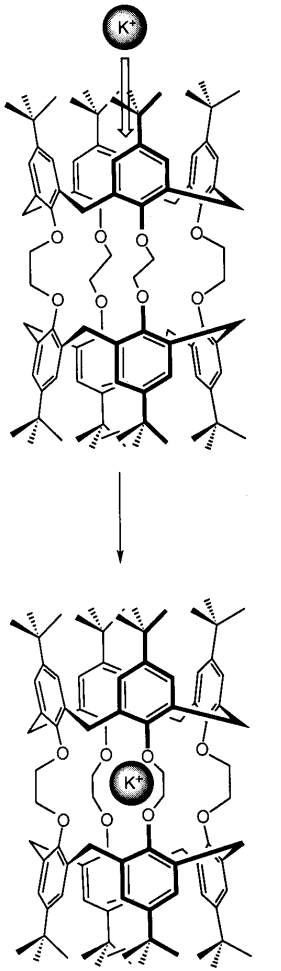


Figure 4. Structure of the K^+ complex **4** of the calix[4]tube **3** in crystals of **4**·I·3 $CHCl_3$·4 CH_3OH·H_2O. A potassium ion is located in the center of **3**, and two methanol molecules in the cone cavities. Ellipsoids are drawn at 30% probability. Hydrogen atoms are included with small arbitrary radii. The chloroform and water solvent molecules are not shown.

Calix-tubes



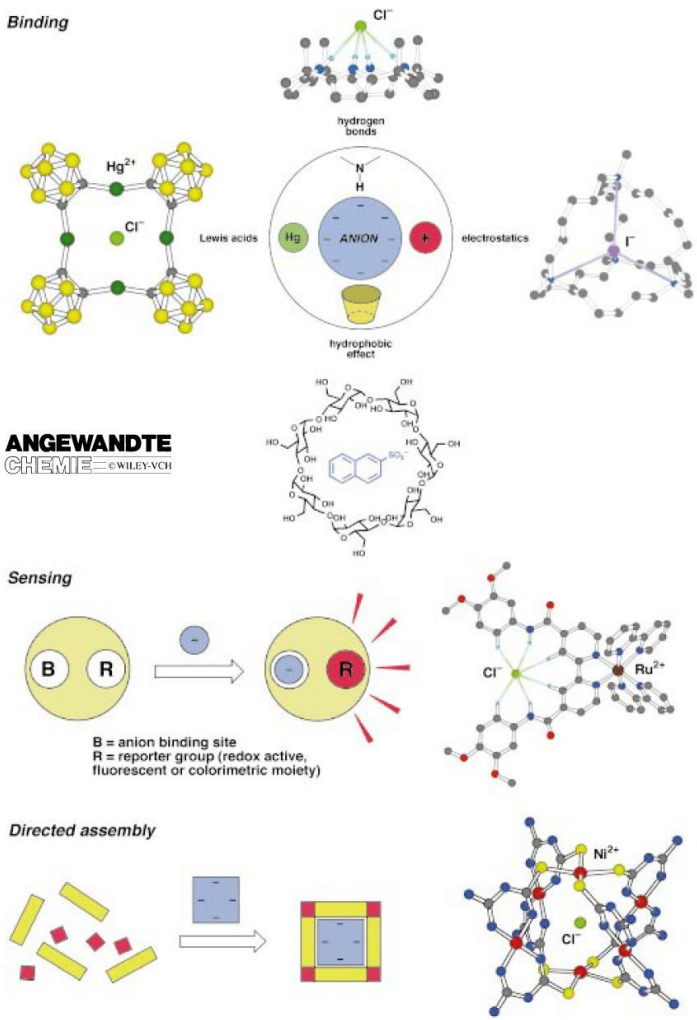


Potassium encapsulation in calix[4]tube

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

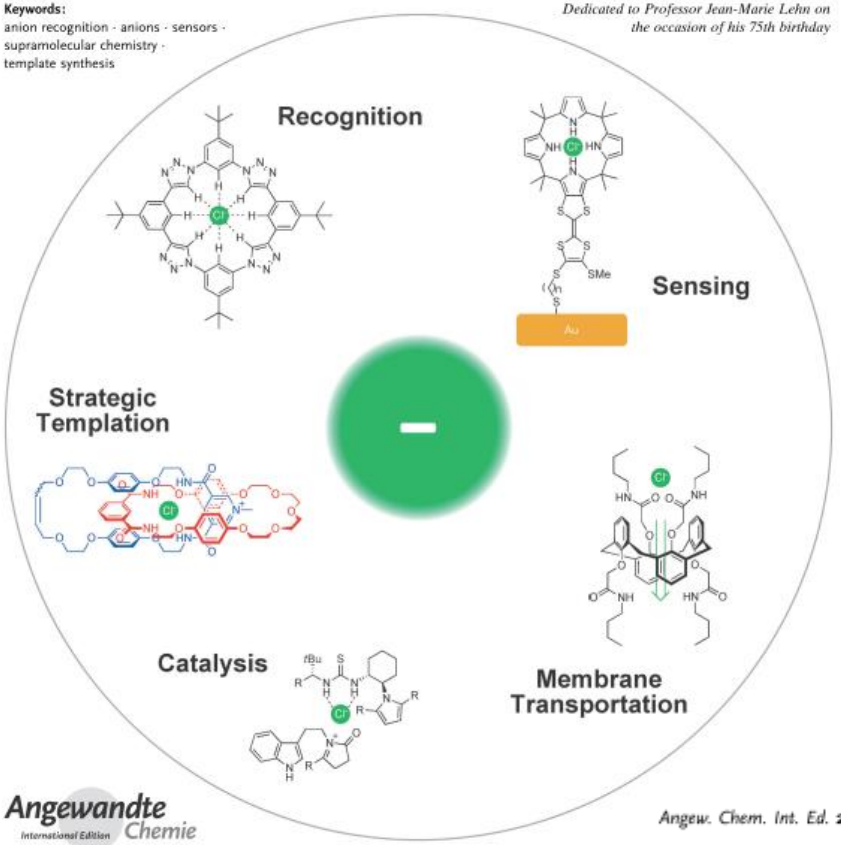
Supramolecular Chemistry of Anions

Advances in Anion Supramolecular Chemistry: From Recognition to Chemical Applications

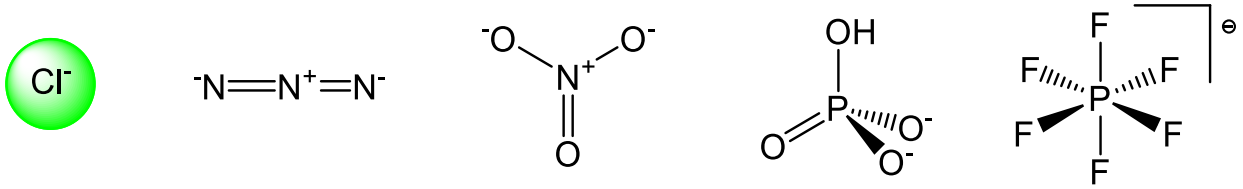
Nicholas H. Evans and Paul D. Beer**

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 - $r(F^-) \approx rK^+$
- large diversity of shapes and geometries (spherical, linear, trigonal, tetrahedral…)



- high free energies of hydration

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

spherical

F^-, Cl^-, Br^-, I^-

linear

N_3^-, CN^-, SCN^-, OH^-

trigonal planar

CO_3^{2-}, NO_3^-

tetrahedral

PO_4^{3-}, VO_4^{3-}, SO_4^{2-},
MoO_4^{2-}, SeO_4^{2-}, MnO_4^-

octahedral

$[Fe(CN)_6]^{4-}$, $[Co(CN)_6]^{3-}$

complex shapes

DNA double helix

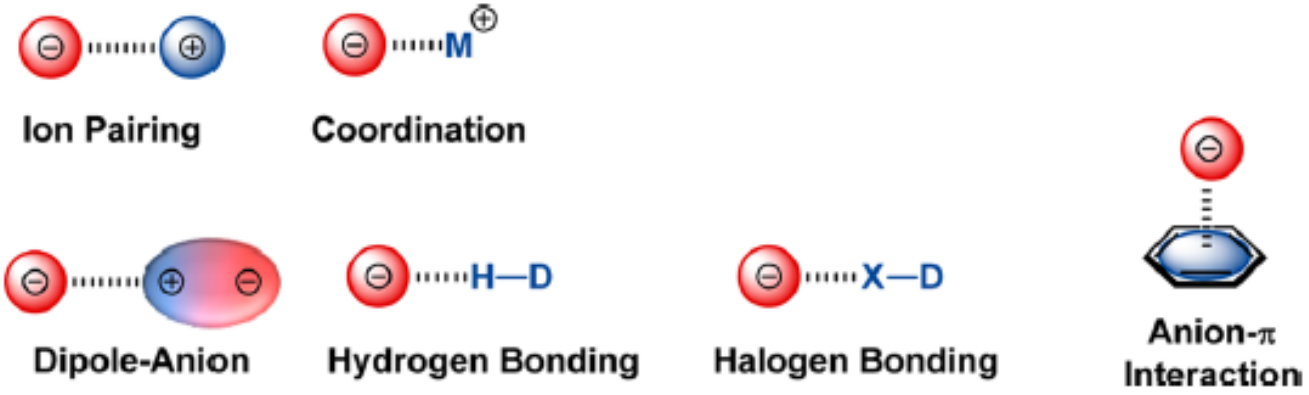
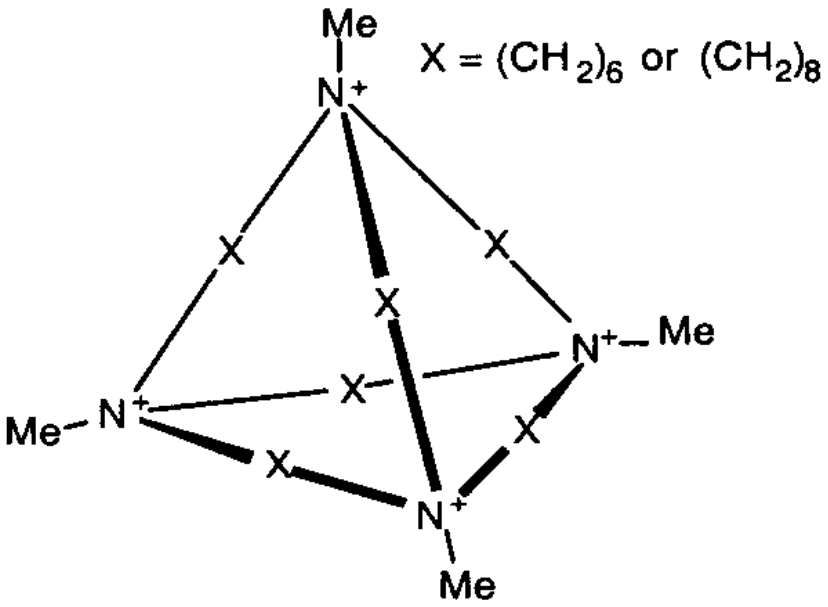


Figure 1. Representation of different interactions found in anion sensing and recognition.

Host cationici



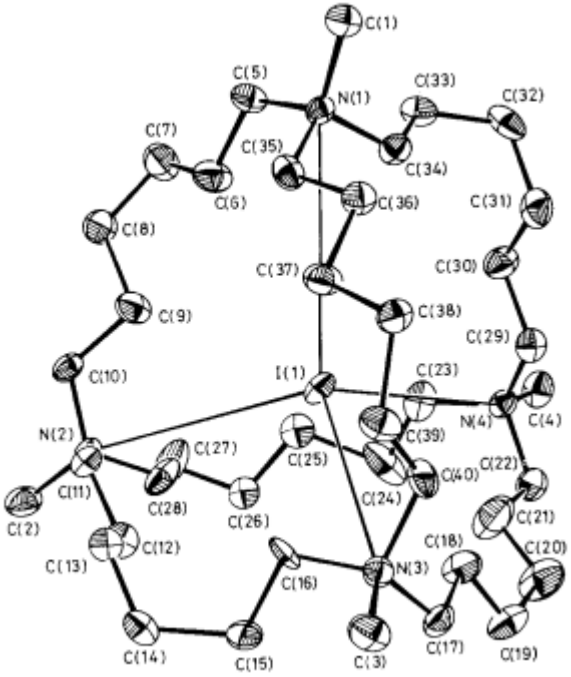
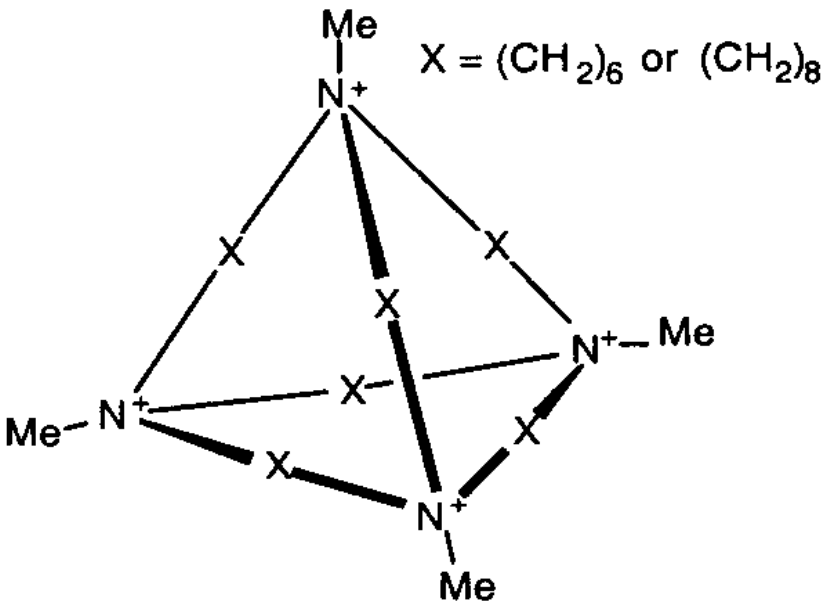


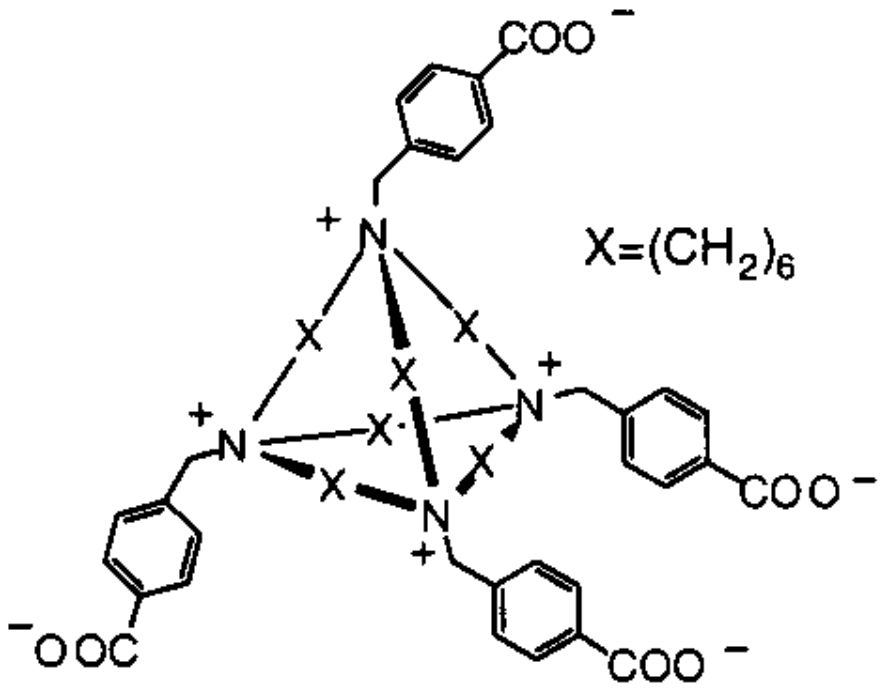
Figure 2. The X-ray crystal structure of the iodide complex of receptor **1**

Schmidtchen

Host cationici



Host zwitter-ionici

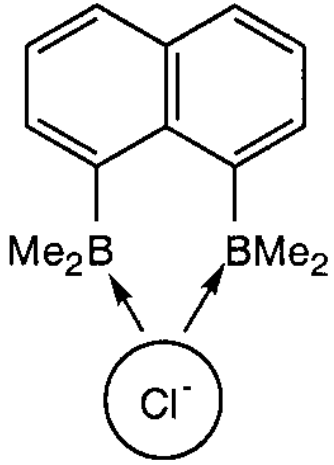


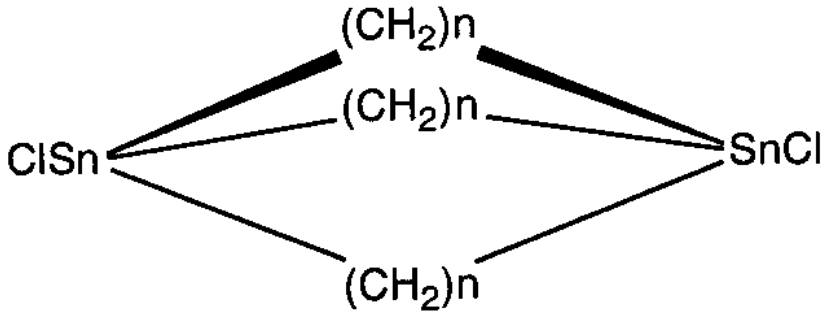
$K(Br^-) = 1020$ (H_2O)

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

Selettività <<

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

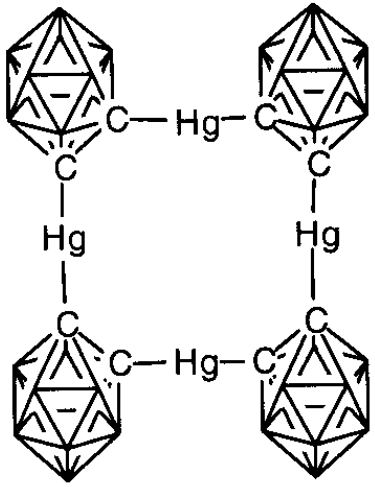




n= 6 , 8

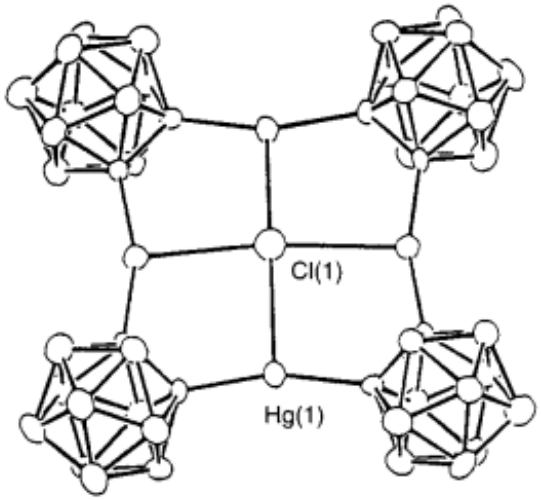
Organotin cryptand encapsulates fluoride anions.

Organo-Boro



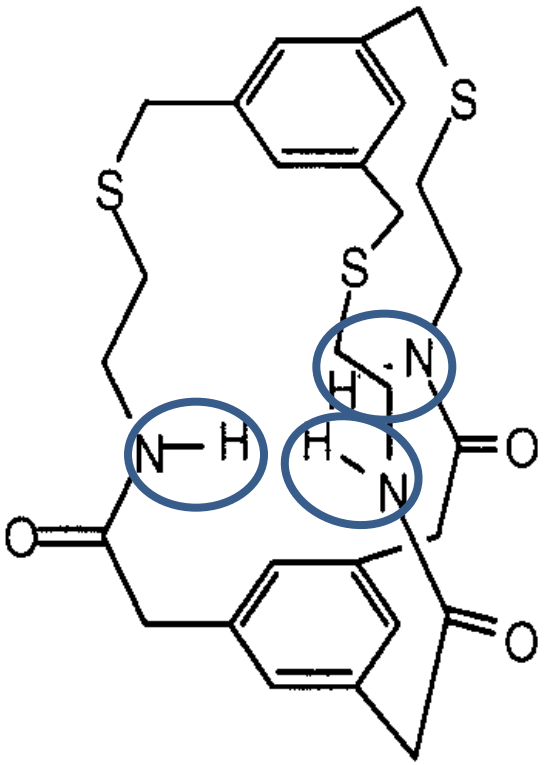
Organo-Sn(IV)

Organo-Hg(II)



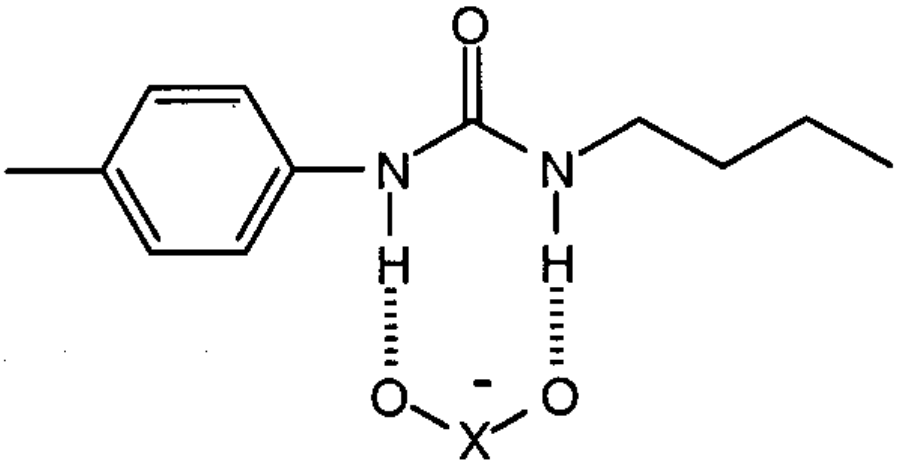
= $B_{10}C_2$

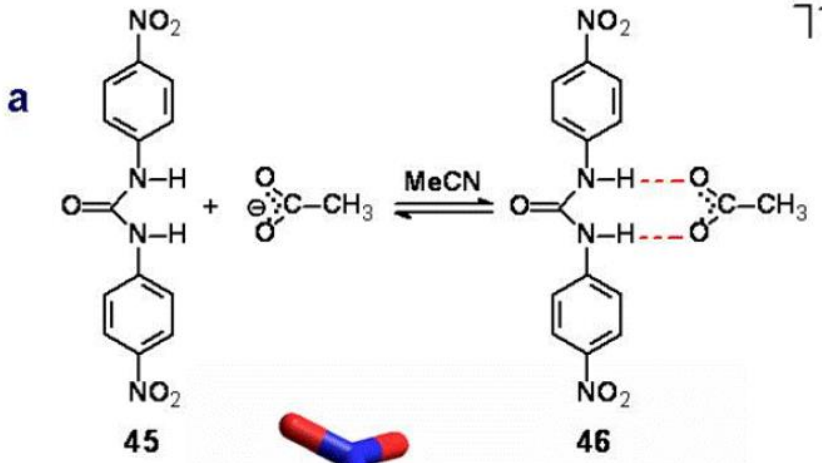
Hawthorne

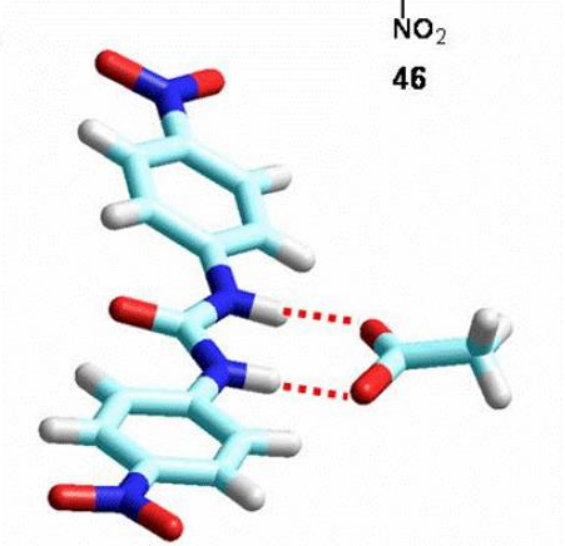


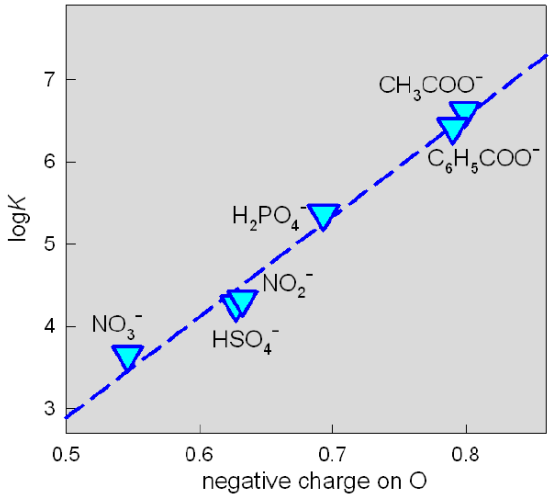
Hydrogen bonding receptor for fluoride anions.

Pascal

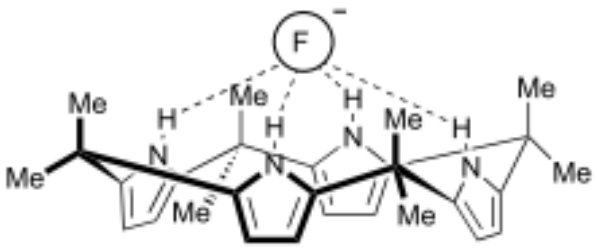


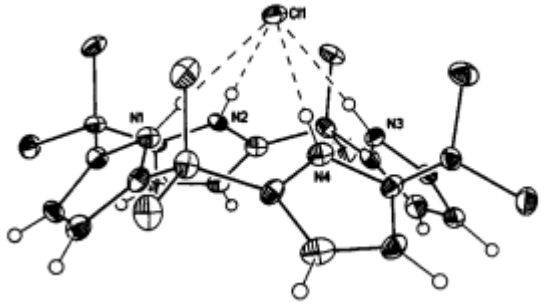

a
NO2
N–H
N–H
NO2
MeCN
C–CH3
45
46

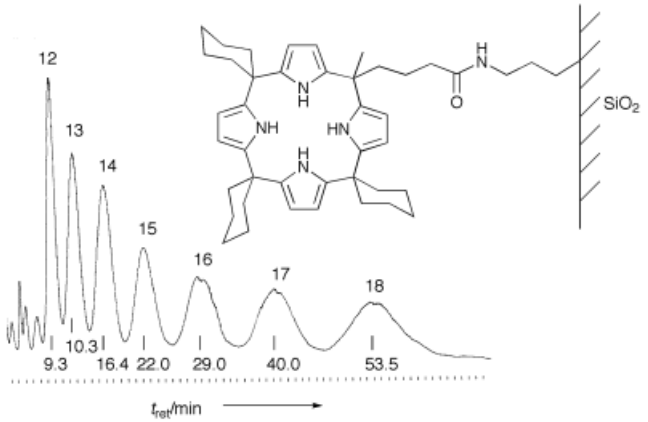

b


logK
negative charge on O
CH3COO-
C6H5COO-
H2PO4-
NO2-
HSO4-
NO3-
7
6
5
4
3
0.5
0.6
0.7
0.8

Fabrizzi

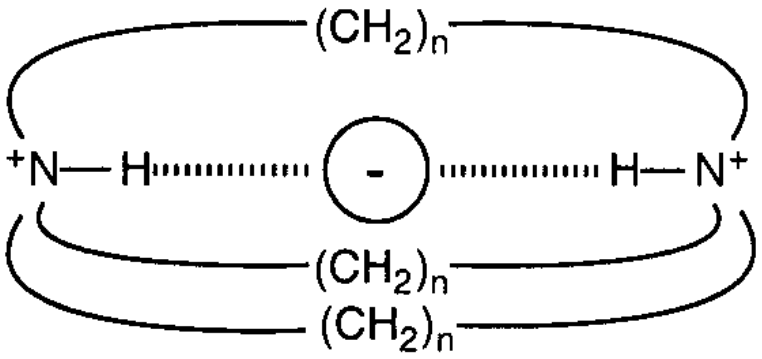




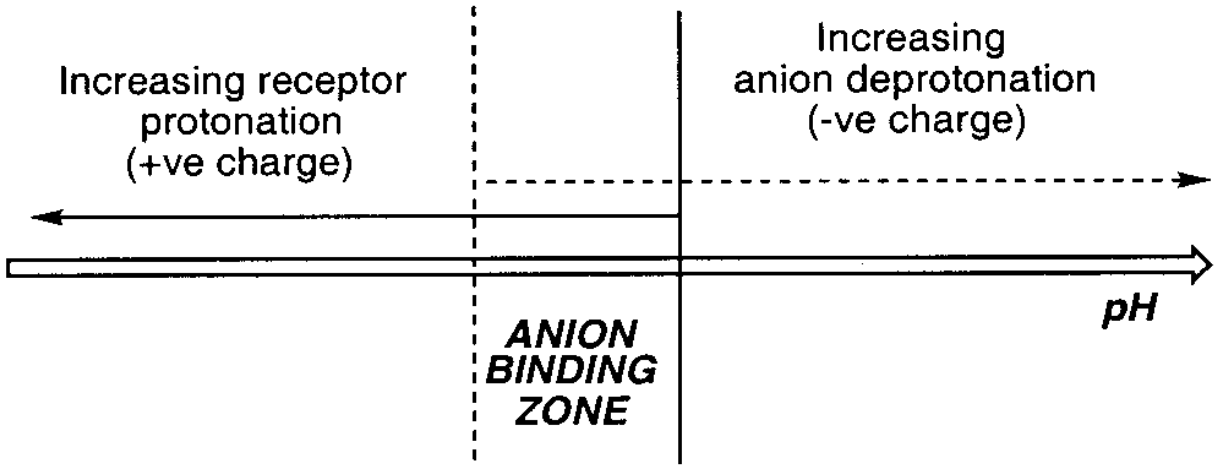


HPLC Separation of oligonuclotides of different lenght

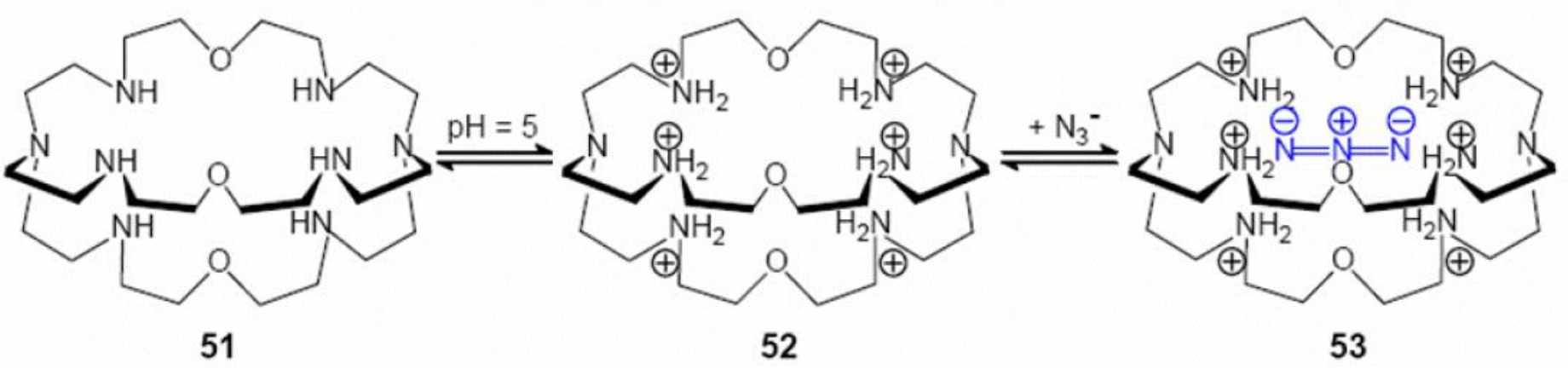
Sessler

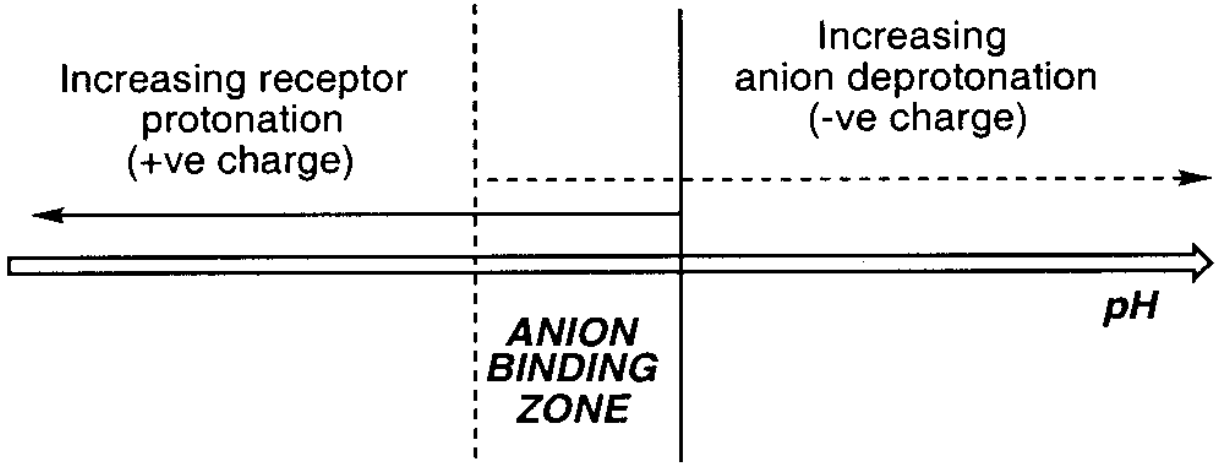


poliazamacrocicli

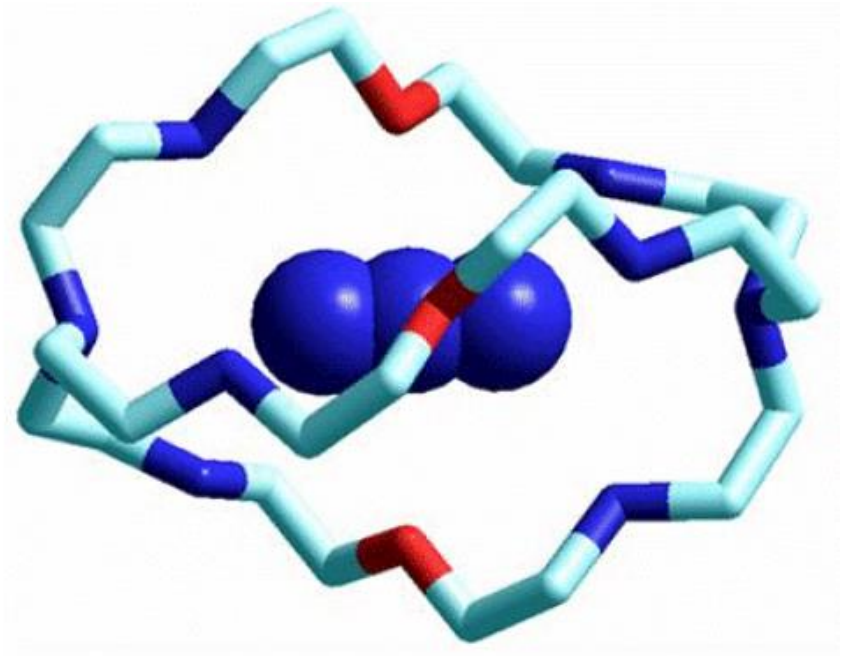


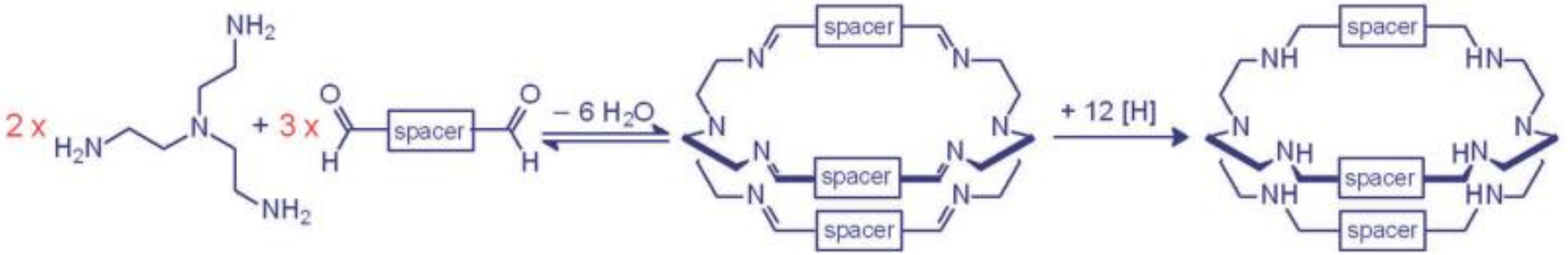
Balance between host protonation and guest deprotonation.

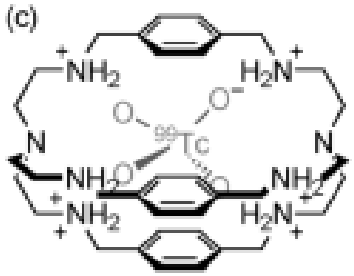




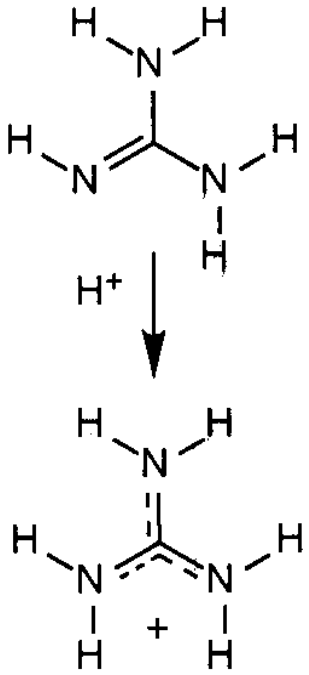
Balance between host protonation and guest deprotonation.



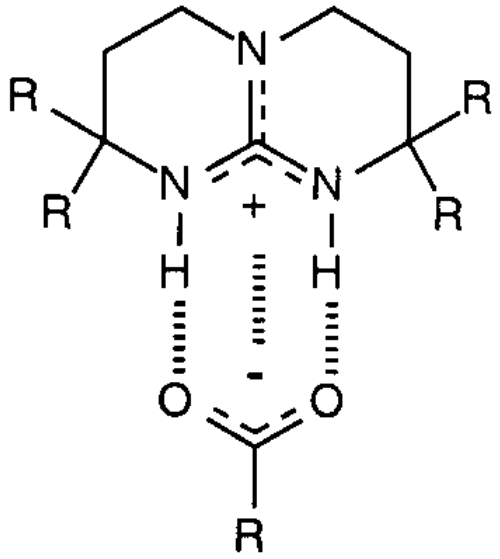

2 x
NH2
H2N
N
NH2
+ 3 x
O
H
spacer
O
H
– 6 H2O
spacer
N
N
N
N
N
N
spacer
spacer
+ 12 [H]
spacer
NH
HN
N
N
NH
HN
NH
HN
spacer
spacer


(c)
NH2
H2N
O
O
99
Tc
O
O
N
N
NH2
NH2
NH2
H2N

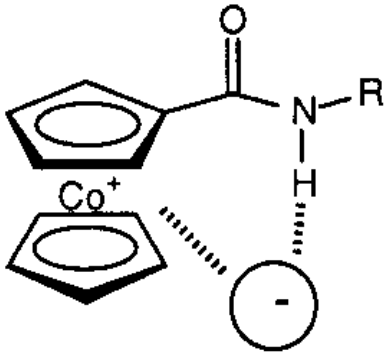
Fabrizzi



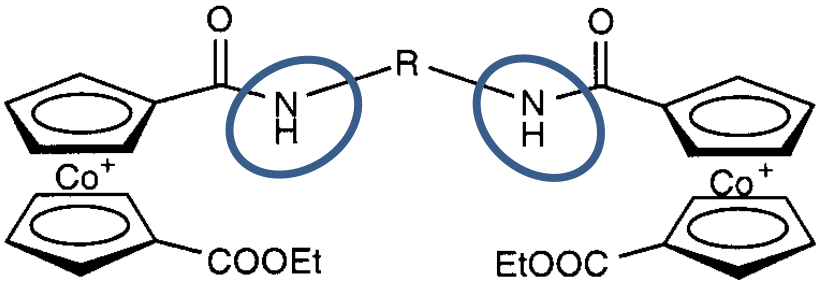
pKa = 13.6



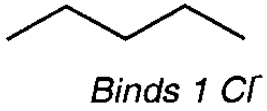
Bicyclic guanidinium is preorganized and complementary for binding bidentate anions.



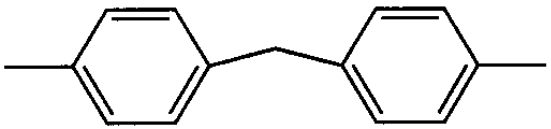
Amide functionalized cobaltocenium binds anions.



—R— =



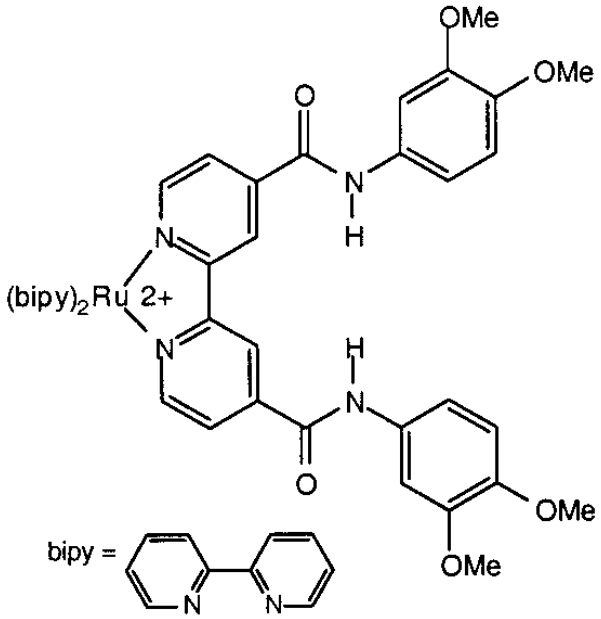
Binds 1 Cl⁻

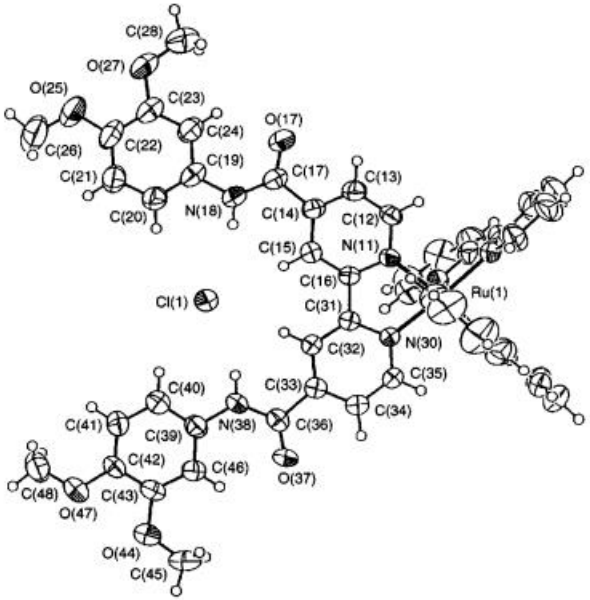


Binds 2 Cl⁻

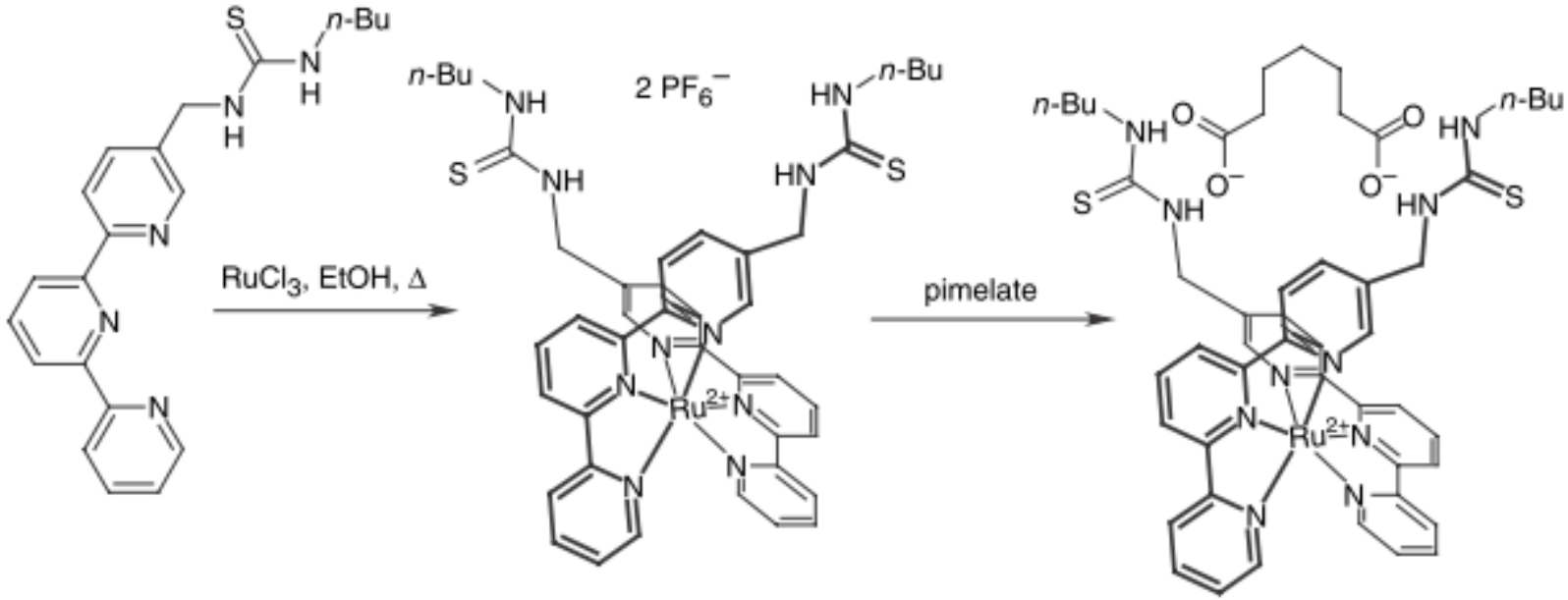
Cobaltocenium based anion receptors have easily tunable binding sites.

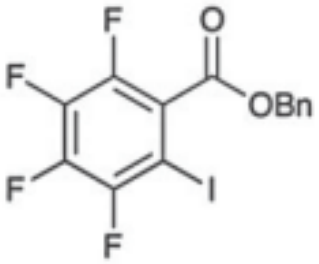
Beer

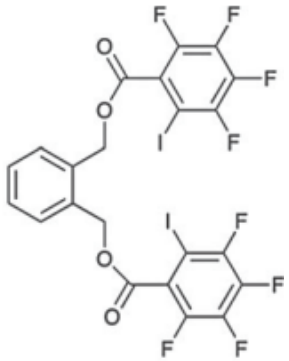

OMe
OMe
O
N
H
N
(bipy)2Ru 2+
N
H
N
O
OMe
OMe
bipy =
N
N

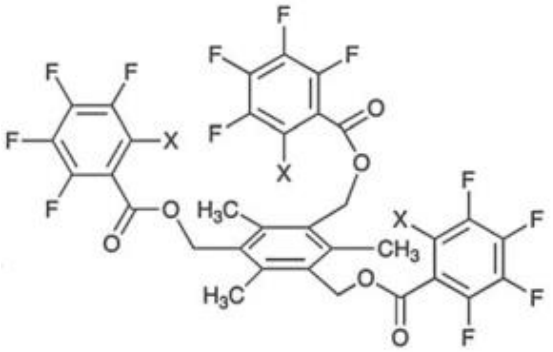

C(28)
O(27)
O(25)
C(23)
C(24)
O(17)
C(26)
C(22)
C(19)
C(17)
C(13)
C(21)
C(20)
N(18)
C(14)
C(12)
C(15)
N(11)
C(16)
Cl(1)
C(31)
Ru(1)
C(32)
N(30)
C(35)
C(40)
C(33)
C(41)
N(38)
C(36)
C(34)
C(39)
C(42)
C(46)
O(37)
C(48)
C(43)
O(47)
O(44)
C(45)

Beer

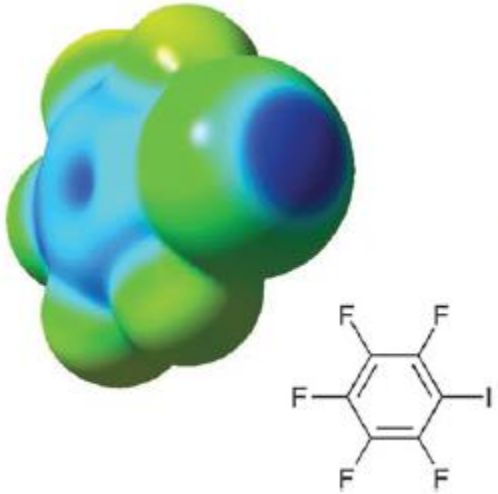

S
n-Bu
N
H
N
H
N
N
N
RuCl3, EtOH, Δ
n-Bu
NH
S
NH
2 PF6−
HN
n-Bu
HN
S
N
N
N
Ru2+
N
N
N
pimelate
n-Bu
NH
S
NH
O
O−
O
O−
HN
n-Bu
HN
S
N
N
N
Ru2+
N
N
N



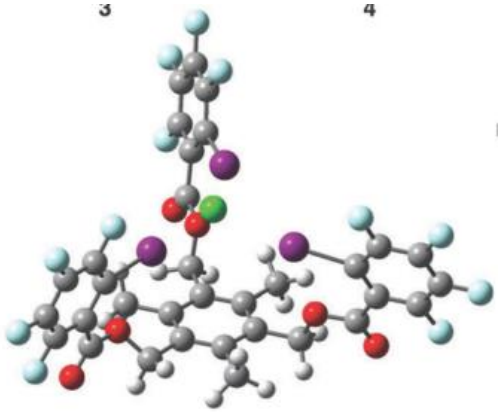




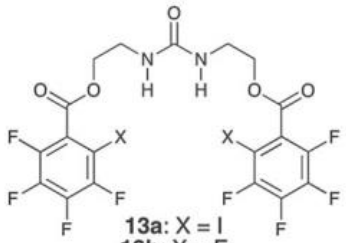
ortho-substituted iodotetrafluroroarenes on to trimethylbenzene scaffold



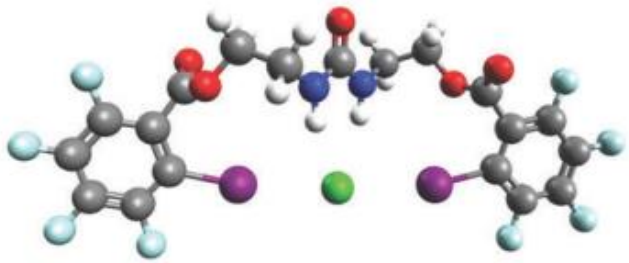
In acetone: $Cl^- > Br^- > I^-$

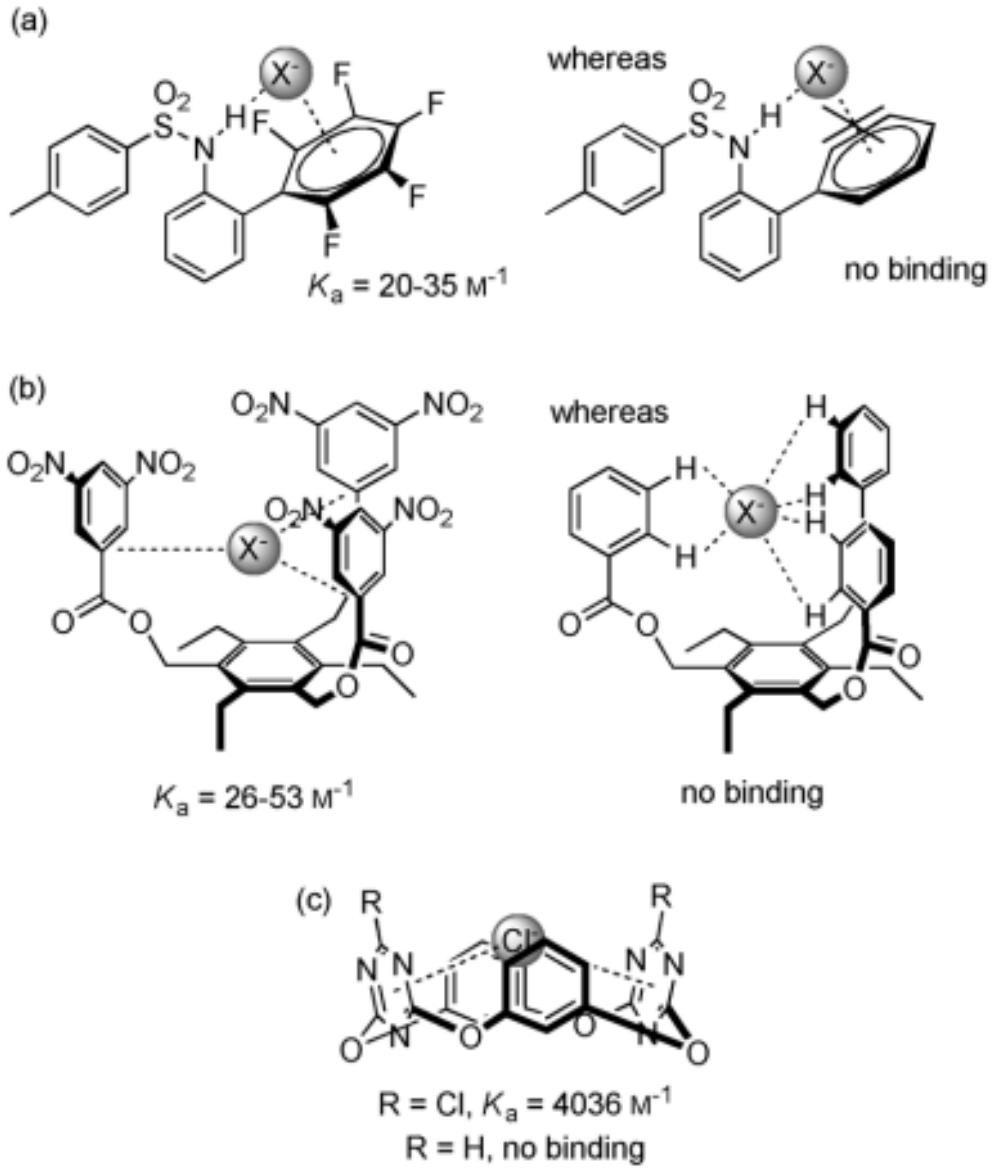


Taylor



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




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

Berryman

(a)

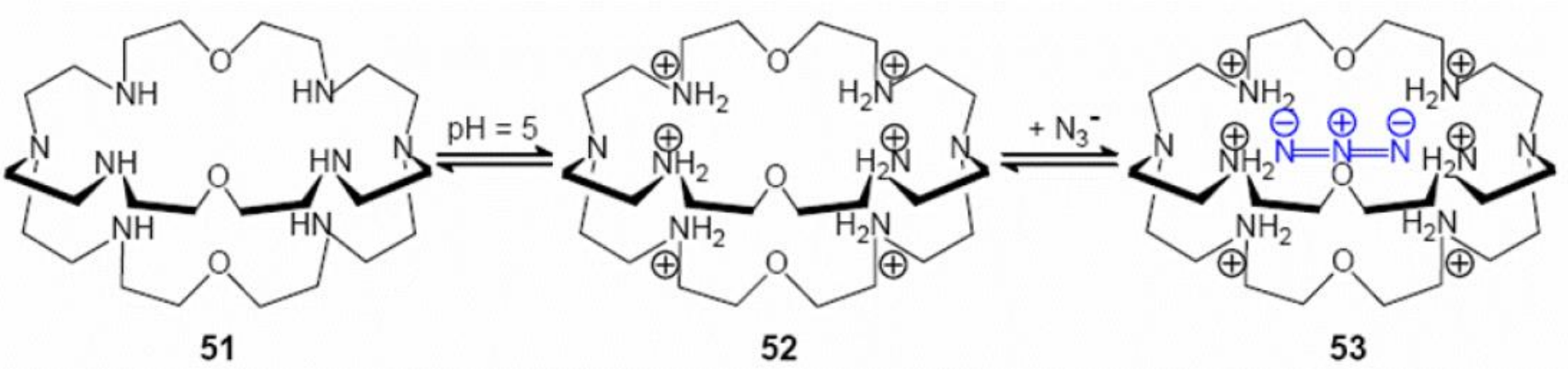
A cascade complex.

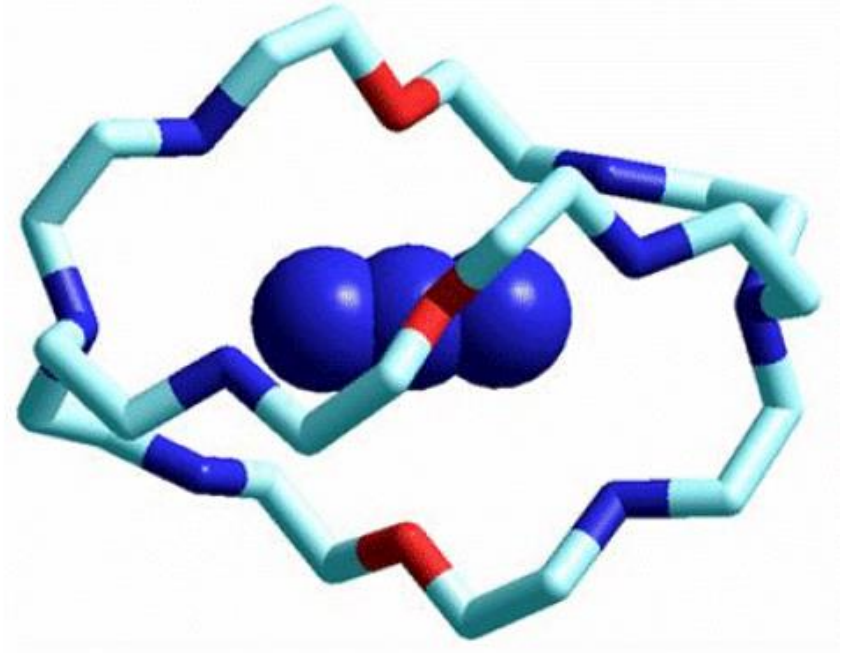
(b)

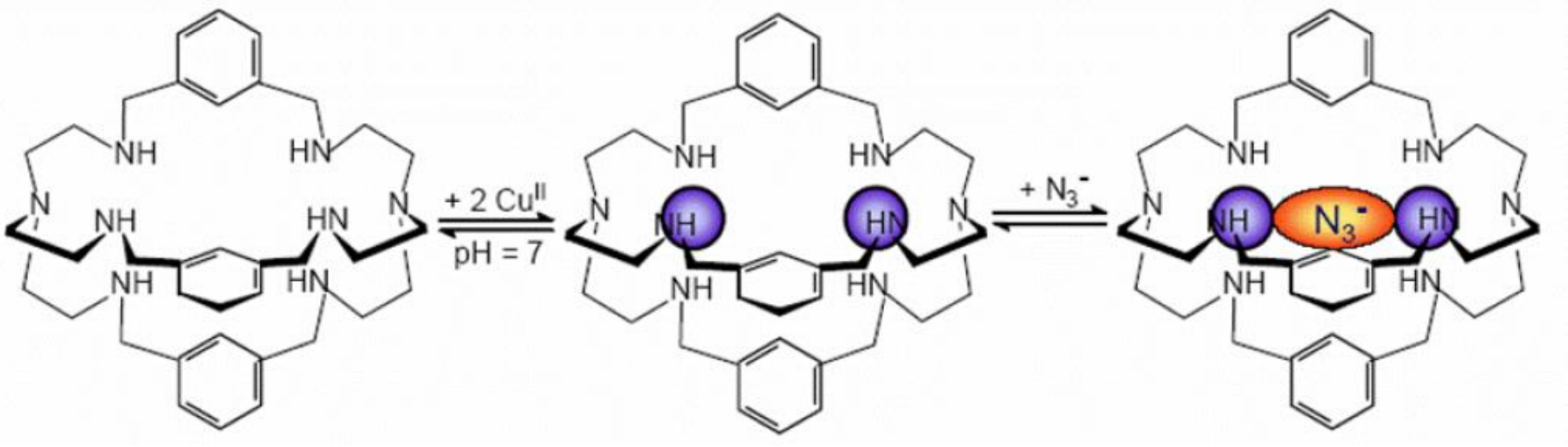
Receptor with individual cation and anion recognition sites.

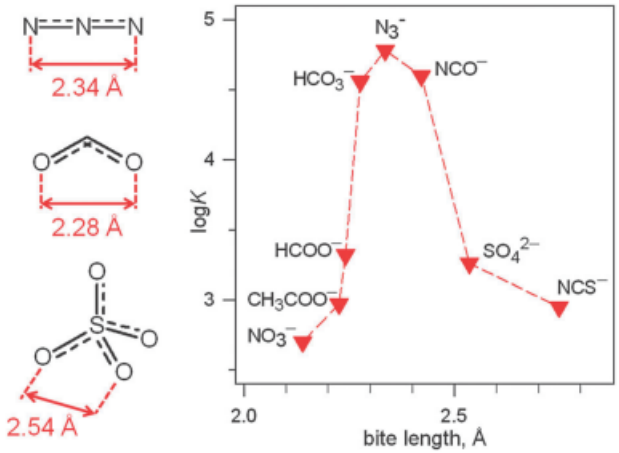
(c)

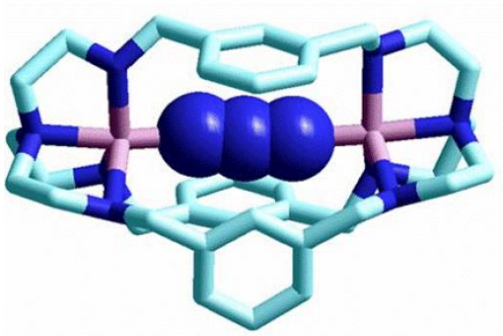
Receptor for zwitterionic guests.

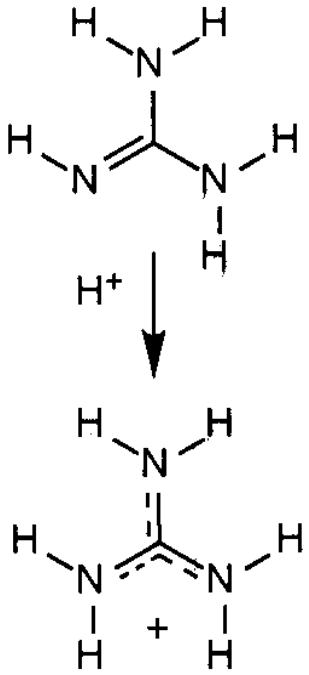

pH = 5
+ N_3^-
51
52
53



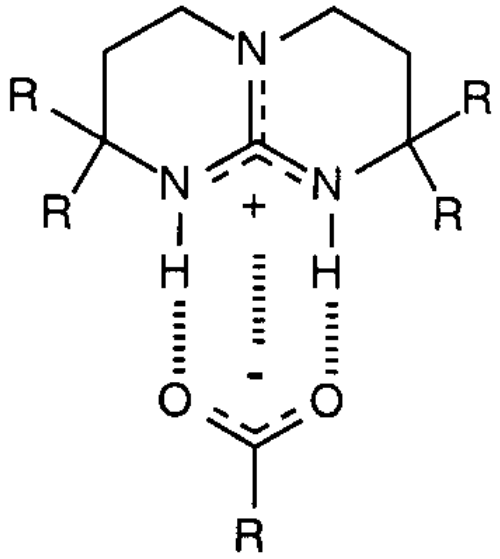

NH
HN
N
+ 2 Cu^II
pH = 7
+ N3-
N3-


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



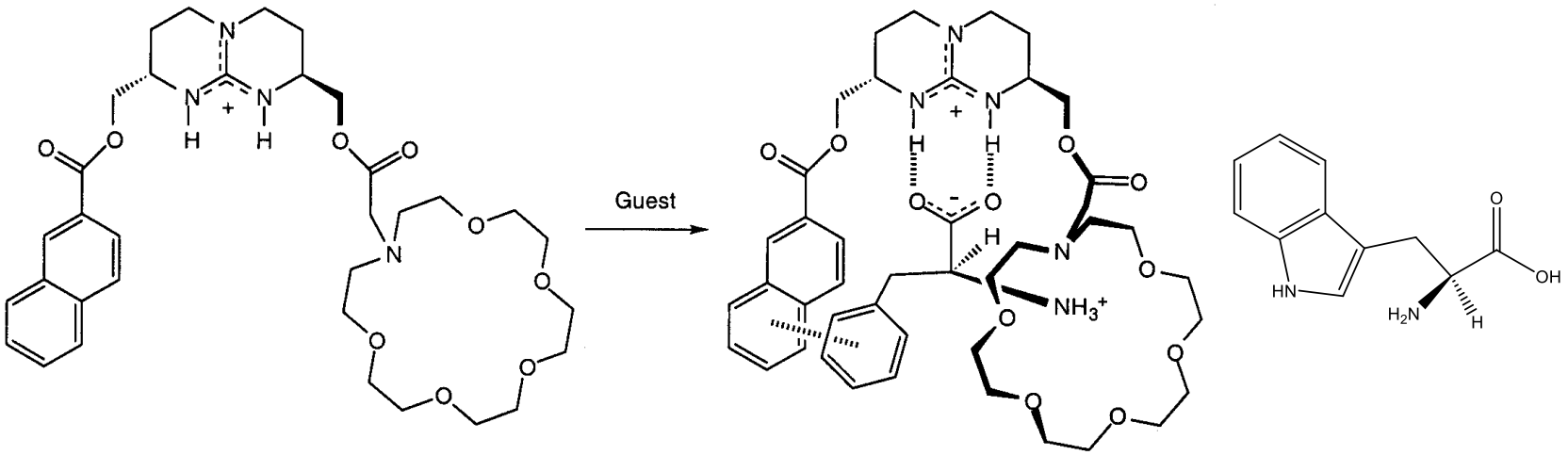


pKa = 13.6



Bicyclic guanidinium is preorganized and complementary for binding bidentate anions.

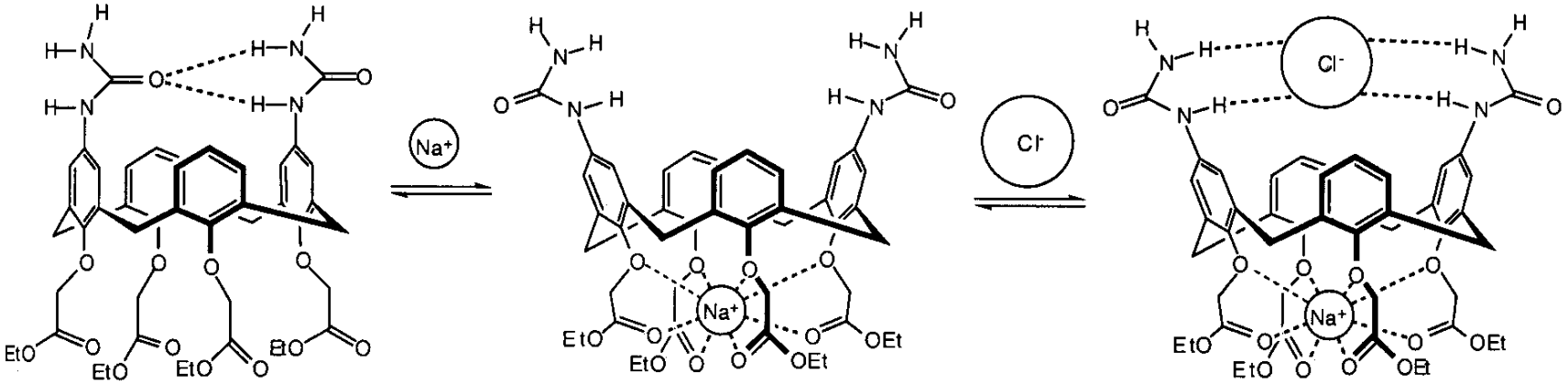
Estrazione di aa con catene laterali aromatiche (Phe, Trp) in CH_2Cl_2

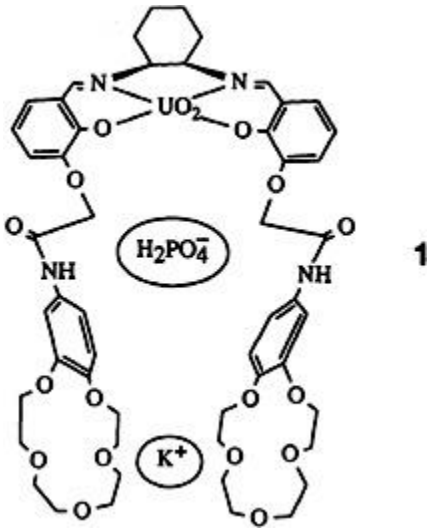


Three point receptor for the selective recognition and extraction of zwitterionic amino acids.

Solubilization of NaX Salts in Chloroform by Bifunctional Receptors**

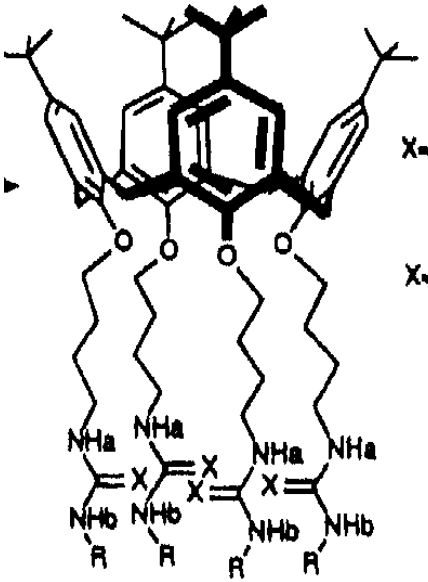
Jurgen Scheerder, John P. M. van Duynhoven, Johan F. J. Engbersen, and David N. Reinhoudt*





1

The Lewis acidic uranyl center and the amide units of receptor **1** bind the anion of the hydrophilic, biologically relevant salt KH_2PO_4 specifically, and simultaneously the crown ether units bind the cation. The complexation properties of **1** were studied with NMR spectroscopy, mass spectrometry, and cyclic voltammetry. The recognition demonstrated for this simple salt could be of great importance for membrane transport, extraction, and sensor technology.



3

X=O; 5a R=phenyl
5b R=n-propyl
5c R=n-octyl
5d R=t-butyl
X=S; 6 R=phenyl

Functionalization of the lower rim of *p-tert*-butylcalix[4]arene with four (thio)urea groups, results in a class of receptors selective for spherical *anions* that are bound *exclusively through hydrogen bonding*. ^1H NMR spectroscopy in $CDCl_3$ reveals a selectivity for Cl^- over Br^- and I^-. The stoichiometry is 1:1 in all cases as was confirmed by Job plots. The association constants are strongly dependent on the nature of the substituent at the urea moiety. The bidentate phenylurea derivative **9** shows the strongest complexation (K_{ass}, $Cl^- = 7.1 \times 10^8\ M^{-1}$) and the largest selectivity for Cl^-.

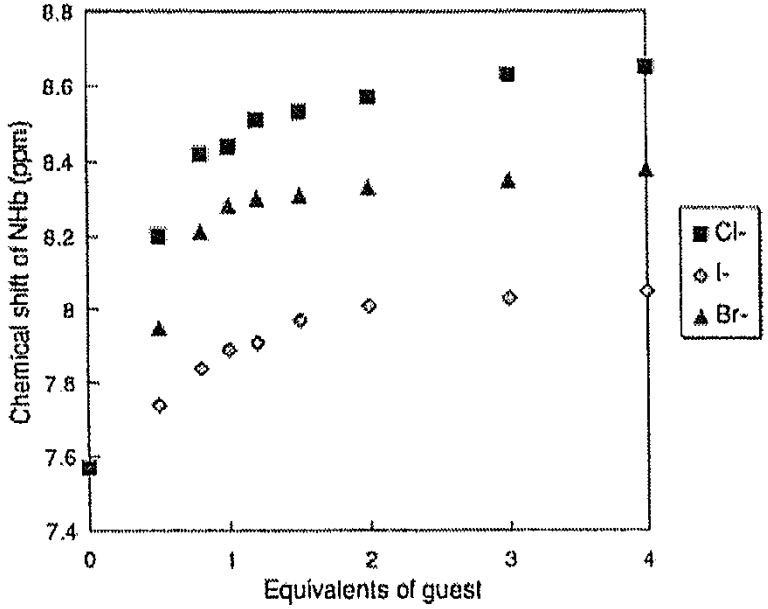


Figure 1. Titration curve of tetraphenylurea calix[4]arene **5a** with Bu_4NCl, Bu_4NBr, and Bu_4NI in $CDCl_3$. Concentration host is 5 mM.

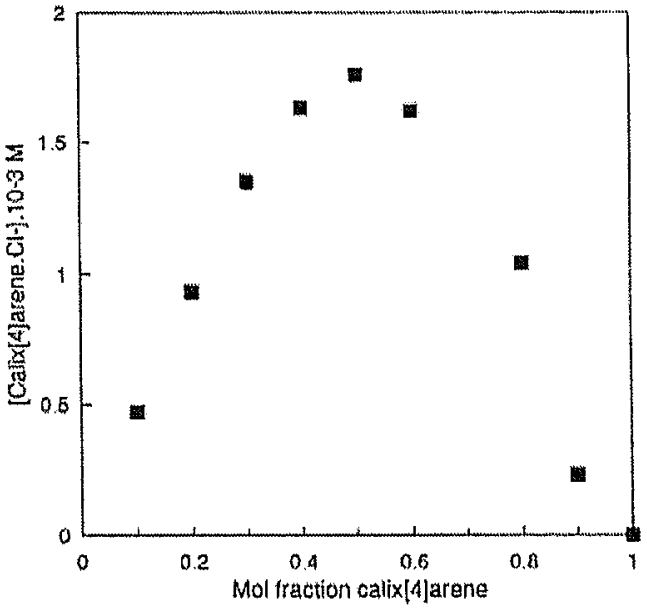
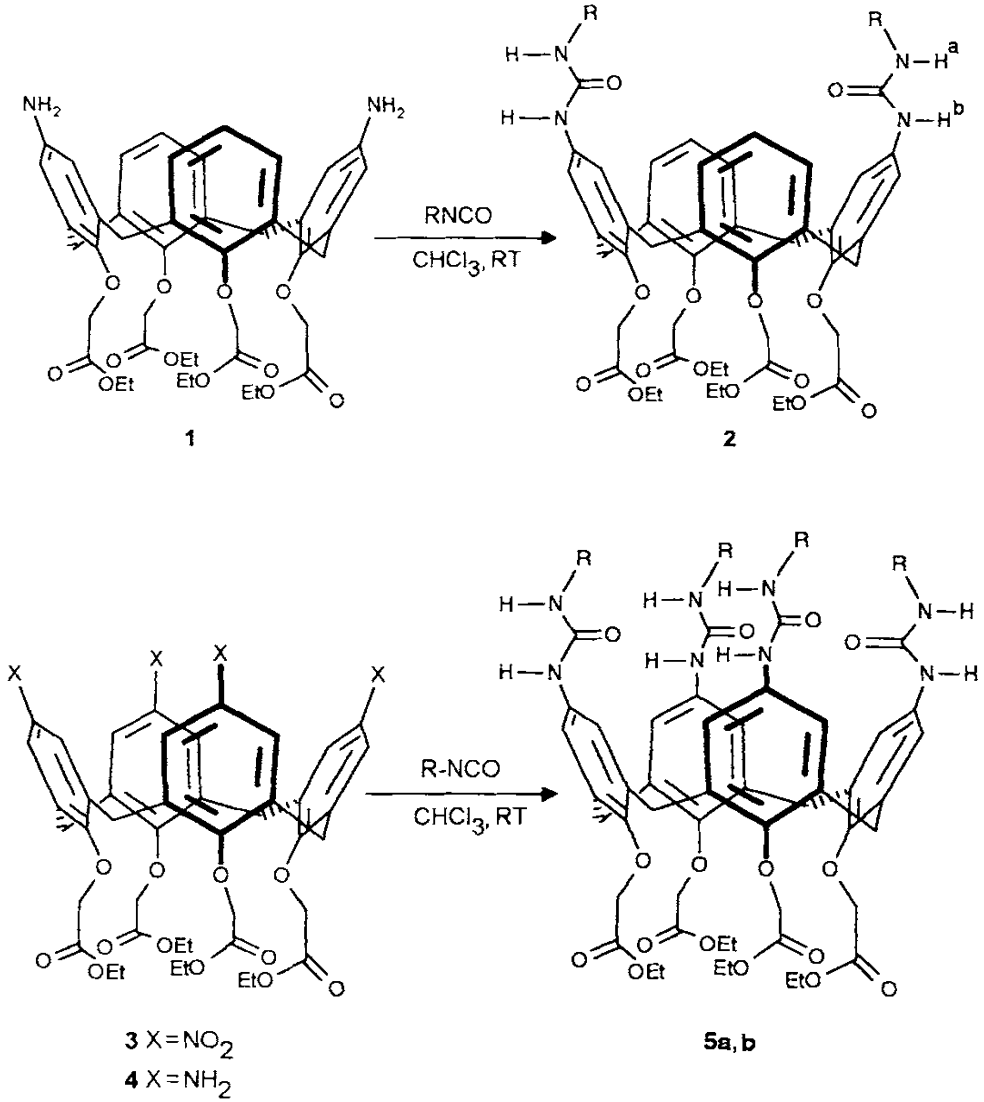
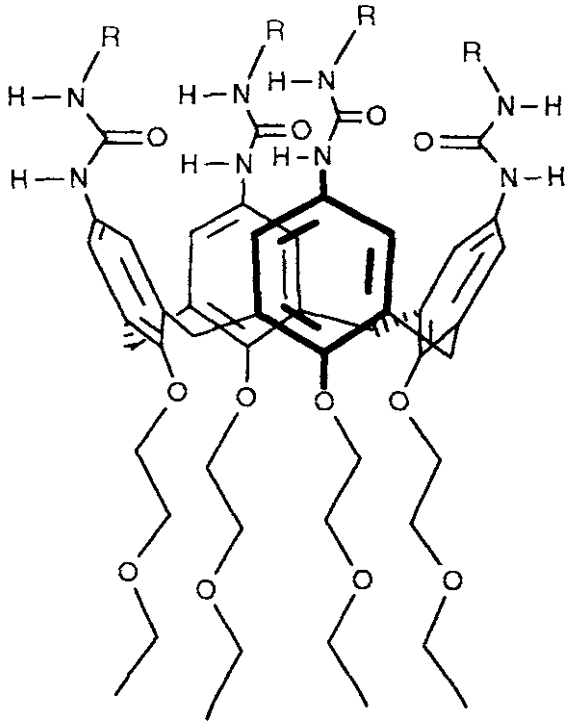


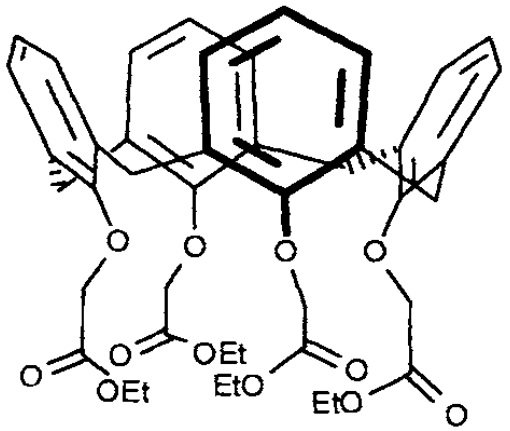
Figure 2. Job plot of the titration of 5 mM Bu_4NCl in $CDCl_3$ with 5 mM tetraphenylurea calix[4]arene **5a** in $CDCl_3$.



Scheme 1. Synthesis of **2** (R = *n*-octyl), **5a** (R = *n*-octyl), and **5b** (R = *tert*-butyl). The labels on the amide protons are used for the assignment of the NMR spectra in Figure 1. RT = room temperature.



6



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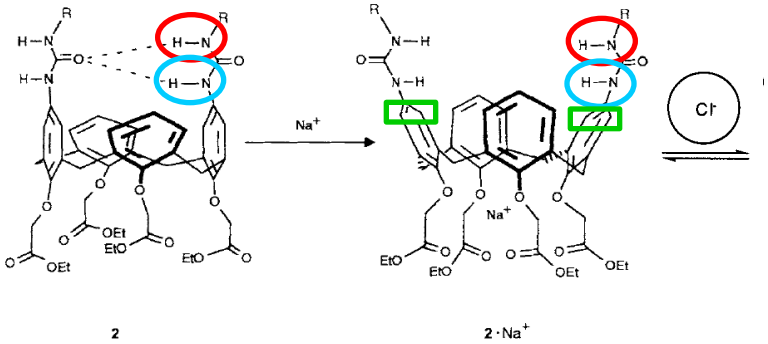
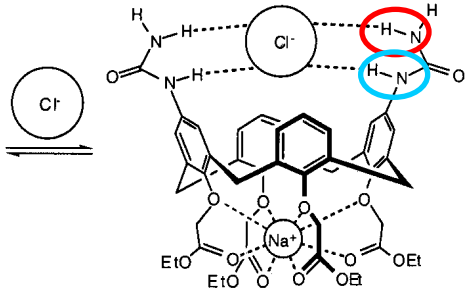




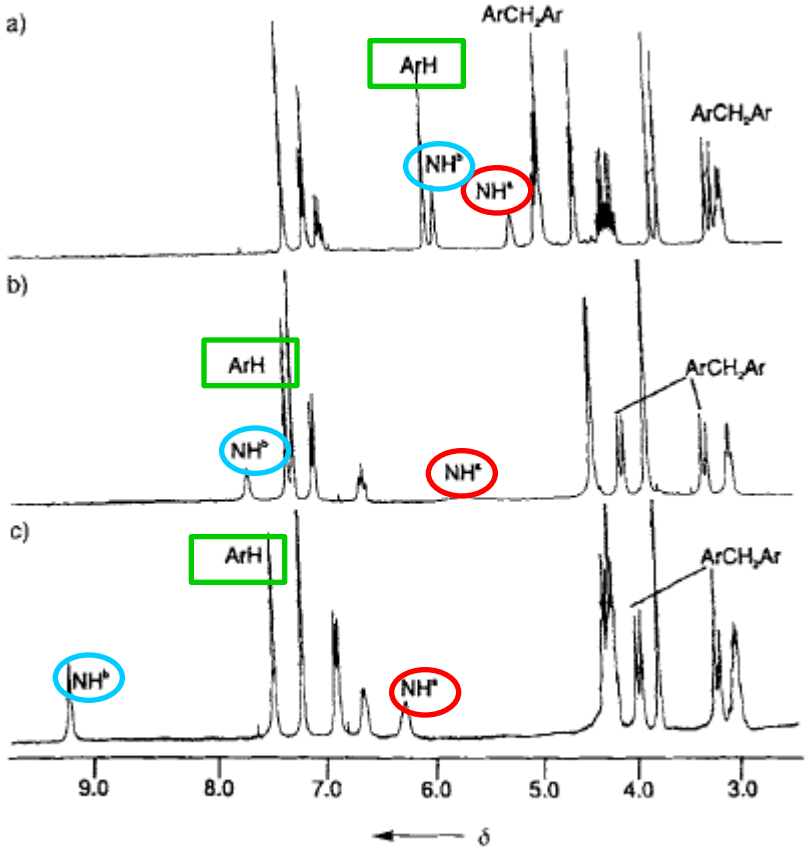
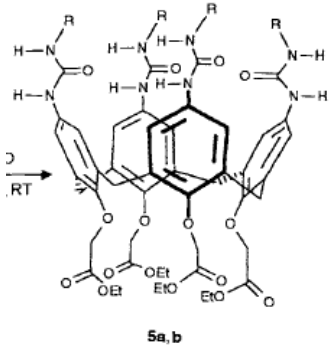


Fig. 1. ^{1}H NMR spectra of **2** ($CDCl_3$, 5 mM). a) Uncomplexed, b) [**2**·Na]ClO_4, c) [**2**·NaCl]. For NH^a and NH^b see Scheme 1; for ArH and $ArCH_2Ar$ see the text or ref. [14].



5a,b

5a (R = n-octyl); **5b** (R = *tert*-butyl).

[14] NOESY experiments with **5a,b** reveal through-space connectivities between the aromatic hydrogens of the calix[4]arene skeleton and the $NH^a CH_2 CH_2$ and $NH^a CH_2 CH_2$ hydrogens of **5a** and the *tert*-butyl hydrogens of **5b**. These connectivities cannot result from through-space interactions within a single molecule since in the same molecule these hydrogens are not close enough [14a]. Consequently, these NOE connectivities must result from intermolecular interactions. Furthermore, the sign of the NOE connectivities is positive, suggesting that slow-tumbling entities with increased molecular mass (≥ 2000) are present

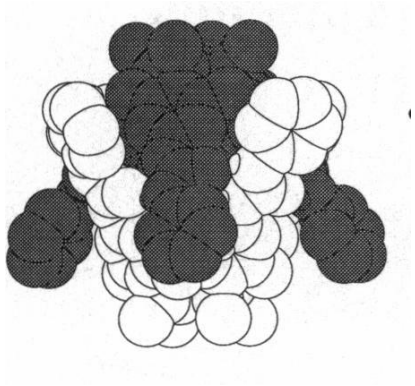


Table 1. Percentage of MX complex formed with **2** and **5a,b** after L–S extraction [a].

	2			**5a**			**5b**		
	Na^+	K^+	Cs^+	Na^+	K^+	Cs^+	Na^+	K^+	Cs^+
Cl^-	100	–	–	100	29	–	100	30	–
Br^-	100	16	–	100	62	–	100	75	–
I^-	100	100	–	100	100	–	100	100	–

[a] The concentration of **2** and **5a,b** is 5 mM in $CDCl_3$. See also ref. [18].

[18] A 5 mM solution (0.5 mL) of **2** or **5a,b** in $CDCl_3$ was stirred with an excess of MX for 24 h. The organic layer was separated and the relative amount of complex formed was determined on basis of the intensities of the ^1H NMR signals for the bridging calix[4]arene methylene hydrogens of the complex and the free ligand.