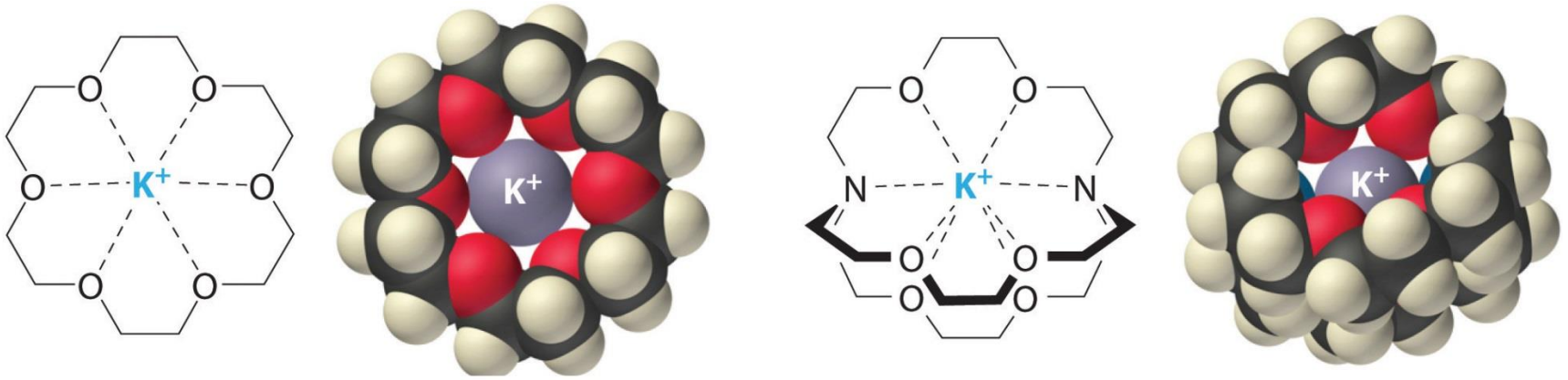
Cation Receptors



Solvation Enthalpy of the Alkali Metal Ions

The dissolution of NaCl in water requires at least three separate processes to occur:

A: Water organization must be disrupted by H-bond scission

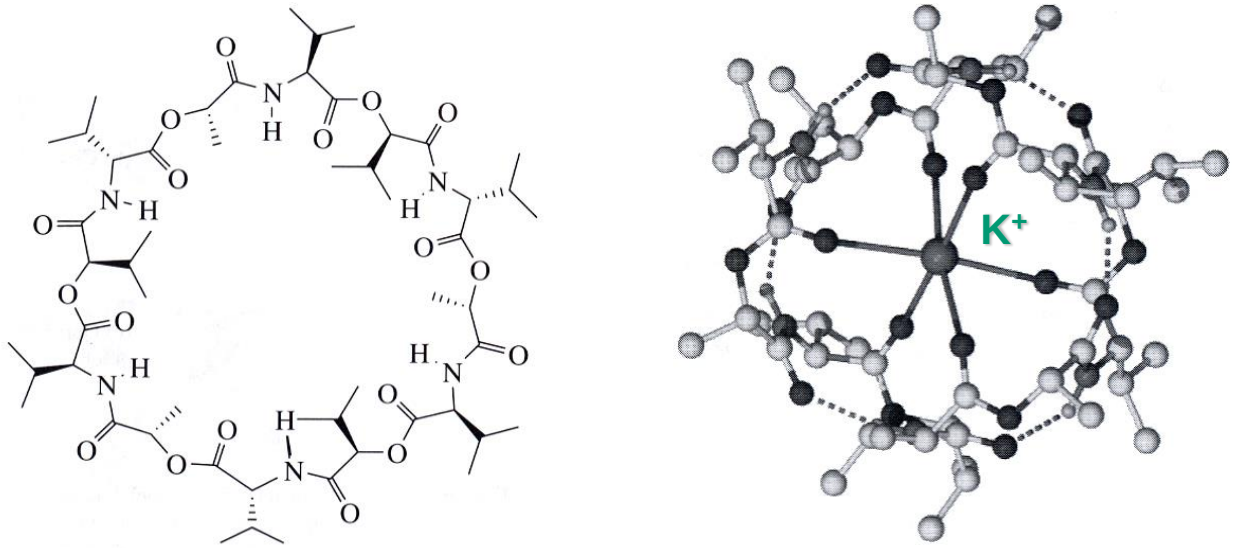
B: Sodium cations and chloride anions must be separated, *i.e.*, the lattice must be broken

C: Stabilizing ion-dipole interactions between Na, Cl, and H_2O must be established.

Ion	kJ/mol	kcal/mol
Li^+	-515	-123
Na^+	-405	-97
K^+	-321	-77
Rb^+	-296	-71
Cs^+	-263	-63

Ionophore

Ionophore (literally ‘‘ion bearer’’) is a name given to the family of compounds with the principal characteristic that is to ‘‘promote the transfer of ions from aqueous medium into a hydrophobic phase.’’ The *Shorter Oxford English Dictionary* gives the following definition: ‘‘An agent which is able to transport ions across a lipid membrane, in a cell.’’



Valinomycin, a natural ionophore for K^+

Pedersen's Seminal Publication

Early in 1967, a paper from Charles J. Pedersen, a chemist at the DuPont Experimental Station, landed on the desk of the editor of the *Journal of the American Chemical Society*. It represented more than five years of laboratory work accomplished entirely by Pedersen with the assistance of a single technician, Ted Malinowski. In the paper, Pedersen reported the discovery of a novel class of chemical compounds called macrocyclic polyethers, which he dubbed the "crown ether" because of their molecular shape.

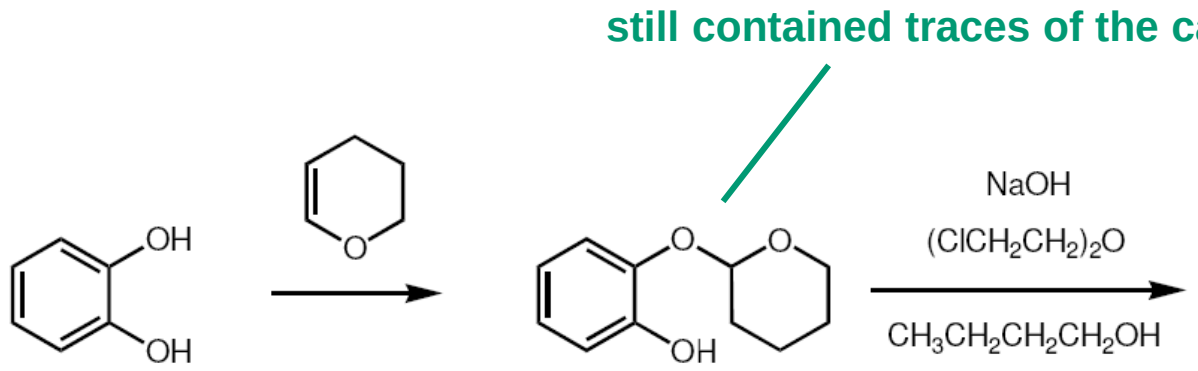
The editor and the still-anonymous referee who reviewed the paper pointed out that many researchers would have managed half a dozen articles out of a similar quantity of data.

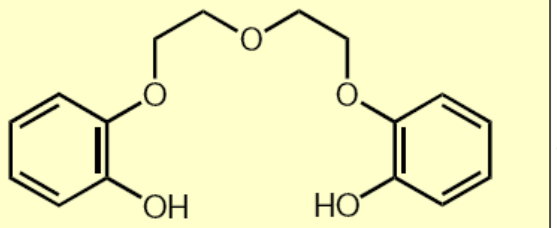
The article has since become known to Pedersen's colleagues simply as "the blockbuster."

C. J. Pedersen

'Macrocyclic Polyethers for Complexing Metals'
C. J. Pedersen *J. Am. Chem. Soc.* **1967**, *89*, 7017.

Pedersen's 'Accidental' Crown Ether Synthesis

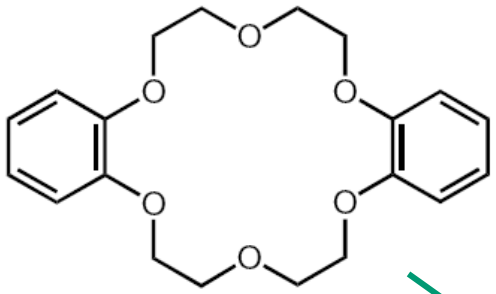




desired product

(an open-chained complexing agent)

+



by-product

dibenzo-18-crown-6

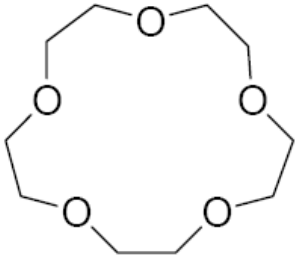
formed in only 0.4 % yield

Crown Ethers

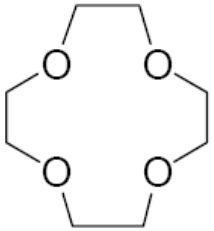
Structure: cyclic polyethers derived from repeating —OCH_2CH_2— units.

Properties: form stable complexes with metal ions.

Applications: synthetic reactions involving anions; phase-transfer catalysis.

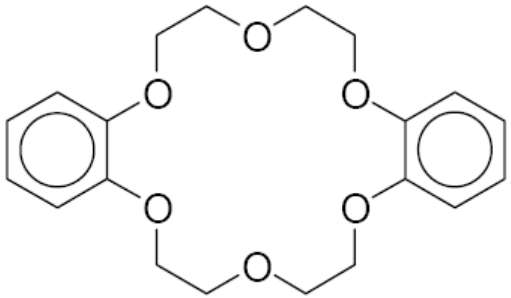


15-crown-5

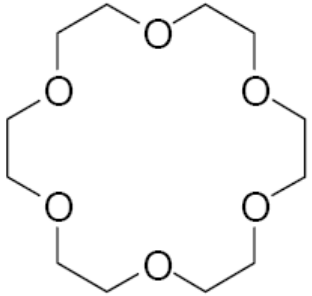


12-crown-4

(or [12]crown-4)



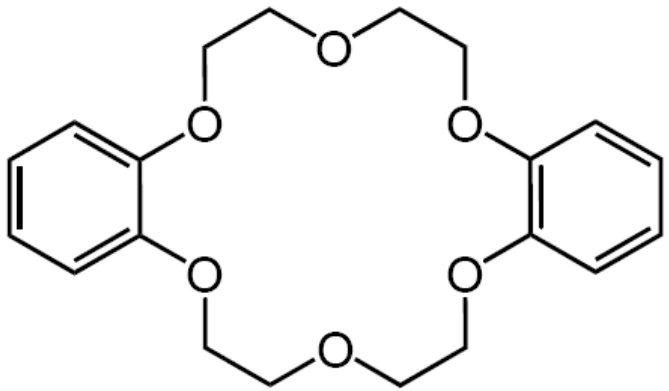
dibenzo-18-crown-6



18-crown-6

Nomenclature

- The first number in the crown designates the number of atoms in the ring (sometimes given in square brackets).
- The second number gives the number of oxygen or other donor atoms.
- Substituents are denoted with a prefix such as benzo-, dicyclohexano-, etc.

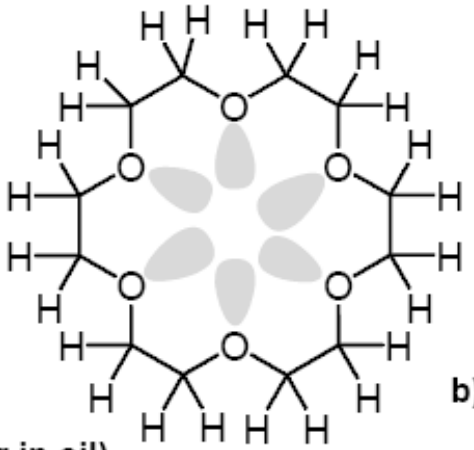


Dibenzo[18]crown-6

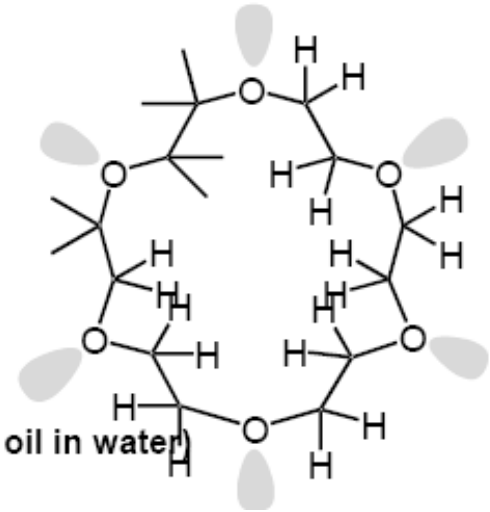
Solution Behavior of Crown Ethers

Crown ethers are soluble in a wide range of solvents from water to alkanes.

solution behavior

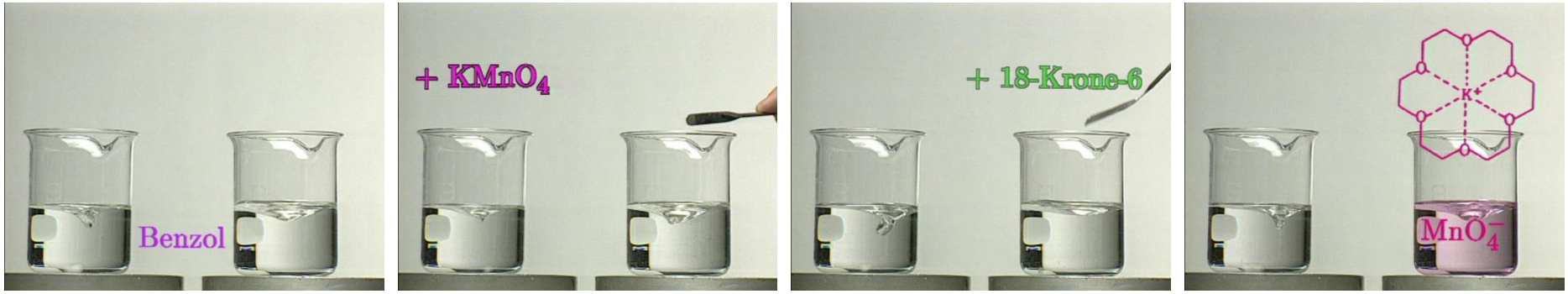


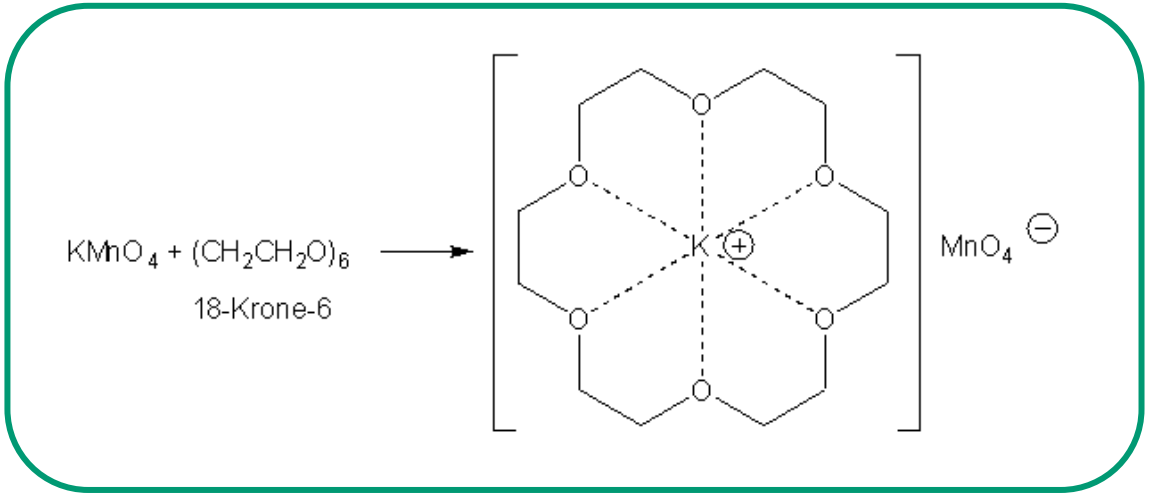
a) in an organic solvent
(like a droplet of water in oil)



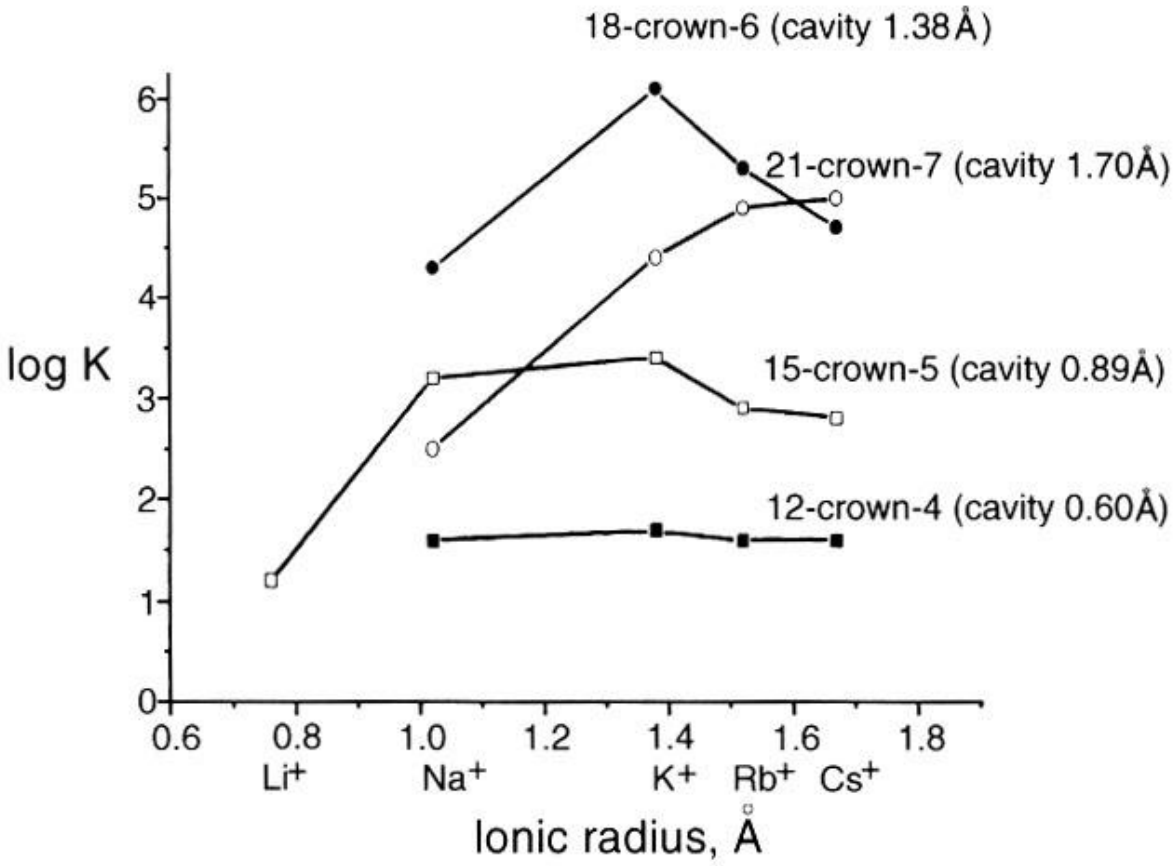
b) in water
(like a droplet of oil in water)

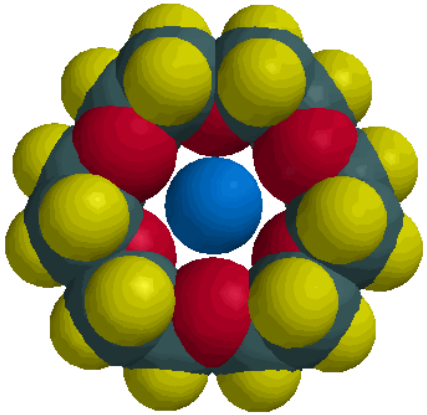
Extraction of $KMnO_4$





Selectivity of Crown Ethers





K^+ complex of 18-crown-6; size match is important

General Considerations

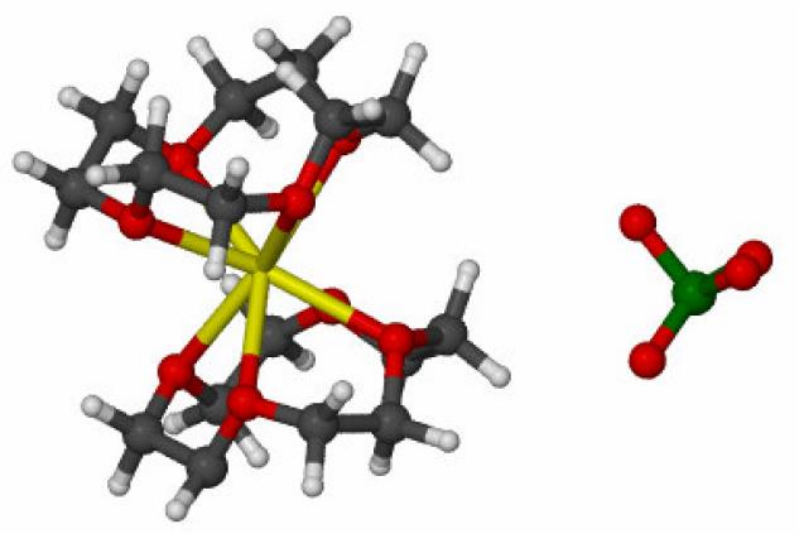
- **Size match between host cavity and guest cation.** In fact, the flexible [18]crown-6 is a reasonably good size match for all of the host cations, although it is optimum for K^+.

- **Number of donor atoms.** In general, supramolecular interactions are additive, hence we expect the larger crown ethers to bind more strongly to metal cations as long as all of the atoms can fit around the metal.

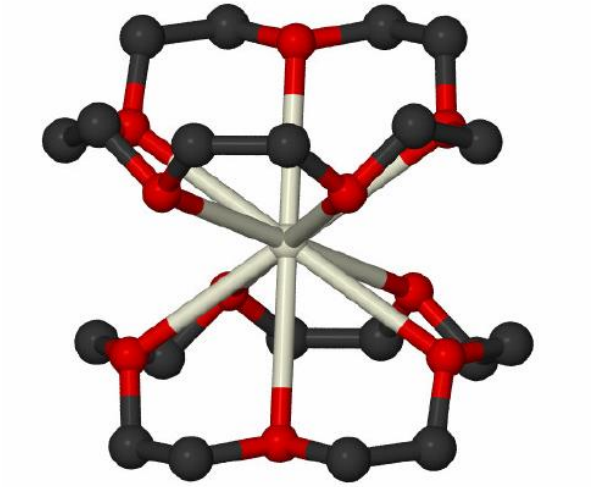
- **Solvation of cation and ligand.** The solvation free energy increases in the order $K^+ < Na^+ < Ca^{2+}$, hence less energy is required to (partially) desolvate K^+ in order to bind it.

- **Chelate ring size (ligand bite angle).** In the complexed species for hosts with ethenyl (two-carbon) bridges, five-membered chelate rings are formed. The small bite angle of the ethylenedioxy unit is suitable for larger cations such as K^+. Smaller metals, particularly Li^+, are less suited to spanning the distance between one donor atom and the next, and hence do not complex as strongly.

Sandwich Complexes



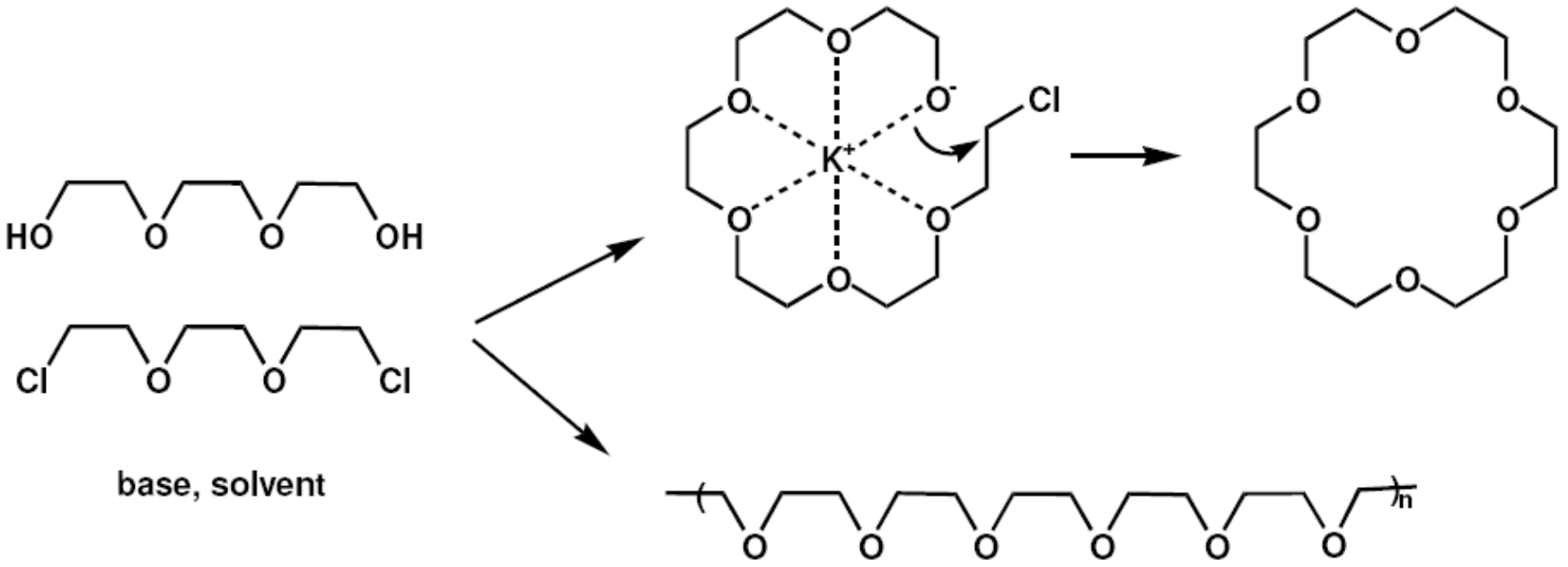
$[Na(12\text{-crown-}4)_2](ClO_4)$



$[Rb(15\text{-crown-}5)_2]^+$
(hydrogens not shown)

Sandwich-type complexes are formed if the size of the cavity is too small.

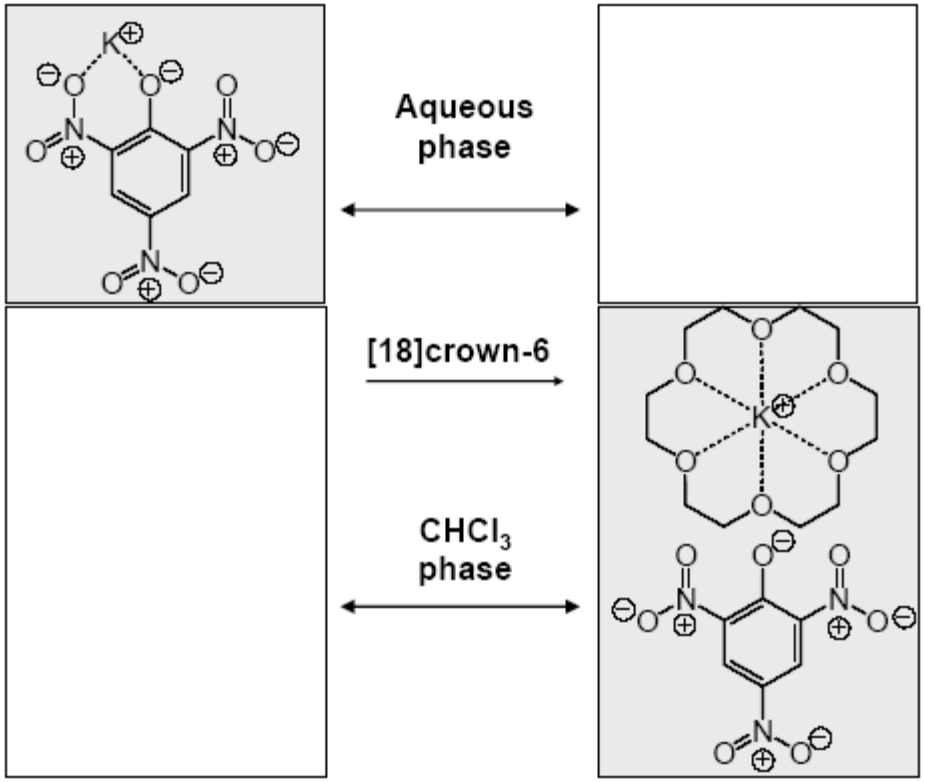
Template Effects in Crown Ether Synthesis



R. N. Greene, *Tetrahedron Lett.* **1972**, *13*, 1793.

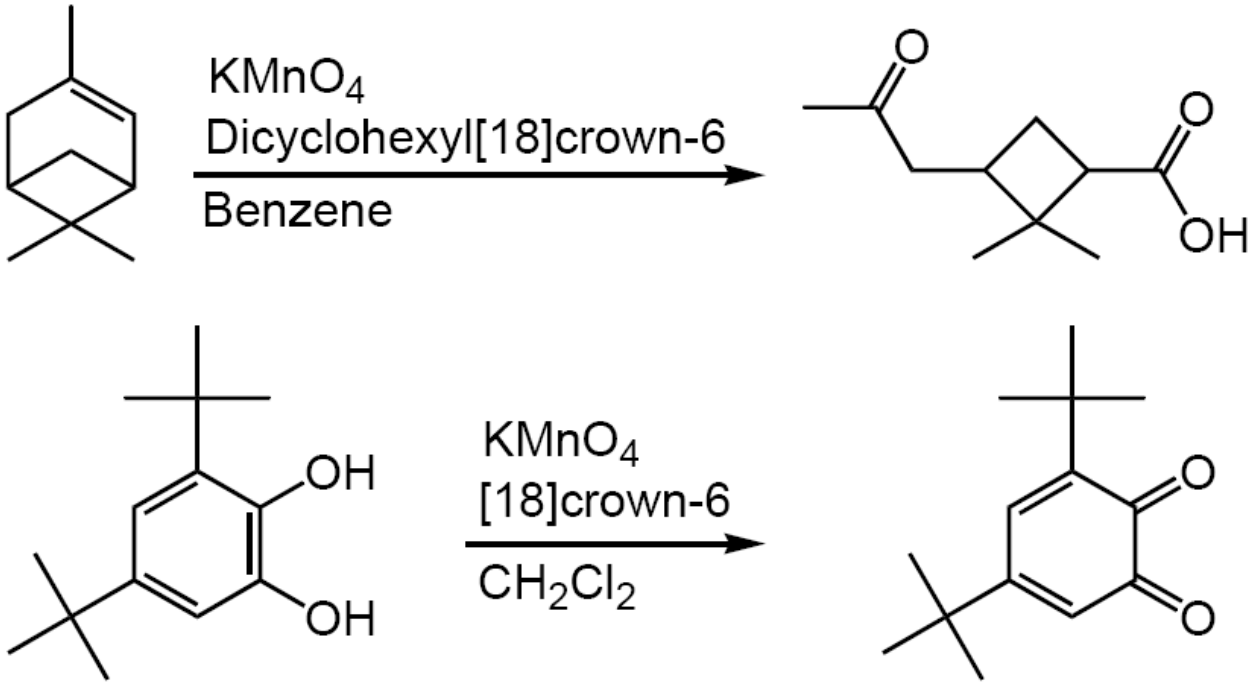
Applications

- Phase transfer catalysis
- Anion activation (‘naked anions’)

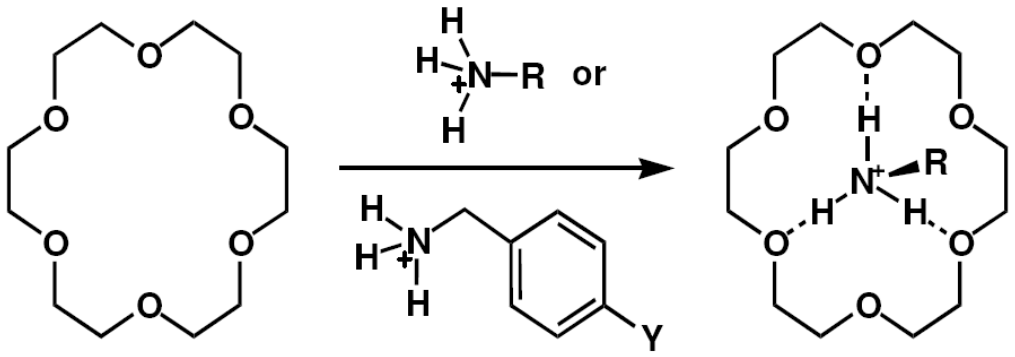


Potassium picrate extraction into an organic solvent

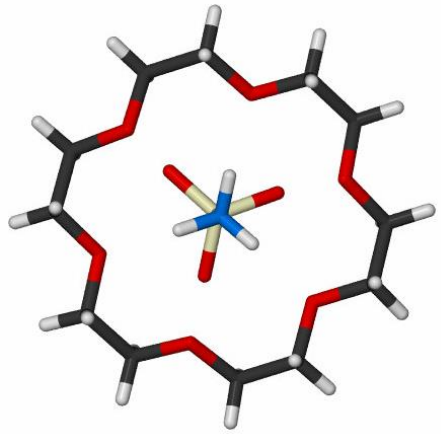
Example: Oxidation of Organic Substrates with $KMnO_4$



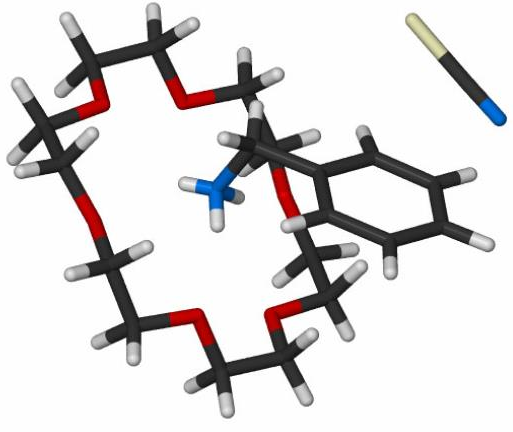
Complexation of Ammonium Ions



Complexation by **ion-dipole interactions** and **hydrogen bonds**.



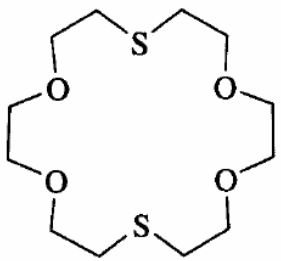
H_3NSO_3 Complex
(X-Ray)



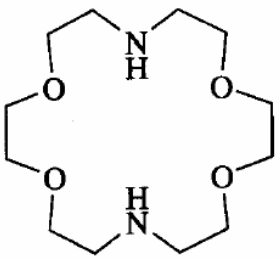
$(BnNH_3)^+(SCN)^-$ Complex
(X-Ray)

Heterocrowns

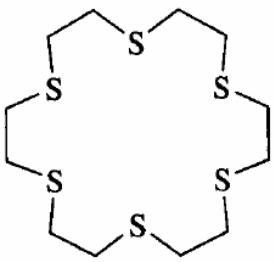
Cation	Ligand						
	[18]crown-6	(3.65)	(3.18)	[15]crown-5	(3.67)	(3.68)	(3.69)
K^+ (methanol)	6.10	1.15	2.04	-	-	-	-
K^+ (water)	2.10	-	<1	0.74	-	1.0	-
Ag^+ (methanol)	4.58	-	-	-	-	-	-
Ag^+ (water)	1.60	4.34	7.80	0.94	5.0	5.85	8.95
Tl^+ (water)	2.27	0.93	1.1	1.23	0.8	-	-
Ba^{2+} (water)	3.78	-	2.51	-	-	1.0	-
Pb^{2+} (water)	4.27	3.13	6.9	1.85	1.65	5.85	5.67



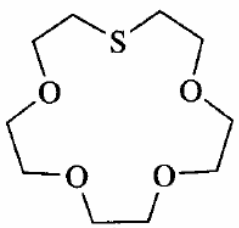
(3.65)



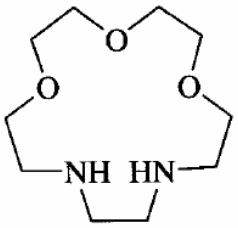
(3.18)



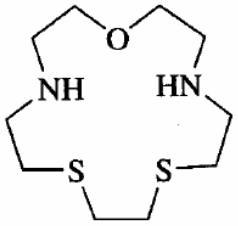
(3.66)



(3.67)

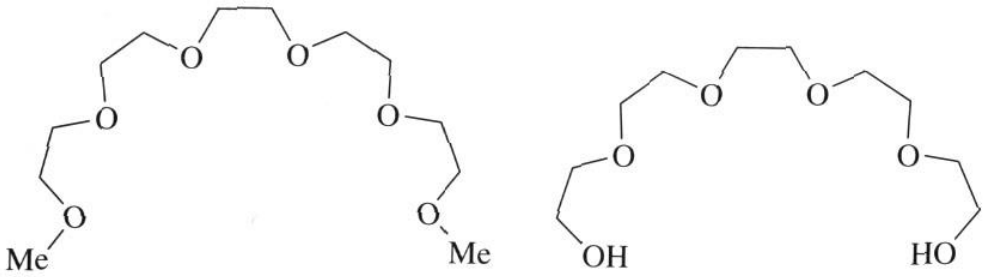


(3.68)



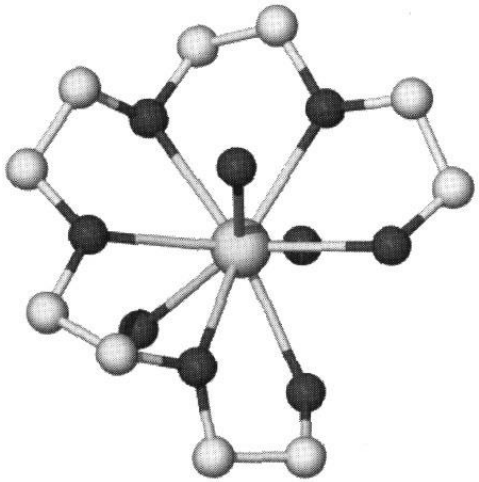
(3.69)

Podands

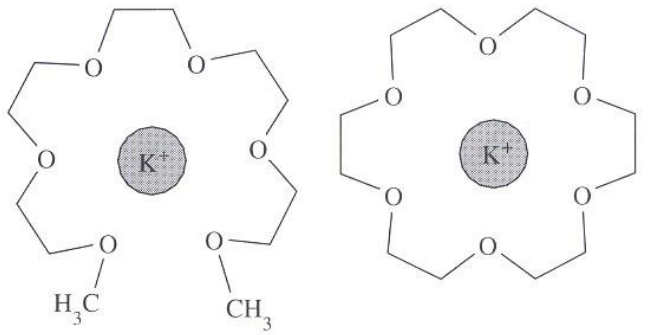


Acyclic hosts with pendant binding sites are termed **podands**. They generally exhibit less cation affinity than their cyclic analogues, as a result of unfavorable enthalpic and entropic effects.

X-ray crystal structure of an europium(III) podand complex

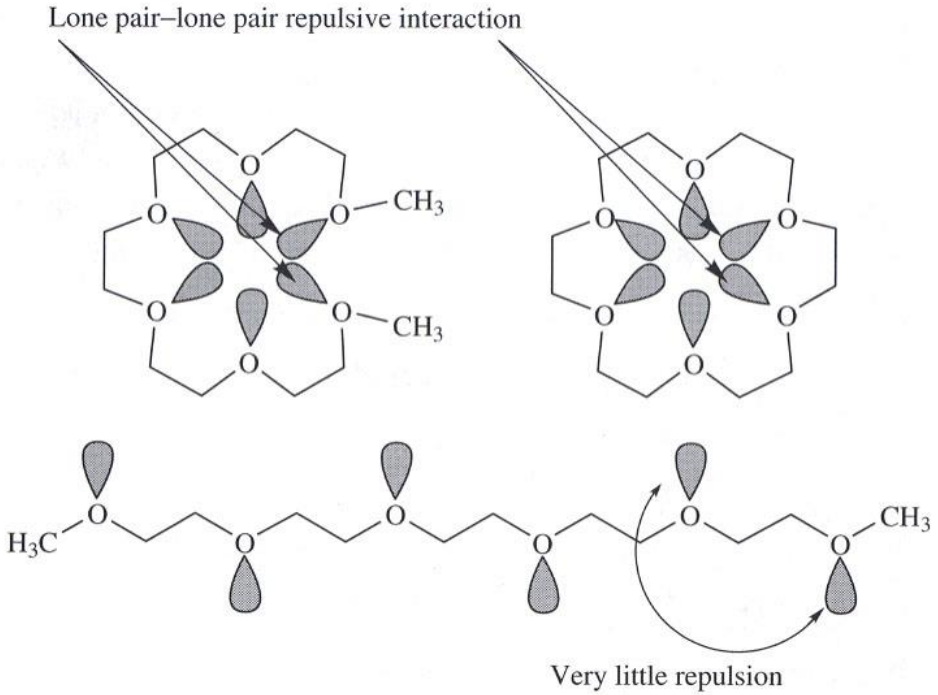


The Macrocyclic Effect



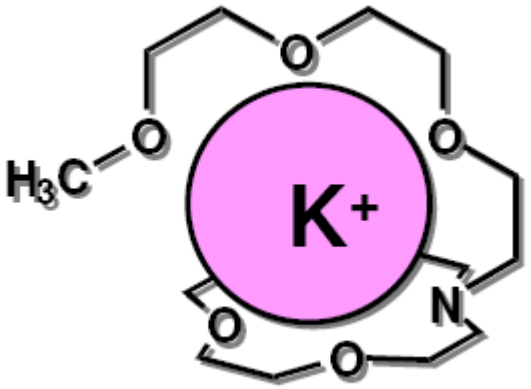
p*K* = 2.0 p*K* = 6.1

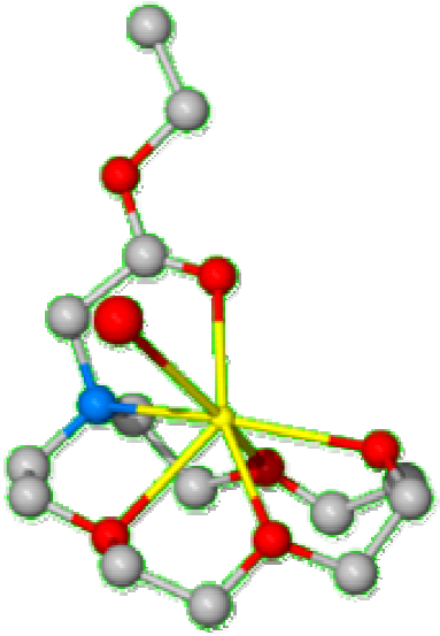
(MeOH, 25 °C)

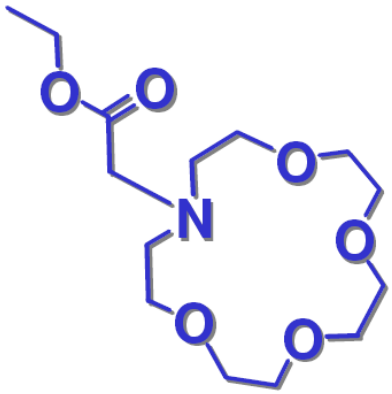


Lariat Ethers

'Lariat' (engl) = 'Lasso' (fran)





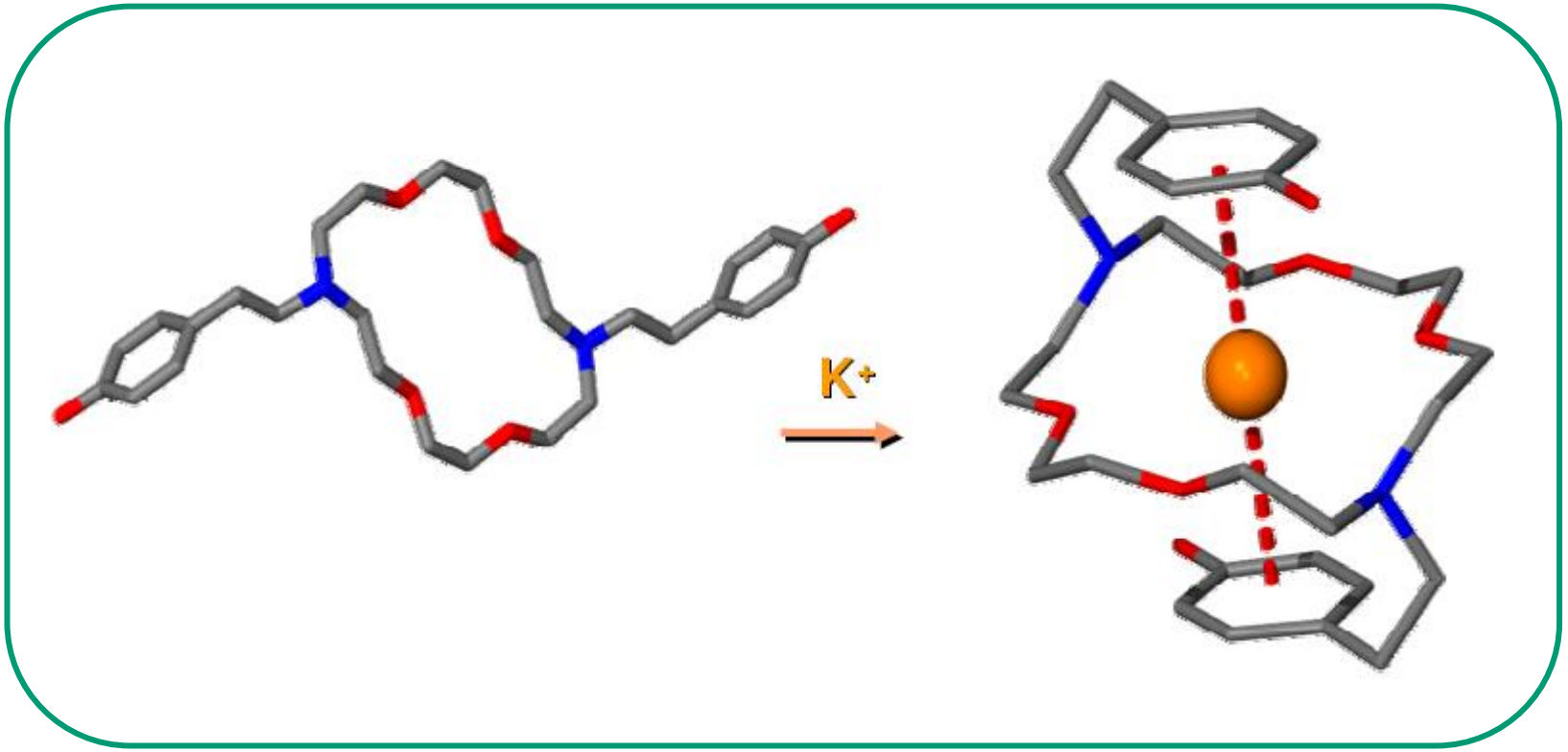


15-crown-5 Na^+ Br^- complex showing lariat ether sidearm participation in complexation

'Lariat Ethers: From Simple Side Arms to Supramolecular Systems'

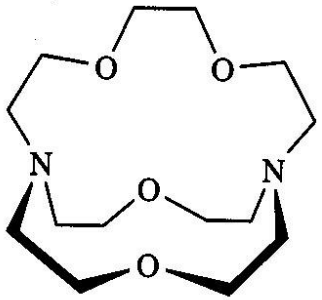
G. W. Gokel, *Coord. Chem. Rev.* **2000**, *205*, 3.

Lariat Ethers to Probe Cation-π Interactions

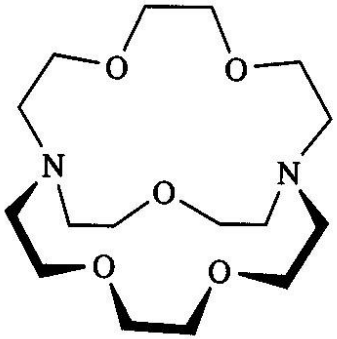


'Macrocyclic polyethers as probes to assess and understand alkali metal cation-π interactions'
G. W. Gokel, *Coord. Chem. Rev.* **2001**, *222*, 127.

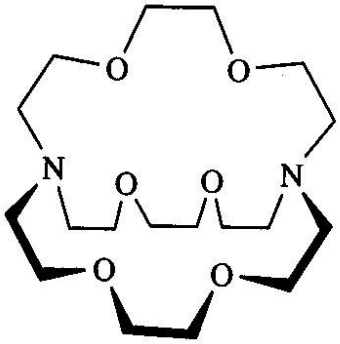
Cryptands



[2,1,1]Cryptand



[2,2,1]Cryptand



[2,2,2]Cryptand

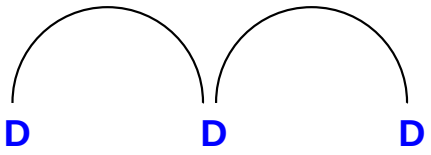
From the Greek *kruptus* meaning ‘hidden’.

Sold commercially under the trade name ‘*Kryptofix’*.

J.-M. Lehn

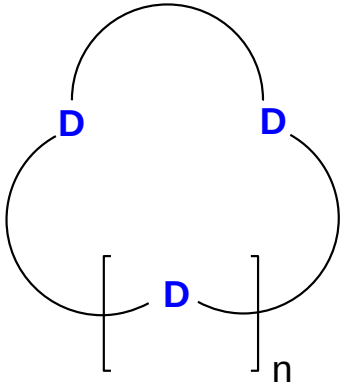
Nomenclature

Open-chain



‘Podand’

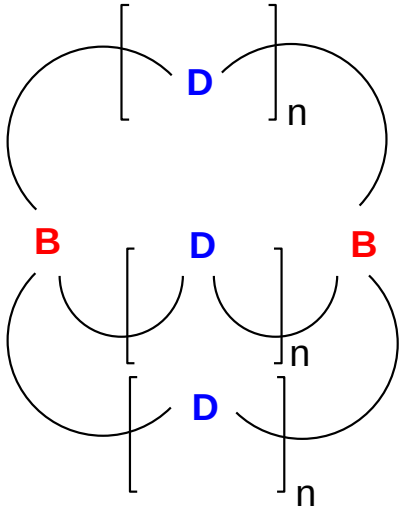
Cyclic



(D = O: ‘crown ether’)

‘Coronand’

3-Dimensional



‘Cryptand’

D = donor atom
B = bridgehead atom

K^+ Complexation by Cryptands

K^+ Binding in water (w) or methanol (m)

Receptor	$k_{complex}$	$k_{release}$	K_S (M^{-1})
18-Crown-6 (w)	4.3×10^8	3.7×10^6	115
[2.2.2] (w)	7.5×10^6	38	2.0×10^5
[2.2.2] (m)	4.7×10^8	0.018	2.6×10^{10}
Valinomycin (m)	4.0×10^7	1300	3.1×10^4

Size-Match Relationship for Cryptands

Log *K* values for the interaction of cryptands with metal ions.

	Li^+ (0.68)	Na^+ (0.95)	K^+ (1.33)	Rb^+ (1.48)	Cs^+ (1.69)	Mg^{2+} (0.66)	Ca^{2+} (0.99)	Sr^{2+} (1.13)	Ba^{2+} (1.35)
[1.1.1][b] (~0.5)	1.7	0.8	–	–	–	–	1.3	–	–
[2.1.1][c] (0.8)	5.5	3.2	<2	<2	<2	2.5	2.50	<2	<2
[2.2.1][c] (1.1)	2.50	5.40	3.95	2.55	<2	<2	6.95	7.35	6.30
[2.2.2][c] (1.4)	1.25	3.9	5.4	4.35	<2	<2	4.4	8.0	9.5
[3.3.2][d] (2.1)	–	3.2	6.0	6.15	>6	–	–	–	–
[3.3.3][d] (2.4)	–	2.7	5.4	5.7	5.9	–	–	–	–

[a] Values (in Å) of radii of cryptand cavities and of metal ions (in parentheses) are from Ref. [13] and Handbook of Chemistry and Physics, R.C. Weast (ed.), 66th ed., CRC Press, Boca Raton, FL, 1985, p. F-164.

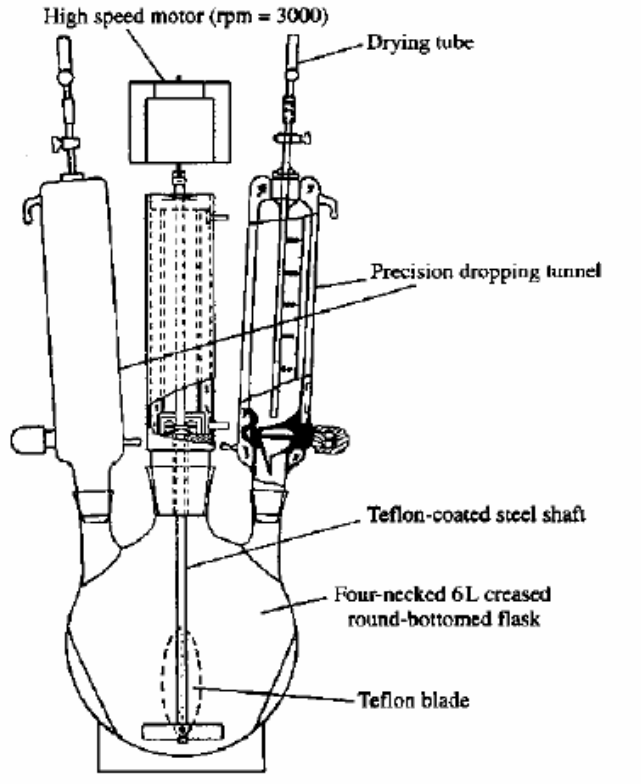
[b] Ref. [18]. Determined in dimethylformamide at 20 °C.

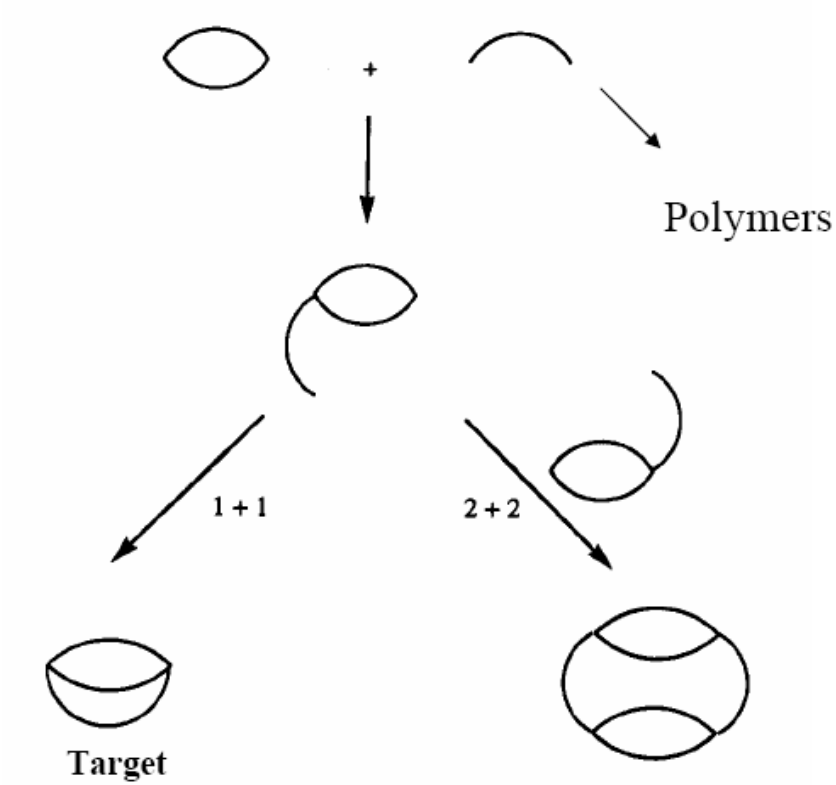
[c] Refs. [17,19]. Determined in water at 25 °C.

[d] Ref. [17]. Determined in methanol at 25 °C.

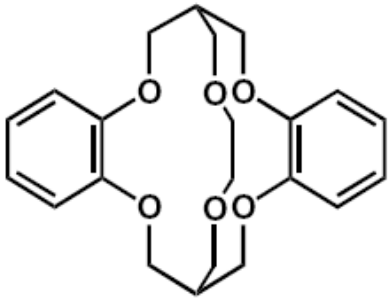
High Dilution Technique

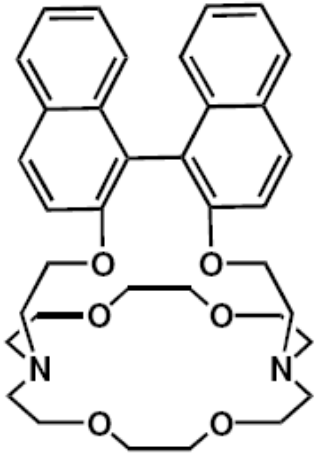
Why? Intramolecular ring closure is a 1st order reaction, its rate proportional to concentration; Intermolecular condensation is 2nd order, its rate proportional to [concentration]^2.

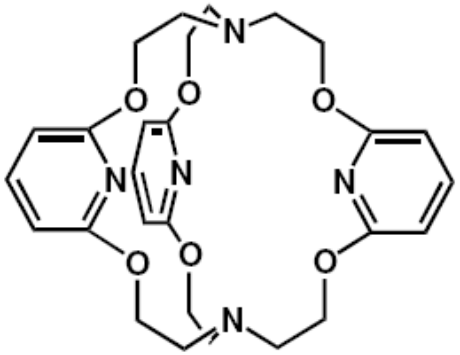


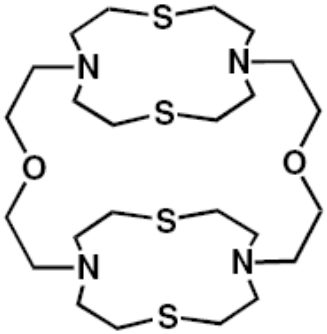


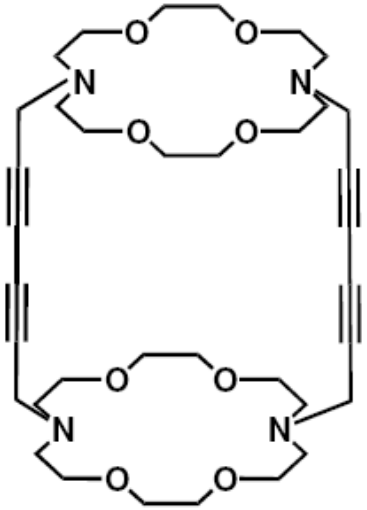
Alternative Cryptand Structures

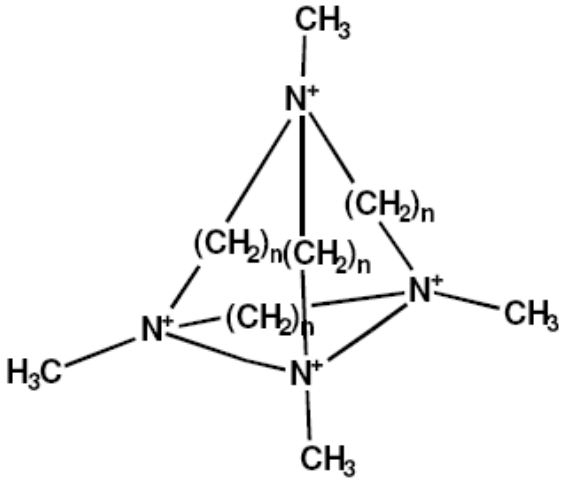




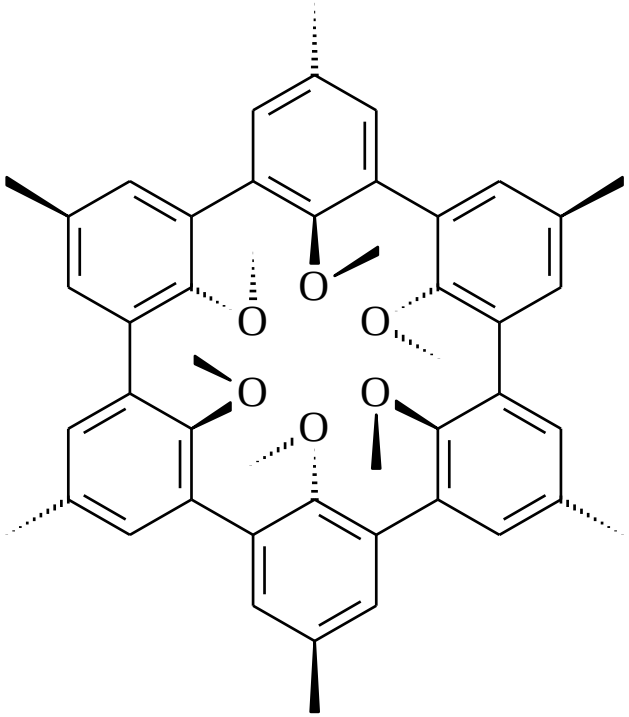


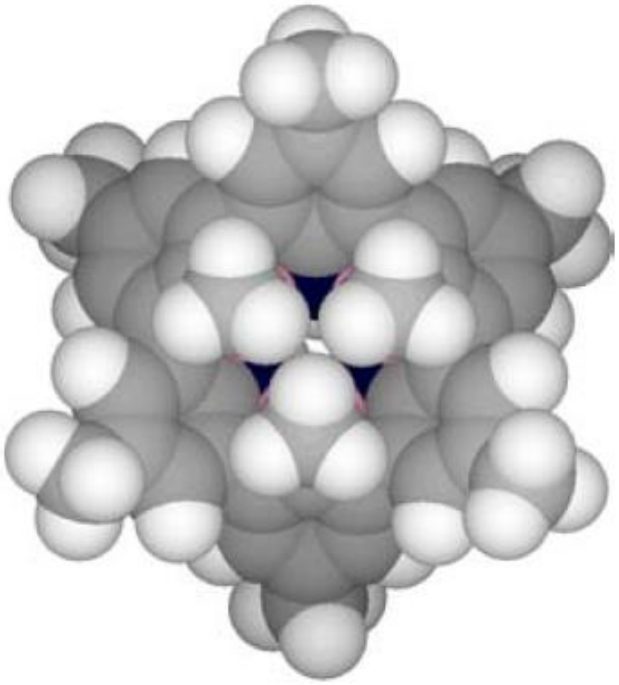




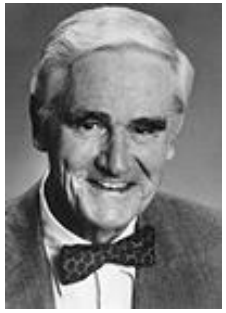


Spherand



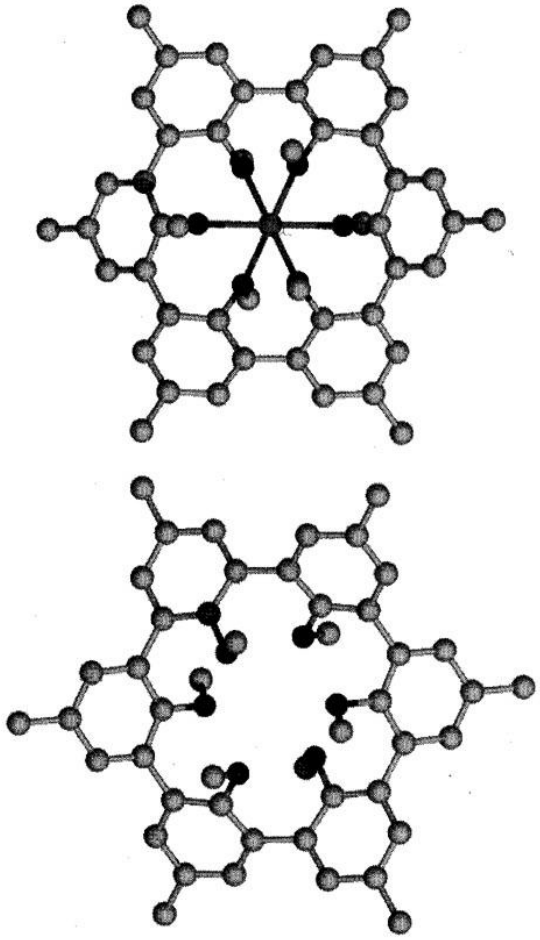


Rigid, 3-dimensional host with highly preorganized O-donor atoms.

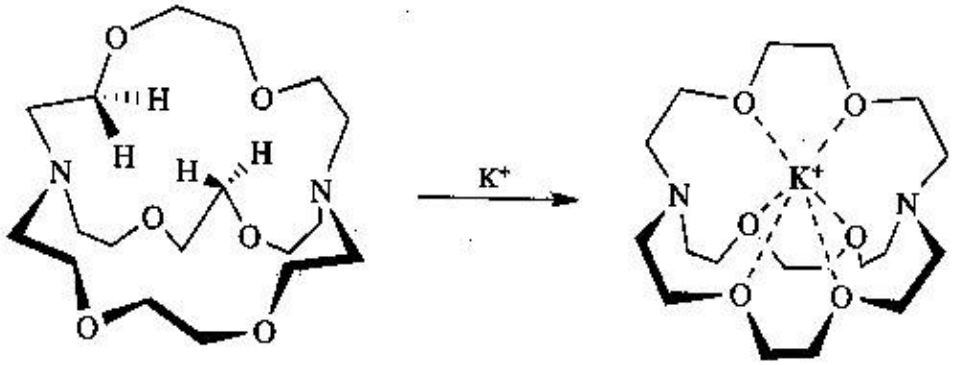


D. Cram

The Importance of Preorganization



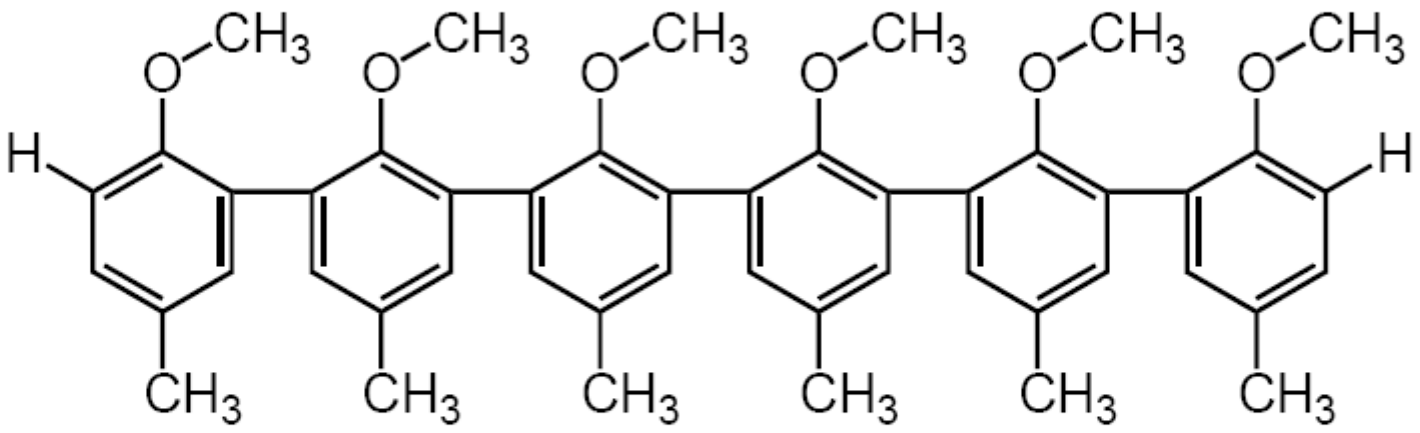
(X-ray)



The complexation of K^+ requires a **reorganization** and a **desolvation** of the cryptand.

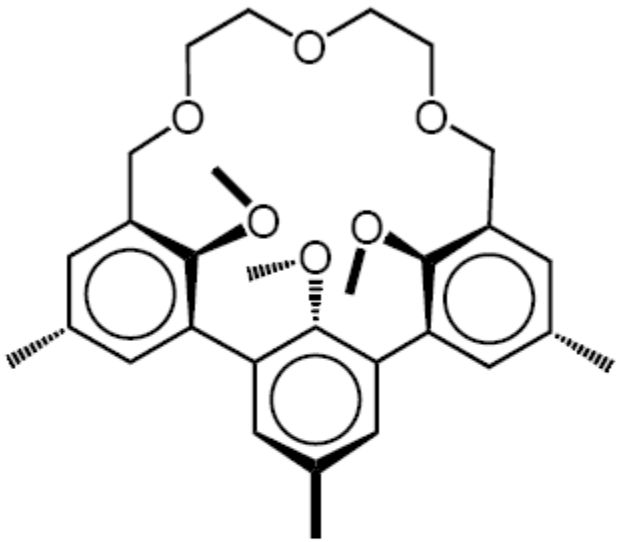
The Importance of Preorganization

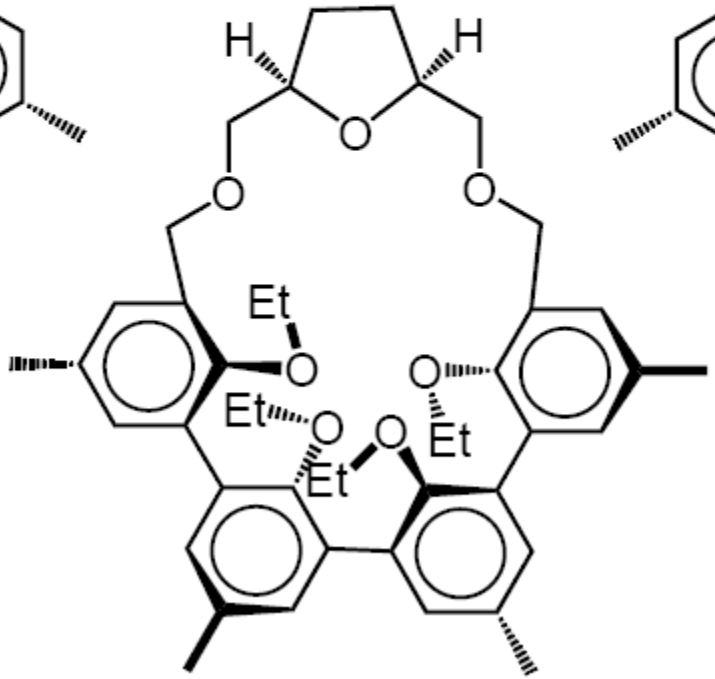
Spherand binds Li^+ more than 10^{12} times more efficiently than:

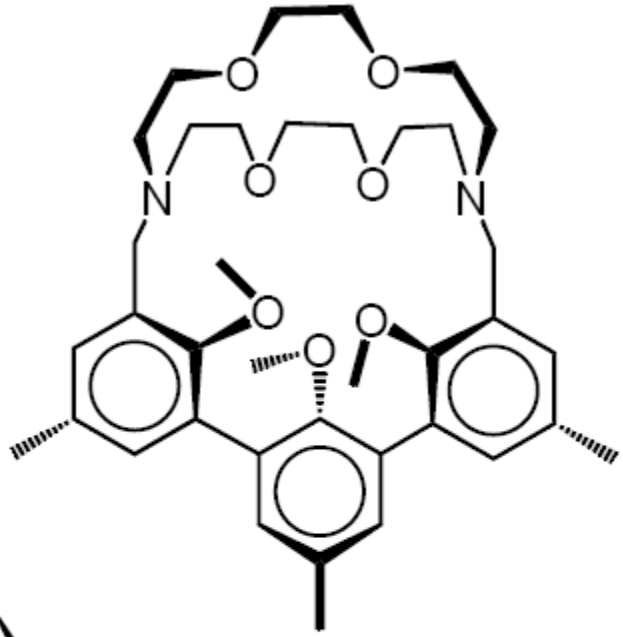


- more than 10000 possible conformations
- Only two of which can bind cations in a convergent manner

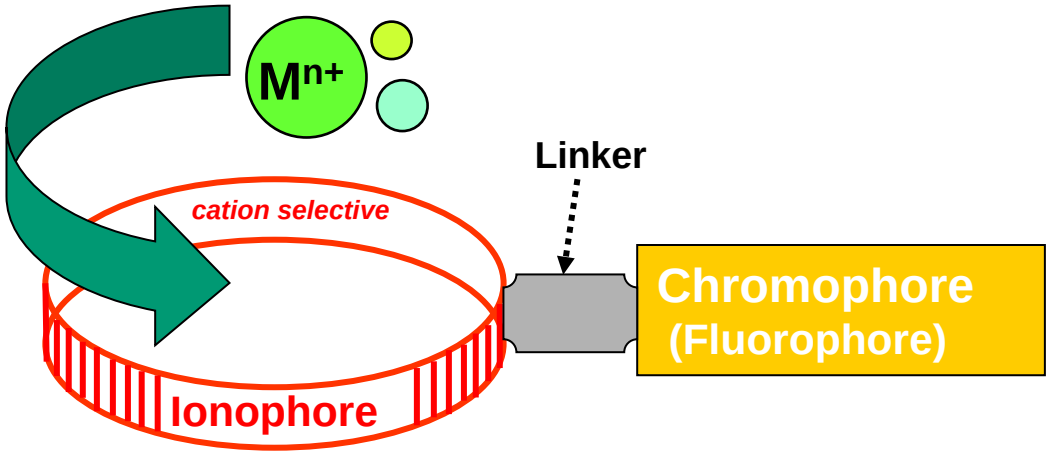
Hybride-Hosts



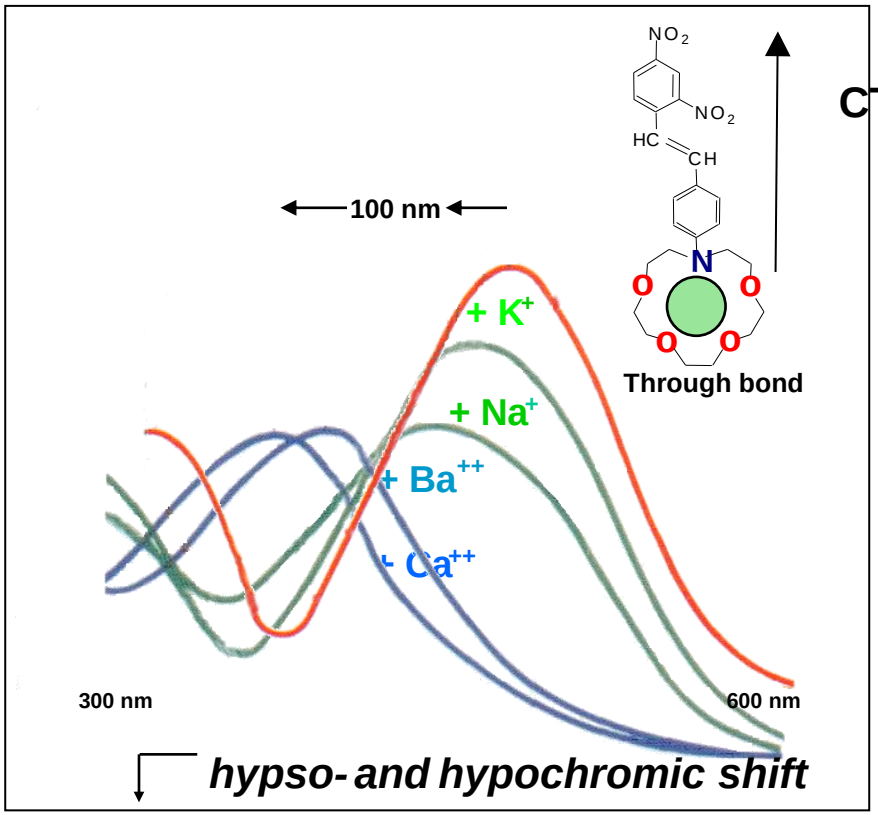




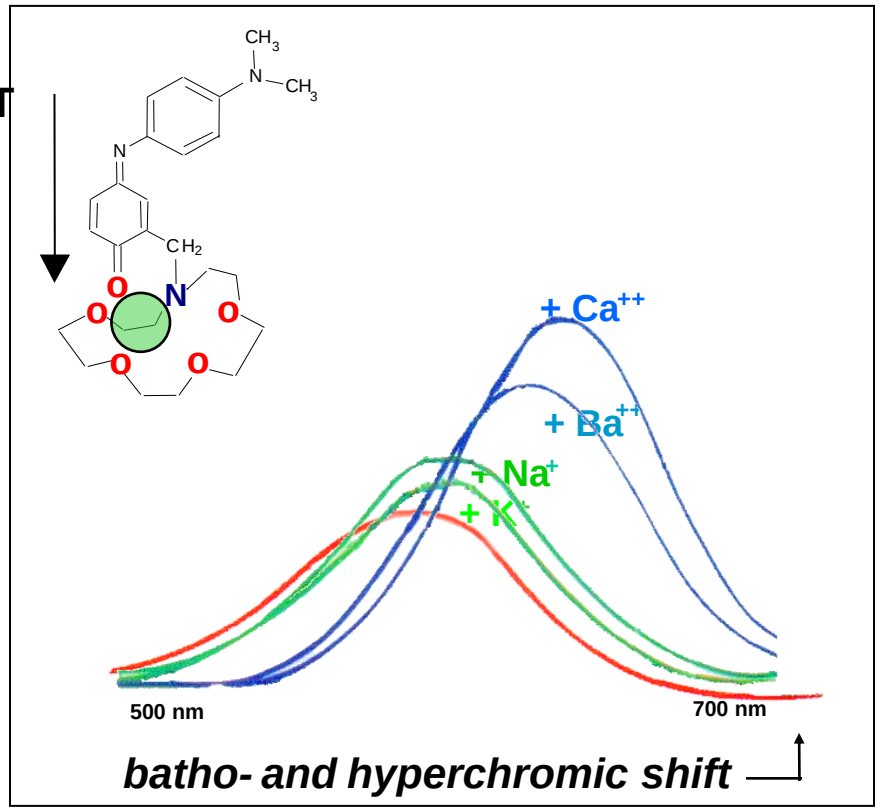
Chromo-Ionophores



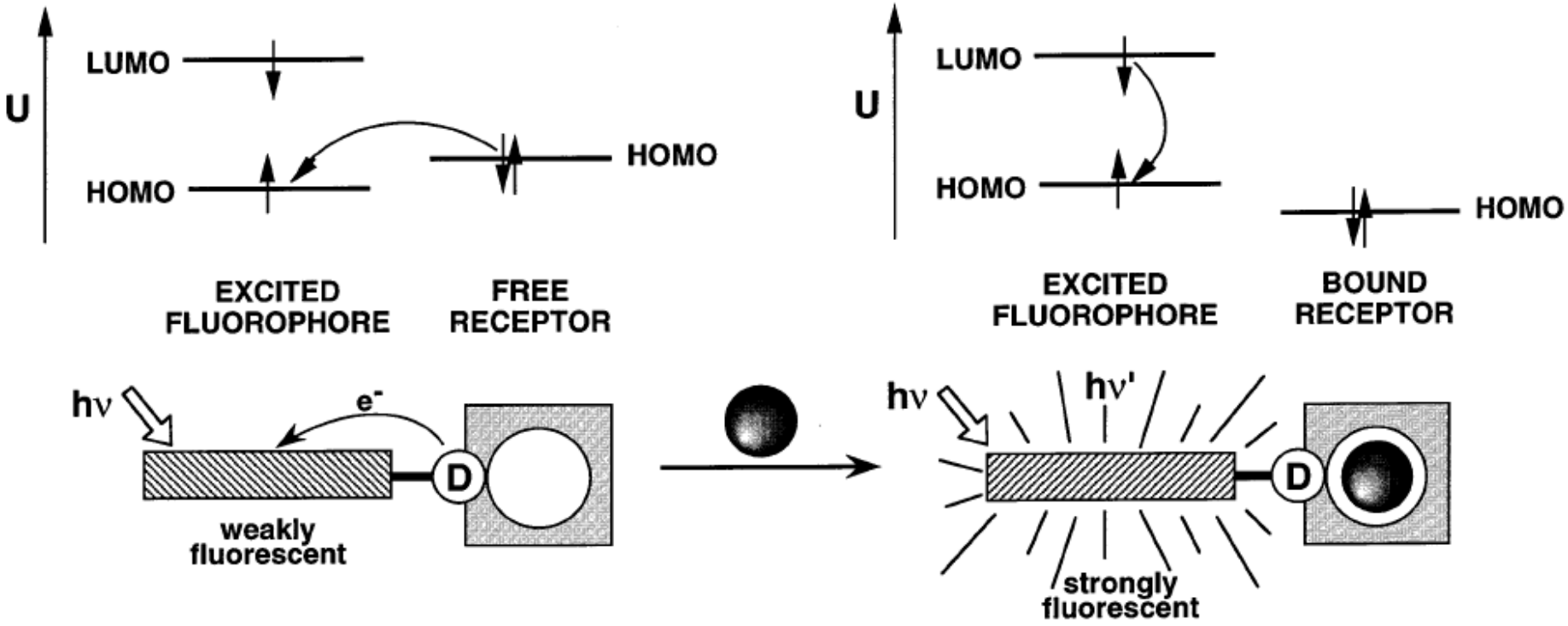
Chromo-Ionophores



CT

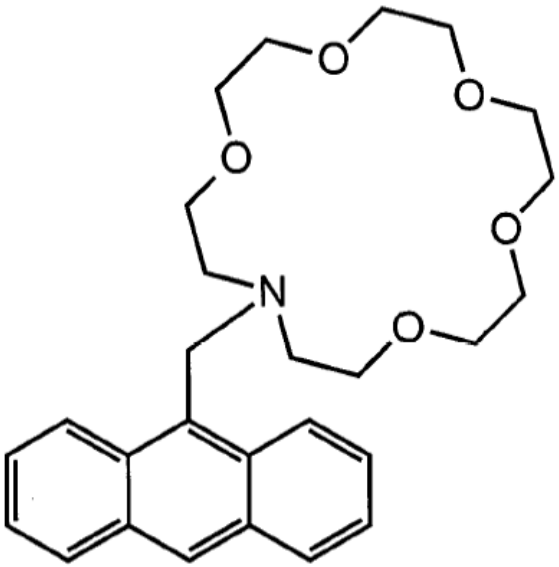


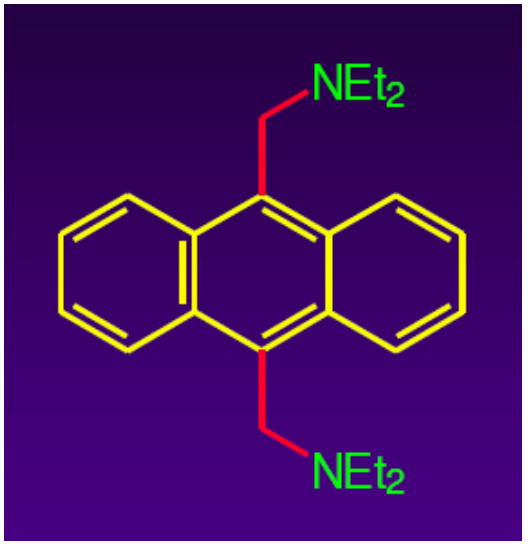
Cation Recognition by Fluorescence
PET (Photoinduced Electron Transfer) Sensors



'Design principles of fluorescent molecular sensors for cation recognition'
B. Valeur et al. *Coord. Chem. Rev.* **2000**, *205*, 3.

Examples of Fluorescence PET Sensors



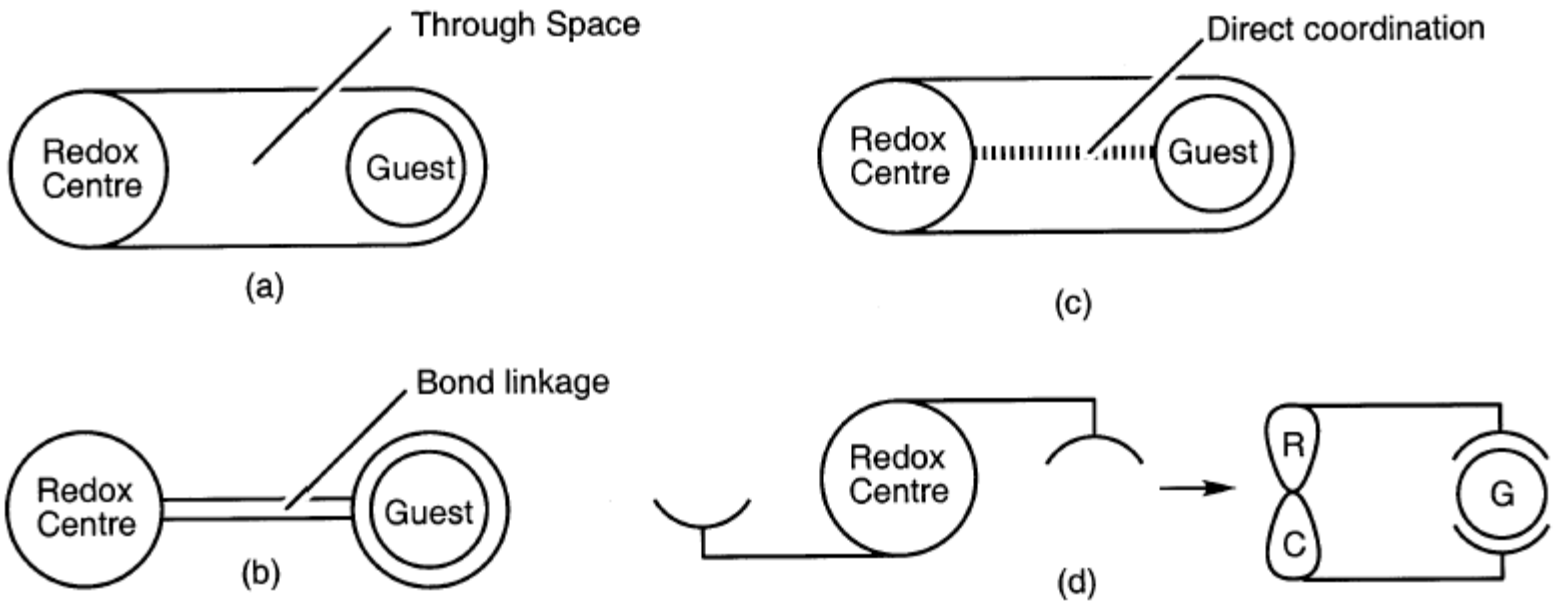


For alkali metal ions

For protons

The electron transfer from the amine to the anthracene is energetically disfavored when the amine is coordinated to a metal cation or a proton.

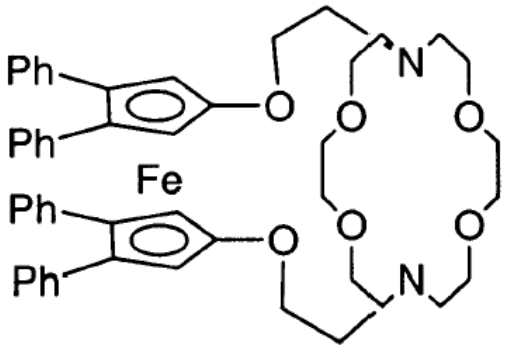
Redox-Responsive Ionophores

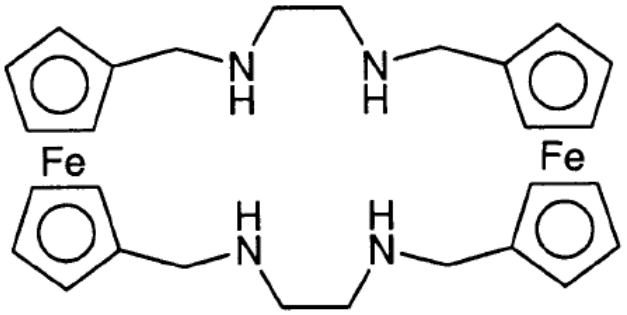


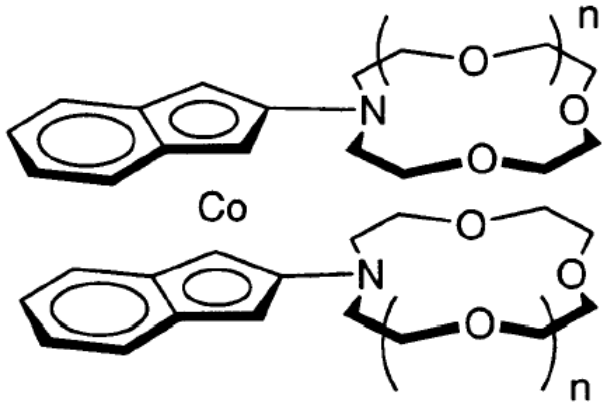
‘Mechanisms of electrochemical recognition of cations, anions and neutral guest species by redox-active receptor molecules’

Paul D. Beer et al. *Coord. Chem. Rev.* **1999**, *185-186*, 3.

Examples of Redox-Responsive Ionophores







The redox-potential of the metallocene changes upon complexation of cations.