Supramolecular receptors

- Multiple interactions
- Complementarity
- Preorganization

} **Cooperativity**

- Macrocycles
- Clefts
- Tweezers

Convergence: the binding entities of the host point toward a common area, creating a binding site

Supramolecular receptors

Classifications

- By substrate
  - Cations
  - Anions
  - Neutral molecules
- By interaction
  - Electrostatic (ion pairing, ion-dipole)
  - H-bonds
  - Donor-acceptor
  - π interactions
- By structure
  - macrocycles
  - Cavitands and clefts
  - Tweezers and cavitands

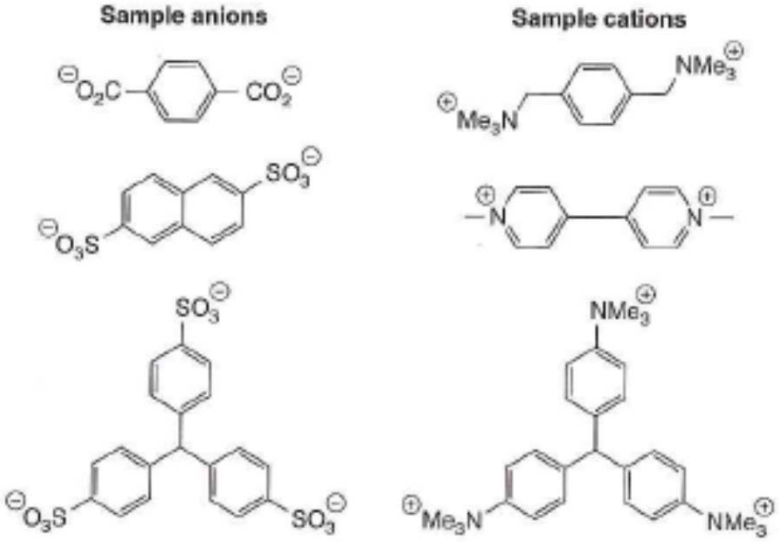
Cations

Guest features

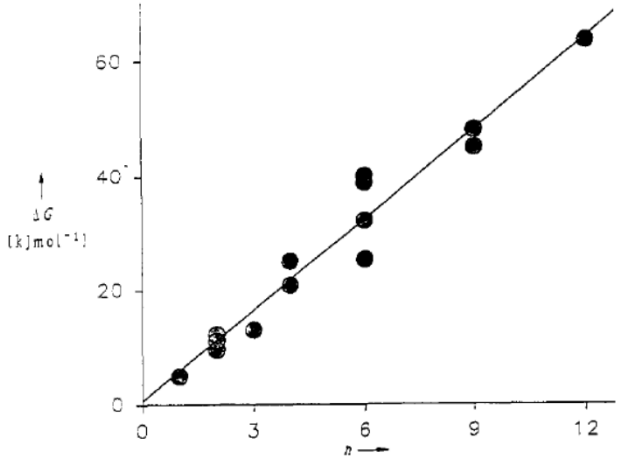
- Metal ions
  - Spherical symmetry
  - Electrostatic interaction (including π)
  - Covalent interactions (donor-acceptor)
- Organic cations
  - Different shapes
  - Electrostatic interactions (including π)
  - H-bonds

Cation binding: ion pairs

Ion pair recognition: cation binding in water



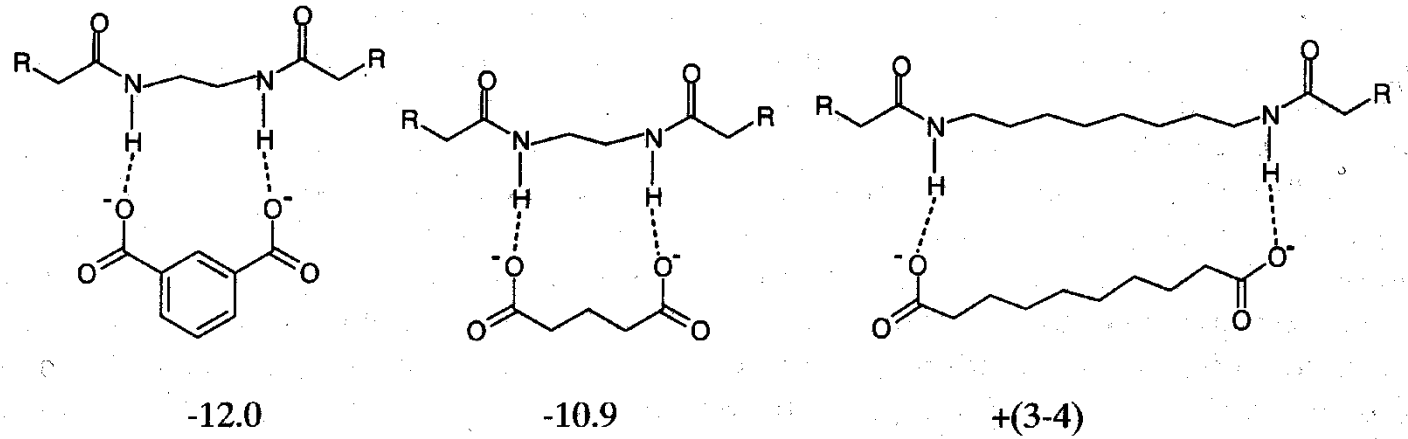
Simple ions to probe ion pairing



ΔG increases by 1.2 ± Kcal/mol per salt bridge

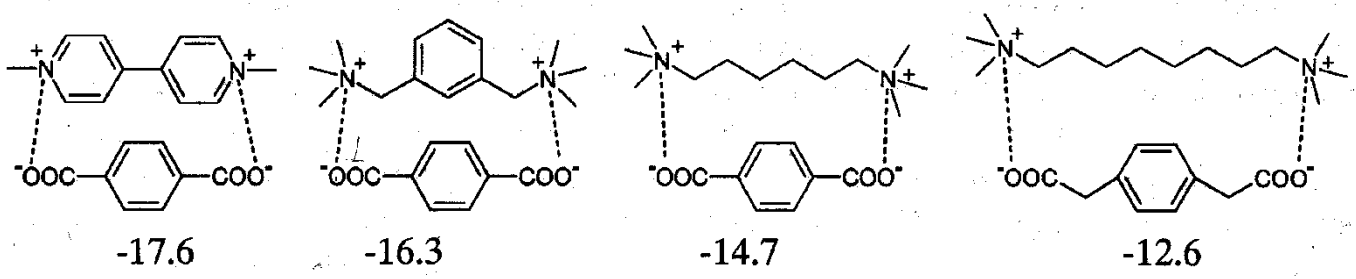
Cation binding: ion pairs

Ion pair recognition: cation binding in water



ΔG in kJ mol^{-1}

Ion pairs (in water at zero ionic strength)



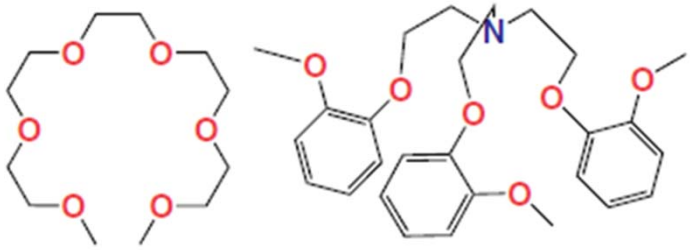
Ion pair interaction has much smaller pre-organization requirements than H-bonding

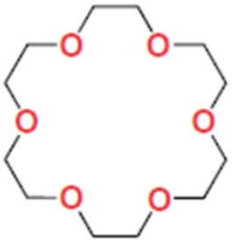
Cations binding

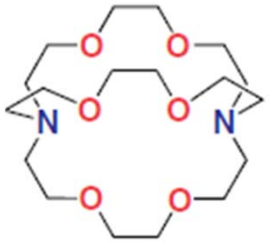
At the edge between coordination an supramolecular chemistry

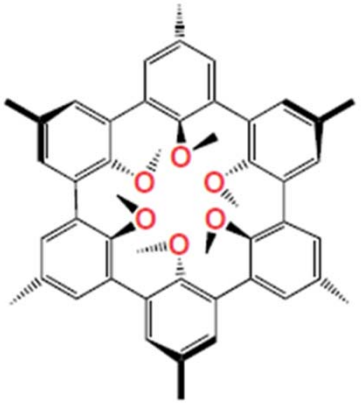
Oxygen-based receptors for hard metal ions: ion-dipole interaction

- Podands
- Crown Eters
- Lariat eters
- Cryptands
- Spherands



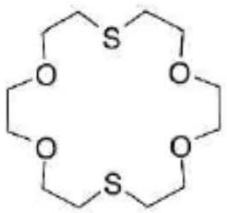




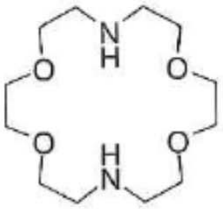


Cations binding: dipolar and donor-acceptor interactions

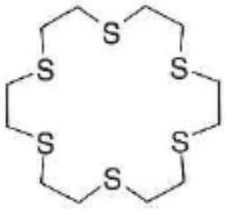
Nitrogen and sulfur analogs of crown ethers



3.64



3.18



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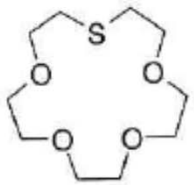

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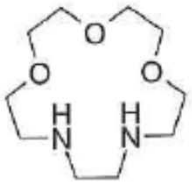

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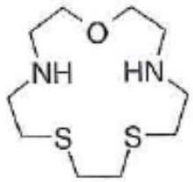


3.68

Table 3.12 Comparative binding constants (log K_{11}) for hard and soft metal ions with various ligands.

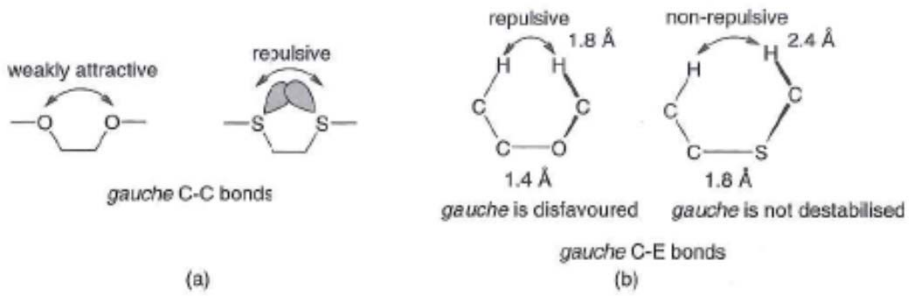
	Ligand						
Cation	[18]crown-6	**3.64**	**3.18**	[15]crown-5	**3.66**	**3.67**	**3.68**
K^+ (methanol)	6.10	1.15	2.04	–	–	–	–
K^+ (water)	2.0	–	<1	0.74	–	1.0	–
Ag^+ (methanol)	4.58	–	–	–	–	–	–
Ag^+ (water)	1.60	4.34	7.80	0.94	5.0	5.85	8.95
Tl^+ (water)	2.27	0.93	1.1	1.23	0.8	–	–
Ba^{2+} (water)	3.78	–	2.51	–	–	1.0	–
Pb^{2+} (water)	4.27	3.13	6.9	1.85	1.65	5.85	5.67

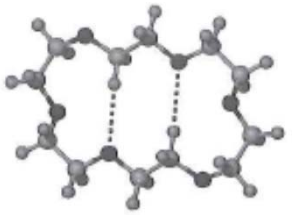
Cations binding: dipolar and donor-acceptor interactions

Nitrogen and sulfur analogs of crown ethers

Table 3.13 thermodynamic parameters for Ag^+ binding by various ligands in methanol at 25 °C

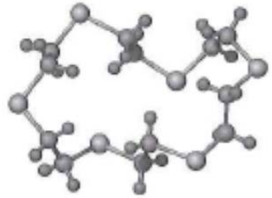
Ligand	Log K	$-\Delta H$ (kJ mol^{-1})	$T\Delta S$ (kJ mol^{-1})
[18]ane-N_4S_2	14.1	77	3.3
[18]ane-N_4O_2	11.2	59.5	4.4
[18]ane-N_2O_4	10.0	51.4	5.7
[18]ane-N_2S_4	13.7	83.2	−5.0
[18]ane-S_2O_4	10.3	64.0	−5.3
[18]crown-6	4.58	38.3	−12.1
[2.2.1]cryptand	14.4	81.9	0.1
[18]ane-$(NMe)_2N_2O_2$	13.4	84.3	−7.8
[18]ane-$(NMe)_2N_2S_2$	14.6	102.1	−18.7





[18]crown-6

[18]ane-S_5



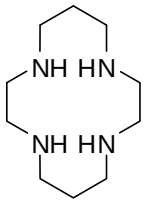
[18]ane-S_6

Cations binding: donor acceptor-interactions

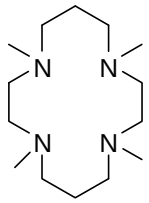
Azamacrocycles

Table 3.15 Comparison of the binding constants (log K_{11}) of cyclam and tetramethyl cyclam for various transition metals (water, 25 °C).[26]

Metal ion	Cyclam	Tetra-N-methylcyclam	Ionic radius (Å)
Cu(II)	27.2	18.3	0.65
Ni(II)	22.2	8.6	0.69
Co(II)	12.7	7.6	0.72
Zn(II)	15.5	10.4	0.74
Cd(II)	11.7	9.0	0.97
Pb(II)	11.3	(~7.5)	1.21



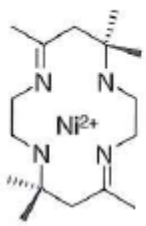
cyclam



Me_4-cyclam

Cations binding: donor acceptor interactions

Shiff bases

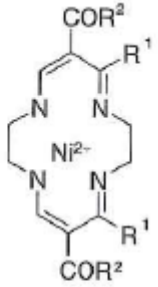


Curtis 1961

Aldol condensation of acetone and $[Ni(en)_3]^{2+}$

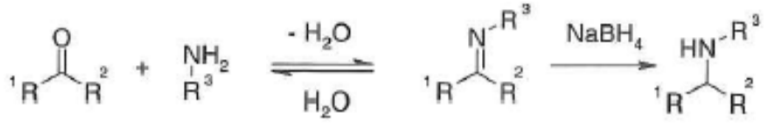
Busch 1964

Fe(II) templated condensation of 2,6-diacetylpyridine with diethylene tetramine.



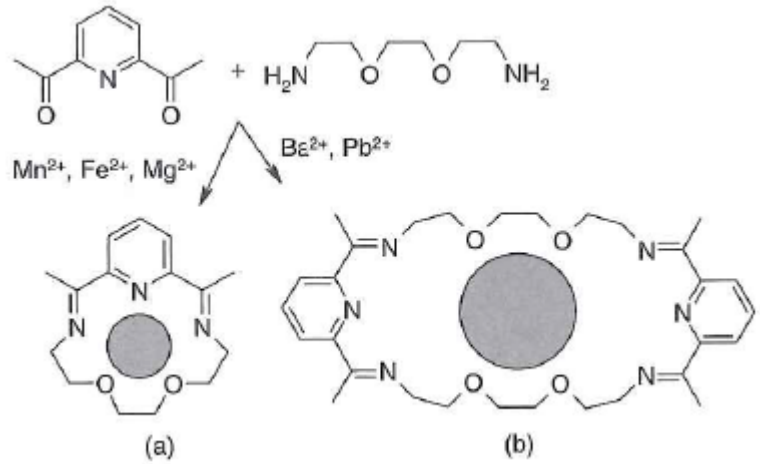
Jäger 1964

Metal templated reaction of β-ketoiminato complexes with 1,2-diaminoethane (en)



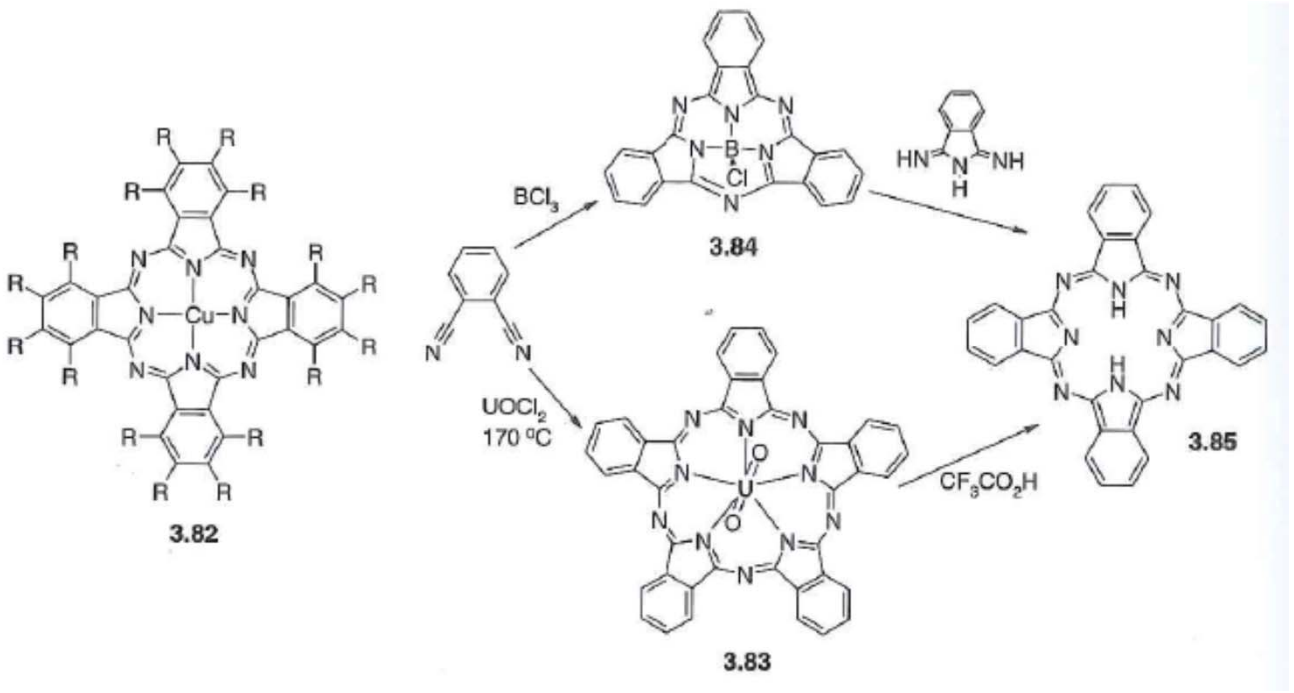
Cations binding: donor acceptor interactions

Shiff-bases



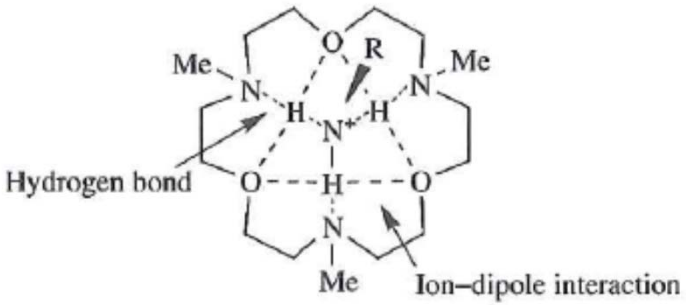
Cations binding: donor acceptor interactions

Phtalocyanines



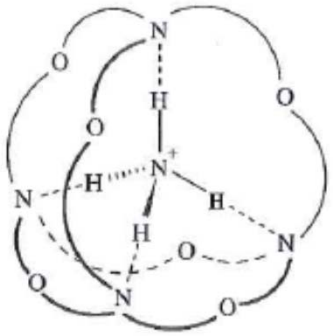
Organic cations binding: H-bonds

Crown ethers

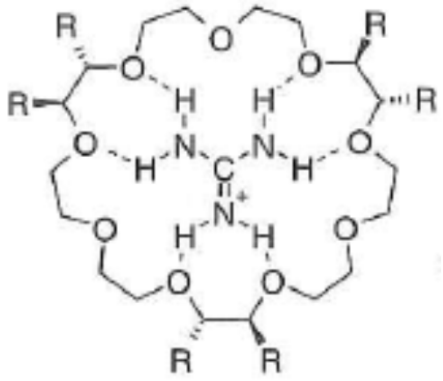


18-crown-6 binds K^+ better than NH_4^+

18ane-O_3N_3 binds NH_4^+ better than K^+



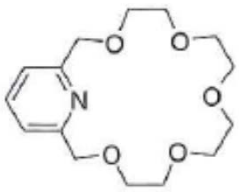
$pK_a \sim 17$



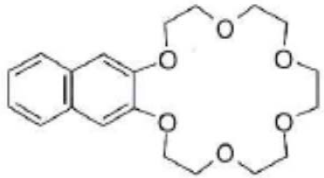
3.98 R = CO_2^-

Organic cations binding: H-bonds

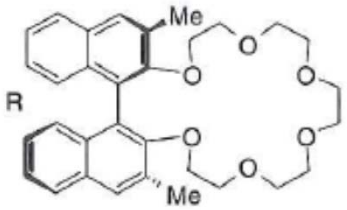
Ditopic receptors



3.94



3.95



3.96

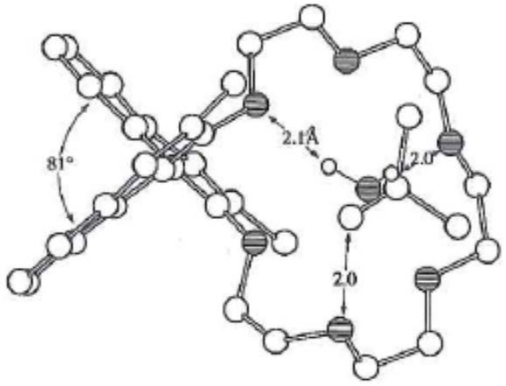
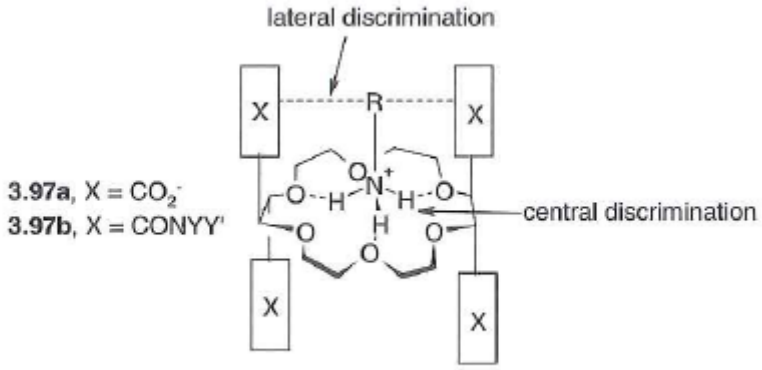


Table 3.17 Complexation free energies for corand receptors with ammonium ions.

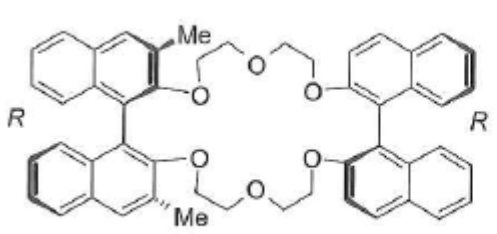
	$-\Delta G°$ (kJ mol^{-1})		
Host	NH_4^+	$CH_3NH_3^+$	$(CH_3)_3CNH_3^+$
3.94	43.9	37.7	34.7
3.95	39.7	31.4	28.9
3.96	37.2	28.9	26.8



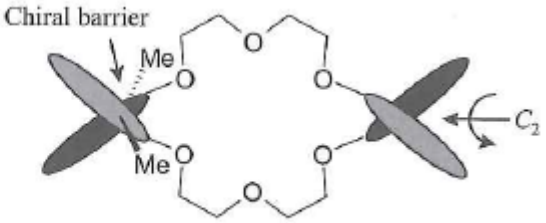
Lateral and Central discrimination.

Organic cations binding: H-bonds

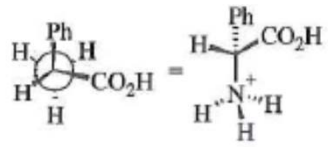
Chiral recognition

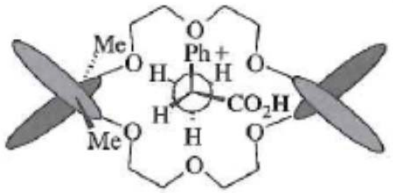


3.106



(*R*,*R*)

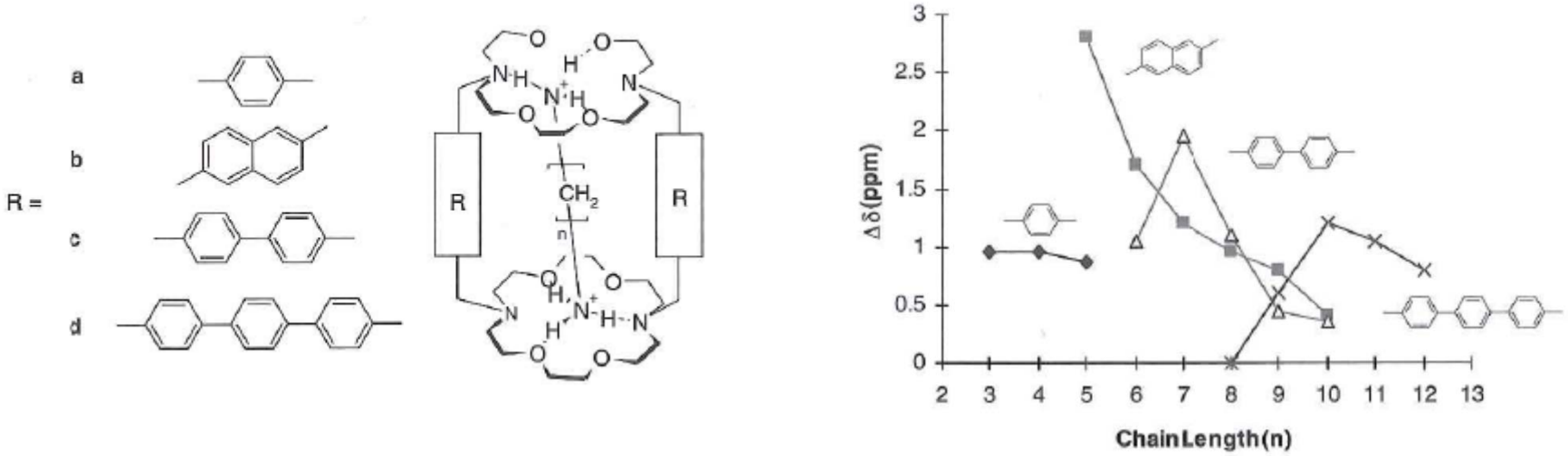




(*R*,*R*)

Organic cations binding: H-bonds

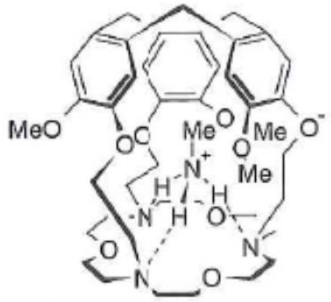
Ditopic receptors



A ditopic receptor is a receptor that possess two remote binding regions. In principle, affinity for the guest should be higher as result of a greater number of interactions and possibly of cooperation, and selectivity can be designed by placement and spacing and of the binding sites

Organic cations binding: H-bonds

Amphiphilic receptors

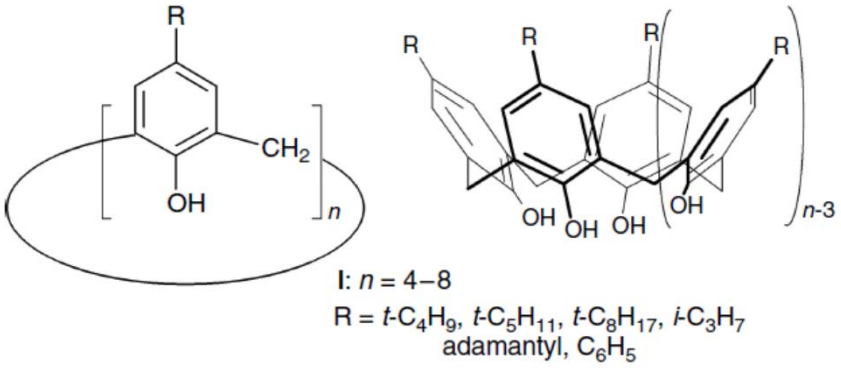


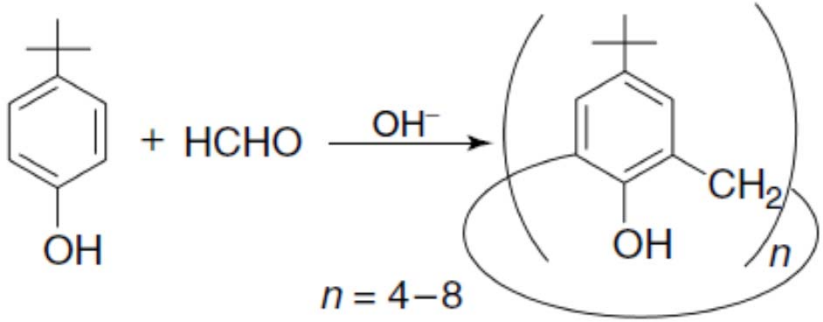
Hydrophobic interaction
π-cation interaction
H-bonding
Size selectivity

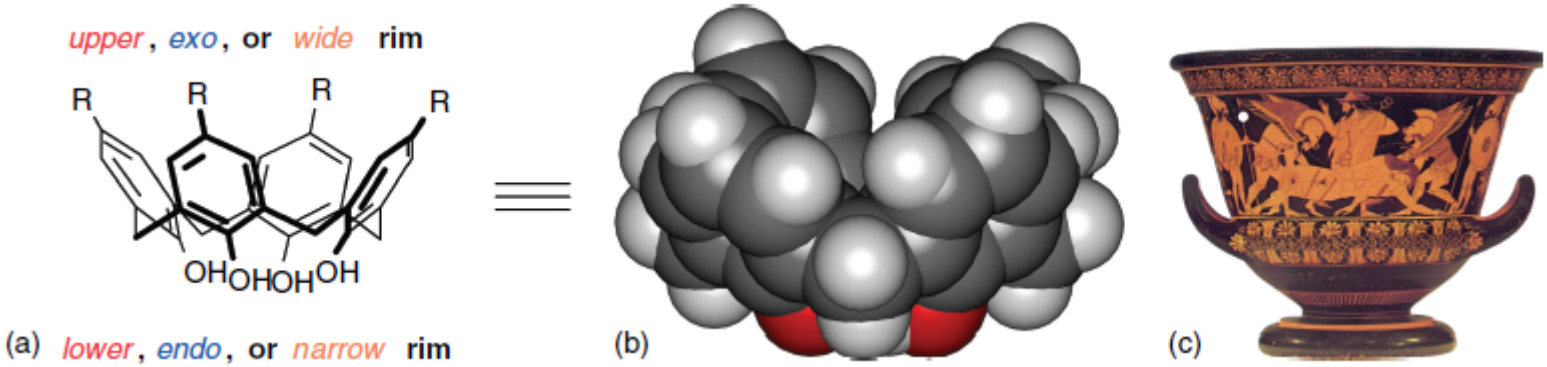
An amphiphilic receptor combines two or more forms of guest recognition sites, which should result into a synergic enhancement of the binding

Cations binding

Amphiphilic receptors: calix[n]arenes

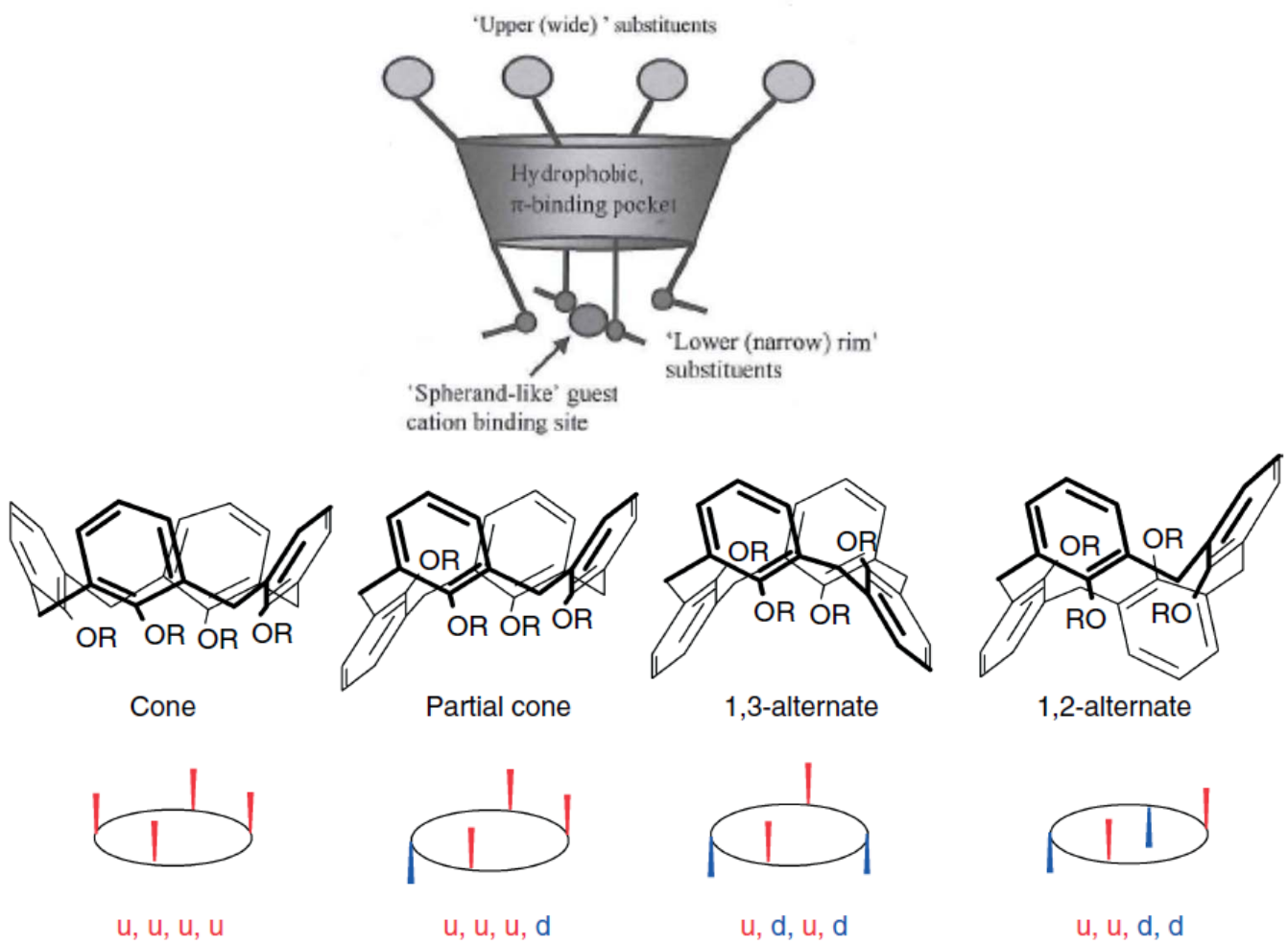






Cations binding

Amphiphilic receptors: calix[n]arenes

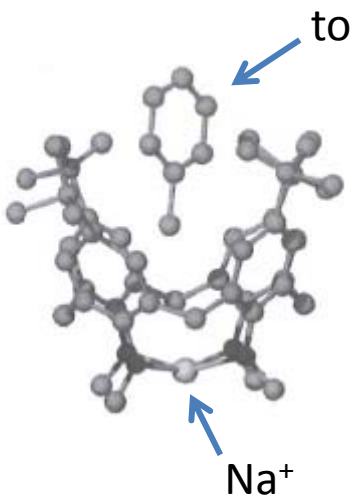


Conformationally mobile for R = H, Me, Et

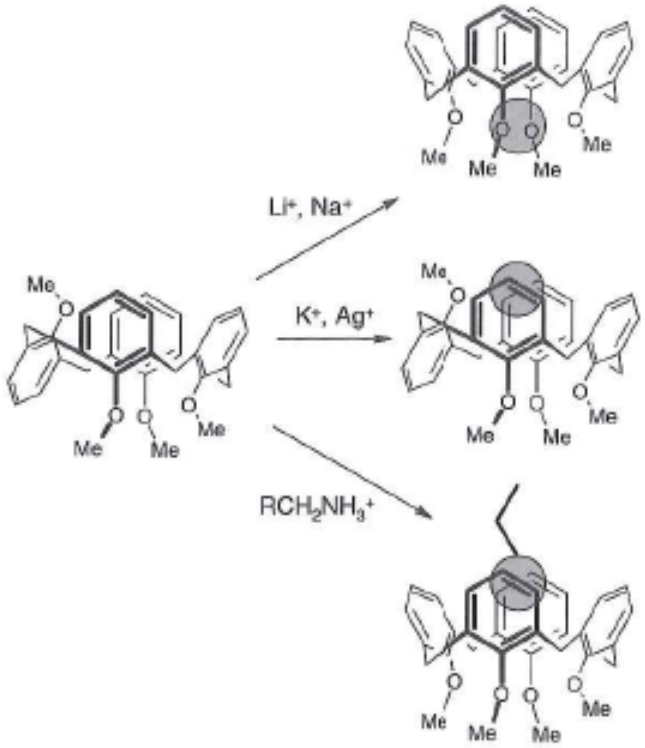
Cone stabilized by H-bonds for R = H and preferred in polar solvents

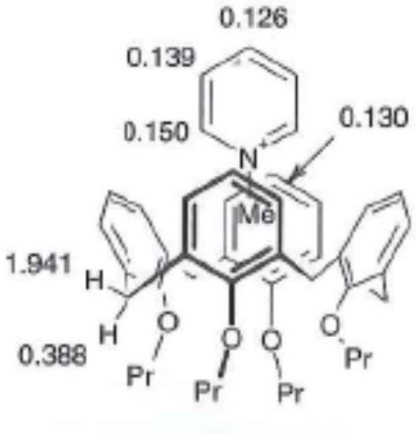
Cations binding

Amphiphilic receptors: calix[n]arenes



Lower rim coordination: metal ions





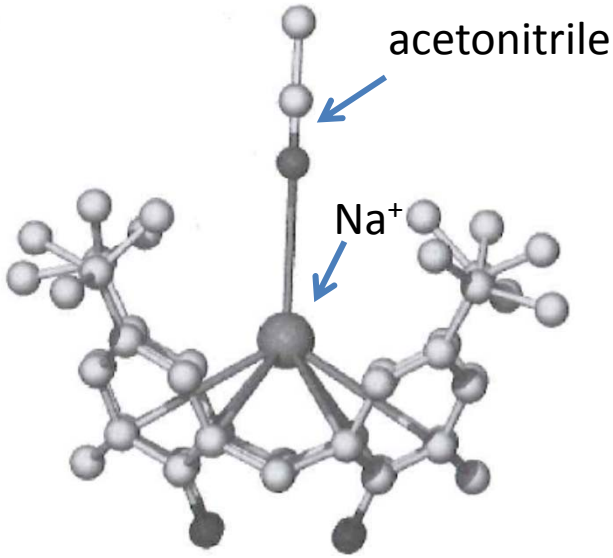
π-poket coordination: metal ions

Cations binding

Amphiphilic receptors: calix[n]arenes

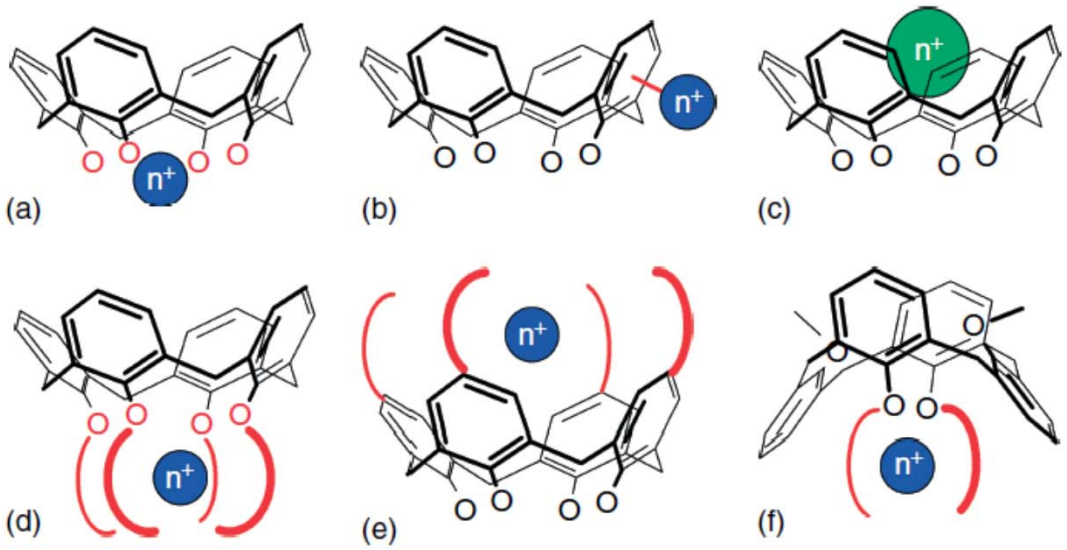
Table 3.20 Selective phase transport of metal cations by calixarenes from basic aqueous solution. The data represent the rate of cation transport (flux) across the phase boundary in moles s^{-1} $m^2 \times 10^8$.

		p-t-butylcalix[n]arene		
Metal salt	Cation diameter	n = 4	n = 6	n = 8
Lower rim anulus diameter (Å)		1.0	2.4	4.8
LiOH	1.52	–	10	2
NaOH	2.04	2	22	9
KOH	2.76	<0.7	13	10
RbOH	3.04	6	71	340
CsOH	3.40	260	810	996
$Ba(OH)_2$	2.70	1.6	3.2	–



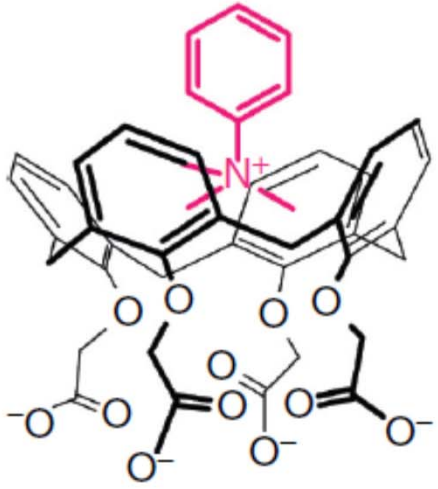
Cations binding

Possible binding sites

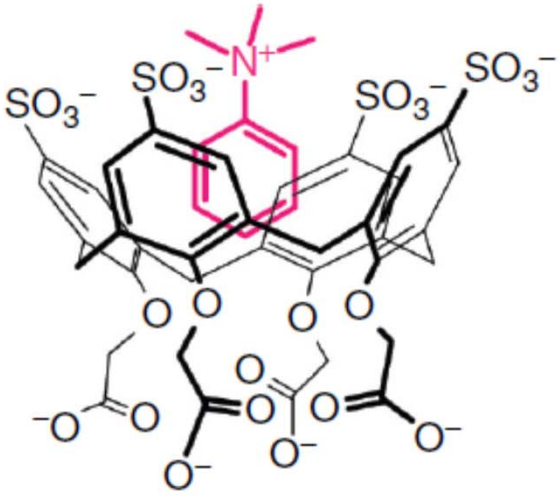


Cations binding

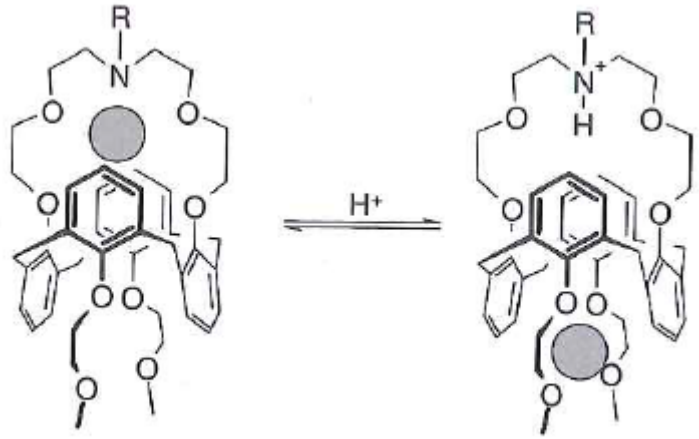
Amphiphilic receptors: calix[n]arenes



10·TMA



11·TMA



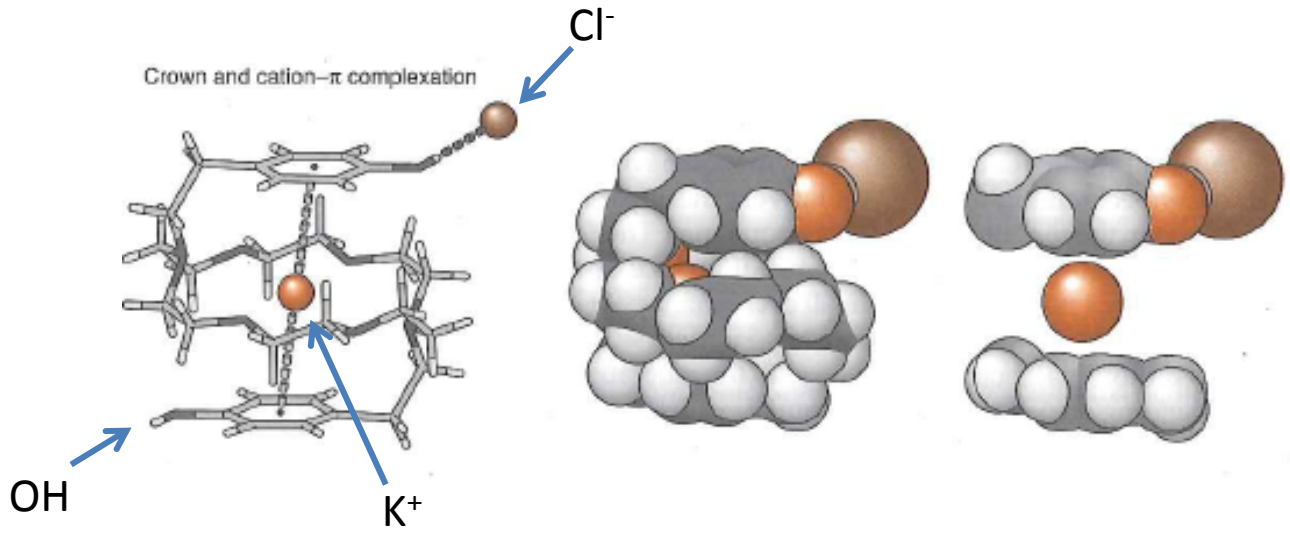
3.131

Cations binding

Amphiphilic receptors: calix[n]arenes

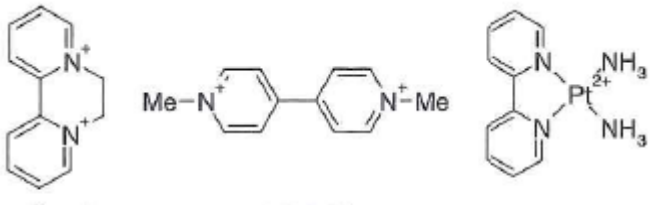
3.134a n = 1
3.134b n = 2

3.135

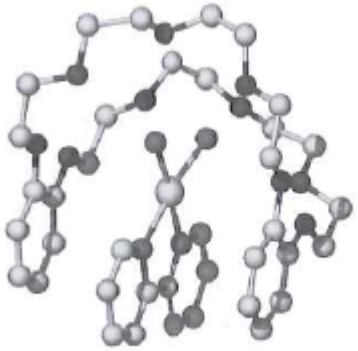


Organic cations binding

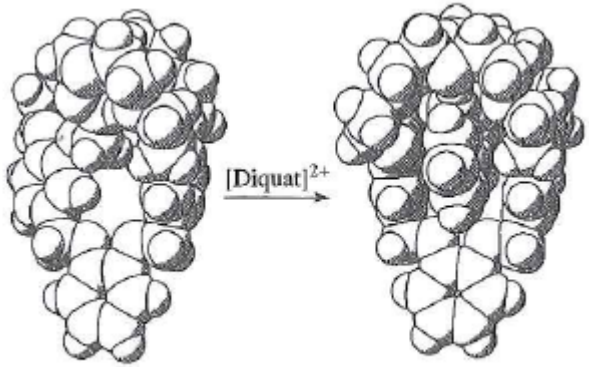
Case study: erbicide



Dibenzo[30]crown-10

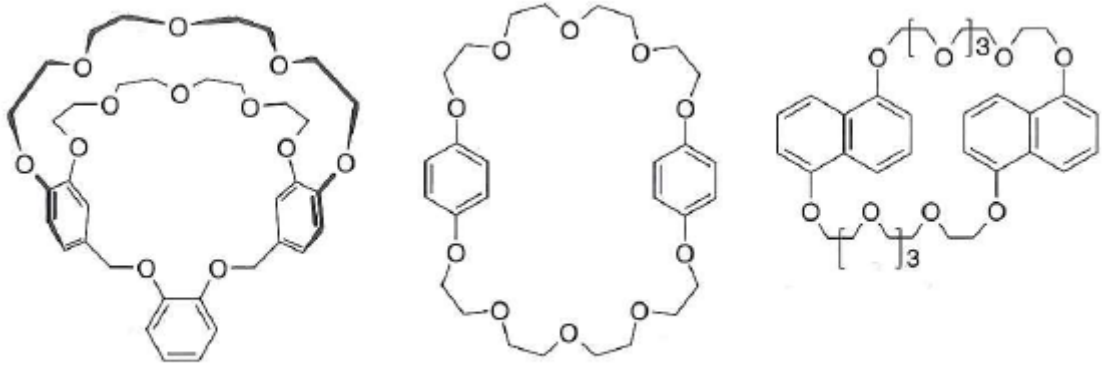


(a)



(b)

1.7×10^4 M^{-1} (acetone, 25 °C)



3.115 3.116 3.117

$>9 \times 10^5$ M^{-1} (acetone, 25 °C)

Anions

Guest features

- Halides
- Oxides
- Organic anions

- Coordinatively saturated
- Lewis bases
- Larger than cations
- Highly polarisable
- Different shapes and geometries
- Higher free energy of solvatation
- Protonation

Anions vs cations

Table 4.1 Properties of some common anions and cations (ionic radii in part from Reference 4).

Ion	Radius (Å)	$\Delta G_{hydration}$ (kJ mol^{-1})	pK_a (298K)
F^- (6 coord.)	1.33	−465	3.3
Cl^- (6 coord.)	1.81	−340	Low
Br^- (6 coord.)	1.96	−315	Low
I^- (6 coord.)	2.20	−275	Low
ClO_4^-	2.50	−430	–
NO_3^-	1.79	−300	−1.4
CO_3^{2-}	1.78	−1315	6.4, 10.3
SO_4^{2-}	2.30	−1080	Low, 2.0
PO_4^{3-}	2.38	−2765	2.1, 6.2, 12.4
$H_2PO_4^-$	2.00	−465	2.1, 6.2, 12.4
$PdCl_6^{2-}$	3.19	−695	–
Na^-	2.2	n/a	–
Cs^-	3.5	n/a	–
Li^+ (6 coord.)	0.76	−475	–
Na^+ (6 coord.)	1.02	−365	–
K^+ (6 coord.)	1.38	−295	–
Cs^+ (6 coord.)	1.67	−250	–
Ca^{2+} (6 coord.)	1.00	−505	–
Zn^{2+} (6 coord.)	0.74	−1955	–
Al^{3+} (6 coord.)	0.54	−4525	–
La^{3+} (6 coord.)	1.03	−3145	–
NH_4^+	1.48	−285	9.3

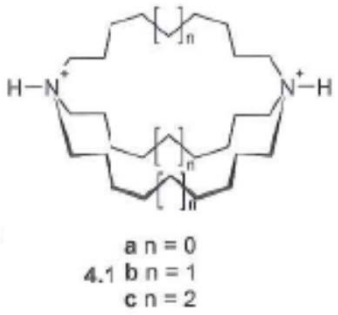
Table 4.2 The Hofmeister Series

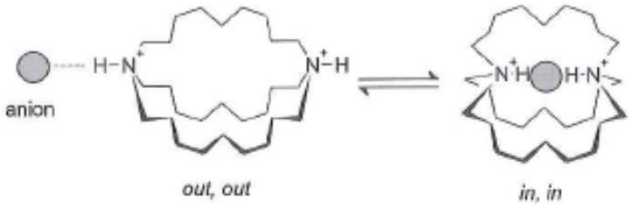
Weakly hydrated (hydrophobic)	Strongly hydrated (hydrophilic)
Anions: organic anions > ClO_4^- > I^- > SCN^- > NO_3^- > ClO_3^- ···	
> Br^- > Cl^- >> F^-, IO_3^- > $CH_3CO_2^-$, CO_3^{2-} > HPO_4^{2-}, SO_4^{2-} > citrate^{3-}	
Cations: $N(CH_3)_4^+$ > NH_4^+ > Cs^+ > Rb^+ > K^+ > Na^+ > H^+ > Ca^{2+} > Mg^{2+}, Al^{3+}	

Precipitate proteins

Dissolve proteins

The first receptor: katapinands

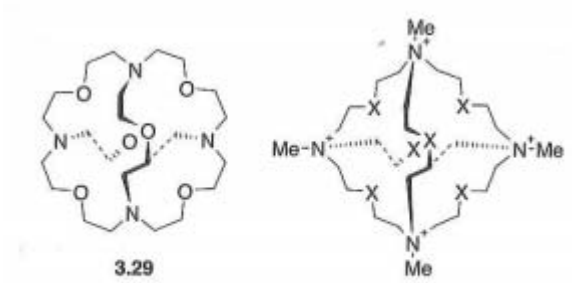




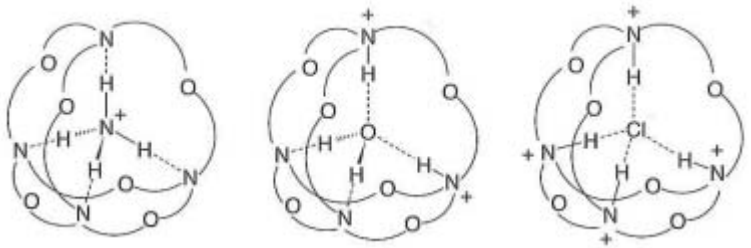
Cl--H-N = 3.10 A

- Reported on November 1967 by Park and Simmons (Du Pont)
- 8,8,8 katapinand does not bind halide anions
- 9,9,9 katapinand binds Cl^- in water/TFA with $K_a = 10^2\ M^{-1}$ and 8-fold selectity over Br^-
- 10,10,10 katapinand binds Cl^-, Br^- and I^- with little selectivity
- scarce reports up to late 80s

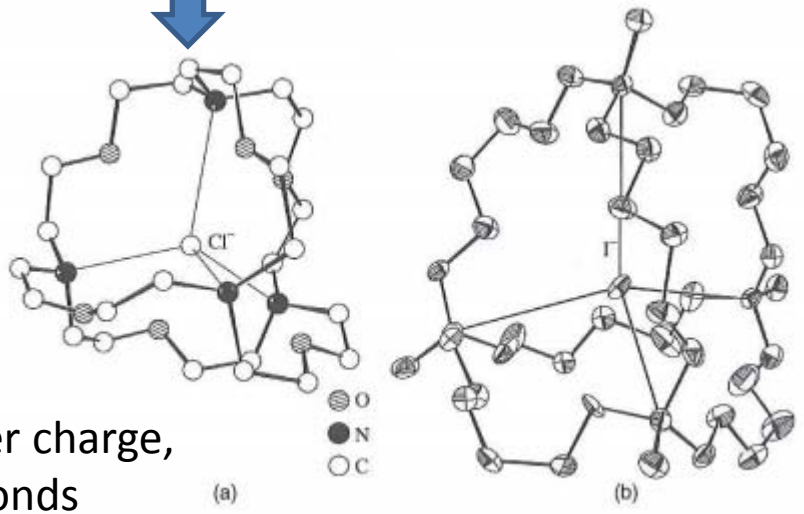
Converting cation hosts into anion hosts



Larger size (methyls outward)
Log K_{ass} (I^-) = 2.25 (water)



Log K_{ass} (Cl^-) > 4 (MeOH)
Selectivity over Br^- ~50

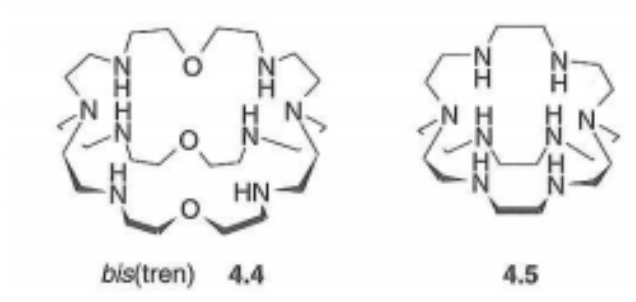


Cl--H-N = 3.09 A

Better preorganization, higher charge,
Greater number of H-bonds

Shape selectivity

The roles of complementarity and preorganization

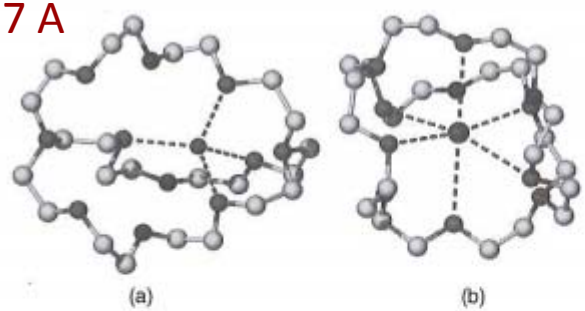


Anion	4.4-6H$^+$	4.5-6H$^+$
F^-	4.19	11.2
Cl^-	3.0	
Br^-	2.6	
I^-	2.15	
N_3^-	4.3	

Log K_{ass} (water)

F--H-N = 2.7 A

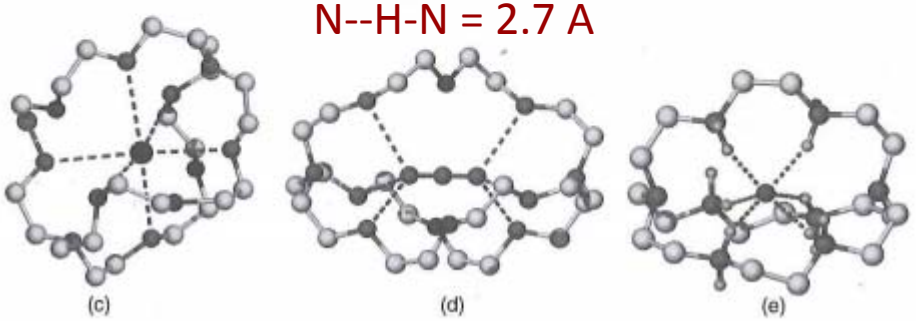
4.4-6H$^+$⊂F$^-$



Cl--H-N = 3.3 A

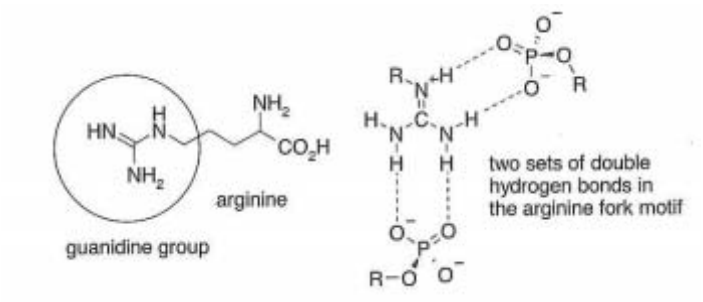
4.4-6H$^+$⊂Cl$^-$

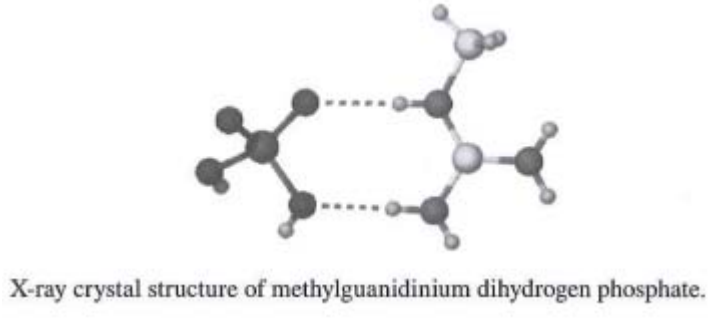
N--H-N = 2.7 A



4.4-6H$^+$⊂Br$^-$ 4.4-6H$^+$⊂N_3^- 4.5-6H$^+$⊂F$^-$

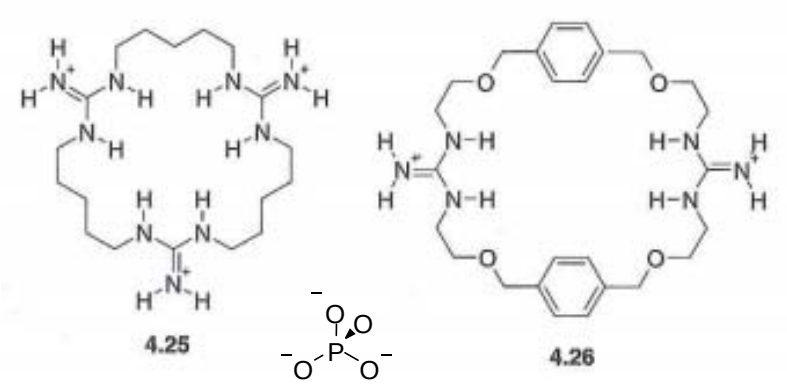
Guanidinium as a natural binding site





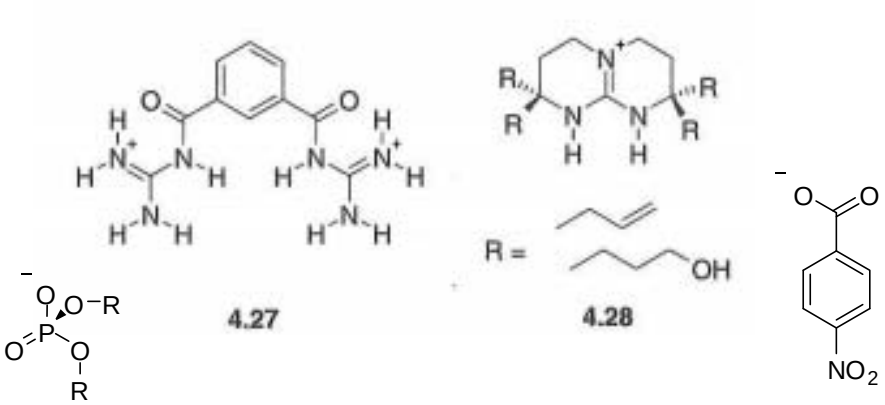
X-ray crystal structure of methylguanidinium dihydrogen phosphate.

pK_a = 13.5



2.4 1.7

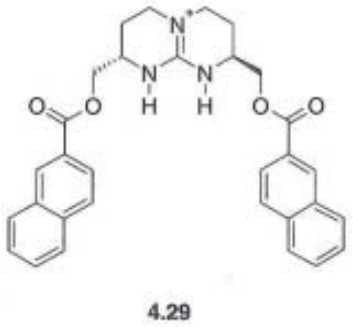
Log K_{ass} (water)



4.7 (acetonitrile) 5.15 (chloroform)

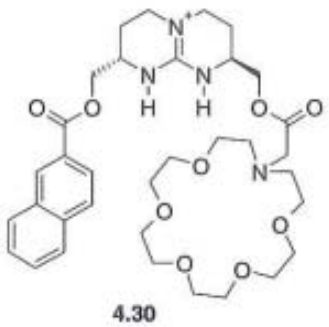
Log K_{ass}

Shape selectivity



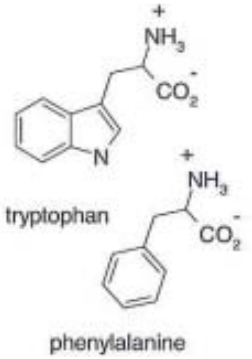
4.29

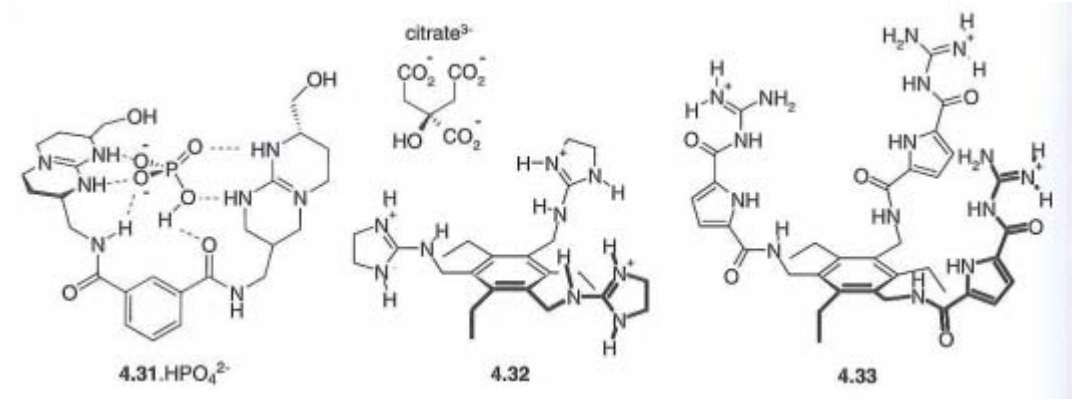
de 17%



4.30

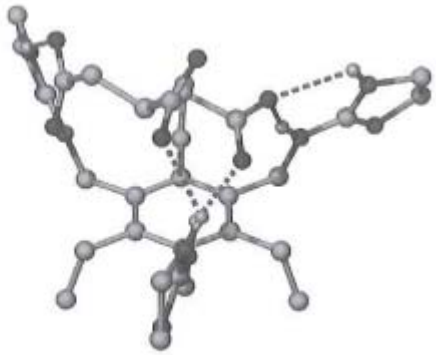
de 80%





4.31.HPO_4^{2-} 4.32 4.33

Log K_{ass} = 3.8
(water)

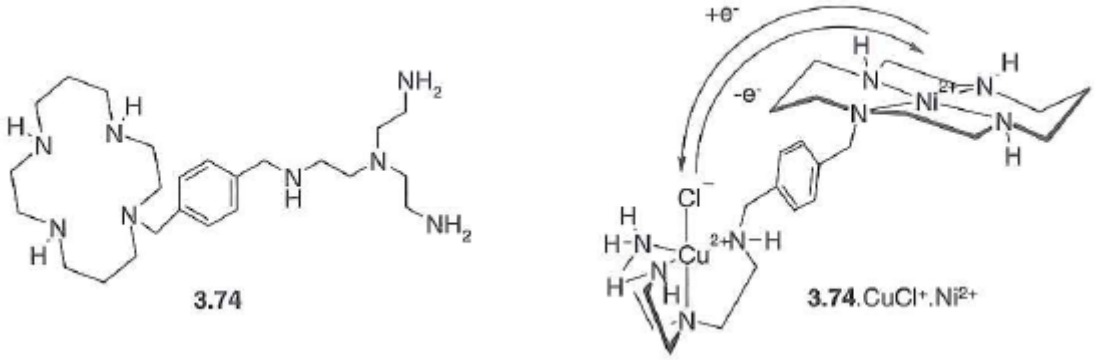


X-ray crystal structure of the citrate complex of **4.32**.[31]

Log K_{ass} > 5
(water)

Metal based-receptors

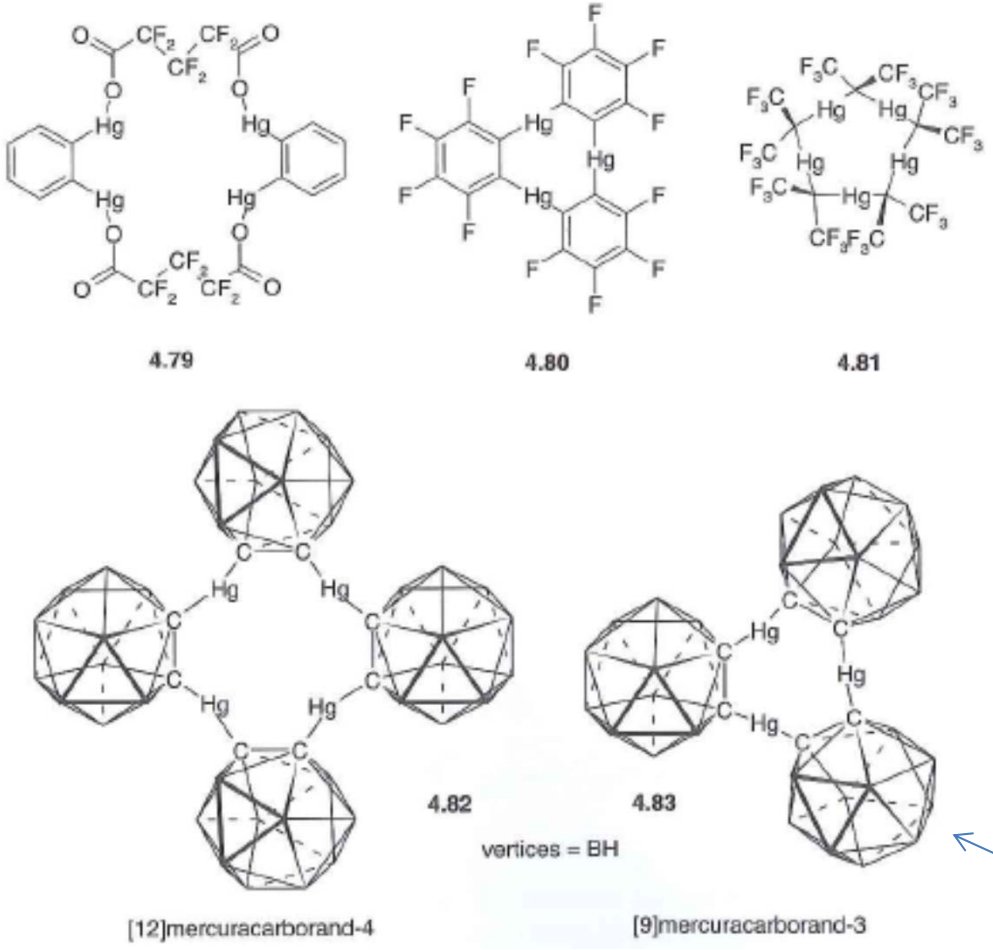
Azamacrocycles

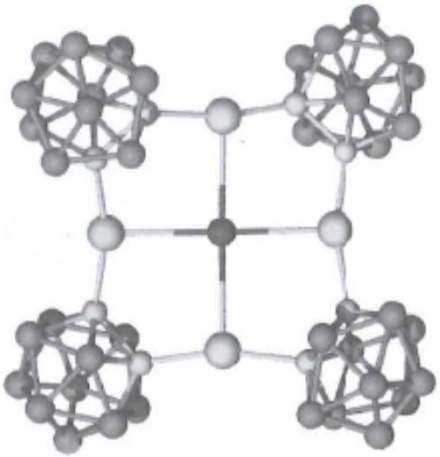


Anion translocation

Metal based-receptors

Anticrowns





Included in ion selective electrods:

Log K_{ass} = 13.2 (sensor saturation)

Log K_{ass} > 5.67 (dodecanethiol)