Anion Recognition and Binding*

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*Based on project DE-FG07-96ER62307 "Supramolecular Chemistry of Selective Anion Recognition for Anions of Environmental Relevance"

Introduction

A three pronged approach is being used to design highly selective receptors for a variety of anions of environmental significance. Initial target receptors are polyamine macromono- and macro-bicycles. Amide-based receptors which promise to be more robust and pH insensitive are also being designed and synthesized. Target anions to date have primarily included nitrate, phosphate, and more recently fluoride. The suitability of receptors to bind specific anions is being probed by solution (potentiometric, nmr and ITIES*), solid state (x-ray crystallographic) and theoretical (molecular dynamics) studies.

Applications oriented studies are also being explored using promising receptors from the aforementioned studies as templates. The fabrication of anion selective electrodes is in progress. "Switchable" receptors, which may have greater applicability in separations, are being designed and synthesized.

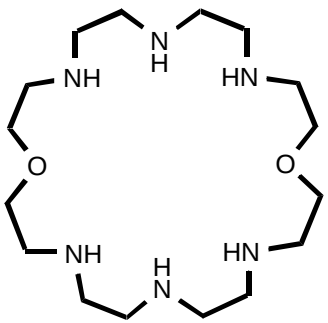
Because of very recent findings of an unusual encapsulation of two nitrates in a bicyclic receptor, the remainder of this poster will focus primarily on nitrate binding.

*Interface between Two Immiscible Electrolyte Solutions

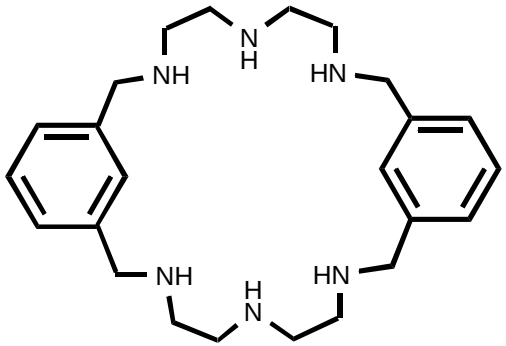
Synthesis

Macrocycles which were originally designed for the project were based on [24]N_6O_2 (**1**), which had been extensively studied in our research group as a phosphoryl transfer catalyst and ATPase mimic. The synthesis of this and related macrocycles is extremely tedious and time consuming, with relatively small yields.

Hence, during year 1 of the project we explored whether macrocycles obtained by much simpler Schiff base condensations could also be viable receptors (**2**). We have now concluded that these new macrocycles are also excellent candidates for selective recognition of target anions.

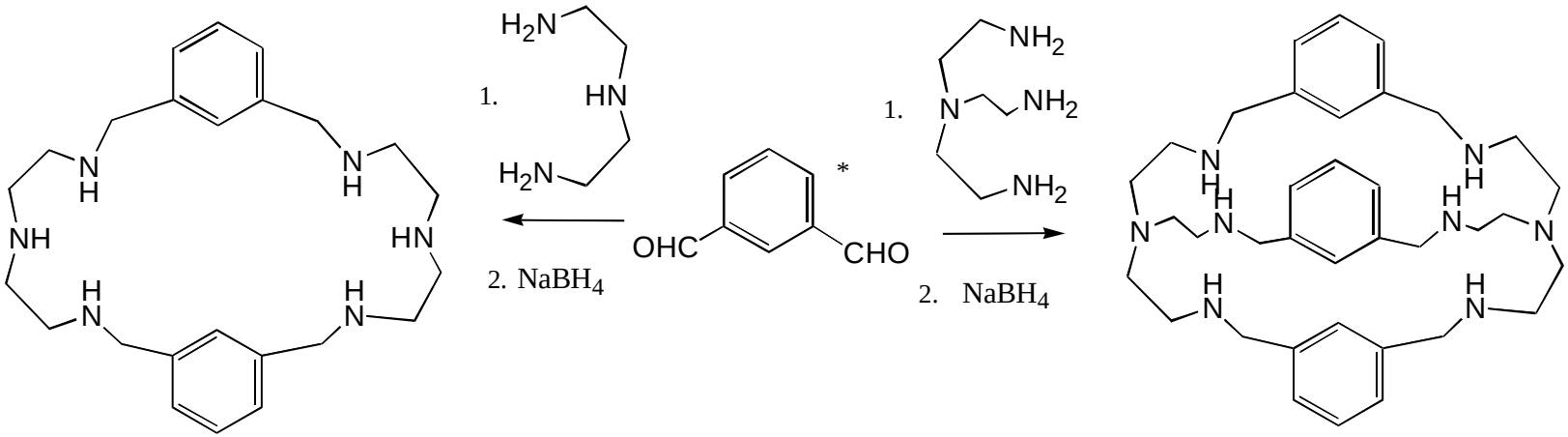


1



2

Synthetic Routes

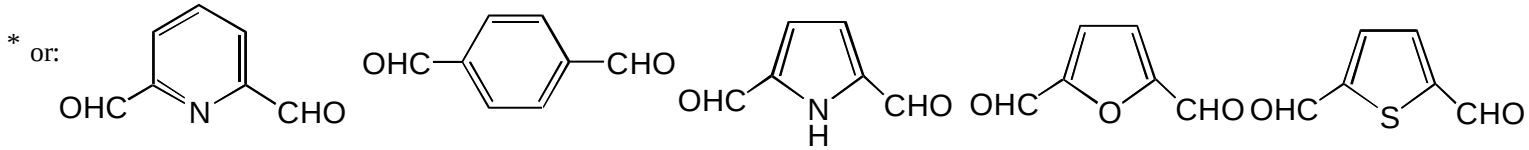


2

Overall Yield ~50-60%

3

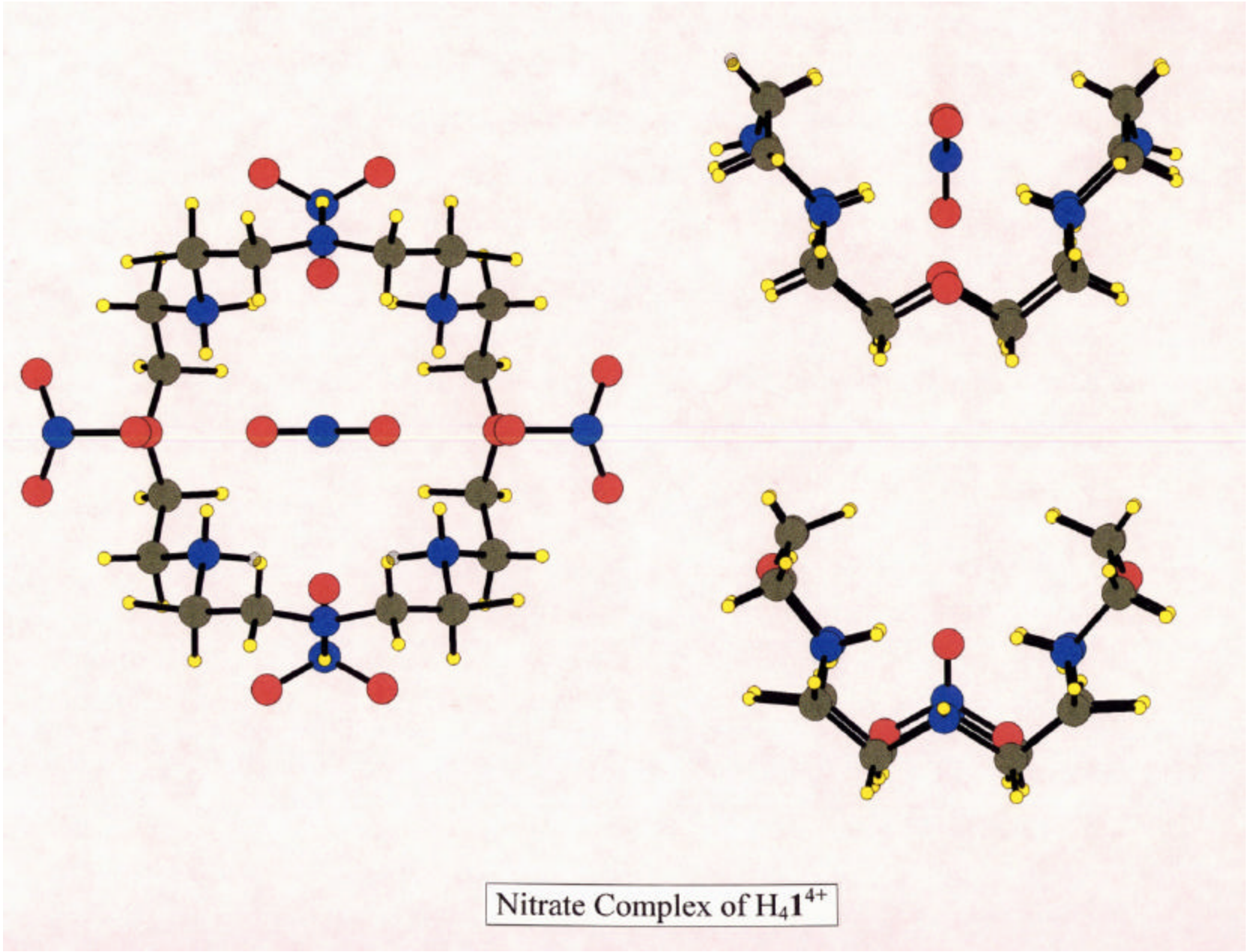
Overall Yield ~40-50%



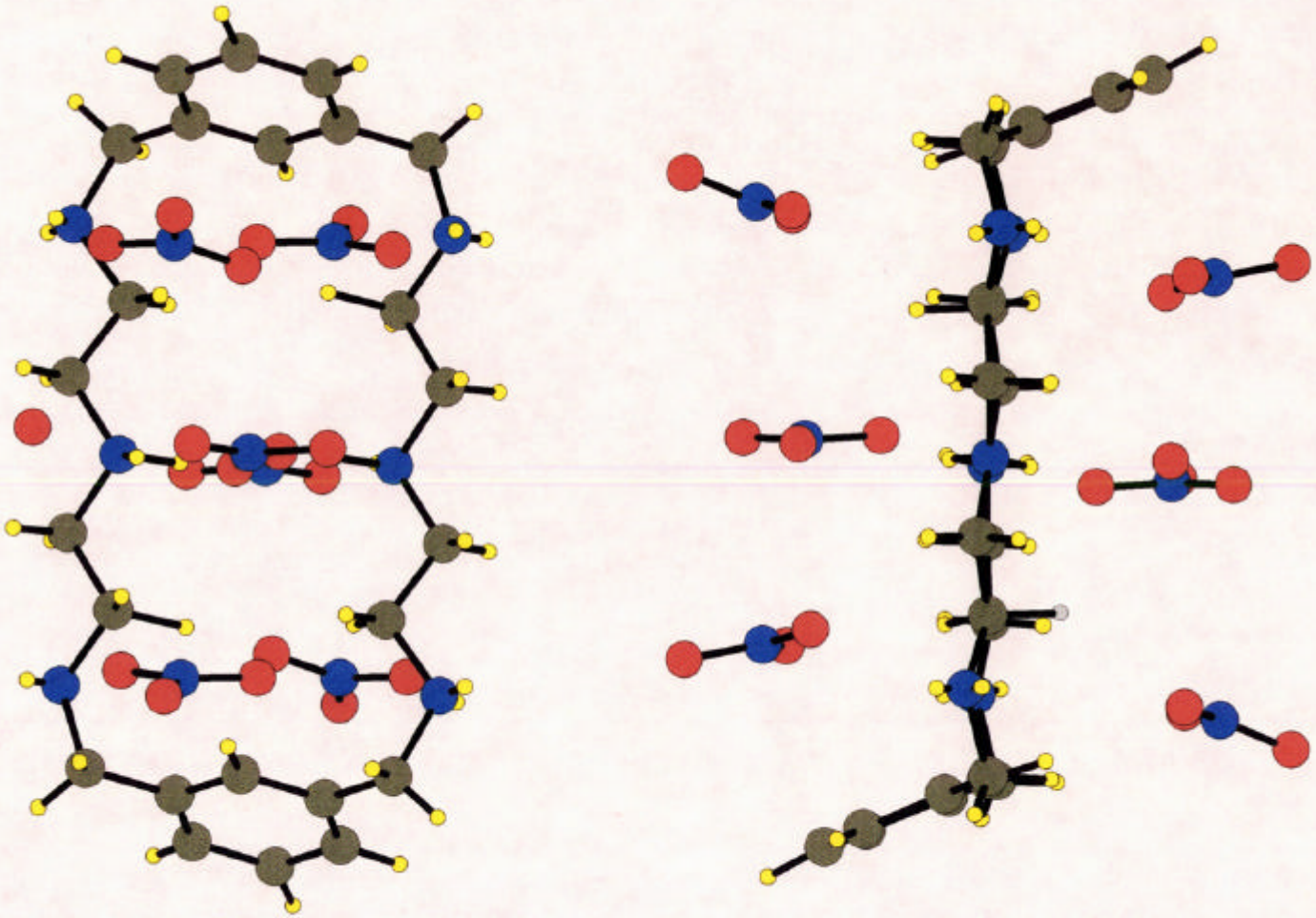
Crystal Structures I
Monocycles

Crystal structures have been obtained for seven macromonocycles with nitrate. Overall findings for monocycles indicate that it is rare that the anion is incorporated "into" the cavity (structures which we call "inclusion"). In fact, only in the nitrate complex of **1** was nitrate directly within the macrocycle. Rather, in other structures the ions hover above and below the macrocyclic plane. This particular finding, in conjunction with molecular dynamics simulations, led us to investigate bicyclic systems, which are constrained to maintain the same approximate shape in both solid and solution states.

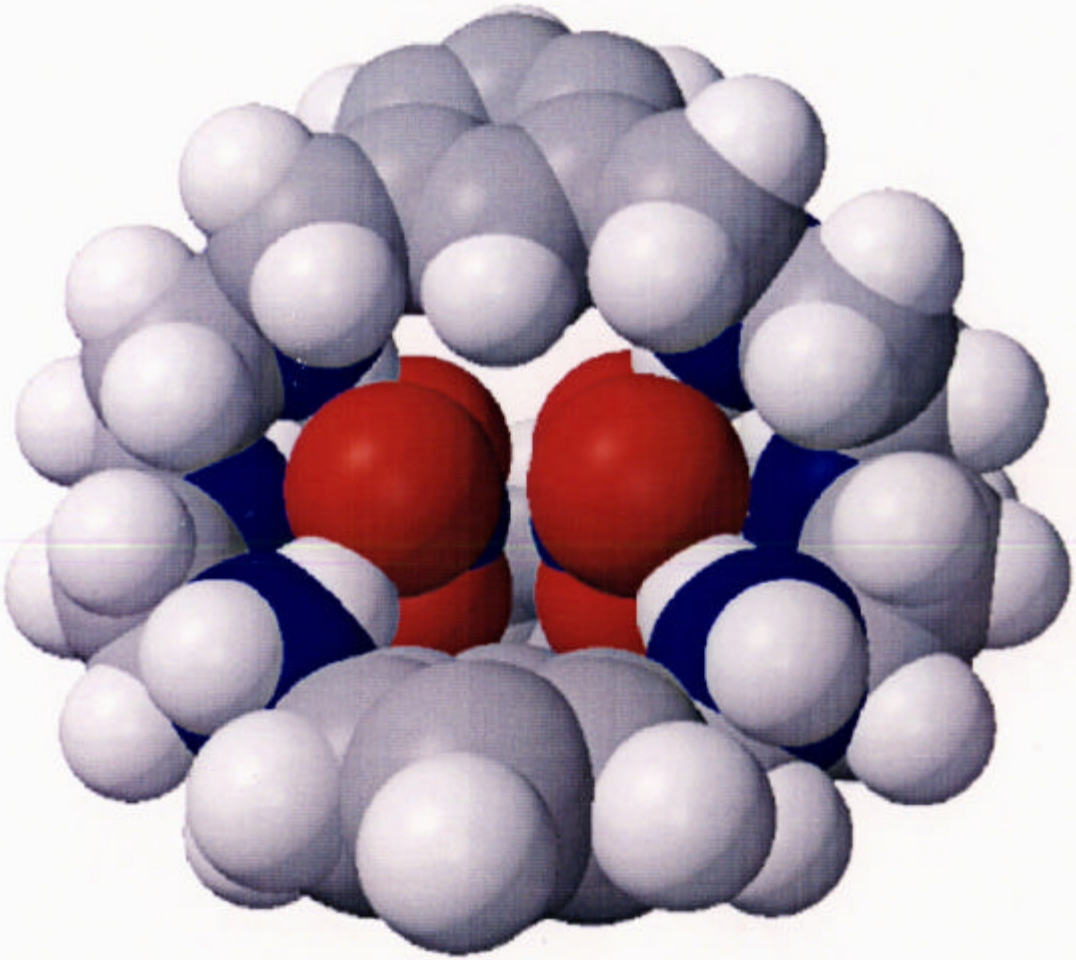
The next slide shows two representative structures: (1) the nitrate structure of **1** revealing the four-fold hydrogen bonding network holding the nitrate in the macrocyclic cavity and (2) the nitrate structure of **2**, in which the nitrates are held proximal to the macrocycle via hydrogen bonding interactions with the macrocyclic amines.



Nitrate Complex of $H_4\mathbf{1}^{4+}$



Nitrate Complex of $H_6\mathbf{2}^{6+}$

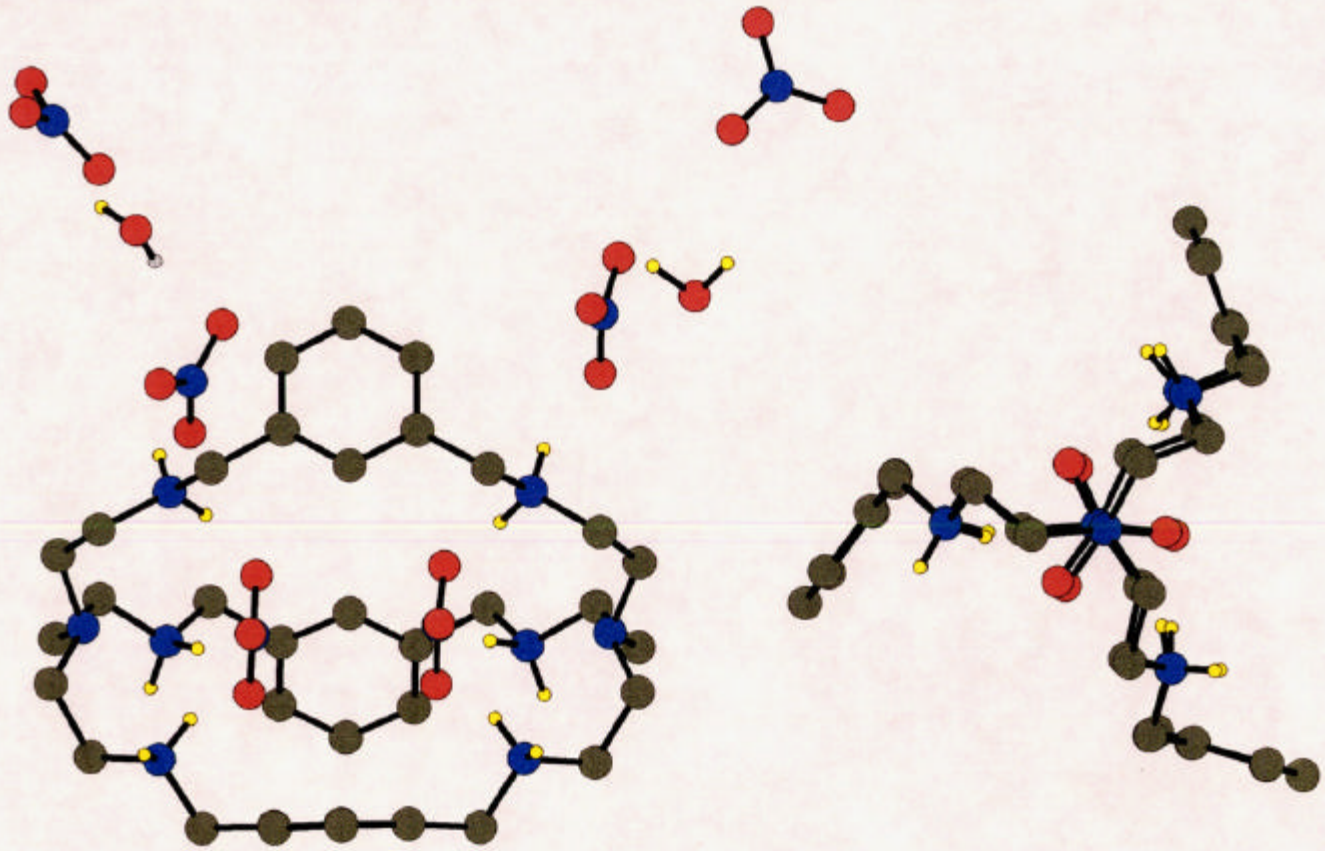


Inclusion Complex Containing Two Nitrate Ions

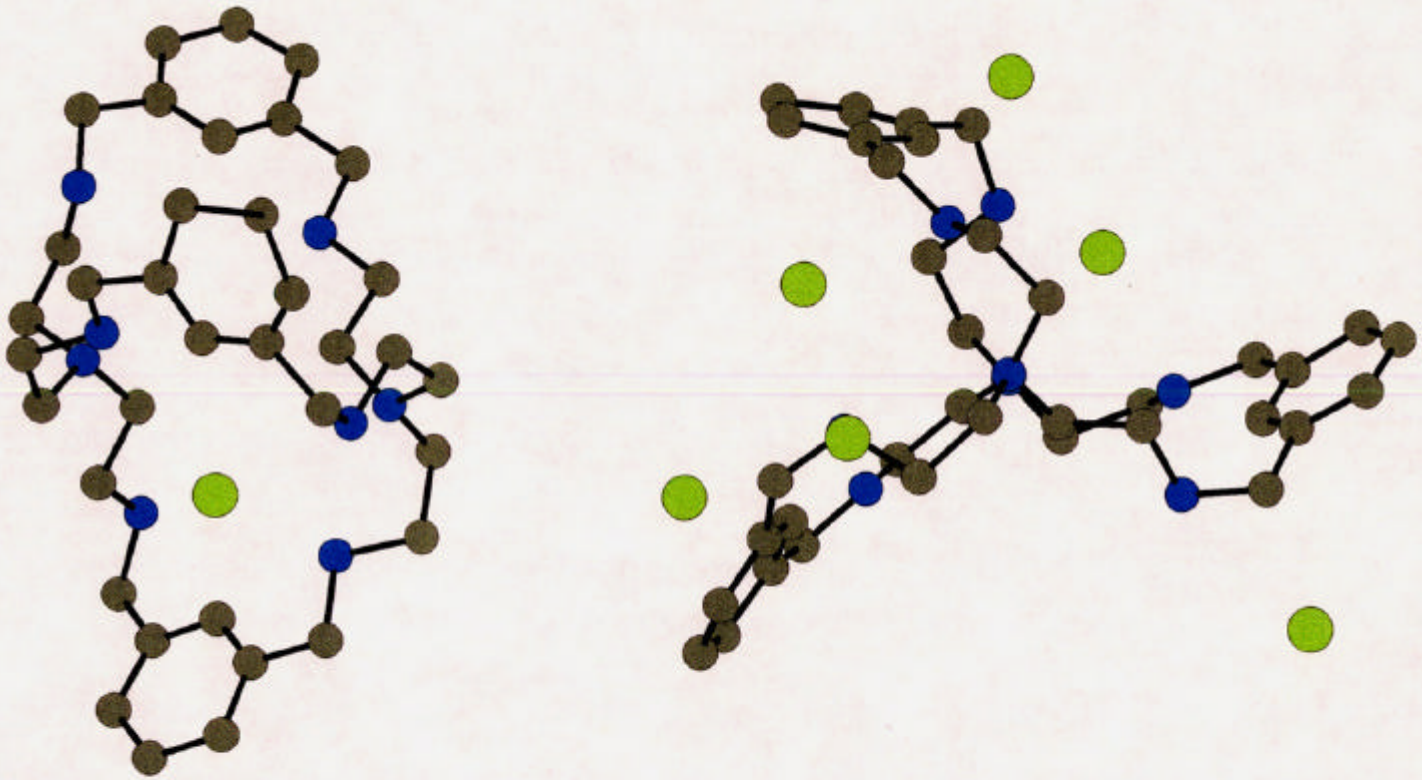
Crystal Structures II
Bicycles

The structural findings for bicycles have been very exciting. To date we have three crystal structures of **3**: the nitrate, chloride, and fluoride salts. While in the chloride structure the chlorides are outside of the macrocyclic cavity, to our amazement, the structure of the nitrate complex with **3** showed not just one, but two nitrates encapsulated in the macrocyclic cage.

In the nitrate structure, both of the nitrate nitrogen atoms exhibit rather short interactions with the apical nitrogens of the macrocycle (N---NO_3 = 3.067(4) Å and 3.090(4) Å), and are separated from eachother by 3.339(4) Å. Strong hydrogen bonding contacts between the trigonally- oriented macrocycle amines and the internal nitrate oxygen atoms are clearly responsible for stabilizing thestructure.



Nitrate Complex of $H_6\mathbf{3}^{6+}$

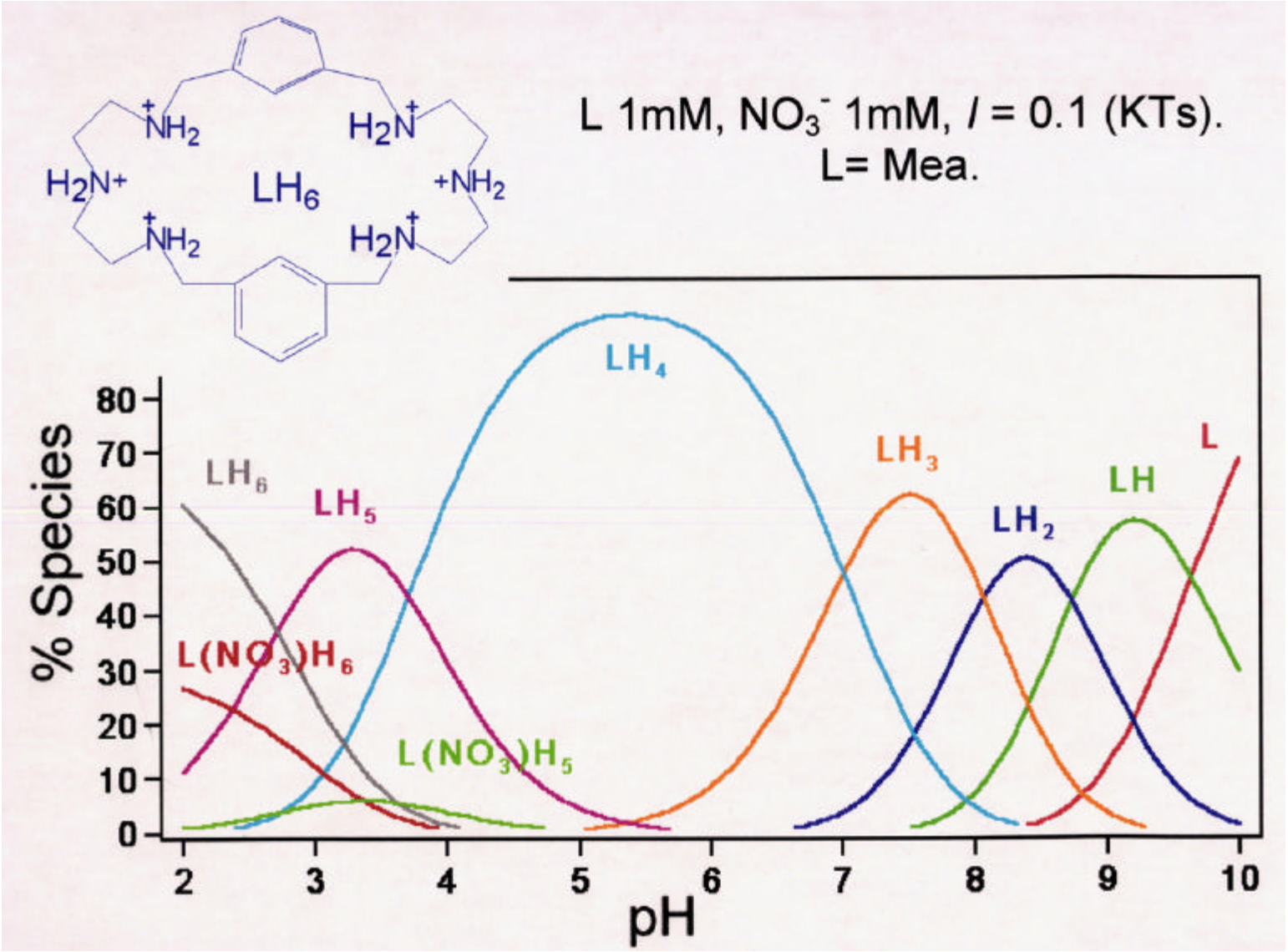


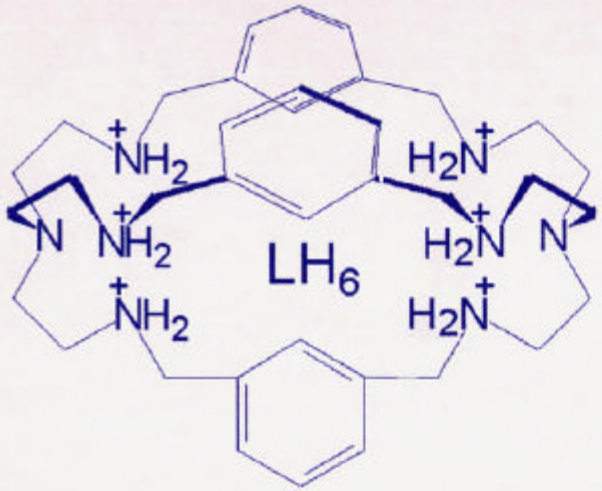
Chloride Complex of $H_6\mathbf{3}^{6+}$

Potentiometric Studies

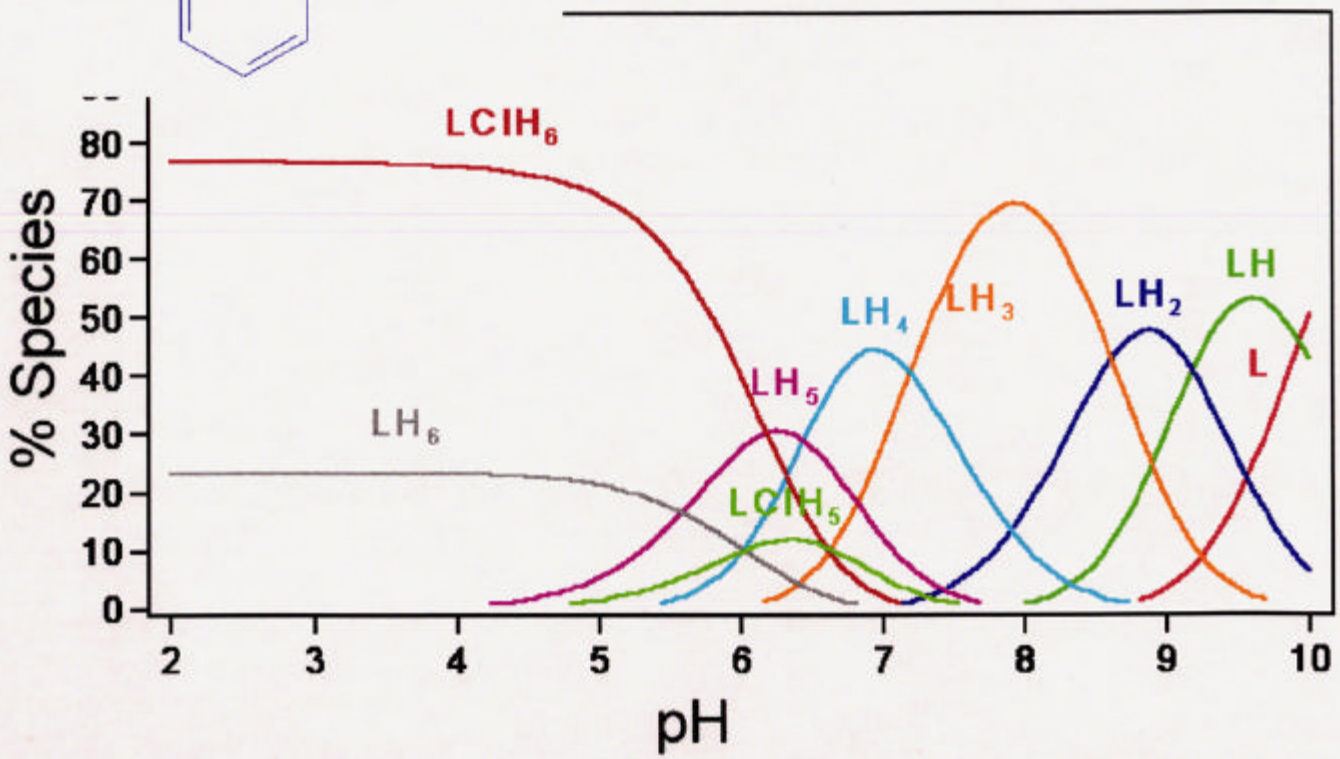
pH titrations were made in the absence and presence of anions. The titration curves are shown for the monocycle **2** and bicycle **3**. To summarize, the monocycle binds nitrate in the hexaprotonated form and to a lesser extent in the pentaprotonated form. The bicycle binds chloride in the hexa-, penta-, and tetraprotonated forms, but only shows binding of one chloride ion. The bicycle binds nitrate only when in the fully protonated form, but binding of two nitrates is distinctly observed as in the crystal structure.

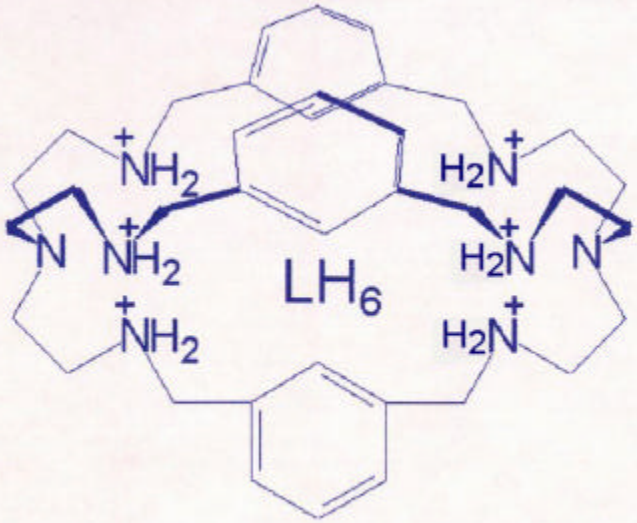
Equilibrium	Monocycle **2**	Bicycle **3**	
	log K (A = NO_3^-)	log K (A = Cl^-)	log K (A = NO_3^-)
$LH_6 + A = LH_6A$	2.31(4)	3.43(3)	3.02(3)
$LH_6A + A = LH_6A_2$	--------	--------	2.38(8)
$LH_5 + A = LH_5A$	1.66(6)	2.40(7)	--------
$LH_4 + A = LH_4A$	--------	1.9(1)	--------


L 1mM, NO3- 1mM, I = 0.1 (KTs).
L= Mea.
LH6
% Species
pH
LH6
LH5
LH4
LH3
LH2
LH
L
L(NO3)H6
L(NO3)H5
0
10
20
30
40
50
60
70
80
2
3
4
5
6
7
8
9
10

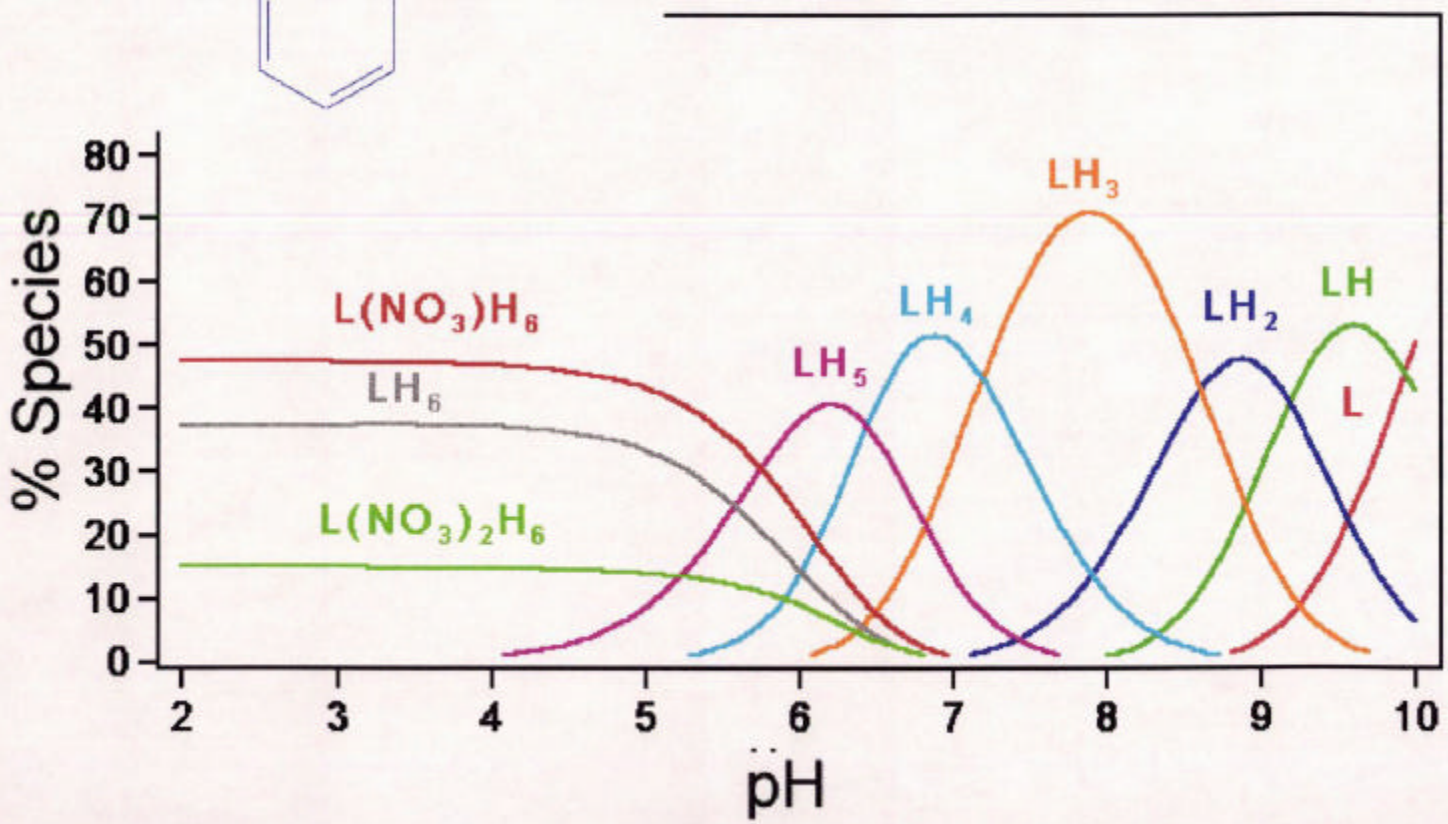


L 1mM, Cl^- 2mM, I = 0.1 (KTs).
L= Meacrp.





L 1mM, NO_3^- 2mM, I = 0.1 (KTs).
L= Meacrp.



Information Access

- *Supramolecular Chemistry of Anions***,** Bianchi, A.; Bowman-James, K.; García-España, E.; Wiley-VCH: New York; 1997461 pp. (ISBN 0-471-19622-8).
- Papoyan, G.; Gu, K.; Wiorkiewicz-Kuczera, J.; Kuczera, K.; Bowman-James, K., Molecular Dynamics Simulations of Nitrate Complexes with Polyammonium Macrocycles: Insight on Phosphoryl Transfer Catalysis Crystal Structure of a Nitrate Inclusion Complex, *J. Am. Chem. Soc.* **1996**, *118*, 1354-1364.
- Mason, S.; Clifford, T.; Seib, L.; Kuczera, K.; Bowman-James, K., Unusual Encapsulation of Two Nitrates in a Single Bicyclic Cage, *J. Am. Chem. Soc.*, in press.
- Wiórkiewicz-Kuczera, J.; Kuczera, K.; Bazzicalupi, C.; Bencini, A.; Valtancoli, B.; Bianchi, A; Bowman-James, K., Solution and Solid State: Molecular Dynamics Simulations and Crystal Structure of the Nitrate Salt of an Octaazamacrocycle, submitted for publication.

- The structure of the nitrate inclusion complex of **3** may be viewed at: http://129.237.102.17/~kuczera/kristin/animate.html.

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Conclusions

- We have succeeded in identifying a more facile and higher yield route to macromonocycles and macrobicycles using Schiff base condensations.

- Crystallographic findings indicate that for monocycles, “incorporation” of anions into the ring is not common.

- Crystallographic findings for bicycles indicate that anions can be more readily incorporated into the ring. An especially relevant finding is the incorporation of two nitrates in the ring of **2**. This is to our knowledge the first example of two discrete anions incorporated into a single cavity.

- Potentiometric studies indicate significant binding constants for both one and two nitrates in **2** when it is in the hexaprotonated form. The monocycle **1** binds nitrate to a lesser extent, however, it show some binding in both the hexa- and penta-protonated forms.