

# Environmental Management Science Program

**Project ID Number 54864**

## **Supramolecular Chemistry of Selective Anion Recognition for Anions of Environmental Relevance**

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## Supramolecular Chemistry of Selective Anion Recognition for Anions of Environmental Relevance

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### Research Objective

This project has as its focus the design and synthesis of polyammonium macrocyclic receptors for oxoanions of environmental importance. The basic research aspects of this project involve: (1) synthesis (and the search for improved synthetic methods); (2) solid state structure determination and thermodynamics studies (to ascertain structural criteria for and strength of anion binding); and (3) molecular dynamics simulations (to assess solution characteristics of the interactions between anions and their receptors). Applications-oriented goals include the fabrication of more selective anion-selective electrodes and the use of these compounds in liquid-liquid separations. The latter goal comprises the subcontract with Dr. Bruce Moyer at Oak Ridge National Laboratory.

### Research Progress and Implications

This report summarizes work after 1 year and 7 months of a 3-year project. To date, we have focussed on the design and synthesis of selective receptors for nitrate and phosphate.

**Synthesis.** The synthesis of polyaza macrocycles, which are the focus of these studies, is in many cases tedious and time-consuming. For example, the synthesis of **1** can take as long as one month because of purifications required during the synthetic route. A major breakthrough in year one of the project was to identify other polyaza macrocycles which bind the desired anions, but which are simpler to synthesize via two step Schiff base/reduction processes with high yields. This is truly significant since now we can obtain large quantities of the macrocycles and can do a variety of studies at the same time. During year one most of our studies focused on monocyclic systems containing two diethylenetriamine units separated by spacers, **2** - **6**. In year two (as a result of findings from molecular dynamics simulations), we began to examine bicyclic macrocycles, **7** - **11**, which can be synthesized by the same method starting with the tetraamine known as *tren*.

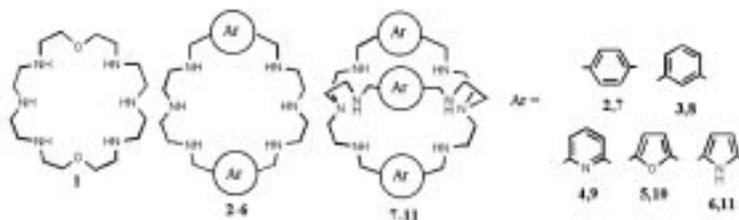


Figure 1

This year we have also have begun the exploration of the synthesis of receptors which have “switching” capabilities, including redox switches (disulfide [oxidized form] and sulfhydryl [reduced form]) and photochemical switches (azobenzenes). This work is currently in progress.

**Structural studies.** (1) *Anions.* We now have eleven crystal structures of nitrate complexes with polyaza macrocycles, seven with monocycles and four with bicycles. We have one monocycle structure with phosphoric acid/dihydrogen phosphate. The latter is unique in that phosphoric acid is actually part of the structure.

The very recent (March 1998) isolation and structural characterization of a bicycle, **8**, with threefold symmetry containing two encapsulated nitrate ions is our most significant finding, which impacts the existing base of knowledge concerning anion receptors. Two nitrates were found to crystallize inside the macrocyclic cavity in an eclipsed conformation, separated by only 3.33 Å. In addition to being the first instance of nitrate bound within a receptor cavity, this is the first example of a receptor incorporating two discrete anions within a single cavity. This finding is truly significant since all anion binding studies to date assume that a only one discrete anion will be bound within a cavity. We now have strong evidence, including NMR, potentiometric titration, and x-ray crystallographic, that this is not necessarily the case. This exciting result indicates that these C<sub>3</sub> bicycles hold considerable promise as receptors for trigonal anions, and furthermore that we are not limited to just one anion for incorporation into the cavity. We also have evidence that the furan analog (**10**) incorporates nitrate within the cavity, but the structure appears to be disordered and we are still working on it.

(2) *Schiff base macrocycles.* We have completed structures of some of the anion free macromonocycles formed by the initial condensation of dien with dialdehydes. These interesting structures shed light on mechanistic considerations involved in the Schiff base condensations.

(3) *Switches.* We have obtained a crystal structure of a prototype disulfide switch macrocycle.

**Molecular dynamics (MD) studies.** Simulations on several complexes using the program CHARMM indicate that hydration effects tend to govern the structure of the receptor in solution so that it becomes relatively planar even if the solid state structure indicates a folded conformation. Also all of the dihedral angles NCCN tend to adopt the *trans* configuration (*ca.* 180° C), which tends to minimize the repulsive electrostatic interactions between the positively charged amino groups. MD studies have also indicated that in solution water plays an important role in forming relay networks to the macrocycle from surrounding nitrates. The results of the theoretical computations pointing to a preference for planarity in monocycles led us to explore bicyclic compounds, which would presumably be forced to maintain a relatively spherical shape in solution. As noted above, this led to the isolation and structural characterization of the encapsulated dinitrate complex.

**Potentiometric studies.** Protonation constants are being determined for each of the macrocycles, and binding constants are being determined for selected anionic substrates. An important experimental finding was that the use of the hexahydrochloride salt in these studies was not recommended, as complex formation tends to influence the pK<sub>s</sub> as well as subsequent binding constants for nitrate. Hence, the *p*-toluenesulfonate macrocyclic salts were obtained assuming that the large counterion would be more "benign", and data were considerably improved and are very reproducible. The results of the potentiometric studies indicate that for monocycles, association constants are disappointingly low (*ca.* 10<sup>-10</sup>-10<sup>-100</sup>), undoubtedly due to the interfering or competing influence of hydration as noted in the MD studies. However, affinities of the bicyclic receptors for nitrate are considerably larger (*ca.* 10<sup>-3-5</sup>). We have just completed the binding studies with the bicycle **8**, and the potentiometric curves show the formation of both the mono-nitrate and di-nitrate complexes ( $\log [LH(NO_3)]/[LH][NO_3] = 2.94(8)$  and  $\log [LH(NO_3)_2]/[LH][NO_3]^2 = 5.70(8)$ ) at pHs up to 6. (Our studies with monocycles indicate that these receptors only form complexes with nitrate at pHs less than 4.)

**Electrode studies.** A comprehensive study on optimizing the conditions for the electrode films has just been completed. These studies are considerably more difficult than for analogous cation selective electrodes because of tricky solubility problems. Findings indicate that 1,2-dimethyl-3-nitrobenzene and 2-fluorophenyl-2-nitrophenyl ether are improved plasticizers over 1-decanol. Preliminary studies using the bicyclic macrocycles as ionophores have just commenced and initial findings indicate promising selectivities for nitrate, but not yet at the level of the commercially available electrodes.

## Planned Activities

**Oak Ridge. Separations studies.** (Subcontract with Bruce Moyer at Oak Ridge National Laboratory) Studies at Oak Ridge will begin this summer now that several promising receptors have been identified. One of my postdoctoral associates will go to Oak Ridge for these studies. Since these studies were delayed the first year, there will be considerable interaction with the Oak Ridge group in probing the utility of these complexes in separations technology in the coming year.

**University of Kansas.** We will continue to investigate multiple binding and incorporation of anions within bicycle cavities. As part of this study we will also probe the chemistry, i.e., because of the short N—N separation for the two nitrates, they may be activated chemically. New amide based receptors, designed along the same lines as the bicyclic polyamines, are being synthesized and will be tested in the separations studies this summer. It is desirable to obtain receptors which are active at higher pHs (for radioactive waste remediation), and amides may meet this goal. Continuing efforts in the design and synthesis of switches are ongoing and will be accelerated when a new postdoctoral associate arrives next month. In the next and last year of the project, we will explore receptor design for the other oxoanions that were targeted in the proposal as well as for photo- and redox-activated switches. We will continue in applications oriented studies including separations and ion selective electrodes.

## Other Access To Information

### Book

*Supramolecular Chemistry of Anions*, Bianchi, A.; Bowman-James, K.; García-España, E. Wiley-VCH: New York; 1997, 461 pp. (ISBN 0-471-19622-8). This is the first comprehensive text reviewing the current state-of-the-art in anion chemistry.

### Publications

Papoyan, G.; Gu, K.; Wiorcikiewicz-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, under revision as a communication in *J. Am. Chem. Soc.*

Wiorkiewicz-Kuczera, J.; Kuczera, K.; Bazzicalupi, C.; Bencine, 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, to be submitted to *J. Am. Chem. Soc.*

### Web site

The structure of the bicycle with two nitrates may be viewed at the following web site: <http://129.237.102.17/~kuczera/kristin/animate.html>.