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Unusual Encapsulation of Two Nitrates in a Single Bicyclic Cage

Susan Mason, Thomas Clifford, Larry Seib,
Krzysztof Kuczera, and Kristin Bowman-James*

Department of Chemistry, University of Kansas
Lawrence, Kansas 66045

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An unusual anion complex consisting of a bicyclic polyammonium receptor with C_3 symmetry and two encapsulated nitrate ions has been isolated and structurally characterized. Anion coordination chemistry is a rapidly emerging field, spurred on by a timely interest in anions from environmental, industrial, and health-related perspectives.[1] While seemingly straightforward, the design of systems for selective recognition is not necessarily so simple. As a general rule, selectivities for simple anions usually follow the Hofmeister series, which is a recognition pattern based on decreasing hydrophobicities: $ClO_4 > SCN^- \approx I^- > NO_3^- \approx Br^- > Cl^- > HCO_3^-$. Because of our interest in designing selective receptors for various oxygen-containing anions of environmental relevance, we have undertaken an examination of systems capable of forming complexes with nitrate.[2] Not only has nitrate been implicated in groundwater contamination as a contributing factor in high incidences of lymphomas,[3] but it is also found in enormous quantities in radioactive tank wastes as at the Hanford site.[4]

Our initial studies indicated that, while simple polyammonium macromonocycles can fold about a nitrate ion in the solid state,[2] most of the crystallographic results for these receptors show nitrates hovering above and below relatively planar macrocycles.[2,5] Simple modeling studies in our laboratory indicated that *bicylic* polyammonium macrocycles with C_3 symmetry might be more effective in binding the trigonal planar nitrate ion. This hypothesis was supported by earlier work of Martell and Lehn in a study on bis(tren) chelates[6] and more recently by the elegant C_3 symmetrical amide receptor reported by Anslyn and co-workers.[7]

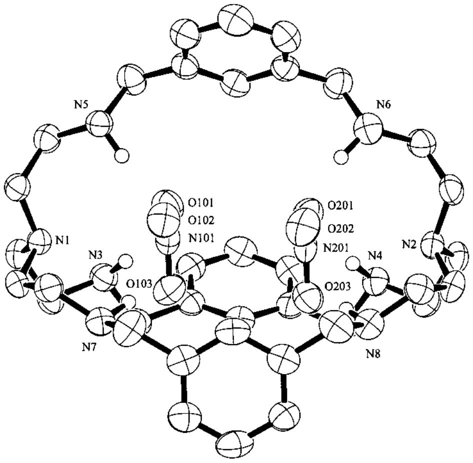

Figure 1. ORTEP view of H_6**1** and the two internal nitrates.

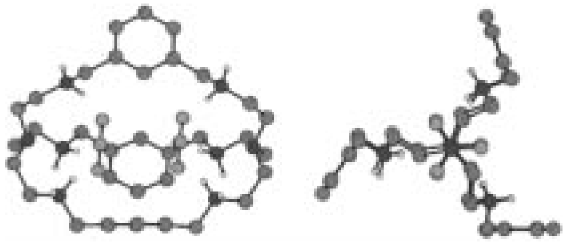

Figure 2. Side-on and end-on perspective views obtained by 90° rotations of the $H_6 \cdot$**1**$\cdot(NO_3)_2$ portion of the nitrate complex with **1**.

In an examination of a series of bicyclic macrocycles obtained from simple Schiff base condensations between tren (2,2′,2″-triaminotriethylamine) and dicarboxaldehydes, we isolated crystals of the nitrate complex of the bicyclic macrocycle, **1**, with bridging *m*-phthalaldehyde spacers. Surprisingly, crystallographic results indicated a unique encapsulation of two nitrate ions within the bicyclic cavity. To our knowledge, this is the first example of two discrete anions bound in such a fashion.[8]

The macrocycle was synthesized according to published procedures[9] with slight modifications, and the nitrate complex was obtained by an anion exchange reaction of $AgNO_3$ with the hydrochloride salt.[10] X-ray analysis of the crystalline product showed the complex to be the hexahydronitrate salt of the macrocycle with two molecules of water.[11] While four of the nitrates were associated via predominantly electrostatic and hydrogen bonding interactions outside of the macrocyclic cavity, two nitrates were snugly nestled inside the cavity in an eclipsed conformation (Figures 1−3). From Figure 2 and the space-filling model, Figure 3, showing just the macrocycle and nitrates, it can be seen that the C_3 symmetry of the bicycle presents an ideal environment for hydrogen bonding interactions with the incorporated anions.

Although there is no crystallographically imposed symmetry, the environment about each of the internal nitrates is almost identical. Both of the nitrate nitrogen atoms exhibit rather short

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[1] For selected reviews see: (a) In *Supramolecular Chemistry of Anions*; Bianchi, A., Bowman-James, K., García-España, E., Eds.; Wiley-VCH: New York; 1997, p 461. (b) Mertes, M. P.; Mertes, K. B. *Acc. Chem. Res.* **1990**, *23*, 413−418. (c) Beer, P. D.; Wheeler, J. W.; Moore, C. In *Supramolecular Chemistry*; Balzani, V.; De Cola, L., Eds.; Kluwer Academic Publishers: Netherlands; 1992; pp 105−118. (d) Katz, H. E. In *Inclusion Compounds*; Atwood, J. L., Davies, J. E. D., MacNichol, D. D., Eds.; Oxford University Press: Oxford; 1991; pp 391−405. (e) Dietrich, B.; Guilhem, J.; Lehn, J.-M.; Pascard, C.; Sonveaux, E. *Helv. Chem. Acta* **1984**, *67*, 91−104. (f) Dietrich, B. *Pure Appl. Chem.* **1993**, *65*, 1457−1464. (g) Izatt, R. M.; Pawlak, K.; Bradshaw, J. S.; Bruening, R. L. *Chem. Rev.* **1991**, *91*, 1721−2085. (h) Vögtle, F.; Sieger, H.; Müller, W. M. *Top. Curr. Chem.* **1981**, *98*, 107−161. (i) Kimura, E. *Top. Curr. Chem.* **1985**, *128*, 113−114. (j) Sessler, J. L.; Cyr, M.; Furuta, H.; Král, V.; Mody, T.; Morishma, T.; Shionoya, M.; Weghorn, S. *Pure Appl. Chem.*, **1993**, *65*, 393−398.

[2] Papoyan, G.; Gu, K.; Wiórkiewicz-Kuczera, J.; Kuczera, K.; Bowman-James, K. *J. Am. Chem. Soc.* **1996**, *118*, 1354−1364.

[3] *Sci. Am.* **1996**, *275*, 24.

[4] "Facts About Hanford," First Hanford Separation Science Workshop, July 23−25, 1991.

[5] (a) Cullinane, J.; Gelb, R. I.; Margulis, T. N.; Zompa, L. J. *J. Am. Chem. Soc.* **1982**, *104*, 3048−3053. (b) O. Gerasimchuk, Ph.D. Thesis, University of Kansas, 1997. (c) A pyridinium-containing macrocycle was reported which folds around two nitrates, one above and one below the macrocycle in a pincerlike conformation (Cramer, R. E.; Fermin, V.; Kuwabara, E.; Kirkup, R.; Selman, M., Akoi, K.; Adeyemo, A.; Yamazaki, H. *J. Am. Chem. Soc.* **1991**, *113*, 7033−7034). (d) Wiórkiewicz-Kuczera, J.; Kuczera, K.; Bazzicalupi, C.; Bencini, A.; Valtancoli, B.; Bianchi, A.; Bowman-James, K., submitted for publication.

[6] Motekaitis, R. J.; Martell, A. E.; Lehn, J.-M.; Watanabe, E.-I. *Inorg. Chem.* **1982**, *21*, 4253−4257.

[7] Bisson, A. P.; Lynch, V. M.; Monahan, M.-K. C.; Anslyn, E. V. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2340−2342.

[8] A related report on the crystallographic structural findings for bicycles derived from the reduction products of Schiff base condensations with furan and pyridine dialdehydes has been published, in which a single ClO_4^- in the former instance, and a single SiF_6^- in the latter case, are bound within the cavity (Morgan, G.; McKee, V.; Nelson, J. *J. Chem. Soc., Chem. Commun.* **1995**, 1649−1652).

[9] Chen, D.; Martell, A. E. *Tetrahedron* **1991**, *47*, 6900−6901.

[10] For the specific conditions of the anion-exchange reaction, see the Supporting Information. Crystals suitable for X-ray diffraction were grown by ether diffusion into a water/ethanol solution of the complex.

[11] Crystal structure data: $C_{36}H_{60}N_{14}O_{20}$, $M_w = 1012.99$, triclinic $P\bar{1}$ (No. 2) with $a = 10.396(2)$ Å, $b = 25.633(2)$ Å, $c = 10.240(1)$ Å, $\alpha = 95.045(9)^o$, $\beta = 117.766(9)^o$, $\gamma = 80.464(9)^o$, $V = 2381.1(6)$ Å^3, $d_{calc} = 1.41$ g cm^{-3}, $Z = 2$, R ($I > 3.00\sigma(I)$) = 0.056, $R_w = 0.072$, and GOF = 2.35.

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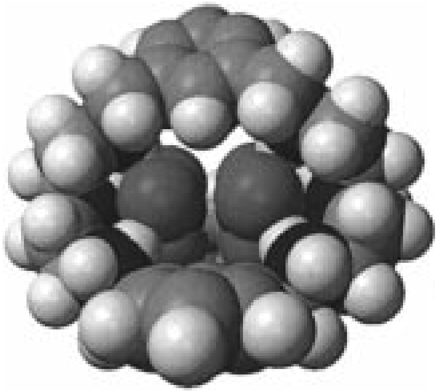

Figure 3. CPK model of $H_6 \cdot \mathbf{1} \cdot (NO_3)_2$ showing hydrogen bonding interactions between the ammonium ions and the internally coordinated nitrates.

Table 1. Selected Interatomic Distances for the Internally Bound Nitrates (Å)

atoms	distances	atoms	distances
Interatomic Contacts			
N(1)−N(101)	3.090(4)	N(2)−N(201)	3.067(4)
N(101)−N(201)	3.339(4)	O(101)−O(201)	3.396(4)
O(102)−O(202)	3.384(4)	O(103)−O(203)	3.356(4)
Hydrogen Bonding Interactions			
O(101)−N(3)	2.904(4)	O(101)−N(5)	2.955(4)
O(102)−N(5)	2.901(4)	O(102)−N(7)	3.020(4)
O(103)−N(7)	2.870(4)	O(103)−N(3)	3.031(4)
O(201)−N(4)	2.851(4)	O(201)−N(6)	2.975(4)
O(202)−N(6)	2.925(5)	O(202)−N(8)	3.035(4)
O(203)−N(8)	2.877(4)	O(203)−N(4)	3.000(4)

interactions with the apical nitrogens of the macrocycle (N···N = 3.067(4) Å and 3.090(4) Å), and are separated from each other by 3.339(4) Å (Table 1). Clearly of major importance to the stabilization of the structure, however, are the hydrogen bonding contacts between the trigonally oriented macrocycle amines and the internal nitrate oxygen atoms. These interactions may also be responsible for the "tugging" of each of the oxygen atoms away from its "twin" counterpart giving O···O distances ranging from 3.356(4) Å to 3.396(4) Å, compared to the somewhat shorter N(101)···N(201) distance (Figure 3, Table 1). Each of these oxygens exhibits an asymmetric bifurcated hydrogen bond between two of the protonated macrocyclic amines, which ties them firmly in place inside the cavity (Table 1). Four additional nitrates and two water molecules lie outside the macrocyclic cavity and will be discussed more fully elsewhere.

To assess the energetics of the unanticipated binding of two nitrates within the same macrocycle in eclipsed conformations, interactions were modeled using the CHARMM molecular simulation package.[12] In our initial approximate model only the macrocycle and two internal nitrates were considered in a vacuum. An unconstrained energy minimization starting from the crystallographic coordinates converged to an almost superimposable structure with an rms deviation from the crystal structure of 0.23 Å for non-hydrogen atoms.

Within the CHARMM optimized structure, the macrocycle−nitrate interactions were found to be −364 kcal mol^{-1} for each of the NO_3- ions, while the nitrate−nitrate repulsion was only 60 kcal mol^{-1}. Thus assuming no changes in the geometries of the components upon binding ("rigid geometry" model), estimates of the binding energy $E_{b1} = -364$ kcal mol^{-1} for the first nitrate, $E_{b2} = -304$ kcal mol^{-1} for the second nitrate, and total binding $E_{b1+b2} = -668$ kcal mol^{-1} are obtained. Interestingly, the repulsion between two like monovalent atomic ions at a distance of 3.3 Å in a vacuum may be estimated at about 100 kcal mol^{-1} using Coulomb's Law. The fact that the nitrate−nitrate repulsion at this same distance in the macrocycle is calculated to be significantly less is due to the redistribution of the overall charge over four atoms in the model. In view of the simplified model and rigid geometry assumption, our energetic results are only qualitative. However, they do indicate that the macrocycle−nitrate attraction in this system is much stronger than the nitrate−nitrate repulsion, allowing the two anions to reside in proximity within the macrocycle.

That the binding of two nitrate ions within the cavity is indeed favorable is supported by potentiometric studies, in which the hexahydrotosylate salt of the macrocycle was titrated in the presence and absence of KNO_3. The protonation constants determined[13] were in agreement with those determined earlier by Martell and co-workers under slightly different conditions.[14] Of particular interest, however, was the finding that the binding of both of the nitrates was observed for the hexaprotonated macrocyclic species. Binding for the mononitrate complex ($\log([LH_6(NO_3)]/[LH_6][NO_3])$) was found to be $\log K_1 = 3.02 \pm 0.03$, and binding of the second nitrate ($\log([LH_6(NO_3)_2]/[LH_6(NO_3)][NO_3])$) was determined to be $\log K_2 = 2.38 \pm 0.08$. The equilibrium model is further supported by NMR titrations, which will be reported elsewhere.

In conclusion, this is a very unusual finding, a receptor capable of binding two discrete anionic guests within a single cavity. The almost ideal D_{3h} geometry and the trigonal positioning of the protonated amines serves to "tie-back" the nitrate oxygen atoms via hydrogen bonding, which allows for a substantial reduction in anion−anion repulsion. Further investigations are ongoing on this and related systems in order to obtain better and more selective receptors for a variety of anionic guests.

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Supporting Information Available: Experimental and crystallographic details and tables (37 pages, print/PDF). See any current masthead page for ordering instructions and Web access information.

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[12] Brooks, J. P.; Bruccoleri, R.; Olafson, B.; States, D.; Swaminathan, S.; Karplus, M. *J. Comput. Chem.* **1983**, *4*, 187−217. Parameters, atomic charges, and topology were previously developed for this class of systems and are described in more detail in the Supporting Information.[2]

[13] Titrations were determined potentiometrically using a glass electrode and SCC standard electrode, with $pK_w = -13.79$, $I = 0.1(KTs)$, $T = 25.00 \pm 0.05$ °C. Titrations were done using NaOH, and data were processed in HYPERQUAD. Specifics details are provided in the Supporting Information.

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