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Bistripodand Amide Host for Compartmental Recognition of Multiple Oxyanions

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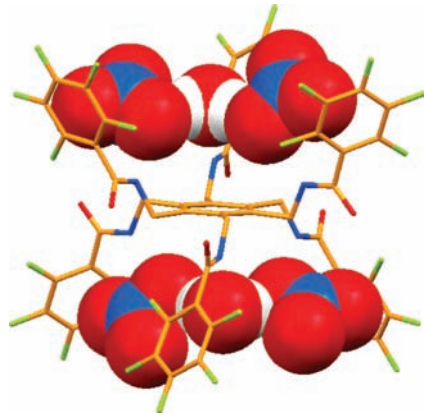
ABSTRACT



A new benzene-based hexasubstituted bistripodal receptor is synthesized and explored as a new generation receptor for multiple anion binding. The solid state crystal structure showed the encapsulation of four nitrate anions in a bistripodand fashion with "*ababab*" conformation of the receptor, and upon complexation with acetate anions, the receptor adopted less favorable "*aaabbb*" conformation with two encapsulated acetate ions.

In recent years, considerable efforts have been made in elucidating the coordination chemistry of anions.[1] Oxyanions like nitrate, acetate, and phosphate recognition are very important because of their vital roles in biological systems, medicine, catalysis, and environmental issues.[1] For example, the carboxylate anions exhibit specific biochemical behaviors in enzymes and antibodies and are also critical components of numerous metabolic processes. So the recognition of the acetate ion is considered to be important among other biologically functional anions.[2] On the other hand, the nitrate anion is implicated in groundwater contamination and present in high concentration in certain wastewaters such as nuclear waste streams, and therefore it raises environmental problems.[3] To date, however, reports on receptors for nitrate are

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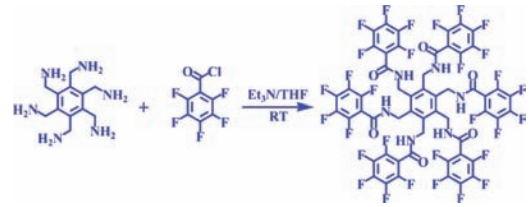
small in number which includes polyammonium macrocycles/macrobicycles,[4] metal organic frameworks,[5] and ion-pair[6] receptors. Very few reports on nitrate binding in a neutral receptor have been demonstrated in the literature.[7,8a] These studies have shown mostly single-anion and in rare cases two-anion binding,[4d,f] and to increase the guest to host ratio, the receptor should recognize multiple anions rather than a single anion. In this context, the designing of the receptor should possess multiple anion binding sites/compartments, larger cleft/cavity in the receptor, and hence higher numbers of guests could be accommodated in a single host. Herein, we show compartmental recognition of two or more anions in a neutral receptor **L** in both solution and solid states. We also structurally demonstrate the compartmental encapsulation of four nitrate anions in **L** (**L**:NO_3 = 1:4), where each compartment holds two nitrate anions in a cascade fashion bridged by a water molecule. Further, a solid state study shows the isolation of unfavorable conformation of **L** in its acetate complex. To the best of our knowledge, this study reports the first example of encapsulation of four nitrate ions in a neutral receptor.

In search of a new higher-generation neutral anion receptor (i.e., receptor with the ability to encapsulate multiple anions), we have chosen substituted benzene[8] as a platform to decorate the amide recognition element for multiple anion binding. The hexasubstituted amide receptor **L** was synthesized in good yield by the simple reaction of hexakis(aminomethyl)benzene[8c] with 6 equiv of pentafluorobenzoyl chloride in the presence of triethylamine in tetrahydrofuran (THF) (Chart 1) and crystallized in dimethyl sulfoxide (DMSO).

Chart 1. Synthesis of **L**



To explore the anion complexation and conformational flexibility of this newly synthesized hexapodal amide, **L** is treated with tetrabutylammonium (TBA) salts of nitrate and acetate. The nitrate complex, **1**, is obtained by adding excess (10 equiv) TBA−NO_3 to the THF solution of **L**, whereas the acetate complex **2** is obtained from acetone solution upon charging TBA−OAc. The single-crystal X-ray structure of complexes **1** and **2** confirms the versatility of **L** as an anion receptor. To avoid the steric disturbances, the arms of **L** may orient in *ababab* or *aaabbb* conformation as shown in Figure 1a and 1b, respectively. As the receptor is more flexible, **L** could adjust its arms to a favorable conformation for the recognition of anions. The solid state structure of complex **1** revealed the unusual encapsulation of four nitrate anions and two water molecules in a single receptor (*ababab* conformation), indicating 1:4 binding of **L** to nitrate (Figure 1c,d) and encapsulation of two acetate anions at two clefts of **L** having *aaabbb* conformation in complex **2** (Figure 2a).

Figure 1c,d shows an *ababab* type of conformation like the case in Figure 1a, upon encapsulating two nitrate anions and a water molecule as guests in each of the clefts. In fact, the benzene center plate acting as a common platform for two equivalent guests bound clefts, making the hexasubstituted host like a "double-decker" anion receptor. Hexapodal molecules generally adopt a conformation in which the arms alternate in positions above and below the plane of the central benzene ring (Figure 1a). On the other hand, very recently polymorphism of the hexapodal molecule, i.e., different alternative conformations, has also been observed crystallographically which also includes the situation like Figure 1b.[9] However, DFT calculations on a benzene platform based hexanonanamide receptor predict that it exists as a bowl, with all six substituents intramolecularly H-bonded together on one side of the benzene plane which failed to bind the anionic guest.[8c] This type of benzene-based octopus-like hexasubstituted receptor was initially demonstrated for the solution state binding of the cationic guests.[8i] In the tripodal

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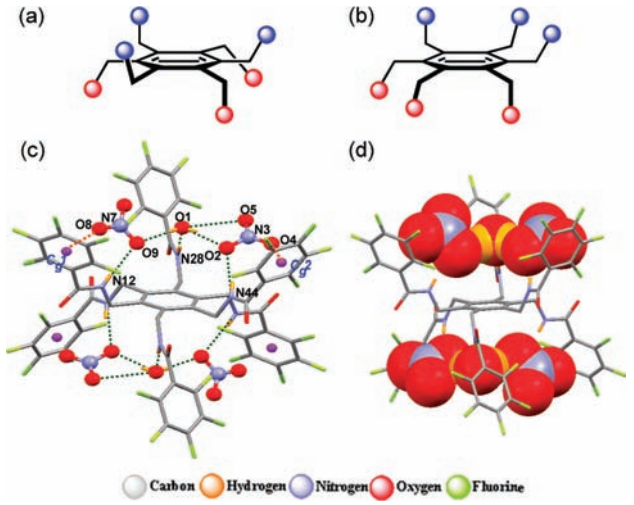

Figure 1. Pictorial view of (a) *ababab* and (b) *aaabbb* of bistripodand conformation. Blue and red balls are the arms extending above and below the central benzene scaffold. (c) View of encapsulated nitrate anions and water molecules above and below the benzene scaffold of **L**. (d) Space filling view of the encapsulated nitrates and water molecules inside the double-decker host. All the nonbonding hydrogen atoms and TBA cations were omitted for clarity.

cleft of complex **1**, each nitrate anion binds via one N−H···O interaction from two different arms, whereas a water guest binds via N−H···O interaction with the third arm. Interestingly, the encapsulated water molecule (O1) further hydrogen bonded to both the nitrate anions in a cascade fashion. In fact, this water molecule is acting as a curtain in between the closely recognized two nitrate anions. Detailed hydrogen bonding interactions are in the Supporting Information (Table S2). Further, the nitrate ions are in short contact with the CH_2 protons of the TBA cations which are located in the crystal lattice. In addition to these hydrogen bonding interactions, the nitrate anions are in short contacts with the π-cloud of the electron-deficient pentafluoro phenyl moiety.[10] These interactions are shown in Figure 1c with a centroid Cg1···O8 distance of 3.201 Å and a centroid Cg2···O8 distance of 3.511 Å. In an earlier report, we have showed the enhanced anion binding of the pentafluoro aryl-substituted tripodal ligands toward halides compared to the simple phenyl substitution.[10e] To check the role of pentafluorophenyl in **L**, we attempted to synthesize its phenyl analogue. Due to lack of solubility in common organic solvents, we are unable to characterize and perform the anion binding studies with the phenyl analogue of **L**.

(10) These weak interactions could be regarded as anion···π interactions though the concept of anion···π interactions in the nonspherical anion is not clear from the presently available literature. In the case of spherical halides, Hay et al. have differentiated between the halide···π vs anionic σ-complex based on d_{offset} values. (a) Hay, B. P.; Bryantsev, V. S. *Chem. Commun.* **2008**, 2417–2428. (b) Schottel, B. L.; Chifotides, H. T.; Dunbar, K. R. *Chem. Soc. Rev.* **2008**, *37*, 68–83. (c) Berryman, O. B.; Bryantsev, V. S.; Stay, D. P.; Johnson, D. W.; Hay, B. P. *J. Am. Chem. Soc.* **2007**, *129*, 48–58. (d) Albrecht, M.; Wessel, C.; Groot, M. D.; Rissanen, K.; Lüchow, A. *J. Am. Chem. Soc.* **2008**, *130*, 4600–4601. (e) Lakshminarayanan, P. S.; Ravikumar, I.; Suresh, E.; Ghosh, P. *Inorg. Chem.* **2007**, *46*, 4769–4771.

In the case of the geometrically equivalent planar anion acetate, complex **2**, pale pink colored crystals were obtained which are suitable for single-crystal X-ray study. Solid state structural analysis revealed 1:2 binding of host to acetate complexation (Figure 2a). Interestingly, in this case, the

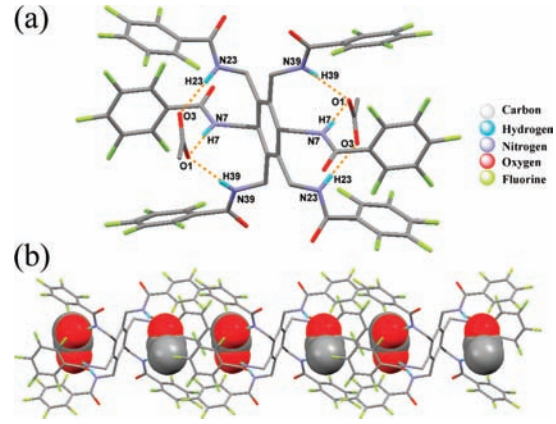

Figure 2. (a) View of **2** showing the encapsulated acetate ions above and below the benzene scaffold of **L**. (b) Packing diagram of **2** showing two tripodal clefts from two receptors holding two acetate ions in the pseudo cage. All the nonbonding H atoms and the TBA cations are omitted for clarity.

receptor moiety **L** in the acetate bound state adopted *aaabbb* conformation like Figure 1b. Therefore, complex **2** also formed two independent tripodal clefts, but cleft pattern is different from complex **1** (Figure 1a vs Figure 1b). In complex **2**, each cleft encapsulates single acetate anions resulting in two acetate anions encapsulation per receptor molecule, and the TBA cations are located in the crystal lattice. AcO^- in each cleft is binding with all three of the amide−NH protons via N−H···O interactions (Figure 2a). Detailed hydrogen bonding interactions are mentioned in the Supporting Information (Table S3). The packing diagram of the complex **2** shows that two units of the receptor form a pseudo cage, composed of six arms that hold two acetate anions inside the cage (Figure 2b) which are separated by 6.101 Å. The driving force of this pseudo cage formation is probably due to four intermolecular C−F···F−C interactions with F···F distance of 2.938 Å.

The anion binding ability of **L** in solution was validated by ^{1}H NMR experiments in acetone-d_6 or DMSO-d_6 at 25 °C in the presence of TBA salts of AcO^-, NO_3^-, and $H_2PO_4^-$ anions. In qualitative ^{1}H NMR studies, AcO^- and $H_2PO_4^-$ showed a downfield shift in the signals of −NH (0.86 ppm for AcO^- and 1.16 ppm for $H_2PO_4^-$) and upfield shift of $-CH_2$ signals (0.17 ppm for AcO^- and 0.21 ppm for $H_2PO_4^-$), whereas there was no chemical shift with NO_3^- in DMSO-d_6. In acetone-d_6, all three anions AcO^-, NO_3^-, and $H_2PO_4^-$ anions showed an appreciable change in chemical shifts of −NH and $-CH_2$ signals (Supporting Information). These preliminary studies indicated the binding of AcO^-, NO_3^-, and $H_2PO_4^-$ in the solution state. For detailed solution state binding of AcO^-, NO_3^-, and $H_2PO_4^-$

with **L** in solution, we have carried out ^{1}H NMR titration experiments in acetone-d_6 at 25 °C. Upon gradual addition of aliquots of TBA−OAc/NO_3^-/$H_2PO_4^-$, changes in chemical shifts were observed for −NH and $-CH_2$ signals of **L** (Figure S18−S22, Supporting Information). In the case of NO_3^- the amide−NH and for AcO^- and $H_2PO_4^-$ ions $-CH_2$ proton signals were monitored for Job plot analysis. The Job plot for **L** with AcO^- and $H_2PO_4^-$ showed host−guest stoichiometry 1:4, and NO_3^- showed 1:2 host−guest binding in solution (Figure 3). Figure 3c showed the stepwise curve in the Job plot for the binding of the $H_2PO_4^-$ ion with **L**. Careful analysis of the corresponding NMR spectra also indicates a special behavior. The signals of the $-CH_2$ protons sequentially become broad, narrow, broad, and finally narrow again. Up to the addition of 1 equiv of $H_2PO_4^-$, the signals become broad, and with further addition up to 2 equiv, it gets sharper. From 2 to 3 equiv of $H_2PO_4^-$, it gets broad again, and further addition of aliquots of $H_2PO_4^-$ up to 4 equiv showed sharpening of the $-CH_2$ signals (Figure S22, Supporting Information). This type of stepwise binding in solution could be attributed to the complex nature of the anion binding induced conformational changes of the receptor or could be due to the presence of multiple equilibria in the system. The association constants for the 1:2 (host:guest) complex for NO_3^- was calculated by EQNMR.[11] The association constants log K_1 and log K_2 for **L** with NO_3^- are 2.83 and 4.91 M^{-1}.[11] We also performed Job plot analysis of AcO^- binding in DMSO-d_6, which further supported 1:4 (host:guest) binding (Figure S17, Supporting Information). The differences in the propensity of **L** to bind four acetate anions in solution as opposed to two anions in the solid state as well as two nitrates in solution and four nitrates in the solid state might be due to variable conformational changes of **L** in solution and solid state and is not uncommon for the systems with multiple binding sites like **L**.[8a,j]

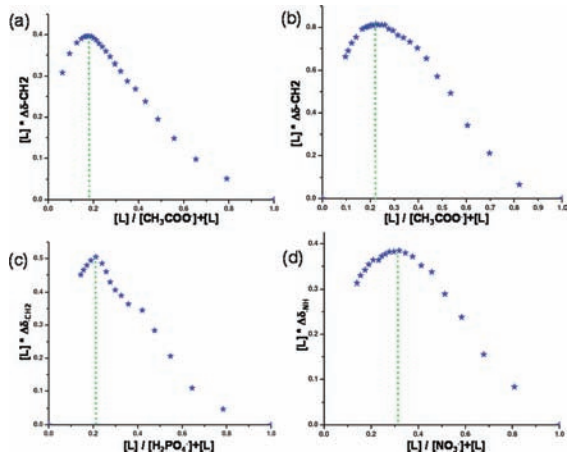

Figure 3. (a) Job's plot for **L** with TBA−OAc in acetone-d_6 ([**L**] is varied from 1.53 mM to 0.98 mM by the addition of aliquots of 40.3 mM TBA−OAc). (b) Job's plot for **L** with TBA−OAc in DMSO-d_6 ([**L**] is varied from 7.91 to 4.25 mM by the addition of aliquots of 85.9 mM TBA−OAc). (c) Job's plot for **L** with TBA−H_2PO_4 ([**L**] is varied from 1.55 to 1.23 mM by the addition of aliquots of 36.8 mM TBA−H_2PO_4) in acetone-d_6. (d) Job's plot for **L** with TBA−NO_3 ([**L**] is varied from 1.98 to 1.38 mM by the addition of aliquots of 27.2 mM TBA-NO_3) in acetone-d_6.

In conclusion, we have utilized the hexasubstituted host as a newer and higher generation of anion receptor. Solution state binding studies of different anions with this new host indicate the binding of multiple anionic guests. Solid state structural evidence of the nitrate complex shows encapsulation of four nitrate anions inside a single receptor. The compartmental anion recognition would lead further to utilizing the hexasubstituted host molecules as new generation receptors for different anionic guests. As a demonstration, we have also shown the anion-dependent conformational changes of the hexa-host. Importantly, the solid state structure of the acetate complex shows the isolation of the unfavorable conformation of the hexasubstituted benzene receptor. We are currently developing other multiarmed higher-generation receptors by incorporating different binding elements for selective anion recognition with higher guest:host ratios and their conformational changes upon guest binding.

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Supporting Information Available: Synthetic procedures,−characterization data, crystallographic information files, crystallographic refinement details, and ^{1}H NMR titration data. This material is available free of charge via the Internet at http://pubs.acs.org.

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