Recognition of nitrates in a discrete dimeric capsular assembly of a triamide half-capsule

M Arunachalam & Pradyut Ghosh*
Department of Inorganic Chemistry, Indian Association for the Cultivation of Science,
2A & 2B Raja S. C. Mullick Road, Kolkata 700 023, India
Email: icpg@iacs.res.in

Received 4 May 2011; accepted 24 June 2011

A newly synthesized tripodal amide receptor for the recognition of planar anions such as nitrate and acetate is described. The tripodal host, \(L_1\), features a 1,3,5-substituted 2,4,6-trimethylbenzene scaffold bearing three convergent amide hydrogen bonding functionality and electron-withdrawing \(p\)-cyanobenzoyl terminals. The single-crystal X-ray crystallographic analysis on crystals obtained upon complexation of \(L_1\) with tetrabutylammonium nitrate in acetone shows the encapsulation of two \(\text{NO}_3^-\) ions inside the staggered dimeric capsular assembly of \(L_1\). On the other hand, complexation with tetrabutylammonium acetate in the same solvent system shows non-capsular recognition of acetate and a water molecule inside the receptor bowl. The \(p\)-cyano substitution in the aryl terminals assists the formation of dimeric capsular assembly of \(L_1\) by enhancing the hydrogen bonding tendency of the aryl C-H protons. Though \(L_1\) demonstrates capsule formation upon complexation with \(\text{NO}_3^-\), the geometrically similar \(\text{AcO}^-\) shows non-capsular recognition in the solid state, which may be due the structural difference between the two anions.

Keywords: Coordination chemistry, Dimeric capsules, Anion recognition, Molecular recognition, Tripodal receptors, Nitrates, Acetates

Significant effort has been made to reveal the coordination behaviour of anions with synthetic receptor systems due to their critical role in environmental, medicinal and biological issues.\(^1\)\(^-\)\(^3\) Self-assembled capsules of cavitand molecules with interior guest binding elements have been studied on several occasions due to their possible application in molecular storage, drug delivery, catalysts and molecular reactors.\(^4\)\(^-\)\(^9\) Self-complementary units of capsular assemblies are usually based on constrained frameworks such as calixarenes/resorcinarenes,\(^10\)\(^-\)\(^11\) glycolurils,\(^12\)\(^-\)\(^13\) and tripodal derivatives. Very recently, we have shown the first report of dimeric capsular assembly by the hexapodal receptor.\(^21\)

Among the tripodal systems, 1,3,5-trialkylbenzene core provides some degree of preorganization into a conical conformation with all three binding arms projected in one direction.\(^17\)\(^-\)\(^20\) Recently, we have shown the anion-assisted capsular assembly and disassembly processes by 1,3,5-trialkylbenzene-based tripodal receptor functionalized with benzimidazole units. Various artificial anion receptors with polyammonium, amide/urea, and pyrrole/indole groups decorated on suitable supramolecular frameworks have been studied for their binding towards anionic species. Carboxylate anions exhibit specific biochemical behavior in enzymes and antibodies and are also critical components of numerous metabolic processes.\(^30\) Therefore, the recognition of acetate ion is considered to be important among other biologically functional anions.

On the other hand, nitrate anion contaminates the groundwater and is present in high concentration in certain waste waters such as nuclear waste streams and therefore it raises environmental problems.\(^31\) There are reports in the literature on the binding of nitrate, based on charged/electrostatic interactions.\(^32\)\(^-\)\(^37\) A few reports on nitrate binding in a neutral receptor have been demonstrated in the literature by us and others.\(^38\)\(^-\)\(^44\) We have demonstrated the recognition of \(\text{NO}_3^-\) and \(\text{AcO}^-\) ions by the \(C_3\)-symmetric neutral tripodal receptors \(L_2\) and \(L_3\) (refs 18 & 19). Our report on the first hexapodal anion receptor showed the unusual recognition of four nitrates in a single hexapodal receptor in its bistripodand conformation.\(^45\) Receptors \(L_2\) and \(L_3\) bind with hydrated halides as well as planar oxyanions such as \(\text{NO}_3^-\) and \(\text{AcO}^-\). An interesting observation from these reports is that, though the cavity of the receptors is the same, the
mode of anion binding with these receptors is different. For instance, \( L_2 \) shows selective dimeric capsule formation upon encapsulating \([F_2(H_2O)_6]^{2-}\) cluster in the dimeric assembly, whereas non-capsular assembly is observed upon its complexation with \( \text{Cl}^- \), \( \text{AcO}^- \) and \( \text{NO}_3^- \) ions. On the other hand, \( L_3 \) shows the recognition of \([F_2(H_2O)_6]^{2-}\), \([\text{Cl}_2(H_2O)_4]^{2-}\), \([\text{AcO}_2(H_2O)_4]^{2-}\) and two nitrates inside the capsular dimer. At this juncture, it is important to investigate the role of electron withdrawing substituents in the mode of assembly of the triamide receptors upon anion binding. Herein, we demonstrate that the \( p \)-cyanobenzoyl-substituted tripodal amide receptor \( L_1 \) as a versatile host for encapsulation of two nitrate ions through capsular assembly and non-capsular recognition of acetate ion as observed in the single crystal X-ray structures.

Ligand design and synthesis
For a synthetic receptor to bind with the anionic species, it should possess complementary binding sites incorporated on a suitable platform/framework. The designing principles of receptors \( L_1 \) are (i) benzene core provides a rigid platform, (ii) triamide clefts to provide complementary binding sites for anions, and, (iii) proper choice of aryl terminals with \( p \)-cyano substituent to enhance the binding ability of the receptor toward anions. It has been well established from our previous results that the electron-withdrawing substituents on the benzene ring assist the active participation of the aryl -CH protons toward anion binding via C-H···anion interactions.\(^{18,19}\) Considering the above points, we have designed and synthesized the tripodal amide receptor \( L_1 \) on the benzene platform for anion binding studies.

Materials and Methods
All reagents, tetrabutylammonium salts, and solvents for syntheses were purchased from commercial sources and used as received. 1,3,5-Tris(aminomethyl)-2,4,6-trimethylbenzene was prepared as per the modified literature procedure,\(^{46}\) except that 1,3,5-tris(bromomethyl)-2,4,6-triethylbenzene was used instead of 1,3,5-tris(bromomethyl)-2,4,6-trimethylbenzene.

\(^1\)H NMR spectra were recorded with 300 MHz Bruker DPX-300 NMR spectrometer. \(^13\)C NMR spectra were obtained at 75.47 MHz. HRMS experiments were carried out on a Waters QtoF (model YA 263) mass spectrometer in positive ESI mode.

Synthesis of \( L_1 \)
1,3,5-Tris(aminomethyl)-2,4,6-trimethylbenzene (0.414 g, 2 mmol) and 0.8 mL of triethylamine were dissolved in 100 mL of chloroform, and the mixture was stirred at 0 °C in an ice bath for 25 min under nitrogen atmosphere. 4-Cyanobenzoyl chloride (0.994 g, 6 mmol, 3 equiv.) was added under nitrogen atmosphere with constant stirring. The formation of a white precipitate in the reaction mixture was observed immediately. The reaction mixture was gradually brought to room temperature and was stirred for 24 h. The precipitate was filtered, and the residue was washed with plenty of water to remove triethylammonium chloride. Then the residue was washed with diethyl ether and dried in air to give 0.94 g of an off-white powder of \( L_1 \). Yield: 79 %. \(^1\)H NMR (300 MHz, DMSO-\( d_6 \); \( \delta \) (ppm)): 2.40 (s, 9H, -CH\(_3\)), 4.56 (d, 6H, -CH\(_2\)), 7.92 (d, 6H, -CHAr), 7.95 (d, 6H, -CHAr), 8.67 (t, 3H, -NH).

Syntheses of complexes (1) and (2)
Preparation of \( \text{TBA.NO}_3\subset \subset L_1 \), (1)
Complex (1) was prepared by charging an excess (15 equiv.) of tetrabutylammonium nitrate into a suspension of \( L_1 \) (60 mg, 0.1 mmol) in 15 mL of acetone. After addition of tetrabutylammonium nitrate the suspension turned clear and the solution was warmed to ~ 40 °C; then the solution was filtered and allowed to slowly evaporate at room temperature. After 3-4 days, colorless crystals of (1) were obtained.
Yield: 51 %. $^1$H NMR (300 MHz, DMSO-$d_6$; $\delta$ (ppm)): 0.84 (t, 12H, -NCH$_2$CH$_2$CH$_2$H), 1.22 (q, 8H, -NCH$_2$CH$_2$CH$_2$H), 1.49 (m, 8H, -NCH$_2$CH$_2$CH$_2$H), 2.40 (s, 9H, -CH$_3$), 3.09 (t, 8H, -NCH$_2$CH$_2$CH$_2$H), 4.56 (d, 6H), 7.92 (d, 6H, -CHAr), 7.95 (d, 6H, -CHAr), 8.7 (3H, -NH).

$^1$C NMR (75 MHz, DMSO-$d_6$; $\delta$ (ppm)): 14.06, 16.62, 19.79, 23.67, 38.13, 123.82, 129.49, 132.84, 140.63, 149.42, 165.18.

**Preparation of L$^1$.TBA.AcO.H$_2$O (2)**

Complex (2) was prepared by charging an excess (10 equiv.) of tetrabutylammonium acetate into a suspension of L$^1$ (60 mg, 0.1 mmol) in 15 mL of acetone. After addition of tetrabutylammonium acetate, the suspension turned clear and the solution was warmed to $\sim 40^\circ$C. Then solution was filtered and allowed to slowly evaporate at room temperature. After 2-3 days, colorless crystals of (2) were obtained.

Yield: 32 %. $^1$H-NMR (300 MHz, DMSO-$d_6$) $\delta$ (ppm): 0.93 (12H, -NCH$_2$CH$_2$CH$_2$CH$_3$), 1.30 (8H, -NCH$_2$CH$_2$CH$_2$CH$_3$), 1.56 (b, 8H,-NCH$_2$CH$_2$CH$_2$CH$_3$ and CH$_2$COO), 1.61 (s, 3H, CH$_2$COO), 2.51 (s, 9H,-CH$_3$), 3.15 (t, 8H, -NCH$_2$CH$_2$CH$_2$H), 4.55 (b, 6H, -NHCH$_2$), 7.90 (d, 6H, -CHAr), 7.98 (d, 6H, -CHAr), 8.77 (t, -NH).

$^1$C NMR (75 MHz, DMSO-$d_6$; $\delta$ (ppm)): 14.06, 16.62, 19.79, 23.67, 25.56, 58.19, 113.99, 119.00, 129.04, 132.72, 132.83, 137.59, 139.01, 165.18.

**NMR studies**

Solution-state $^1$H NMR (300 MHz, Bruker) experiments of L$^1$ with $[n$-Bu$_4$]$_2$N$^+$NO$_3^-$ and $[n$-Bu$_4$]$_2$N$^+$Ac$^-$ were carried out in DMSO-$d_6$ at 25 $^\circ$C. $^1$H NMR titration experiments were performed for L$^1$ with TBA-AcO in DMSO-$d_6$ at 25 $^\circ$C. The initial concentration of L$^1$ was 16.6 mM. Aliquots of anions were added from 82.6 mM stock solutions, and the titration was performed at room temperature.

**X-ray crystallographic analysis**

The crystallographic data and details of data collection for the complexes (1) and (2) are given in Table 1. In each case, a crystal of suitable size was selected from the mother liquor, immersed in Paratone oil, and then mounted on the tip of a glass fiber and cemented using epoxy resin. Intensity data for all four crystals were collected using Mo-K$_\alpha$ ($\lambda = 0.7107$ Å) radiation on a Bruker Smart Apex diffractometer equipped with a CCD area detector at 100 K. The data integration and reduction were processed with SAINIT software. An empirical absorption correction was applied to the collected reflections with SADABS. The structures were solved by direct methods using SHELXTL and were refined on $F^2$ by the full-matrix least-squares technique using the SHELXL-97 program package. Graphics were generated using PLATON and MERCURY. In all the cases, non-hydrogen atoms were treated anisotropically. All the hydrogen atoms attached to carbon atoms were geometrically fixed. Wherever possible, the amide hydrogen atoms were located from the Fourier map.

**Results and Discussion**

A C$_3$-tripodal amide receptor L$^1$ is synthesized easily from 1,3,5-tris(aminomethyl) 2,4,6-trimethylbenzene and 4-cyanobenzoyl chloride in good yield. L$^1$ possesses a preorganized C$_3$-symmetric cleft with amide NH protons suitable for anion recognition. When L$^1$ is treated with excess of tetrabutylammonium salts of NO$_3^-$ and AcO, complexes 2TBA.[L$^1$.NO$_3$]$_2$ (1) and TBA.[L$^1$.AcO.H$_2$O] (2) are isolated as crystals suitable for single crystal X-ray studies in moderate to good yields.

<table>
<thead>
<tr>
<th>Table 1—Crystallographic parameters of complexes (1) and (2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complex (1)</td>
</tr>
<tr>
<td>Empirical formula</td>
</tr>
<tr>
<td>Formula weight</td>
</tr>
<tr>
<td>Crystal system</td>
</tr>
<tr>
<td>Space group</td>
</tr>
<tr>
<td>$a$ (Å)</td>
</tr>
<tr>
<td>$b$ (Å)</td>
</tr>
<tr>
<td>$c$ (Å)</td>
</tr>
<tr>
<td>$\alpha$ (deg.)</td>
</tr>
<tr>
<td>$\beta$ (deg.)</td>
</tr>
<tr>
<td>$\gamma$ (deg.)</td>
</tr>
<tr>
<td>$V$ (Å$^3$)</td>
</tr>
<tr>
<td>$Z$</td>
</tr>
<tr>
<td>$d_{calc}$ (g/cm$^3$)</td>
</tr>
<tr>
<td>Crystal size (mm$^3$)</td>
</tr>
<tr>
<td>$F(000)$</td>
</tr>
<tr>
<td>$\mu$ (Mo-K$_\alpha$) (mm$^{-1}$)</td>
</tr>
<tr>
<td>$T$ (K)</td>
</tr>
<tr>
<td>$2\theta$ max</td>
</tr>
<tr>
<td>Obs. reflections</td>
</tr>
<tr>
<td>Parameters refined</td>
</tr>
<tr>
<td>$R_1$</td>
</tr>
<tr>
<td>$GOF$ ($F^2$)</td>
</tr>
</tbody>
</table>
Complex \(\text{TBA}_2[\text{L}_1\cdot\text{NO}_3]_2\) (1)

Complex (1) crystallizes in triclinic system with \(P\overline{1}\) space group. The solid state structure of (1) revealed a dimeric capsular assembly of \(\text{L}_1\) along with two encapsulated \(\text{NO}_3^-\) ions where all the three arms of the ligand projected in one direction to form a bowl shaped cavity and two such bowls intercalated to form the dimeric assembly. The \(\text{NO}_3^-\) guest is in hydrogen-bonding interaction with the -NH and aryl -CH protons of \(\text{L}_1\) (Fig. 1). Oxygen atoms labelled as O2, O3 and O4 of the encapsulated \(\text{NO}_3^-\) ion interact with amide nitrogen atoms labelled as N46, N31 and N16 respectively via hydrogen bonding interactions with \(\text{N} \cdots \text{O}\) bond distances ranging from 3.044 Å to 3.077 Å. Cyanato substituent in the aryl terminals increases the hydrogen bond donor ability of the C-H protons (Table 2). The encapsulated \(\text{NO}_3^-\) ions are also in hydrogen bonding interactions with the inwardly projected aryl-C-H protons in the \textit{meta}-position of the cyano group resulting in three C-H \cdots O interactions. Oxygen atoms of \(\text{NO}_3^-\) ion labeled as O2, O3 and O4 are in C-H \cdots O hydrogen-bonding interactions with C40, C27 and C12. In addition to the C-H \cdots O interactions with the parent receptor, the encapsulated \(\text{NO}_3^-\) ion is also hydrogen bonded with the aryl \(\text{CH}\) protons \textit{ortho} to the cyano substituent of the other molecule via C-H \cdots O interactions. Oxygen atoms of \(\text{NO}_3^-\) ion labeled as O2, O3 and O4 are in C-H \cdots O hydrogen-bonding interactions with C13, C39, and C28 of the dimeric partner. These intermolecular hydrogen bonding interactions are the driving force in the formation of a staggered dimeric capsular assembly in complex (1). Details of these interactions are mentioned in Table 2. In addition to all these hydrogen bonding interactions, the encapsulated nitrate ion is in short contact with the \(\pi\) cloud of the aryl platform, where the distance between the centroid of aryl platform and the nitrogen atom (N1) of the nitrate ion is 3.172 Å. The distance between the central nitrogen atoms of two \(\text{NO}_3^-\) is 3.426 Å, which is almost comparable with the unusual encapsulation of two nitrate anions reported previously in a protonated polyammonium macrobicyclic receptor \(^{53}\) and in our recent report \(^{19}\) on \(\text{L}_2\). The distance between the centroids of apical benzene caps is 9.749 Å, which is also comparable to our recent report \(^{19}\).

**Complex \(\text{TBA}_2[\text{L}_1\cdot\text{TBA}\cdots\text{OAc}\cdots\text{H}_2\text{O}]\) (2)**

Complex (2) crystallizes in the monoclinic system in the \(P\overline{2}_1/c\) space group along with two water molecules as the solvent of crystallization. The solid-state crystal structure of (2), obtained from acetone,
revealed the non-capsular assembly of L¹ with cleft bound AcO and a cavity encapsulated water molecule (Fig. 2). The anion is bound with the receptor system via N-H···O and C-H···O interactions with L¹ in addition to the hydrogen-bonding interactions with the encapsulated water molecule. Oxygen atoms labelled as O1 and O3 of the encapsulated AcO⁻ ion interact with amide nitrogen atoms labelled as N39 and N17 via hydrogen bonding interactions with N···O bond distances of 3.187 Å to 2.795 Å respectively. Cyanomethyl in the aryl terminals increases the hydrogen bond donor ability of the C-H protons (Table 2). The encapsulated AcO⁻ ions are also in hydrogen bonding interactions with the inwardly projected aryl-C-H protons in the meta-position of the cyano group resulting in two C-H···O interactions. Oxygen atoms of AcO⁻ ion labeled as O5 are hydrogen bonded with the encapsulated water molecule via O-H···O hydrogen bonding interactions. One more water molecule with oxygen atom labeled as O5 is hydrogen bonded with the encapsulated AcO⁻ ion via O-H···O hydrogen bonding interactions with the aryl C-H proton of the receptor bowl as well as the C-H protons of the acetate ion. Details of these interactions are given in Table 3.

Though both nitrate and acetate ions are geometrically equivalent, their modes of binding vary in the solid state and provide entirely different assemblies in the solid state. Our previous report showed that L² also encapsulates AcO⁻ ion along with a water molecule inside the tripodal bowl with a different binding pattern where the methyl group of the acetate ion is projected inside the cavity of the tripodal. In complex 2, in addition to the hydrogen bonding interactions with the receptor bowl, the encapsulated acetate ion and the water molecule also participated in intermolecular hydrogen bonding interactions with the other receptors via C-H···O and O-H···O interactions as shown in Fig 3. These intermolecular interactions lead to the formation of hydrogen bonded infinite polymeric network with intercalated arms (Fig. 3).

The difference in the mode of binding of nitrate and acetate in this case can be justified based on the structural difference between nitrate and acetate. In the case of nitrate, the C₃-symmetric anion fits well in the cavity of the C₃-symmetric receptor. The size and shape complementarity of nitrate and L¹ facilitate the positioning of anion in the centre of the tripodal cavity. On the other hand, since the acetate ion has the Y-shaped hydrogen bond acceptor fragments, it can effectively hydrogen bond with two of the amide N-H protons and form N-H···O hydrogen bonding interactions, and leaving the other N-H proton without direct coordination. This assists the encapsulation of a water molecule inside the cavity and displace the acetate ion towards the cleft of the receptor.

Solution-state anion binding studies

Qualitative ¹H NMR experiments were performed with TBA salts of AcO⁻ and NO₃⁻ to probe the solution-state behavior of L¹ in the presence of these anions. Addition of TBA-OAc to the solution of L¹ in

<table>
<thead>
<tr>
<th>D-H···A</th>
<th>D-H (Å)</th>
<th>H···A (Å)</th>
<th>D···A (Å)</th>
<th>∠D-H···A (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>O6-H6A···O3¹</td>
<td>0.85</td>
<td>1.90</td>
<td>2.716</td>
<td>160</td>
</tr>
<tr>
<td>O6-H6B···O16²</td>
<td>0.86</td>
<td>1.92</td>
<td>2.742</td>
<td>159</td>
</tr>
<tr>
<td>N17-H17···O3³</td>
<td>0.93</td>
<td>1.90</td>
<td>2.795</td>
<td>162</td>
</tr>
<tr>
<td>N24-H24···O6⁴</td>
<td>0.81</td>
<td>2.06</td>
<td>2.860</td>
<td>173</td>
</tr>
<tr>
<td>N39-H39···O1⁵</td>
<td>0.85</td>
<td>2.33</td>
<td>3.187</td>
<td>176</td>
</tr>
<tr>
<td>C32-H32···O6⁵</td>
<td>0.93</td>
<td>2.30</td>
<td>3.192</td>
<td>160</td>
</tr>
<tr>
<td>C47-H47···O1⁶</td>
<td>0.93</td>
<td>2.38</td>
<td>3.175</td>
<td>143</td>
</tr>
</tbody>
</table>

1: x, y, z; 2: 1+x, y, z; 3: x, y, z; 4: x, 1+y, z; 5: x, 1+y, z;

Fig. 2—View showing the hydrogen-bonding interactions of acetate ion and the encapsulated water molecules with L¹ in (1). Tetrabutylammonium cation and nonbonding hydrogen atoms have been omitted for clarity.
DMSO-$d_6$ showed downfield shift in the chemical shift of N-H protons, while in the case of NO$_3^-$ ion, no change in the chemical shift was observed under the present experimental conditions. Hence, we have carried out the $^1$H NMR titration experiments to probe the binding of AcO$^-$ with $L^1$ in DMSO-$d_6$. The $^1$H NMR titration experiments of AcO$^-$ with $L^1$ showed 1:3 host to guest binding in solution (Fig. 4), whereas the solid-state single-crystal X-ray study showed 1:1 binding. Similar solution-state binding was also observed in the case of $L^2$ and $L^3$ with AcO$^-$ in DMSO-$d_6$. Here, the difference in binding of three acetate anions in solution versus one acetate in the solid state may be due to multiple equilibria or side cleft binding of anions in the solution state, which could allow multiple anion interactions with a single receptor. Moreover, while crystallization was carried out in acetone solution, NMR titration experiments were carried out in DMSO. Solvent polarity may have played a crucial role in the mode of binding of anions with the receptor.

**Conclusions**

In summary, $L^1$, a newly synthesized tripodal amide receptor showed capsular encapsulation of nitrate ions and non-capsular binding of acetate ion upon complexation. Structurally similar triamide receptor with $p$-nitrobenzoyl terminal showed capsular recognition for both nitrate and acetate ion in the dimeric capsular assembly. Simple alteration of the electron withdrawing groups in the aryl terminals showed an abrupt change in the mode of anion recognition in the $C_3$-symmetric tripodal amide receptor. Further studies need to be carried out to generalize the anion binding behaviour of tripodal amide receptors of this kind.

**Supplementary Data**

Crystallographic data for the structural analysis of complexes (1) and (2) have been deposited with the CCDC (Cambridge Crystallographic Data Centre, under CCDC No. 830838 and 830839. Copy of this information may be obtained free of charge from www.http://www.ccdc.cam.ac.uk.

**Acknowledgement**

PG gratefully acknowledges the Department of Science and Technology (DST), New Delhi, India, for financial support (grant no SR/S1/IC-16/2008). X-ray crystallography studies were performed at the DST-funded National Single Crystal X-ray Diffraction Facility at the Department of Inorganic Chemistry, IACS, Kolkata, India.

**References**

ARUNACHALAM & GHOSH: RECOGNITION OF NITRATES IN A DISCRETE DIMERIC CAPSULAR ASSEMBLY


52 Mercury 23, supplied with Cambridge Structural Database; CCDC, Cambridge, UK.