Anion complexation of a pentafluorophenyl-substituted tripodal urea receptor in solution and the solid state: selectivity toward phosphate†

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Received 13th November 2008, Accepted 19th March 2009
First published as an Advance Article on the web 20th April 2009
DOI: 10.1039/b820322a

The binding and selectivity of halides (spherical) and oxyanions (tetrahedral) toward a recently reported pentafluorophenyl-substituted tripodal urea-based receptor $\mathbf{L}^1$ are examined thoroughly in the solid state by single-crystal X-ray crystallography as well as in solution by multinuclear NMR techniques. Crystallographic results show proof of a fluoride encapsulation in the cavity of $\mathbf{L}^1$ in complex $[\mathbf{L}^1(F)][Bu_4N]$, **1**. Fluoride encapsulation inside the C_{3v} symmetric cleft is observed *via* six hydrogen bonds to all six urea protons of the receptor. In case of complex **2** crystallographic results show encapsulation of sulfate ion inside a supramolecular cage formed upon 1 : 2 (guest–host) complex formation between sulfate and $\mathbf{L}^1$. Sulfate encapsulation is observed *via* fourteen hydrogen bonding interactions from all six urea moieties of two $\mathbf{L}^1$ units. Our effort to isolate single crystal of halides/oxyanions complexes of $\mathbf{L}^2$ always yield single crystals of free $\mathbf{L}^2$ though literature shows anion binding with this receptor in solution. Solution state binding studies of $\mathbf{L}^1$ are carried out by ^{1}H-NMR titration to calculate binding constants, which show the following anion binding sequence $H_2PO_4^- > SO_4^{2-} > CH_3COO^- > F^- > Cl^- >> Br^-$ whereas there is no binding with I^-, NO_3^- and ClO_4^- guests. Comparison of phosphate and sulfate binding in $\mathbf{L}^1$ and $\mathbf{L}^2$, show higher binding with the pentafluorophenyl substituted receptor, $\mathbf{L}^1$. Further ^{19}F and ^{31}P-NMR experiments in solution are also carried out to probe the binding of F^- and $H_2PO_4^-$ with $\mathbf{L}^1$, respectively. Extensive ^{1}H-NMR experiments in solution and crystallization in the presence of multiple anions are also undertaken to evaluate the selectivity of $H_2PO_4^-$ over other anions.

Introduction

The development of receptors for anions is of considerable current interest in molecular recognition study.[1,2] Tris(2-aminoethyl)-amine, tren, is an important building block in tripodal receptor systems for anions that has been studied by different groups.[3–12] The binding ability of tren-based acyclic tripodal receptors towards anions varies with the attached moiety to the tren (N4) unit, since functional groups modify the hydrogen bonding capability,[10] as well as the conformation of the receptor.[12] Among halides, recognition of the smallest anion, fluoride, is of special interest due to its applications in medical and biological fields and also in drinking water purification process.[13] Similarly, tetrahedral oxyanions, SO_4^{2-} and $H_2PO_4^-$ recognition are of current interest due to their biological and environmental importance.[14] In general, the binding of spherical shaped and carrying single negative charge halides is achieved by the use of receptors with high positive charge and bearing a pre-organized arrangement of appropriate groups.[15] Therefore, tren has been extensively used as a building block for the synthesis of polyamine cage receptors, which display encapsulation of halides in the receptor cavity upon protonation,[15] among which polyammonium cage receptors for fluoride is also known.[15] Moreover, tren based polyamide cryptands cage,[16] calix pyrrole and silsesquioxane cage,[17] have also shown fluoride encapsulation. Mascal *et al.* have recently reported fluoride inclusion complex with triprotonated cyanuric acid based cylindrophane by a combination of anion-π interactions and ion-pair-reinforced hydrogen bonding.[18]

In case of tetrahedral oxyanions a very few receptor systems are known that have shown crystallographic evidence for SO_4^{2-} encapsulation,[9,19] which also includes tripodal urea-based receptors.[9] In our recent study, we have shown encapsulation of dimers of $H_2PO_4^-$ inside a pseudo dimeric cage of a pentafluorophenyl-substituted tripodal urea receptor $\mathbf{L}^1$ (Scheme 1),[12b] whereas Bowman-James *et al.* have shown pocket binding of this anion in a cyclophane receptor.[20] In 1995, Morán *et al.* demonstrated binding of phosphate and sulfate with the $\mathbf{L}^2$ (Scheme 1) in solution.[5] Whereas the binding of guests within pre-organized macrocyclic systems are relatively straightforward to understand but the binding processes of flexible podand receptors remain more illusive.[21] We report herein, the structural evidence of encapsulated F^- in the C_{3v} symmetric cleft of $\mathbf{L}^1$ *via* 1 : 1 complex formation, and SO_4^{2-} encapsulation inside a supramolecular capsule upon 1 : 2 (SO_4^{2-}:$\mathbf{L}^1$) complex formation.

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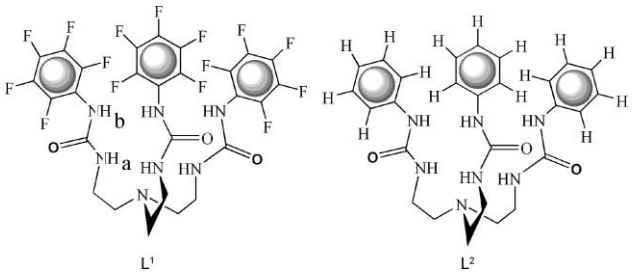
† Electronic supplementary information (ESI) available: ^{1}H-NMR, ^{13}C-NMR and HRMS of $\mathbf{L}^1$, complex **1** and **2**. ^{19}F-NMR spectra of $\mathbf{L}^1$, *n*-$Bu_4N^+F^-$ and $\mathbf{L}^1 + F^-$. ^{1}H-NMR titration curves of $\mathbf{L}^1$ with SO_4^{2-}. Job plots for $\mathbf{L}^1$ with F^-, Cl^-, Br^-, HSO_4^- and SO_4^{2-}. ORTEP diagram of complexes **1** and **2**, and packing diagram of complex **1**. Scatter plot for complexes $H_2PO_4^-$ and fluoride (**1**). CCDC reference numbers 679393 (**1**) and 697104 (**2**). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b820322a



Scheme 1 Tris(2-aminoethyl)amine based pentafluorophenyl and phenyl based tripodal urea receptors $\mathbf{L}^1$ and $\mathbf{L}^2$.

In this work, we also show that $\mathbf{L}^1$ has the highest selectivity toward $H_2PO_4^-$ in solution over other anions like F^-, Cl^-, Br^-, I^-, SO_4^{2-}, ClO_4^-, AcO^- and NO_3^-.

Experimental

Solvents and starting materials

Compounds $\mathbf{L}^1$ and $\mathbf{L}^2$ were prepared as previously described.[5,12b] Tetrabutylammonium salts of fluoride, chloride, bromide, iodide, hydrogensulfate, sulfate (50 wt% in water), dihydrogenphosphate, nitrate, acetate and perchlorate were purchased from commercial sources and used without further purification. The solvents were purified by usual methods prior to use.

Physical methods

HRMS were recorded on a Qtof Micro YA263 mass spectrometer. ^1H, ^{13}C, ^{19}F and ^{31}P-NMR spectra were recorded on Bruker Avance 300, 75 or 500 MHz spectrometers.

Syntheses of tripodal receptors $\mathbf{L}^1$ and $\mathbf{L}^2$

The tripodal receptor $\mathbf{L}^2$ was synthesized following literature procedures and characterization data were matched with the literature data.[5] $\mathbf{L}^1$ was synthesized following our recent report.[12b] 2.6 mL (20 mmol) of pentafluorophenyl isocyanate was dissolved in 25 mL of dry DCM at room temperature in a 100 mL 2-neck round bottomed flask equipped with a dropping funnel. Then tren (1.0 mL, 6.5 mmol) was dissolved in 25 mL of dry DCM and was added drop-wise using a dropping funnel with constant stirring. The resulting solution was stirred for another 1 h at room temperature in N_2 atmosphere. The colourless precipitate formed was filtered off and washed with DCM twice. The precipitate collected was dried in air. Yield of $\mathbf{L}^1$ is 98%. ^1H NMR (300 MHz, DMSO-d_6): δ 2.55 (t, 6 H, NCH_2), 3.15 (t, 6 H, NCH_2CH_2), 6.55 (s, 3 H, NH_a), 8.352 (s, 3 H, NH_b). ^{13}C NMR (75.47 MHz, DMSO-d_6): δ 38.9 (NCH_2), 54.5 (NCH_2CH_2), 115.7 (m of s, Ar, CCF, $J_{CCF} = 15$ Hz), 137.9 (m of d, Ar, CF, $J_{CF} = 247$ Hz), 138.8 (m of d, Ar, CF $J_{CF} = 247$ Hz), 143.6 (m of d, Ar, CF, $J_{CF} = 246$ Hz), 155.4 (s, C=O). HRMS (+ESI) calcd for $[C_{27}H_{19}F_{15}N_7O_3]^+$, $[\mathbf{L}^1 + H]^+$ 774.4609, found 774.2267.

Synthesis of complex 1

75 mg of $\mathbf{L}^1$ was dissolved in 5 mL DMF–MeCN (1 : 1 v/v) binary solvent in a 25 mL beaker. In to this solution, 25 mg of n-$Bu_4N^+F^-$ was added in one shot and mixture was stirred for 5 min at room temperature and slightly warmed for 10 min. The resulting solution was filtered using a filter paper. Filtrate was allowed to evaporate under room temperature. Colourless crystals of the fluoride complex of $\mathbf{L}^1$, $[\mathbf{L}^1(F^-)]\cdot n$-$Bu_4N^+$ (**1**), suitable for X-ray diffraction was obtained after a week. Isolated Yield of **1** is 80%.^1H NMR (300 MHz, DMSO-d_6): δ 1.26 (t, 3 H, $NCH_2CH_2CH_2CH_3$), 1.54 (m, 2 H, $NCH_2CH_2CH_2CH_3$), 1.57 (m, 2 H, $NCH_2CH_2CH_2CH_3$), 2.51 (s, 6 H, NCH_2), 3.13 (s, 6 H, NCH_2CH_2), 3.21 (m, 2 H, $NCH_2CH_2CH_2CH_3$), 7.50 (br, 3 H, NH_a), 10.05 (br, 3 H, NH_b). ^{13}C NMR (200 MHz, DMSO-d_6): δ 13.5 ($NCH_2CH_2CH_2CH_3$), 19.3 ($NCH_2CH_2CH_2CH_3$), 23.2 ($NCH_2CH_2CH_2CH_3$) 36.4 (NCH_2), 51.4 (NCH_2CH_2), 57.6 ($NCH_2CH_2CH_2CH_3$), 115.9 (m of s, Ar, CCF), 137.1 (m, Ar, CF $J_{CF} = 326$ Hz, $J_{CCF} = 18$ Hz), 142.4 (m of d, Ar, CF, $J_{CF} = 318$ Hz), 155.2 (s, C=O). HRMS (+ESI) calcd for $[C_{43}H_{54}F_{16}N_8O_3]^+$, 1034.9151, found 774.2715 $[\mathbf{L}^1 + H^+]$.

Synthesis of complex 2

Complex **2** was synthesized by reacting $\mathbf{L}^1$ and $(n$-$Bu_4N)_2SO_4$/ n-$Bu_4N^+HSO_4^-$. In both the cases, 75 mg of $\mathbf{L}^1$ was dissolved in 10 mL of DMSO in a 25 mL beaker. In the case of the $(n$-$Bu_4N)_2SO_4$ salt, 3 mL of $(n$-$Bu_4N)_2SO_4$ (50 wt% in water) was added to the 10 mL of $\mathbf{L}^1$ solution whereas, in other case 25 mg of n-$Bu_4N^+HSO_4^-$ was added in one shot to the 10 mL of $\mathbf{L}^1$ solution. Then in both cases, the mixtures were stirred for 5 min at room temperature and warmed at 60 °C for 10 min. After cooling to room temperature, both the resulting solutions were filtered using a filter paper. Filtrates were collected in 25 mL beaker and allowed to crystallize at room temperature. From both the solutions colourless crystals of the sulfate complex of $\mathbf{L}^1$, $[2\mathbf{L}^1(SO_4^{2-})]\cdot 2(n$-$Bu)_4N^+$ (**2**), suitable for X-ray diffraction was obtained after three days. Isolated Yield of **2** is 80%.^1H NMR (300 MHz, DMSO-d_6): δ 0.88 (t, 3 H, $NCH_2CH_2CH_2CH_3$), 1.25 (m, 2 H, $NCH_2CH_2CH_2CH_3$), 1.51 (m, 2 H, $NCH_2CH_2CH_2CH_3$), 2.32 (s, 6 H, NCH_2), 2.95 (s, 6 H, NCH_2CH_2), 3.11 (m, 2 H, $NCH_2CH_2CH_2CH_3$), 7.42 (br, 3 H, NH_a), 8.86 (br, 3 H, NH_b). ^{13}C NMR (75.47 MHz, DMSO-d_6): δ 13.9 ($NCH_2CH_2CH_2CH_3$), 19.7 ($NCH_2CH_2CH_2CH_3$), 23.5 ($NCH_2CH_2CH_2CH_3$) 38.3 (NCH_2), 54.9 (NCH_2CH_2), 58.0 ($NCH_2CH_2CH_2CH_3$), 115.8 (m of s, Ar, CCF, $J_{CCF} = 15$ Hz), 137.3 (m of d, Ar, CF, $J_{CF} = 244$ Hz), 138.0 (m of d, Ar, CF $J_{CF} = 246$ Hz), 143.2 (m of d, Ar, CF, $J_{CF} = 246$ Hz), 155.1 (s, C=O). HRMS (+ESI) calcd for $[C_{59}H_{90}F_{15}N_9O_7S]^+$, 1354.4441, found 774.0027$[\mathbf{L}^1 + H^+]$.

^{1}H-NMR studies

Binding constants were obtained by ^1H NMR (300 MHz Bruker) titrations of $\mathbf{L}^1$ with $[n$-$Bu]_4N^+A^-$ (A^-: F^-, Cl^-, Br^-, SO_4^{2-}, HSO_4^-, $H_2PO_4^-$ and AcO^-) in DMSO-d_6 at 25 °C. The initial concentration of $\mathbf{L}^1$ was 20 mM. Aliquots of anions were added from two different stock solutions 25 mM and 50 mM of anions (host–guest = up to 1 : 1, 25 mM stock solution was used, and above 1 : 1 ratio higher concentration anion was used) for all the anions except SO_4^{2-} and HSO_4^-. For these two anions initial concentration of $\mathbf{L}^1$ was 20 mM and aliquots of either SO_4^{2-}/HSO_4^- was added from a stock solution of 5 mM. Tetramethylsilane (TMS) in DMSO-d_6 was used as an internal reference, and each titration was performed by 15 measurements at room temperature. All proton signals were referred to TMS. The association constant,[23] K values were

calculated by fitting the change in the N–H chemical shift with a 1 : 1 association model with non-linear least square analysis for F^-, Cl^-, Br^-, $H_2PO_4^-$ and AcO^- whereas 1 : 2 association model was fitted for sulfate.

The equation $\Delta\delta = \{([A]_0 + [L^1]_0 + 1/K) \pm (([A]_0 + [L^1]_0 + 1/K)^2 - 4[L^1]_0[A]_0)^{1/2}\}\Delta\delta_{max}/2[L^1]_0$ was used to determine the K values. ^{31}P-NMR spectra were recorded at 500 MHz on a Bruker. Chemical shifts in ppm were relative to an external reference of 85% H_3PO_4 in DMSO-d_6 at 25 °C. ^{19}F-NMR spectra were recorded at Bruker 500 MHz spectrometer. Chemical shifts in ppm were relative to an internal standard of trifluoro-toulene in DMSO-d_6 at 25 °C.

Single-crystal X-ray studies

The crystallographic data and details of data collection and refinement for complexes **1** and **2** are listed below.‡ In each case, a single crystal of suitable size was selected from the mother liquor and immersed in Paratone oil and then mounted on the tip of a glass fibre and cemented using epoxy resin. Intensity data for these two crystals were collected using Mo Kα (λ = 0.7107 Å) radiation on a Bruker SMART APEX diffractometer equipped with CCD area detector at 100 K. Reflections were measured from a hemisphere of data collected with each frame covering 0.5° in ω. The data integration, reduction and structure solutions/refinements were carried out using the software package of Bruker SMART APEX. Graphics were generated using PLATON[24] and MERCURY 1.3.[25] In complexes **1** and **2**, the non-hydrogen atoms were refined anisotropically until convergence. Even though the data for complex **2** was collected at 100 K, two fluorine atoms, F6 and F8 were found to be disorder. However, we were unable to model the disorder, as the thermal parameters for the rest of the phenyl ring were in agreement with the model. As a result, the F6 and F8 were considered non-disordered (and planar to the ring) and were refined anisotropically till convergence. Hydrogen atoms attached to the urea nitrogen atoms of complex **1** and **2** were located from the difference Fourier map and refined isotropically. The remainder of the hydrogen atoms in these complexes were geometrically fixed at idealized positions.

Results and discussion

The tripodal urea-based receptors L^1 and L^2 are obtained by reaction between tris(2-aminoethyl)amine and three equiv. of pentafluorophenyl isocyanate and phenyl isocyanate, respectively, in dry CH_2Cl_2.[12b,5] In the case of complex **1** preparation, L^1 is treated with n-$Bu_4N^+F^-$ in N,N-dimethyl formamide (DMF)–acetonitrile (MeCN) (1 : 1 v/v) binary solvent and resulting solution yielded crystals suitable for single-crystal X-ray analysis. Complex **2** is isolated following two different approaches by treating L^1 with bis-(tetrabutylammonium) sulfate (50 wt% in water) and tetrabutylammonium hydrogensulfate. Irrespective of tetrabutylammonium salts, complex **2** is isolated as crystals suitable for single-crystal X-ray studies. Syntheses of the receptor L^1, the fluoride complex **1**, and sulfate complex **2** are straightforward, resulting high yield.

Single-crystal X-ray structural studies of 1

We attempted to grow single crystal of complexes formed with L^1 and n-$Bu_4N^+X^-$ (X = F, Cl, Br, I). But single crystals suitable for crystallographic analysis are only obtained in case of the fluoride complex $[L^1(F)][n\text{-}Bu_4N]$, **1** from a DMF/MeCN binary solvent system upon slow evaporation. Complex **1** crystallizes in the triclinic space group $P\bar{1}$. The crystal structure of compound **1** reveals that the fluoride anion is encapsulated inside the tripodal cavity, with hydrogen bonds to all six urea protons.[22] Structural analysis shows that encapsulation of F^- inside the receptor cavity is governed by six intramolecular N–H···F^- interactions from three urea moieties of the tripodal receptor (Table 1 and Fig. 1a). A correlation of the N–H···F angle *vs.* H···F distance (Fig. 2 and Table 1) shows that all are in the strong hydrogen bonding interaction region of $d_{H\cdots F} < 2.2$ Å and $d_{N\cdots F} < 3.0$ Å. The geometry around fluoride is distorted trigonal prismatic (Fig. 1b and c), with a twist angle averaging 4.28° from the regular trigonal prism, which is quite uncommon in anion complexes.[1e,16] In cases of polyamide cryptands, Bowman-James *et al.* have also reported this uncommon geometry around fluoride in two complexes with a larger twist angles of 36.6°,[16a] and 35°[16b] A further two units of fluoride encapsulated L^1 are held together *via* two intermolecular C–F···F–C contacts (Fig. 1d). Details of these C–F···F–C interaction is the interaction of C8–F4···F14–C26 where F4/F14···F14′/F4′ = 2.811 Å, ∠C8–F4···F14′/∠C8′–F4′···F14 = 165.82° and ∠C26–F14···F4′/∠C26′–F14′···F4′ = 123.84°. In the dimeric pseudo cage of L^1 two fluoride ions are separated at a distance of 13.242 Å whereas distance between the two bridgehead nitrogen centres is 19.824 Å.

The packing diagram of the compound viewed down b-axis with various hydrogen bonding interactions is depicted in the Fig. S22 of the ESI.† The 2_1 screw related tripodal ligands are arranged along c-axis with opposite orientation along with screw related tetrabutylammonium cations between the tripodal ligand involving in C-H···O and C–H···F interactions generating H-bonded layers along ac-plane. Details of these H-bonding interactions are given in Table 2.

Table 1 H-bonding interactions of F^- in complex **1**

D–H···A	d(H···A)/Å	d(D···A)/Å	∠D–H–A/°
N2–H2C···F16	2.10(3)	2.865(3)	149(3)
N3–H3C···F16	2.02(3)	2.793(3)	160(3)
N4–H4C···F16	2.15(3)	2.884(3)	150(3)
N5–H5C···F16	1.90(3)	2.700(3)	165(3)
N6–H6C···F16	2.05(3)	2.835(3)	153(3)
N7–H7C···F16	2.01(4)	2.790(3)	153(3)

‡ Crystal data for **1**: $C_{43}H_{54}F_{16}N_8O_3$, M_r = 1034.94, triclinic, space group $P\bar{1}$, a = 12.9366(13), b = 13.3131(13), c = 15.2703(15) Å, α = 108.729(2), β = 92.717(2), γ = 108.518(2)°, V = 2328.8(4) Å^{-3}, Z = 2, ρ_{calcd} = 1.476 g cm^{-3}, μ = 0.138 mm^{-1}, T = 100(2) K, 16 364 reflections measured, 6755 observed ($I > 2\sigma(I)$) 659 parameters; R_{int} = 0.0292, R_1 = 0.0551; wR_2 = 0.1268 ($I > 2\sigma(I)$), R_1 = 0.0680; wR_2 = 0.1329 (all data) with GOF = 1.095 $I > 2\sigma(I)$, $\Delta\rho_{min}$/e Å^{-3} = –0.242 and $\Delta\rho_{max}$/e Å^{-3} = 0.324. Crystal data for **2**: $C_{86}H_{108}F_{30}N_{16}O_{10}S$, M_r = 2127.94, monoclinic, space group $C2/c$, a = 21.2559(15), b = 19.5053(13), c = 23.6564(17) Å, α = 90.00, β = 95.377(10), γ = 90.00°, V = 9764.8(12) Å^{-3}, Z = 4, ρ_{calcd} = 1.447 g cm^{-3}, μ = 0.155 mm^{-1}, T = 100(2) K, 24 105 reflections measured, 7052 observed ($I > 2\sigma$ (I)) 691 parameters; R_{int} = 0.0356, R_1 = 0.0787; wR_2 = 0.1798 ($I > 2\sigma(I)$), R_1 = 0.0942; wR_2 = 0.1893 (all data) with GOF = 1.065 $I > 2\sigma(I)$, $\Delta\rho_{min}$/e Å^{-3} = –1.035 and $\Delta\rho_{max}$/e Å^{-3} = 1.171.

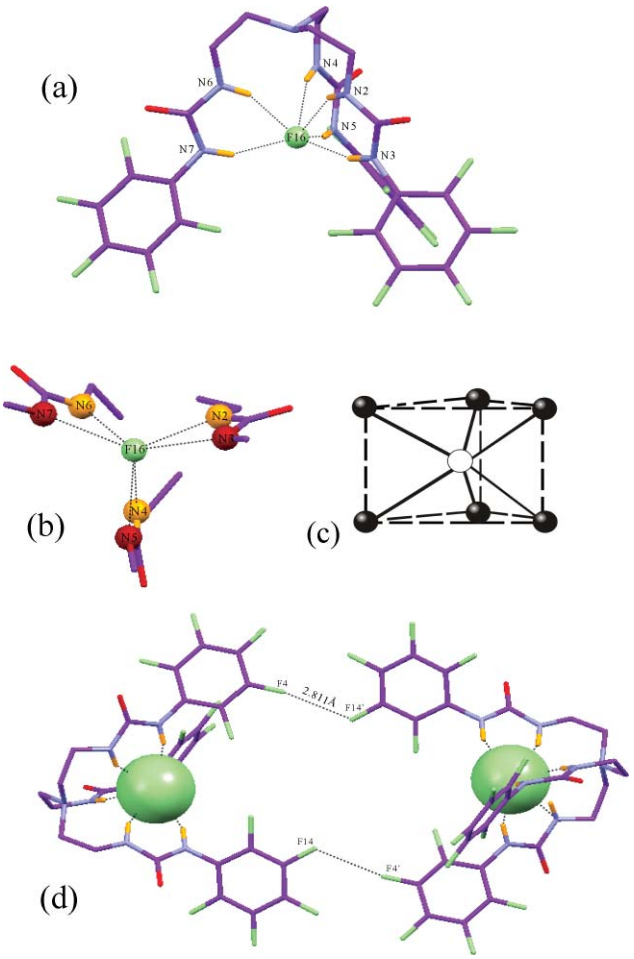


Fig. 1 (a) Perspective of $[\mathbf{L}^1(F)]^-$ showing encapsulation of F^- ion (green, ball and stick) inside the tripodal cavity where dotted lines represent the $(N–H)\cdots F^-$ interactions green F, red O, blue N. The tetrabutylammonium cation and the hydrogens other than urea groups are omitted for clarity, (b) and (c) showing distorted trigonal prismatic geometry around fluoride. (d) Dimer of complex **1** *via* C–F···F–C interaction.

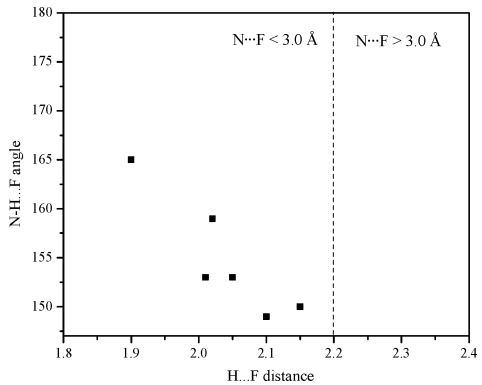


Fig. 2 The scatter plot of N–H···F angle *vs.* H···F distance of the hydrogen bonds in complex **1**.

Single-crystal X-ray studies of complex 2

Efforts have been made to grow single crystal of complexes of L^1 with the n-$Bu_4N^+X^-$ (X = AcO, HSO_4, H_2PO_4) as well as $(n\text{-}Bu_4N^+)_2SO_4^{2-}$ (50 wt% in water). But the single crystal suitable for crystallographic analysis are obtained in cases of sulfate/bisulfate and dihydrogenphosphate complexes of $\mathbf{L}^1$ as $[\mathbf{2}\cdot\mathbf{L}^1(SO_4)][n\text{-}Bu_4N]_2$ and $[\mathbf{L}^1(H_2PO_4)][n\text{-}Bu_4N]\cdot DMF$ from DMSO and DMF/MeCN solvent systems respectively upon slow evaporation. In case of AcO^- crystallization process, a semisolid is isolated upon repeated attempt. In our previous communication we have shown structural details of dihydrogenphosphate complex of $\mathbf{L}^1$.[12b] The complex $[\mathbf{2}\cdot\mathbf{L}^1(SO_4)][n\text{-}Bu_4N]_2$, **2** crystallizes in monoclinic system with $C2/c$ space group. Two inversion-symmetric molecules of $\mathbf{L}^1$ form a cavity that encapsulates a sulfate anion (disordered) in its centre *via* hydrogen bonding to the six urea groups (Fig. 3a). There are total fourteen hydrogen bonding interactions between the twelve NH groups of two L^1 moieties and four O atoms of SO_4^{2-} (Fig. 3b).

Two of the oxygen atoms O5 and O5A accepts four hydrogen bonds each and the other two O atoms (O4 and O6) form three N–H···O contacts each with the urea protons of $\mathbf{L}^1$ (Table 3). A correlation of N–H···O angle *vs.* H···O distance (Fig. 5) shows that in the strong hydrogen bonding interaction region of $d_{H\cdots O} < 2.5$ Å and $d_{N\cdots O} < 3.2$ Å there are twelve contacts. Out of twelve contacts only one contact has an N–H···O angle smaller than 140°, which is N7–H7C···O4 with a N7–H7–O4 angle 135° but $d_{N\cdots O}$ is 2.852 Å. One hydrogen bonding interaction fall in the weak interaction zone ($2.5 < d_{H\cdots O} < 2.8$ Å, and $3.2 < d_{N\cdots O} < 3.5$ Å) where the angle is not smaller than 140° (Table 4). Similar correlation has been done by Wu *et al.* in case of sulfate binding with the tripodal pyridyl urea based metal–organic frame work, which shows eleven strong and six weak hydrogen bonding interactions with the encapsulated sulfate.[9d]

Among the reported three examples of sulfate encapsulation with similar tris(urea) receptors, two are based on metal–organic framework,[9a,c,d] and third one is purely organic based.[9b] Encapsulation of sulfate in our work (*i.e.* receptor to anion binding 2 : 1)

Table 2 Intermolecular C–H···O and C–H···F interactions in **1** with symmetry code

D–H···A	d(H···A)/Å	d(D···A)/Å	∠D–H–A/°
C28–H28A···O3[b]	2.19	3.116(3)	158
C28–H28B···O2[a]	2.23	3.162(3)	161
C32–H32A···O1[c]	2.35	3.305(3)	167
C32–H32B···F5[d]	2.51	3.185(3)	126

[a] x, y, z. [b] $-x, 1-y, 1-z$. [c] $-x, -y, 1-z$. [d] $x, y, 1+z$.

Table 3 Hydrogen bonding parameters in complex **2** with symmetry code

D–H···A	d(H···A)/Å	d(D···A)/Å	∠D–H–A/°
N2′–H2C···O5	2.21 (5)	2.892 (7)	143 (5)
N2–H2C···O4[a]	2.26 (5)	3.034 (6)	163 (5)
N3–H3C···O6	2.13 (5)	2.905 (6)	168 (4)
N3′–H3C···O6[a]	2.12 (5)	2.880 (6)	164 (4)
N4′–H4C···O5	2.16 (5)	2.958 (6)	171 (4)
N4–H4C···O5A	2.44 (5)	3.165 (6)	152 (4)
N5′–H5C···O4	2.07 (5)	2.778 (6)	158 (5)
N5–H5C···O6	2.32 (5)	3.001 (6)	153 (5)
N6′–H6C···O5	2.25 (4)	3.062 (6)	163 (4)
N6–H6C···O5A	2.14 (4)	2.962 (6)	164 (4)
N7–H7C···O4[a]	2.25 (5)	2.852 (6)	135 (4)
N7′–H7C···O5A	2.52 (5)	3.217 (6)	151 (4)
N7′–H7C···O5A[a]	2.13 (5)	2.851 (7)	156 (4)

[a] Atoms related by the symmetry code: $-x, y, 1/2-z$.

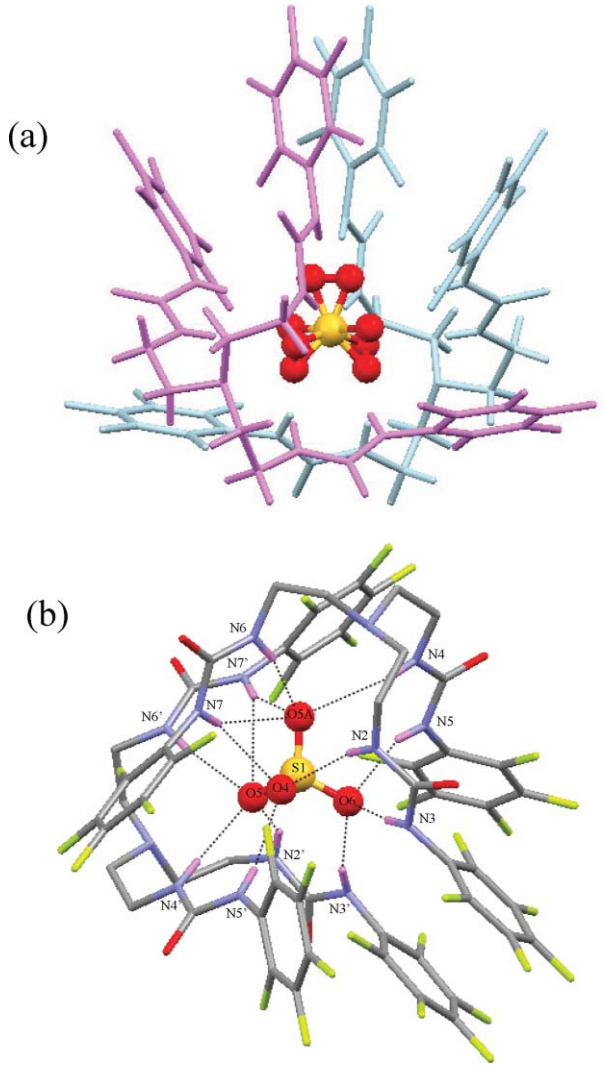


Fig. 3 (a) Crystal structure of **2**, showing two inversion related $\mathbf{L}^1$ molecules and encapsulated disordered sulfate ion. (b) Depiction of sulfate encapsulation by 14 hydrogen bonds (dashed lines) from six urea groups; yellow S, red O, and blue, N. The tetrabutylammonium cations and hydrogens other than urea groups are omitted for clarity.

Table 4 Intermolecular C–H···O and C–H···F interactions in complex **2** with symmetry code

D–H···A	d(H···A)/Å	d(D···A)/Å	∠D–H–A/°
C28–H28A···O1[a]	2.548	3.395 (4)	146.0
C36–H36A···O3[b]	2.386	3.296 (5)	156.2
C36–H36B···O1[a]	2.387	3.304 (4)	157.4
C41–H41B···O1[a]	2.405	3.267 (4)	147.8
C32–H32A···O2[c]	2.361	3.284 (5)	158.7
C28–H28B···O3[b]	2.574	3.473 (5)	154.1
C1–H1A···F11[d]	2.473	3.275 (5)	139.9

[a] x, 1-y, −1/2 + z. [b] −x, −1 + y, 1/2 − z. [c] 1/2 − x, −1/2 + y, 1/2 − z. [d] −x, 2 − y, 1 − z.

is also purely organic based but pattern is quite different from the reported work, which shows sulfate–water–sulfate encapsulation with the capsule of two receptor units (*i.e.* receptor to anion binding 1 : 1).[9b] Whereas, this encapsulation pattern is quite similar

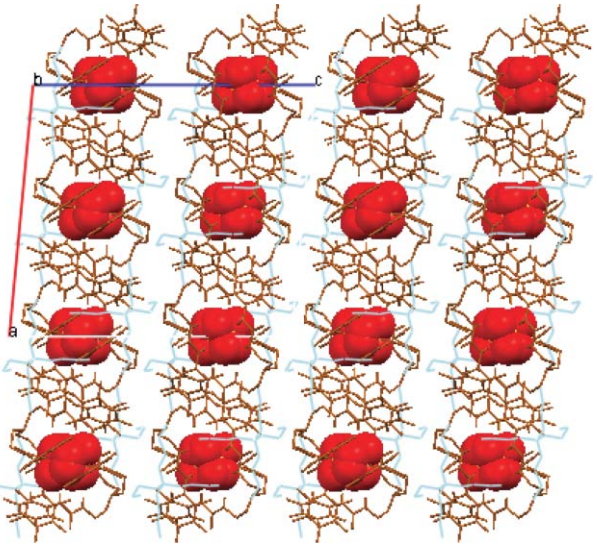


Fig. 4 A slice of the hydrogen-bonded framework obtained by the self assembly of anionic capsules along *b*-axis.

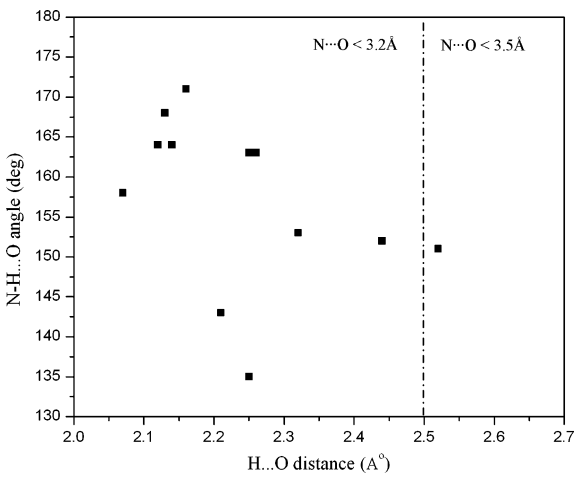


Fig. 5 The scatter plot of N–H···O angle *vs.* H···O distance of the hydrogen bonds in complex **2**.

to the reported metal–organic frameworks but packing of sulfate capsules in the crystal lattice are *via* C–H···O and C–H···F interactions generating H-bonded layers along *ac*-plane (Fig. 4 and Table 4). Table 4 also shows that there are three strong and two weak C–H···O interactions between urea oxygen atoms and methylene hydrogen of tetrabutylammonium cation along with one C–H···F interaction.

Halide binding studies in solution

The binding properties of $\mathbf{L}^1$ with halides in solution state are investigated by ^{1}H NMR experiments in DMSO-d_6 in the presence of various halides as their n-$Bu_4N^+X^-$ salts (where $X^- = F^-$, Cl^-, Br^- and I^-). Fig. 6 shows the chemical shift changes found by the addition of different halides to the urea ligand, $\mathbf{L}^1$ in DMSO-d_6. The most substantial changes are observed for the urea protons ($-NH_a$ and $-NH_b$), indicating that this urea –NH provides the sites of interaction between the ligand and the anions. The large

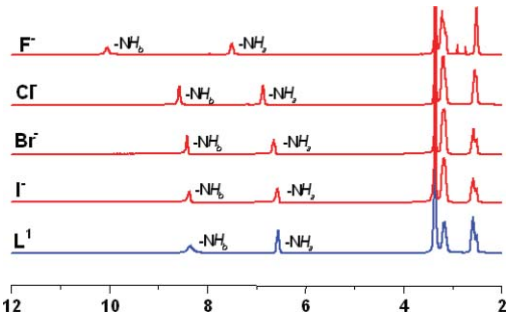


Fig. 6 Partial ^{1}H NMR spectra (300 MHz, DMSO-d_6, 298 K) of $\mathbf{L}^1$ and downfield shift of urea NH groups upon addition of F^-, Cl^-, Br^- and I^- as their tetrabutylammonium salts.

downfield shift of the urea protons $\Delta\delta$ –NH_a 0.681 and –NH_b 1.186 in the case of fluoride; $\Delta\delta$ –NH_a 0.307 and –NH_b 0.206 for chloride; $\Delta\delta$ –NH_a 0.106 and –NH_b 0.047 in the case of bromide are observed. There are no considerable changes in the chemical shift of the urea protons with iodide suggesting that the interaction of $\mathbf{L}^1$ with iodide is energetically unfavourable. Based on the relationship between the $\Delta\delta$ values for urea protons and the ionic radius of halides supports the most significant change is observed for the smallest anion, fluoride.

To evaluate the halide binding, ^{1}H-NMR titration is carried out with F^-, Cl^- and Br^- (Fig. 7). The titration curve gives the best fit for 1 : 1 binding model for host to guest, in agreement with Job plots indicating a maximum $\Delta\delta$ at 0.5 = $[L^1]/([L^1]+[A^-])$,† and the association constants are calculated using EQNMR.[23] The stability constant results evaluated are summarized in Table 5. The stability constant and change in free energy data show that $\mathbf{L}^1$ binds very strongly towards F^- than any other halides having log $K > 4.0$ M^{-1} (Table 5). However Cl^- also displays significant binding but Br^- has much weaker binding with $\mathbf{L}^1$ in DMSO-d_6.

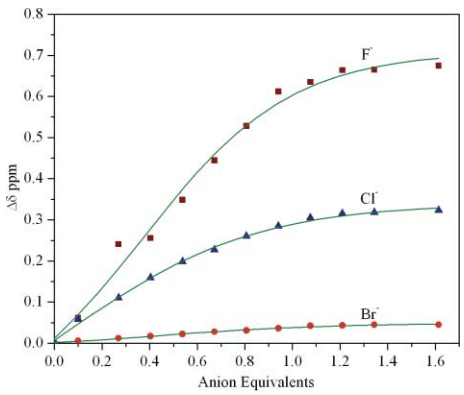


Fig. 7 Plot of change in chemical shift of the urea NH groups of $\mathbf{L}^1$ with increasing amounts of [n-$Bu_4N^+X^-$] in DMSO-d_6 at 298 K (X^- = F, Cl, and Br).

Table 5 Binding constants and free energy change of $\mathbf{L}^1$ with different halides in DMSO-d_6 at 25 °C

Anions	log K/M^{-1}	ΔG/kcal mol^{-1}
F^-	4.06	−5.5
Cl^-	3.42	−4.7
Br^-	1.27	−1.7
I^-	—	—

Therefore, with the increasing size/decreasing basicity of halides the association constant regularly diminishes. Our previous study on protonated pentafluorophenyl substituted tripodal amine receptor having tetrafluoroborate counter ions shows log K values 2.68 and 2.15 M^{-1} for Cl^- and Br^-, respectively, in same solvent system,[12a] indicative of relatively flexible nature of tripodal ammonium receptor as well as its functionality, which can assist to bind with larger guest, bromide with a higher binding constant compared to tripodal urea receptor where difference in binding constants with chloride and bromide is relatively large.

The ^{19}F-NMR spectra in DMSO-d_6 revealed that the encapsulation of fluoride anion might persist in solution too (Fig. 8). A free fluoride resonance for n-tetrabutylammonium fluoride in DMSO-d_6 appears at –98.04 ppm. The addition of $\mathbf{L}^1$ to the solution of tetrabutylammonium fluoride in DMSO-d_6 results in the downfield shift of ~5 ppm of free fluoride resonance indicating the participation of anion in hydrogen bonding with –N*H* of the receptor $\mathbf{L}^1$. The downfield shift observed here may be due to the deshielding effect caused by the ring currents of in-plane pentafluorophenyl units. In case of macrobicyclic amide receptor Bowman-James *et al.* have reported a larger down field shift of free fluoride signal about 8 ppm.[16b] Moreover, ^{19}F-NMR data of $\mathbf{L}^1$ shows three peaks at −163.024, −159.302 and −145.217 ppm corresponding to the fluorine signals of –C_6F_5 unit whereas $\mathbf{L}^1$ in presence of tetrabutylammonium fluoride shows appreciable changes in the –C_6F_5 signal pattern (peaks at −164.182, −146.187 and −141.502).† This may be attributed due to the existence of C–F ··· F–C interaction in the solution state as observed in the crystal structure.

Oxyanion binding studies in solution

In our earlier communication, solution state binding properties of $\mathbf{L}^1$ with $H_2PO_4^-$ and other oxyanions such as CH_3COO^-, NO_3^-, ClO_4^- are reported by ^{1}H-NMR titration experiments in DMSO-d_6.[12b] The binding properties of $\mathbf{L}^1$ with sulfate in solution state is investigated by ^{1}H NMR experiments in DMSO-d_6 in the presence of (n-$Bu_4N^+)_2SO_4^{2-}$. Fig. 9 shows the chemical shift changes found by the addition of different oxyanions to the urea ligand, $\mathbf{L}^1$ in DMSO-d_6. The large downfield shift of the urea protons $\Delta\delta$ –NH_a 1.256 and –NH_b 1.943 ppm in the case of acetate; $\Delta\delta$ –NH_a 0.870 and –NH_b 0.508 ppm for sulfate; in the case of phosphate both the –NH peaks are broad and there are upfield shift of –NH_a resonance by 0.441 ppm and –NH_b resonance show 0.611 ppm downfield shifts, whereas no shift is observed for NO_3^- and ClO_4^- anions. The opposite nature of –NH_a resonance in case of phosphate suggests that this anion bind with the receptor predominatly by the –NH_b, the upfield shift of the –NH_a protons caused presumably due to either desolvation effect as DMSO is displaced from the cavity by the anion or a conformational change in the receptor.[26] The –NH peaks shifts by AcO^-, SO_4^{2-} and H_2PO4^- are characteristic to differentiate each others in solution.

^{1}H-NMR titrations for these three oxyanions are carried out to evaluate the binding constants and stoichiometry. The addition of aliquots of n-tetrabutylammonium salts of SO_4^{2-}, $H_2PO_4^-$ and CH_3COO^- to the solutions of the receptor led to the best fit for 1 : 1 stoichiometry of host to guest,[12b] in agreement with the Job plots in cases of $H_2PO_4^-$ and CH_3COO^- whereas best fit for 1 : 2

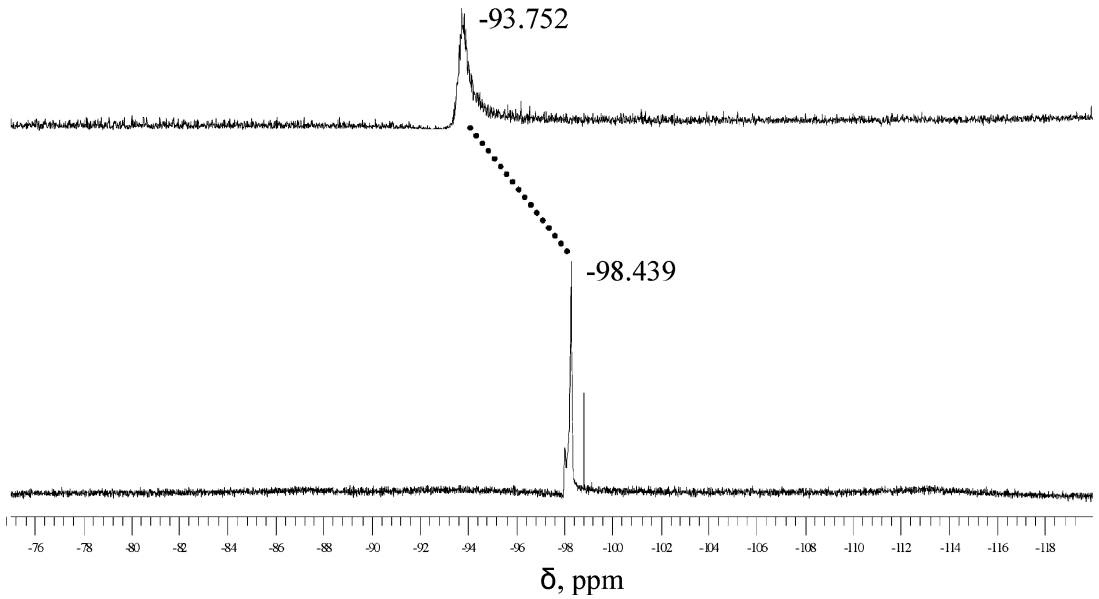


Fig. 8 Partial ^{19}F NMR spectra (500 MHz, DMSO-d_6, 298 K) of *n*-$Bu_4N^+F^-$ and downfield shift of F^- resonance upon addition of $\mathbf{L}^1$.

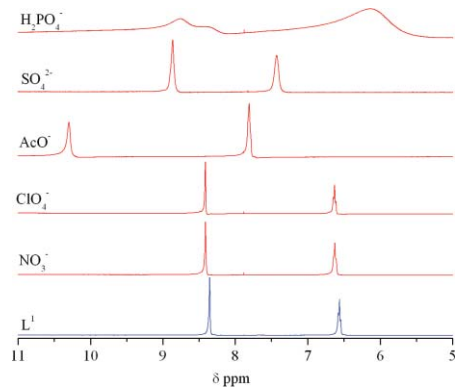


Fig. 9 Partial ^{1}H NMR spectra (300 MHz, DMSO-d_6, 298 K) of $\mathbf{L}^1$ and downfield shift of urea NH groups upon addition of NO_3^-, ClO_4^-, AcO^-, SO_4^{2-}, and $H_2PO_4^-$ as their tetrabutylammonium salts.

stoichiometry of guest to host, is observed in case of SO_4^{2-} binding (Fig. 10).†

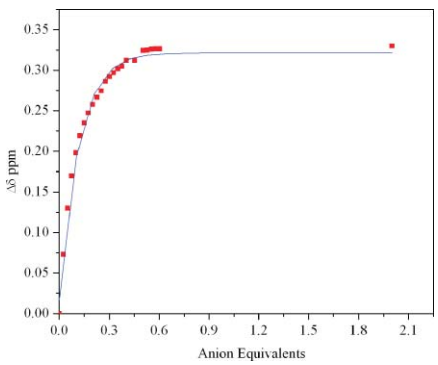


Fig. 10 Plot of change in chemical shift of the urea NH groups of $\mathbf{L}^1$ with increasing amounts of $[n\text{-}Bu_4N^+]_2SO_4^{2-}$ in DMSO-d_6 at 298 K.

The association constants (log *K* in M^{-1}) of $\mathbf{L}^1$ with SO_4^{2-}, $H_2PO_4^-$ and CH_3COO^- are 4.73 M^{-1}, 5.52 M^{-1} and 4.45 M^{-1}, respectively. Since complex **2** is also obtained upon treating $\mathbf{L}^1$ with tetrabutylammonim bisulfate, we have carried out ^{1}H-NMR titration experiments with this salt too. The mode of binding (1 : 2) and binding constant (4.77 M^{-1}) calculated using bisulfate salt are almost same as in the case of SO_4^{2-} binding.† These results indicate that in solution state also bisulfate converts to sulfate in our experimental conditions, support the solid state formation of complex **2** when $\mathbf{L}^1$ is treated either with tetrabutylammonium salt of SO_4^{2-} or HSO_4^-

The binding of $H_2PO_4^-$ to $\mathbf{L}^1$ is also followed by changes in the chemical shifts of ^{31}P NMR signals of *n*-$Bu_4N^+H_2PO_4^-$. The addition of $\mathbf{L}^1$ to a solution of *n*-$Bu_4N^+H_2PO_4^-$ in DMSO-d_6 showed a significant down field shift ($\Delta\delta$ = 8.33 ppm) in the ^{31}P resonances of the *n*-$Bu_4N^+H_2PO_4^-$ with respect to anion in the absence of the receptor (Fig. 11), indicating the formation of a strong complex between the anionic dihydrogenphosphate and the urea groups of the receptor.

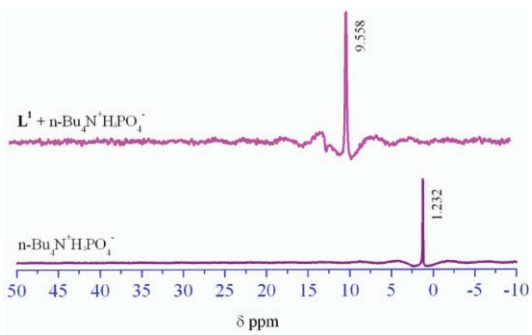


Fig. 11 Partial ^{31}P NMR spectra (500 MHz, DMSO-d_6, 298 K) of *n*-$Bu_4N^+H_2PO_4^-$ and downfield shift of ^{31}P resonance upon addition of $\mathbf{L}^1$.

Competitive binding studies of different anions

In our previous communication we have showed that selectivity of dihydrogenphosphate in presence of other oxyanions like NO_3^-, AcO^-, and ClO_4^- in DMSO-d_6.[12b] Herein we have accounted

a large spectrum of anions like all halides, above oxyanions along with sulfate for selectivity studies of **L**[1] in solution. Detailed ^{1}H-NMR titration experiments showed the binding order of different anions towards **L**[1] is $H_2PO_4^-$ > SO_4^{2-}> CH_3COO^- > F^- > Cl^- >> Br^- which supports Hofmeister-like response whereas there is no binding with I^-, NO_3^- and ClO_4^- guests. To probe the highest selectivity of **L**[1] towards $H_2PO_4^-$ over F^-, Cl^-, Br^-, I^-, AcO^-, ClO_4^-, NO_3^- and SO_4^{2-} we have carried out a series of ^{1}H-NMR experiments in the presence of multiple anions (Fig. 12). Fig. 12 shows the chemical shift changes in the urea protons (–NH_a and –NH_b) found by the addition of several combination of anions to the urea ligand, **L**[1] in DMSO-d_6. In case of the spectrum showed in Fig. 12b, the experiment is carried out upon addition of equivalent amount of tetrabutylammonium fluoride to the solution of **L**[1] containing chloride in DMSO-d_6. When fluoride salt is added to the **L**[1] solution in presence of chloride (with chemical shifts of urea protons $\Delta\delta$ –NH_a 0.307 and –NH_b 0.206 corresponds to chloride complex) shows the chemical shifts which matches with the complex **1**. This experiment indeed suggests the selectivity of **L**[1] to smallest anion, fluoride over chloride as well as other halides in the solution phase. Whereas, chemical shifts of urea protons of **L**[1] in presence of F^- or AcO^- changes to the value corresponds to that of SO_4^{2-} when tetrabutylammonium sulfate is added to the respective solutions (Fig. 12c and d) indicate the selectivity of sulfate over fluoride and acetate. Finally, when $H_2PO_4^-$ is added to the **L**[1] solution containing F^- and SO_4^{2-} or AcO^- and SO_4^{2-} or F^-, AcO^- and SO_4^{2-} chemical shifts of urea protons (Fig. 12e) are similar as observed in case of **L**[1] in presence of $H_2PO_4^-$ (Fig. 8) supports the highest selectivity of **L**[1] toward this particular oxyanion.

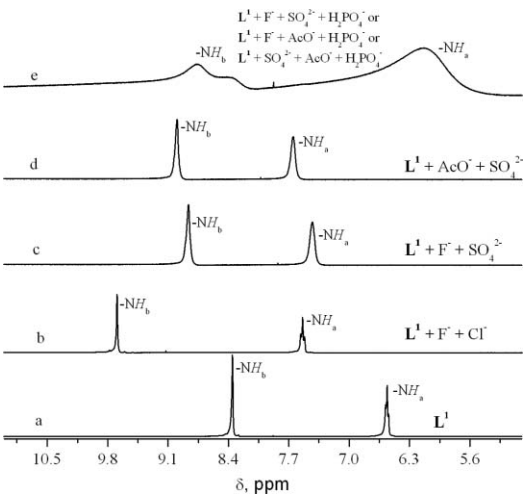


Fig. 12 Partial ^{1}H NMR spectra (300 MHz, DMSO-d_6, 298 K) of **L**[1] (a) and shift of urea NH groups upon addition of different combinations of anions as their tetrabutylammonium salts as mentioned in the individual spectra.

We have also performed crystallization from a mixture of anions to probe the selectivity in solid state too. We tried three different combinations which are: (i) **L**[1] in presence of tetrabutylammonium salt of fluoride and chloride which results fluoride complex **1**, (ii) **L**[1] in presence of tetrabutylammonium salt of fluoride and dihydrogenphosphate which results dihydrogenphosphate complex,[12b] and (iii) **L**[1] in presence of tetrabutylammonium salt of acetate, nitrate, perchlorate and dihydrogenphosphate, which also results dihydrogenphosphate complex.[12b] Therefore, both solution and solid state data confirms selectivity of **L**[1] toward dihydrogenphosphate over halides and other oxyanions.

Comparative studies of L[1] and L[2]

Literature report shows the binding constants for **L**[2] with SO_4^{2-} as bis(tetramethylammonium)sulfate and PO_4^{3-} as tris(tetramethylammonium)phosphate by ^{1}H-NMR titration, which are 3.48 M^{-1} and 4.04 M^{-1} in DMSO-d_6.[5] These data clearly indicate that **L**[1] binds to the phosphate or sulfate more strongly than **L**[2] in DMSO. The enhanced binding of these oxyanions in the case of **L**[1] may be attributed to the significantly more acidic nature of –NH in **L**[1], due to the electron withdrawing character of the $-C_6F_5$ units compared to $-C_6H_5$. In case of the anionic complexes of **L**[1] we have X-ray crystallographically shown the complete encapsulation of anionic guest inside the C_{3v} symmetric cleft where all the amide protons are directed towards the cavity. But no structural evidence of anion complex of **L**[2] is known till date. At this juncture, we tried to isolate single crystal of anion complexes of **L**[2]. In our repeated attempt to grow single crystals of **L**[2] receptor with above oxyanions or halides complexes is unsuccessful. We always isolated free **L**[2] as single crystal upon treating **L**[2] with tetrabutylammonium salt of different anions. This indicate in solution state **L**[2] might be in equilibrium with anion complex, which shows the shift in –NH resonance but in solid state complexes are not stable enough, resulting single crystals of **L**[2]. Both solution state and/or solid state studies also indicate the involvement of intermolecular C–F···F–C and C–F···H–C interactions between **L**[1] moieties in complexes **1**, **2** and reported dihydrogenphosphate complex.[12b] Further, $-C_6F_5$ moieties, which are arranged at the open side of the bowl shaped receptor, could facilitate the anion to encapsulate in the C_{3v} symmetric cavity of **L**[1] *via* electrostatic attraction. In case of non-fluorinated receptor, **L**[2], all the above interactions, electronegative effect, as well as positive cloud effect are not operative which justify our isolation of **L**[2] from its solution state anion complexes.

Conclusions

In conclusion, solution state studies on tren-based tripodal urea receptor **L**[1] shows strong binding affinity towards fluoride among halides. In cases of oxyanions binding order is $H_2PO_4^-$ > SO_4^{2-} > AcO^- and no binding is observed with ClO_4^- and NO_3^-. In solution SO_4^{2-} shows 1 : 2 guest to host binding whereas all other anions indicate 1 : 1 complex formation. Competitive ^{1}H-NMR experiments as well as ^{1}H-NMR titration data suggest selectivity order of **L**[1] towards different anions which follows the Hofmeister series like $H_2PO_4^-$ > SO_4^{2-}> CH_3COO^- > F^- > Cl^- >> Br^- and highly selective receptor for $H_2PO_4^-$. The pentafluorophenyl substituted tripodal receptor **L**[1] shows higher binding toward oxyanions than its non-fluorinated analogue **L**[2]. Further, single-crystal X-ray study confirms complete encapsulation of the fluoride ion in **L**[1] and supports 1 : 1 complex formation. This also represents first structural report on encapsulation of this ion in a tripodal system. In case of sulfate complex **2**, structural analysis shows the formation of a capsule, which confirms the solution state finding of 1 : 2 complex formations (SO_4^{2-} : **L**[1]). Anion encapsulation by **L**[1] tripodal receptor represents another

class of neutral system for recognition studies of spherical as well as oxyanions.

Acknowledgements

P. G. gratefully acknowledges the Department of Science and Technology (DST), New Delhi, India for financial support. Crystallography of complex **2** is performed at the DST-funded National Single-Crystal X-Ray Diffraction Facility at the Department of Inorganic Chemistry, IACS. The authors would like to acknowledge the NMR Research Centre, IISc Bangalore, India, for the ^{19}F-NMR analysis. PSL and MA would like to acknowledge CSIR, New Delhi, India for Senior Research Fellowship.

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