Trapped inorganic phosphate dimer†

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Single crystal X-ray crystallographic signature of the pentafluorophenyl substituted tripodal urea-based receptor shows formation of a pseudo dimeric cage which also encapsulates a phosphate dimer *via* numerous hydrogen bonding and anion···π interactions.

The design and syntheses of receptors for recognition and sensing of inorganic phosphate are of considerable current interest due to its biological and environmental importance.[1] Development of neutral receptors for this ion have been made by different laboratories using amide,[2] sulfonamide,[2a] ferrocene amide,[2e] urea,[3] pyrrole,[4a–c,f] indole,[4d] and carbazole,[4e] as recognition elements, other than ammonium-based,[5] and metal-based polyamine[6] receptors. For tetrahedral phosphate anion encapsulation, tripodal receptors, having complementary shape to this anion, were used to create a C_{3v} symmetric cavity.[2e,3a,c,6b] In 1995, Morán *et al.* demonstrated tris(2-aminoethyl)amine based urea receptor, $\mathbf{L^1}$ (Chart 1) for phosphate binding using ^{1}H-NMR study.[3a] In this study the authors proposed 1 : 1 complex formation upon binding of receptor and dihydrogen phosphate *via* six hydrogen bonds inside the cleft of C_{3v} symmetric cavity. Similar binding of $[H_2PO_4]^-$ with $\mathbf{L^2}\cdot H^+$ was also proposed by another group.[3c] Unfortunately, X-ray structures of $[H_2PO_4]^-$ bound to neutral receptor molecules are limited and none of this structure showed guest encapsulation inside the receptor cavity,[3d,4b,d] though $[SO_4{}^{2-}]$ encapsulation has been structurally demonstrated recently.[3e,f] As well as having enjoyed a rich history in bio-inorganic and medicinal chemistry, recent studies on the receptors containing fluorine substituted phenyl moiety have shown interesting binding properties with different anionic guests .[7,8] Herein, we report a new pentafluorophenyl substituted tripodal urea receptor, **L**, and its $H_2PO_4{}^-$ complex, **1**. Structural analysis shows the formation of a cage type dimer of **L** *via* different non-bonding interactions of pentafluorophenyl units. Further, two units of C_{3v} symmetric host **L**, encapsulate a dimer of $[H_2PO_4]^-$ as a guest *via* sixteen hydrogen bonding and two anion···π interactions.

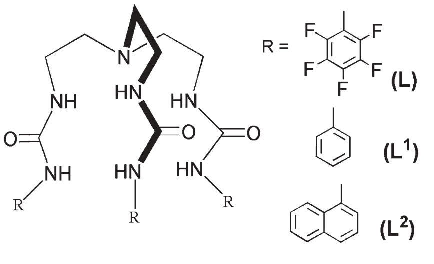

Chart 1 Tripodal urea having pentafluorophenyl substitution **L**, phenyl substitution $\mathbf{L^1}$, and napthyl substitution $\mathbf{L^2}$.

Tripodal urea-based receptor **L** is obtained by reaction between tris(2-aminoethyl)amine and 3 equiv. of pentafluorophenyl isocyanate in dry CH_2Cl_2 and crystals are grown from dimethylformamide (DMF)†. The crystals of complex $[\mathbf{L}(H_2PO_4)][N(Bu)_4]\cdot$DMF (**1**) are obtained upon reaction of **L** with tetrabutylammonium dihydrogen phosphate in DMF/MeCN (1 : 1) upon slow evaporation†. The structures of **L** and **1** have been determined by X-ray crystallography studies.‡ The crystal structure of **L** revealed that O3 of one arm is involved in two intramolecular N–H···O hydrogen bondings with diamide hydrogen H2C and H3C of another arm where H3C is involved in N–H···F interaction with the aryl fluorine atom F11 (Fig. 1).

Further two units of **L** are held together *via* intermolecular C–F···F–C and C–F···Cg (Cg1 and Cg1* represent centroid of $–C_6F_5$ units of two molecules) contacts forming a pseudo dimeric cage in the solid state (Fig. 1). In the dimeric ligand, F13/F13* from one unit of **L** is involved in a bifurcated, C–F···Cg (F13···Cg1*/F13*···Cg1 = 3.027 Å) and C–F···F–C (F13···F1*/F13*···F1 = 2.741 Å) interactions, whereas F2 is involved in C–F···F–C (F2···F9* = 2.753 Å) interaction with F9* of the other **L** unit and *vice versa*. Details of these H-bonding and non-bonding contacts are given in supporting information (Table 2S and 3S)†.

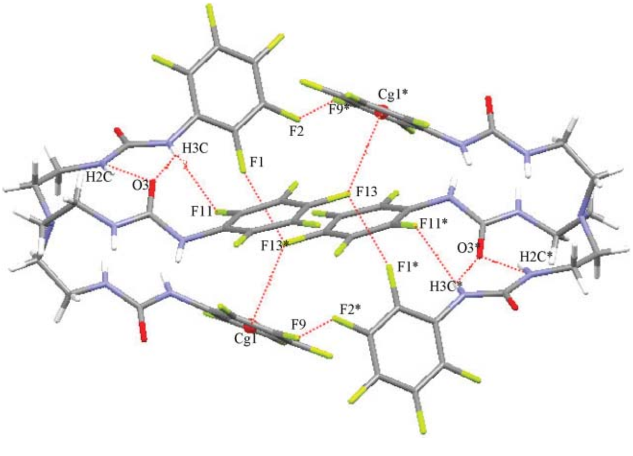

Fig. 1 Intramolcular N–H···O and N–H···F along with intermolecular C–F···Cg and C–F···F–C interactions in **L** showing the formation of a pseudo cage structure. The atoms flagged with an asterisk (*) are at equivalent position (−*x*, 2 − *y*, 1 − *z*).

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† Electronic supplementary information (ESI) available: synthesis and characterization of **L**, and complex **1**, along with the crystallographic data and CIF files for Ligand **L** and complex **1**, and ^{1}H-NMR titration details with anions and **L**. See DOI: 10.1039/b713365k

Complex **1** crystallizes in triclinic system with $P\bar{1}$ space group along with one DMF as solvent of crystallization. It is interesting to note that the $[H_2PO_4]^-$ is located inside the cleft of C_{3v} symmetric **L** (Fig. 2a). The encapsulated $[H_2PO_4]^-$ is oriented in such a way that H6D hydrogen of (O6) forming a strong hydrogen bond *via* O–H···O interaction with O7″ of the other encapsulated $[H_2PO_4]^-$ unit and H6D″ of this $[H_2PO_4]^-$ is further hydrogen bonded to O7 of the first $[H_2PO_4]^-$ unit, forming a hydrogen bonded centrosymmetric dimer of $[H_2PO_4]^-$, as depicted in Fig. 2b and 2c.

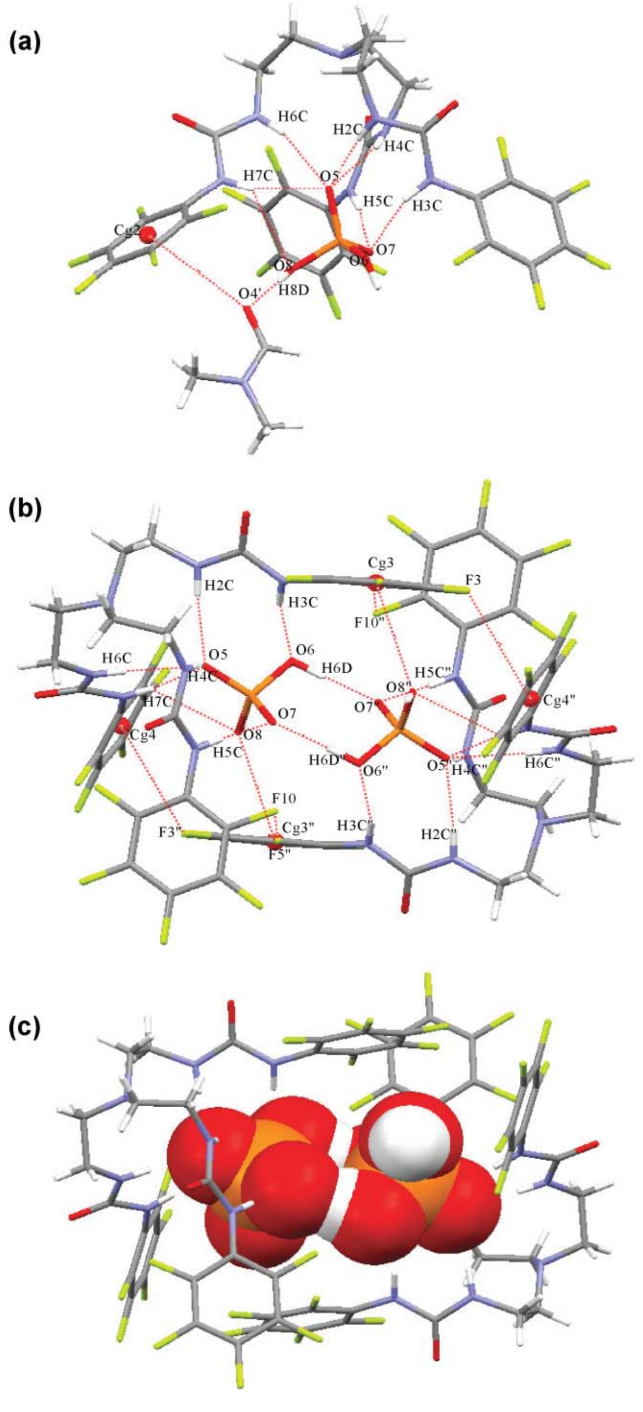

Fig. 2 Binding of (a) $H_2PO_4^-$ with **L**·DMF inside the C_{3v} symmetric cavity of **L**, single prime (′) character indicates that this atom is at equivalent position ($-1 + x,y,z$) (b) $H_2PO_4^-$ dimer inside the pseudo cage of dimer of **L**·DMF. DMF is omitted for clarity, the atoms flagged with a double prime (″) character are at equivalent position ($-x,1 - y,-z$) (c) Space filling presentation of dimeric $H_2PO_4^-$ inside the pseudo cage.

Fig. 2a shows that the $[H_2PO_4]^-$ is bound strongly *via* seven (N–H···O) hydrogen bonds with all three urea moieties of **L**. Thus O5 of $[H_2PO_4]^-$ is involved in four point contacts with the hydrogen atoms of urea, H2C, H4C, H6C and H7C where as H5C and H3C make contacts with O7 and O6 of the anion respectively. Further, H7C which is involved in H-bonding with the O5 makes an additional H-bonding contact with O8 *via* bifurcated N–H···O interaction. Subsequently, O8 also acts as a donor in O–H···O interaction with the lone pair of O4′ oxygen of the lattice DMF which further makes a contact with centroid of the tethered C_6F_5 arm (O4′···Cg2 = 3.474 Å). Thus the encapsulated $[H_2PO_4]^-$ is involved in eight hydrogen bonding interactions with **L**, in addition to the dimeric association among $[H_2PO_4]^-$ units. In biological systems, phosphate-binding proteins provide a classical example of higher coordination number as observed in **1**.[9] The binding of dimer of $[H_2PO_4]^-$ with the dimer of **L** (Fig. 2b) involves two additional intermolecular anion···π interactions. One –C_6F_5 unit of the phosphate encapsulated receptor **L** is making relatively closer approach towards O8 of the encapsulated $[H_2PO_4]^-$ guest of the other unit, making two intermolecular H–O···Cg contacts (Cg3···O8″/Cg3″···O8 = 3.420 Å) with a shortest distance C8···O8/O8″ = 3.002 Å where Cg3/Cg3″ is the centroid of the C_6F_5 ring C4–C9. Therefore, $[H_2PO_4]^-$ dimer is involved in altogether eighteen coordination with the dimer of **L**·DMF. Various hydrogen bonding interactions for the encapsulated dihydrogen phosphate anions with symmetry code are given in supporting information (Table 5S and 6S†). An earlier report on the crystal structure of an $[H_2PO_4]^-$ dimer binding with urea based ligand showed four coordination outside the receptor moiety which is the only urea-based structure known to date.[3d]

Detailed crystallographic analysis on **1** shows two other intermolecular C–F···Cg (F3″···Cg4/F3···Cg4″ = 3.545 Å with <C–F···Cg = 124.9°) and two C–F···F–C (F5···F10″/F5″···F10 = 2.872 Å) contacts with the associated dimer of **L**. These intermolecular interactions and intermolecular anion···π interactions might have also played a role for dimeric association of [**L**(H_2PO_4)·DMF] in solid state.

Solution state binding properties of **L** with $H_2PO_4^-$ and other oxyanions such as CH_3COO^-, NO_3^-, ClO_4^- are investigated by ^{1}H- NMR titration experiments in DMSO-d_6. The addition of aliquots of n-tetrabutyl ammonium salts of $H_2PO_4^-$ and CH_3COO^- to the solutions of the receptor led to the downfield shift of –NH resonance, whereas there is no considerable shift observed for nitrate and perchlorate anions. The titration data gave the best fit for 1 : 1 stoichiometry of host to guest, in agreement with the Job plots in cases of $H_2PO_4^-$ and CH_3COO^- (Fig. 3).

The association constants (log K in M^{-1}) of **L** with $H_2PO_4^-$ and CH_3COO^- are 5.52 and 4.45 M^{-1} respectively. Binding constants calculated for $\mathbf{L^1}$ with $H_2PO_4^-$ by ^{1}H-NMR titration is 4.04 M^{-1} whereas in case of $\mathbf{L^2}$ calculated binding constant using fluorescence titration is 4.60 M^{-1}. The receptor **L** binds $H_2PO_4^-$ more strongly than $\mathbf{L^1}$ or $\mathbf{L^2}$ in DMSO. The enhanced binding of $H_2PO_4^-$ in the case of **L** may be attributed to the significantly more acidic nature of –NH in **L**, due to the electron withdrawing

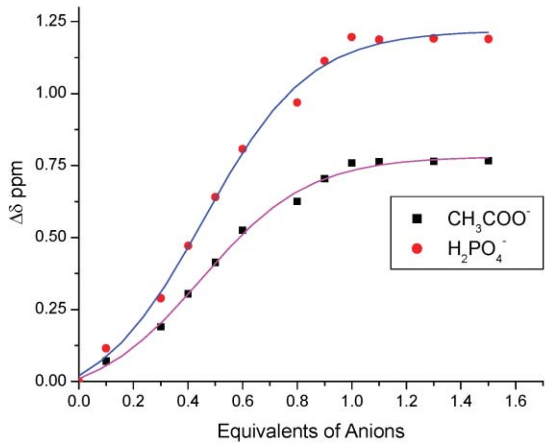

Fig. 3 Chemical shift of the –NH protons of **L** (20 mM) with increasing [n-$Bu_4N^+X^-$] in DMSO-d_6 (X^- = $H_2PO_4^-$, CH_3COO^-).

character of the –C_6F_5 units as well as additional coordination *via* anion···π interaction as observed in the crystal structure. Further, the highest selectivity of **L** towards the binding of $H_2PO_4^-$ over other anions like NO_3^-, ClO_4^- and CH_3COO^- is confirmed *via* a set of ^{1}H-NMR experiments in the presence of different combinations of these anionic mixtures in solution (supporting information Fig. 7S†). In the presence of anionic mixtures the ^{1}H-NMR spectra of **L** closely represent the ^{1}H-NMR spectrum of **L** in presence of $H_2PO_4^-$.

In conclusion, this is a new urea based tripodal anion receptor that shows a significantly high binding constant for dihydrogen phosphate. To the best of our knowledge, this is the first structural evidence of $H_2PO_4^-$ encapsulation inside the C_{3v} symmetric cavity of a neutral receptor. The present mode of encapsulation of dihydrogen phosphate has not been predicted theoretically nor previously reported experimentally. We are currently probing this tripodal urea receptor for encapsulation and binding of other anionic guests having different shapes and sizes.

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Notes and references

‡ Crystal data for **L**: $C_{27}H_{18}F_{15}N_7O_3$, M_r = 773.48, triclinic, space group $P\bar{1}$, a = 9.2984(10), b = 13.3540(14), c = 13.7161(14) Å, α = 118.317(2)°, β = 90.295(2)°, γ = 96.329(2)°, V = 1487.0(3) Å^{-3}, Z = 2, ρ_{calcd} = 1.728 g cm^{-3}, μ = 0.179 mm^{-1}, T = 100(2) K, $R1$ = 0.0582, w$R2$ = 0.1215, GOF = 1.081 $I > 2\ \sigma(I)$. Crystal data for **1**: $C_{46}H_{63}F_{15}N_9O_3P_1$, M_r = 1186.02, triclinic, space group $P\bar{1}$, a = 13.3363(11), b = 14.0385(11), c = 15.5942(13) Å, α = 99.391(2)°, β = 95.841(2)°, γ = 108.885(2)°, V = 2687.8(4) Å^{-3}, Z = 2, ρ_{calcd} = 1.465 g cm^{-3}, μ = 0.163 mm^{-1}, T = 100(2) K, $R1$ = 0.0640, w$R2$ = 0.1252, GOF = 1.117 I > 2 σ(I). CCDC-655559 (**L**), and CCDC-655560 (**1**). For crystallographic data in CIF or other electronic format see DOI: 10.1039/b713365k

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