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Synthesis and anion binding studies of tris(3-aminopropyl)amine-based tripodal urea and thiourea receptors: proton transfer-induced selectivity for hydrogen sulfate over sulfate†

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Tris(3-aminopropyl)amine-based tripodal urea and thiourea receptors, tris([(4-cyanophenyl)amino]propyl)-urea (**L1**) and tris([(4-cyanophenyl)amino]propyl)thiourea (**L2**), have been synthesized and their anion binding properties have been investigated for halides and oxoanions. As investigated by ^{1}H NMR titrations, each receptor binds an anion with a 1 : 1 stoichiometry *via* hydrogen-bonding interactions (NH···anion), showing the binding trend in the order of $F^- > H_2PO_4^- > HCO_3^- > HSO_4^- > CH_3COO^- > SO_4^{2-} > Cl^- > Br^- > I$ in DMSO-d_6. The interactions of the receptors were further studied by 2D NOESY, showing the loss of NOESY contacts of two NH resonances for the complexes of F^-, $H_2PO_4^-$, HCO_3^-, HSO_4^- or CH_3COO^- due to the strong NH···anion interactions. The observed higher binding affinity for HSO_4^- than SO_4^{2-} is attributed to the proton transfer from HSO_4^- to the central nitrogen of **L1** or **L2** which was also supported by the DFT calculations, leading to the secondary acid–base interactions. The thiourea receptor **L2** has a general trend to show a higher affinity for an anion as compared to the urea receptor **L1** for the corresponding anion in DMSO-d_6. In addition, the compound **L2** has been exploited for its extraction properties for fluoride in water using a liquid–liquid extraction technique, and the results indicate that the receptor effectively extracts fluoride from water showing *ca.* 99% efficiency (based on **L2**).

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Introduction

Anion coordination chemistry is a major area of research in supramolecular chemistry, since anions play critical roles in many biological, chemical and environmental applications.[1–7] As learned from nature, hydrogen-bonding interactions are key factors in controlling many important functions of biomolecules, *e.g.* information storage, signal transfer, replication and catalysis.[8] In order to understand and mimic the natural interactions involved in complex living systems, several types of neutral synthetic molecules including amides,[9] thioamides,[10] ureas,[11] thioureas,[12] pyrroles,[13] and indoles[14] have been broadly employed as effective receptors for a variety of anions in solution and solid state.

Among these various receptors that possess hydrogen bonding capabilities in anion binding *via* NH···anion interactions, urea-based receptors have received much attention recently, due to the acidic nature and directional properties of NH groups for anionic guests.[11a,15] An early example reported by Hamilton *et al.* demonstrated that a simple acyclic urea containing a single urea functionality showed an affinity for acetate ($K = 45\ M^{-1}$) in DMSO.[16] Fabbrizzi *et al.* synthesized a bis(4-nitrophenyl) urea receptor that formed a strong complex with fluoride ($K = 2.40 \times 10^7\ M^{-1}$) in CH_3CN.[17] Gale *et al.* developed a urea-based receptor linked with indole groups that formed a carbonate complex stabilized by NH donor groups from both indole and urea functional groups.[18] Johnson *et al.* reported a rigid dipodal urea linked with acetylene groups, which was shown to form a five-coordinate chloride complex.[19]

Recently, a number of urea- and thiourea-based receptors have been developed based on the use of tris(2-aminoethyl)-amine (tren) as a framework appended with different aromatic groups.[20,21] For example, a *m*-cyanophenyl-based tripodal urea reported by Custelcean *et al.* was shown to form a silver-based MOF that encapsulated sulfate by a total of twelve hydrogen bonds.[20a] Wu *et al.* reported a 3-pyridyl-based tripodal urea that also showed strong affinity for sulfate.[20b] Ghosh *et al.*

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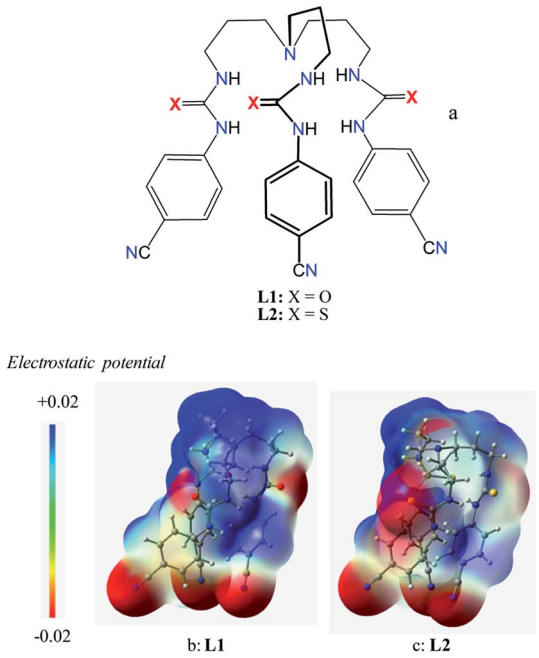
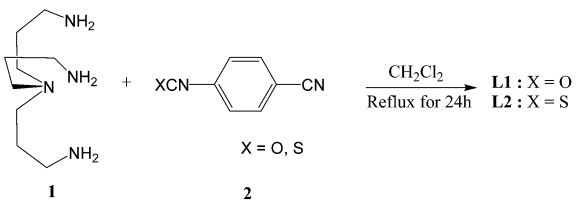
reported a pentafluorophenyl-based tripodal urea for the selective binding of phosphate.[20c] A *m*-nitrophenyl substituted tripodal urea synthesized by Das *et al.* was found to form capsular complexes with carbonate and sulfate.[20h] The progression from urea to thiourea leads to an enhanced acidity of a NH group in the later, thereby a thiourea could have a stronger affinity for an anion than its urea analogue.[22] Gale *et al.* reported a phenyl-based thiourea tripodal receptor that formed a carbonate complex from a mixture of the host with $[Et_4N]$-$[HCO_3]$.[21a] The compound was able to transport bicarbonate across lipid membranes. While fluorinated tripodal ureas and thioureas were shown to transport chloride anions through a lipid bilayer.[21b] In the case of *p*-fluorophenyl tripodal thiourea, an encapsulated chloride complex and a sulfate capsular complex were structurally characterized.[21b] A tren-based tris-(thiourea) receptor substituted with *p*-nitrophenyl groups was shown to form a rigid dimeric capsule with trivalent phosphate.[21c] Our group has recently reported a *p*-cyanophenyl tripodal urea for sulfate forming a seven coordinate sulfate complex.[23a] Further work on this receptor for halides has demonstrated the binding trend in the order of fluoride > chloride > bromide > iodide in solution.[23b] Ghosh *et al.* has recently reported that the thiourea analogue *p*-cyanophenyl tripodal receptor is capable of forming a 1 : 1 complex with fluoride and 2 : 1 complex with sulfate, showing moderate extraction efficiencies for fluoride and sulfate from aqueous solutions.[21d]

Our continued interests in the development of urea/thiourea-based anion receptors[24] have led us to use a slightly larger tripodal framework as tris(3-aminopropyl)amine linked with three *p*-cyanophenyl groups. Because of the longer chain in the propylene group as compared to the ethylene chain analogue, such receptors are expected to provide larger and flexible cavities; which could affect their selectivity patterns for an anion. The choice of cyanophenyl-substituted spacers was derived from their ability to act as electron-withdrawing groups, which was further supported by DFT calculations, showing the highest electron potential on cyano-groups. In particular, recent studies showed that the structural manipulation of simple receptors with variable lengths, sizes, functional groups and spacers can lead to selective binding of a particular anion.[15] Herein, we report the synthesis of two propylene-linked new receptors **L1** and **L2** (Scheme 1), and their comparative anion binding studies by ^{1}H NMR titrations and 2D NOESY experiments in DMSO-d_6, showing the unusual selectivity for hydrogen sulfate than sulfate. In addition, **L2** was further used for the extraction of fluoride in water using a liquid–liquid extraction technique.



Scheme 1 Schematic representation of chemical structures of **L1** and **L2** (a), and electrostatic potential map for **L1** (b) and **L2** (c) calculated at M06-2X/6-31G(d,p) level theory (red is negative potential and blue is positive potential).



Scheme 2 Synthetic pathway of **L1** and **L2**.

Results and discussion

Synthesis

The synthesis of **L1** (urea) and **L2** (thiourea) was accomplished from the reaction of tris(3-aminopropyl)amine (**1**) with three equivalents of 4-cyanophenyl isocyanate/isothiocyanate (**2**) in CH_2Cl_2 (Scheme 2), following the similar method as reported before for ethylene chain analogues.[23,24] In general, a higher yield was achieved for urea-based receptor (90%) than the thiourea-based receptor (73%). Attempts to obtain X-ray quality crystals of free receptors or anion complexes were unsuccessful.

NMR titration studies

The binding properties of the new receptors (**L1** and **L2**) for a number of anions including F^-, Cl^-, Br^-, I^-, ClO_4^-, NO_3^-, HSO_4^-, $H_2PO_4^-$, CH_3COO^-, HCO_3^- and SO_4^{2-} were investigated by ^{1}H NMR studies in DMSO-d_6. Initially, the anion binding abilities of **L1** and **L2** were screened by the addition of one equivalent of the respective anion to a host solution.

As shown in Fig. 1, two NH protons of urea group of **L1** appeared at 8.94 ppm (H1) and 6.37 ppm (H2). These protons shifted downfield after the addition of oxoanions including HSO_4^-, $H_2PO_4^-$, CH_3COO^-, HCO_3^- and SO_4^{2-}. However, no appreciable shift was observed in the presence of ClO_4^-, NO_3^-, Br^- and I^-. Among the all anions, the highest shift of NH's was observed for fluoride followed by $H_2PO_4^-$ and CH_3COO^-. The addition of F^- or $H_2PO_4^-$ to **L1** resulted in the broadening of NH peaks.[25] Such a significant downfield shift of both NH resonances for an anion is attributed to the direct involvement

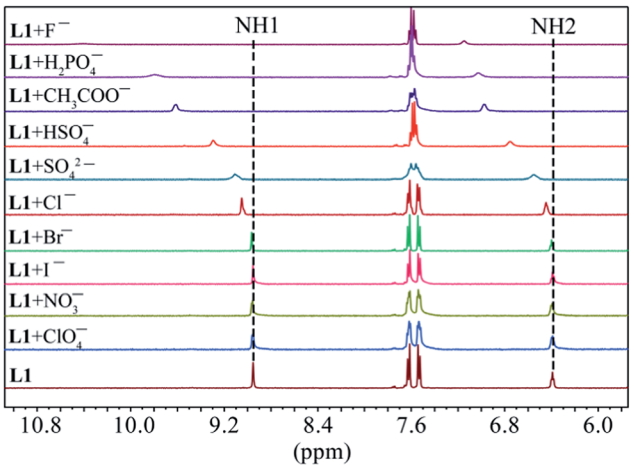


Fig. 1 Partial ^{1}H NMR spectra of **L1** (2 mM) in the presence of one equivalent of different anions in DMSO-d_6 (H1 = CONHAr, H2 = CH_2NHCO).

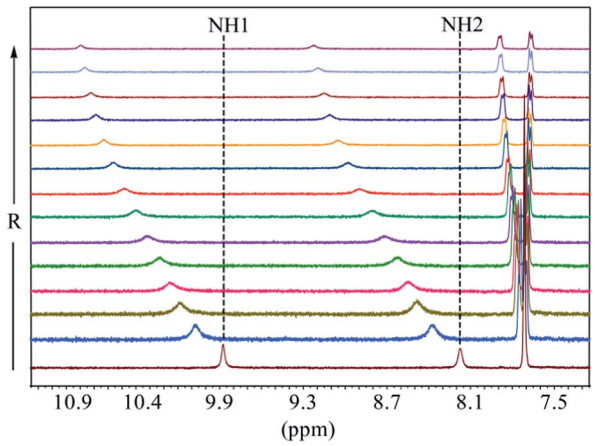


Fig. 3 Partial ^{1}H NMR titration of **L2** showing changes in the NH chemical shifts of the receptor with an increasing amount of HSO_4^- in DMSO-d_6. (H1 = CSNHAr and H2 = CH_2NHCS).

of the NH groups in anion binding *via* NH···anion interactions. For the thiourea-based receptor **L2**, two corresponding NH protons that appeared at 9.86 ppm (H1) and 8.17 ppm (H2) were also found to respond with different anions exhibiting the similar trend (Fig. 2) as observed for **L1** (Fig. 1). However, a higher downfield shift was observed for **L2** with oxoanions and halides as compared to **L1** with the corresponding anions. In the case of F^- and $H_2PO_4^-$ and HCO_3^- with **L2**, peak broadening of NHs occurred similar to that observed for **L1**.

The binding constants of **L1** and **L2** for different anions were measured by ^{1}H NMR titration experiments in DMSO-d_6. Fig. 3 shows a representative example of ^{1}H NMR titration spectra obtained from the incremental addition of hydrogen sulfate to **L2**, displaying a gradual shift change in both NH's resonances. The changes in the chemical shifts of NH's of **L1** or **L2** were plotted with an increasing amount of an anion, providing the best fit for a 1 : 1 binding model for the anions,[26] as shown in

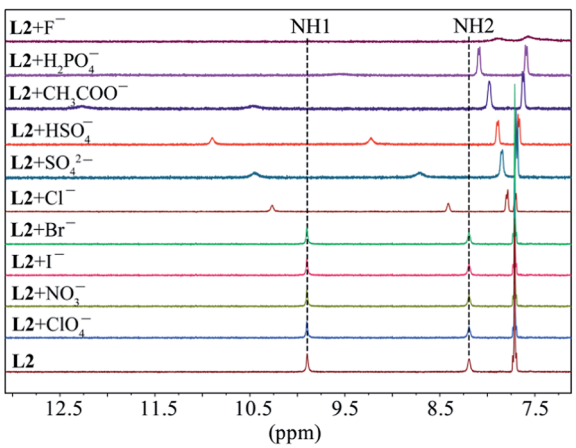


Fig. 2 Partial ^{1}H NMR spectra of **L2** (2 mM) in the presence of one equivalent of different anions in DMSO-d_6 (H1 = CSNHAr, H2 = CH_2NHCS).

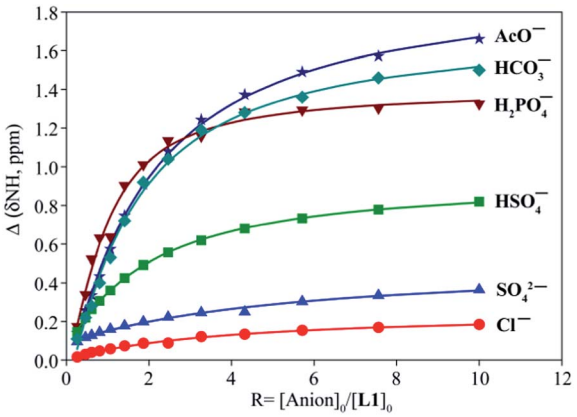


Fig. 4 ^{1}H NMR titration plot of changes in the NH (CH_2NHCO) chemical shifts of **L1** with an increasing amount of different anions in DMSO-d_6.

Fig. 4 for **L1** and Fig. 5 for **L2**. The 1 : 1 stoichiometry was further verified by a Job plot, showing a maximum at a 0.5 mole fraction for each anion (Fig. S30–35 in ESI†). Because of the peak broadening of NH's after the addition of F^- to both receptors, the binding constants for fluoride were determined from shift changes of aromatic CH protons (Fig. 6).

The binding constants of **L1** and **L2** for different anions determined from nonlinear regression analyses of chemical shift changes are listed in Table 1. An inspection of the binding data suggests that both receptors show a similar trend of binding for the investigated anions exhibiting the highest affinity for F^-. In general, the thiourea-based receptor **L2** exhibits higher affinity for an anion as compared to **L1**, which is due to the enhanced acidity of NHs in **L2** incorporated with thiourea groups, as expected.[12b] Both receptors, however, show negligible affinity for other halides. For oxoanions, the highest binding was achieved for $H_2PO_4^-$, followed by HSO_4^-, HCO_3^-, CH_3COO^- and SO_4^{2-}. The observed binding constants broadly reflect the influence of relative basicity of the anions.[27] However,

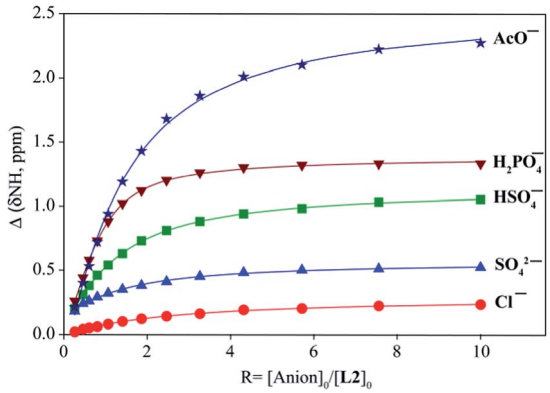


Fig. 5 ^{1}H NMR titration plot of changes in the NH (CH_2NHCS) chemical shifts of **L2** with an increasing amount of different anions in DMSO-d_6.

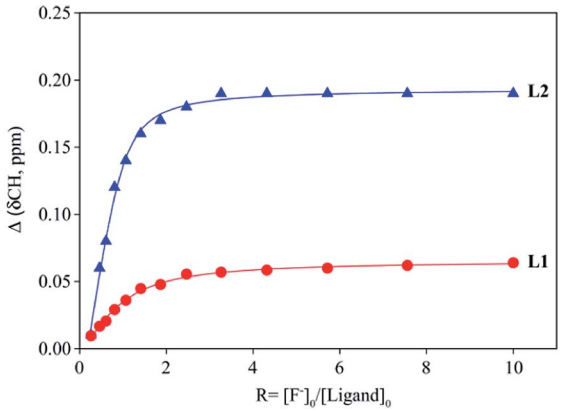


Fig. 6 ^{1}H NMR titration plot of changes in the aromatic CH chemical shifts (*CH*CNH) of **L1** and **L2** with an increasing amount of F^- in DMSO-d_6.

Table 1 Binding constants of **L1** and **L2** in DMSO-d_6

Anion	**L1** (log *K*)	**L2** (log *K*)
F^-	3.16	3.81
Cl^-	1.96	2.34
Br^-	1.75	[a]
I^-	<1	<1
$H_2PO_4^-$	3.02	3.35
HSO_4^-	2.56	2.82
SO_4^{2-}	1.61	1.89
CH_3COO^-	2.50	2.75
HCO_3^-	2.55	3.24
ClO_4^-	<1	<1
NO_3^-	<1	<1

[a] Chemical shift changes were too small to calculate the *K*.

the higher binding constants of both receptors for HSO_4^- as compared to the corresponding values for SO_4^{2-} were somewhat unanticipated, although SO_4^{2-} is more basic than HSO_4^- and has a higher charge. Such a discrepancy could be attributed to acid–base interactions of the central amine group of **L1** or **L2** with the acidic HO group of HSO_4^-,[28] providing a secondary interaction of $N^+\cdots H–O$ that was also verified by DFT calculations (discussed in later). Previously reported urea-based receptors linked with ethylene chains showed stronger binding for SO_4^{2-} than HSO_4^-, in DMSO-d_6.[20h,23a] Thus, the expansion of the tripodal cavity with propylene chains leads to the change of the selectivity patterns for HSO_4^- and SO_4^{2-}, showing greater selectivity for HSO_4^-. As compared to ethylene-chain analogues,[20h,23a,b] the propylene chains in **L1** and **L2** might result in the higher basicity of the central nitrogen, which could be due to the weaker inductive effect[29] of urea/thiourea groups through the longer propylene chains. Thus the central nitrogen can act as a base to transfer a proton from HSO_4^-. Both receptors showed higher binding for HCO_3^- as well, supporting this assumption. For highly basic acetate anion, the non-compliment shape of CH_3COO^- with the tripodal binding pocket might be a probable reason lowering the binding constant than that of $H_2PO_4^-$. In general, the propylene-based receptors showed lower binding affinity for anions as compared to ethylene-based analogues, which could be due to the flexible nature of the cavity and enhanced basicity of the central nitrogen in **L1** or **L2**.

NOESY NMR experiments

2D NOESY NMR experiments were performed to characterize the structures and conformational changes of the complexes in solution. Previous studies by us[23a,b] and others[20h] suggested that 2D NOESY NMR can effectively be used to evaluate the binding strength. In order to corroborate the data from NMR titrations, all 2D NOESY spectra were recorded for free **L1** and **L2** and their spectra were compared after the addition of one equivalent of the respective anions in DMSO-d_6 at room temperature (Fig. 7 and Fig. S36–55 in ESI†). The Fig. 7a and b show the NOESY NMR spectra of free **L1** and **L2**, respectively, each displaying a strong NH1⋯NH2 NOESY contact. After the addition of one equivalent of hydrogen sulfate, the NOESY contacts for both receptors completely disappeared (Fig. 7c and d), indicating the interactions of NHs with the added anion and a possible anion-induced conformational change of the receptors.[23a,30] Similar spectral changes in NOESY were previously reported for anion complexes with tren-based receptors by us,[23a,b] Schneider[30] and Das.[20h,21c] Indeed, both receptors show appreciable affinities for HSO_4^- as measured from ^{1}H NMR titrations in DMSO-d_6 (Table 1). We also observed a similar loss of NOESY signals for **L1** in the presence of certain anions including F^-, $H_2PO_4^-$, CH_3COO^- and SO_4^{2-}, and for **L2** in the presence of SO_4^{2-} (ESI†). However, the spotting of NH1⋯NH2 NOESY signals was hampered for **L2** in the presence of F^-, $H_2PO_4^-$ and CH_3COO^- due to the broadening of NH resonances of the receptor (ESI†). The addition of chloride or bromide to the receptors results in the weakening of NH1⋯NH2 NOESY signals. In contrast, the corresponding signals for both receptors were almost unchanged after the addition of one equivalent of I^-, NO_3^- and ClO_4^-. This observation suggests the absence of interactions of the NHs with added anions, which is in agreement with the results obtained from NMR titrations (Table 1).

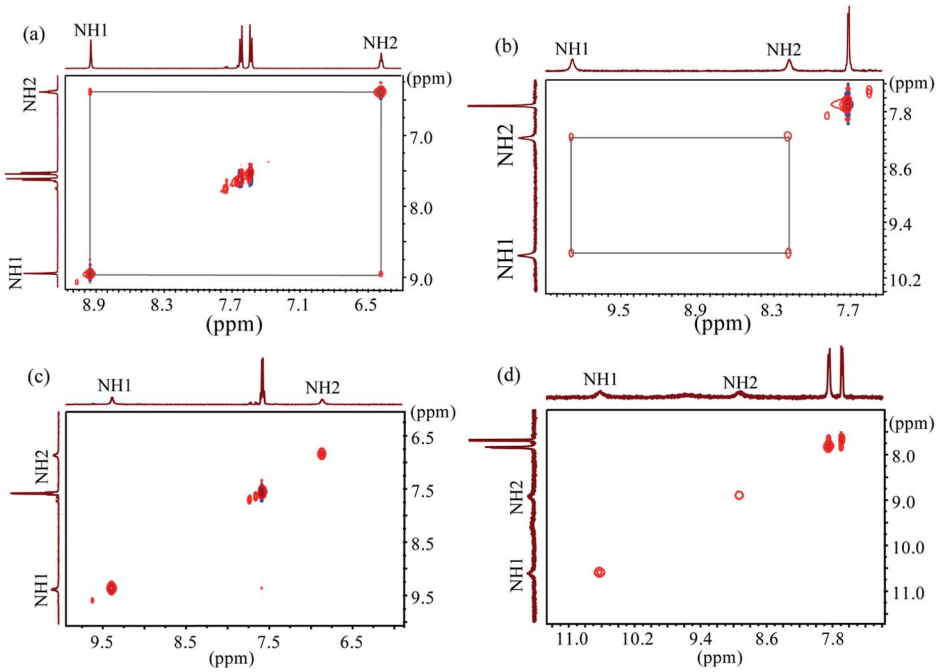


Fig. 7 2D NOESY NMR of (a) free **L1**, (b) free **L2**, (c) **L1** + HSO_4^- (1 eq.) and (d) **L2** + HSO_4^- (1 eq.) (H1 = ArN*H* and H2 = CH_2NH).

DFT calculations

In order to evaluate the binding discrepancies of the receptors for SO_4^{2-} and HSO_4^-, theoretical calculations were performed by density functional theory (DFT) with hybrid meta exchange-correlation functional M06-2X,[31] using the Gaussian 09 package of programs.[32] Molecular geometries were fully optimized without symmetry constraints at the M06-2X/6-31G(d,p) level of theory[33] in gas phase and also in a polarizable continuum model (PCM) solvent model to approximate a DMSO environment (dielectric constant = 46.8). The binding energies (ΔE) of **L1** and **L2** were calculated for SO_4^{2-} and HSO_4^-, using the equation: $\Delta E = E(\text{complex}) - E(\text{receptor}) - E(\text{anion})$. The results show that the binding energies ΔE of $[\mathbf{L1}(SO_4)]^{2-}$ and $[\mathbf{L1}(HSO_4)]^-$ are −173.0 and −74.4 kcal mol^{-1}, respectively in gas phase; while, as expected, the corresponding values are much lower in solvent phase, which are −42.1 and −37.8 kcal mol^{-1}, respectively. The higher binding energies for SO_4^{2-} is the effect of two charges on this anion as compared to one charge on HSO_4^-. On the other hand, the binding energies of $[\mathbf{L2}(SO_4)]^{2-}$ and $[\mathbf{L2}(HSO_4)]^-$ are −200.0 and −94.5 kcal mol^{-1}, respectively in gas phase. In solvent phase the ΔE of $[\mathbf{L2}(SO_4)]^{2-}$ and $[\mathbf{L2}(HSO_4)]^-$ are −55.5 and −47.4 kcal mol^{-1}. It is obvious that the binding energies of **L2** are higher for both anions than those of **L1**, agreeing with the trend of experimental binding constants obtained from ^1H NMR titrations (Table 1).

As shown in Scheme 1b and c, a strong electrostatic positive potential is created inside the cavities due to the presence of cyano-groups on aromatic rings, making them potential to host an anion. Fig. 8a and b show the optimized structures of the free receptors **L1** and **L2** in the solvent phase. For both cases, one NH group of an arm is hydrogen-bonded to oxygen/sulfate of another arm *via* NH···O/S interactions, thus creating a suitable cavity for guest. We previously observed similar hydrogen bonding interactions in a free *p*-cyanophenyl tripodal urea.[23a] The optimized structures of **L1** and **L2** complexes with SO_4^{2-} are shown in Fig. 9, while those with HSO_4^- are displayed in Fig. 10. The corresponding hydrogen bonding distances are listed in Table 2. It is noteworthy to mention that both receptors are deformed in order to interact with SO_4^{2-} or HSO_4^- through NH binding sites. In the sulfate complexes of **L1** and **L2**, one sulfate is encapsulated within the cavity *via* a total six NH···O bonds, exhibiting a 1 : 1 binding for each case. Such a binding mode is in consistence with that observed in solution binding studies in DMSO-d_6. Interestingly, in the optimized complexes with HSO_4^- as shown in Fig. 10, one proton from HSO_4^- is

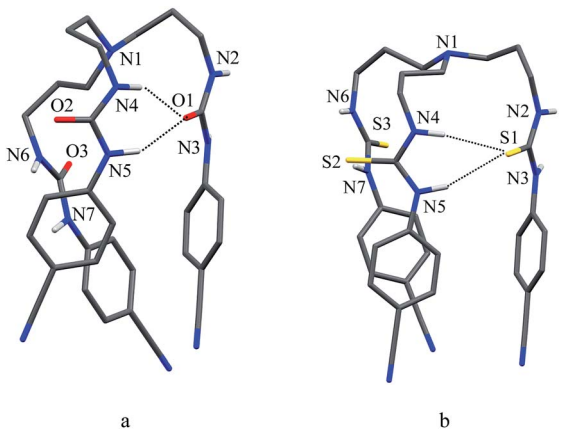


Fig. 8 Optimized structures of (a) **L1** and (b) **L2** calculated at the M06-2X/6-31G(d,p) level of theory.

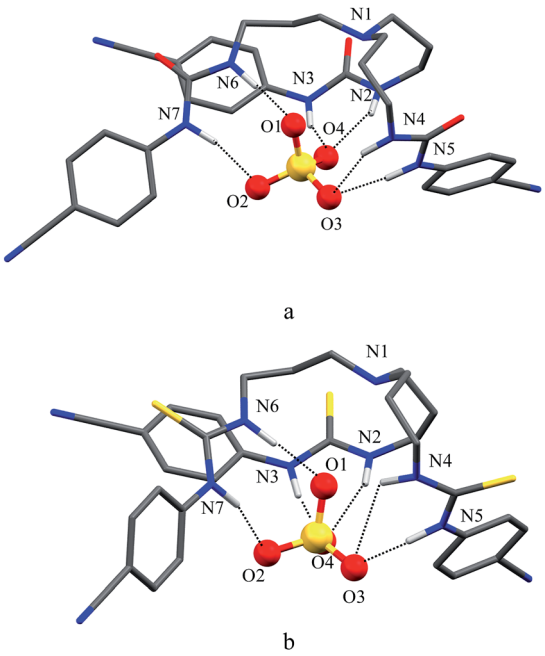


Fig. 9 Optimized structures of (a) $[\mathbf{L1}(SO_4)]^{2-}$ and (b) $[\mathbf{L2}(SO_4)]^{2-}$ calculated at the M06-2X/6-31G(d,p) level of theory.

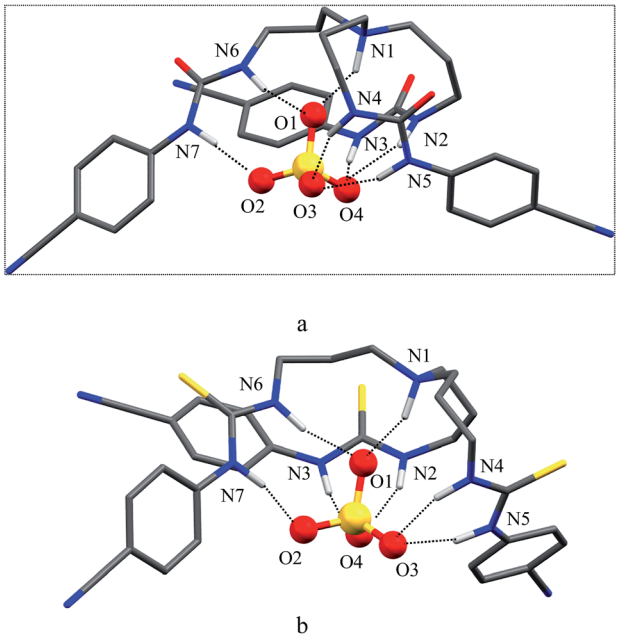


Fig. 10 Optimized structures of (a) $[\mathbf{L1}(HSO_4)]^{-}$ and (b) $[\mathbf{L2}(HSO_4)]^{-}$ calculated at the M06-2X/6-31G(d,p) level of theory.

transferred to the bridgehead nitrogen of **L1** or **L2**, providing an additional binding site as NH^+ to the receptor. Thus the anion is held *via* a total of seven NH···O bonds, supporting the higher binding for HSO_4^- determined in solution by ^1H NMR titrations. Such a proton transfer was previously observed experimentally[23a] as well as theoretically.[34]

Table 2 Hydrogen bonding interactions (Å, °) for the complexes of **L1** and **L2** with sulfate and hydrogen sulfate calculated with DFT at M06-2X/6-31G(d,p)

	L1		**L2**	
Complex	D–H···A	D···A (Å, °)	D–H···A	D···A (Å, °)
SO_4^{2-}	N2–H···O4	2.936	N2–H···O4	2.994
	N3–H···O4	2.758	N3–H···O4	2.742
	N4–H···O3	2.946	N4–H···O3	3.280
	N5–H···O3	2.962	N5–H···O3	2.785
	N6–H···O1	2.792	N6–H···O1	2.875
	N7–H···O2	2.937	N7–H···O2	2.827
HSO_4^-	N1–H···O1	2.738	N1–H···O1	2.705
	N2–H···O4	2.902	N2–H···O4	2.913
	N3–H···O4	2.835	N3–H···O4	2.813
	N4–H···O3	2.934	N4–H···O3	2.853
	N5–H···O3	2.902	N5–H···O3	2.854
	N6–H···O1	2.945	N6–H···O1	2.909
	N7–H···O2	2.812	N7–H···O2	2.819

Fluoride extraction studies

The fluoride extraction studies of **L2** were successfully performed by liquid–liquid extraction technique using tetrabutylammonium iodide as the anion exchanger and the phase transfer agent, following the methods reported previously.[21d,35] For a typical extraction experiment, distilled water solution (5 mL) of sodium fluoride (44.9 mg, 1 mmol) was added to the mixture of **L2** (66.89 mg, 0.1 mmol) and tetrabutylammonium iodide (36.94 mg, 0.1 mmol) in chloroform (5 mL). The biphasic solution was mixed for 3 hours, and the two layers formed were separated. After the evaporation of the organic phase, the white solid product was washed with diethyl ether to remove the remaining tetrabutylammonium iodide, and collected after drying. The extraction efficiency was calculated gravimetrically as 99%. Fig. 11 represents the comparative ^1H NMR spectra of the free receptor, extracted fluoride complex and **L2** in presence of one equivalent of $[n\text{-}Bu_4N]^+F^-$ in DMSO-d_6. The ^1H NMR spectra of the extracted fluoride complex shows broadening and

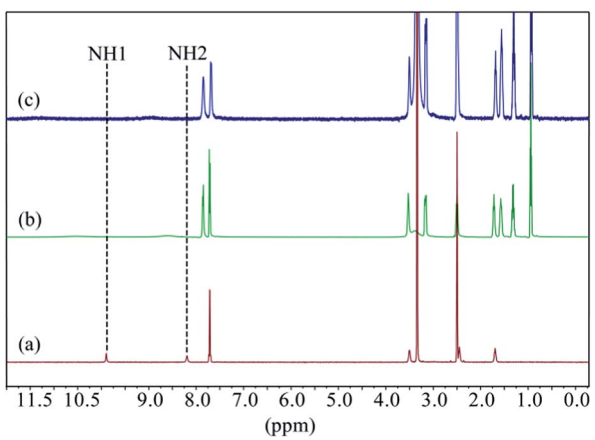


Fig. 11 Comparative ^1H NMR spectra of (a) **L2**, (b) extracted fluoride–**L2** complex, (c) **L2** in the presence of one equivalent of $[n\text{-}Bu_4N]^+F^-$ in DMSO-d_6. (H1 = CSN*H*Ar and H2 = CH_2N*H*CS).

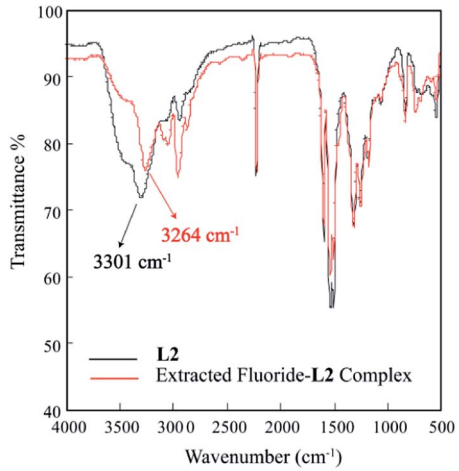


Fig. 12 Comparative FT-IR spectra of L2 (black) and extracted fluoride–L2 complex (red).

significant downfield shifting of NH peaks ($\Delta\delta = 0.67$ and 0.43 ppm) with respect to receptor **L2**, which is very similar to the one obtained after adding one equivalent of $[n\mathrm{Bu_4N}]^+\mathrm{F}^-$ to the receptor. This result clearly indicates the formation of fluoride complex after performing the liquid–liquid extraction by **L2**.

The solid state FT-IR analysis was also performed to examine the interactions of the receptor with fluoride in the extracted complex. The significant downward shift ($\Delta\nu_{(\mathrm{N-H})} = 37\ \mathrm{cm}^{-1}$) of broad NH's stretching frequency from 3301 cm^{-1} (**L2**) to 3264 cm^{-1} (extracted fluoride complex) was observed,[36] suggesting the strong N–H···F^- interactions between NH groups and the fluoride and ultimately deprotonation of the receptor by highly basic fluoride anion (Fig. 12).

Conclusions

In summary, we report two simple acyclic tripodal urea/thiourea-based receptors containing propylene chain-induced cavity, showing strong selectivity for fluoride and dihydrogen phosphate in DMSO-d_6. ^{1}H NMR titrations suggest that both receptors show a similar binding trend for investigated anions following the order of: $\mathrm{F}^- > \mathrm{H_2PO_4}^- > \mathrm{HCO_3}^- > \mathrm{HSO_4}^- > \mathrm{CH_3COO}^- > \mathrm{SO_4}^{2-} > \mathrm{Cl}^-$. Further 2D NOESY was used as a probe showing an obvious encapsulation of certain anions by the receptors *via* NH···anion interactions. Because of the enhanced acidity of NH's, the thiourea receptor showed higher binding affinity for anions as compared to the corresponding urea receptor. As opposed to the commonly observed binding trend for ethylene chain analogues[20h,23a] for $\mathrm{HSO_4}^-$ and $\mathrm{SO_4}^{2-}$, the present binding data suggests that the selectivity patterns of new tripodal receptors can be influenced by the chain length and cavity size, showing the higher binding constant for singly charged $\mathrm{HSO_4}^-$ than that for doubly charged $\mathrm{SO_4}^{2-}$. We assume that the higher binding affinity for $\mathrm{HSO_4}^-$ than $\mathrm{SO_4}^{2-}$ is due to the acid–base interactions[18] between the acidic $\mathrm{HSO_4}^-$ and the basic tertiary amine of urea/thiourea. This assumption was further supported by DFT calculations of the complexes with $\mathrm{HSO_4}^-$, revealing that a proton from $\mathrm{HSO_4}^-$ is transferred to the tertiary nitrogen of each receptor, providing an additional binding site to a receptor. Further, the thiourea-based receptor has successfully been used for liquid–liquid extraction of biologically and environmentally important fluoride anion from aqueous phase with high efficiency.

Experimental

General

All reagents and solvents were purchased as reagent grade and were used without further purification. Nuclear magnetic resonance (NMR) spectra were recorded on a Varian Unity INOVA 500 FT-NMR. Chemical shifts for samples were measured in DMSO-d_6 and calibrated against sodium salt of 3-(trimethylsilyl) propionic-2,2,3,3-d_4 acid (TSP) as an external reference in a sealed capillary tube. NMR data were processed and analyzed with MestReNova Version 6.1.1-6384. The IR spectra was recorded on a Perkin Elmer-Spectrum One FT-IR spectrometer with KBr disks in the range of 4000–400 cm^{-1}. The melting point was determined on a Mel-Temp (Electrothermal 120 VAC 50/60 Hz) melting point apparatus and was uncorrected. Mass spectral data were obtained at ESI-MS positive mode on a TSQ Quantum GC (Thermo Scientific). Elemental analysis was carried out by Columbia Analytical Services (Tucson, AZ 85714).

Synthesis

L1. Tris(3-aminopropyl)amine (526 μL, 2.52 mmol) was added to *p*-cyanophenyl isocyanate (1.12 g, 7.57 mmol) in dichloromethane (400 mL) at room temperature under constant stirring. The mixture was refluxed for 24 hours. A white precipitate formed and was collected by filtration. The residue was washed with dichloromethane and dried under vacuum for overnight to give the tripodal host (**L1**). Yield: 1.40 g, 90%. ^{1}H NMR (500 MHz, DMSO-d_6, TSP): δ 8.94 (s, 3H, Ar-N*H*), 7.62 (d, J = 8.50 Hz, 6H, Ar*H*), 7.53 (d, J = 8.55 Hz, 6H, Ar*H*), 6.37 (s, 3H, $\mathrm{CH_2NH}$), 3.10 (m, J = 6.20 Hz, 6H, $\mathrm{NHCH_2}$), 2.38 (t, J = 6.68 Hz, 6H, $\mathrm{NCH_2}$), 1.56 (m, J = 6.68 Hz, 6H, $\mathrm{CH_2CH_2CH_2}$). ^{13}C NMR (125 MHz, DMSO-d_6): δ 155.32 (C=O), 145.38 (Ar-*C*), 133.77 (Ar-*C*H), 119.62 (Ar-*C*N), 117.88 (Ar-*C*H), 102.96 (Ar*C*-CN), 51.38 ($\mathrm{NHCH_2}$), 37.92 ($\mathrm{NCH_2}$), 27.68 ($\mathrm{CH_2CH_2CH_2}$). ESI-MS (+ve): m/z 620.4 $[\mathrm{M}]^+$. Mp: 210–211 °C. Anal. calcd for $\mathrm{C_{33}H_{36}N_{10}O_3}$: C, 63.86; H, 5.85; N, 22.57. Found: C, 63.91; H, 5.96; N, 22.59. IR frequencies (KBr): $\nu_{(\mathrm{N-H})}$ 3315 cm^{-1}; $\nu_{(\mathrm{CN})}$ 2207 cm^{-1}; $\nu_{(\mathrm{C=O})}$ 1225 cm^{-1}.

L2. Tris(3-aminopropyl)amine **1** (526 μL, 2.52 mmol) was added to *p*-cyanophenyl isothiocyanate (1.24 g, 7.57 mmol) in dichloromethane (400 mL) at room temperature under constant stirring. The mixture was refluxed for 24 hours. A white precipitate formed and was collected by filtration. The residue was washed with dichloromethane and dried under vacuum for overnight to give the tripodal host (**L2**). Yield: 1.24 g, 73%. ^{1}H NMR (500 MHz, DMSO-d_6, TSP): δ 9.86 (s, 3H, Ar-N*H*), 8.17 (s, 3H, $\mathrm{CH_2NH}$), 7.71 (s, 12H, Ar*H*), 3.51 (broad s, 6H, $\mathrm{NHCH_2}$), 2.45 (t, J = 6.97 Hz, 6H, $\mathrm{NCH_2}$), 1.70 (m, J_1 = 6.90 Hz, J_2 = 7.15 Hz, 6H, $\mathrm{CH_2CH_2CH_2}$). ^{13}C NMR (125 MHz, DMSO-d_6): δ 179.87

(*C*=S), 143.99 (Ar-*C*), 132.80 (Ar-*C*H), 121.21 (Ar-*C*N), 119.10 (Ar-*C*H), 104.58 (Ar*C*-CN), 51.06 (NH*C*H_2), 42.57 (N*C*H_2), 25.71 ($CH_2CH_2CH_2$). ESI-MS (+ve): *m*/*z* 668.7 $[M]^+$. Mp: 120 °C. Anal. calcd for $C_{33}H_{36}N_{10}S_3$: C, 59.25; H, 5.42; N, 20.94. Found: C, 59.31; H, 5.56; N, 20.98. IR frequencies (KBr): $\nu_{(N-H)}$ 3301 cm^{-1}; $\nu_{(CN)}$ 2231 cm^{-1}; $\nu_{(C=S)}$ 1176 cm^{-1}.

NMR binding studies

Binding constants were obtained by ^{1}H NMR titrations of **L1** and **L2** using$[n\text{-}Bu_4N]^+A$ (F^-, Cl^-, Br^-, I^-, ClO_4^-, NO_3^-, HSO_4^-, $H_2PO_4^-$, CH_3COO^-, HCO_3^- and SO_4^{2-}) in DMSO-d_6. Initial concentrations were $[host]_0$ = 2 mM, and $[anion]_0$ = 20 mM. Sodium salt of 3-(trimethylsilyl)-propionic-2,2,3,3-d_4 acid (TSP) in DMSO-d_6 was used as an external reference in a capillary tube. Each titration was performed by 13 measurements at room temperature. The association constant *K* was calculated by fitting of several independent NMR signals with a 1 : 1 association model using Sigma Plot software, from the following equations: $\Delta\delta = ([A]^0 + [\mathbf{L}]^0 + 1/K - (([A]^0 + [\mathbf{L}]^0 + 1/K)^2 - 4[\mathbf{L}]^0[A]^0)^{1/2})\Delta\delta_{max}/2[\mathbf{L}]^0$ (where, **L** = receptor and A = anion). Error limit in *K* was less that 10%.

DFT calculations

DFT calculations were performed using the M06-2X hybrid functional which incorporates an improved description of dispersion energies. From the equilibrium geometry, anion was added at the center of the receptor's cavity. The geometries of the anion–receptor complexes were then optimized at the M06-2X/6-31g(d,p) level of theory in gas phase and also in DMSO solvent (dielectric constant = 46.8). All the calculations were carried out using Gaussian 09 package of programs.[32]

Fluoride extraction studies

Distilled water solution (5 mL) of sodium fluoride (44.9 mg, 1 mmol) was added to the mixture of **L2** (66.89 mg, 0.1 mmol) and tetrabutylammonium iodide (36.94 mg, 0.1 mmol) in chloroform (5 mL). The biphasic solution was mixed for 3 hours. Then the two layers were separated. After solvent evaporation of the organic phase, the white solid product was washed with diethyl ether to remove the remaining tetrabutylammonium iodide, and collected after drying. Yield: 92.3 mg, 99%. ^{1}H NMR (500 MHz, DMSO-d_6, TSP): δ 10.53 (broad s, 3H, Ar-N*H*), 8.60 (broad s, 3H, CH_2N*H*), 7.85 (d, J = 8.10 Hz, 6H, Ar*H*), 7.71 (d, J = 8.65 Hz, 6H, Ar*H*), 3.53 (broad s, 6H, NHCH_2), 3.17 (t, J = 8.32 Hz, 8H, NC$H_2$$CH_2CH_2CH_3$), 2.50 (broad s, 6H, NC$H_2$), 1.72 (m, J = 6.65 Hz, 6H, $CH_2CH_2CH_2$), 1.57 (m, 8H, $NCH_2CH_2CH_2CH_3$), 1.32 (m, 8H, $NCH_2CH_2CH_2CH_3$), 0.94 (t, J = 7.32 Hz, 12H, NCH_2CH_2-CH_2CH_3). IR frequencies (KBr): $\nu_{(N-H)}$ 3264 cm^{-1}; $\nu_{(CN)}$ 2231 cm^{-1}; $\nu_{(C=S)}$ 1176 cm^{-1}.

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