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Recent developments in anion induced capsular self-assemblies

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This feature article covers recent developments in anion induced capsular self-assemblies, with particular focus on important reports from 2011-2013. Contemporary studies on the capsular binding of environmentally and biologically relevant anions in aqueous medium are described. Emerging reports of such systems reveal their potential utility towards various functional aspects like anion separation, CO₂ fixation, hydrated halide recognition and anion transportation. This article also highlights potential applications of anion induced molecular capsules.

1. Introduction

Non-covalent synthesis of supramolecular structures with an internal cavity to accommodate guest molecules has attracted much attention in recent times. This is because, these aggregates are important in molecular recognition, selective guest-inclusion and in the catalysis of specific reactions. In particular, anions have shown to be very versatile templates for the synthesis of a wide range of supramolecular assemblies over the last ten years. This article aims to present a comprehensive update on the most important reports on capsular recognition of anions published in the last few years. As a proceeding of our previous article, more importance will be given to studies in aqueous solvents and potential application towards environmental and industrial issues.

In recent times, new platforms are introduced to design synthetic receptors for capsular recognition of anions which will be a part of our discussion. Nature’s sulfate binding protein binds SO₄²⁻ in its synthetic pocket via neutral functionalities which indeed inspires researchers to design synthetic neutral receptors for capsular recognition of anions in highly competitive aqueous medium. Thus, special attentions are also directed towards recognition of anions in aqueous medium by capsular assemblies which may resemble to the natural-world. However, there are other systems for anion recognition studies in aqueous medium which are not included in this article.

One of the major reasons for global warming is due to the increase of CO₂ concentration in the atmosphere. Metal-organic frameworks (MOFs), organic cages, zeolites, amines etc. are widely explored for the removal and storage of CO₂. One of the possible remedies to control aerial CO₂ concentration is its chemical conversion to other species. Synthetic anion receptors are emerging to accomplish this purpose via CO₂ encapsulation from aerial CO₂. On the other hand, anions present in groundwater, specifically, few inorganic oxyanions can be toxic to the human health even at submicromolar concentrations. Removal of SO₄²⁻ from radioactive nuclear waste is essential for improved vitrification of the waste and excess SO₄²⁻ is also responsible for permanent hardness of water. Competitive crystallization technique or liquid-liquid anion exchange technology provides suitable strategy for SO₄²⁻ removal using synthesized anion receptors. Importance will be given to studies which have potential applications towards the above mentioned environmental and industrial issues. In that direction, interesting properties of capsular assemblies such as capsular binding of CO₃²⁻ via sequestration of aerial CO₂ and separation of SO₄²⁻ from water will be discussed in separate sections (Chart 1). Anion binding within covalent capsules and metal-coordinated capsules will not be the part of our discussion.

2. Anion induced dimeric capsular assembly

In this section, recent development of anion receptors on different platforms namely (i) tris(2-aminomethyl)amine (tren), (ii) rigid platforms like benzene, cyanuric acid, triazine and iii) macrocyclic backbone which are relevant in capsular assembly will be discussed.

2.1 TREN based tripodal anion receptors

Literature survey reveals tren scaffold based tripodal receptors are widely used in the formation of anion induced capsular assemblies. Straightforward synthesis of tren based receptors and their complementarity with certain class of anions make them...
attractive scaffolds in anion coordination chemistry. A recent review has elaborated the development of self-assembled capsules of tren based urea/thiourea receptors towards tetrahedral oxyanion recognition and their separation.\(^{27}\) Generally, tripodal ammonium and amide receptors on tren scaffold do not have the tendency to form capsular assembly upon anion binding.\(^{36}\)–\(^{40}\) We have extended our investigation on the solid and solution states binding properties of triprotonated tripodal amine 1 (Chart 2) with wide varieties of anions. Tripodal amine 1 has previously shown monotopic recognition of Cl\(^{-}\) and Br\(^{-}\) in its triprotonated state.\(^{41}\) Recently, it has been found that \([\text{H}_3\text{I}]^{3+}\) also shows monotopic F\(^{-}\) encapsulation via \(C_3N\)-symmetric cleft formation as usual for spherical anion (Fig. 1a).\(^{42}\) Interestingly, octahedral SiF\(_6^{2-}\) dianion induces dimeric capsule assembly of \([\text{H}_3\text{I}]^{3+}\) via multiple N-H–F and C-H–F interactions (Fig. 1b). Monotopic F\(^{-}\) encapsulation vs. SiF\(_6^{2-}\)- induced capsule assembly by \([\text{H}_3\text{I}]^{3+}\) could be due to the difference in charge and shape of the encapsulated guest. However, potentiometric titration of \([\text{H}_3\text{I}]^{3+}\) in MeOH/H\(_2\)O solvent shows high affinity towards more basic F\(^{-}\) and AcO\(^{-}\) over other anions.

Fig. 1 Single crystal X-ray structures of anion complexes of \([\text{H}_3\text{I}]^{3+}\) showing a) monotopic F\(^{-}\) encapsulation by \([\text{H}_3\text{I}]^{3+}\) and b) encapsulation of SiF\(_6^{2-}\) in the dimeric capsular assembly of \([\text{H}_3\text{I}]^{3+}\). Non-bonding hydrogens and lattice anions are omitted for clarity.

Sun and Singh have employed tren based extended tripod amide receptor 2 (Chart 2) towards solvent dependent reversible nitrate binding and dimeric capsule formation.\(^{43}\) Reaction of methanolic solution of 2 with aqueous HNO\(_3\) yields 2-HNO\(_3\), which is structurally characterised as a NO\(_3^-\) encapsulated complex of [H2I]\(^+\). Tris-amide 2 forms a mixture of NO\(_3^-\) complex of 2 and 3 upon treatment with HNO\(_3\) in methanol/chloroform binary solvent. On the contrary, when HNO\(_3\) is added to acetonitrile solution of 2, formation of 3-HNO\(_3\) is observed as evident from NMR and ESI-MS studies. Titration of 3-HNO\(_3\) in DMSO-\(d_6\) with less polar CDCl\(_3\) results the formation of homodimeric capsular assembly of 3 with release of NO\(_3^-\) as evident from \(^1\)H-NMR, ESI-MS studies (Chart 3). Upon lowering the solvent polarity, intramolecular H-bonding interactions between amide –NH and O atom of ortho-nitro group predominate over the interactions between amide and NO\(_3^-\), thus, facilitate the formation of a homodimer 3\(_2\) with the release of NO\(_3^-\). Evaporation of CDCl\(_3\) regenerates the NO\(_3^-\) encapsulated product 3-HNO\(_3\), which suggests the reversibility of the process. Interestingly, upon standing of DMSO/CHCl\(_3\) solution of 3-HNO\(_3\), formation of NO\(_3^-\) trapped self-assembled capsule, [NO\(_3^-\)H\(_2\)I\(_3^{-}\)]\(^2-\) is observed, which is described as a thermodynamically stable product.

Apart from the works by Sun and co-workers, Das et al. have reported halide induced dimeric capsular assembly of a tren based extended amide receptor 4 (Chart 2).\(^{44}\) They have designed tren scaffold based highly organized amide receptor 4 where the amide groups are placed far away from the bridgehead nitrogen. Upon protonation of the bridgehead nitrogen with HCl/HBr, dimeric capsular assembly of \([\text{H}_4\text{I}]^{+}\) is observed. Dimeric assemblies are found to encapsulate a halide-water cluster with the composition \([\text{X}_2(\text{HAO})_2]^{2-}\) (X= Cl\(^-\), Br\(^-\)) (Fig. 2a,b). Widely spaced amide groups in 4 are forced to bind planar parallelogram shaped \([\text{X}_2(\text{H}_{\text{X}}\text{O})_2]^2\) cluster rather than a single halide anion. Dimension of the capsular assemblies vary from 20.62 Å to 20.75 Å moving from smaller Cl\(^-\) to Br\(^-\) anion. Authors have claimed...
solution state existence of \([X_2(H_2O)_2]\) clusters by 2D-NOESY NMR, where strong NOE coupling between the amide NH and the encapsulated water is observed. However, \(I\) induces polymeric assembly of \([H_4I]\) with the rearrangement of \(C_{2v}\) conformation of the receptor. Squaramide functionalization on tren scaffold also results suitable receptors for different oxyanions in solution. Squaramide-based tripodal receptor 5 (Chart 2) forms the dimeric pseudo-capsular assembly with \(SO_4^{2-}\) (Fig. 3), where the \(SO_4^{2-}\) binding occurs in the cleft of 5 in 2:2 (host/guest) stoichiometry. Solution state selective binding of \(SO_4^{2-}\) is observed via 1:1 (host/guest) stoichiometry. \(^{35}\)

![Fig. 2 X-ray crystal structures of dimeric capsular assemblies of \([H_4I]\) showing encapsulation of a) \(([Cl_4(H_2O)_3]\) and b) \([Br_4(H_2O)_3]\) cluster. Non-bonding hydrogens are omitted for clarity.](Image 104x305 to 258x406)

![Fig. 3 View of binding of two \(SO_4^{2-}\) in the dimeric assembly of 5. Non-bonding hydrogens and counterions are omitted for clarity.](Image 321x535 to 558x741)

Tren based urea/thiourea receptors are the intriguing class of anion receptors, particularly, towards the tetrahedral oxyanions.\(^{37}\) Dimeric assembly of this class of receptors assisted by encapsulated tetrahedral anions is the most common feature observed in the reported anion complexes. From the first report of anion binding tren-based urea/thiourea receptors by Morán et al.\(^{38}\) many groups have established 2:1 (host/guest) complexation with tetrahedral oxyanions. Recently, Gale et al. have reported the solid and solution states anion binding affinity of a series of fluorinated tren based urea/thiourea receptors 6-13 (Chart 4) and also studied their transmembrane transport activity.\(^{47} \) Synthesis and anion binding studies of tren-urea 12 are well studied by our group previously.\(^{48-50}\) Structural analysis reveals tendency of the thiourea receptors to form dimeric capsular assembly upon tetrahedral anion encapsulation. Both the sulfate and phosphate complexes of thiourea 7 show \(SO_4^{2-}\) and \(PO_4^{3-}\) templated dimeric assemblies of the receptor (Fig. 4a,b).

Dimension of the dimeric capsules are quite similar, 10.06 Å for \(SO_4^{2-}\) and 10.03 Å for \(PO_4^{3-}\), as measured from the apical N···N distances. Tris-urea receptor 10 forms dimeric capsular assembly upon encapsulation of \(CO_3^{2-}\), which is similar to our previously reported \(CO_3^{2-}\) complex of 12 (Fig. 4c).\(^{30}\) Thiourea analogue of 10 i.e. 11 forms \(PO_4^{3-}\) templated dimeric capsular assembly of 10.13 Å (Fig. 4d). Single crystal X-ray structural analysis of phosphate complex of 13 shows encapsulation of two \(H_2PO_4\) anions in the pseudo-capsular assembly of 13 (Fig. 5a) like [(\(H_2PO_4\)\_12)]\(^{2-}\) via multiple N-H···O and anion–π interactions.\(^{48}\) Encapsulated \(H_2PO_4\) anions are hydrogen bonded to each other as that observed in case of [(\(H_2PO_4\)\_12)]\(^{2-}\). On the other hand, \(SO_4^{2-}\) encapsulation by 13 is found to be assisted by two tetrabutylammonium counterions along with the urea –NH group of 13 (Fig. 5b). All the receptors show strong binding with \(SO_4^{2-}\) (log \(K >10^4\)) in DMSO-d\(_6\)/0.5\%D\(_2\)O solvent with 1:1 host-guest stoichiometry as evident from \(^1H\)-NMR titration study. \(^{55}\) Dihydrogenphosphate also shows moderate binding affinities even in highly competitive solvent medium. All the tris-urea receptors show higher binding affinity than the corresponding more acidic thiourea receptor. Furthermore, the binding affinities of the receptors decrease with the addition of increasingly electron-withdrawing groups. This reverse trend is rationalised by favourable interaction of the more electron-withdrawing groups with polar DMSO-d\(_6\)/D\(_2\)O solvent mixture.

Our continuous investigation of anion binding properties of tris-urea 12 have resulted many interesting properties like \(H_2PO_4\)\(^-\) encapsulation,\(^{49}\) \(CO_3\) fixation\(^{50}\) etc. Phosphate selectivity pattern of 12 is also established by \(^1H\)-NMR titration study. Further we have demonstrated acid/base controllable capsular size modulation of phosphate capsules of 12.\(^{50}\) Crystallization of \(H_2PO_4\) complex with TBAOH results the formation of \(HPO_4^{2-}\) encapsulated tight dimeric capsular assembly of 12 (Fig. 6b). \(HPO_4^{2-}\) encapsulation in 12 is observed via fifteen hydrogen bonding interactions. Capsular size of \(HPO_4^{2-}⊂12\) is measured as 9.92 Å higher than \(CO_3^{2-}\) and \(SO_4^{2-}\) encapsulated capsules. Interestingly, \(H_2PO_4\) pseudo-capsule of 12 can be regenerated upon simple acid treatment of the \(HPO_4^{2-}⊂12\) capsule (Chart 5).
Capsular transformation of the phosphate capsules are corroborated by $^{31}$P-NMR in DMSO-d$_6$. H$_2$PO$_4^-$ complexation of 12 is demonstrated by 8.33 ppm ($\Delta \delta$) downfield shift in $^{31}$P resonance w.r.t the signal of free TBAH$_2$PO$_4$; whereas upon addition of 12 to 1:1 mixture of TBAOH and TBAH$_2$PO$_4$ results a downfield shift of 3.55 ppm ($\Delta \delta$) w.r.t 1:1 mixture of TBAOH and TBAH$_2$PO$_4$. Finally, the addition of perchloric acid to the above mixture shows regeneration of [H$_2$PO$_4$]$^{2-}$c$_{12}$ as revealed by $^{31}$P-NMR signal. We have also shown the first report of hydroxide (OH) encapsulation by tris-urea 12 upon reaction with TBACN. Hydroxide (OH) encapsulation in the dimeric pseudo-assembly of 12 is achieved by six N-H···O interactions in 2:2 (host/guest) stoichiometry (Fig. 6a). We have reasoned possible deprotonation of the acidic –NH proton by CN$^-$ followed by the encapsulation of a H$_2$O molecule in the tris-urea cavity of 12. Finally, in situ generation and the encapsulation of OH are explained by protonation of deprotonated 12 with H$_2$O molecule.

Kinetic and thermodynamic parameters of anion binding properties of 12 with different anions are demonstrated by ITC study in DMSO, which closely resemble with the $^1$H-NMR titration data.

Recently, we have explored tris-urea 12 towards the binding of environmentally relevant and toxic arsenate$^{51}$ in aqueous medium. Hydrogenarsenate (HAsO$_4^{2-}$) and hydrogenphosphate (HPO$_4^{2-}$) have remarkable similarity in terms of charge, thermodynamic radii, pK$_a$ values, and binding modes.$^{52}$ HAsO$_4^{2-}$ encapsulated complex of the tris-urea 12 is isolated by the reaction of 12, TBAI and Na$_3$HAsO$_4$ in DMSO/5%H$_2$O solvent mixture. HAsO$_4^{2-}$ is found to be encapsulated in the dimeric capsular assembly of 12 via eleven N-H···O and one O-H···O interactions (Fig. 6c).$^{53}$ Capsular dimension of HAsO$_4^{2-}$c$_{12}$ is similar to that of the HPO$_4^{2-}$c$_{12}$ capsule but higher than that of SO$_4^{2-}$c$_{12}$ and CO$_3^{2-}$c$_{12}$. HAsO$_4^{2-}$c$_{12}$ capsule represents the first example of the structural evidence of arsenate binding by any synthetic neutral anion receptor. Solution state selectivity of 12 towards HAsO$_4^{2-}$ is observed over HPO$_4^{2-}$, SO$_4^{2-}$ and CO$_3^{2-}$ in semi-aqueous solvent mixture [DMSO-d$_6$/D$_2$O (9:1, v/v)]. Thus, a general trend of dimeric pseudo-capsular vs capsular assembly formation is established for tris-urea 12 via uni-negative vs dinegative anion encapsulation respectively (Fig. 7).
Fig. 6 View of X-ray crystal structures of a) OH⊂12, b) HPO₄²⁻⊂12 and c) HAsO₄²⁻⊂12. Non-bonding hydrogens and countercations are omitted for clarity.

Presence of non fluorinated electron-withdrawing groups can also provide suitable anion receptors for capsular recognition of anions (Chart 6). Nitro-substituted urea/thiourea receptors on tren scaffold are reported for the encapsulation of various tetrahedral oxyanions. Thiourea receptor 15 is found to encapsulate PO₄³⁻ inside the π-stacked dimeric capsular assembly of 15 (Fig. 8a) via twelve strong hydrogen bonding interactions. Planar oxanion CO₃²⁻ also assists the formation of dimeric assembly of 15 (Fig. 8b) assembled by intermolecular C-H···O and C-H···S interactions. On the other hand, F⁻ and SO₄²⁻ lead to the formation of unimolecular capsules of 15 via the participation of external solvent/countercation, which will be discussed later. Interestingly, selective formation of PO₄³⁻⊂15 capsule is demonstrated in the presence of excess HSO₄⁻, HCO₃⁻, NO₃⁻, CH₃COO⁻, F⁻ and Cl⁻ by ¹H and ³¹P-NMR studies. ¹H-NMR titration study of 15 with H₂PO₄⁻ shows switching of the equilibrium from 1:2 to 2:1 (host/guest) stoichiometry upon gradual addition of H₂PO₄⁻. Chemical shift values of NH protons at 2:1 equilibrium closely resemble the ¹H-NMR spectrum of PO₄³⁻⊂15, which confirms the formation of PO₄³⁻⊂15 capsule in solution. Similarly, 2:1 (host/guest) stoichiometry is observed for HSO₄⁻. Both F⁻/Cl⁻ binds in 1:1 stoichiometry, whereas 1:2 binding pattern is observed of CH₃COO⁻. ¹H-NMR titration studies result the following trend of binding affinity: H₃PO₄⁻ >CH₃COO⁻ >F⁻ >HSO₄⁻ >Cl⁻. 3-nitro substituted urea receptor 16 also forms dimeric capsular assembly upon CO₃²⁻, SO₄²⁻ and HPO₄²⁻ encapsulation (Fig. 8c,d). CO₃²⁻ complexation study through the fixation of aerial CO₂ will be discussed later. ¹H-NMR titration studies have shown 1:1 binding of 16 with all the anions in DMSO-d₆ with the selectivity towards SO₄²⁻. Further, oxanion encapsulation by 16 is confirmed by 2D NOESY NMR. First example of thiosulfate (S₂O₃²⁻) encapsulation in the dimeric capsular assembly of a trisurea receptor 17 (Fig. 9a) have been reported by Das et al. Dimeric capsular assembly is also observed for the SO₄²⁻ complex of 17 (Fig. 9b). Solution state ¹H-NMR study of 17 shows selectivity for SO₄²⁻ over S₂O₃²⁻ in 1:1 (host/guest) stoichiometry. On the other hand, cyano terminal tris-urea receptor 18 fails to encapsulate anions as evident from the solid state structure from Cl⁻, Br⁻ and HSO₄⁻ complexes of [HI] ⁶¹ However, tris-urea 18 shows 1:1 binding with all the anions in DMSO-d₆ with high binding affinities for F⁻ (4.51) and SO₄²⁻ (4.70). We have established thiourea analogue, 19 towards efficient encapsulation of anions as determined by solid and solution state studies.
Solution state binding of 19 towards anions by ITC measurement in acetonitrile shows the selectivity towards F⁻ which is well supported by ¹H-NMR titration study in DMSO-d₆. Structural characterisation of SO₄²⁻ and CO₃²⁻ complexes reveal anion assisted dimeric assemblies of 19 with capsular and sandwich modes respectively (Fig. 10a). On the other hand, monoprotic encapsulation of spherical F⁻ is observed by 19 via six N-H···F interactions (Fig. 10b). Structural features of SO₄²⁻ complex and the liquid-liquid extraction of SO₄²⁻ by 19 will be discussed in section 5.2.

Recently, we have structurally demonstrated an interesting example of conformer discrimination of oxalate by two structurally analogous urea receptors 20 and 21. Oxalate (C₂O₄²⁻) complexes of tris-urea 20 and 21 obtained from DMSO/5% H₂O solvent show C₂O₄²⁻ assisted dimeric capsular assembly of the receptors in 2:1 (host/guest) stoichiometry. C₂O₄²⁻ encapsulation in both C₂O₄²⁻⊂20₂ and C₂O₄²⁻⊂21₂ are facilitated by twelve N-H···O interactions (Fig. 11 and 12). The geometry of the encapsulated C₂O₄²⁻ marks their conformational differences in the C₂O₄²⁻ capsules. Simplest dicarboxylate, C₂O₄²⁻ exists in two different conformer namely planar and staggered conformers with 2-6 kcal/mol rotational energy barriers. Although, staggered conformer is stable in solution, most of the structural reports reveal isolation of planar conformer. Receptor 20 shows encapsulation of staggered C₂O₄²⁻ conformer with 68.8° torsion angle in C₂O₄²⁻⊂20₂, whereas in C₂O₄²⁻⊂21₂, 21 encapsulates planar C₂O₄²⁻ conformer with 0.02° torsion angle (Fig. 11 and 12). Thus, by simply tuning the receptor functionality from –CN (20) to –F (21), discrimination of two C₂O₄²⁻ conformers is possible in the molecular capsular assembly. However, in solution 1:1 association is observed between 20/21 and C₂O₄²⁻ with high binding affinities (~10⁵) in DMSO-d₆/D₂O (9:1, v/v) solvent.
2.2 Tripodal anion receptors with rigid platforms

Apart from the flexible tren platform, rigid platforms like 1,3,5 trilalkyl benzene, triazine and cyanuric acid scaffolds are also emerging in the rapidly growing field of anion coordination chemistry. Anion assisted capsular assemblies of benzene based tripodal and hexapodal receptors till 2011 are discussed thoroughly in our previous article. In the next section, we will discuss the current reports on anion-induced capsular assemblies of systems based on such rigid platforms.

2.2.1 Tripodal receptors phenyl bridgehead

Anion assisted capsular assembly and disassembly processes of benzene platform based protonated benzimidazole receptors 24-26 (Chart 7) are reported by our group. Dimeric capsular assembly of tripotontated 24 is previously observed via encapsulation of nitrate-water cluster. Variation in anion dimensionality and the receptor functionality result the formation of different supramolecular architectures. Tripotontated receptor 24 forms a discrete staggered dimeric capsular assembly, templated by four CF₃COO⁻ and two water molecules via multiple N-H⁻·O and CH⁻·O interactions (Fig. 14b). Similarly, tripotontated form of 24 shows discrete dimeric capsular assembly stitched by six ClO₄⁻ and two encapsulated water molecules (Fig. 14a). Capsular dimension of the dimeric capsular assembly of [(H₃₂₄₃)(CF₃COO)₂(H₂O)₂]²⁻ and [(H₂₂₄₃)(ClO₄)·(H₂O)₂] are measured as 11.5 and 11.0 Å respectively. It is worth mentioning that [H₄₂₄₃]⁰ forms six nitrate-two water zipped discrete dimeric capsular assembly of dimension 11.14 Å. On the other hand, tripotontated receptor 25 shows polymeric assembly with NO₃⁻, ClO₄⁻ and I⁻, thus establish...
Benzene platform based neutral amide receptors have shown impart aqueous solubility, and the possibility of an ion binding in aqueous medium. Recently, we have shown NO$_3^-$ encapsulation in the presence of ClO$_4^-$ with a binding constant of $K = 10^{26}$ M$^{-1}$. The cooperative self-assembly of two molecules of analogues dipodal receptor $[H_2]$ is formed where two $[H_2]$···$HClO_4$ counterions and thus forms a heterotetrameric assembly.

Interestingly, when a mixture of tripodal receptor $[H_3]$ and two molecules of $[H_2]$ in the presence of ClO$_4^-$ is formed where two $[H_2]$···$HClO_4$ counterions and thus forms a heterotetrameric assembly.

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Fig. 15 X-ray crystal structures of a) \((\text{NO}_3)_2\subset\text{27}_2\), b) \([\text{F}_2(\text{H}_2\text{O})_4]\subset\text{28}_2\), c) \([\text{Cl}_2(\text{H}_2\text{O})_4]\subset\text{28}_2\) and d) \([\text{SiF}_6(\text{H}_2\text{O})_2]\subset\text{28}_2\). Non-bonding hydrogens, countercations and lattice solvents are omitted for clarity.

2.2.2 Tripodal receptors with cyanuric acid platform

Cyanuric acid platform is a hybrid system having the rigidity in platform like benzene and flexibility in side arms like tren. However, it is poorly explored unlike the other platforms.\(^{76,77}\) We have shown selective monotopic recognition of \(\text{F}^-\) in the \(\text{C}_{3v}\) symmetric cleft of a cyanuric acid platform based tris-amide receptor.\(^{78}\) On the other hand, urea-functionalization (Chart 8) on cyanuric acid platform prefers tetrahedral \(\text{SO}_4^{2-}\) anion which is established for tris-urea \(\text{30}\) via \(\text{SO}_4^{2-}\) encapsulated unimolecular capsule formation.\(^{79}\) Recently, we have shown \(\text{SO}_4^{2-}\) encapsulation in the staggered dimeric capsular assembly of cyan terminal tris-urea \(\text{31}\) (Fig. 16) via twelve N-H···O interactions.\(^{80}\) Thus, higher coordination number of \(\text{SO}_4^{2-}\) is furnished by either coordination from countercations in case of \(\text{30}\) or dimeric assembly of the receptor for \(\text{31}\). This observation encourages us to develop second generation hexaurea receptor \(\text{33}\) with six chelating urea groups, which eventually shows monotopic \(\text{SO}_4^{2-}\) encapsulation in its cavity by ten N-H···O interactions.

Fig. 16 View of \(\text{SO}_4^{2-}\) encapsulation in dimeric capsular assembly of \(\text{31}\). Non-bonding hydrogens, solvent and countercations are omitted for clarity.
2.3 Receptors with macrocyclic platforms

Macrocyclic platform based receptors such as resorcin[4]arenes are suitable for capsular recognition of anions, cations and also neutral molecules due to the presence of bowl-shape cavity and phenolic functions. In 2011, Paek and co-workers have reported synthesis of resorcin[4]arenes modified tetra-amidocavitand 34 (Chart 9) and studied the solution state dimeric capsular assembly with suitable anionic guests. Two monomeric units of 34 forms dimeric capsular assembly upon encapsulation of CH₃OSO₂⁻ and BF₄⁻, as evident from ¹H-NMR study in CD₂Cl₂ solvent. Monomeric unit of 34 in 2CH₃OSO₂⁻/BF₄⁻ capped capsules are held together by multiple intermolecular and intramolecular N-H···O interactions, as suggested by molecular modelling study. ¹H-NMR and 2D-DOSY NMR studies in CD₂Cl₂ with CH₃OSO₂⁻ and BF₄⁻ guests show slow guest exchange and encapsulation of two anionic guests in the dimeric capsular assembly, which is confirmed by diffusion coefficient value of the capsule. Dissociation of the capsule in CD₃OD and non-capsular pattern with carboxylates, halides, PF₆⁻ validate the necessity of proper solvent choice and host/guest complementarity towards dimeric capsule formation.

Rebek and co-workers have reported the encapsulation of a pair of ion-pair in a self assembled molecular capsule of fourteen components. Previously, neutral cylindrical capsule 35 (Chart 9) has reported for the encapsulation of two neutral molecule of picoline. Interestingly, upon addition of trifluoroacetic acid (TFA) and glycouril 36 (Chart 9) to the above assembly generates the extended assembly with composition 35-36:35. ¹H-NMR analysis of the assembly reveals significant downfield shift of the acidic proton (18.7 ppm), which actually suggests protonation of picoline nitrogen with TFA and thus, concomitant encapsulation of picoline-TFA ion pair. Further, ¹H/¹⁹F-DOSY NMR studies confirm guest encapsulated capsular assembly.

Very recently, hybrid squaramide-calix[4]arene regioisomers 37 and 38 (Chart 9) are reported for capsular dimerization assisted by spherical anion encapsulation. Both the distal isomer 37 and proximal isomer 38 form dimer capsular assemblies with spherical Br⁻ and Cl⁻ anion as suggested by ¹H-NMR, ESI-MS and molecular modelling studies. In addition, 38 shows dimeric capsular assemblies with planar oxyanions like nitrate and benzoate unlike 37. Presence of favourable intramolecular H-bonding interactions and greater complimentarity with planar guests facilitate the formation of dimeric capsules with nitrate and benzoate in case of 38. Electron rich tetrathiofulvalene-functionalised fluxional calix[4]pyrrole macrocycles are known to adopt unidirectional cone structure from thermodynamically stable 1,3-alternate conformation during anion complexation. Further, anion directed cone conformation can accommodate a cationic guest of suitable size. Based on this concept, Sessler et al. have demonstrated iodide (as TBA salt) assisted dimeric assembly of cone conformer of 39 (Chart 10), which completely encapsulates a bismethylpyridinium-functionalized calix[4]pyrrole (G1) cationic guest (Fig. 17). The self-assembled system functions as NAND logic gate, where the logic operations are triggered via changing the counterion inputs. Varying the counterion from TBA to TEA, dimeric assembly of 39 rearranges to a TEA encapsulated monomeric unit. Further, changing the anion from iodide to non coordinating tetrakis[bis(3,5-trifluoromethyl)phenyl]borate, formation of 1,3 alternate conformation of 39 with encapsulated G1 is observed. Further, the logic operations are nicely corroborated by UV-Vis spectral data.

Fig. 17 View of encapsulation of two G1 molecules in the dimeric capsular assembly of [I₃9]. Non-bonding hydrogens and lattice solvents are omitted for clarity.
Sessler et al. have reported construction of anion directed formation of supramolecular architectures with tetracationic imidazolium macrocycles.\textsuperscript{87} Complexation of 40 with dicarboxylate G2 (Chart 10) reveals stepwise formation of 1:1 (host/guest) complex to 2:3 (host/guest) adducts.\textsuperscript{88} This stepwise host/guest complexation is supported by job’s plot analysis of \(^1\)H-NMR titration data in DMSO-\(d_6\). Structural analysis shows the formation of a dimeric capsular assembly of the flexible macrocycle 40 with one encapsulated G2 (Fig. 18), while the remaining G2 binds outside. Although, the dimeric assembly is more like a pseudo-capsular assembly rather than a capsule.

Fig. 18 View of crystal structure of G2⊂38. Non-bonding hydrogens and outside G2 molecules are omitted for clarity.

Wang et al. have reported an interesting example of anion directed self-assembly of a oxacalix[2]arene[2]triazine receptor 41 (Chart 11) via anion-\(\pi\) interaction.\textsuperscript{89} Two molecules of 41 forms a dimeric assembly that encapsulates one \([\text{Cl}_4\text{H}_2\text{O}_2]\)^2- rectangular cluster via Cl···\(\pi\) (triazene), \(\pi\)-O-H (H\(\text{H}_2\text{O}\)) and Cl···H-O (H\(\text{H}_2\text{O}\)) interactions (Fig. 19a). Anion binding properties of 41 are monitored by fluorescence quenching emission upon addition of anion in acetonitrile. All the anions show 1:1 binding stoichiometry in solution. \(^1\)H-NMR studies with anions induce no noticeable changes, which further confirm binding mode via anion-\(\pi\) interactions. Recently, synthesis of a triazinonide based shape persistent tetrakisimidazolium macrocycle 42 (Chart 11) is described for anion recognition in water via fluorescence output.\textsuperscript{90} Fluorescence titration via emission enhancement results the selective binding of SO\(_4\)\(^-\) in water with very high binding constant (~10\(^{5}\)). Structural analysis of the crystals grown from a mixture of 42 and excess Na\(\text{SO}_4\) shows trapping of SO\(_4\)\(^-\) in the sandwich type dimeric assembly of 42 (Fig. 19b) via charge assisted strong C-H···O interactions. Further, the receptors in the sandwich assembly are held together via \(\pi\)-\(\pi\) stacking between the phenyl and the triazinonide rings.

Fig. 19 Crystal structures of a) [Cl\(_4\)H\(_2\)O\(_2\)]\(^2-\)⊂41 and b) SO\(_4\)\(^-\)⊂42. Non-bonding hydrogens and counterions are omitted for clarity.

Chart 12

3. Anion binding in unimolecular capsules

Construction of unimolecular capsule from a single receptor can be achieved by i) sealing the receptor cavity with anion, ii) binding of anion followed by intramolecular hydrogen bonding within the receptor, iii) stopping the anion encapsulated receptor with cation/solvent. Literature examples of above classes of unimolecular capsules reported by Atwood, Steed and our group are discussed in our previous article.\textsuperscript{29} Some recent reports of such single molecule capsules, aiming towards recognition of anion, mainly covers the last category of the above mentioned strategies.

Tren based L-alanine amino acid backboned electron-withdrawing group attached hexa-amide receptors 43-47 (Chart 12) are explored by our group towards anion binding.\textsuperscript{91} Appreciable binding between receptors and Cl\(^-\), AcO\(^-\), BzO\(^-\), HSO\(_4\)^- with 1:1 (host/guest) stoichiometry is revealed by detailed ITC studies. Furthermore, this class of receptors show selectivity towards AcO\(^-\) over other investigated anions. Solid state structural evidence of Cl\(^-\) complex of the pentafluorophenyl attached receptor 43 shows the formation of Cl\(^-\) encapsulated unimolecular capsule (Fig. 20). Cl\(^-\) is encapsulated in the C\(_{5v}\)-symmetric cleft of 43 by three N-H···Cl interactions. One tetra-butylammonium counterion seals the cavity of Cl⊂43 via C-H···O and C-H···F interactions with the receptor, thus, results the formation of an unimolecular capsule. Further the role of counterion in Cl\(^-\) binding is verified by solution state ITC experiments, by varying the counterion. In cases of all the hexa-amides higher binding affinity is measured for Cl\(^-\) with TBA counterions over TEA and TMA counterions, which further validates the cooperative effect of ion-pairing.
Halide recognition properties of tris-amide 48 (Chart 12) have been utilized towards liquid-liquid extraction of potassium fluoride/chloride via the formation of halide encapsulated 1D-polymeric assembly. Very recently, we have reported fluoride recognition properties of tris-amides 48 and 49 in solution and solid state structural studies. Structural analysis of both F− and Cl− complexes of 48 show the formation of F−/Cl− encapsulated unimolecular capsules (Fig. 21), where one chloroform molecule seals the capsular cavity. Encapsulated F− in F⊂48 is hydrogen bonded by three N−H···F interactions from amides and one C−H−F interactions from CHCl3 (Fig. 21a), whereas the Cl atoms of CHCl3 `cap’ are in short contact with the −C=O ring. Thus, a solvent capped F− encapsulated single molecule capsule of 48 is described by single crystal X-ray study. Similarly, ditopic recognition of Cl− and CHCl3 via three N−H−Cl and one C−H−Cl interactions via unimolecular capsule formation is observed in case of Cl⊂48 (Fig. 21b). Selective recognition of F− is established for both 48 and 49 in CDCl3 as determined by 1H-NMR titration study.

Apart from the amide receptors, few urea receptors are also accounted for anion recognition via unimolecular capsule formation. Das et al. have reported the formation of solvent/cation sealed unimolecular capsule of 15 (Fig. 22) toward the encapsulation of F− and SO42−.57 PO43− and CO32− induced dimeric capsule assemblies formation of 15 are already demonstrated in the section 2.1. Monotropic F− encapsulation in F⊂15 is facilitated by six N−H−F interactions with the urea groups of the tris-urea. Furthermore, one DMSO/CH3CN solvent seals the cavity via C−H−O interactions, leading toward the formation of F− bound unimolecular capsule (Fig. 22a) in both the cases. SO42− encapsulation in 15 is assisted by nine N−H−O interactions with 15 and one C−H−O interaction from the TBA cation. Thus, the TBA cation acts as a stopper of the SO42− capsular assembly of thiourea 15. Non-bonding hydrogens and countercations are omitted for clarity.

We have reported the formation of SO42− encapsulated unimolecular capsule by a cyanuric acid based tris-urea receptor 32.30 Crystal structure of SO42− complex shows a partial encapsulation of SO42− via six N−H−O interactions. One TBA countercation seals the cavity of the SO42−⊂32 via one C−H−O interaction, thus, generates the unimolecular capsule (Fig. 23). This structure resembles our previously reported two TBA capped SO42− encapsulated complex of tris-urea 30.79

4. Sizes of dimeric capsular assemblies

Comparative capsular sizes of various anion assisted dimeric capsules are summarized in table 1. Dimeric capsular assemblies reported for tren based receptors are generally formed through 2:1 and 1:1 (host/guest) stoichiometry via the encapsulation of one and two anionic guest(s) respectively. In cases of extended tris-amide 4, capsular sizes slightly vary from 20.6 to 20.7 Å with the change of encapsulated guest from [ClI(H2O)2]2− to [BrI(H2O)3]2−.44 Dimeric capsules of tris-urea 12 show significant size variation with anions of different size and shape. Capsular sizes of HAsO42−⊂12 and HPO42−⊂12 capsules are measured as 10.22 and 9.92 Å respectively, which are reasonably higher than SO42−⊂12 and CO32−⊂12 capsules.30 Pseudo-capsular assembly of 12 with both OF− and H2PO4− show higher capsular sizes as 14.95 Å and 13.79 Å respectively. Thus, the inherent flexibility of the tren scaffold is reflected in the capsular size of anion complexes of tris-urea 12. Interestingly monoanionic H2PO4− also induces pseudo-capsular assembly of thiourea 13 with the similar capsular size of 13.44 Å like that of 12. Similar capsular sizes of ~9.1 Å are measured for carbonate capsules for tris-urea 10, 12 and 16. PO43− encapsulated dimeric capsules of thiourea 7 and 11 also
show similar capsular size of ~10.1 Å. Thus, size and shape of the anions also contribute to the size variation of the dimeric capsules. Capsular size and anion selectivity relationship is nicely depicted by Custelcean et al. in the anion complexes of tris-urea based tripodal receptors is revealed by the significant similarities of NO$_3^-$ anions such as NO$_3^-$ (11.14 Å), ClO$_4^-$ (11.02 Å) and CF$_3$COO$^-$ (11.51 Å) The slight differences in the capsular size may be due to the variation of shape of the anion and associated water molecules. In cases of the benzene platform based tris-amide receptors dimeric capsules are generally formed via encapsulation of one anionic guest in each half capsule irrespective of the functionality of the receptor. Capsular size of (NO$_3^-$)$_2$ is $27\bar{2}$ capsule is measured as 9.75 Å which resembles the same to the NO$_3^-$ trapped dimeric assembly of para-nitro substituted tris-amide receptor (10.01 Å). Capsular size of [F$_3$(H$_2$O)$_4$]$_2^-$ cluster templated diamic capsules of 28 is measured as 9.41 Å which is remarkably similar to the fluoride-water cluster encapsulating ortho-nitro (9.19 Å) and para-nitro (9. 45 Å) substituted tris-amide receptors. Similar trend is also observed in capsular sizes of $[\text{Cl}_2(\text{H}_2\text{O})\text{F}]_{2}^-$ capsules (9.65 Å) and hydrate-chloride trapped para-nitro substituted tris-amide receptor (9.57 Å). Thus, inherent rigidity of the benzene based triposal receptors is revealed by the significant similarities in capsular size of the dimeric capsules despite the differences in substituent and composition of the encapsulated guest.

### 5. Potential applications

#### 5.1 Anion recognition in aqueous media

Synthetic polyamine and polypeptide-based receptors are popular for anion recognition in aqueous medium. However, neutral receptors have also shown their potentiality in this aspect. In fact, tren based first urea/thiourea receptor developed by Morán et al. is reported to bind anions in DMSO-water solvent. Recently, tren based urea/thiourea receptors have emerged as effective anion receptor via complete encapsulation of anions in aqueous media in their complementary binding site. Fluorinated urea/thiourea receptors reported by Gale et al. have shown binding of anions in DMSO-$d_6$/0.5%D$_2$O solvent. HAsO$_4^{2-}$ and ura/thiourea receptors reported by Gale et al. have shown binding of anions in DMSO-$d_6$/0.5%D$_2$O solvent. Findings of Custelcean and Wu groups reveal the formation of anion encapsulated capsules of 22 and 23 from highly competitive aqueous media. On the other hand, benzene platform based tris-amide and hexa-amides have shown their interest for recognition of hydrated halides via capsule formation. In particular, encapsulation of fluoride-water cluster by tris-amide 28 in highly competitive acetone/water (1:1) solvent confirms functional aspects of molecular capsules. All these results suggest the scope of further exploration of these receptors towards anion separation, transportation etc.

#### 5.2 Anion separation

Custelcean et al. have pioneered separation of SO$_4^{2-}$ study by encapsulation of SO$_4^{2-}$ in crystalline capsule. They have extensively employed tren scaffold based 3-pyridyl functionalised tris-urea 22 for the selective SO$_4^{2-}$ encapsulation from a mixture of competitive aqueous solution through size, shape and charge discrimination. Related solid and solution states binding properties are discussed in our previous article. However, SO$_4^{2-}$ separation from highly alkaline aqueous solution is more appealing as it would be a practical solution to the problem of

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Platform</th>
<th>Guest and capsular size (Å)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tren-amine</td>
<td>SiF$_4$</td>
<td>8.75</td>
</tr>
<tr>
<td>Tren-amide</td>
<td>Cl$^-$ (20.62), Br$^-$ (20.75)</td>
<td></td>
</tr>
<tr>
<td>Tren-thiourea</td>
<td>SO$_4^{2-}$ (10.06), PO$_4^{3-}$ (10.03)</td>
<td></td>
</tr>
<tr>
<td>Tren-urea</td>
<td>CO$_3^{2-}$ (9.16)</td>
<td></td>
</tr>
<tr>
<td>Tren-thiourea</td>
<td>PO$_4^{3-}$ (10.13)</td>
<td></td>
</tr>
<tr>
<td>Tren-urea</td>
<td>H$_2$PO$_4^-$ (13.79), SO$_4^{2-}$ (9.18), CO$_3^{2-}$ (9.17), HPO$_4^{2-}$ (9.92), HaSO$_4^{2-}$ (10.22), OH$^-$ (14.95)</td>
<td></td>
</tr>
<tr>
<td>Tren-thiourea</td>
<td>H$_2$PO$_4^-$ (13.44)</td>
<td></td>
</tr>
<tr>
<td>Tren-thiourea</td>
<td>PO$_4^{3-}$ (9.59), CO$_3^{2-}$ (7.93)</td>
<td></td>
</tr>
<tr>
<td>Tren-urea</td>
<td>CO$_3^{2-}$ (9.06), SO$_4^{2-}$ (9.60), HPO$_4^{2-}$ (9.86)</td>
<td></td>
</tr>
<tr>
<td>Benzene-amine</td>
<td>NO$_2^-$ (11.14), ClO$_4^-$ (11.02), CF$_3$COO$^-$ (15.11)</td>
<td></td>
</tr>
<tr>
<td>Benzene-amide</td>
<td>NO$_2^-$ (9.75)</td>
<td></td>
</tr>
<tr>
<td>Cyanuric-urea</td>
<td>SO$_4^{2-}$ (10.39)</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Capsular size of dimeric capsules having various anionic guests.

- a: Na$^+$, b: K$^+$, c: Mg$^{2+}$, d: Na$^+$, e: K$^+$, f: Mg$^{2+}$ as countercations.
SO$_4^{2-}$ separation from nuclear waste.\textsuperscript{35} In this direction, Custelcean \textit{et al.} have reported SO$_4^{2-}$ encapsulation in two new crystalline capsules self-assembled from tris-urea 22 and Na$_2$SO$_4$/K$_2$SO$_4$.\textsuperscript{95} Crystalline capsules with compositions [Na$_2$(H$_2$O)$_4$]$[\text{K}^+\text{SO}_4(22)\text{H}_2\text{O}]_2$ and [K$_2$(H$_2$O)$_4$]$[\text{Na}^+\text{SO}_4(22)\text{H}_2\text{O}]_2$ are obtained in good yields from aqueous methanol solution. In both cases, SO$_4^{2-}$ encapsulation is found to be assisted \textit{via} twelve complementary hydrogen bonding interactions in the dimeric capsular assemblies of 22 (Fig. 24a,b). However, differences are observed in the coordination environment of countercations. Presence of [Na$_2$(H$_2$O)$_4$]$[\text{Na}^+\text{SO}_4(22)\text{H}_2\text{O}]_2$ vs [K$_2$(H$_2$O)$_4$]$[\text{K}^+\text{SO}_4(22)\text{H}_2\text{O}]_2$ cluster is observed in Na and K-based system respectively, both of which eventually lead to the formation of NaCl-type framework like Mg-based structure of 22.\textsuperscript{35} Capsular dimensions vary from 9.51 Å to 9.20 Å moving from Na to K-based capsule. Interestingly, the SO$_4^{2-}$ encapsulated Na-based system can be selectively crystallized in 90% yield from highly alkaline aqueous solutions (pH = 14) in presence of competitive anions. Further, the 22 can be recycled by simple water-treatment of the capsule that leaves sodium sulfate in solution.

Fig. 24 X-ray crystal structures of SO$_4^{2-}$⊂22 capsules with a) [Na$_2$(H$_2$O)$_4$]$[\text{Na}^+\text{SO}_4(22)\text{H}_2\text{O}]_2$ and b) [K$_2$(H$_2$O)$_4$]$[\text{K}^+\text{SO}_4(22)\text{H}_2\text{O}]_2$ cluster. Coordination mode and water hydrogen bonding interactions are presented.

On the other hand, designing of anion receptor aiming toward liquid-liquid extraction of SO$_4^{2-}$ from water is highly challenging due to its large hydration energy.\textsuperscript{66,97} Moyer \textit{et al.} have designated a successful extractant, which has solubility in a water-immiscible solvent, salt water insolubility and a provision for maintaining phase charge neutrality.\textsuperscript{35} Due to the importance of SO$_4^{2-}$ separation from nitrate-rich mixtures in the remediation of nuclear waste, several synthetic receptors and different approaches have been developed in recent times. Sessler and Moyer \textit{et al.} have widely utilized dual-host and ion-exchange strategies for SO$_4^{2-}$ extraction.\textsuperscript{35,98} Wu \textit{et al.} have demonstrated efficient extraction of SO$_4^{2-}$ from water by a neutral hexa-urea receptor 50 (Chart 13) using tetrabutylammonium chloride as a phase-transfer agent.\textsuperscript{99} SO$_4^{2-}$ selectivity pattern of 50 in aqueous medium (DMSO-d$_6$/10% D$_2$O) is explored towards liquid-liquid extraction of SO$_4^{2-}$: Addition of TBAI causes CHCl$_3$ solubility of 50 and possible exchange between Cl/SO$_4^{2-}$ in L-L extraction process. Structural analysis of the SO$_4^{2-}$ complex reveals monotopic encapsulation of SO$_4^{2-}$ in the cavity of 50 (Fig. 25) \textit{via} twelve N-H···O interactions.

Fig. 25 View of monotopic SO$_4^{2-}$ encapsulation in the cavity of hexa-urea 50. Non-bonding hydrogens and countercations are omitted for clarity.

We have employed a similar strategy for liquid-liquid extraction of anions by 19 using tetrabutylammonium iodide as phase transfer agent.\textsuperscript{62} Solution state F$^-$ selectivity pattern of 19 is established by $^1$H-NMR and ITC studies. Further, we have shown liquid-liquid extraction of F$^-$ and SO$_4^{2-}$ by 19 \textit{via} anion exchange technique using tetrabutylammonium iodide as phase transfer agent. The CHCl$_3$/CH$_2$Cl$_2$ solubility of 19 is achieved by adding TBAI, followed by usual liquid-liquid extraction, which result ~70% and 40% extraction of F$^-$ and SO$_4^{2-}$ respectively. Crystallization of extracted mass shows SO$_4^{2-}$ encapsulation \textit{in} the dimeric capsular assembly of 19 (Fig. 26) \textit{via} fifteen N-H···O interactions. Capsular dimension of SO$_4^{2-}$⊂19 is measured as 9.51 Å, which is similar to the tren based urea/thiourea capsules. In this context, Moyer \textit{et al.} have demonstrated the role of cations in the liquid-liquid extraction SO$_4^{2-}$ by a calix[4]pyrrole receptor 51 with lipophilic anion exchanger.\textsuperscript{100} Superior extraction of SO$_4^{2-}$ is reported with the methyl substituted cations, which is supported by the formation of thermodynamically stable ion-pair complex of SO$_4^{2-}$.

Fig. 26 Single crystal X-ray structure of SO$_4^{2-}$⊂19 dimeric capsule. Non-bonding hydrogens and countercations are omitted for clarity.

Recently, we have demonstrated a rather unique approach for L-L extraction of SO$_4^{2-}$ using the CO$_3^{2-}$ complex of tris-urea 12. Quantitative formation of carbonate capsules [12$_2$CO$_3$]$_6$ \textit{via} aerial CO$_2$ fixation and its solubility in water-immiscible solvent like CHCl$_3$/CH$_2$Cl$_2$, encourage us to investigate L-L extraction of...
SO₄²⁻ by [12₃CO₃]²⁻. In fact, quantitative (~99%) extraction of SO₄²⁻ as [12₃SO₄]²⁻ capsule is observed by [12₃CO₃]²⁻ via CO₃²⁻/SO₄²⁻ exchange process. Further, this anion exchange process in the capsule is clearly visible through the pink colouration of the aqueous phase in presence of phenolphthalein after L-L extraction. Although, use of Cl⁻ as anion exchanger causes impure extraction of SO₄²⁻ for 12 unlike that of 19 and 51 (Chart 14). Carbonate capsule [12₃CO₃]²⁻ is an exact (2:1) complex of 12 and CO₃²⁻ which rules out possibility of any excess of CO₃²⁻ (phase transfer agent) in the organic layer in case of 12.

![Chart 14 Schematic presentation of CO₃ fixation and SO₄²⁻ extraction cycles of 12 via molecular capsule formation.](image)

5.3 Other relevant applications

Synthetic receptors reported for aerial CO₂ fixation by Gunnlaugsson, Gale and our group are generally obtained from basic DMSO solvent. Encapsulation of such aerially sequestered CO₂ as CO₃²⁻ in a dimeric capsular assembly is well studied in case of tris-urea 12. Tren scaffold based 3-nitrophenyl functionalised tris-urea 16 has recently been established as potential system for the fixation of aerial CO₂ as CO₃²⁻ by Das et al. Crystallization of 16 with TBAF/TABOH in DMSO yields CO₃²⁻ encapsulated complex of 16 in 90% yield. Structural analysis shows CO₃²⁻ templated formation of dimeric capsular assembly of 16 (Fig. 27). Each oxygen atom of CO₃²⁻ is involved in four N-H-O interactions, thus results a twelve coordinated CO₃²⁻ complex. ¹H-NMR titration study of 16 with HCO₃⁻ shows 1:1 (host/guest) association in solution as evident from job’s plot analysis. Association constant value of HCO₃⁻ with 16 is estimated to be 4.15, which resembles the same of tris-urea 12 (4.04) in DMSO-d₆.

![Fig. 27 X-ray crystal structure showing CO₃²⁻⊂16.](image)

Structural evidence of CO₃²⁻ complexes reveals the necessity of higher coordination for CO₃²⁻. Very recently, Hossain et al. have reported CO₂ fixation as CO₃²⁻ by a tren based tripodal hexa-urea 52 (Chart 15) having chelating urea groups. Attempt to grow crystals from mixture of 52 and TBAF in DMSO generates the CO₃²⁻ complex of 52 in quantitative yield like that of 12. CO₃²⁻ complex of 52 shows monotropic encapsulation of CO₃²⁻ inside the highly organised cavity of hexa-urea 52 (Fig. 28) via twelve N-H-O interactions. However, ¹H-NMR titration study shows lower binding affinity for HCO₃⁻ with hexa-urea 52 (log K = 2.35) with 1:1 binding stoichiometry compared to the CO₃²⁻ encapsulating tris-urea receptors.

![Chart 15](image)

![Fig. 28 View of monotropic encapsulation of CO₃²⁻ in the cavity of hexa-urea 52.](image)

6. Conclusions

Development of anion receptors for the binding and transportation of anions across lipid membranes has attracted much attention in recent years. Effective transport of bicarbonate by antiport mechanism is demonstrated for tren based phenyl terminal thiourea receptor by Gale et al. Encapsulation of CO₃²⁻ is observed in the dimeric capsular assembly of the thiourea in solid state. Fluorinated urea/thiourea receptors (Chart 4) have been reported for better transmembrane transport activity for chloride/nitrate, chloride/sulfate and chloride/bicarbonate antiport over their non-fluorinated analogues due to the high lipophilicity of fluorinated receptors. Capsular recognition of various anions in solid state are observed in cases of this urea/thiourea receptors which are described in section 2.1.
practical application of molecular capsules through anion recognition. Utility of anion binding in molecular capsules can be explored in new directions which are initiated in recent years. Suitable functionality on new platforms have revealed many interesting properties such as capsular size modulation, different halide-water cluster encapsulation, CO$_2$ fixation, SO$_4^{2-}$ extraction, anion transportation etc. In particular, simple anion receptors have shown efficiency towards aerial CO$_2$ sequestration as CO$_2$ in the molecular capsules. Competitive crystallization and liquid-liquid extraction have emerged as efficient technique to achieve the challenging task of SO$_4^{2-}$ extraction from water in recent years. A vital task for moving towards the practical application is the construction of molecular capsule for the recognition of anions in aqueous media. Encapsulation of toxic HA$\text{SO}_4^{2-}$ in the dimeric capsular assembly of a simple tripodal urea receptor in aqueous medium is also demonstrated in recent times. However, selective binding and removal of such toxic anions like HA$\text{SO}_4^{2-}$, CrO$_4^{2-}$ from water either by selective crystallization or solvent extraction are yet to be reported. Thus, drinking water purification by removing toxic and hazardous anions using simple anion receptor chemistry is one of the exciting prospects of future work.

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Notes and references

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Pradyut Ghosh is currently a Professor in the Department of Inorganic Chemistry, Indian Association for the Cultivation of Science (IACS), India. He received his PhD in Chemistry from Indian Institute of Technology, Kanpur, under the direction of Parimal K. Bharadwaj in 1998. He spent two years as a post-doctoral fellow at Texas A&M University with Richard M. Crooks and he was an Alexander von Humboldt Fellow at University of Bonn, Germany, in Fritz Vögtle’s group. Upon his return to India, he joined CSMCRI, India, and in 2007 he moved to IACS. His present research interests are recognition, extraction and chemical sensing of ions of environmental and biological relevance, supramolecular aggregation and interlocked molecules.
Recent developments in anion induced capsular self-assemblies

Ranjan Dutta and Pradyut Ghosh*