Recognition and complexation of hydrated fluoride anion: $F_2(H_2O)_6{}^{2-}$ templated formation of a dimeric capsule of a tripodal amide†

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An arene based tripodal amide receptor shows selective dimeric capsule formation templated by fluoride–water cluster, $[F_2(H_2O)_6]^{2-}$, and non-capsular aggregation for chloride, nitrate and acetate anions.

Molecular capsules are an intriguing class of compound achieved by both covalent binding and self-assembly through noncovalent interactions.[1] One of the most fascinating features of molecular capsules is their ability to isolate the encapsulated guests from the bulk. This may even allow stabilization of the reactive intermediates and intermediates in catalytic reactions.[2] Self-complementary units of a molecular capsule are generally based on conformationally restricted systems such as calixarenes,[3a,b] resorcinarenes,[3c] glycoluril[3d] and tripodal[3e,f] derivatives. Among tripodal systems the trialkylbenzene core provides some degree of preorganization into a conical conformation with all three binding arms projected in one direction.[4] In recent times anions have been explored in the area of supramolecular syntheses and assemblies such as molecular capsules.[5]

Fluoride recognition is an area of immense research interest to the scientific community due to its role in chemical, industrial, food and toxicity.[6] Fluoride is one of the most challenging targets for anion recognition because of its high hydration enthalpy. In a recent feature article on fluoride binding, Cametti and Rissanen rightly mentioned—"in principle, a partially hydrated fluoride could be thought of as the target species instead of a naked fluoride anion".[6a] Herein, we structurally demonstrate selective hydrated fluoride anion, $F_2(H_2O)_6{}^{2-}$, cluster templated dimeric capsule formation of a newly synthesized arene based tripodal amide receptor, **L**. Further, anions like nitrate, acetate and chloride prefer non-capsular aggregation of **L**, whereas exchange of these anions with fluoride, resulted in the hydrated fluoride encapsulated complex.

The tripodal receptor **L** (Chart 1) is based on a 1,3,5-methyl substituted arene having amide functionality with nitro substituted (electron deficient) aryl terminals. **L** is synthesized by the reaction of 1,3,5-tris(aminomethyl)-2,4,6-trimethylbenzene[4d] with three equivalents of 2-nitrobenzoyl chloride in presence of triethylamine in chloroform. The reaction mixture is filtered and washed with plenty of water to remove the triethylammonium chloride and dried under vacuum to yield the white solid of **L**. Further, **L** is treated with an excess of tetrabutylammonium (TBA) salts of F^-, Cl^-, $NO_3{}^-$ and AcO^- in dioxane to get the corresponding anion complexes as crystals suitable for single crystal X-ray studies.‡

Upon complexation with fluoride in dioxane, the receptor **L** yielded complex **1** which possesses two units of [$L\cdot TBAF\cdot 3H_2O\cdot$dioxane] in an asymmetric unit. The X-ray crystal structure of **1** revealed the dimeric capsular assembly of the receptor **L** with encapsulated hydrated fluoride, $[F_2(H_2O)_6]^{2-}$, as a guest in the capsule (Fig. 1). The source of water in the crystal could be from the hydrated TBAF salt and atmospheric moisture. It is worth mentioning that selective binding of $Cl(H_2O)_4{}^-$ in a metal–organic framework has also been demonstrated previously.[7]

In our case, probably the $[F_2(H_2O)_6]^{2-}$ cluster has acted as a template in the formation of the dimeric capsule, where all the three arms of **L** projected in one direction to form a bowl shaped cavity and two such bowls intercalate to form the dimeric assembly. Fig. 1b and 2 show the hydrogen bonding pattern of the $[F_2(H_2O)_6]^{2-}$ cluster. This template is formed *via* strong fluoride–water interactions. The cluster possesses a tricyclic arrangement where two fluoride ions are in the apex of the tricycle and are bridged by two water dimers and two molecules of water (Fig. 1b). Therefore, each fluoride is hydrogen bonded with four water molecules with an average hydrogen bonding distance of 2.748 Å ranging from 2.655 Å to 2.912 Å (Fig. 2). Two fluoride ions (F1) and four water oxygen atoms (designated by O4 and O7) of $[F_2(H_2O)_6]^{2-}$ are in two N–H···F and four N–H···O interactions respectively with amide centers of **L** as shown in Fig. 2 and Table 1.

In addition to the conventional hydrogen bonding interactions, fluoride ion (F1) and two waters (designated by O7) of $[F_2(H_2O)_6]^{2-}$ are in interactions with aryl-C–H protons, resulting in two C–H···F and two C–H···O interactions. Nitro group substitution in the aryl terminals increases the aryl C–H acidity which facilitate these C–H···F and C–H···O interactions between the two bowls in present study. Probably

Chart 1 Synthesis of triamide **L**.

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† Electronic supplementary information (ESI) available: Experimental, characterization data for **L**, **1**, **2**, **3** and **4** and crystallographic refinement details for **1**, **2**, **3** and **4**. CCDC 733118–733121. For ESI and crystallographic data in CIF or other electronic format, see DOI: 10.1039/b910014h

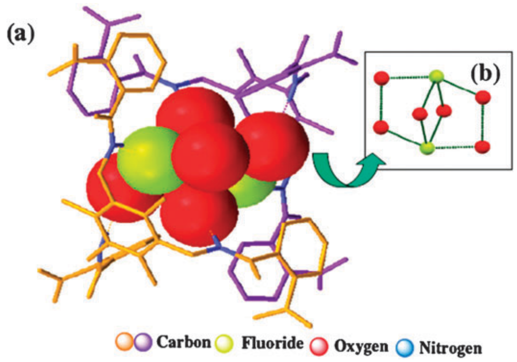

Fig. 1 (a) Space-filled view of the $[F_2(H_2O)_6]^{2-}$ cluster inside the dimeric capsule **1**, (b) inset showing the $[F_2(H_2O)_6]^{2-}$ cluster. One of the two units has been described here and TBA counter cations, lattice dioxane and the hydrogen atoms are omitted for clarity.

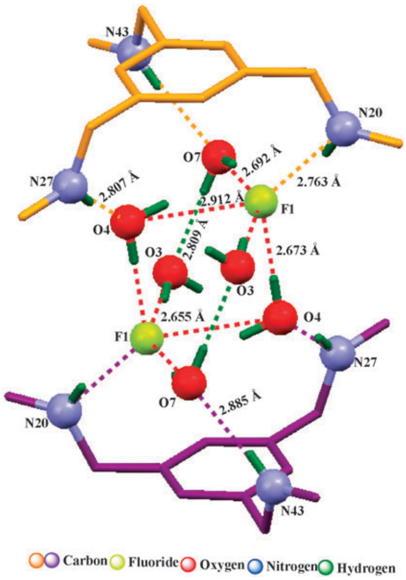

Fig. 2 Partial structure of **1** showing the hydrogen bonding pattern of the $[F_2(H_2O)_6]^{2-}$ cluster and its interactions with **L**.

Table 1 Crystallographic bond parameters of the interactions of the $[F_2(H_2O)_6]^{2-}$ cluster with **L**

D–H···A	D–H/Å	H···A/Å	D···A/Å	∠D–H···A/°
N20–H20···F1	0.860	1.95	2.763(4)	157.6
N27–H27···O4	0.860	1.96	2.807(5)	168.6
N43–H43···O7	0.860	2.03	2.884(5)	170.5
C31–H31···O7	0.931	2.689	3.380	131.68
C16–H16···F1	0.930	2.548	3.347	144.19

these are the driving force in the formation of the staggered dimeric capsular assembly (Fig. S12a, ESI†). Details of all these H-bonding interactions are listed in Table 1. It is worth mentioning that C–H···anion hydrogen bonds draw increasing attention among various anion binding interactions.[8] Further, $[F_2(H_2O)_6]^{2-}$ templated capsules are connected *via* C–H···O interactions between O7 oxygen of $[F_2(H_2O)_6]^{2-}$ and the C–H proton of the aryl terminal group of another capsule (Fig. S12b, ESI†).

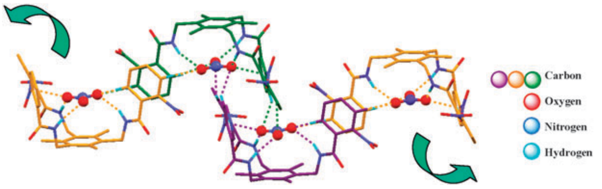

Fig. 3 View of the zipper-like assembly of **3** upon nitrate encapsulation. Tetrabutylammonium counter anions and the non-bonded hydrogen atoms are omitted for clarity.

To understand the assembly with a higher homologous spherical anion, complexation with chloride has been performed. The single crystal X-ray analysis of the chloride complex **2**, [**L**·TBACl·H_2O] revealed discrete dimeric non-capsular assembly (Fig. S13, ESI†). To study the role of the geometry of the anions in the self-assembly processes of **L**, we have synthesized two complexes, **3** and **4**, for planar anions, nitrate and acetate respectively. The single crystal X-ray analysis of **3** and **4** revealed the encapsulation of the respective anion having similar aggregational patterns. As a representative of planar anion complexes, details of complex **3**, [**L**·$TBANO_3$], are presented here. Nitrate is recognized in the bowl shaped cleft of **L** *via* three strong N–H···O interactions between amide protons of **L** and oxygen atoms of nitrate, and also *via* one intramolecular C–H···O interaction between aryl-C–H and one of the oxygen atoms of nitrate (Fig. 3). Two such bowl shaped nitrate encapsulated **L** are held together *via* intermolecular aryl-C–H···O interactions between two of the nitrate oxygens of one bowl and two aryl-C–H of the other bowl. Further, one of the oxygen atoms of the encapsulated nitrate is in intermolecular aryl-C–H···O interactions with the third bowl in the lattice and leads to a infinite zipper-like assembly where nitrate is all together seven coordinate (Fig. 3). Details of these interactions are available in the ESI (Table S3).†

In the case of acetate complex **4**, [**L**·TBAOAc·H_2O], due to the planar shape, the acetate anion prefers to bind with three receptor molecules and that directs the infinite zipper-like aggregation *via* various NH···O and C–H···O interactions upon anion encapsulation (Fig. S14, ESI†). In the solid state crystal structure, along with the acetate anion, a disordered water molecule is also located in the cleft of **L**. When anions are an integral part of supramolecular aggregates, it is expected that if the templating anion is exchanged by other anions it might reorient the assembly. To demonstrate the anion dependent aggregation of **L**, here we have carried out the following two proof-of-concept experiments: (a) added tetrabutylammonium fluoride to the crystals of complex **3** in dioxane and allowed for crystallization, and (b) charged a mixture of fluoride and acetate (1 : 1) with **L** in dioxane. Interestingly, in both cases we isolated crystals suitable for single crystal X-ray studies and confirmed the isolated crystals as complex **1**, *i.e.* $[F_2(H_2O)_6]^{2-}$ templated dimeric capsules of **L**. These results indeed prove that fluoride is preferred over other anions and assists capsular assembly over other aggregation observed for planar anions.

Qualitative ^{1}H-NMR experiments were performed with tetrabutylammonium salts of F^-, Cl^-, AcO^- and NO_3^- to understand the solution state behaviour of **L** in the presence of these anions. Disappearance of the amide –NH signal is observed immediately after the addition of $(n\text{-}Bu)_4N^+F^-$ to the DMSO-d_6 solution of **L** (Fig. S15, ESI†), whereas a very slight downfield shift (0.03 ppm) of the –NH proton is observed in the case of $(n\text{-}Bu)_4N^+Cl^-$ and $(n\text{-}Bu)_4N^+NO_3^-$. In the case of $(n\text{-}Bu)_4N^+CH_3COO^-$, the chemical shift position of the amide –NH protons shifted 0.2 ppm downfield and we have performed ^{1}H-NMR titration experiments of $(n\text{-}Bu)_4N^+CH_3COO^-$ with **L** (Fig. S16, ESI†). A Job's plot analysis of the titration data showed a 1 : 3 host to guest binding in solution whereas the solid state single crystal X-ray study showed 1 : 1 binding. A difference in binding pattern in solid and solution states is not uncommon.[9] Here, the difference in the binding of three acetate anions in solution *versus* one acetate in the solid state may be due to side clefts binding anions in solution which could allow multiple anions interaction with a single receptor. In the solid state, the receptor is more organized and prefers anion encapsulation in the cavity of the three arms of tripodal system **L** and the binding of a single anion can be observed. Further, solvent systems (dioxane *vs.* dimethyl sulfoxide) might have played an important role in imposing different binding patterns in solid and solution states.

In conclusion, the arene capped amide based tripodal receptor showed encapsulation of fluoride hydrate selectively inside the capsule whereas infinite zipper-like aggregates were formed for chloride, nitrate and acetate. Our approach of recognizing the partially hydrated fluoride anion could motivate the development of a new generation of fluoride receptors. Presently, we are working on other rigid/semi-rigid systems using the above approach to develop fluoride receptors in aqueous/semi-aqueous media.

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Notes and references

‡ Crystallographic data for: **1**: $C_{106}H_{160}F_2N_{14}O_{28}$, $M = 2116.48$, triclinic, space group $P\bar{1}$, $a = 12.9823(7)$, $b = 20.3519(12)$, $c = 23.1725(13)$ Å, $\alpha = 105.659(2)$, $\beta = 92.575(2)$, $\gamma = 105.648(2)°$, $V = 5630.8(5)$ Å^3, $D_c = 1.248$ g cm^{-3}, $Z = 2$, $\lambda = 0.71073$ Å, $T = 100(2)$ K, 54 203 reflections, 14 944 independent ($R_{int} = 0.0676$), and 9162 observed reflections [$I \geq 2\sigma(I)$], 1388 refined parameters, $R = 0.0759$, w$R2 = 0.2118$. Data collected on several crystals of complex **1** did not show diffraction beyond theta (max) = 22.67°.

2: $C_{49}H_{68}ClN_7O_{10}$, $M = 950.55$, triclinic, space group $P\bar{1}$, $a = 12.945(2)$, $b = 14.4605(10)$, $c = 15.5879(12)$ Å, $\alpha = 117.393$, $\beta = 95.911(2)$, $\gamma = 101.767(2)°$, $V = 2470.5(5)$ Å^3, $D_c = 1.278$ g cm^{-3}, $Z = 2$, $\lambda = 0.71073$ Å, $T = 100(2)$ K, 19 525 reflections, 6810 independent ($R_{int} = 0.0401$), and 5194 observed reflections [$I \geq 2\sigma(I)$], 631 refined parameters, $R = 0.0415$, w$R2 = 0.0873$. Data collected on several crystals of complex **2** did not show diffraction beyond theta (max) = 22.95°.

3: $C_{49}H_{66}N_8O_{12}$, $M = 959.10$, triclinic, space group $P\bar{1}$, $a = 12.922(6)$, $b = 14.152(7)$, $c = 15.351(7)$ Å, $\alpha = 116.614(6)$, $\beta = 92.811(7)$, $\gamma = 101.864(7)°$, $V = 2424(2)$ Å^3, $D_c = 1.314$ g cm^{-3}, $Z = 2$, $\lambda = 0.71073$ Å, $T = 100(2)$ K, 21 099 reflections, 7484 independent ($R_{int} = 0.0963$), and 4320 observed reflections [$I \geq 2\sigma(I)$], 641 refined parameters, $R = 0.0732$, w$R2 = 0.1747$.

4: $C_{51}H_{71}N_7O_{12}$, $M = 974.15$, triclinic, space group $P\bar{1}$, $a = 12.9277(19)$, $b = 14.647(2)$, $c = 15.513(2)$ Å, $\alpha = 62.355(2)$, $\beta = 73.693(2)$, $\gamma = 77.867(2)°$, $V = 2486.4(6)$ Å^3, $D_c = 1.301$ g cm^{-3}, $Z = 2$, $\lambda = 0.71073$ Å, $T = 100(2)$ K, 23 294 reflections, 8696 independent ($R_{int} = 0.0388$), and 6356 observed reflections [$I \geq 2\sigma(I)$], 650 refined parameters, $R = 0.0529$, w$R2 = 0.1383$.

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