RSC Advances

RSC Advances

COMMUNICATION

Anion directed conformational diversities of an arene based hexa-amide receptor and recognition of [F4(H2O)6]4- cluster

Sourav Chakraborty,[a] Ranjan Dutta,[a] Bryan M. Wong[b] and Pradyut Ghosh *[a]

A benzene platform based new hexa-amide receptor (**L**) has shown conformational diversities *via* isolation of *aaabbb* (*A*), *aabaab* (*B*) and *aaaaaa* (*C*) conformers upon recognition of acetate, nitrate and hydrated-fluoride [F4(H2O)6]4-
10 respectively in solid state. Solution and DFT calculation studies show fluoride binding selectivity of **L**.

Receptors based on (tris-2-aminoethylamine) TREN[1], arene[2], cyanuric acid[3] and calix pyrrole[4] platforms are popular for recognition of anions. But arene platform based hexapodal
15 receptors are scarcely reported in the anion recognition literature.[5] In the year 1974, Vögtle *et al.* first reported an octopus like hexapodal ligand that forms a cation complex.[6] Later, after thirty four years DFT calculation study by Allen *et al.* showed that six alkyl substituted hexa-amide orients in the same direction
20 forming a bowl shaped conformer that binds chloride and triflate with low binding affinity.[7] In 2010 our group reported the first example of compartmental recognition of nitrate/acetate by a pentafluorophenyl substituted hexa-amide receptor.[8a] Later on we have shown recognition of [(F)4(H2O)10]4- cluster in the dimeric
25 capsular assembly of a *m*-nitrophenyl substituted hexa-amide where all the six arms are in unidirectional conformation.[8b] Recognition of hydrated fluoride could be a practical approach towards removal of fluoride from water due to its high hydration energy. In principle, hydrated fluoride may exist in various
30 cluster compositions and thus practically could act as guest in fluoride recognition.[9a] Various fluoride-water clusters have been trapped which includes [F(H2O)]4-,[9b] [F(H2O)4]-,[9c] [(F)2(H2O)6]2-,[2a] [(F)4(H2O)10]4-,[8b] and [(F)2(H2O)4]2-.[2f] On the other hand, polymorphism of hexa-host receptors and their
35 solvated inclusion complexes have also been demonstrated.[10] Herein we report the single crystal X-ray structural evidence on anion-dependent trapping of unusual conformers of 2-(trifluoromethyl)phenyl substituted hexa-amide by hydrated fluoride (*aaaaaaa*), nitrate (*aabaab*) and acetate (*aaabbb*).
40 Furthermore, we show recognition of a new fluoride-water cluster [(F)4(H2O)6]4- in the dimeric capsular assembly of the hexa-amide along with fluoride binding selectivity.

The hexa-amide receptor **L** has been synthesized following the previously published procedure (Scheme. 1).[8] **L** is crystallized
45 from dioxane-water (3:1, v/v) binary solvent mixture in *aaabbb* conformation (*A*). Complexation of **L** with acetate, nitrate and fluoride have resulted complexes **1**; [(**L**)·(CH3COO)2·(TBA)2], **2**; [(**L**)·(NO3)·(TBA)] and **3**; [(**L**)2·(F)4·(H2O)6·(TBA)4] respectively.
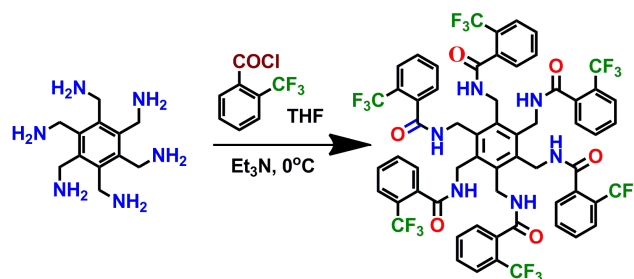
50 **Scheme 1.** Synthesis of **L**.

Structural analysis of **L** has shown orientation of three consecutive arms in one direction *versus* the other three arms directed towards opposite direction, resulting in a chair-like conformation (*aaabbb*, conformer *A* in Fig. 1S, ESI†). The solid
55 state structure of **L** shows one of the amide protons (N3-H3A) is intra-molecularly hydrogen bonded to the carbonyl oxygen (O1) of another arm and one amide –NH proton is directed towards the cavity composed of three arms (Fig. 16S, ESI†). However, this clearly suggests that two tripodal clefts of hexapodal receptor
60 with *aaabbb* conformation are complimentary towards compartmental guest recognition. During complexation with acetate (complex **1**), all three amide –NH protons are oriented towards the cavity of the tripodal cleft to bind acetate where stoichiometry of binding is found to be 1:2 (host/guest) (Fig. 16S,
65 ESI†). The oxygen atom O2 of acetate is in strong hydrogen bonding interactions with two amide –NH centres N1-H1 and N3-H3 whereas O1 is hydrogen bonded to the third amide centre N2-H2 (Table 3S, ESI†). In complex **1**, the distances between the amide nitrogen centres are quite similar to **L**. Several
70 intermolecular C-H···O interactions between acetate and aryl C-H protons of **L** result in the formation of a 1D-polymeric capsular assembly in complex **1** where the distance between two acetates is 6.8 Å. Similar *aaabbb* (*A*) conformer was also observed in case of acetate complexes of pentaflurophenyl[8a] and *m*-nitrophenyl[8b]
75 substituted hexa-amide receptors.

Interestingly, when the guest is changed from acetate to nitrate, **L** shows different structural conformer in single crystal X-ray study. The nitrate complex of **L**, i.e. complex **2** [(**L**)·(NO3)·(TBA)], shows 1:1 (host/guest) recognition where
80 NO3- is recognized in a tetrapodal cleft with overall *aabaab* (*B*) conformation (Fig. 1a). Hence, upon changing the guest we have observed that both the host conformation as well as the stoichiometry of binding is altered. In the tetrapodal cleft of
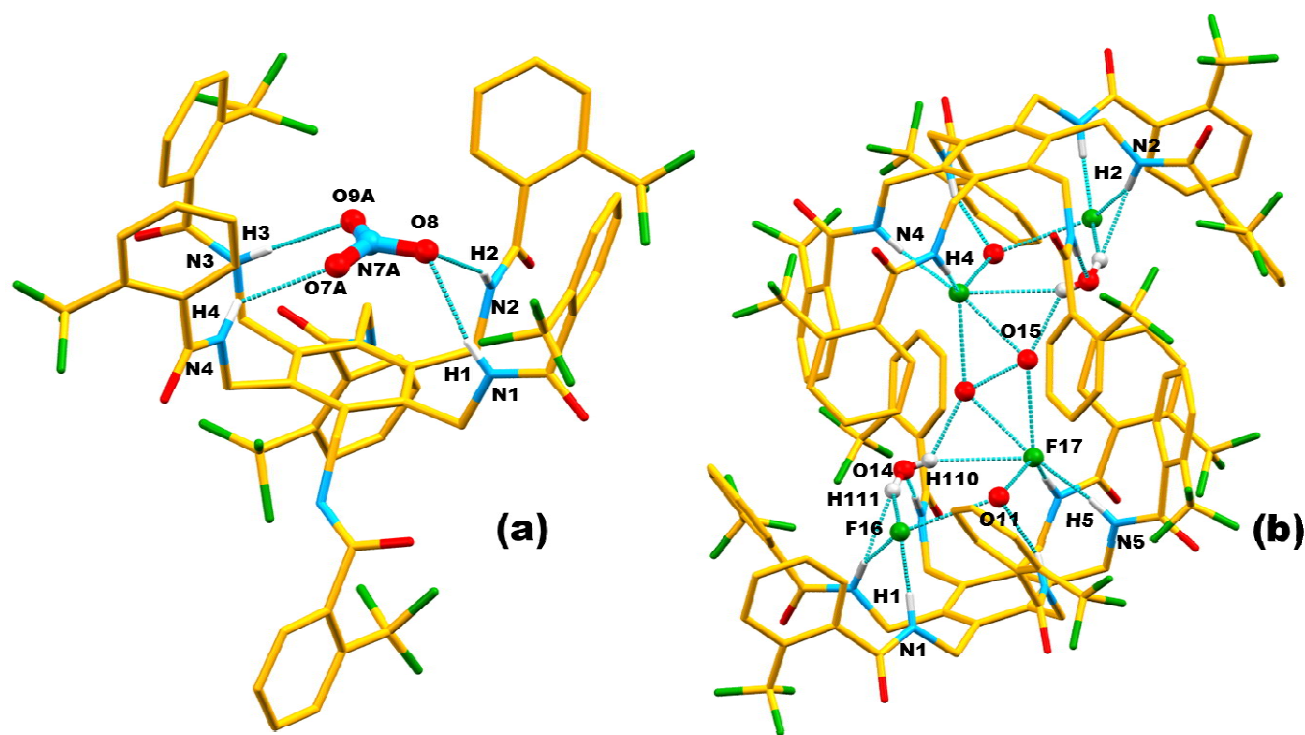
COMMUNICATION

Fig.1 (a) Complex **2** shows recognition of nitrate in unusual **B** conformation by **L**; (b) [F$_4$(H$_2$O)$_6$]$^{4-}$ cluster inside the dimeric capsular assembly of **L** in complex **3** in **C** conformer. Hydrogen atoms on the phenyl rings are removed for clarity.

complex **2**, the NO$_3^-$ is recognized by four strong N-H⋯O hydrogen bonding interactions from all four amide centres (Table 4S, ESI†). The remaining two arms of **L** in **B** conformer point toward opposite direction forming a dipodal cleft without any guest binding. This is an unusual conformation (*aabaab*) that is definitely stabilized upon recognition of guest like nitrate although same receptor preferred *aaabbb* conformation in both free ligand and in its acetate complex (**1**).

Interesting result on the anion directed conformational study is found in case of hydrated fluoride recognition by **L** in complex **3**. Upon changing the guest from planar anions (acetate, nitrate) to spherical anion fluoride, we have observed trapping of very unusual conformer of **L** i.e. *aaaaaa* (**C**) that has recognised [F$_4$(H$_2$O)$_6$]$^{4-}$ in the large cavity of the dimeric capsular assembly of **L** (Fig. 1b). The asymmetric unit of complex **3** possesses one *aaaaaa* conformer of **L**, two fluoride, five water, three dioxane and two TBA counter-cations. The capsular dimension of complex **3** measured from the bridgehead arenes centroid is found to be 11.901Å. **L** in complex **3** is able to encapsulate two F$^-$ and two water molecules, [F$_2$(H$_2$O)$_2$]$^{2-}$ in its bowl shaped cavity (half capsule). This [F$_2$(H$_2$O)$_2$]$^{2-}$ unit is further hydrogen bonded to another [F$_2$(H$_2$O)$_2$]$^{2-}$ unit through two bridging water molecules (O15) to form [F$_4$(H$_2$O)$_6$]$^{2-}$ cluster in the cavity of a dimeric capsular assembly of **L** (Fig. 1b). Encapsulation of

[F$_4$(H$_2$O)$_6$]$^{4-}$ cluster is assisted by multiple N-H⋯F, O-H⋯F and N-H⋯O strong interactions where the hydrogen bonding distances range from 2.62Å to 2.81Å (Table 5S, ESI†). The fluoride ion labelled F16 is hydrogen bonded to amide centres N1-H1 and N2-H2 whereas fluoride ion labelled F17 is hydrogen bonded to amide centres N4-H4 and N5-H5. The other two amide centres namely N3-H3 and N6-H6 are hydrogen bonded to O11 and O14 of [F$_2$(H$_2$O)$_2$]$^{2-}$ unit respectively. Interestingly, the coordination environments of two fluorides (F16 and F17) are different in complex **3**. Thus [F$_4$(H$_2$O)$_6$]$^{4-}$ cluster acts as a template to form a dimeric capsular assembly *via* various hydrogen bonding interactions which orients all the six amide arms in the same direction. However, the unidirectional pattern of all six arms of hexapodal receptors in its native state is very unusual and highly disfavoured in terms of thermodynamics. Thus hydrated fluoride cluster traps one of the most unfavourable conformers in case of arene platform based hexa-amide receptor. It is noteworthy to mention that recognition of [(F)$_4$(H$_2$O)$_{10}$]$^{4-}$ cluster in the dimeric capsular assembly of a *m*-nitrophenyl substituted hexa-amide in *aaaaaa* (**C**) conformation was previously reported by our group.[8b]

DFT studies have been employed to find the binding energies of these three anion complexes (**1**, **2** & **3**). Table 8S (ESI†) summarizes the binding energies for the complexes calculated at

RSC Advances Accepted Manuscript

COMMUNICATION
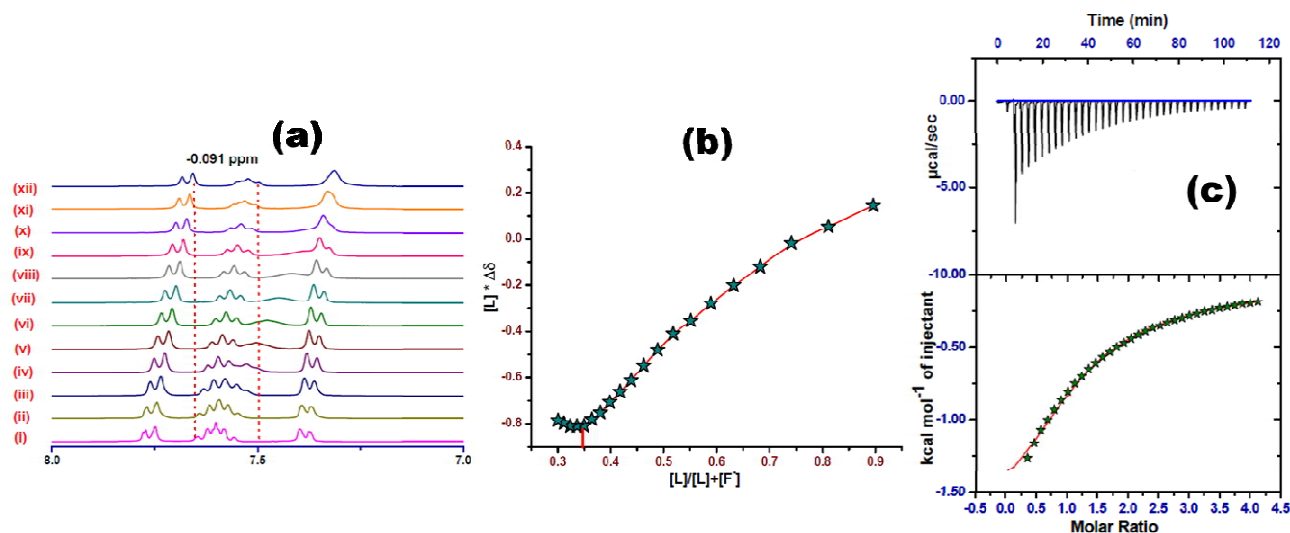
Fig.2 (a) Partial ^{1}H-NMR (300 MHz) spectral changes of **L** in DMSO-d_6 with added F$^-$ in DMSO-d_6 (298K), [**L**] = 10.05mM. The respective ratio of concentrations are [F$^-$]/[**L**]: (i) 0, (ii) 0.20, (iii) 0.46, (iv) 0.70, (v) 0.93, (vi) 1.16, (vii) 1.39, (viii) 1.62, (ix) 1.85, (x) 2.20, (xi) 2.55, (xii) 2.90. (b) Job's plot for **L** with F$^-$ in DMSO-d_6 which shows a 1:2stoichiometry. (c) Representative ITC titration profile of **L** (0.745mM) with TBAAcO (14.45 mM) in DMSO at 298 K; Thermodynamic parameters associated with this titration are, K1 = 4.17E3 ± 1.1E2 M^{-1}, ΔH1 = -1795 ± 18.7 cal/mol, ΔS1 = 10.5 cal/mol/deg, K2 = 2.34E2 ± 8.3 M^{-1}, ΔH2 = -2360 ± 84.5 cal/mol, ΔS2 = 2.92 cal/mol/deg, Chi^2/DOF = 200.4.

the M06-2X/6-31G(d,p) level of theory. Among all three complexes, complex **3** (136.50 kcal/mol) have the largest binding energy where each of the six arms of hexa-amides are in the *aaaaaa* (**C**) conformation to form strong hydrogen bond with a fluoride ion in the center of the complex. It is important to note that all of these calculations were carried out in the gas phase,and the large binding energy arises from the strong columbic attraction of the negatively-charged anion with the hydrogen atoms of the receptor. The presence of explicit solvent molecules would effectively screen the charge of the anion and lower the binding energy; however, the size of these complexes is too prohibitively large to include explicit solvent. Next in the line of decreasing binding energies is complex **1** (77.44 kcal/mol) with *aaabbb* conformation (**A**) where three arms of the ligands are hydrogen bonded to an acetate anion. On a mechanistic level, the binding energy of complex **1** is smaller than the binding energy for complexes **3** for two reasons: (i) complex **1** only involves the interaction of three ligand functional groups with the anion in the *aaabbb* conformation, whereas complex **3** involves attractive interactions with all six arms in the *aaaaaa* conformation; (ii) the fluoride anion is significantly more electronegative than the acetate ion, leading to a much higher binding energy for complex **3**. Interestingly, DFT calculation studies on our previously reported [(F)$_4$(H$_2$O)$_{10}$]$^{4-}$ cluster encapsulation by *m*-nitrophenyl substituted hexa-amide receptor[8b] showed binding energy of 136.86 kcal/mol (Figure 21S and table 12S, ESI†) which is almost equal in magnitude with complex **3**. Following the previously discussed systems, complex **2** possess the next binding energy (71.09 kcal/mol) and involves in hydrogen bonding

interactions with a nitrate anion in *aabaab* (**B**) conformation. The details of the coordinates and optimized structures are mentioned in ESI† (Fig. 18S-21S, Table 9S-11S).

Anion binding propensities of the receptor is evaluated by Isothermal Titration Calorimetry (ITC) and ^{1}H-NMR titration studies. Qualitative ^{1}H-NMR studies of anions (F$^-$, Cl$^-$, Br$^-$, I$^-$, NO$_3^-$, CH$_3$COO$^-$) with **L** are carried out in DMSO-d_6 which reveals only binding of F$^-$ and CH$_3$COO$^-$ in solution (Fig. 14S, ESI†). Both acetate and fluoride have shown 1:2 binding stoichiometry which is evident from the job's plot analysis which supports the solid state binding pattern. **L** has shown binding with acetate with downfield shift of –NH proton upto 0.565 ppm (Fig. 13S, ESI†). Acetate shows the association constant 5.97E5 M^{-2} (Table 7S, ESI†). During the binding constant estimation of fluoride, we have monitored the shift of aromatic –CH protons as broadening and subsequent disappearance of amide –NH signal is observed. The association constant estimated by ^{1}H-NMR titration for fluoride is found to 4.14E7 M^{-2} with upfield shift of –CH proton up to 0.091 ppm (Fig. 2a & 2b). Measureable data in ITC study are only obtained for acetate with **L** in DMSO (Fig. 2c). Unfortunately, binding of TBANO$_3$ with hexa-amides in DMSO turned out to be too weak to be reliably quantified by ITC measurements. In the case of fluoride the ITC profiles have shown fitting in a 1:2 (sequential sites) model with high Chi^2/DoF values and thus are not included. The thermodynamic and kinetic parameters associated with acetate to **L** binding obtained from both ITC and ^{1}H-NMR titration studies are tabulated in Table 6S & 7S, ESI†. **L** has shown exothermic binding pattern towards acetate binding (Fig. 2c). This titration

data fit well to a sequential binding model where binding sites are taken as two. During titration with acetate we have observed no heat pulse beyond 2 equivalents of anions that also confirms the choice of model for data fitting. The binding of the first acetate is found to be entropy ($\Delta H1$ = -1795 cal/mol, $\Delta S1$ = 10.5 cal/mol/deg) driven whereas binding of the second acetate is enthalpy ($\Delta H2$ = -2360 cal/mol, $\Delta S2$ = 2.92 cal/mol/deg) driven. The association constant estimated for acetate binding is 9.76E5 M^{-2} which invariably matched with the ^{1}H-NMR data. The solution state studies have shown selectivity towards fluoride over acetate and justified the solid state binding stoichiometry.

In conclusion, we have shown binding of anions and hydrated anions of different dimensionalities to a hexa-amide receptor with different structural arrangements (conformers *A*, *B*, *C*) in single crystal X-ray structural studies. Anion directed conformational diversity is observed in case of **L**, where we have observed the *A* conformer both in free ligand state and with acetate, *B* conformer with nitrate and thermodynamically highly unfavorable *C* conformer with fluoride through the isolation of discrete $[F_4(H_2O)_6]^{4-}$ cluster. The solution state ^{1}H-NMR titration and ITC studies have shown 1:2 binding stoichiometry with fluoride and acetate with fluoride selectivity. DFT calculations for each of the studied complexes have shown binding energies are sensitive to particular conformation (i.e., *aaaaaa vs. aaabbb*) as well as the electronegativity of the enclosed anion.

Acknowledgements

Notes and references

^{a} Department of Inorganic Chemistry Indian Association for the Cultivation of Science, 2A & 2B Raja S. C. Mullick Road, Kolkata 700032, India. Fax: (+91) 33-2473-2805, E-mail: icpg@iacs.res.in
^{b} Department of Chemical & Environmental Engineering and Materials Science & Engineering Program, University of California, Riverside, Riverside, California 92521, United States

† Electronic Supplementary Information (ESI) available: [Characterisation data of **L** & complex **1-3**, Experimental section, H-Bonding table of complexes, ITC titration profile, Qualitative ^{1}H-NMR spectra, ^{1}H-NMR titration profiles, Job's plots and Anion equivalents plot of receptors with CH_3COO^- & F^-, DFT optimized structures of complexes **1–3** and Cartesian coordinates.]. See DOI: 10.1039/b000000x/ CCDC numbers of the structures: 944132- complex **1**, 944135- complex **2**, 996874- complex **3**, 996875- Free receptor(**L**).

‡Color codes: Carbon: Yellow, Oxygen: Red, Hydrogen: Gray, Nitrogen: Cyan, Fluorine: Dark green.

1. (a) I. Ravikumar and P. Ghosh, *Chem. Commun*., 2010, **46**, 1082–1084; (b) P. Bose, I. Ravikumar and P. Ghosh, *Inorg. Chem.,* 2011, **50**, 10693–10702; (c) M. Li, B. Wu, C. Jia, X. Huang, Q. Zhao, S. Shao and X.-J. Yang, *Chem.–Eur. J*., 2011, **17**, 2272–2280; (d) N. Busschaert, M. Wenzel, M. E. Light, P.-I. Hernández, R.-P. Tomás and P. A. Gale, *J. Am. Chem. Soc.,* 2011, **133**, 14136–14148; (e) S. K. Dey, R. Chutia and G. Das, *Inorg. Chem*., 2012, **51**, 1727–1738; (f) B. Akhuli, I. Ravikumar and P. Ghosh, *Chem. Sci.,* 2012, **3**, 1522– 1530; (g) P. Bose, R. Dutta, S. Santra, B. Chowdhury and P. Ghosh,

Eur. J. Inorg. Chem., 2012, 5791–5801; (h) M. A. Saeed, A. Pramanik, B. M. Wong, S. A. Haque, D. R. Powell, D. K. Chand and M. A. Hossain, *Chem. Commun.*, 2012, **48**, 8631-8633; (i) A. Pramanik, D. R. Powell, B. M. Wong and M. A. Hossain, *Inorg. Chem.,* 2012, **51**, 4274-4284.

2. (a) M. Arunachalam and P. Ghosh, *Chem. Commun*., 2009, 5389–5391; (b) P. Mateus, R. Delgado, P. Brandão and V. Fèlix, *J. Org. Chem.*, 2009, **74**, 8638−8646; (c) M. Arunachalam and P. Ghosh, *Inorg.Chem*., 2010, **49**, 943–95; (d) P. Mateus, R. Delgado, P. Brandão and V. Fèlix, *J. Org. Chem.*, 2012, **77**, 4611−4621; (e) N. L. Bill, D. –S. Kim, S. K. Kim, J. S. Park, V. M. Lynch, N. J. Young, B. P. Hay, Y. Yang, E. V. Anslyn and J. L. Sessler, *Supramolecular Chemistry*, 2012, **24**, 72-76. (f) S. Chakraborty, R. Dutta, M. Arunachalam and P. Ghosh, *Dalton Trans.*, 2014, **43**, 2061–2068.

3. (a) F. Hettche, R. W.Hoffmann, *New J.Chem.*, 2003, **27**, 172–177; (b) A. Frontera, F. Saczewski, M. Gdaniec, E. Dziemidowicz-Borys, A. Kurland, P. M. Deyà, D. Quiñonero and C. Garau, *Chem. Eur. J.* 2005, **11**, 6560–6567; (c) I. Ravikumar and P. Ghosh, *Chem. Commun.,* 2010, **46**, 6741–6743; (d) R. Dutta and P. Ghosh, *Eur. J. Inorg. Chem.*, 2013, 2673–2681.

4. (a) W. E. Allen, P.A. Gale, C. T. Brown, V. M. Lynch and J. L. Sessler, *J. Am. Chem. Soc.,* 1996, **118**, 12471-12472; (b) G. Cafeo, F. H. Kohnke, G. L. L. Torre, A. J. P. White and D.J. Williams, *Chem. Commun.*, 2000, 1207–1208; (c) A. Aydogan, D. J. Coady, S. K. Kim, A. Akar, C. W. Bielawski, M. Marquez and J. L. Sessler, *Angew. Chem. Int. Ed.,* 2008, **47**, 9648–9652; (d) M. Ménand and I. Jabin, *Org. Lett*., 2009, **11**, 673–676; (e) G. Cafeo, H. M. Colquhoun, A. Cuzzola, M. F. Gattuso, H. Kohnke, L. A. Valenti and J. P. White, *J. Org. Chem.*, 2010, **75**, 6263–6266; (f) S.K. Kim, J. L. Sessler, D. E. Gross, C.-H. Lee, J. S. Kim, V. M. Lynch, L. H. Delmau and B. P. Hay, *J. Am. Chem. Soc.,* 2010, **132**, 5827–5836.

5. (a) Supramolecular Chemistry of Anions, ed. A. Bianchi, K. Bowman-James and E. Garcia-España, Wiley-VCH, New York, 1997; (b) P. D. Beer and P. A. Gale, *Angew. Chem., Int. Ed.*, 2001, **40**, 486–516; (c) K. Bowman-James, *Acc. Chem. Res*., 2005, **38**, 671–678; (d) J. L. Sessler, P. A. Gale and W.-S Cho, Anion Receptor Chemistry: Monographs in Supramolecular Chemistry, RSC Publishing, Cambridge, UK, 2006; (e) S. O. Kang, R. A. Begum and K. Bowman-James, *Angew. Chem., Int. Ed.*, 2006, **45**, 7882–7894; (f) E. Garcia-España, P. Díaz, J. M. Llinares and A. Bianchi, *Coord. Chem. Rev.*, 2006, **250**, 2952–2986; (g) C. A. Schalley, Analytical Methods in Supramolecular Chemistry; Ed.; Wiley-VCH: Weinheim, 2007; (h) E. V. Anslyn, *J. Org. Chem.*, 2007, **72**, 687-699; (i) P. A. Gale, S. E. García-Garrido and J. Garric, *Chem. Soc. Rev.*, 2008, **37**, 151–190; (j) S. Merchant and D. Asthagiri, *J. Chem. Phys.*, 2009, **130**, 195102 –195111; (k) S. Kubik, *Chem. Soc. Rev.* 2009, **38**, 585–605; (l) P. Ballester, *Chem. Soc. Rev.*, 2010, **39**, 3810–3830; (m) Supramolecular chemistry of anionic species themed Issue: *Chem. Soc. Rev.*, 2010, **39**, 3581–4008; (n) M. Arunachalam and P. Ghosh, *Chem. Commun*., 2011, **47**, 8477–8492; (o) A. E. Hargrove, S. Nieto, T. Zhang, J. L. Sessler and E. V. Anslyn, *Chem. Rev.*, 2011, **111**, 6603–6782; (p) Anion Coordination Chemistry, ed. K. Bowman-James, A. Bianchi and E. Garcia-España, Wiley-VCH, New York, 2012; (q) M. Cametti and K. Rissanen, *Chem. Soc. Rev.*, 2013, **42**, 2016–2038.

6. F. Vögtle and E. Weber, *Angew. Chem. Int. Ed. Engl.,* 1974, **13**, 814–816.

7. J. V. Gavette, A. L. Sargent and W. E. Allen, *J. Org. Chem.,* 2008, **73**, 3582–3584.

8. (a) M. Arunachalam and P. Ghosh, *Org. Lett.*, 2010, **12**, 328–331; (b) M. Arunachalam and P. Ghosh, *Chem. Commun.,* 2011, **47**, 6269–6271.

9. (a) M. Cametti and K. Rissanen, *Chem. Commun.*, 2009, 2809–2829; (b) M. A. Hossain, M. A. Saeed, A. Pramanik, B. M. Wong, S. A. Haque and D. R. Powell, *J. Am. Chem. Soc.*, 2012, **134**, 11892-11895; (c) Q. –Q. Wang, V. W. Day, K. Bowman-james; *J. Am. Chem. Soc.* 2013, **135**, 392−399.

10. (a) D. Das and L. J. Barbour, *J. Am. Chem. Soc.*, 2008, **130**, 14032–14033; (b) D. Das and L. J. Barbour, *Chem. Commun.*, 2008, 5110–5112; (c) D. Das and L. J. Barbour, *Cryst. Growth Des.*, 2009, **9**, 1599-1604.
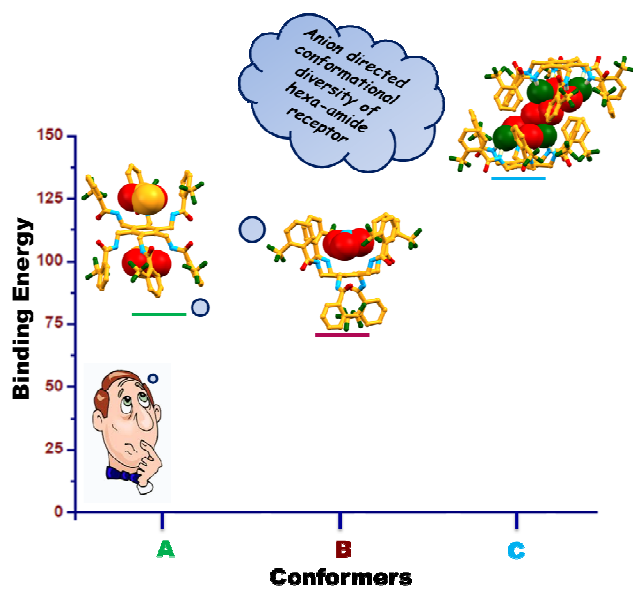
Table of Content:

The TOC shows difference in binding energies between different conformers after binding with anions of different dimensionalities and conformers *A*, *B* & *C* show structural diversities with anions in case of **L**.