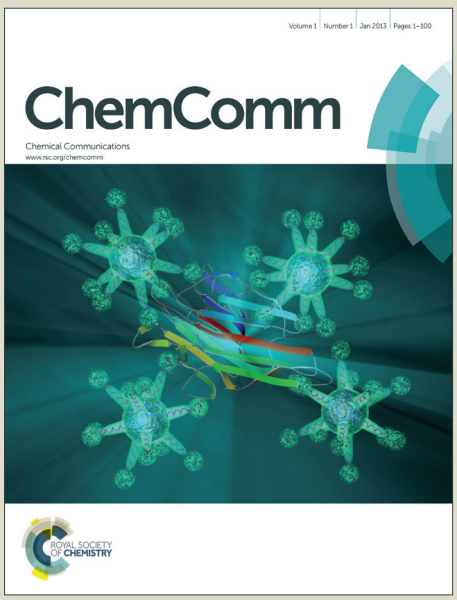
ChemComm

Accepted Manuscript



ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/chemcomm

Journal Name

COMMUNICATION

Selective Recognition and Extraction of KBr via Cooperative Interactions with a Urea Functionalized Crown Ether Dual-host

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

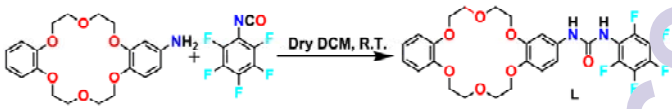
www.rsc.org/

Bidyut Akhuli[a] and Pradyut Ghosh[a,*]

Selective solid-liquid extraction of KBr is demonstrated for the first time with a crown ether based pentafluorophenyl urea functionalized dual-host receptor. ^{1}H-NMR and ITC studies have been carried out to elustrate the effect of cooperativity towards the recognition of alkali metal salts.

The extraction of alkali metal salts from liquid/solid sources is an important aspect in the field of supramolecular chemistry because of its wide application in chemical, biological, medical, environmental and industrial processes.[1-12] Selective recognition of KBr is very important because wide use of pure KBr as an antiepileptic drugs and a sedative.[13] A lot of effort has been made to develop synthetic dual-host receptors for the recognition and extraction of different alkali metal salts.[14-34] For instance, Sessler and Beer have demonstrated the extraction of different alkali metal salts via cooperative interactions with calix[4]pyrrole and calix[4]quinone based dual-host receptors respectively.[35-38] Previously, we have shown the liquid-liquid extraction of KCl and KF by using receptors for cations and anions separately.[34] In spite of the great development of different synthetic dual-host receptors for the extraction, solubilization and separation of different alkali metal salts, selective liquid-liquid or solid-liquid extraction of KBr is rare in the literature.[31] Smith and co-workers have shown solid-liquid extraction of LiBr, NaBr and KBr, though the selectivity is observed for LiBr.[31] Ensafi *et al.* have demonstrated a selective extraction method for bromide that is based on an oxidation-reduction mechanism.[39] Further, the extraction of salts from water to organic phase is a difficult task because of the high hydration energy of most common anions and cations.[40] This difficulty can be overcome if one can extract a particular salt selectively from its solid state, i.e. by solid-liquid extraction. Though, lattice energy plays a governing role towards the solid-liquid extraction of alkali metal salts. Thus, subtle balance between the lattice energy of the salts and the potentiality of the synthetic dual-host receptors can give raise an effective solid-liquid extraction of a particular salt selectively. Herein we report simple dibenzo-18-crown-6 ether based dual-host urea receptor and explored towards solid-liquid extraction of KBr selectively in presence of KCl and KNO_3. Moreover, detailed ^{1}H-NMR titration experiments and ITC studies are presented to establish the effect of cooperative interaction towards the recognition and extraction of alkali metal salts. Here it is important to mention that Barboiu *et al.* and others have shown the recognition and transportation of different alkali metal salts by utilising 15-crown-5 ether based urea/thiourea receptors.[32, 41-46]

For the extraction of alkali metal salts by a dual-host receptor, ligands should composed of metal ion as well as anion binding sites either separated by a spacer or integrated into a unit. The designing principle of **L** is as follows: (i) 18-crown-6 is known for K^+ selective receptor via coordination of suitable number of ethereal oxygen atoms with K^+ ion; (ii) pentafluorophenyl substituted urea is popular for strong H-bond donor unit to anions; and (iii) the lipophilic character of the pentafluorophenyl moiety also enhances the probability of salt extraction through the bilayer membrane. The synthesis of **L** is accomplished by a simple one step reaction of pentafluorophenyl isocyanate with 4′-aminodibenzo-18-crown-6 in dry DCM, in quantitative yield (Scheme 1).



Scheme 1. Synthesis of ligand **L**.

Receptor **L** was examined by ^{1}H-NMR study to probe the extraction ability of solid Na^+/K^+ salts of F^-, Cl^-, Br^-, I^-, NO_3^-, HSO_4^-, $H_2PO_4^-$ and AcO^- into CD_3CN solution (ESI†). After 1h of sonication and stirring, a solution of **L** in the presence of different Na-salts, ^{1}H-NMR spectra of extracted solutions show negligible change when compared to ^{1}H-NMR of free **L** that indicates inability of the receptor towards extraction of any Na-salt into the organic phase. In contrast, in the presence of

[a] Department of Inorganic Chemistry, Indian Association for the Cultivation of Science, 2A & 2B Raja S. C. Mullick Road, Kolkata 700 032, India.
[b] † Electronic Supplementary Information (ESI) available: synthesis and characterisation data of L, ESI-MS spectra, SEM-EDX data, ^{1}H-NMR and ITC titration details. See DOI: 10.1039/x0xx00000x

K-salts like KCl / KBr / KI / KNO_3, the urea-NH_a signal shows considerable downfield shifts of 2.048, 1.779, 1.219 and 1.208 ppm respectively, which indicate strong hydrogen-bonding interactions of **L** with the respective anions (Cl^- /Br- / I^- / NO_3^-) (Figure 1). However, in cases of KF, $KHSO_4$, KH_2PO_4 and KOAc, no such change in the chemical shifts of urea-NH protons of **L** is observed, which suggest that the extraction of these salts in the organic layer is energetically unfavourable probably due to high lattice energy of these salts.

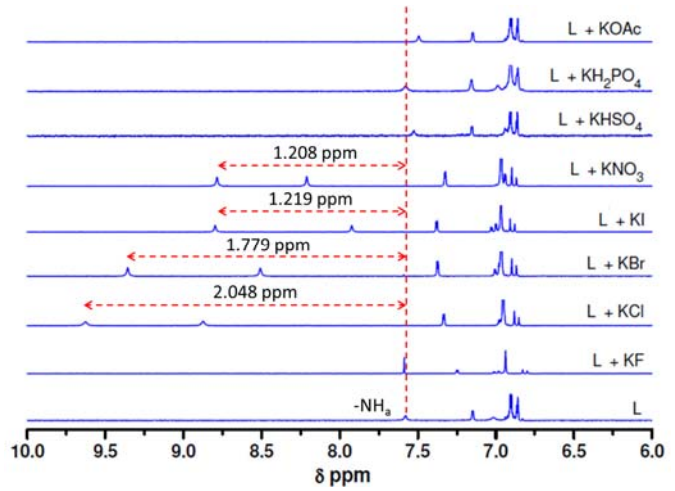


Figure 1. Changes in chemical shifts of urea-NH_a of **L** after solid-liquid extraction with different K-salts; **L** is taken in CD_3CN (~2 mM) and K-salts are taken as solid in excess (5 eqv. with respect to **L**).

Further, Electron Spray Ionisation Mass Spectrometric (ESI-MS, -Ve) experiments of the extracted mass clearly show characteristic peak (*m/z*) appear at 617.61, 661.47 and 644.53 which corresponds to **L**@Cl^-, **L**@Br^- and **L**@NO_3^- respectively (Figure 2). On the other hand, for free ligand, the base peak (*m/z*) is appeared at 581.74. The experimental isotope patterns match well with those calculated on the basis of

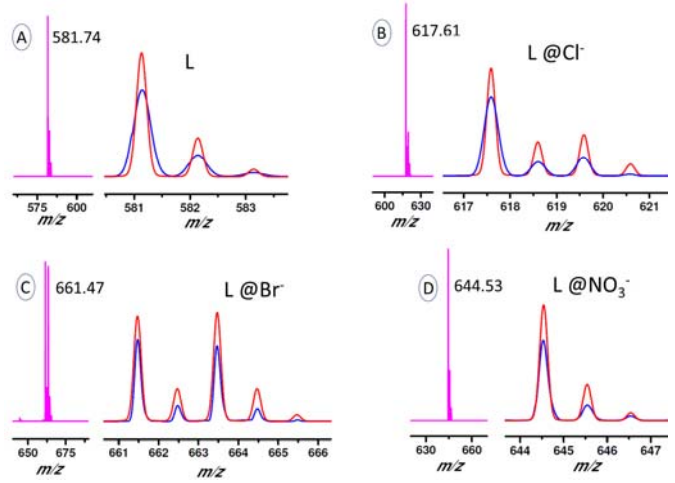


Figure 2. ESI-MS(-Ve) spectra of **L** (A) and the extracted solution of **L** with KCl(B), KBr(C) and KNO_3(D) respectively showing the base peaks and isotopic distribution patterns (red and blue lines are the simulated and experimental isotopic distribution patterns respectively).

natural abundances. No other characteristic peak related to **L**$_2$@Cl^- or **L**@Cl^-_2 is observed at higher *m/z* region that suggest the formation of only 1:1 ligand: anion complexation during solid-liquid extraction. When **L** is subjected to the same solid-liquid extraction experiment with the mixtures of KCl, KBr and KNO_3, interestingly, Br^- is selectively extracted in to the organic layer. The ESI-MS (-ve) spectrum of the extracted mass shows base peak (*m/z*) at 661.47 (Figure S8, ESI†) which corresponds to **L**@Br^-. No other peaks correspond to **L**@Cl^- and **L**@NO_3^- is observed in the mass spectrum that indicates selective extraction of Br^- from mixtures. The ^{1}H-NMR spectrum of the extracted mass obtained from the solid-liquid extraction of **L** in presence of mixture of KCl, KBr and KNO_3 matches well with the ^{1}H-NMR spectrum of extracted mass obtained from same extraction experiment of **L**, only with KBr (Figure S9, ESI†). Further, the element detection Scanning Electron Microscopy Energy Dispersive X-ray (SEM-EDX) analysis of the extracted mass confirmed the presence of only Br (no trace of Cl is detected) along with K in addition to N, F and O (Figure S10, ESI†). Thus, all these results clearly suggest the selective extraction of Br^- from the mixtures of Cl^- and NO_3^-.

The binding properties of **L** with Cl^-, Br^-, NO_3^-, HSO_4^- anions accompanied with bulky non-interacting TBA^+ cation are determined by ^{1}H-NMR titration experiments in CD_3CN at RT. Other anions such as F^-, $H_2PO_4^-$ and AcO^- are avoided because these highly basic anions deprotonate the urea-NH of **L**. The changes in the chemical shift upon addition of different anions into the solution of **L** in 1:1 ratio in CD_3CN are shown in Figure S11, ESI†. The most substantial changes are observed for the urea–NH protons, indicating that this urea–NH provides the site of interaction between the ligand and the anions. The large downfield shifts of the urea–NH_a proton are observed for Cl^-, Br^-, NO_3^- and HSO_4^- ($\Delta\delta$ = 1.358 ppm for Cl^-; $\Delta\delta$ = 0.925 ppm for Br^-; $\Delta\delta$ = 0.475 ppm for NO_3^- and $\Delta\delta$ = 0.542 ppm for HSO_4^-).

To evaluate the association constants of anion binding with **L**, ^{1}H-NMR titration experiments were carried out with Cl^-, Br^-, NO_3^-, HSO_4^- (Figure S12-S15, ESI†). The gradual addition of anions to a ~2 mM solution of **L** in CD_3CN causes nonlinear downfield shifts of the urea-NH and aromatic protons. One of the urea–NH protons (-NH_a) is monitored to determine the association constant. The titration curve gives the best fit for 1:1 binding model for host to guest which is in agreement with the anion equivalence plot (Figure 3). Association constants in absence of K^+ are summarized in Table 1 which shows that **L** binds strongly with Br^- compared to other investigated anions. However, Cl^- also displays high binding constant close to Br^-. On the other hand, NO_3^- and HSO_4^- show lower binding constants with **L** in CD_3CN. Thus, following binding order is observed in case of **L**: Br^- > Cl^- > HSO_4^- > NO_3^-, different from Hofmeister series of anions binding (SO_4^{2-} > Cl^- > NO_3^- > Br^-)[47, 48]. This difference can be attributed to the size and charge density of Br^- ion for better fit in the cavity created by **L** as well as overall electronic property exerted by the pentafluorophenyl substituted urea moiety. However, the smaller size of the Cl^- and larger size of the SO_4^{2-} are the determinant factor towards ineffective recognition process by **L**.

To evaluate the cooperative effect of alkali metal ions towards anion recognition in dual host system, ^{1}H-NMR titrations of

receptor **L** are carried out with the previously investigated anions in the presence of one equivalent of KPF_6 (Figures S16-S19, ESI†). Association constants in presence of K^+ calculated from the above titration experiments are listed in Table 1.

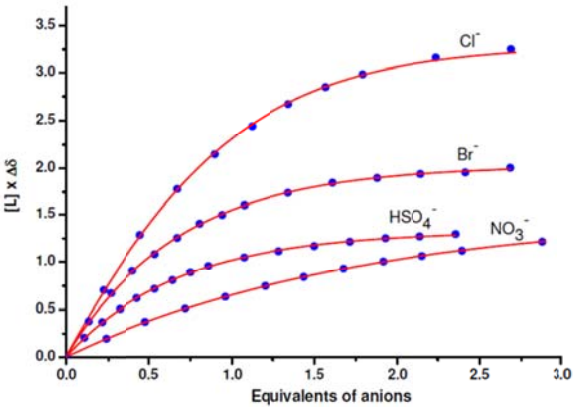


Figure 3. Plot of change in chemical shift of the urea-NH groups of **L** with increasing amounts of TBA^+X^- in CD_3CN at 298 K (X^- = Cl^-, Br^-, NO_3^- and HSO_4^-).

Table 1. Association constants (K_a) for interactions of **L** with various anions both in absence and presence of 1 equiv. of K^+.[a]

Anions	Binding constant in absence of K^+ (K; M^{-1})	Binding constant in presence of K^+ (K_{K+}; M^{-1})	K_{K+} / K
Cl^-	741	1288	1.74
Br^-	851	2455	2.88
NO_3^-	87	324	3.72
HSO_4^-	501	575	1.15

[a] ^1H NMR, solvent: CD_3CN, temperature 298 K, [$\mathbf{L^1}$] = ~2.0 mM, K^+ added as PF_6^- salts and anions added as TBA salts [TBAX] ~10-20 mM, errors < 10%.

Table 1 reveals a number of facts. Firstly, except HSO_4^- the binding constants of Cl^-, Br^- and NO_3^- ions are increased considerably in presence of K^+ which indeed justifies the positive cooperative effect of K^+ in anion binding process. Secondly, in the presence of K^+, the value of the association constant for NO_3^- increases almost 4-folds that indicates large contribution of K^+ binding with the crown-ether of the dual host towards the overall association constant. In cases of Cl^- and Br^-, 2 to 3 folds increase in the binding constant are also noticeable. Interestingly, overall binding constants trend follows the same order as observed in absence of K^+ in the system. The maximum positive cooperative factor is found to be in case of simultaneous binding of NO_3^- and K^+ with **L**.

Further, in order to get more insight into the thermodynamic contribution in the cooperative effect for the recognition of anions, we have undertaken isothermal titration calorimetric (ITC) study of Cl^- (as TBA salt) with **L** both in absence and in presence of K^+ in CH_3CN at RT (298 K) (Figure 4 and Figure S20-S21, ESI†). However, we are unsuccessful to carry out the same study with other anions (Br^-, NO_3^- and HSO_4^-) by ITC even after repeated trial. This could be due to inherent problem associated with those anions and the receptor therefore we are unsuccessful to calculate the binding constants of other anions.

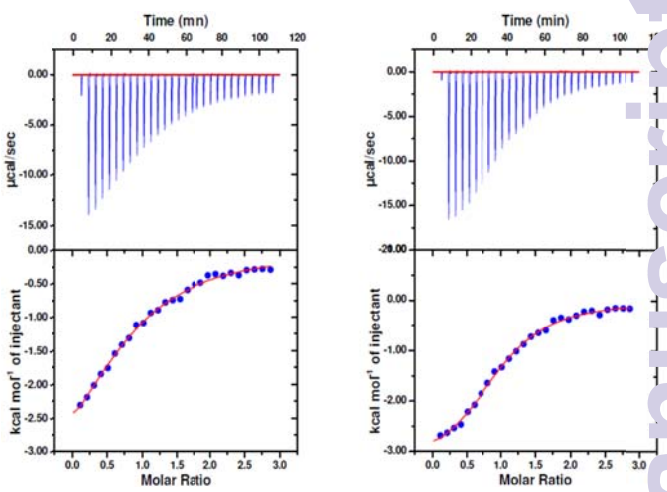


Figure 4. ITC profile of Cl^- (14.1048 mM) binding to host **L** (1.006 mM) in dry CH_3CN at 298 K in absence of K^+ (left) and in presence of 1 equiv. K^+ (right). The upper panel shows the heat pulses experimentally observed in each titration step. The lower panel reports the respective time integrals translating as the heat absorbed for each aliquot and its coherence to a 1:1 binding model.

ITC studies of Cl^- with **L** provide the thermodynamic fingerprints of the binding processes and the different contributions to the total free energy of chloride binding. For both the cases, in absence and in presence of K^+, we find strong exothermic binding. Careful observation of the thermodynamic parameters in Table 2, the contribution of enthalpy (ΔH) towards the total free energy (ΔG) of Cl^- binding in both the cases is almost same (-3490 and -3344 cal mol^{-1} respectively), but the effect of positive entropy in case of Cl^- binding in presence of one equivalent K^+ ($T\Delta S$ = 1686.68 cal mol^{-1}) is considerably large in comparison to Cl^- binding in absence of K^+ ($T\Delta S$ = 783.74 cal mol^{-1}), which can be attributed to the willingness of Cl^- to enter and fit in the host cavity via suitable hydrogen bonding interactions upon binding of K^+ in the crown cavity. Thus, this result suggests that the positive co-operativity of anion binding to **L** is due to the entropic reason. However, the ^1H-NMR titration data gave a relatively low binding constant value for Cl^-, compared to the value obtained in ITC measurement.

Table 2. Thermodynamic parameters for binding of Cl^- (as TBA salt) with **L** in dry CH_3CN at 298 K in absence and in presence of K^+.

TBACl	n	TΔS [cal/mol]	ΔH [cal/mol]	ΔG [cal/mol]	K_a [ITC]
Absence of K^+	1.21 ± 0.05	783.74	-3490 ± 69.90	-4273.74	1288
Presence of K^+	1.01 ± 0.01	1686.68	-3344 ± 39.88	-5030.68	4898

In conclusion, we have demonstrated the design and synthesis of a simple dual-host receptor, dibenzo-18-crown-6 based pentafluorophenyl substituted urea **L** that shows solid- liquid extraction of K-salts of Cl^-, Br^- and NO_3^-. It has been found that in absence of K^+, **L** shows highest selectivity towards Br^- over other anions with following order $Br^- > Cl^- \sim NO_3^- > HSO_4^-$. The positive cooperative effect of K^+ towards the recognition of Br^-, Cl^- and NO_3^- is clearly evident from the association constants of

these anions in presence of K^+. ITC studies further demonstrate that the cooperative effect towards the recognition of chloride is due to positive entropy contributions.

P. G. gratefully acknowledges the Department of Science and Technology (DST), New Delhi, India for financial support through Swarnajayanti Fellowship (DST/SJF/CSA-01/2008-2009). B.A. would like to acknowledge IACS, Kolkata, India, for fellowship.

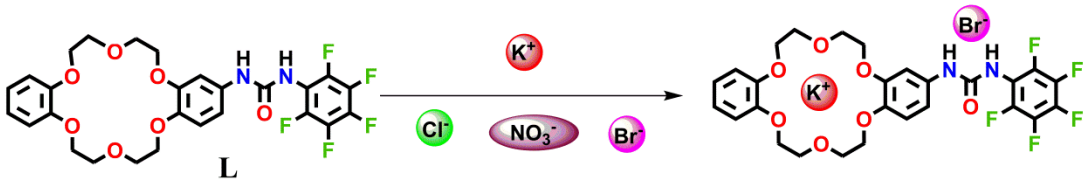
Notes and references

1. A. J. McConnell and P. D. Beer, *Angew. Chem., Int. Ed.*, 2012, **51**, 5052-5061.
2. S.-K. Kim and J. L. Sessler, *Chem. Soc. Rev.*, 2010, **39**, 3784-3809.
3. J. W. Steed, J. L. Atwood and Editors, *Supramolecular Chemistry, Second Edition*, John Wiley & Sons, Ltd., 2009.
4. P. Molina, A. Tarraga and M. Alfonso, *Dalton Trans.*, 2014, **43**, 18-29.
5. B. A. Moyer, F. V. Sloop, Jr., C. J. Fowler, T. J. Haverlock, H.-A. Kang, L. H. Delmau, D. M. Bau, M. A. Hossain, K. Bowman-James, J. A. Shriver, N. L. Bill, D. E. Gross, M. Marquez, V. M. Lynch and J. L. Sessler, *Supramol. Chem.*, 2010, **22**, 653-671.
6. J. W. Steed, D. R. Turner, K. J. Wallace and Editors, *Core Concepts in Supramolecular Chemistry and Nanochemistry*, John Wiley & Sons Ltd., 2007.
7. B. A. Moyer, R. P. Singh and Editors, *Fundamentals and Applications of Anion Separations.* Kluwer Academic/Plenum Publishers, 2004.
8. K. Gloe, H. Stephan and M. Grotjahn, *Chem. Eng. Technol.*, 2003, **26**, 1107-1117.
9. P. A. Gale, *Coord. Chem. Rev.*, 2003, **240**, 191-221.
10. J. M. Lehn, *Supramolecular Chemistry: Concepts and Perspectives*, VCH, 1995.
11. J. M. Mahoney, J. P. Davis, A. M. Beatty and B. D. Smith, *J. Org. Chem.*, 2003, **68**, 9819-9820.
12. J. M. Mahoney, K. A. Stucker, H. Jiang, I. Carmichael, N. R. Brinkmann, A. M. Beatty, B. C. Noll and B. D. Smith, *J. Am. Chem. Soc.*, 2005, **127**, 2922-2928.
13. G. Goodman, *"chapter 10: Hypnotics and Sedatives". The Biological Basis of Therapeutics (4th ed.). London: MacMillan.*, 1970, 121-122.
14. J. Romanski and P. Piatek, *Chem. Commun.*, 2012, **48**, 11346-11348.
15. J. M. Mahoney, R. A. Marshall, A. M. Beatty, B. D. Smith, S. Camiolo and P. A. Gale, *J. Supramol. Chem.*, 2003, **1**, 289-292.
16. M. Ciardi, A. Galan and P. Ballester, *J. Am. Chem. Soc.*, 2015, **137**, 2047-2055.
17. J. E. Redman, P. D. Beer, S. W. Dent and M. G. B. Drew, *Chem. Commun.*, 1998, 231-232.
18. H. Miyaji, D.-S. Kim, B.-Y. Chang, E. Park, S.-M. Park and K. H. Ahn, *Chem. Commun.*, 2008, 753-755.
19. Z.-H. Sun, F.-F. Pan, Triyanti, M. Albrecht and G. Raabe, *Eur. J. Org. Chem.*, 2013, **2013**, 7922-7932.
20. L. H. Uppadine, J. E. Redman, S. W. Dent, M. G. B. Drew and P. D. Beer, *Inorg. Chem.*, 2001, **40**, 2860-2869.
21. J. M. Mahoney, A. M. Beatty and B. D. Smith, *J. Am. Chem. Soc.*, 2001, **123**, 5847-5848.
22. P. Lu, W. Feng, Y. Meng and J. Xie, *Mol. Simul.*, 2013, **39**, 621-628.
23. V. Arens, C. Dietz, D. Schollmeyer and K. Jurkschat, *Organometallics*, 2013, **32**, 2775-2786.
24. 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.
25. P. Piatek, M. Karbarz and J. Romanski, *Dalton Trans.*, 2014, **43**, 8515-8522.
26. E. N. W. Howe, M. Bhadbhade and P. Thordarson, *J. Am. Chem. Soc.*, 2014, **136**, 7505-7516.
27. A. Kumar and S. K. Menon, *Supramol. Chem.*, 2010, **22**, 46-56.
28. S. K. Kim, G. I. Vargas-Zuniga, B. P. Hay, N. J. Young, L. H. Delmau, C. Masselin, C.-H. Lee, J. S. Kim, V. M. Lynch, B. A. Moyer and J. L. Sessler, *J. Am. Chem. Soc.*, 2012, **134**, 1782-1792.
29. I.-W. Park, J. Yoo, B. Kim, S. Adhikari, S. K. Kim, Y. Yeon, C. J. E. Haynes, J. L. Sutton, C. C. Tong, V. M. Lynch, J. L. Sessler, P. A. Gale and C.-H. Lee, *Chem. - Eur. J.*, 2012, **18**, 2514-2523.
30. J. M. Mahoney, G. U. Nawaratna, A. M. Beatty, P. J. Duggan and B. D. Smith, *Inorg. Chem.*, 2004, **43**, 5902-5907.
31. J. M. Mahoney, A. M. Beatty and B. D. Smith, *Inorg. Chem* 2004, **43**, 7617-7621.
32. M. Barboiu, G. Vaughan and A. Van Der Lee, *Org. Lett.*, 2003, **5**, 3073-3076.
33. L. A. J. Chrisstoffels, F. de Jong, D. N. Reinhoudt, S. Sivelli, L. Gazzola, A. Casnati and R. Ungaro, *J. Am. Chem. Soc.*, 1999, **121**, 10142-10151.
34. I. Ravikumar, S. Saha and P. Ghosh, *Chem. Commun.*, 2011, **47**, 4721-4723.
35. S. C. Picot, B. R. Mullaney and P. D. Beer, *Chem. - Eur. J.*, 2012, **18**, 6230-6237.
36. S. K. Kim, H. G. Lee, G. I. Vargas-Zuniga, V. M. Lynch, C. Kim and J. L. Sessler, *Chem. - Eur. J.*, 2014, **20**, 11750-11759.
37. P. R. A. Webber and P. D. Beer, *Dalton Trans.*, 2003, 2249-2252.
38. A. J. McConnell, C. J. Serpell and P. D. Beer, *New J. Chem.*, 2012, **36**, 102-112.
39. A. A. Ensafi and H. Eskandari, *Sep. Sci. Technol.*, 2001, **36**, 81-89.
40. R. Custelcean and B. A. Moyer, *Eur. J. Inorg. Chem.*, 2007, 1321-1340.
41. S. Mihai, A. Cazacu, C. Arnal-Herault, G. Nasr, A. Meffre, A. van der Lee and M. Barboiu, *New J. Chem.*, 2009, **33**, 2335-2343.
42. M. Barboiu, S. Cerneaux, A. van der Lee and G. Vaughan, *J. Am. Chem. Soc.*, 2004, **126**, 3545-3550.
43. A. Cazacu, C. Tong, A. Van der Lee, T. M. Fyles and M. Barboiu, *J. Am. Chem. Soc.*, 2006, **128**, 9541-9548.
44. M. Barboiu, D. Dumitrescu and A. van der Lee, *Cryst. Growth Des.*, 2014, **14**, 3062-3068.
45. N. Hovnanian, S. Cerneaux and P. Dieudonne, *J. Sol-Gel Sci Technol.*, 2004, **31**, 353-358.
46. S. Cerneaux and N. Hovnanian, *J. Membr. Sci.*, 2005, **247**, 87-94.
47. F. Hofmeister, *Arch. exper. Path. Pharm.*, **24**, 247-260.
48. Z. Yang, *J. Biotechnol.*, 2009, **144**, 12-22.

Journal Name

COMMUNICATION

TOC



Selective solid-liquid extraction of KBr is demonstrated for the first time with crown ether based pentafluorophenyl urea functionalised dual-host receptor.