### Accepted Manuscript

Synthesis, crystal structures and competitive binding property of a family of calix[4]arene-biscrown-5/6 and their application in extraction of alkali metal ions from sea bittern

Vallu Ramakrishna, E. Suresh, Vinod P. Boricha, Anjani K. Bhatt, Parimal Paul

PII:	\$0277-5387(15)00356-3
DOI:	http://dx.doi.org/10.1016/j.poly.2015.07.001
Reference:	POLY 11387
To appear in:	Polyhedron
Received Date:	27 April 2015
Accepted Date:	2 July 2015



Please cite this article as: V. Ramakrishna, E. Suresh, V.P. Boricha, A.K. Bhatt, P. Paul, Synthesis, crystal structures and competitive binding property of a family of calix[4]arene-biscrown-5/6 and their application in extraction of alkali metal ions from sea bittern, *Polyhedron* (2015), doi: http://dx.doi.org/10.1016/j.poly.2015.07.001

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

# Synthesis, crystal structures and competitive binding property of a family of calix[4]arene-biscrown-5/6 and their application in extraction of alkali metal ions from sea bittern

Vallu Ramakrishna<sup>a</sup>, Suresh E<sup>a,b</sup>, Vinod P Boricha<sup>a</sup>, Anjani K Bhatt<sup>a</sup> and Parimal Paul<sup>\*,a,b</sup>

<sup>a</sup>Analytical Division and Centralized Instrument Facility, CSIR-Central Salt and Marine Chemicals Research Institute, G. B. Marg, Bhavnagar 364002, India. <sup>b</sup>Academy of Scientific and Innovative Research (AcSIR), CSIR-CSMCRI, G. B. Marg, Bhavnagar 364002, India.

#### Abstract

A family of calix[4]arene compounds containing crown moieties at both the upper and lower rims of the calix unit with different substituents attached to the nitrogen atom of the aza-crown moiety have been synthesized, characterized and their competitive binding property towards Li<sup>+</sup>, Na<sup>+</sup>, K<sup>+</sup>, Mg<sup>2+</sup>, Ca<sup>2+</sup> and Sr<sup>2+</sup> in aqueous media has been investigated. These ionophores exhibit high selectivity towards K<sup>+</sup>, assessed by two-phase extraction method followed by ion chromatographic assay of the metal ions in the extract. Isothermal calorimetric titration for complex formation with K<sup>+</sup> was carried out to evaluate stoichiometry, binding constant and other thermodynamic parameters ( $\Delta$ H,  $\Delta$ S and  $\Delta$ G). For structural elucidation in solution, detail <sup>1</sup>H NMR study was carried out and K<sup>+</sup> complexes were isolated for solid state characterization. Molecular structures of two of the ionophores and K<sup>+</sup>-complex of

one of the ionophores has been established by single crystal X-ray study. <sup>1</sup>H NMR, ITC and single crystal XRD studies suggest 1:1 complex formation with encapsulation of  $K^+$  in the crown-6 ring at the upper rim. These ionophores have been applied for extraction of metal ions from bittern.

**Keywords:** Calixarenes; Crystal structures; Selectivity; Isothermal calorimetry; Two-phase extraction; Alkali metal ions.

\*Corresponding author. E-mail: ppaul@csmcri.org (P. Paul); Tel.: +91 278 2565180.

#### 1. Introduction

Calixarenes are versatile class of macrocyclic compounds, which have been extensively used in the areas of host-guest chemistry, supramolecular chemistry, molecular sensors, coordination chemistry etc. [1-7]. This chemistry has become more versatile because of the ease with which calixarene can be modified depending on the requirement. These modified calixarenes provide a highly preorganized architecture for the assembling of converging binding sites [8-14]. By the appropriate choice of the substituents, they can be made selective binders for metal ions, anions and neutral molecules [15-21]. Among the calixarene derivatives, a new class of hybrid molecules has been developed by incorporating crown ethers moiety into calix[4]arene and it has attracted intense interest because of their complexation ability with alkali and alkaline earth metal ions [22-31]. The ion selectivity of this class of compounds depends mainly on the conformation of the calixarene moiety, the size of the crown ether ring and substituents attached with the calixarene or crown moiety. In this calix-crown

hybrid family, another type of molecules has been developed by incorporating azacrown ring, the advantage of this class of compound is that any desire substituents can be easily attached with the nitrogen atom of the ring and it can act like lariat crown ether making three dimensional cavities for metal ions and also it can impose control steric crowding to tune selectivity [32-35]. This chemistry has been further extended incorporating two crown moieties at the opposite sides of the calixarene unit with 1,3alternate conformation [25,32,36]. It provides the possibility of complex formation with two metal ions at the two crown rings and it can also facilitates complexation with polymeric network structures [16,37].

One of the important applications of these calix-crown hybrid ionophores is to use them as sensor/complexing reagent for alkali and alkaline earth metal ions [38-43]. If good selectivity for a particular metal ion is found, these ionophores can be used for recovery/extraction of that specific metal ion. In this regard, K<sup>+</sup> is most important as it uses as fertiliser and has demand worldwide and India imports its entire requirement [44-46]. The present work is aimed to develop  $K^+$  selective ionophore, which may find potential application in recovery of this metal ion from natural sources such as sea bittern. As the ionic size of  $K^+$  matches very well with the ring size of crown-5/6, so the ionophores reported in the present study is designed incorporating crown -5/6 to make them selective towards K<sup>+</sup> among the other metal ions present in bittern with significant concentration (Na<sup>+</sup>, K<sup>+</sup>, Mg<sup>2+</sup>, Ca<sup>2+</sup>). Substituents such as 2-hydroxy-5nitrobenzyl, ethyl acetate and acetyl groups, which contain donor atom and can act as lariat moiety, are attached with the nitrogen atom of the aza-crown ring. For the determination of selectivity, most of the cases in the literature, the interaction of the ionophore with individual metal ion and comparison of their binding constants has been reported to evaluate the selectivity [25,27]. However, for practical use it is better

to prepare an artificial solution containing mixture of constituent metal ions and to study the competitive complexing property of the ionophore using this solution. With this idea, the competitive binding ability towards Li<sup>+</sup>, Na<sup>+</sup>, K<sup>+</sup>, Mg<sup>2+</sup>, Ca<sup>2+</sup> and Sr<sup>2+</sup> has been investigated using equimolar mixture of these metal ions by two-phase extraction method using picrate as counter anion. Picrate anion makes strong ion-pair interaction, which facilitates transport of metal complex from aqueous to non-aqueous media [24,35].

In this paper, we report synthesis and characterization of four calix-bis-crown ethers, their competitive complexation ability from the equimolar mixture of the above-mentioned metal ions in aqueous media and also from sea bittern as real sample. Metal extraction was carried out by two-phase extraction procedure followed by estimation of the concentration of metal ions in the extract (organic phase) by ion chromatographic assay. The binding constants and other thermodynamic parameters were determined by the isothermal calorimetric titration, stoichiometry of the complexes formed was determined from ESMS data and <sup>1</sup>H NMR spectral change was used to investigate binding sites of the metal ions. For solid state structural characterization, the molecular structures of two of the ionophores and K<sup>+</sup>-complex of one of them have been determined by single crystal X-ray study and reported herein.

#### 2. Experimental

#### 2.1. Materials

The compound 2-hydroxy-5-nitrobenzyl bromide was purchased from Sigma-Aldrich and other chemicals were purchased from S.D Fine chemicals. All the solvents were of analytical grade and purified by standard procedures before use [47]. Milli-Q (Millipore Corporation) water was used for extraction and ion chromatography. Metal

picrate salts were prepared by the reaction of picric acid and metal hydroxide in aqueous media. The reagents 2-(2-chloroethoxy)ethyl, 4-methylbezene sulfonate and pentaethyleneglycolditosylate were prepared following the literature procedures [48]. The starting materials such as *p*-tert-butyl calix[4]arene [49], dealkylated calix[4]arenes [50], calix[4]arene-bis-crown ether were synthesized following the literature procedures [32,39].

#### 2.2. Physical measurements

Elemental analyses (C, H & N) were performed on a model Vario Micro CUBE elemental analyzer. Mass spectra were recorded on a Q-TOF Micro<sup>TM</sup> LC-Ms instrument. Infrared spectra were recorded on a Perkin-Elmer spectrum GX FT-system as KBr pellets. NMR spectra were recorded on models DPX200 and Avance II 500 Brucker FT-NMR instruments. The UV/vis spectra were recorded on a CARY 500 scan Varian spectrophotometer. The cation concentration was measured with a Dionex 500 ion chromatography. Single crystal X-ray structures were determined using a Bruker SMART1000 (CCD) diffractometer. Thermodynamic parameters were determined using isothermal titration calorimetry (ITC200) provided by Microcal Company.

#### 2.3. Synthesis of compounds

#### 2.3.1. Synthesis of calix[4]arene-crown-6-aza-crown-5 (1)

This compound was synthesised following a modified literature procedure [32]. In a typical procedure, N-tosylated calix[4]arene-crown-6-aza-crown-5 (2.72 g) dissolved in 1,4-dioxane (100 mL) and methanol (20 mL) was taken and Na<sub>2</sub>HPO<sub>4</sub> (0.91 g) and 6% Na/Hg amalgam (10.0 g) were added into this solution and the reaction mixture

was heated to reflux at 80 °C for 48 h under nitrogen atmosphere. The solution was evaporated under reduced pressure and the residue was extracted with dichloromethane and saturated aqueous solution of NaHCO<sub>3</sub>, the organic layer thus separated was dried with anhydrous MgSO<sub>4</sub>. The compound thus obtained was purified by column chromatography using neutral silica gel as column material and chloroform as eluent. The compound was recrystallized from ethyl acetate by slow evaporation, which gave colourless crystals suitable for single crystal X-ray study. Yield: 60 % (1.35 g). <sup>1</sup>H NMR (CD<sub>3</sub>CN):  $\delta$  7.14 (d, J = 6.0 Hz, 8H, Ar-Hm-calix), 6.92 (t, J = 7.5 Hz, 2H, Ar-Hp-calix), 6.76 (t, J = 7.5 Hz, 2H, Ar-Hp-calix), 3.70 (s, 12H, Ar-CH<sub>2</sub>-Ar, OCH<sub>2</sub>CH<sub>2</sub>O-azacrown-5), 3.66 (s, 8H, OCH<sub>2</sub>CH<sub>2</sub>O), 3.62 (s, 4H, OCH<sub>2</sub>CH<sub>2</sub>O-crown-6), 3.59 (tt, 4H, Ar-OCH<sub>2</sub>CH<sub>2</sub>O-azacrown-5), 3.5 (br, 4H, Ar-OCH<sub>2</sub>CH<sub>2</sub>O-azacrown-5), 3.51 (t, J = 9.5 Hz, 4H, ArOCH<sub>2</sub>CH<sub>2</sub>O-crown-6), 3.47 (t, J = 5.25 Hz, 4H, Ar-OCH<sub>2</sub>CH<sub>2</sub>O-crown-6), 2.70 (t, J = 5.2 Hz, 4H, -CH<sub>2</sub>CH<sub>2</sub>NH). IR (selected bands): 3210 sh cm<sup>-1</sup>, v (N-H). ES-MS: m/z = 784.53 (100%), calcd. for [1+H<sup>+</sup>]<sup>+</sup> 784.89. Anal. Calcd. for C<sub>46</sub>H<sub>57</sub>NO<sub>10</sub>: C, 70.48; H, 7.32; N, 1.78. Found: C, 69.83; H, 7.09; N, 1.60.

2.3.2. Synthesis of calix[4]arene-crown-6-N-(2-hydroxy-5-nitrobenzyl)aza-crown-5(2)

To a solution of freshly distilled 100 mL tetrahydrofuran (THF), 0.6 g (0.765 mmol) of compound **1**, 0.4 mL (0.153 mmol) of triethylamine was added and stirred for 1 h at 0  $^{\circ}$ C and then 0.354 g (0.153mmol) of N-(2-hydroxy-5-nitrobenzyl) bromide was added and stirring was continued for 4 h at 0  $^{\circ}$ C and then it was slowly heated to 65  $^{\circ}$ C and the stirring was continued for 48 h maintaining the same temperature. The solution was then evaporated under reduced pressure, which gave yellow oil. The crude

product was purified by column chromatography using silica gel as column material and chloroform-methanol (1:0.5) as eluent. Yield: 63.0 % (0.45 g). <sup>1</sup>H NMR (CD<sub>3</sub>CN):  $\delta$  8.08 (d, J = 2.5 Hz, 1H, Ar*H*-chromogenic part), 8.06 (d, J = 2.5 Hz, 1H, Ar*H*-chromogenic part), 7.98 (d, J = 2.5 Hz, 1H, Ar*H*-chromogenic part), 7.11(dd, J =4Hz, 8H, Ar*H*<sub>m</sub>-calix), 6.88 (t, J = 7.5 Hz, 4H, Ar*H*<sub>p</sub>-calix), 3.94 (s, 2H, N-*CH*<sub>2</sub>Ar), 3.82 (s, 8H, Ar-*CH*<sub>2</sub>Ar), 3.63 (s, 4H, Ar-O*CH*<sub>2</sub>*CH*<sub>2</sub>O-crown-6), 3.60 (t, J = 4.5 Hz, 4H, Ar-O*CH*<sub>2</sub>*CH*<sub>2</sub>O-crown-5), 3.56-3.52 (m, 12H, O*CH*<sub>2</sub>*CH*<sub>2</sub>O-crown-6), 3.32 (t, 4H, J = 4.75 Hz, Ar-O*CH*<sub>2</sub>*CH*<sub>2</sub>O-crown-6), 3.25 (t, J = 4.75 Hz, 4H, Ar-O*CH*<sub>2</sub>*CH*<sub>2</sub>Ocrown-5), 3.16 (t, J = 4.75 Hz, 4H, Ar-O*CH*<sub>2</sub>*CH*<sub>2</sub>O-crown-5), 2.68 (t, J = 4.7Hz, 4H, O*CH*<sub>2</sub>*CH*<sub>2</sub>N-). IR (selected band): 3433 cm<sup>-1</sup>, v (O-H); 1514 and 1334 cm<sup>-1</sup>, NO<sub>2</sub> (2hydroxy-5-nitrobenzyl). ES-MS: m/z: found 935.93, calcd. for [**2**+H<sup>+</sup>]<sup>+</sup> 936.00. Anal. Calcd. for C<sub>53</sub>H<sub>62</sub>N<sub>2</sub>O<sub>13</sub>: C, 68.08; H, 6.68; N, 2.99. Found: C, 67.06; H, 6.68; N, 3.14.

#### 2.3.3. Synthesis of calix[4]arene-crown-6-N-ethylester-aza-crown-5 (3)

This compound was synthesized from 1 following the same procedure as described for 2, except ethylbromoester was used instead of N-(2-hydroxy-5-nitrobenzyl) bromide. The crude product was purified by column chromatography using silica gel and hexane-chloroform (1:2) as eluent. The product was recrystallized from acetonitrile to obtain colourless crystals suitable for single crystal X-ray study. Yield: 60.0 % (0.4 g). <sup>1</sup>H NMR (CD<sub>3</sub>CN):  $\delta$  7.10 (dd, *J* = 5.0 Hz, 8H, Ar-*Hm*-calix), 6.87 (tt, *J* = 7.5 Hz, 4H, Ar*H*<sub>p</sub>-calix), 4.14 (q, *J* = 7.33 Hz, 2H, -*CH*<sub>2</sub>-ester part), 3.78 (s, 8H, Ar-*CH*<sub>2</sub>-Ar), 3.64 (s, 4H, Ar-O*CH*<sub>2</sub>*CH*<sub>2</sub>O), 3.57 (overlapped, 8H, O*CH*<sub>2</sub>*CH*<sub>2</sub>O-crown-6 and O*CH*<sub>2</sub>*CH*<sub>2</sub>O-azacrown-5), 3.53 (t, *J* = 4.5 Hz, 4H, Ar-O*CH*<sub>2</sub>*CH*<sub>2</sub>O-crown-6), 3.50 (t, *J* = 5.0 Hz, 4H, Ar-O*CH*<sub>2</sub>*CH*<sub>2</sub>O-), 3.40 (s, 2H, -*CH*<sub>2</sub>CH<sub>3</sub>), 3.31 (q, 8H, Ar-O*CH*<sub>2</sub>*CH*<sub>2</sub>O-crown-6 and Ar-O*CH*<sub>2</sub>*CH*<sub>2</sub>O-azacrown-5), 3.26 (t, *J* = 6.0 Hz, 4H, Ar-O*CH*<sub>2</sub>*CH*<sub>2</sub>O-azacrown-5), 3.26 (t, *J* = 6.0 Hz,

5), 2.74 (s, 4H, O*CH*<sub>2</sub>*CH*<sub>2</sub>NH), 1.26 (t, *J* = 7.25 Hz, -*CH*<sub>3</sub>). IR (selected band): 1737 cm<sup>-1</sup>, v (C=O, ester). ES-MS: *m/z*: found 870.72, calcd for [**3**+H<sup>+</sup>] 870.97. Anal. Calcd. for C<sub>50</sub>H<sub>63</sub>NO<sub>12</sub>: C, 69.03; H, 7.30; N, 1.61. Found: C, 68.30; H, 7.41; N, 1.57.

#### 2.3.4. Synthesis of calix[4]arene-crown-6-N-acetyl aza-crown-5 (4)

This compound was synthesized from **1** following similar procedure as described for **2** except, acetyl chloride was used instead of N-(2-hydroxy-5-nitrobenzyl) bromide. The crude product was purified by column chromatography using silica gel and hexane-chloroform (1:2) as eluent. Yield: 63.0 % (0.2 g). <sup>1</sup>H NMR (CD<sub>3</sub>CN):  $\delta$  7.13-7.10 (m, 8H, Ar*Hm*-calix), 6.91-6.88 (tt, 2 H, Ar*Hp*-calix), 6.82 (t, *J* = 7.5 Hz, 2H, Ar*Hp*-calix), 3.77 (s, 8H, Ar-*CH*<sub>2</sub>-Ar), 3.64 (s, 4H, O*CH*<sub>2</sub>*CH*<sub>2</sub>O-crown-6), 3.63-3.59 (m, 12H, O*CH*<sub>2</sub>*CH*<sub>2</sub>NH, O*CH*<sub>2</sub>*CH*<sub>2</sub>O-crown-6), 3.56-3.51 (m, 4H, Ar-O*CH*<sub>2</sub>*CH*<sub>2</sub>O-azacrown-5), 3.41-3.38 (m, 8H, -O*CH*<sub>2</sub>*CH*<sub>2</sub>O-, ArO*CH*<sub>2</sub>*CH*<sub>2</sub>O-azacrown-5), 3.35-3.29 (m, 6H, overlapped, -*CH*<sub>2</sub>*CH*<sub>2</sub>O-, -O*CH*<sub>2</sub>*CH*<sub>2</sub>O-azacrown-5), 3.24 (t, *J* = 6.25 Hz, 4H, O*CH*<sub>2</sub>*CH*<sub>2</sub>O-), 2.07 (s, 3H, -NCH<sub>3</sub>). IR (selected band): 1677 cm<sup>-1</sup>, v (C=O, acetate). ES-MS: *m/z:* found 826.67, 848.66, 865.63, and 866.63; calcd for [**4**+H<sup>+</sup>]<sup>+</sup> 826.92, [**4**+Na<sup>+</sup>]<sup>+</sup> 848.91, [**4**+K<sup>+</sup>]<sup>+</sup> 865.01, [**4**+H<sup>+</sup>+K<sup>+</sup>]<sup>+</sup> 866.02. Anal. Calcd. for C<sub>48</sub>H<sub>59</sub>NO<sub>11</sub>: C, 69.80; H, 7,19; N, 1.69; found: C, 70.10; H, 7.30; N, 1.70.

#### 2.4. Selectivity study by two-phase extraction method

Selectivity of the ionophores towards Li<sup>+</sup>, Na<sup>+</sup>, K<sup>+</sup>, Mg<sup>2+</sup>, Ca<sup>2+</sup> and Sr<sup>2+</sup> were determined by two-phase extraction method using aqueous solution of the equimolar mixture of these metal ions with picrate as counter anion. In a typical experiment, equal volume (10 mL) of aqueous solution of equimolar mixture of alkali metal picrate (Li<sup>+</sup>, Na<sup>+</sup>, K<sup>+</sup>, Mg<sup>2+</sup>, Ca<sup>2+</sup> and Sr<sup>2+</sup>, 0.1 M each) and CH<sub>2</sub>Cl<sub>2</sub> solution (10 mL) of the

required ionophore (0.002 M) were mixed and vigorously shaken in a vortex mixture for 30 min and the solution was transferred to a separating funnel and allowed to stand for 4 h. The metal ions added with stoichiometric amount and also with 25, 50, 75 and 100 times excess compared to the concentration of ionophores. After settling down, the dichloromethane layer was separated and transferred to a crucible, the solvent was evaporated by gentle heating on a water bath, and then heated in a furnace at 550 °C for 5 h. The residue was dissolved in deionized water (~ 5 mL) and filtered on 0.2  $\mu$ m filter paper. The relative concentrations of the cations in the filtrate were determined by ion chromatography using Ion Pac CS12 (2 mm) analytical column and 20 mM methanesulphonic acid as eluent with a flow rate of 0.25 mL/min. Quantification was made using a standard solution containing a mixture of LiCl, NaCl, KCl, MgCl<sub>2</sub>, CaCl<sub>2</sub> and SrCl<sub>2</sub> (10 ppm each).

#### 2.5. Application for extraction of metal ions from bittern

The ionophores were applied for extraction of metal ions from bittern using the similar procedure as described for selectivity study, except bittern and picric acid were used instead of mixture of the picrate salts of different metal ions. The concentration of metal ions in the organic phase were analysed by ion chromatography as described above.

#### 2.6. Synthesis of $K^+$ complexes of the ionophores **1-4**

Metal ( $K^+$ ) complexes of all the ionophores were synthesised following the similar procedure. In a typical experiment, a mixture of 0.05 mmol of the ionophores (1/2/3/4) and  $K^+$  picrate (0.5mmol, ten-fold excess) was stirred in chloroform at room temperature for 24 h. The reaction mixture was then filtered to remove unreacted picrate salt and the complex was obtained by removing the solvent from the filtrate

under vacuum. The yellow complex thus obtained was dissolved in a minimum volume (ca. 3 mL) of dichloromethane (in which  $K^+$  picrate is almost insoluble) followed by filtration to remove trace quantities of unreacted  $K^+$  picrate. The solution was then evaporated to dryness to get yellow product. The <sup>1</sup>H NMR spectra of the complexes did not show any signal corresponding to free ionophore or excess picrate anion, which confirmed the complete complexation. Yield: 90–95%. For the  $K^+$  complex of the ionophore **1**, crystals suitable for the single crystal X-ray study were grown from ethyl acetate by slow evaporation.

#### 2.7. Characterization data

[1.K<sup>+</sup>.Pic<sup>-</sup>].HPic.EtAc.H<sub>2</sub>O: <sup>1</sup>H-NMR (CD<sub>3</sub>CN):  $\delta$  8.82 (br,1H, -NH), 8.63 (s,4H, picrate), 7.31 (d, *J* = 7.5 Hz, 4H, Ar*Hm*-calix), 7.20 (d, *J* = 7.5 Hz, 4H, Ar*Hm*-calix), 7.03 (t, *J* = 7.5 Hz, 2H, Ar*Hp*-calix), 6.95 (t, *J* = 7.5 Hz, 2H, Ar*Hp*-calix), 3.92-3.91 (m, 4H, OCH<sub>2</sub>CH<sub>2</sub>O-crown-6), 3.83 (br, 4H, Ar-OCH<sub>2</sub>CH<sub>2</sub>O-crown-6), 3.80 (d, *J* = 4.5 Hz, 8H, Ar-*CH*<sub>2</sub>-Ar), 3.72 (overlapped s, 16H, O*CH*<sub>2</sub>*CH*<sub>2</sub>O, Ar-O*CH*<sub>2</sub>*CH*<sub>2</sub>O-crown-5), 3.68 (br, 8H, Ar-O*CH*<sub>2</sub>*CH*<sub>2</sub>NH), 3.10 (s, 4H, OCH<sub>2</sub>*CH*<sub>2</sub>*NH*). IR (selected band): 1559 and 1362 cm<sup>-1</sup> (NO<sub>2</sub>, picrate). ES-MS: *m/z*: found 822.55, calcd for [1+K<sup>+</sup>]<sup>+</sup> 822.99. Anal. calcd. for C<sub>64</sub>H<sub>72</sub>N<sub>7</sub>O<sub>25</sub>K: C, 55.70; H, 5.26; N, 7.11. Found: C, 55.51; H, 5.47; N, 6.94.

[2.K<sup>+</sup>.Pic<sup>-</sup>].HPic: <sup>1</sup>H NMR (CD<sub>3</sub>CN):  $\delta$  8.63 (s, 2H, picrate), 8.12 (d, J = 2.5 Hz, 1H, Ar*H*-chromogenic part), 8.10 (d, J = 2.5 Hz, 1H, Ar*H*-chromogenic part), 8.02 (d, J = 2.5 Hz, 1H, Ar*H*-chromogenic part), 7.42 (d, J = 7.5Hz, 4H, Ar*Hm*-calix), 7.35 (d, J = 7.5Hz, 4H, Ar*Hm*-calix), 7.10 (t, J = 13.0 Hz, 4H, Ar*Hp*-calix), 4.12 (s, 2H, N-CH<sub>2</sub>Ar), 4.02 (s, 4H, Ar-OCH<sub>2</sub>CH<sub>2</sub>O-crown-6), 3.88 (overlapped d, J = 13.5 Hz, 8H, Ar-CH<sub>2</sub>-Ar, 8H Ar-OCH<sub>2</sub>CH<sub>2</sub>O-azacrown-5), 3.74 (overlapped d, J = 12.0Hz, 16H,

 $OCH_2CH_2O$ -crown-6, 4H,  $OCH_2CH_2O$ -azacrown-5), 2.64 (t, J = 4.7Hz, 4H,  $OCH_2CH_2N$ -). IR (selected band): 1560 and 1362 cm<sup>-1</sup> (NO<sub>2</sub>, picrate). ES-MS: *m/z*: found 973.55, calcd for [**2**+K<sup>+</sup>]<sup>+</sup> 974.09. Anal.calcd. for C<sub>65</sub>H<sub>67</sub>N<sub>8</sub>O<sub>27</sub>K: C, 54.54; H, 4.72; N, 7.82. Found: C, 53.97; H, 4.57; N, 7.63.

[3.K<sup>+</sup>.Pic<sup>-</sup>].Hpic: <sup>1</sup>H NMR (CD<sub>3</sub>CN):  $\delta$  8.61 (s, 2H, picrate), 7.31 (d, J = 7.5 Hz, 4H, Ar-*Hm*-calix), 7.23 (d, J = 7.5 Hz, 4H, Ar*Hm*-calix), 7.03 (t, J = 7.5 Hz, 2H, Ar*Hp*calix), 6.98 (t, J = 7.5 Hz, 2H, Ar*Hp*-calix), 4.21 (q, J = 7.16 Hz, 2H, -*CH*<sub>2</sub>-ester), 3.91 (br, 4H, Ar-O*CH*<sub>2</sub>*CH*<sub>2</sub>O-azacrown-5), 3.80 (s, 8H, Ar-*CH*<sub>2</sub>-Ar), 3.75 (br, 4H, Ar-O*CH*<sub>2</sub>*CH*<sub>2</sub>O-azacrown-5), 3.70 (br s, 4H, O*CH*<sub>2</sub>*CH*<sub>2</sub>O-crown-6 and O*CH*<sub>2</sub>*CH*<sub>2</sub>Oazacrown-5), 3.67 (overlapped s, 8H, O*CH*<sub>2</sub>*CH*<sub>2</sub>O-crown-6 and O*CH*<sub>2</sub>*CH*<sub>2</sub>O-azacrown-5), 3.61 (br, 8H, Ar-O*CH*<sub>2</sub>*CH*<sub>2</sub>O-crown-6), 3.55 (br, 4H, Ar-O*CH*<sub>2</sub>*CH*<sub>2</sub>O-), 3.50 (s, 2H, -*CH*<sub>2</sub>CH<sub>3</sub>), 2.93 (br, 4H, O*CH*<sub>2</sub>*CH*<sub>2</sub>N-), 1.3 (t, J = 7.0 Hz, 3H, -*CH*<sub>3</sub>). IR (selected band): 1557 and 1361 cm<sup>-1</sup> (NO<sub>2</sub>, picrate). ES-MS: *m*/*z*: found 908.63, calcd for [**3**+K<sup>+</sup>]<sup>+</sup> 909.06. Anal.calcd. for C<sub>62</sub>H<sub>68</sub>N<sub>7</sub>O<sub>26</sub>K: C, 54.51; H, 5.01; N, 7.17. Found: C, 54.21; H, 4.96; N, 6.95,

[4.K<sup>+</sup>.Pic<sup>-</sup>].Hpic.H<sub>2</sub>O: <sup>1</sup>H NMR (CD<sub>3</sub>CN):  $\delta$  8.61(s,2H, picrate),7.30 (d, J = 7.5 Hz, 4H, Ar*Hm*-calix), 7.21 (t, J = 6.75,4H, Ar*Hm*-calix) 6.93 (tt,4H, Ar*Hp*-calix), 3.87 (br, 4H, OCH<sub>2</sub>CH<sub>2</sub>O-crown-6), 3.80 (d, J = 3Hz, 8H, Ar-CH<sub>2</sub>-Ar), 3.72 (d, J = 5, 20H, OCH<sub>2</sub>CH<sub>2</sub>O-crown-6, ArOCH<sub>2</sub>CH<sub>2</sub>O-azacrown-5), 3.60 (broad s, 4H, Ar-OCH<sub>2</sub>CH<sub>2</sub>O-azacrown-5), 3.40 (d, J = 5.5 Hz, 2H, azacrown-5), 3.35 (t, 6H, Ar-OCH<sub>2</sub>CH<sub>2</sub>O-azacrown-5), 2.10 (s, 3H, -NCH<sub>3</sub>). IR (selected band): 1553 and 1361 cm<sup>-1</sup> (NO<sub>2</sub>, picrate). ES-MS: *m/z*: found 864.38, calcd for [4+K<sup>+</sup>]<sup>+</sup> 865.019. Anal. calcd. for C<sub>60</sub>H<sub>66</sub>N<sub>7</sub>O<sub>26</sub>K: C, 53.75; H, 4.96; N, 7.31. Found: C, 53.45; H, 5.14; N, 7.13.

#### 2.8. Isothermal calorimetric titration

The stoichiometry of the complexes formed, binding constant, thermodynamic parameters such as enthalpy change ( $\Delta H$ ), entropy change ( $\Delta S$ ) and free energy change  $(\Delta G)$  for the reaction of the ionophores with K<sup>+</sup>Pic<sup>-</sup> in acetonitrile were determined by isothermal calorimetric titration (ITC). In a typical procedure, first a blank experiment was carried out using solute and solvent (without taking ionophore) and this data was subtracted from the titration data for complex formation for curve fitting. For complexation study, 1 mM solution of the respective ionophore in dry acetonitrile was taken in the cell and 7 mM solution of Kpic in the same solvent was taken in the syringe. The solution of the Kpic was then added maintaining the successive additions of 2 µL, spacing 180 second intervals to allow the exothermic peak resulting from the interaction to return to the baseline. All these calorimetric studies were performed at 298 K. The blank data was then subtracted from the ITC data for complex formation and the resultant data was fitted with the aid of Origin 7 provided by MicroCal by using one set of sites curve fitting model. This computational plot gave the values of stoichiometry (n), binding constant (Ks), enthalpy change ( $\Delta H$ ), entropy change ( $\Delta S$ ) and free energy change  $(\Delta G)$  was calculated using the equation  $\Delta G = \Delta H - T\Delta S$ .

#### 2.9. Single Crystal X-Ray Study

Crystals of suitable size of the compounds **1**, **3** and the complex  $[\mathbf{1}.K^+.Pic^-]$  were selected, immersed in partone oil and then mounted on the tip of a glass fibre using epoxy resin. Intensity data for all three crystals were collected at 100 K using graphite monochromatised MoK<sub> $\alpha$ </sub> ( $\lambda = 0.71073$ Å) radiation on a Bruker SMART APEX diffractometer equipped with CCD area detector. The data integration and reduction were processed with SAINT software [51]. An empirical absorption correction was applied to the collected reflections with SADABS [52]. The structures were solved by

direct methods using SHELXTL [53] and refined on  $F^2$  by the full-matrix leastsquares technique using the SHELXL-97 [54] package. Graphics are generated using PLATON [55] and MERCURY 1.3 [56]. Even though data was collected under 150 K, in the case of compound 1 some of the atoms in the crown moiety showed dynamic disorder and the occupancy factor and positions for the disordered atoms were determined using FAVR and PART command. In all the compounds non-hydrogen atoms were refined anisotropically till convergence is reached and the hydrogen atoms attached to the ligand moieties were stereochemically fixed. Crystallographic parameters for both the compounds are given in Table 2.

NAT

#### 3. Results and discussion

#### 3.1. Synthesis of ionophores (1-4)

The compound calix[4]arene crown-6 aza-crown-5 (1) was synthesized following the modified literature procedure [32,39], details of the steps involved in this reaction is given in Scheme S1 (ESI) and the characterization data are given in the Experimental Section. The proton of the N-H group of **1** was substituted by 2-hydroxy-5-nitrobenzyl (**2**), ethyl acetate (**3**) and acetyl (**4**) groups, as shown in Scheme 1 and details of synthetic procedure and characterization data are given in the Experimental Section. The compounds **2-4** were obtained from **1** by the reaction with 2-hydroxy-5-nitrobenzyl bromide, ethylbromoester and acetyl chloride, respectively in presence of a base (Et<sub>3</sub>N) in dry THF and were purified by column chromatography using silica gel as column material and chloroform/hexane/methanol of different compositions as eluent. The C, H and N analysis of these compounds are in excellent agreement with the composition of the compounds. The ES-MS spectra of all these four compounds are submitted as ESI (Figs. S1-S4) and the *m/z* values are matched well with that of

calculated values; 784.53 for 1 (calculated for  $[1+H^+]^+$  is 784.89), 935.93 for 2 (calculated for  $[2+H^+]^+$  is 935.99), 870.72 for 3 (calculated for  $[3+H^+]^+$  is 870.97) and 826.67 for 4 (calculated for  $[4+H^+]^+$  is 826.92). The structures of the compounds 1-4 in solution have been assigned on the basis of <sup>1</sup>H NMR spectra (Figs. S5-S8, ESI), the data of which with assignment of peaks are given in the Experimental Section. The 1,3-alternate conformation of the calix moiety is confirmed from the appearance of Ar-CH<sub>2</sub>-Ar methylene protons (8H) as a singlet at  $\delta = 3.70, 3.82, 3.79$  and 3.78 for 1-4, respectively [32]. For the attached 2-hydroxy-5-nitrobenzyl moiety of 2, the methylene protons appeared at  $\delta = 3.94$  (2H) as singlet and the aromatic protons appeared as singlet at 7.98 (1H) and two doublets at  $\delta = 8.07$  (1H) and 8.08 (1H) ppm. For 3, the peaks at  $\delta = 2.74$  (t, 4H), 3.40 (s, 2H) and 4.14 (q, 2H) are due to ester group attached with the nitrogen atom. The methyl protons of the acetyl moiety of 4 appeared as a singlet at  $\delta = 2.07$  (3H) ppm. The signals assigned for the aromatic protons of the calix moiety and for ethylene groups of the crown rings are given in the Experimental Section, overlap of different signals in a few cases have also been noted. In the solid state, structural characterization of two compounds, 1 and 3, were carried out on the basis of single crystal X-ray study, which discussed in the latter section.

#### 3.2. Competitive Complexation Study of the Ionophores (1-4)

These ionophores were synthesised with the aim to use them for selective extraction of industrially important metal ion like  $K^+$  from natural sources such as brine and bittern, which mainly contain Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>2+</sup> and Mg<sup>2+</sup> and small amount of Li<sup>+</sup> and Sr<sup>2+</sup> [57]. It is therefore necessary to investigate competitive complexing ability of these ionophores using these metal ions in aqueous media. It has been carried out by two-phase extraction in water-dichloromethane using equimolar mixture of these metal

ions and picrate as counter anion, which facilitates transfer of metal complex from aqueous to non-aqueous media by strong ion-pair interaction [24]. The concentration of the metal ions in the extract was determined by ion chromatographic assay, a detail of the procedure has given in the Experimental Section. The ion chromatography of the solution containing equimolar amount of Li<sup>+</sup>, Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>2+</sup>, Mg<sup>2+</sup> and Sr<sup>2+</sup> and that in the extract after two-phase extraction using the ionophore 3 are shown in Fig. 1. Ion chromatographs for the metal ions in the extracts obtained using the ionophores 1, 2 and 4 have given as ESI (Figs. S9-S11). The ion chromatographs suggest that all the four ionophores exhibited very high selectivity towards K<sup>+</sup> (83.5, 74.4, 85.6, 81.9%), it also showed some amount of Na<sup>+</sup> (12.1, 13.2, 10.3, 10.3, %) and trace amount of Ca<sup>2+</sup> and Mg<sup>2+</sup>, however no Li<sup>+</sup> and Sr<sup>2+</sup> was detected in the extract. The observed selectivity ratios of the metal ions in the extract are shown in Table 1. The fraction of metal ions extracted from the solution containing equimolar (0.1 M) amount of Li<sup>+</sup>,  $Na^+$ ,  $K^+$ ,  $Ca^{2+}$ ,  $Mg^{2+}$  and  $Sr^{2+}$  using all the four ionophores (0.002 M) expressed in the form of a bar diagram is shown in Fig. 2. The data in Table 1 and also the bar diagram clearly show that these ionophores prefer to bind K<sup>+</sup> ion over the other metal ions used in this study. All of these ionophores exhibited very high selectivity towards K<sup>+</sup> and therefore we were interested to investigate interaction of these ionophores with  $K^{+}$  in solution with the aid of <sup>1</sup>H NMR spectroscopy and solid state structural study of the K<sup>+</sup> complex.

#### 3.3. NMR study

The <sup>1</sup>H NMR spectra of **1-4** were recorded with incremental addition of K<sup>+</sup>-picrate (0 to 8.95 molar equivalents) in CD<sub>3</sub>CN. The spectra for all the four ionophores exhibited significant changes in chemical shifts for almost all the peaks. The spectral change for

**3** is shown in Fig.3 and that of **1**, **2** and **4** are submitted as ESI (Figs. S12-S14). It may be noted that substantial changes in chemical shifts were observed in both aliphatic and aromatic regions and also a new peak appeared around  $\delta = 8.6$ , which is due to picrate anion [15,24]. It is interesting to note that upon addition of metal ion, a few new peaks generated at the expense of the original signals, indicating that the size of the metal ion fits well in the calix-crown cavity making strong interaction with the donor atoms forming stable complex [25,27,58]. The NMR data therefore, clearly supports the high selectivity for these ionophores towards  $K^+$ . The change in chemical shifts for the signals in the entire spectra is because of the distribution of positive charge of K<sup>+</sup> throughout the molecule by  $\pi$ -interaction and also due to conformational change of the ionophores due to complex formation. These ionophores form 1:1 complex (discussed in the later sections), therefore it is important to know where the metal ion has encapsulated out of the two crown rings. From the present NMR data it is difficult to make an unambiguous assignment for the location of  $K^+$ , as the methylene protons of the two crown moieties overlapped in many places and also most of the peaks have shifted. The crystal structures of the  $K^+$  complex of 1 (discussed in the later section) showed that the metal ion has encapsulated in the crown ring at the upper rim (not aza-crown). On the basis of crystal structure, it is therefore, proposed that the metal ion has encapsulated in the crown ring at the upper rim.

#### 3.4. Isolated $K^+$ complexes of the ionophores 1-4

For solid state characterization,  $K^+$  complexes of **1-4** were synthesised by the reaction of appropriate ionophore and  $K^+$  picrate in chloroform at room temperature, as described in the Experimental Section. These complexes were characterized on the basis of elemental analysis, mass, IR and <sup>1</sup>H NMR spectral data, details of which are

given in the Experimental Section. The C, H and N analysis suggested 1:1 complex formation with picrate as counter anion and a picric acid as an inclusion. Selected portion of the ES-MS spectrum of the K<sup>+</sup> complex of **3** is shown in Fig. 4 and that of the ionophores **1**, **2** and **4** are submitted as ESI (Figs S15-17). The *m/z* values for all of the four complexes are in excellent agreement with the calculated values for **1**:1 complex with picrate counter anion. The values are 822.55 for  $[1+K^+]^+$  (calculated 822.98), 973.55 for  $[2+K^+]^+$  (calculated 974.09), 908.63 for  $[3+K^+]^+$  (calculated 909.06) and 864.38 for  $[4+K^+]^+$  (calculated 865.02). Selected IR bands with assignment are given in the Experimental Section, the notable new bands appeared around 1560 and 1361cm<sup>-1</sup> are due to picrate anion [42]. Molecular structure of the K<sup>+</sup>-complex of **1**,  $[1+K]^+$ pic<sup>-</sup>, has been established by single crystal X-ray study and described below.

#### 3.5. Crystal structures

Single crystal X-ray structures of two of the four ionophores (1 and 3) and the K<sup>+</sup> complex of 1 have been determined and details of crystallographic parameters are given in Table 2. The crystal of 1 was grown with the aid of picric acid and obtained as a co-crystal composed of one molecule each of 1 and picric acid, it also contains a water molecule as solvent of crystallisation. The ionophore 1 with picric acid crystallised in orthorhombic system with  $P2_12_12_1$  space group. The crystal structure clearly shows that the calix-crown moiety has adopted the 1,3-alternate conformation (Fig. 5). The water molecule is held via intermolecular H-bonding interaction involving N-H...O and O-H...O contacts and encapsulated in the tethered aza-crown moiety, as depicted in Fig. 5. The Packing diagram viewed down a-axis shows alternate layers of calix crown moiety and picric acid oriented along b-axis, as shown

in Fig. 6. It is interesting to note that one picric acid moiety is involved in six Hbonding interactions with four different calix-crown moieties, as depicted in Fig. S18 (ESI). Thus nitro oxygen atoms O12 and O16 act as acceptors and involved in three and two C-H...O contacts, respectively and the acidic proton H11c from the picric acid makes O-H...N contact with the amino nitrogen of the calix moiety bridging the adjacent layers in generating a two dimensional hydrogen bonded network. Details of all these pertinent H-bonding interactions with symmetry code are given in Table 3.

The ionophore **3** crystallized in orthorhombic system (Pna21 space group) with 1,3alternate conformation of the calix moiety with two crown rings at the opposite side of the calix moiety, as depicted in Fig.7. The intramolecular C-H...O interaction between oxygen atoms and phenyl/methylene hydrogen atoms play important role in adopting 1,3-alternate conformation of the calix moiety. Details of these C-H...O contacts with symmetry code is given in Table 3. The packing viewed down b-axis shows the layered orientation of the molecules along *ac*-plane (Fig. 8). Detail analysis of the packing revealed intermolecular C-H... $\pi$  interaction between the phenyl ring (C1 to C6 with C1g centroid) with methylene hydrogens H39A and H39B, which stabilised the molecule in the crystal lattice. Different parameters of these interactions with symmetry codes are: (C(39)-H(39A)....Cg(1): H(39A)....Cg(1) = 3.288 Å; C(39)....Cg(1) = 3.652Å; <C(39)-H(39A)....Cg(1) = 104.40°; symmetry code: -1/2+x,-1/2-y,z and C(39)-H(39B)....Cg(1): H(39B)....Cg(1) = 3.153Å; C(39)....Cg(1) = 3.652Å; <C(39)-H(39B)....Cg(1) = 113.62°; symmetry code=-1/2+x,-1/2-y,z).

For the K<sup>+</sup> complex of 1, ( $[1+K]^+$ pic<sup>-</sup>), suitable crystals for X-ray study were grown from dichloromethane/ethyl acetate and the compound crystalized in monoclinic system with P21/c space group. As depicted in Fig. 9, the K<sup>+</sup> ion is encapsulated in the crown ring at the upper rim making interaction with four oxygen atoms of the crown

moiety and with the deprotonated phenolic oxygen atom from the picrate anion. The aza-crown moiety encapsulated a water molecule making O-H...O interaction with the oxygen atoms of the crown ring. In addition to the complex formed, one molecule each of picric acid and ethyl acetate are found in the crystal lattice. The K...O distance ranges from 2.14 to 2.56 Å, which is well within the range for previously reported complexes [24,42]. The packing diagram viewed down a-axis with various inter molecular H-bonding interactions are shown in Fig.10. It shows that the complex molecules with opposite orientations are aligned along the layers along c-axis and the picric acid and ethyl acetate are oriented between the adjacent layers of the complex generating ABAB... motifs as depicted in Fig.10. The picric acids in the lattice are associated by  $\pi$ ... $\pi$  stacking interactions with the centroid...centroid distance between the phenyl rings 3.65 Å. The picric acid and ethyl acetate (B layers) are involved in C-H...O contacts linking the AA motifs via C-H...O and N-H...O contacts with the complex generating hydrogen bonded 2D supramolecular network. Details of all these H-bonding interactions and symmetry code are given in Table 3.

#### 3.6. Isothermal calorimetric titration study

For determination of association constant ( $K_a$ ), stoichiometry of the complexes formed (n) and other thermodynamic parameters, isothermal calorimetric titration (ITC) for the reaction of all of the four ionophores with potassium picrate was carried out in dry acetonitrile at 298 K. Detail experimental procedure has given in the Experimental Section. The ITC titration profiles for all the four ionophores are presented in Fig. 11 and the data such as association constant ( $K_a$ ), stoichiometry (n), entropy change (T $\Delta$ S), enthalpy change ( $\Delta$ H) and free energy change ( $\Delta$ G) are summarized in Table 4. The 'n' values in the table are in the range 0.71 to 1.04, which suggests 1:1 K<sup>+</sup>-

ionophore complex formation and the thermodynamic parameters indicate that the binding process is exothermic. The log values of the association constants (log  $K_a$ ) are in the range 4.14 to 5.92, which indicates strong binding of the metal ion with the ionophore. This observation is consistent to the finding noted in NMR spectral changes, where new peaks appeared at the cost of original peaks due to strong complex formation. The thermodynamic parameters obtained (Table 4) suggests that this reaction is enthalpy driven, which partially compensated by negative entropy changes for 1-3. Since the ITC data suggest 1:1 complex formation, therefore we propose that the metal ion is encapsulated in the 6-membered crown ring at the upper rim. Slight variation in association constant and thermodynamic parameters is probably due to different substituents attached with the aza- nitrogen atom, which might have induced conformational changes in the calixarene-biscrown skeleton.

#### 3.7. Comparative study

Metal binding property of calix-crown and calix-bis-crown hybrid molecules has been studied substantially in different context. The aim of the present study is to develop calix-crown based systems, which can be applied for extraction of  $K^+$  from a mixture of metal ions in aqueous media. To develop such a system, three important factors to be considered, high selectivity towards  $K^+$  in presence of mixture of metal ions, it must form strong complex with  $K^+$  and the system must work in aqueous media. To the best of our knowledge, there is no report in the literature, except one from us [42], where mixture of metal ions has been used for competitive complexation study and selectivity has been determined on the basis of analysis of metal ions in the isolated extract. In our earlier reported calix-crown-6 systems [42], the best selectivity ratio obtained for  $K^+/Na^+$  is 1.08. In the present work, the selectivity ratios for  $K^+/Na^+$ 

obtained are in the range 3.30 - 4.89, which suggest that the performance of the present systems are much better than the earlier systems. Since there is no other report on selectivity study with mixture of metal ions, therefore no comparison on this aspect can be made. It may be noted that discrimination of Na<sup>+</sup> is difficult compared to Ca<sup>2+</sup> and  $Mg^{2+}$ , that is why comparison is made only with selectivity ratio of K<sup>+</sup> to Na<sup>+</sup>. There are number of reports with calix-bis-crown systems, where association constant with various individual metal ions have been determined using methods such as twophase extraction, NMR titration, fluorescence titration, ITC etc., mostly in nonaqueous solvents and the log K values were compared to get an idea about selectivity. The ratios of  $\log K$  of K<sup>+</sup> to Na<sup>+</sup> for some of the calix-bis-crown-systems containing crown-6 moiety are 1.88 and 2.68 [59], 1.17 [60], 1.26 and 1.74 [61], 0.98 - 1.20 [62], a system where apparently Na<sup>+</sup> could not be detected and log K for K<sup>+</sup> is 4.6 [63]. There are number of calix-mono-crown systems, where the ratios are comparable to bis-crown systems, one of such recent example shows the ratios 1.69 to 2.01 [64]. It is not appropriate to compare these values with that of the present work as it has been estimated following a completely different procedure, however it looks like the ionophores reported here are better than many other reported systems. Moreover, the method applied in the present study can be applied for practical application for extraction of metal ions from a real system, which is distinctly different from other reports.

#### 3.8. Application

High selectivity of these ionophores towards  $K^+$  motivated us to use these ionophores for extraction of  $K^+$  from a natural source such as sea bittern (concentrated sea water obtained after removal of common salt). This sea bittern mainly contains Na<sup>+</sup> = 6.8 %,

 $K^+ = 1.4 \%$ ,  $Mg^{2+} = 3.6 \%$ ,  $Ca^{2+} = 0.02 \%$  and trace amount of other metal ions such as Li<sup>+</sup>,  $Sr^{2+}$  etc.. However concentration of these metal ions may vary slightly depending on the conditions under which bittern is collected. The experiments were carried out following the procedure similar to that described for equimolar mixture of metal ions, except bittern is used instead of mixture of metal ions. The bar diagram showing the fraction of metal ions in bittern and that in the extract from bittern using all the four ionophores is shown in Fig.12 and the ion chromatogram showing the metal ions in the extract obtained by two-phase extraction using the ionophore **3** is shown in Fig. S19 and the data are given in Table 5. It may be noted that in the case of bittern, like artificial mixture of metal ions, the selectivity towards K<sup>+</sup> is very high and ionophore **3** exhibited maximum selectivity (86.1 %). These ionophores may therefore find application in extraction of K<sup>+</sup> from aqueous solution, particularly in presence of Na<sup>+</sup>, Mg<sup>2+</sup> and Ca<sup>2+</sup>.

#### 4. Conclusions

A series of 1,3-alternate calixarene derivatives with a crown-6 moiety at one side of the calix unit and a aza-crown moiety with different substituents at the aza nitrogen atom on the other side have been synthesized, characterized and their competitive metal binding property with alkali and alkaline earth metal ions in aqueous media has been investigated. The selectivity has been investigated with equimolar mixture of Li<sup>+</sup>, Na<sup>+</sup>, K<sup>+</sup>, Mg<sup>2+</sup>, Ca<sup>2+</sup> and Sr<sup>2+</sup> in aqueous media using picrate as counter anion following two-phase extraction method followed by ion chromatographic assay of metal ions' concentrations in the extract (organic phase). All the four ionophores exhibit K<sup>+</sup> selectivity >75 % with highest selectivity (85.6 %) for the ionophore having ethyl ester substituent at the aza nitrogen atom. Binding constants for all the ionophores with K<sup>+</sup>, stoichiometry of the complexes formed and thermodynamic

parameters such as entropy change, enthalpy change and free energy change have been evaluated by isothermal calorimetric titration and the data exhibit most favourable reaction for the ionophore with ethyl ester substituent at the aza nitrogen atom (**3**). For structural elucidation in solution, detail <sup>1</sup>H NMR study was carried out. Molecular structures of the two ionophores (**1** and **3**) and the K<sup>+</sup>-complex of the ionophore **1** have been established by single crystal X-ray study. On the basis of the structural information, it has been concluded the K<sup>+</sup> ion is encapsulated in the crown-6 cavity at the upper rim. The high selectivity of these ionophores for K<sup>+</sup> is basically due to sizematching factor, the size of the K<sup>+</sup> ion matched very well with the cavity size of the crown-6, it is also evident from NMR study. These ionophores have also exhibited high selectivity towards K<sup>+</sup> when applied for extraction of metal ions from bittern.

#### Appendix A. Supplementary data

CCDC 1040795, 1040794 and 1040796 contains the supplementary crystallographic data for the ionophores 1.pic, 3 and the complex [1.K<sup>+</sup>.Pic<sup>-</sup>].HPic.EtAc.H<sub>2</sub>O, These data respectively. obtained can be free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, from the Cambridge or Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

#### Acknowledgements

CSIR-CSMCRI publication No.: 223/2014. Financial assistance received in the form of Network Project CSC 0105 from CSIR, New Delhi is gratefully acknowledged. V. R gratefully acknowledges the CSIR for awarding Senior Research Fellowship (SRF).

We thank Dr. Babulal Rebary, Mr. A. K. Das, and Mr. V. Vakani for recording ion chromatography, mass and FT-IR spectra, respectively.

Acceleration

#### References

- [1] W. Sliwa, J. Inclusion Phenom. Macrocycl. Chem. 52 (2005) 13.
- [2] J. Yoon, S. K. Kim, N. J. Sing, K. S. Kim, Chem. Soc. Rev. 35 (2006) 355.
- [3] J.S. Kim, D.T. Quang, Chem. Rev. 107 (2007) 3780.
- [4] L.P. Kwan, M.S. Wong, Sensors. 8 (2008) 5313.
- [5] B.S. Creaven, D.F. Donlon, J. McGinley, Coord. Chem. Rev. 253 (2009) 893.
- [6] H.J. Kim, M.H. Lee, L. Mutihac, J. Vicens, J.S. Kim, Chem. Soc. Rev. 41 (2012) 1173.
- [7] J. Harrowfield, Chem. Commun. 49 (2013) 1578.
- [8] S.E. Matthews, P. Schmitt, V. Felix, M.G.B. Drew, P.D. Beer, J. Am. Chem. Soc. 124 (2002) 1341.
- [9] P.R.A. Webber, A. Cowley, G.B. Drew, P.D. Beer, Chem. Eur. J. 9 (2003) 2439.
- [10] K. Ohto, T. Matsufuji, T. Yoneyama, M. Tanaka, H. Kawakita, T. Oshima, J. Inclusion Phenom. Macrocyclic Chem. 71 (2011) 489.
- [11] H. Dube, J.Jr. Rebek, Angew. Chem. Int. Ed. 51 (2012) 3207.
- [12] D.S. Su, S. Perathoner, G. Centi, Chem. Rev. 113 (2013) 5782.
- [13] S.B. Nimse, T. Kim, Chem. Soc. Rev. 42 (2013) 366.
- [14] G. Horvat, V. Stilinović, T. Hrenar, B. Kaitner, L. Frkanec, V. Tomišic, Inorg. Chem. 51 (2012) 6264.
- [15] J.S. Kim, O.J. Shon, J.W. Ko, M.H. Cho, I.Y. Yu, J. Vicens, J. Org. Chem. 65 (2000) 2386.
- [16] J.Y. Lee, H.J. Kim, J.H Jung, W. Sim, S.S. Lee, J. Am. Chem. Soc. 130 (2008)13838.
- [17] S. Patra, E. Suresh, P. Paul, Polyhedron. 26 (2007) 4971.

- [18] M. Yuan, W. Zhou, X. Liu, M. Zhu, J. Li, X. Yin, H. Zheng, Z. Zuo, C. Ouyang,
  H. Liu, Y. Li, D. Zhu, J. Org. Chem. 73 (2008) 5008.
- [19] X. Liu, K. Surowiec, R.A. Bartsch, Tetrahedron. 65 (2009) 5893.
- [20] L.-L. Liu, H.-X. Li, L.-M. Wan, Z.-G. Ren, H.-F. Wang, J.-P. Lang, Chem. Commun. 47 (2011) 11146.
- [21] T. Yoneyama, H. Sadamatsu, S. Kuwata, H. Kawakita K. Ohto, Talanta. 88 (2012) 121.
- [22] I. Leray, Z. Asfari, J. Vicens B. Valeur, J. Chem. Soc., Perkin Trans. 2 (2002) 1429.
- [23] S.K. Kim, G.I. Vargas-Zúñiga, B.P. Hay, N.J. Young, L.H. Delmau, C. Masselin,
   C.-H. Lee, J.S. Kim, V.M. Lynch, B.A. Moyer, J.L. Sessler, J. Am. Chem. Soc.
   134 (2012) 1782.
- [24] P. Agnihotri, E. Suresh, P. Paul, P.K. Ghosh, Eur. J. Inorg. Chem. (2006) 3369.
- [25] S. Patra, P. Paul, Dalton Trans. (2009) 8683.
- [26] J.P. Chinta, B. Ramanujam, C. P. Rao, Coord. Chem. Rev. 256 (2012) 2762.
- [27] S. Patra, D. Maity, A. Sen, E. Suresh, B. Ganguly, P. Paul, New J. Chem. 34 (2010) 2796.
- [28] K. Takahashi, A. Gunji, D. Guillaumont, F. Pichierri, S. Nakamura, Angew. Chem. Int. Ed. 3 (2000) 2925.
- [29] S. Patra, D. Maity, R. Gunupuru, P. Agnihotri, P. Paul, J. Chem. Sci. 124 (2012)1287.
- [30] H. Zhou, K. Surowiec, D.W. Purkiss, R.A. Bartsch, Org. Biomol. Chem. 3 (2005) 1676.
- [31] S. Patra, R. Gunupuru, R. Lo, E. Suresh, B. Ganguly, P. Paul, New J. Chem. 36 (2012) 988.

- [32] J.S. Kim, W.K. Lee, N. Kwanghyun, Z. Asfari, J. Vicens, Tetrahedron Lett. 41 (2000) 3345.
- [33] I. Oueslati, Tetrahedron. 63 (2007) 10840.
- [34] O. Sahin, Y. Mustafa, Tetrahedron Lett. 53 (2012) 2319.
- [35] J.-P. Malval, I. Leray, B. Valeur, New J. Chem. 29 (2005) 1089.
- [36] J.S. Kim, O.J. Shon, S.H. Yang, J.Y. Kim, M.N.J. Kim, J. Org. Chem. 67 (2002) 6514.
- [37] J.Y. Lee, S.Y. Lee, P. Sunhong, J. Kwon, W. Sim, S.S. Lee, Inorg. Chem. 48 (2009) 8934.
- [38] H.M. Chawla, G. Hundal S. Kumar, P. Singh, J Incl Phenom Macrocycl Chem. 72 (2012) 323.
- [39] J.S. Kim, K.H. Noh, S.H. Lee, S.K. Kim, S.K. Kim, J. Yoon, J. Org. Chem. 68 (2003) 597.
- [40] V. Arora, H.M. Chawla, S.P. Singh, ARKIVOC. (2007) 172.
- [41] A. Grun, V. Csokai, G. Parlagh, I. Bitter, Tetrahedron Lett. 43 (2002) 4153.
- [42] V. Ramakrishna, S. Patra, E. Suresh, A.K. Bhatt, P.A. Bhatt, A. Hussain, P. Paul, Inorg. Chem. Commun. 22 (2012) 85.
- [43] A. Casnati, N. Della Ca, F. Sansone, F. Ugozzoli, R. Ungaro, Tetrahedron. 60 (2004) 7869.
- P.K. Ghosh, K.J. Lingalia, M.R. Gandhi, R.H. Dave, H.L. Joshi, R.N. Vohra,
   V.P. Mohandas, S. Daga, K. Halder, H.H. Deraiya, R.D. Rathod, A.U. Hamdani,
   US. Pat. B2 (2006) 7041268.
- [45] E. Suresh, P. Agnihotri, B. Ganguly, P. Bhatt, P.S. Subramanian, P. Paul, P.K Gosh, Eur. J. Inorg. Chem. (2005) 2198.

- [46] P. Paul, P.K. Ghosh, K.J. Lingalia, P.S. Subramanian, E. Suresh, S. Patra, P. Agnihotri, US, Pat. A1 (2010) 2010/0266482.
- [47] D.D. Perrin, W.L.F. Armarego, D.R. Perri, Purification of Laboratory Chemicals,
   2<sup>nd</sup> ed. Pergamon Press, Oxford, U. K. (1980).
- [48] M. Ouchi, Y. Inoue, T. Kanzaki, T. Hakushi, J. Org. Chem. 49 (1984) 1408.
- [49] C.D. Gutsche, M. Iqbal, Organic Syntheses. 68 (1990) 234.
- [50] C.D. Gutsche, J.A. Levine, P.K. Sujeeth, J. Org. Chem. 50 (1985) 5802.
- [51] G.M. Sheldrick, SAINT 5.1 ed, Siemens Industrial Automation Inc, Madison, WI. (1995).
- [52] SADABS, Empirical Absorption Correction Program; University of Göttingen: Göttingen, Germany. (1997).
- [53] G.M. Sheldrick, SHELXTL Reference Manual, Version 5.1, Bruker AXS, Madison. WI (1997).
- [54] G.M. Sheldrick, SHELXL-97, Program for Crystal Structure Refinement, University of Göttingen, Göttingen, Germany. (1997).
- [55] A.L. Spek, Acta Cryst. D65 (2009) 148.
- [56] Mercury 1.3, Supplied with Cambridge Structural Database, CCDC, Cambridge, U.K. (2003).
- [57] Ugo Bardi, Sustainability 2 (2010) 980.
- [58] B.B. Adhikari, M. Gurung, H. Kawakita, O. Keisuke, Analyst 136 (2011) 3758.
- [59] J.S. Kim, W.K. Lee, Do.Y. Ra, Y-III. Lee, W.K. Choi, K.W. Lee, W.-Z. Oh, Microchem. J. 59 (1998) 464.
- [60] J.S. Kim, W.K. Lee, W. Sim, J.W. Ko, M.H. Cho, Do.Y. Ra, J.W. Kim, J. Incl Phenom. Macrocycl .Chem. 37 (2000) 359.
- [61] S.H. Lee, J.Y. Kim, J. Ko, J.Y. Lee, J.S. Kim, J. Org. Chem. 69 (2004) 2902.

- [62] K. Salorinne, M. Nissine, J. Incl. Phenom. Macrocycl. Chem. 61 (2008) 11.
- [63] K.N. Koh, K. Araki, S. Shinkai, Z. Asfari, J. Vicens, Tetrahedron Lett. 36 (1995) 6095.
- Acceleration [64] J. Wang, R.A. Bartsch, Supramolecular Chem. 26 (2014) 526.

29

#### **Scheme and Figure Captions**

Scheme 1. Route for the synthesis of ionophores (2-4), reagents/ solvents: a) Et3N/2hydroxy-5-nitrobenzyl bromide, THF b) Et3N/ Ethylbromoester, THF c) Et3N/ acetyl chloride, THF.

**Fig. 1.** Ion chromatograms of (a) solution containing equimolar mixture of  $Li^+$ ,  $Na^+$ ,  $K^+$ ,  $Mg^{2+}$ ,  $Ca^{2+}$  and  $Sr^{2+}$  (0.0005 M each) and (b) that of the extract obtained after two-phase extraction using the ionophore **3**.

**Fig. 2.** Bar diagram showing the fraction of metal ions extracted from the solution containing equimolar amount of  $Li^+$ ,  $Na^+$ ,  $K^+$ ,  $Mg^{2+}$ ,  $Ca^{2+}$  and  $Sr^{2+}$  (0.1M each) metal ions using the ionophores (0.002 M).

**Fig. 3**. Relevant portion of the <sup>1</sup>H NMR spectra for ionophore **3** upon addition of 0.08 (a), 0.24 (b), 0.48 (c), 0.80 (d) 1.20 (e), 1.68 (f), 2.24 (g) and 2.88 (h) molar equivalent amounts of K-picrate; new peaks are growing with the disappearance of the peaks of the original complex.

Fig. 4. Relevant portion of the ES-MS spectrum of the complex  $[3+K^+]^+$  pic<sup>-</sup> recorded in acetonitrile.

**Fig. 5.** Ball and stick diagram of compound **1** and the hydrogen bonding interaction of encapsulated water molecule with the ether moiety and the amino hydrogen is shown (other hydrogen atoms and the picric acid moiety are omitted for clarity).

**Fig. 6**. Packing diagram for **1** viewed down a-axis showing the alternate layers of calix moiety (red) and picric acid (blue) oriented along b-axis (hydrogen atoms are omitted for clarity).

**Fig. 7.** Mercury diagram for the crystal structure of 3 with atom numbering scheme (only hydrogen atoms involved in intramolecular H-bonding are shown for clarity)

Fig. 8. Packing diagram for 3 viewed down b-axis depicting the orientation of the molecules in ac-plane along with intermolecular C-H... $\pi$  interaction between the methylene hydrogen H39B with the centroid of the phenyl ring along a-axis are shown.

**Fig. 9**. Ball and stick diagram for the  $[1.K^+.pic^-.H_2O]$  complex depicting the coordination of  $K^+$  and the hydrogen bonding interaction of the encapsulated water molecule with the azacrown moiety (only the nitrogen and oxygen atoms are labelled for clarity).

**Fig. 10.** Packing and hydrogen bonding interaction in  $[1.K^+.pic^-.H_2O]$ . Hpic.ethyl acetate depicting the orientation of alternate of complex layers and lattice guests (picric acid and ethyl acetate) are shown.

**Fig. 11.** ITC titration profiles of ionophores **1-4** (1 mM) in acetonitrile at 298 K with Kpic (7 mM), the upper panel shows the heat pulses experimentally observed in each titration. The lower panel shows the heat evolved *vs.* mole ratio of K<sup>+</sup>/ionophores, the solid line in the lower panel is a best fit, obtained upon using the one site model.

**Fig. 12**. Bar diagram showing the fraction of metal ions in bittern and that in the extract obtained from bittern using the ionophores **1-4**.

CC

#### Tables

Table 1. Selectivity ratio of metal ions in the extract obtained from equimolar mixture of ions by two-phase extraction.<sup>a</sup> 3022

	Se	electivity ra	atio <sup>b</sup>
Ionophores	K <sup>+</sup> /Na <sup>+</sup>	$K^+/Mg^{2+}$	K <sup>+</sup> /Ca <sup>2+</sup>
1	4.73	33.51	42.72
2	3.30	18.46	25.52
3	4.89	52.70	78.36
4	4.04	50.13	62.34

<sup>a</sup>Concentration (%) of metal ion in the original solution (before extract),  $Li^+ = 3.18$ ,  $Na^+ =$ 10.4,  $K^+ = 17.7$ ,  $Mg^{2+} = 10.9$ ,  $Ca^{2+} = 18.1$  and  $Sr^{2+} = 39.5$ ; <sup>b</sup> the selectivity ratio is calculated by [% of  $K^+$  in the extract] [% of  $M^{n+}$  in the original solution]/[% of  $M^{n+}$  in the extract][% of K<sup>+</sup> in the original solution]

	Table 2. Crystal data and refinement	parameters for ionophores 1	and <b>3</b> and for the complex
--	--------------------------------------	-----------------------------	----------------------------------

[1.K <sup>+</sup> .	pic]
---------------------	------

Ide	entification code	Ionophore 1.pic	Ionophore 3	[1.K+.Pic-].HPic.
Che	emical formula	C52H62N4O18	C <sub>50</sub> H <sub>63</sub> NO <sub>12</sub>	EtAc.H20 C <sub>62</sub> H <sub>72</sub> KN <sub>7</sub> O <sub>27</sub>
For	rmula weight	1031.06	870.01	1386.37
Cry	ystal Colour	yellow	Colourless	yellow
Cry	ystal Size (mm)	0.33 x 0.27 x 0.12	0.48 x 0.40 x 0.24	0.23 x 0.12 x 0.04
Ter	mperature (K)	110(2)	110(2)	110(2)
Spa	ace Group	P212121	Pna21	P-1
a(Å	Å)	15.918(3)	15.099(3)	10.2997(11)
b(Å	Å)	16.590(4)	13.739(3)	13.7378(15)
c(Å	Á)	18.741(4)	21.624(4)	22.775(2)
α (	°)	90	90	80.307(2)
β (	°)	90	90	83.653(2)
γ (°	?)	90	90	83.533(2)
Ζ		4	4	2
V(A	Å <sup>3</sup> )	4949.0(19)	4485.8(15)	3142.5(6)
De	nsity (Mg/m <sup>3</sup> )	1.384	1.288	1.465
μ(	(mm <sup>-1</sup> )	0.105	0.091	0.180
F(0	000)	2184	1864	1456
Ret	flections Collected	23456	24459	22521
Ind	lependent Reflections	8693	5352	10963
$R_{in}$	t	0.0450	0.0347	0.0364
Nu	mber of parameters	718	569	912
GC	<b>DF</b> on $F^2$	1.054	1.040	1.053
Fin	alR1/wR2 (I $\geq 2 \sigma$ (I)	0.0626/ 0.1597	0.0484 / 0.1275	0.0712 / 0.1688
We	eighted $R_1/wR_2$ (all	0.0710/ 0.1687	0.0530 / 0.1342	0.0974 / 0.1827
dat	a)			
CC	DC number	CCDC 1040795	CCDC 1040794	CCDC 1040796
	$R = \Sigma   Fo  -$	$ Fc    / \Sigma  Fo  ; wR = [\Sigma$	$\Sigma w(Fo2 - Fc2)2/\Sigma w(Fo2 - Fc$	Fo2)2]1/2

Compound	D-HA	d(HA)(Å)	d(DA) (Å)	<d-ha (°)<="" th=""></d-ha>
	N(1)-H(1C) O(18) <sup>1</sup>	1.79(5)	2.665(4)	168(5)
	O(11)-H(11C)O(12) <sup>1</sup>	2.05(2)	2.702(3)	136(3)
	$O(18)-H(18C)O(7)^{1}$	2.13(4)	2.881(4)	180(3)
1	$O(18)-H(18D)O(10)^1$	2.07(4)	2.821(4)	157(4)
1	$C(14)-H(14B)O(16)^2$	2.59(3)	3.543(4)	167(2)
	$C(23)$ -H(23) $O(13)^1$	2.45(3)	3.169(4)	134(3)
	$C(30)-H(30B)O(13)^3$	2.54(3)	3.435(6)	154(3)
	$C(34)-H(34A)O(13)^{1}$	2.55(3)	3.455(6)	156(4)
	$C(39)-H(39B)O(16)^2$	2.57(3)	3.530(6)	172(2)
S	Symmetry code: 1.x,y,z ; 2.	1-x,-1/2+y,3/2-z;	3. 1-x,1/2+y,3/2-	-Z.
	C(23)-H(23) O(5) <sup>1</sup>	2.453	3.271(4)	146.76
2	$C(33)-H(33A)O(2)^{1}$	2.399	2.968(4)	117.01
3	$C(34)-H(34A)O(5)^{1}$	2.498	3.132(4)	122.87
	$C(44)$ -H(44A) $O(10)^1$	2.576	3.152(4)	118.23
	Symmetry	y code : 1) x,y,z.		
	$O(18)-H(18C)O(19)^1$	2.05 (3)	2.731(4)	139(4)
	$O(27) - H(27C) O(7)^{1}$	2.15(4)	2.812(4)	161(5)
	O(27) - H(27D) O(10) <sup>1</sup>	2.12(5)	2.887(4)	173(5)
	C(10)- H(10) O(17) <sup>1</sup>	2.45(4)	3.294(5)	159(4)
	C(29)- H(29B) O(12) <sup>1</sup>	2.45(4)	3.107(5)	125(3)
	N(1) - H(1C) O(18) <sup>2</sup>	2.02(4)	2.740(4)	160(4)
	$C(33)$ - $H(33A)$ $O(25)^3$	2.54(3)	3.35 1(5)	141(3)
[1 K <sup>+</sup> nic <sup>-</sup> ]	C(36)- H(36B) O(12) <sup>4</sup>	2.54(3)	3.415(6)	150(3)
	$C(37) - H(37A) O(12)^4$	2.52(4)	3.271(6)	134(3)
	C(39) - H(39A) O(15) <sup>5</sup>	2.49(3)	3.240(5)	135(3)
	C(39) - H(39B) O(26) <sup>6</sup>	2.36 (4)	3.109(6)	134(3)
	$C(41) - H(41A)O(24)^{2}$	2.42(3)	3.144(5)	131(2)
	$C(41)$ - $H(41B)$ $O(21)^7$	2.57(3)	3.395(5)	143(2)
	$C(44) - H(44B)O(19)^2$	2.56 (3)	3.520(5)	169(2)
	$C(59) - H(59B) O(16)^8$	2.56(3)	3.294(6)	134(3)
Symmetry co	ode: 1.x,y,z ; 2. x,-1+y,z; 3.	x,1+y,z; 41+x	,y,z; 5. 2-x,1-y,1	-z; 6. 1+x,y,z;
7. 1+x,-1+y,	z 8. 1-x,1-y,1-z			

Table 3. Details of H-bonding interactions with symmetry code for 1, 3 and [1.K<sup>+</sup>.pic].

	Isothe	rmal calorimetric ti	trations' data fo	or K <sup>+</sup> ion	
Ionophore	$\log K_a$	п	$\Delta H$	ΤΔS	$\Delta G$
		(stoichiometry)	$(\text{kcal mol}^{-1})$	(kcal mol <sup>-1</sup>	(kcalmol <sup>-1</sup> )
1	5.80	0.85	-17.40	-9.24	-7.92
2	4.14	0.71	-8.89	-3.25	-5.64
3	5.92	0.84	-23.28	-15.20	-8.08
 4	4.70	1.04	-4.26	2.16	-6.41

Table 4. Binding constant (Ka), stoichiometry and other thermodynamic parameters obtained from isothermal calorimetric titration for **1-4** with K<sup>+</sup>.pic<sup>-</sup>.

Table 5.	Fraction	of meta	l ion i	n bittern	and	that in	the	extract	obtained	from	bittern	by
two-pha	se extract	tion usir	ng all t	ne four i	onop	hores						

	Samples	Concer	ntration o	f metal i	on (%)			
		Na <sup>+</sup>	$K^+$	Mg <sup>2+</sup>	Ca <sup>2+</sup>			
	In bittern	57.65	11.56	30.69	0.14			<b>V</b>
	In the extra	ct						
	1	9.54	82.78	1.80	5.86			
	2	15.47	77.38	2.63	4.50		G	
	3	10.81	86.06	0.15	2.96	C		
	4	9.13	80.43	0.14	3.28			
		6						
6								







Figure 2.



Figure 3.



Figure 5.







Figure 9.







Figure 11.



# Graphical Abstract for Table of Contents (Abstract)

Competitive metal ion binding property of a family of calix-crown hybrid ionophore has been reported. <sup>1</sup>H NMR, ITC and crystal structure studies were carried out for structure elucidation and to determine thermodynamic parameters for complexation. The ionophores were applied for extraction of K<sup>+</sup> from a natural source such as sea bittern.

### Graphical Abstract for Table of Contents (Pictograph)

