Chapter VI

Summary of the work and future prospects
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6.1. Summary of the work

The aim of the work presented in this thesis was to develop calix-crown based hybrid ionophore, which can selectively detect and possibly extract alkali and alkaline earth metal ion(s) from their mixture in aqueous media. Special emphasis was for potassium, as it is an industrially important metal ion and our country imports its entire requirement of potash. For this purpose, series of calix-crown hybrid ionophores with different conformations, cavity size and substituents attached to crown ring were synthesised and characterized. The competitive ion-binding property of these ionophores towards alkali and alkaline earth metal ions such as Li$^+$, Na$^+$, K$^+$, Mg$^{2+}$, Ca$^{2+}$, and Sr$^{2+}$ has been investigated in aqueous media. Many of these systems were also applied for determination of selectivity towards metal ions present in sea-bittern.

The calix-crown hybrid ionophores synthesized are, a series of calixarene derivatives with variation in the size of the crown rings, calix[4]arene-crown-n (n = 4, 5 and 6). The second series of ionophores designed and synthesized were calix-bis-crown ethers, incorporating crown-5/6 to make them selective towards K$^+$ among the other metal ions present in bittern. In this series of ionophores, substituents such as 2-hydroxy-5-nitrobenzyl, 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. The next series of ionophores synthesized were a family of calix-crown hybrid ionophores incorporating benzocrown-6 with cone and 1, 3-alternate conformations of the calix moiety and in addition to the benzocrown-6, crown-5/6 have also been incorporated at the upper rim of 1,3-alternate calixarene forming calix[4]arene biscrown-5/6 making the possibility of complexation with two metal ions. Finally, a calix-crown hybrid ionophore with anthraquinone moiety attached to the crown ring was synthesized. Anthraquinone is a bulky rigid moiety with keto group, the oxygen atom of which may interact with the metal ion through axial position and at the same time it may impose certain steric crowding controlling the selectivity of the ionophore. It was therefore interesting to see how this molecule behaves towards complexation with alkali and alkaline earth metal ions. All of these ionophores were characterized on the basis of various analytical and spectroscopic techniques such as elemental analysis, mass spectrometry, FT-NMR, FT-IR and UV-VIS
spectrophotometry. Molecular structures of some of the ionophores were established by single-crystal X-ray study.

The competitive complexation property/selectivity of all of these ionophores towards alkali and alkaline earth metal ions were then investigated in aqueous media by two-phase extraction method using equimolar mixture of Li$^+$, Na$^+$, K$^+$, Mg$^{2+}$, Ca$^{2+}$, and Sr$^{2+}$ in presence of picrate anion. The concentrations of metal ions in the organic extract were estimated by ion chromatographic assay or inductively coupled plasma (ICP). Association constant with some strongly interacting metal ions were determined by UV-VIS spectrophotometry, NMR and isothermal calorimetric titration (ICT). Thermodynamic parameters were also evaluated from the ITC data.

For solid state characterization of metal complexes, K$^+$ and Na$^+$ (in a few cases) complexes were synthesised and characterized on the basis of analytical and spectroscopic data. Molecular structures of a number of complexes were determined by single crystal X-ray study. Both mono- and bi-metallic complexes were obtained and detail analysis of coordination pattern and intra- and intermolecular interactions have given many useful information about coordination geometry and structural features.

The high selectivity of some of the ionophores towards K$^+$, as found in the competitive complexation study, has motivated to use these ionophores for extraction of K$^+$ from a natural source such as sea bittern. The experiments were carried out following the procedure similar to that described for equimolar mixture of metal ions, except bittern is used instead of equimolar mixture of metal ions. Analysis of the data revealed that most of the cases it exhibited high selectivity towards K$^+$, similar to that observed for mixture of ions. In a few cases the selectivity towards K$^+$ is found to be ~ 86.0 %. These ionophores may therefore find application in extraction of K$^+$ from aqueous solution, particularly in presence of Na$^+$, Mg$^{2+}$ and Ca$^{2+}$.

Data analysis such as selectivity, binding constants, thermodynamic parameters etc. revealed that factors such as size matching between ionic diameter of metal ion and cavity size, conformation of the calixarene, substituents with additional coordination property and steric crowding etc. influence selectivity and complexation property. Picrate anion also plays important role, some cases it has coordinated the metal ion making polymeric
chain and almost all cases it makes strong ion pair with cationic chromophore through non-bonding interaction, which facilitates transportation of complex from aqueous to non-aqueous medium.

6.2. Future prospects

Potassium is one of the most important metal ions as it use as fertiliser, and has demand worldwide; our country imports its entire requirement. Brine, concentrated sea water, is one of the main natural sources of potassium and efforts are going on to recover K$^+$ from brine. In this direction, one of the important possibilities is the selective extraction of K$^+$ using suitable extractants. Therefore, designing of extractants/ligands, which can extracts K$^+$ from brine is an important area of research with tremendous potential of application. In this context designed calixarene can play important role and also it find application as extractant.

The work reported in this thesis clearly shows the factors, which influence selectivity and binding capability. Therefore, calixarene derivatives with variation in substituents, conformation and steric crowding can be developed to improve selectivity (> 95 %). Another important aspect, which has not been studied here, is the recovery of K$^+$ from the complex following demetallation procedure and recycle of the extractants. This can be studied to develop suitable method(s) to recover metal ions and to recycle the ligand. Another important aspect is the solubility; efforts should be made to develop water soluble extractant incorporating suitable substituents such as sulphonic acid, carboxylic acid etc. (Fig.6.1), so that extraction can be made in complete aqueous media.

![Fig.2. Water soluble calix[4]arene hybrid ionophores](image-url)
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2 Synthesis, characterization, crystal structures and metal-ion binding property of calix[4]arene-biscrown and their application for extraction of metal ion from sea-bittern
   Vallu Ramakrishna, V.P.Boricha, E. Suresh, Anjani K. Bhatt, and Parimal Paul *(Submitted)*

3 Synthesis crystal structures and study on ion-selectivity of a series of calix[4]arene based ionohore containing benzocrown ether at lower rim and crown ethers of different sizes in upper rims
   Vallu Ramakrishna, V.P.Boricha, E. Suresh, Anjani K. Bhatt, and Parimal Paul *(Submitted)*

4 Synthesis and competitive binding property of calix[4]arene incorporated alizarin crown-6 as an ionophore
   Vallu Ramakrishna, Anjani K. Bhatt, and Parimal Paul *(Submitted)*

**Papers presented in Conferences/ Symposium:**

1. Symposium on Modern trends in Inorganic Chemistry-XV (MTIC-XV) at Department of chemistry, Indian institute of Technology Roorkee on December 13-16, 2013

2. International Conference on Supramolecules and Nanomaterials-Research and Applications (ICSNA 2012) at Department of chemistry, Gujarat University, Ahmadabad on February 6-8, 2012

3. International Conference on Structural and Inorganic Chemistry at Department of chemistry, NCL-Pune, Pune, on December 4-5, 2014. (ICSIC-2014)
Synthesis, crystal structures and competitive binding property of a family of functionalized calix[4]arene ionophores

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ABSTRACT

A family of calix-crown hybrid molecules incorporating crown-4, crown-5 and crown-6 moieties as ionophore has been synthesized to evaluate their competitive complexing and extracting abilities towards different alkali and alkaline earth metal ions. Selectivity of these ionophores towards Li⁺, Na⁺, K⁺, Ca²⁺, Mg²⁺ and Sr²⁺ has been evaluated with aqueous solution containing equimolar mixture of these ions. The concentration of metal ion in the extract (organic phase) has been estimated by ion chromatographic assay. Two of the ionophores show strong complexation with Na⁺ and K⁺, whereas the third ionophore exhibits no complexation with any metal ions used in this study. Association constants (Kₐ) for the binding of Na⁺ and K⁺ with two of these ionophores have been determined spectrophotometrically. Molecular structures of the Na⁺ and K⁺ complexes of these ionophores have been established by single crystal X-ray study. ¹H NMR study of the ionophores and their complexes has also been carried out to investigate conformational behavior of the ionophores and their metal complexes in solution. Results have been discussed in light of various factors that contribute to determine ion-selectivity.

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In this communication, we report competitive complexation property of calix[4]arene-crown-n (n = 4, 5 and 6, Fig. 1) with the metal ions Li⁺, Na⁺, K⁺, Ca²⁺, Mg²⁺ and Sr²⁺. Selectivity of these ionophores towards the above-mentioned metal ions has been evaluated by two-phase extraction using aqueous solution containing equimolar mixture of these ions. The concentration of metal ion in the extract (organic phase) has been estimated by ion chromatographic assay. Association constants for strongly interacting metal ions were also determined. The molecular structures of the Na⁺ and K⁺ complexes of the two ionophores were also determined by single crystal X-ray study.

The ionophores 1–3 were synthesized following the modified published procedures [29,30,40], route followed for the synthesis [Scheme S1, ESI] and details of the synthetic procedures [S2, ESI] are available as ESI. These compounds were characterized on the basis of elemental analysis, mass spectrometry, IR and ¹H NMR data [S2, ESI]. Elemental analysis and mass data are in excellent agreement with the calculated values. It may be noted that the m/z values for 1 appeared as [1 + Na]⁺, whereas for 2 and 3, it appeared as both Na⁺ and K⁺ salt, [2/3 + Na]⁺ and [2/3 + K]⁺, with different intensity of peaks. Association with different cations in ESI-MS depends on complexation ability of the ligand with various metal ions, and the variation in peak intensity depends on the stability of the complex formed. Ion-binding property of 1–3 towards alkali and alkaline earth metal ions was evaluated by two-phase extraction method using equimolar mixture of metal ions. The experiments were carried out with an aqueous solution containing equimolar amounts of Li⁺, Na⁺, K⁺, Mg²⁺, Ca²⁺ and Sr²⁺ as their picrate salts and the respective ionophore dissolved in dichloromethane [29]. The metal ions

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added with stoichiometric amount and also with 25, 50, 75 and 100 times excess with respect to the concentration of ionophore used [S3, ESI]. The organic phase containing the complex formed was separated and the metal ions in the extract were determined by ion chromatographic assay [S4, ESI]. It may be noted that the extract obtained from ionophore 1 exhibited only trace amount of a few metal ions, indicating poor complexing ability of this ionophore towards the metal ions tested. It was also examined with the aid of $^1$H NMR study, the spectra of 1 and that in presence of metal ions were recorded in CDCl$_3$. The $^1$H NMR spectra recorded in presence of metal ions did not show any significant change compared to that of 1, indicating that no considerable amount of complex is formed with the metal ions used for this study. This is probably due to cavity size of crown-4, which is not large enough to allow the entry of the hydrated metal ion for complex formation. The organic extracts of 2 and 3 showed the presence of Na$^+$, K$^+$, Mg$^{2+}$ and Ca$^{2+}$, and the distributions of metal ions in the extract, together with values of the observed selectivity ratios, are shown in Table 1. The plot of the metal fraction of the metal ions extracted against concentration of metal ions used in the extraction process is shown in Fig. 2 for ionophore 3, similar plot for 2 is given as ESI (S5). The result clearly suggests that these two ionophores prefer to bind Na$^+$ and K$^+$ over the other metal ions; Mg$^{2+}$ and Ca$^{2+}$ also form considerable amount of complexes but Li$^+$ and Sr$^{2+}$ do not form any complex with these ionophores. Small size and high hydration enthalpy ($-520$ and $-1443$ kJ mol$^{-1}$ for Li$^+$ and Sr$^{2+}$, respectively) are likely the factors, which prevented this metal ion to form complex. For Sr$^{2+}$, probably the large size of the hydrated metal ion also played important role to prevent its entry into the cavity of the ionophore to form complex. The other notable observation is that the selectivity ratio (K$^+$/Na$^+$) for 2 towards K$^+$ and Na$^+$ ions is 0.84 (Table 1), whereas the same for 3 is 1.08, indicating that the selectivity towards K$^+$ over Na$^+$ is significantly high for 3, which is due to better size matching for K$^+$ with the crown-6 cavity. For structural elucidation of these complexes, we synthesized both Na$^+$ and K$^+$ complexes of the ionophores 2 and 3.

These complexes were synthesized by stirring the solution of Na$^+$ or K$^+$ picrate and the ionophore in chloroform–methanol (5:1) at room temperature for 24 h and purified from dichloromethane [S6, ESI]. These complexes were characterized on the basis of elemental analysis, mass spectrometry, IR and $^1$H NMR data and finally molecular structures were determined by single crystal X-ray study. It is interesting to note that the ESI-MS of all the four complexes exhibited m/z values corresponding to both Na$^+$ and K$^+$ complexes; however the peak with 100% intensity corresponds to the complex, which used is for measurement, i.e., for Na$^+$ complexes the 100% peak corresponds to [2/3Na$^+$] and for K$^+$ complexes the 100% peak corresponds to [2/3K$^+$] [S6, ESI]. To check purity of the complexes, powder X-ray diffraction patterns of all the four complexes were recorded and these patterns were compared with those obtained by simulation from single crystal X-ray data, good matching of both the patterns (S7 and S8, ESI) suggests that the molecular structures determined from single crystal X-ray analysis (described below) represent the bulk complexes. Suitable crystals for X-ray study of these complexes were grown from THF–toluene (2:3), except K$^+$ complex of 3, which was grown from dichloromethane–toluene (1:1). The $^1$H NMR spectra of the ionophore 3 and that of its Na$^+$ and K$^+$ complexes (3Na$^+$–pic and 3K$^+$–pic) are shown in Fig. 3. It may be noted that in the $^1$H NMR spectra of the ionophore, a typical AB pattern was observed for the methylene bridge (ArCH$_2$Ar) protons of the calix moiety, that is two widely separated doublets at $\delta = 3.90$–4.65 and 3.12–3.36 ppm ($J = 12$–13.8 Hz), which suggests that these ionophores exist in cone conformation in solution [29,41,42]. The low-field doublet is due to axial hydrogen atom, and the high-field doublet is due to equatorial hydrogen atoms of the methylene bridge. These doublets are also observed in the Na$^+$ and K$^+$ complexes with slight change in chemical shifts, indicating that the cone conformation of the calix moiety is retained in the complexes. The chemical shifts of the signals due to crown moiety ($\delta = 3.71$–4.15) changed significantly upon complexation with metal ion (Fig. 3), indicating that the metal ion encapsulated in the crown cavity to form the complex. A few changes in chemical shifts are also noted in the aromatic

Table 1

<table>
<thead>
<tr>
<th>Compound</th>
<th>Concentration (%) of metal ion in the extract</th>
<th>Selectivity ratio$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Li$^+$</td>
<td>Na$^+$</td>
</tr>
<tr>
<td>2</td>
<td>Trace</td>
<td>34.42</td>
</tr>
<tr>
<td>3</td>
<td>Trace</td>
<td>32.09</td>
</tr>
</tbody>
</table>

$^a$ 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. $^b$ The ratio is calculated by [% of K$^+$ in the extract] [% of M$^{2+}$ in the original solution] / [% of M$^{2+}$ in the extract] % of K$^+$ in the original solution].
region ($\delta = 6.67\text{–}7.06$), which is due to overall conformational change of the molecule because of the complexation with metal ion. A new peak appeared at $\delta = 8.85$ in the complexes due to picrate counter anion. The $^1$H NMR spectra of 2 and 3 are, therefore, consistent to the formation of complexes encapsulating metal ion in the calix-crown cavity.

Molecular structures of the Na$^+$ and K$^+$ complexes of 2 ($2$.Na$^+$.pic and $2$.K$^+$.pic) and 3 ($3$.Na$^+$.pic and $3$.K$^+$.pic) were determined from single crystal X-ray study, and details of unit cells are available as ESI [S9]. Suitable crystals for X-ray study were grown from THF/CH$_2$Cl$_2$-toluene, and the analysis of the data revealed the structures shown in Figs. 4 and 5 (hydrogen atoms and lattice solvent molecules are omitted for clarity). In all of these complexes, the metal ion is coordinated to one of the phenolic OH of the calix moiety and with oxygen atoms from picrate anion and crown moiety. The picrate anion is coordinated in a bidentate fashion using the oxygen atom of the deprotonated OH and one of the oxygen atoms of an adjacent nitro group. The Na$^+$ ion is six coordinated in $2$.Na$^+$.pic and seven coordinated in $3$.Na$^+$.pic, whereas K$^+$ is seven coordinated in $2$.K$^+$.pic and eight coordinated in the complex, $3$.K$^+$.pic. It is interesting to note that for Na$^+$, two of the oxygen atoms of the crown moiety and for K$^+$, one of the oxygen atoms of the crown ring do not participate in coordination. This is because of the size of the metal ions and this constrain, which the crown ring is expected to experience for coordination of all of the oxygen atoms to the same metal ion. The larger K$^+$ ion is better fitted in the cavity as evident from higher coordination number compared to Na$^+$ in the same crown ring. For 3, due to more flexibility of the larger crown ring (crown-6), more oxygen atoms could come closer to metal ion for coordination. It is noteworthy that the cone conformation of the calixarene moiety, found in the ionophore, is retained even after complexation with metal ion. The Na$^+$...O and K$^+$...O distances in both the complexes are found in the ranges 2.279(4) to 2.698(6) and 2.630 (3) to 2.938(4)Å, respectively. In all of these complexes, there are several intra- and intermolecular O—H...O and C—H...O interactions, in which picrate anion is also involved. In an attempt to understand the interaction between the $2$Na$^+$pic with lattice host p-xylene and $2$K$^+$pic with lattice host toluene, packing and hydrogen bonding interaction has been analyzed in detail (Table S1). Packing diagrams with hydrogen bonding between $2$Na$^+$pic and p-xylene viewed down b-axis, and the interaction between $2$K$^+$pic and toluene viewed down c-axis are given in supplementary data (S10 and S11). In the case of $2$K$^+$pic, the dimeric complex is involved in inter and intramolecular C-H...O and O—H...O H-bonding generating a corrugated layer along ab plane. Lattice toluene guest molecules are located in the clefts of the corrugated layer and anchored by C—H...π interactions between the phenyl hydrogen H9 of the calix ring with the centroid of the toluene guest with C1g...H9 distance 3.21Å. For the Na$^+$pic complex, host moiety is...
Table 2
Molar ratio of picrate to host in organic layer (R) and association constants (Kd) for 2 and 3 with Na⁺ and K⁺.

<table>
<thead>
<tr>
<th>Compound</th>
<th>R</th>
<th>Na⁺</th>
<th>K⁺</th>
<th>Na⁺</th>
<th>K⁺</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>0.19</td>
<td>0.34</td>
<td>1.47 × 10⁶</td>
<td>2.6 × 10⁶</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0.14</td>
<td>0.37</td>
<td>9.6 × 10⁴</td>
<td>4.9 × 10⁶</td>
<td></td>
</tr>
</tbody>
</table>

Details of the determination of different parameters of Eq. (1) are given as ESI [S12] and the association constant thus determined are given in Table 2. The data show that the association constant for K⁺ is significantly higher compared to that of Na⁺, which is due to strong complexing ability of the larger K⁺ because of the better size-matching factor plays the predominant role in ion-selectivity.

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Appendix B. Supplementary data

CCDC 834098, 834099, 834100 and 834101 contain the supplementary crystallographic data for 2.Na⁺.pic, 2.K⁺.pic, 3.Na⁺.pic and 3.K⁺.pic, respectively. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Other supplementary data associated with this article can be found in the online version. Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.inoche.2012.05.028.

References


