CHAPTER-V

SYNTHESIS OF ALIZARIN-CROWN-6 INCORPORATED CALIX[4]ARENÉ AND THEIR INTERACTION WITH ALKALI AND ALKALINE EARTH METAL IONS IN AQUEOUS MEDIA
## CONTENTS

**Chapter: V** Synthesis of alizarin-crown-6 incorporated calix[4]arene and their interaction with alkali and alkaline earth metal ions in aqueous media

5.1 Introduction 1

5.2 Experimental section 1

5.2.1. Materials 1

5.2.2. Physical measurement 1

5.2.3. Synthesis of anthraquinone substituted calix[4]arene-crown-6 ether (I) 2

5.2.4. Determination of selectivity 2

5.2.5. Determination of binding constant by NMR titration 2

5.2.6. Synthesis of metal complexes 3

5.3. Results and discussions 5

5.3.1. Synthesis and characterization of the ionophore (1) 5

5.3.2. Selectivity study 7

5.3.3. NMR titration for determination of binding constant 7

5.3.4. Isolated complexes of the ionophore 1 11

5.4. Conclusions 13

References 14
5.1. Introduction

In the earlier chapters, calix[4]arene-crown hybrid ionophores with variation in size of the crown rings, type of the crown moieties and substituents in the crown/calix moieties with their competitive complexation property towards alkali and alkaline earth metal ions have been reported. In this chapter, a calix-crown hybrid ionophore with anthraquinone moiety attached to the crown ring with its complexation property has been reported. 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.\textsuperscript{1-25} It is therefore interesting to see how this molecule behaves towards complexation with alkali and alkaline earth metal ions under similar conditions as used for other ionophores.

In this chapter, synthesis and characterization of the anthraquinone substituted calix[4]arene-crown-6 ether its selectivity and complexation property has been reported. Binding constant with strongly interacting metal ions, determined by NMR titration has also been reported.

5.2. Experimental section

5.2.1. Materials

The compound 1,2-dihydroxy-9,10-anthraquinone was purchased from S.D Fine chemicals. The other starting materials were purchased from the same source as described in the earlier Chapters. Starting compounds were also prepared following the literature procedure as mentioned in the earlier Chapters. The 1, 2-dihydroxy anthraquinone modified pentaethylene glycol ditosylate was prepared following the literature procedure.\textsuperscript{26}

5.2.2. Physical measurement

For physical measurements, same instruments as described in Chapters II-IV are used.

In a typical procedure, calix[4]arene, (0.937 g, 2.2 mmol) and 1,2-dihydroxy anthraquinone modified pentaethylene glycol ditosylate (1.6 g, 2.2 mmol) and K$_2$CO$_3$ (0.3 g, 2.2 mmol) were taken in 100 mL dry acetonitrile and heated under reflux for 72 h under nitrogen atmosphere. Then the solvent of the reaction mixture was removed under reduced pressure and the crude product thus obtained was dissolved in 100 mL dichloromethane and was treated with 100 mL 1N HCl. The organic layer was then separated and dried with anhydrous Mg(SO)$_4$ and the solution was then evaporated under reduced pressure. The crude product thus obtained was purified by column chromatography using 1:2 ethylacetate and hexane. Yield: 40%. Elemental analysis for C$_{50}$H$_{44}$O$_{10}$, C, 74.76; H, 6.27; Found: C, 74.32; H, 6.52. ES-MS: m/z = 843.64 (100%), calcd. for [1+K$^+$]+ 843.92. Selected IR band (KBr pellet, cm$^{-1}$) 3387 $\tilde{\nu}$(OH), 2928–2874 $\tilde{\nu}$(C=C, aromatic), 1671 $\tilde{\nu}$(C=O).

$^1$H NMR (CD$_3$CN) δ: 8.20 (t, J = 6.5 Hz, 2H, H$_3$H$^4$) (see Fig.5.2 for naming), 7.96 (d, J = 9.0 Hz, 1H, H$^5$), 7.82 (s, 2H, ArOH-calix, H$^{15}$), 7.36 (d, J = 9.0 Hz 1H, H$^6$), 6.98 (d, J = 6.5 Hz, 2H, ArHp-calix, H$^{17}$), 6.94 (t, J = 7.5 Hz, 6H, ArHm-calix, H$^{18}$), 6.75 (q, J = 5.0 Hz, 2H, ArHm-calix, H$^{16}$), 6.50 (t, J = 7.5 Hz, 2H, ArHp-calix, H$^{19}$), 4.43 (t, J = 4.5 Hz, 2H, anthraquinone-OCH$_2$, H$^7$), 4.40 (t, J = 4.75 Hz, 2H, ArOCH$_2$, H$^{14}$), 4.31 (dd, J = 12.16 Hz, 4H, ArCH$_2$Ar, H$^{20}$), 4.24 (t, J = 5.0 Hz, 2H, anthraquinone-OCH$_2$, H$^8$), 4.14 (t, J = 4.5 Hz, 2H, anthraquinone-crown, H$^{12}$), 4.09 (broad s, 6H, anthraquinone crown, H$^9$,H$^{10}$,H$^{11}$), 4.03 (t, J = 4.5 Hz, 2H, ArOCH$_2$, H$^{13}$), 3.32 (d, J = 13.0 Hz, 4H, ArCH$_2$Ar, H$^{21}$).

5.2.4. Determination of selectivity

Selectivity of the ionophore 1 was examined with alkali and alkaline earth metal ions in aqueous media using equimolar mixture of metal ions and various concentrations of metal ions present in bittern solution following the similar procedure as described in Chapter IV.

5.2.5. Determination of binding constant by NMR titration

For NMR titration, stock solutions of the picrate salts of the metal ions Na$^+$/ K$^+$/ Ca$^{2+}$ were prepared in CD$_3$CN. $^1$H NMR spectra of the solutions containing 2 mg of ionophore 1, dissolved in 0.5 mL of the same solvent, was recorded. Into this
solution, required amount of stock solution containing desired metal salt was added by micro syringe to make the concentrations of the desired concentrations of the metal ion in the solution and the spectra of the resulting solutions were recorded. Upon addition of increasing concentration of cations, gradual shift of certain signals were noted. Using this gradual change in chemical shift, binding constants were calculated using the literature procedure.27,28

5.2.6. Synthesis of metal complexes

The metal complexes were synthesized following a general procedure. In a typical experiment, a mixture of 0.05 mmol of the ionophore and Na+/K+/Ca2+ picrate (0.5 mmol, ten-fold excess) was stirred in chloroform at room temperature for 24 h. The solution was then filtered and the solvent from the filtrate was removed under reduced pressure. The yellow complex was then purified by dissolving it in dichloromethane, filtered and removing the solvent. Yield: 80–90%.

Characterization data

[1.Na+pic].H2O.H2O, Elemental analysis for C50H48O12Na, C, 69.52; H, 5.60; Found: C, 69.13; H, 5.65. ES-MS: m/z = 827.52 (100%), calcd. for [1+Na+] 827.81. Selected IR band (KBr pellet, cm⁻¹) 3424 ν (OH), 2925-2856 ν (C=C, aromatic), 1671 ν (C=O), 1633. ¹HNMR (CD3CN) δ: 8.63 (s, 2H, picrate), 8.23 (d, J = 7.5 Hz, 1H, anthraquinone, H3), 8.20 (d, J = 6.0 Hz, 1H anthraquinone, H4), 7.96 (d, J = 9.0 Hz, 1H anthraquinone, H5), 7.91 (s, 2H, ArOH-calix, H15), 7.88-7.84 (m, 2H, anthraquinone,H1, H2), 7.37 (d, J = 9.0 Hz, 1H anthraquinone,H6), 6.93 (d, J = 7.5 Hz, 2H, ArHp-calix, H17), 6.86 (t, J = 8.5 Hz, 4H, ArHm-calix, H18), 6.79 (t, J = 6.5 Hz, 2H, ArHm-calix, H16), 6.71 (t, J =7.5Hz, 2H, ArHm-calix, H16), 6.34 (t, J =7.5Hz, 2H, ArHp.calix), 4.52 (t, J = 4.25Hz, 2H, anthraquinone-OCH2, H3), 4.38 (t, J = 4.25Hz, 2H, Ar-OCH2H14), 4.29 (Overlapped t, J = 6.5Hz, 2H, ArCH2Ar, H20), 2H, anthraquinone-OCH2, H3; 2H, anthraquinone-crown, H15), 4.21(t, J = 4.0 Hz, 2H, anthraquinone-crown, H9), 4.14 (t, J = 4.25Hz, 2H, anthraquinone-crown, H10), 4.11(Overlapped t, J = 4.25Hz, 2H, ArCH2Ar, H20, 2H, anthraquinone-crown, H11), 3.94 (t, J = 4.25 Hz, 2H, -anthraquinone-crown, H13), 3.33 (dd, J = 12.0 Hz, 4H, ArCH2Ar, H21).
Chapter-V

[1.K+pic].H₂O.H₂O, Elemental analysis for C₅₀H₄₈O₁₂K, C, 68.24; H, 5.49; Found: C, 68.05; H, 5.71; ES-MS: m/z = 843.76 (100%), calcd. for [1+K⁺] 843.92; Selected IR band (KBr pellet, cm⁻¹) 3391 ν (OH), 2925-2856 ν (C=C, aromatic), 1671 ν (C=O), 1632. ¹HNMR (CD₂CN) δ: 8.61 (s, 2H, picrate), 8.23 (d, J = 6.0Hz, 1H, anthraquinone, H³), 8.18 (d, J = 6.0 Hz, 1H anthraquinone, H⁴), 7.93 (d, J = 8.5 Hz, 1H anthraquinone, H⁵), 7.90-7.86 (m, 2H, anthraquinone, H¹, H²), 7.37 (d, J = 8.5 Hz, 1H anthraquinone, H⁶), 7.13 (s, 2H, ArOH-calix,H¹⁵), 6.85 (overlapped t, J = 7.5Hz, 2H, ArHp-calix, H¹⁷; 2H, ArHm-calix, H¹⁸), 6.75 (t, J = 7.5 Hz, 1H, ArHm-calix, H¹⁶), 6.71 (d, J = 7.0Hz, 4H, ArHm-calix, H¹⁸), 6.64 (t, J=7.5Hz, 1H, ArHm-calix, H¹⁶), 6.31(t, J=7.5Hz, 2H, ArHp-calix, H¹⁹), 4.60 (t, J = 4.25Hz, 2H, anthraquinone-OCH₂, H⁷), 4.34 (d, J = 3.0Hz, 2H, anthraquinone-OCH₂, H¹⁴; 2H, ArOCH₂, H⁸), 4.24 (Overlapped d, J = 7.5Hz, 2H, ArCH₂Ar, H²⁰; 2H, anthraquinone-crown, H⁹), 4.21(t, J = 2.25Hz, 4H, anthraquinone-crown, H¹²,H¹¹), 4.05 (t, J = 4.25Hz, 2H, anthraquinone crown, H¹⁰), 3.96 (d, J = 13 Hz, 2H, ArCH₂Ar, H²⁰), 3.85 (t, J = 3.75 Hz, 2H, ArOCH₂, H¹³), 3.38 (d, J = 13.5 Hz, 2H, ArCH₂Ar, H²¹), 3.27 (d, J = 13.5 Hz, 2H, ArCH₂Ar, H²¹).

[1.Ca²⁺(pic)₂].H₂O Elemental analysis for C₅₀H₄₆O₁₁Ca, C, 69.59; H, 5.37; Found: C, 69.12; H, 5.60; ES-MS: m/z = 843.86, calcd. For [1+Ca²⁺-H⁺]⁺ 843.89; Selected IR band (KBr pellet, cm⁻¹) 3398 ν (OH), 2925-2856 ν (C=C, aromatic), 1671 ν (C=O); ¹HNMR (CD₂CN) δ: 8.70 (s, 4H, picrate), 8.18 (d, J = 7.5Hz, 1H, anthraquinone, H³), 8.15 (d, J = 8.0 Hz, 1H, anthraquinone, H⁴), 7.98 (d, J = 8.5 Hz, 1H anthraquinone,H⁵), 7.87-7.81 (m, 2H, anthraquinone, H¹, H²), 7.73 (s, 2H, ArOH-calix, H¹⁵), 7.32 (d, J = 8.5 Hz, 1H anthraquinone, H⁶), 7.02 (Overlapped dd, J = 7.0 Hz, 2H, ArHm-calix, H¹⁷, 2H, ArHp-calix, H¹⁸), 6.93 (dd, J = 7.5 Hz, 4H, ArHm-calix, H¹⁸), 6.79-6.73 (m, 2H, ArHm-calix, H¹⁶), 6.55 (t, J =7.5Hz, 2H, ArHp-calix, H¹⁹4.62(br s, 2H, anthraquinone-OCH₂H⁷), 4.52 (t, J = 3.75Hz, 2H, ArOCH₂, H¹⁴), 4.35 (t, J = 3.5Hz, 2H, anthraquinone-OCH₂H⁸), 4.32 (t, J = 4.0 Hz, 2H, anthraquinone-crown, H¹²), 4.25 (dd, J = 13.0Hz, 4H, ArCH₂Ar, H²⁰), 4.19 (t, J = 3.75Hz, 2H, -OCH₂CH₂O-crown, H⁹), 4.10 (t, J = 4.25Hz, 2H, -OCH₂CH₂O-crown, H¹⁰), 4.02 (t, J = 4.0Hz, 2H, -OCH₂CH₂O-crown,H¹¹), 4.00 (t, J = 4.25Hz, 2H, Ar-OCH₂, H¹³).
5.3. Results and discussions

5.3.1. Synthesis and characterization of the ionophore (1)

Ionophore 1 has been synthesized by the reaction of 1,2-dihydroxyanthraquinone modified pentaethylene glycolditosylate and calix[4]arene in the presence of two equivalents of K₂CO₃ as a base following the route shown in Scheme 1 and detail procedure has given in the Experimental Section. Elemental analysis, given in the Experimental Section, is in excellent agreement with the composition of 1. The ES-MS spectrum of 1 is shown in Fig.5.1, the \( m/z \) value of which (843.64) matched very well with the calculated value (843.92) for \([1+K^+]^+\). The \(^1\)H NMR spectrum of 1 with assignment of signals is shown in Fig.5.2 and the data are presented in the Experimental Section. The anthraquinone moiety exhibited signals at \( \delta = 8.20, 7.96, 7.82 \) and 7.36

![Scheme 1](image-url)

**Scheme 1.** The route followed for the synthesis of ionophore 1, reagents/solvents: a) chloroethoxyethanol/acetonitrile/K₂CO₃/reflux for 72h, b) TsCl/THF/0°C for 24h, c) 1,2-dihydroxy-9,10-anthraquinone modified pentaethylene glycolditosylate/acetonitrile/reflux for 72h.
Fig. 5.1. ES-mass spectrum of the ionophore 1, recorded in CD₃CN[1+K⁺]⁺

Fig. 5.2. ¹H NMR spectrum of ionophore 1 recorded in CD₃CN
and the phenolic OH of calixarene moiety appeared at δ = 7.83.\textsuperscript{29,30} The protons for the methylene bridge of the calixarene moiety appeared at 4.32 (dd, 4H) and 3.32 (d, 4H), which suggests cone conformation for the calixarene molecule.\textsuperscript{31} On the basis of these data the molecular structure assigned for 1 is shown in Scheme 1.

5.3.2. Selectivity study

Selectivity of the ionophore 1 was investigated by two phase extraction method following the similar procedure described in the earlier Chapters and mentioned in the Experimental Section. The concentration of metal ions in the extract, determined by ICP, exhibited \( K^+ = 42, \text{Ca}^{2+} = 24, \text{Na}^+ \% \) and trace amount of \( \text{Mg}^{2+} \), which indicates that this ionophore can extract \( \text{Na}^+ \), \( K^+ \) and \( \text{Ca}^{2+} \) and not highly selective for any particular metal ion when mixture of metal ions are present. On the basis of this information, the binding constants of 1 with all of these three metal ions were determined by NMR titration.

5.3.3. NMR titration for determination of binding constant

The method followed for NMR titration is described in the Experimental Section and the \( ^1\text{H} \) NMR spectral change for 1, recorded with incremental addition of picrate salts of the metal ions (\( \text{Na}^+/\text{K}^+/\text{Ca}^{2+} \)) in CD\(_3\)CN are shown in Figs.5.3-5.5. The spectra for all the three metal ions exhibited significant changes in chemical shifts for many of the signals. It may be noted that substantial changes in chemical shifts for all of the metal ions is observed in the aliphatic region, where signals due to crown moiety appears. It suggests that the crown moiety is involved in interaction with metal ions, in other words the metal ions are encapsulated in the calix crown cavity. In the aromatic region, the signals due to anthraquinone moiety is least affected, which indicates that this moiety is not involved in making interaction with metal ions. The chemical shift of the OH proton has shifted most for \( K^+ \) ion, moderate shift has noted with \( \text{Ca}^{2+} \), whereas no significant change for \( \text{Na}^+ \) has noted, suggesting that the OH group makes interaction with the encapsulated \( K^+ \) and \( \text{Ca}^{2+} \) ions but \( \text{Na}^+ \) does not interact with the OH group. Both in the aliphatic and aromatic regions, the signals due to calixarene moiety exhibited considerable changes, which is maximum for \( K^+ \). It may be attributed to the overall conformational change of the ionophore due to complexation with metal ions.
Fig. 5.3. $^1$H NMR spectral change for ionophore 1 upon addition of Na$^+$Pic, 0.06 (a), 0.18 (b), 0.36 (c), 0.60 (d) 0.90 (e), 0.96 (f), 1.44 (g) and 2.04 (h) 2.76 (i) 3.6 (j) 4.56 (k) 5.52 (l) molar equivalent amounts of Na-picrate.

Fig. 5.4. $^1$H NMR spectral change for ionophore 1 upon addition of K$^+$Pic, 0.06 (a), 0.18(b), 0.36 (c), 0.60 (d) 0.90 (e), 1.26 (f), 1.70(g)2.40 2.98 (h) 3.61(i) 4.54 (j) 5.78 (k) and 8.09(l) molar equivalent amounts of K-picrate.
Fig. 5.5. $^1$H NMR spectral changes for ionophore 1 upon addition of Ca(Pic)$_2$ 0.06 (a), 0.18 (b), 0.36 (c), 0.60 (d) 0.90 (e), 1.26 (f), 1.74 (g) and 2.34 (h) 4.86 (i) 5.94 (j) molar equivalent amounts of metal salt.

Binding constants for Na$^+$, K$^+$ and Ca$^{2+}$ ions were determined using the NMR titration data. Considering the gradual change in chemical shift of a particular signal upon addition of incremental amount of metal ion, the binding constants were calculated using the program developed by Hirose. The non-linear least square fit with Na$^+$, K$^+$ and Ca$^{2+}$ are presented in Figs. 5.6-5.8, and the binding constants obtained are given in Table 1. The data suggests that K$^+$ binds strongly followed by Ca$^{2+}$ and then Na$^+$ ion.

Table 1. Binding constants ($K_s$) for the ionophores 1 with different metal ions.

<table>
<thead>
<tr>
<th>Ionophore</th>
<th>Metal ion</th>
<th>Binding constant ($K_s/M^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Na$^+$</td>
<td>$1.471 \times 10^2$</td>
</tr>
<tr>
<td></td>
<td>K$^+$</td>
<td>$1.625 \times 10^3$</td>
</tr>
<tr>
<td></td>
<td>Ca$^{2+}$</td>
<td>$5.673 \times 10^2$</td>
</tr>
</tbody>
</table>
Fig. 5.6. The non-linear least square fit from $^1$H NMR titration data for the ionophore 1 with Na$^+$Pic in CD$_3$CN at room temperature.

Fig. 5.7. The non-linear least square fit from $^1$H NMR titration data for the ionophore 1 with K$^+$Pic in CD$_3$CN at room temperature.
Fig.5.8. The non-linear least square fit from $^1$H NMR titration data for the ionophore 1 with Ca$^+$ (Pic$^-$)$_2$ in CD$_3$CN at room temperature.

5.3.4. Isolated complexes of the ionophore 1

For solid state characterization, Na$^+$, K$^+$ and Ca$^{2+}$ complexes of 1 were synthesized, detail procedure and characterization data are given in the experimental section. Elemental analysis is in excellent agreement with the calculated values. The ES-MS spectra for all the three complexes are shown in Figs.5.9-5.11, the $m/z$ values 827.52, 843.64 and 843.86 for Na$^+$, K$^+$ and Ca$^{2+}$ ions respectively, matched very well with the calculated values for [1+Na$^+$]$^+$ (827.81), [1+K$^+$]$^+$ (843.10), and [1+Ca$^{2+}$-H$^+$]$^+$ (843.89), respectively. The elemental analysis, mass and $^1$H NMR data, therefore confirmed the formation of these complexes.
Fig. 5.9. ES-mass spectrum of the complex [1+Na⁺].Pic⁻ in CH₂CN

Fig. 5.10. ES-mass spectrum of the complex [1+K⁺].pic⁻ in CH₂CN
5.4. Conclusions

An anthraquinone substituted calix[4]arene-crown-6 hybrid ionophore has been synthesised and characterized on the basis of elemental analysis, mass and NMR spectroscopic data. The selectivity of this ionophore towards alkali and alkaline earth metal ions in aqueous media has been investigated and it exhibits complexation with Na\(^+\), K\(^+\) and Ca\(^{2+}\) and not highly selective for any particular metal ion in presence of mixture of metal ions. The complexation property of this ionophore towards the three strongly interacting metal ions has also been investigated by \(^1\)H NMR titration and the data has been used to calculate binding constant. The binding constant values suggest moderate to strong binding of metal ions, in which K\(^+\) exhibited highest binding constant. Metal-complexes of this ionophore with the metal ions Na\(^+\), K\(^+\) and Ca\(^{2+}\) have been synthesised, isolated in solid state and characterized. Apparently, the bulky and rigid substituent such as anthraquinone at the crown ring could not provide a conformational arrangement with controlled steric crowding, which can preferentially binds a particular metal ion, showing very high selectivity.
References