CHAPTER 4

STUDIES ON THE COMPLEXES OF CALIXARENE SULFONAMIDE WITH METAL IONS OF BIOINORGANIC IMPORTANCE
RESUME

Neutral bidentate chelate complexes of metal ions viz. Mn(II), Fe(II), Co(II), Ni(II), Cu(II) and Zn(II) have been prepared using calix[6]arene sulfonacetamide. These complexes have been characterized by elemental analysis. Cyclic Voltammetric data for complexes have been studied and the waves show that the metal goes to higher oxidation state or reduced to lower oxidation state.
INTRODUCTION

Sulfonamide derivatives exhibit versatile pharmacological activity and in particular, a cytostatic effect. Transition metal complexes of sulfonamides also find application in chemotherapy. Complexes of aromatic sulfonamides have been intensively studied as carbonic anhydrase inhibitors. Studies on their metal chelates could have been much physiological and pharmacological relevance because the metal chelates of sulfadugs have been found to be more bacteriostatic than the drugs themselves. Several authors have reported the antimicrobial activities of sulfonamides and their metal complexes.

Coordination complexes of Fe(III) with Schiff's based derived from sulfonamide drugs were reported. Metal complexes of peptide derivative such as complex formation of Cu(II) with N-benzene sulfonylglycine was prepared. A macrocyclic ligand containing two sulfonamide groups was synthesized and used for cation transportation. Mn(II), Fe(II), Co(II), Ni(II), Cu(II) and Zn(II) complexes of sulfonamide derivatives have been synthesized by H. Singh et al. and their fungitoxicity was studied. Studies on the interaction of biological metal ions with sulfonamide drugs such as sulfapyridine, sulfadiazine and sulfathiazole was performed.

It would be interesting to attach simplest sulfonamides to the calixarenes and resultant derivatives may complex with the transition metal ions selectively and efficiently. Electrochemical investigation of calixarene sulfonamide metal complexes may reveal the binding behaviour of the metal ions and their interactions as well redox behaviour in biological systems (biological oxidoreduction processes) may be understood by the help of such synthetic model systems with important features such as three dimensionality of ligand structure with a hydrophobic pocket as present in many biological systems. Biologically potent sulfonamide group containing ligating arms may be added to the special features which may preorganize to bind with metal ions and
affect their reactivity. With this in view, simplest biologically active sulfonamide groups were introduced on the upper rim of the calixarene to study the behaviour of bioinorganic metal ions viz. Mn(II), Fe(II), Co(II), Ni(II), Cu(II) and Zn(II) by solid complexation.
EXPERIMENTAL

CHEMICALS

All the chemicals are of Analytical grade of E. Merck unless otherwise specified.

APPARATUS

Melting points are taken in a sealed capillary tube using a Toshniwal (India) melting point apparatus and are uncorrected. Cyclic Voltammograms were recorded on CH Instruments Model 605A attached to 384B EG & G Par Polarographic Analyzer with glassy carbon or Pt wire counter electrode. The potential was scanned in the range of $-1.8 \text{V}$ to $+1.5 \text{V}$ at scanning rate $0.1 \text{V.s}^{-1}$

Preparation of Ligand

The ligand calix[6]arene sulfonacetamide was prepared as described in Chapter 2.

Preparation of Solid Metal complexes of Calix[6]arene sulfonacetamide with Mn(II), Fe(II), Co(II), Ni(II), Cu(II) and Zn(II)

0.01M ligand solution was prepared by dissolving appropriate amount of calix[6]arene sulfonacetamide into analytical grade dimethylformamide.

Equal volumes of 0.01M calix[6]arene sulfonacetamide solution and 0.1M metal solutions were taken in a round bottomed flask. The reaction mixture was reflux for three hours on a water bath. The solid thus obtained were filtered through a sintered glass crucible of porosity G-4 and washed thoroughly with hot double distilled water. The metal complexes thus obtained were dried.
Digestion of Metal Complexes of calix[6]arene sulfonacetamide

Known amount of calix[6]arene sulfonacetamide was weighted and digested with the acid mixtures of nitric acid and hydrochloric acid in 3:1 ratio. Metal ion contents in the digested solutions were determined by standard volumetric methods, titrating with EDTA and appropriate indicator. % amount of metal ions found in the solutions were listed in Table 1.

Electrochemical Studies

The electrochemical studies were performed by Cyclic Voltammetry. Electrochemical data were obtained from the isolated complexes of Mn(II), Fe(II), Co(II), Ni(II), Cu(II) and Zn(II) in DMF and data were compared with the cyclic voltammetric response of free metal ions. The cyclic voltammetric responses recorded for free metal ions in 0.5M LiCl supporting electrolyte with a scan rate of 0.1 V.s\(^{-1}\).
Table 1: Physical Properties of Metal Complexes of Calix[6]arene sulfonacetamide with Mn(II), Fe(II), Co(II), Ni(II), Cu(II) and Zn(II)

<table>
<thead>
<tr>
<th>No.</th>
<th>Metal Complex</th>
<th>Colour</th>
<th>mp °C</th>
<th>Elemental analysis %</th>
<th>% of Metal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>%C</td>
<td>%H</td>
</tr>
<tr>
<td>1</td>
<td>[C₆₄H₅₀O₂₂N₄S₂]Mn</td>
<td>off White</td>
<td>126 d</td>
<td>56.94</td>
<td>(57.10)</td>
</tr>
<tr>
<td>2</td>
<td>[C₆₄H₅₀O₂₂N₄S₂]Fe</td>
<td>off White</td>
<td>213 d</td>
<td>56.93</td>
<td>(57.06)</td>
</tr>
<tr>
<td>3</td>
<td>[C₆₄H₅₀O₂₂N₄S₂]Co</td>
<td>Light Green</td>
<td>247 d</td>
<td>56.85</td>
<td>(56.93)</td>
</tr>
<tr>
<td>4</td>
<td>[C₆₄H₅₀O₂₂N₄S₂]Ni</td>
<td>Off White</td>
<td>260 d</td>
<td>56.88</td>
<td>(56.94)</td>
</tr>
<tr>
<td>5</td>
<td>[C₆₄H₅₀O₂₂N₄S₂]Cu</td>
<td>Light Yellow</td>
<td>220 d</td>
<td>56.43</td>
<td>(56.74)</td>
</tr>
<tr>
<td>6</td>
<td>[C₆₄H₅₀O₂₂N₄S₂]Zn</td>
<td>Off White</td>
<td>188 d</td>
<td>56.23</td>
<td>(56.66)</td>
</tr>
</tbody>
</table>

The calculated values are in parenthesis.
Table 2: Cyclic Voltammetric Studies of Solid Complexes of Calix[6]arene sulfonacetamide with Mn(II), Fe(II), Co(II), Ni(II), Cu(II) and Zn(II)

<table>
<thead>
<tr>
<th>No.</th>
<th>Sample</th>
<th>Cathodic Potential $E_{Pc}$ (V)</th>
<th>Anodic Potential $E_{Pa}$ (V)</th>
<th>$\Delta E_{Pc}$ (V)</th>
<th>$\Delta E_{Pa}$ (V)</th>
<th>$E_{1/2}$ (V)</th>
<th>Cathodic Current $i_{pc}$</th>
<th>Anodic Current $i_{pa}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Zn(II) Salt</td>
<td>-1.25</td>
<td>-0.77</td>
<td>0.45</td>
<td>0.64</td>
<td>-1.01</td>
<td>1.56</td>
<td>-0.29</td>
</tr>
<tr>
<td></td>
<td>Zn(II) Complex</td>
<td>-1.70</td>
<td>-1.41</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Fe(II) Salt</td>
<td>0.37</td>
<td>0.43</td>
<td>1.17</td>
<td>1.05</td>
<td>0.40</td>
<td>1.20</td>
<td>-1.24</td>
</tr>
<tr>
<td></td>
<td>Fe(II) Complex</td>
<td>-0.80</td>
<td>-0.31</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Co(II) Salt</td>
<td>-0.64</td>
<td>-0.32</td>
<td>0.18</td>
<td>0.04</td>
<td>-0.48</td>
<td>1.33</td>
<td>-0.12</td>
</tr>
<tr>
<td></td>
<td>Co(II) Complex</td>
<td>-0.82</td>
<td>-0.36</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Ni(II) Salt</td>
<td>-0.83</td>
<td>-0.12</td>
<td>0.03</td>
<td>0.15</td>
<td>-0.48</td>
<td>0.90</td>
<td>-0.15</td>
</tr>
<tr>
<td></td>
<td>Ni(II) Complex</td>
<td>-0.86</td>
<td>-0.27</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Cu(II) Salt</td>
<td>-0.85</td>
<td>-0.02</td>
<td>0.01</td>
<td>0.04</td>
<td>-0.44</td>
<td>1.12</td>
<td>-0.10</td>
</tr>
<tr>
<td></td>
<td>Cu(II) Complex</td>
<td>-0.86</td>
<td>-0.06</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
RESULTS AND DISCUSSION

The physical properties of the metal complexes of calix[6]arene sulfonacetamide with Mn(II), Fe(II), Co(II), Ni(II), Cu(II) and Zn(II) have been listed in Table 1. The elemental analysis is in agreement with the calculated values and confirms the stoichiometry of metal to ligand is 1:1.

Cyclic Voltammetric Studies of Calix[6]arenesulfonacetamide and their complexes with metal ions viz. Mn(II), Fe(II), Co(II), Ni(II), Cu(II) and Zn(II)

Cyclic Voltammetric data for complexes have been studied. The cyclic voltammograms of free metal ions and the complexes are given in Fig. 2 to Fig. 6. The waves show that the metal goes to higher oxidation state or reduced to lower oxidation state.

The divalent metal ions under study showed redox type behaviour with a change in their potential upon binding with calix[6]arene sulfonacetamide.

Zn(II) Complex

Cathodic peak potential for Zn(II) was observed at -1.25V, when Zn(II) is reduced to lower oxidation state. This peak was observed at lower potential of -1.70V upon complexation with calix[6]arene sulfonacetamide. Anodic peak potential [Zn to Zn(II)] was observed at -0.77V, which was due to the transition of metal to the higher oxidation state. This wave was appeared at -1.41V upon complexation. Difference in the Cathodic peak potential of complex and the free metal ($\Delta E_{pc}$) was 0.45 V.

Current peak current was also found to decrease upon complexation. Cathodic peak current for Zn(II) was found to be $1.56 \times 10^{-4}$ A, which was lowered to $1.23 \times 10^{-4}$ A upon complexation. Anodic peak current for Zn(II) was found at $-0.29 \times 10^{-4}$ A and that of complex was obtained at $-0.04 \times 10^{-4}$ A.
Fig. 2a: Cyclic Voltammogram of Zn(II) ion

Fig. 2b: Cyclic Voltammogram of Calix[6]arene sulphonacetamide–Zn(II) Complex
Fig. 3a: Cyclic Voltammogram of Fe(II) Ion

Fig. 3b: Cyclic Voltammogram of Calix[6]arene sulphonacetamide- Fe(II) Complex
Fig. 4a: Cyclic Voltammogram of Co(II) Ion

Fig. 4b: Cyclic Voltammogram of Calix[6]arene sulphonacetamide- Co(II) Complex
Fig. 5a: Cyclic Voltammogram of Ni(II) Ion

Fig. 5b: Cyclic Voltammogram of Calix[6]arene sulphonacetamide- Ni(II) Complex
Fig. 6a: Cyclic Voltammogram Cu(II) Ion

Fig. 6b: Cyclic Voltammogram of Calix[6]arene sulphonacetamide- Cu(II) Complex
Fe(II) Complex

Largest potential difference was observed for Fe(II)-calix[6]arene complex ($\Delta E_{pc}=1.17$) Reductive voltammetric wave was observed at 0.37V cathodic peak potential [Fe(II) to Fe], which was significantly decreased to $-0.80$ upon complexation with the disappearance of original reductive voltammetric wave at 0.37V. Similarly, Oxidative voltammetric wave [Fe to Fe(II)] was observed at anodic peak potential of 0.43V for Fe(II) salt, which was lowered to $-0.31$V upon complexation. The largest difference of $\Delta E_{pc}= 1.17$V and $\Delta E_{pa}= 1.05$V suggest strong complexation, compare to other metal complexes.

Cathodic peak current for Fe(II) salt was found to be $1.20 \times 10^{-4}$A, which was lowered to $1.74 \times 10^{-4}$A upon complexation. Anodic peak current for Fe(II) was obtained at $-1.24 \times 10^{-4}$A, which shifted at $-0.16 \times 10^{-4}$A after complex formation takes place.

Co(II) Complex

Cathodic peak potential for Co(II) salt was observed at $-0.64$V and that of metal-ligand complex was observed at $-0.82$V, this voltammetric wave is due to the reduction of Co(II) to Co. Anodic peak potential was observed at $-0.32$V for Co(II) and shifted to $-0.36$V after complexation, which is due to the oxidation of Co to Co(II).

Cathodic and anodic peak current for Co(II) were observed at $i_{pc}= 1.33 \times 10^{-4}$A and $i_{pa}= -0.12 \times 10^{-4}$A, respectively. After complex formation, these values were found at $0.49 \times 10^{-4}$A for cathodic current and $-0.09 \times 10^{-4}$A for anodic current.

Ni(II) Complex

Reductive voltammetric wave(cathodic peak potential) was observed at $-0.83$V and that of metal-ligand complex was observed at $-0.86$V. Oxidative
voltammetric wave (Anodic peak potential) was observed at -0.12V for metal ion and that of the complex was found at -0.27V.

Cathodic and anodic peak currents were found at $0.90 \times 10^{-4}$A and $-0.15 \times 10^{-4}$A for Ni(II) and shifted to $0.52 \times 10^{-4}$A and $-0.05 \times 10^{-4}$A, respectively.

**Cu(II) complex**

Reductive voltammetric wave was appeared at a cathodic peak potential ($E_{pc}$) of -0.85V and a minor decrease was observed with a value -0.86V for metal-ligand complex. Cu(II) is reduced to Cu(I) and as a result Reductive voltammetric wave is observed. Anodic peak potential for Cu(II) was recorded at -0.02V and that of complex was at -0.06V.

Cathodic peak current for Cu(II) was found at $1.12 \times 10^{-4}$A. The current peak height was decreased to $0.43 \times 10^{-4}$A. Anodic peak current was observed at $-0.10 \times 10^{-4}$A, which was found at $-0.05 \times 10^{-4}$A, after complexation.

The values obtained from Cyclic Voltammetric experiments are noted in the Table-2. Difference in cathodic peak potential ($\Delta E_{pc}$) and anodic peak potential ($\Delta E_{pa}$) are also listed in Table-2.
M-L type 1:1 complexation between Calix[6]arene sulfonacetamide and Metal ions may be predicted as shown in the following figure.

Fig 1: M-L type complex of Calix[6]arene sulfonacetamide with metal ions
REFERENCES