SYNTHESIS, IR, EPR, UV-VISIBLE CHARACTERIZATION AND IN VITRO ANTIMICROBIAL ACTIVITY OF MACROCYCLIC SCHIFF’S BASE AND ITS METAL COMPLEXES OF Mn(II) AND Co(II)

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ABSTRACT

Novel macrocyclic Schiff’s base ligand and its transition metal complexes of Mn(II), and Co(II) have been synthesized and characterized. Mn(II) and Co(II) metal complexes of chelating macrocyclic Schiff’s base ligand have been synthesized using acetates and chlorides of the metals. All metal complexes were characterized by elemental analyses, molar conductance, magnetic moment measurements and spectral (UV-Vis, IR, and ESR) studies. The macrocyclic ligand acted as tetradentate ligand and coordinate with metal ions through nitrogen and oxygen atoms. The low molar conductance values in DMF indicated that the metal complexes were non-electrolyte in nature. The magnetic moments and electronic spectral data suggested octahedral geometry for the Mn(II) and Co(II) complexes. The ligand and metal chelates were screened in-vitro for antibacterial and antifungal activity. Well diffusion method was used for antibacterial and antifungal activity.

Key Words: Schiff’s base ligand, Mn(II), Co(II), complexes, spectral studies, octahedral, antibacterial, antifungal.

INTRODUCTION

The coordination chemistry has been significantly enriched due to the synthesis of metal complexes, in which the metal is coordinated through sulphur, nitrogen and oxygen donor
Metal chelation is involved in many essential biological processes where the coordination can occur between metal ions and donor atoms present in ligand. In coordination chemistry, macrocyclic complexes have paying attention of both inorganic and bioinorganic researchers. Aza-oxo group containing ligands come into view, that these types of ligands their metal complexes are very potential and used as, antibacterial, and antifungal, anticancer, antifertile agents due to their other biological properties. Macrocyclic complexes are best prepared with the aid of metal ions as templates to direct the condensation reaction which ultimately ends with ring closure.

This research article focused on the template synthesis of $N_2O_2$ donor macrocyclic Schiff’s base ligand and its metal complexes of Mn(II) and Co(II) ions derived from 1,4-bis(2-formylphenoxy)butane and thiourea in the presence of divalent metal salts in 1:1:1 ratio. The formation of the complexes was confirmed on the basis of spectral studies. The *in vitro* antibacterial and antifungal activities against bacterial stains *E.coli*, *B.cereus* and fungus *A. niger*, *F.oxysporum*, and *A.brassicae* were also tested.

**MATERIALS AND METHODS**

All used chemicals were commercial products and used as supplied. Salicylaldehyde, 1,4-dibromobutane and thiourea were of AR grade and procured from Sigma Aldrich, Bangalore, India. Metal salts were purchased from E. Merck, India and were used as received. All used solvents were of spectroscopic grade.

**Synthesis of 1,4-bis(2-formylphenoxy)butane**

To a stirred solution of salicylaldehyde (24.4 g, 0.2 mol) and $K_2CO_3$ (13.8 g, 0.1 mol) in DMF (25 mL), 1,4-dibromobutane (21.6 g, 0.1 mol) was added drop wise. The reaction was refluxed for 10 hrs at 150-155°C and then for 5 hrs. at room temperature. Reaction solution was put in a refrigerator. One hour later, the precipitate was formed, it was filtered off, and washed with ethanol, distilled water, recrystallized from ethanol and dried in vacuum (Fig1).
Synthesis of macrocyclic metal complexes

All complexes were synthesized by the template method, *i.e.*, by condensation of 1,4-bis(2-formylphenoxy)butane and thiourea in the presence of divalent metal salts in 1:1:1 ratio. In hot methanolic solution of 1,4-bis(2-formylphenoxy)butane (1.0 mmol) methanolic solution of divalent metal salt of Mn(II), and Co(II) (1.0 mmol) was added. The resulting solution was refluxed for 5 hrs, after that thiourea (1.0 mmol) was added to the above solution and then refluxed continue for 8-12 hrs. On overnight cooling, a coloured precipitate was formed which was filtered, washed with methanol, and dried in vacuum. The obtained yield was about 55-65 %.

The template condensation of 1,4-bis(2-formylphenoxy)butane and thiourea in the presence of bivalent metal salts, in the molar ratio 1:1:1 is represented in Fig 2.

Physical measurements

Elemental study (CHN) was analyzed on Carlo-Erba 1106 elemental analyzer. Molar conductance was measured on the ELICO (CM82T) conductivity bridge. Magnetic susceptibility was measured at room temperature on a Gouy balance using CuSO₄·5H₂O as calibrant. IR spectra were recorded on FT-IR spectrum BX-II spectrophotometer in KBr pellet. The electronic spectra were recorded in DMSO on Shimadzu UV-visible mini-1240 spectrophotometer. Electronic impact mass spectrum was recorded on JEOL, JMS-DX-303 Mass Spectrometer. EPR spectra of all complexes were recorded at room temperature (RT) on E₄-EPR spectrometer using the DDPH as the g-marker at SAIF, IIT Bombay.
Fig 2: Template synthesis of transition metal complexes

(M = Mn(II), Co(II) and X = Cl\(^-\), CH\(_3\)COO\(^-\))

**Antibacterial activity:** Synthesized transition metal complexes were examined for their antibacterial activity against *E.coli* and *B.cereus*. Antibacterial activity was performed by using the well diffusion method \(^{[10]}\). Two test tubes containing microorganism in nutrient broth were sterilized in an autoclave. Sterilized swabs were dipped into the nutrient broth, containing the micro-organism and used to rub the surfaces of the plates of media. The tested complexes were dissolved in DMSO. Well were made at equidistance on the plate and complex was poured into each well. The plates were incubated. After 24 hrs the zones of inhibition were measured. Neomycin was taken as positive control.

**Antifungal activity:** Culture of *A. niger*, *F.oxysporum*, and *A.brassicae* were selected for antifungal activity. The sensitivity test was used to test the effects of the complexes on the fungi using well diffusion method. DMSO and Captan were employed as a control and standard fungicide, respectively. The inhibition of growth of fungi was expressed in percentage and determined by using following relation

\[
I(\%) = \frac{(CT)}{C} \times 100
\]

Where I = % Inhibition, C = Radial diameters of the colony in control, T = Radial diameter of the colony in test compound.

**RESULTS AND DISCUSSION**

The macrocyclic transition metal complexes were prepared by reacting of 1,4-bis(2-formylphenoxy)butane and thiourea in the presence of metal salts in 1:1:1 ratio in methanol.
The molar conductance values of complexes in DMF were found in range of 25-45 Ω^−1 cm^2 mol^−1 corresponding to non-electrolyte nature of complexes\(^{[11]}\). Metal complexes were sparingly soluble in water, ethanol, and in most of the organic solvents but highly soluble in DMSO and DMF. All metal complexes were stable in air. Based on elemental analysis, the complexes were assigned the composition as shown in Table 1.

**Table 1: Physical properties and analytical data of Mn(II) and Co(II) complexes**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Colour</th>
<th>M.P (°C)</th>
<th>M. Wt</th>
<th>Molar conductance</th>
<th>Yield (%)</th>
<th>Elemental Analysis calculated (found)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,4-bis (2-formylphenoxy)butane (C(<em>{19})H(</em>{18})N(_2)O(_4))</td>
<td>Light brown</td>
<td>85</td>
<td>298</td>
<td>-</td>
<td>68</td>
<td>C</td>
</tr>
<tr>
<td>[Mn(C(<em>{19})H(</em>{18})N(_2)O(_2)S)Cl(_2)]</td>
<td>Off white</td>
<td>&gt;200</td>
<td>463.9</td>
<td>27</td>
<td>60</td>
<td>H</td>
</tr>
<tr>
<td><a href="OAc">Mn(C(<em>{19})H(</em>{18})N(_2)O(_2)S)</a>(_2)</td>
<td>Creemish</td>
<td>&gt;120</td>
<td>510.9</td>
<td>33</td>
<td>49</td>
<td>N</td>
</tr>
<tr>
<td>[Co(C(<em>{19})H(</em>{18})N(_2)O(_2)S)Cl(_2)]</td>
<td>Dark pink</td>
<td>&gt;360</td>
<td>467.9</td>
<td>45</td>
<td>57</td>
<td>M</td>
</tr>
<tr>
<td>[Co(C(<em>{19})H(</em>{18})N(_2)O(_2)S)(OAc)(_2)]</td>
<td>pink</td>
<td>&gt;340</td>
<td>514.9</td>
<td>25</td>
<td>63</td>
<td>C</td>
</tr>
</tbody>
</table>

OAc = CH\(_3\)COO

**Fig 3: IR Spectrum of [Co(C\(_{19}\)H\(_{18}\)N\(_2\)O\(_2\)S)(OAc)\(_2\)] Complex**

**IR spectra:** In IR spectrum of metal complexes bands in the region 2846-2888 cm\(^{-1}\), 1586-1638 cm\(^{-1}\), and 746-798 cm\(^{-1}\), corresponding to the presence of the aromatic stretching,
azomethine group (C=N), stretching vibration of C=S group \[^{12, 13}\]. This binding of donor atoms to metal ion was also supported by the appearance of new IR bands at 434-475 and 580-615 cm\(^{-1}\) due to \(\nu(M-N)\) and \(\nu(M-O)\) vibrations, respectively \[^{14,15}\]. This discussion revealed that the nitrogen atom of azomethine group and oxygen atoms of macrocyclic moiety coordinated to metal ions. However, a strong absorption band in the range of 750-780 cm\(^{-1}\) remained as such in IR spectra of all metal complexes, indicated that C=S not coordinated to metal ion. In IR spectra of chloride complexes, bands corresponding to (M-Cl) were observed at 340-335 cm\(^{-1}\). The acetato complexes gave IR bands in the region 1401-1438 cm\(^{-1}\) and 1290-1330 cm\(^{-1}\) due to \(\nu_\text{as}(OAc)\) and \(\nu_\text{s}(OAc)\) stretching vibrations, respectively. The value of \(\Delta\nu\) lies in the range of 187-212 cm\(^{-1}\), which suggested the unidentate behaviour of acetate ion (Fig 3) \[^{16}\].

**Magnetic Moment:** The magnetic moment observed for Mn(II) complexes lies in the range 5.92-5.95 BM corresponding to five unpaired electrons. The Co(II) complexes showed magnetic moments in well within the expected range 4.7-5.2 BM for octahedral complexes \[^{17}\].

**Electronic Spectra:** Electronic spectra of Mn(II) complexes exhibited four weak intensity absorption bands in the range 17850-18502, 23031-24082, 26801-28185, and 34487-37740 cm\(^{-1}\). These bands assigned to the \(^6A_{1g}\rightarrow^4T_{1g} (4G)\), \(^6A_{1g}\rightarrow^4E_g\), \(^4A_{1g}\ (4G)\) and \(^6A_{1g}\rightarrow^4E_g\) and \(^6A_{1g}\rightarrow^4T_{1g} (4P)\) transitions, respectively, corresponding to an octahedral geometry Fig 4a \[^{18}\]. Fourth transition was due to charge transfer. The electronic spectra of Co(II) complexes exhibited absorption bands in the region 9559-10521, 17638-18612, 22282-23378 and 37568-37720 cm\(^{-1}\) corresponded to \(\nu_1\) and \(\nu_3\) transitions, respectively \(^4T_{1g}\rightarrow^4T_{2g} (F)\), \(^4T_{1g} (F)\rightarrow^4T_{1g}\)
These bands were characteristic of high spin octahedral Co(II) complexes Fig 4b [19]. The ligand field parameters Dq, B, LFSE were calculated using the procedure given by Drago [20].

Table 2: Electronic spectral data of the complexes and magnetic Moment

<table>
<thead>
<tr>
<th>Complexes</th>
<th>Transitions</th>
<th>µ BM</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Mn(C_{19}H_{18}N_{2}O_{2}S)Cl_{2}]</td>
<td>17850, 23031, 26801, 34487</td>
<td>5.92</td>
</tr>
<tr>
<td><a href="OAc">Mn(C_{19}H_{18}N_{2}O_{2}S)</a>_{2}</td>
<td>18502, 24082, 28185, 37740</td>
<td>5.95</td>
</tr>
<tr>
<td>[Co(C_{19}H_{18}N_{2}O_{2}S)Cl_{2}]</td>
<td>9559, 18612, 23378, 37720</td>
<td>5.2</td>
</tr>
<tr>
<td>[Co(C_{19}H_{18}N_{2}O_{2}S)(OAc)_{2}]</td>
<td>9965, 17638, 22282, 37568</td>
<td>4.7</td>
</tr>
</tbody>
</table>

Table 3: Ligand field parameter of complexes

<table>
<thead>
<tr>
<th>Complexes</th>
<th>Dq</th>
<th>B'</th>
<th>β</th>
<th>C</th>
<th>F2</th>
<th>F4</th>
<th>LFSE (KJ mol⁻¹)</th>
<th>hₛ</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Mn(C_{19}H_{18}N_{2}O_{2}S)Cl_{2}]</td>
<td>1785</td>
<td>402</td>
<td>0.51</td>
<td>3806</td>
<td>942</td>
<td>107</td>
<td>-</td>
<td>7</td>
</tr>
<tr>
<td><a href="OAc">Mn(C_{19}H_{18}N_{2}O_{2}S)</a>_{2}</td>
<td>1850</td>
<td>521</td>
<td>0.64</td>
<td>3775</td>
<td>1057</td>
<td>104</td>
<td>-</td>
<td>4.8</td>
</tr>
<tr>
<td>[Co(C_{19}H_{18}N_{2}O_{2}S)Cl_{2}]</td>
<td>955</td>
<td>887</td>
<td>0.77</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>135</td>
<td>-</td>
</tr>
<tr>
<td>[Co(C_{19}H_{18}N_{2}O_{2}S)(OAc)_{2}]</td>
<td>996</td>
<td>745</td>
<td>0.65</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>141</td>
<td>-</td>
</tr>
</tbody>
</table>

Electronic Paramagnetic Resonance: An EPR spectra was readily detected even for large zero-field splitting, because d⁴ was an odd electron system whose ground state was a kramer’s doublet and whose degeneracy is only completely removed by a magnetic field. The broad signal in the polycrystalline EPR spectra of Mn(II) complexes was attributed to forbidden transitions, where \( M = \pm 1 \) (\( M = \) electron spin quantum number). The broadening of spectra was due to immobilization of Mn(II) ion in the ligand resulted because the rotational motion of Mn(II) is highly restricted. Another origin of line broadening is due to spin relaxation, which is temperature dependent. All the Mn(II) complexes, under study, shows isotropic, when recorded as polycrystalline sample [21]. The X-band EPR spectra of the Co(II) complexes were recorded at liquid nitrogen temperature in polycrystalline form. The EPR spectra of Co(II) complexes with \( g_{iso} = 2.00-2.03 \) correspond to the octahedral symmetry around the Co(II) ion Fig 5 [22].

Table 4: EPR spectral data of the Mn(II) and Co(II) complexes

<table>
<thead>
<tr>
<th>Complexes</th>
<th>( g_1 )</th>
<th>( g_⊥ )</th>
<th>( g_{iso} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Mn(C_{19}H_{18}N_{2}O_{2}S)Cl_{2}]</td>
<td>-</td>
<td>-</td>
<td>2.19</td>
</tr>
<tr>
<td><a href="OAc">Mn(C_{19}H_{18}N_{2}O_{2}S)</a>_{2}</td>
<td>-</td>
<td>-</td>
<td>2.18</td>
</tr>
<tr>
<td>[Co(C_{19}H_{18}N_{2}O_{2}S)Cl_{2}]</td>
<td>2.32</td>
<td>1.89</td>
<td>2.00</td>
</tr>
<tr>
<td>[Co(C_{19}H_{18}N_{2}O_{2}S)(OAc)_{2}]</td>
<td>2.40</td>
<td>1.86</td>
<td>2.03</td>
</tr>
</tbody>
</table>
Antibacterial Screening: Complex [Co(C_{19}H_{18}N_2O_2S)(OAc)_2] and [Co(C_{19}H_{18}N_2O_2S)(OAc)_2] inhibited the tested microorganism in appreciable extent. [Mn(C_{19}H_{18}N_2O_2S)(OAc)_2] complex showed activity against *B. Cereus* only. [Mn(C_{19}H_{18}N_2O_2S)Cl_2] Complex not showed any activity. The difference in activity depends on their impermeability of the cell or the differences in ribosomes in microbial cell \(^{[23]}\). It was observed that liposolubility is an important factor, which effect antimicrobial activity \(^{[24]}\).

Antifungal Activity: Transition metal complexes were tested against the fungus *A. niger*, *F. oxysporum*, and *A. brassicae*. Each macrocyclic complexes (100 mg/ml) were used for determination of their potency against tested pathogens and compared with antibiotic. All the complexes have good antifungal activity but cobalt(II) complex showed strong activity Fig 6. Further, on the basis of chelation theory, antifungal activity of the metal complexes can be explained. Chelation may enhance the biochemical potential of bioactive species. Because on chelation, the polarity of the metal ion will be reduced due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Hence macrocyclic complexes become very stable due to delocalization of \(\pi\)-electrons. It enhances the penetration of the complexes into lipid membranes and blocking of the metal binding sites in the enzymes of microorganisms \(^{[25]}\).
Fig 6: Antifungal activity of transition metal complexes against fungi *F. oxysporum* at concentration 1000 ppm (a) standard (b) [Co(C$_{19}$H$_{18}$N$_2$O$_2$S)Cl$_2$]  (c) [Co(C$_{19}$H$_{18}$N$_2$O$_2$S)(OAc)$_2$]  (d) [Mn(C$_{19}$H$_{18}$N$_2$O$_2$S)Cl$_2$]

**CONCLUSION**

Mn(II) and Co(II) transition metal complexes were synthesized and characterized analytically, and spectroscopically. On the basis of spectroscopic studies octahedral geometry
is assigned for Mn(II), and Co(II) complexes (Figure 7). Metal complexes were studied for antimicrobial activity including antibacterial, and antifungal. Among all Complexes \([\text{Co(C}_{19}\text{H}_{18}\text{N}_{2}\text{O}_{2}\text{S})\text{Cl}_{2}]\) showed good results.

**ACKNOWLEDGEMENT**

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