Synthesis and Antifungal Activity of Complexes of Cu(II), Co(II) and Fe(III) with Quaternary Ammonium Salts Derivatives of Diethylaminoethyl Methacrylate Containing Acetic Acid Group

ZAHRA OULD KADA1, TAHAR BENAISSA2, SOFIANE DAOUDI2 and MOHAMED MAKHLOUFIA2

1Department of Chemistry, University Djillali Liabes of Sidi Bel Abbes 22000, Algeria
2Physical Chemistry Studies Laboratory, University of Dr. Moulay Tahar, Saida 20000, Algeria
daoudi_20@yahoo.fr

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Abstract: In the present paper the synthesis and characterization of three new metal complexes of Cu(II), Fe(III) and Co(II), with quaternary ammonium salts used as ligand derived from 2-(diethylamino)ethylmethacylate (DEAEMA) have been successfully prepared in alcoholic medium. The ligand has got -COOH moiety which is capable of chelation. The ligand and its metal complexes were characterized by conductivity measurements, FTIR spectroscopy, electronic spectroscopy, 1H and 13C NMR spectroscopies and have been screened for their antifungal activities

Keywords: Quaternary ammonium salts, DEAEMA, Cu(II), Co(II), Fe(III) complexes, Antifungal activity

Introduction

Metal complexes offer a platform for the design of novel therapeutic compounds1. They are play essential role in pharmaceutical industry and in agriculture2. The coordination chemistry of oxygen donor ligands is an active area of research they have been widely studied for their biological activities as Antimicrobial3,4, Antitubercular5,6, Antiviral7, Anticonvulsant8,10, Antitumor11,12, Antitumor11,12, And anti-inflammatory activities13,14.

Quaternary ammonium salts (QAS) are used successfully as extractants15 are widely used as phase transfer catalysts in the field of organic synthesis16, QAS have gained great importance because of their diverse biological properties, such as antibacterial17,19 and antifungal20,21. The correlation of QAS with antifungal activity is related to fungal phospholipase inhibition22. Generally, the chelating ligand is a polyfunctional molecule which can encase the metal in an organic sphere23. A quaternary ammonium halides containing COOH group can be considered as bifunctional compounds24. Following all these
observations, we report here the synthesis and structural studies on the complexes of Cu(II), Co(II) and Fe(III) with quaternary ammonium salts derivatives of diethylaminoethyl methacrylate containing acetic acid moiety.

**Experimental**

All the solvents and reagents used in this study were obtained from Sigma Aldrich and BIOCHEM. Metal salts of Cu(II), Co(II) and Fe(III) were used as nitrates. The reaction progress was monitored by Thin layer chromatography (TLC) was performed throughout the reaction to optimized the reaction for purity and completion of reaction on Merck silica gel using CHCl₃ as the eluting solvent system, and spots were observed using iodine as visualizing agent. All the melting points were determined in open capillary tubes using BÜCHI 540 apparatus and are uncorrected. UV-Visible spectra were measured in DMSO solution at 10⁻² molar concentration using Shimadzu UV-Visible recorder spectrophotometer with 1 cm matched quartz cells. The IR spectra in the range of 4000-400 cm⁻¹ were recorded as potassium bromid disc on Shimadzu FTIR-8300 Fourier transform infrared spectrophotometer. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker Avance 300 MHz spectrometer, using TMS as internal standard and CD₃OD as a solvent, chemical shifts in ppm. Molar conductances of the solution of the metal complexes were determined with a conductivity meter type inoLab Level 1 Multiparameter. All measurements were carried out at room temperature with freshly prepared solution.

**Chemical Synthesis**

*Synthesis of the ligand HL*

According to the procedure adopted by Guiqian Lu et al., a mixture of tertiary amines 2-(diethylamino)ethylmethacrylate (3 g, 0.016 mol) and bromoacetic acid (2.36 g, 0.017 mol) dissolved in dry acetone (40 mL), in the presence of hydroquinone was gently refluxed for 40 hours on water bath. After cooling to room temperature, the solvent was evaporated and the residue were simply filtered and washed with cold diethyl ether. The synthesis of the ligand may be represented as follows:

\[
\text{Br} \quad \text{O} \quad \text{H} \\
\text{N} \quad \text{C₂H₅} \\
\text{C₂H₅ OC} \\
\text{H₂O} \\
\text{O} \quad \text{H} \\
\text{OC} \quad \text{H₃} \\
\text{H₅C₂} \\
\text{Br} \\
\text{Acetone} \\
50 ^\circ \text{C}
\]

Scheme 1. Synthesis of ligand

*Synthesis of the metal complexes*

To a methanolic solution (0.01 mol in 20 mL) of the required metal was added a methanolic solution (0.02 mol in 20 mL) of ligand HL in a 1:2 (metal: ligand) molar ratio for Cu(II), Co(II) metal, and 1:3 (metal : ligand) molar ratio for Fe(III) metal. Then the mixture was gently heated under reflux for 30 minutes and a crystalline colored precipitate was formed at room temperature. The precipitates were filtered out, washed with cold diethyl ether and dried in desiccators.

**Results and Discussion**

The formations of the ligand and its metal complexes were detected by thin layer chromatography (TLC) via their Rₜ which were different from starting materials. The complexes are of various colours varied from lawn green, dark green and brownish colour different from the colour of the ligand indicating that the colours formed depend on the
metal ions. The melting points of the complexes are different (higher) than that of the ligand, an evidence for complexation. The physical and analytical data of all the compounds studied has been summarized in Table 1.

Table 1. Physical properties and analytical data of the ligand and its complexes

<table>
<thead>
<tr>
<th>Compound</th>
<th>Color</th>
<th>%Yield</th>
<th>Melting Point °C</th>
<th>Molar conductivity µS.cm⁻¹</th>
<th>Rf Value</th>
<th>Solvent system</th>
<th>Suggest formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>HL</td>
<td>White</td>
<td>76</td>
<td>104-105</td>
<td>34.5</td>
<td>0.42</td>
<td>CHCl₃</td>
<td>C₁₂H₂₂BrNO₄</td>
</tr>
<tr>
<td>Cu L₂(1)</td>
<td>lawn green</td>
<td>65</td>
<td>134-135</td>
<td>43</td>
<td>0.46</td>
<td>CHCl₃</td>
<td>C₂₄H₄₂Br₂CuN₂O₈</td>
</tr>
<tr>
<td>Co L₂(2)</td>
<td>dark green</td>
<td>68</td>
<td>182-183</td>
<td>27.7</td>
<td>0.61</td>
<td>CHCl₃</td>
<td>C₂₄H₄₂Br₂CoN₂O₈</td>
</tr>
<tr>
<td>FeL₃(3)</td>
<td>brown</td>
<td>54</td>
<td>154-155</td>
<td>36.8</td>
<td>0.38</td>
<td>CHCl₃</td>
<td>C₃₆H₆₃Br₃FeN₃O₁₂</td>
</tr>
</tbody>
</table>

UV spectral studies of the ligand and its metal complexes

The electronic spectra for the ligand and its metal complex shows that the absorption bands in the UV region can be expressed as $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transition, the absorption data for the ligand and its metal complex are given in Table 2. The electronic spectrum of the ligand HL shows two bands at 287.5 and 220.5 nm assigned to $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ respectively, the complex Cu(II) exhibited absorption bands at 217.50 nm which may be assigned to transition $\pi \rightarrow \pi^*$, And the Co(II) complex displayed an electronic spectrum with transitions at 214nm, these bands may be assigned to the transition $\pi \rightarrow \pi^*$. The electronic spectrum of the Fe(III) shows bands at 208 nm assigned to the $\pi \rightarrow \pi^*$ transitions.

Table 2. Electronic spectral data of the ligand and its metal complexes 1 to 3 in DMSO

<table>
<thead>
<tr>
<th>Compound</th>
<th>Absorption bands (nm)</th>
<th>ABS</th>
<th>Assigned transition</th>
</tr>
</thead>
<tbody>
<tr>
<td>HL</td>
<td>220.5 - 287.5</td>
<td>3.4367</td>
<td>$\pi \rightarrow \pi^<em>$, $n \rightarrow \pi^</em>$</td>
</tr>
<tr>
<td>CuL₂(1)</td>
<td>217.50</td>
<td>3.2439</td>
<td>$\pi \rightarrow \pi^*$</td>
</tr>
<tr>
<td>CoL₂(2)</td>
<td>214.00</td>
<td>3.1177</td>
<td>$\pi \rightarrow \pi^*$</td>
</tr>
<tr>
<td>FeL₃(3)</td>
<td>208.00</td>
<td>3.0683</td>
<td>$\pi \rightarrow \pi^*$</td>
</tr>
</tbody>
</table>

Infrared spectra studies of the ligand and its metal complexes

The IR spectra in the (4000–400 cm⁻¹) region provide information regarding the coordination mode in the complexes were analyzed by comparison with the data for the free ligand. The IR data of the ligand and complexes are shown in Table 3. The infrared spectrum of HL showed some characteristic stretching bands at 3431.1, 1745.5, 1635.5, 1164.9 cm⁻¹ and assigned to $\nu$(OH), $\nu$(COO)as, $\nu$(C=C)s, $\nu$(C-O-C)s. The $\nu$ (O-H) band of the HL appeared at 3431.1 cm⁻¹ was absent in the infrared spectra of complexes 1 to 3, indicating the deprotonation and coordination of the carboxylate anions to the metal atom moiety. And formation of M–O bond via deprotonation at 592–675.0 cm⁻¹.

Table 3. The characteristic infrared absorptions of the ligand and its metal complexes

<table>
<thead>
<tr>
<th>Compound</th>
<th>$\nu$(OH)</th>
<th>$\nu$(COO)as</th>
<th>$\nu$ C=C</th>
<th>$\nu$(COO)s</th>
<th>$\nu$ (C–O–C)</th>
<th>$\nu$ (M-O)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HL</td>
<td>3431.1</td>
<td>1745.5</td>
<td>1635.5</td>
<td>1305.7</td>
<td>1164.9</td>
<td>–</td>
</tr>
<tr>
<td>Cu L₂ (1)</td>
<td>–</td>
<td>1741.6</td>
<td>1624.0</td>
<td>1384.8</td>
<td>1168.8</td>
<td>596.0</td>
</tr>
<tr>
<td>Co L₂ (2)</td>
<td>–</td>
<td>1745.4</td>
<td>1620.1</td>
<td>1380.9</td>
<td>1168.8</td>
<td>592.0</td>
</tr>
<tr>
<td>FeL₃ (3)</td>
<td>–</td>
<td>1743.5</td>
<td>1654.8</td>
<td>1379.0</td>
<td>1163.0</td>
<td>675.0</td>
</tr>
</tbody>
</table>
NMR Analysis studies of the ligand and its metal complexes

The $^1$H and $^{13}$C NMR chemical shifts of free ligand in CD$_3$OD at room temperature show the following signals.

$^1$H NMR (300MHz), $\delta$ (ppm): 7.568 (1H, OH), 6.104 (1Hb, C1), 5.785 (1Ha, C1), 4.635 (2H, C5), 4.184 (2H, C9), 3.346 (2H, C6), 2.982 (2H, C7), 1.805 (3H, C3), 1.564 (3H, C8).

$^{13}$C NMR chemical shifts are given in the following signals $^{13}$C-NMR (300MHz), $\delta$ (ppm): 165.032 (C4), 164.591 (C10), 134.062 (C2), 124.707 (C1), 59.241 (C6), 57.632 (C5), 48.838 (C9), 46.972 (C7), 15.239 (C3), 6.492 (C8).

In $^{13}$C NMR spectra of free ligand C9, C10 of the carboxymethyl moieties were observed in 48.838 and 164.591 ppm respectively, indicated the formation of the ligand. The $^1$H NMR spectra of complexes 1 to 3 gave an additional support for the formation of the complexation. The spectra of ligand, HL showed a sharp peak, $\delta$(OH) at 7.568 ppm which was absent in the spectra of the complexes 1 to 3 and indicated the deprotonation and complexation of carboxylate anions to metal ions. On the basis of the preceding discussion, the structure of the ligand and its metal complexes may be suggested as follows, the proposed structures are presented in Figures 1-4.

Antifungal activities tests

The antifungal activities of the synthesized ligand HL and his metal complexes were studied in different concentrations (50, 100, 250 and 500 ppm) against three phytopathogenic fungal strains namely Fusarium oxysporum, Fusarium commune and Fusarium rodelens. The antifungal activity was determined by the radial growth method. In this technique, sterilized hot PDA nutrient medium (composition: potato (200 g), dextrose (20 g), agar (15 g) and distilled water 1000 mL) and 4 mm diameter hole punch were used, on the PDA. After solidification of media, respective fungal spore suspensions were transferred to petri plates. Each test compound was dissolved in water and then diluted at the desired concentration. The fungal cultures were incubated at 37 °C for 4 days. Finally the zones of inhibition were carefully measured. The antifungal activity data are listed in Table 4.

![Figure 1. Structure of the ligands](image1.png)

![Figure 2. Proposed structure metal complexes of CuL2](image2.png)
As indicated in Table 4, at the concentration of 500 ppm, all of the tested compounds exhibited good inhibitory effects against *Fusarium oxysporum*. The Cu(II) and Co(II) complex showed moderate inhibition with *Fusarium commune* at the concentration of 500 ppm, the ligand and Cu(II), Co(II) complex showed a weak inhibition against *Fusarium rodelens*. The Fe(III) complex showed higher activities against all the tested strains.

**Conclusion**

In summary, we have described the synthesis of the ligand HL and his metal complexes, IR, UV-Visible, NMR spectral techniques were used to confirm their formation. The synthesized compounds showed promising antifungal potential against the phytopathogenic test fungi at high concentrations.
Acknowledgement
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References