Synthesis and antifungal activity of novel metal chelates containing heterocyclic azo dyes

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ABSTRACT

The biologically potent ligand 2,4-dihydroxy-5-((5-phenyl-1,3,4-oxadiazol-2-yl)diazenyl)phenyl)(phenyl)methanone (DAPOBR) was prepared by diazotization reaction of diazonium salt of 2-Amino-5-phenyl-[1,3,4]-Oxadiazole (APO) and benzoresorcinol (BR). The Cu(II) complexes have been synthesized by mixing an aqueous solution of metal salts in 1:2 molar ratios with 1,3,4-oxadiazole ligands. Characterization of novel ligand was carried out by CHN, FT-IR, NMR and mass spectral analysis, while structures and geometry of metal chelates viz. Cu2+, Ni2+, Co2+, Mn2+ and Zn2+ was confirmed by CHN analysis along with reflectance spectroscopies and magnetic moment studies. Also the antifungal activity of DAPOBR and its metal chelates was examined against various fungus.

Keywords: 1,3,4-Oxadiazole, Benzoresorcinol, Diazotization reaction, Reflectance spectroscopies study and Antifungal properties.

INTRODUCTION

Benzoresorcinol (2,4-dihydroxybenzophenone) and its derivatives find wide application in transition metal chemistry as well as in pharmaceutical chemistry [1-3]. Recently, the studies on synthesis and properties of benzoresorcinol derivatives and their metal chelates have attracted much [4,5]. Also the excellent research on synthesis and biological applications of various transition metal chelates of heterocyclic compounds has been found in recent years [6,7].

Compounds containing 1,3,4-oxidiazoles are studied extensively for their wide spectrum of bioactivities such as antibacterials, antifungals, antituberculosis, anti-inflammatory, anti-HIV and anticancer agents [8-11], as well as in the synthesis of corrosion inhibitors and pharmaceutical agents [12-14].

The reaction of oxadiazole derivatives with benzoresorcinol has not been reported so far. Hence, in continuous of our previous work [15,16], it was thought of interest to merge both of benzoresorcinol and 2-Amino-5-phenyl-[1,3,4]-Oxadiazole (APO) moieties also prepared their metal chelates which may enhance the biological activity of compound to some extent and or they might possess some of the above mentioned biological activities. Hence the present communication comprises the synthesis, characterization and biological activities of 2,4-dihydroxy-5-((5-phenyl-1,3,4-oxadiazol-2-yl)diazenyl)phenyl)(phenyl)methanone (DAPOBR) and their metal chelates. The synthetic approach is shown in scheme-1.
MATERIALS AND METHODS

2-Amino-5-phenyl-[1,3,4]-Oxadiazole (APO) was prepared according to reported method [17]. All other chemicals and solvents used were of laboratory grade.

Synthesis of 2,4-dihydroxy-5-((5-phenyl-1,3,4-oxadiazol-2-yl)diazenyl)phenyl)(phenyl)methanone (DAPOBR):

2-Amino-5-phenyl-[1,3,4]-Oxadiazole (APO) (0.01 mole) was dissolved in a mixture of H$_2$SO$_4$ (12 ml) and water (15 ml) and cooled to 0°C in ice bath. To this solution a cold aqueous solution of sodium nitrite (0.04 mole) was added. The diazonium salt solution of APO was filtered into a cooled solution of Benzoresorcinol (0.01 mole) at 0-5°C. The resulting solid azo dye was washed with water, dried and recrystallized from, MeOH. Yield: 71%, M.P. 285-287°C (decompose) uncorrected.

![Reaction Scheme](image-url)
Elemental Analysis

<table>
<thead>
<tr>
<th>Empirical Formula</th>
<th>Mol. Wt.</th>
<th>Yield (%)</th>
<th>Elemental Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>C%</td>
</tr>
<tr>
<td>DAPOBR</td>
<td>386</td>
<td>71</td>
<td>65.28</td>
</tr>
<tr>
<td>(DAPOBR)(\text{Cu}^{2+})</td>
<td>834</td>
<td>70</td>
<td>60.47</td>
</tr>
<tr>
<td>(DAPOBR)(\text{Co}^{2+})</td>
<td>829</td>
<td>66</td>
<td>60.80</td>
</tr>
<tr>
<td>(DAPOBR)(\text{Mn}^{2+})</td>
<td>825</td>
<td>67</td>
<td>61.40</td>
</tr>
<tr>
<td>(DAPOBR)(\text{Ni}^{2+})</td>
<td>829</td>
<td>66</td>
<td>60.82</td>
</tr>
<tr>
<td>(DAPOBR)(\text{Zn}^{2+})</td>
<td>836</td>
<td>63</td>
<td>60.33</td>
</tr>
</tbody>
</table>

Measurements:
The elemental contents were determined by Thermo Finigen Flash1101 EA (Itally) the metals were determined volumetrically by Vogel’s method [18]. To a 100 mg chelate sample, each 1 ml of HCl, \(\text{H}_2\text{SO}_4\) and HClO\(_4\) were added and then 1 g of NaClO\(_4\) was added. The mixture was evaporated to dryness and the resulting salt was dissolved in double distilled water and diluted to the mark. From this solution the metal content was determined by titration with standard EDTA solution. Infrared spectra of the synthesized compounds were recorded on Nicolet 760 FT-IR spectrometer. NMR spectrum of DAPOBR was recorded on 60 MHz NMR spectrophotometer. Magnetic susceptibility measurement of the synthesized complexes was carried out on Gouy Balance at room temperature. Mercury tetrathiocyanatocobalate (II) \(\text{Hg}[\text{Co(NCS)}_4]\) was used as a calibrant. The electronic spectra of complexes in solid were recorded on at room temperature. MgO was used as reference. Antifungal activity of all the samples was monitored against various organisms, following the method reported in literature [19].

RESULTS AND DISCUSSION

Present studies describe the synthesis of 2,4-dihydroxy-5-((5-phenyl-1,3,4-oxadiazol-2-yl)diazenyl)phenyl) (phenyl)methanone (DAPOBR) and their metal chelates. The structures of the ligand and their metal chelates were investigated and confirmed by the elemental analysis, FT-IR, \(^1\)H NMR, \(^{13}\)C NMR, mass spectral, reflectance and magnetic moment studies. The resulted DAPOBR ligand was an amorphous brown powder. The C,H,N contents of DAPOBR (Table-1) are consistent with the predicted structure (Scheme-1). The IR spectrum
of DAPOBR comprises the important bands due to CO and OH group of benzoresorcinol. The broad band due to –OH group appeared at around 3450, 1320, 880 and 720 cm\(^{-1}\) [20] are attributed to OH stretching, bending, rocking and wagging vibrations, respectively while the band for CO stretching of diaryl was found at 1630 cm\(^{-1}\). Also the bands for azo group, C-O-C stretching and aromatic stretching supports the structure of synthesized ligand (DAPOBR).

The NMR spectrum of DAPOBR in DMSO clarify that the spectrum shows singlet of 2H at 5.3 δ ppm due to –OH group. The aromatic protons are appeared in multiplicity at 6.84-8.12 δ. Thus the structure of DAPOBR is confirmed as shown in Scheme-I.

## TABLE-2: SPECTRAL FEATRUES AND MAGNETIC MOMENT OF DAPOBR METAL CHELATES

<table>
<thead>
<tr>
<th>Metal Chelates</th>
<th>µeff (BM)</th>
<th>Electronic spectral data (cm(^{-1}))</th>
<th>Transition</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAPOBR-Cu(^{2+})</td>
<td>2.51</td>
<td>23435, 13201</td>
<td>Charge transfer (^{2}B_{1g} \rightarrow {^{1}A_{1g}})</td>
</tr>
<tr>
<td>DAPOBR-Co(^{2+})</td>
<td>4.75</td>
<td>23736, 19112, 8920</td>
<td>(^{4}T_{1g}(F) \rightarrow {^{2}T_{2g}}(F)), (^{4}T_{1g}(F) \rightarrow {^{2}T_{2g}}(P))</td>
</tr>
<tr>
<td>DAPOBR-Mn(^{2+})</td>
<td>5.52</td>
<td>23239, 19022, 16850</td>
<td>(^{6}A_{1g} \rightarrow {^{4}A_{2g}}(G)), (^{6}A_{1g} \rightarrow {^{4}T_{1g}}(PC))</td>
</tr>
<tr>
<td>DAPOBR-Ni(^{2+})</td>
<td>3.70</td>
<td>22584, 15359</td>
<td>(^{3}A_{1g} \rightarrow {^{3}T_{1g}}(P)), (^{3}A_{1g} \rightarrow {^{3}T_{1g}}(F))</td>
</tr>
<tr>
<td>DAPOBR-Zn(^{2+})</td>
<td>Diamag.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The elemental analysis and metal contents of metal chelates of DAPOBR (Table-1) are also consistent with the predicted structure. All the metal chelates The results show that the metal: ligand (M:L) ratio for all divalent metal chelate is 1:2.

The IR spectra of DAPOBR ligand and its metal chelates are almost identical in all aspects. The only discernible differences in the spectra of metal chelates are the band due to -OH group is narrow compared to that of parent ligand. This may be due to metal-oxygen band. The other bands are at their respective positions as appeared in the spectrum of parent ligand. Also the band due to (M-O) band supports the coordination. The important IR Spectral data are shown in Table-2.

Electronic spectral data along with magnetic measurement gave enough support to determine the geometry of metal complexes. Magnetic moments of all metal chelates are given in Table-2. The diffuse electronic spectrum of Cu\(^{2+}\) chelates shows two broad bands around 13201 and 23435 cm\(^{-1}\). The first band may be due to \(^{2}B_{1g} \rightarrow {^{1}A_{1g}}\) transition, while the second band may be due to charge transfer. These bands along with higher value of the magnetic moment of the Cu\(^{2+}\) chelate supports the distorted octahedral structure for the Cu\(^{2+}\) metal chelates [21]. The Co\(^{2+}\) metal chelate gives rise to two absorption bands at 23736 and 19112cm\(^{-1}\), which can be assigned \(^{4}T_{1g}(F) \rightarrow {^{2}T_{2g}}(P)\), \(^{4}T_{1g}(F) \rightarrow {^{2}T_{2g}}(G)\) transitions, respectively. These absorption bands and the µeff value indicate an octahedral configuration of the Co\(^{2+}\) metal chelate [22]. The spectrum of Mn\(^{2+}\) metal chelate comprised two bands at 19022cm\(^{-1}\) and 23239cm\(^{-1}\). These bands may be assigned to \(^{6}A_{1g} \rightarrow {^{4}T_{2g}}(G)\) and \(^{6}A_{1g} \rightarrow {^{4}A_{2g}}(G)\), transitions, respectively. The high intensity of the bands suggests that they may have some charge transfer character. The electronic spectrum of the Ni(II) complex exhibits two bands at 15,359 and 22,584 cm\(^{-1}\), attributed to \(^{3}A_{1g} \rightarrow {^{3}T_{1g}}(P)\), \(^{3}A_{1g} \rightarrow {^{3}T_{1g}}(F)\) transitions, respectively, for an octahedral Ni(II) complex [23], while Zn\(^{2+}\) metal chelate is diamagnetic in nature and its electronic spectra do not furnish any characteristic d-d transitions.

The magnetic moment is found to be lower than normal range. In the absence of low temperature measurement of magnetic moment it is difficult to attach any significance to this. The observed µeff values in the range 2.51-5.52 B.M are consistent with the above moiety [22].
TABLE-3: ANTIFUNGAL ACTIVITY OF DAPOBR LIGAND AND ITS METAL CHELATES

<table>
<thead>
<tr>
<th>Sample</th>
<th>Nigrospora Sp.</th>
<th>Botrydepliai thiobromine</th>
<th>Aspergimus niger</th>
<th>Rhisopus Nigricans</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAPOBR</td>
<td>50</td>
<td>58</td>
<td>45</td>
<td>52</td>
</tr>
<tr>
<td>DAPOBR-Cu&lt;sup&gt;2+&lt;/sup&gt;</td>
<td>78</td>
<td>72</td>
<td>71</td>
<td>75</td>
</tr>
<tr>
<td>DAPOBR-Co&lt;sup&gt;2+&lt;/sup&gt;</td>
<td>65</td>
<td>67</td>
<td>62</td>
<td>69</td>
</tr>
<tr>
<td>DAPOBR-Mn&lt;sup&gt;2+&lt;/sup&gt;</td>
<td>70</td>
<td>67</td>
<td>69</td>
<td>65</td>
</tr>
<tr>
<td>DAPOBR-Ni&lt;sup&gt;2+&lt;/sup&gt;</td>
<td>61</td>
<td>65</td>
<td>62</td>
<td>66</td>
</tr>
<tr>
<td>DAPOBR-Zn&lt;sup&gt;2+&lt;/sup&gt;</td>
<td>68</td>
<td>72</td>
<td>60</td>
<td>69</td>
</tr>
</tbody>
</table>

CONCLUSION

On the basis of these studies it is clear that ligand coordinated to metal atoms in a bidentate mode, by oxygen donor system. The examination of antifungal activity of DAPOBR ligand and its all metal chelates (Table-3) shows clear enhancement of activity upon coordination with metal ion. Among all the chelates the Cu<sup>2+</sup> chelate is more active against fungus.

Acknowledgement

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REFERENCES