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## 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)diazanyl)phenyl)(phenyl)methanone (DAPOBR) was prepared by diazotization reaction of diazonium salt of 2-Amino-5-phenyl-[1,3,4]-Oxadiazole (APO) and benzoorsorcinol (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-oxidazole 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. Cu<sup>2+</sup>, Ni<sup>2+</sup>, Co<sup>2+</sup>, Mn<sup>2+</sup> and Zn<sup>2+</sup> 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, Benzoorsorcinol, Diazotization reaction, Reflectance spectroscopies study and Antifungal properties.

### INTRODUCTION

Benzoorsorcinol (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 benzoorsorcinol 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].

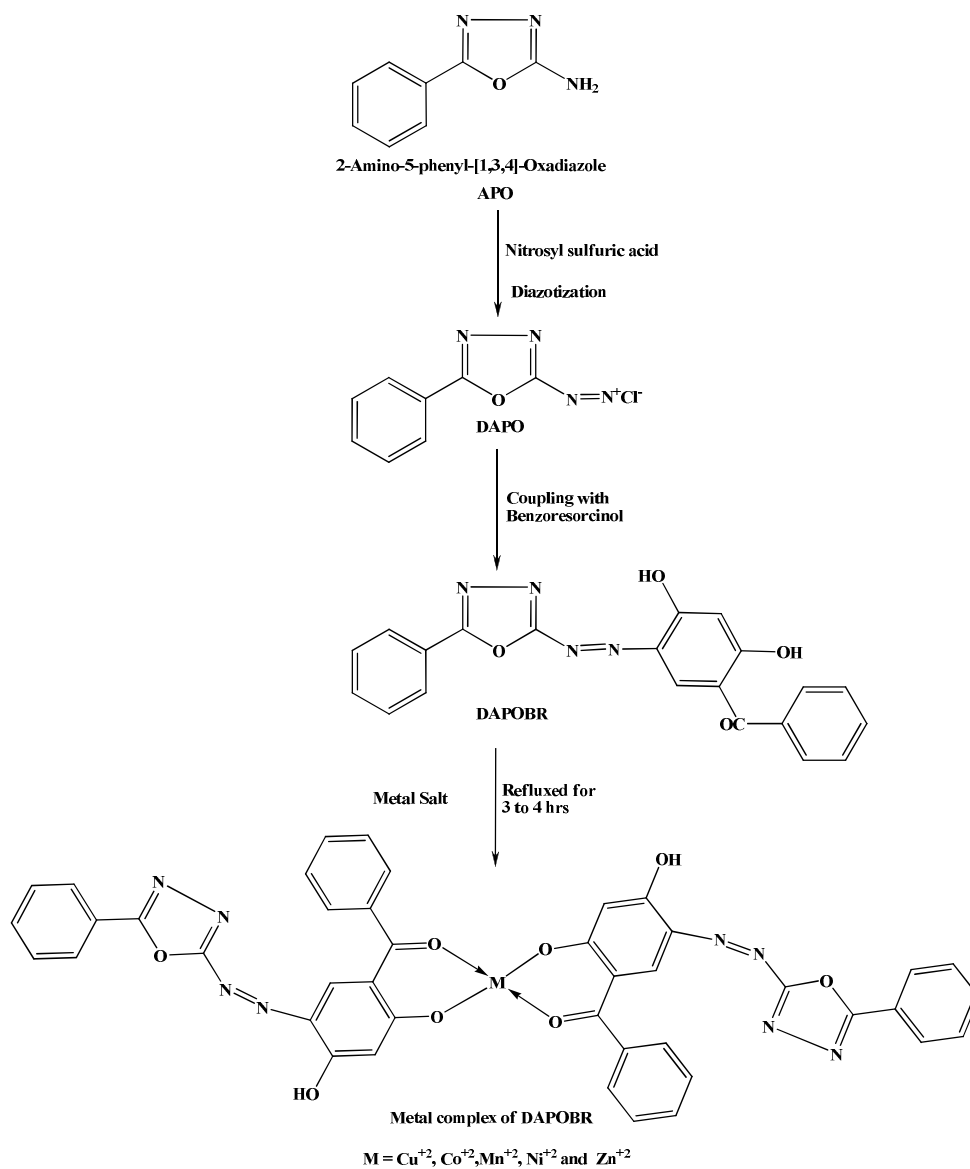
Compounds containing 1,3,4-oxadiazoles are studied extensively for their wide spectrum of bioactivities such as antibacterials, antifungals, antituberculosis, anti-inflammatory, anti-HIV and anticancer agents [8-11], as well as in the synthesis of corrosion inhibitors and pharmacological agents [12-14].

The reaction of oxadiazole derivatives with benzoorsorcinol has not been reported so far. Hence, in continuous of our previous work [15,16], it was thought of interest to merge both of benzoorsorcinol 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)diazanyl)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) (0.01mole) was dissolved in a mixture of  $\text{H}_2\text{SO}_4$  (12ml) and water (15ml) and cooled to  $0^\circ\text{C}$  in ice bath. To this solution a cold aqueous solution of sodium nitrite (0.04mole) was added. The diazonium salt solution of APO was filtered into a cooled solution of Benzoescorcinol (0.01mole) at  $0-5^\circ\text{C}$ . The resulting solid azo dye was washed with water, dried and recrystallized from, MeOH. Yield: 71%, M.P.285-287 $^\circ\text{C}$  (decompose) uncorrected.



Scheme - 1

**Elemental Analysis**

	C%	H%	N%
<b>C<sub>21</sub>H<sub>14</sub>N<sub>4</sub>O<sub>4</sub> (386)</b>			
<b>Calculated:</b>	65.28	3.65	14.50
<b>Found :</b>	65.2	3.6	14.4
<b>IR Spectral Features:</b>	2950- 2850		Ar C-C
(cm <sup>-1</sup> )	1630, 1575		Azo group
	3450		OH
	1350		C-O-C
<b>NMR :</b>	δ ppm 6.51-8.02 (m, 12H, Ar-H), 5.30 (s, 2H, OH).		

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

The metal chelates of DAPOBR with Cu<sup>2+</sup>, Co<sup>2+</sup>, Zn<sup>2+</sup>, Mn<sup>2+</sup>, and Ni<sup>2+</sup> metal ions were prepared in two steps. The general procedure for the metal chelates is as follows;

**(I) Preparation of DAPOBR solution:**

DAPOBR (0.05 mol) was taken in 500 ml beaker and formic acid (85% v/v) was added up to slurry formation. To this slurry water was added till the complete dissolution of DAPOBR. It was diluted to 100 ml.

**Synthesis of DAPOBR-metal-chelates:**

In a solution of metal acetate (0.005 mol) in acetone: water (50:50 v/v) mixture (40 ml) the 20 ml of above mentioned DAPOBR solution (i.e. containing 0.01 M DAPOBR) was added with vigorous stirring at room temperature. The appropriate pH was adjusted by addition of sodium acetate for complete precipitation of metal chelate. The precipitates were digested on a boiling water bath. The precipitates of chelate were filtered off, washed by water and air-dried.

**Table-1: Elemental analysis of DAPOBR ligand and its transition metal chelates**

Empirical Formula	Mol. Wt.	Yield (%)	Elemental Analysis							
			C%		H%		N%		M%	
			Cald	Found	Cald	Found	Cald	Found	Cald	Found
DAPOBR	386	71	65.28	65.2	3.65	3.6	14.50	14.4	-	-
(DAPOBR) <sub>2</sub> Cu <sup>2+</sup>	834	70	60.47	60.4	3.14	3.1	14.36	14.3	7.62	7.5
(DAPOBR) <sub>2</sub> Co <sup>2+</sup>	829	66	60.80	60.7	3.16	3.1	13.51	13.4	7.10	7.0
(DAPOBR) <sub>2</sub> Mn <sup>2+</sup>	825	67	61.10	61.1	3.17	3.1	13.57	13.5	6.65	6.6
(DAPOBR) <sub>2</sub> Ni <sup>2+</sup>	829	66	60.82	60.8	3.16	3.1	13.51	13.4	7.08	7.0
(DAPOBR) <sub>2</sub> Zn <sup>2+</sup>	836	63	60.33	60.3	3.13	3.0	13.40	13.3	7.82	7.6

**Measurements:**

The elemental contents were determined by Thermo Finigen Flash1101 EA (Italy) the metals were determined volumetrically by Vogel's method [18]. To a 100 mg chelate sample, each 1 ml of HCl, H<sub>2</sub>SO<sub>4</sub> and HClO<sub>4</sub> were added and then 1 g of NaClO<sub>4</sub> 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) Hg[Co(NCS)<sub>4</sub>] 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, <sup>1</sup>H NMR, <sup>13</sup>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 benzoorsorcinol. The broad band due to –OH group appeared at around 3450, 1320, 880 and 720  $\text{cm}^{-1}$  [20] are attributed to OH stretching, bending, rocking and wagging vibrations, respectively while the band for CO stretching of diaryl was found at 1630  $\text{cm}^{-1}$ . 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  $\delta$  ppm due to –OH group. The aromatic protons are appeared in multiplicity at 6.84-8.12  $\delta$ . Thus the structure of DAPOBR is confirmed as shown in **Scheme-I**.

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

Metal Chelates	$\mu_{\text{eff}}$ (BM)	Electronic spectral data ( $\text{cm}^{-1}$ )	Transition
DAPOBR- $\text{Cu}^{2+}$	2.51	23435 13201	Charge transfer ${}^2\text{B}_{1g} \rightarrow {}^2\text{A}_{1g}$
DAPOBR- $\text{Co}^{2+}$	4.75	23736 19112 8920	${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}(\text{F})$ ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}$ ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}(\text{P})$
DAPOBR- $\text{Mn}^{2+}$	5.52	23239 19022 16850	${}^6\text{A}_{1g} \rightarrow {}^6\text{A}_{2g}$ ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{2g}(\text{4G})$ ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{1g}(\text{PG})$
DAPOBR- $\text{Ni}^{2+}$	3.70	22584 15359	${}^3\text{A}_{1g} \rightarrow {}^3\text{T}_{1g}(\text{P})$ ${}^3\text{A}_{1g} \rightarrow {}^3\text{T}_{1g}(\text{F})$
DAPOBR- $\text{Zn}^{2+}$	Diamag.		-----

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  $\text{Cu}^{2+}$  chelates shows two broad bands around 13201 and 23435  $\text{cm}^{-1}$ . The first band may be due to a  ${}^2\text{B}_{1g} \rightarrow {}^1\text{A}_{1g}$  transition, while the second band may be due to charge transfer. These bands along with higher value of the magnetic moment of the  $\text{Cu}^{2+}$  chelate supports the distorted octahedral structure for the  $\text{Cu}^{2+}$  metal chelates [21]. The  $\text{Co}^{2+}$  metal chelate gives rise to two absorption bands at 23736 and 19112  $\text{cm}^{-1}$ , which can be assigned  ${}^4\text{T}_{1g} \rightarrow {}^2\text{T}_{2g}$ ,  ${}^4\text{T}_{1g} \rightarrow {}^4\text{T}_{1g}(\text{P})$  transitions, respectively. These absorption bands and the  $\mu_{\text{eff}}$  value indicate an octahedral configuration of the  $\text{Co}^{2+}$  metal chelate [22]. The spectrum of  $\text{Mn}^{2+}$  metal chelate comprised two bands at 19022  $\text{cm}^{-1}$  and 23239  $\text{cm}^{-1}$ . These bands may be assigned to  ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{2g}(\text{G})$  and  ${}^6\text{A}_{1g} \rightarrow {}^4\text{A}_{2g}(\text{G})$  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  $\text{cm}^{-1}$ , attributed to  ${}^3\text{A}_{1g} \rightarrow {}^3\text{T}_{1g}(\text{P})$ ,  ${}^3\text{A}_{1g} \rightarrow {}^3\text{T}_{1g}(\text{F})$  transitions, respectively, for an octahedral Ni(II) complex [23], while  $\text{Zn}^{+2}$  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  $\mu_{\text{eff}}$  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

Sample	Zone of inhibition of fungus at 1000 ppm (%)			
	<i>Nigrospora Sp.</i>	<i>Botrydeplaiia thiobromine</i>	<i>Asperginus niger</i>	<i>Rhisopus Nigricans</i>
DAPOBR	50	58	45	52
DAPOBR-Cu <sup>2+</sup>	78	72	71	75
DAPOBR-Co <sup>2+</sup>	65	67	62	69
DAPOBR-Mn <sup>2+</sup>	70	67	69	65
DAPOBR-Ni <sup>2+</sup>	61	65	62	66
DAPOBR-Zn <sup>2+</sup>	68	72	60	69

### 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.

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