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SYNTHESIS, CHARACTERIZATION AND ANTIFUNGAL ACTIVITY OF METAL CHELATES OF 2-PHENYL-5-(8-HYDROXYQUINOLIN-5-YL)OXAZOLE

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ABSTRACT:
2-Phenyl-5-(hydroxyquinolin-5-yl)oxazole (PHQO) was prepared by condensation of 5-chloroacetyl-8-hydroxy quinoline and benzyl amine. The various transition metal chelates of PHQO with Co^{2+}, Zn^{2+},Ni^{2+},Cu^{2+},Mn^{2+} metal ions were prepared and characterized. The antifungal activity of all these derivatives was evaluated against various fungi.

KEYWORDS: Oxazole,8-hydroxyquinoline; Metal Chelates; spectral studies; magnetic properties and Anti-fungal activity.

INTRODUCTION:

Number of heterocyclic compounds reported for good complexing agents [v,vi]. Among them 8-Hydroxy quinoline(8HQ) reported for different biological activities as well as therapeutic activities such as antitumor, antiseptic, antioxidant, antimicrobial, anti-HIV, anti-inflammatory, antiviral, anti-diabetic, anti-asthmatic, anti-neurodegenerative and analgesic [i-vii]. 8-Hydroxy quinoline(8HQ) has a coordinating ability and good metal recognition properties [viii-ix]. The derivatives of 8HQ have good chelating capability toward an enormous quantity of metal cations [x-xi]. The approach to the preparation of potential biologically active metal complexes, the present work designed the synthetic route of some novel Metal Chelates shown in scheme-1. The synthesized compounds were evaluated for its antifungal activity.

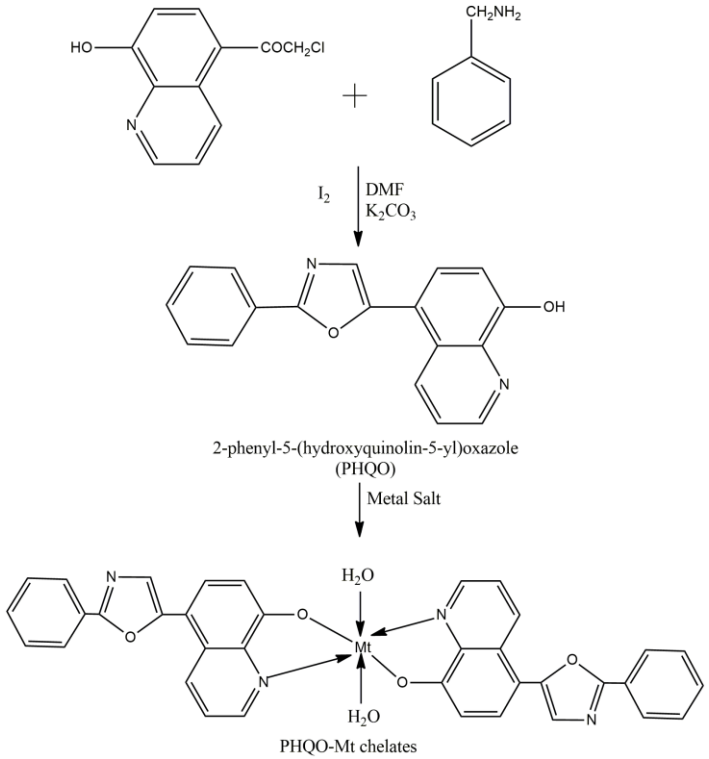
EXPERIMENTAL SECTION:

The entire chemicals used were of laboratory grade. 5-chloroacetyl-8-hydroxy quinoline was prepared by reported method [xii,xiii].

Synthesis of 2-phenyl-5-(8-hydroxyquinolin-5-yl)oxazole (PHQO)

To a suspension of 5-chloroacetyl-8-hydroxy quinoline (0.15 mole) in ethyl acetate solvent, benzyl amine (0.15mole) was added in 100 ml of DMF. Dry K_2CO_3 (0.30 mole) was added as an acid acceptor. The whole reaction mixture was refluxed on a sandbath for 3.5-4 hrs. The solid separated was collected by filtration, dried and washed by ethyl acetate. The filtrate was concentrated and the residue was extracted with petroleum ether and the solution filtered.

Concentration of the filtrate gave 77% yield, m.p.119-120° C. Recrystallization from petroleum ether (b.p.60-68°C).



Scheme-1

Anal. Calcd. for $C_{18}H_{12}N_2O_2$(288):%C, 74.99; %H, 4.20; %N, 9.72. Found: %C, 74.9; %H, 4.1; %N,9.7. IR Spectral Features (cm-1) shows at 3302-2765 (OH),3058, 2872, 1625,1456(C-H),1624, 1580, 1478 and 755(8-Hydroxy quinoline),1280(C-N), 1150 (C-O) and NMR Signals (δ ppm) at 4.85 (s,1H,OH), 7.10-8.92(m,5H, Quinoline), 7.12 (1H,s,CH of oxazole) and 7.45-8.12 (5H,m,Aromatic C-H).

Synthesis of metal chelates of PHQO:

The metal chelates of PHQO with Cu^{2+}, Co^{2+}, Ni^{2+}, Mn^{2+}, Zn^{2+} and Cd^{2+} metal ions were prepared in two steps.

Step-I Preparation of PHQO solution:

PHQO (0.1 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 PHQO. It was diluted to 100 ml.

Step-II Synthesis of PHQO-metal-chelates:

In a solution of metal acetate (0.01 mol) in acetone: water (50:50 v/v) mixture (40 ml), the 20 ml of PHQO solution (containing 0.02 M PHQO) 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: ANALYSIS OF PHQO LIGAND AND ITS METAL CHELATES

Empirical Formula	Mol. Wt. gm/mole	Yield (%)	Elemental Analysis			
			% C	% H	% N	% M
			Cald Found	Cald Found	Cald Found	Cald Found
$C_{18}H_{12}N_2O_2$	288	77	74.99 74.9	4.20 4.1	9.72 9.7	-
$C_{36}H_{22}N_4O_4Cu^{+2}2H_2O$	673.54	72	64.14 64.1	3.86 3.8	8.31 8.2	9.43 9.4
$C_{36}H_{22}N_4O_4Co^{+2}2H_2O$	668.94	75	64.58 64.5	3.89 3.8	8.37 8.3	8.81 8.8
$C_{36}H_{22}N_4O_4Ni^{+2}2H_2O$	668.71	69	64.60 64.5	3.89 3.8	8.37 8.3	8.78 8.7
$C_{36}H_{22}N_4O_4Mn^{+2}2H_2O$	664.94	72	64.97 64.9	3.91 3.8	8.42 8.4	8.26 8.2
$C_{36}H_{22}N_4O_4Zn^{+2}2H_2O$	675.38	76	63.96 63.9	3.85 3.8	8.29 8.2	9.68 9.6

MEASUREMENTS:

The elemental contents were determined by Thermo Finigen Flash1101 EA (Itally) the metals were determined volumetrically by Vogel's method [xiv]. To a 100 mg chelate sample, each 1 ml of HCl, H2SO4and HClO4 were added and then 1 g of NaClO4 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 PHQO was recorded on 60 MHz NMR spectrophotometer. Magnetic susceptibility measurement of the synthesized complexes was carried out on Gouy Balance at room temperature. Mercury tetrathio cynato cobalate (II) Hg[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 fungi, following the method reported in literature [xv].

RESULTS AND DISCUSSION:

The synthesis of 2-Phenyl-5-(8-hydroxyquinoline-5-yl)oxazole (PHQO) was prepared by condensation of 5-Chloromethyl-8-hydroxyquinoline (CMQ) hydrochloride with benzyl amine. The resulted PHQO ligand was an amorphous brown powder. The C, H, N contents of PHQO (Table-1) are consistent with the structure predicted (Scheme-1). The IR spectrum of PHQO comprises the important bands due to 8-hydroxyquinoline. The bands were observed at 1640, 1580, 1475 and 755 cm^{-1}.

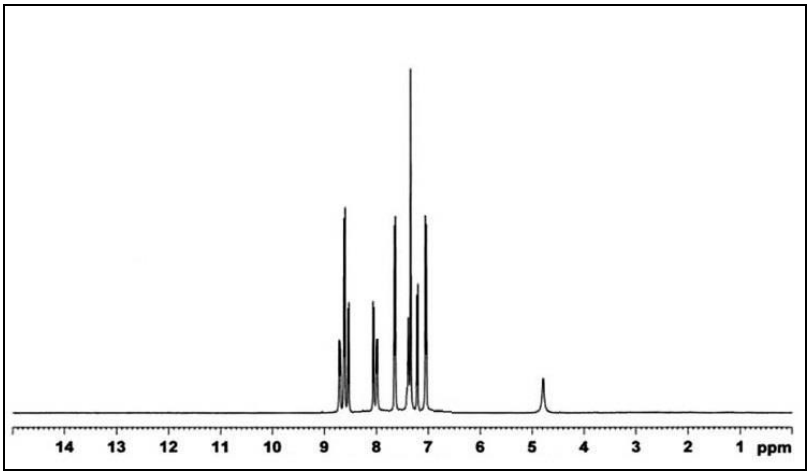


Fig. 1 NMR of PHQO

The broad band due to –OH group appeared at 3302-2765 cm-1. The NMR spectrum of PHQO in DMSO indicates that the singlet of 1 H at 7.12 for CH of oxazole. While the singlet at 4.85 δ ppm due to –OH group. The quinoline protons are appeared in multiplicity at 7.10-8.92 δ and Aromatic proton shows multiplet at 7.45-8.12 δ. Thus the structure of PHQO is confirmed as shown in Scheme-I.

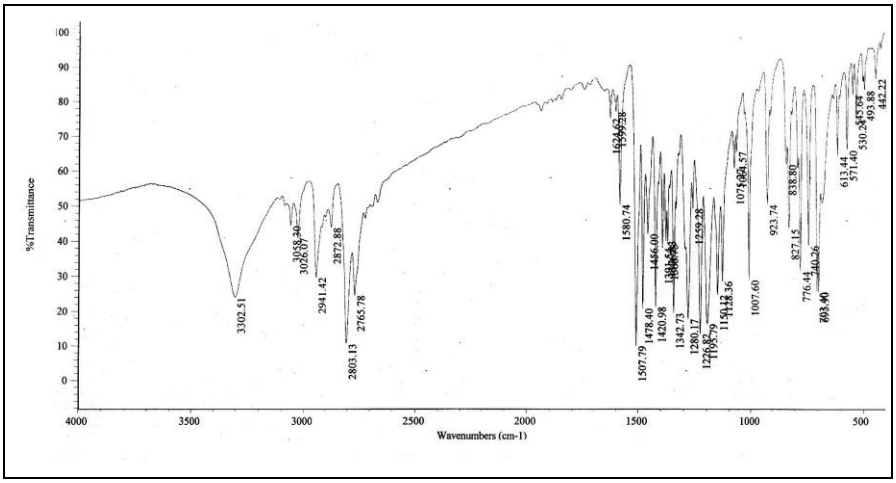


Fig. 2 IR of PHQO

The metal and C, H, N contents of metal chelates of PHQO (Table-I) are also consistent with the predicted structure. The results show that the metal: ligand (M:L) ratio for all divalent metal chelate is 1:2.

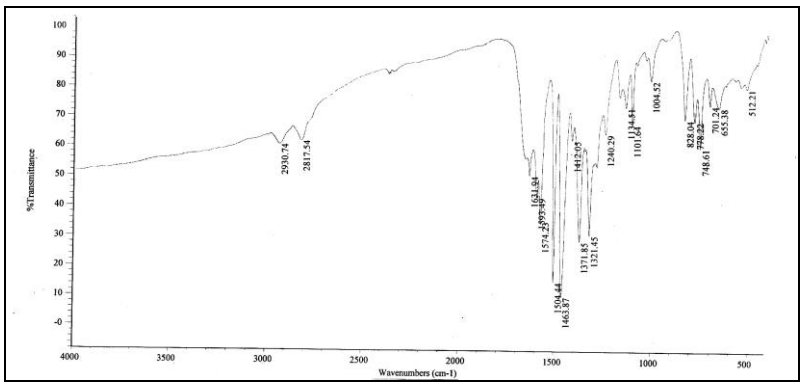


Fig. 3 IR of PHQO-Cu^{+2}

The infrared spectra of all the chelates are identical and suggest the formation of the entire metalo cyclic compound by the absence of band characteristic of free –OH group of parent PHQO. The other bands are almost at their respectable positions as appeared in the spectrum of parent-PHQO ligand. However, the band due to (M-O) band could not be detected as it may appear below the range of instrument used. The important IR Spectral data are shown in Table-2.

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

Metal Chelates	**μ_{eff} (BM)**	**Electronic spectral data (cm^{-1})**	**Transition**
PHQO-Cu^{+2}	2.54	23451 15874	Charge transfer $^2B_{1g} \rightarrow {}^2A_{1g}$
PHQO-Ni^{+2}	3.70	22583 15372	$^3A_{1g} \rightarrow {}^3T_{1g}(P)$ $^3A_{1g} \rightarrow {}^3T_{1g}(F)$
PHQO-Co^{+2}	4.63	22725 15260 8940	$^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ $^4T_{1g}(F) \rightarrow {}^4T_{2g}$ $^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$
PHQO-Mn^{+2}	5.54	23857 18348 16820	$^6A_{1g} \rightarrow {}^6A_{2g}{}^4E_g$ $^6A_{1g} \rightarrow {}^4T_{2g}$ (4G) $^6A_{1g} \rightarrow {}^4T_{1g}$(PG)
PHQO-Zn^{+2}	Diamag.	-	-

The data of electronic transitions and magnetic moments of metal chelates are summarized in Table-2. The observed μeff values in the range 2.54-5.54 B.M are consistent with the above moiety. The value of magnetic moments and reflectance spectral data of each chelates co-relates with structure assigned as the octahedral geometry [xvi,xvii].

The examination of antifungal activity of PHQO ligand and its all chelates (Table-3) reveals that the ligand is moderately toxic against fungi, while all the chelates are more toxic than ligand. Among all the chelates the Cu+2 chelate is more toxic against fungi.

TABLE-3: ANTIFUNGAL ACTIVITY OF PHQO LIGAND AND ITS METAL CHELATES

Sample	**Zone of inhibition of fungus at 1000 ppm (%)**			
	Aspergillus Niger	***Botrydepladia Thiobromine***	***Nigrospora Sp.***	***Fusarium oxyporium***
PHQO	63	67	61	69
PHQO-Cu^{+2}	79	84	76	82
PHQO-Ni^{+2}	77	79	71	78
PHQO-Co^{+2}	76	81	74	80
PHQO-Mn^{+2}	75	77	75	80

PHQO-Zn^{+2}	73	78	76	81

CONCLUSION:

Novel Ligand having 8-hydroxy quinoline and oxazole moieties was prepared from 5-chloroacetyl-8-hydroxyquinoline. The ligand was used to synthesis various transition metal chelates. All the chelates are found with 1:2 metal:ligand ratio. The spectral features of all the compounds are consistent with predicted structure. The compounds behave good antimicrobial activity as expected.

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