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Studies on Metal Complexes of Pyrazole Bearing Ligand with Their Antimicrobial Screening

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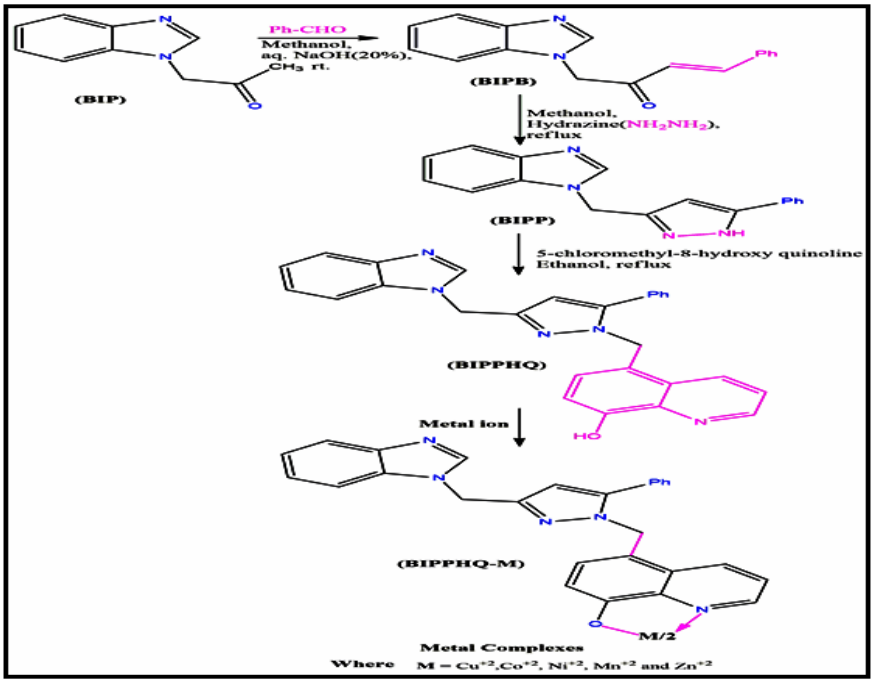
ABSTRACT

In present research article, we reported the synthesise of novel hetertocyclic ligand namely, 5-((3-((1H-benzimidazol-1-yl)methyl)-5-phenyl-1H-pyrazol-1-yl)methyl)-8-hydroxy quinoline (BIPPHQ) from 5-chloro methyl-8-hydroxy quinoline and 1-((5-phenyl-1H-pyrazol-3-yl) methyl)-1H-benzimidazole (BIPP). The BIPP was synthsised by the reaction between hydrazine hydrate with 1-(1H-benzimidazol-1-yl)-4-phenylbut-3-en-2-one (BIPB), which was synthesisd from 1-(1H-benzimidazol-1-yl)propan-2-one (BIP) and benzaldehyde. The transition metal complxes of 5-((3-((1H-benzimidazol-1-yl)methyl)-5-phenyl-1H-pyrazol-1-yl)methyl)-8-hydroxy quinoline (BIPPHQ) were sythsised and analysed with the help of elemen conten analysis, spectroscopic data analysis, ratio of metal and ligand and also magneic parameters. The BIPPHQ and etal coplexes also screened for antimicrobial study.

Keywords: Pyrazole,8-hydroxy quinoline, Metal complex, Spectral analysis, Magnetic properties, Antibacterial and Antifungal activity screening.

INTRODUCTION

Nowadays Metals complexes become very important in the field of medicinal chemistry[1,2]. The divalent transition metals show various biochemical reactions[3]. The researchers synthesised number of metal complexes having organic ligands due to their various biological activities[4-6]. 8-Hydroxy quinoline (8-HQ) is a significant heterocyclic compound in metal complexation due to their medicinal properties like antibacterial, anti-fungal, anti-malaria, anti-HIV anti-cancer[7-11]. By chelation process 8- Hydroxy quinoline form metal complexes with divalent transition metal ions[12]. 8-HQ shows potential therapeutic effect for the treatment in metabolism problem occurs due to of irregularity of metal and/or imbalance in metal ion problem in human body[13,14]. Hence, we synthesis metal complexes based on heterocyclic ligand and screened them for their antimicrobial activity.



Scheme 1. Whole research work

EXPERIMENTAL

1-(1H-benzimidazol-1-yl) propan-2-one (BIP) was synthesised from reported method[13,14]. Laboratory grade chemicals were usd. The present element were analysed by titrimertically method[15]. For IR and NMR spectra study Nicolet 760 FT-IR spectrometer and 60 MHz NMR spectrophotometer were used. The electronic spectra studied carried out using MgO. The evaluation of antimicrobial screening was analysed by Broth Dlution method[16,17]. The whole reaction work is summarized in following Scheme 1.

Synthesis of 1-(1H-benzimidazol-1-yl)-4-phenyl but-3-en-2-one (BIPB)[18,19]

A mixture of 1-(1H-benzimidazol-1-yl) propan-2-one (BIP) (1mmol) and benzaldehyde (1mmol) in C_2H_5OH (20 mL), was added dropwise to alkali solution of KOH, and stirred for 1 day at 25°C. The reaction mixture added into ice cold water containing beaker with stirring. The resultant solid separated out and crystallized by R-sprit. The Yield was 76% and m.p. was 123-124°C. The elemental analysis for $C_{17}H_{14}N_2O$ (262 g/mol), Cal.(Found)% C-77.84(77.8); %H-5.38(5.3) and %N-10.68(10.6). IR spectra (cm^{-1}, KBr): 3021 (Aromatic C-H Str.), 2900, 2820, 1500, 1380(C-H Str.), 1660 (CO), 1600 (N=C), 1580 (C=C). ^{1}HNMR (δ,ppm): 7.02-8.12 (m, 10H,benzimidazole, Aromatic-H), 4.96 (s, 2H,-N-CH_2-CO-), 6.47, 8.51(d, 2H, ethylene); ^{13}C NMR (ppm): 196.51(CO), 112.31-138.25 (Ar-C), 58.34(CH_2), 148.88, 154.06 (C=C). Mass (m/z) : 263 $(M+1)^+$.

Synthesis of 1-((5-phenyl-1H-pyrazol-3-yl) methyl)-1H-benzimidazole (BIPP)[19,20]

Reflux a mixture of 1-(1H-benzimidazol-1-yl)-4-phenyl but-3-en-2-one (BIPB) (0.5 mmol) in ethanol (5 mL), hydrazine hydrate(1.5 mmol) for 4-5 hours. Aftyer completion of reaction, it was cooled at 0°C for overnight. The formed product was filtered, washed, dried and recrystallized from C_2H_5OH. 82% yield and m.p. 160–161°C. The elemental analysis for $C_{17}H_{14}N_4$(274 g/mol), Cal.(Found)% C-74.43(74.4); %H-5.14(5.1) and %N-20.42(20.4). IR spectra KBr (cm^{-1}): IR (KBr): ν 3425 (NH), 3020 (Aromatic C-H Str.), 2900, 2820, 1530, 1370(C-H Str.),1600 (C=N). ^{1}HNMR (δ,$CDCl_3$,TMS): 7.29-7.87 (m,10H,Ar-H), 6.09 (s, 1H, NH), 4.82(s,2H,CH_2), 5.15 (s, 1H, Hpyraz). ^{13}C NMR: δ 113.7-148.8 (Ar-C), 57.8 (CH_2),103.2(pyraz C-H), Mass (m/z) : 275 $(M+1)^+$.

Synthesis of 5-((3-((1H-benzimidazol-1-yl) methyl)-5-phenyl-1H-pyrazol-1-yl) methyl) -8-hydroxy quinoline (BIPPHQ)[19]

A mixture of triethyl amine (0.5 mmol) and 5-chloromethyl-8-hydroxy quinoline (0.5 mmol) was added with stirring to a cold mixture of 1-((5-phenyl-1H-pyrazol-3-yl) methyl)-1H-benzimidazole (BIPP) (0.5 m mol) in dry acetone (5 mL) at 0°C. Whole mixture was continuous stirred for 2 h 25°C. The solid product was separated out, it was filtered and recrystallized from C_2H_5OH. yield was 70% and m.p. was 178–1789°C. The elemental analysis for $C_{27}H_{21}N_5O$ (431 g/mol),Cal.(Found)% C-75.16(75.1); %H-4.91(4.9) and %N-16.23(16.2). IR spectra (KBr, cm^{-1}) 3298(-OH),2932(CH_2), 3028 (Aromatic C-H Str.), 2932, 2840,1508 (C-H Str.),1619, 1576, 1508, 1456(8-HQ moiety), 1508 (C=C), 1456 (C-C), 1576 (C=N), 1275-1298(C-N). ^{1}HNMR (δ,$CDCl_3$,TMS): δ 7.29-7.98 (m,15H,Ar-H), 4.77-4.42 (s,4H,CH_2), 5.11 (s, 1H, Hpyraz), 9.51(s,1H,-OH). ^{13}C NMR: δ 116.1-152.2 (Ar-C), 51.9,58.7 (CH_2),105.6 (pyraz C-H). Mass (m/z):432 $(M+1)^+$.

Synthesis of Metal complexes of 5-((3-((1H-benzimidazol-1-yl)methyl)-5-phenyl-1H-pyrazol-1-yl)methyl)-8-hydroxy quinoline (BIPPHQ)

The metal complexes of BIPPHQ (i.e. of Ni(II), Zn(II), Cu(II), Mn(II) and Co(II) ions) were prepared by similar manner. The method as follow, A preheated solution of salt of M(II) (2.5mmol) in aqueous formic acid (1:1,2.5 mL) was added to the preheated aqueous formic acid solution (20%, 20 mL) of BIPPHQ (5mmol) with stirring. Adjust the pH with NH_4OH (50%) solution and digested for 4 hours. The resultant product was filtered, washed and air-dried. All complexes were prepared and isolated in amorphous shape.

Thermogravimetric analysis of synthesised BIPPHQ and metal complexes were carried out by Du point Thermo-gravimetric analyzer.

Table 1: Analysis of BIPPHQ and Its Metal Complex

Ligand and Metal complexes	Mol. Wt.	Color	Yield%	Elemental analysis (%) %C Calc. Found	%H Calc. Found	%N Calc. Found	%M Calc. Found
$C_{27}H_{21}N_5O$	431	White	70	75.16	4.91	16.23	-
			75.1	4.9	16.2	-	
$C_{54}H_{40}N_{10}O_2Cu(II).2H_2O$	960.54	Pale	67	67.52	4.62	14.58	6.62
	white		67.5	4.6	14.5	6.6	
$C_{54}H_{40}N_{10}O_2Ni(II).2H_2O$	955.71	Greenish	64	67.87	4.64	14.66	6.14
	white		67.8	4.6	14.6	6.1	
$C_{54}H_{40}N_{10}O_2Co(II).2H_2O$	955.94	Off	68	67.85	4.64	14.65	6.17
	white		67.8	4.6	14.6	6.1	
$C_{54}H_{40}N_{10}O_2Zn(II).2H_2O$	962.38	Pale	62	67.39	4.61	14.55	6.79
	yellow		67.3	4.6	14.5	6.7	
$C_{54}H_{40}N_{10}O_2Mn(II).2H_2O$	951.94	Off	65	68.13	4.66	14.71	5.77
	white		68.1	4.6	14.7	5.7	

Table 2: Electronic spectral data and magnetic properties of metal complexes of BIPPHQ

Metal complexes	μeff (B.M.)	Electronic spectral data (cm^{-1})	Transition
BIPPHQ-Cu(II)	1.92	23985	CT
		15763	$^2B_{1g} \rightarrow {}^2A_{1g}$
BIPPHQ-Ni(II)	3.23	22239	$^3A_{2g} \rightarrow {}^3T_{1g}$ (P)
		15790	$^3A_{2g} \rightarrow {}^3T_{1g}$ (F)
BIPPHQ-Co(II)	4.82	23955	$^4T_{1g}$(F) → 6T2g(υ1)
		18118	$^4T_{1g}$(F) → 4A2g(υ2)
		8742	$^4T_{1g}$(F) → $^4A_{2g}$(υ2)
BIPPHQ-Mn(II)	5.52	23887	$^6A_{1g} \rightarrow {}^6A_{1g}(^4E_g)$
		18340	$^6A_{1g} \rightarrow {}^4T_{2g}(^4G)$
		16845	$^6A_{1g} \rightarrow {}^4T_{1g}(^4G)$
BIPPHQ-Zn(II)	Diamagnetic	-	-

Table 3: Thermogravimetric analysis of BIPPHQ and metal complexes

Ligand/Metal chelates	%Weight loss at various temperature(°C)						
	100	200	300	400	500	600	700
BIPPHQ	-	8.90	10.46	24.60	29.80	32.09	35.25
BIPPHQ-Cu(II).2H_2O	0.04	5.73	12.33	27.88	33.59	37.14	39.9
BIPPHQ-Ni(II).2H_2O	3.21	16.45	20.12	37.77	53.95	66.35	69.57
BIPPHQ-Co(II).2H_2O	2.53	13.70	25.36	39.83	53.63	65.32	68.86
BIPPHQ-Zn(II).2H_2O	7.46	16.05	32.20	37.49	56.26	67.35	70.12
BIPPHQ-Mn(II).2H_2O	3.26	10.56	14.66	35.85	54.44	67.04	69.56

RESULTS AND DISCUSSION

The synthesis of 5-((3-((1H-benzimidazol-1-yl)methyl)-5-phenyl-1H-pyrazol-1-yl)methyl)-8-hydroxy quinoline (BIPPHQ) synthesisd from 1-(1H-benzimidazol-1-yl) propan-2-one (BIP) and benzaldehyde. Table 1 data consist with the structure of synthesised compounds (Scheme 1). The most unique IR bands of BIPPHQ shows which may be due to 8-hydroxy quinoline, which are presented at 3298 (-OH), 2932(CH_2), 1576 (C=N) cm^{-1}.

BIPPHQ shows NMR peak at 9.51 for OH. The methylene proton shows singlet at 4.77-4.41 δ. It confirmed the structure of BIPPHQ.

The elemental ananalysis (Table 1) are confirmed that the all metal complexed are divalent.

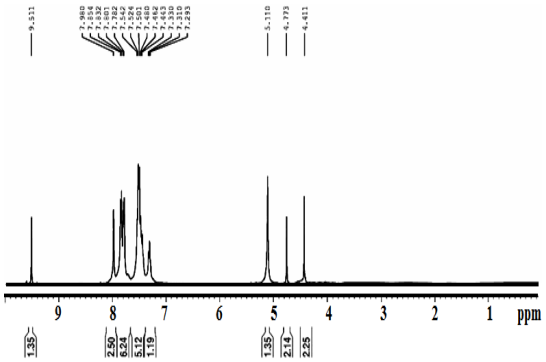


Fig. 1. ^{1}H NMR of BIPPHQ

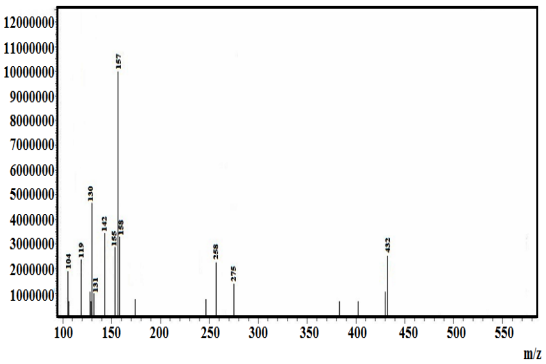


Fig. 2. LC-MS of BIPPHQ

The significant differnece in IR of Ligand and metal complexes is the band of hydroxyl group at 3298 cm^{-1}, which is absent in metal complexe may be due to complextion loos of hydrogen of hgydroxyol group[21,22].

Table 2 shows the electronic spectral data and magnetic properties of metal complexes of BIPPHQ, which are shows the octahedral geometry of metal complexes[21-23].

Table 4: Antibacterial activity of BIPPHQ and metal complexes

Compounds	MIC, μgmL^{-1}			
	Gram-positive		*Gram-negative*	
	B. megaterium	*S. aureus*	*E. coli*	*P. aeruginosa*
BIPPHQ	150	125	150	150
BIPPHQ-Cu(II)	25	50	25	50
BIPPHQ-Ni(II)	75	100	100	75
BIPPHQ-Co(II)	50	50	75	75
BIPPHQ-Zn(II)	75	100	100	100
BIPPHQ-Mn(II)	100	125	125	125
Amoxillin	250	150	250	200

Antibacterial and antifungal screening of BIPPHQ and metal complexes (Table 3 and 4) shows that the metal complexes are more toxic than BIPPHQ, out of them metal complexes of Cu(II) is most toxic.

Table 5: Antifungal activity of BIPPHQ and metal complexes

Compounds	Minimum Inhibitory Concentration (MIC, μgmL^{-1})			
	Penicillium Expansum	BotrydepladiaThiobromine	Nigrospora Sp.	Fusarium oxyporium
BIPPHQ	150	150	125	150
BIPPHQ-Cu(II)	25	50	25	50
BIPPHQ-Ni(II)	125	100	100	125
BIPPHQ-Co(II)	100	125	100	125
BIPPHQ-Zn(II)	75	50	75	75
BIPPHQ-Mn(II)	150	125	100	125
Nystatin	300	200	250	200

CONCLUSION

The novel hetertocyclic ligand containing metal complxes of 5-((3-((1H-benzeimidazol-1-yl)methyl)-5-phenyl-1H-pyrazol-1-yl)methyl)-8-hydroxy quinoline (BIPPHQ) were sythsised. All the characterization method predicted the structure of synthesised compounds. Antimicrobial screening of BIPPHQ and metal complexes were shows good effectiveness.

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Conflict of interest

The author declare that we have no conflict of interest.

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