Nigerian Research Journal of Chemical Sciences **(ISSN: 2682-6054)**
Vol. 7, 2019

SYNTHESIS, CHARACTERIZATION AND ANTIBACTERIAL ACTIVITY OF 2-PHENYLBUT-2-ENAL ISONICOTINOYL HYDRAZONE (PINH) COMPLEXES WITH Co(II), Cu(II), Mn (II) AND Zn(II) IONS

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ABSTRACT

A novel hydrazone, 2-Phenylbut-2-enal isonicotinoyl hydrazone (PINH) was synthesized and characterized by elemental analysis, melting point, electronic and infrared spectral studies. Its complexes with Mn(II), Co(II), Cu(II) and Zn(II) nitrates were also synthesized and characterized by elemental analysis, melting point, conductance, magnetic susceptibility, electronic and infrared spectral studies. Infrared data suggest that the ligand is neutral bidentate donor, ligating through the carbonyl oxygen and the azomethine nitrogen towards the metal ions. The nitrate ion is in the outer coordination sphere in the complexes. The magnetic and electronic spectral data indicate octahedral structures for the divalent M(II) ions. Octahedral geometry has been suggested for all the metal (II) complexes synthesized. Antibacterial activity of the ligand PINH and that of its metal complexes were studied against gram-positive bacteria: *Streptococccus pyogenes*, *Staphylococcus aureus;* and gram-negative bacteria: *Escherichia coli and Shigella species.* The results showed that the metal complexes have better antibacterial activities than 2-Phenylbut-2-enal isonicotinoyl hydrazone ligand.

Keywords: Antibacterial; complexes; hydrazones; spectroscopy; transition metals.

INTRODUCTION

Over the years, much attention has been paid to investigate the chemistry of transition metal complexes with large number of hydrazones as ligands [1], especially heterocyclic containing hydrazones [1, 2]. Hydrazone ligands create an environment similar to the one present in biological systems usually by making coordination through oxygen and nitrogen atoms. Various important properties of hydrazones, along with their applications in medicine and analytical chemistry, have led to an increased interest, in the complexation of their characteristics with

transition metal ions [3-5]. The hydrazones offer a number of attractive features such as degree of rigidity, a conjugated-system and NH unit that readily participate in hydrogen bonding and may be a site of deprotonation. It is well established that the formation of metal complexes plays an important role in enhancing the biological activity of free hydrazones [6].

Heterocyclic hydrazones are promising compounds from the view point of coordination chemistry because of their ability towards complexation and their biological properties. Thus, the chemistry of transition metals with hydrazones has been of interest to coordination as well as bio-inorganic chemists due to their different bonding modes with metal ions [7].

The structural motif present in heterocyclic hydrazones is a remarkable tool for the development of multifunctional organic receptors that find applications in chemical, environmental and biological sciences. Heterocyclic hydrazones constitute an important class of active drugs that attracted the attention of medicinal chemists due to their wide ranging pharmacological properties like antifungal, antibacterial and anticonvulsant

compounds [8]. Hydrazones and their transition metal complexes derived from various acid hydrazides and salicylaldehyde have attracted much attention recently. The complexes of hydrazones derived from 2-furic acid hydrazide have rarely been reported and are expected to have interesting coordination modes and promising biological application [10].

In the present work, we describe the condensation of isonicotinic acid hydrazide and 2-phenylbut-2-enal to yield 2-Phenylbut-2-enalIsonicotinoyl hydrazone (PINH). Some transition metal complexes of 2-phenylbut-2-enal isonicotinoyl hydrazone were synthesized, characterized and evaluated for their antibacterial activities.

MATERIALS AND METHODS

All chemicals used were reagent grade from Sigma-Aldrich or B.D.H companies, used as supplied.

The infrared spectra of the ligand and complexes were recorded as KBr pellets on a (4000-350cm^{-1}) FTIR-8400S Fourier Transform Infrared spectrophotometer (Germany). The UV-vis spectra of the complexes were recorded at room temperature on UV-2500PC spectrophotometer (Japan), using absolute ethanol as solvent in 1cm quartz curettes. Molar conductance of the complexes was determined in absolute ethanol at room temperature using CON 6/TDS 6 hand-held conductivity meter (USA). The melting point was determined using AAR 3235 Gallenkamp

melting point apparatus and the C.H.N. elemental analysis was performed on AA-7000 Atomic absorption spectrophotometer (Turkey). These instruments were obtained from National Research Institute for Chemical Technology, Zaria, Kaduna State, Nigeria. Magnetic susceptibilities of the complexes were measured at room temperature using the HO-EM-08 magnetic susceptibility balance (India) at the Chemistry Department, Kwara State University, Molete, Kwara State. The necessary diamagnetic corrections for ligands were done using Pascal's table.

The metal content of complexes [Co(II), Cu(II), Mn(II), Zn(II)] was determined spectrophotometrically using Varian AA240 Atomic absorption spectrophotometer (USA) and the nitrates content of complexes was also determined spectrophotometrically [11] using PD303 UV spectrophotometer (Japan) at Springboard Research Laboratories, Awka, Anambra State, Nigeria.

Preparation of the Ligand

Preparation of 2-phenylbut-2-enal isonicotinoyl hydrazone (PINH)

The hydrazone was prepared by the condensation reaction of isonicotinic acid hydrazide (INH) and 2-phenylbut-2-enal [12]. 9.6 g (0.07 mol) of isonicotinic acid hydrazide dissolved in 40 ml absolute ethanol was added to 10 ml (10.34 g, 0.07 mol) of 2-phenyl but-2-enal. The mixture was refluxed for about 4 hours in a 250 ml round bottom flask after which it was poured in a beaker and left for the crystals to form. The crystals obtained were recrystallized with minimum quantity of ethanol, dried over calcium chloride in a desiccator and weighed. The reaction is shown in (Fig. 1).

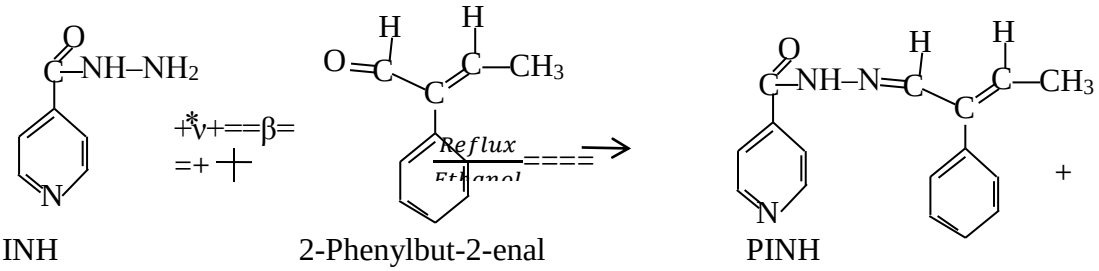

Fig. 1: Schematic diagram showing the synthesis of the ligand PINH

Preparation of metal nitrate complexes

The appropriate metal nitrates (0.012 mol) [3.5 g $Co(NO_3)_2.6H_2O$, 2.2 g $MnNO_{3(aq)}$, 3.0 g $Cu(NO_3)_2.3H_2O$, 3.6 g $Zn(NO_3)_2$] in (10 ml) absolute ethanol were heated under reflux with constant stirring with (1.5 g, 0.006 mol) of the ligand PINH in (10 ml) absolute ethanol for about 2 hours. The solid complexes formed were then separated by filtration, washed with ethanol (5 ml) and finally dried and kept in a dessicator.

Antibacterial activity

This was evaluated using agar diffusion method [13]. Gram-positive bacteria: *Streptococccus pyogenes, Staphylococcus aureus*; and Gram-negative bacteria: *Escherichia coli, Shigella species,* were cultivated in nutrient agar on petri dishes. The test solution was prepared by dissolving 10 mg of each of the tested compound in 1 ml acetone. A 6 mm diameter filter paper discs were socked in the tested solutions. After 24 hours cultivation at 37 °C, diameters of zones of inhibition were determined. Acetone was used as control and was inactive under applied conditions.

RESULTS AND DISCUSSION

The reaction of PINH with the metal nitrates, [metal= Co(II), Mn(II), Cu(II), and Zn(II)] in (1:2) molar ratios gave the complexes Table (1).

The physical properties and chemical analysis of the complexes are given in Tables 1 and 2 and it is in good agreement with the proposed formulas. All the complexes are non-hygroscopic solids and stable in air. They are insoluble in water, sparingly soluble organic solvents like formalin but soluble in acetone and moderately soluble in ethanol and methanol.

The molar conductance values (Table 1) of the metal complexes in ethanol are in the ranges of 0.02-1.60 ohm^{-1} cm^2 mol^{-1} indicating non-electrolyte nature of these complexes [14]. The molar conductance values reveal that the metal nitrate complexes are non-electrolytic complexes [15].

Table 1: Physical properties and analysis data of the ligand and its complexes

Complex	Formula	Formula weight ($gmol^{-1}$)	Colour	M.P ^oC	%Yield	Solubility	Molar conductivity ($ohm^{-1}\ cm^2\ mol^{-1}$)
PINH	$C_{16}H_{15}N_3O$	265.0	Pale yellow	161	74.4	Ethanol	0.03
Zn-PINH	$C_{32}H_{34}N_8O_{10}Zn$	755.40	Orange	245	71.4	Ethanol	0.15
Cu-PINH	$C_{32}H_{34}N_8O_{10}Cu$	753.50	Dark green	230	94.9	Ethanol	0.07
Co-PINH	$C_{32}H_{34}N_8O_{10}Co$	748.93	Dark brown	220	84.9	Ethanol	0.13
Mn-PINH	$C_{32}H_{34}N_8O_{10}Mn$	744.93	Yellow	190	88.9	Ethanol	0.57

Table 2: Elemental analyses of some of the prepared complexes

Compound	Molecular Formula	Mol. Wgt	Elemental analysis: Found (calculated) %				
			Metal	C	H	N	NO_3^-
PINH	$C_{16}H_{15}N_3O$	265.00	–	72.50 (72.45)	5.52 (5.66)	16.16 (15.85)	–
Zn-PINH	$C_{32}H_{34}N_8O_{10}Zn$	755.40	9.74 (8.66)	51.07 (50.83)	4.52 (4.50)	14.58 (14.83)	15.91 (16.42)
Cu-PINH	$C_{32}H_{34}N_8O_{10}Cu$	753.50	7.09 (8.43)	51.29 (51.05)	4.79 (4.51)	14.87 (14.86)	16.37 (16.46)
Co-PINH	$C_{32}H_{34}N_8O_{10}Co$	748.93	7.57 (7.87)	51.17 (51.27)	4.65 (4.54)	14.63 (14.96)	16.93 (16.56)
Mn-PINH	$C_{32}H_{34}N_8O_{10}Mn$	744.93	8.24 (7.37)	51.67 (51.55)	4.67 (4.56)	15.73 (15.04)	15.87 (16.65)

Infrared Spectra

The main frequencies of the i.r. spectra of the ligand and its complexes and their tentative assignments are shown in Table 3. The spectrum of the free ligand PINH showed characteristic absorption bands at 956 cm^{-1}, 1707 cm^{-1}, 1582 cm^{-1}, 3055 cm^{-1} and 1160 cm^{-1} which are due to ν(N–N), ν(C=O), ν(C=N), ν(N–H) and ν(C–N) respectively. The IR spectra of the complexes were compared with those of the free ligand in order to determine the involvement of coordination sites in the complexes. In the spectra of metal nitrate complexes, the ν(N–H) band is almost unaltered or shifted to higher frequencies indicating non-involvement of this group in coordination and a decrease in hydrogen bonding on complexation may occur. A considerable shift (63-109cm^{-1}) in ν(C=O) was observed indicating a decrease in the force constant of (C=O) bond as a consequence of coordination through the carbonyl oxygen atom in these complexes. The shift of the imino group i.e ν(C=N) bands to lower wave numbers in the complexes of the ligand by about 8-20 cm^{-1} indicates the involvement of the azomethine nitrogen in bonding [16]. The coordination through the azomethine nitrogen atom was further supported by the shift of the ν(N–N) vibration observed at 956cm^{-1} in the spectrum of the PINH ligand to higher frequency in the complexes by 72-92 cm^{-1}. This is due to the reduction of ions pair repulsive forces in the adjacent nitrogen atoms [17].

The metal complexes also exhibited a very strong band at the region 1350-1380 cm^{-1}which are attributed to the ν_3 vibrations of uncoordinated nitrate ion of D_{3h} symmetry [18].

The appearance of broad band at 3408 – 3420 cm^{-1} in the complexes have been assigned to ν(OH) which is associated with coordinated or solvated water molecules which is indicative of the presence of water molecules in the complexes and this implies that water molecules held by a crystal lattice is present in the complexes [19].

Evidence of the bonding is also shown by the observation that new bands appear in the spectra of the complexes at about 533-603 cm^{-1} and 392-412 cm^{-1} which are assigned to ν(M-O) and ν(M-N) stretching vibrations respectively [16, 20] which are not observed in the spectra of the ligand, because there is no metal coordinated to nitrogen and to oxygen in the ligand [21, 22].

Table 3: Infrared Spectra of the Ligand and Metal Complexes

Compound	ν(N-N)	ν(C=N)	ν(C=O)	ν(C-N)	ν(N–H)	ν(H_2O)	ν(NO_3^-)	ν(M-N)	ν(M-O)
PINH	956	1582	1707	1160	3055	–	–	–	–
Cu-PINH	1028	1568	1644	1123	3084	3408	1352	412	583
Zn-PINH	1041	1562	1648	1408	3109	3420	1367	407	596
Co-PINH	1034	1574	1651	1291	3114	3408	1380	392	533
Mn-PINH	1048	1569	1598	1304	3211	3416	1373	395	603

Electronic Spectra and Magnetic Properties:

The room temperature (25 °C) magnetic moments and the electronic spectral data of the complexes are listed in Table 4. The PINH ligand spectrum in ethanol showed strong bands at 13514 cm^{-1} and 15848 cm^{-1} due to n →π * and π→π * transitions. These bands shift to lower wave numbers in the electronic spectra of most of the complexes at the regions 13, 477cm^{-1} and 12723cm^{-1} may indicate the coordination of the hydrazone to the metal ions.

The magnetic moment value of Co-PINH is 4.45 B.M suggesting octahedral geometry for Co(II)ion [16]. The electronic spectra of Co-PINH shows two absorption bands at 13,477cm^{-1} and 12723cm^{-1} due to $^4T_{1g} \rightarrow {}^4A_{2g}$ and $^4T_{1g}(F) \rightarrow {}^4T_{2g}$ transitions respectively, corresponding to three unpaired electrons and favouring octahedral geometry around the metal ion [23, 24].

The electronic spectra of Cu-PINH show a single band at 13477 cm^{-1} and assigned to $^2E_g \rightarrow {}^2T_{2g}$ favouring octahedral geometry. The magnetic moment of the complexes was found to be 2.07 B.M corresponding to one unpaired electron [23].

The electronic spectra of manganese complex is consistent with spectra of Mn(II) ions with chelates, weak bands of low intensities. The spectra show single band at 13514 cm^{-1} Mn-PINH is assigned to $^6A_{1g} \rightarrow {}^4T_{1g}(G)$ transition favoring octahedral geometry. The magnetic moment of the

complexwas found to be 5.65B.M corresponding to five unpaired electrons present in tits atomic structures [23].

The diamagnetic Zn(II) complex shows no prominent absorption in the visible region because of d^{10} and configuration for Zn(II) ions. Zn-PINH complex showed absorption band at 13,477cm^{-1} with no significant shift from that of the ligand. This absorption band is assigned to $^1A_{1g} \rightarrow {}^1A_{1g}$ transition and the complex is expected to have an octahedral geometry. The magnetic data of the zinc complex confirmed that they are essentially diamagnetic because all the d electrons are completely filled and it lies within the octahedral range [23].

Table 4: Electronic spectral and magnetic susceptibility data of the ligand and its complexes

Compound	μeff B.M.	Electronic spectra cm^{-1}	Assignment	Geometry
PINH	–	13514 15848	$n \rightarrow \pi^*$ $\pi \rightarrow \pi^*$	–
Cu-PINH	2.07	13477	$^1A_{1g} \rightarrow {}^1A_{1g}$	Octahedral
Zn-PINH	Diamagnetic	13477	$^2E_{2g} \rightarrow {}^2T_{2g}$	Octahedral
Co-PINH	4.45	12723, 13477	$^4T_{1g}(F) \rightarrow {}^4T_{2g}$	Octahedral
Mn-PINH	5.65	13514	$^6A_{1g} \rightarrow {}^4T_{1g}(G)$	Octahedral

Antibacterial Activity

The ligand PINH and its complexes were tested against two Gram positive bacteria: *S. aureus* and *S. pyogenes* and two Gram-negative bacteria*: E.coli* and *Shigella spp*. The results are shown in Table 5. The results indicate that the metal complexes of the hydrazone ligand (PINH) are more active towards the bacteria tested than the ligand. The results also show that complex formation of the ligand with metal ions increases its antibacterial activity since the complexes showed more activity than the ligand against the tested bacteria. Cu(II) and Zn(II) complexes showed higher bacteria activity than those of Mn(II) and Co(II) complexes [25].

Table 5: Antibacterial effects of the investigated compound

Compound	Gram positive bacteria		Gram negative bacteria	
	S. pyogenes	*S. aureus*	*E. coli*	*Shigella spp*
PINH	+++	+++	++	++
Zn-PINH	++++	++++	++	+++
Cu-PINH	++++	+++	++	++
Co-PINH	++	+++	++	++++
Mn-PINH	+++	+++	++	++

Note: ++++ = very high activity, +++ = high activity, ++ = moderate activity, + = some activity

CONCLUSION

The ligand 2-phenylbut-2-enal isonicotinoyl hyrazone (PINH) was successfully synthesized. It formed complexes with Co(II), Cu(II),Mn(II) and Zn(II) nitrates. The ligand acted as neutral bidentate donor, coordinating via the carbonyl oxygen and the azomethine nitrogen. Metal-ligand complexes all show 1:2 molar ratios on complexation. Octahedral geometry is suggested for all the synthesized Co(II), Cu(II), Mn(II) and Zn(II) complexes. The anions (nitrate ions) appear to be in the outer coordination sphere of the complexes.

Generally, the ligand and complexes showed fairly comparable behaviour towards the test organisms. PINH have considerable good antibacterial activity and the antibacterial properties of the ligand were enhanced on coordination with transition metal (II) ions.

On the basis of their physicochemical properties, the structure proposed for the complexes is presented in Fig 2.

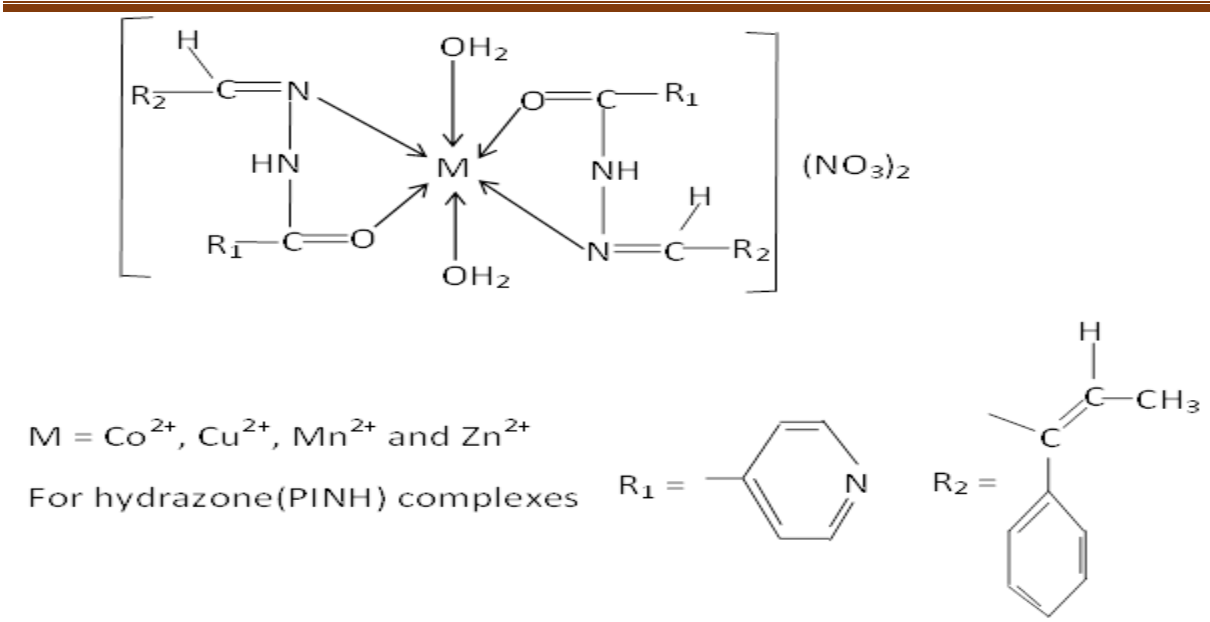

Figure 2: Proposed structure for the hydrazone(PINH) metal (II) complexes

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