

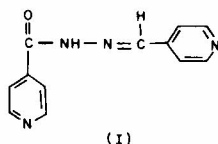
## Synthesis, Characterization & Antibacterial Studies of Iron(II), Cobalt(II), Nickel(II), Copper(II) & Zinc(II) Complexes of Pyridine-4-carboxaldehyde Isonicotinoyl Hydrazone

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Pyridine-4-carboxaldehyde isonicotinoyl hydrazone (4-PINH) forms complexes of the types  $M(4-PINH)X_2$  [ $X = Cl, Br$  and  $M(II) = Fe, Co, Ni, Cu$  &  $Zn$ ],  $M(4-PINH)SO_4 \cdot 2H_2O$  [ $M(II) = Fe, Co, Ni$ ],  $M(4-PINH)_2(NCS)_2$  [ $M(II) = Co, Ni$ ] and  $M(4-PINH)_2 \cdot nH_2O$  [ $PIN =$  deprotonated ligand,  $n = 2$  for  $Co(II)$  &  $Ni(II)$  and  $n = 0$  for  $Cu(II)$  &  $Zn(II)$ ]. Magnetic and electronic spectral studies suggest octahedral geometry for  $Fe(II)$ ,  $Co(II)$ ,  $Ni(II)$  and  $Cu(II)$  complexes except for  $Cu(4-PIN)_2$ , which is square-planar. ESR studies of  $Cu(II)$  complexes show that  $Cu(4-PINH)Cl_2$  is dimeric or polymeric in nature, and the unpaired electron is present in the  $d_{x^2-y^2}$  orbital of  $Cu(II)$ .  $^1H$  NMR and infrared spectral studies suggest uninegative bidentate behaviour of the ligand in the  $M(4-PIN)_2 \cdot nH_2O$  complexes and neutral bidentate behaviour in rest of the complexes. The bonding sites are the carbonyl/enolic oxygen and azomethine nitrogen. The ligand and its  $Co(II)$ ,  $Ni(II)$  and  $Zn(II)$  complexes show good antibacterial activity against *Klebsiella pneumoniae*, *E. coli* and *Staphylococcus aureus*.

Hydrazones derived from the condensation of isonicotinic acid hydrazide (INH) with pyridine aldehydes have been found to show better antitubercular activity than INH<sup>1</sup>. Although 3d-metal complexes of pyridine carboxylic acid hydrazides and their hydrazone derivatives with acetone<sup>2-4</sup> and salicylaldehyde<sup>5</sup> have been reported, no work has appeared on the complexes of the biologically active ligands obtained from the condensation of pyridine carboxylic acid hydrazides with pyridine carboxaldehydes. Further, these ligands are expected to exhibit variable bonding and stereochemical behaviour in their complexes because of the presence of as many as five potential donor sites and the possibility of keto-enol tautomerism. The present paper describes the results of our investigation on the complexes of pyridine-4-carboxaldehyde isonicotinoyl hydrazone (4-PINH, I).



### Materials and Methods

All the chemicals used were BDH reagents or reagents of equivalent purity. INH was obtained from M/s Sigma Chem. Co., U.S.A. Pyridine-4-carboxaldehyde was prepared by the literature method<sup>6</sup>. Pyridine-4-carboxaldehyde isonicotinoyl hydrazone was obtained by the condensation of INH with pyridine-4-carboxaldehyde, as reported in literature, m.p. 231° (lit.<sup>7</sup> 232°).

Compounds of the type  $M(4-PINH)X_2$  ( $X = Cl, Br, 1/2 SO_4$ ) and  $M(4-PINH)_2(NCS)_2$  were prepared by mixing the ethanolic solution of the respective metal(II) salt and the ligand in the 1:1 molar ratio. Complexes of the type  $M(4-PIN)_2 \cdot nH_2O$  were prepared by mixing an aqueous ethanolic solution of the metal(II) acetate and the ligand in 1:2 molar ratio followed by the addition of requisite amount of sodium acetate. Zinc-doped copper(II) complexes were prepared just like the respective pure copper(II) complexes employing 5:95 molar ratio of  $Cu(II)$  and  $Zn(II)$  chlorides/acetates. All the complexes, which precipitated immediately or on stirring the reaction mixture for sometimes, were digested on a water-bath for ~30 min, cooled, suction filtered, washed with hot ethanol and dried *in vacuo*.

The complexes were analysed for their metal, anion, nitrogen and hydrazine contents employing standard literature procedures<sup>8</sup>. The metal analyses were done after destroying the organic matter at first with aqua-regia and then with conc.  $H_2SO_4$ . Nitrogen was estimated by microanalysis.

The methods and apparatus employed for studying molar conductance, magnetic susceptibility, electronic and infrared spectra and the procedures for calculating the ligand-field parameters were the same as described elsewhere<sup>9</sup>.

ESR spectra of  $[Cu(4-PINH)Cl_2]$  and  $[Cu(4-PIN)_2]$  doped in the diamagnetic host lattice of  $[Zn(4-PINH)Cl_2]$  and  $[Zn(4-PIN)_2]$ , respectively, were recorded at 77 K on a Varian E-12 Spectrometer using TCNE ( $g = 2.00277$ ) as the standard.  $^1H$  NMR spectra of 4-PINH and  $Zn(4-PIN)_2$  were recorded in  $DMSO(d_6)$  on a Bruker NH-270 FT NMR Spectrometer.

The antimicrobial action of the compounds under investigation was studied *in vitro* against three bacteria species, viz., *Klebsiella aerogenes*, *Escherichia coli* and *Staphylococcus aureus* in DMSO at 10, 5 and 1 mg/ml by paper-disc method using peptone-water for making inoculum (~24 hr culture). Nutrient broth agar was used for testing the bacteria.

### Results and Discussion

The analytical data (Table 1) show that 4-PINH yields two types of complexes: (i)  $M(4\text{-PINH})X_2$  ( $X = \text{Cl, Br, } 1/2 \text{ SO}_4$ ) and  $M(4\text{-PINH})_2(\text{NCS})_2$  where it acts as a neutral ligand, and (ii)  $M(4\text{-PIN})_2 \cdot n\text{H}_2\text{O}$  where it acts in a deprotonated form. The former type of complexes are formed at pH 3-4 while the latter type result at pH 6-7, by the loss of one proton from the ligand in presence of a base. The complexes do not melt upto 300°C except a few which melt with decomposition in the range 200-300 °C. All the complexes are insoluble in water except  $\text{Co}(4\text{-PINH})\text{Br}_2$ , a few are slightly soluble in ethanol and

methanol and most of the halide, thiocyanate and  $M(4\text{-PIN})_2 \cdot n\text{H}_2\text{O}$  complexes are soluble in DMF and DMSO. Molar conductance values of the soluble complexes in DMF show that the Co(II) and Zn(II) chloride complexes are non-electrolytes.  $\text{Co}(4\text{-PINH})\text{Br}_2$  and Co(II) and Ni(II) thiocyanate complexes show molar conductivities which are lower than that required for the 1:1 electrolytic<sup>10</sup> behaviour but indicate some ionic dissociation in DMF as shown below:



The corrected magnetic moments of Co(II) and Ni(II) complexes and  $\text{Fe}(4\text{-PINH})\text{SO}_4 \cdot 2\text{H}_2\text{O}$  indicate that they are spin-free octahedral complexes. The subnormal magnetic moment of  $\text{Fe}(4\text{-PINH})\text{Cl}_2$  may be due to metal-metal interaction. The magnetic moments of Cu(II) complexes are normal and correspond to the presence of one unpaired electron without giving specific information about their stereochemistry.

Table 1—Characterization Data of Pyridine-4-carboxaldehyde Isonicotinoyl Hydrazone Complexes

Compound	Colour (m.p., °C)	Found (Calc.), %				$\mu_{eff}$ (B.M.)	$\Lambda_M$ (mhos cm <sup>2</sup> mol <sup>-1</sup> )
		Metal	Anion	N	Hydrazine		
$\text{Fe}(4\text{-PINH})\text{Cl}_2$	Chocolate (> 300)	15.35 (15.70)	19.56 (20.13)	15.80 (15.90)	—	4.34	—
$\text{Co}(4\text{-PINH})\text{Cl}_2$	Yellowish-green (> 300)	16.25 (16.56)	19.50 (19.95)	15.45 (15.73)	8.95 (8.99)	4.80	30.35
$\text{Ni}(4\text{-PINH})\text{Cl}_2$	Green (> 300)	16.20 (16.51)	19.75 (19.94)	15.54 (15.76)	8.95 (9.00)	2.92	—
$\text{Cu}(4\text{-PINH})\text{Cl}_2$	Green (~ 267)	17.50 (17.64)	19.23 (19.66)	15.40 (15.53)	—	1.72	—
$\text{Zn}(4\text{-PINH})\text{Cl}_2$	Yellow (> 300)	17.95 (18.04)	19.55 (19.56)	15.25 (15.45)	8.75 (8.83)	diamagnetic	18.30
$\text{Co}(4\text{-PINH})\text{Br}_2$	Light-yellow (> 300)	13.17 (13.25)	35.50 (35.93)	12.43 (12.59)	7.05 (7.19)	5.23	42.07
$\text{Ni}(4\text{-PINH})\text{Br}_2$	Yellow (> 300)	13.15 (13.20)	35.45 (35.96)	12.55 (12.60)	7.15 (7.20)	3.22	—
$\text{Co}(4\text{-PINH})_2(\text{NCS})_2$	Light-yellow (~ 244)	9.25 (9.40)	18.45 (18.50)	22.05 (22.33)	10.16 (10.21)	5.03	53.37
$\text{Ni}(4\text{-PINH})_2(\text{NCS})_2$	Green (> 300)	9.10 (9.37)	18.40 (18.51)	22.39 (22.34)	10.16 (10.21)	2.63	45.12
$\text{Fe}(4\text{-PINH})\text{SO}_4 \cdot 2\text{H}_2\text{O}$	Brick-red (> 300)	13.12 (13.39)	23.26 (23.23)	13.52 (13.52)	—	4.98	—
$\text{Co}(4\text{-PINH})\text{SO}_4 \cdot 2\text{H}_2\text{O}$	Light-pink (> 300)	14.10 (14.14)	22.95 (23.03)	13.25 (13.43)	7.56 (7.67)	4.37	—
$\text{Ni}(4\text{-PINH})\text{SO}_4 \cdot 2\text{H}_2\text{O}$	Light-green (> 300)	13.85 (14.09)	23.75 (23.04)	13.35 (13.44)	7.45 (7.68)	2.98	—
$\text{Co}(4\text{-PIN})_2 \cdot 2\text{H}_2\text{O}$	Golden-yellow (> 300)	10.58 (10.82)	—	20.15 (20.55)	11.50 (11.74)	4.18	—
$\text{Ni}(4\text{-PIN})_2 \cdot 2\text{H}_2\text{O}$	Yellow (> 300)	10.68 (10.77)	—	20.25 (20.56)	11.45 (11.75)	2.84	—
$\text{Cu}(4\text{-PIN})_2$	Green (~ 220)	12.15 (12.38)	—	21.50 (21.81)	—	2.02	—
$\text{Zn}(4\text{-PIN})_2$	Yellow (> 300)	12.25 (12.69)	—	21.55 (21.73)	11.75 (12.42)	diamagnetic	—

[Fe(4-PINH)Cl<sub>2</sub>] and [Fe(4-PINH)SO<sub>4</sub>·2H<sub>2</sub>O] yield one broad band at 10530 and 9750 cm<sup>-1</sup>, respectively, which may be assigned to <sup>5</sup>T<sub>2g</sub>→<sup>5</sup>E<sub>g</sub>(D) transition in an octahedral geometry around Fe(II)<sup>11</sup>.

The spectra of all the cobalt(II) complexes show two bands in the regions 8160-9350 and 17390-19050 cm<sup>-1</sup> which may be assigned to <sup>4</sup>T<sub>1g</sub>(F)→<sup>4</sup>T<sub>2g</sub>(F)(ν<sub>1</sub>); →<sup>4</sup>T<sub>1g</sub>(P)(ν<sub>3</sub>) transitions, respectively, in an octahedral environment around Co(II)<sup>12</sup>.

Ni(II) complexes exhibit two bands in the regions 8475-10200 and 14080-16000 cm<sup>-1</sup> attributable to <sup>3</sup>A<sub>2g</sub>(F)→<sup>3</sup>T<sub>2g</sub>(F)(ν<sub>1</sub>) and <sup>3</sup>A<sub>2g</sub>(F)→<sup>3</sup>T<sub>1g</sub>(F)(ν<sub>2</sub>) transitions, respectively, in an octahedral geometry around Ni(II)<sup>13</sup> (Table 2).

The spectrum of Cu(4-PIN)<sub>2</sub> shows a broad band at 15380 cm<sup>-1</sup> while that of Cu(4-PINH)Cl<sub>2</sub> yields two bands at 10810 and 12700 cm<sup>-1</sup>. The above spectral features suggest a square-planar geometry<sup>14,15</sup> for the former complex and a distorted octahedral geometry for the latter<sup>16</sup>.

The high energy band occurring in the region 21740-27780 cm<sup>-1</sup> in these complexes may be assigned to a charge-transfer or intra-ligand transition.

ESR spectrum of Cu(4-PIN)<sub>2</sub> at 77 K shows a high field transition around 3200 g (ΔMS=1) with the parallel, perpendicular and average g values of 2.18, 2.05 and 2.09, respectively, while the spectrum of Cu(4-PINH)Cl<sub>2</sub> shows a half-field signal around 1500 G (ΔMS=2) with g=4.17. The 77 K spectrum of this compound shows somewhat improved resolution as compared to the 300 K spectrum. The presence of half-field signal around 1500 g shows the dimeric or polymeric nature of Cu(4-PINH)Cl<sub>2</sub><sup>17</sup>. The trend g<sub>||</sub> > g<sub>⊥</sub> > g<sub>e</sub> (free-ion value) shows that the unpaired electron is in the d<sub>x<sup>2</sup>-y<sup>2</sup></sub> orbital of Cu(II).

<sup>1</sup>H NMR spectrum of 4-pyridine carboxaldehyde isonicotinoyl hydrazone in DMSO (d<sub>6</sub>) shows signals at δ 8.12 ppm for -CH=N proton, at δ 7.86 ppm for -NH proton, and two quartets at δ 8.47-8.83 ppm and 7.47-7.84 ppm for the two pyridine ring protons.

In the spectrum of Zn(4-PIN)<sub>2</sub>, the signal due to -CH=N proton shows down-field shift and appears at δ 8.49 ppm indicating coordination through azomethine nitrogen. The signals due to pyridine ring protons occur as quartets at δ 8.71-8.82 ppm and δ 7.56-8.12 ppm, respectively<sup>18</sup>. The disappearance of signal due to -NH proton shows the removal of this proton via enolisation.

The infrared spectrum of 4-PINH in nujol and KBr shows a band at 3190 cm<sup>-1</sup> assigned to ν(N-H) which remains practically unchanged in the spectra of the complexes of type (i) and disappears in the spectra of complexes (ii). This indicates that imino nitrogen is not involved in bonding in the complexes (i) while the proton of this group is involved in enolization and is subsequently deprotonated on coordination to the metal ions in the latter type of complexes (type ii).

The bands occurring at 1680 and 1270 cm<sup>-1</sup> may be attributed to amide-I (νC=O) and amide-III modes, respectively. The corresponding bands in the spectra of all the adducts are observed in the regions 1630-1670 and 1275-1285 cm<sup>-1</sup>, respectively. A negative shift in amide-I (νC=O) and a positive shift in amide-III bands indicate coordination through carbonyl oxygen<sup>19</sup>.

In the spectra of the complexes of type (ii), the disappearance of ν(C=O) and appearance of a new band due to ν(NCO) at ~1500 cm<sup>-1</sup> confirm the enolisation of the keto group and its deprotonation on complex formation. Further, the spectra of these

Table 2—Electronic Spectral Data and Ligand-field Parameters of Pyridine-4-carboxaldehyde Isonicotinoyl Hydrazone Complexes

Complex	λ <sub>max</sub> (cm <sup>-1</sup> )	D <sub>q</sub> (cm <sup>-1</sup> )	B (cm <sup>-1</sup> )	β	β° (%)	LFSE (kJ/mol)
Fe(4-PINH)Cl <sub>2</sub>	10530	1053	—	—	—	50.39
Fe(4-PINH)SO <sub>4</sub> ·2H <sub>2</sub> O	9750	975	—	—	—	46.16
Co(4-PINH)Cl <sub>2</sub>	8700,20000	978	823	0.85	16	93.58
Co(4-PINH)Br <sub>2</sub>	8300,19000,23800	963	770	0.79	21	92.17
Co(4-PINH)SO <sub>4</sub> ·2H <sub>2</sub> O	8330,19050,25000	946	788	0.81	19	90.53
Co(4-PINH)(NCS) <sub>2</sub>	8160,17390,22220	922	683	0.70	30	88.24
Co(4-PIN) <sub>2</sub> ·2H <sub>2</sub> O	9350,18180,22730	1015	646	0.66	34	97.14
Ni(4-PINH)Cl <sub>2</sub>	8930,14930,22220	893	1021	0.96	4	128.2
Ni(4-PINH)Br <sub>2</sub>	8475,14080	848	916	0.86	14	121.7
Ni(4-PINH)SO <sub>4</sub> ·2H <sub>2</sub> O	9430,15620,27780	943	993	0.94	6	135.4
Ni(4-PINH) <sub>2</sub> (NCS) <sub>2</sub>	10000,16000,23260	1000	800	0.76	24	143.5
Ni(4-PIN) <sub>2</sub> ·2H <sub>2</sub> O	10200	1020	—	—	—	146.4
Cu(4-PINH)Cl <sub>2</sub>	10810,12900,21740	1290	—	—	—	92.58
Cu(4-PIN) <sub>2</sub>	15380,22990	1538	—	—	—	110.4

complexes show a negative shift of 20-30  $\text{cm}^{-1}$  in  $\nu(\text{C}=\text{N})$  and a positive shift of 5-15  $\text{cm}^{-1}$  in  $\nu(\text{N}-\text{N})$  modes indicating coordination through azomethine nitrogen. The pyridine ring vibrations remain practically unaltered indicating non-involvement of pyridine nitrogen in the complexes. The infrared spectral studies thus show neutral and uninegative bidentate behaviour of the ligand in complexes of types (i) and (ii), respectively. The bonding sites are azomethine nitrogen and carbonyl or enolic oxygen. The spectra of the chloro complexes show two split bands at  $\sim 175$  and  $\sim 190 \text{ cm}^{-1}$ , characteristic of bridged chlorine<sup>20</sup>. In the thiocyanate complexes, an intense band occurs at  $\sim 2080 \text{ cm}^{-1}$  due to  $\nu(\text{C}\equiv\text{N})$ ; a sharp band at  $\sim 480 \text{ cm}^{-1}$  and a weak band around  $780 \text{ cm}^{-1}$  corresponding to  $\delta(\text{NCS})$  and  $\nu(\text{C}-\text{S})$  modes, respectively showing that the thiocyanate is N-bonded in the complexes<sup>21</sup>.

In the spectra of  $[\text{Co}(4\text{-PINH})\text{SO}_4 \cdot 2\text{H}_2\text{O}]$  and  $[\text{Ni}(4\text{-PINH})\text{SO}_4 \cdot 2\text{H}_2\text{O}]$ ,  $\nu_1$  mode of the sulphate group appears as a medium intensity band at  $971 \text{ cm}^{-1}$  while  $\nu_3$  mode splits into three bands appearing around 1160, 1095 and  $1050 \text{ cm}^{-1}$  suggesting that the symmetry of the sulphate group is lowered and probably reduced to  $\text{C}_{2v}$ . Thus, the sulphate group in these complexes behaves as a bridging bidentate<sup>22</sup> moiety.

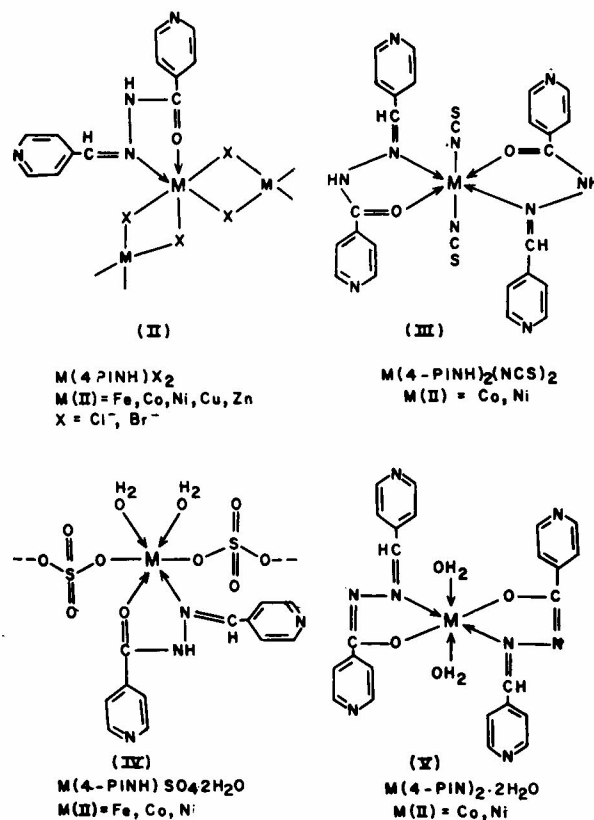
The infrared spectra of the hydrated complexes contain a broad band in the range 3350-3420 and a weak band in the range 680-700  $\text{cm}^{-1}$  assignable to  $\nu(\text{OH})$  and  $\rho_r(\text{H}_2\text{O})$  modes of coordinated water<sup>21</sup>, which are absent in the anhydrous complexes. The non-ligand bands occurring in the ranges 290-300 and 325-330  $\text{cm}^{-1}$  are tentatively assigned to  $\nu(\text{M}-\text{O})$  and  $\nu(\text{M}-\text{N})$  modes, respectively<sup>23</sup>.

Based on the analytical data and physicochemical studies discussed above, the structures of the complexes may be represented by II-V.

#### Antibacterial activity

The results of the study on antibacterial activity show almost complete inhibition of bacterial growth at all the three concentrations of the compounds. Pyridine-4-carboxaldehyde isonicotinoyl hydrazone (4-PINH) and  $\text{Ni}(4\text{-PINH})_2(\text{NCS})_2$  show good antibacterial activity against all the three bacteria at all the concentrations, while  $\text{Zn}(4\text{-PINH})\text{Cl}_2$  shows good inhibition only at two concentrations i.e., 5 and 1 mg/ml but no inhibition at higher concentration i.e., 10 mg/ml.  $\text{Co}(4\text{-PINH})_2(\text{NCS})_2$  shows inhibition against *Klebsiella pneumoniae* and *E. coli* and no inhibition against *Staphylococcus aureus* at all the concentrations<sup>24</sup>.

Thus, the results indicate that the ligand and its Ni(II) and Co(II) complexes show better inhibitory



effects as compared to zinc(II) complex, against all the bacteria tested and at all the concentrations used.

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