

Synthesis, Characterization and Antimicrobial Activity of Transition Metal Complexes of Hydrozone of Isonicotinic Acid Hydrazone

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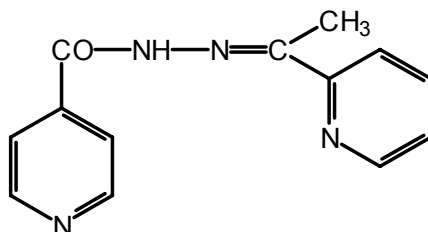
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The transition metal complexes of hydrazone of isonicotinic acid hydrazone, viz., 1NH-AP of the type M-3(1NH-AP) (M = Mn, Fe, Co, Ni, Cu and Zn) have been synthesized and characterized by infrared and magnetic susceptibility measurements and probable structures assigned to them.

Key Words: Isonicotinic acid hydrazone, 2-Acetyl pyridine, Schiff base, IR data.

INTRODUCTION

Derivatives of isonicotinic acid (isoniacin) and its hydrazone (isoniazid) are well known for their high specific antitubercular activity, but their metal complexes have not attracted much attention. The coordination chemistry of isoniazid has been reported by Cymerman-Craig *et al.*¹. Some complexes of transition metals with Schiff bases derived from this hydrazone have been mentioned in the literature²⁻⁴. The coordination compounds of aroylhydrazones have been reported to act as enzyme inhibitors¹ and are useful due to their pharmacological applications⁵⁻⁷. In view of the increasing interest in hydrazones, on account of the structural, analytical and pharmacological importance of their metal complexes, the synthesis of hydrazone (1NH-AP) (**I**) and its metal complexes are reported.



(I) (1NH-AP)

EXPERIMENTAL

All the chemicals used were of either BDH or NICE. Solvents and the metal salts were used without further purification.

Isonicotinic acid hydrazide (1 mmol) and 2-acetyl pyridine (1 mmol) were refluxed together for 3 h in the presence of a drop of conc. HCl. The volume of the mixture was reduced to half. It was then cooled in a refrigerator, when light yellow crystals separated. It was filtered, washed several times with cold ethanol and finally dried.

Preparation of the complexes: The complexes were prepared by two methods. (i) By reacting stoichiometric amounts of the Schiff base and the metal salts. (ii) By carrying out the *in situ* reaction of amine, 2-acetyl pyridine and the metal salts. However, in both the cases, complexes of the same stoichiometry were isolated. We have adopted the *in situ* reaction in the present investigation as exemplified below.

Isonicotinic acid hydrazide (1 mmol) and 2-acetyl pyridine (1 mmol) were taken together in ethanol (30 mL) and refluxed for 0.5 h after which manganese sulphate (1 mmol) in ethanol was added and reflux continued for another 3 h. Upon cooling, microcrystalline manganese complex precipitated. It was filtered, washed thoroughly with ethanol and dried. All other complexes were prepared in an identical manner.

The IR spectra in KBr pellets were recorded on a Perkin Elmer spectrophotometer. Magnetic susceptibility was measured by Gouy method.

Antimicrobial activity of the ligand and its complexes: The main characteristics of the medium were to support the growth of the organisms normally tested and not contain antagonist of antimicrobial activity. The medium must allow free diffusion of plant extract from the well.

The sterilized medium was poured into a Petri dish in a uniform thickness and kept aside for solidification. Using sterilized swabs, even distribution of lawn culture was prepared using bacteria and fungi chosen in Muller Hinton Agar (MHA) plates and Sabouraud's dextrose (SDA) agar, respectively.

Well method: Mueller Hinton agar (MHA) and Sabouraud's dextrose (SDA) agar were prepared with lawn culture using desired test organisms. The inoculated plates were kept aside for few minutes. Using well cutter 2 wells are made in those plates at required distance. In each step of well cutting, the well cutter was thoroughly wiped with alcohol. Using sterilized micropipette, 20 μ L of compound extract was added in to one well and in another well the same volume of corresponding controls (solvent without chemical extract) were added.

After diffusion, the plates were incubated at 37 °C for 24 h. After incubation, the inhibition of growth was analyzed and results were recorded.

RESULTS AND DISCUSSION

The reaction of non-aqueous solutions of metal salts with 1NH-AP resulted in the formation of complexes of the composition M-3L (L = 1NH-AP; M = Mn, Fe, Co, Ni, Cu and Zn). The complexes are highly stable under laboratory conditions and can be stored for a long time in a desiccator. They are coloured solid and have high melting point.

The ligand is expected to be tridentate, the possible coordination sites being the pyridine-nitrogen, the azomethine-nitrogen and the amide group. A study and comparison of the IR spectra of the ligand and its complexes imply that the ligand is bidentate with carbonyl-oxygen and exocyclic azomethine nitrogen as the two coordination sites.

The NH stretching absorption of free ligand occurs at 3465 cm^{-1} which has undergone shift to lower wave number suggesting⁸⁻¹¹ the coordination through the imine nitrogen is absent in the complex. The ligand band due to $\nu(\text{C=O})$ undergo a shift to lower frequency region suggesting^{11,12} coordination of the carbonyl oxygen in the complex. The band due to $\nu(\text{C=N})$ mode also undergo a shift to lower frequency and is observed as a strong peak in the region 1548 cm^{-1} suggesting^{8,11-13} participation of exocyclic azomethine nitrogen in the complex formation. All other complexes exhibit an identical pattern suggesting them to be isostructural (Table-1).

TABLE-1
IR DATA (cm^{-1}) OF THE LIGAND AND ITS COMPLEXES

Ligand	Complex						Assign- ment	Ref.
	Mn(II)	Fe(II)	Co(II)	Ni(II)	Cu(II)	Zn(II)		
3465	3421	3401	3401	3437	3421	3437	$\nu(\text{N-H})$	8-11
1670	1634	1636	1638	1631	1637	1634	$\nu(\text{C=O})$	11,12
1575	1548	1562	1537	1532	1537	1530	$\nu(\text{C=N})$	8,11-13

The magnetic moments of the present complexes at room temperature have been calculated^{12,14,15} and the values are given in Table-2 and expected for six coordinated spin free species.

TABLE-2
MAGNETIC MOMENT DATA OF COMPLEXES

Magnetic moment value (BM)	Found (Theo.)						
	Mn(II)	Fe(II)	Co(II)	Ni(II)	Cu(II)	Zn(II)	
μ_{eff}	5.3 (5.9)	4.08 (5.1-5.5)	4.19 (4.1-5.2)	2.96 (2.8-4.0)	1.71 (1.7-2.2)		Diamag.

Antimicrobial activity: The complexes have been screened as possible fungitoxides and bacteria. The susceptibility of a certain bacterial and fungal strains towards an antibacterial and antifungal drug can be measuring the diameter shows all the complexes are high sensitive against bacteria and fungal pathogen chosen. The results are summarized in Table-3.

TABLE-3
ANTIMICROBIAL ACTIVITY DATA OF LIGAND AND ITS COMPLEXES

Name of the organism	Zone of inhibition (mm)						Ligand
	Mn(II)	Fe(II)	Co(II)	Ni(II)	Cu(II)	Zn(II)	
<i>Staphylococcus epidermidis</i>	15	6	20	20	12	15	9
<i>Shigella sonnei</i>	22	14	11	11	15	21	15
<i>Salmonella typhi</i>	23	20	15	15	18	23	22
<i>Pseudomonas aeruginosa</i>	17	15	18	15	20	17	23
<i>Candida Krusei</i>	19	22	13	22	18	19	17
<i>Candida parapsilopsis</i>	15	24	12	23	14	15	19
<i>Aspergillus flavus</i>	6	17	11	17	8	14	11
<i>Penicillium notatum</i>	8	19	20	19	8	18	11

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