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3-Chlorobenzalaldehyde Isonicotinic Acid Hydrazone Evaluate the Biological Activity of Transition Metal Complexes and Schiff Bases with Ligands

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ABSTRACT

In present paper, synthesis and spectral characterization of Schiff base complexes of 3-chlorobenzaldehyde isonicotinic acid hydrazone with a series of transition metal complexes of Ti (III), V(III), Mn(III), Ru(III), Co(II), Ni(II), Zn(II), Cd(II) etc., have been done. Pure powered form of the complexes have been suitably synthesized and isolated in the study. The values of molar conductance suggest their 1:1 electrolyte nature.

Keywords: IR spectra, Isonicotinic acid, Hydrazone, Antimicrobial activity, Schiff bases

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INTRODUCTION

Hydrazones belongs to Schiff base compounds family with the structure $R_2C{=}NR_2$. Schiff base is similar to an aldehyde or ketone in which C=O group is replaced by C=N-R group. This Schiff base is prepared by the process of condensation of an aldehyde or ketone with a primary amine according to the Eqn. 1.

$$ {}^{R\setminus}_{R/}C = O + R'NH_2 \rightarrow {}^{R\setminus}_{R/}C = N - R' + H_2O \qquad (1)$$

In Eqn. 1, R stands for an alkyl or an aryl group. Shiff base may be prepared with either aryl or alkyl substituent. Schiff bases having aryl substituent are substantially more stable and more readily synthesized compare to the Schiff bases having alkyl substituent that are relatively unstable. As a result, Schiff bases of aliphatic aldehydes are relatively unstable and readily polymerizable 1,2 and Schiff bases of aromatic aldehydes are relatively more stable with its effective conjugation. The Schiff base has prepared with the help of an aldehydes or ketones by the reversible reaction in presence of either acid/base catalysis or upon heating. The process continues to its final stage and assumed to be complete after the separation of either product or removal of water or both together. With the reaction of aqueous acid or base, many Schiff bases can be hydrolyzed back to their aldehydes or ketones and amines. The reaction of aldehydes and ketones with ammonia or 1° amines forms amine derivatives also known as Schiff bases (compounds having a C=N function). Eqn. 2 represents the chemical formation of a Schiff base by the condensation process of hydrazine with aldehydes or ketones as shown in Eqn. 2.

$$ {}^{R\setminus}_{R/}C = O + H_2N - NH_2 \rightarrow {}^{R\setminus}_{R'/}C = N - NH_2 + H_2O \qquad (2)$$

Hydrazone

In Pal [1], it has been mentioned that hydrazones derived from condensation of isoniazid with pyridine aldehyde & ketones show better antitubercular activity rather than isonicotinic hydrazone and this is because of its ability to form stable complexes with d and f block metal ions [2-4]. Hydrazones based studies have a significant interest from the past because of its dependence on their mode of chelation and transition metal ions present in the living system [5,6]. The Schiff bases compounds of aroylhydrazones have been synthesized to act as enzyme inhibitors and are useful due to their pharmacological activities [7].

Biological activities of many of these compounds were shown to be related to their metal chelating abilities in the past [8]. The available papers support the facts that Schiff base complexes have a significant role for the development of co-ordination chemistry [9]. It is also reported in different studies that certain Schiff bases exhibit anti-tubercular activities [10]. More experimental work is still needed to be done regarding ligand bonding molecular structure and the thermal behaviors of these compounds so as to have a better understanding of the subject.

MATERIALS AND METHODS

Elemental analyses have been done with these complexes and the metal has been estimated gravimetrically. The molar conductance of the complexes was measured at 10^{-3} dilution in DMSO/methanol or both dilutions at 25°C indicate its 1:2 electrolytic nature. The magnetic properties of the complexes, infrared and visible spectra were recorded [11]. The complexes also subjected to the thermo gravimetric analyses. The colors of complexes were observed and their melting point was estimated [12]. Elemental analyses were performed on a Perkin-Elmer-24°C model at the Central Drug Research Institute (CDRI), Lucknow. The Infra-red studies of the complexes were recorded with Perkin Elmer spectrophotometer model 651 in KBr or Nujol phase from 4000-250 cm^{-1} at R.S.I.C, CRDI, and Lucknow. Conductivity measurements were completed by Philips at Chemistry Department of Bareilly College, Bareilly affiliated with MJP Rohilkhand University, Bareilly. The complex conductance was measured with in methanol and DMSO. The magnetic susceptibility was determined by Gouy's method using $CuSO_4.5H_2O$ as calibrant. Beckmann-DU spectrometer is used for recording electronic spectra of the complexes. In the present work, analytical grade chemicals have been taken. The elemental analysis was carried out at CDRI, Lucknow. Perkin Elmer spectrophotometer model 651 in KBr or Nujol phase available at RSIC, CDRI, and Lucknow is used to record IR spectra of the complexes. A Stahl type applicator was used for coating adsorbent on glass plates (20 × 20 cm^2). Glass chambers (12 × 24 × 24 cm^2) were used for development and the plates were dried in electric air driver. The adsorbent used was silica gel G of B.D.H grade.

Synthesis of ligand

Isonicotinic acid hydrazide (10 g) was dissolved in 100 ml of distilled water and was mixed with 100 ml of methanol in which s-chlorobenzaldehyde (9 g) was dissolved in a 500 ml Round Bottom Flask (RBF). A few drops of 10% NaOH solution were added to the mixture as a catalyst and the flask was shaken vigorously. The hydrazone, formed as shown in Figure 1, was filtered off and dried. It was then recrystallized from methanol.

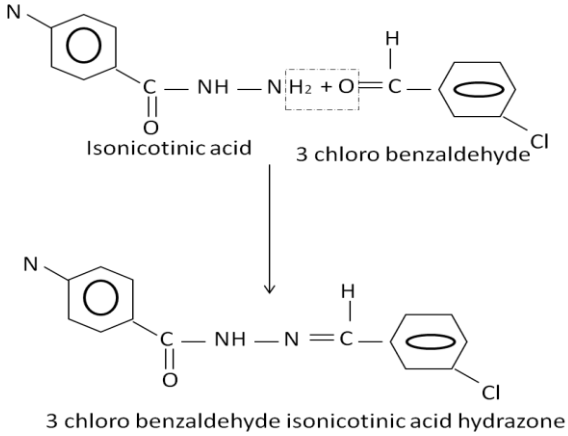

Figure 1: Formation of ligand

Characterization of ligand

The molecular composition of ligand is investigated wit Nujol the help of elemental analyses of carbon, hydrogen and nitrogen (C, H and N). IR spectra of the ligand were recorded in KBr phase. The melting point of the ligand was determined by open capillary method & uncorrected. Table 1 represents the detail about the ligand formed and shown in Figure 1.

Table 1: Ligand characterization detail

S. No.	Name and molecular formula of the ligands	Color	M.P/D.T	Elemental analyses					Solubility
				% of C	% of H	% of N	% of C	% of Cl	
1.	3-chloro benzaldehyde isonicotinic acid hydrazone (INH)	Colorless	171	60.00 (59.50)	3.80 (3.40)	16.00 (15.70)	6.10 (5.60)	13.68 (12.70)	DMSO

Synthesis of metal complexes

For preparing the metal complexes, solution of the ligand is added in appropriate solvent to form the solution of the respective metal. Titanium was prepared by dissolving in requisite amount of $TiOCl_2.8H_2O$ (B.D.H) in distilled water. Metal contents of solution were determined gravimetrically analysis. The preparation of all the complexes is done by using the available general method. The solution of the metal salt was added drop wise to the hot ethanolic solution of the ligand in the molar ratio of 2:1 with constant stirring when the complex was precipitate. The obtained coloured product was separated by filtration washed with distilled water and then with methanol. Finally it is dried under vacuum. The metal complexes are finally achieved by the Recrystallization of hot methanol [13,14].

Characterization of metal complex

The characterization of the metal complex formed is represented in Table 2.

Table 2: Characterization of metal complex

Name and molecular formula of complex	**3-Chlorobenzaldehyde isonicotinic acid hydrazone titanium (III) chloride ($[C_{13}H_{10}N_3OCl].2CH_3OH.TiCl_3$)**				
Colour	Orange				
M.P/D.T	235				
Elemental analyses	**% of C**	**% of H**	**% of N**	**% of M**	**% of O**
	45.62 (44.42)	3.80 (2.60)	11.40 (10.58)	6.38 (5.28)	24.10 (23.12)
Molar conductance	**Methanol**	**DMF**		**DMSO**	
	105	60		42	
Magnetic moments in B.M.	1.70				

Table 3: Antimicrobial activity of ligand and metal complex

S. No.	**Ligand/Complex**	**Antifungal activity zone of inhibition (mm)** ***Aspergillus awamori***
1	3- chloro benzaldehyde isonicotinic acid hydrazone	20
2	3-Chlorobenzaldehyde isonicotinic acid hydrazone Titanium (III) Chloride	14

RESULTS AND DISCUSSION

Results obtained from this paper may be summarized according to the following points as mentioned below:

Elemental analysis

The elemental analyses for C, H and N and the gravimetric estimation of the titanium metal give a formula of $[C_{13}H_{10}N_3OCl].2CH_3OH.TiCl_3$ to the complex. This shows that the ligand has reacted with the metal in 2:1 molar ratio. The difference in melting points of the ligand and its corresponding metal complex indicates the formation of the complex [15].

Molar conductance

The molar conductance values in DMF and DMSO at 10^{-3} M dilution at 25°C indicate its 1:3 electrolytic nature of the complex.

Magnetic properties

The measurement of magnetic properties gives a value of 1.70 B.M. for the magnetic moments of the complex [16]. This value is very close to that expected for Ti^{+3} (d^1 system).

Electronic spectra

The electronic spectra of the complex show band at 17880 cm^{-1} which may be assigned to d-d transition [17]. The value of d-d transition corresponds to crystal field splitting energy. The spectrum of the complex also show a weak band at 22727 cm^{-1} with a shoulder in the region of 1770 $cm^{-1.}$These bands have been assigned to $2B_{1g} \leftarrow 2B_{2g}$ and $2A_1 \leftarrow 2B_{2g}$ transitions respectively [18].

Infra-red (IR) spectroscopy

The I.R spectrum of the ligand shows important peaks at 3400 cm^{-1} and 1645 cm^{-1}, which may be assigned to N-H and C=O vibrations respectively. Another important band appears at 1600 cm^{-1} which may attributed to νC=N vibrations [19,20]. The 1,3-disubstitution pattern of phenyl nucleus is represented by the peak appearing at 775 $cm^{-1.}$ This data indicate that isonicotinic acid hydrazide has undergone condensation with 3-chlorobenzaldehyle. The peaks at 1645 and 1600 cm^{-1} have shifted to 1665 and 1620 cm^{-1} respectively in the I.R. spectrum of the complex. This indicates that the co-ordination has occurred through oxygen atom of C=O group and nitrogen atom of azomethine group. Thus the ligand is behaving in bidentate manner.

Co-ordination of water

The peaks observed in the spectrum of the metal complex at 2970 and 2890 cm^{-1} corresponding to the $-CH_3$ asymmetric and symmetric vibrations, it did not appear in the spectrum of the free ligand indicating co-ordination of the solvent molecules to the metal ion [21,22]. It appears, therefore that the complex has octahedral geometry. Out of six positions four are occupied by two bidentate ligand molecules and two by solvent molecules.

Antibacterial activity

The antibacterial activity of the Co(II), Ni(II), Zn(II) Ti(III) complexes were studied against *Escherichia coli, Aeromonas hydrophila, Salmonella typhi* and *Bacillus cereus* using a nutrient agar medium by disc diffusion method [23]. The sterilized (autoclaved at 121°C for 15 min) medium (40-55°C) was poured into the petri dishes to give a depth of 3-4 mm and allowed to solidify. The suspension of the micro-organism then streaked on plates. The plates were pre-incubated for that room temperature and incubated at 38°C for 24 h. The results of the antibacterial activity studies for the complexes and standard antibiotic tetracycline were evaluated by Muller Hinton agar diffusion method and serial dilution sensitivity test against [24] both Gram-positive and Gram-negative bacteria. DMSO solvent was also used as control. The variation in the effectiveness of different compounds against different organism depends either on impermeability of cells or the microbe of difference in ribosome of microbial cells [25]. Antimicrobial activity of ligand and metal complex are given in Table 3.

CONCLUSION

On the basis of above mentioned facts the complex appears to have octahedral geometry, three co-ordination sites are occupied by tridentate ligand molecule and the remaining three by water molecules. The structure of the complex may therefore, be represented as in Figure 2.

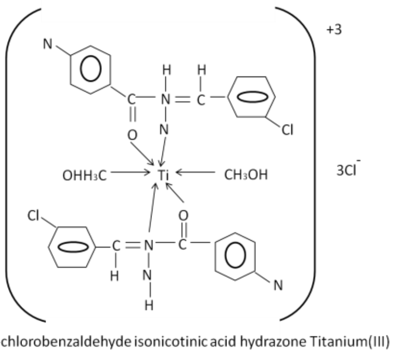

Figure 2: Proposed structure for prepared complex

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