Research Article

Synthesis, Characterisation and Antimicrobial Study of Cobalt (II) Complex of a Schiff Base Derived from Isonicotinic acid Hydrazide and 4-Chlorobenzaldehyde

Kumble Divya*, Gayathri B. H
Assistant Professor, Post Graduate Department of Chemistry, B.M.S College for women, Basavanagudi, Bengaluru, Karnataka, India.
***Corresponding author's E-mail:** kumbledivya71088@gmail.com

Received: 21-08-2020; **Revised:** 16-10-2020; **Accepted:** 28-10-2020; **Published on:** 15-11-2020.

ABSTRACT

New Schiff base ligand N'-[(4-chlorophenyl) methylidene] pyridine-4-carbohydrazide has been synthesized and complexed to Co(II) metal ion. The Schiff base ligand was synthesized by the condensation of Isonicotinoyl hydrazone with 4-chlorobenzaldehyde. The ligand and their metal complex is characterized by C, H, N analysis, IR spectra and UV-Vis for tentative structure proposal. The ligand is coordinated to Co(II) metal ion through the enolic oxygen and azomethine nitrogen resulting in a square planar geometry. The ligand and metal complex were studied for their antimicrobial activities against gram positive and gram-negative bacteria. The metal complex shows more potent activities compared with Schiff base ligand.

Keywords: Schiff Base, Metal – organic frame work, IR spectra, UV-Visible, Antimicrobial.

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DOI: 10.47583/ijpsrr.2020.v65i01.011

DOI link: http://dx.doi.org/10.47583/ijpsrr.2020.v65i01.011

INTRODUCTION

Synthesis of metal complexes attained increasing interest owing to their versatile coordination behaviour and in the understanding of molecular processes[1]. Metal complexes are of significant attention in terms of its structural and coordination chemistry. They display diverse chemical, optical and magnetic properties by tailoring with different ligands. In specific, the study of metal complexes of Schiff base (SB) ligands appears to be fascinating in terms of unusual structure and stability[2]. SB complexes are considered to be among the most important stereo chemical models in transition metal coordination chemistry due to their preparative accessibility, structural variability[3,4]. SB are condensation product of primary amines and carbonyl compounds. SB is an analogue of a ketone/ aldehyde in which the carbonyl group has been replaced by an azomethine group. SB are important intermediates for the synthesis of various bioactive compounds[5]. They show a variety of biological activities including antibacterial, antifungal, anti-cancer etc. Schiff base is an important intermediate in many enzymatic reactions[6].

Recently a great deal of interest have been developed in the synthesis and characterization of transition metal complexes containing SB as ligands due to their variety of applications in biological, clinical, analytical and industrial fields[7]. Among these, SB ligands and their metal complexes do have significant interest because of their pharmacological activities[8]. Furthermore, the enhanced biological activity of these complexes has extended much attention due to their possible applications as new therapeutic agents[9]. SB derived from an amino and carbonyl compound are an important class of ligands that coordinate to metal ions via azomethine nitrogen[10]. It was found in the literature that presence of C, N linkage in azomethine derivatives, was responsible for remarkable antibacterial, antifungal, anticancer and antimalarial activities[11].

Isonicotinoyl hydrazide (INH) is a first reported antituberculosis drug[12], synthesized from isonicotinic acid which is produced from 4- methylpyridine[13]. Hydrazide moiety present in the molecule of INH can readily undergo SB condensation with compounds containing carbonyl function to form their corresponding hydrazones. Literature survey documented for high bactericide and fungicide properties of INH based SB[14].

Thus, in the present work INH based SB is synthesized and complexed with cobalt. The coordination chemistry of cobalt has a considerable interest since cobalt complexes derived from SB are reported to be biologically active[15]. The cobalt SB complexes are also an important class of coordination compounds, not only because of their involvement in Vitamin B_{12} models and oxygen carrier properties, but also due to their interesting magnetic and spectroscopic as well as diverse binding ability[16]. A large number of reports on the antibacterial properties of cobalt complexes reported in the literature, presumably due to their aqueous stability, availability, and ease of synthesis[17].

Keeping the above facts in mind in our present work we have chosen to synthesize SB derived from INH and 4-chlorobenzaldehyde followed by its complexation with Co(II) metal. The ligand and its metal complexes were also screened for *in vitro* antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*. Studies show

that the metal complexes of SB ligand have better antimicrobial activities as compared to SB.

MATERIALS AND METHODS

All the reagents were used namely INH, 4-chlorobenzaldehyde, cobalt chloride, ethanol are of synthetic grade.

Elemental microanalysis of the compounds, C, H and N were performed using Shimadzu elemental vario EL III model elemental analyser. Melting points of the ligand and its complexes were recorded on an OMEGA melting point apparatus. The pH measurement was done on the Elico-16 pH meter. The IR spectra were obtained in a KBr disk using a BIO-RAD FTS 135 spectrometer, the UV-VIS spectra were recorded in PC based double beam spectrophotometer 2202 in N,N'-dimethylformamide (DMF) solution.

Synthesis of schiff base

The SB (ligand) was prepared by mixing a warm dilute ethanoic solution of INH (0.01M) with ethanoic solution of 4-chlorobenzaldehyde (0.01M) under reflux for 4-5 hours in a water bath. The clear solution was poured into cold water (500 ml) and the solid precipitated was then filtered, washed with cold water, dried and then recrystallized. The prepared compounds were checked for purity by TLC using glass plates percolated with silica gel 60 GF254 and suitable solvent system as mobile phase.

Synthesis of metal complex

The SB was taken in alcohol (0.02M, 50 cm^3) and stirred gently for one hour to give a homogeneous solution and then mixed with alcoholic solution of metal salt i.e., Cobalt (II) chloride (0.01M, 25 cm^3). The resulting solution was refluxed for 6–8 hrs. The mixture was concentrated to half of its initial volume and kept in a desiccator for two days over anhydrous $CaCl_2$. The complex was then filtered, washed with ethanol and dried. The complex was soluble in DMF but sparingly soluble in other common organic solvents and water.

Biological assay: preparation of nutrient broth

Nutrient broth gel was prepared to study antimicrobial activity of the synthesised compounds. Different concentrations of metal complex in a test tube (0.05, 0.1, 0.15, 0.2, and 0.25 M) were taken for gram positive and gram negative bacteria respectively. Nutrient broth gel was added to each test tube and covered with cotton plug. The solution is then kept in an autoclave about an hour and after autoclaving it is cooled at room temperature. By using Broth Dilution Method it was tested for gram positive bacteria *Staphylococcus aureus* and gram negative bacteria *Escherichia coli.* Added two drops of SB solution and complex solution to each test tube using pipette and stirred well before keeping it in BOD incubator. After 24 hours microbial growth was examined by comparing it with the control solution. Both showed positive results.

RESULTS AND DISCUSSION

Physical measurements

The physical properties and the microanalytical data of the ligand and metal complexes are summarized in the Table 1. The analytical results show (1:2) metal ligand ratio, i.e., ML_2 type. The colour change from ligand to metal complexes is in support of metal ligand interaction which is further reinforced by conductivity and pH measurements. The ligand is soluble in ethanol. The complex is soluble in DMF. Molecular formulae of the ligand and metal are proposed based on the results of microanalytical tool in combination with spectral techniques. The experimental molar conductivity data of metal complexes is found in the range of 6.6–33.2 μS/cm which suggests their nonelectrolytic nature of the complex. The pH of ligand and complexes was almost in the neutral range.

Table 1: Physical data of the synthesised compound

Compound	Formula	Colour	M.P (°c)	Yield %	Cal(found) %			UV(λ_{max}) (nm)
					C	H	N	
L=(Schiff base)	$C_{14}H_{13}N_3O_2Cl$	Off white	208-212	78	60.12 (60.02)	3.88 (3.98)	16.18 (16.01)	410
[Co(L) Cl_2H_2O	$[Co(C_{56}H_{52}N_{12}O]$ $Cl_2.H_2O$	Dark brown	320-330	80	60.16 (60.24)	3.78 (3.88)	16.15 (16.13)	540

Chemistry and electronic spectra

The condensation reaction of INH and 4-chlorobenzaldehyde under reflux conditions results in the formation of the SB ligand namely N'-[(4-chlorophenyl) methylidene] pyridine-4-carbohydrazide. The ligand is subsequently reacted with chloride salts of Co(II) to give corresponding metal complex. The proposed synthetic route of the ligand and the Co(II) complexes are given in Scheme 1.

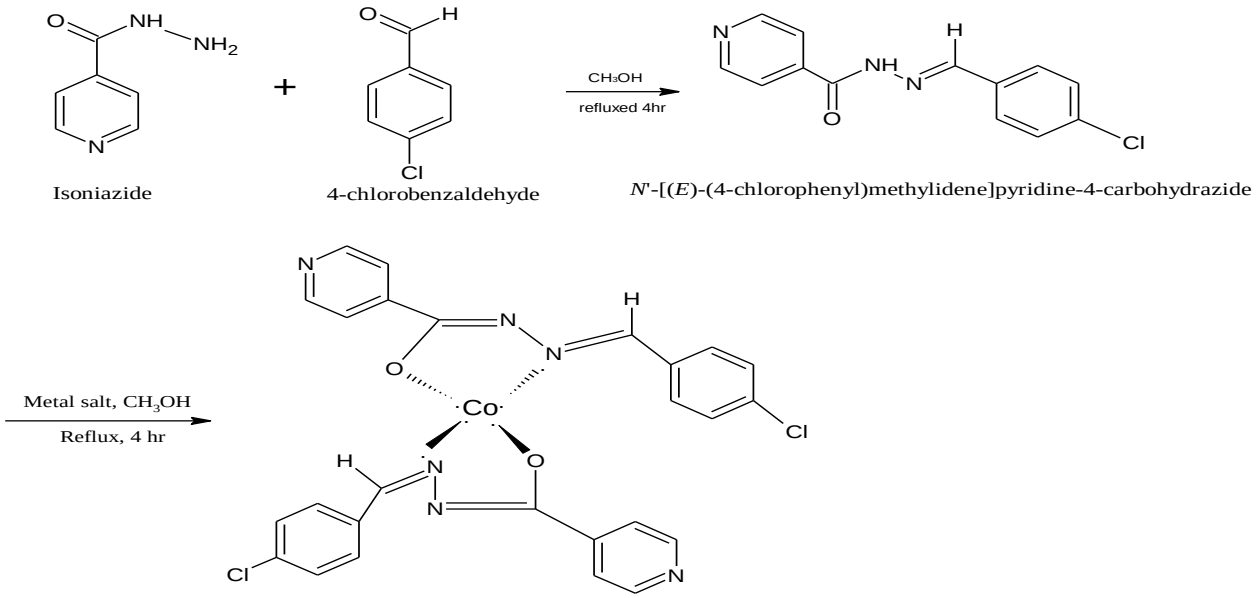
The ligand and metal complexes are of different colours, the ligand is off-white while the complexes of Co(II) are dark brown in colour. The ligand is soluble in ethanol while the metal complex is only soluble in DMF. The SB melted at 208-212°C and the complex have melting point above 320°C. The structures of the products are confirmed by the elemental analysis, which shows that the difference between the found values and calculated values of carbon, hydrogen and nitrogen elements are situated within the range which confirms the correctness of the suggested structures of the prepared compounds. The Schiff base

ligand shows absorption band at 410 nm is assigned to n-π* transition. On complexation the absorption band was shifted to 540 nm (Figure 2a) due to the formation of coloured complex.

Stoichiometry of the reaction product

Complex obtained is studied in DMF solution to determine the M/L ratio in the complex by Job's Method[18]. A series of solutions were prepared with a constant concentration (10^{-3} M) of the metal ion and ligand, SB. The M/L ratio was determined from the relationship between the absorption of the absorbed light and the mole ratio of M/L. The study shows that the metal to ligand, ratio was 1:2. In view of this result, a reaction mechanism is proposed and metal to ligand ratio is to be considered as 1:2.

Overall scheme



Scheme 1: Reaction of INH with 4-chlorobenzaldehyde followed by the complex formation

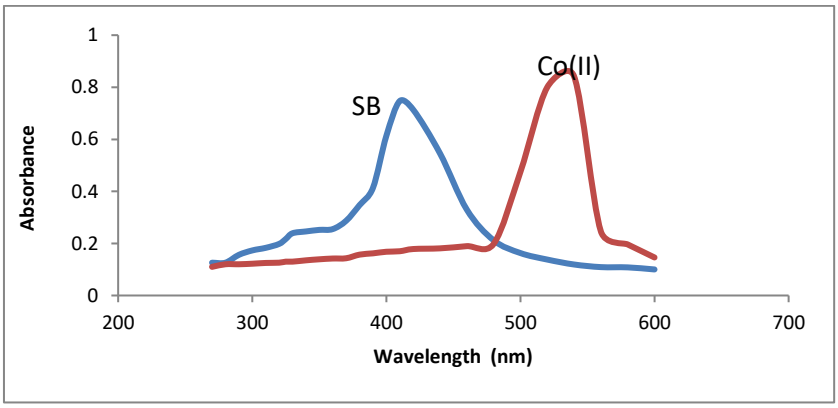


Figure 2a: UV Graph of Schiff base and metal complex

Infrared spectroscopy

The IR spectra of the SB ligand exhibited bands in the region 1591cm^{-1} (Figure 2b) which is due to the stretching frequency of C=N group[19]. On complexation, the positional shift have been observed from 1591 to 1550 cm^{-1} for the band C=N in the complex (Figure 2c). The sharp band in the region 1666 cm^{-1} was assigned for the presence of C=O group in the ligand was shifted to lower frequency upon complexation[20]. All the values are shown in table 2.2.

Table 2: IR result of Schiff base and its complex

Ligand/complex	ν (C=N)	ν (NH)	ν (C=O)	ν (M-N)	ν (M-O)	Ligand/complex
L=(Schiff base)	1591	3469	1666	-	-	L=(Schiff base)
[Co(L) Cl_2H_2O	1550	-	-	511	420	[Co(L) Cl_2H_2O

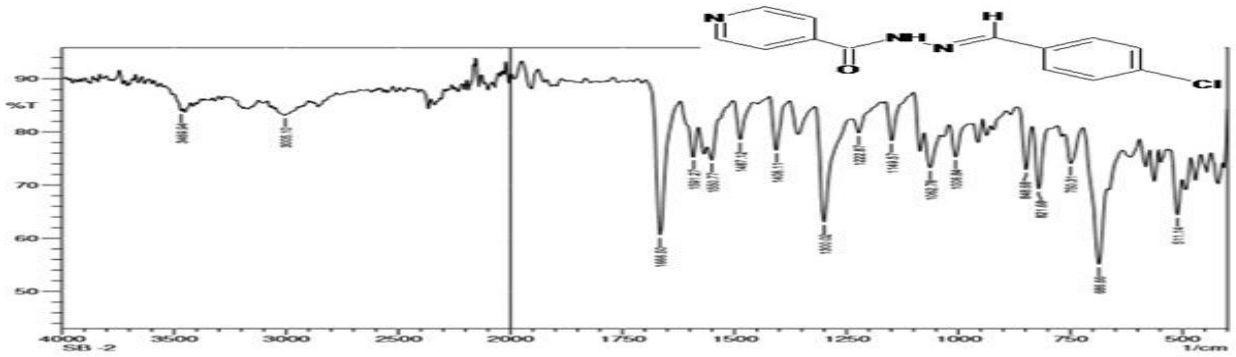
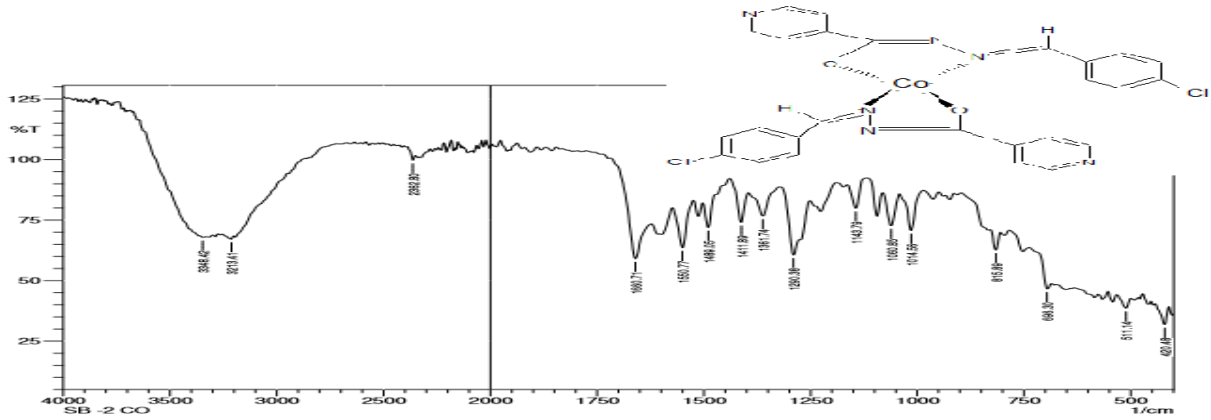


Figure 2b: IR Spectra of Schiff base



2c: IR Spectra of complex

Antibacterial activity

The synthesized ligand and Co(II) complex was screened for antibacterial activity against Gram positive bacteria *Staphylococcus aureus* and Gram-negative bacteria *Escherichia coli by using* Broth Dilution Method. It is noticed that metal complex shows better inhibitory activity than SB due to the enhanced biochemical potential of bioactive organic species upon Chelation[21]. The higher activity of the metal complex may be due to the effect of metal ions on the normal cell membrane. According to Tweedy's chelation theory[22], complexation results in the overlapping of ligand orbital with the metal orbitals and partial sharing of positive charge of metal ion with donor groups of the ligand which reduces the polarity of the metal orbitals[23]. This enhances the delocalization of the pi electrons over the entire complex ring thereby promoting the lipophilicity of the chelate[24]. Therefore, chelation enhances the lipophilic character of the metal complex. This favours the complex permeation through the lipid layers of the cell membrane of the bacteria.

Table 3: antimicrobial study of SB and complex

Compound name	*Escherichia coli* (Gram negative)						*Staphylococcus aureus* (Gram positive)					
SB	++	++	+ -	+ -	- -	- -	++	++	++	+ -	- -	- -
Cobalt complex	++	+ -	- -	- -	- -	- -	++	+ -	- -	- -	- -	- -

++ = High growth *+ - = Mild growth* *- - = No growth*

CONCLUSION

The SB ligand N'-[(4-chlorophenyl) methylidene] pyridine-4-carbohydrazide was successfully synthesized and complexed with Co(II) metal ion. The metal complex was characterized by elemental analysis, FT-IR and UV-Visible spectra. The IR spectra of ligand shows that the coordination to Cobalt is via C=N and C-O. On complexation the absorption band was shifted to higher wavelength due to the formation of coloured complex. The proposed structure says the complex has square planar geometry. Synthesized SB and metal complex were screened for its antimicrobial activity. Also, from this study it can be concluded that the antibacterial growth inhibition ability of the synthesized complex increases upon complexation.

Acknowledgments: The authors are thankful to B M S College for Women, Bengaluru for providing the lab facilities to carry out the research work.

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Source of Support: None declared.

Conflict of Interest: None declared.