

# Synthesis, physical characterization and antimicrobial activity of copper(II) and cobalt(II) complexes with new Schiff base ligand containing thiocarbonohydrazide

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**ABSTRACT:** The synthesis and biological studies of some metal complexes of thiocarbonohydrazone ligand are described. The ligand is obtained by condensation of thiocarbonohydrazide with nicotinaldehyde. The metal complexes of Co(II) and Cu(II) with 1,5-bis(pyridin-3 ylmethylene) thiocarbonohydrazide were synthesized and isolated as solid products and characterized by analytical means as well as by spectral techniques such as FT-IR, UV-Vis, microanalysis and molar conductivity. Also the synthesized complexes and ligand were screened for their antibacterial activity against *Escherichia coli*, *Serratia marcescens*, *Staphylococcus aureus*, and *Proteus vulgaris* and results showed that the all complexes have antibacterial effects.

**Keywords:** Synthesis, Schiff Base, thiocarbonohydrazide, nicotinaldehyde, antibacterial activity.

## INTRODUCTION

During the last several years, coordination chemistry has been considerably enriched due to the synthesis and characterization of a large number of transition metal complexes in which the metal is coordinated by sulfur, nitrogen and oxygen. Metal complexes of ligands containing ONS donors have antibacterial (1–3), antifungal (4,5) and antitumour activities (6–8). Metal complexes of thiocarbonohydrazones have attracted much attention due to their biological activity (9–11). Thiocarbonohydrazides are an important class of compounds which possess applications in many fields. The chemistry of thiocarbonohydrazides has gained increased interest in both synthetic organic chemistry and biological fields and has considerable value in many useful applications such as the assessment process of the three-dimensional ultrastructure examination techniques of interphase nuclei and tissues, besides their therapeutic importance (12). In the study reported in this article we synthesized Schiff-base 1, 5-bis(pyridin-3 ylmethylene) thiocarbonohydrazide ligand. The metal(II) Schiff-base complexes using Co(II) and Cu(II) metals salts were prepared using the Schiff-base ligand. The ligand and the respective metal complexes were characterized by means of physical and spectral analyses. Also the synthesized complexes were screened for their antibacterial activity against *Escherichia coli* (Lio), *Serratia marcescens* (PTCC 1330), *Staphylococcus aureus* (ATCC 6633), and *Proteus vulgaris* (Lio).

## Experimentals

### Materials

The metal salts  $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$  and  $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$  were purchased from Merck, nicotinaldehyde and 2-chloroethanol, carbon disulfide and Hydrazine hydrate were purchased (synthetic grade) from Sigma–Aldrich and Merck,. All the solvents (AR grade) used in the synthesis and analysis were procured from Merck and used without any further purification.

### Physical and spectral measurements

Melting points were measured using electrothermal digital melting point apparatus and molar conductivity was measured by CARISON GLP32 conductivimeter. Elemental analyses were performed in a Carlo-Erba EA microanalyser. FT-IR spectra were recorded on the Perkin-Elmer FT-IRGX in the range of 400–4000  $\text{cm}^{-1}$  using a KBr disc. UV-Vis Spectra were recorded on the Varian Cary 50 Spectrophotometer (range 200–900 nm) using methanol as a solvent. The  $^{13}\text{C}$  and  $^1\text{H}$  NMR Spectra were recorded using Bruker DPX 300 with  $\text{d}_6\text{-DMSO}$  being the solvent containing tetra-methyl-silane (TMS) as the internal standard.

### Procedure for the preparation of thiocarbohydrazide

Hydrazine hydrate (80%, 18 mL, 0.3 mol) and 2-chloroethanol (1 mL, 0.015 mol) were added to a three-neck flask. Then carbon disulfide (6 mL, 0.1 mol) was added dropwise under stirring with cooling using an ice-water bath, and yellow solid was formed. After adding NaOH (0.6 g, 0.015 mol), the reaction mixture was exposed to microwave irradiation at 400 W for 15 min. Then it was cooled to room temperature. The solid thus obtained was collected by filtration, washed by methanol and recrystallized from water. White granule crystal was obtained. m.p. 171–172 °C (lit. (13) m.p. 170 °C), yield 88%.

### Synthesis of 1, 5-bis(pyridin-3 ylmethylene) thiocarbohydrazide (L)

nicotinaldehyde (10 mmol, 1.07 g) was added to the thiocarbohydrazide (5 mmol, 0.536 g) in hot methanolic solution with 1 mL HCl (0.1 N). The mixture was heated to reflux in the water bath for 4 h (Fig. 1). The pale yellow precipitate was formed by ice cooling. This (precipitate) was filtered off, washed with methanol and petroleum ether. Re-crystallization was carried out in methanol and a yellow amorphous compound was obtained, which was subsequently dried over anhydrous  $\text{CaCl}_2$  under vacuum (m.p. 208 °C, yield 74%).

### Synthesis of metal complexes

All the metal complexes were synthesized by adding the methanolic solution of metal (II) salts (0.5 mmol) to the hot homogeneous solution of the ligand (0.5 mmol) in the methanol. The mixture of the metal and the ligand was heated to reflux with constant stirring in a water bath for 6 h. At room temperature, the product was filtered off. The obtained products were dried over anhydrous  $\text{CaCl}_2$  under vacuum.

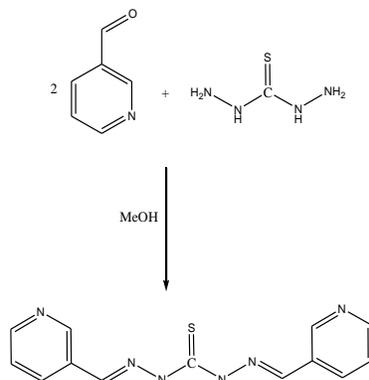


Figure 1. Synthesis of the Schiff Base ligand (L).

### Antibacterial study

## MATERIALS AND METHODS

### Test organisms for antibacterial assay

The standard strains of the following microorganisms were used as test organisms: Escherichia coli (Lio), Serratia marcescens (PTCC 1330), S. aureus (ATCC 6633), and Proteus vulgaris (Lio). Some microorganisms were obtained from Persian Type Culture Collection, Tehran, Iran and others locally isolated (Lio). The organisms were sub-cultured in nutrient broth and nutrient agar (Oxoid Ltd.) for using in experiments, while diagnostic sensitivity test agar (DST) (Oxoid Ltd.) was used in antibiotic sensitivity testing.

### Sensitivity testing

For bioassays, suspension of approximately  $1.5 \times 10^8$  cells per mL in sterile normal saline was prepared as described by Forbes et al. (14). The sensitivity testing was determined using agar-gel diffusion method ((15,16)). In each disks 30  $\mu$ L of chemicals were loaded. The isolated bacterial strains were first grown in nutrient broth for 18 h before use. The inoculums suspensions were standardized and then tested against the effect of the chemicals at amount of 30  $\mu$ L for each disk in DST medium. The plates were later incubated at  $37 \pm 0.5$  °C for 24 h after which they were observed for zones of inhibition. The effects were compared with the standard antibiotic chloramphenicol at a concentration of 1 mg/mL (17).

Table 1. Physical properties of the ligand (L) and its metal complexes

Compound	L	(LCoCl <sub>2</sub> ).3H <sub>2</sub> O	(LCuCl <sub>2</sub> ).2H <sub>2</sub> O
Colour	Yellow	Rad	green
mp(°C)	205	267	288
Yield%	74	52	48
Conductivity $\mu$ S/cm( $10^{-3}$ )	-	137	139
C%.Obs(Cal)	54.4(54.91)	33.4(33.35)	34.4(34.48)
H%.Obs(Cal)	4.5 (4.25)	4.1(3.87)	3.8(3.12)
N%.Obs(Cal)	28.7(29.56)	17.3(17.95)	18.0(18.56)

## RESULTS AND DISCUSSION

All the metal complexes were synthesised with an equimolar ratio of ligand and metal salts in methanol. The ligand (L) was synthesized by the condensation of diamine and aldehyde, and characterized by UV-Vis, IR, <sup>1</sup>H and <sup>13</sup>C NMR and CHN. The complexes formed were (LCoCl<sub>2</sub>).3H<sub>2</sub>O and (LCuCl<sub>2</sub>).2H<sub>2</sub>O. Due to the amorphous nature of the complexes, all the efforts were in vain to develop the crystal. The binding and coordination modes of the ligand and its metal complexes were determined by spectral data studies. Table 1 represents the preliminary observations of the synthesized compounds with respect to colour, melting point (mp), yield, conductivity and Elemental analysis of the compounds that was conducted and the findings. The complexes are insoluble in water; however, they are sparingly soluble in DMSO. The complexes show low molar conductivity indicating their non-electrolytic behaviour (18).

### IR spectroscopy

The infrared spectral data of the Schiff-base ligand show the characteristic peaks for the functional groups like -CH=N-, C=S, N-H, and N-N group at 1611 cm<sup>-1</sup>, 786 cm<sup>-1</sup>, 3133 cm<sup>-1</sup> and 1116 cm<sup>-1</sup> respectively; and thioamide vibrations at 1115-1532 cm<sup>-1</sup> were observed in the ligand (18–21).

The IR spectra of the metal(II) Schiff-base complexes show a broad band at ~3450 cm<sup>-1</sup> for the  $\nu$ (OH) group of coordinated water. The  $\nu$ (N-H) group vibration bands in complexes shifted or even disappeared or appeared to be very weak due to resonance and hyper conjugation between the C=S and C=N with N-H. The azomethine (HC=N) vibration band in the Co and Cu complexes shifted to a higher frequency at 1618 and 1622 cm<sup>-1</sup> due to the increase in bond length through coordination with the metal(II) centre. The  $\nu$ (C=S) vibration in the Co and Cu complexes at 768 and 770 cm<sup>-1</sup> shifted to a lower frequency in the metal complex due to the coordination of the sulphur to the metal centre. Their new band appeared in the Co and Cu complexes at 504 and 507 cm<sup>-1</sup> due to the  $\nu$ (M-N) vibration, suggesting the bonding between the nitrogen and metal(II) ion.

Table 2. UV-Vis Spectral data (nm) for L and its metal complexes (methanol 200–900 nm)

Compound	(HC=N) $n \rightarrow \pi^*$ (nm)	(N-N) $n \rightarrow \sigma^*$ (nm)	Intra-Ligand charge transfer(nm)	d→d(nm)
L	344	276	-	-
(LCoCl <sub>2</sub> ).3H <sub>2</sub> O	352	258	301	531
(LCuCl <sub>2</sub> ).2H <sub>2</sub> O	356	262	-	427

### UV-Vis spectroscopy

The UV-Vis spectral data of the ligand and its metal complexes are given in Table 2. Two absorption bands were observed for the ligand corresponding to  $n \rightarrow \pi$  and  $n \rightarrow \pi^*$  bands at 344 nm and 276 nm for azomethine (HC=N) and (N-N) chromophores, respectively.

The Co(II) complex showed the <sup>4</sup>T<sub>1g</sub>(F) → <sup>4</sup>A<sub>2g</sub>(F) d-d transition bands at 531 nm. The 12 nm shift to a higher wavelength was attributed to the azomethine band observed at 356 nm as a result of the coordination with C=N in the Co(II) complex. The charge transfer band for the S → Co(II) could be seen at 301 nm and there was also a 18 nm lower wavelength shift observed in the N-N chromophore bands of 276 nm of free ligand which was observed

at 258 nm. The Co(II) metal is coordinated to three donor sites of the ligand and has assumed a square pyramidal geometry (19). The UV-Vis spectra of the Cu(II) complex showed peaks at 356 nm and 427 nm. The azomethine band was shifted to higher wavelength in the Cu(II) complex. The new band was at 427 nm assigned to the S → Cu(II) showing the coordination. The C=N and C=S groups are coordination sites of the ligand in Cu(II) complex. The ligand is coordinated to copper by the two C=N and one C=S, and two chloride ions from the metal salts making a five coordination sphere around the Cu(II). From the above data and lack of the characteristic peak of Cu(II) at around ~800 nm the trigonal bipyramidal geometry is proposed for the Cu(II) complex (19,20).

### **<sup>1</sup>H and <sup>13</sup>C NMR spectroscopy**

<sup>1</sup>H NMR spectral data of the ligand in d<sub>6</sub>-DMSO shows that the signal at the 8.66 ppm was assigned to the azomethine (HC=N) proton. The NH proton is assigned at the 8.91 ppm. The aromatic region signal was observed from 7.24 ppm to 8.55 ppm. In <sup>13</sup>C NMR spectra Two peaks were observed for the C=S and C-SH at 175.48 cm<sup>-1</sup> and 176.73 cm<sup>-1</sup>, respectively. the signals of aromatic rings carbons appear at 124.31ppm to 155.63 ppm.

Table 3. Inhibition Zones (mm) of complexes against bacterial strains

Complex	E.coli	S.marcescens	S. aureus	P.vulgaris
L	12	10	10	11
(LCoCl <sub>2</sub> ).3H <sub>2</sub> O	18	16	13	14
(LCuCl <sub>2</sub> ).2H <sub>2</sub> O	17	18	12	15
Choloramphenicol	20	22	15	15

### **Antibacterial activities**

Antibacterial activities of the chemicals were studied against four bacterial strains (Table 3). The all prepared chemicals inhibited the growth of bacterial strains producing a zone diameter of inhibition from 10.0 to 18.0 mm, depending on susceptibility of the tested bacteria. Free Schiff base ligand shows weak activity; Compare of Schiff base ligand and its related complexes show that such complexes have higher antibacterial activity than that of the respective free ligand against the same microorganism under identical experimental conditions (22–30). Such an increased activity for the metal chelates as compared to the free ligand can be explained on the basis of chelation theory (31). Chelation considerably reduces the polarity of the metal ion because of the partial sharing of its positive charge with the donor groups and possible π-electron delocalization over the chelate ring. Such chelation could increase the lipophilic character of the central metal atom, which subsequently favours the permeation through the lipid layer of cell membrane (32-34).

## **CONCLUSION**

The work described in this paper involved the synthesis and spectroscopic characterization of cobalt and copper complexes with a new Schiff-base ligand having the coordinating group like CH=N, C=S and N-NH. These complexes were characterized by using different physiochemical techniques. Also, Results of this research showed that all prepared chemicals have relatively antibacterial effects against the studied bacterial strains.

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