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## Synthesis and characterization of Schiff base metal complexes derived from imidazole-2-carboxaldehyde with L-phenylalanine

R. Selwin Joseyphus\*<sup>1</sup>, C. Shiju<sup>1</sup>, J. Joseph<sup>2</sup>, C. Justin Dhanaraj<sup>3</sup> and K. C. Bright<sup>4</sup>

<sup>1</sup>Department of Chemistry, Mar Ivanios College (Autonomous), Thiruvananthapuram, Kerala, India

<sup>2</sup>Department of Chemistry, University College of Engineering, Anna University, Nagercoil, Tamil Nadu, India

<sup>3</sup>Department of Chemistry, Noorul Islam University, Kumaracoil, Tamil Nadu, India

<sup>4</sup>Department of Physics, St. John's College, Anchal, Kollam, Kerala, India

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### ABSTRACT

The Schiff base ligand, derived from imidazole-2-carboxaldehyde with L-phenylalanine and the Co(II), Ni(II), Cu(II) and Zn(II) complexes were synthesized. The synthesized ligand and its complexes were characterized by elemental analysis, molar conductance, magnetic moment, <sup>1</sup>H NMR, <sup>13</sup>C NMR, IR, UV-Vis., ESR, mass spectra, TGA, CV and powder XRD. The analytical data shows that the metal to ligand ratio is 1:1. The molar conductance data reveal that all the complexes are non-electrolytes. The results show that the ligands act as a tridentate monobasic donor coordinating through the azomethine nitrogen, imidazole nitrogen and carboxylato oxygen atoms. The TGA data indicates the presence of coordinated water molecules in these complexes. The crystallinity of these compounds was proved by the powder XRD pattern. Antimicrobial studies indicate that the complexes exhibit more activity than the ligand.

**Keywords:** Schiff base, NMR, XRD, UV-Vis., XRD

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### INTRODUCTION

Transition metal complexes with Schiff base ligands have been extensively investigated as antimicrobial and anticancer agents. Schiff base complexes derived from amino acids are important due to their ability to possess unusual configurations and biological importance [1-8]. Schiff bases have appeared to be important intermediates in a number of enzymatic reactions involving interaction of an enzyme with an amino- or carbonyl group of the substrate. Transaminases are found in mitochondria and cytosole of eukaryotic cells [9]. Polydentate ligands such as Schiff bases, assisted by metal ions, provide highly organized supramolecular metal complexes. Such complexes possess binding sites and cavities for various cations, anions, and organic molecules [10]. Imidazole-2-carboxaldehyde with amino acids derivatives are reported to exhibit analgesic, anti-inflammatory, anticancer and herbicidal activities. Some of the Schiff base complexes containing N and O donor atoms are effective as stereospecific catalysts for oxidation, reduction, hydrolysis, biocidal activity, other organic and inorganic transformations [11-15]. These complexes are considered as good models to study metal-ligand interactions in metalloproteins and metalloenzymes [16, 17]. In addition, some of these complexes have been shown to exhibit interesting physical, chemical, and potentially beneficial chemotherapeutic properties [18-22]. Varied properties of this type of complexes prompted us to synthesize, characterize and to investigate the biological activity of these complexes.

## MATERIALS AND METHODS

All the chemicals used were of Analar grade. Imidazole-2-carboxaldehyde, L-phenylalanine, metal(II) chlorides were obtained from E-Merck, India. The solvents were dried and distilled before use according to the standard procedures.

The elemental analysis was carried out using a Perkin-Elmer 2400 CHN instrument. The metal content present in the complexes were determined by EDTA titration [23]. Molar conductance was measured ( $10^{-3}$  M) using a Coronation digital conductivity meter. The mass spectra were recorded using JEOL JMS600H mass spectrometer. The NMR spectra were recorded using JEOL GSX 400 FT-NMR spectrometer in DMSO- $d_6$  with TMS as the internal standard. FT-IR spectra were recorded by employing JASCO FT/IR-410 spectrometer using KBr pellet technique (4000-400  $\text{cm}^{-1}$ ). The electronic absorption spectrum was recorded using Thermo Scientific UV-VIS spectrophotometer (190-1100 nm). Magnetic measurements were performed using Guoy's balance by making diamagnetic corrections using Pascal's constant at room temperature. The X-band ESR spectrum of the copper(II) complex was recorded by a Varian E112 X-band spectrometer. Cyclic voltammetry measurements were carried out in a Bio-Analytical System model CV-50W electrochemical analyzer. For this three electrode cells comprised of a reference Ag/AgCl, auxiliary platinum and working glassy electrodes were used. Again tetrabutylammonium perchlorate was used as a supporting electrolyte. The thermal data was analyzed by Thermogravimetric SDT Q 600/V8.3 build 101 thermal analyzer. The synthesized compound was subjected to XRD using Rigaku D<sub>max</sub> X-ray diffractometer with Cu-K $\alpha$  radiation.

### Synthesis of ligand

L-phenylalanine (2 mmol) and KOH (2 mmol) were dissolved in methanol (25 mL) and stirred for about 1 h. Then a solution of imidazole-2-carboxaldehyde (2 mmol) dissolved in absolute methanol (25 mL) was added slowly. Again the stirring is continued at an optimum temperature for about 60 °C until the mixture was reduced to half of its initial volume and then ether was added. The yellow precipitate was obtained immediately, which was washed several times with ether and then dried *in vacuo* over anhydrous CaCl<sub>2</sub>. Yield: 78%. C<sub>13</sub>H<sub>12</sub>N<sub>3</sub>O<sub>2</sub>K, Anal. Calcd.: C, 55.92; H, 3.98; N, 15.07. Found: C, 55.92; H, 4.30; N, 14.94.

### Synthesis of metal complexes

The Schiff base ligand (2 mmol) dissolved in methanol (25 mL), with Co/Ni/Cu/Zn(II) chloride (2 mmol) dissolved in aqueous methanol (20 mL) was added dropwise. The above mixture was magnetically stirred for about 2 h. The precipitate obtained was filtered off, washed with ethanol, ether and then dried *in vacuo* over anhydrous CaCl<sub>2</sub>. Yield: 63-75%.

C<sub>13</sub>H<sub>16</sub>N<sub>3</sub>O<sub>4</sub>ClCo, Anal. Calcd.: C, 41.22, H, 4.10, N, 11.87; Found: C, 41.90, H, 4.33, N, 11.28. C<sub>13</sub>H<sub>16</sub>N<sub>3</sub>O<sub>4</sub>ClNi, Anal. Calcd.: C, 41.34, H, 4.93, N, 11.79; Found: C, 41.92, H, 4.33, N, 11.27.

C<sub>13</sub>H<sub>16</sub>N<sub>3</sub>O<sub>4</sub>ClCu, Anal. Calcd.: C, 41.57, H, 4.76, N, 11.84; Found: C, 41.39, H, 4.27, N, 11.14. C<sub>13</sub>H<sub>16</sub>N<sub>3</sub>O<sub>4</sub>ClZn, Anal. Calcd.: C, 41.90, H, 4.89, N, 11.75; Found: C, 41.18, H, 4.25, N, 11.08.

### Antimicrobial activity

The ligand and its complexes were tested *in vitro* against the bacterial species; *E. coli*, *B. subtilis*, *P. aeruginosa*, *S. aureus*; fungal species; *A. niger*, *A. flavus*, and *C. albicans* by disc diffusion method. The test organisms were grown on nutrient agar medium in petri plates. The compounds were prepared in DMSO and soaked in filter paper disc of 5 mm diameter and 1 mm thickness. The discs were placed on the previously seeded plates and incubated at 37 °C and the diameter of inhibition zone around each disc was measured after 24 h for antibacterial and 72 h for antifungal activities. The MIC was determined by serial dilution technique [24].

## RESULTS AND DISCUSSION

The ligand is yellow in colour and soluble in some common organic solvents. The metal complexes are soluble in DMSO and DMF. The purity of the product was monitored by TLC using silica gel. The elemental analysis data of ligand is in good agreement with those calculated for the suggested formula. The synthesized compound is shown in Scheme 1. The analytical data show that the metal to ligand ratio is 1:1 in all the complex systems. The composition of the complexes is [ML(H<sub>2</sub>O)<sub>2</sub>Cl] where L= *imidazole-2-carboxaldehyde with L-phenylalanine*. The low molar

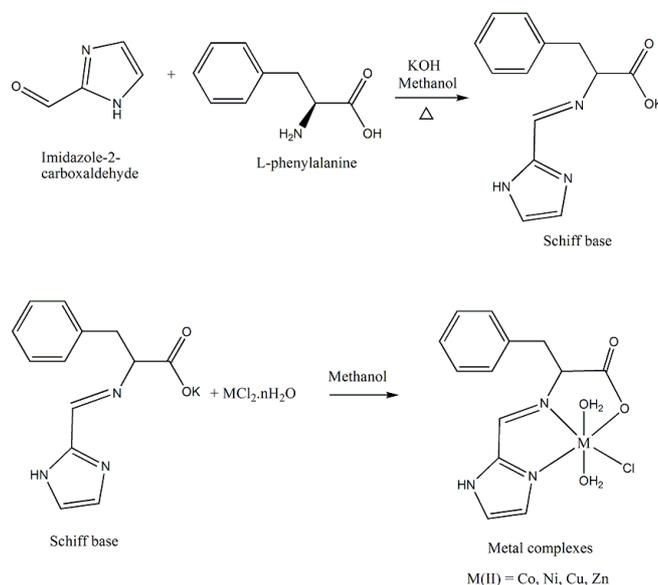
conductance values ( $15\text{-}26 \text{ Ohm}^{-1}\text{cm}^2\text{mol}^{-1}$ ) of the metal complexes reveal their non-electrolytic nature [26]. The ligand shows a molecular mass ion peak at  $m/z = 282 [M^+ (28\%)]$  which coincides with the formula weight of the ligand. The molecular ion peaks at  $m/z 373 (M^+ + 1, 10\%)$ ,  $372 (M^+, 13\%)$ ,  $376 (M^+ + 1, 10\%)$ ,  $377 (M^+ + 1, 14\%)$  respectively, which coincide with the formula weight of the Co(II), Ni(II), Cu(II) and Zn(II) complexes.

### NMR spectra

In the  $^1\text{H}$  NMR spectrum of ligand the azomethine proton exhibits a singlet signal at 8.6 ppm. The aromatic ring proton exhibited signals at 7.8-8.2 ppm and the methylene protons in the imidazole ring signal appeared at 7.2-7.4 ppm. The proton nearer to the carboxylate group appeared at 3.1 ppm and the methyl proton exhibit a doublet signal at 3.6 ppm. In the  $^{13}\text{C}$  NMR spectrum of the ligand displayed signals at 168 and 176 ppm corresponds to the azomethine carbon and carboxylate carbon atoms respectively. The aromatic carbons are also appeared at 132-145 ppm and the carbon atoms present in the imidazole ring resonate at 126-138 ppm. The azomethine carbon atom adjacent to the carboxylate carbon appears at 76 ppm and the other methyl carbon displayed at 54 ppm.

### IR spectra

The IR spectrum of the ligand display band at  $1662 \text{ cm}^{-1}$  is the stretching frequency of azomethine group. The ligand exhibit a band at  $1634 \text{ cm}^{-1}$  can be assigned to an asymmetric stretching frequency of the carboxylate group of the ligand. The ligand also display bands at  $1382 \text{ cm}^{-1}$  are due to symmetric stretching vibration of the carboxylate group [25]. Sharp bands present in the region  $\sim 3368$  and  $\sim 1520 \text{ cm}^{-1}$  is due to peptide N-H stretching frequencies [25]. The azomethine group of free ligand was shifted to lower frequency  $\sim 1643\text{-}1656 \text{ cm}^{-1}$  in the complexes confirm the coordination of the azomethine nitrogen atom to the metal ion. The new broad band appeared at  $\sim 3400 \text{ cm}^{-1}$  in the metal complexes can be attributed to the stretching vibration of the coordinated water molecules. Also a band at  $\sim 850 \text{ cm}^{-1}$  in the complexes is assigned to coordinated water molecule [27]. On complexation, the asymmetric and symmetric stretching bands of carboxylate groups were shifted to lower frequency, which reveals the formation of a linkage between the metal ion and carboxylate oxygen atoms. Moreover, the difference ( $\sim 200 \text{ cm}^{-1}$ ) between the asymmetric and symmetric stretching modes indicates the monodentate binding of the carboxylate group in the complexes [28]. The new bands appeared in the regions,  $548\text{-}585$  and  $434\text{-}457 \text{ cm}^{-1}$ , which may probably be due to the formation of M-O and M-N bands respectively [26].



### Electronic spectra and magnetic measurements

The electronic spectrum of the ligand exhibit an absorption band at 336 nm is attributed to the  $\pi\text{-}\pi^*$  transition of the azomethine chromophore. The electronic spectrum of Co(II) complex exhibit two absorption bands at 523 and 658 nm, which are assignable to the overlap of transitions  $^4T_1g(F) \rightarrow ^4A_2g(F)$  and  $^4T_1g(F) \rightarrow ^4T_2g(F)$  indicating an octahedral environment [29,30]. The electronic spectrum of Ni(II) complex give three absorption bands at  $\sim 1000$ , 624 and 361 nm attributable to  $^3A_2g(F) \rightarrow ^3T_2g(F)$ ,  $^3A_2g(F) \rightarrow ^3T_1g(F)$ , and  $^3A_2g(F) \rightarrow ^3T_1g(P)$  transitions, suggesting an octahedral geometry [28]. The Cu(II) complex displayed broad band  $\sim 720 \text{ nm}$  region, which can be assigned to

${}^2E_g \rightarrow {}^2T_{2g}$  transition, indicating the complex to have distorted octahedral geometry [29]. In octahedral complexes, the Jahn–Teller effect is the most pronounced when an odd number of electrons occupy the  $E_g$  orbitals. The magnetic moment value of cobalt complex is 5.06 BM, (normal range for octahedral Co(II) complex is 4.3–5.2 BM), which indicates an octahedral geometry [31]. The nickel complex exhibit 3.22 BM, which are in the normal range (2.9–3.3 BM) observed for octahedral [31] nickel complexes. The magnetic moment value of copper complex is 1.97 BM, which is normally observed for octahedral [30] Cu(II) complex. Zn(II) complex is diamagnetic and it would have an octahedral geometry. The X-band ESR spectrum of Cu(II) complex was recorded at room temperature. The spectrum shows one intense absorption band at high field, which is isotropic due to the tumbling of the molecule. Moreover, the absence of a half field signal at 1600 G indicates the absence of any Cu–Cu interaction in the complex [32].

#### Cyclic voltammetry

The metal complexes were recorded in DMSO solution in the potential range -2V to +2V at a scan rate of 50 mVs<sup>-1</sup>. The Co(II) and Ni(II) complexes displayed one irreversible reduction peak at -560 and -290 mV of anodic waves in all scan rates. Cu(II) complex exhibits a pair of cathodic and anodic peak potentials at -55 and 285 mV, respectively, representing the Cu(II)/Cu(I) couple. The peak-to-peak separation ( $\Delta E_p = 340$  mV) indicates a quasi-reversible, one electron transfer process. Similarly, the Zn(II) complex displayed a pair of cathodic and anodic peak potentials at -260 and -165 mV respectively, representing the Zn(II)/Zn(I) couple. The separation ( $\Delta E_p = 95$  mV) indicates a quasi-reversible, one electron transfer process.

#### TG analysis

The thermal stability of the complexes undergoes decomposition steps mainly in three stages. The TG curve of metal complexes shows a weight loss 11.49%, (Cal. 9.68%), 10.63% (Cal. 9.70%), 10.81% (Cal. 9.57%) and 10.31% (Cal. 9.55%) in the temperature ranges from 125–220, 145–215, 140–210 and 135–210 °C respectively. These are due to the loss of two coordinated water molecules. The second decomposition stage starts in the temperature ranges from 220–515, 215–660, 210–670 and 210–640 °C bringing a weight loss of 68.80% (Cal. 70.18%), 68.65% (Cal. 70.37%), 67.35% (Cal. 69.44%) and 68.45% (Cal. 69.25%) respectively for the metal complexes which correlates with the loss of coordinated organic ligand. Above this temperature, a horizontal thermal curve has been observed due to the formation of the metal oxide as the final residue.

#### Powder XRD

Powder XRD pattern of the metal complexes were recorded in the range  $2\theta=0-80^\circ$ . The metal complexes possess sharp crystalline peaks indicate their crystalline nature. The grain size of these complexes was calculated using Scherrer equation [33] has the average grain size values of 37-58 nm, suggesting that the complexes are in nanocrystalline regime.

#### Antimicrobial activity

The amikacin and nystatin were used as positive standards for antibacterial and antifungal studies. Comparatively a better activity is found for the bacteria rather than the fungi. The compounds exhibit moderate to strong antimicrobial activity. The copper complex exhibits a higher activity than the other metal complexes towards fungal species. The Cu(II) complexes show remarkable activity, especially against the Gram-negative bacteria such as *E. coli*. Similar antibacterial activities of copper complexes have been reported [34–36]. Again the Cu(II) complex shows equal or better activity compared to the positive controls such as amikacin. The Ni(II) complex displays moderate activity against the bacterial species. The complexes exhibit greater activity than those of the free ligand; this indicates that the complexation to metal enhances the activity of the ligand. This is explained on the basis of Overtone's concept and chelation theory [37]. Chelation tends to make the ligand a more powerful and potent bacterial agent. A possible explanation for this increase in the activity upon chelation is that, in a chelated complex, the positive charge of the metal is partially shared with donor atoms present in the ligands and there is an electron delocalization over the whole chelated ring. This, in turn, increases the lipid layers of the bacterial membrane. Generally, it is suggested that the chelated complexes deactivate various cellular enzymes, which play a vital role in various metabolic pathways of these microorganisms. Other factors such as solubility, conductivity, and dipole moment that are affected by the presence of metal ions may also be the possible reasons for increasing the biological activity of the metal complexes as compared to the ligand from which they are derived [38]. Search for new antitumor depends basically on the line of antibiotics affecting Gram-negative bacteria. In our case, the Cu(II) complex shows a strong activity, especially against the Gram-negative bacteria such as *E. coli*. Thus the compounds synthesized by us may have antitumor effect [39].

## CONCLUSION

The synthesized Schiff base metal complexes possess an octahedral geometry. The electrochemical process in these complexes is quasi reversible and involves one electron transfer. Presence of coordinated water molecules and thermal stability were confirmed by the TG analysis. Powder XRD results show that the complexes are nanocrystalline. The antimicrobial studies reveal that the complexes are more active than the ligand.

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