Indian Journal of Chemistry
Vol. 64, May 2025, pp. 496-499
DOI: 10.56042/ijc.v64i5.12769

Synthesis, characterization and biological activity of metal complexes and their Schiff base ligands

K Ramya Charitha & P Kavitha*
Department of Chemistry, Chaitanya (Deemed to be University), Hyderabad 506 001, Telangana, India
E-mail: kavithapingili04@gmail.com

Received 26 July 2024; accepted (revised) 28 April 2025

Schiff base ligands have been chemically synthesized from 6-aminopyrimidine-4-thiol and 4-formyl-2-hydroxybenzonitrile in a 2:1 stoichiometric ratio (2L:M) along with their corresponding Cu(II) and Zn(II) complexes. Thermo gravimetric analysis, ^1H and ^{13}C NMR, FT-IR, UV-Visible and MS spectroscopic techniques have been used to analyze the structures of all the synthesized substances. Additionally, the antibacterial activity of the ligands (L) and their metal complexes has been examined *in vitro* against several pathogens. Comparing the activity to the MIC and zone of inhibition allows for a quantitative and qualitative evaluation. Research has shown that metal (II) complexes are more effective than ciprofloxacin against selected microbes.

Keywords: Pyrimidine, Metal complexes, Antibacterial activity, Ciprofloxacin

The synthesis of Schiff base ligand and metal complexes is an important topic of current study with implications for both theoretical and applied domains[1]. The important role of Schiff bases which are readily modifiable and synthesized is one of the interesting subjects in coordination chemistry[2,3]. A simple synthetic technique involves reacting an amine with a carbonyl molecule to produce the majority of Schiff bases. Coordination chemists rely heavily on Schiff base ligands because they provide a solid foundation for developing other ligand systems with the potential to selectively bind to metal ions[4-6]. Biology and pharmacology researchers have mostly been looking into a few Schiff base complex classes. Some of these molecules have shown progress in medicines[7,8].

The several research domains that have discovered applications for metal complexes generated from Schiff bases include the reversible binding of oxygen, catalytic activity in the hydrogenation of olefins, photo chromic properties, and the capacity to complex with certain metals[9,10]. Several physiologically relevant Schiff bases have been described in the literature to exhibit antimicrobial, antibacterial, antifungal, anti-inflammatory, anticonvulsant, anticancer, and anti-HIV properties[11-16]. Researchers have been quite interested in heterocyclic compounds and their biological and therapeutic effects in the last few decades. Numerous biological activities have been shown by heterocyclic moiety and its derivatives including antibacterial, antifungal, antioxidant, antimalarial, and antileishmanial activities[17-22].

As a result of these considerations and our ongoing interest in the subject, the current work details an investigation into the synthesis, spectroscopic characterization, thermal study and biological activities of Cu(II), Zn(II) complexes with Schiff base ligands derived from 6-aminopyrimidine-4-thiol and 4-formyl-2-hydroxybenzonitrile.

Experimental Section

Materials and methods

The compounds were acquired from Sigma-Aldrich and used without undergoing further purification. Metal salts and solvents were procured from E. Merck and used without undergoing purification. The reaction was monitored using thin layer chromatography (TLC) on pre-coated silica-gel plates (Merck, India) to ensure its completion. A Perkin Elmer FT-IR type 1650 spectrophotometer was used to capture infrared spectra in the 4000-400 cm^{-1} range using KBr pellets. A Varian 300MHz was used to record the ^1H and ^{13}C NMR spectra in DMSO-d_6, with tetramethylsilane serving as an internal reference. The Agilent technologies (HP) 5973 mass spectrometer, which operates at an ionization potential of 70 eV, was used to record the mass spectra. A UV 1800 spectrophotometer (Shimadzu) was used to record the electronic absorption spectra. Thermo gravimetric analysis (TGA) was performed using a Universal TGA Q50 equipment that heated samples at a rate of 2°C/min from 30 to 1000°C.

Mass spectrometry

The MS technique was used to confirm the formation of the ligand and associated metal complexes. The presence of ligand was confirmed when the molecular ion peak was identified at *m/z* 256.04, which is in agreement with the molecular weight of the ligand. The molecular ion peaks at *m/z* 571.09, 572.02 in the mass spectra of complexes provide confirmation of the coordination of Cu, Zn ions with the ligand.

NMR spectroscopy

The ligand (L) was analysed using ^{1}H and ^{13}C NMR spectra in DMSO-d_6 solvent. At δ 8.69, the doublet signal was ascribed to the resonance of the CH=N group hydrogen. At δ 7.01-8.69, the Aryl-H signals were detected. The phenolic proton (OH) resonance for ligand L was observed at 9.17 in the ^{1}H NMR spectrum.

The structure of the L was evaluated further using ^{13}C NMR. The signal at δ 196.02 was attributed to (-CH=N). The group (CN) carbon was observed at δ 160.78 for L. The peaks of other aromatic ring carbons were observed at δ 117.68–150.15. The peak at δ 165.62 was corresponding to -COH group. These peaks confirm the formation of Schiff base ligand (L). Metal complexes of zinc and copper exhibit aromatic peaks at δ 7.52–7.72 and 7.42–7.73 respectively in ^{1}H NMR. Whereas the absence of the -OH and -SH peaks in metal complexes revealed additional confirmation of ligand binding with these complexes.

FT-IR spectroscopy

The synthesis of the ligand and its complexes was confirmed by comparing the infrared spectra of the Schiff base ligand with those of the corresponding metal complexes. The observed infrared stretching frequencies of the metal complexes and free ligand are shown in Table 1. The stretching frequency of the C-N bonds is attributed to the free ligand IR band at 1610 cm^{-1}. The stretching vibrations of the O-H and S-H groups are corresponding to the peak at 3071 and 1280 cm^{-1}, respectively. These stretching frequencies provide significance to the ligand development.

The presence of new bands at certain frequencies in the infrared spectra of metal complexes is evidence of the development of a coordination link between the ligand and metal. The stretching vibrations at 577 cm^{-1}, 479 cm^{-1} and 440 cm^{-1} corresponds to M-O, M-N and M-S metal bonds of Cu(II) complex. It was believed that the presence of additional bands at these stretching frequencies demonstrated interaction between the metal ions and sulfur, nitrogen and oxygen. The azomethine group of L was responsible for the IR band at 1640 cm^{-1}. The stretching vibrations at 542 cm^{-1}, 476 cm^{-1} and 431 cm^{-1} corresponds to M-O, M-N and M-S metal bonds of Zn(II) complex. The other stretching vibrations are shown in Table 1.

UV–Visible spectra

Ligands and the complexes they produce UV-visible spectra from 200 to 700 nm were obtained in DMSO solutions at ambient temperature. The two bands in the free ligand at 310 and 316 nm were found to be the $n \rightarrow \pi^*$ transition of the azomethine group and the $\pi \rightarrow \pi^*$ transition of the heterocyclic moiety respectively. Coordination with the metal centre the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions in metal complexes were shifted to longer wavelengths. Complexes exhibiting Cu(II) and Zn(II) transitions at $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ respectively seen in the bands at 318 and 329 nm. The $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions were shifted to longer wavelengths in these compounds. A cooperative association between M and L has been formed.

Thermal analysis

The Cu(II) complex undergoes a three-step degradation process. It is probable that the reduction of water molecules triggered the first step of deterioration, which occurred up to 180°C. The second phase, which begins at temperatures ranging from 190 to 390°C, is the degradation of the organic portion of a molecule. The third phase of breakdown starts at 398°C and finishes at about 620°C, when L is dissolved (42% of the total) and metal oxide is formed.

There are three separate steps in dissolving the Zn(II) complex. The first stage's disintegration up to 240°C is probably caused by the loss of water molecules. Temperatures between 240 and 290°C mark the second step of a molecule's organic moiety disintegration. At 290°C and continuing until roughly 430°C, the third stage of decomposition starts

Table 1 — IR spectral data of ligand L and its complexes in cm^{-1}

S. No.	Compd	C=N	C-O	O-H	C=C	C-S	M-O	M-N	M-S
1	Ligand	1610	1180	3071	1563	765	–	–	–
2	Zn(II)	1618	1165	3050	1518	724	542	476	431
3	Cu(II)	1604	1187	3082	1510	753	577	479	440

breaking down L (discovered 40%) and then forms metal oxide.

Results and Discussion

Synthesis of ligand (L)

The compound 4-((E)-(6-mercaptopyrimidin-4-ylimino)methyl)-2-hydroxybenzonitrile (L) was prepared by combining 1.34 g of 6-aminopyrimidine-4-thiol with 1.33 g of 4-formyl-2-hydroxybenzonitrile in an equimolar ratio. The reaction was carried out in a round-bottom flask. The reaction mixture became yellow after 6 hours of refluxing in an acidic medium. To monitor the progress of the reaction, TLC was used. The procedure for carrying out the reaction included reducing the pressure of the solution during evaporation, washing the yellow precipitate with ethanol, filtering and then recrystallizing the product with ethanol (Scheme 1).

Synthesis of metal complexes

Metal salts Cu(II) and Zn(II) were reacted with the ligand (2.49 g, 0.01 M) (L) in a 2:1 molar ratio to produce a variety of complexes. Ethanol was used to dissolve the ligands and metal chlorides separately (0.98 g, 0.01 M). Before adding metal salt solutions drop by drop to the ethanolic ligand solution, a few drops of sodium acetate solution were added to maintain a steady *p*H. After stirring the mixture for four hours, the precipitate formed. After removing the precipitate by filtration we cleaned it with ethanol and allowed to dry (Scheme 2).

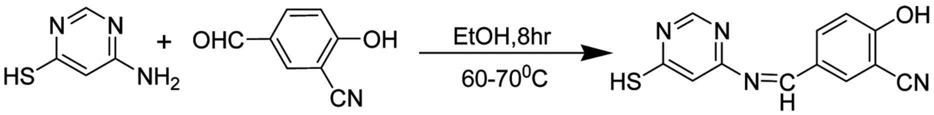
The present study involved the selection of three Gram positive bacteria, namely *Bacillus cereus*, *Micrococcus luteus* and *Staphylococcus aureus*, as well as six Gram negative bacteria namely *Klebsiella pneumonia*, *Enterobacter aerogenes*, *Escherichia coli*, *Pseudomonas fluorescens*, *Pseudomonas aeruginosa* and *Salmonella enteritidis*.

Biological activity

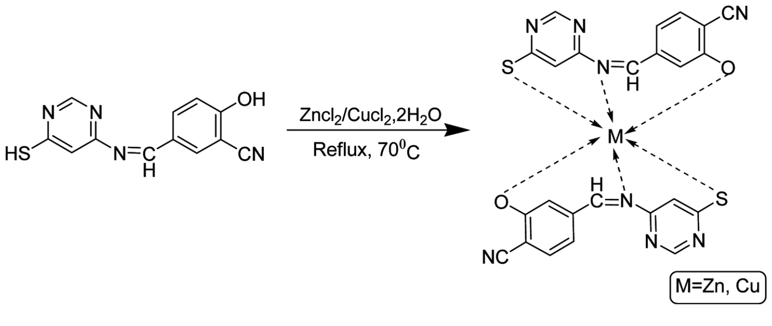
Antibacterial activity

The bacteria chosen for this study are Gram positive (*Bacillus cereus, Micrococcus luteus, Staphylococcus aureus*) and Gram negative (*Klebsiella pneumoniae, Enterobacter aerogenes, Escherichia coli, Pseudomonas fluorescens, Pseudomonas aeruginosa, Salmonella enteritidis)*. The bacterial stock cultures were kept at 4°C in a freezer after being cultivated on nutrient agar for 24 hours at 37°C. The ligand and its complexes were tested for antibacterial activity using the antibacterial agar well diffusion assay, which was slightly modified from the original methodology. Inoculating nutrient agar with nine food pathogenic bacterial strains was performed. Following that, sterilized discs (6 mm in diameter) containing samples (1 mg/mL) were deposited on inoculated nutritional agar medium.

After being saturated with DMSO, the discs were dried, then put on inoculation plates and left to incubate at 37°C for 24 to 48 hours. The disc's inhibitory zones diameter was measured in millimetres. The minimum inhibitory concentration (MIC) was used to assess the lowest concentration sufficient to inhibit the growth of the organism. The positive control and negative control consisted of dimethyl sulfoxide (DMSO) (1 mg/mL). Zn(II) showed high activity in all organisms when compared



Scheme 1 — Synthetic route of Schiff base ligand (L)



Scheme 2 — Synthetic route of Schiff base Metal complexes

Table 2 — The minimum inhibitory concentration values (MIC) of ligand and its complexes

		MIC^a(in mg/mL) Std. ciprofloxacin	Ligand(L)	Cu(II)	Zn(II)
Gram positive	*Bacillus cereus*	1.41 ± 1.06	2.65 ± 0.16	NA	3.21 ± 1.58
	Micrococcus luteus	2.22 ± 0.52	NA	6.11 ± 1.05	4.54 ± 0.25
	Staphylococcus aureus	3.17 ± 0.56	4.11 ± 0.12	NA	2.54 ± 1.10
Gram negative	*Klebsiella pneumoniae*	4.14 ± 0.32	NA	4.10 ± 0.02	4.83 ± 1.46
	Enterobacter aerogenes	2.12 ± 0.22	4.16 ± 0.12	NA	5.20 ± 0.20
	Escherichia coli	1.18 ± 0.54	NA	2.24 ± 1.06	5.97 ± 0.15
	Pseudomonas fluorescens	3.07 ± 0.70	NA	NA	5.36 ± 2.46
	Pseudomonas aeruginosa	2.45 ± 0.60	3.16 ± 0.12	NA	3.25 ± 0.28
	Salmonella enteritidis	2.11 ± 0.16	NA	2.34 ± 1.06	7.36 ± 0.70

NA: Not active.

to ciprofloxacin metal (II) complexes have much stronger antibacterial effects shown in Table 2.

Conclusion

In conclusion, we have created 4-((E)-(6-mercaptopyrimidin-4-ylimino)methyl)-2-hydroxy-benzonitrile (L) and the complexes with Cu(II), Zn(II). The spectral properties of Ligand and its metal complexes have been extensively studied. *In vitro* antibacterial activity against nine food pathogens was evaluated for the Schiff base ligand and their complexes. The antibacterial effects of the complexes were greater than those of the comparable ligand. The zinc complex was one of the compounds that showed promising antibacterial activity.

Supplementary Information

Supplementary information is available in the website http://nopr.niscpr.res.in/handle/123456789/58776.

Acknowledgment

The authors would like to extend their appreciation to the Director of the Indian Institute of Chemical Technology in Hyderabad. Chaitanya Deemed to be University's Principal, Hyderabad. Director of the Centre for Cellular and Molecular Biology, Hyderabad. For providing spectral information and biological activity.

Conflict of Interest

The author's confirmed that there is no conflicts of interest.

References

1 Al Zoubi W & Ko Y G, *Appl Organomet Chem*, 31 (2017) 3574.

2 Zhang J, Xu L & Wong WY, *Coord Chem Rev*, 355 (2018) 180.

3 Jia Y & Li J, *Chem Rev*, 115 (2014) 1597.

4 Das M, Baig F & Sarkar M, *RSC Adv*, 63 (2016) 57780.

5 Prasad K S, Castro J O, Frau J, Flores-Holgu N, Shruthi G, Shivamallu C & Glossman-Mitnik D, *J Mol Struc*, 1191 (2019) 17.

6 Wood J M, *Natur Wissen Schaften*, 62 (1975) 357.

7 Jarrahpour A, Khalili D, De Clercq E, Salmi C & Brunel J, *Molecules*, 12 (2007) 1720.

8 Wang Q, Wang Y & Yang Z Y, *Chem Pharm Bull,* 56 (2008) 1018.

9 Johari R, Kumar G, Kumar D & Singh S, *J Ind Coun Chem*, 26 (2009) 23.

10 Mittal P & Uma V, *Der Chemica Sinica*, 1 (2010) 124.

11 Kesharwani R & Singh P, *Asian J Chem*, 12 (2000) 23.

12 Kumar H, Chaudhary R, *Der Chemica Sinica*, 1 (2010) 55.

13 Habib S I, Baseer M A & Kulkarni P A, *Der Chemica Sinica*, 2 (2011) 27.

14 Bajpai P, Agrawal P K, Vishwanathan L, *J Sci Indust Res,* 41 (2011) 185.

15 Sullivan J F, *J Nutr,* 109 (1979) 1432.

16 Alaaddin C, IbrahimY, Habibe O & Misir A, *Trans Met Chem*, 27 (2002) 171.

17 Patel A D & Joshi J D, *Synth React Inorg Met-Org Nano-Met Chem*, 25 (1995) 991.

18 Kriza A, Reiss A, Forea S & Carproin T, *J Ind Chem Soc*, 77 (2000) 207.

19 Fujita M, Kwon Y J, Washizu S & Ogura K, *J Amer Chem Soc*, 116 (1994) 1151.

20 Konstantinovic S S, Radovanovic B C, Cakic Z & Vasic V, *J Serb Chem Soc*, 68 (2003) 641.

21 Farooque M A, Mosaddik M A, Islam M S, Alam M S, Bodruddoza M A K, *Online J. Bio Sci*, 2 (2002)797.

22 Patel K M, Patel K N, Patel N H, Patel M N, *Synth React Inorg Met-Org Nano-MetChem*, 31 (2001) 239.