

Green Chemistry Approach: Synthesis of Schiff Base Ligand Derived from 4-Hydroxy-3-Methoxybenzaldehyde and Glycine and its Cu (II), Zn (II) Complexes

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ABSTRACT

This study presents the green synthesis and characterization of a Schiff base ligand derived from 4-hydroxy-3-methoxybenzaldehyde and glycine, along with its Copper (II) and Zinc (II) complexes, employing a mechanochemical approach. This method aligns with green chemistry principles by minimizing waste and energy consumption, and avoiding hazardous reagents. The Schiff base ligand and metal complexes were synthesized through solvent-free grinding, producing a milky-colored ligand and distinctively colored complexes: dark green for Cu (II) and white for Zn (II). The synthesized compounds demonstrated high yields: 96% for the ligand, 98% for the Cu (II) complex, and 97% for the Zn (II) complex. Spectroscopic analyses, including infrared (IR) and ultraviolet-visible (UV-Vis) spectroscopy, confirmed the formation of the Schiff base and its metal complexes, revealing the presence of functional groups and electronic transitions indicative of complexation. The IR spectra showed characteristic bands for hydroxyl (O-H), imine (C=N), carbonyl (C=O), and aromatic groups, as well as metal-ligand (M-N, M-O) interactions. UV-Vis spectra indicated $\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$, and d-d transitions, suggesting conjugated π -systems and electronic transitions within the metal ions. This study underscores the efficacy and environmental benefits of the mechanochemical method in synthesizing Schiff base ligands and their metal complexes.

Key words: Green synthesis, mechanochemical, glycine, Schiff base complex

INTRODUCTION

Green synthesis of Schiff base compounds focuses on environmentally friendly methods that minimize waste, reduce energy consumption, and avoid hazardous reagents. Various methods include, mechanochemical Synthesis that utilizes mechanical force to drive chemical reactions, significantly reducing solvent waste and energy use. Solvent-Free Reactions which involves conducting reactions without solvents, which eliminates solvent-related hazards and disposal issues. Use of Renewable Resources Employing natural starting materials to create sustainable and biodegradable products. Catalyst-Free Methods entails avoiding toxic and expensive catalysts by using alternative activation methods like microwaves or ultrasound, which also often reduce reaction times. Energy-Efficient Techniques which involves Implementing microwave or ultrasonic irradiation to accelerate reactions, thereby reducing energy consumption and improving reaction efficiency. Aqueous or Green Solvents, when solvents are necessary, using water or other green solvents like ethanol to minimize environmental impact.

These green approaches not only make the synthesis of Schiff base compounds more sustainable but also

enhance safety and cost-effectiveness, aligning with the principles of green chemistry.

A condensation process occurs when the nucleophilic nitrogen atom of an amine attacks the electrophilic carbon atom of an aldehyde or ketone. This reaction results in the replacement of the C=O group with a C=N group in the final product. This product is known as a Schiff base, imine, azomethine, or anil. Named after Hugo Schiff, a Schiff base has the general structure $R_2C=NR^*$, where R^* is an alkyl or aryl group ($R^* \neq H$) and R may be a hydrogen (H) or another substituent (Ishaq *et al.*, 2020)

Schiff bases, characterized by the -N=CH- (imine) group, have been extensively used as chelating ligands in coordination chemistry. Their metal complexes are of significant interest due to their diverse chemical, structural, and biological properties. These complexes have industrial, antifungal, antibacterial, anticancer, and herbicidal applications. Chelating ligands with N, S, and O donor atoms are particularly interesting for their biological activity and versatility in bonding to metal ions, which can enhance their effectiveness (Aziz, 2010).

Vanillin, a phenolic aldehyde organic compound with the molecular formula $C_8H_8O_3$, contains aldehyde, ether, and phenol functional groups. It is the primary component of vanilla bean extract. The condensation of vanillin with amino acids produces a binucleating Schiff base, characterized by a bridging group that can span two metals, demonstrating strong complexation ability with metal ions (Sulaiman 2022). This study aimed to synthesize and characterize Schiff base ligand derived from 4-hydroxy-3-methoxybenzaldehyde and glycine and its copper(II) and Zinc(II) complexes using mechanochemical method.

In recent years, Schiff bases have experienced significant advancements, resulting in innovative applications across various scientific fields. These developments underscore their versatility in addressing contemporary challenges. Drug Delivery Systems: Schiff bases have been utilized to create advanced drug delivery systems, enabling the controlled encapsulation and release of therapeutic agents. Nanomaterials and Nanotechnology: Incorporated into nanomaterials, Schiff bases play a role in nanotechnology applications such as nanocatalysis, nanosensors, and drug delivery platforms. Biological Imaging: As fluorescent probes, Schiff bases are used in biological imaging to accurately visualize cellular processes and structures. Supramolecular Chemistry: Photodynamic Therapy: Schiff bases are explored in photodynamic therapy for cancer treatment, leveraging their photosensitive properties to target and destroy cancer cells. Catalytic Applications: Recent studies highlight the use of Schiff bases as catalysts in various reactions, including asymmetric synthesis, cross-coupling reactions, and sustainable catalysis. Smart Materials: Advances in Schiff bases have led to smart materials that respond to external stimuli like light, pH, or temperature, suitable for sensing and responsive technologies. Computational Approaches: Computational chemistry is employed to design Schiff bases with specific properties, speeding up the discovery of new compounds with tailored functionalities.

Recent research and discoveries have expanded the applications, synthetic methodologies, and properties of Schiff bases, continuing their evolution as a versatile class of compounds (Abou-Omar *et al.*, (2021); Fatima *et al.*, (2020); Iye EN *et al.*, (2019); Chen *et al.*, (2019); Leelanada *et al.*, (2016).

MATERIALS AND METHOD

In the synthesis of the Schiff base and its corresponding metal complexes; analytical grade chemicals were obtained from Sigma Aldrich and used without further purification. Glycine and vanillin served as the starting materials for the Schiff base preparation, while anhydrous $ZnCl_2$ and hydrated copper (II) chloride dihydrate were utilized as the metal salts for the complexation.

All glassware was thoroughly washed with detergent, soaked in 5% nitric acid, rinsed with distilled water, and dried in an oven (Sulaiman *et al.*, 2022). All weighing were performed using an electric balance. Melting points were determined with a digital melting/boiling point apparatus. Infrared spectral analyses were conducted using attenuated total reflectance in the range of 400-4000 cm^{-1} with a Perkin Elmer infrared spectrophotometer. Electronic spectra of the ligand and complexes were analyzed using a UV-Vis spectrophotometer in the range of 200-400 cm^{-1} and 400-900 cm^{-1} respectively. The solubility of the compounds was tested in various solvents including n-hexane, ethanol, water, chloroform, DMSO, DMF, methanol, benzene, acetone, and diethyl ether.

Synthesis of Schiff base Ligand

The Schiff base was synthesized using a modified procedure reported by Zhong and Qin (2014) as referenced in Sulaiman et al. (2022). Glycine (6.6 mmol) was weighed and placed in an agate mortar and pestle, then ground continuously for 30 minutes until the mixture became sticky. Vanillin (6.6 mmol) was then added and the grinding continued until the reactants turned milky color, resulting in a loose solid powder after about 1 hour. The reaction was conducted at room temperature. The product was dried in a hot air oven drying at 40 °C for approximately 10 minutes.

Synthesis of Cu (II) complex

Equimolar quantities (0.23 g, 3 mmol) of glycine, 4-hydroxy-3-methoxybenzaldehyde (0.46 g, 3 mmol), and copper (II) chloride dehydrate (0.51 g, 3 mmol) were combined in a agate mortar and ground with a pestle for 45 minutes. The resulting green-colored paste gradually transformed into a solid powder upon continuous grinding for an additional 15 minutes. A dark green solid product was obtained and subsequently dried in a hot air oven, then stored in a desiccator over anhydrous calcium chloride.

Synthesis of Zn (II) complex

Equimolar quantities (0.23 g, 3 mmol) of glycine, 4-hydroxy-3-methoxybenzaldehyde (0.46 g, 3 mmol), and anhydrous Zinc (II) chloride ((0.41 g, 3 mmol) were combined in agate mortar and ground with a pestle for 45 minutes. White-colored solid powder upon continuous grinding for an additional 15 minutes were obtained. The white solid product was subsequently dried in a hot air oven, and then stored in a desiccator over anhydrous calcium chloride.

RESULT AND DISCUSSION

The ligand and metal complexes were soluble in DMSO, DMF, and ethanol but insoluble in acetone, chloroform, n-hexane, diethyl ether, water and methanol. These compounds exhibit high stability in solid and dry atmospheres except Cu (II) complexes which are hygroscopic at lower temperatures. Consequently, they were stored in a desiccator over CaCl₂. The mechanochemical technique used for synthesizing the compounds yielded a milky-colored ligand, and white and dark green complexes for Zn (II) and Cu (II), respectively. The non-hygroscopic crystalline Schiff base exhibited a melting point range of 210-212°C. The complexes were quantitatively obtained through manual grinding of solid metal salts and Schiff base at room temperature, with impressive yields of 98% for the Cu (II) complex, 97% for the Zn (II) complex, and 96% for the ligand, as shown in Table 1. The solubility in polar solvents can be attributed to the polar nature of the synthesized compounds.

Table 1. Physical properties of Ligand and metal (II) complexes

Compound	Colour	Melting point °C	% Yield
Ligand	Milky	210-212	96
Cu (II) complex	dark green	>300	98
Zn (II) complex	white	>300	97

S. Ishaku *et al.*, 2024

Infra-red and Uv-Vis Spectra

The infra-red spectra of the Schiff base ligand and the metal (II) complexes showed important bands as recorded in table 2. The infrared (IR) and ultraviolet (UV) spectral data provide valuable insights into the functional groups and electronic transitions in the Schiff base compound. For the IR- spectral bands, νO-H

(3308 cm^{-1}), this band corresponds to the stretching vibration of the hydroxyl (O-H) group. It indicates the presence of hydroxyl groups, which are typically found in phenols or alcohols. $\nu\text{C-H}$ (2891 cm^{-1}), this band is due to the stretching vibrations of C-H bonds in aldimines. It indicates the presence of C-H bonds, usually from the aldehyde or aromatic ring. $\nu\text{C=N}$ (1675 cm^{-1}), this band corresponds to the stretching vibration of the imine (C=N) group. The presence of this band is a key characteristic of Schiff bases, indicating the formation of the imine linkage. $\nu\text{C=O}$ (1689 cm^{-1}), this band represents the stretching vibration of the carbonyl (C=O) group in the acidic end of the amino acid glycine. The $\nu\text{C=C}$ (1581 cm^{-1}) band corresponds to the stretching vibration of the carbon-carbon double bond (C=C). $\nu\text{C-O}$ (1282 cm^{-1}) band is due to the stretching vibration of the carbon-oxygen (C-O) bond, indicating the presence of ether or phenol groups. While, $\nu\text{C-N}$ (1114, 1170 cm^{-1}) band correspond to the stretching vibrations of the carbon-nitrogen (C-N) bonds. They are typically found in amines or imines, reinforcing the presence of the imine linkage in the Schiff base. The Ultraviolet (UV) Spectral Peaks of 262 nm (38167 cm^{-1}) absorption peak is indicative of $\pi \rightarrow \pi^*$ transitions. It is typically associated with the conjugated system of double bonds, such as those in aromatic rings or C=C bonds. While, 334 nm (29940 cm^{-1}) absorption peak is likely due to $n \rightarrow \pi^*$ transitions. These are common in compounds with non-bonding electrons, such as those found in carbonyl (C=O) and imine (C=N) groups.

The Infrared (IR) Spectral Data for Copper (II) Complex showed important bands at $\nu\text{O-H}$ (3367 cm^{-1}), this band corresponds to the stretching vibration of the hydroxyl (O-H) group. In the context of a metal complex, it may indicate the presence of coordinated water molecules or hydroxyl groups of carboxylic acid. $\nu\text{C-H}$ (2994 cm^{-1}), band is attributed to the stretching vibrations of C-H bonds. $\nu\text{C=N}$ (1675 cm^{-1}) band corresponds to the stretching vibration of the imine (C=N) group. It confirms the presence of the Schiff base ligand in the complex, as the C=N bond is a characteristic feature of Schiff bases. $\nu\text{C=O}$ (1580 cm^{-1}) this band represents the stretching vibration of the carbonyl (C=O) group. In metal complexes, the position of this band shift slightly compared to the free ligand, indicating coordination through the oxygen atom of the carbonyl group. $\nu\text{C=C}$ (1517 cm^{-1}) This band corresponds to the stretching vibration of the carbon-carbon double bond (C=C), typically associated with aromatic rings or alkenes. $\nu\text{C-O}$ (1282 cm^{-1}) is due to the stretching vibration of the carbon-oxygen (C-O) bond, indicating the presence of ether or phenol groups in the complex. While $\nu\text{C-N}$ (1105 cm^{-1}) band corresponds to the stretching vibration of the carbon-nitrogen (C-N) bond, which is present in the Schiff base ligand. The $\nu\text{M-N}$ (637 cm^{-1}) band represents the stretching vibration of the metal-nitrogen (M-N) bond. It indicates that the nitrogen atom of the Schiff base is coordinated to the copper (II) ion and $\nu\text{M-O}$ (574 cm^{-1}) band corresponds to the stretching vibration of the metal-oxygen (M-O) bond. It indicates coordination through the oxygen atom, likely from the hydroxyl or carbonyl group, to the copper (II) ion. Ultraviolet (UV) Spectral Peaks 269 nm (37174 cm^{-1}) Uv absorption peak is indicative of $\pi \rightarrow \pi^*$ transitions. It suggests the presence of conjugated systems, and 345 nm (281985 cm^{-1}) UV absorption peak likely corresponds to $n \rightarrow \pi^*$ transitions, common in compounds with non-bonding electrons, such as carbonyl and imine groups. 432 nm (23148 cm^{-1}) uv absorption is may be due to charge transfer.

The Infrared (IR) Spectral Bands of Zn (II) complex showed bands at $\nu\text{O-H}$ (3372 cm^{-1}) the stretching vibration of hydroxyl (O-H) groups possibly from coordinated water or hydroxyl-containing ligands. $\nu\text{C-H}$ (2889 cm^{-1}) likely the stretching vibrations of C-H bonds, $\nu\text{C=N}$ (1674 cm^{-1}) band is due to the stretching vibration of the imine (C=N) group, characteristic of Schiff bases. $\nu\text{C=O}$ (1580 cm^{-1}) band represents the stretching vibration of the carbonyl (C=O) group. $\nu\text{C=C}$ (1517 cm^{-1}) band corresponds to the stretching vibration of carbon-carbon double bonds (C=C), typically found in aromatic rings or alkenes. $\nu\text{C-O}$ (1281 cm^{-1}) band indicates the stretching vibration of carbon-oxygen (C-O) bonds, suggesting the presence of ether or phenol groups in the compound. $\nu\text{C-N}$ (1107 cm^{-1}) band represents the stretching vibration of carbon-nitrogen (C-N) bonds, indicating the presence of nitrogen-containing groups such as imines or amines. $\nu\text{M-N}$ (641 cm^{-1}) band corresponds to the stretching vibration of metal-nitrogen (M-N) bonds, showing coordination of the nitrogen atoms in the ligand to the metal ion while, $\nu\text{M-O}$ (572 cm^{-1}) band represents the stretching vibration of metal-oxygen (M-O) bonds, indicating coordination through oxygen atoms, possibly from carbonyl or hydroxyl groups, to the metal ion. Ultraviolet (UV) Spectral Peaks at 253 nm (39525 cm^{-1}) Uv absorption peak is associated with $\pi \rightarrow \pi^*$ transitions, 342 nm (29239 cm^{-1}) This peak likely corresponds to $n \rightarrow \pi^*$ transitions, which are common in compounds with non-bonding electrons, such as those in carbonyl and imine groups while 614 nm (16286 cm^{-1}) peak is typically associated with d-d transitions of the metal ion, indicating electronic transitions within the metal ion's d orbitals in the coordination environment. The IR

spectral data confirm the presence of key functional groups and metal-ligand interactions in the copper (II) and Zn (II) complex. The shifts in the positions of the C=N and C=O bands compared to the free ligand indicate coordination through these groups. The presence of M-N and M-O bands further confirms the coordination of the Schiff base ligand to the copper (II) ion. The UV spectral data suggest the presence of conjugated π -systems and d-d transitions, providing additional insights into the electronic structure of the complex.

Table 2: Infra-red Spectra data for ligand and metal(ii) complexes

Compound	$\nu(\text{O-H})$ (cm^{-1})	$\nu(\text{C-H})$, (cm^{-1})	$\nu(\text{C=N})$, (cm^{-1})	$\nu(\text{C=O})$ (cm^{-1})	$\nu(\text{C=C})$ (cm^{-1})	$\nu(\text{C-O})$ (cm^{-1})	$\nu(\text{C-}),$ (cm^{-1})	$\nu(\text{M-N})$ (cm^{-1})	$\nu(\text{M-O})$ (cm^{-1})
Ligand	3308	2891	1675	1689	1581	1282	1169	-	-
Cu (II) complex	3371	2994	1675	1580	1517	1282	1105	637	574
Zn (II) complex	3372	2892	1674	1580	1517	1281	1107	641	572

S. Ishaku *et al.*, 2024.

Antimicrobial Assay Schiff Base Ligand and Metal Complexes

The results of the antimicrobial screening of the Schiff base and its metal complexes at a concentration of 30mg/mL (0.03g/mL) in DMSO against five (5) antibacterial strains were analyzed. The inhibition Zone was measured in millimeters. The results indicated that the ligands and Co (II) complexes showed susceptibility against all the bacteria isolates of Escherichia Coli, Staphylococcus aureus, Klebsiella pneumoniae and Pseudomonas aeruginosa except Salmonella typhi which showed resistance to the metal complexes and the ligand. In general, at 30mg/mL concentrations Schiff base ligand and Co (II) complexes showed activity in comparison with the standard drug ciprofloxacin.

CONCLUSION

This study demonstrates the successful synthesis of Schiff base ligands and their metal complexes through a mechanochemical approach. The ligand and metal complexes exhibit solubility in solvents such as DMSO, DMF, and ethanol, while insoluble in non-polar solvents like acetone, chloroform, n-hexane, diethyl ether, and methanol including water. Notably, the ligand and Cu (II) complexes are hygroscopic at lower temperatures, necessitating storage in a desiccator over CaCl_2 .

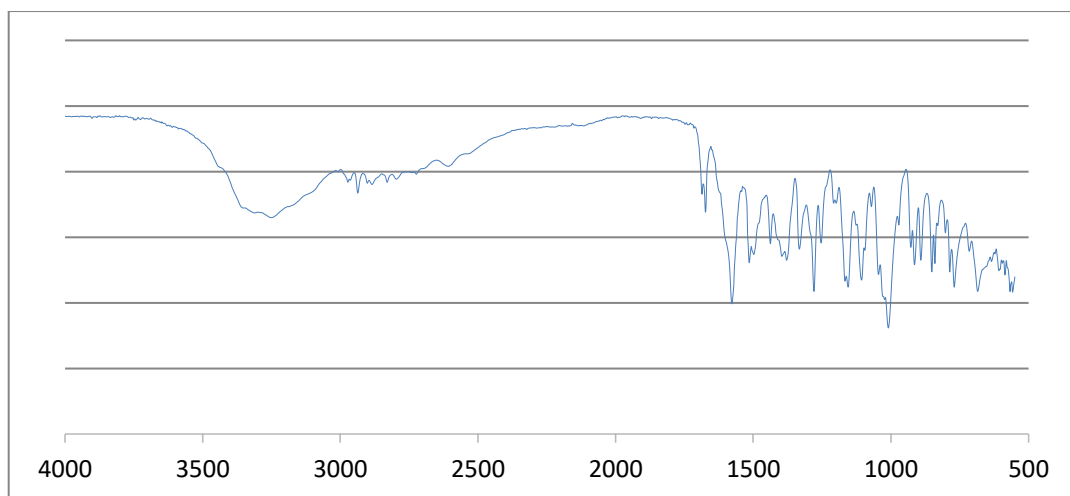
The mechanochemical synthesis produced a milky-colored ligand and distinctively colored Zn (II) (white) and Cu (II) (dark green) complexes. The crystalline Schiff base exhibited a melting point range of 210-212°C. The high yields of the synthesized compounds—98% for the Cu (II) complex, 97% for the Zn (II) complex, and 96% for the ligand—underscore the efficiency of the mechanochemical method.

Infrared (IR) and ultraviolet-visible (UV-Vis) spectroscopy provided critical insights into the structural and electronic properties of the synthesized compounds. The IR spectra confirmed the presence of key functional groups, including hydroxyl, imine, carbonyl, and aromatic rings, as well as metal-ligand interactions. The UV-Vis spectra revealed $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions, along with d-d transitions in the metal complexes, highlighting the conjugated π -systems and electronic transitions within the metal ions' coordination environment.

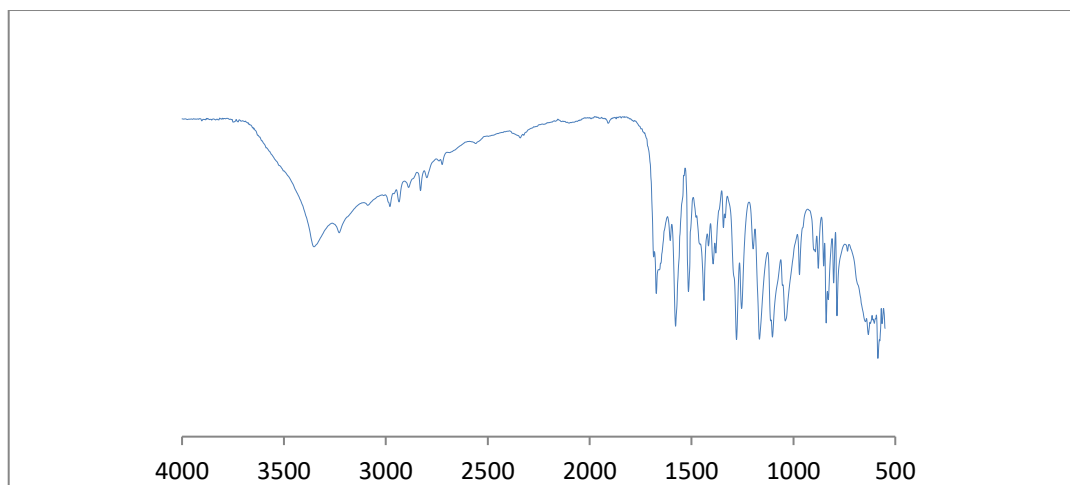
The antimicrobial screening of the ligand and metal (II) complexes of Cu and Zn showed promising result of high susceptibility than the standard drug ciproflaxin

In summary, mechanochemical methods for Schiff base synthesis offer substantial environmental advantages

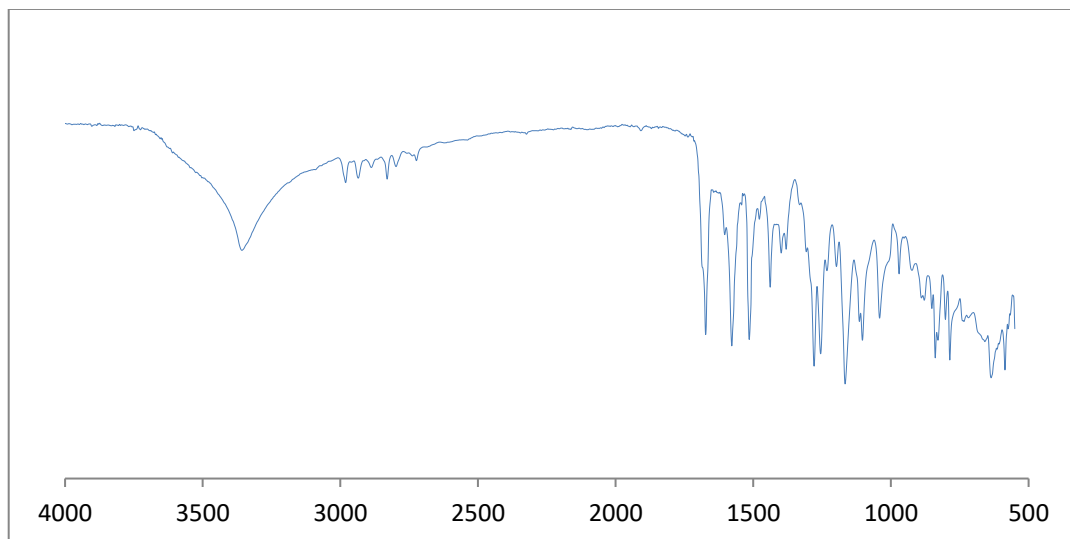
over traditional methods by reducing solvent use, minimizing waste, enhancing energy efficiency, improving safety, and promoting sustainable catalysis. These benefits align with the principles of green chemistry, making mechanochemical methods a more eco-friendly alternative for chemical synthesis. It is therefore recommended that, further studies be carried out to ascertain the potency of these compounds as antiviral, anticancer and antifungal agents to enhance and ascertain its usability and applicability.



Ligand (L) spectra



Cu (II) complex spectra



Zn (II) complex spectra

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