

Ni(II) Complex of a Novel Schiff Base Derived from Benzaldehyde and Sulphathiazole: Synthesis, Characterization and Antibacterial Studies

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Abstract: New Schiff base and its Ni(II) complex, were synthesized using benzaldehyde and sulphathiazole. They were characterized using elemental analyser, UV-visible spectrophotometer, FTIR, ¹H-NMR and ¹³C-NMR spectroscopy. IR spectral data suggested that the ligand coordinated to nickel ions through two azomethine nitrogen, and one amine nitrogen. Electronic spectral measurement indicated the occurrence of ligand to metal charge transfer. Based on the continuous variation method, metal: ligand ratio of 1:1 was proposed. Elemental analysis and spectroscopic studies suggested that the Schiff base behaved as a tridentate ligand towards nickel ion. Antibacterial sensitivity of the ligand and its Ni (II) complex were assayed in vitro against *Staphylococcus aureus*, *Echerichia coli*, *Pseudomonas aeruginosa* and *Salmonella typhi*. It was observed that the Ni(II) complex was more potent than the Schiff base against the bacterial strains used. Therefore, the Schiff base and its Ni(II) complex may inhibit bacterial infections caused by *E.coli*, *P.aeruginosa*, *S. typhi* and *S.aureus*. The Ni(II) complex showed enhanced antibacterial activity when compared with the pure the Schiff base.

Key Words: Schiff base, synthesis, benzaldehyde, sulphathiazole, Ni²⁺, characterization, antibacterial assay.

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1.0 Introduction

A Schiff base is a compound formed from the condensation of either an aldehyde or a ketone with a primary amine. The carbonyl group of the aldehyde gives aldimines while that of ketone gives ketoimines. They are condensation products of ketones (or) aldehydes with primary amines (Zhang *et al.*, 2006). The application of inorganic chemistry in medicine can be divided into two main categories. In the first class, ligand serves as drugs and function by targeting a metal ion of one form or the other (free or bound). The second class involves metal-based drugs and imaging agents in which the central metal atom is usually the key feature of the mechanism of action. The development in the field of bio-inorganic chemistry has attracted researches in synthesis and applications of Schiff bases because most Schiff bases have been identified as models for biologically important species. Schiff bases are special class of ligands with a variety of donor atoms that enhances coordination modes towards various metals. Schiff base ligands containing NO, NS, NNO and SNO donor systems are ubiquitous in coordination chemistry and are use in synthesis of most transition metal complexes, which remains an important area of research due to their simplify synthetic route, good yield, high purity and wide range of applications (Shebl, 2008). The study of Schiff bases has received great impetus in recent years due to their remarkable stereochemical, electrochemical and electronic properties. Schiff

bases with hetero atoms (N, S and O), which often acts as donor atoms, have been found to exhibit excellent biological activity that has been linked to their binding mode to metal (Shebl, 2008). Schiff bases have structural similarities with neutral biological systems and due to the presence of imine group, they are useful in elucidating the mechanism of transformation of racemization reaction in biological system (Wu and Yuan, 2004; Keskioglu *et al.*, 2008).

Several researches have confirmed that most metals interact with Schiff base to form chelates. For example, Xishi *et al.* (2003), reported the synthesis and characterization of a novel Schiff base ligand from the condensation of 2,2-bis (p-methoxyphenylamine) and salicylaldehyde. Its Mn (II), Co(II) and Cu(II) complexes were also synthesized by interacting them with the synthesized Schiff base. Ben Saber *et al.* (2005), reported the synthesis and characterization of Cr(III), Fe(III), Co(II) and Ni(II) complexes of a Schiff base derived from 4- dimethylamino benzaldehyde and primary amines, Other studies have also been reported and in most cases, the synthesized Schiff bases were also reacted with some metal ions to form complexes (Otuokere and Chinweuba., 2011)

The growing interest in transition metal complexes containing Schiff base antibiotics is derived from their functions and well-established chemical in biological systems as well as their pharmaceutical and catalytic applications (Rehder *et al.*, 2003; Rehder, 2003). Schiff's bases represent an important class of pharmacologically active molecules of significant interest because of their useful pharmacological properties. A number of Schiff's base derivatives have been reported to exert excellent antibacterial (Amir *et al.*, 2002; More *et al.*, 2002; Chohan *et al.*, 2010), antifungal, antitubercular, antitumor, antileishmanial and DNA-binding activities (Rajendran and Karvembu, 2002). Schiff base compounds have been the subject of great interest in fungicidal studies (Chohan *et al.*, 2005; Otuokere and Chinweuba, 2011), biological studies (Ergene *et al.*, 2010; Abd El-halim *et al.*, 2011), antimicrobial studies (Da Silva *et al.*, 2011) and antibacterial studies (Lekha *et al.*, 2014).

Several Schiff bases have been synthesized and tested for microbial activities. Umendra and

Sulekh, (2011) synthesized Schiff base complexes of Ni(II) ion and reported that they demonstrated good antifungal activities against pathogenic fungi and were much better than those of standard fungicide chlorothalonil. Rakesh *et al.*, (2015) investigated the antifungal activity of N-(2-hydroxy-1-naphthalidene) phenylglycine and its transition metal complexes. They investigated and concluded that the activity of the ligand was increased upon complexation with Cu (II), Ni (II) and Co (II) ions. Therefore, the metal Schiff base complexes displayed better antifungal activity compared to the ligand. Metal (II) coordination compounds of Mn, Co and Cu with a Schiff base derived from the condensation of cinnamaldehyde antibiotic with ethylenediamine were synthesized and characterized by Anacona and Santaella (2013) and were found to displayed good antimicrobial activities. Some Schiff based of benzaldehyde or sulphathiazole derivatives have also been synthesized, characterized and tested for antimicrobial activities. Seng (2006) synthesized Schiff base by coupling benzol acetone with sulfathiazole and characterized it through elemental analysis, FTIR and H NMR. Antioxidative and antimicrobial actions of the metal Schiff bases were enhanced more than that of the Schiff base itself. Anacona *et al.* (2018) synthesized metal coordination compounds of a cephalixin base derived from the condensation of cephalixin antibiotics with sulphathiazole and were characterized by elemental and thermal analysis, molar conductance and magnetic susceptibility measurements, electronic, FT-IR, EPR and ¹H NMR spectral studies. The biological activities of the metal Schiff bases complexes were also found to be better than those of the free ligand. Iqbal and Hoque. (2016) synthesized, characterized and investigated antimicrobial properties of Schiff base derived from amoxicillin and benzaldehyde. Screening of the Schiff base for antibacterial and antifungal activities revealed strong inhibition zones that were better than the antibiotics alone. Similar findings have been reported by Kshash (2010) for Schiff bases synthesized by direct condensation of cefotaxime and benzaldehyde and by Sinthuja and Kumari (2013).

Anacona and Lopez (2012) synthesized nickel (II) complexes containing sulfathiazole and cephalosporin antibiotics. They characterize the



complexes and tested for their antimicrobial activities and the results indicated the effectiveness of these complexes as comparable to some commercial cephalosporins. Abdulghani and Hussain (2015) and Osigbemhe *et al.* (2020), also made similar conclusion based on their study that involves the same compounds except benzaldehyde replaces sulfathiazole. In our research group, we also reported that Ni(II) complex of (3,3-dimethyl-7-oxo-6-(2-Phenylacetamido)-4-thia1-azabicyclo-[3.2.0]heptane-2-carboxylic acid exhibited anti-microbial activities (Otuokere *et al.*, 2020). Arising from the fact that Schiff bases of nickel(II) complexes and those coupled with either sulfathiazole or benzaldehyde have shown great performance against microbial activity, it becomes interesting to note that to the best of our knowledge neither Schiff base produced by coupling sulfathiazole with benzaldehyde nor their Ni(II) complexes have been reported elsewhere. Therefore, the present study is aimed at synthesizing, characterizing and antimicrobial assay of Ni(II) Schiff base derived from sulfathiazole with benzaldehyde.

2.0 Materials and Methods

2.1 Instrumental analysis

The chemicals and solvents used in this study were of analytical grade and were used as obtained without further purification. The melting points and decomposition temperature of the novel Schiff base ligand and the Ni(II) complex were determined using Gallenkamp melting point apparatus. The solubility of the novel Schiff base ligand and Ni(II) complex were determined in n-hexane, methanol, petroleum ether and dimethylsulfoxide. The molar conductance of the novel Schiff base

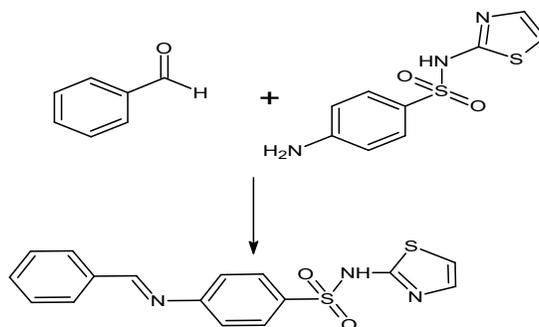
ligand and the Ni(II) complex were measured at room temperature in a concentration of 10^{-3} M DMSO solution using Jenway Conductivity Meter 4510. Nickel analyses were carried out on AAS spectrophotometer (Buck210). The elemental analysis for C, N, H and S were obtained using a Perkin-Elmer 240B elemental analyzer. The stoichiometry of the complex was determined using continuous variation method as described by Tirmizi *et al.*, (2012). The UV-Vis spectral measurement was determined using UV-1800 series. The solvent used was DMSO. FTIR spectra were obtained on a Perkin Elmer Spectrum BX FT-IR spectrophotometer ($4400-350\text{ cm}^{-1}$) in KBr pellets. The NMR spectral measurements were recorded on nuclear magnetic resonance Bruker spectrophotometer using tetramethylsilane internal standard and DMSO- d_6 as solvent.

2.2 Synthesis of the novel Schiff base ligand, 4-[(E)-phenylmethylidene]amino}-N-(1,3-thiazol-2-yl)benzene sulfonamide (PTBS)

The synthesis was carried out according to the method of Zahid, (2012) with slight modification. Sulphathiazole (5.11 g; 2 mmol) in ethanol (45 cm^3) solution was added to 2.03 cm^3 (2 mmol) of benzaldehyde. The solution was stirred and refluxed for 3 hours. The product was filtered off, washed several times with H_2O , cold ethanol and dried in a desiccator. The yield was calculated as shown in Equation 1.

$$\text{Percent (\%)}\text{Yield} = \frac{\text{Actual Yields (in g)}}{\text{Theoretical Yield (in g)}} \times 100(\%) \quad (1)$$

The propose scheme for the synthesis of the Schiff base is shown in Scheme 1.



Scheme 1: Synthesis of 4-[(E)-phenylmethylidene]amino}-N-(1,3-thiazol-2-yl)benzenesulfonamide Schiff base ligand (PTBS)



2.3 Synthesis of 4-[(E)-phenylmethyldiene]amino-N-(1,3-thiazol-2-yl)benzene sulfonamide-Ni(II) complex

To 45 cm³ hot ethanol solution of (6.87 g; 2 mmol) PTBS, 45 cm³ aqueous solution of (4.75 g; 2 mmol) NiCl₂.2H₂O was added and refluxed for 2 hours. The solution obtained were filtered and evaporated to half of its volume. The concentrated solutions were left overnight at room temperature for precipitation to take place. The product was filtered off, washed several times with H₂O, cold ethanol and dried in an oven and the yield was calculated using equation 1.

2.4 Antibacterial sensitivity test

The organisms used were gram-negative *E.coli* and *P. aeruginosa*. The gram-positive bacterial strains were *S. aureus* and *S. typhi*. The organisms were clinical isolates obtained from Federal Medical Centre, Umuahia, Abia State. Antibacterial activity of the samples were determined by using agar well diffusion method while bacterial growth were subcultured on nutrient broth for their *in vitro* testing which were prepared by dissolving (24 g) of nutrient broth. The mixture was autoclaved for 15 minutes at 120 °C. Stock solution for *in vitro* antibacterial activity was prepared by dissolving 5 mg of compound in 9 cm³ of DMSO. Inoculation was done with the help of micropipette with sterilized tips in which 100 µL of activated strain was placed onto the surface of agar plate. It was spread over the whole surface and then two wells having diameter of 10 mm were dug in media and incubated at 37 °C for 48 hours. Activity was determined by measuring the diameter of zone showing complete inhibition and has been expressed in mm.

3.0 Results and Discussion

Table 1 presents results obtained for physicochemical parameters of PTBS and [Ni(PTBS)]. Since the complexes are coloured, it indicates that complexation occurred. The melting point of the complex was higher than that of the Schiff base ligand because the metals have closed packed structures, so they have strong metallic bond and small atomic radii, they need more energy to break the bonds (Nadiyah and Uwaisulqarni, (2013). However, the conductivities of PTBS and [Ni(PTBS)] were 10.5 and 10.7 Sm²mol⁻¹ respectively. These values are low and point toward weak electrolytic systems Geary

(1971) reported that coordination compounds with molar conductance above 100 Ohm⁻¹mol⁻¹cm⁻¹ are electrolytes, indicating that those below this threshold value are weak electrolyte. The elemental analysis results were in good agreement with the calculated value. Based on the continuous variation method, metal: ligand ratio of 1:1 was proposed.

Table 1: Some physicochemical parameters of PTBS and [Ni(PTBS)]

Properties	PTBS	[Ni(PTBS)]
Colour	Greenish-brown	Green
M.P. (°C)	244-246	280 -282
Yield (%)	96.1	85.4
Conductance (Sm ² mol ⁻¹)	10.5	10.7
Metal: ligand	-	1:1
C Found (Calc.)	55.92 (55.71)	47.91 (47.04)
H Found (Calc.)	3.79 (3.72)	3.02 (3.07)
Ni Found (Calc.)	-	14.63 (14.55)
N Found (Calc.)	12.21 (12.27)	10.48 (10.41)
O Found (Calc.)	9.30 (9.38)	7.98 (7.92)
S Found (Calc.)	18.63 (18.57)	15.99 (15.78)

Table 2 present solubility profile of the Schiff base and its complex. The Schiff base and its Ni(II) complex were insoluble in methanol, slightly soluble in n-hexane, slightly soluble in petroleum ether and very soluble in DMSO. The solubility profile suggested that PTBS and [Ni(PTBS)] are moderately polar compounds. They were soluble in DMSO was because it is an important polar aprotic solvent that dissolves both polar and non-polar compound.

The FTIR spectra of PTBS and [Ni(PTBS)] are shown in Fig. 1. The FTIR spectral of PTBS and [Ni(PTBS)] were compared and used to ascertain the binding mode of the nickel ions at donor sites of the ligand. Information concerning the coordination of metal ions with nitrogen was revealed by the appearance of a medium intensity band at 457.00 cm⁻¹, which was assigned to ν(M-N) stretching vibration (Najlaa *et al.*, 2020).



Table 2: Solubility profile of PTBS and [Ni(PTBS)] in various solvents

Ligand/complex	n-Hexane	Methanol	Petroleum ether	DMSO
PTBS	SS	IS	SS	VS
[Ni(PTBS)]	SS	IS	SS	VS

****IS-Insoluble, SS-Slightly Soluble, VS-Very soluble**

The FTIR of the PTBS Schiff base showed absorption band at 1697.90 cm^{-1} which was assigned to azomethine $\nu(\text{C}=\text{N})$ stretching mode. On comparison with [Ni(PTBS)] it was deduced that this peak was shifted to lower wavenumber (i.e., 1625.66 cm^{-1}) indicating the participation of the azomethine nitrogen in coordination. Similar shift was reported by Narendra and Parashuram, (2014) in the formation of metal complexes of Schiff base derived from streptomycin and amoxicillin. Canpolat, (2014) reported that in the IR spectrum of the dioxouranium (VI) Schiff base complexes, the $\nu(\text{C}=\text{N})$ azomethine stretching band appearing at ca. $1617\text{-}1644\text{ cm}^{-1}$ in the ligands are shifted ca. $1599\text{-}1619\text{ cm}^{-1}$ for the complexes. The absence of band characteristics of $\nu(\text{C}=\text{O})$ confirms the formation of the proposed Schiff base framework. The band at 3361.79 cm^{-1} was assigned to $\nu(\text{N-H})$ stretch in the PTBS ligand. In the complex, the $\nu(\text{N-H})$ stretch was absent which suggested deprotonation during coordination to Ni(II) ion. The vibration frequency observed at 1414.30 cm^{-1} was assigned to $\nu(\text{S}=\text{O})$ of the Schiff base. This functional group remained unchanged 1419.00 cm^{-1} in the spectrum of [Ni(PTBS)] suggesting that this group was not involved in coordination to Ni(II) ion.

The electronic spectra of Schiff base PTBS and [Ni(PTBS)] are shown in Fig.2. Comparison of the electronic spectra of Schiff base PTBS and [Ni(PTBS)] were made. The Schiff base PTBS and [Ni(PTBS)] showed absorption maxima at 207.50, 216.50, 229.50, 240.50, 244.50, 254.50, 261.50, 271.50, 280.50 and 284.50 nm. The transitions were assigned to intra ligand charge transfer (ILCT). These were due to $n - \pi^*$ and $\pi - \pi^*$ transitions in $\text{C}=\text{N}$ and $\text{C}=\text{C}$ chromophores. [Ni(PTBS)] showed an additional peak at 320 nm.

This absorption band was assigned to ligand to metal charge transfer (LMCT). This transition suggested the formation of the nickel complex.

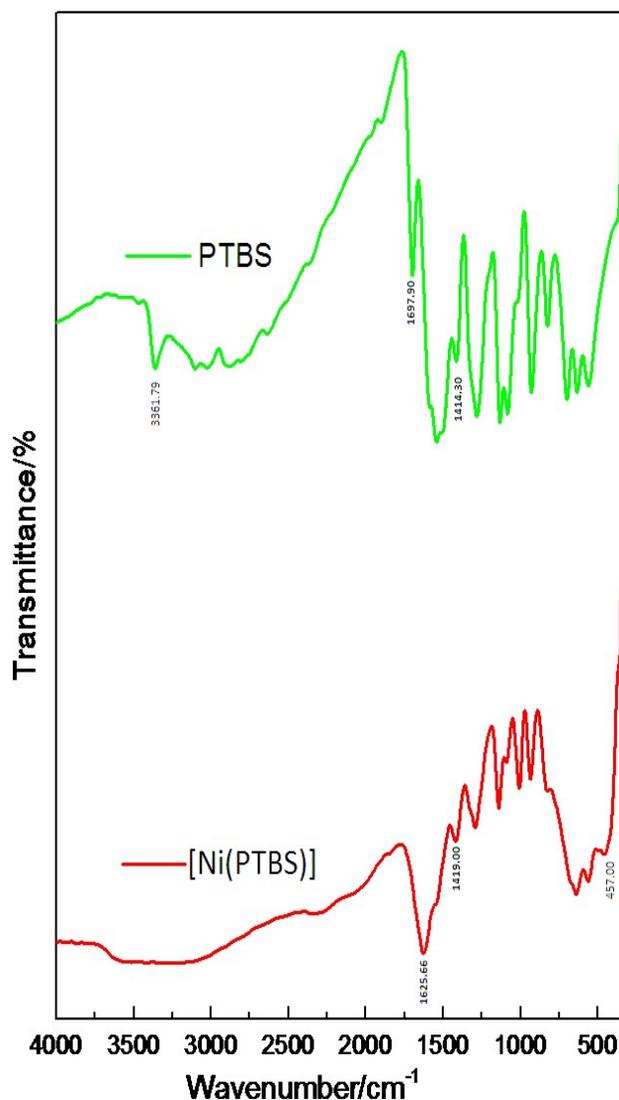


Fig. 1: FTIR spectra of PTBS and [Ni(PTBS)]



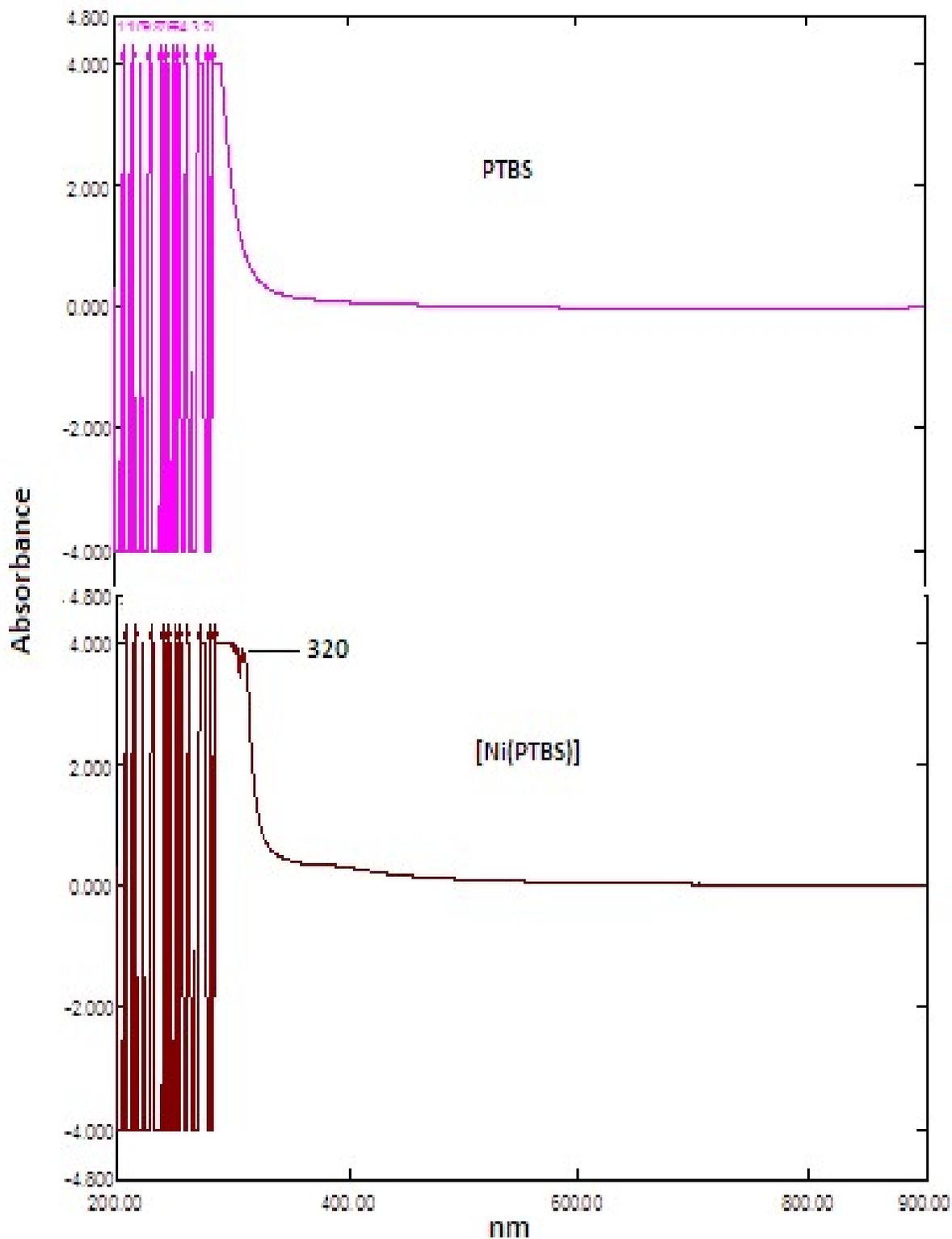


Fig. 2: Uv-Vis spectra of PTBS and [Ni(PTBS)]



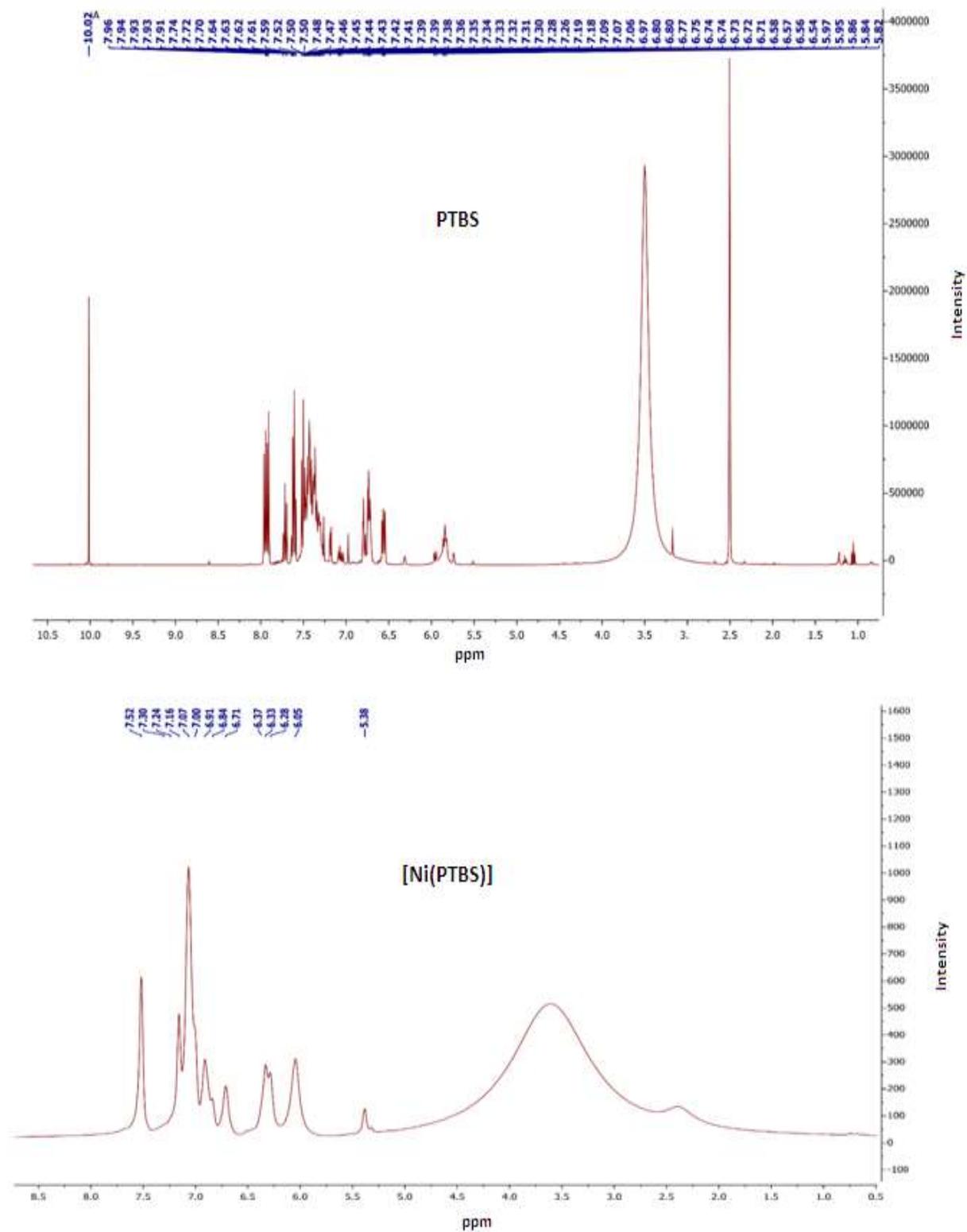


Fig. 3: ¹H-NMR spectra of PTBS and [Ni(PTBS)]



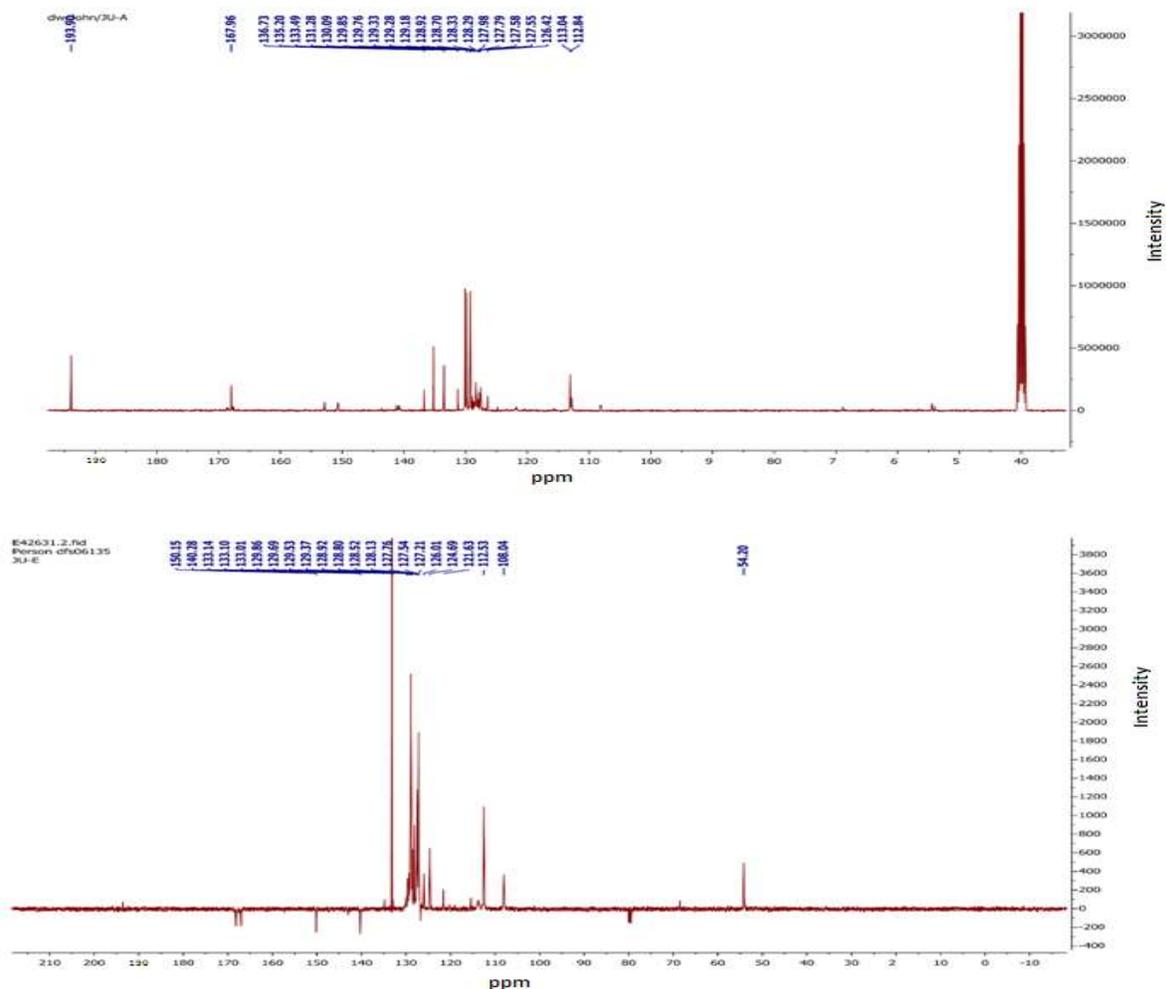


Fig. 4: ^{13}C -NMR spectra for PTBS and [Ni(PTBS)]

Based on continuous variation method, elemental analysis, FTIR, UV-Vis, ^1H -NMR and ^{13}C -NMR spectroscopy, the proposed structure for the newly synthesized Schiff base ([Ni(PTBS)]) is shown in Fig. 5.

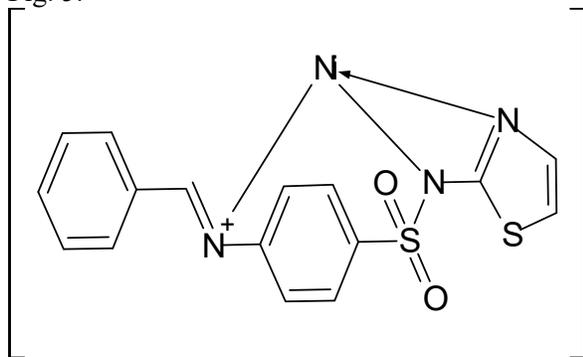


Fig. 5: Proposed structure of [Ni(PTBS)]

The zone of inhibition (mm) of PTBS and [Ni(PTBS)] on some bacterial species are shown in Table 3. The data showed that all compound exhibited varying degree of inhibitory results on the growth of different tested bacterial strains. [Ni(PTBS)] showed a higher significant activity ($p < 0.05$) when compared to PTBS. [Ni(PTBS)] showed higher significant activity ($p < 0.05$) against *E. Coli*, *P. aeruginosa* and *S. typhi* bacterial strain when compared to PTBS.

The significant antibacterial activity is attributed to the chelation of the ligand with metal ions. It has been reported that in a complex, coordination could augment the lipophilic character of the central metal atom, which favours its permeability through the lipid layers of the cell membrane and disturbing the metal binding sites on enzymes of the organism, hence the enhanced antibacterial activity (Angelo, 2020; Angelo *et al.*, 2020).



Table 3: Zone of inhibition (mm) of PTBS and [Ni(PTBS)] on some bacterial species

Ligand/complex	Gram Positive		Gram Negative	
	<i>E. Coli</i>	<i>P. aeruginosa</i>	<i>S. typhi</i>	<i>S. aureus</i>
PTBS	13.00 ± 0.02 ^a	16.00 ± 0.04 ^a	14.00 ± 0.01 ^a	17.00 ± 0.03 ^b
[Ni(PTBS)]	19.00 ± 0.01 ^b	20.00 ± 0.02 ^b	22.00 ± 0.01 ^b	12.00 ± 0.03 ^a

**Values are mean ±SD of 3 replicates, mean within the rows with different superscripts differ significantly (P<0.05).

4.0 Conclusion

New Ni(II) complex of Schiff base was synthesized from the novel ligand derived from benzaldehyde and sulphathiazole. The melting point of the complex when compared to the ligand are higher. Low conductivity value indicated the weak electrolytic nature of the Schiff base and its Ni(II) complex. Spectroscopic studies indicated that PTBS coordinated to Ni ion through the -NH group and two C=N groups. The PTBS behaved as a tridentate ligand. A trigonal geometry has been proposed for the metal complex. The ligand showed significant activity against one gram-negative and two gram-positive bacterial strains. In overall, the metal complex showed enhanced antibacterial activity. Finally, they were proved to be active against all bacterial strains.

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