

SYNTHESIS, CHARACTERIZATION AND ANTIBACTERIAL ACTIVITY EVALUATION OF METAL(II) COMPLEXES DERIVED FROM (E) –N-BENZYLIDIENE ACETAMIDE SCHIFF BASE

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Abstract:

Metal (II) complexes of Co and Ni with schiff base derived from (E)-N-benzylideneacetamide were synthesized using microwave irradiation method and characterized on the basis of FT-IR, molar conductance, melting point, decomposition temperature and solubility test. The spectroscopic data indicated that the Schiff base ligand acted as a bidentate and coordinated to the metal via imine nitrogen and deprotonated oxygen atom. Also, the Schiff base ligand have melting point of 80-81^oC, the molar conductance values were found to be within 15.0-20.0ohm⁻¹cm²mol⁻¹ indicating that they are non electrolytic in nature. The solubility test of the compound indicated that then compounds are soluble in water, acetone, DMF and DMSO but completely insoluble in methanol, ethanol and methylated spirit. The synthesized ligand and their metal(II) complexes were studied for their *in vitro* antibacterial activity against two bacterial strains; *P. Aenoginosa* and *E. Coli*. The result indicated that the complexes exhibited better activity than the ligand but less compared to the standard drug (amoxicilin).

Keywords — (E)-N-benzylidene acetamide, benzaldehyde, acetamide, Schiff base and antibacterial activity.

1.0 INTRODUCTION

The antimicrobials become resistant, and therefore they do not act on the antibiotics as expected. Thereby making treatment ineffective and this become one of the world's most pressing public health threats, with the drug resistant bacteria causing huge number of deaths annually [1]. This is against the backdrop that the pharmaceutical and biotechnology industries are investing less and less in antibiotic discovery due to the challenges and complexities in the process, the difficulty and unpredictability of gaining regularly approval among other challenges. The accompanying loss of expertise in the sector only elevates the threat in the battle with antimicrobial resistant (AMR). Therefore, synthesis and study of coordination compounds containing biologically important ligands have been an area of interest in recent years because of their numerous applications in biology, environment and other systems [2]. The transition metals and their ions have much higher tendency to form coordination compounds as compared to the s- and p- block elements. It is because of their relatively smaller sizes, higher ionic charges and the availability of *d* orbital for bond formation. Coordination compounds, unlike normal compounds, retain their identity even when dissolved in water or any other suitable solvent. The properties of these compounds are totally different from those of their constituents [3].

Schiff base compound was first discovered and named after German Chemist Hugo Schiff in 1864, having the functional group C=N in the structure [4]. Schiff bases can be synthesised using various methods such as microwave irradiation method [5], condensation method and solvent free method [6]. A Schiff base known as imine, is a compound formed by condensation reaction of aldehyde or ketone with a primary amine as shown in scheme below; where R₁, R₂ and R₃ can be aryl or an alkyl group.

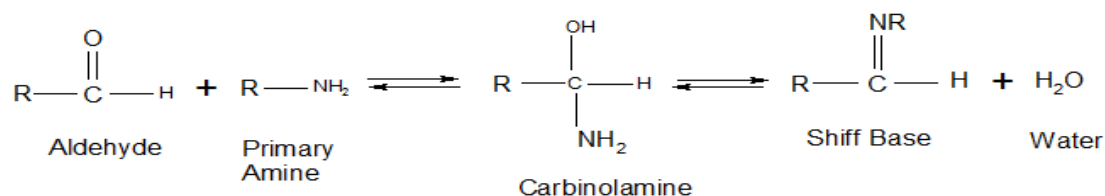


Figure 1. Mechanism of Schiff base formation

Schiff base with an aryl R group is more stable and can be easily synthesised compared to Schiff base with alkyl R substituent. The nitrogen atom of the Schiff base contain a long pair of electron with an sp² hybridized of latal that contributes to various biological and chemical properties, which is very important [7]. Thus, this research is designed to maximise the chance of harnessing a group of under exploited antimicrobial inorganic compounds and their biosynthetic agent to generate antimicrobial compounds libraries capable of arresting this microbial challenge and for structure activity studies.

2.0 MATERIALS AND METHODS

The following materials were used; fume cupboard, capillary tube, thermometer, Kern ABS-N analytical balance, FT-IR (Cary 630, Agilent), Conductivity meter (Jenway 4020), melting point apparatus, beakers, conical flasks, stirrer, magnetic bead, filter paper, glass funnel and dropper etc. And all glass wares used in this research work were properly washed with detergent, rinsed with distilled water and dried in an oven at 110⁰C. The reagents used were of analytical grade which Include; acetamide, benzyaldehyde, nickel(II) chloride hexahydrate, NiCl₂·6H₂O, and cobalt(II) chloride hexahydrate, CoCl₂·6H₂O and were used without further purification.

2.1 Synthesis of Schiff base ligand

The Schiff base ligand was synthesized by microwave Irradiation method reported by [8]. It is a temperature controlled method used to reduce the reaction time and give high yield. The process involves the condensation reaction of acetamide (2.95 g, 0.05 moles) with benzyaldehyde (5.3 g, 0.05 moles), in 10 mLof ethanol, few drops of 10% NaOH were added to adjust the pH of the solution. The reaction mixture in the conical flask was introduced into the microwave oven. Irradiated for 8 min, allowed to cool and precipitate was formed, filtered, and recrystallized from ethanol and dried at room temp.

2.2 Synthesis of metal complexes

The Co(II) complex was synthesized by the dissolution of Co(II) salt (5.15g, 0.025 moles) in 10 mL of ethanol, (7.35 g, 0.05 mol) of the synthesized Schiff base ligand was added to the solution in metal to ligand ratio of 1:2. Few drops of 10% NaOH were added to the reaction mixture to maintain a pH of about 6.0-7.0 and introduced into the microwave oven. Irradiated for 8 min, allowed to cool and the obtained precipitate was collected by filtration, dried and recrystallized from ethanol and kept in a

dessicator for further analysis. The same procedure was used to synthesize the Ni(II) complex using the same Schiff base ligand.

2.3 Evaluation of antibacterial activity

The *in vitro* antibacterial screening effects of the investigated compounds were tested against the two bacterial strains namely; *Pseudomonas aeruginosa* and *Escherichia coli*, were carried out using disk diffusion technique, with Nutrient Agar as the medium [9]. The stock solution (5 and 10 mM) of the synthesized compounds was prepared by dissolving the compounds in DMSO. In the typical procedure, a well was made on the agar medium inoculated with microorganisms, filled with the test solution using a micropipette and the plate was incubated for 24 h at 37 °C. During this period, the test solution diffused and the growth of the inoculated microorganisms was affected. The results were recorded by measuring the growth inhibition surrounding the disk.

3.0 RESULTS AND DISCUSSION

3.1 Physical properties of the Synthesized Schiff base ligands and the complexes

The physical properties of the Schiff base ligand and its Co(II) and Ni(II) complexes reported in (Table 1) showed that the compounds are coloured and stable at room temperature and this may be attributed to the higher decomposition temperatures which suggested a good thermal stability of the compounds [10]. The percentage yield of the ligands and complexes were obtained in a moderately good yield (65 -70 %) as presented in Table 1 and these are in close agreement with (60-70%) reported by [11].

Table 1 Physical properties of Schiff base ligand and their Ni(II) and Co(II) complexes

Compounds	M.W (gmol^{-1})	M.P ($^{\circ}\text{C}$)	D.T ($^{\circ}\text{C}$)	Colour	% yield
Schiff base	147	80-81	--	white	65
Ni(II)complex	232	--	150-160	pale green	68
Co(II)complex	206	--	170-175	Pale brown	70

Key: M.W = Molecular Weight, M.P= Melting Point, D.T= Decomposition Temperature

3.2 Infrared spectral data

The IR spectral data presented in Table 2 provide valuable information regarding the nature of the functional group attached to the compounds. The infrared spectra of the ligand showed a band at 1627 cm^{-1} which was attributed to $\nu(\text{C}=\text{N})$ band of the ring and was observed to have slightly shifted to lower wave numbers of 1537 and 1587 cm^{-1} for Ni(II) and Co(II) complexes respectively, almost between 10 and 40 cm^{-1} reduction indicating the involvement of $\nu(\text{C}=\text{N})$ nitrogen in coordination to the metal ion [12]. The bands in the region $3300\text{-}3400\text{ cm}^{-1}$ in the spectra of the ligand and the complexes were accorded to $\nu(\text{OH})$ stretching vibrations which indicates that the $-\text{OH}$ group does not participate in bond formation. The considerable changes in frequencies observed by phenolic C-O stretches in the spectra of the ligand and complexes may be due to the participation of phenolic oxygen in the complexation with the metals via deprotonation [11]. Accordingly, the ligand acted as a bidentate chelating agent, bonded to the metal ion via the azomethine nitrogen and deprotonated oxygen atoms respectively. Thus confirming the complexation of the metals with the ligands by the appearance of new peak intensity ligands bands in the region $540\text{-}510\text{ cm}^{-1}$ and $485\text{-}450\text{ cm}^{-1}$ in the spectra of the complexes which are assigned to $\nu(\text{M-O})$ and $\nu(\text{M-N})$ vibrations respectively.

Table 2 FTIR spectra data of Schiff base ligand and their Ni(II) and Co(II) complexes

Compounds	$\nu(\text{C}=\text{N})$ (cm^{-1})	$\nu(\text{OH})$ (cm^{-1})	$\nu(\text{C}-\text{O})$ (cm^{-1})	$\nu(\text{M}-\text{O})$ (cm^{-1})	$\nu(\text{M}-\text{N})$ (cm^{-1})
Schiff base	1627	3295	1135	--	--
Ni(II)complex	1538	3308	1120	540	485
Co(II)complex	1587	3295	1146	510	450

3.3 Molar conductance

The molar conductivity corresponding to the Ni(II) and Co(II) complexes are 15 and 20 $\text{ohm}^{-1} \text{cm}^2 \text{mn}^{-1}$ respectively, this presents low conductance values and thus structural formula of non-electrolyte for these complexes can be assigned. This indicates the non-electrolytic nature of the complexes and this agrees with the findings of Geary [13].

Table 3 Molar conductance of Ni(II) and Co(II) complexes in ($1 \times 10^{-3} \text{mol dm}^{-3}$) DMSO

Compounds	Specific Conductance (Mol dm^{-3}) $\times 10^{-3}$	Molar Conductance ($\Omega^{-1} \text{cm}^2 \text{mol}^{-1}$)
Ni(II)complex	15×10^{-6}	15
Co(II)complex	20×10^{-6}	20

3.4 Solubility Test

The Solubility test (Table 4) shows that the synthesized Schiff base is soluble in water, acetone, DMF and DMSO but insoluble in methanol, ethanol, N-hexane and methylated spirit, which may be due the polar nature of the solvent. The solubility for its Co(II) complex in the same solvents revealed that the complex was insoluble in acetone, methanol, ethanol, N-hexane, methylated spirit but soluble water, DMF and DMSO. The solubility for its Ni(II) complex was also tested with the same solvents and was found to be soluble in water acetone, N-hexane, DMF, DMSO and methylated spirit but insoluble in methanol and ethanol.

Table 4 Solubility test of Schiff base ligands and its Ni(II) and Co(II) complexes

Solvents	Ligand	Ni(II)complex	Co(II)complex
Water	S	S	S
Methanol	IS	IS	S
Ethanol	IS	IS	IS
Acetone	S	S	IS
n-hexane	IS	S	IS
Methylated spirit	IS	S	S
DMF	S	S	S
DMSO	S	S	S

Key: IS = insoluble S = soluble DMF = Dimethylformamide DMSO = Dimethylsulfoxide

3.5 Antimicrobial Studies

The minimum inhibitory concentration result was presented in Table 5. from the result, the ligand showed inhibitory activity at 50 mg/ml against *P. aeruginosa* whereas the complexes showed lower MIC values of 25 and 12.5 for Co(II) and Ni(II) complexes respectively compared to the MIC value of the ligand, which is higher, it indicate that the complexes exhibited better activity than the ligand. The trend shows that NI(II) has better activity than Co(II) and ligand against the *P.aeruginosa* and *E.coli*. The

improved antibacterial activities of the metal complexes than the ligand may be attributed to the presence of the nitro group which is renowned for its antibacterial activity of Schiff base metal complexes, and their better lipophilic nature [14]. In most cases, the metal complexes are generally more active than the metal free ligand due to chelation which increases antibacterial activity, because of partial sharing of its positive charge with donor groups of the ligand and possible pi-electron delocalisation which increased the lipophilic character [15].

Table 5 Minimum Inhibitory (mg/mL) of the Schiff base ligand and their Ni(II) and Co(II) complexes

Compounds	<i>P. aeruginosa</i>	<i>E.coli</i>
ligand	50	25
Co(II)complex	25	25
Ni(II)complex	12.5	12.5
Amoxicilin	12.5	12.5

3.0 CONCLUSIONS

The Schiff base ligand (E)-N-benzylideneacetamide and the metal(II) complexes have been synthesized and characterized on the basis of solubility testing, molar conductance studies, melting point and decomposition and infrared spectroscopy. The infrared analysis showed that the complexes were coordinated with the ligand via azomethine nitrogen and oxygen of the phenolic group. The molar conductance values of the complexes obtained suggested their non-electrolytic nature. The melting point and decomposition temperatures suggested a good thermal stability. The *in vitro* antibacterial studies showed that the complexes exhibited better activity than the ligands but less compared to the standard drug. Therefore, from those observations, it was concluded that the synthesized metal complexes can be potentially useful as biological agents, thus there is the need to explore this compounds with the view to harnessing its potential as drug.

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