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SOLID STATE SYNTHESIS, CHARACTERIZATION AND ANTI-MICROBIAL STUDIES OF CO(II) AND NI(II) METAL COMPLEXES WITH SCHIFF BASE DERIVED FROM L-VALINE AND VANILLIN.

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ABSTRACT

Two polynuclear metal complexes with general formula $[Ni_4L_4(H_2O)_{12}].2H_2O$ and $[Co_3L_3(H_2O)_9].5H_2O$ have been synthesized via solid state synthesis with Schiff base derived from vanillin and L-valine. The compounds were characterized by elemental analysis, ESI-Mass spectrometry, infrared spectroscopy, thermogravimetric analysis (TGA) and conductivity measurements. Data from experimental results showed that the ligand binds to two metal centers in a tridentate (N O O) manner through the imine nitrogen, phenolic and carboxylic oxygen respectively. Antimicrobial activities of the ligand and its corresponding metal complexes were investigated and found active against some selected bacterial and fungal species.

Keywords: solid–state reaction, polynuclear metal complexes, mass spectrometry, thermal decomposition, antimicrobial activity.

INTRODUCTION

Schiff bases are compounds containing carbon nitrogen double bond generally known as azomethine or imine linkage (Thiery *et al.,* 2018). They are structure-based compounds in which the oxygen atom of the carbonyl group (C=O) of an aldehyde or ketone is replaced by the nitrogen of primary amine (Tidwell, 2008). The beneficial properties of Schiff base compounds are not limited to the azomethine bond, but are structurally enhanced by numerous scaffolds, such as aromatic and substituted aromatic compounds (Brodowska *et al.,* 2016). Also, the presence of electron rich species such as nitrogen (N), oxygen (O) and sulfur (S) in the Schiff base molecule were reported to greatly increase their applications (Rauf *et al.,* 2017). Schiff bases are well-known to have diversified biological activities such as antibacterial (Panneerselvam, *et al.,* 2009; Singh, *et al.,* 2006), antifungal (Mishra and Soni, 2008), antiviral (Kumar, *et al.,* 2010), anti-HIV-1 (Vicini, *et al.,* 2003), anti-proliferative (Cheng, *et al.,* 2010) activities among others.

Schiff bases act as good chelating agents for transition and non-transition metal ions (Nair et *al.,* 2016). Schiff base complexes plays important role in biological processes like activation of enzymes by metals. Such complexes are useful in the storage and transport of active substances through membranes (Agrawal *et al.,* 2013). Schiff base metal complexes have found increasing use because of their high sensitivity and selectivity (Nunez *et al.,* 1986). Studies have shown that amino acid Schiff bases and their metal complexes have antibacterial, anticancer, and antiviral effects, and could also inhibit superoxide anion radicals (Gou *et al.,* 2010). These complexes have also shown catalytic activity in various oxidation reactions of environmental and biological importance (Ajay *et al.,* 2012).

Solid-state synthesis encompasses chemical reactions that are induced by direct absorption of mechanical energy through mixing of two or more solids without a solvent by grinding or milling the solid reagents together (James and Friščić, 2013). The source of mechanical energy use to force molecules to react is obtained by grinding a mixture of two (or more) different solids (Dubois, *et al.,* 2014). The kinetic energy supplied during grinding can have several effects on a crystalline solid including: heating, reduction of particle size with concomitant increase in surface area and generation of fresh surfaces, local melting and even phase changes to alternative polymorphs (Frisˇcˇic, 2019).

Over the years, conventional method for preparing Schiff bases is by refluxing the carbonyl compounds and amines in organic solvents (Jarrahpour and Zarei, 2011). Although the concept is still applied in most reactions, solution synthesis has the disadvantage of long response time, use of solvents that are harmful to the environment, and provide low yield (Zhong and Qin, 2014). Solid-state synthesis on the other hand offers not only a possibility to eliminate the need for bulk solvent use and reduce generation of waste, but it also unlocks the door to a different reaction environment in which synthetic strategies, reactions and molecules previously not accessible in solution, can be achieved (Frisˇcˇic´, 2019).

In 2011, Prakash and Adhikari synthesized a Schiff base derived from 2-hydroxy-5-methylacetophenone and glycine and its transition metal complexes by reflux. The ligand was bacteriostatic against bacterial strains such as *Proteus vulgaris, Shigella flexneri*, and *Bacillus coagulans.* Al-Shaheen and Al-Mula (2015) reported a dinuclear Schiff base complexes of Mn(II) derived from glycine, L-serine, L-tyrosine, and L-phenylalanine, that was synthesized by refluxing the Schiff base and Mn(II) salt with a solvent. Mounika *et al* (2010) reported solution synthesis, characterization and biological activity of a Schiff base derived from 3-ethoxy salicylaldehyde and 2-amino benzoic acid. The chemical structure of the Schiff-base was confirmed by various spectroscopic studies such as IR, ^{1}H NMR, ^{13}C NMR, ESI-mass spectra and elemental analysis. Sallam and Abbas (2012), reported some complexes of Ni(II) with Schiff bases obtained by the condensation of arginine with salicylaldehyde; 2,3-; 2,4-; 2,5-dihydroxybenzaldehyde and o-hydroxy naphtaldehyde using the template method in ethanol or ammonia media.

A survey of the literature reveals limited work has been carried out on the solid state synthesis of metal complexes with Schiff base derived from vanillin and valine. The coordination abilities of Schiff base have attracted our attention and aroused our interest in elucidating the structure of Co(II) and Ni(II) metal complexes. The present study describes the coordination behavior of polynuclear metal complexes synthesized by simple grinding of the solid reactants using pestle and mortar.

MATERIALS AND METHODS

Reagents

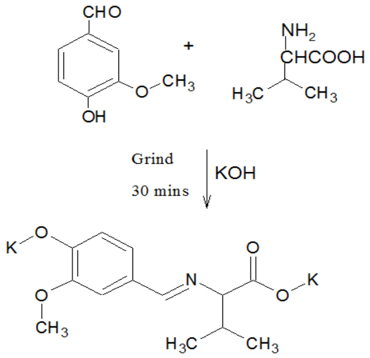
Chemicals (reagent grade) were purchased from sigma Aldrich and Alfa Aesar and were used without further purification. L-valine, vanillin and potassium hydroxide were used as starting materials for the preparation of the Schiff base. The metal salts used were $CoCl_2$ (anhydrous) and $Ni(CH_3COO)_2$. $4H_2O$. All glass wares used were thoroughly washed with detergent, soaked in concentrated nitric acid, rinsed with distilled water and dried in an oven at 110 ^oC.

Instruments

All weighing were carried out on electric balance model AB54, melting points were determined using a digital WRRS-IB Microprocessor melting points apparatus. Infrared spectral analysis were carried out by using KBr pellets in the range (4000-400 cm^{-1}), on a Perkin Infra-red Model 337. Mass spectra were recorded by ESI technique on VG AUTOSPEC mass spectrometer. TGA studies were carried on Mettler Toledo Star system in the temperature range of 0-1000 ^oC. Molar conductance of the metal complexes was determined in DMSO using a coronation digital conductivity meter. Magnetic susceptibility balance Sherwood MK1 was used to measure the magnetic properties of the metal complexes. Antimicrobial studies were carried out at the department of microbiology, Bayero University Kano, Nigeria.

Synthesis of the Schiff Base

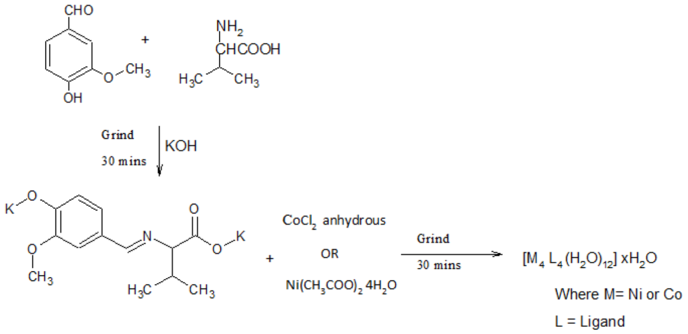
Valine (5 mmol) and potassium hydroxide (5 mmol) were weighed and placed in an agate mortar and continually grinded until the mixture became sticky. Then, vanillin (5 mmol) was added and grinded continuously, until the color of the reactants turned into yellow, and a loose solid powder was obtained after about 30 minutes. The reaction was carried out at room temperature. The products were washed with little cold dehydrated ethanol and recrystallized from hot ethanol which was dried for about 30 minutes in a vacuum drying oven at 40 °C (Zhong and Qin, 2014).



Scheme 1. Synthesis of Schiff Base.

Synthesis of the Metal(II) Complexes

Metal(II) salt (5 mmol) was added to the agate mortar containing the Schiff base and grinded continuously for about 30 minutes. The reaction was carried out at room temperature. The products were washed with little cold dehydrated ethanol, filtered, recrystallized from hot ethanol and dried for about 30 minutes in a vacuum drying oven at 40 °C (Zhong and Qin, 2014).



Scheme 2. Formation of the metal complexes

Anti-microbial screening

The synthesized Schiff base and its corresponding metal complexes were screened for antibacterial activity against bacterial species*: Stapylococcus aureus*, *Escherichia coli*, *Streptococcus pneumoniae* and *Selmonella .typhi* and antifungal activity against *T. capitis* and *T. rubrum.*

Anti-bacterial test

Using an inoculation loop, enough material from an overnight culture of the test organism was transferred into a test tube containing normal saline until the turbidity of the suspension matched the turbidity of the 0.5 Mcfarland standard (as a reference to adjust the turbidity of bacterial suspensions) as described by the national committee for clinical laboratory standard. The standard Inocula of the isolate were swabbed on to the surface area of the prepared agar plates. Nutrient agar was used as the required medium. The Schiff base and each of the two complexes were dissolved in dimethyl sulfur oxide (DMSO) to produce four different concentrations 40, 20, 10 and 5µg per disc. A sterilized forcept was used to place the prepared disc of the Schiff base and the complexes on the already inoculated agar plates at various intervals and then incubated at 37 ^{o}C for 24hrs (Yusha'u and Salisu, 2011).

Anti-Fungal test

For anti-fungal activity, potato dextrose agar (PDA) was used as the required medium. A sterilized forcept was used to place the prepared disc of the Schiff base and the complexes on the already inoculated agar plates at various intervals and was left for 3days at room temperature (Hassan *et al.,* 2006). The inhibition zone of the Schiff base and the corresponding metal complexes were measured (in millimeter) around the disc and were compared with the standard drugs.

RESULTS AND DISCUSSION

The aldehyde group (-CHO) of vanillin and amine group (-NH_2) of valine was utilized for the synthesis of the tridentate Schiff base, which was stable in air and soluble in ethanol, methanol, dimethylformamide (DMF), dimethylsulfuroxide (DMSO) and completely insoluble in chloroform and n-hexane. The metal(II) complexes were stable at room temperature and decomposed on heating at high temperatures. Results of solubility tests of these compounds revealed that they are soluble in methanol, ethanol, DMSO and DMF but insoluble in non-polar solvents such as chloroform and n-hexane. The synthesized Schiff base and its corresponding metal complexes were colored solids with percentage yield in the range 82.89-90.45% (Table 1). The values for the elemental analysis of the Schiff base and its corresponding metal complexes obtained were in good agreement with the theoretical values (Table 1). The low molar conductance values of 10^{-3} M solutions in DMSO indicates both complexes were non electrolytic in nature (Table 1). The results of the infrared spectra, mass spectrometry, conductivity measurements and thermal analysis, led to the possible molecular formulae of the complexes to be $[Co_3(C_{13}H_{10}O_4N)_3(H_2O)_9].5H_2O$ and $[Ni_4(C_{13}H_{10}O_4N)_4(H_2O)_{12}].2H_2O$. The molar ratio of the Schiff base and metal ions of the complexes was found to be 3:3 and 4:4 for complexes of Co(II) and Ni(II) ion respectively.

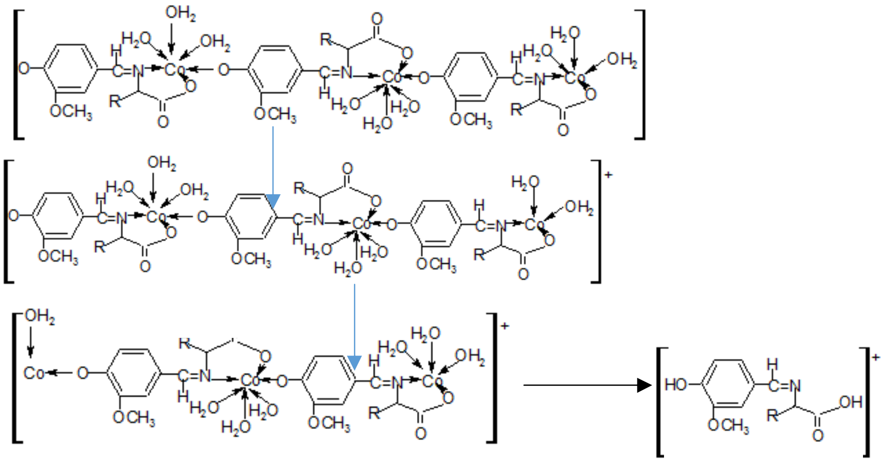
Table 1: Some Physical Properties of the Compounds

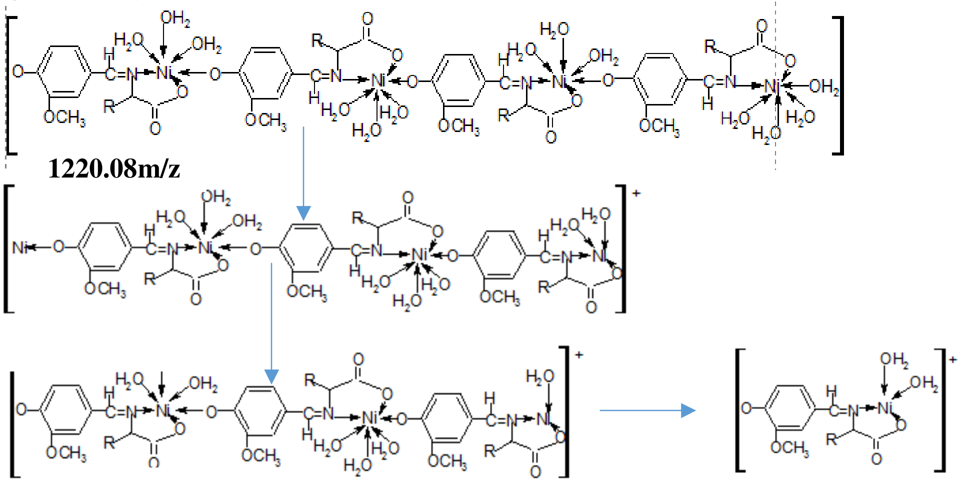
Compound	Molecular Formula	Molecular Weight	Colour	m.p (°C)	Yield (%)	% Elemental Analysis Observed (Calc)			Molar Conductance (Ω^{-1} cm^{2}Mol^{-1})
						C	H	N	
Ligand	$C_{13}H_{10}O_4NK_2$	328.03	Yellow	96	89.04	41.96 (42.09)	3.18 (3.15)	4.89 (4.91)	-
Co(II) complex	$Co_3C_{39}H_{73}O_{26}N_3$	1170.00	Pink	-	82.89	39.69 (39.79)	6.19 (6.25)	3.51 (3.57)	13.25
Ni(II) complex	$Ni_4C_{52}H_{88}O_{30}N_4$	1484.03	Pale Green	-	90.45	42.05 (42.08)	5.93 (5.98)	3.77 (3.78)	25.68

Note: Calculated values are in bracket

Mass Spectrometry-ESI

The mass spectra of Schiff base and its Co(II) and Ni(II) complexes were recorded and their stoichiometric compositions were compared (table 2). The mass spectrum of Schiff base (fig. 1a) shows a well-defined molecular ion peak at m/z 327.8 which coincides with the formula weight of the Schiff base. In the spectra of Co(II) metal complex (fig. 1b), peaks at 1072.99m/z, 804.91m/z and 252.12m/z observed were assigned as $[Co_3L_3(H_2O)_8]^+$, $[Co_3L_2(H_2O)_7]^+$ and $[H_2L]^+$ ions respectively, suggesting a trinuclear metal complex (scheme 3) and were in agreement with the proposed structural formula of the complex given as $[Co_3L_3(H_2O)_9]$. For Ni(II) complex (fig.1c), the base peaks was seen at 1220.08m/z represented as $[Ni_4L_3(H_2O)_{13}]^+$ (table 2). Other important peaks include 1128.08m/z, 1050.66m/z, 326.7m/z representing $[Ni_4L_3(H_2O)_8]^+$, $[Ni_3L_3(H_2O)_7]^+$ and $[NiL(H_2O)_2]^+$ fragments respectively (scheme 4). The data was found to be in good agreement with the proposed structure for the complexes.



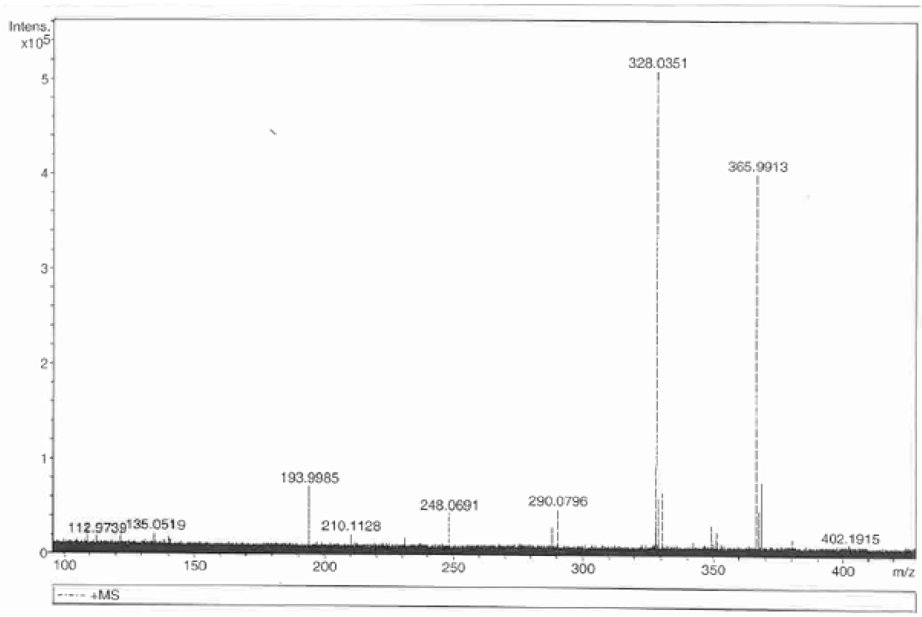


Ta **ectrometry-ESI for the Compounds**

Ligand	328.03	327.46	K_2L
Co(II) complex	1072.99	1071	$[Co_3L_3(H_2O)_8]$
	804.91	803	$[Co_3L_2(H_2O)_7]$
	252.12	252	H_2L
Ni(II) complex	1220.08	1220	$[Ni_4L_3(H_2O)_{12}]$
	1128.08	1128	$[Ni_4L_3(H_2O)_8]$
	1050.66	1051	$[Ni_3L_3(H_2O)_7]$
	326.7	326	$[NiL(H_2O)_2]$

KEY: Ligand (L) = $C_{15}H_{10}O_4N$

(a)



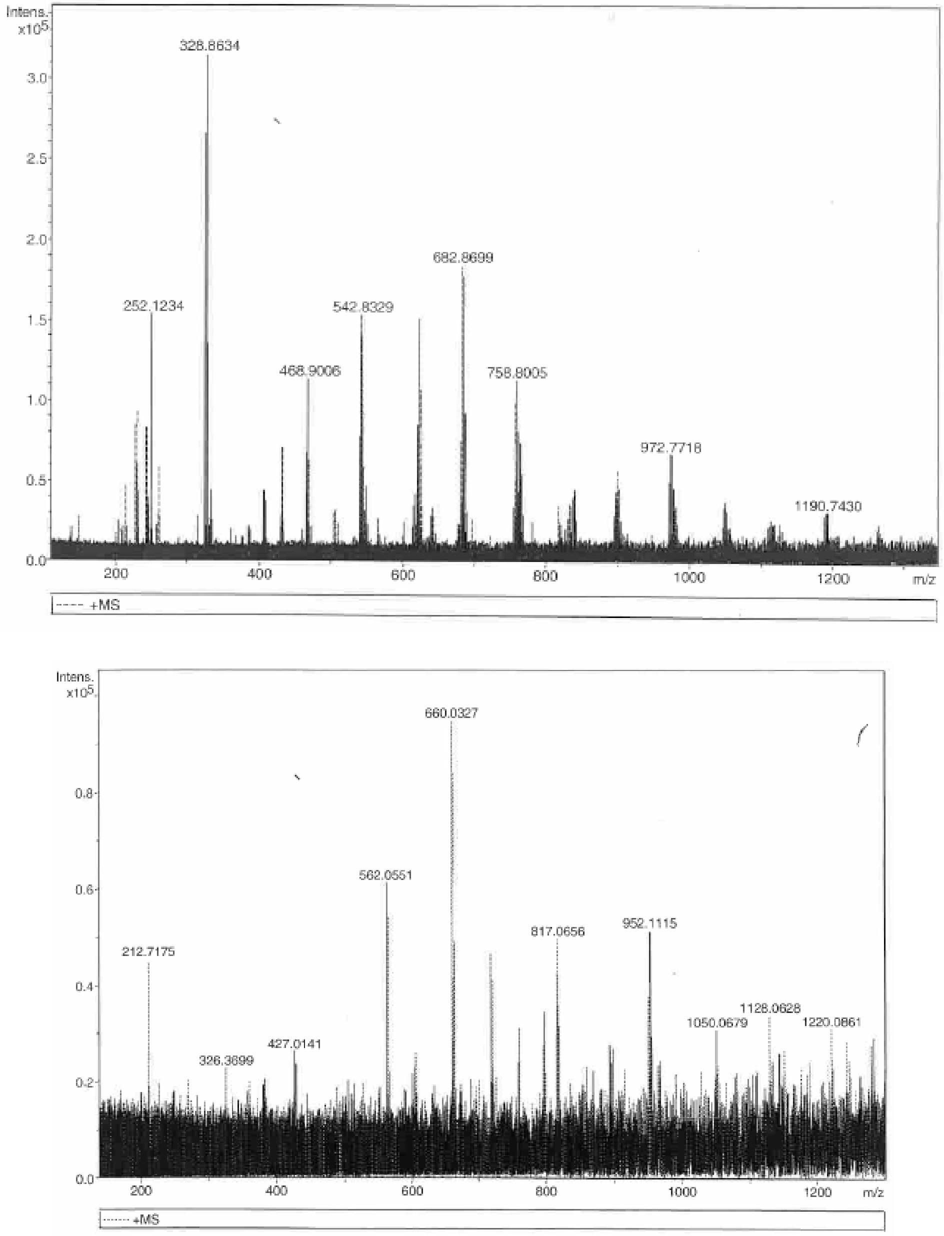


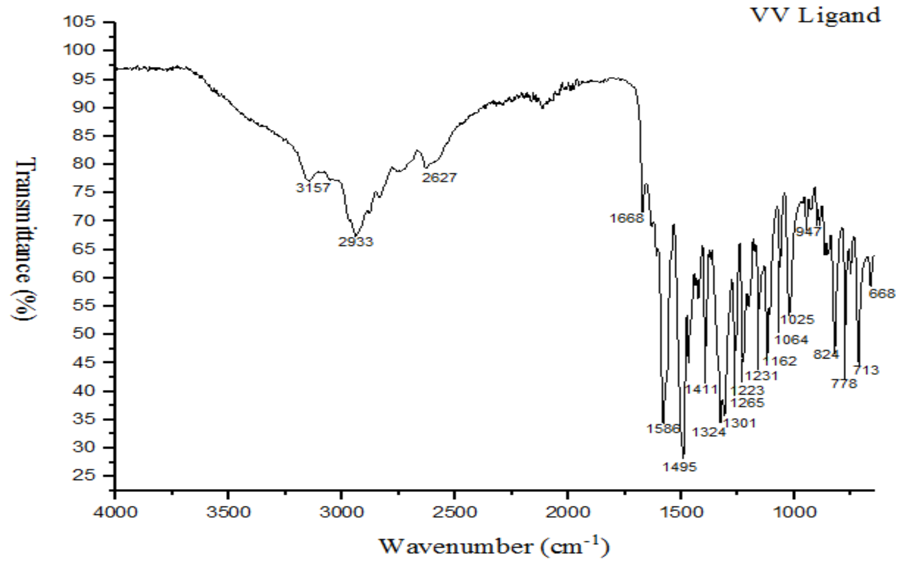
Figure 1: (a) MS-ESI spectra for the Schiff base, (b) $[Co_3 (C_{13}H_{10}O_4N)_3 (H_2O)_9]\ 5H_2O$ and (c) $[Ni_4 (C_{13}H_{10}O_4N)_4 (H_2O)_{12}]\ 2H_2O$

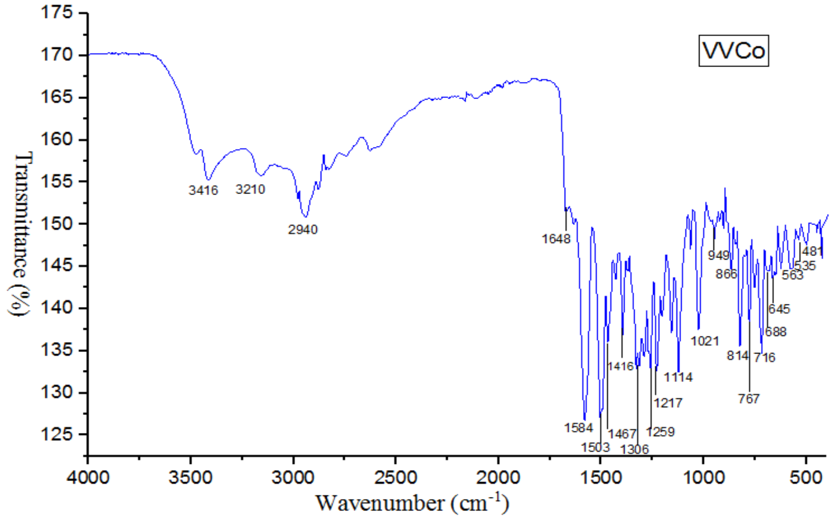
Infra-red Spectroscopy

In the spectra of the Schiff base (fig 2a), band at 1668cm^{-1} was assigned to C=N stretching vibrations. On complexation, a shift to lower frequency (1648 cm^{-1}) was observed in Co(II) complex (fig. 2b) which was in agreement with 1648 cm^{-1} reported by Zhong and Zhong,(2014) for C=N stretching vibrations. A shift to higher frequency with a value of 1677 cm^{-1} was observed in Ni(II) complex (fig. 2c), which was close to 1670 cm^{-1} reported by Tariq, (2010).. These shifts in frequency suggest the coordination of the imino nitrogen to the metal ion. When compared with the spectra of the Schiff base, the band for asymmetric carboxyl stretching *vas*(COO$^-$) at 1586cm^{-1} was shifted to lower frequency in the range of 1558-1564cm^{-1}, and that of symmetric carboxyl stretching *vs*(COO$^-$) at 1411 cm^{1}, was observed at higher frequency in the range of 1416-1422 cm^{-1},which are in line with monodentate bonding of the carboxylate group (Nakamoto, 1986). These values were found similar to 1556 cm^{-1}and 1565 cm^{-1} reported by Mounika *et al.*, (2010), Joseyphus *et al.,* (2006) and Al-Shaheen and Al-Mula, (2015) respectively for *vas*(COO$^-$) stretching vibrations and 1417 cm^{-1} and 1434 cm^{-1} due to symmetric stretching vibrations *vs*(COO^-) in $Na_2[Mn_2(VG)_2(H_2O)_2(NO_3)_2]$and $Na_2[Mn_2(VS)_2(H_2O)_2(NO_3)_2]$ complexes respectively as reported by Al-Shaheen and Al-Mula (2015). These confirms the linkage between the metal ion and carboxylate oxygen atom. The phenolic stretching vibrations of the ligand at 1223 cm^{-1} undergoes a major shift towards higher frequency in the range 1258-1259 cm^{-1}, implying the coordination of phenolic group with the metal ion. These values were found similar to 1263 cm^{-1} (Wang *et al.,* 2011) reported for phenolic *ν*(C-O) stretching vibrations observed in Sm(III) complex with vanillin-tryptophan ligand. Spectral bands in the range 3330-3416cm^{-1} for v(O-H) were assigned to water molecules present in the complexes, which are in agreement with ESI-ms and TG results. In the lower frequency region, the IR bands in the range 481-487 cm^{-1} and 563-565 cm^{-1} arise due to *ν*(M-O) and *ν*(M-N) respectively. Table 3 below shows some important infrared absorption bands of the ligand and its corresponding metal complexes.

Table 3: Infrared Spectra of the Compounds

Compound	v(C=N) (cm^{-1})	v(C-O) (cm^{-1})	vas(COO^-) (cm^{-1})	vs(COO^-) (cm^{-1})	v(H-O) (cm^{-1})	v(M-O) (cm^{-1})	v(M-N) (cm^{-1})
Ligand	1668	1223	1586	1411	-	-	-
Co(II) complex	1648	1259	1564	1416	3416	481	563
Ni(II) complex	1677	1258	1558	1422	3330	487	565





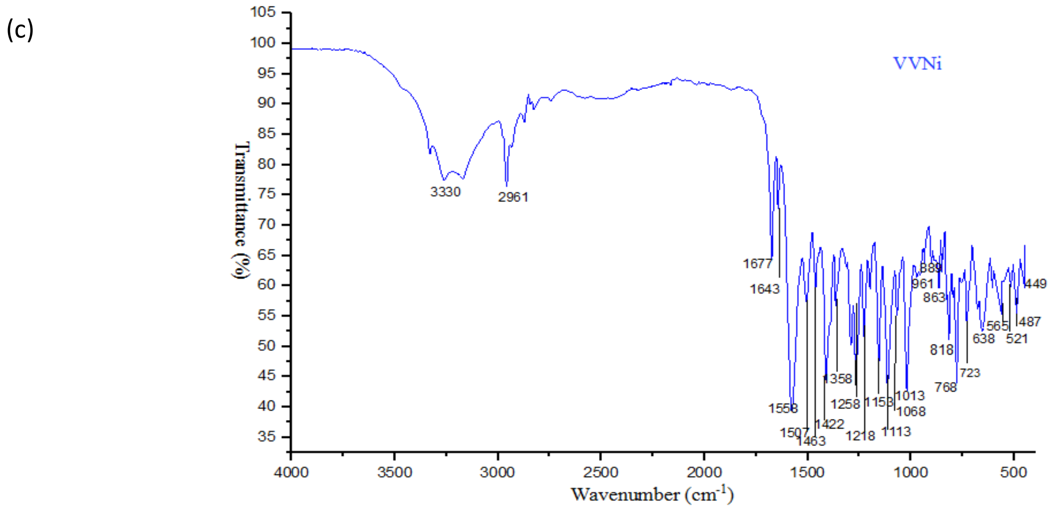


Figure 2: (a) Infrared spectra for the Schiff base,(b) $[Co_3(C_{13}H_{10}O_4N)_3\ (H_2O)_9]\ 5H_2O$ and (c) $[Ni_4(C_{13}H_{10}O_4N)_4(H_2O)_{12}]2H_2O$

Thermogravimetric Analysis

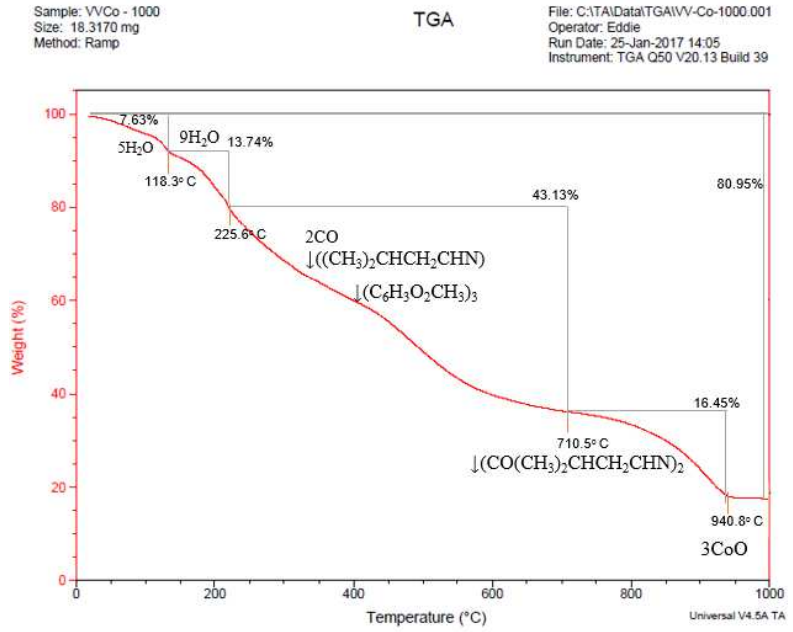
The TGA Curve for Co(II) complex (fig. 3a) shows a loss of five free water molecules within the temperature range of 25-134 ° C with a an experimental weight loss of 7.63 % (calc. 7.64). From 134-225 ° C a weight loss of 13.74 % (calc. 13.73 %) was observed, which could be due to loss of nine coordinated water molecules as seen in the ESI-ms spectra of the metal complex. Further decomposition of the complex was observed within a temperature range of 225-710 ^oC, which can be attributed to the loss of part of the Schiff base ligand as 2CO, $((CH_3)_2CHCH_2CHN)$ and $(C_6H_3O_2CH_3)_3$ groups, corresponding to a weight loss of 43.13 % (calc. 42.92 %). This was followed by the loss of $(CO\ (CH_3)_2CHCH_2CHN)_2$ corresponding to a weight loss of 16.64 % (calc. 16.62%) within a temperature range of 710-940 ^oC. The remained residue of 19.05% (calc. 19.09 %) was observed and was in agreement with the calculated value as 3CoO (table 4).

For Ni(II) complex (fig. 3b), weight loss of 2.43 % was observed within a temperature range of 50-110 ^oC, revealing the release of $2H_2O$ as water of crystallization (calc. 2.43 %). The complex further decomposes, showing a mass loss of 14.48 % within a temperature range of 110-200 ^oC. This mass loss indicates the loss of 12 H_2O as coordinated water (calc. 14.57 %). A mass loss of 38.81 % was observed at a temperature range of 200-450 ^oC, corresponding to the loss of part of the Schiff base ligand as 4CO, $((CH_3)_2CHCH_2CHN)_4$ and $(C_6H_3O_2CH_3)$ (calc. 38.14 %). 24.07% weight loss was observed at higher temperature in the range 450-675 ^oC which corresponds to $(C_6H_3O_2CH_3)$ group. The remained residue of 20.21 % (calc. 20.22 %) was in agreement with the calculated value as metal oxide (4NiO). Table 4 shows the decomposition pattern of the complexes and probable assignment at each stage.

Table 4: Thermal Decomposition Data of the Complexes

Compound	Temp range (° C)	Mass loss from TG (%)	Theoretical mass loss (%)	Weight loss from TG	Theoretical weight loss	Probable assignment	
Co(II) complex	25-120	7.63	7.64	89.9	90	$5H_2O$	Loss of water of crystallization
	120-225	13.74	13.73	161.9	162	$9H_2O$	Loss of coordinated water
	225-710	43.13	42.92	505.5	506	2CO $((CH_3)_2CHCH_2CHN)$ $(C_6H_3O_2CH_3)_3$	Decomposition of the organic ligand
	710-940	16.45	16.62	193.9	196	$2(CO(CH_3)_2CHCH_2CHN)$	
	940-1000	19.05	19.09	224.6	225	3CoO	Residue as metal(II) oxide
		100	**100**	**1175.8**	**1179**	**$[Co_3L_3(H_2O)_9]\ 5H_2O$**	
Ni(II) complex	25-110	2.43	2.43	36.06	36.06	$2H_2O$	Loss or water of crystallization
	110-200	14.48	14.57	214.89	216.22	$12H_2O$	Loss of coordinated water
	200-450	38.81	38.14	575.96	566.01	4CO $4(CH_3)_2CHCH_2CHN$	Decomposition of the ligand
	450-675	24.07	24.64	357.21	365.67	$(C_6H_3O_2CH_3)$ $(C_6H_3O_2CH_3)$	
	675-825	20.21	20.22	299.92	300.07	4NiO	Residue as metal(II) oxide
		100	**100**	**1484.04**	**1484.03**	**$[Ni_4L_4(H_2O)_{12}]\ 2H_2O$**	

(a)



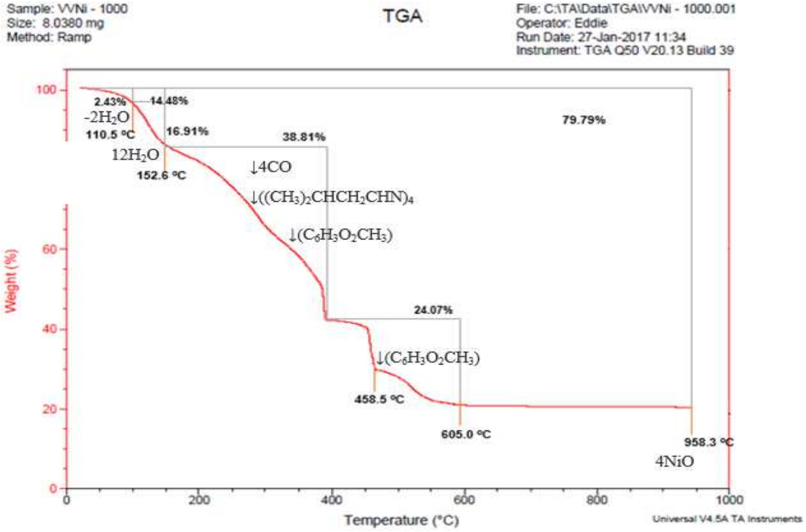


Figure 3: (a) TG curve for [[$Co_3((C_{13}H_{10}O_4N)_3$ $(H_2O)_9$] $5H_2O$ and (b) $Ni_4(C_{13}H_{10}O_4N)_4$ $H_2O)_{12}$] $2H_2O$

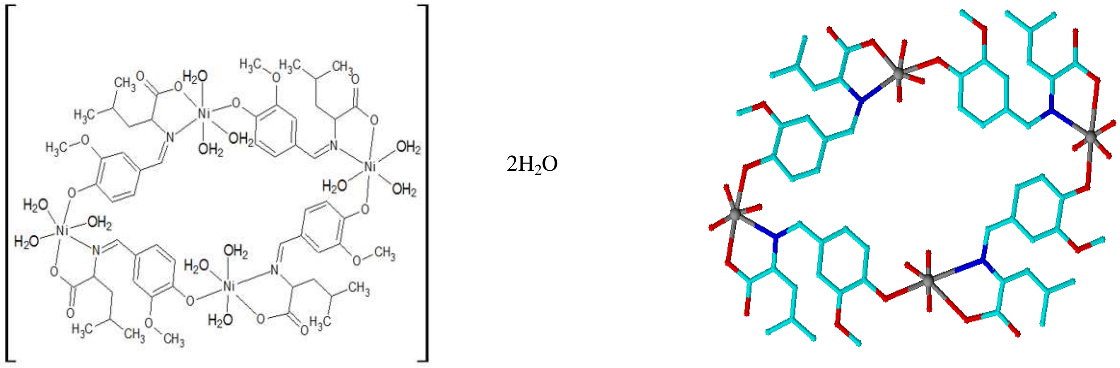


Fig. 4: (a) Proposed structure of Ni(II) complex and (b) 3D Polymeric frame work showing connectivity of Ni(II) complex

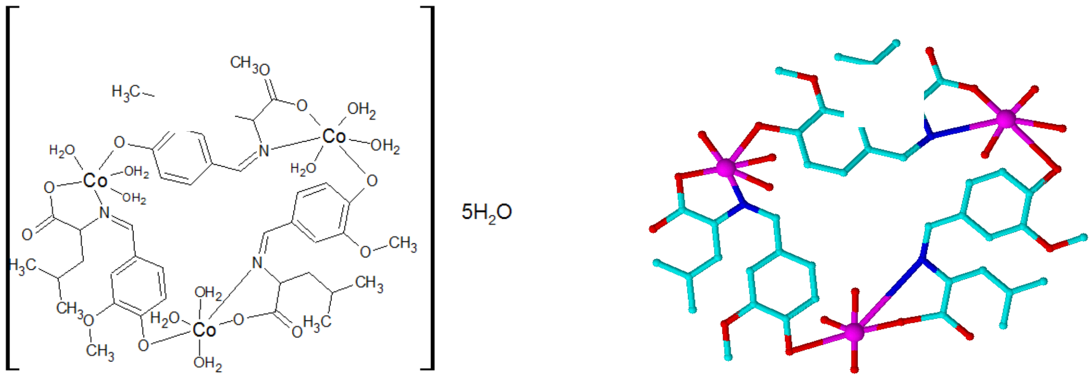


Fig. 5: (a) Proposed structure of Co(II) complex and (b) 3D polymeric frame work showing connectivity of Co(II) complex

Biological Activity

Bioactivity screening for the anti-bacterial and anti-fungal activities of stock solutions of the Schiff base and the complexes was performed qualitatively using disk diffusion assay (Yusha'u, and Salisu, 2011 and Hassan *et al.,* 2006),

(Table 5). Ciprofloxacin and ketoconazole were used as standard drugs. The compounds yielded clear inhibition zones around the disk. Anti-bacterial activities of the Schiff base and its metal(II) complexes were carried out against two Gram positive bacteria (*Staphyloccus aureus* and *Streptococcus pneumoniae)* and two Gram negative bacteria (*Escherichia coli* and *Salmonella typhi*). The two complexes were observed to be active against both Gram positive and Gram negative bacteria while the ligand is inactive against all the selected bacterial strain*s.* For the anti-fungal activity, results showed that the two complexes have significant activity against *Tinea capitis* and *Trichophyton rubrum.* The ligand was found to be less active compared to the metal complexes for activities against *Trichophyton rubrum* and inactive against *Tinea capitis.*

Table 5: Growth Inhibition Zone of Microbes.

Compound	**Concentration (µg/disc)**	**Inhibition Zone (mm)**					
		Anti-bacteria				***Anti-fungal***	
		S.aureus	***S.pneumoniae***	***S. typhi***	***E.coli***	***T.capitis***	***T.rubrum***
Ligand	40	6	6	6	6	6	11
	20	6	6	6	6	6	9
	10	6	6	6	6	6	7
	5	6	6	6	6	6	6
Co(II) complex	40	7	16	14	12	13	14
	20	12	11	11	10	11	12
	10	10	10	9	9	9	10
	5	9	9	8	8	7	9
Ni(II) complex	40	14	10	15	16	12	16
	20	12	9	11	13	9	14
	10	10	8	9	11	8	11
	10	9	7	8	10	7	10
Control	10	24	20	32	37	34	44

1-6mm = inactive active; 7-10 = active; any value greater than 11 very active.

CONCLUSION

The cobalt(II) and nickel(II) complexes of valine-vanillin Schiff base has been synthesized by solid-state reaction at room temperature. The complexes were characterized by elemental The thermal decomposition processes of the complexes include dehydration and pyrolysis of the Schiff base and the final residue were identified to be metal oxide (3CoO or 4NiO). The complexes were found to be biologically active against some selected bacteria and fungi species.

analysis, IR, MS-ESI and TGA and were found to be polynuclear, coordinating in a tridentate manner through imine nitrogen, carboxylic and phenolic oxygen (fig. 4 and 5).

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