

Synthesis, Characterization and Antimicrobial Activity of Metal(II) Complexes of Benzoyl Hydrazide and Its Hydrazone Derivative Mixed with Nicotinamide

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Abstract: The increasing prevalence of antimicrobial resistance has prompted the exploration of alternative antimicrobial agents. In this context, the antimicrobial properties of hydrazide derivatives and their metal complexes have garnered significant interest. In line with this motivation, the present study investigated the antimicrobial activity of Benzoyl hydrazide (BAH) and its hydrazone derivative, acetophenone-benzoylhydrazone (ABH), along with their corresponding metal(II) complexes. Synthesis and characterization of BAH, ABH, and their metal complexes were conducted using a range of spectroscopic techniques. The structural elucidation of the hydrazide and hydrazone compounds involved the utilization of infrared (FT-IR), UV-Visible, and nuclear magnetic resonance (^1H -NMR and ^{13}C -NMR) spectroscopy. Similarly, the characterization of the metal complexes was achieved through infrared (FT-IR) and UV-Visible spectroscopy. The infrared (IR) spectra of the metal complexes exhibited medium bands within the 1624 to 1503 cm^{-1} range, which could be attributed to the stretching vibrations of $\nu\text{C}=\text{N}$. Notably, these bands displayed frequency shifts in both higher and lower directions. Additional weak bands emerged at $692 - 520\text{ cm}^{-1}$ and $584 - 422\text{ cm}^{-1}$, corresponding to the M-O and M-N bonds, respectively. The presence of these bands further supported the formation of the metal complexes. Moreover, the electrolytic nature of the complexes was confirmed by molar conductivity measurements in aqueous solutions, which ranged from 235 to $298\text{ }\Omega^{-1}\text{cm}^2\text{mol}^{-1}$. Investigation into the magnetic properties of the metal complexes showed that, with the exception of the Cu(II) complex of benzoic acid hydrazide mixed with nicotinamide, the complexes demonstrated magnetic dilution. Specifically, the room temperature magnetic moments for the Cu(II) complex were determined as 1.69 B.M and 3.79 B.M , respectively, indicative of an antiferromagnetic behavior. Furthermore, all the complexes exhibited significantly heightened antimicrobial activity compared to their respective ligands, thus highlighting their potential as effective antimicrobial agents against the tested microbes.

Keywords: Benzoyl Hydrazide, Acetophenone-Benzoylhydrazone, Magnetic Moment, Spectroscopic Techniques, Conductivity

1. Introduction

Hydrazones have garnered substantial attention in the field of medicinal chemistry and coordination chemistry due to their versatile nature [1-3]. These compounds serve as valuable models for biologically significant species and exhibit applications as biomimetics. The simplicity of their

synthesis has led researchers to create a myriad of novel hydrazones [4, 5]. Of particular interest is the coordination chemistry of acylhydrazones, which has been explored extensively due to their diverse range of uses, including as drugs, photo-thermochromic compounds, and precursors for organic synthesis [4, 5]. The inclusion of a carbonyl oxygen atom in hydrazones facilitates the formation of chelate binding centers, further enhancing their significance [6].

The bonding of metal ions to biologically active compounds has been recognized to augment their activities [7]. In recent decades, there has been a mounting fascination with compounds containing hydrazide and hydrazone moieties, as well as their complexes with first row transition metal ions. These compounds have found applications in medicine, particularly in the treatment of tuberculosis, as well as in biological systems and analytical chemistry [8]. The coordination chemistry of acylhydrazones has been subject to extensive investigation, resulting in a plethora of transition metal complexes involving these ligands. Previous studies have documented the synthesis and electrochemical examination of dinuclear Cu(II) complexes and several studies have revealed the captivating nature of research concerning hydrazone Schiff bases in combination with entities like azides and bipyridine [9-13].

In this study, we present the synthesis of a novel Schiff base, namely acetophenone-benzoylhydrazone (ABH), originating from benzoyl hydrazide (BAH) as a precursor compound. Subsequently, mixed metal complexes involving the precursor and hydrazone along with nicotinamide (NA) were synthesized. The compounds were subjected to spectral characterization, and their biological activities were thoroughly examined and discussed.

2. Experimental

2.1. Materials and Methods

All the chemicals including solvents and metal salts were of analytical grade supplied by British Drug Houses (BDH)

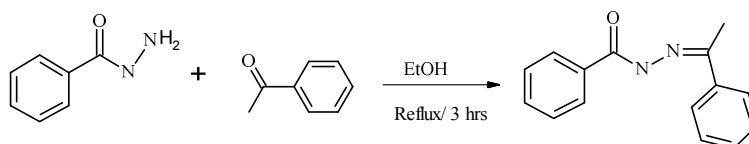


Figure 1. Synthesis of Acetophenone-Benzoylhydrazone.

2.3. Synthesis of Metal Complexes of Benzoylhydrazide Mixed with Nicotinamide

The procedure described by Osowole *et al.*, [15] was used to synthesize the mixed complexes, with slight modification. Solution of copper (II) chloride dihydrate (0.501 g, 2.940 mmol) in 10 mL of methanol was added drop wisely into a homogenous solution of benzoylhydrazide (0.389 g, 2.940 mmol) and nicotinamide (0.728 g, 5.960 mmol) in 50mL of hot methanol and stirred for two hours. The precipitate formed was filtered, washed with methanol and dried over calcium chloride in a desiccator. The same method was repeated for other metal complexes.

2.4. Synthesis of Metal Complexes of Acetophenone-Benzoylhydrazone Mixed with Nicotinamide

Solutions of respective metal salt (0.286 g, 1.680 mmol) in

chemical limited, England except for nicotinamide which was supplied by Bond Pharmacy. The infrared spectra of the ligands and those of the complexes were recorded on Shimadzu FT-IR 8000 Spectrometer using KBr discs. The electronic spectra of ligands and the synthesized complexes were determined in methanol using Shimadzu UV-Vis Spectrometer. Conductivity measurements were done using 1×10^{-3} M water solution of the complexes at 28 °C using HANNA instrument (TDS Conductimeter). The melting point and decomposition temperature of all compounds were determined using the Gallenkamp apparatus. The percentage composition of metal in the complexes was determined by complexometric titration using EDTA. Magnetic susceptibility measurement were done using Guoy balance, Magnetic Susceptometer (Sherwood Scientific Cambridge, UK.).

2.2. Synthesis of Acetophenone-Benzoylhydrazone

The synthesis of the precursor benzoylhydrazide was performed following the procedure outlined in reference [14]. To initiate the reaction, a solution of benzoylhydrazide (6.908 g, 0.0515 mole) in 50 mL of absolute ethanol was added dropwise into an ethanolic solution of acetophenone (6 mL, 0.0515 mole). The resulting mixture was stirred for a short period and then refluxed for a duration of 3 hours. Subsequently, the mixture was allowed to stand overnight in a beaker, leading to the formation of a white crystalline precipitate. This precipitate was separated by filtration, washed with ethanol, and dried using anhydrous calcium chloride in a desiccator [14].

10 mL of methanol was added drop wisely into a homogenous solution of acetophenone-benzoylhydrazone (0.401 g, 1.680 mmol) and nicotinamide (0.410 g, 3.360 mmol) in 50 mL of hot methanol and refluxed for two hours. The precipitate formed, was filtered, washed with methanol and dried over calcium chloride in a desiccator [16].

2.5. Antimicrobial Activity

The synthesized compounds were evaluated for their antimicrobial activity against a panel of 15 microorganisms, including both Gram-negative and Gram-positive bacteria. To assess their efficacy, a concentration of 35 mg/mL of the synthesized compounds was utilized, while ampicillin, a commercially available antibiotic, was employed as the standard control. The compounds were dissolved in distilled water, while BAH, ABH, and $[\text{Cu}(\text{BAH})(\text{NA})_2(\text{H}_2\text{O})_2]\text{Cl}_2$ were dissolved in methanol prior to testing.

3. Results and Discussion

3.1. Physicochemical Properties

The precursor $MCl_2 \cdot xH_2O$ undergoes reflux with BAH and ABH in methanol, resulting in the formation of $[M(BAH)(NA)_2(H_2O)_2]Cl_2$ and $[M(ABH)(NA)_2(H_2O)_2]Cl_2$. The synthetic route utilized in this study is illustrated in Figure 2. These complexes are characterized by their air stability,

diverse range of colors (ranging from pale pink to blue), high melting points, and solubility in water. Table 1 provides the physical properties of Nicotinamide, benzoyl hydrazide, acetophenone-benzoylhydrazone, and their corresponding metal complexes. The molar conductivities of the complexes, measured in distilled water, fall within the range of 235 to 298 $\Omega^{-1}cm^2mol^{-1}$, indicating their behavior as 1:2 electrolytes.

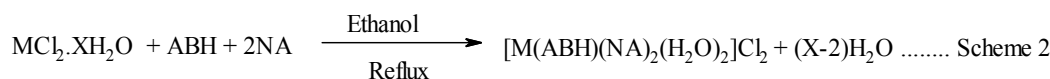


Figure 2. General Representation for the Synthesis of the Complexes.

Table 1. Physical Properties of Nicotinamide, Hydrazide, Hydrazone and the Complexes.

Compound	Formula (formula weight)	Colour	Melting point °C	%Metal found (calcd)	%Yield	$\Lambda_M (\Omega^{-1} \cdot cm^2 \cdot mol^{-1})$
Nicotinamide	$C_6H_6N_2O$ (122.12)	White	130-132	-	-	-
BAH	$C_7H_8N_2O$ (136.14)	White	171-173	-	67	-
$[Mn(BAH)(NA)_2(H_2O)_2]Cl_2$	$MnC_{19}H_{24}N_6O_5Cl_2$ (542.32)	Pale pink	> 360	10.34 (10.35)	76	250.42
$[Co(BAH)(NA)_2(H_2O)_2]Cl_2$	$CoC_{19}H_{24}N_6O_5Cl_2$ (546.31)	Purple	> 360	10.79 (10.80)	81	235.22
$[Ni(BAH)(NA)_2(H_2O)_2]Cl_2$	$NiC_{19}H_{24}N_6O_5Cl_2$ (546.09)	Light green	> 360	10.75 (10.93)	56	246.70
$[Cu(BAH)(NA)_2(H_2O)_2]Cl_2$	$CuC_{19}H_{24}N_6O_5Cl_2$ (550.92)	Blue	290-294	11.50 (11.65)	87	242.45
ABH	$C_{15}H_{14}N_2O$ (238)	White	156-158	-	84	-
$[Mn(ABH)(NA)_2(H_2O)_2]Cl_2$	$MnC_{27}H_{30}N_6O_5Cl_2$ (643.94)	White	> 360	8.83 (8.84)	81	298.71
$[Co(ABH)(NA)_2(H_2O)_2]Cl_2$	$CoC_{27}H_{30}N_6O_5Cl_2$ (648.17)	Purple	318-320	9.10 (9.21)	85	270.12
$[Ni(ABH)(NA)_2(H_2O)_2]Cl_2$	$NiC_{27}H_{30}N_6O_5Cl_2$ (647.71)	Light green	> 360	9.34 (9.59)	54	294.79
$[Cu(ABH)(NA)_2(H_2O)_2]Cl_2$	$CuC_{27}H_{30}N_6O_5Cl_2$ (652.78)	Blue	290-292	9.70 (9.90)	89	255.72

3.2. NMR Spectra of the Hydrazone Ligand

The 1H -NMR spectrum of ABH showed peaks for the aromatic protons between 7.43-7.89 ppm. Therefore, ortho hydrogen couple strongly and resonate at 7.89 ppm ($^3J=7-10Hz$) than meta hydrogen which appears at 7.60, 7.57,

7.55, 7.23 ppm ($^4J=2-3Hz$) which in turn couple more strongly than para hydrogen at 7.50 and 7.43 ($^5J=0-1Hz$). The signal at 10.81ppm correspond to the proton of the amide group. The chemical shift of the methyl proton at 2.39 ppm is due to the deshielding effect because of the $C=N$ group.

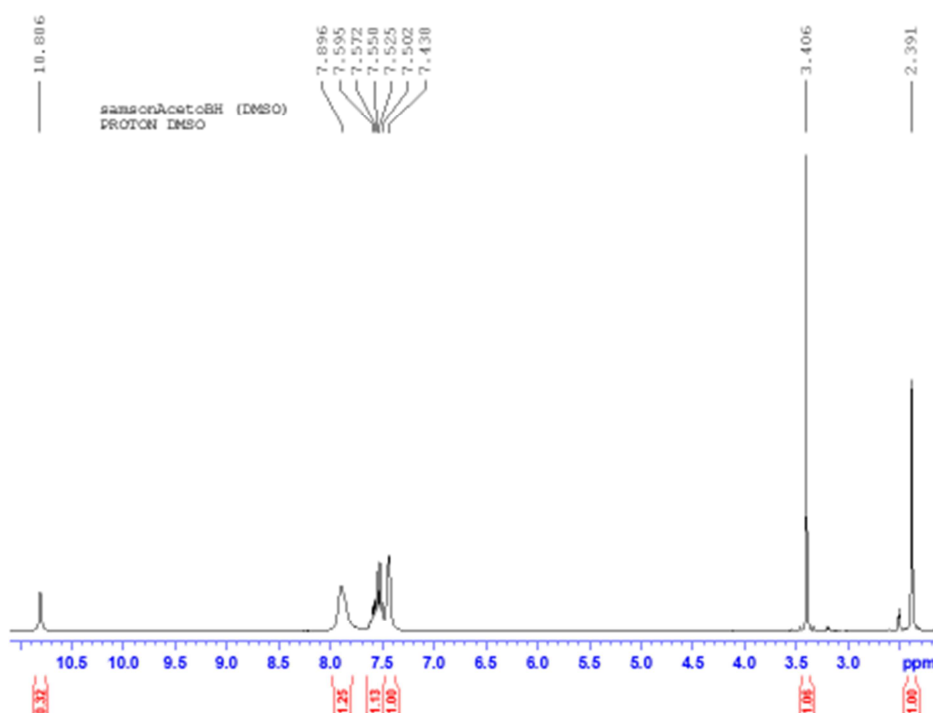
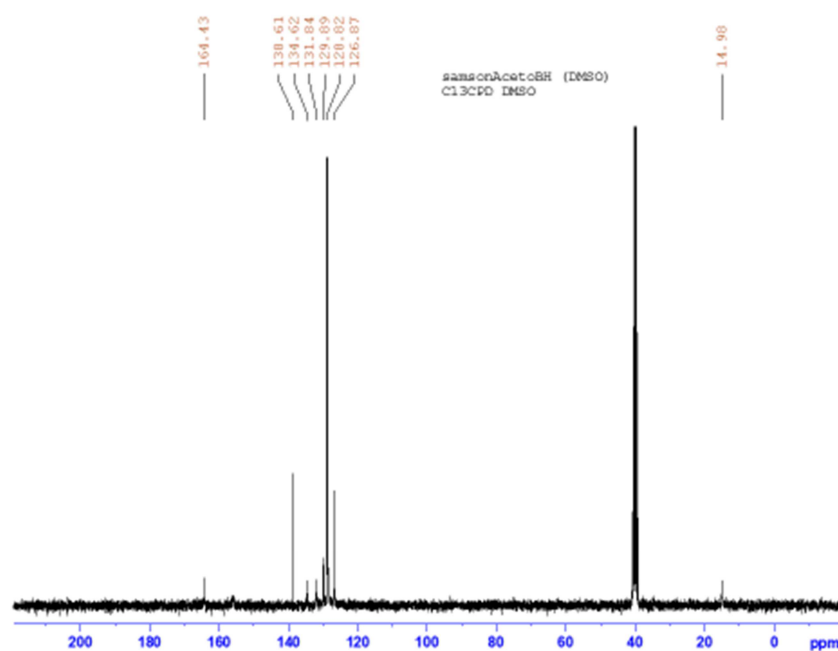


Figure 3. 1H NMR Spectrum of ABH.

Figure 4. ^{13}C NMR Spectrum of ABH.

The singlet observed at 139 ppm arises from the ipso (quaternary) carbon which has no attached hydrogen. Other singlets occur at 135 ppm and 132 ppm due to other quaternary carbons present. There are two larger peaks for the doublet ortho and meta carbon which occurs at 129.8 and 128.82 ppm respectively. A medium sized peak for the para carbon occurs at 126.87 ppm. The signal at 164.43 ppm is attributed to the presence of carbonyl amide. The chemical shift of the methyl carbon at 14.98 ppm shows a deshielding effect due to its attachment to C=N group.

3.3. Infrared Spectra

Table 2 presents the characteristic IR bands identified in the study. The IR spectrum of BAH displayed bands associated with the stretching vibrations of N-H, C=O, and N-N. Specifically, the stretching vibrations of N-H in the secondary amine were observed at 3299 cm^{-1} , while the primary amine exhibited two closely overlapping bands at 3196 cm^{-1} . The C=O group was responsible for a strong band at approximately 1661 cm^{-1} , and the N-N bond was represented by a band at 992 cm^{-1} [19, 20]. Nicotinamide also exhibited characteristic bands at 3351, 1685, and 1381 cm^{-1} , corresponding to the N-H, C=O,

and C=N functional groups, respectively.

Upon complexation, the N-H and C=O vibrations experienced slight shifts to wavenumbers of 3317 - 3304 cm^{-1} and 1673-1623 cm^{-1} , respectively. These shifts indicate the involvement of the nitrogen and oxygen atoms in chelate formation. In the IR spectra of all the complexes, the non-ligand bands observed in the regions of 692 - 626 cm^{-1} and 584 - 203 cm^{-1} can be attributed to the M-O and M-N bonds, respectively [21].

In the complexes, the C=O and N-H vibrations of nicotinamide consistently appeared as strong bands at 1708 - 1670 cm^{-1} and 3424-3403 cm^{-1} , respectively, indicating that the coordination of nicotinamide to the metal occurs through the pyridine nitrogen. The IR spectrum of ABH exhibited diagnostic bands at 1639 cm^{-1} and 1542 cm^{-1} for the C=O and C=N functional groups, respectively. Upon coordination, the carbonyl group frequency shifted to a range between 1674 - 1622 cm^{-1} , and the C=N band at 1542 cm^{-1} disappeared in the spectra of the metal complexes. This suggests that the azomethine group is involved in the coordination [22]. Additionally, new weak sharp bands appeared in the regions of 582 - 422 cm^{-1} for M-N bonds and 688 - 520 cm^{-1} for M-O bonds.

Table 2. Infrared Spectra Data (cm^{-1}) of the Nicotinamide, Hydrazide, Hydrazone and the Metal Complexes.

Compounds	νNH	νNH_2	C-H	$\nu\text{C=O}$	C=N	$\nu\text{M-N}$	$\nu\text{M-O}$
Nicotinamide	-	3351	-	1685	1381	-	-
BAH	3299	3196	3020	1661	-	-	-
[Mn(BAH)(NA) $_2$ (H $_2$ O) $_2$]Cl $_2$	3424	3304,3212	3072	1708,1672	-	503	635
[Co(BAH)(NA) $_2$ (H $_2$ O) $_2$]Cl $_2$	3403	3306,3212	3079	1670,1625	-	584	626
[Ni(BAH)(NA) $_2$ (H $_2$ O) $_2$]Cl $_2$	3406	3317,3212	3079	1669,1625	-	579	692
[Cu(BAH)(NA) $_2$ (H $_2$ O) $_2$]Cl $_2$	3403	3306,3159	3066	1707,1623	-	549	688
ABH	3195	-	3010	1639	1542	-	-
[Mn(ABH)(NA) $_2$ (H $_2$ O) $_2$]Cl $_2$	3425	3298,3203	3072	1707,1672	1433	422	520
[Co(ABH)(NA) $_2$ (H $_2$ O) $_2$]Cl $_2$	3421	3304,3200	3078	1705,1668	1446	430	582
[Ni(ABH)(NA) $_2$ (H $_2$ O) $_2$]Cl $_2$	3408	3321,3213	3080	1670,1626	1446	428	580
[Cu(ABH)(NA) $_2$ (H $_2$ O) $_2$]Cl $_2$	3402	3305,3161	3066	1706,1622	1436	549	688

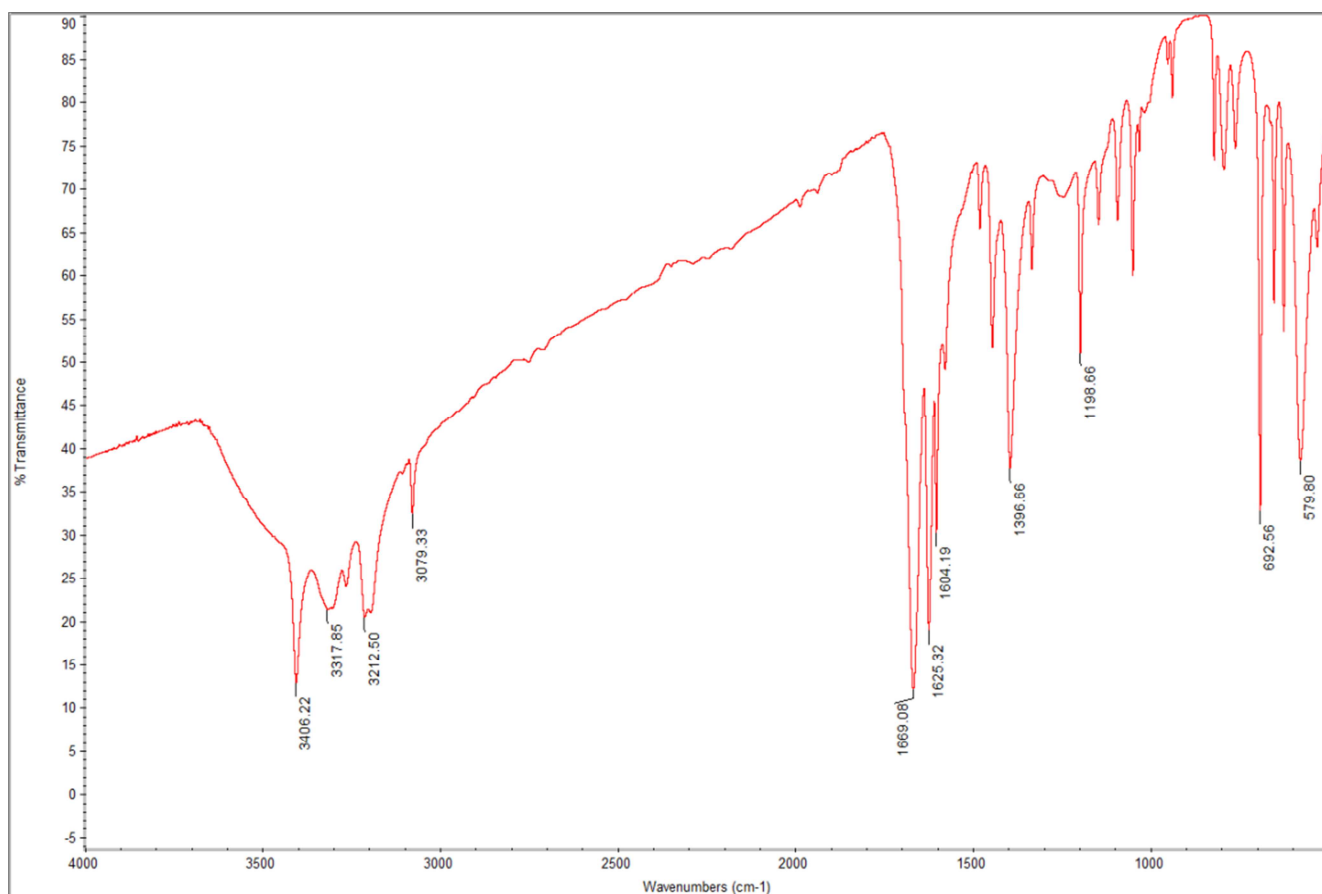


Figure 5. IR spectrum of $[\text{Ni} (\text{BAH}) (\text{NA})_2(\text{H}_2\text{O})_2]\text{Cl}_2$.

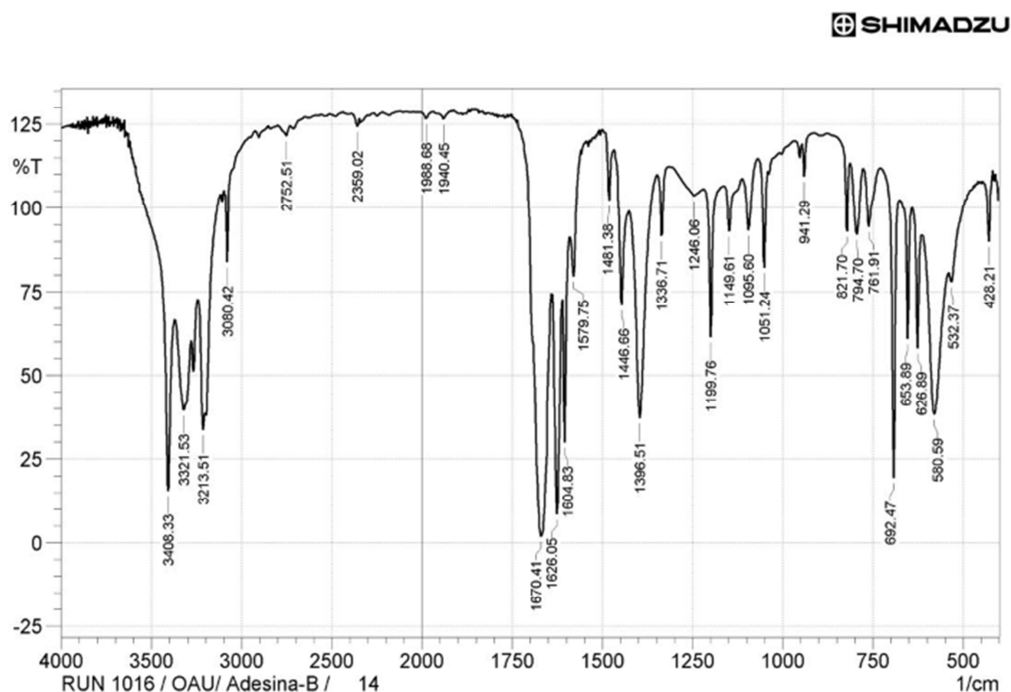


Figure 6. Infrared Spectrum of $[\text{Ni} (\text{ABH})(\text{NA})_2(\text{H}_2\text{O})_2]\text{Cl}_2$.

3.4. Electronic Spectral and Magnetic Moments Data

The electronic spectral and magnetic moments data of

nicotinamide, hydrazide, hydrazone and the metal complexes are presented in Table 3. The ligands (BAH and ABH) and nicotinamide showed intraligand transitions assigned to $\pi\text{-}\pi^*$ and $n\text{-}\pi^*$ between 24 and 280 nm and underwent shifts upon

complexation [23]. The visible spectra of the Cu(II) complexes of BAH showed one broad, structured d-d band centered at 780 nm and a slight shoulder at 963 nm as a result of distortion while that of ABH showed a band at 759 nm and a distortion at 961 nm that is consistent with ${}^2E_g \rightarrow {}^2T_{2g}$ transition in an octahedral environment [24, 25]. The Cu(II) complex of BAH and ABH displayed magnetic moment of 1.73 and 1.76 B.M indicating its mononuclear nature with one unpaired electron [26].

In the ligand field spectrum of Co(II) complex of BAH, three d-d bands (505, 762, and 962 nm) are observed and are attributed to ${}^4T_{1g} \rightarrow {}^4T_{1g}$, ${}^4T_{1g} \rightarrow {}^4A_{2g}$ and ${}^4T_{1g} \rightarrow {}^4T_{2g}$ transitions respectively. The visible spectrum of [Co(ABH)(NA)₂(H₂O)₂]Cl₂ showed the lowest energy band at 936 nm. The multiple band has three peaks at about 761, 645, and 506 nm, while the observed magnetic moment of 4.82 B.M. is attributable to octahedral geometry [27]. The slight reduction of [Co(BAH)(NA)₂(H₂O)₂]Cl₂ at 3.59 B. M compared to the calculated magnetic moment at 3.87 may be as a result of antiferromagnetism.

The visible spectrum of Ni(II) complex of BAH showed three band at 961, 850 and 738 nm assigned to ${}^3A_{2g} \rightarrow {}^3A_{2g}$, ${}^3A_{2g} \rightarrow {}^3T_{1g}$ and ${}^3A_{2g} \rightarrow {}^3T_{1g}$ transitions respectively. A band at 400 nm tending towards the UV region occurs due to charge transfer (LMCT). [Ni(ABH)(NA)₂(H₂O)₂]Cl₂ showed only one d-d transition at 832 nm peculiar of octahedral geometry. Generally, distorted octahedral complexes are paramagnetic with magnetic moments in the range 2.9-3.9; values of 2.65 and 2.84 B.M, for [Ni(BAH)(NA)₂(H₂O)₂]Cl₂, and [Ni(ABH)(NA)₂(H₂O)₂]Cl₂ are consistent with the presence of two unpaired electrons in an octahedral geometry [28].

Mn(II) complex of BAH showed six bands assigned as follows (the wavelength (nm) and transition included: 968 (${}^6A_{1g} \rightarrow {}^4T_{1g}$), 890 (${}^6A_{1g} \rightarrow {}^4T_{2g}$), 691 and 688 (${}^6A_{1g} \rightarrow {}^4E_g$ and ${}^6A_{1g} \rightarrow {}^4A_{1g}$) 640nm (${}^6A_{1g} \rightarrow {}^4A_{2g}$) 597 (${}^6A_{1g} \rightarrow {}^4E_g$), these transitions are forbidden but support Mn(II) complex in an octahedral field [29], while the other band at 443 nm is as a result of charge transfer. Mn(II) complex of ABH showed d-d transitions at 837 nm. The magnetic moment of [Mn(BAH)(NA)₂(H₂O)₂]Cl₂ and [Mn(ABH)(NA)₂(H₂O)₂]Cl₂ which occurs at 4.83 and 4.67 B. M respectively indicate antiferromagnetic interaction between the adjacent metal cations [30].

Table 3. Electronic Spectral and Magnetic Moment Data of Nicotinamide, Hydrazide, Hydrazone and their Metal Complexes.

Compound	Intraligand Transition (nm)	Ligand field transition (nm)	Proposed geometry	μ_{eff} B. M
Nicotinamide	218,280			
BAH	224,268			
[Mn(BAH)(NA) ₂ (H ₂ O) ₂]Cl ₂	214,261	443,597,692,993	Octahedral	4.83
[Co(BAH)(NA) ₂ (H ₂ O) ₂]Cl ₂	214,262	505,762,962	Octahedral	3.59
[Ni(BAH)(NA) ₂ (H ₂ O) ₂]Cl ₂	214,261	738,850,961	Octahedral	2.65
[Cu(BAH)(NA) ₂ (H ₂ O) ₂]Cl ₂	213,262	780,963	Octahedral	1.67
ABH	288,249			
[Mn(ABH)(NA) ₂ (H ₂ O) ₂]Cl ₂	225,262	440,832,996	Octahedral	4.67
[Co(ABH)(NA) ₂ (H ₂ O) ₂]Cl ₂	262	510,961	Octahedral	4.81
[Ni(ABH)(NA) ₂ (H ₂ O) ₂]Cl ₂	225,262	832	Octahedral	2.76
[Cu(ABH)(NA) ₂ (H ₂ O) ₂]Cl ₂	262	759,961	Octahedral	1.76

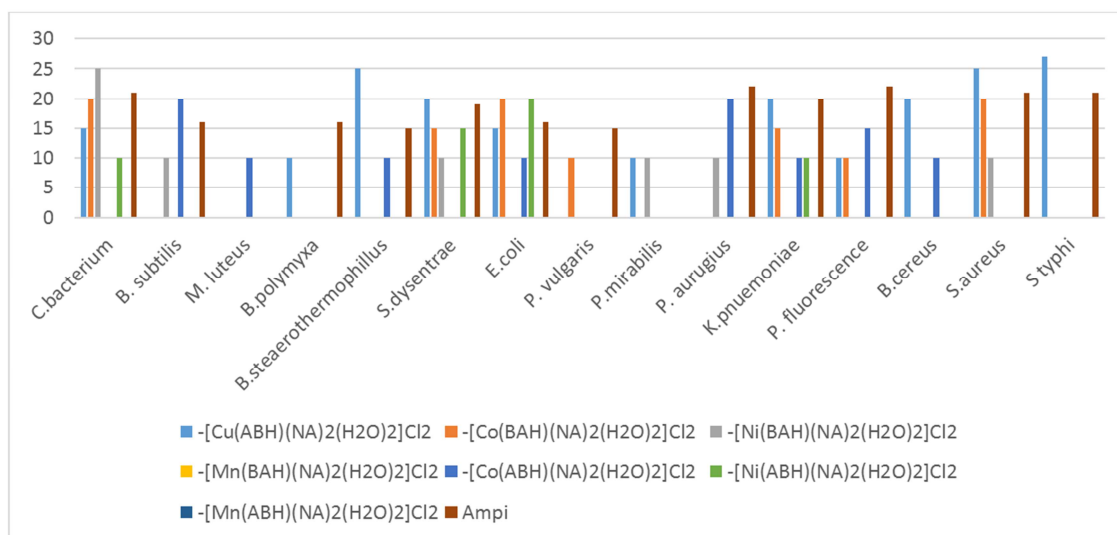


Figure 7. Graph of Zone of Inhibition of Synthesized Ligand Against Micro-Organisms.

3.5. Antimicrobial Activity

The synthesized hydrazide, hydrazone, and their mixed

ligand metal complexes exhibited varying antibacterial activities against the tested bacterial strains. Upon careful examination of the results, it was noted that the ligands

themselves did not demonstrate inhibitory effects against most of the organisms, except for *Corynebacterium*, which was inhibited by ABH, while BAH displayed activity against *Micococcus luteus* and *Bacillus stearothermophilus*. However, the antibacterial activity of the ligands became more pronounced upon coordination with metal ions under the same experimental conditions.

This enhancement in activity can be attributed to a synergistic effect between the metal ion and the hydrazide/hydrazone and nicotinamide ligand. The increased activity is attributed to the decrease in polarity of the ligand resulting from the overlap of the ligand orbital and partial sharing

of the positive charge of the metal ion with an electron-releasing group [31, 32]. Notably, $[\text{Cu}(\text{ABH})(\text{NA})_2(\text{H}_2\text{O})_2]\text{Cl}_2$ exhibited resistance against most bacteria, except for *Bacillus subtilis* and *Micococcus luteus*. Similarly, $[\text{Ni}(\text{BAH})(\text{NA})_2(\text{H}_2\text{O})_2]\text{Cl}_2$, $[\text{Co}(\text{ABH})(\text{NA})_2(\text{H}_2\text{O})_2]\text{Cl}_2$, and $[\text{Co}(\text{BAH})(\text{NA})_2(\text{H}_2\text{O})_2]\text{Cl}_2$ displayed strong inhibitory effects against selected microorganisms.

Overall, the antibacterial activities of all the compounds were comparable to that of ampicillin, which served as the standard. Graphical representations illustrating the zone of inhibition caused by both the ligands and the complexes are presented in Figures 7 and 8, respectively.

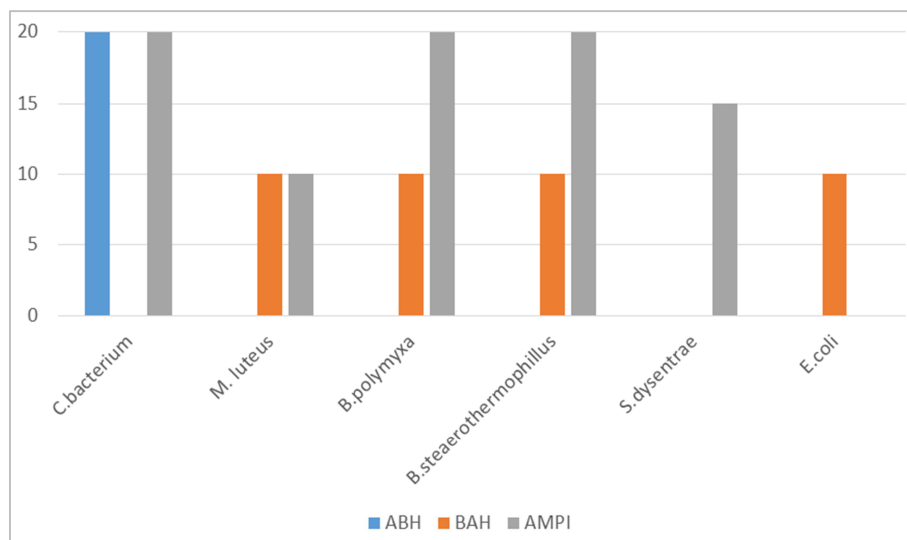


Figure 8. Graph of Zone of Inhibition of Synthesized Metal Complexes Against Micro-Organisms.

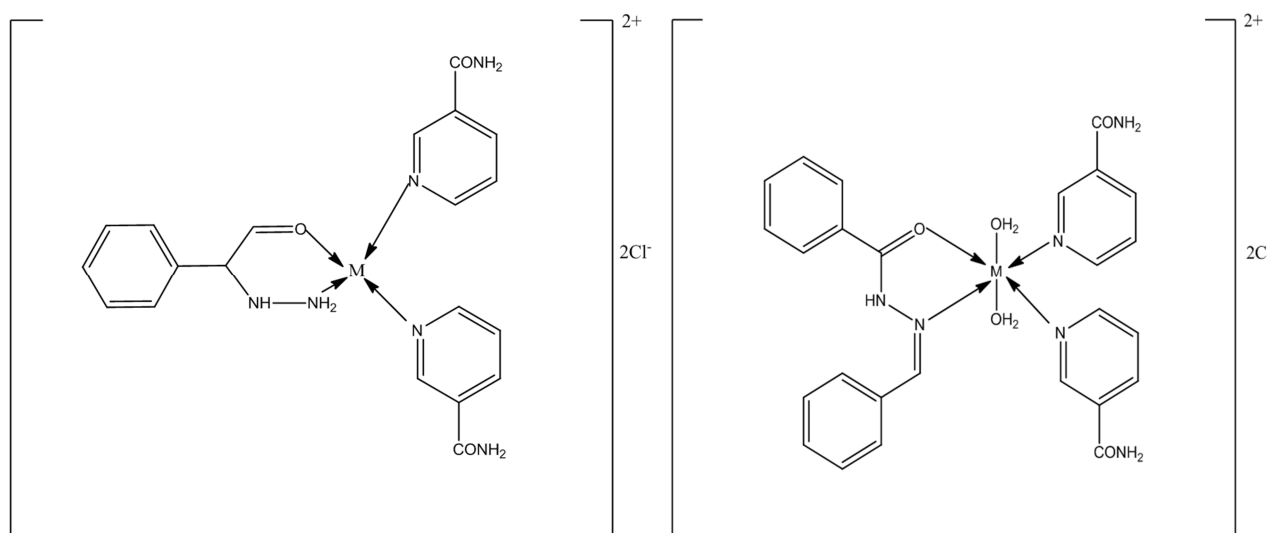


Figure 9. Proposed Structure of Metal Complexes (Mn, Co, Ni and Cu) of ABH and BAH Mixed with Nicotinamide.

4. Conclusion

In conclusion, we have successfully synthesized a new aroylhydrazones (acetophenone-benzoylhydrazones) as well as the mixed Mn(II), Co(II), Ni(II) and Cu(II) complexes of the ligand and its precursor. The coordination sites are consistent

with literature involving the azomethine and carbonyl groups while nicotinamide with one binding site coordinated through the pyridyl nitrogen. The electronic and magnetic moments data indicated six coordinate octahedral geometry with the presence of counter ions outside the coordination sphere as supported by conductivity measurements. All the metal complexes displayed moderate activity against the tested

micro-organisms with $[\text{Ni}(\text{BAH})(\text{NA})_2(\text{H}_2\text{O})_2]\text{Cl}_2$ and $[\text{Cu}(\text{ABH})(\text{NA})_2(\text{H}_2\text{O})_2]\text{Cl}_2$ showing the best antimicrobial activities.

References

- [1] Lazny R. & Nodzevska A. N, N-Dialkylhydrazones in organic synthesis from simple N, N-dimethylhydrazones to supported chiral auxiliaries. *Chem. Rev.* 2010; 110: 1386-1434.
- [2] Loncle J, Brunel M, Vidal N, Dherbomez M. & Letourneux Y. Synthesis and antifungal activity of cholesterol-hydrazone derivatives. *Eur. J. Med. Chem.* 2004; 39: 1067 - 1071.
- [3] Uribe-Romo FJ, Doonan CJ, Furukawa H, Oisaki K. & Yaghi OM. Crystalline covalent organic frameworks with hydrazone linkages. *J. Am. Chem. Soc.* 2011; 133: 11478-11481. [dx.doi.org/10.1021/ja204728y](https://doi.org/10.1021/ja204728y).
- [4] Hidai M. & Mizobe Y. Recent advances in the chemistry of dinitrogen complexes. *Chem. Rev.*, 1999, 95: 1115 - 1133. <https://pubs.acs.org/doi/10.1021/cr00036a008>.
- [5] Kobayashi S, Mori Y, Fossey JS. & Salter MM. Catalytic enantioselective formation of C-C bonds by addition to imines and hydrazones: a ten-year update. *Chem. Rev.* 2011; 111: 2626-2704. doi: 10.1021/cr100204f.
- [6] Tandon SS, Chander S. & Thompson LK. Ligating properties of tridentate Schiff base ligands, 2-[(2-pyridinylmethyl)-imino]methyl phenol (HSALIMP) and 2-[[[2- (2-pyridinyl) ethyl]imino]methyl]phenol (HSALIEP) with zinc(II), cadmium(II), nickel(II) and manganese(III) ions. X-ray crystal structures of the $[\text{Zn}(\text{SALIEP})(\text{NO}_3)_2]$ dimer, $[\text{Mn}(\text{SALIEP})_2](\text{ClO}_4)_2$, and $[\text{Zn}(\text{AMP})_2(\text{NO}_3)_2]$. *Inorg. Chim. Acta*, 2000; 303-302: 683-692. [https://doi.org/10.1016/S0020-1693\(00\)00010-4](https://doi.org/10.1016/S0020-1693(00)00010-4).
- [7] Yildiz M, Dulger B, Koyuncu SY. & Yapici, B. M. (2004). Synthesis and antimicrobial activity of bis (imido) Schiff bases derived from thiosemicarbazide with some 2-hydroxy-aldehydes and metal complexes. *J. Indian Chem. Soc.*, 81, 7-12.
- [8] Ainscough EW, Brodie AM, Denny WA, Finlay GJ, Gothe SA, & Ranford JD. Cytotoxicity of salicylaldehyde benzoyl-hydrazone analogs and their transition metal complexes: quantitative structure-activity relationships. *J. Inorg. Biochem.* 1999; 77: 125-133. DOI: 10.1016/S0162-0134(99)00131-2.
- [9] Hosseini-Monfared H, Kalantari H, Mohammad-Ali K. & Janiak C. Synthesis, Structural Characterization and Electrochemical Studies of a Nicotinamide-bridged Dinuclear Copper Complex derived from a Tridentate Hydrazone Schiff Base Ligand. *Journal of Inorganic and General Chemistry*. 2007; 633: 1945-1948. DOI: 10.1002/zaac.200700238.
- [10] Hosseini-Monfared H, Bikas R, Sanchiz J, Lis T, Siczek M, Tucek J, Zboril R. & Mayer P. Syntheses, structures and magnetic properties of azido- and phenoxo-bridged complexes of manganese containing tridentate aroylhydrazone based ligands. *Polyhedron*, 2013; 61: 45-55. doi/abs/10.1002/ejic.200600552.
- [11] Ajayeoba TA, Akinyele OF. & Oluwole AO. Synthesis, characterisation and antimicrobial studies of mixed nickel (II) and copper(II) complexes of aroylhydrazones with 2, 2'-bipyridine and 1, 10-phenanthroline. *Ife Journal of Science*. 2017; 19: 119-132. <https://dx.doi.org/10.4314/ijss.v19i1.12>.
- [12] Akinyele OF, Fakola EG, Durosinmi LM, Ajayeoba TA. & Ayeni AO. (2019). Synthesis and characterization of heteroleptic metal complexes of isoniazid and metformin. *Ife Journal of Science*, 21 (3): 185-191 <https://dx.doi.org/10.4314/ijss.v21i3.15>.
- [13] Akinyele OF, Fakola EG, Durosinmi LM, Ajayeoba TA. & Ayeni AO. (2020) Synthesis, characterization and antimicrobial activities of heteroleptic metal chelates of isoniazid and 2, 2'-bipyridine Bull. Chem. Soc. Ethiop. 34 (3), 471- 478. DOI: <https://dx.doi.org/10.4314/bcse.v34i34>.
- [14] Sabita S. & Sudha M. Synthesis and Characterization of Copper Complex of Salicylaldehyde Benzoyl Hydrazone. *J. Nepal Chem. Soc.*, 2012; 29: 11-17.
- [15] Osowole AA, Agbaje OB. & Ojo BO. Synthesis, Physicochemical and Antioxidant Properties of Some Metal(II) Complexes of Mixed Drugs, Aspirin and Nicotinamide. *Asian J Pharm Clin Res*, 2014; 7 (3): 145-149. <https://doi.org/10.15436/-2475-6245.16.010>.
- [16] Ekennia AC, Onwudiwe DC, Osowole AA, Olanukanmi LO. & Ekenso EE. Synthesis, Biological, and Quantum Chemical Studies of Zn (II) and Ni(II) Mixed-Ligand Complexes Derived from N, N-Disubstituted Dithiocarbamate and Benzoic Acid. Hindawi Publishing Corporation Journal of Chemistry. 2016, Article ID 5129010, <http://dx.doi.org/10.1155/2016/512901>.
- [17] Ali I, Waseem AW & Saleem K. Empirical formulae to molecular structures of metal complexes by molar conductance. *Synthesis and Reactivity in Inorganic, Metal-Organic, and Nano-Metal Chemistry*. 2013; 43: 1162-1170.
- [18] Geary WJ. (1971). The use of conductivity measurements in organic solvents for characterization of coordination compounds. *J. Coord. Chem. Rev.* 7, 81-83.
- [19] Sutradhar M, Martins LMDRS, Fatima C. Guedes da Silva, & Pombeiro AJL. Oxidovanadium complexes with tridentate aroylhydrazone as catalyst precursors for solvent-free microwave-assisted oxidation of alcohols. *Applied Catalysis A: General*. 2015; 493: 50-57. <http://dx.doi.org/10.1016/j.apcata.2015.01.005>.
- [20] Akinyele OF, Fakola EG, George RC. & Durosinmi LM. (2021). Synthesis, characterization and antibacterial activity of mixed ligand complexes of nicotinamide and 2, 2'-bipyridine. *Ife Journal of Science*, 23 (1): 213 - 222. <https://dx.doi.org/10.4314/ijss.v23i1.18>.
- [21] El-Sherif AA, Shoukry MM. & Mohamed MA. Synthesis, characterization, biological activity and equilibrium studies of metal(II) ion complexes with tridentate hydrazone ligand derived from hydralazine. *Spectrochim. Acta A*. 2012; 98: 307-321. <https://doi.org/10.1016/j.saa.2012.08.034>.
- [22] Olasomi OE, Akinyele OF, Akinkunmi EO, Isabirye DA. & Aiyelabola TO. (2017). Synthesis, characterisation and antimicrobial studies of coordination compounds of l-serine and their mixed ligand complexes with aspartic acid. *Asian Journal of Chemistry*, Vol. 29 (2), 371-374.
- [23] Refat MS. & El-Metwaly NM. Spectral, thermal and biological studies of Mn (II) and Cu(II) complexes with two thiosemicarbazide derivatives. *Spectrochimica Acta Part A*, 2012; 92: 336-346. <https://doi.org/10.1016/j.saa.2012.02.041>.

- [24] Lee, JD. (1996). Concise Inorganic Chemistry, English Language Book Society, London, 374, 834-856.
- [25] Akinyele OF, Akinnusi TO, Ajayeoba TA, Ayeni AO. & Durosinmi LM. (2019). Synthesis, characterization and antimicrobial activities of Cobalt(II), Nickel(II) and Copper(II) complexes of aroylhydrazone mixed with aspirin. *Science Journal of Chemistry*. Vol. 7 (3): 67-71.
- [26] Vrdoljak V, Pavlovi G, Hrenar T, Rubcic M, Siega P, Dreos R. & Cindrica M. Cobalt (III) complexes with tridentate hydrazone ligands: protonation state and hydrogen bond competition. *RSC Adv.* 2015; 5: 104870-104883. DOI: 10.1039/C5RA22068H.
- [27] Akinyele OF, Adejayan SB, Durosinmi LM, Ayeni AO. & Ajayeoba TA. (2020). Interactions of metal ions with trimethoprim and metformin, *International Journal of ChemTech Research*. Vol. 13 (2), 38-45. <http://dx.doi.org/10.20902/IJCTR.2019.130205>.
- [28] Akinyele OF, Olayode SO, Ajayeoba TA, George RC, Famojuro AT, Ogunsakin OE. & Ogundele SB. (2021). Synthesis, characterization and antibacterial activities of mixed ligand metal (II) complexes of substituted benzoic acid hydrazide and isoniazid. *Ife Journal of Science and Technology*. Vol 5 (1), 49–59.
- [29] Bikas R, Ghorbanloo M, Sasani R, Patenburg I. & Meyer G. Manganese (II) complexes of hydrazone based NNO-donor ligands and their catalytic activity in the oxidation of olefins. *Journal of Coordination Chemistry*. 2017; 70: 819-830. doi/abs/10.1080/00958972.2017.1281918.
- [30] Al-Sha'alan NH. Antimicrobial activity and spectral, magnetic and thermal studies of some transition metal complexes of a schiff base hydrazone containing a quinoline moiety. *Molecules*. 2007; 12 (5): 1080-1091. <https://doi.org/10.3390/12051080>
- [31] Abu-Zaid AA, Alopidi MA, El-Sehrawy MH. In vitro antibacterial, anticancer and antioxidant properties of some oil plant extract. *Journal of American Science*. 2013; 9 (11): 83-94. <http://www.jofamericanscience.org>.
- [32] Akinyele OF, Fakola EG, Olasunkanmi OO, George RC, Durosinmi LM, Ayeni AO, Ajayeoba TA. Synthesis, characterization, antibacterial activity and molecular docking of mixed ligand complexes of nicotinamide and isoniazid. *Chemistry Africa*. 2023. <http://doi.org/10.1007/s42250.-023-00701-8>.