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Exploring the synthesis, of transition metal complexes derived from 5-nitrosalicyaldehyde benzoylhydrazone characterization and their antimicrobial activities

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Abstract

Synthesis as well as Characterization of a Hydrazine derivative Schiff Base ($L^{\wedge}$) Derived from 5-Nitrosalicylaldehyde and Benzhydrazides, along with their transition divalent metal chelates of Ni, Cu, and Co. The complex ion were characterized using Melting Temperatures, FT-IR Spectrum Analysis, Magnetic Susceptibility, and UV-Vis Spectroscopy. These vibrant and stable ketimine and chelates remain undissolved in pure water but readily dissolve in organic solvents such as Dimethyl sulfoxide, acetone, and ethanol. The magnetic and spectral measurements suggest an octahedral geometry for the metal ions. The spectral data of the ligand displayed a prominent band at 1580c/m, confirming the presence of the imine group after synthesis. Interestingly, in the chelates, this peaks shifted to a higher spatial frequency*, suggesting coordination of the imine nitrogen with the metal, thus establishing complexation through the N-atom of the imine moiety. The antimicrobial efficacy of the chelation compounds and ligating molecule was evaluated using the disc diffusion method against the bacterial isolates, namely Pseudomonas - aeruginosa, Enterobacter - cloacae, Klebsiella - pneumoniae, as well as Staphylococcus - aureus (G - ve and G +ve respectively), the fungi isolates, Aspergillus - niger as well as Phytopthera - infestans. Comparing the inhibitory effect of the analysis of the ligand (L^1) and its respective chelate molecule demonstrated that the chelates displayed enhanced antimicrobial potency compared to the unbound ligand.*

Keywords: 5-nitrosalicylaldehyde, Antimicrobial activity, Benzhydrazide, Schiff bases, Synthesis.

Introduction

Hydrazone molecules hold significance in both chemistry and biology due to their versatile applications, while the hypotetical and computerized investigations concerning the coordination of metal ions with donor ligands further contribute to the importance of hydrazone as a pivotal subject in chemistry[1].

Due to their intriguing biological features and coordinative ability, novel hydrazine derivatives are constantly attracting the interest of organic and medicinal chemists. Hydrazones exhibit a wide variety of pharmacological activities, including analgesic[2], anti-inflammatory[3], antibacterial[4], antimicrobial, anti-HIV[5], and anticancer[6].

Furthermore, because they effortlessly create stable complexes with a variety of transition metals, hydrazones are among the most extensively utilized ligands. Many researchers have created a variety of substituted derivatives as prospective medications in an effort to improve their medicinal characteristics while lowering their toxicity[7]

In this article, we present synthesis and analysis of the imine derived from 5-nitrosalicyaldehyde as well as benzhydrazide, along with its selected divalent metal chelates of Co, Ni, and Cu. Additionally, we explore their antimicrobial utilization.

Materials and methods

Every piece of glassware employed in this investigation underwent meticulous cleansing using cleanser and subsequent rinsing with purified water. To avert the adhesion of metal particles to the glass surface, the glassware was immersed in a potent nitric acid for approximately 3h. Subsequently, after being washed 4 to 5intervals with pure water, the glassware was withered in a cooker at 110°C. The chemicals as well as diluents employed in the study were of high purity and procured from Sigma Aldrich. They were utilized as received, without the need for further purification. The process of quantifying was conducted using an electronic quantifying B154 balance. IR spectroscopy had been captured using Happ-Genzel balance within the 4000–400c/m range. UV–visible spectra were recorded in Dimethylformamide mixture on a CARY-50 Biophotometer spanning the range of 300–1000 nano meter. MK1 Sherwood amagnetic sensitivity detector was utilized to assess the magnetization capacity of the compounds. The melting temperature of both the complexing agent and the chelates was calculated employing a Gallenkamp melting temperature equipment. The assessment of both antifungal as well as antibacterial efficacy was conducted at the Federal University Dutsin-Ma Katsina, Microbiology Department. The bacterial strains *K. pneumoniae, P. aeruginosa*, *E. cloacae*as

well as *S. aureus* classified as (G- and G+) bacteria, along with the fungal-related organisms *A. niger* along side *P. infestans*, was acquired, subsequently distinguish in the section of the department.

Synthesis of 5-Nitrosalicyaldehyde Benzoylhydrazone ($L^{\wedge}$): When a solution containing the corresponding 1.361g of Benzohydrazides dissolved in 50ml methanol, in a similar mannera combination containing 30ml methanol as well as 1.6710g 5-Nitrosalicylaldehydewas carefully introduced, immediately a deposit is produced. The combination was agitated for half an hour, subsequently kept at ambient temperature for 24 hours, resulting in a complete residue of amber precipitate. Precipitate was sieved, afterward cleansed with concentrated ethyl alcohol, it was dehydrated within an empty desiccator for a certain duration[8].

Synthesis of the metal(II) complexes of Ni, Co and Cu: 100mg of 5nSBH and 96 mg of the salts was dissolved in 20mL methanol. The mixture was then subjected to reflux for 4 hours. Subsequently, the composite was allowed to undergo ambient temperature aging for several days. After filtration, the resulting percipient was washed with ethyl alcohol and diethyl ether before being air-dried at ambient conditions. Similar result was obtained for all other complexes[9]. The complexes were prepared utilizing the salts $NiCl_2.6H_2O$, $Co(NO_3)_2$, and $CuSO_4.5H_2O$.

The antimicrobial study of 5nSBH ligand and its metal - ligand chelate: The synthesized 5nSBH and its metal compounds were assessed for their fungicidal and bactericidal properties using the disc diffusion procedure on aseptic plate containing Mueller Hinton plate (MHP) and Sabouraud agar (SA). Standard solution of the mixture was formulated in Dimethyl sulfoxide at a concentration of 200mg/mL, 40mg/mL, and 8mg/mL, a series of dilutions were made to determine the minimal inhibition concentration values (mg/mL). The effectiveness of the synthetic variants was assessed by incubating two fungal species, A. *niger* and P. *infestans*, along with four bacterial strains: S. aureus K. *pneumoniae*, P. *aeruginosa*, as well as E. cloacae, for 24 and 48 hours, respectively, at 37 degrees Celsius[10]. Fluconazole, an anti-mycotic drug, and abacteriostatic drug Ciprofloxacin were used to gauge the effectiveness of the synthetic variants. They were also evaluated for antimicrobial properties in equivalent concentration and under situation similar to the compounds been studied. Antimicrobial properties were performed in threefold, and the average value was taken as the conclusive result. The diameters of the zones of inhibition were measured around the discs[11] to assess the antimicrobial activity.

The analyses were carried out at the microbiology laboratory Federal University Dutsin-Ma Katsina state.

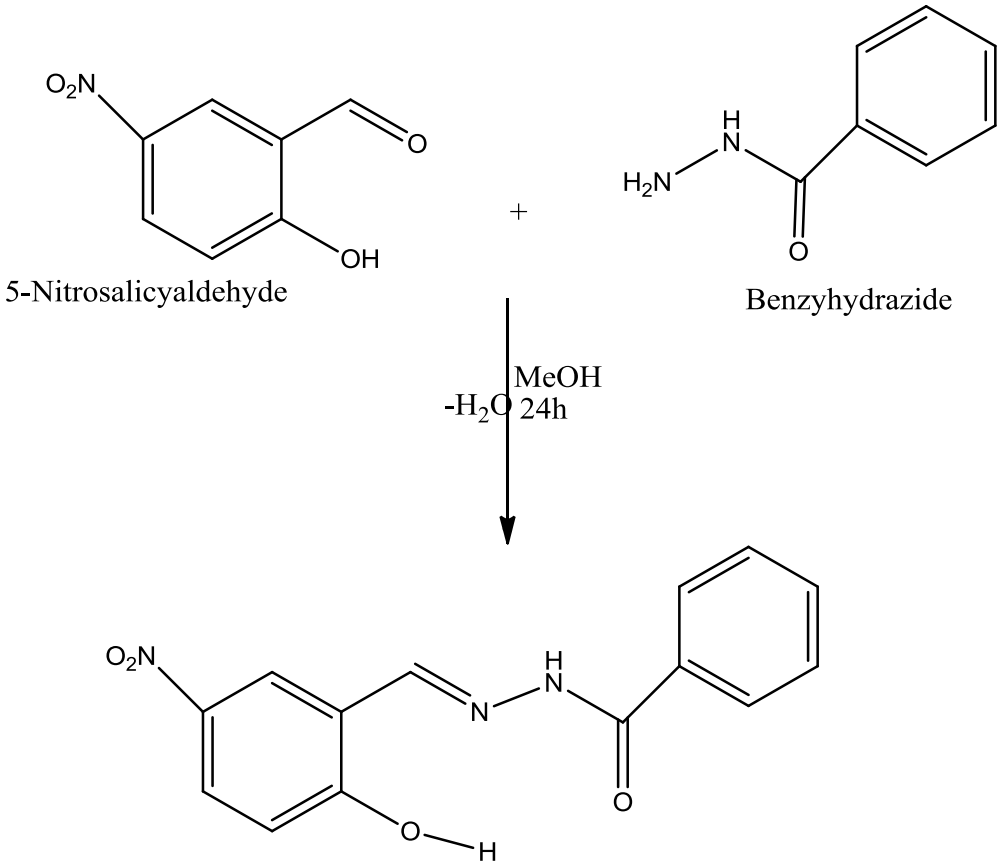

Figure-1: 5-Nitrosalicyaldehyde benzoylhydrazone.

Results and discussion

As depicted in Figure-1, the Schiff base was synthesized by condensing 5-nitrosalicylaldehyde and benzhydrazide in a 1:1 mole ratio. The reaction between 5nSBH and metal salts (Figure-2), as shown in Table-1, gave an output of different colored mixture having substantial yield.

Unlike their insolubility in pure water, the ligand ($L^{\wedge}$) as well as the metal (II) compounds exhibit solubility in hydrocarbon diluents like acetone, ethanol, methanol, n-hexane, and DMSO (Table-2).

IR Spectra studies: The ligand and the complexes' Fourier-transform infrared (FT-IR) spectroscopic data, presented in Table-3, exhibited prominent absorption peaks at 1677, and also 1580c/m in the ligand's IR spectrum. These peaks were ascribed to the extending (stretching) oscillation of the carbonyl group (-CO) and imine group (-CN), respectively. To assess the involvement of the sites of coordination in the compounds, a comparative analysis was conducted between the infrared spectroscopy of the complexes and those of the unbound ligand.

Based on reference[12], complexation takes place through the N-atom of the imine group which is due to a shift in peaks to higher spatial frequency of 1595, 1602, and 1677c/m an indication the coordination of the imine nitrogen to the metal as evidenced by the unchanged or slightly shifted (-NH) band to higher frequencies in the spectrum of metal nitrate and chloride chelate. This observation suggests that the imine nitrogen is engaged in coordination, while the lack of significant changes in the (-NH) band implies a reduction in hydrogen bonding during the chelation process. Hence 3063c/m which is peak displayed for (-OH) it is noteworthy that this shifts towards higher spatial frequency in the spectrum of the ligand when forming complexes, signifying the bond formation of the (-OH) group with the metal ions. This shift clearly indicates coordination of the phenolic oxygen to the metal centers. Additionally, the appearance of new peaks in the chelates' around 7007c/m and likewise 924c/m, which correspond to (-M-N) and (-M-O) vibrations, provides further compelling evidence of bonds interactions[13]. This discovery strengthens the case for successful chelation compounds formation.

Table-1: Physical characteristics of 5nSBH ($L^{\wedge}$) and its coordination species.

Chemical Composition	Molecular notation	Mol. Mass $gmol^{-1}$	Appearance	Percentage Productivity (%)	Melting Temp (^0C)
$L^{\wedge}$	$C_{14}H_{11}N_3O_4$	285.1	Yellow	59	130 – 131
[Ni $L^{\wedge}_2$]	[$NiCl_2.6H_2O$ $(C_{14}H_{10}N_3O_4)_2$]	807.8	Green	71	210 - 211
[Co$L^{\wedge}_2$]	[$Co(NO_3)_2$ $(C_{14}H_{10}N_3O_4)_2$]	753.0	Red	76	209 - 210
[Cu $L^{\wedge}_2$]	[$CuSO_4.5H_2O$ $(C_{14}H_{10}N_3O_4)_2$]	819.6	Blue	67	214 - 215

Table-2: Solubility properties of 5nSBH ($L^{\wedge}$) and their complex ion in different solvents.

Dissolvent Compound	Distilled Water	Methanol	Ethanol	Chloroform	Benzene	DMSO	Hexane	Acetone
$L^{\wedge}$	ISS	SO	SO	SO	SPS	SO	SO	SO
[Ni $L^{\wedge}_2$]	ISS	SO	SO	SPS	SO	SO	SO	SPS
[Co $L^{\wedge}_2$]	ISS	SO	SO	SO	SO	SO	SO	SO
[Cu $L^{\wedge}_2$]	ISS	SPS	SPS	SO	SPS	SPS	SO	SPS

Key: SO- soluble, ISS - insoluble, SPS – sparingly soluble, L^- 5-nitrosalicyaldehyde benzoyl hydrazone.

Table-3: Diagnostic FT-IR bands (cm^{-1}) observed in Ligand ($L^{\wedge}$) and their coordination adduct.

Compound	v CO	v CN	v NH	v OH	v N-N	v M-O	v M-N
L^	1677	1580	3063	3063	1073,1282	-	-
[Ni $L^{\wedge}_2$]	1677,1602	1602	3391,3488	3391	1073,1282	924	7007
[Co $L^{\wedge}_2$]	1677	1595	3414	3181	1282,1073	924	7007
[Cu $L^{\wedge}_2$]	1677	1677	-	3071	1282,1073	924	7007

Antimicrobial property: Antimicrobial properties of the imine ligand (L^) and its respective metal coordination entity was evaluated using the disc diffusion method. Zones of inhibition in diameter (mm) for each treatment were measured. To assess the antifungal and antibacterial effectiveness of the test compounds, fluconazole and ciprofloxacin, both antifungal and antibacterial drugs, respectively, were examined at equivalent concentrations and under identical environmental conditions.

A disc impregnated with Dimethyl sulfoxide was utilized as a negative control. The synthesized ligands and each of its chelates were subjected to antibacterial assessment against *S. aureus, P. aeruginosa, K. pneumoniae*, and finally *E. cloacae* (Table-4). The results revealed that the ligand exhibited minimal to been inert against all validated organisms. The Cu(II) metal complex showed resistance against two bacterial strains of *S. aureus* and *P. aeruginosa*, whereas *K. pneumoniae* was susceptible to attack by all the metal chelates. Notably, *E. cloacae* demonstrated significant activity opposed to the three (3) complex molecule. In comparison, the standard drug Ciprofloxacin displayed robust activity against the verified organisms, with larger zones of inhibition at the same concentrations when compared to both the ligands and the complex molecule.

L^: 5-nitrosalicyaldehyde benzoylhydrazone: Comparably, the fungicidal activity of the ligand as well as its coordination species was evaluated, and the findings are presented in Table-5. It is demonstrated from the results that the ligands exhibited significant fungicidal properties against both fungal strain verified. However, all the metal-ligand chelate displayed appreciable efficacy specifically against the fungal strain *P. Infestans.* Conversely, the complex molecules were found to be dormant in opposition to the fungal pathogen A. niger. Notably, the strain *P. Infestans* displayed resistance to the standard drugs fluconazole, yet it exhibited promising activity against *A. niger*.

Conclusion

The hydrazine derivative Schiff base 5-nitrosalicylaldehyde benzoylhydrazone (5nSBH) and its metal chelates of Co, Ni, and Cu were effectively synthesized and thoroughly analyzed through spectrum and technological based research.

Figure-2 is proposed for all the synthesized coordinating species, which was validated by the spectroscopic data.

The coordination between the molecular complexes and as well as the ligating specie was established through the imine nitrogen and hydroxyl phenyl moiety (OH) of the Schiff's imine. This was confirmed by comparing the infrared spectrum information of the ligating molecule to those of their divalent metal chelating molecules. The coordination process was found to effectively bind the metal with the chelating agent.

Notably, the synthesized divalent metal coordination entity exhibited significant bactericidal and fungicidal properties. The antimicrobial activity of the complexes surpassed that of the free ligand against various strains of bacteria and fungi. This suggests that the formation of complexes with metal ions enhances the ligand's antimicrobial efficacy, leading to improved activity against the tested species of bacteria and fungus.

In conclusion, the successful synthesis and assessment of the hydrazine derivative and its divalent metal coordination entity have provided valuable insights into their structural features and microorganism-inhibiting potential. The observed increased antimicrobial activity of the chelates compared to the free ligand emphasizes their potential applications as potent anti-pathogenic agents. These findings contribute to the understanding of metal-ligand interactions and support the development of new antimicrobial agents for combating bacterial and fungal infections.

Table-4: Antibacterial assessment of ligand L^ and their coordination entity against selected bacterial strains.

Organism Conc. (mg/ml)	*S. Aureus* 8.00 40.0 200	*P. Aeruginosa* 8.00 40.0 200	*E. Cloacae* 8.00 40.0 200	*K. Pneumonicae* 8.00 40.0 200
L^	- - -	2.00 6.00 7.00	- - -	- - -
Co $L^{\wedge}_2$	18.0 19.0 21.0	22.0 22.0 22.0	17.0 19.0 21.0	12.0 17.0 17.0
Ni $L^{\wedge}_2$	11.9 12.9 13.0	17.0 19.0 20.0	19.0 22.0 23.0	9.00 10.0 10.0
Cu $L^{\wedge}_2$	3.80 4.00 4.00	- - -	18.0 18.0 18.0	9.00 14.0 15.0
Ciprofloxacin	35.0 37.0 39.0	44.0 45.0 46.0	37.0 38.0 42.0	35.0 35.0 36.0

Table-5: The fungicidal property of ligand 5nSBH and their chelation compound.

Organism/compound Conc.(mg/ml)	*A. niger* 8.00	40.0	200	*P. Infestans* 8.00	40.0	200
L^	35.0	35.0	36.0	33.0	36.0	37.0
Co $L^{\wedge}_2$	-	-	-	26.0	26.0	29.0
Ni $L^{\wedge}_2$	-	-	-	21.0	24.0	26.0
Cu $L^{\wedge}_2$	-	-	-	18.0	19.0	22.0
Fluconazole	32.0	33.0	39.0	-	-	-

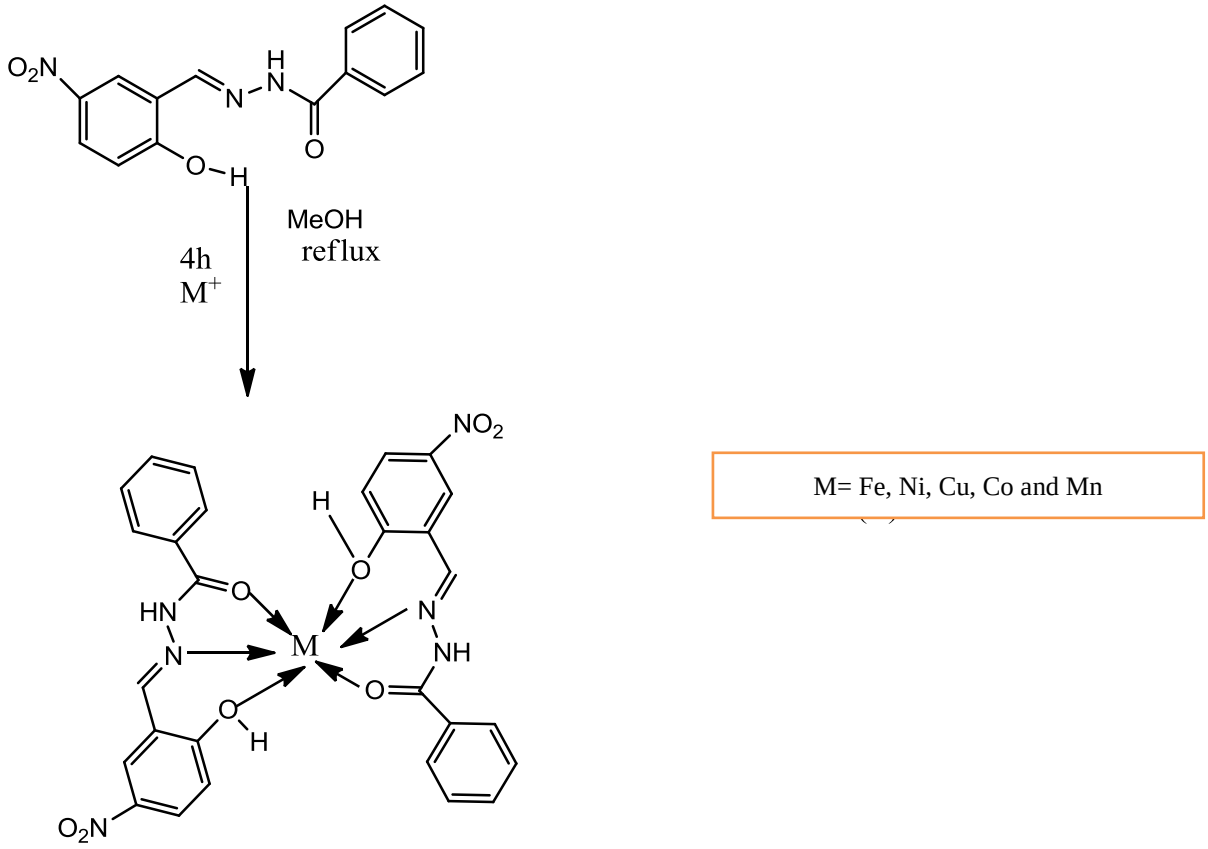

Figure-2: Proposed structure of metal (II) complex.

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