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NOVEL SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL STUDIES OF SCHIFF BASE COMPLEXES OF 4-PYRIDINE CARBOXALDEHYDE

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ABSTRACT

In the present study an intermolecular reductive Schiff base formation from 4-nitro pyridine and 4 pyridine carboxaldehyde carried out in the presence of iron powder and dilute acid. The Schiff base and metal complexes have been characterized by elemental analysis, molar conductance, molecular weight determination, IR, XRD and SEM. The biological activities have also been studied for the synthesized compounds. The Schiff base and its metal complexes show a good activity against the bacteria *Staphylococcus aureus*, *E.coli*, *Klebsiella*, *Pneumonia* and fungi like *Candida albicans*, *Apergillus niger* and Pencillium sp. The antimicrobial results also indicate that the metal complexes are better antimicrobial agents as compared to the Schiff base.

Keywords: 4-Nitropyridine, 4-Pyridinecarboxaldehyde, Antimicrobial activity.

INTRODUCTION

During the past three decades considerable attention has been paid to the chemistry of the complexes of the Schiff base containing nitrogen and other donors. Heterocyclic compounds are widely distributed in nature and essential to much biochemical Process. These compounds are worth attention because of their biological activities and clinical usage Schiff base ligand forms a stable complex with different transition metal ions and has been the subject for thorough investigation because of their extensive application in wide ranging areas from material science to biological sciences

Schiff bases are important intermediates for the synthesis of various bioactive compounds. Furthermore, they are reported to show a variety of biological activities including antibacterial, antifungal, anti-cancer and herbicidal activities [1-5].

Schiff base (azomethine) derivatives, the C=N linkage is essential for biological activity, several azomethines were reported to possess remarkable antibacterial, antifungal, anticancer and diuretic activities [6-9].

Traditional formation of Schiff bases from nitroarene starting materials requires a two-step process in which the nitroarene is first reduced to the aniline, then isolated, and subsequently condensed with the desired carbonyl. Recently, catalytic Schiff base formation from nitroarenes and carbonyls has been reported [10, 11].

Recent years have witnessed a major drive to increase the efficiency of organic transformations while lowering the amount of waste materials.

All the facts discussed above plus the increased interest in environmental protection issues inspired us to develop an efficient, mild and practical one pot synthesis of imines from aromatic nitro compounds.

Tandem nitroarene reduction and intramolecular Schiff base condensation to give heteroarenes has been reported using iron in aqueous media. [12-14] surprisingly, the breadth of this methodology in an intermolecular application has not been previously reported.Korich developed a facile; an intermolecular reductive Schiff base formation from nitroarenes and benzaldehydes to yield diarylimines is carried out in the presence of iron powder and dilute acid. [15]

In this paper we describe the synthesis and characterization of Schiff base ligand prepared by condensation of 4-pyridinecarboxaldehyde with 4-nitropyridine and its complexes with Co(II), Ni(II), Cu(II) and Zn(II) ions. The metal in the Schiff base complex is hexa coordinated binds through pyridine nitrogen and azomethine nitrogen.

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MATERIALS AND METHODS

All the chemicals and solvents used were of AR grade. All the reagents used for the preparation of the Schiff bases were obtained from Sigma Aldrich. Metal salts were purchased from Loba Chemie. IR spectra of the ligand and their complexes have been recorded in KBr pellets at Shimadzu FT-IR 8201 spectrophotometer in 4000-200cm^{-1}. Elemental analyses were performed with Perkin Elmer 240 analyzer. Molecular weight determination was done by Rast micro method using diphenyl as solvent. The surface morphology of the complexes was studied using JSM-5610 scanning electron microscope.

Preparation of Schiff base ligand

Hydrochloric Acid (4.5 mmol) was added to a mixture of 4-nitro pyridine (0.72 mmol), 4 pyridine carboxaldehyde (0.72 mmol), and iron powder (7.32 mmol) in 26 mL of EtOH–H2O (2:1 v/v) solution. The reaction was heated to 65°C for 4.5 h before being filtered while hot. The filtrate was extracted using CH2Cl2 (3 × 25 mL) after which the organic layers were combined, dried over MgSO4, filtered, and concentrated in vacuo to yield pale Yellow-orange crystals dried in dessicator over phosphorous pentaoxide yield 80%; MP-168^{0}C

Preparation of the Schiff base metal complexes

Schiff base metal complexes were prepared by the addition of hot ethanolic solutions (600C) of ligand and aqueous solution nitrates of Co(II), Ni(II), Cu(II) and Zn(II) in drop by drop in 2:1 molar ratio. The mixture was stirred for 8 hours at 600C. The precipitated solids were washed thoroughly by ethanol and then by diethyl either. The solid complexes were dried in vacuum desiccator.

Determination of antimicrobial activity

The in-vitro biological activity of the Schiff base and its metal complexes in DMSO were tested against the bacteria *Staphylococus aureus, E.coli, Klebsiella pneumonia* and the fungi *Candida albicans*, *Aspergillus niger*, *Pencilium* sp. by disc diffusion method using nutrient agar as medium and Amikacin, Flucanazole as control. The inhibition zone was developed at which the concentration was noted. The antimicrobial activity was estimated based on the size of inhibition zone in the discs [16-19].

RESULTS AND DISCUSSION

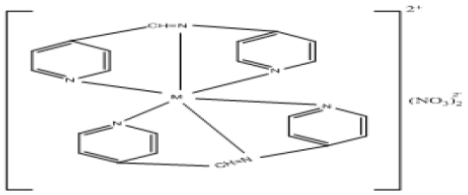
All the metal complexes prepared above are coloured while Zn(II) complex is colourless and are stable towards air and have high melting point. The complexes are insoluble in water and common organic solvents but are soluble in DMF and DMSO.

The magnetic susceptibility values of Co(II) and Ni(II) complexes were found to be 5.0 BM, and 3.1 BM indicating an octahedral geometry around the metal ion. The magnetic susceptibility value of Cu(II) complex was found to be 1.8 BM indicates the octahedral nature of the complexes. The results also indicate the mononuclear and paramagnetic nature of Co(II), Ni(II), Cu(II) complexes, while Zn(II) complex was diamagnetic

In the IR spectrum of ligand, the absorption at 855 cm-, 1384 cm-1 are due to the vibration of 4-substituted pyridine and C-H stretching vibration. The presence of –CH=N group, C–O group, and C–H group are identified by the presence of absorption at 1744 cm-1, 2854 cm-1 and 2925 cm-1 respectively. The IR spectrum of the free ligand is compared with the spectra of metal complexes. The characteristic absorption bands 3451–3345 cm-1 is assigned to –OH group of coordinated water. The absorption bands in the range 2864–2810 cm-1 are due to the presence of C-H group. The band absorbed at 1457 cm-1 is shifted to higher frequencies at 1643 cm-1– 1676 cm-1 in the complexes. This suggests that the nitrogens of pyridine ring are coordinated to the metal ion. Another absorption bands in the range 781-720 cm-1 is assigned to the (M-N bond) group with the central metal atom.

Based on the above observations, the proposed structure of metal-Schiff base complex

Structure 1. Structure of metal-Schiff base complex



M = Co(II), Ni(II), Cu(II) and Zn(II)

XRD Analysis

The powder XRD analysis of Ni(II) complex was carried out to find the crystalline or amorphous nature of the complex. The strong and broad peak confirms the complex formation and the appearance of large feeble peaks indicates that the complex is microcrystalline. The grain size of the complex is calculated using Scherer's formula. The calculated grain size 0.68 nm suggested that the complex is in microcrystalline state. The Cu(II) complex is microcrystalline in nature. The Cu(II) complex showed cocoon like appearance on higher magnification. Lower magnification showed grain like appearance.

Antimicrobial Activity

The antimicrobial study showed that Co(II), Ni(II), Cu(II) and Zn(II) complexes have active against the tested organisms. Such enhancement in biological activity of metal complexes can be explained on the basis of Overtone's concept and chelation theory. The present investigation suggest that all the metal complexes of the ligand bearing metal ion, pyridine ring, -N=CH- group, have comparatively more biological activity. This antibacterial activity serves as a basis for the chemical modification directed towards the development of new class of antimicrobial agents.

Figure 1. XRD Spectrum of Ni(II) complex

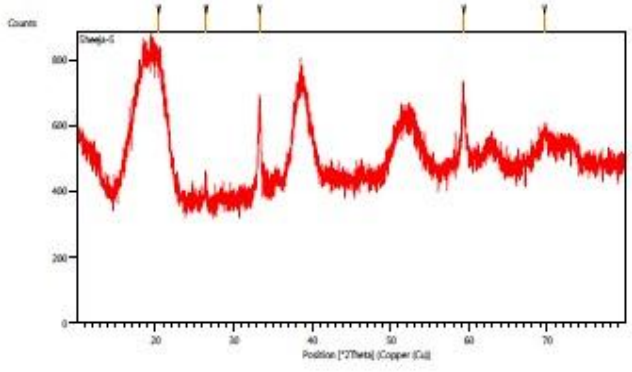


Figure 2. SEM Analysis

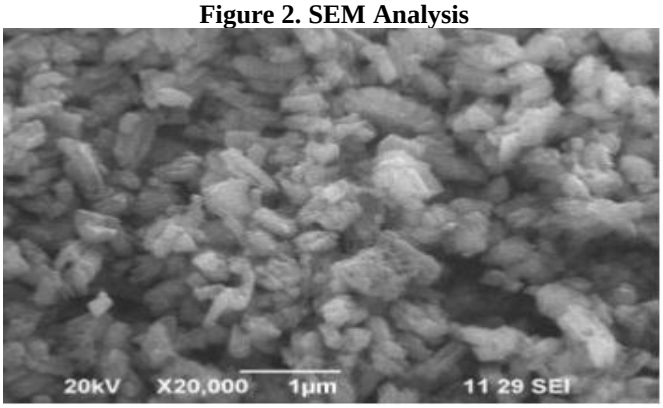


Table 1. Physical characteristics and analytical data of ligand and its complexes

Compound	Color Yield	Chemical formula	Molecular weight	Melting point	Elemental analysis (calculated) found			
					C	H	N	M
Schiff base ligand	Pale yellow 80%	$C_{11}H_9N_3$	183	168-170	72.14 69.79	4.93 4.57	22.93 22.87	---
SCB Co	Brownish black 57%	$CoC_{22}H_{18}N_8O_6$	548	212-220	48.05 47.87	3.29 3.16	20.42 20.68	10.75 10.44
SCB Ni	Green 50%	$Ni\ C_{22}H_{18}N_8O_6$	548	207-210	48.15 47.82	3.25 3.19	20.49 20.62	10.70 10.40
SCB Cu	Light green 70%	$CuC_{22}H_{18}N_8O_6$	553	220-225	47.05 47.67	3.20 3.10	20.40 20.62	11.75 10.49
SCB Zn	Off white 65%	$ZnC_{22}H_{18}N_8O_6$	555	195-200	49.05 47.80	3.29 3.18	20.42 20.68	10.75 10.41

Table 2. Magnetic susceptibility data for the Schiff base complex systems

Schiff base	Magnetic susceptibility (BM)
SCB Co	**5.0**
SCB Ni	**3.1**
SCB Cu	**1.8**
SCB Zn	Diamagnetic

Table 3. The selected IR spectral data of the ligand and complexes

Compound	√(C=N) (cm^{-1})	√(C-O) (cm^{-1})	√(OH-(H20) (cm^{-1})	√(C-H (cm^{-1})	√(M-N) (cm^{-1})
Schiff base	1744.43	2854	3348	2925	---
SBCCo	1660	2810	3358	2922	780
SBC Ni	1649	2852	3450	2915	765
SBCCu	1650	2865	3455	2930	744
SBC Zn	1655	2850	3348	2922	735

Table 4. Antimicrobial activities of ligand and its complexes

Compound	Anti-bacterial activity			Anti-fungal activity		
	Staphylococcus aureus	***E.Coli***	***Klebsiella pneumonia***	***Candida albicans***	***Aspergillus niger***	***Pencilium* sp**
Schiff base	9	8	10	12	8	8
SCB Co	12	11	10	8	9	9
SCB Ni	10	8	8	11	10	9
SCB Cu	9	8	9	8	7	8
SCB Zn	9	9	10	10	7	10
Amikacin	30	25	30	-	-	-
Flucanazole	-	-	-	20	30	25

CONCLUSION

Schiff base have been prepared by a simple and environmentally friendly reductive imination procedure. This process tolerates various functional groups and often proceeds quantitatively with no need for purification. This methodology uses only Fe powder in acidic EtOH/H2O as a reducing agent for nitro derivatives which upon reduction spontaneously condense with an aldehyde in situ.

The antimicrobial study showed that Co(II), Ni(II), Cu(II) and Zn(II) complexes have moderately active against the tested organisms. The synthesized compounds therefore, present a new scaffold that can be used to yield potent antimicrobial compounds. It can be concluded that these compounds certainly holds great promise towards good active leads in medicinal chemistry.

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