



RESEARCH ARTICLE

Synthesis, Characterization, Antifungal, Antibacterial Studies of Heterocyclic Schiff Base Metal Complexes

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ABSTRACT

Co (II), Ni (II), Cu (II) and Zn (II) complexes of the Schiff base derived from indole-3-carboxaldehyde and m-nitro benzoic acid were synthesized and characterized by elemental analysis, molar conductance, IR, UV-Vis, magnetic moment, powder XRD and SEM. Powder XRD and SEM indicate the crystalline state and surface morphology studies of the complexes. The antimicrobial activity of the synthesized ligand and its complexes were screened by disc diffusion method.

KEYWORDS

Indole-3-carboxaldehyde, m-nitrobenzoic acid, Schiff base, XRD, SEM, Anti fungal, Anti bacterial studies

INTRODUCTION

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, anticancer and herbicidal activities¹⁻⁵

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

Schiff base derived from indoline-2, 3-dione and 2- amino benzoic acid and its Tin complex showed antibacterial activity against Staphylococcus aureus. Synthesis, spectroscopic characterization, redox, and biological screening studies of some Schiff bases transition metal (II)

complexes derived from salicylidene-4-aminoantipyrine and 2-aminophenol, 2-aminothiophenol were studied by Raman et al⁷⁻⁹

In view of these facts we can clear about that Schiff base are important not only in medical chemistry, but also in organic synthetic chemistry. Schiff base perhaps are synthesized in various method.

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}

The present investigation deals with the synthesis, characterization and antimicrobial studies of the Schiff base derived from indole-3-carboxaldehyde and m-nitrobenzoic acid and its Co (II), Ni (II), Cu (II) and Zn (II) complexes.

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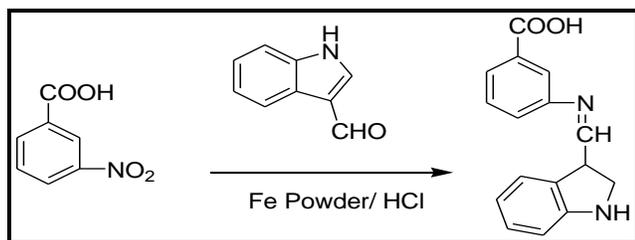
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EXPERIMENTAL

All the chemicals used were of Analar grade. Indole-3-carboxaldehyde and m-nitrobenzoic acid were respectively obtained from Fluka and Lancaster. Co (II)/Ni (II)/Cu (II)/Zn (II) chlorides were purchased from Merck. Solvents were purified and distilled before use. The metal content present in the complexes was determined by EDTA titration (Vogel, 1978).

Synthesis of Schiff base 3-(indolin-3-ylmethyleamino) benzoic acid



Hydrochloric acid (0.13 mL, 4.5 mmol) was added to a mixture of 3 nitro benzoic acid (1.20 gr, 0.72 mmol) Indole-3-carboxaldehyde (1.045gr, 0.72 mmol), and iron powder (0.419 g, 7.32 mmol) in 24 mL of EtOH–H₂O (2:1 v/v) solution. The reaction was heated to 65°C for 3h before being filtered while hot. The filtrate was extracted using CH₂Cl₂ (2 × 25 mL) after which the organic layers were combined, dried over MgSO₄, filtered, and concentrated in vacuo to yield 1.764g (80%).

Preparation of Metal Schiff Base Complexes

To the Schiff base ligand (2 mmol) dissolved in methanol, Co(II)/Ni(II)/Cu(II)/Zn(II) chloride (1 mmol) dissolved in methanol was added dropwise. The above mixture was magnetically stirred and refluxed for 1 h. The complexes obtained were filtered, washed with methanol and dried (yield: 75–80%).

Physical Measurements

Elemental analysis was obtained using a Perkin-Elmer elemental analyzer. Conductivity measurements were made on freshly prepared 10⁻³ M solutions in DMSO at room temperature with a coronation digital conductivity meter. The IR spectra were recorded on a JASCO FT/IR-410 spectrometer

in the range 4000–400 cm⁻¹ using KBr disc method. Electronic spectra were recorded on a Perkin Elmer Lambda-25 UV/ VIS spectrometer in the range 200–900 nm. The room temperature magnetic measurements were carried out using Guoy balance and the diamagnetic corrections were made using Pascal's constant. Powder XRD was recorded on a Rigaku Dmax X-ray diffractometer with Cu Ka radiation. SEM images were recorded in a Hitachi SEM analyzer.

In Vitro Antimicrobial Studies

The ligand and its complexes were tested against the bacterial species: Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Proteus vulgaris and Pseudomonas aeruginosa; and the fungal species: Candida albicans, Rhizopus stolonifer, Aspergillus flavus, Aspergillus niger and Rhizoctonia bataicola. These studies were carried out using Kirby Bayer Disc diffusion method¹².

Chloroamphenicol and Nystatin were used as the standard antibacterial and antifungal agents. The test organisms were grown on nutrient agar medium in petri plates. The compound was dissolved in DMF solution and soaked in filter paper disc of 5 mm diameter and 1 mm thickness. The discs were placed on the previously seeded plates and incubated at 37°C and the diameter of inhibition zone around each disc was measured after 24 h for bacterial and 72 h for fungal species. The minimum inhibitory concentration (MIC) value of the compounds was determined by serial dilution technique.

RESULTS AND DISCUSSION

The analytical data and physical properties of the ligand and its complexes are listed in Table 1. The Schiff base ligand (L) is soluble in common organic solvents. The resultant Schiff base complexes are soluble in DMF and DMSO and insoluble in other common organic solvents.

The analytical data (Table 1) indicate that the metal to ligand ratio is 1:2 for all the complex systems. The molar conductance of all the complexes was measured in DMSO using 10⁻³ M solutions at room temperature.

Table 1: Physico-analytical data of the Schiff base and Schiff base complexes

Compound	Empirical formula/color	Elemental analysis, calcd (found)%			AcO ⁻ 1cm ⁻² mol ⁻¹	$\mu_{\text{eff}}^{(\text{BM})}$
		C	H	N		
Schiff base	C ₁₆ H ₁₂ N ₂ O ₂ , yellow	72.99(72.11)	4.10(4.21)	10.64(10.43)	--	----
[CoL2]	C ₃₂ H ₂₂ N ₄ OCo, dark green	65.67(65.30)	3.79(3.53)	9.57(9.55)	11.0	4.47
[NiL2]	C ₃₂ H ₂₂ N ₄ O ₄ Ni, yellow	65.65(65.39)	3.69(3.55)	9.58(9.60)	8.6	3.33
[CuL2]	C ₃₂ H ₂₂ N ₄ O ₄ Cu, blakish green	65.13(65.21)	3.76(3.51)	9.49(9.14)	10.2	1.88
[ZnL2]	C ₃₂ H ₂₂ N ₄ O ₄ Zn, yellow	64.93(64.34)	3.74(3.98)	9.50(9.49)	5.2	dia

Table 2: Infrared spectral data of Schiff base and Schiff base metal complexes cm⁻¹

Compound	$\nu(\text{C}=\text{N})$	$\nu_{\text{as}}(\text{COO}^-)$	$\nu_{\text{s}}(\text{COO}^-)$	$\nu(\text{M}-\text{O})$	$\nu(\text{M}-\text{N})$
Schiff base	1660	1561	1377	---	----
CoL2	1646	1573	1388	555	430
NiL2	1655	1578	1396	574	464
CuL2	1645	1569	1385	551	455
ZnL2	1650	1574	1384	550	459

Table 3: MIC values of Schiff base metal complexes against the growth of fungi ($\mu\text{g/ml}$)

Compound	A.niger	R.stolonifer	A.flavus	R.bataicola	C.albicans
Schiff base	85	90	95	80	95
CoL2	54	35	54	39	65
NiL2	34	28	55	44	40
CuL2	30	33	35	36	36
ZnL2	30	37	25	33	29
Nystatin	10	15	09	12	15

Table 4: MIC values of Schiff base metal complexes against the growth of bacteria ($\mu\text{g/ml}$)

Compound	E.Coli	K.pneumoniac	P.vulgaris	P.aeruginosa	S.areus
Schiff base	20	55	55	80	95
CoL2	09	19	54	29	65
NiL2	18	20	25	44	40
CuL2	10	30	35	26	36
ZnL2	80	23	25	33	29
chloramphenicol	05	10	09	08	15

The low molar conductivity values of the metal complexes (Table 1) suggest the non-electrolytic nature.¹³

Infrared Spectra

The IR spectral data of the ligand and its complexes were given in Table 2. The IR spectrum of the free ligand exhibits a sharp band at 1660 cm^{-1} , due to the azomethine group vibration. On complexation this band was shifted to lower frequency in the $1655\text{--}1644\text{ cm}^{-1}$ range indicating the coordination of the azomethine nitrogen atom to the metal ion. For the free ligand, the observed bands at 1561 and 1377 cm^{-1} can be respectively ascribed to asymmetric carboxyl (COO^-) and symmetric carboxyl (COO^-) groups.¹⁴

During complexation these bands were shifted to higher frequency by $5\text{--}16\text{ cm}^{-1}$ range indicating the linkage between the metal ion and carboxylato oxygen atom. The large difference between the (COO) and (COO) value of 200 cm^{-1} indicates the monodentate binding nature of the carboxylato group in the complexes. In the lower frequency region the weak bands observed at $573\text{--}550$ and $461\text{--}430\text{ cm}^{-1}$ have been assigned respectively to the ($\text{M}\text{--}\text{O}$) and ($\text{M}\text{--}\text{N}$) vibrations. Accordingly, one can deduce that the ligand binds the metal ion as bidentate fashion (NO). The bonding sites are the azomethine nitrogen and the carboxylato oxygen atoms.

Electronic Spectra and Magnetic Studies

The electronic spectrum of free Schiff base ligand shows a broad band at 348 nm , which is assigned to $p\text{--}p^*$ transition of the C,N chromophore. On complexation this band was shifted to lower wavelength region suggesting the coordination of azomethine nitrogen to the central metal ion.

The electronic spectrum of tetrahedral Co(II) complexes is reported to have only one absorption band in the visible region due to $4A_2(F) \rightarrow 4T_1(P)$ transition.¹⁵

The spectrum of the present Co(II) complex has only one band in the visible region at 693 nm ,

which indicates tetrahedral geometry for the complex.

The electronic spectrum of the Ni(II) complex shows an intense absorption band at 604 nm , which is due to the $3T_1(F) \rightarrow 3T_1(P)$ transition indicating tetrahedral geometry.

The electronic spectrum of Cu(II) complex exhibits a broad band centered at 616 nm due to $2B_1g \rightarrow 2A_1g$ transition corresponding to square planar geometry.

Generally, Zn(II) complexes does not exhibit any d-d electronic transition due to its completely filled d^{10} electronic configuration, however often exhibit charge transfer spectra.

The Zn(II) complex shows an absorption band at 414 nm attributed to the $L \rightarrow M$ charge transfer transition, which is compatible with this complex having a tetrahedral geometry.¹⁶

The Co(II) complex has a magnetic moment value of 4.47 BM , which is in agreement with the reported value for tetrahedral.¹⁷

Generally, square planar Ni(II) complexes are diamagnetic while tetrahedral complexes have moments in the range $3.2\text{--}4.1\text{ BM}$.

The Ni(II) complex reported herein has a room temperature magnetic moment value of 3.33 BM , which is within the normal range observed for tetrahedral Ni(II) complex.

The magnetic moment value of the Cu(II) complex was observed to be 1.88 BM , which indicates that the complex is monomeric and paramagnetic.

From the results obtained from elemental analysis, conductance, infrared, electronic and magnetic moment studies, the proposed geometry of the complexes were assigned.

Powder XRD

Powder XRD patterns of Co(II), Ni(II), Cu(II) and Zn(II) complexes recorded in the range ($2\theta = 0\text{--}80$) were shown in Fig. 1 XRD patterns of the metal complexes show the sharp crystalline peaks indicating their crystalline phase. The average crystallite size (dXRD) of the

complexes was calculated using Scherer's formula.¹⁸

The Co(II), Ni(II), Cu(II) and Zn(II) complexes have an average crystallite size of 79, 80, 85 and 59 nm, respectively.

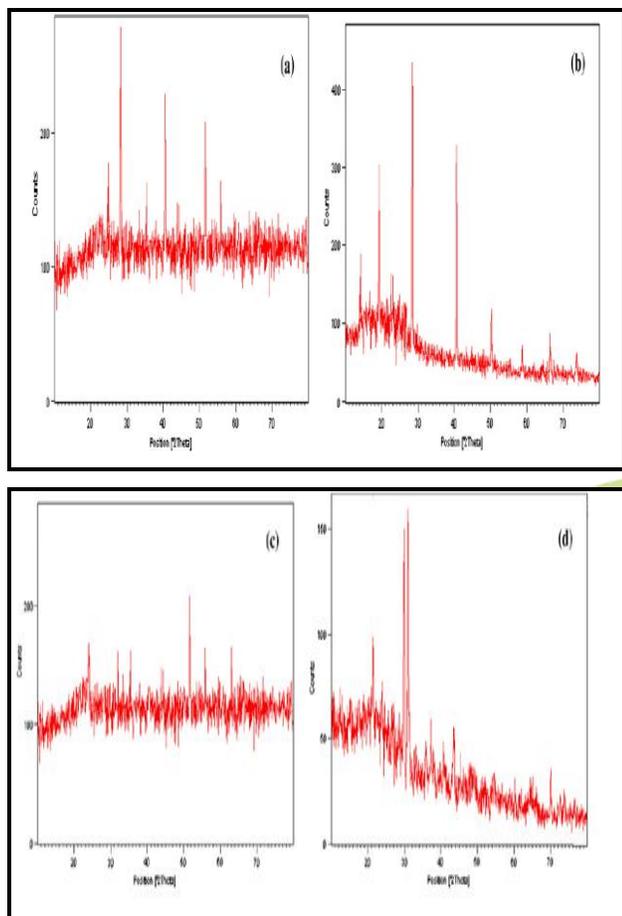


Figure 1: XRD pattern of Co(II), Ni(II), Cu(II) and Zn(II) complexes

SEM

SEM picture of the metal complexes show that the particles are agglomerated with controlled morphological structure and the presence of small grains in non-uniform size. The SEM images of Co(II) and Ni(II) complexes exhibit irregular shaped grains, whereas Cu(II) and Zn(II) complexes show sharp crystalline species.

The average grain size (35, 45, 75 and 100 nm, respectively for Co (II), Ni(II), Cu(II) and Zn(II) Schiff base complexes) found from SEM shows that the complexes are polycrystalline with micrometer sized grains.

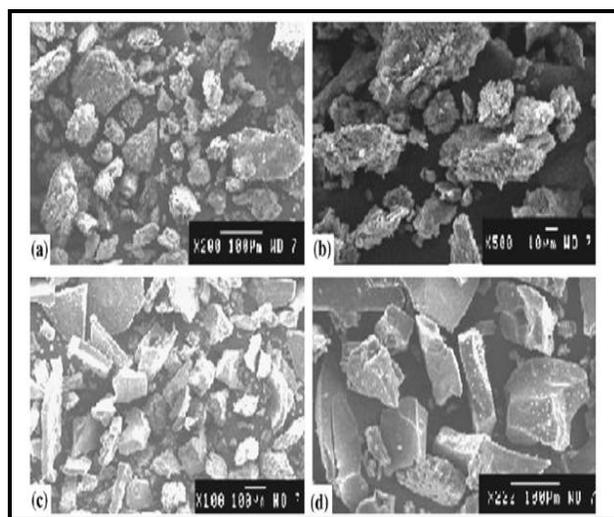


Figure 2: SEM micrographs of the Co(II), Ni(II), Cu(II) and Zn(II) complexes

In Vitro Antimicrobial Studies

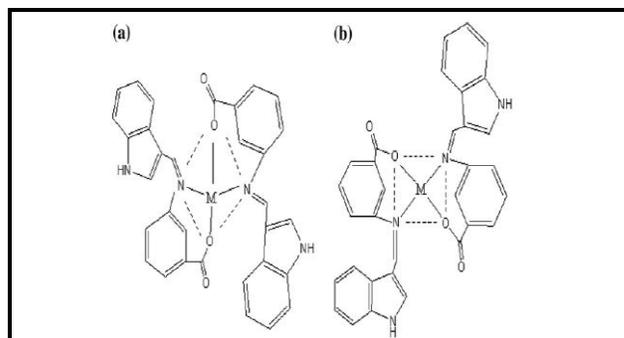
Antifungal

The in vitro antifungal and antibacterial screening results are given in Tables 3. The standard error for the experiment is ± 0.001 cm and the experiment is repeated three times under similar conditions. DMF is used as negative control and Nystatin for antifungal activities.

Anti Bacterial

The in vitro antibacterial screening results are given in 4. The standard error for the experiment is ± 0.001 cm and the experiment is repeated three times under similar conditions. DMF is used as negative control and chloramphenicol is used as positive standard for antibacterial.

Proposed structure of Schiff base metal complexes (a) tetrahedral geometry for Co (II), Ni (II) and Zn (II) complexes and (b) square planar geometry for Cu (II) complex.



CONCLUSION

This type reaction is economically attractive method for synthesis of Schiff base compounds and their derivatives. 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.

Schiff base and its metal complexes were prepared and characterized using the microanalytical, conductance, electronic and vibrational spectral analysis. IR spectral data demonstrates the ligand to act as bidentate, coordinating through azomethine nitrogen and carboxylato oxygen atoms. Magnetic and electronic spectral studies reveal tetrahedral geometry for Co (II) and Ni (II) complexes while Cu (II) complex possess square planar geometry. XRD and SEM analysis suggests the crystalline and morphological structural studies of the complexes. These observations show that the majority of the compounds are more active than their respective Schiff base. The activity with respect to the metal in the complexes follow the order: Cu(II) > Co(II) > Ni(II) > Zn(II) > L.

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