

Synthesis, Complexation, Spectral and Antimicrobial Study of Some Novel 5-Bromo-2-Fluorobenzaldehydeoxime

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ABSTRACT

In this newly approached method a novel series of Transition metal complexes were synthesized by the reaction of 5-bromo-2-fluorobenzaldehyde (1) react with hydroxylamine in ethanolic solution at room temperature. Mononuclear complexes were synthesized by reaction with Cu(II), Zn(II) and Hg(II) chloride salts. The complexes were characterized by elemental analysis, Ultraviolet, Infra-red and ^1H NMR spectral studies. The antimicrobial activities of the ligand and its metal complexes were estimated.

Keywords: Substituted benzaldehyde; metals; complexes; antibacterial and antifungal activity

1. INTRODUCTION

In recent years, the chemistry of coordination compounds has shown rapid development in diverse disciplines as a result of possible use of these new compounds in biological applications. Transition metal complexes with potential biological activity are the main focus of extensive investigation. The biological importance of oximes and their complexes is very well known. Metal complexes with ligands containing nitrogen and oxygen donor atoms have act as the fungicidal agents.

Synthesis of oximes, and their complexes with different transition metals are reported in the literature¹⁻⁹ and found to be active as antibacterial, antitubercular⁸, antilepral¹⁰, antiviral¹¹, antimalarial¹² and active against certain kinds of tumours^{13,14}. In this paper, a novel series of transition metal complexes with oxime were synthesized and they were screened for antimicrobial activities. Most of the complexes were shown moderate to good antibacterial and antifungal activity.

2. EXPERIMENTAL METHODS

The chemicals such as 5-bromo-2-fluorobenzaldehyde, cobalt chloride, Mercury chloride and Zinc chloride were procured from Sigma-Aldrich Chem, Bangalore. Melting

points were observed in open capillaries and were uncorrected. IR spectra of all compounds were recorded in Perkin-Elmer 883 spectrometer using KBr pellets. The antibacterial and antifungal activities of all compounds were observed using cup-plate method¹¹.

3. RESULTS AND DISCUSSION

General method for synthesis of 5-bromo-2-fluorobenzaldehyde oxime (I)

A mixture of 5-bromo-2-fluorobenzaldehyde (0.02 mol) in 15mL ethanol was added to aqueous solution of hydroxylamine hydrochloride (0.08 mol) and sodium acetate (0.1 mol).

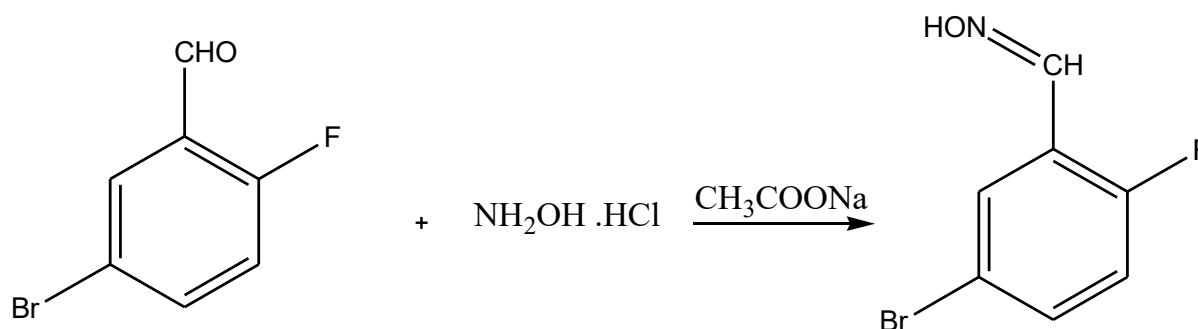
This mixture was stirred continuously for 10 minutes at room temperature and then allowed to cool. The precipitated compound 5-bromo-2-fluorobenzaldehydeoxime was collected and purified by crystallization method using ethanol (yield: 84.3%).

General method for synthesis of Complexes of 5-bromo-2-fluorobenzaldehydeoxime with Co(II), Hg(II) and Zn(II).

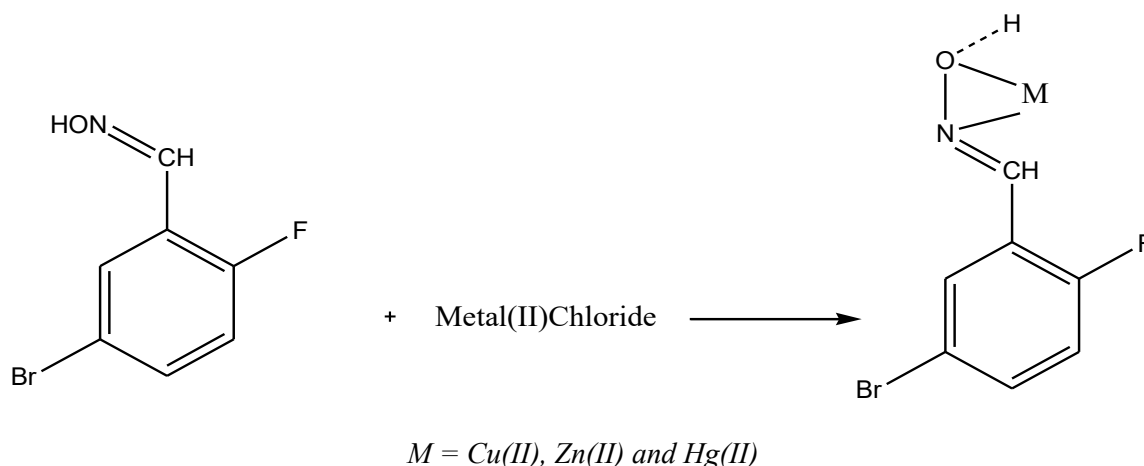
5-bromo-2-fluorobenzaldehydeoxime (0.002 mol) was dissolved in 15 mL ethanol and was added to dissolved cobalt, nickel and copper chloride (0.001 mol) in 15 mL ethanol. The mixture was heated at 60 °C for 2 h and then left to cool.

The precipitate was collected and purified by crystallization from ethanol to give compounds as crystals, yields, 73.1, 65.7 and 80.1 % respectively.

SCHEME : I



SCHEME : II

**Table 1.** Physical and analytical data of complexes

Compounds	Color	M. P (°C)	Elemental analysis (found) %		
			C	H	N
Ligand	White	82 - 86	35.50% (35.68)	2.0% (2.98)	6.15% (6.56)
Cu(II)	Pale green	108 - 112	29.24 (29.30)	1.86 (1.94)	5.98 (6.02)
Zn(II)	White	>250	29.38 (29.44)	1.90 (1.96)	5.46 (5.54)
Hg(II)	Pale white	>250	29.52 (29.60)	1.81 (1.89)	5.77 (5.82)

*() = Calculated value

Table 2. The electronic spectra of all the complexes were recorded in ethanol

S. No	Compound name	λ_{max}
1	Ligand	310, 297 and 250 nm
2	Co(II) complexe	211 to 249, 297 to 307 and 326 to 588
3	Zn(II) complexe	212 to 251, 297 to 307
4	Hg(II) complexes	250 to 297 , 307 to 517

From the spectra of free ligand, $\pi \rightarrow \pi^*$ transitions were obtained. Then $n \rightarrow \pi^*$ transitions were also associated with nitrogen of the azomethine and oxime group in the free ligand. In the complexes, the $n \rightarrow \pi^*$ transition was shifted to higher energy level. These results were indicated that the nitrogen and /or oxygen atom of the oxime groups were coordinated to the metal ions. These bands were assigned to both a charge transfer transition from the metal to anti-bonding orbital of the ligand and to spin allowed transition of the ligand. The observed absorptions of ligand such as 310, 297 and 250 nm were assigned to the $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions¹⁵.

Table 3. IR spectra

Compounds	$\nu(\text{O-H})$	$\nu(\text{C=N})$	$\nu(\text{N-O})$	$\nu(\text{N-M})$	$\nu(\text{M-O})$
Ligand	3294	1633	972	-	-
Cu(II)	-	1593	975	464	526
Zn(II)	-	1591	974	462	526
Hg(II)	3522	1614	970	460	524

The infrared spectra of free ligand shown broad band at 3294 cm^{-1} which correspond to $-\text{OH}$ group of oxime. The IR frequency of all the complexes were shifted to lower frequencies for $-\text{OH}$ of oxime. This may be due to formation of coordinate covalent bond through oxygen atom of hydroxyl group to metal. The IR frequency at 1633 cm^{-1} had indicated the existence of $-\text{C=N}$ group. The IR spectra of all the $-\text{C=N}$ group of azomethine had also shifted to lower frequencies and it was shown the existence of coordinate bond formation with metals through nitrogen atom of azomethine group¹⁵.

4. SPECTRAL STUDIES

5-bromo-2-fluorobenzaldehydeOxime. ¹H NMR (300MHz, CDCl₃): 8.30 s, 2H (CH=NOH), 7.89 -7.48 d,3H (Ar-H) ¹³C-NMR (DMSO, ppm): 161.01 (C=N-OH), 133.30-129.70 (Ar-C).

[5-bromo-2-fluorobenzaldehydeOxime)Cu]: ¹H-NMR (DMSO, ppm): 11.78 s, 1H (O...H), 8.13 s, 1H (CH=NOH), 7.8 d,3H (Ar-H). ¹³C-NMR (DMSO, ppm): 140.84 (C=N-OH), 133.67-129.01 (Ar-C).

[5-bromo-2-fluorobenzaldehydeOxime)Zn]: ¹H-NMR (DMSO, ppm): 11.82 s, 1H (O...H), 8.15 s, 1H (CH=NOH), 7.84 -7.60 d,3H (Ar-H). ¹³C-NMR (DMSO, ppm): 160.04 (C=N-OH), 140.83-133.53 (Ar-C).

[5-bromo-2-fluorobenzaldehydeOxime)Hg]: ¹H-NMR (DMSO, ppm): 11.81 s, 1H (O...H), 8.17 s, 1H (CH=NOH), 7.8 d, 3H (Ar-H). ¹³C-NMR (DMSO, ppm): 140.84 (C=N-OH), 133.62-129.05 (Ar-C).

The $^1\text{H-NMR}$ spectra has provide the evidence for the structural characteristics of the oxime ligand.

The $^1\text{H-NMR}$ chemical shift at 8.30 ppm with sharp singlet had indicated the presence of aldehydic proton, which is lower field shifted to 8.13 ppm in the spectrum of the aldoxime ligand through the oximation reaction¹⁷.

The spectrum of the 5-bromo-2-fluorobenzaldehydeoximeligand exhibited multiplet signals at 7.45-7.60 ppm due to aromatic protons¹⁸.

In addition, the spectrum of the ligand 5-bromo-2-fluorobenzaldehydeoxime showed a singlet signal at 10.20 ppm due to the hydrogen of the $-\text{OH}$ group. The $^1\text{H-NMR}$ spectrum of the ligand exhibited a signal at 14.20 ppm, which can be attributed to the hydrogen bonded OH proton of the hydroxyl imino group.

The coordination of the ligands have been further substantiated by the $^1\text{H NMR}$ spectra of the ligands and some of their complexes with Cu(II) , Zn(II) and Hg(II) .

In the spectra of the ligands, the protons observed at (δ 8.0-8.1 ppm) shift downfield in the spectra of the complexes (δ 8.5-8.6 ppm), this deshielding is possibly due to the donation of the lone pair of electrons by the azomethine nitrogen to the metal atom resulting in formation of a coordination bond.

5. ANTIMICROBIAL ASSAY

Synthesized compounds were tested for inhibition against the human pathogenic bacteria and fungi.

Microbial assay were carried out by disc diffusion technique followed by Kelman *et al.*, 2001. Pathogenic bacterial strains were inoculated in sterile nutrient broth and incubated at 37 °C for 24h.

Pathogens were swabbed on the surface of the Muller Hinton Agar plates and discs (Whatmann No.1 filter paper with 9 mm diameter) were impregnated with the 50 μl of synthesized compound on the surface.

In vitro antifungal activity of synthesized compound was determined against CzapekDox Agar, inoculums of 24h old culture of *Aspergillus flavus* well drained spores were distributed uniformly on the surface of the agar plates with the help of sterile cotton swab.

Fungalstrain, *Mucor* sp. was inoculated by taking a piece of fungal colony using a sterile cotton swab and gently swabbed on the surface of the medium. Control discs were placed with antibiotic and solvents to asses the effect of antibiotic and solvents on pathogens. The plates were incubated at 37 °C for 24h and the antimicrobial activity was measured based on the inhibition zone around the disc impregnated with synthesized compounds.

The zone of inhibition in different bacterial strains against synthesized compounds shown in Table 1.

Among the various bacterial strains maximum zone of inhibition (13 mm) was recorded in *Salmonella typhi* strain and minimum zone of inhibition (2 mm) was observed in *Vibrio cholera*, *Streptococcus pneumonia* and *Staphylococcus aureus* strains.

The antifungal activity of the synthesized compounds shows maximum activity (12 mm) in *Mucor* sp.

Table 4 . Antimicrobial activity of synthesized compounds against human pathogens

S. No.	Human Pathogens	LIGAND	Cu(II)	Zn(II)	Hg(II)
1	<i>Pseudomonas aeruginos</i>	+	+	++	++
2	<i>Vibrio cholera</i>	+	+	+	+
3	<i>Vibrio parahaemolyticus</i>	+	+	+	+
4	<i>Staphylococcus aureus</i>	+	-	++	+
5	<i>Escherichia coli</i>	+	++	+	+
6	<i>Streptococcus pneumonia</i>	+	+	+	-
7	<i>Salmonella typhi</i>	+	+	+	+
8	<i>Klebsiella pneumonia</i>	+	++	+	++
9	<i>Aspergillus flavus</i>	+	+	+	+
10	<i>Mucor sp</i>	+	+	+	+
11	Ampicillin standard	+++	+++	+++	+++

*(+++Very active (Standard) ; (++) active, (+) less active (-) no active

6. CONCLUSIONS

In this paper, we have explored the synthesis and coordination chemistry of some mononuclear complexes derived from the di substituted benzaldehydeoxime ligand. Its containing various transition metal complexes such as Ni(II), Cu(II) and Co(II) were synthesized and evaluated, their antimicrobial activities using disk diffusion method against bacteria and fungi were determined. According to the UV-Vis, IR and NMR data of the azomethine linked oxime ligand, the complexes coordinated to the metal ion through the oxime nitrogen and oxygen atom of the hydroxyl group in substituted benzaldehyde. Based on the obtained results, the structure of the coordination compound under investigation can be formulated as in Scheme II.

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