



Synthesis, Characterization, and Antibacterial Evaluation of Divalent Metal Complexes of Schiff Base [(4-Methoxy- Benzylidene)- Amino]- Acetic Acid



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ABSTRACT

A new Schiff base derived from 4-anisaldehyde and glycine in an ethanolic medium and its complexes with Co (II), Ni (II), Mn (II), and Cd (II) have been prepared. The complexes have been characterized by FTIR, solubility, melting/decomposition temperature determination, conductivity test, and Job's method of continuous variation. The ligand was found to be bidentate as the metals coordinate with the ligand through the carboxylic oxygen and azomethine nitrogen. The *in vitro* antibacterial activity against *Escherichia coli* and *Staphylococcus aureus* strains was studied. The free ligand was found to have no biological activity against any of the strains.

Keywords:

Antibacterial activity,
Schiff base,
FTIR,
4-anisaldehyde.

INTRODUCTION

Schiff bases, containing an imino group ($-RC=N-$), are formed by the condensation of a primary amine with an active carbonyl group. They exhibit a wide range of biological activities, including antibacterial, antifungal, and anticancer properties (Shivakumar, 2008; Tarafder et al., 2000). The biological activity is often linked to the ability of the imino group to form hydrogen bonds with the active sites of cellular constituents (Dharamraj, 2001). Previous studies have indicated that the anti-bacterial activity of Schiff bases is influenced by the position of substituents in the benzene ring, the type of bacteria (whether gram-positive or gram-negative), and the solvent used in the experiment (Ejiah et al., 2013). Metal complexes of Schiff bases have been reported to exhibit enhanced biological activity compared to non-coordinated Schiff bases (Routier et al. 2000). Chelation to the metal ion can be useful in developing cytotoxic drugs, radioactive agents in imaging studies, and radioimmunotherapy (RIT).

In this study, we focused on a Schiff base derived from 4-anisaldehyde and glycine, and its metal complexes with Co(II), Ni(II), Mn(II), and Cd(II). The choice of this particular Schiff base and these metal ions was motivated by several factors. First, 4-anisaldehyde and glycine are readily available and economically feasible starting materials. Second, the resulting Schiff base is expected to exhibit enhanced coordination properties and biological activities when complexed with transition metals. Previous studies have shown that metal complexes often demonstrate higher biological activities compared to their free ligands (Routier et al. 2000). The novelty of our

research lies in the synthesis and characterization of these specific metal complexes, which have not been extensively studied, and their potential antibacterial activity against multidrug-resistant bacterial strains.

The increasing prevalence of infections caused by multidrug-resistant bacteria, such as MRSA and VRE, underscores the urgent need for new antibacterial agents (Guidos 2010). By exploring the antibacterial properties of these newly synthesized metal complexes, our research aims to contribute to the development of alternative therapeutic agents capable of overcoming bacterial resistance.

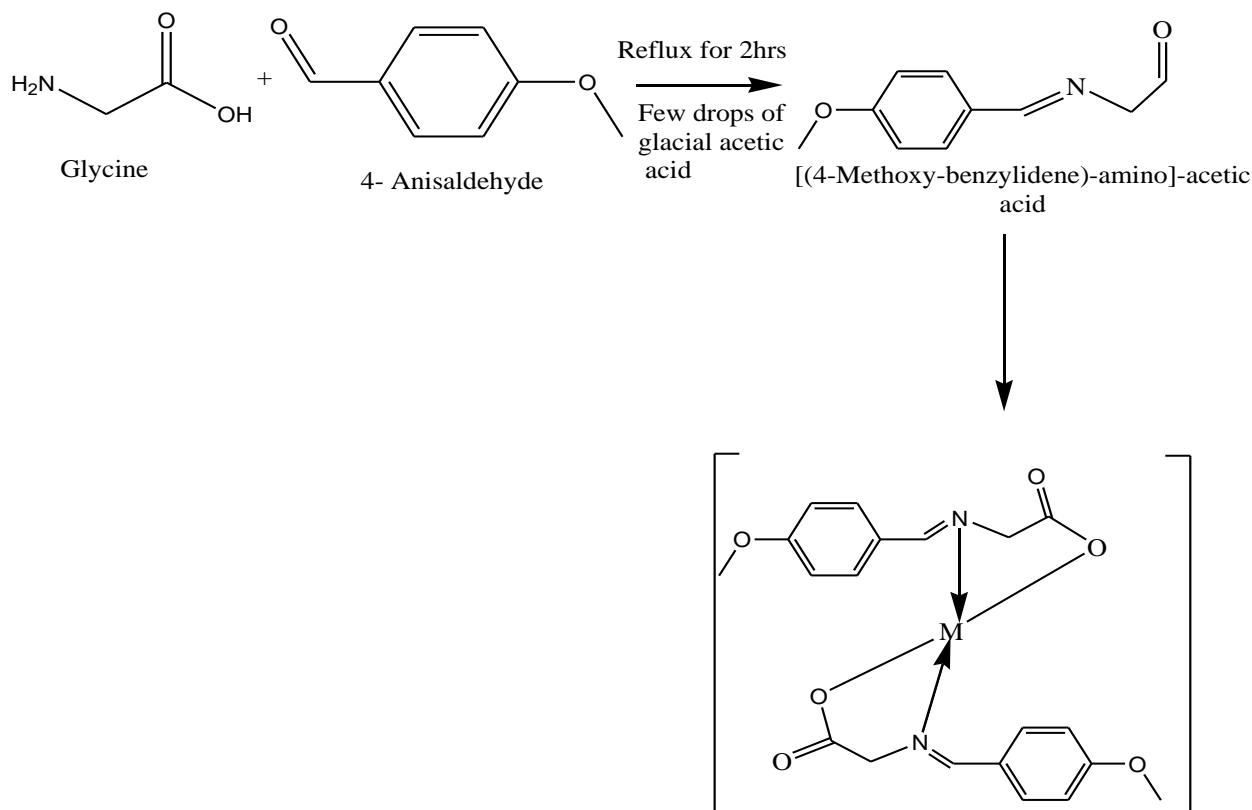
MATERIALS AND METHODS

Chemicals and Instruments

All chemicals and reagents used were of analytical grade and used without further purification. The following instruments were used: BIBBY-Stuart SMP 10 Scientific melting point apparatus, HANNA EC215 conductivity meter, and Thermo Nicolet 100 FTIR spectrophotometer for IR spectral analysis in the $4000-400\text{ cm}^{-1}$ range. All glassware was washed with water, rinsed with ethanol, and dried in an oven before use. Calibration and standardization procedures were followed as per the manufacturers' instructions. For the FTIR spectrophotometer, a background spectrum was taken before each sample to ensure baseline correction. The conductivity meter was standardized with a 0.1 M KCl solution to maintain accuracy.

Preparation of Ligand

A hot ethanolic solution (20 mL) of anisaldehyde (0.13 g, 0.001 mol) and equimolar glycine (0.75 g, 0.001 mol) in 20 mL (5 mL distilled water + 15 mL absolute ethanol) was mixed with constant stirring. The mixture was refluxed at 60°C for 2 hours in the presence of a few drops of glacial acetic acid. The resulting solution was kept overnight at room temperature. The precipitate formed was filtered, washed with cold ethanol, and dried in a desiccator over phosphorus pentoxide.



RESULTS AND DISCUSSION

Solubility and Physical Data

The solubility test of the complexes (Table 1) indicated that the isolated complexes are highly soluble in water and DMSO, and insoluble or slightly soluble in other common organic solvents.

Table 1: Solubility of the synthesized ligand and its metal complexes in various solvents

S/N	Compounds	Water	DMSO	Ethanol	Methanol	Chloroform	Diethyl ether	Acetone	Ethylacetate
1.	C ₁₀ H ₁₁ NO ₃	S	S	S	S	IS	IS	IS	IS
2.	C ₂₀ H ₂₀ CoN ₂ O ₆	S	S	SS	SS	IS	IS	IS	IS
3.	C ₂₀ H ₂₀ NiN ₂ O ₆	S	S	SS	SS	IS	IS	IS	IS
4.	C ₂₀ H ₂₀ MnN ₂ O ₆	S	S	SS	SS	IS	IS	IS	IS
5.	C ₂₀ H ₂₀ CdN ₂ O ₆	S	S	SS	SS	IS	IS	IS	IS

KEY: S = Soluble, SS = Sparingly Soluble, IS = Insoluble

The physical data of the synthesized ligand and its complexes are given in Table 2. The compounds yielded significant amounts between 62-79%. The molar conductance measurement values were quite low, indicating the non-electrolytic nature of the compounds.

The color of the metal complexes was blue for Co (II), green for Ni (II), and white for Mn (II) and Cd (II). This color change is due to charge transfer transitions between the highest occupied ligand molecular orbitals and the lowest empty metal d-orbitals.

Table 2: Physical Data of Synthesized Ligand and Complexes: Yield, molecular weight, melting point, decomposition temperature, conductivity, and color of the ligand and metal complexes

S/N	MOLECULAR FORMULA	YIELD %	MOL. WT	M.P. (°C)	D.T (°C)	Conductivity (ohm ⁻¹ cm ² mole ⁻¹)	COLOUR
1.	C ₁₀ H ₁₁ NO ₃	74	193.20	179	-	-	Cream
2.	C ₂₀ H ₂₀ CoN ₂ O ₆	66	431.13	-	209	9.80	Blue
3.	C ₂₀ H ₂₀ NiN ₂ O ₆	75	430.89	-	267	15.59	Green
4.	C ₂₀ H ₂₀ MnN ₂ O ₆	62	319.04	-	254	13.98	White
5.	C ₂₀ H ₂₀ CdN ₂ O ₆	79	376.52	-	213	14.37	White

The results of the melting/decomposition temperature of the ligand and its metal complexes were found to be between 179°-263°C. The higher decomposition temperature of the complexes compared to the melting point of the ligand indicates high thermal stabilities.

The analysis of Job's method data confirms that the Schiff base ligand forms stable 1:2 complexes with Co(II), Ni(II), Mn(II), and Cd(II) ions. The maximum absorbance at a mole fraction of 0.6 for all complexes indicates efficient coordination and supports the proposed

stoichiometry. These findings are further corroborated by spectroscopic data, which highlight the changes in absorbance associated with complex formation and provide insight into the structural characteristics of the synthesized metal complexes. The trends in absorbance suggest efficient complex formation up to this point, after which the absorbance decreases, indicating excess ligand beyond the optimal stoichiometry does not further contribute to complexation.

Table 3: Job's Method Analysis of Ligand Complexation with Metal Ions

mole fraction, x (total volume = 10ml)	Absorbance at different wavelengths, (λnm)			
	Co(II) (500nm)	Ni(II) (350nm)	Mn(II) (350 nm)	Cd(II) (400 nm)
0.1	0.19	0.20	0.11	0.08
0.2	0.23	0.31	0.19	0.17
0.3	0.47	0.39	0.21	0.32
0.4	0.55	0.48	0.32	0.44
0.5	0.58	0.53	0.35	0.53
0.6	0.88	0.75	0.56	0.68
0.7	0.66	0.36	0.25	0.37
0.8	0.47	0.21	0.16	0.07
0.9	0.12	0.18	0.12	0.06

Spectroscopic Analysis

The FTIR spectra (Table 4) provided further evidence of coordination. The ligand exhibited a strong band at 1603 cm⁻¹, attributed to the ν(C=N) stretching vibration. In the metal complexes, this band shifted to higher wavenumbers (1609-1634 cm⁻¹), indicating coordination through the azomethine nitrogen. Additionally, the

disappearance of the -OH band at 3172 cm⁻¹ in the metal complexes confirmed coordination through carboxylic oxygen. New bands in the regions 607-500 cm⁻¹ and 502-418 cm⁻¹ were assigned to ν(M-N) and ν(M-O) vibrations respectively, further supporting the formation of metal-ligand bonds.

Table 4: Infrared Absorption Frequencies (cm⁻¹): Comparison of IR absorption frequencies for the ligand and its metal complexes, indicating coordination sites

S/N	COMPOUNDS	ASSIGNMENTS					
		v(H ₂ O)	v(O-H)	v(C=N)	Δv(C=N)	v(M-N)	v(M-O)
1.	(C ₁₀ H ₁₁ NO ₃)	-	3172	1603	-	-	-
2.	[Co(C ₂₀ H ₂₀ N ₂ O ₆)]	-	-	1634	31	500	419
3.	[Ni(C ₂₀ H ₂₀ N ₂ O ₆)]	-	-	1609	6	607	502
4.	[Mn(C ₂₀ H ₂₀ N ₂ O ₆)]	-	-	1634	31	586	519
5.	[Cd(C ₂₀ H ₂₀ N ₂ O ₆)]	-	-	1616	13	507	418

Antibacterial Activity

The antibacterial activity (Table 5) of the ligand and its metal complexes was evaluated against Gram-positive (*Staphylococcus aureus*) and Gram-negative (*Escherichia coli*) bacteria using the agar well diffusion method. The ligand alone showed insignificant activity against both strains, with inhibition zones similar to the negative control (distilled water). In contrast, the metal complexes exhibited varying degrees of antibacterial activity, with the Cd (II) complex showing the highest inhibition zones for both bacteria.

The order of antibacterial activity against *Staphylococcus aureus* was Cd > Co > Mn > Ni, while for *Escherichia*

coli, it was Cd > Co > Mn > Ni. The increased activity of the metal complexes compared to the free ligand can be attributed to the metal ions' ability to enhance the lipophilicity of the complexes, facilitating their interaction with the bacterial cell membranes. This increased permeability can lead to disruption of cell processes and ultimately bacterial cell death. The mechanisms of action for these metal complexes could involve the generation of reactive oxygen species (ROS), disruption of membrane integrity, and interference with enzyme function. These potential mechanisms align with previous reports on similar compounds (Agarwal et al., 2014; Valarmathy et al., 2013).

Table 5: Antibacterial Screening Data: Zones of inhibition (mm) for ligand and metal complexes against *Staphylococcus aureus* and *Escherichia coli* at different concentrations.

COMPOUNDS	ANTIBACTERIAL					
	<i>Staphylococcus aureus</i>			<i>Escherichia coli</i>		
	Concentration(μg/mL)	and zone(s)	of inhibition(mm)	Concentration(μg/mL)	and zone(s)	of inhibition(mm)
	10 ⁻¹	10 ⁻²	10 ⁻³	10 ⁻¹	10 ⁻²	10 ⁻³
C ₁₀ H ₁₁ NO ₃	6	6	6	6	6	6
C ₂₀ H ₂₀ CoN ₂ O ₆	15	13	9	16	12	8
C ₂₀ H ₂₀ NiN ₂ O ₆	8	6	6	8	6	6
C ₂₀ H ₂₀ MnN ₂ O ₆	10	8	6	12	10	8
C ₂₀ H ₂₀ CdN ₂ O ₆	18	14	10	20	16	8
Ciprofloxacin	36	-	-	38	-	-
Distilled water	6	6	6	6	6	6

CONCLUSION

The Schiff base ligand and its metal complexes were successfully synthesized and characterized. The ligand acted as a bidentate donor coordinating through the carboxylic oxygen and azomethine nitrogen. The metal complexes exhibited enhanced antibacterial activity compared to the free ligand, making them potential candidates for antibacterial agents.

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