Current Pharma Research
ISSN-2230-7842
CODEN-CPRUE6
www.jcpronline.in/

Research Article

Synthesis and biological activity of novel Schiff base ligand and its transition metal complexes.

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Received 05 May 2019; received in revised form 20 July 2019; accepted 29 July 2019

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ABSTRACT

A Schiff base (Bis-imine) 4,4'-((1E,1'E)-hydrazine-1,2-diylidenebis (methanylylidene)) bis(2-bromo-6-methoxy phenol was synthesized by the condensation of bromo-vanillin with hydrazine hydrate. The bis-imines was further used as ligand for the synthesis of metal complexes with transition metals like Cu(II), Fe(II), Zn(II), Ni(II), Co(II), Mn(II) and Cd(II). All the synthesized metal complexes were characterized by different analytical techniques and screened for antibacterial activities. Some of the derivatives were found to be moderate to excellent active against screened bacteria.

KEYWORDS

Bromo-vanillin, bis-imines, metal complexes.

1. INTRODUCTION

In recent years, there has been considerable interest in the synthesis and use of coordination compounds due to their practical convenience, operational flexibility and interesting structural features. Schiff bases are important intermediates for the synthesis of various bioactive compounds. The antimicrobial activity of the ligands and their transition metal complexes against different bacteria are also reported.

Schiff bases shows variety of biological activities including antibacterial, antifungal, anti cancer and herbicidal activities. Schiff base are important not only in medical chemistry, but also in food industry, dye industry, analytical chemistry, catalysis, fungicidal, agrochemical and biological activities. Modern coordination compounds play a crucial role in biological and other systems. Especially, the synthesis of biologically active compounds such as pharmaceuticals, agrochemicals, flavours and fragrances as well as creation of advanced materials has got great attention.

Schiff bases are important intermediates for the synthesis of various bioactive compounds. The antimicrobial activity of the ligands and their transition metal complexes against different bacteria are also reported. Schiff base reported as versatile antimicrobial activity. Moreover, metal on complex formation increased antimicrobial activity as compared to ligands. Many Schiff base metal complexes with a variety of biological activities have been described in the literature [1-2].

Schiff bases are very significant due to their stability, chelating properties and biological applications [3]. Presence of both nitrogen and oxygen donor atoms in the backbones of these ligands a great deal of attention in this area has been focused on the complexes formed by transition metal ions with Schiff bases. Schiff bases containing halogen groups specially bromine and their metal complexes have a special interest due to their antimicrobial properties [4,5]. It is reported that one or more halo-atoms in the aromatic ring, shows biological activities like antitumor, antibacterial and antifungal activities [6]. Some of Schiff bases and their transition metal complexes have also been used as drugs as bactericidal, fungicidal, anti-tubercular and antiviral agents [7, 8].

Several Schiff bases have been reported for their significant biological activities like antitumor, anti-inflammatory agents, insecticidal, antibacterial, antituberculosis, antimicrobial, anticonvulsant activity. The Schiff bases are also used as versatile components in nucleophilic addition with organometallic reagents and in cycloaddition reactions.

The bis-imines organic compounds represent one of the most employed classes in coordination chemistry due to convenient synthetic preparation and high versatility. These aspects influence to form stable complexes derivatives with the large majority of transitional metal ions. The research area on all sides of the coordination compounds with azomethinic bis-imines as main characters due to their potential significance in different interdisciplinary fields i.e. catalysis, magneto chemistry and bioinorganic.

In addition, these compounds are of a high interest due to their use as starting materials in the synthesis of various heterocyclic compounds like, 4-thiazolidinones, 2-azetidinones, α-

aminophosphonates etc. The synthetic and medicinal importance of Schiff bases and their derivatives promoted us to synthesize Schiff base and their derivatives.

Schiff bases have substituted aliphatic or aromatic side chains which show extensive biological activities. Schiff bases reported in the synthesis of various drugs, important precursors in designing drugs for medical treatment. The biological applications of Schiff bases can be extended from antimicrobial, plant growth regulator, antioxidant, enzymatic, anticancer, anti-inflammatory, anti-malarial, antiviral, neuroprotective, analgesic, anticonvulsant to neurotoxic activities. They also serve as a dominant class of ligands with a variety of binding sites for coordination with metals [9].

Imines and bis-imines is an important class of organic compounds [10]. Bis-imines are generally bi-or-tridentate ligands capable of forming very stable complexes derivatives with transition metals. These bis-imines form stable complexes with the large majority of transitional metal ions [11].

Schiff base heterocyclic metal complex with imine moiety, act as important antimicrobial agents due to their versatile properties such as chelation, adaptability of fine structure for a specific biological action, and chemotheraptic drugs. Schiff base compounds derived from various heterocyclic platforms have been competently reviewed [12].

Schiff base of *o*-vanillin and 2-aminopyridine and their metal complex possess antibacterial activity [13]. The mono and bis-Schiff bases of *o*-vanillin and 2,3-diaminopyridine have been used as ionophores in a Cu(II) selective electrochemical sensor. These compounds as well as their metal complexes have been found to possess biological activity [14]. However, Schiff bases derived from *o*-vanillin have not been investigated so thoroughly.

In view of the above, Herein we report the synthesis, characterization and biological activity of some novel Schiff base derived from isovanillin, bromovanillin and hydrazine hydrate and their metal complexes with transition metals Cu(II), Ni(II), Fe(II), Zn(II), Mn(II). All the synthesized metal complexes were characterized by different spectroscopic methods and screened for antimicrobial activities.

2. MATERIALS AND METHODS

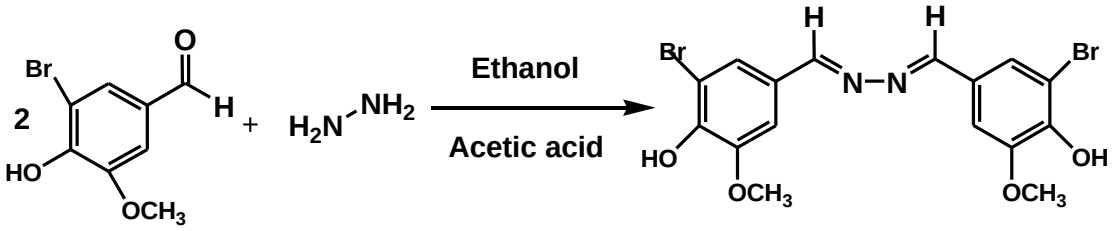
2.1. Materials

All the required chemicals were purchased from S. D. Fine chemicals and used without purifications. Melting points of complexes were taken in open capillaries and are corrected.

2.2. Synthesis of 4, 4'-((1E,1'E)-hydrazine-1,2-diylidenebis(methanylylidene))bis(2-bromo-6-methoxy phenol)

Bromo-vanillin (2mmol) and hydrazine hydrate (1 mmol) were dissolved in ethanol (5 ml). 2-3 drops of glacial acetic acid was added and the mixture was refluxed for 3 hrs. (Table 1). The progress of the reaction was monitored by TLC. After completion of reaction, the content of the flask was poured over crushed ice. The solid obtained was filtered, washed with cold water, dried and recrystallized from ethanol (Scheme 1).

The crude was purified by column chromatography using hexane-ethyl acetate (8:2) as eluent and characterized by comparison of IR, 1H NMR and melting point. The purity of synthesized Schiff base was checked by TLC. The spots were visualized after exposed in iodine chamber or ultra violet light.



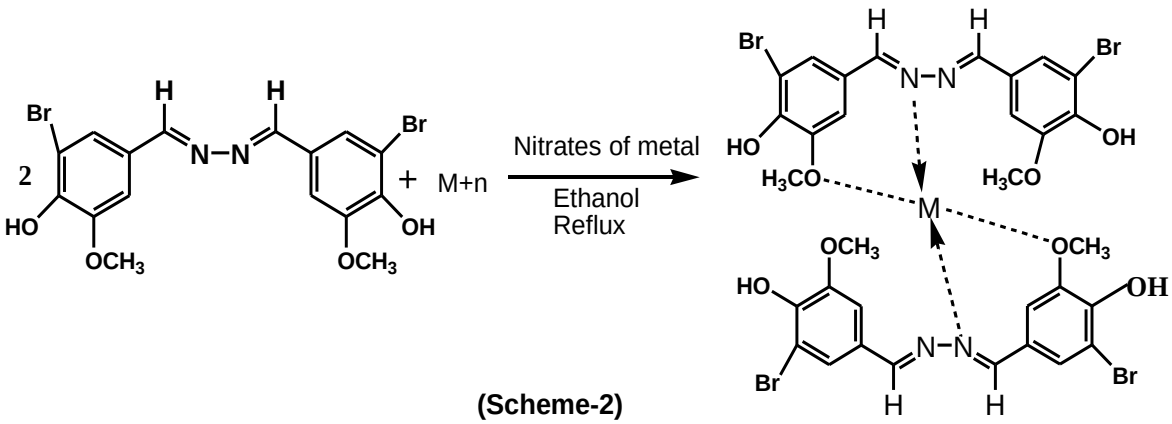
(Scheme-1)

2.3. Spectral Data

Mol. Formula: Analytical cal. $C_{16}H_{14}Br_2N_2O_4$: C, 41.81; H, 3.15; N, 6.19; found: C, 41.81; H, 3.15; N, 6.19.^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 3.73 (s, 6H, 2 × CH_3), 5.76 (s, 1H, –OH), 7.42 (s, 1H, C-2), 7.44 (s, 1H, C-2′), 7.5 (d, 1H, C-6), 7.51 (d, 1H, C-6′), 8.84 (s, 1H, –CH=N_{azine}), 8.87 (s, 1H, –CH=N_{azine}). (EI): (*m*/*z*) 458.9 [$M^{+\cdot}$].

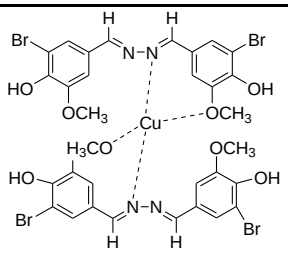
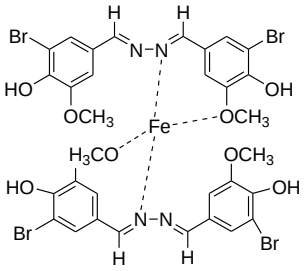
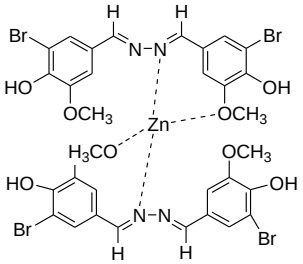
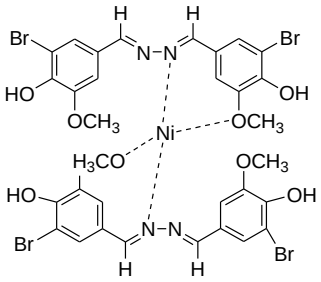
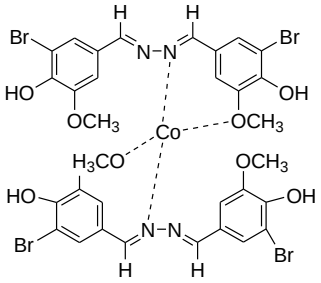
2.4. Synthesis of Metal complex

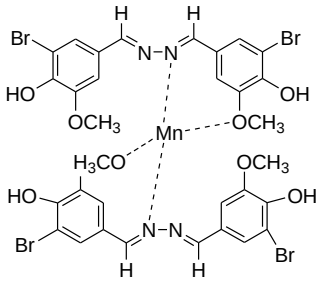
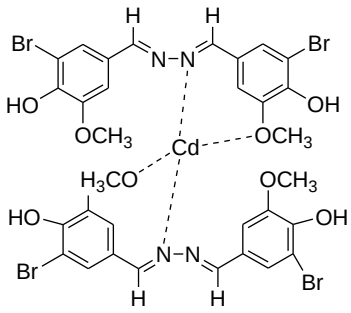
A mixture of 4, 4'-((1E,1'E)-hydrazine-1,2-diylidenebis(methanylylidene))bis(2-bromo-6-methoxy phenol (2mmol), metal salt (1mmol) and ethanol(5ml.) was refluxed for appropriate time **(Table-1)**. After completion of reaction, the content was treated with liquid ammonia to precipitate the solid. Separated solid was filtered, washed with cold water, and dried **(Scheme 2)**.



(Scheme-2)

Table 1. Synthesis of Bromo-vanillin Schiff Base Metal Complexes.

Entry	Schiff Base Metal Complexes	Time (hr)	M. P. (°C)
C1		**3.8**	**270**
C2		**3.6**	**> 300**
C3		**3.7**	**216**
C4		**4.1**	**207**
C5		**3.8**	**256**

C6		**3.9**	**> 300**
C7		**4.7**	**> 300**

3. RESULTS AND DISCUSSION

3.1. Spectral Interpretation

The IR spectrum of complexes showed ν(C=N) band in the range of 1624-1666 cm^{-1}. Lowering in wave number suggests that the azomethine nitrogen is coordinated to metal ions. (Table 2) and UV-Visible spectra of metal complexes were recorded in DMSO solvent at room temperature (Table 3). Electronic spectra of Cu(II), Fe(II), Zn(II), Ni(II), Co(II), Mn(II) and Cd(II) metal complexes displayed the bands in the range 306-344 nm due to charge transfer spectra after complexation indicating the coordination of azomethine nitrogen to metal ion and one peak was found because of d-d transition.

Table 2. IR Absorption Frequencies of Metal Complexes.

Ligand	Metal in Complex	λmax
4,4'-((1E,1'E)-hydrazine-1,2-di ylidenebis(methanylylidene)bis (2-bromo-6-methoxy phenol)	Cu	326.5
	Fe	344.5
	Zn	345
	Ni	343
	Co	343
	Mn	339.5
	Cd	306

Table 3. λmax of Metal Complexes.

Ligand	Metal in Complex	λmax
4,4'-((1E,1'E)-hydrazine-1,2-diylidenebis(methanylylidene)bis (2-bromo-6-methoxy phenol)	Cu	326.5
	Fe	344.5
	Zn	345
	Ni	343
	Co	343
	Mn	339.5
	Cd	306

3.2. Antibacterial Study

The petri-plates were prepared and antibacterial activity has been carried out using known method. Bacteria *Escherichia coli, Bacillus subtilis & Salmonella sp.* were used for the screening purpose. Antibiotic penicillin was used as standard for this biological analysis. All the testing plates were incubated at 37 °C for 24 hours. The results were recorded as zones of inhibition (Table 4) in mm.

Table 4. Anti-bacterial Activity of Metal Complexes.

Sr. No.	Metal Present	*Escherichia coli*	*Pseudomonas aeruginosa*	*Bacillus subtilis*
1	Cu	19mm	19mm	30mm
2	Fe	18mm	19mm	25mm
3	Zn	5mm	8mm	11mm
4	Ni	16mm	13mm	18mm
5	Co	0mm	0mm	0mm
6	Mn	17mm	12mm	18mm
7	Cd	12mm	17mm	19mm
Standard	**Penicillin**	**13mm**	**18mm**	**21mm**

4. CONCLUSION

We reported the synthesis of new ligand. The ligand on reaction with seven metal salts was converted to respective metal complexes. All the synthesized complexes were characterized and screened for biological activity using *Escherichia coli, Bacillus subtilis & Salmonella sp.*

Bacteria. Metal complexes of copper and iron were found to be excellent active against all the three micro-organisms. Remaining complexes showed less to moderate activity.

5. ACKNOWLEDGEMENTS

The authors are thankful to Principal, Vasantrao Naik Mahavidyalaya, Aurangabad for providing the necessary facilities to carry out this work.

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