



# MICROWAVE ASSISTED SYNTHESIS, CHARACTERIZATION AND ANTIBACTERIAL ACTIVITY OF DIOXO MOLYBDENUM(VI) SCHIFF'S BASE COMPLEXES DERIVED FROM 2-HYDROXY- 4-METHYLBENZALDEHYDE AND 4- AMINO BENZENETHIOL

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## Abstract

Molybdenum(VI) complexes with a novel Schiff base ligand derived from condensation reaction of 2-hydroxy-4-methylbenzaldehyde and 4-aminobenzenethiol was synthesized by microwave and investigated and characterized by various physicochemical techniques. The ligands as well as the complex were screened separately for antibacterial activity against two Gram-positive bacteria (*Bacillus subtilis* and *Staphylococcus aureus*) and two Gram-negative bacteria (*Escherichia coli* and *Serratia marcescens*). It was found that metal complex displayed much higher antibacterial activities and better inhibitory effects than that of the Ligand or the free metal ions.

**Keywords:** Antimicrobial activity, broth dilution, disc diffusion, Molybdenum, Schiff base.

## Introduction

Molybdenum has been an important metal due to its capability of forming complexes with variety of ligands [1-4]. It is an essential constituent of recognized enzymes that catalyzes reduction of molecular nitrogen and nitrates in plants and oxidation (hydroxylation) of Xanthine and other Purines as well as aldehydes in animals [5]. Oxo- and dioxo-molybdenum complexes have been generously studied as catalysts for variety of organic transformations, commonly for sulfoxidation of sulfides [5], oxygen atom transfer (OAT) reactions [6-9]; antioxidant activities [10], and also as neutral esterification agents [11]. The variety of transition metal complexes with wide choice of oximes and schiff's bases ligand system and coordination environment have instigated us to undertake research in this area [12].

The Schiff base and their metal complexes have special important in the field of co-ordination chemistry. Ogunniran et al have proved that physical properties and antimicrobial activities are enhanced upon complexation [13]. Amino acids are well known for their tendency to form complexes with metals having biological significance and metabolic enzymatic activities [14]. Schiff base compounds have demonstrated antibacterial, antifungal, antimalarial, antiviral and anticancer activities, which are often enhanced when they are in metal complex form [15-27].

Microwave assisted synthesis has gained importance at present times and as of now it has become the new non-conventional method in organic and inorganic synthesis, replacing the conventional reflux and proving to be eco-friendly, clean, and convenient [18]. The use of microwave irradiation as a heat source not only shortens the reaction time but also enhances product yield as well as enhancing the purity by reducing unnecessary side reactions [19]. Microwave-irradiated reactions are done under solvent free or less solvent conditions. There are a few reports on the synthesis of metal complexes by microwave methods [20-22].

## Experimental

### Materials and instrumentation

All chemicals, reagents and solvents used in the synthesis of the complex were of analytical grade, while L-alanine, salicylaldehyde, ammonium molybdate were obtained from Merck Specialties Private Limited and were used without further purification.  $\text{MoO}_3$  was obtained by heating ammonium molybdate. Carbon, hydrogen and Nitrogen analysis were carried out by micro analytical methods. The analysis of metal Molybdenum was carried out by reported method [23]. The molar conductivity of the complexes was measured at room temperature in DMF solvent using digital conductivity meter CMD-650. The infrared spectra over the region  $4000\text{--}400\text{ cm}^{-1}$  were carried out applying KBr disc technique using IFS-25 DPUS/IR spectrometer. The electronic spectra were measured in DMSO solvent by using a Perkin-Elmer lambda-4 $\beta$  spectrophotometer.

### Preparation of 2-((E)-(4-mercaptophenylimino)methyl)-5-methylphenol (HL) Ligand

It was prepared by slowly adding of 10 mL ethanolic solution of (1.25 g, 10 mmol) of 4-aminobenzenethiol to 10 mL ethanolic solution of (1.36 g, 10 mmol) of 2-hydroxy-4-methylbenzaldehyde, and the mixture was stirred with the help of magnetic stirrer at room temperature until complete dissolution. The reaction mixture was heated in the microwave reactor at  $130^\circ\text{C}$  for 5 minutes. A dirty white precipitate (HL) was filtered off and washed several times using cold ethanol. The precipitate was then dried over anhydrous silica gel. (Yield  $\approx 91\%$ ) m.p.:  $113\text{--}115^\circ\text{C}$ ; molecular formula  $\text{C}_{14}\text{H}_{13}\text{NOS}$ . A perspective view with the atom labeling of the ligand is given in Figure 1.

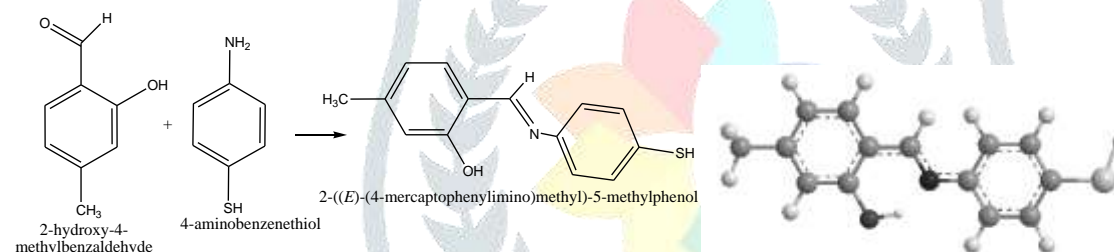


Fig-1: Synthesis and structure of the Schiff base ligand

### Preparation of Metal Complex

The Mo-L complexes was obtained when ligand and metal salts were reacted (molar ratio 1:2) in ethanol solution.  $\text{MoO}_3$ , 0.72g (0.005 mol) was added in 15mL of ethanol and to this a solution of Schiff base ligand (0.01 mol 2.43g in 25mL of ethanol) was added in the presence of 0.01mol of NaOH. The mixture was heated in the microwave reactor at  $150^\circ\text{C}$  for 15 minutes. The solid mass (Mo- complex) so obtained was filtered off, washed several times with ethanol and was finally dried under vacuum. The prepared metal complexes were colored; stable; insoluble in methanol, ethanol, acetonitrile and chloroform; and soluble in DMSO and DMF (Yield: 87%. m.p.:  $>185^\circ\text{C}$ ). Metal complexes were characterized by elemental analysis, conductivity measurements, Fourier-transform infrared spectroscopy (FT-IR), ultraviolet-visible (UV-Visible), and proton nmr spectroscopy. The proposed structure of metal complexes is shown in figure-2.

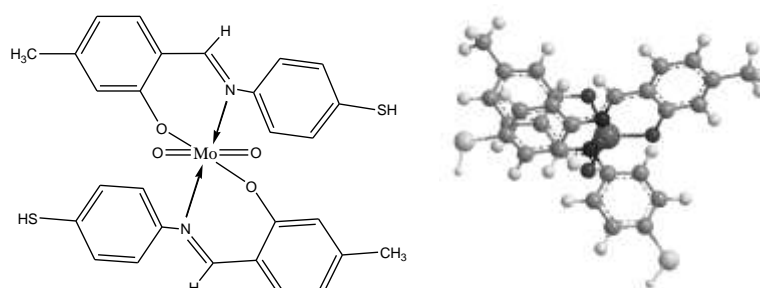


Fig-2: Proposed structure of Molybdenum(VI) complex

## Result and discussion

### Elemental analysis

Elemental analysis differentiates the elemental ratios of pure ligand and their metal complexes. The observed elemental properties give strong support to the data that the complex formation occurred. Physical properties of the synthesized compounds are presented in table-1.

**Table 1: Analytical and Physical data of ligand and complex**

Compound	Colour	Mol. Formula	Formula wt. (g mol <sup>-1</sup> )	Elemental Analysis Found (Cal)					$\lambda_M$ Ohm <sup>-1</sup> cm <sup>2</sup> mol <sup>-1</sup>
				C	H	N	S	Mo	
Ligand (HL)	Dirty white	C <sub>14</sub> H <sub>13</sub> NOS	243.32	79.92 (79.97)	5.41 (5.39)	5.72 (5.76)	13.14 (13.19)	----	----
Mo-L complex	Light Yellow	MoC <sub>28</sub> H <sub>24</sub> N <sub>2</sub> O <sub>4</sub> S <sub>2</sub>	612.57	54.86 (54.90)	3.93 (3.95)	4.48 (4.57)	10.39 (10.47)	15.77 (15.66)	33

### Conductance measurement

The molar conductivity measurement carried in 10<sup>-3</sup>M DMF solution for the Mo-L complex was found to be 33 Ohm<sup>-1</sup>cm<sup>2</sup>mol<sup>-1</sup> which is much less than the value of 70-160 Ohm<sup>-1</sup>cm<sup>2</sup>mol<sup>-1</sup> obtained for 1:1 electrolyte in this solvent. Thus it can be concluded that the complex in study is undissociated which indicates the non-electrolytic nature of this complex.

### Infrared Spectra

The structurally significant IR bands for free ligand and metal-ligand complex are reported in Table 2. The band at 1628 cm<sup>-1</sup> observed in the IR spectra of free ligand can be attributed to  $\nu(\text{C}=\text{N})$  stretching vibration, whereas another band at 3220 cm<sup>-1</sup> in the free ligand is attributed to the free O-H stretching of phenolic moiety whereas the broad band around 2625cm<sup>-1</sup> can be assigned to S-H stretching vibrations and a band at 933 cm<sup>-1</sup> can be assigned to C-S-H bending mode of Ph-SH moiety. [24]. In the complexes, the band due to phenolic O-H vibrations disappeared, indicating deprotonation of the O-H group and subsequent coordination of the oxygen to the metal ion. In addition on complexation the band at 1628 cm<sup>-1</sup> for the benzylidenimin group in the free ligand was shifted to a lower frequency in the range 1562 cm<sup>-1</sup>, indicating the coordination of the benzylidenimin nitrogen atom to the metal ion [25]. Further, the spectrum of the complexes shows new bands at 528 and 465 cm<sup>-1</sup> which may probably be due to the formation of M-O and M-N bonds, respectively. [26].

**Table 2: IR (cm<sup>-1</sup>) and UV (nm) spectral data**

Compound	$\nu(\text{OH})$	$\nu(\text{C}=\text{N})$	$\nu(\text{Mo}-\text{O})$	$\nu(\text{Mo}-\text{O})$	$\lambda_{\text{max}}$
Ligand C <sub>14</sub> H <sub>13</sub> NOS (HL)	3220	1628	---	----	257, 291, 369
Mo- SPEA complex	----	1562	528	465	242, 345, 532

### Electronic spectra

The electronic absorption spectra of the ligand and its metal complexes were recorded in DMSO solution between 200-700nm at room temperature and the data obtained are given in Table 2. The spectra of ligand show three bands in the range 257–369 nm. The former spectral range is assigned to  $\pi-\pi^*$  transitions of the entire p-conjugated system in mercaptophenyl and/or phenylmethyl imino moiety, whereas the bands in the latter range are due to  $n-\pi^*$  transitions of the nonbonding electrons existing on the nitrogen atom of  $-\text{C}=\text{N}$  chromophore. These bands are shifted in the spectra of complex to lower wavelengths indicating the coordination of metal with the ligand. The intense broad band at 532 nm in the spectra of complex may be due to ligand to metal charge transfer (LMCT) [27]. The analytical data suggested the stoichiometry of 1:2 (M: L) for the complex.

### <sup>1</sup>H (proton) NMR spectra

The <sup>1</sup>H (proton) NMR spectral comparison of Ligand (HL) and the diamagnetic Mo(VI) complex using TMS as an internal standard furnishes useful information about the proton environment of ligand and also its mode of ligation in the complex. The spectra of ligand show a sharp singlet peak at  $\delta$  8.39 ppm which has been attributed to the presence of benzylidenimin proton (CH = N) and a multiplet within the range of  $\delta$  7.2–7.46 ppm for aromatic C-H protons whereas peaks at 3.0 ppm and 2.35 ppm can be assigned to aromatic C-SH and for C-H of methyl group

protons [28]. The aromatic hydroxyl group has appeared as a singlet at  $\delta$ 5.0 ppm. A comparison of  $^1\text{H}$  NMR spectrum of Mo(VI) complex has shown a slight upfield shift in benzyliidenimin proton ( $\text{CH} = \text{N}$ ) signal and appears at  $\delta$ 8.61 ppm pointing out the involvement of N in coordination [28, 29]. The peaks due to OH group  $\delta = 5.0$  ppm in the ligand is found to be absent in the spectra of Mo complex indicating the coordination of ligand through O atom of  $-\text{OH}$  group via deprotonation [30]. The peaks due to aromatic C-SH proton, methyl group protons and aromatic hydrogen remain almost unchanged in the complex indicating the non-involvement of these groups in coordination.

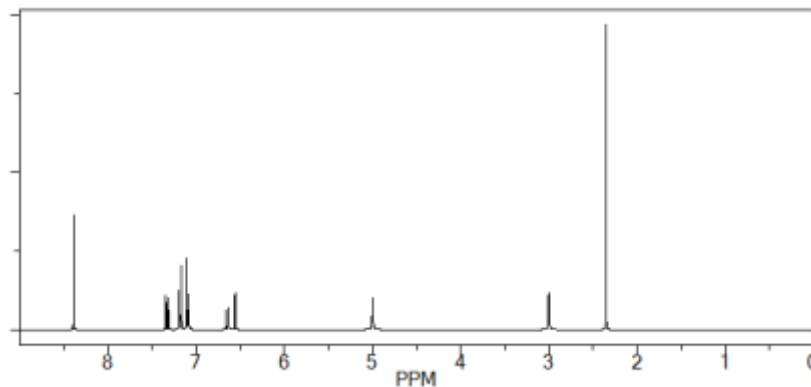


Figure 3.  $^1\text{H}$  NMR spectra of Ligand (HL)

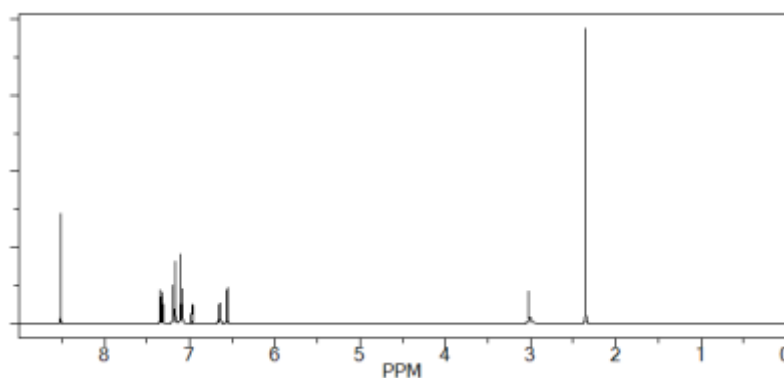


Figure 3.  $^1\text{H}$  NMR spectra of Mo-L Complex.

### Antimicrobial Study

Antibacterial activities of synthesized Ligand and the Mo(VI) complex were evaluated against pathogenic strains by applying agar disc diffusion and broth dilution methods [31,32]. The tests were performed using the methodology described in the guidelines of the Clinical and Laboratory Standards Institute (CLSI). The bacterial pathogens used in this study were *Bacillus subtilis* and *Staphylococcus aureus* as Gram-positive bacteria; and *Escherichia coli* and *Serratia marcescens* as Gram-negative bacteria. Each of the bacterial strains were cultured onto Muller–Hinton agar (MHA) plate and incubated for 18–24 h at 35 °C. The turbidity of all microorganisms was adjusted to 0.5 McFarland turbidity standards to obtain a  $1.5 \times 10^8$  CFU/mL suspension. All the examined samples were prepared by dissolving 20 mg of each compound in 1 mL of DMSO. Thus, DMSO was used as a negative control for all the samples examined. A bacterial culture (which has been adjusted to 0.5 McFarland) was used to lawn Hinton agar plates using a sterile swab. Paper discs of 8 mm diameter were impregnated individually with a constant amount (100  $\mu\text{g}/\text{mL}$ ) of the compounds. Plates were incubated at 37 °C for 18–24 h and the antibacterial activity of each test sample was determined by measuring the diameter of zone of inhibition. The antibacterial behavior of each test sample was repeated twice. No inhibition zone was found for DMSO sample.

Antibacterial activities were also evaluated using the microdilution method. Each test sample was prepared in DMSO to obtain 2000  $\mu\text{g}/\text{mL}$  concentration (stock solution). The aim of the broth micro-dilution method was the evaluation of the lowest concentration of the examined antibacterial agent to inhibit the visible growth of the microorganism being investigated. The highest dilution of active sample to inhibit evident growth of the microorganism was expressed as the MIC. The MIC values calculated for the ligand and its Mo(VI) complex is shown in Table 3. The inhibition zone diameter values obtained for these compounds reveal that the complex shows fairly good activity against all the tested bacterial strains, as compared to ligand or free metal ions. The higher activity of the metal complexes may be owing to the effect of metal ions on the normal cell membrane and can be explained by using overtones concept and chelation theory [31]. The antimicrobial activities are found to increase with increase in concentration of experimental solutions. Metal chelates bear polar and nonpolar properties together; this makes them suitable for permeation to the cells and tissues. In addition, chelation may enhance or suppress the biochemical potential of bioactive organic species. Further, on chelation, metal ion polarity is reduced to a greater extent due to the overlapping of the ligand orbital and partial sharing of positive charge of metal ions with donor groups. Hence, the delocalisation of the  $\pi$ -electrons is increased over the whole chelate sphere which enhances the lipophilicity of the complex. The lipophilic nature of the central metal atom is also increased upon chelation, which

subsequently favours the permeation through the lipid layer of the cell membrane [32]. These metal –ligand complex have an advantage in that the respective bioactivities of the uncoordinated ligands and metal ions are combined which could make them more potent antimicrobial agents.

**Table 3: MIC ( $\mu\text{g mL}^{-1}$ ) values of the ligand, free-metal cations and Mo(VI) complex evaluated by minimum inhibitory concentration (MIC)**

Compound	Antibacterial activity			
	<i>B. subtilis</i>	<i>S. aureus</i>	<i>E. coli</i>	<i>S. marcescens</i>
SPEA	90	104	135	102
Free-metal cations	112	142	168	107
Mo- SPEA Complex	22	29	19	18

## CONCLUSION

Microwave (MW) irradiation is an efficient and environment friendly method to accomplish various inorganic and organic syntheses to afford products in higher yields in shorter reaction periods. In the present studies, we successfully synthesized Mo(VI), complexes with novel Schiff's base ligand derived hydroxy-4-methylbenzaldehyde and 4- aminobenzenethiol. The structure of the parent ligand was investigated by elemental analysis, FTIR and  $^1\text{H-NMR}$ . The corresponding metal complexes were characterized using elemental analysis, conductivity measurements, FTIR, UV-Vis and  $^1\text{H-NMR}$  spectroscopy. The FTIR data showed that the ligand bonds to the metal ions via oxygen atom of O-H group and nitrogen of the benzylideneimin group confirming the bidentate chelating nature of the ligand. The measured molar conductivity of the metal complexes was found to be in the range of  $33 \Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$  which indicated these complexes were non-electrolytes. By comparing the ligand and its metal complexes, it was found that, in general, metal complexes showed better inhibitory effect and also exhibited much lower MIC values against all the tested bacteria strains. The process of chelation dominantly affects the biological activity of the complex that is potent against pathogens. Based on these facts, it could be proposed that this novel complex would be better therapeutic drug for antibacterial treatment.

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