

Synthesis, Characterization and Antimicrobial Studies of Schiff Base Complexes of Arsenic(III), Antimony(III) and Bismuth(III) Chloride

Jain Anita^{1*}, Gupta Meenal², Bhardwaj Arpan¹, Thapak T.R.¹¹Department of Chemistry, Govt. Madhav Science P.G. College, Ujjain, INDIA²School of Studies in Chemistry and Biochemistry, Vikram University, Ujjain, INDIAAvailable online at: www.isca.in, www.isca.meReceived 18th May 2015, revised 29th June 2015, accepted 30th July 2015

Abstract

In this study, thioacetamide and salicylaldehyde were condensed together to form 2-(thioacetylmino)methyl]phenol (LH), which further reacts with metals As (III), Sb(III) and Bi(III) chloride in ratio of 1:1 and 2:1 respectively, to form complexes. All these were characterized by ¹HNMR, ¹³CNMR and IR spectroscopy, elemental analysis and reported literature studies. On the basis of all supporting information, all metal complexes (M/L) in 1:1 (ML₁) and 1:2 (ML₂) showed 4 and 5 coordinated geometry, distorted trigonal bipyramidal and distorted octahedral, respectively. These complexes showed good antibacterial, antifungal and antitubercular activities.

Keywords: Schiff bases, pnictogen complexes, antimicrobial activity and antitubercular activities.

Introduction

Schiff base are the condensation product of aromatic amine and any aldehyde and may acts as bidentate to polydentate ligand depends on the substituent present in it. They may coordinate to central metal ion of transition and P-block metals through azomethine nitrogen, oxygen and sulfur donor atoms to form chelated complexes.

They have been used in various biological activities including carcinogenic, antitumour, antiviral, antifungal, antibacterial and industrial applications¹. They have been used in optical and electrochemical sensors as well as in various chromatographic methods to enable detection of enhanced selectivity and sensitivity. In addition, the presence of nitrogen and oxygen donor atoms in the complexes makes these compounds effective and stereospecific catalysts for many chemical reactions and may also show biological activity and other transformations of organic and inorganic chemistry².

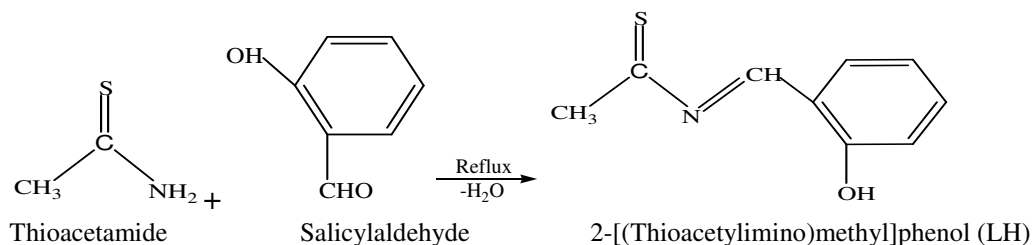
In this study, we report the synthesis and characterization of As (III), Sb(III) and Bi(III)chloride complexes of Schiff base ligand; 2-[(thioacetylmino)methyl]phenol (LH), in 1:1 (ML₁) and 1:2 (ML₂) ratio respectively. The characterization and

identification were done by elemental analysis, IR, ¹H- and ¹³C-NMR spectra and reported literature studies..

Material and Methods

Arsenic trioxide (CDH, AR grade), thionyl chloride (CDH, AR grade), thioacetamide and salicylaldehyde are of AR grade and purchased from Sigma Aldrich. Elemental analysis (C, H, N) were carried out using flash EA 1112 series, thermofinnigan model IIT Bombay. IR spectra were recorded on a 3000 hyperion microscope with vertex 80 FTIR system. ¹H and ¹³C-NMR spectra were recorded on a mercury plus 300 MHz, 75 MHz NMR spectrophotometer.

Preparation of the Schiff base; 2-[(Thioacetylmino)methyl]phenol: 20 cm³ ethanolic solution of salicylaldehyde (5.23 ml, 0.05 mol) and 20 cm³ ethanolic solution of thioacetamide and (3.75 gm, 0.05 mol) are mixed in a 250 ml of round bottom flask. The mixture was stirred for 3-4 hour at 65 °C ccheme- 1. This solution was evaporated under vacuum till remove the solvent after that filtered and washed with several time with ethanol. It was recrystallized from hot ethanol and the colour of the product was obtained as light yellow. The purity of it was checked by TLC (solvent system: Hexane-ethyl acetate).



Scheme-1

Synthesis of metal-complexes: The complexes ML₁ and ML₂ were synthesized by the molar ratio of AsCl₃ (1.81 gm, 0.01 mol), SbCl₃ (2.28 gm, 0.01 mol), and BiCl₃ (3.15 gm, 0.01 mol), with reaction of LH in 1/2 ratio (1.79 gm, 0.01 mol / 3.59 gm, 0.02 mol) in 25 ml of absolute ethanolic solution, respectively.

In this method, the ligand was dissolved by dropwise addition of 25 ml of absolute ethanol with continuous stirring at 60 °C. The complexation takes place immediately upon addition of the metal salt solution slowly. The precipitated complex was filtered off, washed with H₂O, cold EtOH and cold Et₂O several times and dried in vacuum scheme-2.

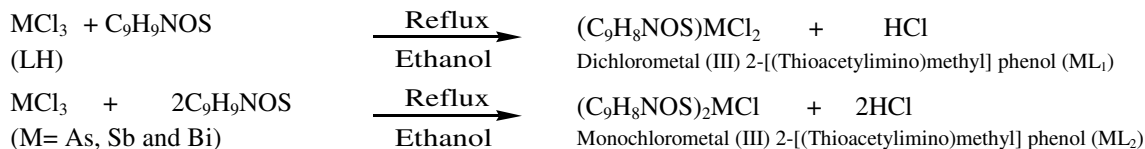
Antimicrobial Screening: Broth Dilution Method: In this method, stock solution of sample is prepared by dissolving 384 mg of sample in 2 ml of DMSO then 4 ml of peptone water was added using fresh pipette. 11 sterile test tubes of 10 ml are properly arranged in the rack, then 4 ml of stock solution was transferred to the first test tube through fresh micro-pipette and 4 ml of peptone water was added to it thus total volume become 8 ml. Again in similar way, 4 ml of solution from first tube was transferred to the second tube and 4 ml of peptone water was added. Continue dilution in this way, will make total volume 8 ml to remaining test tubes. Rest of other two test tubes contained media control (MC) and nutrient broth (GC). The tubes were incubated for 18 hours at 37°C then inoculated a tube containing broth with the organism and kept at 4°C in a refrigerator overnight to be used as standard for the determination of complete inhibition³ figure-1. MIC is expressed as the lowest concentration, which inhibited growth judged by lack of turbidity in the tube⁴ 12.

Well diffusion method: The antimicrobial activities of synthesized (LH) and (ML₂) complexes were studied for their antibacterial and antifungal activities by Muller-Hinton agar and potato dextrose agar respectively. The antibacterial and antifungal activities were done at 0.5 mg/ml concentration in DMF solvent by using two bacteria (Staphylococcus aureus and Echerichia coli) and two fungi (Aspergillus niger and Panicillium notatum) using the diffusing method³ figure-1.

Media Preparations: The antibacterial and antifungal activities were studied by preparing Muller Hinton Media and Potato dextrose sugar media, respectively.

The application of selected strains of bacteria and fungi were inoculated using streak plate method and wells were made on the agar surface with 6 mm cork borer. Then extracts were poured into the well on the plate and were incubated at 37 °C and for 24 hours for bacterial (standard-ciprofloxacin) and 25 °C for 48 hours for fungal activity (standard-flucanazole). Activities were determined by measuring the diameter of the zone showing complete inhibition (mm).

Antitubercular Studies: Due to As, Sb and Bi metal Schiff base complexes, the excellent results of antimicrobial screening were obtained therefore we have studied for their in vitro antituberculosis activity. Complexes were assayed for their inhibitory activity toward *M. tuberculosis* H37Rv in above similar concentration and the results were compared with standard anti-TB drugs namely Pyrazinamide and Streptomycin figure-2,3.



Scheme-2

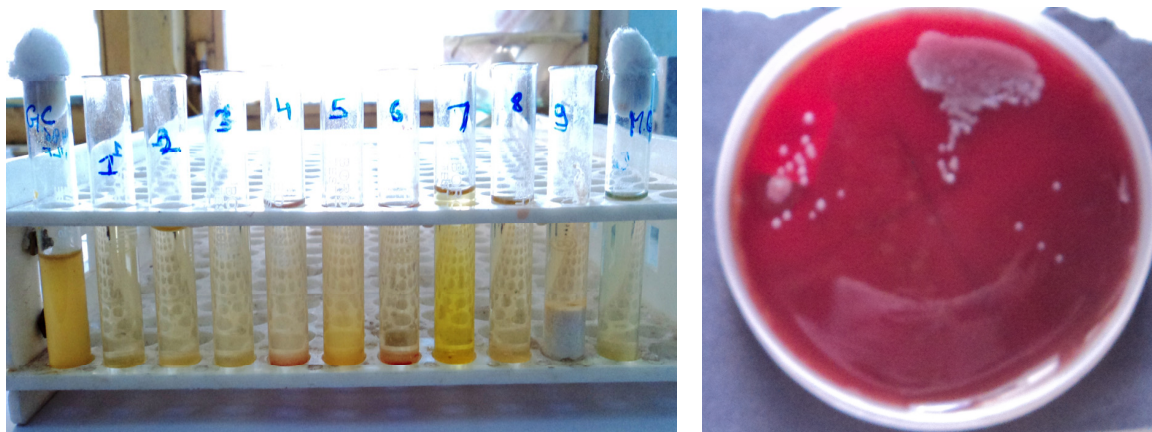


Figure-1
Results of broth dilution and MBC methods

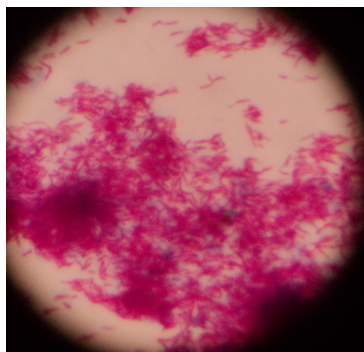


Figure-2
Growth of *Mycobacterium Tuberculin* before complex application

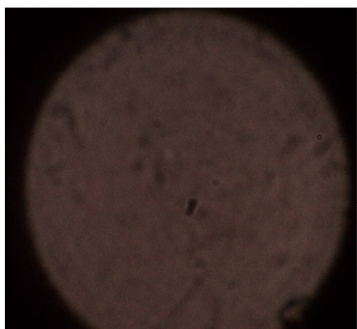
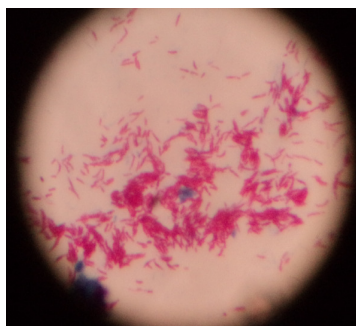


Figure-3
Antitubercular activity of ligand and complexes

Results and Discussion

In the IR spectrum of ligand, the absorption bands appearing at 3360(br), 1590 and 1710 cm^{-1} are respectively, due to $\nu(\text{OH})$ intramolecular hydrogen bond, $\nu(\text{CH}=\text{N})$ azomethine and $\nu(\text{C}=\text{S})$ thio functionalities present in the ligand. The bands observed near 3090 cm^{-1} and 2000-1650 cm^{-1} are due to aromatic C-H stretching vibrations and combination bands of aromatic ring, respectively. Strong absorption band observed at 1662 cm^{-1} is due to C=C stretching vibrations. The absorption bands observed at 2969 and 1472-1430 cm^{-1} are due to C-H stretching and bending vibrations, respectively^{5,6}. In the region of 1479, 1361 cm^{-1} and 1225 cm^{-1} are due to mixed vibrations of N-C=S and C-O moieties present in the ligand.

In the IR spectra of complexes of metals, the absorption band of imino group is shifted to lower wave number at 1586-1580 cm^{-1} , showing shift of band at lower wave number. This indicates that the azomethine nitrogen is coordinated to the metal through its lone pair of electrons^{7,9} table-1.

The absorption band of phenolic group is lost in the spectrum indicates that phenolic -OH group is deprotonated and binds through phenolic oxygen which is further confirmed by presence of absorption band at 1217 - 1210 cm^{-1} respectively. Other low intensity bands in the far IR region at 542.0-539.2 cm^{-1} , 420.1-418.8 cm^{-1} , 276.9-271.6 cm^{-1} , indicating that $\nu(\text{M-O})$, $\nu(\text{M-N})$ and $\nu(\text{M-Cl})$ vibrations respectively. These results show that metal (As, Sb and Bi) is bonded to oxygen and nitrogen atoms in complexation.

In ¹H- NMR spectrum of ligand in DMSO the signal at δ 2.0 is due to thiomethyl group and at δ 6.9 is due to phenolic hydroxyl group present in the ligand. The NMR peak observed at δ 8.4 which is deshielded, indicates that (-CH=N) imino proton is conjugated in the molecule^{10,11}.

In the complex, the nmr peak at δ 8.9- δ 8.7 indicating that imino nitrogen is coordinating to metal ion. The nmr signal at δ 6.9 disappears indicates that deprotonation of phenolic group and bonding takes place through phenoxy group of the ligand to the metal^{12,13}. These spectral data are summarized in table- 2.

Table-1
IR spectral data of ligand and metal complexes (cm^{-1})

Compounds	$\nu(\text{OH})$	$\nu(\text{CH}=\text{N})$	$\nu(\text{C-O})$	$\nu(\text{M-O})$	$\nu(\text{M-N})$
$\text{C}_9\text{H}_9\text{NOS}$	3360	1590	1225	-	-
$(\text{C}_9\text{H}_8\text{NOS})\text{AsCl}_2$	-	1580	1210	540.0	419.3
$(\text{C}_9\text{H}_8\text{NOS})_2\text{AsCl}$	-	1586	1215	542.0	419.1
$(\text{C}_9\text{H}_8\text{NOS})\text{SbCl}_2$	-	1585	1211	543.0	417.8
$(\text{C}_9\text{H}_8\text{NOS})_2\text{SbCl}$	-	1580	1217	541.5	418.8
$(\text{C}_9\text{H}_8\text{NOS})\text{BiCl}_2$	-	1586	1220	538.2	420.3
$(\text{C}_9\text{H}_8\text{NOS})_2\text{BiCl}$	-	1582	1210	539.2	420.1

Table-2
¹H and ¹³C-NMR chemical shifts of ligand and metal complexes

Compound	¹ H NMR Chemical Shift (δ)	¹³ C NMR Chemical Shift (ppm)
C ₉ H ₉ NOS	2.0 (S, 3H, CH ₃), 6.9 (br s, 1H, OH), 6.9-7.2 (m, 5H, Ar-H), 8.4 (S, 1H, CH=N)	142.0 124.0, 127.0 (Ar-c), 149.0 (C _{Ar} -OH), 163.2 (CH=N), 176.0 (C=S), 20.8 (CH ₃)
(C ₉ H ₈ NOS)AsCl ₂	2.1 (S, 3H, CH ₃), 6.9-7.1 (m, 4H, Ar-H), 8.6 (S, 1H, CH=N)	142.0 -124.5, 127.0 (Ar-c), 152.0 (C _{Ar} -OH), 165.1 (CH=N), 176.0 (C=S), 20.9 (CH ₃)
(C ₉ H ₈ NOS) ₂ AsCl	2.1 (S, 6H, 2CH ₃), 6.9-7.1 (m, 8H, 2Ar-H), 8.7 (S, 2H, 2CH=N)	127.2, 123.3, 125.2, 124.4, 127.0 (Ar-c), 152.4 (C _{Ar} -OH), 165.5 (CH=N), 176.0 (C=S), 20.9 (CH ₃)
(C ₉ H ₈ NOS)SbCl ₂	2.0 (S, 3H, CH ₃), 6.9-7.2 (m, 4H, Ar-H), 8.5 (S, 1H, CH=N)	142.0 127.2-124.5 (Ar-c), 151.8 (C _{Ar} -OH), 165.1 (CH=N), 176.0 (C=S), 20.4 (CH ₃)
(C ₉ H ₈ NOS) ₂ SbCl	2.6 (S, 6H, 2CH ₃), 6.9-7.2 (m, 8H, 2Ar-H), 8.8 (S, 2H, 2CH=N)	127.5, 123.7, 125.6, 124.3, 127.0 (Ar-c), 151.8 (C _{Ar} -OH), 165.5 (CH=N), 176.0 (C=S), 20.1 (CH ₃)
(C ₉ H ₈ NOS)BiCl ₂	2.8 (S, 3H, CH ₃), 6.3-7.3 (m, 4H, Ar-H), 3.9 -4.0 (S, 12H, OCH ₃), 8.7 (S, 1H, CH=N)	142.0 127.1-124.0 (Ar-c), 152.1 (C _{Ar} -OH), 165.3 (CH=N), 176.0 (C=S), 20.8 (CH ₃)
(C ₉ H ₈ NOS) ₂ BiCl	2.3 (S, 3H, CH ₃), 6.9-7.2 (m, 8H, Ar-H), 8.9 (S, 2H, 2CH=N), 2.0 (S, 3H, CH ₃)	127.1, 123.4, 125.2, 124.5, (Ar-c), 152.1 (C _{Ar} -OH), 165.7 (CH=N), 176.0 (C=S), 20.7 (CH ₃)

Table-3
Minimum Inhibitory Concentrations (MIC) and Minimum bacterial Concentrations (MBC) of ligand (LH) and metal complexes (ML₂)

Sample	Staphylococcus aureus		Echerichia coli		Klebsiella pneumoniae		Panicillium notatum	
	MIC (mg/ml)	MBC (mg/ml)	MIC (mg/ml)	MBC (mg/ml)	MIC (mg/ml)	MBC (mg/ml)	MIC (mg/ml)	MBC (mg/ml)
LH	1	2	1	2	2	4	2	4
AsL ₂ Cl	0.5	1	0.5	1	1	2	1	2
SbL ₂ Cl	0.5	1	1	2	1	2	0.5	1
BiL ₂ Cl	0.5	1	1	2	0.5	1	1	2

Table-4
Results of antimicrobial and antitubercular Screening of ligand and (ML₂)

Complexes	Growth inhibition against Bacteria and Fungi in (mm)				antitubercular Screening Conc. 1.0/0.5mg/ml
	S. aureus	E. coli	A. niger	P. notatum	
LH	24	21	22	20	- ++
AsL ₂ Cl	29	30	28	30	+++
SbL ₂ Cl	36	33	30	32	++++
BiL ₂ Cl	34	31	26	28	+++
Ciprofloxacin\ Pyrazinamide	20	22	21	20	+++++
Flucanazole\ Streptomycin	21	23	22	20	++++

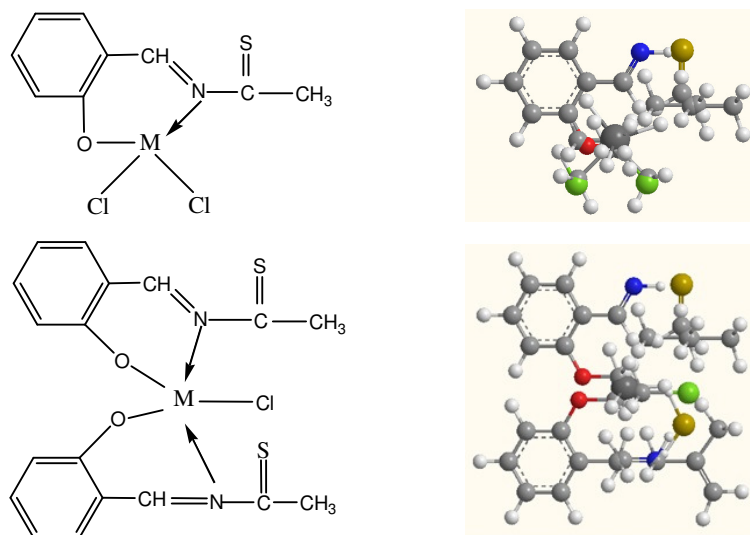
In the ^{13}C - NMR spectrum of ligand, the peaks observed at 149.0, 142.0 and 163.2 ppm are due to phenolic ($\text{C}_{\text{Ar}}\text{-OH}$), quaternary carbon of the aromatic ring and imino ($\text{CH}=\text{N}$) functionalities present in ligand respectively. The rest of the benz-imine ring resonates at 127.0, 123.1, 125.0 ppm and 124.0 ppm. The peaks observed at 176.0, 163.2 ppm and 20.8 ppm are due to thio, imine and methyl groups present¹².

In the complex, the ^{13}C - NMR is similar to the ligand, except that imino carbon appears at 165.8- 165.5 ppm (deshielding) and phenoxide carbon is also deshielded and appears at 152.4-151.8 ppm, indicating that coordination takes place through imino nitrogen and phenolic oxygen to the metal¹³. These spectral data are summarized in table-2.

The results of antimicrobial screening suggested that all metal complexes and ligand show good antibacterial, antifungal as well as antitubercular activities table-3. Antitubercular analysis clearly revealed that ligand (LH) shows inhibition at concentrations with MIC 1.0mg/ml and complexes shows 0.5 mg/m, while As(III), Sb(III) and Bi(III) complexes shows superior activity similar to that of Streptomycin but less than pyrazinamide drug¹⁴ table-4.

Conclusion

On the basis of spectral techniques IR, ^1H -NMR and ^{13}C -NMR and reported literature, it is suggested that ligand acts as bidentate ligand. It is coordinated through sulphur of thio group and lone pair of imino nitrogen atom to the metal (III) chloride. In the complexes (ML_1 and ML_2) the central metal ion appears to acquire the coordination number four and five and most plausible geometry of the complex is distorted trigonal bipyramidal and distorted octahedral figure-3, respectively.



(M= As, Sb and Bi)

Figure-3
Structure of metal complexes (ML_1/ML_2)

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