Microwave Assisted Synthesis, Spectroscopic Characterizations

In-Vitro Antibacterial And Antifungal Properties Of Some Antimony And Bismuth Complexes Derived From N^O And N^S Donor Imines

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ABSTRACT

New series of biologically potent organoantimony(III) and bismuth(III) complexes have been synthesized by thermal as well as microwave assisted synthesis and characterized by their elemental analyses, molar conductance, and IR, NMR (^{1}H and ^{13}C) and electronic spectral studies. The synthesized imines and their new metal complexes have been screened for in-vitro antibacterial activity against Gram-negative (*Escherichia coli*) and Gram-positive (*Staphylococcus aureus*) bacterial strains, and for in-vitro antifungal activity against *Fusarium oxysporum* and *Aspergillus niger*. All compounds showed significant antibacterial and antifungal activities against microbial species. The spectral data suggested for the complexes to have tetra-coordinated environment around the central metal atoms but, due to the stereochemically active lone pair of electrons, distorted trigonal bipyramidal geometry of the said complexes has been proposed. Elemental analyses and NMR spectral data of the ligands and their metal complexes agree with their proposed structures.

INTRODUCTION

Increasing attention for environmental protection during the last decades has led both modern academic and industrial groups to develop chemical processes with maximum yield and minimum cost while using non-toxic reagents, solvents and catalysts. One of the tools used to combine economic aspects with the

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environmental ones is the green chemistry /1/ .This process consists of microwave assisted synthesis /2/ which has been carried out without isolation of any intermediate, thus reducing time, saving money, energy and raw materials. In the last few years there has been an increased interest in the use of microwave heating in organic /3/ and organometallic compound synthesis /4/ and it forms now the basis of a number of commercial systems. Some interesting features of this method are the rapid reaction rates, simplicity, few mL of solvent and the ease of work-up after the reaction. Also, microwave irradiation generates rapid intense heating of polar substances, which result in the reduction of reaction time compared to conventional heating.

Many of the metal complexes with oxygen and sulphur compounds containing NO and NS donor atoms, such as semicarbazones /5,6/ and S-benzyl esters of dithiocarbazic acid /7, 8/ and their metal chelates have been found to exhibit fungicidal, bactericidal, antiviral, and antitubercular activities. Owing to their pharmacological activity, dithiocarbazates are very important compounds in biochemistry and medicine because they possess some degree of cytotoxic activity. So far, the coordination of semicarbazones and dithiocarbazates with transition metals has been explored more thoroughly /9, 10/ than their coordination with nontransition metals. They can also act in a bidentate and / or tetradentate manner, so different stereochemistries were proposed on the bases of spectral and analytical data. Recently, antimony complexes of the salicyladehyde imine of S-benzyldithiocarbazate have been shown to display marked activity against leukemia /11/. Antimony complexes are very interesting due to their fascinating structure /12/, bonding variations /13/ and potential applicability as biocides. Compounds of organoantimony are well known for their applications in chemotherapy /14/, as these compounds exhibit significant antimicrobial, /15/ antiparasitic and antitumor activities, which are associated with cytostatic activity /16-17/. Bismuth compounds have been widely used in the clinic for centuries because of their high effectiveness and low toxicity in the treatment of a variety of microbial infections, including syphilis, diarrhea, gastritis, and colitis. Special emphasis has been placed recently on the use of bismuth for duodenal ulcers, peptic diseases, and the eradication of *Helicobacter pylori* /18/ from patients. Apart from antimicrobial activity /19, 20/, bismuth compounds exhibit anticancer activities. ^{212}Bi and ^{213}Bi compounds have also been used as targeted radio-therapeutic agents for cancer treatment, and furthermore they have the ability to reduce the side-effects of cisplatin in cancer therapy /21/. We describe herein the synthesis of bidentate nitrogen-sulphur and nitrogen-oxygen donor ligands with the non-transition metals antimony(III) and bismuth(III), using microwave assisted synthesis. An attempt has also been made to evaluate their anti-fungal and antibacterial activities.

EXPERIMENTAL

$PhSbCl_2$ and Ph_2SbCl were prepared according to the literature method /22/. 2-Hydroxy benzamide, semicarbazide hydrochloride and trichloro bismuthane were purchased and used as such. All the chemicals were dried and purified before use. All the preparations were done under anhydrous conditions. The purity was checked by thin-layer chromatography (TLC).

Table 1

Synthetic and analytical data of organoantimony(III) and chlorobismuth(III) complexes of hydrazinecarboxamide (L^1H_2) and S-benzyl ester of dithiocarbazic acid (L^2H_2)

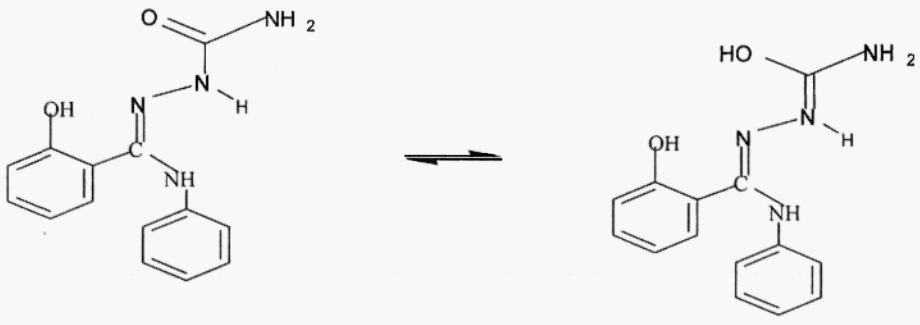
Reactants in g			Molar ratio	Empirical formula of complexes	Colour & State	M Pt. (°C)	Elemental Analysis (%)[a]				Mol. Wt[a]
Starting Material	Ligand	Sodium					N	S	Cl	Sb / Bi	
-	L^1H_2	-	-	$C_{14}H_{14}O_2N_4$	Off white Solid	110	19.9 (20.7)	-	-	-	251.11 (270.27)
Ph_2SbCl (0.76)	L^1H_2 (0.66)	0.056	1:1:1	$C_{36}H_{32}O_2N_4Sb$	Yellow Solid	145	10.01 (10.26)	-	-	22.13 (22.29)	540.16 (546.24)
$PhSbCl_2$ (0.72)	L^1H_2 (0.73)	0.123	1:1:2	$C_{20}H_{17}O_2N_4Sb$	Cherry Solid	158	11.27 (11.99)	-	-	25.90 (26.06)	462.14 (467.12)
$BiCl_3$ (0.82)	L^1H_2 (0.71)	0.118	1:1:2	$C_{14}H_{12}O_2N_4ClBi$	Yellow solid	173	10.14 (10.93)	-	6.29 (6.92)	40.34 (40.76)	507.48 (512.69)
-	L^2H_2	-	-	$C_{21}H_{19}ON_3S_2$	Grey solid	130	10.06 (10.68)	16.15 (16.30)	-	-	386.89 (393.52)
Ph_2SbCl (0.62)	L^2H_2 (0.79)	(0.05)	1:1:1	$C_{53}H_{28}O_2N_3S_2Sb$	Brown Solid	149	6.07 (6.29)	9.22 (9.59)	-	18.10 (18.22)	663.12 (668.46)
$PhSbCl_2$ (0.93)	L^2H_2 (1.36)	(0.16)	1:1:2	$C_{27}H_{22}ON_3S_2Sb$	Black Solid	163[b]	6.85 (7.12)	10.19 (10.86)	-	20.17 (20.62)	584.16 (590.36)
$BiCl_3$ (0.71)	L^2H_2 (0.89)	(0.10)	1:1:2	$C_{21}H_{17}ON_3S_2ClBi$	Light brown solid	197	6.12 (6.61)	9.76 (10.08)	5.27 (5.57)	32.10 (32.86)	629.42 (635.93)

[a]Calculated values are given in parentheses.

[b]Decomposition temperature of the complexes.

Synthesis of the Ligands (L^1H_2 and L^2H_2)

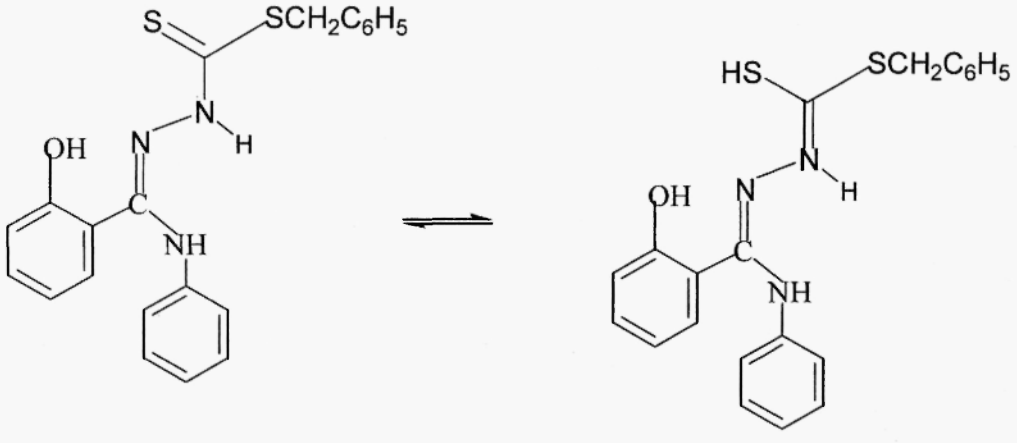
The ligands semicarbazone (L^1H_2) and S-benzyl ester of dithiocarbazate (L^2H_2) (prepared by the reported method /23/) of 2-hydroxy-N-phenyl benzamide were prepared by condensation of 2-hydroxy-N-phenyl benzamide with semicarbazide hydrochloride (in presence of sodium acetate) and S-benzyldithiocarbazate in 1:1 molar ratio using ethanol. The reaction mixture was refluxed over a water bath for 3-4 h and allowed to stand overnight, and the solid separated out was filtered, purified by recrystallization from ethanol and dried *in vacuo*. Their physico-chemical properties and analytical data are given in **Table 1**. The parent ligands exist in the tautomeric forms in absolute alcohol, as shown in **Figure 1**.



Keto form Enol form

L^1H_2

Bifunctional tridentate ligand (HO^N^OH)



Thioketo form Thioenol form

L^2H_2

Fig. 1: Bifunctional tridentate ligand (HO^N^SH)

Table 2

Comparison between conventional and microwave method of synthesis and IR (cm^{-1}) spectra data of the organoantimony(III) and chlorobismuth(III) complexes.

Compound	Yield (%)		Time		ν(C=N)	ν(M←N)	ν(M–S)	ν(M–O)
			(h)	(Min)				
	Thermal	Microwave	Thermal	Microwave				
$Ph_2Sb(O^{\frown}N^{\frown}OH)$	56	76	13	10	1610	410	-	-
$PhSb(O^{\frown}N^{\frown}O)$	61	76	16	13	1595	412	-	510
$ClBi(O^{\frown}N^{\frown}O)$	64	80	16	15	1626	325	-	428
$Ph_2Sb(S^{\frown}N^{\frown}OH)$	55	75	13	10	1610	415	298	-
$PhSb(S^{\frown}N^{\frown}O)$	46	74	14	15	1612	412	295	512
$ClBi(S^{\frown}N^{\frown}O)$	49	83	14	13	1628	329	273	425

M = Sb / Bi

Preparation of the Complexes:

For comparison purpose, two different routes were employed for the synthesis of the antimony and bismuth complexes. A comparison between thermal method /22/ and microwave method /23/ is given in **Table 2**.

(1) Preparation of the organoantimony(III) and chlorobismuth(III) complexes: Microwave Method :

For the synthesis of these complexes, dichloromonophenyl antimony(III), diphenylmonochloroantimony(III) and chlorobismuthane(III) and the sodium salts of the ligands in 1:1:1 and 1:1:2 molar ratios were irradiated inside a microwave oven at 700 W for about 10-15 min. The products were recovered from the microwave oven and dissolved in a few mL of dry methanol. The white precipitate of sodium chloride formed during the course of the reaction was removed by filtration and the filtrate was dried under reduced pressure. The resulting product was repeatedly washed with petroleum ether and then finally dried at 40-60 ^{0}C / 0.5 mm Hg for 3-4 h. The purity was further checked by thin-layer chromatography (TLC). The details of these reactions and the analysis of the resulting products are recorded in **Table 1**.

Thermal Method :

The organoantimony(III) and chlorobismuth(III) complexes were also synthesized by the thermal method. The reaction mixtures were heated under reflux for 13-16 h and, after completion of the reaction, the excess of solvent was distilled off. Finally the reaction mixture was filtered to remove NaCl and the complexes were washed, adopting the same procedure mentioned above.

ANTIFUNGAL ACTIVITY

The antifungal activity was evaluated against *Fusarium oxysporum* and *Aspergillus niger* using agar plate technique. The compounds were directly mixed with the medium in different concentrations. Controls were also run and three replicates were used in each case. The linear growth of the fungus was recorded by measuring the diameter of the fungus colony after four days. The amount of growth inhibition in each of the replicates was calculated by the equation, 100. (C-T) C^{-1}, where C and T are the diameters of the fungus colony in the control and the test plates, respectively /24/.

ANTIBACTERIAL ACTIVITY

Antibacterial activity was evaluated against *Staphylococcus aureus* and *Escherichia coli* by the paper disc plate method. The nutrient agar medium (0.5 %, peptone, 0.15% yeast, 0.15% beef extract, 0.35% NaCl and 0.13% KH_2PO_4) in distilled water (1000 cm^3) was autoclaved for 20 min at 15 *psi before inoculation.* The 5mm diameter paper discs of Whatman No.1 were soaked in different solutions (500 and 1000 ppm) of the

compounds, dried and then placed in the petri plates previously seeded with the test organisms. The plates were incubated for 24 h at 28 ± 2°C and the inhibition zone around each disc was measured /24/.

PHYSICAL MEASUREMENTS AND ANALYTICAL METHODS

The molecular weights were determined by the Rast Camphor /25/ method as well as ebulliometrically. Sulphur and nitrogen were estimated gravimetrically (Messenger's method) as $BaSO_4$ and by Kjeldahl's method, respectively. Chlorine was determined by Volhard's method /25/. Antimony was estimated by oxidation of Sb(III) to Sb(V) on heating with $KMnO_4$, the excess of which was decolorized with H_2O_2. The remaining H_2O_2 was decomposed and Sb(V) then determined iodimetrically. Bismuth was estimated complexometrically /25/. Electronic spectra of the complexes were recorded in methanol on a UV-160A, Shimadzu spectrophotometer in the range 200-600 nm. Infrared spectra of the ligands and their complexes were scanned in the range 4000 – 200 cm^{-1} with the help of a model Nicolet Megna FTIR-550 spectrophotometer and a model FT IR-8400 S spectrophotometer on KBr optics as well as Nujol mulls. NMR spectra were recorded using a JEOL-AL-300 FT NMR spectrometer in DMSO-d_6 using TMS tetra methylsilane as the internal standard. The conductivity of the resulting derivatives was determined at room temperature in dry DMF.

RESULTS AND DISCUSSION

The elemental analysis and spectral data are consistent with the formulation of compounds as $Ph_2Sb(O^{\frown}N^{\frown}OH)$, $PhSb(O^{\frown}N^{\frown}O)$, $ClBi(O^{\frown}N^{\frown}O)$, $Ph_2Sb(S^{\frown}N^{\frown}OH)$, $PhSb(S^{\frown}N^{\frown}O)$, and $ClBi(S^{\frown}N^{\frown}O)$. The unimolar reactions of Ph_2SbCl, $PhSbCl_2$ and $BiCl_3$, with the sodium salt of H_2-Saly.SCTZ (L^1H_2) and H_2-Saly.DTCZ (L^2H_2) in methanol solution proceed with the formation of M←N, M-S and M-O bonds yielding the substitution products. The reactions proceed as shown in equations (1-3).

1. $Ph_2SbCl + HX^{\frown}N^{\frown}OH + Na \rightarrow PhSbCl(X^{\frown}N^{\frown}OH) + NaCl$ (1)

2. $PhSbCl_2 + HX^{\frown}N^{\frown}OH + 2Na \rightarrow PhSb(X^{\frown}N^{\frown}O) + 2NaCl$ (2)

3. $BiCl_3 + HX^{\frown}N^{\frown}OH + 2Na \rightarrow ClBi(X^{\frown}N^{\frown}O) + 2NaCl$ (3)

where X = O (L^1H_2) / S (L^2H_2) and $HO^{\frown}N^{\frown}XH$ is the donor set of the ligand—

The resulting colored solids are monomeric in nature, as evidenced by their molecular weight determinations, and are soluble in most of the common organic solvents. Their low molar conductivity values (8-10 ohm^{-1} cm^2 mol^{-1}) show that they are non-electrolytes in nature.

Metal complexes were also prepared by the microwave method besides by conventional method. The reason for synthesizing metal complexes by microwave method is due to its ecofriendly nature. The reaction time is brought from hours to seconds and a small amount of solvent is required for the reaction completion. Enhancement in the yield of the resulting products is observed /26/. The microwave mediated reactions occur more safely, reduce the amount of waste products and increase the yield of pure required products and thus the results seem to be quite promising.

Electronic Spectra

The electronic spectra of the ligands, L^1H_2, L^2H_2 and their antimony and bismuth complexes have been recorded in dry methanol. In the electronic spectra of the ligands and their complexes, the bands at ca. 264 and 319 nm were assigned to π–π^* electronic transitions. These bands remained unaltered /27/ in the antimony as well as bismuth complexes, whereas an additional band due to n–π^* transitions appears at 350–375 nm due to >C=N group and undergoes a bathochromic shift of ~10–15 nm in the complexes, due to antimony- as well as bismuth-ligand electronic interaction and polarization within the >C=N chromophore resulting after chelation.

Infrared Spectra

The IR spectra of the free ligands and their complexes were scanned in the form of KBr optics as well as Nujol mulls. The IR spectrum of the ligand (L^1H_2) shows a strong band at 1618 cm^{-1} due to the >C=N group, which shifts to the lower wave number (~8-10 cm^{-1}) in the antimony complexes while shifted to a higher wave number (~8-10 cm^{-1}) in the bismuth complexes, indicating the coordination of the azomethine nitrogen to the metal atoms. The band in the region 3300-3100 cm^{-1}, due to the ν(NH) / (OH) mode, disappears in the corresponding complexes. However, two strong bands at *ca* 3485 and 3370 cm^{-1} due to the asymmetric and symmetric vibrations of $-NH_2$ group, remain unaltered in the spectra of the complexes, indicating the non-involvement of this group in the coordination.

In the IR spectra of the ligand L^2H_2 and its antimony(III) and bismuth(III) complexes, a band due to νNH vibrations appears at 3410–3100 cm^{-1}, which is absent in the spectra of the complexes. In the spectra of $Ph_2Sb(X^{\frown}N^{\frown}O)$, $PhSb(X^{\frown}N^{\frown}O)$ and $ClBi(X^{\frown}N^{\frown}O)$ complexes, the νOH band disappears showing metal and oxygen bond formation, while remaining unaltered in $Ph_2Sb(X^{\frown}N^{\frown}OH)$, showing non-involvement of OH in bond formation. Again the band due to >C=N at *ca.* 1620 cm^{-1}, shifts to the lower wave number (~8-10 cm^{-1}) in the antimony complexes and to higher wave number (~8-10 cm^{-1}) in the bismuth complexes. The band due to ν(C=S) in the spectra of the ligand appears at 1025–1055 cm^{-1} and disappears on complexation, showing chelation through the thiolic sulphur.

Some new bands observed in the regions 400-450, 505-515, 370-391, 320-332, 230-265 and 445 cm^{-1} are due to ν(Sb←N) /28/, ν(Sb–O) /28/, ν(Sb–S) /29/, ν(Bi←N) /30/, ν(Bi–S) /30/ and ν(Bi–O) respectively. The band at 450-470 cm^{-1} may be assigned to ν(Sb-Ph) /28/ vibrations.

The free ligand (L^2H_2) displays bands at ~2900 and ~2960 cm^{-1} attributed to symmetric and asymmetric vibration of $-CH_2$ of $SCH_2C_6H_5$ groups and gets reduced to a weak doublet in the spectra of the complexes /23/.

Table 3

^{1}H NMR spectral data (δ, ppm) of the ligands and their corresponding organoantimony(III) and chlorobismuth(III) complexes

Compound	ϕ–NH (bs)	-NH_2	–NH (free) (bs)	ϕ–OH	-SCH_2	Aromatic protons (m)	Ph-Sb
(HO^N^OH)	10.47	2.70	10.60	12.0	-	6.76-8.40	-
Ph_2Sb(O^N^OH)	10.46	2.71	-	12.2	-	6.70-8.12	6.12 – 7.29
PhSb (O^N^O)	10.52	2.76	-	-	-	6.75-8.16	6.45-7.82
ClBi (O^N^O)	10.51	2.71	-	-	-	6.78-8.29	-
(HO^N^SH)	10.46	3.10	12.15	12.11	4.98	6.81-8.35	-
Ph_2Sb(S^N^OH)	10.48	3.08	-	12.09	5.05	6.84-8.32	6.50-8.21
PhSb (S^N^O)	10.48	3.09	-	-	5.08	6.86-8.35	6.13-7.33
ClBi (S^N^O)	10.53	3.09	-	-	5.06	6.70-8.16	-

bs = broad singlet, s = singlet and m = complex pattern pattern.

^{1}H NMR Spectra

The ligand L^1H_2 exhibits a proton signal at δ10.60 ppm due to the ¯NH proton and this disappears in the spectra of the metal complexes, thereby suggesting the deprotonation of the NH group. The NH_2 group gives a singlet at δ 2.70 – 3.10 ppm in the ligands and their metal complexes. This shows that the -NH_2 group is not taking part in the complexation. The ligands show multiplets in the region δ 6.70 – 8.40 ppm attributable to aromatic protons, which appear almost in the same position in their respective complexes.

The ν(OH) proton signals of the ligands resonate at δ12.0 (L^1H_2) and δ12.11 (L^2H_2) ppm, which disappeared in the PhSb(X^N^O) and ClBi(X^N^O) complexes, while they remained as such in Ph_2Sb(X^N^OH) complexes, showing non-participation of OH group in bond formation. The -SCH_2 protons in the L^2H_2 ligand resonate at 4.98 ppm which remains almost same in the complexes. The aromatic protons in the complexes appear at (6.70-8.35 ppm) in almost the same positions as in the ligands. The ^{1}H NMR spectra of the ligands and their complexes are listed in **Table 3**.

^{13}C NMR Spectra

A comparative study of ^{13}C NMR spectra of the ligands with antimony(III) and bismuth (III) derivatives provides useful information about the mode of bonding. Considerable shifts have been observed in the position of Ar-OH group carbon on complexation, indicating that this group is participating in the bonding, while no appreciable shift was observed in the position of Ar-OH groups carbon atoms for those complexes where it does not participate. In ^{13}C NMR spectral data of the ligands (L^1H and L^2H_2) and their corresponding complexes, shifts in the positions of carbon atoms involved in the complex formation clearly indicates the bonding of the azomethine nitrogen (δ 156.20 and δ 157.32 ppm) and amido oxygen / thiolo sulfur (δ 162.35 and δ 165.34 ppm) to the metal (antimony and bismuth) atoms /31/. These signals show a considerable shift in the position as compared to their position in corresponding free imines, indicating the involvement of >C=N group and >C=O / >C=S in bonding, which is further confirmed by the IR spectra due to the M←N, M-O and M-S bonds formation. A new set of four signals observed in the spectra of the complexes in the range ~140.21-130.65 ppm has been assigned to the phenyl carbons attached to the antimony atom. The ^{13}C NMR spectra of the ligands and their complexes also support the authenticity of the proposed structures (**Table 4**).

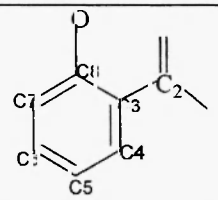
The structures shown in **Figure 2**, in which the central atom (Bi / Sb) aquires pseudo trigonal bipyramidal /31/ geometry, appear to be highly plausible.

ANTIMICROBIAL STUDIES

The antimicrobial activity of the two imines and some of their antimony and bismuth complexes were evaluated against pathogenic fungi and bacteria. The test results are given in **Table 5**. The data indicate that both the imines exhibit moderate antimicrobial activities against these microorganisms, but their antimony

Table 4

^{13}CNMR spectral data (δ, ppm) of the ligands and their organoantimony(III) and chlorobismuth(III) complexes

Compound	Azomethine carbon C_1	Amido / thiolo C_2	Aromatic Carbon 						*Ph-Sb			
			C_3	C_4	C_5	C_6	C_7	C_8	C(i)	C(o)	C(m)	C(p)
(HO^N^OH)	156.20	162.35	128.3	127.3	124.8	127.6	128.7	136.9	-	-	-	-
PhSb(O^N^O)	159.23	165.18	129.2	128.4	125.5	128.4	129.2	137.7	140.21	134.46	131.15	130.65
ClBi(O^N^O)	158.37	164.12	129.58	129.7	126.1	128.3	129.8	138.3	-	-	-	-
(HO^N^SH)	157.32	165.34	143.35	131.24	112.43	128.43	133.14	147.02	-	-	-	-
PhSb(S^N^O)	159.28	166.36	145.26	133.43	113.19	129.06	135.17	148.62	140.13	135.68	132.76	130.17
ClBi(S^N^O)	159.47	167.23	143.53	132.17	113.46	129.17	134.21	147.96	-	-	-	-

*Antimony phenyl carbon values are given in order C(i), C(o), C(m) and C(p), respectively.

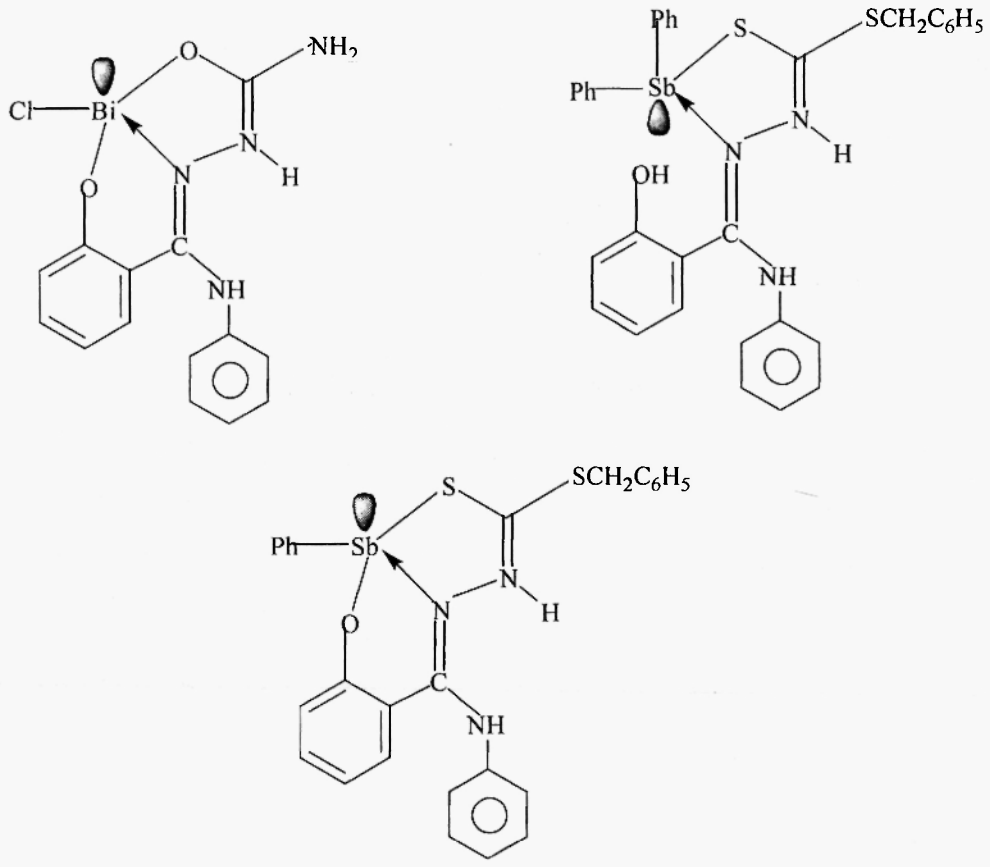


Fig. 2:

and bismuth complexes are much more active than the free ligands. This is in agreement with our previous findings that chelation of dithiocarbazate ligands /23/ by the metal ion (antimony) enhances their activity.

Antimicrobials can attack various targets in microorganisms, as a consequence of which organisms are either destroyed or have their growth inhibited. Since the complexes inhibit the growth of microorganisms, it is assumed that the production of the enzymes is being affected, and hence the microorganisms are unable to utilize their food, or the intake of ion decreases and consequently the growth ceases. At lower concentrations, when the enzyme leaches out, the growth of the microorganism is arrested, though very little enzyme is being produced, but its amount is sufficient to suffice the need of the microorganism to grow, whilst higher concentrations destroy the enzyme mechanisms by blocking any of the metabolism pathways (viz. lipid, carbohydrate and aminoacids) and the organism dies. Inorganic complexes can also affect non-metalloenzymes. Metals can coordinate to the active site residues to block substrate interaction or coordinate to residues outside the active-site to affect structural integrity. The coordination ability of metal also holds the attractive promise of forming stronger attachments through covalent and ionic bonds.

Table 5

Antifungal and antibacterial screening data of the ligands their corresponding organoantimony(III) and chlorobismuth(III) complexes.

Compound	Antifungal Screening						Antibacterial Screening			
	Average inhibition (%) after 96 h (conc. in ppm.)						Diameter of inhibition zone (mm) after 24 h (conc. in ppm)			
	Fusarium oxysporum			*Aspergillus niger*			*Staphylococcus aureus*		*Escherichia coli*	
	50	100	200	50	100	200	500	1000	500	1000
L^1H_2	29	42	65	26	40	62	5	7	4	7
PhSb (O^N^O)	42	51	65	37	35	55	8	9	7	8
ClBi (O^N^O)	46	54	68	40	38	59	11	16	10	11
L^2H_2	68	72	85	68	75	80	8	10	6	8
PhSb (S^N^O)	66	75	86	70	73	85	10	13	8	9
ClBi (S^N^O)	75	78	92	72	79	89	12	17	9	12
Bavistin / Streptomycin	91	100	100	86	98	100	15	17	16	17

The results reveal that there is considerable increase in the toxicity of the complexes as compared to the ligands. On giving a closer look at these results, a common feature appears, which is that the bioactivity enhances due to the following points.

1. The enhancement in the activity can be explained on the basis of chelation theory /32/. Chelation reduces the polarity of the metal ion considerably, mainly because of the partial sharing of its positive charge with donor groups and possible π electron delocalization on the whole chelate ring. The lipid and polysaccharides are some important constituents of cell wall and membranes, which are preferred for metal ion interaction. In addition to this, cell wall also contains many aminophosphates, carbonyl and cysteinyl ligands, which maintain the integrity of the membrane by acting as a diffusion barrier and also provide suitable sites for binding. Chelation can considerably reduce the polarity of the metal ion, which in turn increases the lipophilic character of the chelate. Thus, the interaction between metal ion and the lipid is favored. This may lead to the breakdown of the permeability barrier of the cell, resulting in interference with the normal cell processes. If the geometry and charge distribution around the molecule are incompatible with the geometry and charge distribution around the pores of the bacterial cell wall, penetration through the wall by the toxic agent cannot take place and this will prevent the toxic reaction within the pores.
2. Chelation is not the only criterion for antibacterial activity. Some important factors that contribute to the activity are: nature of the metal ion, nature of the ligand, coordinating sites, geometry of the complex, concentration, hydrophilicity, lipophilicity and presence of co-ligands, solubility, concentration and fineness of the particle size of the metal ion as well as the presence of the bulkier organic moieties, which affect the growth of organisms /33/. Certainly, steric and pharmokinetic factors also play a decisive role in deciding the potency of an antimicrobial agent. The higher toxicity of the metal complex can be attributed to the effect of metal ion on the normal cell processes. The widespread interaction of metal ions with cellular compounds is due to the fact that all these structures contain a variety of functional groups that can act as metal binding ligands. The problem is how to obtain those interactions in cells and organisms where non-polar membrane exist to hinder the movement of charged metal ions into the cell, where myriad of metal binding sites exist to compete for the metal ion, and where specificity of cellular interaction must occur in order to obtain therapeutic value /34/.
3. It is also evident that the complexes having sulphur as a donor atom in the ligand system display higher activity than those which do not have it /32/.
4. It has been found that the gram (+)ve bacteria are more affected than the gram -ve bacteria. The ligands are much more toxic to gram positive bacteria and this toxicity is further enhanced in the complexes /32/.
5. Apart from this, the mode of action of these compounds may also invoke the hydrogen bond though the >C=N-N=C< group with the active centers and thus interfere with normal cell processes. Presence of lypophilic and polar substituents is expected to enhance antibacterial activity. Heterocyclic ligands with multifunctionality have a greater chance of interaction, either with nucleoside bases (even after complexation with metal ion) or with biologically essential metal ions present in the biosystem and can be promising candidates as bactericides since they always look to react especially with some enzymatic

functional groups, to achieve a higher coordination number. Thus, the antibacterial property of metal complexes cannot be ascribed to chelation alone but is an intricate blend of all the above contributions.

CONCLUSIONS

Microwave (MW) irradiation is an efficient and environmentally-benign method to accomplish various inorganic syntheses to afford products in higher yields in shorter reaction periods.

N-phenyl benzamide semicarbazone (HO^N^OH) and N-phenyl benzamide S-benzyldithiocarbazate (HO^N^SH) ligands behave as bidentate as well as tridentate with different metal starting materials in different reaction conditions.

Antimony(III) and bismuth(III) complexes obtained by 1:1:1 and 1:1:2 molar reactions with the sodium salt of the ligand were found to be tetracoordinated, but, due to stereochemically active lone pair of electrons present on the metal atom, trigonal bipyramidal geometry has been tentatively proposed for the said complexes.

Antimicrobial activity of the complexes and the ligands showed that the former are more active than the parent ligands.

The data given in Table 5 reveal that PhSb(O^N^S) and ClBi(O^N^S) complexes were found to be more toxic than the other complexes and the bismuth complexes display better results than the antimony complexes.

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