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PHYSICO-CHEMICAL CHARACTERIZATION OF BIOACTIVE MIXED LIGAND COMPLEXES OF ANTIMONY WITH 3,5-DIARYLSUBSTITUTED PYRAZOLINATES AND O,O'-ALKYLENE DITHIOPHOSPHATES

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Abstract. Antimony(III) complexes of 3(2'-hydroxyphenyl)-5-(4'-substituted phenyl) pyrazolinates and O,O'-alkylene dithiophosphate of the type $[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$ and $[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$ (where GO_2PS_2 – deprotonated O,O'-alkylene dithiophosphate; $C_{15}H_{12}N_2OX$ – deprotonated 3(2'-hydroxyphenyl)-5-(4'-subsitutedphenyl) pyrazolinates; X = –H,–CH_3, –OCH_3 and –Cl; G = –$C(CH_3)_2CH_2CH(CH_3)$–) have been synthesized and characterized by elemental analysis (C, H, N, Cl and Sb), molecular weight study by FAB mass, electronic spectral studies, far and mid IR, multinuclear NMR (^1H,^{13}C and ^{31}P). On the basis of above spectral studies, coordination of dithiophosphate and pyrazolinates along with the compounds structure have been discussed tentatively. All complexes were tested for *in vitro* antibacterial and antifungal activity, exhibiting a very good antibacterial and antifungal activity. Few complexes were also tested for their antiviral activity against papya ringspot virus showing a significant antiviral activity with inhibition of approximately 34.30 %.

Keywords: antibactirial activity, antiviral activity, antimony(III), pyrazolinates, dithiophosphates.

1. Introduction

The chemistry of main group metal compounds derived from nitrogen, oxygen and sulphur donor ligands have been an active area of research [1]. There are several reasons for continuing interest in these compounds, such as organoantimony salts are used medically to treat some tropical disease, especially in the treatment of all forms of leishmaniasis [2]. A series of aryl antimony compounds and their *in vitro* antitumour activities have been reported [3], showing a very high antitumour activity for few of these compounds compared with cisplatin. The synthesis along with spectral studies of dialkyldithiophosphates and dithiophosphinates of arsenic, antimony, bismuth and their organometallic moieties have been reviewed [4]. The interest in the chemistry of main group metals with dithiophosphato ligands arises from their utility as antitumour agents [5].The pyrazolines are an important class of polyazo heterocyclic compounds, showing a wide range of biological activity, such as analgesic [6], antitumor [7], antitussive [8], anti-inflammatory [9], anticonvulsant [10], cardiovascular [11] and antidepressant [12] properties. Pyrazolines are well known for their importance in industries, *e.g.* as dyes, antioxidants in lubricating oils [13], in agriculture as a catalyst for decarboxylation reactions and as inhibitors for plant growth [14-15]. Complexation behavior of 3(2'-hydroxyphenyl)-5-phenyl) pyrazoline and substituted pyrazolines with arsenic antimony and bismuth have been studied in our laboratories [16-18]. Similar types of ligands were also used for the complexes of tin(IV), organotin(IV) and triorganotin(IV) [19-21]. We have also investigated the complexation behavior of antimony(III) complexes with dithiophosphate ligands [22]. In continuation to our previous work, it was though worthwhile to study the complexation behavior of arsenic(III), antimony(III) and bismuth(III) with 3(2'-hydroxyphenyl)-5-(4'-subsitutedphenyl) pyrazolinates and O,O'-alkylene dithiophosphate for comparative bioactivity. In this article, we describe the synthesis, spectral properties and bioactivity of mixed ligand complexes of antimony(III) of 3(2'-hydroxyphenyl)-5-(4'-subsitutedphenyl) pyrazolinates and O,O'-alkylene dithiophosphate.

2. Experimental

2.1. Materials

Solvents (benzene, isopropanol and ethanol) were rigorously dried and purified by standard methods before use. All chemicals were of analytical grade quality.

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Antimony(III) chloride (E. Merck), sodium metal (SD fine), *o*-hydroxyacetophenone (CDH), and benzaldehyde (E. Merck) were used without any further purification. Dichloroantimony(III) 3(2'-hydroxyphenyl)-5-(4'-substitutedphenyl) pyrazolines and chloroantimony(III) 3(2'-hydroxyphenyl)-5-(4'-subsitutedphenyl) pyrazolines were prepared by the reported procedure [16]. O,O'-alkylene dithiophosphate was prepared by the reported procedure [23].

2.2. Synthesis of $[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$

The new mixed ligand complexes of antimony(III) of the general formula $[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$ were prepared by the reaction of dichloroantimony(III) pyrazolinates and ammonium salt of O,O'-alkylene dithiophosphate in 1:1 molar ratio.

$$[(C_{15}H_{12}N_2OX)Sb]Cl_2 + NH_4GO_2PS_2 \xrightarrow{\text{Benzene}} [Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl + NH_4Cl\downarrow$$

where X = –H, $–CH_3$, $–OCH_3$ and –Cl; G = $–C(CH_3)_2CH_2CH(CH_3)–$]; GO_2PS_2 = deprotonated O,O' alkylene dithiophosphate; $C_{15}H_{12}N_2OX$ = deprotonated 3(2'-hydroxyphenyl)-5(4'subsitutedphenyl)pyrazolinates.

The benzene suspension of the antimony(III) pyrazolinates (1.42 g, 3.2 mmol) was added dropwise to a slowly stirred benzene suspension of ammonium salt of O,O'-hexylene dithiophosphate (0.75 g, 3.2 mmol). The reaction mixture was stirred for 9 h to ensure the completion of the reaction. The reaction mixture was filtered to remove precipitated NH_4Cl (0.16 g) and the filtrate was dried under vacuum. The obtained orange colored solid was recrystallized in acetone at room temperature (purity was further checked by silica gel TLC). 1.78 g (89 %) of $[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$ was obtained. Compounds 2-4 were prepared by the same method. The physical and analytical results are presented in Table 1.

Table 1

Synthetic and analytical data for $[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$ and $[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$

Comp.no	Compound	m.p., K	Yield, %	C	H	N	S	Sb	Cl	Mol. weight
				(Found/Calcd.)						
1	$[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$	362	87	41.52 (41.63)	4.10 (4.13)	4.58 (4.62)	10.46 (10.57)	20.02 (20.11)	5.80 (5.86)	606 (606.25)
2	$[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$	355	84	43.48 (43.63)	4.27 (4.36)	4.47 (4.52)	10.24 (10.33)	20.54 (19.66)	5.66 (5.73)	618 (619.25)
3	$[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$	359	90	41.40 (41.55)	4.20 (4.25)	4.34 (4.40)	9.97 (10.07)	19.06 (19.16)	5.49 (5.58)	635 (635.25)
4	$[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$	363	86	39.48 (39.39)	3.68 (4.75)	4.32 (4.37)	9.93 (10.00)	18.97 (19.03)	11.00 (11.09)	639 (639.75)
5	$[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$	348	85	53.40 (53.54)	4.64 (4.71)	6.90 (6.94)	7.85 (7.93)	15.01 (15.09)	–	804 (806.75)
6	$[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$	353	82	54.48 (54.62)	4.98 (5.03)	6.62 (6.70)	7.56 (7.66)	14.43 (14.58)	–	832 (834.75)
7	$[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$	348	83	51.47 (52.61)	4.75 (4.84)	6.39 (6.46)	7.31 (7.38)	13.96 (14.04)	–	865 (866.75)
8	$[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$	352	81	48.27 (49.32)	4.07 (4.11)	6.32 (6.39)	7.25 (7.30)	13.84 (13.90)	7.95 (8.10)	874 (875.75)

Notes: X = H for **1** and **5**; CH_3 for **2** and **6**; OCH_3 for **3** and **7**; Cl for **4** and **8**; G = $–C(CH_3)_2CH_2CH(CH_3)–$

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2.3. Synthesis of $[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$

The new mixed ligand complexes of antimony(III) of the general formula $[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$ were prepared by the reaction of chloroantimony(III) dipyrazolinates and ammonium salt of O,O'-alkylene dithiophosphate in 1:1 molar ratio.

$$[(C_{15}H_{12}N_2O.X)_2Sb]Cl + NH_4GO_2PS_2 \xrightarrow{\text{Benzene}} [Sb(C_{15}H_{12}N_2O.X)_2(GO_2PS_2)] + NH_4Cl \downarrow$$

where X = –H, $–CH_3$, $–OCH_3$, –Cl; G = $–C(CH_3)_2CH_2CH(CH_3)–$; GO_2PS_2 = deprotonated O,O'-alkylene dithiophosphate; $C_{15}H_{12}N_2OX$ = deprotonated 3(2'-hydroxyphenyl)-5-(4'-subsitutedphenyl) pyrazolinates

A benzene solution of antimony(III) dipyrazolinates (1.56 g, 2.4 mmol) was added dropwise to the benzene suspension of ammonium salt of O,O'-hexylene dithiophosphate (0.56 g, 2.4 mmol) under constant stirring. The reaction mixture was stirred for 9 h to ensure the completion of the reaction. The reaction mixture was filtered to remove precipitated NH_4Cl (0.13 g) and the filtrate was dried under vaccum. The dark orange colored solid was recystallized in acetone at room temperature (purity was further checked by TLC). 1.50 g (75 %) of $[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$ was obtained. Compounds 6-8 were prepared by the same method. The physical and analytical results are presented in Table 1.

2.4. Physical Measurements

Chlorine was estimated by Volhard's method [24] and antimony was estimated iodometrically [24]. Infrared spectra were recorded on Varian 3100 FT-IR spectrophotometer in the range of 4000–50 cm^{-1}. The ^1H NMR spectra and proton decoupled ^{13}C NMR spectra were recorded at room temperature in $CDCl_3$ on a JEOL AL 300 spectrometer, operated at 300.1 and 74.45 MHz for ^1H and ^{13}C, using TMS (tetramethylsilane) as internal standard. ^{31}P NMR spectra were recorded in C_6H_6 solution on a Bruker Avance 400 NMR at 161.9 MHz using H_3PO_3 as an internal standard. The elemental analysis (C, H and N) was obtained by using a Coleman CHN analyzer. The specific optical rotations were recorded at 298 K in benzene on Perkin-Elmer polarimeter (model 341) using the sodium D line (λ = 589 nm). Electronic spectra were recorded in benzene solution on Hitachi UV-2000 UV-visible spectrophotometer within the range of 400–200 nm.

2.5. Antimicrobial Studies

Agar disc diffusion technique was used for screening *in vitro* antimicrobial activity [25]. Inoculums of bacteria were prepared in a nutrient broth and fungi in a potato dextrose agar slant. The cultures were inoculated and incubated for 48 h in case of bacteria and 5 days for fungi. Molten Muller Hinton medium was poured in a sterile Petri dish (9 cm in diameter) to get a depth of 5 mm. The medium was left to solidify and then seeded with respective test organisms. For the purpose of seeding, 5 ml of sterile water was added to the agar slant culture of fungi. The culture was scraped to get suspension of fungi spore. A sterile cotton swab was dipped in the culture/suspension and lightly rubbed over the solidified medium. The plate was left for a few minutes and then used for the test. 30 μm of each sample to be tested was dissolved in 1 ml of acetone. 5 mm discs of Whatman filter paper no.40 were cut and sterilized. The filter paper discs were immersed in the solution of a sample, after soaking; the disc was removed and left in a sterile Petri dish to permit the solvent to evaporate. After about 10 min the paper discs were transferred to seeded agar plate. Discs were kept on the seeded agar plates. Finally the dishes were incubated at 310 K for 24 h (for bacteria) and at 303 for 72 h (for fungi), where clear or inhibition zones were detected around each disc. A disc soaked in DMSO alone was used as a control under the same conditions and there was no inhibition zone. Each distinct inhibition zone was measured as a diameter in mm, both antibacterial and antifungal activity was calculated as a mean of three replicates.

2.6. Antiviral Testing

Pure cultures of Papaya ring spot virus (PRSV) were maintained on Carica papaya plants in a glass house. Local lesion bioassay method [26] was performed to study the antiviral properties of the various compounds against the test virus.

Powder samples of compounds were prepared in various dilutions from 1:10 and 1:20 with inoculation buffer. 1 ml was mixed with 1 ml of freshly prepared viral inoculums and incubated for 30 min in cold conditions; later the inoculum was inoculated to local lesion assay seeding by using the small piece of muslin cloth. For control, some of the seedlings were being maintained in insect mesh house for observation. Three independent replications were performed; in each experiment 10 seedlings were used for each dilution for testing of antiviral property.

Local lesions which appeared on tested and control chenopodium plants were counted and per cent antiviral activity was calculated by the formula (1).

$$\text{Percent antiviral activity} = (C–T)/T \cdot 100 \qquad (1)$$

where C is a number of local lesions on control leaves; T is a number of local lesions on tested leaves.

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3. Results and Discussion

All the compounds are orange colored solids, stable at room temperature, soluble in common organic (chloroform, acetone, alcohol) and coordinating solvent (tetrahydrofuran, dimethylformamide and dimethyl-sulphoxide). The FAB mass spectra show the monomeric nature of these compounds. The elemental analysis (C, H, N, P, S, Cl and Sb) data is in accordance with a stoi-chiometry proposed for respective compounds (Table 1).

3.1. Specific Optical Rotation Data

The specific optical rotation values of benzene solution of free pyrazolines and mixed ligand complexes of antimony(III) are not measurable at the concentration of 1.00, 0.50, 0.10 and 0.05 %. All the four free pyrazoline ligands show zero specific optical rotation at 0.02 % concentration. Thus free pyrazolines are racemic mixture. The specific optical rotation values for mixed ligand complexes of antimony(III) in the benzene solution at 0.02 % concentration are also zero indicating the presence of racemic mixture.

3.2. Infrared Spectral Studies

The infrared spectra of the complexes recorded in the range of 4000–50 cm^{-1} and assignments made on the basis of previous reports are summarized in Table 2. All compounds exhibit the band of medium intensity in the region of 3435–3412 cm^{-1} due to υ(N–H) stretching vibrations and band in the region of 1634–1620 cm^{-1} due to υ(C=N) stretching vibrations [16-21, 27-28]. The signal due to υ(O-H) (originally present at ~3085 cm^{-1} in the free pyrazolines) is completely disappeared from the spectra of the complexes. The appearance of two new bands (in comparison to free pyrazolines) in the region of 478–458 and 447–429 cm^{-1} are assigned to υ(Sb–O) and υ(Sb–N) stretching vibrations, respectively [16]. The appearance of two new bands due to Sb–O and Sb–N, as well as the absence of hydroxyl band suggest that pyrazoline behaves as a monobasic bidentate ligand in these compounds.

The infrared spectra of these newly synthesized complexes also show medium to strong intensity bands in the region of 1132–1110 and 898–879 cm^{-1} have been assigned to [(P)–OC] and [P–O(C)] stretching vibrations, respectively [29-30]. A sharp band in the region of 922–910 cm^{-1} was assigned to ring vibrations of dioxaphosphorinane ring [29-30]. The band for [P=S] was found in 687–670 cm^{-1} region and it was observed that, in comparison with the spectra of the parent alkylenedithiophosphoric acids, there is a shifting towards lower frequency [29-30]. This shifting indicates a bidentate chelation of thiophosphoryl sulphurs to antimony. The bands of weak to medium intensities in the region of 598–585 cm^{-1} were due to P–S stretching vibration [29-30]. The O,O'-alkylene dithiophosphate ligands are isodentate in nature but upon coordination with the antimony these ligands shows anisodentate behavior. Distortion in the coordination polyhedra may occur due to the steriochemically active lone pair of electrons and small ligand bite. The band of weak intensity at 387–364 cm^{-1} occurs due to Sb–S stretching vibration [22, 31]. Thus the presence of one new band due to Sb–S and shifting of [P=S] band indicating the bidentate nature of O,O'-alkylene dithiophosphate (Table 2).

Table 2

IR spectral data (cm^{-1}) for $[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$ and $[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$

Comp. no	υ(N–H)	υ(C=N)	υ(C–O)	Y[(P)–O–C]	Ring vibration	υ[P–O–(C)]	υ(P=S)	υ(P–S)	υ(Sb–O)	υ(Sb–N)	υ(Sb–S)	υ(Sb–Cl)
1	3412	1624	–	1125	912	890	680	595	478	447	387	336
2	3435	1632	–	1114	915	889	682	597	467	429	376	338
3	3426	1620	1017	1113	914	898	670	585	465	443	368	321
4	3427	1623	–	1110	920	879	687	598	471	434	364	328
5	3434	1626	–	1120	922	891	683	598	468	443	386	–
6	3427	1628	–	1132	913	886	672	592	476	431	379	–
7	3413	1634	1014	1123	920	890	674	590	472	440	373	–
8	3412	1626	–	1125	910	883	679	592	477	441	381	–

Notes: X = H for **1** and **5**; CH_3 for **2** and **6**; OCH_3 for **3** and **7**; Cl for **4** and **8**; G = $–C(CH_3)_2CH_2CH(CH_3)–$

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3.3. ^{1}H NMR Spectral Studies

The ^{1}H chemical shifts of all compounds are listed in Table 3. In ^{1}H NMR spectra of $[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$ and $[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$, the benzene ring protons were observed as multiplet in the region of 7.9–6.4 ppm [16-21, 27-28]. The peak due to hydroxyl proton (originally present at δ ~11.00 ppm in free pyrazolines) is absent from the spectra of the complexes suggesting the bonding through hydroxyl oxygen atom [16-21, 27-28]. The appearance of a peak at δ = 5.5–5.1 ppm as a broad signal could be assigned to N–H group (originally present at δ = 5.5–5.3 ppm in free pyrazolines) suggesting the non-involvement of N–H group in bond formation [16-21, 27-28]. The skeletal protons of five membered ring are observed at δ = 3.4–3.0 ppm as a triplet and at δ = 2.5–2.0 ppm as a doublet. They could be assigned to CH and CH_2 group, respectively [16-21, 27-28]. The $–CH_3$ and $–CH_2$ protons of alkylene dithiophosphate show multiplet in the region of 1.6–1.1 ppm [29-30] and the –OCH protons coupled with ^{31}P nuclei to get multiplet in the region of 5.0–4.2 ppm [29-30]. The observed integration ratio was found well with the presence of one dithiophosphate and two pyrazoline ligands in the complexes.

Table 3

^{1}H NMR spectral data for $[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$ and $[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$

Comp.no	Compounds	Chemical shift δ, ppm	
		Pyrazoline	Dtp
1	$[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$	7.6–6.8 (13H, m, Ar–H) 5.3 (2H,s, NH) 3.3 (1H, t, CH) 2.5 (2H, d, CH_2)	1.1 (m, 9H $–CH_3$) 4.8 (m, 1H, OCH–)
2	$[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$	7.9–6.4 (13H, m, Ar–H) 5.5 (2H,s, NH) 3.0 (1H, t, CH) 2.3 (2H, d, CH_2) 0.9 (3H, s, CH_3)	1.4 (s, 9H $–CH_3$) 4.9–4.3 (m, 2H, OCH–)
3	$[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$	7.8–6.7 (13H, m, Ar–H) 5.4 (2H, s, NH) 3.1 (1H, t, CH) 2.0 (2H, d, CH_2) 3.6 (3H, s, OCH_3)	1.5 (s, 9H $–CH_3$) 4.9–4.2 (m, 2H, OCH–)
4	$[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$	7.6–6.5 (13H, m, Ar–H) 5.5 (2H,s, NH) 3.3 (1H, t, CH) 2.1 (2H, d, CH_2)	1.6 (s, 9H $–CH_3$) 5.0–4.4 (m, 2H, OCH–)
5	$[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$	7.7–6.8 (13H, m, Ar–H) 5.1 (2H,s, NH) 3.3 (1H, t, CH) 2.3 (2H, d, CH_2)	1.3 (s, 9H $–CH_3$) 4.8–4.4 (m, 2H, OCH–)
6	$[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$	7.6–6.5 (13H, m, Ar–H) 5.2 (2H,s, NH) 3.4 (1H, t, CH) 2.4 (2H, d, CH_2) 0.9 (3H, s, CH_3)	1.6 (s, 9H $–CH_3$) 4.9–4.6 (m, 2H, OCH–)
7	$[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$	7.6–6.7 (13H, m, Ar–H) 5.2 (2H,s, NH) 3.3 (1H, t, CH) 2.5 (2H, d, CH_2) 3.9 (3H, s, OCH_3)	1.5 (s, 9H $–CH_3$) 5.0–4.5 (m, 2H, OCH–)
8	$[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$	7.8–6.6 (13H,m, Ar–H) 5.4 (2H,s, NH) 3.0 (1H, t, CH) 2.3 (2H, d, CH_2)	1.4 (s, 9H $–CH_3$) 4.8–4.3 (m, 2H, OCH–)

Notes: X = H for **1** and **5**; CH_3 for **2** and **6**; OCH_3 for **3** and **7**; Cl for **4** and **8**; G = $–C(CH_3)_2CH_2CH(CH_3)–$; Dtp = O,O'-alkylene dithiophosphate

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Table 4

^{31}C NMR spectral data for [Sb($C_{15}H_{12}N_2OX$)(GO_2PS_2)]Cl and [Sb($C_{15}H_{12}N_2OX$)$_2$(GO_2PS_2)]

Comp.no	Compounds	Chemical shift δ, ppm		
		^{13}C NMR		^{31}P NMR
		Pyrazoline	Dtp	
1	[Sb($C_{15}H_{12}N_2OX$)(GO_2PS_2)]Cl	144.1–124.0(Ar–C) 159.0(C=N) 46.3(CH) 27.8(CH_2)	83.1(OC) 77.4(OCH) 22.0(CH_2) 14.3 (CH_3)	98.2
2	[Sb($C_{15}H_{12}N_2OX$)(GO_2PS_2)]Cl	144.6–124.5(Ar–C) 159.1(C=N) 47.5(CH) 28.4(CH_2) 51.5(CH_3)	84.5(OC) 78.1(OCH) 22.9(CH_2) 13.8 (CH_3)	99.1
3	[Sb($C_{15}H_{12}N_2OX$)(GO_2PS_2)]Cl	143.8–123.9(ArC) 158.4(C=N) 46.4(CH) 27.8(CH_2) 51.3(OCH_3)	83.0(OC) 77.0(OCH) 22.9(CH_2) 14.8 (CH_3)	96.3
4	[Sb($C_{15}H_{12}N_2OX$)(GO_2PS_2)]Cl	144.5–124.9(Ar–C) 157.9(C=N) 46.4(CH) 26.6(CH_2)	84.2(OC) 78.4(OCH) 23.0(CH_2) 14.3(CH_3)	93.8
5	[Sb($C_{15}H_{12}N_2OX$)$_2$(GO_2PS_2)]	143.9–123.9(Ar–C) 157.9(C=N) 46.9(CH) 26.8(CH_2)	85.0(OC) 79.9(OCH) 22.9(CH_2) 14.8(CH_3)	94.5
6	[Sb($C_{15}H_{12}N_2OX$)$_2$(GO_2PS_2)]	143.7–123.9(Ar–C) 158.8(C=N) 47.0(CH) 27.1(CH_2) 13.8(CH_3)	84.9(OC) 78.3(OCH) 23.0(CH_2) 13.5(CH_3)	99.0
7	[Sb($C_{15}H_{12}N_2OX$)$_2$(GO_2PS_2)]	143.5–124.7(Ar–C) 158.0(C=N) 47.1(CH) 23.9(CH_2) 51.2(OCH_3)	84.6(OC) 79.9(OCH) 23.1(CH_2) 14.8(CH_3)	95.7
8	[Sb($C_{15}H_{12}N_2OX$)$_2$(GO_2PS_2)]	144.5–124.3(Ar–C) 157.9(C=N) 47.1(CH) 27.5(CH_2)	85.0(OC) 78.5(OCH) 23.0(CH_2) 13.6(CH_3)	93.0

Notes: X = H for **1** and **5**; CH_3 for **2** and **6**; OCH_3 for **3** and **7**; Cl for **4** and **8**; G = –$C(CH_3)_2CH_2CH(CH_3)$–; Dtp = O,O'-alkylene dithiophosphate

Table 5

Electronic spectral data for [Sb($C_{15}H_{12}N_2OX$)(GO_2PS_2)]Cl and [Sb($C_{15}H_{12}N_2OX$)$_2$(GO_2PS_2)]

Comp.no	Electronic spectral data, nm		
	I (Pyrazoline) ($\pi\rightarrow\pi^*$ and $n\rightarrow\pi^*$)	II (Dithiophosphate) ($\pi\rightarrow\pi^*$ and $n\rightarrow\pi^*$)	III Metal → ligand
1	246	289	368–350
2	245	289	371–349
3	249	299	367–349
4	240	278	364–350
5	239	288	371–345
6	235	286	366–347
7	238	298	364–349
8	235	284	369–349

Notes: X = H for **1** and **5**; CH_3 for **2** and **6**; OCH_3 for **3** and **7**; Cl for **4** and **8**; G = –$C(CH_3)_2CH_2CH(CH_3)$–

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3.4. ^{13}C NMR Spectral Studies

The proton decoupled ^{13}C NMR spectra of $[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$ and $[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$ show the presence of all important signals with reference to $[(SbC_{15}H_{13}N_2OX)]Cl_2$ and $[(SbC_{15}H_{13}N_2OX)_2]Cl$ (Table 4, [16]). The signal observed in the region of 144.6–123.9 ppm as multiplet could be assigned to aromatic carbon [16-21, 27-28]. The signal observed at δ = 158.9–157.9 ppm due to imino carbon of C=N group is shifted to downfield in comparison to the spectra of free pyrazolines (at δ = 143.5–142.8 ppm) suggesting the involvement of imino nitrogen in coordination [16-21, 27-28]. ^{13}C NMR spectrum of the compounds shows all important signals with references to O,O'-alkylene dithiophosphate [31].

3.5. ^{31}P NMR Spectral Studies

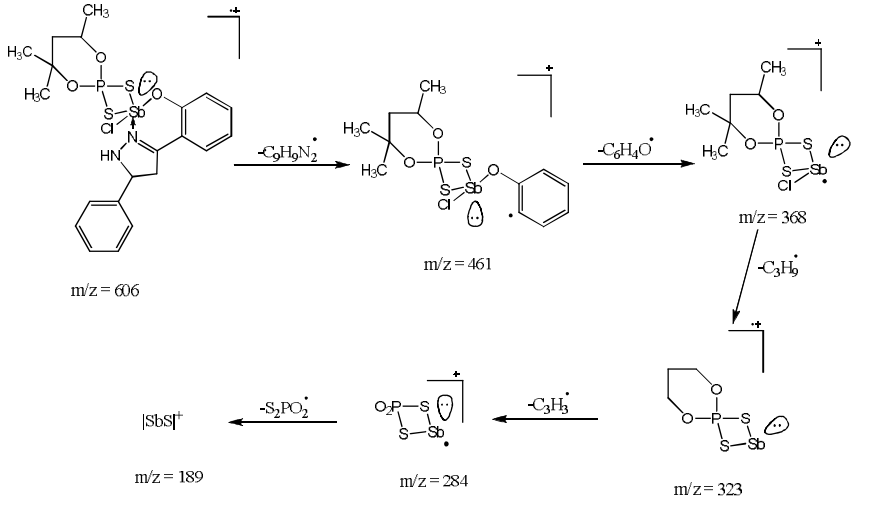
^{31}P NMR chemical shift value showed downfield shifting of about 19–23 ppm in the corresponding dioxaphosphorinane with respect to their parent alkylenedithiophosphoric acids, (77.80–78.58 ppm for dioxaphosphorinane] indicating the bidentate mode of attachment of alkylenedithiophosphate ligand [29-30], (Table 4).

3.6. Electronic Spectral Studies

The electronic spectral data for $[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$ and $[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$ complexes are listed in Table 5. In all the antimony complexes, $\pi\rightarrow\pi^*$ and $n\rightarrow\pi^*$ transitions due to pyrazoline moities exhibit the most intense band in the range of 249–235 nm [32-34]. The band in the region of 299–278 nm may be attributed to intraligand charge transfer due to dithiophosphate ligand [35]. The third band of comparatively low intensity in the range of 371–345 nm is attributed to ligand to the metal charge transfer [36].

3.7. FAB Mass Spectral Studies

The FAB mass of all the compounds gives a characteristic peak at $[M^+]$ along with other peak showing fragmentation (Scheme 1). The mass spectrum of $[Sb(C_{15}H_{13}N_2O)_2(C_6H_{12}O_2PS_2)]$, exhibited the molecular ion peak at m/z = 606 and peaks at 461, 368, 323, 284 and 189 due to successive removal of $-C_9H_9N_2$, $-C_6H_4O$, $-C_3H_9$, $-C_3H_3$ and $-SPO_2$, respectively. The major mass fragment ions are given in Table 6.



Scheme 1. FAB mass fragmentation pattern of $[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$; G = $-C(CH_3)_2CH_2CH(CH_3)-$

Table 6

FAB mass spectra of $[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$

Fragment ion formulae	m/z	
	Compound **1**, X = H (Relative intensity, %)	Compound **3**, X = $-OCH_3$ (Relative intensity, %)
$\|(C_{15}H1_2N_2O.X)SbCl(S_2PO_2C_6H_{12})\|^{.+}$	606 (11)	636 (12)
$\|(C_6H_5O)SbCl(S_2PO_2C_6H_{12})\|^+$	461 (19)	461 (22)
$\|ClSbS_2PO_2C_6H_{12}\|^+$	368 (47)	368 (59)
$\|SbS_2PO_2C_3H_3\|^+$	323 (57)	323 (59)
$\|SbS_2PO_2\|^{.+}$	284 (100)	284 (100)
$\|(SbS)\|^+$	189 (52)	189 (53)

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3.8. Antimicrobial Studies

Comparison of the antimicrobial activity of dichloroantimony(III) pyrazolines, chloroantimony(III) dipyrazolinates, and mixed ligand complexes of antimony(III) with antibiotic terbinafin and kanamycin exhibits the following results (Table 7).

The complexes $[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$ and $[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$ exhibit greater antibacterial effect towards *Bacillus subtilis, Pseudomonas sp., S. aureus*, *K. pneumoniae*, *Vibrio sp.*, and *E. coli* compared to dichloroantimony(III) pyrazolinates and chloroantimony(III) dipyrazolinates and kanamycin (Fig. 1). But their antifungal effect towards *Aspergillus flavus* and *Penicillium chrysogenum* was less compared to chloroantimony(III) dipyrazolinates and terbinafin (Fig. 2). The mixed ligand complexes of antimony(III) also show significant antiviral activity with inhibition of about 34.30 % (Table 8).

Table 7

Antimicrobial activity of the dichloroantimony(III) pyrazolinate, chloroantimony(III) dipyrazolinate, $[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$ and $[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$

Number	Fungi		Gram (+ve) bacteria		Gram (–ve) bacteria			
	A. flavus	*P. chrysogenum*	*S. aureus*	*B.subtilis*	*K. pneumoniae*	*Vibrio spp.*	*E. coli*	*P. aeruginosa*
1	++++	+++	+++	+++	+++	+++	++	++++
2	++	+++	+++	++	++	++	+	++
3	+++	++	+++	+++	+++	+++	++	++
4	++	++	+++	++	+++	++	+	+++
5	++	+++	+++	+++	+++	+++	++	+++

Notes: Inhibition values beyond control are: + 6–10 mm, ++ 11–15 mm, +++ 16–20 mm, ++++ 21–25 mm (the values are including disc diameter).

The standards are in the form of sterile Whatmann's filter paper disc, each disc containing 30 µg of the drug.

1 – Terbinafin (antifungal agent) and kanamycin (antibacterial agent); 2 – dichloroantimny (III) [3(2'-hydroxyphenyl)-5-phenyl pyrazolinate]; 3 – chloroantimny(III) di[3(2'-hydroxyphenyl)-5-phenyl pyrazolinate]; 4 – comp. no. 1 and 5 – comp. no. 5 from Table 1.

Table 8

Antiviral activity of $[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$ and $[Sb(C_{15}H_{12}N_2OX)_2(GO_2PS_2)]$

Comp.no	Compound	Inhibition, %
1	$[Sb(C_{15}H_{13}N_2O)(GO_2PS_2)]Cl$	26.12
3	$[Sb(C_{15}H_{12}N_2OOCH_3)(GO_2PS_2)]Cl$	43.56
5	$[Sb(C_{15}H_{12}N_2OCl)(GO_2PS_2)]$	46.32
7	$[Sb(C_{15}H_{13}N_2O)_2(GO_2PS_2)]$	34.09
8	$[Sb(C_{15}H_{12}N_2OOCH_3)(GO_2PS_2)]$	26.45

Notes: G = $–C(CH_3)_2CH_2CH(CH_3)–$. Inhibition was calculated according to the formula (1)

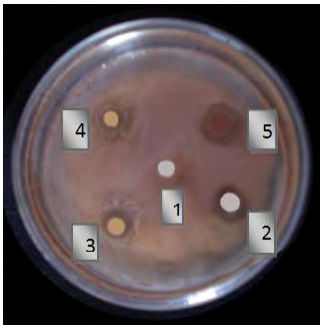

Fig. 1. Antibacterial activity against *Bacillus subtilis*: DMSO (1); kanamycin (2); dichloroantimony(III) pyrazolines (3); chloroantimony(III) dipyrazolinates (4) and $[Sb(C_{15}H_{12}N_2OCl)_2(C_6H_{12}O_2PS_2)]$ (5)

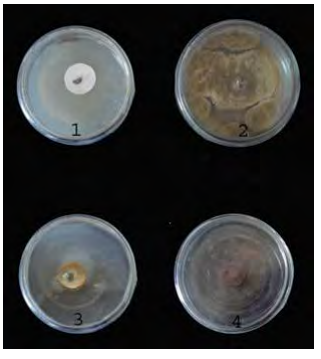

Fig. 2. Antifungal activity against *Aspergillus flavus*: terbinafin (1); DMSO (2); chloroantimony(III) dipyrazolinates (3) and $[Sb(C_{15}H_{13}N_2O)_2(C_6H_{12}O_2PS_2)]$ (4)

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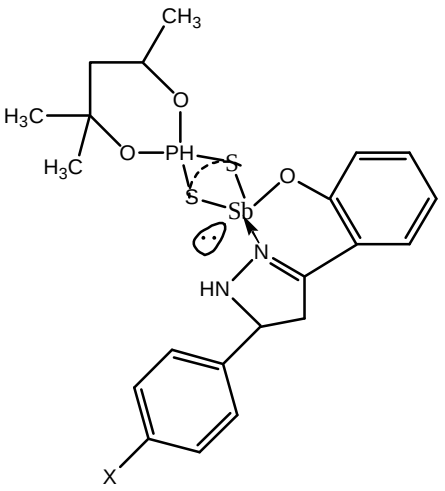

Fig. 3. Proposed structure for $[Sb(C_{15}H_{12}N_2OX)(C_6H_{12}O_2PS_2)]Cl$, where X = –H, $–CH_3$, $–OCH_3$ and Cl

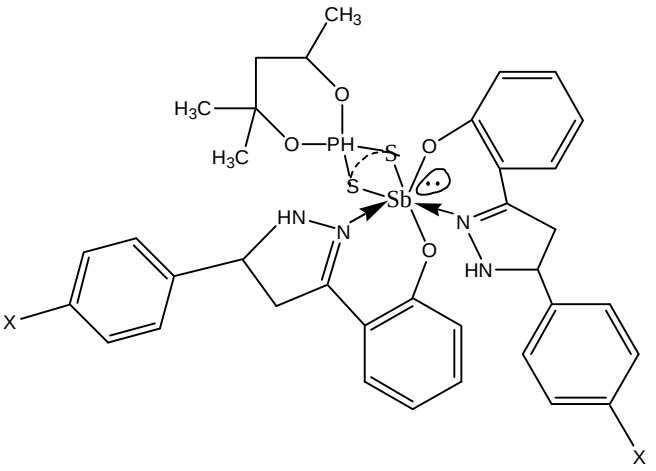

Fig. 4. Proposed structure for $[Sb(C_{15}H_{12}N_2OX)_2(C_6H_{12}O_2PS_2)]$, where X = –H, $–CH_3$, $–OCH_3$ and Cl

So, the geometry for compounds no.1-4 shows a trigonal bipyramidal geometry with coordination number five and compound number 5-8 would be distorted pentagonal bipyramidal geometry with coordination number six (Figs 3-4). Besides this, the synthesized compounds are biologically active.

4. Conclusions

It can be concluded that complexation of substituted antimony(III) moiety with biologically active pyrazoline ligand results in increased activity of these complexes. It appears that when chlorine in chloro-antimony(III) dipyrazolinates is replaced by O,O'-alkylene dithiophosphates moiety, there is a significant change in antimicrobial activity of these complexes. This concludes that antimicrobial activity of these complexes arises from pyrazoline moiety and antimicrobial activity increases when chlorine atom is replaced by the O,O'-alkylenedithiophosphate moiety.

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ФІЗИКО-ХІМІЧНА ХАРАКТЕРИСТИКА БІОАКТИВНИХ ЛІГАНДНИХ КОМПЛЕКСІВ СУРМИ З 3,5-ДІАРИЛЗАМІЩЕНИМИ ПІРАЗОЛІНАТАМИ І О, О'-АЛКІЛЕН ДІТІОФОСФАТАМИ

Анотація. *Синтезовані комплекси сурми 3(2'-гідроксифеніл)-5-(4'-заміщений феніл)піразолінат з О,О'-алкілен дитіофосфатом типу* $[Sb(C_{15}H_{12}N_2OX)(GO_2PS_2)]Cl$ *та* $[Sb(C_{15}H_{12}N_2OX)2(GO_2PS_2)]$ *(де* GO_2PS_2 *– депротонований О,О'-алкілен дитіофосфат;* $C_{15}H_{12}N_2OX$ *– депротонований 3(2'-гідроксифеніл)-5-(4'-заміщений феніл)піразолінат;* $X = –H, –CH_3, –OCH_3$ *та –Cl;* $G = –C(CH_3)_2CH_2CH(CH3)–$*). Проведені дослідження синтезованих сполук за допомогою елементного аналізу (C, H, N, Cl і Sb), бомбардування швидкими атомами, електронних спектральних досліджень, ІЧ-спектроскопії, багатоядерного ЯМР (*^1H, ^{13}C *та* ^{31}P*). На основі одержаних даних розглянуто координацію дитіофосфату та піразолінатів, а також структуру сполук. За результатами тестів* in vitro *встановлено, що синтезовані комплекси мають непогану антибактеріальну та протигрибкову активність. Результати досліджень деяких зразків на активність проти папайського рингпот-вірусу, показали значну антивірусну активність з інгібуванням приблизно 34,30 %.*

Ключові слова: *антибактеріальна активність, антивірусна активність, сурма(III), піразолінати, дитіофосфати.*

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