ORGANOBISMUTHINES CONTAINING AROMATIC HETEROCYCLES: SYNTHESIS AND CHARCTERIZATION

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ABSTRACT

The work presents the synthesis of tertiary bismuthines containing heterocyclic aromatic rings of general formula $(2\text{-}XC_4H_3)_3Bi$ where X = S (**1**); O (**2**) or NMe (**3**). These bismuthines were characterized by IR, Raman, Mass, ^1H, ^{13}C, COSY NMR spectroscopy. Molecular structure of $(2\text{-}C_4H_3O)_3Bi$ (**2**) was determined by X-ray diffraction. Toxicity against larvae of Atremia Salina was determined.

INTRODUCTION

Tertiary bismuthines are little lesser known in comparison to phosphines and arsines [1]. Although there exist a number of reports on phosphines and arsines containing aromatic heterocyclic ring directly attached to P or As respectively [2-5], a few reports are known on the corresponding antimony and bismuth homologues [6-7]. Recently some well characterized stibines containing aromatic heterocycles were reported by our group [8-9]. In early 40s a report has appeared on the synthesis of tris(2-thienyl)bismuthines and tris(2-furyl)bismuthines and characterization was done by elemental analysis only [10,11].

Sidewise bismuth has known for its biological activity and hence its application in medicinal chemistry. A number of organobismuth compounds have been investigated for potential bioactivity. It is the unquestionable antimicrobial activity of some organobismuth compounds at low concentrations, the relatively low human cell cytotoxicity highlights the chemistry of bismuth as an important focus for the development or discovery of new pharmaceutical agents [12-13]. In view of our interest on structural aspects of organoantimony and organobismuth compounds and existence of scanty reports on bismuthines where bismuth is directly attached to an aromatic heterocycle this work was undertaken.

MATERIALS AND METHODS

All the solvents were distilled immediately prior to use. 2-Thienyllithium was purchased from Ahldrich. All the reactions were performed under an atmosphere of oxygen-free, dry nitrogen. Melting points were obtained on a MEL-TEMP II Fisher and are uncorrected. Far IR spectra were recorded in polyethylene on Nicolet –Magna 750 spectrometer. EI and CI mass spectra were recorded on Jeol SX102 double focusing mass spectrometer with reverse geometry using a 6kV Xenon beam (10mA). NMR spectra were collected on Jeol Eclipse 300 (^1H: 300 MHz; ^{13}C: 75 MHz) in chloroform.

X-ray crystallography: Data were collected on a Siemens P4/Pc diffractometer at 293°K using monochromated Mo-Kα radiation (λ = 0.7107 Å). The system used for calculations was Siemens SHELXTL PLUS (PC Version)[14-16] using semi-empirical absorption correction and structure determination was done by direct methods and refinement by a full matrix least squares procedure. The crystallinity of the sample was poor and crystal decayed during collection. Large residual electron density was observed around bismuth atom.

Synthesis of $(2\text{-}C_4H_3S)_3Bi$ (**1**)

A solution of bismuth trichloride (3.22 g, 14.1 mmol) in THF (15 mL) was added dropwise, under a nitrogen atmosphere, to 2-thienyllithium (3.81 g, 42.3 mmol) (1 M in THF) at –20 °C with continuous stirring. The mixture was further stirred for 30 min at room temperature and then quenched with water-ice mixture. After extraction with hexane (3 x 5 mL) and drying over sodium sulfate solvent was removed under vacuum. Slow concentration from chloroform solution yielded the microcrystalline powder. MS (EI) *m/z* (%):, 375 (2.8) $[M\text{-}(2\text{-}SC_4H_3)^+]$, 292 (100) $[M\text{-}(2\text{-}SC_4H_3)^+]$; MS(CI) *m/z* (%): 459 (3.54) $[M^+]$, 375 (95.7) $[M\text{-}(SC_4H_3)^+]$.

Synthesis of $(2\text{-}C_4H_3O)_3Bi$ (**2**)

The compound was synthesized by a similar procedure to **1**. 2-Furyllithium was prepared according to the literature procedure [17]. MS (EI) *m/z* (%): 410(2.12) $[M^+]$, 343(6.4) $[M\text{-}(2\text{-}OC_4H_3)^+]$, 276 (97.8) $[M\text{-}(2\text{-}OC_4H_3)^+]$; MS(CI) *m/z* (%): 411(5.18) $[M^+]$, 343(46.1) $[M\text{-}(OC_4H_3)^+]$, 276 (4.9) $[M\text{-}(2\text{-}OC_4H_3)^+]$.

Synthesis of $(2\text{-}C_4H_3NMe)_3Sb$ (**3**)

The compound was synthesized by a similar procedure [14] to (**1**). 1-Methyl-2-pyrrolyllithium was prepared according to the literature procedure. MS (EI) *m/z* (%): 449(0.7) $[M^+]$, 369 (3.5) [M-

$(C_4H_3NMe)^+$], 289 (59.6) [M-$(2\text{-}C_4H_3NMe)^+$]; MS(CI) *m/z* (%): 450(7.8) [M^+], 369 (21.9) [M-$(C_4H_3NMe)^+$], 289 (7.0) [M-$(2\text{-}C_4H_3NMe)^+$].

Toxicological studies on larvae of Atremia Salina:

The larvae of Atremia Salina were obtained in a 500ml of sea-type water solution (prepared with Instant Ocean Aquatic Systems) with a concentration of 37.5g/L. The eggs of A. Salina were incubated at 25°C for 48 hrs. A stock solution of 20mM in DMSO of these compounds was diluted to 2mM and 1mM in sea type water.

100μ of the larvae solution were placed in a micro plate NUNC with 96 walls to obtain a distribution of 10 larvae/wall and 100μL of stock solution. This last give a total concentration of 1mM and 0.5mM. The cultures were incubated for 24 hr in order to determine the compounds toxicity.

The LC_{50} value was determined according to Reed-Muench (colegate) method and Probit analysis programme. LC_{50} is the lethal concentration with 50% mortality.

RESULTS AND DISCUSSION

The three tertiary bismuthines remain unaffected by water, thus the Bi-C bonds in the above compounds are not hydrolyzed by water alone. These tris(2-heteroaryl) bismuth(III) derivatives behave like other triarylbismuthines and are thermally stable and melt without decomposition. These compounds show very slow degree of decomposition at room temperature in moist atmosphere. The decomposition product could not be characterized because of its insolubility in common solvents.

On the basis of the structure of other tertiary bismuthines [18] a pyramidal structure may be assigned to compound 1-3. m.p., %yield, selected IR and Raman bands data are presented in Table 1. In the far IR spectra and Raman spectra C-Bi vibrations were observed [19] e.g. bands at 619, 565, 466 and 266 cm^{-1} can be assigned to C-Bi vibrations in the far IR spectra of compound (**1**).

Table 1. Elemental analyses and physical properties of triheteroarylstibines and derivatives.

No.	Colour	m.p. (°C)	Yield (%)	Selected far IR (Raman bands)
(1)	white	136-137	55	619,(620),565,(498),466,(220),216
(2)	white	115	49	746,(746),(615),597(599), (256)246,(229)
(3)	light brown	109-110	47	673,(671),604,406,(398),256,(251),220,(221)

EI mass spectral analyses of triheteroarylbismuth derivatives show some common fragmentation pattern. The fragmentation peaks observed for heterocyclic part are not of much importance and are according to those reported in the literature [20]. In the EI mass spectra of tris(2-thienyl)bismuth(III) molecular ion peak could not be observed while for the compound (2) and (3) the molecular ion peak percentage was very low, CI mass spectra were obtained for these compounds to confirm the molecular ion.

^1H and ^{13}C chemical shifts are reported in Table 2. The proton NMR spectra of these compounds show a characteristic pattern of three multiplets in the aromatic region. In all the cases assigning individual protonic signal was based on J_{HH} coupling constant values [21] and was confirmed by COSY.

For 5 membered heterocycle substituted at 2nd position by bismuth, it was observed that H^3 and H^5 are more deshielded comparatively to the parent unsubstituted heterocycle which may be due to the pπ-dπ bonding as reported earlier for phosphines and stibines [2,8]. Four ^{13}C signals were observed for these compounds in the aromatic region. Similarly to proton NMR, C^3 and C^5 carbon show more pronounced shift in comparison to C^4 and C^2 carbons in the ^{13}C NMR spectra

Table 2. ^1H and ^{13}C NMR shifts for tris(2-heteroaryl)bismuthines(III)

Compound	δH^3	δH^4	δH^5	δC^2	δC^3	δC^4	δC^5
				J(in Hz)			
(1) $(C_5H_3S)_3Bi$	7.45 J_{34} (3.3)	7.19 J_{35} (0.84)	7.69 J_{45} (4.68)	145.65	129.30	133.04	137.91
(2) $(C_5H_3O)_3Bi$	6.67 J_{34} (3.3)	6.48 J_{35} (0.90)	7.69 J_{45} (1.8)	125.02	124.49	11.03	147.99
(3) $(C_5H_3NMe)_3Bi$	6.15 J_{34} (3.5)	6.10 J_{35} (1.6)	6.82 J_{45} (2.7)	121.63	122.62	110.34	126.12
	δ_{Me} 3.56			δ_{Me} 38.34			

*Values of δ (ppm) for unsubstituted heterocycles are: thiophene (H2 7.18, H3 6.99), furan (H^2 7.29, H^3 6.24), 1-Methylpyrrole (H^2 6.74, H^3 6.28)

To best of our knowledge this appears to be the first report on the molecular structure of bismuthine containing aromatic heterocycles. X-ray diffraction parameters and selected bond lengths and angles for compound **2** are listed in Table 3 and 4 respectively. The molecular structure and unit cell packing are shown in Figure 1 and 2 respectively.

Table 3. Selected bond lengths (Å) and bond angles (°) for Compound (2)

Bi(1)-C(10)	2.20(3)	C(10)-Bi(1)-C(6)	90.0(13)
Bi(1)-C(2)	2.22(2)	C(10)-Bi(1)-C(2)	92.4(9)
Bi(1)-C(6)	2.21(3)	C(6)-Bi(1)-C(2)	91.3(9)
O(1)-C(2)	1.35(3)	O(3)-C(10)	1.33(3)
O(3)-C(13)	1.35(3)	O(2)-C(9)	1.46(4)
O(1)-C(5)	1.36(4)	O(2)-C(6)	1.32(4)

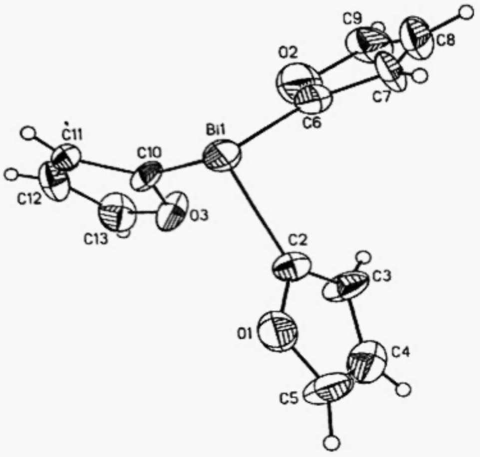

Figure 1 Moecular structure of tris(2-furyl)bismuthine (2)

Trifurylbismuth has pyramidal configuration about the bismuth atom as in triphenylbismuth [22] with a stereochemically active lone pair defining the fourth position. The average C-Bi-C is 91.2° which is slightly smaller than found in Ph_3Bi (93.6°) and which is significantly smaller than the tetrahedral angle suggesting the poor percentage s-character for the orbitals of bismuth. This is not altogether unexpected in view of high stability of the 6s orbital. The molecule as a whole possesses no symmetry because of unequal rotation of furyl groups about their respective Bi-C bonds.

The mean Bi-C bond length is 2.21Å, which is slightly shorter than that found in other bismuthines containing aromatic ring e.g. 2.23(3)Å in Ph_3Bi[223]; 2.24(3) Å in $(4\text{-}Me_2N\text{-}C_6H_4)_3Bi$[24]; 2.26(8)Å in $(2,6\text{-}F_2C_6H_3)_3Bi$[25] and 2.26(2)Å in $(2,4,6\text{-mesitil})_3Bi$[26]. This observation also supports a more important $p\pi$-$d\pi$ interaction in these bismuthines containing aromatic heterocyclic rings thus shortening of bond. Similar results were reported for stibines containing these groups. There exists a very weak intermolecular interaction between the central metal bismuth and two oxygen atoms of different furyl groups of another molecule The Bi....O bond distance is 3.53 Å, which is close to the sum of Van der Waals radii (3.60 Å).

The toxicity of these compounds on larvae of Artemia Salina, LC_{50} values were determined. For tris (2-theinyl) bismuth(III). The LC_{50} value was >1000 and no toxic activity was observed even at high concentration (1000 μM): its effect on larvae was insignificant. On the other hand, tris (2-furyl)bismuth(III) exhibited high toxicity with a LC_{50} value of 99 while tris (N–Methyl pyrrolyl) bismuth showed an intermediate toxicity (LC_{50} 598).

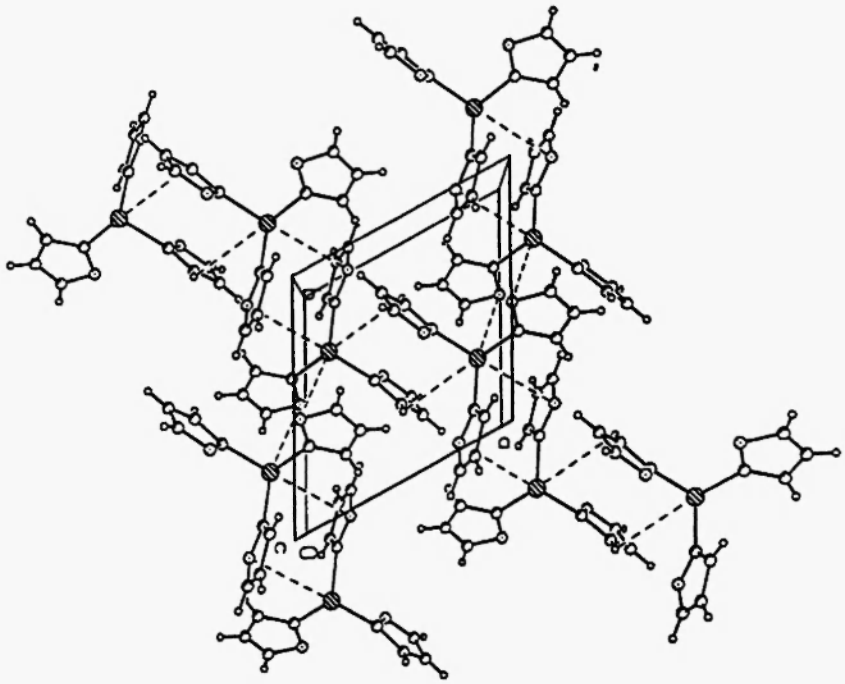

Figure 2 Unit cell of tris(2-furyl)bismuthine (2)

Table 5. Crystal data for compound (2)

Compound $(2\text{-}C_4H_3O)_3Bi$ (2)			
Empirical formula	$C_{12}H_9O_3Bi$	Formula weight	410.17
Crystal system	Triclinic	Crystal size (mm)	0.36 x 0.20 x 0.16
Space group	P⊏	a (Å)	8.533(1)
b (Å)	8.782(1)	c (Å)	8.901(1)
α (°)	88.471(1)	β (°)	85.129(1)
γ (°)	63.078(1)	Z	2
μ[MoKα] (mm^{-1})	14.866	V (Å^3)	592.52(2)
2θ (°)	2.3 to 25.0	D_{calc} (g cm^{-3})	2.299
Reflections collected	2194	Unique reflections	2046
R_{int}	0.050	$R[I>2\sigma(I)]$	0.080
Refinement method	Full matrix least square	Method of solution	SHELXS-97
Extinction Coeffcient	0.0026(2)	Max/min $\Delta\rho$ (e Å^{-3})	3.24 / -4.11
S [goodness-of-fit]	1.00	Deposition number	CCDC 171426

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