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Synthesis, crystal structures and in vitro antitumor activities of some organoantimony arylhydroxamates

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Abstract

A series of novel organoantimony arylhydroxamates with the formulae $[Ar_3SbL_2]^-[HNEt_3]^+$ (LH = arylhydroxamic acid; Ar = C_6H_5, 4-$CH_3C_6H_4$, 3-$CH_3C_6H_4$, 4-ClC_6H_4, 4-FC_6H_4) and $(4\text{-}CH_3C_6H_4)_4SbL$ were synthesized and characterized by elemental analysis, IR, ^1H NMR and mass spectroscopy. The crystal structures of $(4\text{-}CH_3C_6H_4)_4SbL$ and $[Ph_3SbL_2]^-[HNEt_3]^+$ were determined by X-ray diffraction. The in vitro antitumor activities of all compounds against three human cancer cells are reported.

Keywords: Organoantimony; Arylhydroxamic acid; Crystal structures; Antitumor activity

1. Introduction

A great number of references describing synthesis and biological activities of organoantimony carboxylates with the general formula $Ar_nSbX_{(5-n)}$ ($n = 3, 4$; X = carboxylate) have already appeared in the literature [1–8]. However, the published data on the antitumor activity of these compounds are relatively limitied [9,10]. In recent years some organoantimony (III) derivatives have been reported to exhibit marginal antitumor activities [11–14], at the same time we have found that some organoantimony (V) derivatives exhibit high in vitro antitumor activity against human tumor cell lines and often higher than cisplatin [15–17]. Arylhydroxamic acids are important ligands, because they are often included in the active sites of some biological enzymes [18] and have a wide range of biological activity, including antitumor activity [19–22]. Therefore, we have synthesized a series of arylantimony derivatives of arylhydroxamic acid in order to investigate whether including arylhydroxamate groups in organoantimony (V) derivatives can improve their antitumor properties. In addition, we are also interested in studying the nature of bonding and the structure of these compounds.

2. Results and discussion

2.1. Preparations

The title compounds are synthesized under anhydrous condition. All compounds are white crystals and stable under ordinary conditions. They are soluble in organic solvents such as THF, dichloromethane, chloroform, acetone, methanol and dimethyl sulfoxide, but not soluble in benzene, hexane and petroleum ether. The general reaction is shown as follows:

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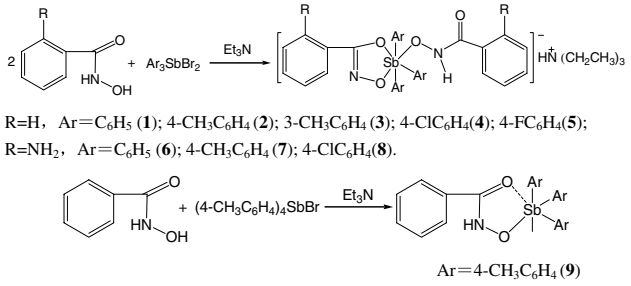

R=H, Ar=C_6H_5 (**1**); 4-$CH_3C_6H_4$ (**2**); 3-$CH_3C_6H_4$ (**3**); 4-ClC_6H_4(**4**); 4-FC_6H_4(**5**);
R=NH_2, Ar=C_6H_5 (**6**); 4-$CH_3C_6H_4$ (**7**); 4-ClC_6H_4(**8**).

Ar=4-$CH_3C_6H_4$ (**9**)

2.2. IR

The IR spectra of these compounds have been recorded in the range of 4000–400 cm^{-1}. The important IR data of the free ligands and the title compounds are summarized in Table 1. The IR spectroscopic data provide further support for the molecular constitution of the title compounds. In majority of organoantimony (V) compounds the antimony has generally a coordination number of five. Because the vacant 5d orbital of antimony atom can accept lone electron pairs of ligands, in some cases the antimony may have a coordination number of six [23,24] or seven [9,25]. When there are interactions between the antimony atom and the carbonyl oxygen atom of the hydroxamate group, the absorption vibration frequencies [ν(C=O)] decrease. In the title compounds, the very strong stretching vibrations ν(C=O) is displaced to lower frequency between 1615 and 1628 cm^{-1}, so we can assume that there are coordination interactions between the antimony atom and the carbonyl oxygen atom of the hydroxamate group (see the crystal structures of compounds **1** and **9**). In addition, the frequencies of Sb–C deformations appear between 453 and 504 cm^{-1} which is consistent with the literature [6].

2.3. ^1H NMR

The ^1H NMR data of the title compounds are listed in Table 2. The chemical shifts of the protons of CH_3 appear between 0.92 and 1.05 ppm. The protons of CH_2 appear between 2.61 and 2.82 ppm. The protons of Ar show a complex multiplet between 6.51 and 8.00 ppm. The amino hydrogen is so active that its displacement cannot be assigned. All the protons in the compounds have been identified and the total number of protons calculated from the integration curve tallies with what was expected from the molecular formula.

Table 1
IR data of the compounds (cm^{-1})

Compound	ν(C=O)	ν(N–O)	ν(Sb–C)
1	1622	907	460
2	1622	906	487
3	1629	909	471
4	1624	905	489
5	1628	907	510
6	1619	907	464
7	1621	907	485
8	1615	907	491
9	1595	907	489
PhCONHOH	1639	898	
2-$NH_2C_6H_4$CONHOH	1632	903	

2.4. Mass spectra

The main mass spectra data of compound **1** are listed in Table 3. Although there is no molecular ion peak, the fragment ions found are in agreement with the expected structure of the compound. The $PhCO^+$ (m/z = 105) is the base peak. The breakdown of Sb–O and Sb–C bonds are the principle breakdown patterns for the compound.

2.5. Crystal structures

2.5.1. Crystal structure of compound *1*

The colorless crystals of compound **1** were obtained from CH_2Cl_2–petroleum ether. One of the approximate dimensions $0.18 \times 0.14 \times 0.10$ mm was mounted in a glass capillary and used for data collection. Fig. 1 shows the molecular structure of compound **1** and gives the atom numbering scheme. The selected bond distances and angles are listed in Table 4.

Hydroxamates are versatile ligands which can be either unidentate or bidentate. Antimony–oxygen bond lengths in organoantimony compounds are extremely

Table 2
^1H NMR data of the compounds

Compound	Ar	CH_2	CH_3
1	7.31–8.00 (25 H, m)	2.70–2.78 (6 H, q)	0.99–1.04 (9 H, t)
2	7.15–7.96 (22 H, m) 2.32 (9 H, s)	2.67–2.74 (6 H, q)	0.96–1.01 (9 H, t)
3	7.15–7.95 (22 H, m) 2.27 (9 H, s)	2.72–2.80 (6 H, q)	0.98–1.03 (9 H, t)
4	7.33–7.96 (22 H, m)	2.75–2.82 (6 H, q)	0.99–1.03 (9 H, t)
5	7.04–7.97 (22 H, m)	2.74–2.81 (6 H, q)	0.98–1.03 (9 H, t)
6	6.51–7.90 (23 H, m)	2.71–2.78 (6 H, q)	1.00–1.05 (9 H, t)
7	6.64–7.90 (20 H, m) 2.37 (9 H, s)	2.61–2.69 (6 H, q)	0.98–1.03 (9 H, t)
8	6.52–7.81 (20 H, m)	2.70–2.77 (6 H, q)	0.92–0.97 (9 H, t)
9	7.03–7.45(21 H, m) 2.28 (12 H, s)		