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Synthesis and Biological Activity of Some Triarylantimony Dipyrazolecarboxylates

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ABSTRACT: *A series of triarylantimony dipyrazolecarboxylates was synthesized by the reaction of pyrazolecarboxylic acid with triarylantimony dibromides in the presence of potassium hydroxide. The structures of the title compounds were confirmed by elemental analysis, ^1H NMR, IR, and mass spectra. Some of these compounds were found to possess antibacterial activity.* © 2002 Wiley Periodicals, Inc. Heteroatom Chem 13:299–301, 2002; Published online in Wiley Interscience (www.interscience.wiley.com). DOI 10.1002/hc.10033

INTRODUCTION

Triorganoantimony dicarboxylates of the type $R_3Sb(O_2CR')_2$ have been widely studied because of their range of applications, such as biological and catalytic activity [1–4]. It is well known that pyrazole derivatives have a broad spectrum of biological activities [5–6]. However, studies of the derivatives of pyrazole carboxylic acids with main group metalloids are relatively few. In order to investigate their biological activity we describe in this paper the synthesis, characterization, and antibacterial activity of a series of triarylantimony dicarboxylates, which contain two active centers, namely the triarylantimony(V) moiety and the pyrazolecarboxylate group (Fig. 1).

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RESULTS AND DISCUSSION

The title compounds were synthesized as shown in Eq. (1). These triarylantimony dipyrazolecarboxylates have been successfully synthesized by stirring 1:1 equivalent of triarylantimony(V) dibromides and the ligand in the presence of potassium hydroxide in toluene under mild condition. When each reaction had been completed, the products were easily purified by recrystallization from CH_2Cl_2 and petroleum ether. Most of the complexes are white crystalline solids (only compound **3** is a colorless adhesive oil), which are soluble in methanol, chloroform, THF, benzene, and toluene, and insoluble in petroleum ether and water. They are unaffected by atmospheric moisture, showing no decomposition over a period of several weeks. The yields and elemental analyses of the compounds are given in Table 1.

$$Ar_3SbBr_2 + 2\,RCO_2H \xrightarrow{\text{base}} Ar_3Sb(O_2CR)_2 \qquad (1)$$

IR

The infrared spectra of these compounds were recorded over the range 400–4000 cm^{-1}. Tentative assignments have been made on the basis of earlier publications and the important data are listed in Table 2. The infrared spectra of all of the organoantimony(V) compounds do not show a strong band in the 3500–3300 cm^{-1} region, due to ν(OH), indicating deprotonation and coordination of the carboxylate group.

The vacant 5d orbital of the antimony atom tends towards high coordination with ligands containing lone electron pairs. The IR stretching

TABLE 1 Physical Constants of Products

Compound	R^1	R^2	Ar	Yield (%)	m.p. (°C)	Elemental Analyses (%) Found (Calcd.) C	H	N
1	Ph	OPh	4-$CH_3C_6H_4$	97.0	234–236	66.93 (67.29)	4.63 (4.83)	5.37 (5.71)
2	Ph	OPh	3-$CH_3C_6H_4$	71.3	194–198	67.96 (67.29)	4.75 (4.83)	4.94 (5.71)
3	Ph	OPh	2-$CH_3C_6H_4$	79.5	*	67.78 (67.29)	5.13 (4.83)	5.03 (5.71)
4	Ph	OPh	4-ClC_6H_4	69.2	249–252	59.58 (59.88)	3.92 (3.67)	5.48 (5.37)
5	Me	Cl	Ph	22.2	286–288	50.16 (51.46)	4.22 (3.89)	7.01 (8.00)

*Adhesive oil.

frequencies of the carboxylate groups are very important for the determination of their structures: when there are interactions between the carbonyl oxygen atoms of the carboxylate groups and the antimony atom, the asymmetric absorption vibration frequencies $\nu_{asy}(CO_2)$ of carboxylate groups decrease and the symmetric absorption frequencies $\nu_{sym}(CO_2)$ increase. Their difference $[\Delta\nu(CO_2)]$ therefore decreases [1,7,8]. In the IR spectra of the title compounds the carboxylate bands are observed in the characteristic regions for $\nu_{asy}(CO_2)$ between 1640 and 1591 cm^{-1} and $\nu_{sym}(CO_2)$ between 1352 and 1327 cm^{-1} (see Table 2). On the basis of the difference of $\Delta\nu(CO_2)$ (between 302 and 241 cm^{-1}) values, these compounds can be divided into two classes: compounds **1, 2**, and **4** show relatively low $\Delta\nu(CO_2)$ values (between 243 and 241 cm^{-1}), while compounds **3** and **5** show high values (292, 302 cm^{-1}). We can assume that in compounds **1**, **2**, and **4** there are interactions between the carbonyl oxygen atoms of the carboxylate groups and the antimony atom, while in other compounds there are weaker interactions or no interactions between the carbonyl oxygen atoms of the carboxylate groups and the antimony atom [2]. When Ar is 2-$CH_3C_6H_4$, compound **3** shows a relatively high $\Delta\nu(CO_2)$ value, and this may be attributed to the steric effect of the *o*-methyl group which weakens the Sb—C(Ph) bond and decreases the capacity of the antimony atom to accept lone electron pairs from the carbonyl oxygen atoms. In addition, the frequencies ν_{asy}[Sb—C(Ph)] appear between 478 and 502 cm^{-1}; this is consistent with literature values [2,7].

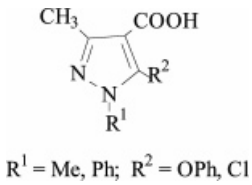

FIGURE 1 Structure of the ligands.

^1H NMR

The chemical shifts of various protons in the compounds are listed in Table 3. The conclusions drawn from the ^1H NMR spectral studies lend further support to the mode of bonding discussed above. The absence of signals between 10.00 and 13.00 ppm because of the CO(OH) proton tends to confirm the deprotonation of the carboxylic group of the ligands. The signals of the aromatic protons of organoantimony pyrazolecarboxylates are complex and are observed between 6.35 and 8.06 ppm. All protons in the compounds have been identified and agree with those calculated from the expected molecular formula.

MS

The mass spectra of compound **5** are recorded. The molecular ion peak is not observed. The Ph—Ph (*m*/*z* 154) is the base peak. Decarboxylation and dephenylation from the antimony atom are the two main breakdown patterns for this compound [e.g. (*m*/*z*, relative intensity): $Ph_3SbO_2CR^+$ (527, 1), Ph_3Sb^+ (352, 1), Ph_2Sb^+ (275, 5), $PhSb^+$ (198, 28), $Ph—Ph^+$ (154, 100), and Sb^+ (121, 5)].

Antibacterial Activity

Compounds **1–4** were evaluated for their antibacterial activity by the usual agar plate technique [9] against the bacteria *Gibbereila zeae, Alternaria*

TABLE 2 The Important IR Data of the Compounds (cm^{-1})

Compound	ν_{asy} (CO_2)	ν_{sym} (CO_2)	$\Delta\nu$ (CO_2)	ν_{asy} [Sb—C(Ph)]
1	1595	1352	243	486
2	1591	1350	241	502
3	1640	1338	302	489
4	1593	1352	241	488
5	1619	1327	292	478

TABLE 3 ^{1}H NMR Data of Products (ppm)

Compound	*Ar*	*R^1*	*R^2*	*$CH_3C{=}N$*
1	6.65–7.47 (12H, m), 2.34 (Me, 9H, s)	6.65–7.47 (10H, m)	6.65–7.47 (10H, m)	2.31 (6H, s)
2	6.60–7.58 (12H, m), 2.30 (Me, 9H, s)	6.60–7.58 (10H, m)	6.60–7.58 (10H, ,m)	2.34 (6H, s)
3	6.35–7.87 (12H, m), 2.34 (Me, 9H, s)	6.35–7.87 (10H, m)	6.35–7.87 (10H, m)	2.24 (6H, s)
4	6.65–7.48 (12H, m)	6.65–7.48 (10H, m)	6.65–7.48 (10H, m)	2.39 (6H, s)
5	7.45–8.06 (15H, s)	3.70 (6H, s)	–	2.24 (6H, s)

solani, Rhizoctonia solani, and Physolospora piricola at 50 ppm concentration in acetone as the solvent in vitro. The results of the antibacterial activity are given in Table 4. Preliminary tests indicated that these compounds exhibit, to a certain extent, antibacterial activity against the four bacteria. The data in Table 4 show that the activity of triarylantimony dipyrazolecarboxylates is affected by the nature of the aryl group: for example, compounds **3** (Ar = 2-$CH_3C_6H_4$) and **4** (Ar = 4-ClC_6H_4) exhibit a relatively lower antibacterial activity.

EXPERIMENTAL

Material and Methods

All operations were performed in an atmosphere of dry argon using Schlenk and vacuum techniques. All solvents were dried by standard methods and distilled prior to use. Elemental analyses were determined on a Yanaco CHN Corder MT-3 elemental analyzer. IR spectra were recorded on a Bruker Equinox 55 spectrometer in KBr discs. ^{1}H NMR spectra were measured on a Bruker AC-200 spectrometer in $CDCl_3$ solution with TMS as the internal standard. Mass spectra were recorded on a HP-5988A mass spectrometer at 70 eV with the temperature of ionization being 200°C. Pyrazolecarboxylic acid was prepared according to earlier references [5,10]. Triarylantimony dibromides were synthesized by standard methods [11].

TABLE 4 Antibacterial Activity of Selected Compounds

	Inhibition Ratio (%)			
Compound	Gibberelia zeae	Alternia solani	Rhizoctonia solani	Physolospora piricola
1	40.0	33.3	31.4	66.7
2	48.0	40.0	40.0	29.2
3	28.0	13.3	28.6	12.5
4	28.0	20.0	25.7	12.5

Synthesis of the Organoantimony Complexes

Pyrazolecarboxylic acid (1 mmol) and potassium hydroxide (0.056 g, 1 mmol) were stirred in 20 ml of toluene at room temperature for 4 h to prepare the potassium salt. The triarylantimony dibromides (0.5 mmol) were added to the suspension of the potassium salt of pyrazolecarboxylic acid in toluene. The mixture was stirred overnight at room temperature. Then the solvent was evaporated under reduced pressure. The obtained solid (except compound **3**) was recrystallized from CH_2Cl_2/petroleum ether (1:3, v/v) and dried in vacuo.

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