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Synthesis, Structural Characterization and *in vitro* Antitumour Properties of Triorganoantimony(V) Disalicylates: Crystal and Molecular Structures of [5-Y-2-(HO)-$C_6H_3COO]_2SbMe_3$ (Y = H, Me, MeO)

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Triorganoantimony(V) salicylates, [5-Y-2-(HO)-$C_6H_3COO]_2SbR_3$ (R = Me, Ph; Y = H, Me, MeO), were obtained by reacting R_3SbCl_2 with the appropriate sodium salt. The compounds have been characterized by IR, MS, ^1H and ^{13}C NMR spectroscopy. The molecular structure of the three substituted trimethylantimony(V) disalicylates has been determined by X-ray diffraction. The salicylate ligands are mono-coordinated to antimony through an oxygen atom of each carboxylate, leading to a trigonal bipyramidal geometry, with the antimony-methyl groups in equatorial positions and the oxygen atoms in axial positions. The trimethylantimony compounds tested *in vitro* against a series of human tumour cell lines were found to be inactive.

Keywords: organoantimony; carboxylate; crystal structure; antitumour

INTRODUCTION

Metal compounds have received much attention in recent years as potential antitumour agents.[1,2] Platinum compounds occupy a key position owing to their clinical use, but numerous main-group metal derivatives have also been screened for potential anticancer activity. Among these, organotin(IV) carboxylates have been most extensively investigated and several dibutyltin(IV) salicylates and substituted salicylates were reported to exhibit *in vitro* antitumour activity against human tumour cell lines, often higher than cisplatin.[3–7] In contrast, organoantimony compounds have received much less attention as potential antitumour drugs.[1] Only recently some diphenylantimony(III) derivatives of dithiophosphorus ligands have been reported to exhibit marginal *in vitro* and *in vivo* antitumour activity (Ehrlich ascites tumour, P388 leukemia).[8–12] Therefore, it was thought worthwhile to explore whether other organoantimony compounds exhibit antitumour properties, and in particular to study the effect of substituting the organotin(IV) moiety for an organoantimony group. We report in this paper the synthesis of some substituted triorganoantimony(V) disalicylates, [5-Y-2-(HO)-$C_6H_3COO]_2SbR_3$ (R = Me, Ph; Y = H, Me, MeO), their structural characterization, including the molecular structures of the three trimethylantimony(V) derivatives determined by X-ray crystallography, and the *in vitro* antitumour activity of the trimethylantimony compounds against MCF-7 and EVSA-T (breast cancers), WiDr (a colon carcinoma), IGROV (an ovarian cancer), M19 MEL (a melanoma) and A498 (a renal cancer) was determined.

EXPERIMENTAL

Chemicals and instruments

Ph_3SbCl_2 and Me_3SbCl_2 were prepared according to literature methods.[13,14] Salicylic acid and its 5-substituted derivatives were commercial rea-

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gents and were used as received. IR spectra (4000–200 cm^{-1}) were recorded on a Perkin–Elmer 283B instrument, using KBr pellets. Electron impact (EI) Mass spectra (70 eV) were obtained using a Hewlett-Packard MS-598 apparatus. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solutions using a Bruker AC250 spectrometer operating at 250.13 MHz proton frequency, equipped with a QNP (^{1}H, ^{13}C, ^{19}F, ^{119}Sn) probe head.

General procedure for the synthesis of [5-Y-2-(HO)-$C_6H_3COO]_2SbR_3$

Stoichiometric amounts of sodium methoxide (MeONa) and carboxylic acid (1:1 molar ratio) were stirred in methanol (MeOH) for 1 h, after which 2 equivalents of R_3SbCl_2 were added. The reaction mixture was refluxed for 6 h and the solvent was removed in vacuum to dryness. The resulting solid was mixed with 100 ml $CHCl_3$, and the insoluble NaCl filtered off. The clear filtrate was concentrated in vacuum to *ca* 10–15 ml. Upon addition of ethanol or diethyl ether the triorganoantimony(V) salicylates were deposited as white crystaline solids. Details concerning the synthesis are presented in Table 1.

X-Ray crystallography for [5-Y-2-(HO)-$C_6H_3COO]_2SbMe_3$

Intensity data for colourless crystals were measured at room temperature on a Rigaku AFC6R diffractometer fitted with MoKα radiation (graphite monochromator, $\lambda = 0.71073$ Å); in each case the ω:2θ scan technique was employed and θ_{max} was 27.5°. No decomposition of the crystals occurred during their respective data collections and the data sets were corrected for Lorentz and polarization effects,[15] and for absorption employing an empirical procedure.[16] Crystal data are summarized in Table 2. The structures were solved by direct methods[17] and each was refined by a full-matrix least-squares procedure based on *F*.[15] Non-hydrogen atoms were refined with anisotropic thermal parameters and carbon-bound hydrogen atoms were included in the models at their calculated positions. The OH atoms were located from a difference map for the Y = Me and MeO compounds but their positions were not refined; the OH atoms were not located in the analysis of the Y = H compound. The refinements were continued until convergence, and final refinement details are collected in Table 2. The systematic absences in the data set for the Y = H compound were consistent with the monoclinic

Table 1 Preparation of [5-Y-2-(HO)-$C_6H_3COO]_2SbR_3$

Starting materials					
R_3SbCl_2 [g, (mmol)]	5-Y-2-(HO)$C_6H_3CO_2H$ MeONa [g, (mmol)]	Product	Yield [g (%)]	M.p. (°C)	Recrystallization solvent
R = Ph	Y = H	[2-(HO)-$C_6H_4COO]_2SbPh_3$	1.86	200–202	$CHCl_3$–EtOH
1.41 (0.33)	0.92 (0.66)		(89)		
	0.36 (0.66)				
R = Ph	Y = Me	[5-Me-2-(HO)-$C_6H_3COO]_2SbPh_3$	1.29	185–187	$CHCl_3$–EtOH
1.06 (0.25)	0.76 (0.50)		(79)		
	0.27 (0.50)				
R = Ph	Y = MeO	[5-MeO-2-(HO)-$C_6H_3COO]_2SbPh_3$	1.65	182–184	$CHCl_3$–EtOH
1.06 (0.25)	0.84 (0.50)		(96)		
	0.27 (0.50)				
R = Me	Y = H	[2-(HO)-$C_6H_3COO]_2SbMe_3$	1.50	123–124	EtOH–Et_2O
0.95 (0.40)	1.10 (0.80)		(85)		
	0.43 (0.80)				
R = Me	Y = Me	[5-Me-2-(HO)-$C_6H_3COO]_2SbMe_3$	1.25	160–162	$CHCl_3$–Et_2O
0.79 (0.33)	1.01 (0.66)		(80)		
	0.36 (0.66)				
R = Me	Y = MwO	[5-MeO-2-(HO)-$C_6H_3COO]_2SbMe_3$	1.71	202–204	$CHCl_3$–EtOH
0.95 (0.40)	1.34 (0.80)		(85)		
	0.43 (0.80)				

Table 2 Crystallographic data for $[5\text{-Y-2-(HO)-C}_6\text{H}_3\text{COO}]_2\text{SbMe}_3$

	Compound		
	Y = H	Y = Me	Y = MeO
Formula	$C_{17}H_{19}O_6Sb$	$C_{19}H_{23}O_6Sb$	$C_{19}H_{23}O_8Sb$
Mol. wt	441.1	469.1	501.1
Crystal system	monoclinic	monoclinic	monoclinic
Space group	*Cc*	$P2_1/n$	$P2_1/c$
a (Å)	17.732(2)	10.196(2)	15.079(3)
b (Å)	7.957(2)	13.479(2)	10.314(4)
c (Å)	12.665(2)	14.824(3)	12.865(7)
β (deg)	97.72(1)	106.13(2)	90.52(3)
V (Å^3)	1770.8(6)	1957.2(7)	2000(2)
Z	4	4	4
D_c (g cm^{-3})	1.654	1.592	1.663
F(000)	880	944	1008
Crystal size (mm^3)	0.05 × 0.18 × 0.29	0.24 × 0.32 × 0.40	0.06 × 0.32 × 0.40
μ (cm^{-1})	15.84	14.38	14.20
Transmission factors	0.936–1.024	0.889–1.053	0.889–1.057
No. of data collected	2340	5149	5255
No. of unique data	2266	4889	5043
No. of unique reflections used with $I \geq 3.0\,\sigma(I)$	1873	3166	2995
R	0.027	0.035	0.037
R_w	0.030	0.037	0.036
Residual ρ_{max} (e Å^3)	0.50	0.41	0.77

space groups *Cc* and *C*2/*c*. The subsequent refinement confirmed the choice of the non-centrosymmetric space group, a choice supported by the distribution of *e*-statistics; the absolute configuration was determined by refining the inverted structure and comparing the residuals. Final fractional atomic coordinates for the non-hydrogen atoms are listed in Tables 3–5 and the numbering schemes employed are shown in Figs 1–3, which were drawn with ORTEP.[18] Data manipulations were performed with the teXsan programme[15] installed on an Iris Indigo workstation. Other crystallographic details, comprising thermal parameters, H-atom parameters, all bond distances and angles, and tables of observed and calculated structure factors, are available on request (E.R.T.T.).

RESULTS AND DISCUSSION

The title compounds were obtained by reacting triorganoantimony(V) dichlorides with the appropriate sodium salicylates (prepared *in situ* from sodium methoxide and the free acid) according to Eqn [1].

$$2\,\text{MeONa} + 2[5\text{-Y-2-(HO)-C}_6\text{H}_3\text{COOH}] \xrightarrow{-2\text{MeOH}} 2[5\text{-Y-2-(HO)-C}_6\text{H}_3\text{COONa}] \xrightarrow[-2\text{NaCl}]{+\text{R}_3\text{SbCl}_2} [5\text{-Y-2-(HO)-C}_6\text{H}_3\text{COO}]_2\text{SbR}_3 \quad [1]$$

All the compounds are white crystalline solids, readily soluble in chloroform. The trimethylantimony(V) derivatives are also soluble in ethanol, and do not precipitate when water is added to the ethanolic solution. Preparative details, melting points and solvents used for recrystallization are given in Table 1.

The compounds were characterized by infrared, mass spectrometry and NMR (^{1}H and ^{13}C). The molecular structures of the trimethylantimony(V) derivatives were determined by X-ray diffraction.

The absorption bands in the infrared spectra of organoantimony(V) salicylates (Table 6) were assigned by comparison with the spectra of starting materials and literature data.[19–23] All compounds showed strong absorption bands in the

Table 3 Fractional atomic coordinates for $[2\text{-}(HO)\text{-}C_6H_4COO]_2SbMe_3$

Atom	*x*	*y*	*z*
Sb	0.4388(—)	0.07361(5)	0.7319(—)
O(11)	0.4933(3)	0.2479(6)	0.6436(4)
O(12)	0.4913(3)	0.4465(7)	0.7641(5)
O(13)	0.5695(4)	0.7087(8)	0.7552(5)
O(21)	0.3987(3)	−0.1196(7)	0.8214(4)
O(22)	0.2936(3)	−0.1565(8)	0.7061(4)
O(23)	0.1975(3)	−0.3775(7)	0.7402(4)
C(1)	0.3452(4)	0.2190(11)	0.7429(8)
C(2)	0.4383(5)	−0.0734(10)	0.5992(6)
C(3)	0.5287(4)	0.0794(10)	0.8507(6)
C(11)	0.5144(4)	0.3896(9)	0.6827(6)
C(12)	0.5688(4)	0.4877(9)	0.6291(6)
C(13)	0.5943(5)	0.6430(10)	0.6687(7)
C(14)	0.6440(4)	0.7338(10)	0.6173(7)
C(15)	0.6696(5)	0.6679(12)	0.5301(7)
C(16)	0.6466(5)	0.5160(13)	0.4900(7)
C(17)	0.5981(6)	0.4254(10)	0.5413(8)
C(21)	0.3348(4)	−0.1988(9)	0.7876(6)
C(22)	0.3137(4)	−0.3372(8)	0.8526(6)
C(23)	0.2460(4)	−0.4214(9)	0.8255(5)
C(24)	0.2262(4)	−0.5526(9)	0.8873(6)
C(25)	0.2739(5)	−0.5975(10)	0.9754(7)
C(26)	0.3408(5)	−0.5139(10)	1.0055(6)
C(27)	0.3605(4)	−0.3855(9)	0.9434(6)

1660–1580 and 1390–1340 cm^{-1} regions, due to stretching vibrations of the carboxyl groups. The ν(C—O) bands are shifted to higher wavenumbers, indicating a single bond between each salicylate group and antimony through one oxygen of the COO^- group. This correlates with the appearance of new bands in the 400–300 cm^{-1} region which were assigned to Sb—O stretching vibrations. Moreover, the $\Delta\nu = [\nu(C{=}O) - \nu(C{-}O)]$ values are higher than 200 cm^{-1}, confirming monodentate coordination of the carboxylate ligands.[24] However, weak intramolecular Sb···O=C interactions, as revealed by an X-ray crystal structure of $(CH_3COO)_2SbPh_3$,[25] cannot be ruled out on this basis only.

For the trimethylantimony(V) derivatives, a medium to strong band at *ca* 870–860 cm^{-1} was assigned to the rocking vibration of the Me_3Sb fragment, and only one band of medium intensity (*ca* 600–580 cm^{-1}) was observed, assigned to the SbC_3 asymmetric stretch. This is consistent with the expected planar arrangement of the SbC_3 moiety, in a highly symmetric D_{3h} point group, in which the symmetric SbC_3 stretching frequency is IR-inactive.[23]

On the basis of infrared data, a trigonal bipyramidal configuration (with oxygen atoms in axial positions) can be considered for the trimethylantimony(V) salicylates. For the triphenylantimony(V) analogues a similar coordination polyhedron around the central antimony atom can be envisaged. However, the coupling between Sb—Ph stretching and phenyl ring vibrations results in the breakdown of the local symmetry;[21,22] accordingly, two bands of medium intensity (290 and 240 cm^{-1}) are assigned to asymmetric and symmetric SbC_3 stretching vibrations.

In the 70 eV EI mass spectra (Table 7) the molecular ion cannot be observed, but all compounds display a fragment ion resulting from the loss of one salicylate moiety, i.e. $Y(HO)C_6H_3COOSbR_3^+$. For the trimethylantimony(V) salicylates the base peak is always a non-metal ion resulting from the salicylate ligand, while for the triphenylantimony(V) derivatives the base peak is either $PhSb^+$ or Ph_2^+.

The ^1H and ^{13}C NMR data are listed in Tables 8 and 9. The assignment of signals was made by

Table 4 Fractional atomic coordinates for $[5\text{-}Me\text{-}2\text{-}(HO)\text{-}C_6H_3COO]_2SbMe_3$

Atom	*x*	*y*	*z*
Sb	0.25590(3)	0.01725(2)	0.16174(2)
O(11)	0.0908(3)	−0.0817(2)	0.1410(2)
O(12)	0.2188(3)	−0.2072(2)	0.1236(3)
O(13)	0.1053(4)	−0.3689(2)	0.0531(3)
O(21)	0.3905(3)	0.1365(2)	0.1799(2)
O(22)	0.5687(3)	0.0450(3)	0.1795(3)
O(23)	0.7867(3)	0.1292(3)	0.1681(2)
C(1)	0.1167(5)	0.1271(4)	0.1647(4)
C(2)	0.2851(5)	−0.0170(4)	0.0337(4)
C(3)	0.3636(5)	−0.0526(4)	0.2832(3)
C(11)	0.1069(5)	−0.1725(3)	0.1221(3)
C(12)	−0.0171(4)	−0.2341(3)	0.0959(3)
C(13)	−0.0104(5)	−0.3293(3)	0.0623(3)
C(14)	−0.1283(6)	−0.3846(3)	0.0362(3)
C(15)	−0.2467(5)	−0.3469(4)	0.0457(3)
C(16)	−0.2564(4)	−0.2541(3)	0.0804(3)
C(16′)	−0.3866(5)	−0.2161(4)	0.0928(4)
C(17)	−0.1389(4)	−0.1981(3)	0.1056(3)
C(21)	0.5141(4)	0.1262(3)	0.1765(3)
C(22)	0.5840(4)	0.2176(3)	0.1663(3)
C(23)	0.7172(4)	0.2148(4)	0.1611(3)
C(24)	0.7798(5)	0.3012(5)	0.1475(4)
C(25)	0.7146(6)	0.3882(5)	0.1420(4)
C(26)	0.5817(5)	0.3952(4)	0.1474(3)
C(26′)	0.5113(7)	0.4912(4)	0.1421(4)
C(27)	0.5194(4)	0.3081(3)	0.1596(3)

Table 5 Fractional atomic cordinates for $[5\text{-MeO-2-(HO)-C}_6\text{H}_3\text{COO}]_2\text{SbMe}_3$

Atom	*x*	*y*	*z*
Sb	−0.24374(2)	0.03353(3)	0.24476(3)
O(11)	−0.3687(2)	0.0514(4)	0.1743(2)
O(12)	−0.4369(2)	−0.0687(4)	0.2910(3)
O(13)	−0.6026(2)	−0.1185(4)	0.2647(3)
O(16)	−0.6130(2)	0.2491(4)	−0.0393(3)
O(21)	−0.1183(2)	0.0492(4)	0.3167(2)
O(22)	−0.0483(2)	−0.0763(4)	0.2053(3)
O(23)	0.1159(2)	−0.1276(4)	0.2371(3)
O(26)	0.1215(2)	0.2450(4)	0.5374(3)
C(1)	−0.2864(3)	0.1407(6)	0.3707(4)
C(2)	−0.2462(4)	−0.1657(5)	0.2476(5)
C(3)	−0.1974(3)	0.1271(6)	0.1136(4)
C(11)	−0.4381(3)	0.0013(5)	0.2135(4)
C(12)	−0.5225(3)	0.0340(5)	0.1607(3)
C(13)	−0.6000(3)	−0.0274(6)	0.1882(3)
C(14)	−0.6777(3)	0.0029(5)	0.1385(4)
C(15)	−0.6790(3)	0.0953(5)	0.0638(4)
C(16′)	−0.5395(4)	0.3221(6)	−0.0659(5)
C(16)	−0.6025(3)	0.1583(5)	0.0359(4)
C(17)	−0.5241(3)	0.1274(5)	0.0837(3)
C(21)	−0.0481(3)	−0.0046(5)	0.2813(4)
C(22)	0.0350(3)	0.0259(5)	0.3368(3)
C(23)	0.1119(3)	−0.0352(6)	0.3112(3)
C(24)	0.1893(3)	−0.0049(5)	0.3646(4)
C(25)	0.1891(3)	0.0877(5)	0.4386(4)
C(26)	0.1127(3)	0.1520(5)	0.4638(4)
C(26′)	0.0484(4)	0.3182(6)	0.5635(5)
C(27)	0.0357(3)	0.1207(5)	0.4139(4)

comparison with the spectra of previously reported organotin(IV) analogues.[5,6] A singlet resonance at *ca* 11 ppm assigned to the hydroxylic proton is in agreement with the coordination of the salicylate through its carboxylate group only. All carbon types display only single resonances, which is consistent with weak intramolecular Sb···O=C interactions being absent in solution.

Crystal and molecular structures of $[5\text{-Y-2-(HO)-C}_6\text{H}_3\text{COO}]_2\text{SbMe}_3$

The crystal structures of the trimethylantimony derivatives [Y = H (**1**), Me (**2**) and MeO (**3**)] have been determined at room temperature; selected interatomic parameters for all three determinations are listed in Table 10. The molecular structure of compound **1** (Y = H) is shown in Fig. 1. The structure is molecular, there being no significant intermolecular contacts in the lattice; the closest non-hydrogen contact occurs between the O(13) and C(3)′ atoms of 3.31(1) Å (symmetry operation: x, $1+y$, z). The antimony atom exists in a distorted trigonal bipyramidal geometry with the equatorial plane occupied by the three methyl groups (the sum of the trigonal angles is 360.1°). The Sb and three carbon atoms are coplanar to ±0.002(8) Å. The axial positions are occupied by the oxygen atoms derived from two monodentate carboxylate ligands; the O(11)–Sb–O(21) angle is 171.9(2)°. The two Sb—O bond distances are equal within experimental error. The pendant O(12) and O(22) atoms are 3.120(6) and 3.140(5) Å, respectively, from the antimony atom. These long distances are shorter than the sum of van der Waals radii, estimated as $\Sigma r_{vdW}(\text{Sb, O}) = 3.8$ Å, and suggest some interaction, even if weak, between these atoms. The narrow range of C–Sb–C angles [i.e. 117.8(4)–122.4(4)°] indicates that no significant expansion in a C–Sb–C angle results from the proximity of either of the O(12) and O(22) atoms

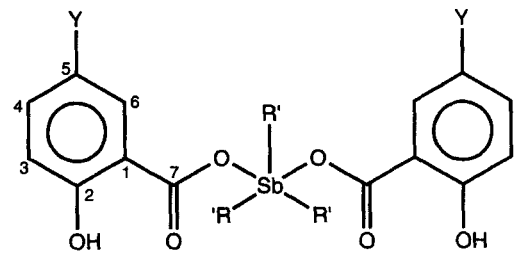
Table 6 Infrared data for $[5\text{-Y-2-(HO)-C}_6\text{H}_3\text{COO}]_2\text{SbR}_3$ (in cm^{-1})

R, Y	ν(C=O)	ν(C—O)	δ(SbMe)	$\nu_{as}(\text{SbC}_3)$	$\nu_s(\text{SbC}_3)$	ν(SbO)
Ph, H	1630s	1375s	—	290m–s	240m–s	400m
	1590s	1350s				340w
Ph, Me	1640s	1380s	—	290m	240m	420m–s
	1590s	1345s				340m
Ph, MeO	1580s	1370s	—	290m	240m	380m
		1350s				
Me, H	1630s	1380s	865s	585m	—	410m–s
	1595s	1350s				320w–m
Me, Me	1640s	1390s	860m	595m	—	420m–s
	1580s	1340s				340m
Me, MeO	1580s	1375s	870m	600m	—	380w–m
		1355s				

Table 7 70 eV EI mass spectra for $[5\text{-Y-2-(HO)-C}_6\text{H}_3\text{COO}]_2\text{SbR}_3$ [*m/z*, (%)]

	R, Y					
	Ph, H	Ph, Me	Ph, MeO	Me, H	Me, Me	Me, MeO
$Y(HO)C_6H_3COOSbR_3^+$	489 (2)	503 (3)	519 (2)	303 (30)	317 (37)	333 (23)
$Y(O)C_6H_3COOSbR_3^+$	488 (5)	502 (11)	518 (5)	302 (4)	316 (17)	332 (14)
$Y(O)C_6H_3COOSbR_2^+$	411 (3)	425 (6)	441 (2)	287 (5)	301 (7)	317 (11)
$Y(O)C_6H_3COOSbR^+$	—	—	364 (3)	272 (2)	286 (13)	302 (19)
$Y(O)C_6H_3COOSb^+$	—	—	—	257 (2)	271 (6)	287 (6)
R_3SbOH^+	—	369 (2)	—	183 (42)	183 (48)	183 (25)
R_3Sb^+	352 (4)	352 (3)	352 (2)	166 (6)	166 (16)	166 (6)
R_2Sb^+	275 (13)	275 (24)	275 (13)	151 (26)	151 (47)	151 (51)
RSb^+	198 (71)	198 (100)	198 (96)	136 (11)	136 (16)	136 (18)
Ph_2^+	154 (100)	154 (99)	154 (100)	—	—	—
$Y(HO)C_6H_3COOH^+$	—	152 (39)	168 (14)	138 (28)	152 (22)	168 (35)
$YC_6H_3CO_2^+$	120 (3)	134 (3)	150 (32)	120 (44)	134 (100)	150 (100)
$Y(O)C_6H_3^+$	92 (17)	106 (9)	122 (5)	92 (100)	106 (53)	122 (18)
Ph^+	77 (50)	77 (60)	77 (59)	—	—	—

Table 8 ^{1}H NMR data for $[5\text{-Y-2-(HO)-C}_6\text{H}_3\text{COO}]_2\text{SbR}_3$



	Chemical shifts, δ (ppm), and H–H coupling constants (Hz)							
R, Y	HO	H(3)	H(4)	H(5)	H(6)	CH_3	CH_3O	R—Sb
Ph, H	11.29 s	6.91 dd $^3J = 8.4$ $^4J = 1.2$	7.38 ddd $^3J = 7.2, 8.4$ $^4J = 1.8$	6.85 ddd $^3J = 7.2, 7.8$ $^4J = 1.8$	7.89 dd $^3J = 7.8$ $^4J = 1.8$	—	—	8.15 m[a] 7.55 m[b]
Ph, Me	10.98 s	6.79 d $^3J = 8.2$	7.18 dd $^3J = 8.2$ $^4J = 2.1$	— —	7.59 d $^4J = 2.1$	2.27 s	—	8.13 m[a] 7.55 m[b]
Ph, MeO	10.69 s	6.79 d $^3J = 9.2$	6.97 dd $^3J = 9.2$ $^4J = 3.4$	—	7.31 d $^4J = 3.4$	—	3.72 s	8.13 m[a] 7.55 m[b]
Me, H	11.50 s	6.94 dd $^3J = 8.4$ $^4J = 1.2$	7.38 ddd $^3J = 7.2, 8.4$ $^4J = 1.8$	6.81 ddd $^3J = 7.2, 7.9$ $^4J = 1.2$	7.76 dd $^3J = 7.9$ $^4J = 1.8$	—	—	2.10 s
Me, Me	11.295	6.84 d $^3J = 8.2$	7.19 dd $^3J = 8.2$ $^4J = 2.1$	—	7.55 d $^4J = 2.1$	2.27 s	—	2.10 s
Me, MeO	11.02 s	6.86 d $^3J = 8.9.$	7.01 dd $^3J = 8.9$ $^4J = 3.1$	—	7.24 d $^4J = 3.1$	—	3.76 s	2.1 s

[a] *ortho*, [b] *meta* + *para*. m, complex pattern; s, singlet; d, doublet.

Table 9 ^{13}C NMR data for [5-Y-2-(HO)-$C_6H_3COO]_2SbR_3$

R, Y	Chemical shifts, δ (ppm)									
	C(7)	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	CH_3	CH_3O	R—Sb
Ph, H	173.0	114.4	161.4	116.9	134.7	118.3	130.4	—	—	136.3[a]
										133.4[b]
										131.4[c]
										129.5[d]
Ph, Me	173.5	114.3	159.7	117.0	135.9	127.7	130.6	20.5	—	137.1[a]
										133.8[b]
										131.7[c]
										129.8[d]
Ph, MeO	172.9	114.5	156.0	118.0	122.5	151.8	113.9	—	55.9	136.5[a]
										133.8[b]
										131.9[c]
										129.9[d]
Me, H	174.3	114.6	162.0	117.3	135.1	118.7	130.7	—	—	12.0
Me, Me	174.3	114.1	159.8	117.0	136.0	127.7	130.5	20.4	—	12.0
Me, MeO	173.9	114.2	156.3	118.1	122.7	151.8	113.7	—	55.9	12.0

[a] *ipso*. [b] *ortho*. [c] *meta*. [d] *para*

to the antimony atom, stressing the weak nature of these intramolecular interactions. The positions of the OH atoms were not located from the X-ray analysis; however, their positions are suggested to lie between the pendant carboxylate oxygen atoms and the hydroxyl oxygen atoms by analogy with the other two structures (see below); the O(12)···O(13) and O(22)···O(23) separations are 2.516(8) and 2.527(7) Å, respectively. Each of the carboxylate residues is planar with the mean deviation from the least-squares plane through the six-membered ring (and the hydroxyl oxygen atom) being 0.009 and 0.010 Å, respectively; similar observations are found in the carboxylate residues in **2** and **3**. The O(11)/C(11)/C(12)/C(13) and O(21)/C(21)/C(22)/C(23) torsion angles of −179.5 (7)° and 176.9(6)°, respectively, reflect the coplanarity between the CO_2 group and the rest of the carboxylate residue in each ligand. The two carboxylate groups are not coplanar, however, with the dihedral angle between the two CO_2 moieties being 68.5°; the two non-coordinating oxygen atoms lie on opposite sides of the molecule.

The molecular structure of the compound **2** (Y = Me) is shown in Fig. 2. This structure is molecular with the closest non-hydrogen contact in the lattice being 3.250(6) Å, which occurs between the O(23) and C(2)′ atoms (symmetry operation: $1-x$, $-y$, $-z$). The geometry about the antimony atom in **2** is essentially as found in the structure of **1**; the antimony atom and three methyl groups are planar to ±0.010(4) Å and the O(11)–Sb–O(21) axial angle is 168.8(1)°. The Sb—O bonds are slightly disparate at 2.102(3) and 2.082(3) Å in this structure in contrast to that found in **1**. The presence of significant intramolecular hydrogen bonding contacts are indicated in the O(12)···H(13) separation of 1.63 Å [O(12)···O(13) is 2.551(5) Å] and the O(23)···H(23) distance of 1.59 Å [O(22)···O(23) is 2.544(5) Å]. The O(21) and O(22) atoms are separated from the antimony atom by 3.082(3) and 3.148(3) Å, respectively. Interestingly, the disparity between the long and short C—O bond distances are similar (i.e. 0.05 and 0.06 Å) in the two carboxylate ligands, in contrast to **1** where the corresponding values are 0.02 and 0.09 Å, despite the relatively high errors associated with the latter parameters. The major structural change in **2**, compared with **1**, is the relative orientation of the carboxylate residuals. The dihedral angle between the two CO_2 groups is 160.5° in **2** and the two non-coordinated oxygen atoms lie to the same side of the molecule. The O(11)/C(11)/C(12)/C(13) and O(21)/C(21)/C(22)/C(23) torsion angles of 171.2(4)° and −179.5(4)°, respectively, suggest a significant twist about the C(11)–C(12) bond.

The structure of the third compound characterized crystallographically, **3** (Y = MeO), is shown in Fig. 3. The closest non-hydrogen contact in the lattice occurs between the O(23) and C(3)′ atoms,

of 3.400(7) Å (symmetry operation: $2-x$, $-0.5+y$, $0.5-z$). The immediate geometry about the antimony atom in **3** is as described above for **1** and **2**. The antimony and three methyl groups are coplanar within ±0.001(8) Å and the O(11)–Sb–O(21) angle is 170.5(1)°; the weak secondary interactions Sb···O(12) and Sb···O(22) separations are 3.159(4) and 3.202(4) Å, respectively. The presence of intramolecular hydrogen-bonding contacts are indicated by the O(12)···H(13) separation of 1.69 Å [O(12)···O(13) is 2.571(5) Å] and the O(22)···H(23) separation of 1.66 Å [O(22)···O(23) is 2.561(5) Å]. The O(11)/C(11)/C(12)/C(13) and O(21)/C(21)/C(22)/C(23) torsion angles of 171.8(5)° and 174.1(5)°, respectively, indicate small but significant twists about the O_2C—C bonds. The dihedral angle between the two CO_2 groups is 74.4°, indicating that the relative disposition of the carboxylate ligands is similar to that reported for **1**.

Table 10 Selected interatomic parameters (Å, deg) for [5-Y-2-(HO)-$C_6H_3COO]_2SbR_3$

	Compound		
	Y = H	Y = Me	Y = MeO
Sb—O(11)	2.098(5)	2.102(3)	2.092(3)
Sb—O(21)	2.090(5)	2.082(3)	2.104(3)
Sb—C(1)	2.043(8)	2.060(5)	2.069(6)
Sb—C(2)	2.047(8)	2.053(5)	2.056(5)
Sb—C(3)	2.040(7)	2.058(5)	2.071(5)
O(11)–C(11)	1.267(9)	1.276(5)	1.274(5)
O(12)–C(11)	1.244(9)	1.228(5)	1.231(5)
O(21)–C(21)	1.317(8)	1.283(5)	1.282(5)
O(22)–C(21)	1.229(8)	1.223(5)	1.227(6)
O(13)–C(13)	1.34(1)	1.335(5)	1.362(6)
O(23)–C(23)	1.334(8)	1.342(6)	1.350(6)
O(16)–C(16′)	—	—	1.386(6)
O(26)–C(26′)	—	—	1.353(6)
O(11)–Sb—O(21)	171.9(2)	168.8(1)	170.5(1)
O(11)–Sb—C(1)	95.7(3)	86.0(2)	90.4(2)
O(11)–Sb—C(2)	83.8(3)	92.2(2)	94.6(2)
O(11)–Sb—C(3)	90.5(3)	92.8(2)	85.1(2)
O(21)–Sb—C(1)	92.3(3)	82.8(2)	84.2(2)
O(21)–Sb—C(2)	93.5(3)	91.9(2)	94.9(2)
O(21)–Sb—C(3)	84.6(3)	93.9(2)	90.8(2)
C(1)–Sb—C(2)	117.8(4)	117.3(2)	120.9(3)
C(1)–Sb—C(3)	119.9(4)	120.9(2)	119.9(2)
C(2)–Sb—C(3)	122.4(4)	121.8(2)	119.1(3)
Sb—O(11)–C(11)	120.9(5)	119.6(3)	122.2(3)
Sb—O(21)–C(21)	121.1(5)	122.0(3)	123.5(3)
O(11)–C(11)–O(12)	122.3(7)	122.5(4)	123.5(4)
O(11)–C(11)–C(12)	117.9(7)	116.5(4)	115.6(4)
O(12)–C(11)–C(12)	119.8(7)	121.0(4)	120.8(4)
O(21)–C(21)–O(22)	122.0(6)	122.5(4)	123.2(4)
O(21)–C(21)–C(22)	117.0(6)	115.4(4)	116.0(4)
O(22)–C(21)–C(22)	121.0(7)	122.1(4)	120.8(4)

The immediate geometry about the antimony atoms in all three compounds **1**–**3** is essentially the same. Whereas there was some disparity in the Sb—O bonds in the structure of **2**, the range of Sb—O bond distances in the three compounds was found to be narrow at 2.082(3)–2.104(3) Å, i.e. equivalent to the 5σ level. This result indicates that the variable substitution in the 5-position does not result in a significant change in the donor ability of the carboxylate ligand. In no case were the intramolecular Sb···O interactions, which ranged from 3.082(3) to 3.202(4) Å, considered significant. The weak nature of the Sb···O secondary interactions may be traced, in part, to the presence of intramolecular hydrogen-bonding contacts between the OH atoms and the pendant oxygen atoms (see later). Such contacts have been observed previously in the related organotin compounds n-$Bu_2Sn[O_2CC_6H_4(2\text{-}OH)]_2$[26] and n-$Bu_2Sn[O_2CC_6H_3(2\text{-}OH)(5\text{-}Cl)]_2$.[27] Interestingly, in the two organotin compounds mentioned, there are additional, intermolecular hydrogen-bonding contacts leading to loosely associated dimers; no such association occurs in the trimethylantimony compounds described herein, possibly owing to steric crowding about the antimony atom. The major difference between the three structures is found in the relative orientations of the carboxylate residues. In the structures of **1** and **3** there is no significant dihedral angle between two carboxylate groups, whereas in **2**, the two carboxylate groups are nearly planar. There are two other trimethylantimony dicarboxylate structures available for comparison.

In the structure of $(2\text{-}NC_5H_4CO_2)_2SbMe_3$[28] each antimony atom (there are two molecules in the crystallographic asymmetric unit) exists in a trigonal bipyramidal geometry with Sb(1)—O(11) 2.121(4), Sb(1)—O(21) 2.132(4), Sb(2)—O(31) 2.123(3) and Sb(2)—O(41) 2.120(3) Å; the secondary Sb···O contacts range from 3.012(4) to 3.112(4) Å. The molecules differ in the relative orientations of the carboxylate residues. In the first molecule, the two carboxylate ligands lie to the same side of the molecule in the fashion indicated in the structure of **2**, and the dihedral angle between the two carboxylate residues is

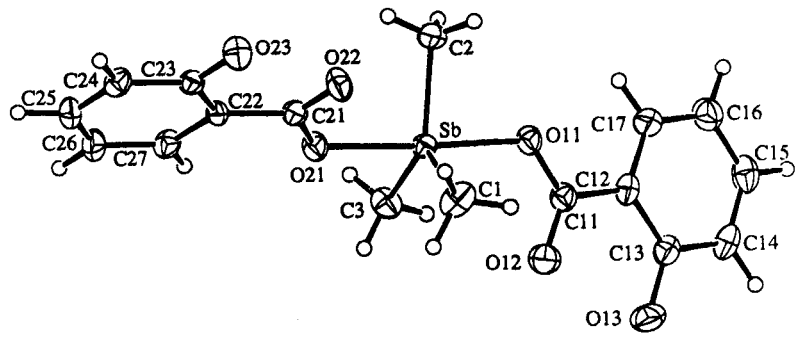


Figure 1 Molecular structure and crystallographic numbering scheme for $[2\text{-}(HO)\text{-}C_6H_4COO]_2SbMe_3$. The OH atoms were not located in the X-ray analysis.

176.5°, whereas in the second the comparable dihedral angle of 54.9° suggests a conformation as found in the structures of **1** and **3**. Clearly, there is little energy difference between the two conformations. In the structure of $(SC_4H_3CO_2)_2SbMe_3$[29] the Sb—O(11) and Sb—O(21) bond lengths are 2.136(6) and 2.124(6) Å, respectively, the O(11)–Sb–O(21) angle is 170.1(2)°, and the secondary Sb···O interactions are 3.093(7) and 3.066(7) Å. The dihedral angle between the carboxylate groups is 170.0°, i.e. resembling that found in **2**. The degree of asymmetry in the Sb—O bonds formed in the latter two structures, where no intramolecular hydrogen-bonding contacts are found, resembles that found in **1**, **2** and **3**. This observation suggests that the presence of the intramolecular hydrogen-bonding contacts do not have a significant effect on the mode of coordination of the carboxylate residues. In addition to these trimethylantimony compounds, there are also several triphenylantimony structures available in the literature.

The structure of $(CH_3COO)_2SbPh_3$,[25] $(C_6H_5COO)_2SbPh_3$,[30] $(CF_3COO)_2SbPh_3$[31] and $(SC_4H_3COO)_2SbPh_3$[32] each features a trigonal bipyramidal C_3SbO_2 geometry and monodentate carboxylate ligands. It is noteworthy that, except for the $(CF_3CO_2)_2SbPh_3$[31] compound, the disparity between the short and long Sb–O interactions in the triphenylantimony compounds is significantly less than in the trimethylantimony derivatives. This reflects the positive inductive effect of the methyl groups compared with the phenyl groups. The exception is the compound with the strongly electron-withdrawing CF_3 groups. Particularly notable among the triphenylantimony compounds, however, is the structure of $(2\text{-}NC_5H_4CO_2)_2SbPh_3$,[28] in which the carboxylate ligands coordinate the antimony atom in a different way. One ligand coordinates the antimony atom employing one oxygen atom only, with the second Sb···O contact being weak. The second ligand again coordinates via one oxygen atom only; however, the weak intramolecular contact involves the pyridine nitrogen atom. This behaviour contrasts that found in the trimethyl

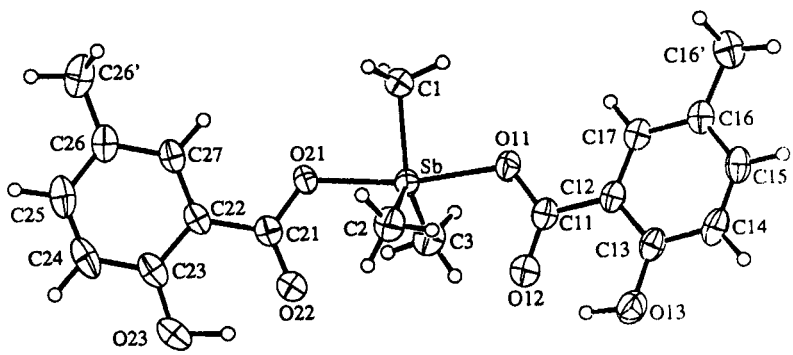


Figure 2 Molecular structure and crystallographic numbering scheme for $[5\text{-}Me\text{-}2\text{-}(HO)\text{-}C_6H_3COO]_2SbMe_3$.

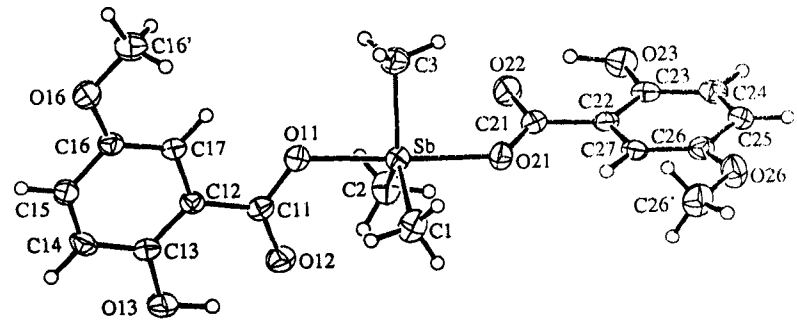


Figure 3 Molecular structure and crystallographic numbering scheme for [5-MeO-2-(HO)-$C_6H_3COO]_2SbMe_3$.

analogue.[29] Such structural diversity resembles that found in the structures of tin, and in particular organotin, carboxylates.[33,34]

In vitro antitumour screening

The compounds 5-Y-2-(HO)-$C_6H_3COO]_2SbR_3$ (R = Me; Y = H, Me, MeO) were screened against a panel of human tumour cell lines. All three were found to be inactive against the six tumour types used, giving ID_{50} values often >60 000 ng ml^{-1}, and never <11 000 ng ml^{-1}.

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