

# Synthesis, characterization and antitumor activity of some arylantimony triphenylgermanylpropionates and crystal structures of $\text{Ph}_3\text{GeCH}(\text{Ph})\text{CH}_2\text{CO}_2\text{SbPh}_4$ and $[\text{Ph}_3\text{GeCH}_2\text{CH}(\text{CH}_3)\text{CO}_2]_2\text{Sb}(4\text{-ClC}_6\text{H}_4)_3$

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## Abstract

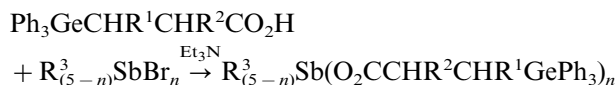
A series of novel arylantimony(V) triphenylgermanylpropionates with the formula  $(\text{Ph}_3\text{GeCHR}^1\text{CHR}^2\text{CO}_2)_n\text{SbAr}_{(5-n)}$  ( $\text{R}^1 = \text{H}$ ,  $\text{Ph}$ ;  $\text{R}^2 = \text{H}$ ,  $\text{CH}_3$ ;  $n = 1, 2$ ) were synthesized and characterized by elemental analysis, IR,  $^1\text{H-NMR}$ ,  $^{13}\text{C-NMR}$  and mass spectroscopy. The crystal structures of  $\text{Ph}_3\text{GeCH}(\text{Ph})\text{CH}_2\text{CO}_2\text{SbPh}_4$  and  $[\text{Ph}_3\text{GeCH}_2\text{CH}(\text{CH}_3)\text{CO}_2]_2\text{Sb}(4\text{-ClC}_6\text{H}_4)_3$  were determined by X-ray diffraction. The in vitro antitumor activities of some selected compounds against five cancer cells are reported. © 2001 Elsevier Science B.V. All rights reserved.

**Keywords:** Antimony; Germanium; Crystal structures; Antitumor activity

## 1. Introduction

A substantial number of references describing synthesis and applications of  $\text{R}_n\text{SbX}_{5-n}$  ( $\text{R} = \text{alkyl, aryl}$ ;  $\text{X} = \text{carboxylate}$ ;  $n = 3, 4$ ) have appeared in the literature [1–20]. To the biological activity of some organoantimony carboxylates Bajpai and co-workers [2] considered that the activity was not significantly affected by the nature of the R groups at Sb. However, Singhal and co-workers [3] found that the effect of the nature of R groups on the activity was relatively complex. As we know very well, organogermanium has a wide range of biological activities [21–24]. Therefore, we have prepared nine new arylantimony  $\beta$ -triphenylgermanylpropionates in order to examine whether including organogermanium in organoantimony compounds improves their antitumor properties and to investigate the influence of the organic ligands at Sb on their biological activity. At the same time we were also interested in studying the nature of bonding and structure of these compounds.

These arylantimony triphenylgermanylpropionates were synthesized by the reaction of triphenylgermanylpropionic acid with  $\text{Ar}_n\text{SbBr}_{(5-n)}$  in the presence of triethylamine. The general reaction scheme is shown as follows:



For compounds **I**:  $n = 1$ ,  $\text{R}^3 = \text{Ph}$ ,  $\text{R}^1 = \text{R}^2 = \text{H}$  (**I**<sub>1</sub>);  $\text{R}^1 = \text{H}$ ,  $\text{R}^2 = \text{CH}_3$  (**I**<sub>2</sub>);  $\text{R}^1 = \text{Ph}$ ,  $\text{R}^2 = \text{H}$  (**I**<sub>3</sub>). For compounds **II**:  $n = 2$ ,  $\text{R}^1 = \text{H}$ ,  $\text{R}^2 = \text{CH}_3$ ,  $\text{R}^3 = 4\text{-CH}_3\text{C}_6\text{H}_4$  (**II**<sub>1</sub>);  $4\text{-ClC}_6\text{H}_4$  (**II**<sub>2</sub>);  $\text{R}^1 = \text{Ph}$ ,  $\text{R}^2 = \text{H}$ ,  $\text{R}^3 = 4\text{-ClC}_6\text{H}_4$  (**II**<sub>3</sub>);  $\text{Ph}$  (**II**<sub>4</sub>);  $3\text{-CH}_3\text{C}_6\text{H}_4$  (**II**<sub>5</sub>);  $\text{R}^1 = \text{R}^2 = \text{H}$ ,  $\text{R}^3 = \text{Ph}$  (**II**<sub>6</sub>).

## 2. Results and discussion

### 2.1. Preparations

The compounds are prepared under mild condition. All compounds are white crystals and stable under ordinary conditions. They are easily soluble in organic

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solvents such as benzene, toluene, chloroform, and dimethyl sulfoxide, but not soluble in acetone, ether, methanol, ethanol, and petroleum ether.

The reaction of triarylantimony dichloride with arylmagnesium bromide represents a satisfactory method of preparation of salts such as tetraphenylstibonium bromide. We use toluene instead of benzene and less ether than in the Ref. [4]. The product was precipitated during this period, whereas in Ref. [4] that is in solution as ether–benzene. However, this method has been proved to be unsatisfactory for the preparation of quaternary stibonium salts having two or more different aryl groups bonded to antimony, mainly because of the occurrence of exchange reactions between the Grignard reagent and tetraarylstibonium cation.

## 2.2. IR

The IR spectra of these compounds have been recorded in the range of 4000–400  $\text{cm}^{-1}$ . The absorption bands can be assigned on the basis of earlier publications and the important data are listed 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 [5,6] or seven [7]. The IR stretching vibration frequencies of carbonyl groups in organoantimony carboxylates are very important for determining their structures: When there are interactions between the antimony atom and the carbonyl oxygen atoms of the carboxylate groups, the asymmetric absorption vibration frequencies [ $\nu_{\text{asy}}(\text{CO}_2)$ ] of carbonyl groups decrease and the symmetric absorption vibration frequencies [ $\nu_{\text{sym}}(\text{CO}_2)$ ] increase. Therefore their differences [ $\Delta\nu(\text{CO}_2)$ ] decrease [3,8,9]. In the IR spectra of the title compounds the carboxylate bands are observed in the characteristic regions:  $\nu_{\text{asy}}(\text{CO}_2)$  between 1670 and 1622  $\text{cm}^{-1}$  and

$\nu_{\text{sym}}(\text{CO}_2)$  between 1377 and 1291  $\text{cm}^{-1}$ . On the basis of the difference  $\Delta\nu(\text{CO}_2)$  these compounds can be divided into two classes: Compounds **I**<sub>1</sub>, **I**<sub>2</sub> and **I**<sub>6</sub> show low  $\Delta\nu(\text{CO}_2)$  values (280, 271 and 283  $\text{cm}^{-1}$ , respectively) while all other compounds show high  $\Delta\nu(\text{CO}_2)$  values (between 310 and 349  $\text{cm}^{-1}$ ). To the former we can assume that there are stronger interactions between the carbonyl oxygen atoms of the carboxylate groups and the antimony atom (confirmed by crystal structure of compound **I**<sub>2</sub>). To the latter we can assume that there are weaker interactions or no interaction between the antimony atom and the carbonyl oxygen atoms of the carboxylate groups. (See the crystal structure of compound **I**<sub>3</sub>). In addition, the frequencies  $\nu_{\text{asy}}(\text{Sb}-\text{C})$  appear between 458 and 472  $\text{cm}^{-1}$ , this is consistent with the literature [8].

## 2.3. <sup>1</sup>H-NMR

The <sup>1</sup>H-NMR data of the title compounds are listed in Table 2. The <sup>13</sup>C-NMR data of the three compounds are given in Table 3. From the Table 2 we find when one  $\beta$  proton is substituted with a phenyl group there is a significant downfielding shift for  $\alpha$  and  $\beta$  protons due to the deshielding effects. C(1) is a chiral center and C(2) is a prochiral center. The three hydrogens on C(1) and C(2) comprise an ABX system. However, the ABX system can not be identified in 90 MHz spectra. Here the three hydrogens show a multiplet in most cases. 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.

## 2.4. Mass spectra

The main mass spectra data of compound **I**<sub>3</sub> and **I**<sub>6</sub> are listed in Table 4. For both there is no molecular ion peak. But the fragment ions found are in agreement with the expected structure of the compounds. Decarboxylation and dephenylation from metal atom are the main breakdown patterns for the two compounds.

## 2.5. Crystal structure

### 2.5.1. Structure of $\text{Ph}_3\text{GeCH}(\text{Ph})\text{CH}_2\text{CO}_2\text{SbPh}_4$

A colorless crystal was recrystallized from  $\text{CH}_2\text{Cl}_2$ – $\text{CH}_3\text{OH}$ . One of the approximate dimensions 0.30  $\times$  0.25  $\times$  0.20 mm was mounted in a glass capillary and used for data collection. Fig. 1 shows the molecular structure of compound **I**<sub>3</sub> and gives the atom numbering scheme. The selected bond distances and angles are listed in Table 5. The Ge–C bonds are consistent with the literature [25]. The stereochemistry of germanium is typically tetrahedral geometry. As usual (see Table 6) the apical Sb–C distance (2.151 Å) is longer than the

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

Compound	$\nu_{\text{asy}}(\text{CO}_2)$	$\nu_{\text{sym}}(\text{CO}_2)$	$\Delta\nu(\text{CO}_2)$	$\nu_{\text{asy}}(\text{Sb}-\text{C})$
<b>I</b> <sub>1</sub>	1627	1347	280	466
<b>I</b> <sub>2</sub>	1635	1306	329	462
<b>I</b> <sub>3</sub>	1636	1326	310	466
<b>II</b> <sub>1</sub>	1662	1341	321	466
<b>II</b> <sub>2</sub>	1610	1339	271	472
<b>II</b> <sub>3</sub>	1649	1329	320	467
<b>II</b> <sub>4</sub>	1645	1291	349	458
<b>II</b> <sub>5</sub>	1648	1335	313	465
<b>II</b> <sub>6</sub>	1645	1362	283	462

Table 2  
<sup>1</sup>H-NMR data of the compounds

Compound	GeCHR <sup>1</sup>	CHR <sup>2</sup> CO	Ph <sub>3</sub> Ge	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>
<b>I<sub>1</sub></b>	1.42–1.62(2H,t)	2.08–2.24 (2H,t)	7.40–7.80 (15H,m)			7.40–7.80 (20H,m)
<b>I<sub>2</sub></b>	1.18 –1.90(2H,m)	2.15–2.52 (1H,m)	7.31–7.78 (15H,m)		0.68–0.77 (3H,d)	7.31–7.78 (20H,m)
<b>I<sub>3</sub></b>	3.51–3.72(1H,t)	2.58–2.72 (2H,d)	7.22–7.58 (15H,m)	6.80–7.05 (5H,m)		7.22–7.58 (20H,m)
<b>II<sub>1</sub></b>	1.20–1.85 (4H,m)	2.25–2.60 (2H,m)	7.21–7.95 (30H,m)		0.75–0.82 (6H,d)	7.21–7.95 (12H,m), 2.38 (9H,s)
<b>II<sub>2</sub></b>	1.19–1.82 (4H,m)	2.16–2.60 (2H,m)	7.32–7.90 (30H,m)		0.72–0.80 (6H,d)	7.32–7.90 (12H,m)
<b>II<sub>3</sub></b>	3.34–3.44 (2H,m)	2.52–2.80 (4H,m)	7.14–7.32 (30H,m)	6.76–7.01 (10H,m)		7.14–7.32 (12H,m)
<b>II<sub>4</sub></b>	3.44–3.52 (2H,m)	2.60–2.75 (4H,m)	7.16–7.45 (30H,m)	6.72–7.02 (10H,m)		7.16–7.45 (15H,m)
<b>II<sub>5</sub></b>	3.42–3.62 (2H,m)	2.68–2.80 (4H,t)	7.18–7.50 (30H,m)	6.70–7.04 (10H,m)		7.18–7.50 (12H,m), 2.22 (9H,s)
<b>II<sub>6</sub></b>	1.41–1.65 (4H,t)	2.18–2.38 (4H,t)	7.28–8.04 (30H,m)			7.28–8.04 (15H,m)

Table 3  
 The <sup>13</sup>C-NMR data (ppm) for compounds **I<sub>3</sub>**, **II<sub>1</sub>** and **II<sub>6</sub>**

Compd.	GeC	C=O	CHC=O	Ph <sub>3</sub> Ge	ArSb	Others
<b>I<sub>3</sub></b>	33.1	175.9	38.8	135.9( <i>i</i> ), 135.2 ( <i>o</i> ), 128.6( <i>p</i> ), 127.9( <i>m</i> )	142.8( <i>i</i> ), 135.6( <i>o</i> ), 130.0( <i>p</i> ), 128.8( <i>m</i> )	138.5 (Ph)
<b>II<sub>1</sub></b>	9.3	178.5	31.1	136.1( <i>i</i> ), 134.8( <i>o</i> ), 128.9( <i>p</i> ), 128.2( <i>m</i> )	138.7( <i>i</i> ), 133.9( <i>o</i> ), 130.9( <i>p</i> ), 129.1( <i>m</i> )	–
<b>II<sub>6</sub></b>	18.3	180.8	19.6	135.1( <i>i</i> ), 134.8( <i>o</i> ), 128.7( <i>p</i> ), 128.0( <i>m</i> )	140.8( <i>p</i> ), 137.1( <i>i</i> ), 133.8( <i>o</i> ), 130.0( <i>m</i> )	21.4(CH <sub>3</sub> Ph), 37.0(CH <sub>3</sub> CH)

Table 4  
 Fragment ions observed for compounds **I<sub>3</sub>** and **II<sub>6</sub>**

<b>I<sub>3</sub></b>			<b>II<sub>6</sub></b>		
<i>M/z</i>	Fragment	Intensity	<i>M/z</i>	Fragment	Intensity
453	Ph <sub>3</sub> GeCH(Ph)CH <sub>2</sub> CO <sub>2</sub> <sup>+</sup>	5	352	Ph <sub>3</sub> Sb <sup>+</sup>	5
429	Ph <sub>4</sub> Sb <sup>+</sup>	35	305	Ph <sub>3</sub> Ge <sup>+</sup>	87
305	Ph <sub>3</sub> Ge <sup>+</sup>	98	301	[Ph <sub>3</sub> Ge-4H] <sup>+</sup>	100
275	Ph <sub>2</sub> Sb <sup>+</sup>	13	275	Ph <sub>2</sub> Sb <sup>+</sup>	8
227	[Ph <sub>2</sub> Ge-H] <sup>+</sup>	20	227	[Ph <sub>2</sub> Ge-H] <sup>+</sup>	19
198	PhSb <sup>+</sup>	74	198	PhSb <sup>+</sup>	69
154	Ph-Ph <sup>+</sup>	70	151	PhGe <sup>+</sup>	46
121	Sb <sup>+</sup>	6	121	Sb <sup>+</sup>	6
77	Ph <sup>+</sup>	100	74	Ge <sup>+</sup>	3
74	Ge <sup>+</sup>	7			

equatorial Sb–C distance (mean value 2.102 Å). Although the Sb–C distances found here are typical of Sb-aryl bonds, the Sb(1)–O(1) distance is 2.289 Å [longer than typical Sb–O distance (2.05 Å), (see Table 6)]. In Ph<sub>4</sub>SbOC(O)H the Sb–O distance is 2.222 Å also longer than the typical Sb–O value [17]. Similarly, very long apical Sb–X bonds are also found in Ph<sub>4</sub>SbCl,

Ph<sub>4</sub>SbBr and Ph<sub>4</sub>SbOSO<sub>2</sub>Ph in Table 6. If the normal Sb–O distance is taken as 2.05 Å [17], the percentage elongation of Sb–O bonds in Ph<sub>4</sub>SbX, for X = OMe, OC(O)H, OSO<sub>2</sub>Ph, Ph<sub>3</sub>GeCHPhCH<sub>2</sub>CO<sub>2</sub>, are 1, 8, 22 and 12%, respectively.

The crystal structure of compound **I<sub>3</sub>** can be reported as monomeric. The C–O distances of the carboxyl

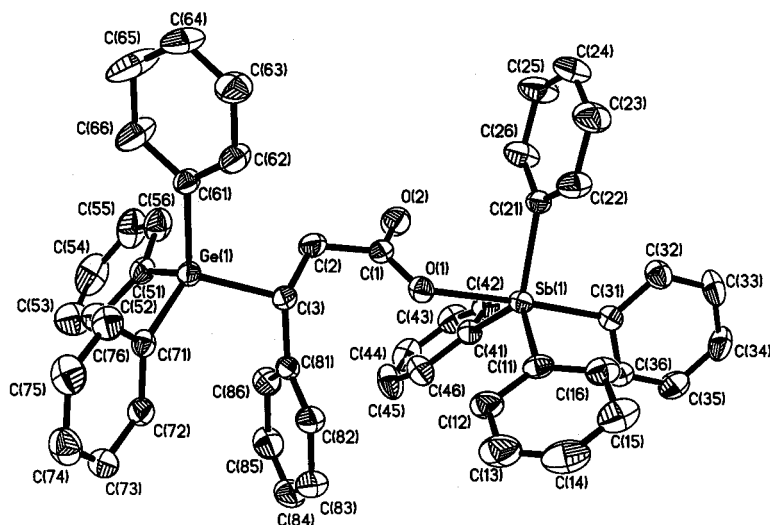


Fig. 1. The molecular structure of  $\text{Ph}_3\text{GeCH}(\text{Ph})\text{CH}_2\text{CO}_2\text{SbPh}_4$ .

group are 1.231 and 1.300 Å, respectively, which are typical bond lengths for C=O and C–O groups. The distance between Sb and the carbonyl oxygen is 3.233 Å (cf.  $\text{Ph}_4\text{SbOCOH}$ , 3.291 Å) which shows a much lower degree of interaction between the non-bonded oxygen atom and antimony atom. This is still well within the sum of the van der Waals' radii [10]. The smaller Sb⋯O interaction leads to a much smaller variation in the equatorial angles of compound **I**<sub>3</sub> [C(41)–Sb(1)–C(11) 120.54, C(11)–Sb(1)–C(21) 111.79, C(41)–Sb(1)–C(21) 125.08°, in all 357.41°]. The antimony atom is displaced by 0.1975 Å towards C(31) from the plane described by the equatorial carbon atoms C(21), C(41) and C(11). At the same time, the mean  $C_{\text{eq}}\text{–Sb–}C_{\text{ap}}$  angle is 95.4° representing a deviation of the equatorial  $\text{SbC}_3$  fragment from the planar arrangement of a regular trigonal bipyramid. However, the geometry of compound **I**<sub>3</sub> is clearly a distorted trigonal bipyramidal with a relatively small distortion towards tetrahedral.

### 2.5.2. Structure of $[\text{Ph}_3\text{GeCH}_2\text{CH}(\text{CH}_3)\text{CO}_2]_2\text{Sb}(4\text{-ClC}_6\text{H}_4)_3$

The colorless crystal of  $[\text{Ph}_3\text{GeCH}_2\text{CH}(\text{CH}_3)\text{CO}_2]_2\text{Sb}(4\text{-ClC}_6\text{H}_4)_3$  was obtained from a  $\text{CH}_2\text{Cl}_2$ –*n*-hexane solution. The molecular structure with the atom numbering scheme is depicted in Fig. 2. The selected bond distances and angles are listed in Table 7.

Carboxylates are versatile ligands which can be either unidentate or bidentate. The molecule consists of a monomer with a seven-coordinated antimony atom surrounded by four oxygens and three phenyl groups. The coordination geometry of antimony can be described as a distorted pentagonal bipyramid with the plane being defined by four oxygens from two asymmetrically chelating carboxylate groups and one carbon atom from one phenyl group, while the other phenyl groups occupying the axial positions.

The Sb(1)–O(2) and Sb(1)–O(4) distances [2.129(3), 2.146(3) Å] are significantly different from the corresponding distances in  $\text{Ph}_3\text{Sb}(\text{O}_2\text{CCHCM}_2\text{CM}_2)_2$  [both 2.106(3) Å] [18] and  $\text{Ph}_3\text{Sb}(\text{O}_2\text{C-}2\text{-C}_4\text{H}_3\text{S})_2$  [2.145(4), 2.095(4) Å] [7]. In this compound there are relatively strong bonding interactions between Sb(1) and the carbonyl oxygens of the carboxylates. The Sb(1)–O(1) and Sb(1)–O(3) distances [2.739(3), 2.647(3) Å] are also different from the corresponding distances in  $\text{Ph}_3\text{Sb}(\text{O}_2\text{CCHCM}_2\text{CM}_2)_2$  [both 2.800(2) Å] and  $\text{Ph}_3\text{Sb}(\text{O}_2\text{C-}2\text{-C}_4\text{H}_3\text{S})_2$  [2.744(4), 2.949(4) Å], which are considerably shorter than the sum of the covalent radii (3.60 Å) [19]. This indicates that there are coordination interactions between the carbonyl oxygens of the two asymmetrical triphenylgermanylpropionate groups and the antimony atom. The C(5)–O(1) and C(5)–O(2)

Table 5  
Selected bond distances and bond angles of compound **I**<sub>3</sub>

Bond	Distances (Å)	Bond	Angles (°)
Sb(1)–O(1)	2.289(3)	C(31)–Sb(1)–O(1)	177.00(14)
Sb(1)–O(2)	3.233(3)	C(41)–Sb(1)–C(11)	120.54(19)
Sb(1)–C(41)	2.121(5)	C(41)–Sb(1)–C(21)	125.08(19)
Sb(1)–C(11)	2.122(5)	C(11)–Sb(1)–C(21)	111.79(18)
Sb(1)–C(21)	2.123(4)	C(41)–Sb(1)–C(31)	94.07(17)
Sb(1)–C(31)	2.170(5)	C(11)–Sb(1)–C(31)	96.36(18)
Ge(1)–C(71)	1.948(5)	C(21)–Sb(1)–C(31)	95.75(16)
Ge(1)–C(61)	1.951(4)	C(41)–Sb(1)–O(1)	83.78(15)
Ge(1)–C(51)	1.959(5)	C(11)–Sb(1)–O(1)	82.98(16)
Ge(1)–C(3)	2.000(5)	C(21)–Sb(1)–O(1)	87.21(14)
O(1)–C(1)	1.300(6)	C(71)–Ge(1)–C(61)	110.04(19)
C(1)–O(2)	1.231(6)	C(71)–Ge(1)–C(51)	108.0(2)
C(1)–C(2)	1.514(7)	C(61)–Ge(1)–C(51)	109.9(2)
C(2)–C(3)	1.508(7)	C(71)–Ge(1)–C(3)	111.84(19)
C(3)–C(81)	1.518(6)	C(61)–Ge(1)–C(3)	107.86(19)
		C(51)–Ge(1)–C(3)	109.2(2)
		C(1)–O(1)–Sb(1)	118.6(3)
		O(2)–C(1)–O(1)	123.7(4)

Table 6  
Comparison of mean distances in some trigonal bipyramidal antimony compounds

	$d(\text{SbC})_{\text{ap}}$	$d(\text{SbC})_{\text{eq}}$	$d(\text{SbX})_{\text{ap}}$ (Å)	C–Sb–X (°)	Ref.
Ph <sub>4</sub> SbOH	2.128	2.131	2.048	175.4 (O)	[11]
Ph <sub>4</sub> SbOMe	2.199	2.119	2.061	178.1 (O)	[12]
Ph <sub>4</sub> SbOC(O)H	2.176	2.109	2.222	–	[13]
Ph <sub>4</sub> SbOSO <sub>2</sub> Ph	2.131	2.108	2.506	176.0 (O)	[14]
Ph <sub>5</sub> Sb	2.243	2.133	–	178.7 (C)	[15]
Ph <sub>4</sub> SbCl	2.15	2.10	2.74	–	[16] <sup>a</sup>
Ph <sub>4</sub> SbBr	2.151	2.102	2.965	175.5 (Br)	[17]
I <sub>3</sub>	2.170	2.122	2.289	177.0 (O)	This work

<sup>a</sup> Geometry at Sb intermediate between tetrahedral SbC<sub>4</sub> and trigonal bipyramidal SbC<sub>4</sub>X.

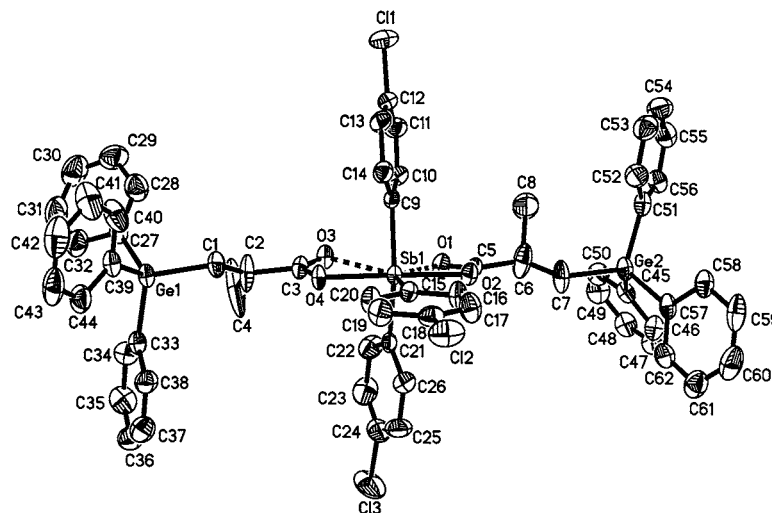


Fig. 2. The molecular structure of [Ph<sub>3</sub>GeCH<sub>2</sub>CH(CH<sub>3</sub>)CO<sub>2</sub>]<sub>2</sub>Sb(4-ClC<sub>6</sub>H<sub>4</sub>)<sub>3</sub>.

distances [1.208(5), 1.294(6) Å] are different from C(3)–O(3) and C(3)–O(4) distances [1.231(5), 1.286(5) Å]. They are also different from those in Ph<sub>3</sub>Sb(O<sub>2</sub>CCHMe<sub>2</sub>CMe<sub>2</sub>)<sub>2</sub> [1.229(6), 1.301(6) Å] and Ph<sub>3</sub>Sb(O<sub>2</sub>C-2-C<sub>4</sub>H<sub>3</sub>S)<sub>2</sub> [1.226(6), 1.305(6), 1.215(6), 1.309(6) Å]. The O(3)–Sb(1)–O(1), O(3)–Sb(1)–O(4) and O(1)–Sb(1)–O(2) angles are 79.3, 53.0 and 51.6°, respectively. The plane angles are 360.3° in all. The C(9)–Sb(1)–C(21) angle, which is affected by adjacent O(1) and O(3), is increased to 149.86°, while the C(15)–Sb(1)–C(21) and C(15)–Sb(1)–C(9) angles are decreased to 104.33(19)° and 105.81(18)°, respectively. The corresponding angles in Ph<sub>3</sub>Sb(O<sub>2</sub>C-2-C<sub>4</sub>H<sub>3</sub>S)<sub>2</sub> are 145.9(2), 104.4(2) and 109.5(2)°, which in Ph<sub>3</sub>Sb(O<sub>2</sub>CCHMe<sub>2</sub>CMe<sub>2</sub>)<sub>2</sub> are 150.0(3), 105.1(2) and 105.1(2)°. These differences can be attributed to the –I effect of Cl of the aryl groups and the steric effect of the two bulky triphenylgermylpropionate groups in the molecule. The –I effect of Cl enhances the Lewis acidity of Sb and leads to the stronger Sb⋯O=C coordination [20]. The atoms Sb(1), O(1), O(2), O(3), O(4) and C(15) are coplanar within 0.0703 Å.

In the unit cell there is a surprising weak intermolecular interaction between the Cl atom of aryl group and

carbonyl oxygen of a neighbouring molecule. The Cl(2)–O(3) distance is 3.198 Å.

Table 7  
Selected bond distances and bond angles of compound II<sub>2</sub>

Bond	Distances (Å)	Bond	Angles (°)
Sb(1)–O(2)	2.129(3)	C(9)–Sb(1)–C(21)	149.86(19)
Sb(1)–O(4)	2.146(3)	C(21)–Sb(1)–C(15)	104.33(19)
Sb(1)–O(1)	2.739(3)	C(9)–Sb(1)–C(15)	105.81(18)
Sb(1)–O(3)	2.647(3)	O(2)–Sb(1)–O(4)	176.42(13)
Ge(1)–C(33)	1.951(5)	C(9)–Sb(1)–O(2)	90.45(15)
Ge(1)–C(1)	1.965(5)	C(9)–Sb(1)–O(4)	90.78(15)
Ge(2)–C(57)	1.947(6)	C(21)–Sb(1)–O(4)	89.41(15)
Ge(2)–C(7)	1.970(5)	C(33)–Ge(1)–C(39)	109.5(2)
O(1)–C(5)	1.208(5)	C(51)–Ge(2)–C(7)	109.7(3)
O(3)–C(3)	1.231(5)	O(3)–C(3)–O(4)	120.5(4)
O(2)–C(5)	1.294(6)	O(1)–C(5)–O(2)	122.2(4)
O(4)–C(3)	1.286(5)	C(15)–Sb(1)–O(2)	87.92(15)
Cl(2)–O(3)	3.198	C(21)–Sb(1)–O(2)	91.21(15)
		C(15)–Sb(1)–O(4)	88.51(15)
		O(3)–Sb(1)–O(1)	79.3(4)
		O(3)–Sb(1)–O(4)	53.0(4)
		O(1)–Sb(1)–O(2)	51.6(4)

Table 8  
Yields and elemental analyses of the compounds

Compound	Yield (%)	M.p. (°C)	Elemental analysis: found (calcd.) (%)		Formula for calc.
			C	H	
I <sub>1</sub>	61.8	160–162	66.99 (67.05)	4.92 (4.88)	C <sub>45</sub> H <sub>39</sub> GeO <sub>2</sub> Sb
I <sub>2</sub>	51.3	173–175	67.16 (67.36)	5.01 (5.04)	C <sub>46</sub> H <sub>41</sub> GeO <sub>2</sub> Sb
I <sub>3</sub>	86.3	168–170	68.94 (69.43)	5.02 (4.91)	C <sub>51</sub> H <sub>43</sub> GeO <sub>2</sub> Sb
II <sub>1</sub>	85.4	208–210	66.57 (66.44)	5.11 (5.40)	C <sub>65</sub> H <sub>63</sub> Ge <sub>2</sub> O <sub>4</sub> Sb
II <sub>2</sub>	91.6	160–161	60.06 (60.23)	4.13 (4.40)	C <sub>62</sub> H <sub>54</sub> Cl <sub>3</sub> Ge <sub>2</sub> O <sub>4</sub> Sb
II <sub>3</sub>	43.1	190–192	63.50 (63.56)	4.45 (4.30)	C <sub>72</sub> H <sub>58</sub> Cl <sub>3</sub> Ge <sub>2</sub> O <sub>4</sub> Sb
II <sub>4</sub>	73.1	209–211	68.65 (68.79)	5.04 (4.89)	C <sub>72</sub> H <sub>61</sub> Ge <sub>2</sub> O <sub>4</sub> Sb
II <sub>5</sub>	64.7	179–181	69.25 (69.33)	5.05 (5.20)	C <sub>75</sub> H <sub>67</sub> Ge <sub>2</sub> O <sub>4</sub> Sb
II <sub>6</sub>	62.6	208–209	64.74 (65.22)	4.90 (4.83)	C <sub>60</sub> H <sub>53</sub> Ge <sub>2</sub> O <sub>4</sub> Sb

### 3. Experimental

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. <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra were measured on a Bruker AC-200 spectrometer or JEOL-FX-90Q spectrometer in CDCl<sub>3</sub> solution with TMS as internal standard. Mass spectra were recorded on a HP-5988A mass spectrometer (EI) at 70 eV, the temperature of ionization was 200°C. All the reactions involving metal halides were carried out under anhydrous and oxygen-free argon atmosphere. Solvents were purified, dried, and stored by literature methods.

#### 3.1. Reagents

The substituted β-triphenylgermanylpropionic acids were synthesized via the following reaction [25,26]. R<sub>3</sub>SbBr<sub>2</sub> was prepared by the method reported by W.J. Lice and co-workers [27]. R<sub>3</sub>Sb was converted into the corresponding dibromide by direct bromination, and the solid product was recrystallized from toluene–petroleum ether mixture. To prepare Ph<sub>4</sub>SbBr an adaptation of the method of W.E. McEwen and co-workers [4] was used. A suspension of 25.4 g (0.06 mol) of triphenylantimony dichloride in a mixture of ether (160 ml) and toluene (80 ml) was added slowly with stirring to a solution of phenylmagnesium bromide (0.18 mol) in 250 ml of ether. The mixture was stirred occasionally, and allowed to remain at room temperature (r.t.) for 6 days. A large amount of product had precipitated during this period. To the stirred mixture was added slowly 20 g ice and 26 ml of 40% hydrobromic acid, and the mixture were stirred overnight. After filtration and recrystallization of the precipitate from water–ethanol (3:2), the tetraphenylstibonium bromide weighed 16.6 g (54.4%) and had a m.p. 212–214°C (lit. 210–215°C).

Table 9  
Crystallographic data for compound II<sub>2</sub> and I<sub>3</sub>

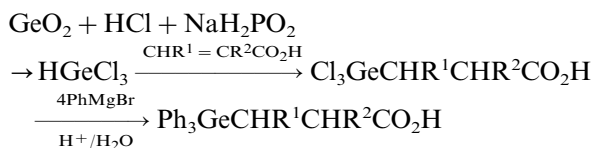
Compound	II <sub>2</sub>	I <sub>3</sub>
Formula	C <sub>62</sub> H <sub>54</sub> Cl <sub>3</sub> Ge <sub>2</sub> O <sub>4</sub> Sb	C <sub>51</sub> H <sub>43</sub> GeO <sub>2</sub> Sb
Temperature (K)	298	298
Wavelength (Å)	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic
Space group	<i>P</i> 2(1)/ <i>n</i>	<i>C</i> 2/ <i>c</i>
Unit cell dimensions		
<i>a</i> (Å)	13.2650	16.2787
<i>b</i> (Å)	23.5968	22.946
<i>c</i> (Å)	18.5131	26.013
$\alpha$ (°)	90	90
$\beta$ (°)	106.1420	107.640
$\gamma$ (°)	90	90
Volume (Å <sup>3</sup> )	5566.4	9259.9
<i>Z</i>	4	8
Density (Mg mm <sup>-3</sup> )	1.474	1.353
Absorption coefficient (mm <sup>-1</sup> )	1.745	1.276
<i>F</i> (000)	2492	3348
Crystal size (mm)	0.20 × 0.25 × 0.30	0.30 × 0.25 × 0.20
$\theta$ Range for data collection (°)	1.69–25.03	1.58–25.03
Limiting indices	–15 ≤ <i>h</i> ≤ 10, –27 ≤ <i>k</i> ≤ 28, –20 ≤ <i>l</i> ≤ 22	–19 ≤ <i>h</i> ≤ 15, –27 ≤ <i>k</i> ≤ 27, –30 ≤ <i>l</i> ≤ 30
Reflection collected	22 885	19 138
Independent reflections	9785 ( <i>R</i> <sub>int</sub> = 0.0477)	8191 ( <i>R</i> <sub>int</sub> = 0.0416)
Completeness to $\theta = 25.03^\circ$	99.5%	100.0%
Absorption correction	None	SADABS
Refinement method	Full-matrix least-squares on <i>F</i> <sup>2</sup>	Full-matrix least-squares on <i>F</i> <sup>2</sup>
Goodness-of-fit on <i>F</i> <sup>2</sup>	0.972	1.063
Final <i>R</i> indices [ <i>I</i> > $\sigma$ ( <i>I</i> )]	<i>R</i> <sub>1</sub> = 0.0412, <i>wR</i> <sub>2</sub> = 0.0884	<i>R</i> <sub>1</sub> = 0.0456, <i>wR</i> <sub>2</sub> = 0.1232
<i>R</i> indices (all data)	<i>R</i> <sub>1</sub> = 0.0860, <i>wR</i> <sub>2</sub> = 0.1053	<i>R</i> <sub>1</sub> = 0.0599, <i>wR</i> <sub>2</sub> = 0.1313
Large difference peak and hole (e Å <sup>-3</sup> )	1.077 and –0.890	1.150 and –0.771

Table 10  
Antitumor activity of the selected compounds in vitro

Compound	$X \pm \text{S.D.}^a$ , inhibition ratio (%) (10 $\mu\text{M}$ )				
	HL-60 cells	EJ cells	Skov3 cells	Hela cells	BGC-823 cells
<b>I</b> <sub>2</sub>	1.522 $\pm$ 0.179, 31.7	–	0.62 $\pm$ 0.037, 14.5	2.006 $\pm$ 0.091, 13.6	0.705 $\pm$ 0.026, 15.1
<b>I</b> <sub>3</sub>	2.246 $\pm$ .404, –24.8	1.074 $\pm$ 0.065, 8.5	0.674 $\pm$ 0.027, 10.9	1.591 $\pm$ 0.439, 27.9	0.662 $\pm$ 0.017, 22.5
<b>II</b> <sub>2</sub>	0.719 $\pm$ .025, 67.7	0.23 $\pm$ 0.034, 80.5	0.5 $\pm$ 0.013, 30.8	2.083 $\pm$ 0.241, 9.83	0.54 $\pm$ 0.078, 37.2
<b>II</b> <sub>4</sub>	0.295 $\pm$ 0.041, 46.7	0.911 $\pm$ 0.32, 22.4	0.553 $\pm$ 0.025, 26.9	1.227 $\pm$ 0.017, 44.4	0.833 $\pm$ 0.048, 8.2
<b>II</b> <sub>5</sub>	1.387 $\pm$ 0.286, 30.0	–	0.606 $\pm$ 0.091, 19.9	1.165 $\pm$ 0.268, 47.2	2.129 $\pm$ 0.076, 1.0
<b>II</b> <sub>6</sub>	1.944 $\pm$ 0.068, 12.71	1.088 $\pm$ 0.026, 7.33	–	1.842 $\pm$ 0.227, 16.54	0.803 $\pm$ 0.071, 6.52
<b>a</b> <sup>b</sup>	0.9	7.9	5.8	0.3	–

<sup>a</sup>  $X \pm \text{S.D.}$ , the observed mean values and the standard deviation.

<sup>b</sup>  $\text{Ph}_3\text{GeCH}_2\text{CHCH}_3\text{CO}_2\text{H}$ .



### 3.2. Synthesis of the title compounds

The title compounds were synthesized by a more convenient method. Typically, to  $\beta$ -triphenylgermanylpropionic acid (1 mmol) and triethylamine (0.8 ml) in toluene (40 ml) was added 0.5 mmol of  $\text{R}_3\text{SbBr}_2$  (or 1 mmol of  $\text{Ph}_4\text{SbBr}$ ). The reaction mixture was stirred at r.t. for 6–8 h and filtered. The filtrate was evaporated in vacuo. The obtained solid was recrystallized from  $\text{CH}_2\text{Cl}_2$ –petroleum ether. The yields, melting points and elemental analysis of the prepared compounds are given in Table 8.

### 3.3. Crystal structure determination

Diffraction measurements of compounds **I**<sub>3</sub> and **II**<sub>2</sub> were carried out at 298 K on a Bruker Smart 1000 diffractometer (graphite-monochromatized Mo– $\text{K}\alpha$  radiation,  $\lambda = 0.71073 \text{ \AA}$ ). The crystal class, orientation matrix and accurate unit-cell parameters were determined by standard procedures. The intensities were corrected for absorption using SADABS program. The structure was solved by heavy atom method and refined by a full-matrix least square procedure based on  $F^2$ . Non-hydrogen atoms were refined with anisotropic thermal parameters. Crystal data are summarised in Table 9.

## 4. Antitumor activity

The antitumor activity was assayed by the MTT or SRB methods [28]. Antitumor activities of some selected compounds were listed in Table 10. The results of bioassay showed that these compounds exhibit cer-

tain activities against cancer cells in vitro. The compounds including organoantimony moiety have relatively higher antitumor activities than triphenylgermanylpropionic acid. The antitumor data indicate that the antitumor activities are affected by the nature of the aryl and the triphenylgermanylpropionic acids, for example, when  $\text{R}^3$  is 4- $\text{ClC}_6\text{H}_4$  compound **II**<sub>2</sub> has relatively higher antitumor activity.

## 5. Supplementary material

Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre, CCDC no. 146615 for compound **I**<sub>3</sub> and CCDC no. 146616 for compound **II**<sub>2</sub>. Copies of this information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

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