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Studies of bimetallic carboxylates: their synthesis, characterization, biological activity and X-ray structure

Imtiaz-ud-Din [a], M. Mazhar [a,*], Khalid M. Khan [b], M.F. Mahon [c], K.C. Molloy [c]

[a] Department of Chemistry, Quaid-i-Azam University, Islamabad 45320, Pakistan
[b] HEJ Research Institute of Chemistry, International Center for Chemical Sciences, University of Karachi, Karachi 75270, Pakistan
[c] Department of Chemistry, University of Bath, Bath BA2 7AY, UK

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Abstract

Ten novel diorganotin dicarboxylates containing germanium in the carboxylate ligand have been synthesized and their structures have been characterized by IR, Mössbauer and multinuclear NMR (^{1}H, ^{13}C, ^{119}Sn) spectroscopies and X-ray diffraction. Also, the twodiastereotopic protons of the methylene group which are directly attached to the chiral center in these compounds have been successfully analyzed for the first time. The resulted ABX system gives three coupling constants and three chemical shifts. The single crystal X-ray analysis of precursor (p-$CH_3C_6H_4$)$_3$GeCH(p-$CH_3C_6H_4$)CH_2COOH revealed the dimeric structure of the molecule through H-bonding between carboxylic acid groups in a conventional manner. The results of their biological activity suggest that the materials have potential to be used as drugs.

Keywords: Synthesis; Diorganotindicarboxylates; Germanium; Spectroscopy; Diastereotopy; X-ray structure; Biological activities

1. Introduction

Organotin compounds show a diversity of applications which exist for its constituent compounds. There are now more organometallic compounds of tin in commercial use than any other element, covering a spectrum of fields of both biologically related and non-biological applications [1]. The dialkyltin compounds have lowest mammalian toxicity and exhibit greater antitumour activity than the corresponding mono- and tri-alkyl derivatives [2]. It has been reported that germanium-substituted organotin carboxylates possess potential activity against certain bacteria [3]. To further widen the scope of biological activity of diorganotin compounds, there is a need to prepare new series of diorganotin carboxylates containing germanium as a part of carboxylate ligand. The introduction of germanium in these compounds is primarily an attempt to achieve lower toxicity, high biological activity and strengthen body immune system [4,5]. Unfortunately, epidemic diseases, in different parts of the world, are spreading as a result of non-availability of the highly priced drugs or more seriously due to the development of parasitic resistance against the available drugs. In view of this situation, there is a need to develop new drugs that are low priced, easily available and safe to administer. We, therefore, have been motivated to search for new compounds to overcome these problems and report here synthesis, characterization and biological activities of some new diorganotin carboxylates containing germanium of general formula:

$$[R^4]_2Sn[OOCCH(R^3)CH(R^2)Ge(R^1)_3]_2$$

where $R_1 = p$-$CH_3C_6H_4$, C_6H_5; $R^2 = C_6H_5$, o-$CH_3C_6H_4$, p-$CH_3C_6H_4$, p-$CH_3OC_6H_4$; $R^3 = H$, CH_3; $R^4 = n$-C_4H_9, n-C_8H_{17}.

Another fascinating feature exhibited by such compounds is that of the presence of a chiral center in the vicinity of the methylene group which may cause 'non-equivalence' of the two methylene protons in the ^{1}H NMR spectra, a phenomenon commonly termed as diastereotopic effect [6]. The spin coupling in the NMR

* Corresponding author. Tel.: 92519219811; fax: 925128273869.
E-mail address: mazhar42pk@yahoo.com (M. Mazhar).

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Table 1
The yields and elemental analysis of $(R^1)_3$ Ge–CH(R^2)–CH(R^3)COOH

Compound no.	R^1	R^2	R^3	Yield (%)	Physical state	MP (°C)	Elemental analysis found (calc.) (%)	
							C	H
$\mathbf{I}_1$	p-$CH_3C_6H_4$	C_6H_5	H	65.0	Crystalline solid	180–182	72.40 (72.73)	6.29 (6.06)
$\mathbf{I}_2$	p-$CH_3C_6H_4$	p-$CH_3C_6H_4$	H	73.0	Crystalline solid	218–219	72.41 (73.08)	6.21 (6.29)
$\mathbf{I}_3$	p-$CH_3C_6H_4$	o-$CH_3C_6H_4$	H	74.0	Crystalline solid	210–212	73.20 (73.08)	6.42 (6.29)
$\mathbf{I}_4$	p-$CH_3C_6H_4$	p-$CH_3OC_6H_4$	H	69.5	Crystalline solid	192–194	70.97 (70.85)	6.23 (6.10)
$\mathbf{I}_5$	p-$CH_3C_6H_4$	C_6H_5	CH_3	68.8	Crystalline solid	174–175	72.98 (73.08)	6.89 (6.29)
$\mathbf{I}_6$	C_6H_5	C_6H_5	CH_3	71.6	Crystalline solid	150–151	71.98 (71.94)	5.69 (5.57)

spectra of these organometallics has been used for the first time for the characterization of organic portion present in these compounds and the complex NMR spectrum of methylene group corresponding to ABX system. The geminal coupling constant (J_{gem}) in a diastereotopic methylene group, besides other factors, may depend upon the HCH-bond angle and the neighboring substituents [7]. The magnitude of (J_{gem}) for sp^3-hybridized carbon, with an HCH-bond angle of 109°, lies between 11 and 17 Hz [23]. This phenomenon is quite fairly found in naturally occurring biologically active compounds [8]. Spin–spin coupling in NMR spectroscopy also help in investigating various dynamic processes taking place in these compounds.

2. Experimental

Dibutyltin oxide and dioctyltin oxide were purchased from Aldrich (Germany) while germanium dioxide (99.9% purity) was procured from Peoples Republic of China and were all used as received. All chemical reactions were carried out in organic solvents, which were dried before used in accordance to standard methods [9].

Elemental analyses were carried out at Midwest Microlab Indianapolis, USA. Melting points were determined with a Mitamura Riken Kogyo (Japan) apparatus and are uncorrected. Infrared spectra were recorded on Bio-Rad Excalibure FTIR Model FTS 3000 MX as KBr pellets. ^1H and ^{13}C NMR spectra in solution ($CDCl_3$) were recorded at ambient temperature on a Bruker 300 Spectrometer operating at 300 and 75 MHz, respectively, using TMS as a reference. Details of our Mössbauer spectrometer and related procedures are given elsewhere [10].

2.1. Synthesis

The precursors, triorganogermyl (substituted) propanoic acids were prepared according to [11,12]. The physical properties, yields and elemental analysis of the precursors are given in Table 1.

The compounds (**I**–**X**) were prepared by the following procedure.

In a two necked 100 cm^3 flask, fitted with Dean-Stark apparatus, reflux condenser and magnetic stirrer, was added 2.00 mmol of the appropriate germanium substituted propanoic acid and 1.00 mmol of diorganotin oxide in toluene (50 cm^3). The contents were refluxed for 8–9 h by continuous removal of water, then allowed to cool at room temperature and toluene was removed under reduced pressure. The resulting solid was recrystallized in chloroform/pet-ether mixture (1:3) to yield the product as white crystalline solid. The physical and analytical data of the prepared organotin compounds are given in Table 2.

2.2. X-ray crystallography

The methodology of [12] was followed to obtained a crystal suitable for X-ray diffraction. Crystallographic and experimental details are given in Table 2. For the precursor, (p-$CH_3C_6H_4)_3GeCH(p$-$CH_3C_6H_4)CH_2COOH$, the dataset was collected on a crystal of size $0.25 \times 0.25 \times 0.25$ mm at 150 K on a Nonius Kappa CCD

Table 2
Crystallographic data for compound $\mathbf{I}_2$

Empirical formula	$C_{31}H_{32}GeO_2$
Formula weight	509.16
Crystal system	triclinic
Space group	$P\bar{1}$
a (Å)	10.2070(2)
b (Å)	10.8370(2)
c (Å)	13.4580(2)
α (°)	109.449(1)
β (°)	99.039(1)
γ (°)	105.394(1)
V (Å^3)	1303.05(4)
Z	2
μ(Mo Kα) (mm^{-1})	1.200
Reflections collected	26,372
Independent reflections	7597 [$R_{int} = 0.0376$]
Reflections observed (>2σ)	6447
Goodness-of-fit on F^2	1.028
Final R_1, wR_2 indices [$I > 2\sigma(I)$]	0.0347, 0.0796
R_1 wR_2 indices (all data)	0.0463, 0.0841

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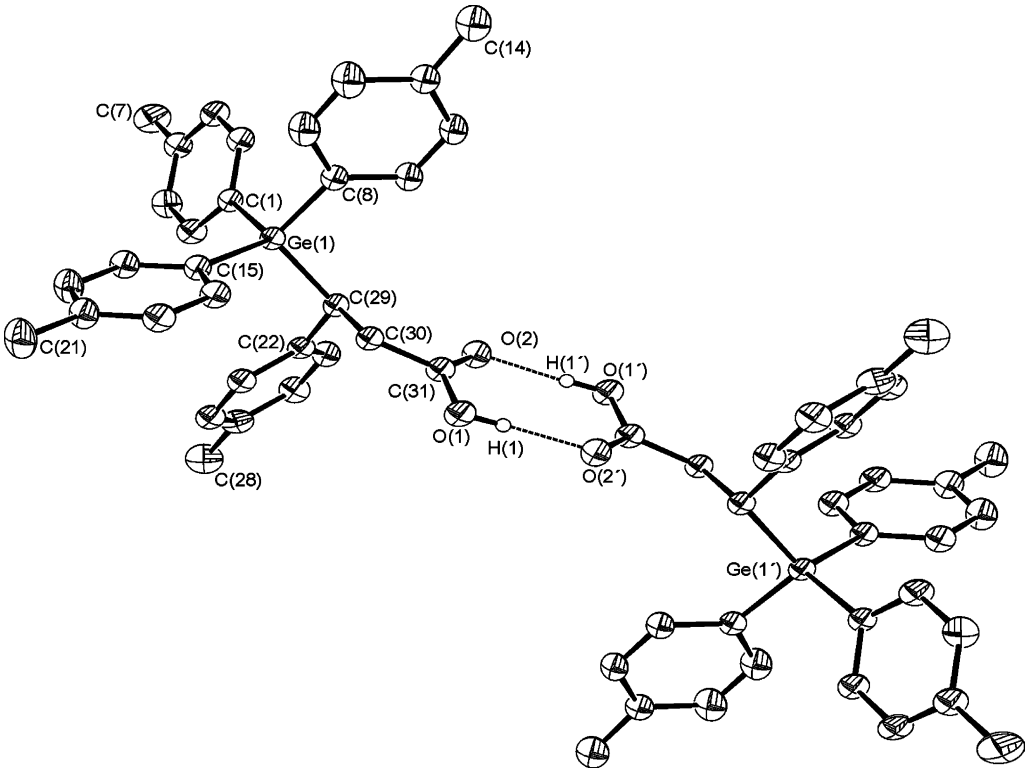


Fig. 1. The structure of compound ($\mathbf{I}_2$). Primed atoms are related to their unprimed counterparts by the operation $2-x,-y,-z$. Selected geometric data: Ge(1)–C(1) 1.951(2), Ge(1)–C(8) 1.948(2), Ge(1)–C(15) 1.952(2), Ge(1)–C(29) 1.983(2), O(1)–C(31) 1.321(2), O(2)–C(31) 1.217(2) Å; C(1)–Ge(1)–C(8) 108.29(7)°, C(1)–Ge(1)–C(15) 110.57(6)°, C(1)–Ge(1)–C(29) 110.69(6)°, C(8)–Ge(1)–C(15) 109.74(7)°, C(8)–Ge(1)–C(29) 105.89(6)°, C(15)–Ge(1)–C(29) 111.50(6)°.

diffractometer using Mo Kα radiation; Lp and absorption corrections (semi-empirical from equivalents) were applied. Refinement was full-matrix least-squares on F^2. Hydrogen atoms were included at calculated positions, save for the acid hydrogen which was located and refined at fixed distance (0.89 Å) from O1. The dimeric structure of ($\mathbf{I}_2$) along with selected geometric data are given in Fig. 1.

Software used: SHELXS 86 [13], SHELXL 97 [14], ORTEX [15].

2.3. Biological studies

Biological activities of these diorganotin dicarboxylates containing germanium were determined against various bacteria and fungi by the "agar well diffusion method" [16]. Cytotoxicity data for these collected by "Brine Shrimp method" [17].

3. Discussion

Ten germanium substituted di-*n*-butyltin and di-*n*-octyltin dipropionates were synthesized by the condensation of di-*n*-butyltin oxide or/and di-*n*-octyltin oxide and triorganogermyl (substituted) propanoic acids in 1:2 mol ratio, respectively, by use of a Dean and Stark apparatus. The reaction proceeds a follows:

$$(R^4)_2SnO + HO_2CCH(R^3)CH(R^2)Ge(R^1)_3 \xrightarrow[\text{Toluene}]{\text{Reflux}} (R^4)_2Sn[OOCCH(R^3)CH(R^2)Ge(R^1)_3]_2 + H_2O$$

The yield obtained for these diorganotin derivatives are 70–80%. The compounds are soluble in chloroform and toluene and are air and moisture stable (see Table 3).

The infrared spectrum of these compounds has been recorded in the range of 4000–400 cm^{-1}. The absorption bands can be assigned on the basis of earlier publications [3,18] and important data are listed in Table 4. In the spectra, medium to weak bands in the region 471–491 cm^{-1} are assigned to Sn–O whereas those in the region 580–593 cm^{-1} indicate the presence of Sn–C bond [19]. The complexation by deprotonation of substituted germyl propanoic acid ligand has been evidenced by the absence of ν(OH) band at ca. 3400 cm^{-1}. Furthermore, a new peak in the range of 471–491 cm^{-1} indicates the presence of Sn–O–C unit in all the compounds. Another evidence of tin–carboxylate bond formation comes from parameter $\Delta\nu[\Delta\nu = \nu(COO)_{asy} - \nu(COO)_{sym}]$ which is also used to determine the nature of bonding of the carboxylate to tin(IV) [20]. It has been observed that

Table 3
The yields, melting points, elemental analysis and R′ groups discription of diorganotindicarboxylates $(^4R)_2Sn[OOCH(^3R)CH(^2R)Ge(^1R)_3]_2$

Compound no.	^1R	^2R	^3R	^4R	MP (°C)	Analysis found (calc.) (%)		Yield (%)
						C	H	
I	p-$CH_3C_6H_4$	C_6H_5	H	n-C_4H_9	148–150	67.00 (66.89)	6.7 (6.4)	78.6
II	p-$CH_3C_6H_4$	p-$CH_3C_6H_4$	H	n-C_4H_9	175–176	67.10 (67.25)	6.38 (6.41)	80.5
III	p-$CH_3C_6H_4$	o-$CH_3C_6H_4$	H	n-C_4H_9	208–209	67.21 (67.25)	6.42 (6.41)	83.7
IV	p-$CH_3C_6H_4$	p-$CH_3OC_6H_4$	H	n-C_4H_9	140–141	65.43 (65.57)	6.45 (6.25)	76.5
V	p-$CH_3C_6H_4$	C_6H_5	CH_3	n-C_4H_9	228–230	67.44 (67.25)	6.56 (6.41)	72.8
VI	C_6H_5	C_6H_5	CH_3	n-C_4H_9	210–211	65.26 (65.87)	5.94 (5.83)	75.2
VII	p-$CH_3C_6H_4$	C_6H_5	H	n-C_8H_{17}	170–172	68.51 (68.42)	6.85 (6.90)	71.4
VIII	p-$CH_3C_6H_4$	p-$CH_3C_6H_4$	H	n-C_8H_{17}	118–120	68.48 (68.77)	7.02 (7.05)	79.8
IX	p-$CH_3C_6H_4$	o-$CH_3C_6H_4$	H	n-C_8H_{17}	134–135	68.82 (68.77)	7.10 (7.05)	81.5
X	p-$CH_3C_6H_4$	p-$CH_3OC_6H_4$	H	n-C_8H_{17}	128–130	67.15 (67.19)	7.97 (6.89)	74.8

Table 4
Characteristic IR absorption frequencies (cm^{-1}) of diorganotin dicarboxylates of general formula $(^4R)_2Sn[OOCH(^3R)CH(^2R)Ge(^1R)_3]_2$

Compound	ν_{asym}(COO)	ν_{sym}(COO)	$\Delta\nu$	ν(Ge–C)	ν(Sn–O)	ν(Sn–C)
I	1596	1375	221	664	482	589
II	1605	1370	235	669	491	590
III	1604	1376	228	670	489	589
IV	1608	1378	230	661	480	588
V	1634	1398	236	698	484	580
VI	1636	1404	232	682	485	586
VII	1593	1385	210	662	478	593
VIII	1597	1382	215	669	471	590
IX	1592	1379	213	670	478	588
X	1598	1380	218	668	475	588

$\nu(COO)_{asym}$ occurred in the range of 1580–1681 cm^{-1} and $\nu(COO)_{sym}$ in the range of 1375–1408 cm^{-1}. The $\Delta\nu$ values (210–236 cm^{-1}) reveal that carboxylate groups behave as bidentate ligand in all these compounds.

^1H NMR data of the compounds (**I**–**X**) are presented in Tables 5 and 6. All the protons in the compounds have been identified by intensity and multiplicity patterns and the total number of protons calculated from the integration curve are in agreement with the expected molecular composition. The di-*n*-butyltin derivatives (**I**–**VI**) show a multiplet in the region 0.54–1.07 ppm for butyl protons with a well-defined triplet around 0.54–0.68 ppm due to the terminal methyl protons with (^1H–^1H) coupling constant at nearly 6.8 Hz [21]. Similarly, di-*n*-octyltin derivatives (**VII**–**X**) exhibited a multiplet in range 0.82–1.25 ppm for octyl protons with a well-defined triplet around 0.82–0.86 ppm which is due to the terminal methyl protons having (^1H–^1H) coupling constant at about 7.5 Hz. Aromatic protons are observed to be resolved in two distinct of multiplets in aromatic region due to the presence of two aromatic groups (R^1 and R^2).

In **I**–**X** (except **V** and **VI**) the CHGe is a chiral center, the CH_2 is a prochiral center and three hydrogens, CH_2CHGe unit, comprise an ABX system which appears as two multiplets in region of 2.81–2.98 and 3.32–3.76 ppm, respectively. Sub-spectral analysis of ABX spectra revealed that the eight lines portion of the spectrum is made up of two AB sub-spectra whereas the X-part of the spectrum consists of only four detectable lines. The two protons of the methylene group(A,B), being diastereotopic, coupled to the third proton(X) of the chiral center giving three chemical shifts ν_A, ν_B and ν_X and three suitable coupling constants, J_{AB}, J_{AX} and J_{BX}. The three chemical shifts for these compounds along with geminal coupling constant (J_{AB}) and two different vicinal coupling constants (J_{AX} and J_{BX}) are given in Table 6. The methylene protons show J_{AB} value of 15 ± 1 Hz [22] and J_{BX} fall in range 4 ± 1 Hz, J_{AX} value of 12 ± 1 Hz. Another important observation in this system is the extent of diastereotopy ($\Delta\delta = \delta_A - \delta_B$) which is typically about 0.07 ppm [23] but increases when influenced by the π-electrons of the substituents attached at the chiral center. The $\Delta\delta$ values for these compounds range 0.09–0.16 ppm which signified the increased extent of diastereotopy. For **V**, **VI**, one of the methylenic proton is replaced by CH_3 group and the unit $CH(CH_3)CHGe$ no longer belongs to ABX system and the two hydrogens appear as multiplets in close vicinity.

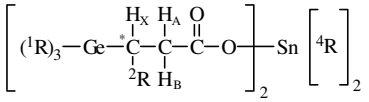
The ^{13}C NMR spectral data for compounds (**I**–**X**) have been presented in Table 7. The carbon attached to

Table 5
^{1}H NMR data of diorganotin dicarboxylates of general formula[a,b,c,d] $[(R^1)_3GeCH(R^2)CH(R^3)COO]_2Sn(R^4)_2$

Compound no.	R^2	R^1	R^4		CH–R^3	CH
			CH_3	$(CH_2)_3$		
I	6.81–6.90 (10H, m)	7.08–7.18 (24H, m) 2.34[a] (18H, s)	0.68 (6H, t) (6.9)	0.86–1.07 (12H, m)	2.85 (4H, m)	3.58 (2H, m)
II	6.78–6.85 (8H, m) 2.22[a] (6H, s)	7.11–7.18 (24H, m) 2.33[a] (18H, s)	0.67 (6H, t) (6.9)	0.87–1.05 (12H, m)	2.89 (4H, m)	3.54 (2H, m)
III	6.55–6.59 (8H, m) 1.79[a] (6H, s)	6.79–6.94 (24H, m) 2.18[a] (18H, s)	0.54 (6H, t) (6.8)	0.70–0.85 (12H, m)	2.81 (4H, m)	3.65 (2H, m)
IV	6.60–6.80 (8H, m) 3.70[a] (6H, s)	7.12–7.18 (24H, m) 2.33[a] (18H, s)	0.68 (6H, t) (6.8)	0.87–1.04 (12H, m)	2.87 (4H, m)	3.55 (2H, m)
V	−6.90–6.92 (10H, m)	7.06–7.08 (24H, m) 2.33[a] (18H, s)	0.67 (6H, t) (6.9)	0.98–1.05 (12H, m)	3.31 (4H, m) 1.20 (6H, d)	3.32 (2H, m)
VI	6.89–7.04 (10H, m)	7.19–7.28 (30H, m)	0.71 (6H, t) (6.6)	0.89–1.02 (12H, m)	3.32 (4H, m) 1.21 (6H, d)	3.37 (2H, m)
			CH_3	$(CH_2)_7$		
VII	6.84–6.98 (10H, m)	7.07–7.19 (24H, m) 2.32[a] (18H, s)	0.82 (6H, t) (6.9)	0.86–1.23 (28H, m)	3.06 (4H, m)	3.72 (2H, m)
VIII	6.76–6.87 (8H, m) 2.23[a] (6H, m)	7.09–7.19 (24H, m) 2.33[a] (18H, s)	0.86 (6H, t) (6.8)	0.92–1.25 (28H, m)	2.89 (4H, m)	3.57 (2H, m)
IX	6.73–6.93 (8H, m) 1.94 (6H, s)	7.05–7.11 (24H, m) 2.33[a] (18H, s)	0.85 (6H, t) (7.1)	0.89–1.24 (28H, m)	2.83 (4H, m)	3.76 (2H, m)
X	6.60–6.64 (8H, m) 3.7[a] (6H, s)	7.09–7.10 (24H, m) 2.33[a] (18H, s)	0.86 (6H, t) (7.0)	0.88–1.25 (28H, m)	2.87 (4H, m)	2.55 (2H, m)

$R^1 = p\text{-}CH_3C_6H_5$ (for compounds **I**, **II**, **III**, **IV**, **V**, **VII**, **VIII**, **IX**, **X**), C_6H_5 (for compound **VI**).
$R^2 = C_6H_5$ (for compounds **I**, **V**, **VI**, **VII**), $o\text{-}CH_3C_6H_4$ (for compounds **III**, **IX**), $p\text{-}CH_3C_6H_4$ (for compounds **II**, **VIII**), $p\text{-}CH_3OC_6H_4$ (for compounds **IV**, **X**).
$R^3 = H$ (for compounds **I**, **II**, **III**, **IV**, **VII**, **VIII**, **IX**, **X**), CH_3 (for compounds **V**, **VI**).
$R^4 = n\text{-}C_4H_9$ (for compounds **I**–**VI**), $n\text{-}C_8H_{17}$ (for compounds **VII**–**X**).
[a] Substituents on the phenyl rings.
[b] In $CDCl_3$ at 297K.
[c] Chemical shift (δ) in ppm, $^nJ(^1H–^1H)$ in Hz.
[d] Multiplicity is given as: s, singlet; d, doublet; t, triplet; m, multiplet.

Table 6
^{1}H NMR data in $CDCl_3$ for the protons at and around chiral center of diorganotin derivatives with general formula[a,b]



make the CH_2 carbon C_2, so that the designation used in the text is clear

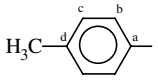
Compound no.	H_A	H_B	H_X	J_{gem} (Hz)	J_{vic} (Hz)	$(\delta H_A - \delta H_B)\ \Delta\delta$
I	3.01 (1H, dd)	2.87 (1H, dd)	3.60 (1H, dd)	15.30	4.22, 12.95	0.14
II	2.93 (1H, dd)	2.84 (1H, dd)	3.56 (1H, dd)	15.11	4.32, 12.88	0.09
III	2.82 (1H, dd)	2.69 (1H, dd)	3.65 (1H, dd)	15.20	4.31, 12.79	0.13
IV	2.94 (1H, dd)	2.84 (1H, dd)	3.54 (1H, dd)	15.27	4.89, 12.14	0.10
VII	3.27 (1H, dd)	3.11 (1H, dd)	3.73 (1H, dd)	15.71	5.01, 12.85	0.16
VIII	2.93 (1H, dd)	2.84 (1H, dd)	3.56 (1H, dd)	16.0	4.16, 12.96	0.09
IX	2.97 (1H, dd)	2.81 (1H, dd)	3.78 (1H, dd)	15.16	4.26, 12.94	0.16
X	2.93 (1H, dd)	2.84 (1H, dd)	3.54 (1H, dd)	15.50	4.71, 12.15	0.09

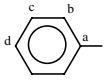
[a] Chemical shifts (ppm), splitting pattern.
[b] Coupling constants in Hz.

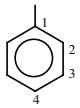
tin and other unique carbons have been explicitly differentiated for these diorganotin derivatives. The α-carbon of the alkyl group attached to tin occurs at ca.25 ppm in both the dibutyl- and dioctyltin(IV) derivatives. The aromatic carbon resonances were assigned by comparison of experimental chemical shift with those calculated from incremental method [24] and with the literature values [3,25]. The group with strong electron withdrawing effect e.g. methoxy, attached to the aromatic ring (^{2}R) resonates at very low field. The measurement of coupling constants $^nJ[^{119}Sn–^{13}C]$ makes it easier to establish molecular structure of tin compounds.

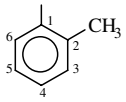
Table 7
^{13}C NMR data for $[(R^1)_3GeCH(R^2)CH(R^3)COO]Sn(R^4)_2$[a,b]

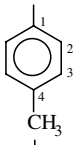
		I	II	III	IV	V	VI	VII	VIII	IX	X
R^1	a	141.3	138.7	138.8	138.7	142.1	142.0	139.5	139.5	138.7	138.7
	b	135.5	135.5	135.4	135.5	135.4	135.6	135.0	135.8	135.5	135.5
	c	128.9	128.3	128.9	129.3	128.8	128.9	128.4	130.3	129.9	129.3
	d	131.6	131.9	139.8	138.4	128.6	128.6	133.8	136.4	131.7	133.4
R^2	1	138.7	138.1	136.3	131.3	138.0	138.6	138.7	138.1	139.8	131.9
	2	128.3	128.6	131.7	128.9	132.4	132.4	127.9	128.6	136.2	128.9
	3	127.9	128.9	130.0	113.4	128.0	128.0	128.9	128.9	128.8	113.4
	4	125.3	134.5	126.7	157.5	125.3	125.3	126.6	134.5	126.7	157.5
	5	–	–	125.0	–	–	–	–	–	124.9	–
	6	–	–	125.8	–	–	–	–	–	125.7	–
R^1–CH_3		21.45	21.45	21.45	21.42	21.38	–	29.68	22.89	21.42	21.48
R^2–CH_3		–	24.78	24.73	–	–	–	–	24.12	24.02	–
R^2–OCH_3					55.07						55.07
R^3–CH		36.57	36.76	36.72	36.93	43.41	43.38	38.40	38.12	36.68	36.92
–CH		32.77	32.30	29.72	31.95	41.21	41.49	34.19	34.67	33.17	33.21
R^3		H	H	H	H	19.43	19.85	H	H	H	H
Sn	1	24.83	20.93	20.19	24.84	24.63	25.11	24.09	24.12	24.03	24.16
		^1J[567.0]	[571.4]	[568.0]	[574]	[568]	[568.2]				
	2	29.71	29.76	27.90	29.71	26.20	30.16	31.92	31.16	31.95	31.90
		^2J[33.4]	[34.2]	[34.0]	[34.9]	[34.5]	[34.1]				
	3	26.18	26.12	26.13	26.10	26.13	26.61	25.10	25.55	25.12	25.27
		^3J[92.0]	[95.1]	[93.4]	[96.3]	[94.2]	[93.8]				
	4	13.2	13.25	13.28	13.25	13.26	13.90	29.34	30.28	29.39	29.37
	5	–	–	–	–	–	–	29.16	29.41	29.22	29.20
	6	–	–	–	–	–	–	28.80	26.58	28.81	28.85
		–	–	–	–	–	–	22.62	22.54	22.64	22.66
	8	–	–	–	–	–	–	14.07	15.57	14.13	14.08
COO		182.91	183.00	183.12	183.00	186.17	186.29	182.8	184.45	183.11	183.00

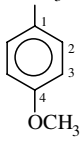
$R^1 =$  (For compounds I, II, III, IV, V, VII, VIII, IX, X).

 (For compound VI).

$R^2 =$  (For compounds I, V, VI, VII).

 (For compounds III, IX).

 (For compounds II, VIII).

 (For compounds IV, X).

$R^3 =$ H (for compounds **I**–**IV** and **VIII**–**X**), CH_3 (for compounds **V**, **VI**).

$R^4 = C_4H_7$ (for compounds **I**–**VI**) Sn–$^1CH_2$–$^2CH_2$–$^3CH_2$–$^4CH_3$ C_8H_{17} (for compounds **VII**–**X**) Sn–$^1CH_2$–$^2CH_2$–$^3CH_2$–$^4CH_2$–$^5CH_2$–$^6CH_2$–$^7CH_2$–$^8CH_3$.

[a] In $CDCl_3$ at 297K.

[b] Chemical shifts in ppm, ^1J[^{119}Sn–^{13}C] in Hz.

Table 8
C–Sn–C angles (°) based on NMR parameters

Compound no.	$^1J[^{119}Sn–^{13}C]$ (Hz)	θ (°)
I	567.0	130.9
II	571.4	131.4
III	571.9	131.5
IV	574.0	131.7
V	568.2	131.1
VI	569.5	131.3

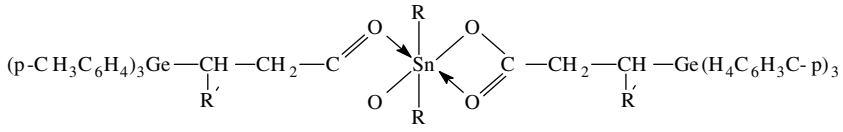
The magnitude of $^1J[^{119}Sn–^{13}C]$ for dibutyltin(IV) derivatives has been found out in range 569 ± 2 Hz which tallies with the literature values [26,27]. The C–Sn–C angle were calculated from ^1J values for dibutyltin derivatives which came out to be around 131° (Table 8). The crystallographic data for **III** and **X** have already been reported [28] which clearly depicted the C–Sn–C at the extreme of data (130–152°). The tin atom geometry is thus best described as based on a skew trapezoidal bipyramid geometry and suggested that two carboxylates chelate the tin with different degrees of asymmetry [29]. The NMR parameters ^1J and θ values support coordination numbers of more than four at tin(IV) in solution (in $CDCl_3$) as delineated by X-ray crystallographic data.

Table 10
Mössbauer data of some selected compounds

Compound code	QS (mm S^{-1})	IS (mm S^{-1})	ρ = QS/IS
I	3.89	1.48	2.62
II	3.73	1.48	2.52
IV	4.09	1.51	2.71
VI	3.79	1.53	2.48
IX	3.78	1.47	2.57

boxylate group and suggested in between penta- and hexa-coordinated geometry around tin in solution despite difference in solid state for these compounds.

^{119m}Sn Mössbauer data for some diorganotin dicarboxylates containing germanium are presented in Table 10. The QS splitting (Δ) values range from 3.73 to 4.09 mm S^{-1} which correspond to monomeric hexa-coordinated *trans*-C_2SnO_4 geometry around tin atom in the solid phase for these compounds. The IS (δ) measurements fall in range 1.48–1.51 mm S^{-1}. The ρ value greater than 2.1 demonstrated a coordination number greater than 4 around the tin atom for diorganotin carboxylates as earlier reports manifested [3,31]. The ρ values for these compounds lie in between 2.48 and 2.71 which support a structure similar to (**1**) as that described by Gielen et al. [32] and Tiekink [33].



(I)

^{119}Sn NMR chemical shift for these compounds is enlisted in Table 9 and exhibits a single resonance in range −145.0 to −150.3 ppm. The shift range of the compounds appears to be penta-coordinated tin as reported earlier [30]. The multinuclear (^{1}H, ^{13}C, ^{119}Sn) NMR data described dynamic behaviour of the car-

Table 9
^{119}Sn NMR data of compounds

Compound code	^{119}Sn δ (ppm)
I	−145.00
II	−146.47
III	−147.24
IV	−147.34
V	−150.37
VI	−150.40
VII	−146.30
VIII	−147.54
IX	−148.60
X	−147.64

R = *n*-Bu, *n*-octyl

R′ = Ph, *p*-MePh, *o*-MePh, *p*-MeOPh

In continuation of our previous reports [12,34], we report here the dimeric structure of (*p*-$CH_3C_6H_4$)GeCH(*p*-$CH_3C_6H_4$)CH_2COOH (**I_2**) (Fig. 1); crystallographic data are given in Table 2. The Ge atom adopts a slightly distorted tetrahedral coordination geometry [C–Ge–C: 108.37(7)–111.5(6)°] in this structure. The Ge–C bond lengths involving the three tolyl groups are identical within experimental error [1.948(2)–1.952(2) Å]. However, Ge–Csp^3 distance [Ge–C(29)] is significantly longer [1.983(2)Å], as observed previously in the related compound **I_3**, **I_5** [34,12]. The molecule forms dimeric pair about crystallographic inversion centers through hydrogen bonding interactions between carboxylic acid groups. The hydrogen bond is relatively strong [O(1)–O(2′): 2.663(2); H(2A)–O(1′): 1.82(4) Å; <O(2)–H(2A)–O(1′): 164(4)°]. The two C–O bond lengths [C(31)–O(2): 1.217(2); C(31)–O(1): 1.3211(9) Å] clearly differentiate

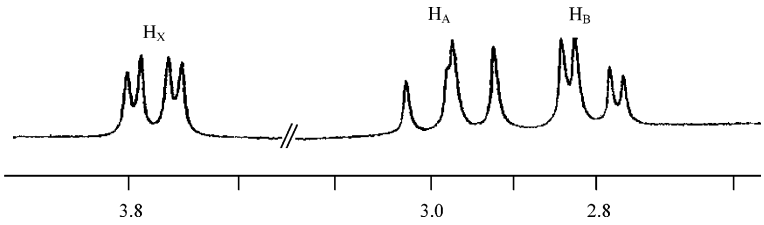


Fig. 2. ^{1}H NMR(300 MHz) demonstrating diastereotopic protons at C_2 in compound **VIII** $[(p\text{-}CH_3C_6H_4)_3GeCH_X(o\text{-}CH_3C_6H_4)CH_AH_BCO_2]_2Sn[n\text{-}C_8H_{17}]_2$.

between single and double bond characters of the two C–O moieties. The related compound $(p\text{-}CH_3C_6H_4)_3GeCH(C_6H_5)CH(CH_3)COOH$ confirmed the mode of dimerization of the compound [12]. The crystal structures of two germanium substituted dibutyltin carboxylates (**III**) and (**V**) have also already been reported [28]. Both structures consist of a monomer with Ge atom occupying tetrahedral geometry whereas the tin atom is distorted towards a skew trapezoidal bipyramid geometry as a result of weakly chelating carboxylate ligands (see Fig. 2)

4. Biological activities

4.1. Antibacterial bioassay

The antibacterial activity was assayed by agar well diffusion method. The results are summarized in Table 11. The activity of these newly synthesized compounds against six different types of bacteria *C. diphtheria*, *B. subtilis*, *S. pyogenes*, *S. aureus*, *P. aeruginosa* and *S. typhi*, relative to reference drug tetracycline, were studied. The antibacterial activity of the reported compounds was compared on the basis of substituent groups particularly R^1, R^2 and R^4 groups. All the compounds show good activity with few exceptions. Generally, when R^4 is dioctyl the range of antibacterial activity of the compounds is significantly increased.

4.2. Antifungal bioassay

The agar tube dilution protocol method was used to test the activity of the compounds against different types of fungi, i.e., *T. longiformis*, *C. albicans*, *A. flavis*, *M. canis*, *F. solani* and *F. moniliformis*, relative to standard drugs, Miconazole and Ketoconazole. The results are given in Table 12. Most of the compounds show no significant activity against fungi. However, some synthesized compounds such as compound (**I**) shows moderate activity against *T. longiformis*, compound (**II**) shows good activity only against **F. solani** and compound (**IX**) shows significant activity against *T. longiformis* and *F. Moniliformis*.

4.3. Cytotoxicity studies

The toxicity of these compounds particularly dioctyltin derivatives has been decreased by the incorporation of germinium. Toxicity of these diorganotin derivatives is measured by Brine Shrimp and bioassay method and their lethal doses (LD_{50}) are given in Table 13. The LD_{50} values for dibutyl derivatives were found in between 0.43 and 4.65 μg/ml which suggested comparatively a high degree of toxicity for these com-

Table 11
Bactericidal data of some diorganotin derivatives[a]

Name of bacteria	Zone of inhibition (mm)										
	I	**II**	**III**	**IV**	**V**	**VI**	**VII**	**VIII**	**IX**	**X**	Ref. drug (mm)
Corynebacterium diphtheriae	15	17	16	16	–	–	17	–	19	18	31
Bacillus subtilis	15	16	15	19	15	13	23	–	17	17	30
Streptococcus pyogenes	25	–	–	15	–	–	22	–	20	15	31
Staphlococcus aureus	15	–	–	14	–	10	19	–	15	15	29
Pseudomonas aeruginosa	15	15	–	–	15	–	17	–	17	18	20
Salmonella typhi	18	16	13	19	15	12	20	–	18	19	29

Reference drug tetracycline.
– No activity.
Size of well = 10 mm (diameter).
[a] (In vitro) concentration = 1 mg/ml of DMSO.

Table 12
Fungicidal screening data[a,b,c]

Compound no.	Human pathogens			Animal pathogens	Plant pathogens	
	Trichophyton logniformis	*Candid albicans*	*Aspergillus flavis*	*Microsporum canis*	*Fusarium solani*	*Fusarium moniliformis*
I	61.04	–	–	–	–	–
II	–	14.7	–	21	81	19
III	–	–	–	–	–	–
IV	–	–	–	–	–	–
V	–	–	–	–	–	–
VI	–	–	–	–	–	–
VII	10.4	–	–	20	10	–
VIII	–	–	–	–	–	–
IX	100	–	–	–	–	100
X	20.8	–	30	–	–	–

% Inhibition after 168 h conc. 200 μg/ml medium SDA.
Std. drugs = Miconazole and Ketoconazole (100%).
[a] in vitro.
[b] Incubation temp. 27 °C (28 ± 1 °C).
[c] Incubation period 7–10 days.

Table 13
Cytotoxicity data of diorganotin derivatives[a]

Sample code	LD_{50} (μg/ml)
I	1.38
II	4.65
III	3.53
IV	0.43
V	3.87
VI	3.74
VII	57.97
VIII	No positive lethality
IX	6.75
X	8.77
Etoposide[b]	0.91

[a] Against Brine Shrimp (Artemia saline).
[b] Reference drug.

pounds. On the other hand the LD_{50} values the dioctyltin derivatives show lower toxicity particularly compounds (**VII**) and (**VIII**) with lethal dose greater than 58 μg/ml but demonstrating enhanced antibacterial activity.

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