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Synthesis, characterisation, and structural elucidation by spectral investigation (FT-IR, multinuclear NMR, mass spectrometry) of biologically active organotin(IV) compounds containing germanium

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A new series of di and tri-organotin(IV) compounds containing germanium with the general formula $R_{4-n}SnL_n$ was synthesised by reaction of 3-triphenylgermanyl-3,3-dimethylpropionic acid with organotin(IV) oxides and organotin(IV) chloride in 2:1 and 1:1 molar ratio, respectively, where R = CH_3, C_2H_5, n-C_4H_9, n-C_8H_{17}, and C_6H_5 n = 1 or 2 and L = triphenylgermanyl acid anion (GeC_{23} H_{23} O_2^-). These compounds were characterised by elemental analyses, FT-IR, multinuclear NMR (^{1}H, ^{13}C, ^{119}Sn), and mass spectrometry. The geometry around the tin atom was determined and compared in both solution and solid states. The spectroscopic results indicated that all the diorganotin(IV) compounds containing germanium possess trigonal-bipyramidal structures in solution and octahedral geometry in the solid state. A linear polymeric trigonal-bipyramidal structure in the solid state and a tetrahedral environment around the tin atom in non-coordinating solvents has been proposed for the triorganotin(IV) compounds. All synthesised compounds were tested in vitro against a number of microorganisms to assess their biocidal properties and to correlate them with the structures of the derivatives. These studies revealed that such compounds show promising activity against different strains of bacteria and fungi using the reference drugs imipenum and miconazole.

Key Words: Bimetallic organotin, germanium carboxylates, microbial activity.

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Introduction

The chemistry of organometallic compounds in general and organotin compounds in particular has witnessed a quantum leap during the last 50 years owing to their potential biological and industrial applications.[1,2] The organotin(IV) compounds have been studied extensively and screened in vitro and in vivo for antitumour activity usually against P388 lymphocytic leukaemia,[3] especially in complexes where tin bonds to electronegative atoms, such as oxygen, nitrogen, and sulphur are present. Organotin compounds have gained an edge over other organometallics due to their bioavailability in the ecosystem and entrance into the food chain. Organotin compounds are now the active components in a number of biocidal formulations, finding applications in such diverse areas as fungicides, miticides, molluscicides, marine antifouling paints, surface disinfectants, and wood preservatives.[4]

Organogermanium compounds, the other class, have received much attention due to their diverse applications in the field of medicine, electronics, and optics.[5,6] Germanium compounds not only proved to be of low toxicity but also helped in developing the immune system in tumour-bearing animals. In 1994, the first organogermanium pharmaceutical propagermane was launched in Japan under the trade name Serocion (Sanwa Kenkyusho Co. Ltd.). Its biological activity spectrum includes protection against viruses, immunostimulation, and hepatoprolation. The introduction of germanium in organotin(IV) compounds is a preliminary attempt to achieve lower toxicity and high biological activity and strengthen the body's immune system.[6] In view of the diverse fields of applications of organotin(IV) and organogermanium compounds, we synthesised a new series of bimetallic organotin(IV) and germanium compounds to study their biocidal activity. All synthesised compounds were characterised by elemental analyses, FT-IR, multinuclear NMR (^{1}H, ^{13}C, ^{119}Sn), and mass spectrometry. After characterisation all synthesised compounds were subjected to antimicrobial studies.

Experimental

Chemicals

3,3-Dimethylpropenoic acid, organotin(IV) oxides, organotin(IV) chloride, and triethylamine were purchased from Aldrich, USA, and used without further purification. Germanium dioxide was purchased from the People's Republic of China. All organic solvents were purchased from E. Merck, Germany, and were dried before use according to the standard methods.[7]

Instrumentation

Melting points were determined using a capillary tube on an electrothermal melting point apparatus, model MP-D Mitamura Riken Kogyo, Japan, and are uncorrected. Elemental analyses were carried out at Midwest Micro lab., Indianapolis, IN. 46250, USA.

Infrared absorption spectra were recorded as KBr discs on a Bio-Rad Excalibur FT-IR Model FTS 3000 MX. The ^{1}H- and ^{13}C-NMR spectra were recorded on a Varian Mercury 300 Spectrometer using deuterated solvent and TMS as a reference operating at 300 and 75.5 MHz respectively. ^{119}Sn-NMR spectra were obtained on a Brucker 250 ARX Spectrometer (Germany) with Me_4Sn as an external reference. Mass spectra were

recorded on MAT 311 A. Finnegan (Germany). The m/z values were computed relative to H = 1, C = 12, O = 16, Cl = 35.5, Ge = 74, Sn = 120.

Synthesis of 3-(Triphenylgermanyl)-3, 3-dimethylpropionic acid

3-(Triphenylgermyl)-3,3-dimethylpropionic acid was synthesised according to the literature method from trichlorogermyl-3,3-dimethyl propionic acid.[8−12] Typically 3-tri-chlorogermanyl-3,3-dimethylpropionic acid was synthesised by hydrogermanation reaction with germanium dioxide, sodium hydrogen phosphinate monohydrate, and 3,3-dimethyl propionic acid in 1:2:1 molar ratio. 3-Trichlorogermyl-3,3-dimethyl propionic acid was converted into 3-triphenylgermyl-3,3-dimethyl propionic acid by reaction with PhMgBr in ether solution in 1:4 molar ratio[12] (Eq. 1 and Eq. 2).

$$GeO_2 + 3HCl + NaH_2PO_2.H_2O \xrightarrow[(CH_3)_2C{=}CHCO_2H]{Et_2O} Cl_3GeC(CH_3)_2CH_2CO_2H \quad (1)$$

$$Cl_3GeC(CH_3)_2CH_2CO_2H + 4PhMgBr \xrightarrow[\text{iii) } H^+ \text{ hydrolysis}]{\substack{\text{i) } 0\ ^\circ C, Et_2O \\ \text{ii) reflux, } 4h}} (Ph)_3GeC(CH_3)_2CH_2CO_2H \quad (2)$$

Synthesis of Sn(IV) compounds containing Ge

Two types of Sn(IV) compounds containing Ge, i.e. diorganotin(IV) derivatives and triorganotin(IV) derivatives containing germanium, were synthesised. Generally diorganotin(IV) derivatives containing germanium were synthesised by the condensation of diorganotin oxide and 3-(triphenylgermyl)-3,3 dimethyl propionic acid in 1:2 molar ratio in a 2-necked flask fitted with a Dean and Stark apparatus, reflux condenser, and magnetic stirrer. The reaction mixture was refluxed for 8-10 h with continuous removal of water formed azeotropically by use of a Dean and Stark apparatus. The reaction mixture was cooled at room temperature. Then it was filtered and toluene was removed under reduced pressure. The thick residue was kept at low temperature for a few days and the resulting solid was recrystallised in a mixture of $CHCl_3$ and petroleum ether (3:1 ratio) to yield a white solid.[13]

$$R_2SnO + 2Ph_3GeC(CH_3)_2CH_2CO_2H \xrightarrow[\text{Reflux 8-10 h}]{\text{Toluene}} (Ph_3GeC(CH_3)_2CH_2CO_2)_2Sn(R)_2 + H_2O \quad (3)$$

$$R = CH_3\mathbf{(1)}, C_2H_5\mathbf{(2)}, n-C_4H_9\mathbf{(3)}, n-C_8H_{17}\mathbf{(4)}, C_6H_5\mathbf{(5)}$$

Triorganotin(IV) derivatives containing germanium were synthesised by reaction of triorganotin(IV) chloride and 3-(triphenylgermyl)-3,3 dimethyl propionic acid in 1:1 molar ratio in the presence of triethylamine in a 2-necked flask fitted with a reflux condenser and magnetic stirrer, containing toluene. The reaction mixture was refluxed for 8-10 h and cooled at room temperature. After cooling triethylamine hydrochloride was filtered off. The solvent was evaporated under reduced pressure and the thick residue kept at room temperature for a few days. The resulting solid was recrystallised in a mixture of $CHCl_3$ and petroleum ether (3:1) to yield a white solid.[14]

$$R_3SnCl + Ph_3GeC(CH_3)_2CH_2CO_2H \xrightarrow[\text{Toluence}]{Et_3N} (Ph_3GeC(CH_3)_2CH_2CO_2)SnR_3 + Et_3N.HCl \qquad (4)$$

$$R = CH_3\textbf{(6)},\ n-C_4H_9\textbf{(7)},\ C_6H_5\textbf{(8)}$$

Methodology of antimicrobial studies

Antibacterial activity

All the new synthesised compounds were screened for their antibacterial activity against 6 different types of bacteria, i.e. *Escherichia coli, Bacillus subtilis, Shigella flexenari, Staphylococcus aureus, Pseudomonas aeruginosa,* and *Salmonella typhi*, by the agar well diffusion method.[15] Imipenum was used as the standard antibiotic. The 24-h-old culture containing approximately 104-106 colony forming units (CFUs) was spread on the surface of Mueller-Hinton Agar (MHA) plates. Wells were created in the medium with the help of a sterile metallic borer. Test samples of different concentrations were added to their respective wells. Experimental plates were incubated at 37 °C for 24 h and zones of inhibition (%) were measured and compared with the standard antibiotic imipenum with zone inhibition of 20 and 22 mm, respectively.

Antifungal activity

The agar tube dilution protocol was applied to study the activity of the compounds against various fungal strains like *Trichophyton longifusus, Candida albicans, Aspergillus flavus, Microsporum canes, Fusarium solani,* and *Candida glaberata.* The standard antifungal drugs used for comparison testing were amphotericin B and miconazole. The tubes containing sterile Sabouraud and dextrose agar were incubated with the test compound at different concentrations and solidified at room temperature. Test fungal cultures were inoculated on the slant, and growth inhibition (%) was observed after incubation for 7 days.[16]

Cytotoxicity

Shrimp larvae were applied as a tool to monitor the cytotoxicity of synthesised compounds using Etoposide as the standard cytotoxic drug.[12] Brine shrimp eggs (50 mg) were placed in a hatching tray half filled with brine solution and incubated for 2 days at 27 °C. Test samples (20 mg) were dissolved in DMSO and diluted to 1000 μg, 100 μg, and 10 μg/mL in 500 μL, 50 μL, and 5 μL vials using a Pasteur pipette. In each vial, 30 larvae were placed and adding seawater made a volume of 5 mL. The contents were incubated at 25-27 °C for 24 h under illumination. The numbers of survivors were counted and compared with the standard cytotoxic drug.[17]

Results and discussion

The physical and analytical data for the investigated compounds are given in Table 1. All compounds are non-hygroscopic and are stable in air and light. The yields obtained for these compounds are 65%-83%. The synthesised compounds are soluble in common organic solvents like $CHCl_3$, CH_2Cl_2, and DMSO.

Table 1. Physical data* of organotin derivatives containing germanium of general formula $[(C_6H_5)_3GeC(CH_3)_2CH_2COO]_{4-n}Sn[R]_n$ n = 2 for compounds 1-5 and n = 3 for compounds 6-8.

Comp. no.	R	Molecular formula	M. Wt.	M.P. °C	Yield %	Solubility	Elemental Analysis Found (Calc.)	
							C %	H %
1	CH_3	$C_{48}H_{52}O_4Ge_2Sn$	957	160-163	81	$CHCl_3$, CH_2Cl_2, DMSO	60.20 (60.25)	5.41 (5.48)
2	C_2H_5	$C_{50}H_{56}O_4Ge_2Sn$	985	138-140	83	''	60.89 (60.97)	5.65 (5.73)
3	n-C_4H_9	$C_{54}H_{64}O_4Ge_2Sn$	1041	165-168	80	''	62.26 (62.30)	6.13 (6.20)
4	n-C_8H_{17}	$C_{62}H_{80}O_4Ge_2Sn$	1153	124-125	76	''	64.49 (64.57)	6.90 (6.99)
5	C_6H_5	$C_{58}H_{56}O_4Ge_2Sn$	1081	170-173	78	''	64.30 (64.44)	5.10 (5.22)
6	CH_3	$C_{26}H_{32}O_2GeSn$	568	174-176	80	''	54.81 (54.99)	5.61 (5.68)
7	C_4H_9	$C_{35}H_{50}O_2GeSn$	694	138-140	79	''	60.49 (60.56)	7.19 (7.26)
8	C_6H_5	$C_{41}H_{38}O_2GeSn$	754	182-185	65	''	65.17 (65.30)	5.01 (5.08)

Infrared spectroscopy

The infrared spectra of compounds **1-8** were recorded in the range of 4000-400 cm^{-1} and important bands for structural assignment are listed in Table 2. Tentative assignments were made on the basis of earlier work.[18,19] The absorptions of interest are those of ν(C=O), ν(Sn-C), ν(Sn-O), and ν(Ge-C).[6,20] The complexation of organotin(IV) with germanium acid ligand is confirmed by the absence of a broad band in the range of 3200-2800 cm^{-1} due to ν(OH). The difference between $\nu(COO)_{asy}$ and $\nu(COO)_{sym}$ has been used to predict the mode of tin and carboxylate interaction.[20] The $\Delta\nu$ values for the diorganotin(IV) compounds (**1-5)** and triorganotin(IV) compounds (**6-8)** lie in the range of 218-225 and 217-218 cm^{-1}, respectively, indicating the bidentate nature of the COO group.[21] There is donation of charge density from C=O to the electropositive tin metal, which slightly increases the C=O bond lengths. Hence the absorption frequency decreases and triphenylgermanyl acid anion ligand acts as a bidentate ligand in the solid state. Therefore, diorganotin(IV) and triorganotin(IV) compounds adopt distorted octahedral geometry and trigonal bipyramidal geometry for around the tin atom, respectively.

Table 2. IR absorption frequencies in cm^{-1} of organotin derivatives containing germanium: $[(C_6H_5)_3GeC(CH_3)_2CH_2COO]_nSn[R]_{4-n}$ n = 2 for compounds 1-5 and n = 1 for compounds 6-8.

Comp.	$\nu(COO)_{asym}$	$\nu(COO)_{sym}$	$\Delta\nu$	ν(Ge-C)	ν(Sn-C)	ν(Sn-O)
1	1617	1399	218	633	567	461
2	1618	1399	219	633	567	462
3	1591	1369	222	672	573	469
4	1618	1398	220	633	565	467
5	1614	1389	225	654	-	465
6	1618	1400	218	622	530	462
7	1617	1400	217	626	568	467
8	1616	1399	217	633	-	461

NMR spectroscopy

^{1}H-NMR

^{1}H-NMR spectral data in $CDCl_3$ solution of the synthesised compounds are given in Table 3 and are interpreted by comparing them with ^{1}H-NMR spectra of germanium acid. The resonance of protons was assigned on the basis of their integration and multiplicity pattern. In di- and triphenyltin(IV) compounds **(5,8)**, a complex pattern of multiplets is observed in the range of 7.00-7.61 and 6.80-6.91 ppm due to aromatic protons of the phenyl group attached to germanium and tin moiety. The di-and tributyltin(IV) derivatives **(3,7)** show a multiplet in the region of 1.08-1.34 ppm for methylene protons with a well defined triplet at 1.21 and 0.08 ppm due to terminal methyl protons with a ^{1}H-^{1}H coupling constant at about 6.91 and 7.11 Hz.[22,23] The dioctyltin(IV) derivative **(4)** exhibited a multiplet in the range of 1.31-1.55 ppm for the methylene protons, with a well defined triplet for terminal methyl at 0.85 ppm having a ^{1}H-^{1}H coupling constant of about 7.20 Hz.

Table 3. ^{1}H-NMR data$^{(a-e)}$ for organotin derivatives containing germanium of general formula: $[(C_6H_5)_3GeC(CH_3)_2CH_2COO]_nSn[R]_{4-n}$.

Comp.	$(CH_3)_2$	CH_2	R	C_6H_5Ge
1	1.25 (s, 12H)	2.56 (s, 4H)	0.84 [(s, 6H)] ^{2}J[72]	6.55-7.15 (m, 30H)
2	1.59 (s, 12H)	2.92 (s, 4H)	1.21 [(t, 6H), ^{3}J(7.14)] 1.45 (m, 4H)	7.00-7.19 (m, 30H)
3	1.60 (s, 12H)	2.95 (s, 4H)	0.85 [(t, 6H), ^{3}J(6.91)] 1.2-1.4 (m, 12H)	7.00-7.20 (m, 30H)
4	1.65 (s, 12H)	2.91 (s, 4H)	0.85 [(t, 6H), ^{3}J(7.20)] 1.31-1.55 (m, 28H)	7.01-7.15 (m, 30H)
5	1.60 (s, 12H)	2.78 (s, 4H)	6.82-6.91 (m, 10H)	7.08-7.61 (m, 30H)
6	1.59 (s, 6H)	2.65 (s, 2H)	0.56 [(s, 9H)] ^{2}J[57]	7.22-7.51 (m, 15H)
7	1.49 (s, 6H)	2.60 (s, 2H)	0.81 [(t, 9H), ^{3}J(7.14)] 1.08-1.34 (m,18H)	7.15-7.45 (m, 15H)
8	1.57 (s, 6H)	2.75 (s, 2H)	6.80-6.94 (m, 15H)	7.11-7.65 (m, 15H)

[a] n = 2 for compounds **1-5**; n = 1 for compounds **6-8**

[b] In $CDCl_3$ at 295 K.

[c] Chemical shifts in ppm. $^{3}J(^{1}H\text{-}^{1}H)$, $^{2}J[^{119}Sn\text{-}^{1}H]$ in Hz.

[d] Multiplicity is given as s = singlet, t = triplet, m = multiplet.

[e] R = CH_3 **(1,6),** C_2H_5 **(2)**, n-C_4H_9 **(3,7)**, n-C_8H_{17} **(4)** and C_6H_5 **(5,8).**

^{13}C-NMR

^{13}C-NMR spectral data of compounds **1-8** are listed in Table 4. The number of signals found corresponds with the presence of magnetically nonequivalent carbon atoms, which were assigned by comparison with literature values.[24] The position of the carboxylate carbon moves to lower field in all complexes as compared with the germanium containing acid ligand, indicating participation of the carboxylic group in coordination to tin(IV).[25] The coupling constant $^{1}J[^{119}Sn\text{-}^{13}C]$ and the values of inter-bond angles, C-Sn-C, are important parameters for structural determination of organotin(IV) carboxylate. The C-Sn-C angles for diorganotin(IV) derivatives are calculated using the ^{1}J value in Lockhart's equation for compounds **1-4**, and lie in the range of 128.82° to 131.25° described as skew trapezoidal bipyramidal geometry of the tin atom in non-coordinated solvents.[26]

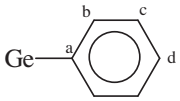
Table 4. ^{13}C-NMR data$^{(a-d)}$ for organotin derivatives containing germanium of general formula: $[(C_6H_5)_3GeC(CH_3)_2CH_2COO]_nSn[R]_{4-n}$.

S. no.	1	2	3	4	5	6	7	8
Ph-Ge a	135.91	136.10	136.02	136.12	136.51	138.33	136.56	138.98
b	133.89	134.11	134.25	134.54	134.45	136.10	134.45	137.04
c	130.18	130.25	129.51	130.25	129.56	130.44	129.54	134.27
d	132.05	132.05	131.25	132.10	132.45	131.15	132.25	136.30
$(CH_3)_2$	25.95	27.05	26.01	25.65	28.43	27.73	27.10	25.82
C$\prime$	30.85	31.45	29.89	30.02	30.21	29.25	30.01	27.53
CH_2	44.95	44.50	45.24	49.05	49.54	47.26	48.55	44.24
COO	182.1	181.5	182	176.98	181.89	179.80	178.79	179.71
Sn-C	4.95 ^1J[612]	17.98 ^1J[535]	25.85 ^1J[577]	25.91 ^1J[561]	136.84	-1.9	18.15	137.36
2	-	9.56 ^2J[18.7]	27.13 ^2J[22]	27.94 ^2J[20]	135.21 135.21	-	29.10	136.56
3	-	-	27.5	31.05	128.17	-	29.55	128.58
4	-	-	14.98	30.02	132.35	-	14.00	129.38
5	-	-	-	28.5	-	-	-	-
6	-	-	-	22.01	-	-	-	-
7	-	-	-	17.5	-	-	-	-
8	-	-	-	14.65	-	-	-	-
^{119}Sn	–145.69	–149.42	–	–150.43	–	131.0	100.29	–

[a] n = 2 for compounds **1-5**; n = 1 for compounds **6-8**

[b] In $CDCl_3$ at 295 K.

[c] Chemical shift in ppm $^nJ[^{119}Sn\text{-}^{13}C]$ in Hz.



[d] R = CH_3 **(1,6)**, C_2H_5 **(2)**, n-C_4H_9 **(3,7)**, n-C_8H_{17} **(4)** and C_6H_5 **(5,8)**

^{119}Sn-NMR

^{119}Sn-NMR chemical shifts for these compounds are listed in Table 4 and exhibited a single resonance at –145.19, –149.42, and –150.43 for diorganotin(IV) and 131.00 and 100.29 for triorganotin(IV) derivatives. The ^{119}Sn chemical shift of these compounds described the pentacordinated and tetrahedral geometry of the tin atom in non-coordinated solvents. It is generally accepted that the compounds with different geometry about the tin atom produce shifts in the well-defined ranges; the range is between +200 to –60 ppm for 4-coordinated compounds and from –90 to –330 ppm for 5-coordinated systems.[8] These results are consistent with the ^{1}H- and ^{13}C-NMR results.

Mass spectrometry

Mass spectral fragmentation pattern and relative abundance (%) of representative compounds **1** and **7** are given in Table 5. The molecular ion peaks of these compounds were not observed, as reported earlier.[27,28] Primary decomposition is

due to the loss of one unit of triphenylgermyl-substituted propionic acid followed by the loss of the alkyl group directly attached to the tin atom or to germanium moiety. The mass fragmentation pattern of triorganotin(IV) containing germanium is quite different from diorganotin(IV) derivatives. The primary fragmentation is due to loss of the alkyl group from tin atom. Secondary decomposition is due to loss of triphenylgermyl-substituted propionic acid followed by successive cleavage of R group and ending at Sn^+ (m/z = 120) and in some cases as SnH^+ (m/z = 121). A second fragmentation pathway is by loss of R groups by different routes followed by liberation of CO_2. This route is more probable than the first one. Thus, the mass spectral data for both di- and triorganotin(IV) carboxylates containing germanium support the proposed structure of the compounds.

Table 5. Fragments observed for compounds 1 and 7.

Compound 1			Compound 7		
m/z	Fragments	Intensity %	m/z	Fragments	Intensity %
1044	$[((C_6H_5)_3GeC(CH_3)_2CH_2COO)_2Sn(C_4H_9)_2]^+$	n.o	696	$[((C_6H_5)_3GeC(CH_3)_2CH_2COO)Sn(n\text{-}C_4H_9)_3]^+$	(n.o)
639	$[(C_6H_5)_3GeC(CH_3)_2CH_2COOSn(C_4H_9)_2]^+$	10.28	666	$[((C_6H_5)_3GeCHCH_2COOSn(C_4H_9)_3]^+$	15.72
405	$[(C_6H_5)_3GeC(CH_3)_2CH_2COO]^+$	32.14	405	$[(C_6H_5)_3GeC(CH_3)_2CH_2COO]^+$	35.71
361	$[(C_6H_5)_3GeC(CH_3)_2CH_2]^+$	19.2	361	$[HCCH_2COOSn(C_4H_9)_3]^+$	34.21
305	$[(C_6H_5)_3Ge]^+$	100	331	$[(C_6H_5)_3GeCCH_2]^+$	25.46
304	$[CCH_2CO_2Sn(C_4H_9)_2]^+$	77.1	329	$[(C_6H_5)_3GeC{\equiv}C]^+$	100
234	$[Sn(C_4H_9)_2]^+$	22.4	305	$[(C_6H_5)_3Ge]^+$	18.51
228	$[(C_6H_5)_2Ge]^+$	51.4	291	$[Sn(C_4H_9)_3]^+$	55.19
177	$[Sn(C_4H_9)]^+$	7.71	234	$[Sn(C_4H_9)_2]^+$	45.63
151	$[(C_6H_5)Ge]^+$	5.78	228	$[(C_6H_5)_2Ge]^+$	29.6
121	$[SnH]^+$	15.1	227	$[(C_6H_5)_2Ge{-}H]^+$	16.42
74	$[Ge]^+$	11.52	177	$[Sn(C_4H_9)]^+$	35.61
57	$[C_4H_9]^+$	61.21	151	$[(C_6H_5)Ge]^+$	35.94
			121	$[SnH]^+$	6.14
			114	$[(C_4H_9)_2]^+$	74.39
			77	$[C_6H_5]^+$	55.61
			74	$[Ge]^+$	3.15
			57	$[(C_4H_9)]^+$	64.37

Evaluation of antimicrobial activity

Antibacterial activity

Organotin(IV) carboxylates containing germanium were tested for their activity against various bacteria adopting the agar well diffusion method.[16] The bacteria cultures used were *Escherichia coli, Bacillus subtilis, Shigella flexenari*, and *Salmonella typhi*. Imipenem was used as standard antibiotic. The results are summarised in Table 6. Screening tests among diorganotin(IV), bis[3-(triphenylgermyl)-3,3-dimethylpropionato]-di-n-octyltin(IV) show better activity than the other members of the series, while tri-butyl and tri-phenyl tin carboxylates (**6, 7)** is the most potent candidates against all types of tested bacteria. Biocidal activity of triorganotin(IV) derivatives is related to their structure by the fact that the species generating a tetrahedral structure in solution are more active.[29]

Table 6. Antibacterial activity data[(a−c)] of organotin derivatives containing germanium (in vitro).

Name of Bacteria	Zone of Inhibition of Samples (mm)							Zone of Inhibition of Std. Drug (mm)
	1	2	3	4	5	7	8	
Escherichia coli	26	28	22	28	29	27	30	30
Bacillus subtilis	25	28	26	29	22	-	27	31
Shigella flexenari	-	5	10	10	-	-	-	33
Staphylococcus aureus	42	40	42	40	42	38	41	43
Pseudomonas aeruginosa	20	24	20	22	21	19	24	25
Salmonella typhi	40	38	38	41	37	35	40	41

[a]Concentration of sample = 3 mg/mL

[b]Concentration of standard drug (imipenum) = 10 μg/disc

[c](-) = No activity

Antifungal screening

The synthesised organotin(IV) derivatives containing germanium were screened against various fungal strains like *Trichophyton longifusus, Candida albicans, Aspergillus flavus, Microsporum canis, Fusarium solani*, and *Candida glaberata*, by agar tube dilution.[16] The standard antifungal drugs used were amphotericin B and miconazole for the comparison test. The results obtained are given in Table 7. Earlier reports showed that higher antifungal activities were associated with tributyl and triphenyltin (IV) derivatives.[30] Our screening results are quite consistent with the earlier reports. Most of the synthesised compounds showed significant activity against the tested fungi. Trimethyltin(IV) and tributyltin(IV) derivatives containing germanium are highly active against all tested fungi except *Candida albicans*. Diphenyltin(IV) derivatives are as active against *Candida glaberata* as is the reference drug, miconazole. Thus the increased fungicidal activity of trimethyltin(IV) derivatives is due to the triarylgermyl substituted propionate group, which could act as carrier in this series.[31]

Table 7. Antifungal activity data[(a−c)] of organotin derivatives containing germanium (in vitro).

Name of Fungus	% Inhibition of Samples							Std. Drug MIC μg/mL	% μg/mL
	1	2	3	4	5	7	8		
Trichophyton ongifusus	68	64	69	65	54	66	69	Miconazole	70
Candida albicans	101	103	105	109	-	35	99	〃	110
Aspergillus flavus	-	-	-	-	-	-	-	Amphotericin B	20
Microsporum canis	92	96	90	99	78	89	96	Miconazole	98
Fusarium solani	70	69	71	72	68	60	71	〃	73
Candida glaberata	101	104	101	108	92	95	109	〃	110

[a]Concentration of sample = 400 μg/mL of DMSO

[b]Incubation temperature (period) = 27 ± 1 °C (7 days)

[c](–) = No activity

Conclusions

The elemental analyses results of all synthesised compounds are comparable with calculated and found values of carbon and hydrogen atoms, which confirmed the formation and purity of compounds. The $\Delta\nu$ values for the diorganotin(IV) compounds (**1-5)** and triorganotin(IV) compounds (**6,8)** indicated the bidentate nature of the COO group containing germanium. Diorganotin(IV) and triorganotin(IV) compounds containing triphenylgermanyl acid adopt distorted octahedral geometry and trigonal bipyramidal geometry for around the tin atom, respectively. The spectroscopic results indicated that diorganotin(IV) derivatives containing germanium adopted skew trapezoidal bipyramidal geometry around the tin atom, while a linear polymeric trigonal-bipyramidal structure in the solid state and a tetrahedral environment around the tin atom in non-coordinating solvents have been proposed for the triorganotin(IV) compounds. Mass spectral data reveal that thefragment ions formed are in agreement with the expected structure and proposed molecular formula of all synthesised compounds. Biological screening of these compounds demonstrated their promising activity against different microbes.

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