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Synthesis, Spectroscopic Characterization, and Biological Activity Studies of Organotin(IV) Derivatives of (*E*)-3-(3-Fluorophenyl)-2-phenyl-2-propenoic Acid. Crystal and Molecular Structure of $Et_2Sn[OCOC(C_6H_5)=CH(3\text{-}FC_6H_4)]$

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ABSTRACT: *The complexes Me_2SnL_2 (**I**), Me_3SnL (**II**), Et_2SnL_2 (**III**), $n\text{-}Bu_2SnL_2$ (**IV**), $n\text{-}Bu_3SnL$ (**V**), $n\text{-}Oct_2SnL_2$ (**VI**), Bz_2SnL_2 (**VII**), and Ph_3SnL (**VIII**), where "L" is (E)-3-(3-fluorophenyl)-2-phenyl-2-propenoate, have been prepared and structurally characterized by means of elemental analysis, infrared, mass, and multinuclear (^1H, ^{13}C, ^{119}Sn) NMR spectral techniques. The spectroscopic results showed that the geometry around the Sn atom in triorganotin(IV) derivatives is four-coordinated in noncoordinating solvent and behaves as five-coordinated linear polymers with bridging carboxylate groups or five-coordinated monomers, both acquiring trans-R_3SnO_2 geometry for Sn in the solid state. While all the diorganotin(IV) derivatives may acquire trigonal bipyramidal structures in solution due to collapse of the Sn←O=CO interaction and octahedral geometries in the solid state, which have been confirmed by the X-ray crystallographic data of the compound* **III**. *The crystal structure of Et_2SnL_2 (**III**) has been determined by X-ray crystallography and is found skew-trapezoidal bipyramidal, which substantiates that the ligand acts as an anisobidentate chelating agent, thus rendering the Sn atom six coordinated. The crystal is monoclinic with space group $C2_1/n$. All the investigated compounds have also been screened for biocidal and cytotoxicity data.* © 2006 Wiley Periodicals, Inc. Heteroatom Chem 17:420–432, 2006; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20243

INTRODUCTION

Organotin(IV) carboxylates form an important class of compounds and have been receiving increasing attention in recent years not only because of their intrinsic interest but also owing to their varied applications [1]. Organotin compounds have also

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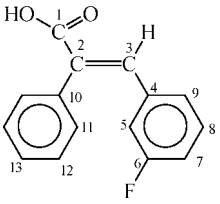


FIGURE 1 Numbering scheme of (*E*)-3-(3- uorophen yl)-2-phenyl-2-propenoic acid (**HL**).

been studied as possible candidates for antitumor activity, chemotherapy, leishmaniasis, and helminthes and parasitic infection of the skin [2,3]. Some examples find wide use as catalysts and stabilizers, and certain derivatives are used as biocides, as antifouling agents, and as wood preservatives [4]. From the data available in the literature, it has been identified that some of the organotin(IV) carboxylates with ligands bearing fluorine proved to be active against tumors [5,6].

Encouraged by the above findings, it was thought of interesting to explore the properties of organotin(IV) derivatives of (*E*)-3-(3-fluorophenyl)-2-phenyl-2-propenoic acid (Fig. 1) as a continuation of our studies of organotin chemistry [7–9]. The newly synthesized organotin(IV) derivatives have been structurally characterized by means of elemental analysis, infrared, ^{1}H, ^{13}C, and ^{119}Sn NMR spectroscopic studies and mass spectrometric analysis, while the crystal and molecular structure of diethyltin(IV)-di-(*E*)-3-(3-fluorophenyl)-2-phenyl-2-propenoate (**III**) is described. Bioassay tests against various bacteria and fungi were carried out to investigate their biological significance. Their cytotoxicity has also been studied.

RESULTS AND DISCUSSION

The reactions of R_2SnCl_2 and R_3SnCl with the silver salt of (*E*)-3-(3-fluorophenyl)-2-phenyl-2-propenoic acid (**HL**) have been carried out in 1:2 and 1:1 molar ratios in dry chloroform, respectively, resulting in the isolation of R_2SnL_2 and R_3SnL solids (Eqs. (1) and (2)). Di-*n*-octyltin(IV) derivative (**VI**) was synthesized by the reaction of **HL** and di-*n*-octyltin(IV) oxide in 1:2 molar ratio, respectively, in dry toluene using Dean and Stark apparatus (Eq. (3)). The ligand acid (**HL**) was synthesized by using a reported procedure [10]. The composition of complexes and the nature of bonding were recognized by spectroscopic characterization and X-ray crystallographic data.

$$R_2SnCl_2 + 2AgL \rightarrow R_2SnL_2 + 2AgCl \qquad (1)$$

where R is Me (**I**), Et (**III**), *n*-Bu (**IV**), and Bz (**VII**).

$$R_3SnCl + AgL \rightarrow R_3SnL + AgCl \qquad (2)$$

where R is Me (**II**), *n*-Bu (**V**), and Ph (**VIII**).

$$R_2SnO + 2HL \rightarrow R_2SnL_2 + H_2O \qquad (3)$$

where R is *n*-Oct (**VI**).

All the compounds are air stable and soluble in common organic solvents. The physical data are given in Table 1.

Infrared Spectroscopy

The infrared spectra of investigated compounds have been recorded in the range 4000–400 cm^{-1} as KBr pellets or as neat liquids (compounds **VI** and **VII**) using KBr cells. The absorption frequencies of interest are ν(COO), ν(Sn—O), and ν(Sn—C) and are reported together with frequency difference, $\Delta\nu = \nu_{asym}(COO) - \nu_{sym}(COO)$ in Table 2. The explicit feature observed in the spectra of the synthesized compounds is the absence of the broad band in the range 3073–2504 cm^{-1}, which appears in the free ligand acid (**HL**) as the ν(O—H) vibration, thus indicating Sn—OCO bond formation through this site. Similarly, absorption bands in the range 483–446 and 552–521 cm^{-1}assigned to Sn—O and Sn—C bonds, respectively, also support the formation of the complexes [11].

The ν_{asym}(COO) and ν_{sym}(COO) bands appear at 1583–1571 and 1398–1370 cm^{-1}, respectively; and the $\Delta\nu$ values, which are within the range of silver salt of the ligand acid, indicate a bidentate coordination mode for the carboxylate ligand in organotin(IV) carboxylates [12]. These results suggest that the Sn atom in diorganotin(IV) dicarboxylates approaches six-coordination (Figs. 2a and 2b), which is totally consistent with the skew-trapezoidal structure of compound **III**, obtained from X-ray crystallographic data. In the same way, the $\Delta\nu$ values for the investigated triorganotin(IV) carboxylates suggest a linear polymeric structure with bidentate bridging ligands (Fig. 2e) or monomers (Fig. 2d), both leading to *trans*-R_3SnO_2 geometry for Sn [13].

NMR Spectroscopic Studies

^{1}H NMR. The ^{1}H NMR spectra of the ligand acid (**HL**) and its corresponding organotin(IV) complexes were recorded in $CDCl_3$ solution, and data are reported in Table 3.

The assignment of the protons of phenyl moieties of the ligand resonances was achieved on the basis of their distinct multiplicities, $^{n}J[^{1}H, ^{19}F]$ coupling constant values and by comparing with the results

TABLE 1 Physical Data of the Investigated Organotin(IV) Derivatives of (*E*)-3-(3-Fluorophenyl)-2-phenyl-2-propenoic Acid[a]

Compound	*Compound (Formula Weight)*	*MP (°C)*	*Yield (%)*	*%C Calcd (Found)*	*%H Calcd (Found)*
I	Me_2SnL_2 $C_{32}H_{26}F_2O_4Sn$ (631)	135—137	80.3	60.86 (60.88)	4.12 (4.14)
II	Me_3SnL $C_{18}H_{19}FO_2Sn$ (405)	153—155	90.5	53.33 (53.29)	4.69 (4.70)
III	Et_2SnL_2 $C_{34}H_{30}F_2O_4Sn$ (659)	115—117	80.0	61.91 (62.00)	4.55 (4.52)
IV	*n*-Bu_2SnL_2 $C_{38}H_{38}F_2O_4Sn$ (715)	105—107	83.0	63.78 (63.69)	5.31 (5.35)
V	*n*-Bu_3SnL $C_{27}H_{37}FO_2Sn$ (531)	Liquid	75.0	61.02 (61.10)	6.70 (6.66)
VI	*n*-Oct_2SnL $C_{46}H_{54}F_2O_4Sn$ (827)	Viscous liquid	70.0	66.75 (66.68)	6.53 (6.48)
VII	Bz_2SnL_2 $C_{44}H_{34}F_2O_4Sn$ (783)	Viscous liquid	60.6	67.43 (67.33)	4.34 (4.40)
VIII	Ph_3SnL $C_{33}H_{25}FO_2Sn$ (591)	360—361	65.0	67.01 (66.99)	4.23 (4.31)

[a]In all other tables, the formulation and number of the compounds are the same as given in this table.

obtained from the incremental method [14]. In all compounds, the olefinic proton appears as a sharp singlet at 7.25–7.95 ppm [15–17].

The methyl protons of dimethyl- and trimethyltin(IV) derivatives appear as sharp singlets at 1.08 and 0.58 ppm with well-defined satellites at 81.1 and 57.6 Hz, respectively. The α-CH_2 protons of diethyltin(IV) derivative resonate as a quartet at 1.73 ppm with $^3J[^1H, ^1H] = 7.9$ Hz. While β-CH_3 protons resonate as a triplet at 1.35 ppm with $^3J[^1H, ^1H] = 7.9$ Hz. The protons of *n*-butyltin and of the phenyl moieties of the triphenyltin and tribenzyltin(IV) show a complex pattern and were assigned according to the literature [18,19]. Despite the complex pattern of ^1H NMR spectra of di- and tri-*n*-butyltin(IV) derivatives, a clear triplet due to terminal methyl group appears in both at 0.90 and 0.92 ppm, respectively, with $^3J[^1H, ^1H] = 7.3$ Hz.

The α-CH_2 to γ-CH_2 protons of *n*-octyltin(IV) moiety in compound **VI** appear as multiplet at 0.55–0.65 ppm and are compatible with the calculated values [14]. However, the δ′-CH_3 protons resonate as a triplet at 0.16 ppm with $^3J[^1H, ^1H] = 6.8$ Hz.

The dibenzyltin(IV) moiety of compound **VII** also involves a complex pattern due to the aromatic protons of the ligand and phenyl groups. However, α^*-CH_2 protons of the benzyl moiety show a singlet at 2.84 ppm.

Various literature methods have been applied to calculate the C—Sn—C bond angles in solution, based on $^2J[^{119}Sn, ^1H]$ coupling constant as given in Table 5 [20–22]. The coupling constants and the calculated C—Sn—C bond angles support the five-coordinated geometry for the diorganotin(IV) and a four-coordinated for the triorganotin(IV) carboxylates in noncoordinating solvents [21,22].

TABLE 2 Infrared Data (cm^{-1}) of Organotin(IV) Derivatives of (*E*)-3-(3-Fluoro phenyl)-2-phenyl-2-propenoic Acid[a]

	ν(COO)				
Compound	*Asym.*	*Sym.*	*Δν*	*ν(Sn—C)*	*ν(Sn—O)*
I	1580 s	1398 s	182	510 m	455 w
II	1571 s	1370 s	201	552 m	463 w
III	1583 s	1381 s	202	550 w	463 w
IV	1580 s	1389 s	191	522 w	451 m
V	1582 s	1380 s	202	522 w	451 m
VI	1580 s	1391 s	189	542 m	483 w
VII	1576 s	1398 s	178	521 m	450 m
VIII	1582 s	1393 s	189	—	446 s
HL (Acid)	1677 s	1420 s	257	—	—
AgL	1581 s	1376 s	205	—	—

[a]s = strong; m = medium; w = weak.

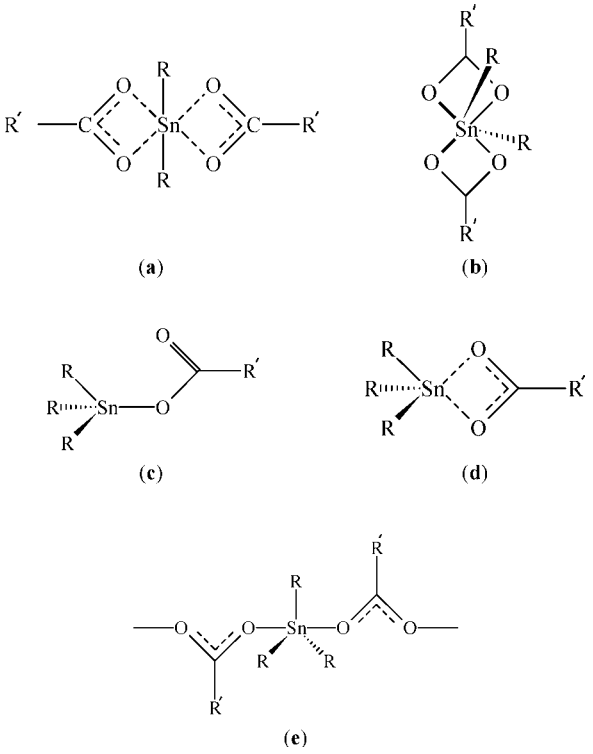


FIGURE 2 Proposed structures (a) and (b) for diorganotin(IV) derivatives, and (c), (d), and (e) for triorganotin(IV) carboxylates.

^{13}C NMR. ^{13}C NMR data (in $CDCl_3$) for the ligand and its di- and triorganotin(IV) derivatives are given in Table 4.

The signals of R groups attached to Sn atom, where R is Me, Et, *n*-Bu, *n*-Oct, Bz and Ph, were assigned by comparison with their homologues, combined with the $^nJ[^{119}Sn, ^{13}C]$ coupling constants [18,23,24]. The assignment of the ^{13}C resonances associated with the carboxylate ligand is based on (i) comparison with the results obtained from the incremental method [25] and (ii) the values of the coupling constants, $^nJ[^{119}Sn, ^{19}F]$ [14,26]. Involvement of the carboxyl (COO) group in bonding to Sn atom is confirmed by the resonance ascribed to carboxyl carbon, which (except in compounds **II** and **V**) exhibits the greatest shift upon coordination [27]. In compounds **II** and **V**, the COO carbon usually undergoes a minor up-field shift due to (i) electron with donating effect of the R (Me and *n*-Bu, respectively) groups and (ii) collapse of the Sn···O=C interaction by the noncoordinating solvents, which cause partial shielding of the carboxylate carbon, compared to their diorganotin(IV) counterparts.

The magnitudes for $^nJ[^{119}Sn, ^{13}C]$ coupling in compounds **II, III**, and **V** are also observed as given in Table 4. In addition to $^nJ[^{119}Sn, ^1H]$, the coupling constants, $^nJ[^{119}Sn, ^{13}C]$ are also important parameters for the structure elucidation of organotin(IV) compounds. For triorganotin(IV) compounds, the magnitudes of $^1J[^{119}Sn, ^1H]$ coupling suggest the typical tetrahedral geometry around the Sn atom in solution [18,28]. As far as geometry of the diorganotin(IV) dicarboxylates in noncoordinating solvents is concerned, it is not defined with certainty due to fluxional behavior of the carboxylate oxygen in their coordination with the Sn atom [29]. However, earlier reports suggest that geometry lies between penta- and hexa-coordination [30].

^{119}Sn NMR. The ^{119}Sn chemical shift data obtained from $CDCl_3$ solutions of di- and triorganotin(IV) compounds (**I–VIII**) are listed in Table 4. A single resonance in the range of 231.3 to –121.0 ppm for di- and 139.0 to –110.3 ppm for triorganotin(IV) (**II, V**, and **VIII**, respectively) derivatives, compatible with the 5-4 coordinated geometries proposed for the solution structure, is observed for each compound [31,32].

These data and the information obtained from the $^1J[^{119}Sn, ^{13}C]$ and $^2J[^{119}Sn, ^1H]$ coupling constants and C–Sn–C bond angles calculated from the ^1J and ^2J values of the representative compounds (Table 5) [20,27] tend to confirm penta-coordinated geometry for the diorganotin(IV) dicarboxylates and tetra-coordinated geometry for triorganotin(IV) derivatives in the solution [32].

Mass Spectrometry

The important fragmentation patterns of the mass spectra of di- and triorganotin(IV) compounds at 70 eV are given in Schemes 1 and 2, and data are reported in Tables 6 and 7, respectively.

The molecular ion peak, $[M^+]$, of low intensity is observed only for some of the compounds and thus supporting the earlier reports [28]. The fragmentation pattern depends on the structure of the compounds. Therefore, in all the synthesized compounds, the base peak is due to the ligand moiety after the loss of CO_2, $[C(C_6H_5)=CH(3\text{-}FC_6H_4)]$ (R′) with only exception of compound **VI**, where the base peak is obtained by the loss of an R group.

Diorganotin(IV) derivatives as compared to triorganotin(IV) carboxylates follow a complex pattern. However, according to the earlier reports [33,34], the synthesized compounds were found to lose a ligand or an alkyl or an aryl radical first, followed by elimination of CO_2 and other neutral species, ultimately giving $[Sn^+]$. Another route, mostly followed by triorganotin(IV) carboxylates, involves release of the

TABLE 3 ^{1}H NMR Data of Organotin(IV) Derivatives of (*E*)-3-(3-Fluorophenyl)-2-phenyl-2-propenoic acid[a,b,c]

^{1}H No.	***HL*** *Acid*	**I** *Me_2SnL_2*	**II** *Me_3SnL*	**III** *Et_2SnL_2*	**IV** *n-Bu_2SnL_2*	**V** *n-Bu_3SnL*	**VI** *n-Oct_2SnL_2*	**VII** *Bz_2SnL_2*	**VIII** *Ph_3SnL*
3	7.91 (s)	7.94 (s)	7.93 (s)	7.95 (s)	7.90 (s)	7.78 (s)	7.25 (s)	7.90 (s)	7.90 (s)
5	6.90 (d, 7.8)	6.89 (d, 8.2)	6.84 (d, 7.7)	6.89 (dd, 1.9, 8.1)	6.88 (d, 7.7)	6.86 (d, 8.2)	6.20 (d, 7.0)	6.79 (d, 6.4)	6.87 (d, 11.6)
7	6.70 (d, 10.2)	6.70 (d, 10.2)	6.66 (d, 10.5)	6.69 (tt, 1.83, 3.6, 10.3)	6.68 (d, 10.2)	6.69 (d, 10.4)	6.01 (d, 10.4)	6.60 (d, 8.3)	6.67 (d, 9.6)
8	7.15 (dd, 7.9, 14.1)	7.14 (dd, 7.8, 14.1)	7.10 (dd, 8.0, 14.1)	7.13 (tt, 1.9, 7.3, 10.0)	7.14 (dd, 7.3, 14.1)	7.10 (dd, 7.3, 14.1)	6.43 (dd, 6.1, 7.7)	6.91 (dd, 7.1, 11.3)	7.10 (d, 6.0)
9	6.94 (dd, 2.1, 8.3)	6.93 (bd, 2.9)	6.87 (d, 2.3)	6.91 (dd, 2.2, 8.2)	6.91 (dd, 1.9, 8.4)	6.83 (d, 1.9)	6.22 (dd, 2.7, 7.7)	6.88 (bd, 7.7)	7.04 (d, 6.8)
11	7.37—7.42 (m)	7.37—7.38 (m)	7.30—7.35 (m)	7.35—7.40 (m)	7.37—7.38 (m)	7.27—7.37 (m)	6.68—6.70 (m)	7.27 (m)	7.44—7.52 (m)
12	7.37—7.42 (m)	7.37—7.38 (m)	7.30—7.35 (m)	7.35—7.40 (m)	7.37—7.38 (m)	7.27—7.37 (m)	6.68—6.70 (m)	7.27 (m)	7.44—7.52 (m)
13	7.23—7.25 (m)	7.22—7.24 (m)	7.19—7.21 (m)	7.21—7.24 (m)	7.21—7.24 (m)	7.21—7.22 (m)	6.53—6.56 (m)	7.06—7.11 (m)	7.33—7.38(m) (m)
α	—	1.08 (s) (81.1)	0.58 (s) (57.6)	1.73 (q, 7.9)	1.74—1.77 (m)	1.61—1.67 (m)	1.04 (bs)	—	—
β	—	—	—	1.35 (t, 7.9)	1.70—1.73 (m)	1.34—1.39 (m)	1.04 (bs)	7.52—7.55 (m)	7.68—7.80 (m)
γ	—	—	—	—	1.37—1.41 (m)	1.25—1.32 (m)	—	7.52—7.55 (m)	7.68—7.80 (m)
δ	—	—	—	—	0.90 (t, 7.3)	0.92 (t, 7.3)	—	7.36—7.39 (m)	7.22—7.27 (m)
α'—γ'	—	—	—	—	—	—	0.55—0.65(m)	—	—
δ'	—	—	—	—	—	—	0.16 (t, 6.8)	—	—
$\alpha*$	—	—	—	—	—	—	—	2.84 (s)	—

[a]Chemical shifts (δ) in ppm. ^{2}J[^{119}Sn, ^{1}H]; ^{3}J[^{1}H, ^{1}H] in Hz are listed in parenthesis. Multiplicity is given as s = singlet, d = doublet, bd = broad doublet, dd = doublet of doublet, t = triplet, tt = triplet of triplet, q = quartet, m = multiplet.
[b]Numbering is according to Fig. 1.

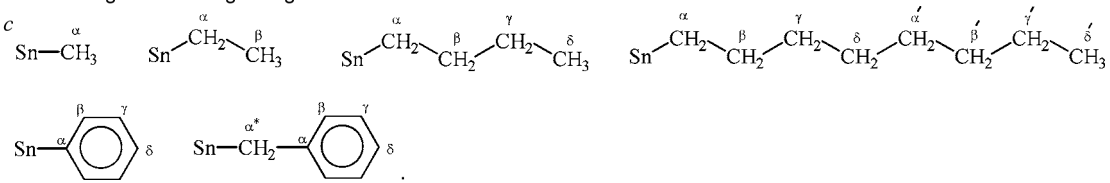
c 

TABLE 4 ^{13}C NMR Data of Organotin(IV) Derivatives of (*E*)-3-(3-Fluorophenyl)-2-phenyl-2-propenoic Acid.[a,b,c]

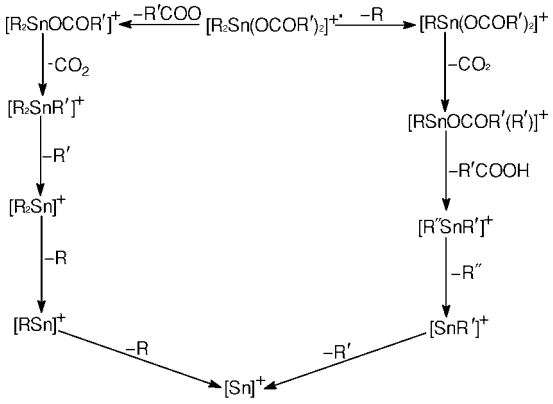
^{13}C No.	***HL*** Acid	**I** Me_2SnL_2	**II** Me_3SnL	**III** Et_2SnL	**IV** $n\text{-}Bu_2SnL$	**V** $n\text{-}Bu_3SnL_2$	**VI** $n\text{-}Oct_2SnL_2$	**VII** Bz_2SnL_2	**VIII** Ph_3SnL
1	172.85	176.83	172.67	176.82	174.84	172.0	176.75	174.76	173.40
2	132.88	133.19	135.66	133.30	133.46	135.60	133.58	134.44	134.29
3	140.97	140.49	138.2, 136.36 (d, 2.4)	140.04, 140.16 (d, 5.0)	140.89, 140.94 (d, 2.6)	137.27, 137.31 (d, 2.7)	139.96	139.97	138.27
4	136.28, 136.41 (d, 8.3)	136.63, 136.76 (d, 8.1)	137.67, 137.80 (d, 7.9)	136.67, 136.80 (d, 8.2)	136.82, 136.94 (d, 7.9)	137.27, 137.39 (d, 7.5)	136.79, 136.91 (d, 7.6)	136.78, 136.91 (d, 8.0)	137.18, 137.34 (d, 9.5)
5	116.81, 117.17 (d, 22.4)	116.65, 117.00 (d, 22.2)	116.73, 117.90 (d, 22.1)	116.56, 116.80 (dd, 3.9, 22.4)	117.06, 117.42 (d, 22.6)	116.10, 116.45 (d, 22.3)	116.55, 116.91 (d, 22.9)	116.65, 117.01 (d, 22.4)	116.56, 116.91 (d, 22.4)
6	160.32, 164.24 (d, 246.1)	160.34, 164.25 (d, 245.8)	160.63, 164.53 (d, 245.2)	160.29, 164.19 (d, 245.6)	160.65, 164.56 (d, 245.8)	160.09, 163.99 (d, 245.4)	160.31, 164.21 (d, 245.7)	160.24, 164.14 (d, 245.1)	160.36, 164.26 (d, 245.4)
7	116.26, 116.60 (d, 21.5)	115.96, 116.30 (d, 21.0)	115.50, 115.84 (d, 21.3)	115.81, 116.15 (d, 21.1)	116.40, 116.74 (d, 21.6)	114.78, 115.12 (d, 21.3)	115.74, 116.08 (d, 21.6)	115.68, 116.02 (d, 21.6)	115.49, 115.84 (d, 21.7)
8	129.65, 129.78 (d, 8.3)	129.59, 129.72 (d, 8.1)	129.69, 129.82 (d, 8.4)	129.51, 129.64 (d, 8.4)	129.93, 130.06 (d, 8.4)	129.09, 129.22 (d, 8.3)	129.61	129.39, 129.52 (d, 7.9)	129.47, 129.61 (d, 8.7)
9	126.77, 126.80 (d, 2.1)	126.55, 126.60 (d, 2.3)	126.53, 126.58 (d, 2.6)	126.50, 126.54 (d, 2.6)	126.99, 127.04 (d, 2.9)	125.95, 125.99 (d, 2.8)	126.44, 126.47 (d, 2.4)	126.51, 126.55 (d, 2.6)	126.39, 126.43 (d, 2.4)
10	134.61	135.20	136.64	135.40	135.30	136.47	135.50	135.66	136.58
11	128.83	128.78	128.80	128.74	129.12	128.19	128.70	128.44	128.52
12	129.55	129.52	129.89	129.40	129.84	129.27	128.06	129.72	130.18
13	128.37	128.22	128.00	128.11	128.59	127.27	128.06	127.86	127.86
α	—	4.81	−1.91 (379.1, 396.7)	17.73 (580.6)	25.67	16.32 (342.0, 357.8)	25.59	137.61	128.35
β	—	—	—	8.93	27.01	27.56 (21.1)	24.55	130.80	139.57
γ	—	—	—	—	26.60	26.71 (61.8, 64.5)	33.15	128.95	136.96
δ	—	—	—	—	13.92	13.39	29.10	128.76	128.92
α'	—	—	—	—	—	—	29.05	—	—
β'	—	—	—	—	—	—	31.79	—	—
γ'	—	—	—	—	—	—	22.59	—	—
δ'	—	—	—	—	—	—	14.04	—	—
α^*	—	—	—	—	—	—	—	34.4	34.37
$\delta - ^{119}$Sn	—	−128.9	139.0	−121.0	−157.1	111.6	−158.1	−231.32	−110.3

[a]Chemical shifts (δ) in ppm. $^nJ[^{117/119}Sn, ^{13}C]$, $^nJ[^{119}Sn, ^{13}C]$, and $^nJ[^{19}F, ^{13}C]$ in Hz are listed in parenthesis.
[b]Numbering is according to Fig. 1.
[c]See footnote 3 of Table 3 for α, β, γ, δ, α', β', γ', δ', and α^*.

TABLE 5 (C—Sn—C) Angles (°) Based on NMR Parameters of Selected Organotin(IV) Derivatives of (*E*)-3-(3-Fluorophenyl)-2-phenyl-2-propenoic Acid

				Angle (°)	
Compound	*Compound*	^1J [^{119}Sn,^{13}C] (Hz)	^2J [^{119}Sn, ^{1}H] (Hz)	^1J	^2J
I	Me_2SnL_2	—	81.1	—	132.2
II	Me_3SnL	396.7	57.6	111.6	110.8
III	Et_2SnL_2	580.6	—	132.8	—
V	*n*-Bu_3SnL	357.8	—	110.5	—

ligand and the stepwise elimination of R groups to give Sn^+ as an end product.

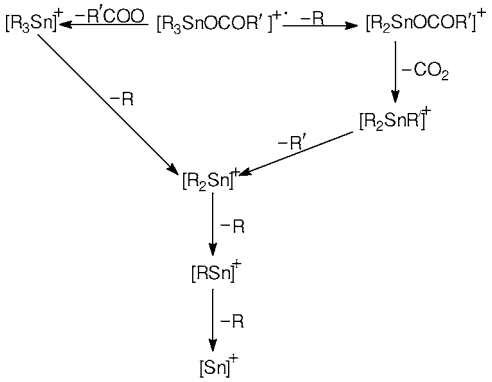


R = CH_3, C_2H_5, *n*-C_4H_9, *n*-C_8H_{17}, $C_6H_5CH_2$

R″= Corresponding alkene, arene or methine

R′= $CH(3\text{-}FC_6H_4)=C(C_6H_5)$

SCHEME 1 Fragmentation pattern of R_2SnL_2.



R = CH_3, *n*-C_4H_9, C_6H_5

R′= $CH(3\text{-}FC_6H_4)=C(C_6H_5)$

SCHEME 2 Fragmentation pattern of R_3SnL.

X-ray Structure

Experimental data pertinent to the X-ray structure analysis of **III** are listed in Table 8, and the selected bond lengths and bond angles are given in Table 9. Figure 3 shows the molecular structure of **III**.

The hexa-coordinated Sn atom is surrounded by four O atoms of the propenoate ligands forming an almost planar base, and the ethyl groups occupy the two remaining positions resulting in a highly distorted octahedral geometry, which may be best described on the basis of the skew-trapezoidal geometry. The symmetry-related propenoates are asymmetrically coordinated to the Sn atom, with Sn—O bond distances of 2.111 (16), 2.112 (17), 2.543 (18), and 2.569 (2) Å; the Sn—C bond distances are 2.121 (3) and 2.122 (2) Å. The molecules are separated by normal Van der Waals contacts in the crystal with no Sn···F interactions. The structure exhibiting similar geometry as found in **III** includes $Et_2Sn(O_2CC_4H_3S)_2$, $Et_2Sn(O_2CC_5H_3NSMe)_2$, and $Et_2Sn(O_2CCH{=}CHC_4H_3S)_2$ [35–37]. The structure of **III** shows anisobidentate mode of coordination of the propenoate ligands accompanied by unequal C—O bond distances; the C—O distances for the weakly coordinated O atoms are being shorter than the C—O distances of the strongly bound O atoms (Table 9).

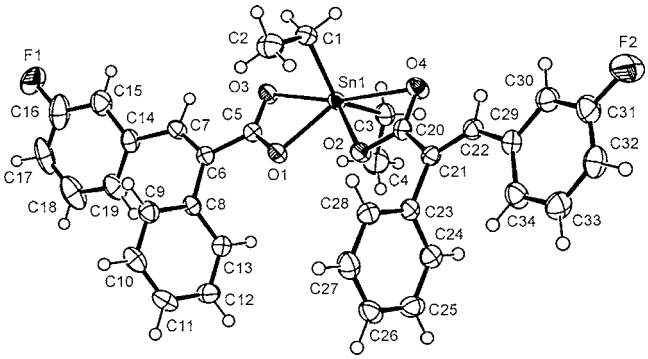


FIGURE 3 ORTEP drawing of the X-ray structure of $C_{34}H_{30}F_2O_4Sn$ (**III**).

The dimensions in the *E*-3-(3-fluorophenyl)-2-phenyl-2-propenoate ligands in **III** are unexceptional with mean bond distances C=C 1.32 (3) and C_{sp2}—C_{sp2} 1.482 (3) Å.

Biological Activity

The in vitro biocidal activities of all complexes, **I–VIII** (including **HL**) were carried out against various bacteria by using the agar well diffusion method [38], and the results obtained are given in Table 10. They were compared with the results obtained for reference drug, imipenum. The activities of the compounds **III**, **V**, **VI**, and **VIII** were found comparable or slightly better than the reference drug against *Escherichia coli*, *Bacillus subtilis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Salmonella typhi*. However, complex **V** showed good activity only against *Bacillus subtilis* and compound **VI** exhibited the highest activity against *Escherichia coli*, *Bacillus subtilis*, and *Pseudomonas aeruginosa*, better than reference drug (imipenum). The results obtained for compound **VI** contradict the assessment that diorganotin(IV) compounds have low-biological activity [39], and an increase in the number of carbon atoms in the R groups decreases the antimicrobial activity of the organotin(IV) compounds [40]. This substantiates that the anionic group may also share some role in the biocidal activity of organotin(IV) complexes [39]. But all these synthesized compounds were found inactive against the bacterium *Shigella flexenari* (Table 10).

The fungicidal screening data for the compounds tested by using tube diffusion test [41] are listed in Table 11. The investigation showed that triorganotin compounds are more active than diorganotin(VI) derivatives and the ligand itself, particularly against *Trichophyton longifusus*, *Aspergillus flavusi,* and *Microsporum canis*. This supports the assessment that the biocidal activity of organotin(IV) compounds is related to their geometry, and the species generating a tetrahedral structure in solution is more active. This can also be best explained on the basis of a triorganotin-ligand behavior, which dictates that the function of an ionic group is to be transportation of the active organotin(IV) moiety to the site of the action [39]. It is observed that the ligand acid (**HL**) and its organotin complexes are inactive against *Candida glaberata*. Compounds **II** and **V** showed good activity against *Trichophyton longifusus* and *Microsporum canis*; while complexes **III, VII, VIII**, and ligand acid (**HL**) gave better activity only against *Microsporum canis*, which is comparable to the activity of miconazole (reference drug), while showing moderate or no activity against the other tested fungi (Table 11).

The cytotoxicity data (LD_{50} values) collected by brine-shrimp lethality bioassay method [42] are summarized in Table 12. The results demonstrate that the compounds **II, III,** and **VIII** showed positive lethality with LD_{50} values in the range 1.7248–35.8900 μg/mL. Thus, the compound **VIII** was found to be the least toxic and compound **II** was the most toxic of all the synthesized organotin(IV) derivatives of (*E*)-3-(3-fluorophenyl)-2-phenyl-2-propenoic acid. While the other investigated compounds, including ligand acid (**HL**), exhibited no cytotoxicity (Table 12).

The results so obtained support the earlier findings that toxicological properties of organotin(IV) compounds are affected by both the number of Sn—C bonds in the molecule and the nature of R groups directly bonded to the Sn atom. Thus Sn atom produces maximum biological activity when $n = 3$ as observed in some of the synthesized triorganotin(IV) compounds (**II** and **VIII**) [40]. The toxicity rising to a maximum and then steadily decreasing as the number of carbon atoms increases is a common phenomenon for organotins. It is maximum when R = Et (**III**), and as the number of carbon atoms in R is increased the toxicity is reduced [40]. Furthermore, the degree of toxic action is believed to be controlled by the ease with which the triorganotin(IV) compounds interact with amino acid at certain active sites. Similarly, the diorganotin(IV) compounds, which are less toxic, act by inhibiting mitochondrial oxidative phosphorylation [43].

EXPERIMENTAL

Materials

Organotin chlorides/oxides were purchased from Aldrich, Fluka, or Alfa-Aesar (Johnson Matthey) Chemicals, while dibenzyltin dichloride was prepared by the earlier reported method [44]. The ligand (*E*)-3-(3-fluorophenyl)-2-phenyl-2-propenoic acid was synthesized, using the Perkin condensation method [10]. The organic solvents (chloroform *n*-hexane, etc.) used were from Merck, Germany and dried in situ using the standard procedures [46]. All the other chemicals were of analytical grade and were used without further purification.

General Procedure for Synthesis

Ligand acid (100 mmol) was dissolved in ethanol (350 mL) to which sodium bicarbonate (0.1 mol), dissolved in distilled water (60 mL), was added

TABLE 6 Fragmentation Pattern and Relative Abundance of Diorganotin(IV) Derivatives of (*E*)-3-(3-Fluorophenyl)-2-phenyl-2-propenoic Acid at 70 eV[a]

Fragment Ions	**I***(m/z (%))* $R = CH_3$	**III***(m/z (%))* $R = C_2H_5$	**IV***(m/z (%))* $R = n\text{-}C_4H_9$	**VI***(m/z (%))* $R = n\text{-}C_8H_{17}$	**VII***(m/z (%))* $R = C_7H_7$
$[R_2Sn(OCOR')_2]^+$	–	–	–	828 (2)	784 (2)
$[RSn(OCOR')_2]^+$	617 (3)	631 (53)	659 (2)	715 (100)	693 (4)
$[RSnOCOR'(R')]^+$	573 (3)	587 (1)	–	671 (2)	649 (4)
$[R_2SnOCOR']^+$	391 (48)	419 (42)	475 (12)	587 (34)	543 (3)
$[R_2SnR']^+$	347 (14)	375 (2)	–	543 (1)	499 (1)
$[RSnR']^+$	331 (1)	345 (6)	–	429 (1)	407 (1)
$[Sn\ R']^+$	317 (9)	317 (32)	317 (32)	317 (20)	317 (58)
$[R_2Sn]^+$	150 (6)	178 (12)	–	346 (1)	302 (1)
$[RSn]^+$	135 (7)	149 (8)	177 (16)	233 (3)	211 (4)
$[Sn]^+$	120 (1)	120 (9)	120 (2)	120 (1)	120 (3)
$[R'COOH]^+$	242 (12)	242 (12)	242 (12)	242 (3)	242 (54)
$[R']^+$	197 (100)	197 (100)	197 (100)	197 (36)	197 (100)
$[CH_3(CH_2)_2CH_2]^+$	–	–	57 (40)	57 (11)	–
$[CH_3CH_2CH_2]^+$	–	–	–	43 (16)	–
$[C_6H_5CH_2]^+$	–	–	–	–	91 (54)

[a] $R' = CH(3\text{-}FC_6H_4){=}C(C_6H_5)$.

dropwise with continuous stirring to obtain a clear solution, followed by dropwise addition of silver nitrate (100 mmol) solution in 50 mL of water with constant stirring. The white precipitate so obtained was filtered under suction in dark, washed thoroughly with water and ethanol, respectively, and dried over anhydrous $CaCl_2/P_2O_5$ in dark.

The silver salt (10 mmol) of (*E*)-3-(3-fluorophenyl)-2-phenyl-2-propenoic acid was suspended in 30 mL of dry chloroform in a 250-mL two-necked round bottom flask equipped with all accessories. Diorganotin dichloride (5 mmol) and triorganotin chloride (10 mmol), dissolved in 30 mL chloroform, was added slowly with vigorous stirring. The reaction mixture was refluxed for 7–8 h and was allowed to stand overnight at room temperature. The silver chloride settled was filtered off, and the solvent was removed by rotary evaporator. The product obtained was recrystallized from a mixture of chloroform: *n*-hexane (80:20).

Di-*n*-octyltin(IV) carboxylate (**VI**) was synthesized by the condensation of ligand acid, **HL** (10 mmol) with di-*n*-octytin oxide (5 mmol) in 1:2 molar ratio by heating at reflux temperature for 8–10 h in dry toluene (100 mL) using Dean–Stark apparatus. The water formed during the condensation reaction was removed at intervals and then was cooled to room temperature, and the solvent was removed by the rotary evaporator. The collected solid was recrystallized from chloroform and *n*-hexane mixture (90:10).

TABLE 7 Fragmentation Pattern and Relative Abundance of Trioganotin(IV) Derivatives of (*E*)-3-(3-Fluorophenyl)-2-phenyl-2-propenoic Acid at 70 eV[a]

Fragment Ions	**II***(m/z (%))* $R = CH_3$	**V***(m/z (%))* $R = n\text{-}C_4H_9$	**VIII***(m/z (%))* $R = C_6H_5$
$[R_3SnOCOR']^+$	406 (8)	—	592 (8)
$[R_2SnOCOR']^+$	391 (97)	475 (75)	515 (51)
$[R_2SnR']^+$	347 (65)	—	471 (5)
$[R_3Sn]^+$	165 (90)	291 (3)	351 (43)
$[R_2Sn]^+$	150 (60)	234 (3)	274 (5)
$[RSn]^+$	135 (66)	177 (31)	197 (100)
$[Sn]^+$	120 (42)	120 (8)	120 (8)
$[R'COOH]^+$	242 (8)	242 (9)	242 (2)
$[R']^+$	197 (100)	197 (100)	197 (100)
$[CH_3(CH_2)_2CH_2]^+$	—	57 (40)	—
$[C_6H_5]^+$	—	—	77 (16)

[a] $R' = CH(3\text{-}FC_6H_4){=}C(C_6H_5)$.

Instrumentation

Melting points were determined in a capillary tube using a MPD Mitamura Riken Kogyo (Japan) electrothermal melting point apparatus. The infrared (IR) spectra were recorded as neat liquids, using KBr cells or KBr pellets (for solid compounds) on a Bio–Rad *Excaliber* FT–IR, model FTS 300 MX spectrometer (USA), in the frequency range of 4000–400 cm^{-1}.

TABLE 8 Crystal Data, Data Collection, Structural Solution and Re nement of Compound $C_{34}H_{30}F_2O_4Sn$ (**III**)

Empirical formula	$C_{34}H_{30}F_2O_4Sn$	
Formula weight	659.27	
Temperature (K)	173 (2)	
Wavelength (Å)	0.71073	
Crystal system	Monoclinic	
Space group	$C2_1/n$	
Unit cell dimensions	$a = 10.0900$ (10) Å	
	$b = 9.1290(10)$ Å	$\beta = 91.921(6)^\circ$
	$c = 31.302$ (5) Å	
Volume (Å)^3	2881.7 (6)	
Z	4	
$D_{calc.}$ (g cm^{-3})	1.520	
Absorption coef cient (mm^{-1})	0.94	
$F(000)$	1336	
Crystal size (mm^{-3})	$0.26 \times 0.24 \times 0.20$	
Theta range for data collection (°)	2.6—2.7	
Index ranges	$-12 \le h \le 12$, $-11 \le k \le 11$, $-40 \le 1 \le 40$	
Re ections collected	11536	
Independent re ections	6433 (R(int) = 0.028)	
Re nement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	6433/0/389	
Goodness-of- t on F^2	1.05	
Final R indices ($I > 2\sigma(I)$)	$R_1 = 0.032$, $wR_2 = 0.061$	
R indices (all data)	$R_1 = 0.053$, $wR_2 = 0.067$	
Largest diff. peak and hole	0.52 and −0.64 e.Å^{-3}	

Multinuclear NMR (^{1}H, ^{13}C, ^{119}Sn) spectra were recorded on a Bruker ARX 250-FT-NMR spectrometer using $CDCl_3$ as an internal reference for (δ ^{1}H ($CDCl_3$) = 7.25 and δ ^{13}C ($CDCl_3$) = 77.0). ^{119}Sn NMR spectra were obtained with Me_4Sn as an external reference (Ξ (^{119}Sn) = 37.290665) [47]. Chemical shifts are given in ppm, and coupling constants J are given in Hz. Mass spectral data were taken on a MAT-8500 Finnigan mass spectrometer (Germany). The m/z values were evaluated assuming that H = 1, C = 12, N = 14, O = 16, F = 19, Cl = 35, and Sn = 120.

X-ray single crystal analyses were made on Nonius Kappa CCD diffractometer with graphite-monochromated Mo K_α radiation. The structures were solved by the direct method [48] and expanded using the Fourier techniques [49]. The figures were plotted with the help of ORTEPII [50]. The CCDC deposition number is 271638.

TABLE 9 Selected Bond Distances (Å) and Bond Angles (°) for $C_{34}H_{30}F_2O_4Sn$ (**III**)

Sn(1)—O(2)	2.1112. (16)	O(4)—C(20)	1.242 (3)
Sn(1)—O(1)	2.1124 (17)	C(6)—C(7)	1.342 (3)
Sn(1)—C(3)	2.121 (3)	C(21) —C(22)	1.341 (3)
Sn(1)—C(1)	2.122 (2)	C(6)—C(8)	1.489 (3)
Sn(1)—O(3)	2.5430 (18)	C(7)—C(14)	1.480 (3)
Sn(1)—O(4)	2.5690(2)	C(21)—C(23)	1.490 (3)
O(1)—C(5)	1.295 (3)	C(22)—C(29)	1.468 (3)
O(2)—C(20)	1.304 (3)		
O(2)—Sn(1)—O(1)	82.80 (6)	C(1)—Sn(1)—O(3)	88.23 (9)
O(2)—Sn(1)—C(3)	105.57 (9)	C(5)—O(1)—Sn(1)	101.62 (15)
O(1)—Sn(1)—C(3)	106.24 (9)	C(20)—O(2)—Sn(1)	102.17 (15)
O(2)—Sn(1)—C(1)	106.00 (9)	C(5)—O(3)—Sn(1)	82.94 (14)
O(1)—Sn(1)—C(1)	106.84 (9)	C(2)—C(1)—Sn(1)	114.84 (18)
C(3)—Sn(1)—C(1)	136.42 (10)	C(4)—C(3)—Sn(1)	114.5 (2)
O(2)—Sn(1)—O(3)	138.29 (6)	O(3)—C(5)—O(1)	119.9 (2)
O(1)—Sn(1)—O(3)	55.50 (6)	O(3)—C(5)—C(6)	122.6 (2)
C(3)—Sn(1)—O(3)	87.76 (8)	O(1)—C(5)—C(6)	117.5 (2)

BIOCIDAL STUDIES

Antibacterial Activity

The synthesized compounds were screened for antibacterial activity against *Escherichia coli, Bacillus subtilis, Shigella flexenari, Staphylococcus aureus, Pseudomonas aeruginosa,* and *Salmonella typhi* bacterial strains, using the agar well diffusion method [38]. Imipenum was used as a standard drug, and the wells (6 mm in diameter) were dug in the media with the help of a sterile metallic borer. Two to eight hours old bacterial inoculums containing approximately 10^4–10^6 colony-forming units (CFU)/mL were spread on the surface of a nutrient agar with the help of a sterile cotton swab. The recommended concentration of the test sample (200 mg/mL in DMSO) was introduced into the respective wells. Other wells supplemented with DMSO and reference antibacterial drug served as negative and positive controls, respectively. The plates were incubated immediately at 37°C for 20 h. The activity was determined by measuring the diameter of the inhibition zone (in mm), showing complete inhibition. Growth inhibition was calculated with reference to the positive control. The results of the antibacterial activity so obtained are collected in Table 10.

Antifungal Activity

The synthesized carboxylates were also tested for antifungal activity against six different human, animal, and plant pathogens, namely *Trichophyton longifusus, Candida albicans, Aspergillus flavus, Microsporum canis, Fusarium solani*, and *Candida glaberata* by using the tube diffusion test [41]. Amphotericin B and miconazole were used as standard antifungal agents for the comparison test.

Stock solutions of pure compounds (200 μg/mL) were prepared in sterile DMSO. Sabouraud dextrose agar was prepared by mixing Sabouraud (32.5 g), glucose agar (4%) and agar-agar (4 g) in 500 mL of distilled water followed by dissolution at 90–95°C on a water bath. The media (4 mL) was dispensed into screw-capped tubes and autoclaved at 121°C for 15 min. Test compounds (66.6 μL) were added from the stock solution to nonsolidified Sabouraud agar media (50°C). The tubes were then solidified at room temperature and inoculated with 4 mm diameter portion of inoculums derived from a 7-day old respective fungal culture. For nonmycelial growth, an agar surface streak was employed. The tubes were incubated at 27–29°C for 7–10 days, and growth in the compound containing media was determined by measuring the linear growth (in mm) and growth inhibition with reference to the respective control. The results of the antifungal activity obtained are listed in Table 11.

Cytotoxicity

For all the synthesized complexes, including ligand acid (**HL**), LD_{50} values were measured and compared with standard drug etoposide to evaluate their toxicity. The LD_{50} data were determined by adopting the brine-shrimp lethality bioassay method [42], and the results are summarized in Table 12.

TABLE 10 Antibacterial Activity Data of Organotin(IV) Derivatives of (*E*)-3-(3-Fluorophenyl)-2-phenyl-2-propenoic Acid[a,b]

		Zone of Inhibition (mm)									
Name of Bacterium	*Clinical Implication*	**I**	**II**	**III**	**IV**	**V**	**VI**	**VII**	**VIII**	**HL**	*Ref. Drug*
Escherichia coli	Infection of wounds, urinary tract and dysentery	—	—	14	—	25	75	—	17	—	[30]
Bacillus subtilis	Food poisoning	—	9	15	13	32	65	—	25	9	[31]
Shigella flexenari	Blood diarrhea with fever and severe prostration	—	—	—	—	—	—	—	—	—	[33]
Staphylococcus aureus	Food poisoning, scaled skin syndrome, endrocarditis	11	14	18	12	32	—	14	24	10	[43]
Pseudomonas aeruginosa	Infection of wounds, eyes, septicemia	12	14	13	—	—	35	—	—	11	[25]
Salmonella typhi	Typhoid fever, localized infection	—	—	15	—	16	—	—	—	10	[41]

[a]In vitro, agar well diffusion method, conc. 200 mg/mL of DMSO.
[b]Reference drug, imipenum.

TABLE 11 Antifungal Activity Data of Organotin(IV) Derivatives of (*E*)-3-(3-Fluorophenyl)-2-phenyl-2-propenoic Acid[a,b]

	Percent Inhibition											
Name of Fungus	**I**	**II**	**III**	**IV**	**V**	**VI**	**VII**	**VIII**	**HL**	*Standard Drug*	*Percent Inhibition*	*MIC (μg/mL)*
Trichophyton longifusus	55	90	50	60	90	80	50	55	50	Miconazole	100	70
Candida albicans	40	65	70	—	65	65	55	—	—	Miconazole	100	110.8
Aspergillus flavus	35	75	70	60	70	—	50	65	65	Amphotericin B	100	20
Microsporum canis	—	90	75	30	90	—	90	90	90	Miconazole	100	98.4
Fusarium solani	—	70	—	—	65	40	65	—	—	Miconazole	100	73.25
Candida glaberata	—	—	—	—	—	—	—	—	—	Miconazole	100	110.8

[a]Concentration: 200 μg/mL of DMSO.
[b]MIC = Minimum inhibitory concentration.

TABLE 12 Cytotoxicity Data of Organotin(IV) Derivatives of (*E*)-3-(3-Fluoro-phenyl)-2-phenyl-2-propenoic Acid[a,b,c]

Compound	**I**	**II**	**III**	**IV**	**V**	**VI**	**VII**	**VIII**	**HL**
LD_{50}	—	1.7248	24.766	—	—	—	—	35.8900	—

[a]Against brine-shrimps, Artemia salina (in vitro).
[b]No cytotoxicity for compounds **I**, **IV–VII**, and **HL**.
[c]Reference drug, etoposide.

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