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Organotin(IV) Esters of (*E*)-3-Furanyl-2-phenyl-2-propenoic Acid: Synthesis, Investigation of the Coordination Modes by IR, Multinuclear NMR (^{1}H, ^{13}C, ^{119}Sn) and In Vitro Biological Studies

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ABSTRACT: *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**)], where L is (E)-3-furanyl-2-phenyl-2-propenoate, have been synthesized and structurally characterized by vibrational and NMR (^{1}H, ^{13}C and ^{119}Sn) spectroscopic techniques in combination with mass spectrometric and elemental analyses. The IR data indicate that in both the di- and triorganotin(IV) carboxylates the ligand moiety COO acts as a bidentate group in the solid state. The ^{119}Sn NMR spectroscopic data, $^{1}J[^{119}Sn,^{13}C]$ and $^{2}J[^{119}Sn, ^{1}H]$, coupling constants show a four-coordinated environment around the tin atom in triorganotin(IV) and five-coordinated in diorganotin(IV) carboxylates in noncoordinating solvents. The complexes have been screened against bacteria, fungi, and brine-shrimp larvae to assess their biological activity.* © 2008 Wiley Periodicals, Inc. Heteroatom Chem 19:612–620, 2008; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20488

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INTRODUCTION

The environmental and biological chemistry of organotin(IV) carboxylates is the subject of interest due to their increasingly widespread use in industry and agriculture [1].

In addition, bioorganotin chemistry has also developed a great deal due to the fact that certain organotin(IV) in general and organotin(IV) carboxylates in particular play an important role in anticarcinogenesis [2–6].

Owing to their high biological activity, there is relatively little information available on organotin compounds as anticancer agents in vivo. However, more recently diorganotin compounds are being investigated for their antitumor activity [7–9]. Although tin-based drugs usually are less active than the corresponding platinum antitumor drugs, they have the advantage of lower toxicity [10]. The diorganotin(IV) antitumor complexes are of tetra-coordinated, penta-coordinated, and hexa-coordinated geometries [11]. In general, the biological activity of organotin(IV) compounds is influenced greatly by the structure of the molecule, the coordination number of the tin atom, and also by its mode of action [12,13].

As a part of our continuing program in this area [14–17] and based on the above-mentioned

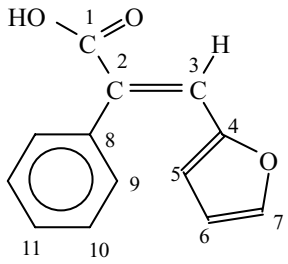


FIGURE 1 Numbering scheme of (*E*)-3-furanyl-2-phenyl-2-propenoic acid.

considerations, we have investigated a series of reactions of di- and triorganotin chlorides/oxides with (*E*)-3-furanyl-2-phenyl-2-propenoic acid. The generic structure of the ligand framework is shown in Fig. 1. The characterization of the compounds is carried out by means of ^{1}H, ^{13}C, ^{119}Sn NMR, and FT-IR spectroscopy, as well as the elemental and mass spectrometric (MS) analyses. The synthesized complexes and ligand acid (**HL**) have been tested for in vitro biological activity.

RESULTS AND DISCUSSION

Reactions of di- and triorganotin chlorides/oxides with stoichiometric amount of silver salt of (*E*)-3-furanyl-2-phenyl-2-propenoic or free ligand acid were carried out at temperature of reflux in dry chloroform (60 mL) or toluene (80 mL), respectively. The ligand acid (**HL**) was synthesized in laboratory using the reported procedure [18]; see Fig. 1.

All the synthesized compounds are stable and soluble in common solvents. The physical data are summarized in Table 1.

Spectroscopic Studies

IR Spectra. The stretching frequencies of interest are those associated with COO, Sn—C, and Sn—O groups and are listed in Table 2. IR spectra of the silver salt, ligand, and the synthesized complexes have been recorded as KBr pellets or neat liquids in the range 4000–400 cm^{-1}.

The assignment of the bands has based on the comparison with spectra of free ligand (**HL**) and its silver salt (**AgL**). The deprotonation of the carboxylic acid is evident from the disappearance of a

TABLE 1 Physical Data of the Synthesized Organotin(IV) Derivatives of 3-Furanyl-2-phenyl-2-propenoic Acid[a,b] $L = R^1CH = C(R^2)COO$

Compound	*Compound (Formula Weight)*	*MP (°C)*	*Yield (%)*	*%C Calcd (Found)*	*%H Calcd (Found)*
I	Me_2SnL_2 $C_{28}H_{24}O_6Sn$ (575)	172–175	81	58.43 (58.23)	4.17 (4.20)
II	Me_3SnL $C_{16}H_{28}O_3Sn$ (377)	95–97	90	50.93 (51.03)	7.42 (4.67)
III	Et_2SnL_2 $C_{30}H_{29}O_6Sn$ (604)	121–123	80	59.60 (59.51)	4.80 (4.95)
IV	*n*-Bu_2SnL_2 $C_{34}H_{36}O_6Sn$ (659)	86–89	78	61.91 (62.01)	5.46 (5.50)
V	*n*-Bu_3SnL C_{25} H_{36} O_3Sn (503)	Liquid	79	59.64 (59.41)	7.16 (7.07)
VI	*n*-Oct_2SnL_2 $C_{42}H_{52}O_6Sn$ (771)	Viscous Liquid	70	65.37 (65.34)	6.74 (6.52)

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

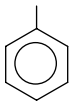
[b] R^1 =  and R^2 = 

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

	ν(COO)				
Compound No.	*Asymmerical*	*Symmerical*	*Δν*	*ν(Sn-C)*	*ν(Sn-O)*
I	1576 s	1383 s	193	597 w	459 w
II	1568 s	1372 s	196	595 w	453 w
III	1575 s	1381 s	194	595 m	493 w
IV	1575 s	1381 s	194	559 w	461 m
V	1587 s	1389 s	198	595 m	460 w
VI	1574 s	1378 m	196	592 w	490 w
HL (Acid)	1672 s	1421 s	251	–	–
AgL	1576 s	1377 s	199	–	–

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

broad band owing to the COOH group in the region 3400–2800 cm^{-1} of the ligand [19]. The asymmetric, ν_{asym}(COO), and symmetric, ν_{sym}(COO), stretching vibrations for the uncomplexed ligand and its silver salt have been detected at 1672, 1421 and 1576, 1377 cm^{-1}, respectively. In the complexes, the carbonyl stretching frequencies are found to be shifted to lower wave numbers, which is ascribed to carboxylate coordination in accordance with earlier reports [20,21]; see Table 2.

The ν_{asym}(COO) and ν_{sym}(COO) bands appear at 1672–1568 and 1421–1372 cm^{-1}, respectively [22]. The values of a difference, $\Delta\nu = \nu_{asym}(COO) - \nu_{sym}(COO)$ in the spectra of the complexes are lower than the values for (*E*)-3-furanyl-2-phenyl-2-propenoic acid ($\Delta\nu$ = 251 cm^{-1}) and are comparable with that observed in the silver salt of the ligand ($\Delta\nu$ = 199 cm^{-1}). These observations suggest anisobidentate nature of the carboxylate ligand [22,23] and support the assessment that diorganotin(IV) carboxylates have hexa-coordinated distorted octahedral motifs (Figs. 2a and 2b) and triorganotin(IV) compounds may acquire polymeric geometries containing bridging COO groups in the solid state (Fig. 2d). This is totally consistent with the earlier reports [14,24]. Diorganotin(IV) carboxylates exhibit the hexacoordinated geometry, whereas triorganotin(IV) shows the trigonal bipyramidal geometry. Polymeric structure is supported by trigonal bipyramidal geometry.

Absorption bands in the region 493–453 cm^{-1} are assigned to the stretching frequencies associated with the Sn—O bonds [25], which substantiate further the formation of tin complexes.

NMR Spectra. Tables 3–5 show the ^{1}H, ^{13}C, and ^{119}Sn NMR chemical shifts of the ligand and its complexes in $CDCl_3$ solution. ^{1}H NMR spectra coincide with the expected integration and peak multiplicities. In the spectrum of free ligand, single resonance is observed at 7.81 ppm, which appeared in the spectra of complexes in the region 7.69–7.89 ppm [14,15–17]; see Table 3. Resonance signals for the protons of furanyl moiety of the ligand were assigned on the basis of $^{3}J[^{1}H, ^{1}H]$ values [26], while that of the phenyl moiety were assigned according to our earlier reports [14,15–17]. The $^{2}J[^{119}Sn, ^{1}H]$ (81 and 57 Hz, respectively) values of dimethyltin(IV), 81 Hz (s, 1.04 ppm) and trimethyltin(IV), 57 Hz (s, 0.58 ppm) derivatives support the five-coordinated and four-coordinated environment around the tin atom in the solution [27]. Moreover, organotin(IV)

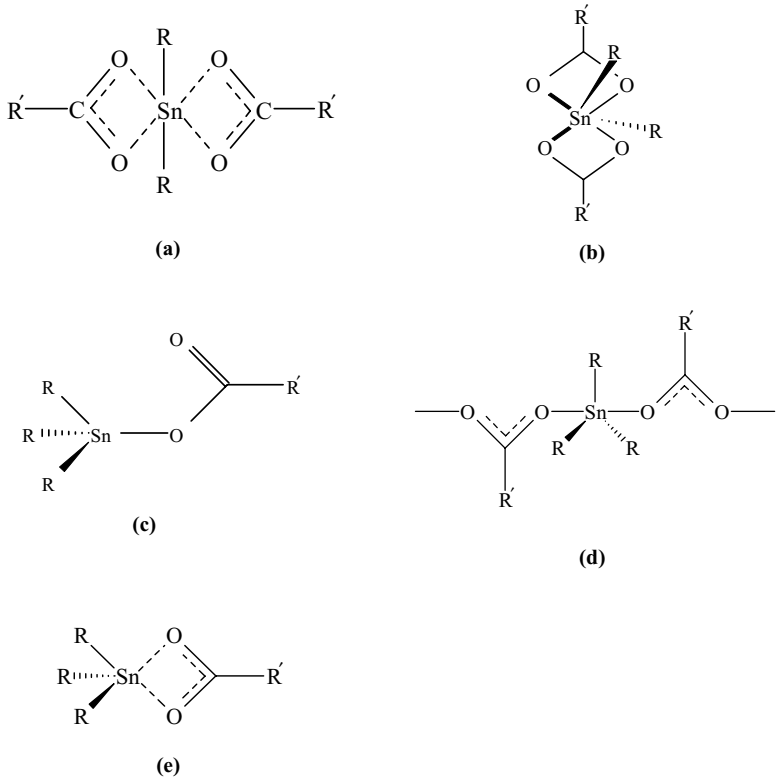
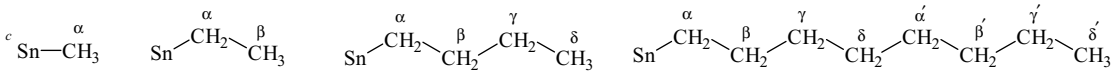


FIGURE 2 Proposed structures (a), (b) for diorganotin(IV) derivatives, and (c), (d), (e) for triorganotin(IV) carboxylates.

TABLE 3 ^{1}H NMR Data of Organotin(IV) Derivatives of (*E*)-3-furanyl-2-phenyl-2-propenoic Acid[a–c]

^{1}H No.	HL Acid	**I** Me_2SnL_2	**II** Me_3SnL	**III** Et_2SnL_2	**IV** $n\text{-}Bu_2SnL_2$	**V** $n\text{-}Bu_3SnL$	**VI** $n\text{-}Oct_2SnL_2$
3	7.81 (s)	7.87 (s)	7.73 (s)	7.89 (s)	7.87 (s)	7.69 (s)	7.87 (s)
5	5.86 (d, 3.5)	5.93 (d, 3.3)	5.79 (d, 3.2)	5.68 (d, 3.4)	5.90 (d, 3.4)	5.76 (d, 3.5)	5.90 (d, 3.3)
6	7.37–7.39 (m)	7.25–7.29 (m)	7.25–7.28 (m)	7.28–7.29 (m)	7.24–7.29 (m)	7.21–7.26 (m)	7.26–7.29 (m)
7	6.27 (d, 1.7)	6.28 (d, 1.7)	6.24 (d, 1.7)	6.27 (d, 1.7)	6.27 (d, 1.7)	6.23 (dd, 0.6, 1.8)	6.27 (d, 1.6)
9	7.43–7.45 (m)	7.41–7.44 (m)	7.39–7.42 (m)	7.41–7.44 (m)	7.41–7.44 (m)	7.37–7.40 (m)	7.39–7.44 (m)
10	7.43–7.45 (m)	7.41–7.44 (m)	7.39–7.42 (m)	7.41–7.44 (m)	7.41–7.44 (m)	7.37–7.40 (m)	7.39–7.44 (m)
11	7.40–7.41 (m)	7.37–7.39 (m)	7.34–7.36 (m)	7.36–7.39 (m)	7.36–7.39 (m)	7.33–7.35 (m)	7.37–7.38 (m)
α	–	1.04 (s), [81]	0.58 (s), [57]	1.69 (q, 8.0), [75]	1.69 (t, 6.2), [81]	1.58–1.69 (m)	1.69 (bs)
β	–	–	–	1.33 (t, 7.9)	1.36–1.40 (m)	1.32–1.37 (m)	1.69 (bs)
γ	–	–	–	–	1.36–1.40 (m)	1.26–1.31 (m)	–
δ	–	–	–	–	0.90 (t, 7.3)	0.89 (t, 7.3)	–
γ-γ'	–	–	–	–	–	–	1.24–1.34 (m)
δ'	–	–	–	–	–	–	0.85 (t, 7.0)

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

[c] 

moieties of the compounds, **III–VI** were assigned as described in the literature [19,15–17]. Chemical shifts of the signals for the ligand moiety of all the investigated complexes appear almost at the same positions as in the free ligand acid (Table 3).

In ^{13}C NMR spectra, the position of phenyl and furanyl carbon signals does not shift significantly on binding to tin as compared with those in the ligand acid. However, position of the carboxylate carbon moved to the lower field region in all the complexes except in the compounds **II** and **V** in comparison with the ligand acid, indicating participation of the carboxylic group in coordination to tin atom (Table 4) [28]. Deshielding of carboxylate carbon

TABLE 4 ^{13}C NMR data of Organotin(IV) Derivatives of (*E*)-3-Furanyl-2-phenyl-2-propenoic Acid[a–c]

^{13}C No.	**HL** Acid	**I** Me_2SnL_2	**II** Me_3SnL	**III** Et_2SnL_2	**IV** $n\text{-}Bu_2SnL_2$	**V** $n\text{-}Bu_3SnL$	**VI** $n\text{-}Oct_2SnL_2$
1	172.87	176.61	172.20	176.89	176.69	171.95	176.69
2	135.37	135.77	136.73	136.29	136.32	137.35	136.09
3	129.95	129.56	130.45	129.19	129.14	131.38	128.68
4	150.77	150.82	151.19	151.14	151.17	151.39	150.95
5	112.38	112.13	111.92	112.13	112.12	111.84	112.10
6	115.69	115.25	113.84	114.94	114.86	113.28	114.97
7	144.68	144.48	143.68	144.31	144.26	143.33	144.30
8	135.37	135.77	136.73	136.29	136.32	137.35	136.09
9	128.69	128.52	128.38	128.56	128.57	128.25	128.52
10	129.31	129.23	129.16	129.35	129.35	129.11	129.21
11	128.18	127.97	127.58	127.94	127.93	127.35	127.89
α	–	4.78	−2.25[380, 397]	17.72 [542, 583]	25.23 [576, 597]	16.63 [342, 358]	25.48 [565, 583]
β	–	–	–	8.95 [41]	26.72 [32]	27.87 [20]	24.50 [37]
γ	–	–	–	–	26.24 [82]	26.99 [62]	33.13 [94]
δ	–	–	–	–	13.58	13.63	29.10 [26]
α'	–	–	–	–	–	–	29.04
β'	–	–	–	–	–	–	31.80 [9]
γ'	–	–	–	–	–	–	22.59 [34]
δ'	–	–	–	–	–	–	14.05
δ ^{119}Sn	–	−130.34	136.31	−166.34	−160.03	107.48	−153.01

[a]Chemical shifts (δ) in ppm. ^{n}J[$^{117/119}$Sn, ^{13}C]; ^{n}J[^{119}Sn, ^{13}C] in Hz are listed in square brackets.
[b]Numbering is according to Fig. 1.
[c]See footnotes of Table 3 for α, β, γ, δ, α', β', γ', δ'.

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

Compound No.	*Compound*	$^{1}J[^{119}Sn, ^{13}C]$ *(Hz)*	$^{2}J[^{119}Sn, ^{1}H]$ *(Hz)*	*Angle (°)*	
				^{1}J	^{2}J
I	Me_2SnL_2	–	81	–	132.1
II	Me_3SnL	397	57	111.6	110.5
III	Et_2SnL_2	583	75	127.9	124.9
IV	*n*-Bu_2SnL_2	597	81	134.6	132.1
V	*n*-Bu_3SnL	358	–	112.3	–
VI	*n*-Oct_2SnL_2	583	–	133.3	–

C (1) observed in complexes **I, III, IV**, and **VI** should be related to the electrophilicity of the tin. A σ-charge donation from the COO donor group to the tin center removes electron density from the carboxylate carbon C (1), produces deshielding, which will attenuate at positions remote from the tin metal. A slight upfield shift observed for C (1) of the compounds **II** and **V** could be due to the flow of charge from the electron with donating methyl (**II**) and *n*-butyl (**V**) groups to the tin, which in turn shifts electron density to the carbon C(1) of the electron with drawing carboxylic (COO) group [14,15–17]. Here again the ^{13}C NMR assignments of organotin moieties of the synthesized complexes are based on those made previously [14,15–17]; see Table 4.

^{119}Sn NMR chemical shifts of the complexes in $CDCl_3$ solution are listed in Table 4. The ^{119}Sn chemical shift values of complexes **II** and **V** are 136.3 and 107.4, respectively. Similarly, in complexes **I, III, IV**, and **VI** ^{119}Sn chemical shift values are found to be in the range of −130.3 to −166.3 ppm. The occurrence of ^{119}Sn chemical shifts in these areas indicates four-coordinated environment in triorganotin(IV) derivatives and five-coordinated in diorganotin(IV) carboxylates around the central tin atoms in these complexes in noncoordinating solvents [29]. This is further supported by the C—Sn—C bond angles (Table 5) calculated from the $^{2}J[^{119}Sn, ^{1}H]$ and $^{1}J[^{119}Sn, ^{13}C]$ values, using the literature methods [28,30]. Furthermore, our recent work on analogous di- and triorganotin(IV) carboxylates has also confirmed this assessment [15–17].

Mass Spectrometric Data

The mass spectral data collected at 70 eV for both the di- and triorganotin(IV) derivatives are reported in Tables 6 and 7, respectively. Although the major fragmentation pattern is shown in Schemes 1 and 2, the molecular ion peak is observed only for methyl derivatives (**I** and **II**) and is consistent with the literature [31].

TABLE 6 Fragmentation Pattern and Relative Abundance of Diorganotin(IV) Derivatives

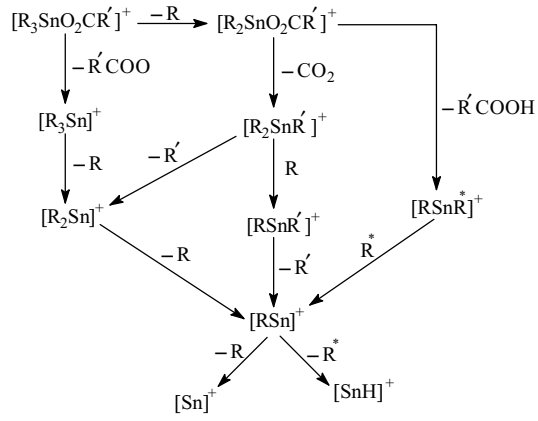
Fragment Ions	***I*** *Int.(%)* $R = CH_3$	***III*** *Int. (%)* $R = C_2H_5$	***IV*** *Int. (%)* $R = n\text{-}C_4H_9$	***VI*** *Int. (%)* $R = n\text{-}C_8H_{17}$
$[R_2Sn(O_2CR')_2]^+$	576 (5)	604 –	660 –	772 –
$[R_2SnO_2CR']^+$	363 (71)	391 (4)	447 (3)	559 (10)
$[RSn(O_2CR')_2]^+$	561 (7)	575 (8)	603 (100)	659 (100)
$[RSnO_2CR'(R')]^+$	517 (4)	531 (8)	559 (10)	615 (2)
$[SnR']^+$	289 (27)	289 (33)	289 (49)	289 (35)
$[R_2Sn]^+$	150 (6)	– –	234 –	– –
$[RSn]^+$	135 (14)	149 (2)	177 (3)	– –
$[^*RSnR']^+$	303 (3)	317 –	345 (2)	– –
$[SnH]^+$	121 –	121 (2)	121 (3)	121 (2)
$[Sn]^+$	120 (2)	120 (5)	120 (3)	120 (2)
$[R'COOH]^+$	214 (17)	214 (10)	214 (13)	214 (21)
$[C_{10}H_5O]^+$	141 (100)	141 (100)	141 (78)	141 (50)
$[R']^+$	169 (76)	169 (49)	169 (75)	169 (51)
$CH_3(CH_2)_2CH_2$	– –	– –	57 (24)	57 (46)

$R' = (C_6H_5)CCH(C_4H_3O)$.
$^*R = CH_2, C_4H_8$.

TABLE 7 Fragmentation Pattern and Relative Abundance of Diorganotin(IV) Derivatives

Fragment Ions	***II*** *Int.(%) R = CH_3*	***V*** *Int.(%) R = n-C_4H_9*
$[R_3SnO_2CR']^+$	378 (3)	504 –
$[R_2SnO_2CR']^+$	363 (12)	447 (100)
$[R_2SnR']^+$	319 (9)	403 (2)
$[RSnR']^+$	–	346 (2)
$[R_3Sn]^+$	165 (10)	291 (8)
$[R_2SnH]^+$	–	235 (3)
$[RSn^*R]^+$	–	233 (6)
$[R_2Sn]^+$	150 (3)	–
$[RSn]^+$	135 (4)	177 (16)
$[SnH]^+$	121 –	121 (13)
$[Sn]^+$	120 (1)	120 (7)
R′COOH	214 (100)	214 –
[R′]	169 (61)	169 (30)
$C_{11}H_9$	141 (69)	141 (14)
C_6H_5	77 (14)	77 –
$CH_3(CH_2)_2CH_2$	–	57 (24)

R′ = $(C_6H_5)CCH(C_4H_3O)$.
*R = C_4H_8.

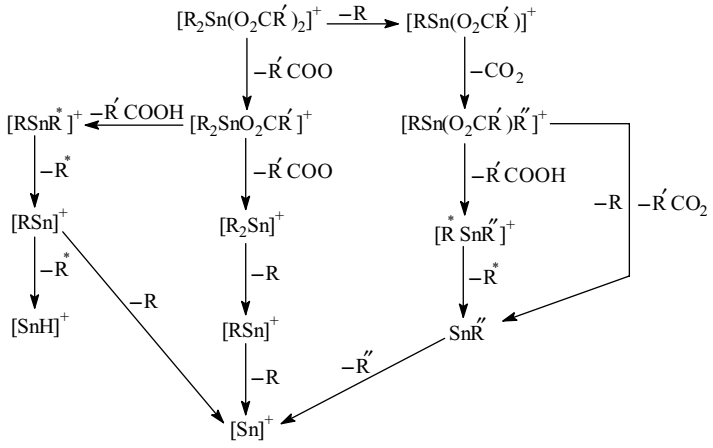


R = CH_3, n-C_4H_9
R^* = C_4H_8
R′ = $(C_6H_5)CCH(C_4H_3O)$
R′CO_2 = Ligand

SCHEME 2 Fragmentation pattern of R_3SnL.

Diorganotin(IV) compounds lose R (Me, Et, *n*-Bu, *n*-Oct) radical or ligand (R′COO) to give $[RSn(O_2CR')_2]^+$ or $[R_2SnO_2CR']^+$ fragment ions. Then loss of CO_2 or R′COO or R′COOH takes place in the secondary fragmentation. The next decomposition step involves a release of ligand acid, R′COOH and gives the $[^*RSnR']^+$ fragment ion, where *R is a corresponding alkene. It is then followed by elimination of *R or R, which ultimately gives $[SnH]^+$ or $[Sn]^+$, respectively (Scheme 1).

Triorganotin(IV) compounds are also observed to follow almost the same fragmentation pattern (Scheme 2). In conclusion, the fragmentation patterns of both, di- and triorganotin(IV) carboxylates obey the established routes described in earlier reports [32].



R = CH_3, n-C_4H_9, n-C_8H_{17}
R^* = CH_2 or C_4H_9
R′ = $(C_6H_5)C{=}CH(C_4H_3O)$
R″ = $(C_6H_5)C{\equiv}C(C_4H_3O)$
R′CO_2 = Ligand

SCHEME 1 Fragmentation pattern of R_2SnL_2.

TABLE 8 Antibacterial Activity Data of Organotin(IV) Derivatives of (*E*)-3-Furanyl-2-phenyl-2-propenoic Acid[a,b]

Name of Bacterium	*Clinical Implication*	*Zone of Inhibition (mm)*							*Ref. Drug*
		I	***II***	***III***	***IV***	***V***	***VI***	***HL***	
Escherichia coli	Infection of wounds, urinary tract and dysentery	–	–	10	–	29	–	–	30
Bacillus subtilis	Food poisoning	12	–	10	15	25	–	–	31
Shigella flexenari	Blood diarrhea with fever and severe prostration	–	–	8	–	–	–	–	33
Staphlococcus aureus	Food poisoning, scaled skin syndrome, endrocarditis	15	–	10	25	35	12	–	43
Pseudomonas aeruginosa	Infection of wounds, eyes, septicemia	–	10	10	16	–	–	–	25
Salmonella typhi	Typhoid fever, localized infection	17	–	–	15	10	–	–	41

[a]In vitro, agar well diffusion method, conc. 1 mg/mL of DMSO.
[b]Reference drug, Imipenum.

Biological Activity

The in vitro biological activities of complexes **I–VI** and the ligand acid (**HL**) were screened against various bacteria and fungi by the "agar well diffusion" [33] and "tube diffusion" [34] methods, respectively. The data obtained are presented in Tables 8 and 9.

For antibacterial activities, the compounds were tested at a concentration of 1 mg/mL of DMSO solution and the susceptibility zones being measured in millimeters (Table 8). The screening results indicate that the activities of complexes, **III–IV** are significantly greater than the other tested compounds but are less than those of the reference drug, imipenum. Compounds **II** and **IV** are inactive except for some activity against *Shigella flexenari*, *Pseudomonas aeruginosa*, and *Staphlococcus aureus*, respectively. Similarly, the compound, **I** was found to be active only against *Bacillus subtillis*, *Staphlococcus aureus*, and *Samonella typhi*. The ligand acid (**HL**) is completely inactive, but some of its organotin(IV) derivatives showed significant antibacterial effects.

The antifungal activity bioassay test indicates that the compounds **I–V** and ligand acid (**HL**) exhibits high antifungal activity against most of the tested fungi, whereas compound **IV** is active only against the *Asperigillus flavus* and *Microsporum canis* (Table 9). In the present analysis, tri-*n*-butyltin(IV) derivative is associated with the highest antifungal activity and is consistent with the earlier reports [17,35] that complexes exhibiting the four coordinated geometry in solution state show more activity.

The cytotoxicity (LD_{50}) data have also been determined using the brin-shrimp (*Artemia salina*) method [36], and results are listed in Table 10.

TABLE 9 Antifungal Activity Data of Organotin(IV) Derivatives of (*E*)-3-Furanyl-2-phenyl-2-propenoic Acid[a,b]

Name of Fungus	*Percent Inhibition*							*Standard Drug*	*Percent Inhibition*	*MIC (μg/mL)*
	I	***II***	***III***	***IV***	***V***	***VI***	***HL***			
Trichophyton longifusus	30	90	60	20	90	–	70	Miconazole	100	70
Candida albicans	–	–	70	85	60	–	–	Miconazole	100	110.8
Aspergillus flavus	40	70	–	70	70	50	20	Amphotericin B	100	20
Microsporum canis	90	90	70	80	90	75	70	Miconazole	100	98.4
Fusarium solani	60	65	–	–	65	–	50	Miconazole	100	73.25
Candida glaberata	–	–	–	–	–	–	–	Miconazole	100	110.8

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

TABLE 10 Cytotoxicity Data of Organotin(IV) Derivatives of (*E*)-3-Furanyl-2-phenyl-2-propenoic Acid[a–c]

Compound	***I***	***II***	***III***	***IV***	***V***	***VI***	***HL***
LD_{50}	–	–	–	54.55	0	–	–

[a]Against brine-shrimps, *artemia salina* (in vitro).
[b]No cytotoxicity for compounds (**I–III**), (**V**), (**VI**) and (HL).
[c]Reference drug, Etoposide.

The highest toxicity is observed for tri-*n*-butyltin(IV) derivative whereas di-*n*-butyltin(IV) compound **IV** was found to be the least toxic, and the other synthesized compounds showed no cytotoxicity (Table 10).

EXPERIMENTAL

Materials and Instrumentations

Di- and triorganotin(IV) chlorides/oxides were produced from Aldrich, Fluka, or Alfa-Aesar Chemicals and were used without further purification. The ligand acid, (*E*)-3-furanyl-2-phenyl-2-propenoic acid, was prepared by the reported method [18]. Organic solvents were used of Merck (Germany) and were dried in situ using standard procedures [37]. Melting points were determined in capillary tubes using an electrothermal melting point apparatus; model MPD Mitamura Riken Kogyo (Japan). Infrared (IR) spectra in the range 4000–400 cm^{-1} 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). The ^{1}H, ^{13}C, and ^{119}Sn NMR spectra were recorded on a Bruker ARX 250 FT-NMR spectrometer (Germany) using $CDCl_3$ as an internal reference [^{1}H ($CDCl_3$) = 7.24; ^{13}C ($CDCl_3$) = 77.0]. ^{119}Sn NMR spectra were obtained with Me_4Sn as an external reference [Ξ (^{119}Sn) = 37.290665] [38]. Mass spectral data were recorded on a MAT 8500 Finnigan mass spectrometer (Germany).

Synthesis

Methyl-, ethyl-, and tri-*n*-butyltin(IV) complexes (**I, III**, and **V**) were synthesized by heating at reflux for 6–8 h the corresponding diorganotin dichloride (3.12 mmol) or triorganotin chloride (6.23 mmol) with the silver salt of (*E*)-3-furanyl-2-phenyl-2-propenoic acid (2.0 g, 6.23 mmol) in 1:2 and 1:1 molar ratio, respectively (Eqs. (1) and (2)) in dry chloroform (60 mL) The synthesis was carried out in a 250-mL two-necked round-bottom flask, fitted with a water condenser and a magnet bar. It was placed overnight at room temperature, and the formed silver chloride (AgCl) was filtered off, and solvent was rotary evaporated.

Di-*n*-butyl- and di-*n*-octyltin(IV) derivatives (**IV** and **VI**) were prepared by the reaction of (*E*)-3-furanyl-2-phenyl-2-propenoic acid (2.0 g, 9.35 mmol) in 2:1 molar ratio by heating at reflux temperature for 8–10 h with di-*n*-butyl- (1.16 g, 4.68 mmol) and di-*n*-octyltin(IV) oxide (1.69 g, 4.68 mmol), respectively in toluene (80 mL). The water formed was removed intervally using Dean and Stark apparatus (Eq. (3)), whereas the solvent was evaporated under the reduced pressure.

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

where R = Me (I), Et (III)

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

where R = Me (II), *n*-Bu (V)

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

R = *n*-Bu(IV), *n*-Oct(VI)

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