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Synthesis, Characterization, and Biological Studies of Tri- and Diorganotin(IV) Complexes with 2′,4′-Difluoro-4-hydroxy-[1,1′]-biphenyle-3-carbolic Acid: Crystal Structure of $[(CH_3)_3Sn(C_{13}H_7O_3F_2)]$

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ABSTRACT: *Eight tri- and diorganotin(IV) carboxylates with general formulae R_3SnL and R_2SnL_2 (where $R = CH_3$, n-C_4H_9, C_6H_5, C_7H_7, and $L = 2',4'$-difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic acid) were synthesized and characterized by UV–vis, IR, conductance, multinuclear (^1H, ^{13}C, and ^{119}Sn) NMR spectroscopy, and mass spectrometry. The crystal structure of $[(CH_3)_3Sn(C_{13}H_7O_3F_2)]$ indicates that the tin atom in the asymmetric unit exists in a trigonal bipyramidal geometry having a space group* Pbca *with an orthorhombic crystal system. These complexes were also screened for their antibacterial and antifungal activities.* © 2002 Wiley Periodicals, Inc. Heteroatom Chem 13:638–649, 2002; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10057

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INTRODUCTION

The biological importance of organotin(IV) halides and their derivatives has been recently reviewed [1]. Organic ligands with sulfur, nitrogen, oxygen, and fluorine as substituents have long been used to increase the biological activity of organotin carboxylates [2]. Organotin compounds with such ligands have widely been tested for their possible use in cancer chemotherapy. A few such compounds where the hydrogen of the organic moiety is substituted by fluorine have proved to be active against tumors [3–5]. Although the Van der Waals radii of fluorine (1.35 Å) and hydrogen (1.20 Å) are comparable, the much higher electronegativity of fluorine also strongly affects the electron density distribution in the molecule. Some work has been done on the synthesis of organotin carboxylates containing mono- or polyfluorophenyl groups [7–11], and their antitumor activity has been studied against two human tumor cells [2]. We have also made a similar attempt to synthesize some organotin(IV) derivatives with 2′,4′-difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic

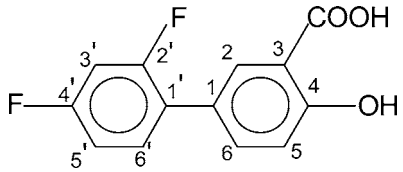


FIGURE 1 Numbering scheme of 2′,4′-difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic acid.

acid (Fig. 1), which is one of the most frequently used analgesic, antipyretic, and anti-inflammatory drugs [12], with the aim that the newly synthesized compounds are supposed to be more active against tumor cells. These complexes were characterized by UV–vis, IR, conductance, multinuclear (^{1}H, ^{13}C, and ^{119}Sn) NMR spectroscopy, and mass spectrometry. The crystal structure of $[(CH_3)_3Sn(C_{13}H_7O_3F_2)]$ is also studied to try to learn more about design the mode of action of the drug supposed to have antitumor activity.

RESULTS AND DISCUSSION

Organotin(IV) derivatives of 2′,4′-difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic acid have been synthesized by the reaction of the silver salt of the ligand acid with the corresponding organotin(IV) chlorides in 1:1 and 1:2 molar ratios in dry chloroform. However, prolonged reflux (8 h) is required for a good yield.

All these complexes are solids, generally with high melting points, which are stable in light and dry air. They are more soluble in polar than in nonpolar solvents. The conductivities of 10^{-3} M solution of the complexes in dimethyl sulfoxide (DMSO) are in the range of 2–8 μs/cm^2 (Table 1) suggesting nonionic species in the solvent used [13,14].

Electronic Spectra

The electronic spectra of the ligand and its derivatives were recorded in DMSO solution. The spectrum of the ligand showed three distinct well defined maxima at 315, 251, and 235 nm. These maxima are consistent with the typical spectrum of benzothiazoline [15,16], and may be attributed to the $\pi \rightarrow \pi^*$ transition of the benzene ring of the ligand moiety. In the corresponding tin(IV) complexes a similar pattern is observed, which indicates a complex formation. This idea is further confirmed by an additional band observed around 275 nm, assigned to the $n \rightarrow \pi^*$ transition of the carbonyl group of the ligand coordinated to the tin atom.

Infrared Spectroscopy

The infrared spectra of compounds I–VIII have been recorded in the range of 4000–400 cm^{-1} using KBr and CsI optics. Tentative assignments have been made on the basis of earlier work and important data are listed in Table 2. The absorptions of interest are those of carbonyl ν(C═O), ν(Sn─C), ν(Sn─O), and ν(─OH). In spectra of the complexes, medium to weak bands in the region 430–480 cm^{-1} are assigned to Sn─O [17] and those in the region of 500–600 cm^{-1} are assigned to the Sn─C bonds [18]. At 2800–3200 cm^{-1} a wide and strong band is assigned to OH stretching of the O─H group attached to the phenyl ring of the ligand moiety, this result confirming that there is no participation of the group in the complex formation.

As we know that the vacant 5d orbital on tin tends to give higher coordination with ligands having

TABLE 1 Physical Data[a–d] for Organotin(IV) Derivatives of 2′-4′-Difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic Acid

No.	*Compound*	*Empirical formula (F. Wt.)*	*Yield (%)*	*m.p. (°C)*	*%C Cald. (Found)*	*%H Cald. (Found)*	*Conductance (μs/cm^2)*
(I)	Bu_2SnL_2	$C_{34}H_{32}O_6F_4Sn$ (731.09)	34.0	120	57.44 (57.50)	5.31 (5.29)	2.8
(II)	Bu_3SnL	$C_{25}H_{34}O_3F_2Sn$ (538.89)	38.36	33–35	56.91 (56.89)	6.92 (6.87)	5.6
(III)	Me_2SnL_2	$C_{28}H_{20}O_6F_4Sn$ (646.69)	46.0	200–202	54.04 (54.00)	4.19 (4.27)	4.6
(IV)	Me_3SnL	$C_{16}H_{16}O_3F_2Sn$ (412.69)	79.64	78–80	48.30 (48.51)	4.73 (4.77)	11.1
(V)	Ph_2SnL_2	$C_{38}H_{24}O_6F_4Sn$ (767.69)	32.0	–	60.75 (60.72)	4.04 (4.12)	6.0
(VI)	Ph_3SnL	$C_{31}H_{22}O_3F_2Sn$ (598.89)	46.09	300 (dec.)	63.13 (63.11)	4.10 (4.08)	4.4
(VII)	Bz_2SnL_2	$C_{40}H_{28}O_6F_4Sn$ (798.69)	46.54	145–147	61.61 (61.55)	4.39 (4.42)	6.6
(VIII)	Bz_3SnL	$C_{34}H_{28}O_3F_2Sn$ (640.69)	52.72	–	61.40 (61.25)	4.90 (4.94)	7.8
L	Ligand	$C_{13}H_8O_3F_2$ (250.20)	–	210–211	–	–	0.6

[a]For ligand see Fig. 1.
[b]Bu, *n*C_4H_9; Me, CH_3; Ph, C_6H_6; Bz, $C_6H_5CH_2$.
[c]Compound V and VIII are semisolid.
[d]Conductance in DMSO at 27°C.

TABLE 2 Infrared Data (cm^{-1}) for Organotin(IV) Derivatives of 2′,4′-Difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic Acid[a]

		ν(COO)				
No.	*Compounds*	*(asy)*	*(sym)*	*Δν*	*ν(Sn—C)*	*ν(Sn—O)*
(I)	Bu_2SnL_2	1636 s	1384 w	252	536 m	477 s
(II)	Bu_3SnL	1637 s	1392 m	245	532 m	478 m
(III)	Me_2SnL_2	1674 s	1390 m	284	532 s	476 s
(IV)	Me_3SnL	1637 s	1379 s	258	532 m	470 m
(V)	Ph_2SnL_2	1631 m	1379 s	252	533 w	476 s
(VI)	Ph_3SnL	1635 s	1383 s	252	532 s	476 m
(VII)	Bz_2SnL_2	1619 s	1379 m	240	530 w	466 s
(VIII)	Bz_3SnL	1623 s	1370 m	253	536 w	470 m
(L)	Ligand	1681 s	1455 m	226	–	–
(L-Ag)	Ligand-Ag	1645 s	1384 m	261	–	–

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

a lone pair of electrons, the IR stretching vibration frequencies of carbonyl groups in organotin carboxylates are important for determining their structures. When the structure changes from four to five coordinated symmetry, the asymmetric absorption vibration frequencies (ν_{asy}) of the carbonyl groups decrease and the symmetric absorption vibration frequencies (ν_{sym}) increase so that the difference $\Delta\nu$(C═O) decreases.

The carbonyl absorption of diorganotin dicarboxylates is apparently more complicated than those of triorganotin carboxylates because of the presence of two carbonyl groups. Now, if the two carbonyl groups have the same environment, there is only one carbonyl absorptions in the IR spectra, but if there are two carbonyl absorptions in the IR spectra, the two carbonyl groups have different coordination environments [19].

Table 2 shows that there is only one type of carbonyl absorption, with $\Delta\nu$ in the range of 240–260 cm^{-1}, which is within the range of the silver salt of the ligand acid. Therefore this carboxylate ion behaves as a bidentate group [20–25], and we suggest the trigonal bipyramidal structure for triorganotin compounds and distorted octahedral geometry for diorganotin(IV) derivatives. These arrangements are further confirmed by the other spectroscopic techniques.

^{1}H NMR Spectroscopy

^{1}H NMR spectral data of tri- and diorganotin(IV) derivatives of 2′,4′-difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic acid are given in Tables 3 and 4 and are interpreted by comparing them with the ^{1}H NMR spectra of the precursors. The signals are assigned by their peak multiplicity, intensity pattern, integration, coupling constants, and the satellites.

In the spectrum of the ligand, the signals at δ 7.09–7.95 with their distinct multiplicity and J value have been assigned to the different protons attached to the biphenyl moiety of the ligand. The analogous pattern of the signals at rather similar positions has been observed for the investigated compounds (Tables 3 and 4). In tri- and diphenyltin the derivatives of 2′,4′-difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic acid, a complex pattern is observed in the range of δ 7.35–7.65 and δ 6.99–7.25 due to the aromatic protons of the ligand and phenyl groups. The phenolic proton appears at almost the same δ value as in the ligand (δ 11.2) showing no participation in the complexation.

The butyl protons show a complex pattern due to $-CH_2-CH_2-CH_2-$ in the range of δ 1.77–0.82 and a clear triplet due to the terminal methyl group in the range of δ 0.82–1.05 [24–26]. In tri- and dibenzyl the methylene protons show singlets at δ 2.92, $^2J[(^{119}Sn\text{-}^1H)] = 60.5$ and δ 2.95, $^2J[(^{119}Sn\text{-}^1H)] = 72.7$ Hz. Similarly, for tri- and dimethyltin dichloride, $^2J[(^{117/119}Sn\text{-}^1H)] = 56.4$, 58.6 Hz and 67.0, 69.5 Hz, respectively [27], while for the trimethyltin derivative of dolobid $^2J[(^{117/119}Sn\text{-}^1H)] = 55.78$, 58.35 Hz, which clearly reflects the tetrahedral geometry of the compound. Using $^2J[(^{117/119}Sn\text{-}^1H)]$ values in Lockhart's equation, the C—Sn—C angle for some organotin derivatives have been calculated and data are reported in Table 7 [28].

^{13}C, ^{119}Sn NMR Spectroscopy

^{13}C NMR spectral data of $CDCl_3$ solutions of the ligand acid and its tri- and diorganotin(IV) derivatives (I–VIII) are given in Tables 5 and 6. The number of signals found correspond with the presence of magnetically nonequivalent carbon atoms, which were assigned by comparison with other related organic

TABLE 3 ^{1}H NMR Data[a–e] for Triorganotin-2′,4′-difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic Acid

H No.	*L (Dolobid)*	*II (Bu_3SnL)*	*IV (Me_3SnL)*	*VI (Ph_3SnL)*	*VIII (Bz_3SnL)*
2	7.86 s	7.91 s	7.99 s	8.1 s	8.0 s
5	6.89 d (8.45)	6.92 d (8.59)	7.00 d (8.6)	6.92 d (8.61)	6.89 d (8.63)
6	7.65 d (8.23)	7.45 d (8.59)	7.53 d (8.37)	7.88 m (–)	7.78 d (6.8)
3′	6.95 s	6.79 s	6.87 s	6.81 s	6.69 s
5′	6.85 d (7.78)	6.85 d (7.78)	6.92 d (7.10)	6.88 d (7.69)	6.83 d (6.8)
6′	7.46 d (8.67)	7.28 d (8.7)	7.35 d (7.25)	7.25 d (8.6)	7.21 d (8.6)
OH	11.2 s	11.9 s	11.2 s	11.6 s	11.9 s
*CH_2	–	–	–	–	2.92 s [60.5]
α	–	1.57 m	0.65 s [55.78, 58.35]	7.75–7.80 m	7.32–7.57 m
β	–	1.28 m	–	7.45–7.65 m	–
γ	–	1.28 m	–	7.35–7.39 m	–
δ	–	0.82 t	–	–	–

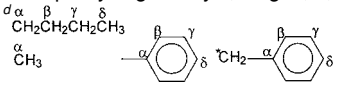
[a]In $CDCl_3$ at 298 K (40%).
[b]Chemical shift (δ) in ppm. $^{3}J(^{1}H, ^{1}H)$ in Hz, $^{n}J[^{117/119}Sn, ^{1}H]$ in Hz.
[c]Multiplicity is given by s, singlet; d, doblet; t, triplet; and m, multiplet.
[d] 
[e]For numbering scheme, see Fig. 1.
[f]Phenyl and benzyl ring protons were difficult to assign.

TABLE 4 ^{1}H NMR Data[a] for Diorganotin(IV) Derivatives of 2′,4′-Difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic Acid

H No.	*I (Bu_2SnL_2)*	*III (Me_2SnL_2)*	*V (Ph_2SnL_2)*	*VII (Bz_2SnL_2)*
2	8.0 s	7.95 s	8.02 s	7.93 s
5	6.96 d (8.64)	7.05 d (8.52)	6.92 d (8.72)	6.85 d (7.99)
6	7.58 d (8.64)	7.72 d (8.45)	7.65 d (8.5)	7.52 d (9.15)
3′	6.87 d (7.57)	6.97 d (7.35)	7.05 d (7.62)	6.63 d (7.7)
5′	6.87 d (6.8)	7.01 d (6.9)	6.92 d (6.9)	6.82 d (6.5)
6′	7.31 d (8.7)	7.41 d (8.5)	7.21 d (8.5)	7.22 d (8.3)
OH	11.8 s	11.5 s	11.3 s	11.2 s
*CH_2	–	–	–	2.95 s (72.79)
α	1.77 t	1.1 [78.5]	6.59–7.25 m	7.29–7.55 m
β	1.64 m	–	–	–
γ	1.32 m	–	–	–
δ	0.82 t	–	–	–

[a]See footnotes in Table 3.

TABLE 5 ^{13}C Data[a] for Triorganotin(IV) Derivatives of 2′,4′-Difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic Acid

C No.	*L (Dolobid)*	*II (Bu_3SnL)*	*IV (Me_3SnL)*	*VI (Ph_3SnL)*	*VIII (Bz_3SnL)*
COOH	171.5	174.0	177.4	175.6	174.52
1	125.1	125.44	125.5	125.74	126.96
2	130.2 (3.2)	131.46	131.36	131.61	131.7
3	113.4	114.57	112.4	113.46	112.7
4	160.7	161.18	161.3	161.18	161.59
5	117.5	117.26	117.32	117.36	117.8
6	135.7 (2.7)	135.23 (3.1)	135.48 (3.23)	137.10	136.8
1′	123.7 (13.8, 3.9)	124.58 (13.85, 3.8)	124.1 (13.7, 3.6)	124.30 (13.6, 3.7)	124.5 (13.6, 3.7)
2′	159.1 (248, 12.7)	159.15 (173.75, 11.7)	158.6 (158.0, 11.6)	157.9 (156.7, 11.5)	158.63 (157.8, 11.9)
3′	104.4 (26.5)	104.28 (26.1)	104.27 (25.3)	104.25 (26.48)	104.28 (24.6)
4′	161.4 (247, 11.8)	162.46 (246, 11.7)	162.3 (246.5, 11.5)	162.60 (245.6, 11.6)	162.34 (246, 11.9)
5′	112.0 (20.9, 3.3)	111.46 (21.05, 3.9)	111.45 (21.07, 3.71)	111.40 (21.06, 3.89)	111.60 (21.9, 3.8)
6′	131.4 (9.8, 4.9)	131.06 (9.4, 5.0)	131.18 (12.17, 5.09)	131.10 (9.4, 4.8)	131.0 (9.43, 4.6)
*CH_2	–	–	–	–	30.12 [350.9]
α	–	26.99	1.95 [355.31]	137.42	127.0–129.76
β	–	27.74	–	136.8	–
γ	–	16.98	–	130.43	–
δ	–	13.49	–	129.03	–

[a]See footnotes in Table 3.

TABLE 6 ^{13}C NMR Data[a] for Diorganotin(IV) Derivatives of 2′,4′-Difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic Acid

C No.	*I (Bu_2SnL_2)*	*III (Me_2SnL_2)*	*V (Ph_2SnL_2)*	*VII (Bz_2SnL_2)*
COOH	177.5	175.7	176.1	174.53
1	126.2	126.7	124.9	126.32
2	131.9	131.9	130.8	131.66
3	112.6	112.8	113.5	112.6
4	161.5	162.2	161.2	160.64
5	117.6	116.9	117.35	117.82
6	136.7 (3.33)	137.0 (3.1)	136.5	136.75
1′	124.0 (13.8, 3.8)	124.0 (13.8, 3.8)	123.7 (12.9, 3.1)	125.53 (13.8, 3.5)
2′	158.8 (158.2, 11.8)	158.8 (158.2, 11.8)	158.7 (155.2, 11.2)	157.78 (157.2, 11.4)
3′	104.3 (25.5)	104.3 (25.5)	104.1 (25.95)	104.14 (24.7)
4′	162.5 (247, 11.7)	162.5 (246.2, 11.7)	161.2 (245.1, 11.4)	162.65 (246.3, 11.72)
5′	111.7 (21.09, 3.9)	111.7 (21.09, 3.9)	112.84 (20.5, 3.75)	111.58 (21.7, 3.5)
6′	131.2 (9.53, 4.9)	131.2 (9.53, 4.9)	131.8 (9.4, 4.5)	131.66 (9.43, 4.3)
*CH_2	–	–	–	30.10 [382.89]
α	26.33 [464.0]	4.5	137.85	127–129.95
β	26.53	–	136.1	–
γ	26.44	–	129.8	–
δ	13.46	–	128.5	–

[a]See footnotes in Table 3.

analogues as model compounds [29,30]. The positions of the phenyl carbon signals remains almost unchanged in the complexes as compared with those in the ligand acid. The position of the carboxylate carbon mover to lower field in all the complexes shifts, as compared with the ligand acid, indicating participation of the carboxylic group in coordination to tin(IV) [31]. The identification of alkyl/phenyl carbons in all the complexes confirms complexation, and the complete assignment of the signals confirms the identity of the compounds. The coupling constants $^1J[^{119}Sn\text{-}^{13}C]$ and the values of the interbond angle C–Sn–C are the most important indicators for the structural evaluation of organotin carboxylate [32–36]. For the trimethyl, dibenzyl, and tribenzyltin derivatives ^1J values lie in the narrow range of 350–382 Hz (Table 7), corresponding to the average value of the angle $\theta = 107$–111°. These values are slightly higher than those corresponding with ideal tetrahedral angle, confirming the pseudotetrahedral geometry of the central tin atom. The coupling constant $^1J[^{119}Sn\text{-}^{13}C]$ of the dibutyl and tributyltin compounds in $CDCl_3$ are in the range of 450–470 Hz, which corresponds to an angle $\theta = 116$–118°. These angles are near to those in an equilateral triangle, and hence fulfil the idea of trans-trigonal bipyramidal geometry for these derivatives.

TABLE 7 (C–Sn–C) Angles (°) Based on NMR Parameters

Compounds	*$^1J(^{119}Sn\text{-}^{13}C)$ (Hz)*	*$^2J(^{119}Sn\text{-}^1H)$ (Hz)*	*Angles (°)*	
			^1J	*^2J*
Bu_2SnL_2	464.0	6.80	117.45	117.45
Bu_3SnL	454.78	7.20	116.63	116.64
Me_3SnL	355.31	31.30	107.92	107.93
Bz_2SnL_2	382.89	20.75	110.34	110.34
Bz_3SnL	350.90	30.12	107.53	107.53

^{119}Sn Chemical shift $\delta(^{119}Sn)$ of organotin compounds cover a range of over 600 ppm and are quoted relative to tetramethytin with downfield shifts from the reference compound having a positive sign. As the electron-releasing power of the alkyl group increases, the tin atom becomes progressively more shielded and $\delta(^{119}Sn)$ value moves to higher field. These values are also dependent upon the nature of the X in R_nSnX_{4-n} and generally move to lower field as the electronegativity of the latter increases. A very important property of the ^{119}Sn chemical shift is that an increase in coordination number of the tin atom from four to five, six or seven usually produces a large upfield shift of $\delta(^{119}Sn)$ [37]. The ^{119}Sn NMR spectra were recorded and the chemical shifts for all the compounds except compound VII lie in the range of tetrahedral geometry where compound VII show higher coordination, probably 5 (Table 8). These values are strongly dependent upon the nature and orientation of the organic groups bonded to tin. The shifts observed in the above cases can be explained quantitatively in terms of an increase in electron density on the tin atom as the coordination number increases [38]. An increase in coordination number is accompanied by an appropriate upfield shift. It is generally accepted that compounds with a specific geometry about the tin atom produce shifts in moderately well defined ranges.

TABLE 8 ^{119}Sn NMR Data for Organotin(IV) Carboxylates

Compounds	*^{119}Sn NMR (ppm)*
I	−122.39
II	135.245
III	165.518
IV	158.378
V	218.253
VI	−93.130
VII	−277.961
VIII	250.603

Mass Spectrometry

The main fragment ions observed in the mass spectra of compounds I–VIII are listed in Tables 9 and 10, and the fragmentation behavior is described in Schemes 1 and 2. The molecular ion peak is observed in all the triorganotin(IV) carboxylates, while it is absent in almost all the diorganotin(IV) carboxylates [39]. The fragmented ions are in good agreement with the expected structures of the compounds. For all the derivatives except III and V the base peak is derived from loss of the organic part of the ligand moiety coordinated to the tin atom. The other fragment ions containing the Sn atom are also quite intense. In triorganotin(IV) carboxylates the primary fragmentation is due to loss of the R group, where the R is methyl, butyl, phenyl, and benzyl, and the same is true for diorganotin(IV) derivatives. However, the secondary and tertiary decomposition is also followed by loss of the R group in triorganotin(IV) derivatives, while diorganotin(IV) derivatives exhibit slightly different patterns of fragmentation. Peaks $[R_2SnC_{13}H_7O_3F_2]^+$, $[R_2SnC_{12}H_7OF_2]^+$, $[RSnC_{12}H_7OF_2]^+$, $[SnC_{12}H_7OF_2]^+$, $[C_{12}H_7OF_2]^+$, and $[C_{13}H_7O_3F_2]^+$ are commonly observed in both tri- and diorganotin(IV) derivatives.

Single Crystal Analysis

The crystallographic numbering scheme for $[(CH_3)_3SnC_{13}H_7O_3F_2]$ is shown in Fig. 2, interatomic parameters being listed in Table 11, and selected bond lengths and bond angles being given in Table 12. The geometry around the tin atom is a trigonal bipyramid. The three methyl groups are located on the basal plane and the more electronegative O atoms from the symmetry related carboxylate ligands occupy the axial positions. The Sn atom is 0.169 Å out of the equatorial plane towards the more strongly bound O1 atom. The three Sn—C distances are equal within the experimental error [2.134 (11), 2.104 (13), and 2.131 (11) Å] and are also in agreement with the values reported for related compounds [40]. The Sn—O bond lengths are significantly different [Sn1—O1 2.205(8) and Sn1—O4 2.374(8) Å]. The longer C4—O1 bond [1.303(12) Å] and the shorter Sn1—O1 bond [2.205(8) Å] share the same O atom and vice versa. This could be interpreted that one of the carboxyl O atoms forms a covalent bond with the Sn atom, but the other carboxyl O atom (double bonded) is coordinated to tin with a longer Sn—O distance because the C—O bond keeps some of its double bond character. The O1—Sn—O4 angle is 173.1(3)°. The central trimethyltin group bridges two neighboring 2′,4′-difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic acid ligands via carboxylate moieties to form a one dimensional polymeric structure (Fig. 3) running along the *a*-axis. Similar polymeric chain structure of triorganotin compounds with carboxylate bridges have also been reported [41–45].

BIOLOGICAL STUDIES

All the synthesized compounds were subjected for screening of their antibacterial activity by using the

TABLE 9 Mass Spectral Data for Triorganotin Complexes with 2′,4′-Difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic Acid

Fragmentation	*Bu (e/m)*	*(%) Int.*	*Me (e/m)*	*(%) Int.*	*Ph (e/m)*	*(%) Int.*	*Bz (e/m)*	*(%) Int.*
$[R_3SnC_{13}H_7O_3F_2]^+$	540	8	414	18	600	8	642	2
$[R_2SnC_{13}H_7O_3F_2]^+$	483	100	399	100	523	18	551	5
$[R_3SnC_{12}H_7OF_2]^+$	439	–	355	38	479	2	507	5
$[RSnC_{12}H_7OF_2]^+$	382	5	340	18	402	2	416	2
$[RSn]^+$	177	18	135	18	197	25	211	2
$[C_{12}H_7OF_2]^+$	205	12	205	10	205	22	205	100
$[C_{13}H_7O_3F_2]^+$	249	14	249	7	249	22	249	2
$[R_3Sn]^+$	291	8	165	23	351	52	393	2
$[R_2Sn]^+$	234	22	150	35	274	23	302	2
$[Sn^+/SnH]^+$	120	5	120	5	120	17	120	5
$[R]^+$	57	22	15	–	77	100	91	22
$[SnC_{12}H_7OF_2]^+$	325	22	325	22	325	1	325	3

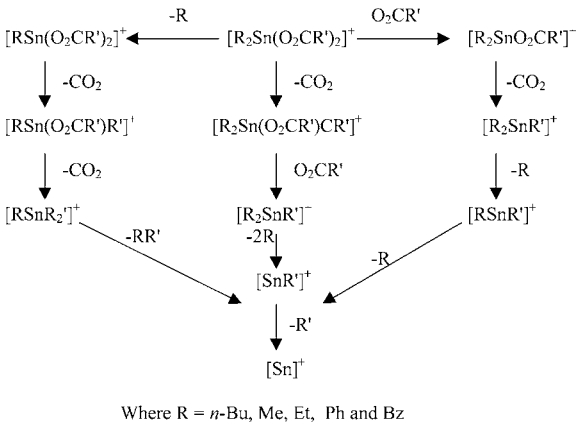
TABLE 10 Mass Spectral Data for Diorganotin Complexes with 2′,4′-Difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic Acid

Fragmentation	*Bu (e/m)*	*(%) Int.*	*Me (e/m)*	*(%) Int.*	*Ph (e/m)*	*(%) Int.*	*Bz (e/m)*	*(%) Int.*
$[R_3SnC_{26}H_{14}O_6F_4]^+$	732	12	647	–	769	–	800	–
$[R_2SnC_{13}H_7O_3F_2]^+$	483	38	398	40	519	24	551	02
$[R_2SnC_{12}H_7OF_2]^+$	439	05	354	25	475	27	507	–
$[RSnC_{12}H_7OF_2]^+$	382	03	339	05	398	08	416	02
$[SnC_{12}H_7OF_2]^+$	325	22	325	28	325	30	325	05
$[C_{12}H_7OF_2]^+$	205	42	205	30	205	45	205	20
$[RSnC_{26}H_{14}O_6F_4]^+$	675	–	632	–	691	01	709	–
$[RSnC_{25}H_{14}O_4F_4]^+$	631	–	588	–	647	02	665	20
$[RSnC_{24}H_{14}O_2F_4]^+$	587	–	544	–	603	05	621	–
$[SnC_{12}H_7OF_2]^+$	325	22	325	28	325	30	325	05
$[C_{13}H_7O_3F_2]^+$	249	15	249	98	249	100	249	55
$[Sn^+/SnH^+]^+$	120	08	120	8	120	10	120	18
$[R]^+$	57	12	15	–	77	52	91	76
$[R_2SnC_{25}H_{14}O_4F_4]^+$	688	–	603	–	724	50	756	–

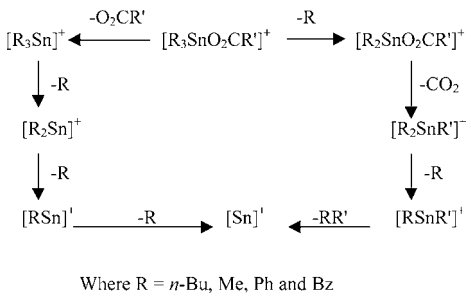
agar well diffusion method [46]. The compounds were tested at a concentration of 100 mg/ml in DMSO solution, the susceptibility zones being measured in millimeters and presented in Table 13. Compounds (I), (II), and (VI) showed a different level of activities against almost all the tested bacteria, while compound (III) was found to be almost inactive except for some activity against *Corynebacterium diphtheriae*, *Klebsiella Pneumoniae,* and *Staphylococcus aureus*. The compound (V) was found to be inactive against *Bacillus cereus*, *Proteus Vulgaris,* and *Streptococcus pyogenes*, whereas it showed a good degree of activity against other tested bacteria. In general, the susceptibility zones were clear around the discs. The ligand was found to be active and its organotin carboxylates showed more significant antibacterial effects.

When the synthesized compounds were screened against different fungal strains using the tube diffusion test [47], it was observed that the ligand along with its organotin carboxylates are significantly active against all of the tested fungal strains. The results of antifungal assay are collected in Table 14.

It has also been reported that, within a given series the triorganotin(IV) derivatives are more active against fungi [48]. Our screening tests are quite consistent with the early reports except that the trimethyltin derivative is also found to be an active fungicide. This can be best explained on the basis of a triorganotin-ligand behavior, which dictates that the



SCHEME 1 Fragmentation pattern of R_2SnL_2.



SCHEME 2 Fragmentation pattern of R_3SnL.

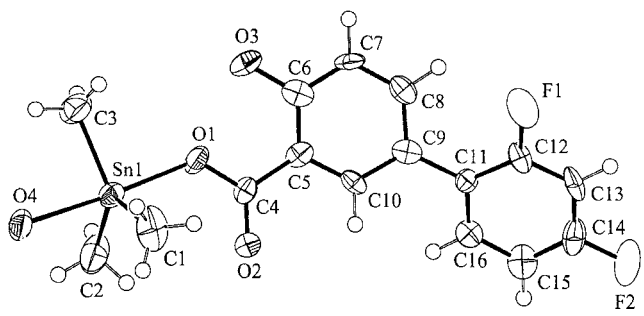


FIGURE 2 X-ray crystal structure diagram of trimethyltin(IV)-2′,4′-difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic acid.

TABLE 11 Atomic Coordinates and B_{iso}/B_{eq} and Occupancy for Trimethyltin(IV)-2′,4′-difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic Acid

Atom	*x*	*y*	*z*	B_{eq}	*occ*
Sn(1)	0.23828 (4)	0.07571 (6)	0.19959 (6)	2.738 (15)	0.740
F(1)	0.0171 (5)	0.4693 (7)	−0.3227 (9)	5.7 (3)	0.370
F(1′)	−0.0242 (10)	0.1407 (13)	−0.2391 (17)	4.9 (6)	
F(2)	−0.1109 (4)	0.2841 (6)	−0.5521 (7)	5.8 (3)	
O(1)	0.1637 (4)	0.1705 (6)	0.1285 (6)	3.3 (2)	
O(2)	0.1398 (4)	0.0822 (6)	−0.0205 (6)	3.6 (2)	
O(3)	0.1340 (4)	0.3426 (6)	0.1429 (7)	3.8 (2)	
O(4)	0.3269 (4)	−0.0099 (6)	0.2758 (6)	4.2 (2)	
C(1)	0.2964 (6)	0.0849 (11)	0.534 (10)	5.1 (4)	
C(2)	0.1795 (7)	−0.0456 (9)	0.2254 (10)	5.1 (4)	
C(3)	0.2520 (8)	0.1778 (9)	0.3300 (9)	4.8 (3)	
C(4)	0.1380 (6)	0.1578 (9)	0.0306 (10)	2.4 (3)	
C(5)	0.1033 (5)	0.2432 (10)	−0.0128 (10)	2.6 (3)	
C(6)	0.1035 (6)	0.3322 (9)	0.0432 (11)	2.8 (3)	
C(7)	0.0723 (6)	0.4106 (9)	−0.0032 (10)	3.2 (3)	
C(8)	0.0396 (6)	0.4027 (9)	−0.1026 (11)	3.1 (4)	
C(9)	0.0368 (6)	0.3140 (9)	−0.1612 (10)	2.5 (3)	
C(10)	0.0707 (5)	0.2369 (9)	−0.1138 (10)	2.3 (3)	
C(11)	−0.0018 (7)	0.3072 (8)	−0.2676 (10)	2.6 (4)	
C(12)	−0.0107 (6)	0.3837 (9)	−0.3397 (10)	2.7 (3)	
C(13)	−0.0472 (6)	0.3772 (10)	−0.4342 (12)	3.6 (4)	
C(14)	−0.0748 (7)	0.2895 (12)	−0.4583 (10)	3.8 (4)	
C(15)	−0.0689 (6)	0.2122 (10)	−0.3888 (12)	3.6 (4)	
C(16)	−0.0317 (6)	0.2213 (8)	−0.2948 (10)	3.1 (3)	
H(1)	0.3053	0.0211	0.0277	6.1542	
H(2)	0.2726	0.1180	−0.0031	6.1542	
H(3)	0.3345	0.1174	0.0694	6.1542	
H(4)	0.1444	−0.0272	0.2756	5.7053	
H(5)	0.1605	−0.0649	0.1571	5.7053	
H(6)	0.2027	−0.0953	0.2578	5.7053	
H(7)	0.2846	0.1547	0.3799	5.9146	
H(8)	0.2648	0.2375	0.3001	5.9146	
H(9)	0.2129	0.1851	0.3707	5.9146	
H(10)	0.0721	0.4714	0.0340	3.9374	
H(11)	0.0179	0.4575	−0.1320	3.7604	
H(12)	0.0715	0.1776	−0.1533	2.8234	
H(13)	−0.0521	0.4313	−0.4825	4.3007	
H(14)	0.0907	0.1536	−0.4051	4.3043	
H(15)	0.3454	−0.0404	0.2268	4.4833	
H(16)	0.3431	−0.0292	0.3342	4.4833	

function of an ionic group is to transport the active organotin moiety to the site of the action. The ligand is displaced from tin, when the organometallic unit is bonded to the active site of the biological system [48], otherwise the ligand may remain bonded to tin until it reaches its receptor site. Under such circumstances, an ionic ligand may well influence the ease with which R_3SnL is transported [48]. Thus the increased fungicidal activity of trimethyltin derivative is probably due to the dolobid group.

EXPERIMENTAL

All the tri- and diorganotin compounds except benzyl were procured from Aldrich or Fluka while tri- and dibenzyltin compounds were prepared by the reported method [49]. All the solvents were dried before use by the literature methods [50]. The ligand 2′,4′-difluoro-4-hydoxy-[1,1′]-biphenyl-3-carboxylic acid was received through the courtesy of MSD pharmaceutical company, Karachi, Pakistan.

General Procedure for the Synthesis

To a suspension of the silver salt of the 2′,4′-difluoro-4-hydoxy-[1,1′]-biphenyl-3-carboxylic acid in dry chloroform (25 ml) contained in a 250 ml two-necked round bottom flask equipped with a water condenser

TABLE 12 Bond Angles (°) and Bond Distances (Å) for Triethyltin(IV)-2′,4′-difluoro-4-hydroxy-[1,1′]-biphyenyl-3-carboxylic Acid

Atoms	*Angle (°)*	*Atoms*	*Angle (°)*
O(1)—Sn(1)—O(4)	173.1 (3)	O(1)—Sn(1)—C(1)	92.5 (4)
O(1)—Sn(1)—C(2)	97.3 (4)	O(1)—Sn(1)—C(8)	88.9 (4)
O(4)—Sn(1)—C(1)	84.7 (4)	O(4)—Sn(1)—C(2)	89.6 (4)
O(4)—Sn(1)—C(3)	86.9 (4)	C(1)—Sn(1)—C(2)	119.8 (6)
C(1)—Sn(1)—C(3)	119.2 (6)	C(2)—Sn(1)—C(2)	120.2 (5)
Sn(1)—O(1)—C(4)	123.7 (8)	O(1)—C(4)—O(2)	124.1 (12)
O(1)—C(4)—C(5)	114.0 (11)	O(2)—C(4)—C(5)	121.9 (11)
C(4)—C(5)—C(6)	122.2 (11)	C(4)—C(5)—C(10)	119.4 (12)
C(6)—C(5)—C(10)	118.3 (13)	O(3)—C(6)—C(5)	121.0 (12)
O(3)—C(6)—C(7)	119.2 (12)	C(5)—C(6)—C(7)	119.9 (13)
C(6)—C(7)—C(8)	121.0 (12)	C(7)—C(8)—C(9)	121.3 (13)
C(8)—C(9)—C(10)	116.2 (12)	C(8)—C(9)—C(11)	119.7 (12)
C(10)—C(9)—C(11)	124.1 (11)	C(5)—C(10)—C(9)	123.3 (12)
C(9)—C(11)—C(12)	123.4 (11)	C(9)—C(11)—C(16)	119.4 (12)
C(12)—C(11)—C(16)	117.6 (12)	F(1)—C(12)—C(11)	122.0 (12)
F(1)—C(12)—C(13)	115.2 (12)	C(11)—C(12)—C(13)	122.8 (13)
C(12)—C(13)—C(14)	117.7 (13)	F(2)—C(14)—C(13)	117.0 (13)
F(2)—C(14)—C(15)	121.0 (15)	C(13)—C(14)—C(15)	122.0 (13)
C(14)—C(15)—C(16)	118.7 (13)	F(1′)—C(16)—C(11)	124.3 (15)
F(1′)—C(16)—C(15)	113.9 (14)	C(11)—C(16)—C(15)	121.7 (12)
Atoms	*Distance (Å)*	*Atoms*	*Distance (Å)*
Sn(1)—O(1)	2.205 (8)	Sn(1)—O(4)	2.374 (8)
Sn(1)—C(1)	2.134 (11)	Sn(1)—C(2)	2.104 (13)
Sn(1)—C(3)	2.131 (11)	F(1)—C(12)	1.337 (14)
F′(1)—C(16)	1.312 (19)	F(2)—C(14)	1.354 (14)
O(1)—C(4)	1.303 (12)	O(2)—C(4)	1.216 (13)
O(3)—C(6)	1.362 (14)	C(4)—C(5)	1.484 (16)
C(5)—C(6)	1.406 (16)	C(5)—C(10)	1.391 (15)
C(6)—C(7)	1.385 (16)	C(7)—C(8)	1.377 (16)
C(8)—C(9)	1.419 (15)	C(9)—C(10)	1.403 (15)
C(9)—C(11)	1.511 (16)	C(11)—C(12)	1.383 (15)
C(11)—C(16)	1.384 (14)	C(12)—C(13)	1.366 (17)
C(13)—C(14)	1.378 (18)	C(14)—C(15)	1.365 (16)
C(15)—C(16)	1.374 (17)		

and magnetic stirring bar, the triorganotin chloride (0.01 mol) or diorganotin dichloride (0.005 mol) in dry chloroform (25 ml) was added dropwise with constant stirring. The reaction mixture was refluxed for 7–8 h, under an inert atmosphere and was allowed to stand overnight at room temperature. Silver chloride that had formed was filtered off and the solvent was removed under reduced pressure. The residual solid mass was recrystallized from dichloromethan/*n*-hexane (1:1) mixture.

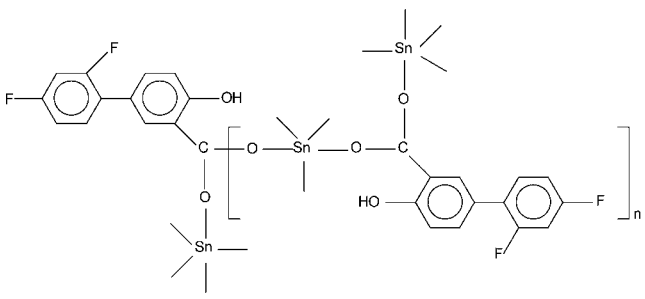


FIGURE 3 Polymeric structure for trimethyltin(IV)-2′,4′-difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic acid.

Instrumentation

Melting points were determined in a capillary tube using a MP. D Mitamura Riken Kogyo (Japan) electrothermal melting point apparatus and are uncorrected. Infrared absorption spectra were recorded as KBr/CsI pellets on a Perkin Elmer Spectrum 1000 FT-IR Spectrometer. ^{1}H, ^{13}C, and ^{119}Sn NMR spectra were recorded on a Brucker AM 250 spectrometer (Germany), using $CDCl_3$ as an internal reference [$\delta\,^{1}H(CDCl_3) = 7.25 : \delta\,^{13}C(CDCl_3) = 77.0$]. ^{119}Sn NMR spectra were obtained with Me_4Sn [(Sn) = 37.296665] as an external reference. Mass

TABLE 13 Antibacterial Activity of Organotin(IV) Derivatives of 2′,4′-Difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic Acid

	Compounds							
Bacteria	*(L)*	*(I)*	*(II)*	*(III)*	*(IV)*	*(V)*	*(VI)*	*(VII)*
Bacillus cereus	*	16	16	*	*	*	17	*
Corynebacterium diptheriae	19	20	35	16	*	17	27	*
Escherichia coli ETEC	15	18	15	*	*	16	20	*
Klebsiella pneumoniac	*	20	*	15	*	14	18	*
Proteus mirabillis	*	20	15	*	*	19	23	*
Pseudomonas aeroginosa	13	23	16	*	*	16	16	*
Salmonella typhi	15	21	16	*	15	16	25	*
Proteus vulgaris	*	19	15	*	*	*	17	*
Staphylococcus aureus	*	20	20	17	*	20	24	*
Streptococcus pyogenes	*	*	*	*	*	*	*	*

*No activity.

spectral data were measured on a MAT 8500 Finnigan mass spectrometer (Germany). UV absorption spectra were recorded on a Perkin Elmer UV–vis Lambda 2S instrument, while conductance measurements were made on a conductometer, model DDS-11A instrument (China) conductometer. X-ray single crystal analysis was made on a Rigaku AFC6S diffractometer with graphite monochromatic Mo Kα radiation.

X-Ray Crystallography

Trimethyltin(IV) (2′,4′-difluoro-4-hydoxy-[1,1′]-biphenyl-3-carboxylate. A crystal of approximate dimension $0.40 \times 0.32 \times 0.22$ mm, grown from a dichloromethane/*n*-hexane mixture (80:20), was used for data collection.

Crystal Data

$C_{16}H_{16}O_3F_2Sn$, $M = 414.00$ orthorhombic, $a = 20.773$ (2) Å, $b = 13.890$ (3) Å, $c = 12.000$ (3) Å, space group *Pbca*, $Z = 8$, $D_c = 1.588$ g/cm^3, μ(Mo Kα) = 15.03 cm^{-1}, $F_{(000)} = 1640.00$.

The data were collected at a temperature of $-103 \pm 1^\circ$C using ω-2θ scan technique to a maximum 2θ value of 50.1° by using a Rigaku AFC6S diffractometer with graphite monochromatic Mo Kα radiation, $\lambda = 0.7016$ Å. A total of 3437 unique reflections were measured (ω-2θ scan technique and $2\theta_{max}$ was 50.1°), of these 1234 satisfied the $I > 3.00\sigma(I)$ criterion of observability and were used in the subsequent analysis. The data were collected for Lorentz and polarization effects and for absorption employing the DIFABS program [51]. The structure was solved by the direct method and refined by a full matrix least-squares procedure based on F [52]. Non-hydrogen atoms were refines anisotropically. The F-atom at the 0-position was disordered over two sites F1 and F1′ with the equivalent occupancy factors. Hydrogen atoms were included at geometrically idealized positions and were not refined. The final residual, after 10 cycles of least squares, were R = 0.041, $R_w = 0.037$,

TABLE 14 Antifungal Studies of Organotin(IV) Derivatives of 2′,4′-Difluoro-4-hydroxy-[1,1′]-biphenyl-3-carboxylic Acid

	Compounds							
Fungi	*(L)*	*(I)*	*(II)*	*(III)*	*(IV)*	*(V)*	*(VI)*	*(VII)*
Epidermophyton floccosun	*	*	*	*	*	*	*	*
Trichophyton schoenleinii	76	63	75	65	66	82	50	50
Trichophyton rubrum	*	*	*	*	*	*	*	*
Pseudallescheria boydii	77	69	61	55	73	77	57	60
Candida albicans	50	62	67	48	48	60	50	50
Aspergillus niger	57	60	76	76	75	80	63	56
Microsporum canis	63	57	67	65	57	75	63	62
Trichophyton simii	63	65	70	50	69	75	*	51
Trichophyton mentagrophytes	*	*	*	*	*	*	*	*
Fusariumoxysporum	56	56	52	57	70	76	55	51
Fusarium solani	*	*	*	*	*	*	*	*
Macrophomina phaseolina	60	60	58	40	67	76	60	60
Rhizoctonia solani	*	*	*	*	*	*	*	*

*No activity.

for a weighting scheme of $w = 1/[\sigma^2 (Fo)^2 + (xP^2 + yP)]$. The analysis of various maps showed no special features and the maximum and minimum residuals in the final difference map were 0.46 and –0.57e-/Å^3. The final fractional atomic coordinates are listed in Table 11 and the crystallographic numbering scheme used is shown in Fig. 2, data manipulation was performed with the texsan package [53] installed on an iris Indigo workstation.

Antibacterial Activity

The synthesized compounds were screened for antibacterial activity against *B. cereus, C. diptheriae, Escherichia coli, K. pneumoniac, Proteus mirabillis, Pseudomonas aeroginosa, Salmonella typhi, P.s vulgaris, S. aureus,* and *S. pyogenes* bacterial strains using the agar well diffusion method [46]. Amoxicillin and amicillin were used as standard drugs. The wells were dug in the media with the help of a sterile metallic borer with centers at least 24 mm apart. 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. Recommended concentration of the test sample (2 mg/ml in DMSO) was introduced into the respective wells. Other wells were supplemented with DMSO and reference antibacterial drugs serving as negative and positive controls, respectively. The plates were incubated immediately at 37°C for 20 h. Activity was determined by measuring the diameter of zones showing complete inhibition (mm). Growth inhibition was calculated with reference to positive control. The results of antibacterial activity are collected in Table 13.

Antifungal Activity

The synthesized compounds were also tested for antifungal activity against six human pathogens namely *Epidermophyton floccosun, Trichophyton schoenleinii, Trichophyton rubrum, Pseudallescheria boydii, Candida albicans, Aspergillus niger,* three animal pathogens *Microsporum canis, Trichophyton simii, Trichophyton mentagrophytes,* and four plant pathogens *Fusariumoxysporum, Fusarium solani, Macrophomina phaseolina, Rhizoctonia solani* by using tube diffusion test [47]. The micoanazole (75 μg/ml), ketocanozole (75 μg/ml), benlate (50 μg/ml), and nabam (50 μg/ml) were used as standard drugs. Stock solutions of pure compounds (12 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 steamed dissolution, 4 ml media being dispensed into screw capped tubes and autoclaved at 121°C for 15 min. Test compound (66.6 μl) was added from the stock solution to nonsolidified Sabouraud agar media (50°C). Tubes were allowed to solidify at room temperature and inoculated with 4-mm-diameter portion of inoculums derived from a 7 days 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 the growth in the compound-containing media was determined by measuring the linear growth (mm) and growth inhibition with reference to the respective control. The results of antifungal activity are shown in Table 14.

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REFERENCES

[1] Molloy, K. C. In The Chemistry of the Metal–Carbon Bond; Hartlay, R. R. (Ed.); Wiley: London, 1989.
[2] Joshi, K. C.; Pathak, V. N.; Panwar, P. Agric Biol Chem 1977, 41, 543–549.
[3] Gielen, M.; Tiekink, E. R. T.; Bouhdid, A.; deVos, D.; Biesemans, M.; Verbruggen, I.; Willem, R. Appl Organomet Chem 1995, 9, 639–648.
[4] Albanus, L.; Bjorklund, N. E.; Gustafson, B.; Johsson, M. Acta Pharmacol Toxicol Suppl 1975, 36, 93–99.
[5] Belsky, I.; Gerther, D.; Zilka, A. J. Med Chem 1968, 11, 92–96.
[6] Welch, J. T. Tetrahedron 1987, 43, 3123–3197.
[7] Gielen, M.; Elkhoufi, A.; Biesemans, M.; Willem, R. Appl Organomet Chem 1993, 7, 119–125.
[8] Gielen, M.; Biesemans, M.; Elkhloufi, A.; Piret, J. M.; Kayser, F.; Willem, R. J Fluorine Chem 1993, 64, 279–291.
[9] Gielen, M.; Elkhloufi, A.; deVos, D.; Kolker, H. J.; Schellens, J. H. M.; Willem, R. Bull Soc Chim Belg 1993, 102, 761–764.
[10] Gielen, M.; Elkhloufi, A.; Biesemans, M.; Kayser, F.; Willem, R. Appl Organomet Chem 1993, 7, 201–206.
[11] Gielen, M.; Boualam, M.; Meriem, A.; Mahieu, B.; Biesemans, M.; Willem, R. Heteroat Chem 1992, 3, 449–452.
[12] Cotton, L. M.; Hux, R. A. Anal Profile Drug Sub 1985, 14, 491–526.
[13] Kettle, S. F. A. Coordination Compounds; Thomas Nelson: London, 1975.
[14] Jolly, W. L. Coord Chem Rev 1974, 13, 47–81.
[15] Biradar, N. S.; Mohale, V. B.; Kulkarni, V. H. Inorg Chim Acta 1973, 7, 267–270.
[16] Bosnich, B. J Am Chem Soc 1968, 90, 627–632.
[17] Deacon, G. B.; Phillips, R. J. Coord Chem Rev 1980, 33, 227–250.

[18] Singh, G.; Gupta, V. D. Natl Acad Sci Lett India 1982, 5, 423–429.
[19] Gielen, M.; Melotte, M.; Atassi, G.; Willem, R. Tetrahedron 1989, 45, 1219–1229.
[20] Molloy, K. C.; Quill, K.; Nowell, I. W. J Chem Soc, Dalton Trans 1987, 101–106.
[21] Holmes, R. R. Acc Chem Res 1989, 22, 190–197.
[22] Saxena, A.; Tandon, J. P.; Molloy, K. C.; Zuckerman, J. J. Inorg Chim Acta 1982, 63, 71–74.
[23] Nath, M.; Sharma, C. L.; Sharma, N. Synth React Inorg Met-Org Chem 1991, 21, 807–824.
[24] Tiwari, R.; Srivastava, G.; Mehrotra, R. C.; Crowe, A. J. Inorg Chim Acta 1986, 111, 167–170.
[25] Saxena, A.; Tandon, J. P. Polyhedron 1984, 3, 681–688.
[26] Smith, P. J. Chemistry of Tin; Chapman and Halls: London, 1998.
[27] Buttrus, N. H.; Suliman; M. M.; Al-Allaf, T. A. K. Synth React Inorg Met-Org Chem 2001, 31, 837–848.
[28] Lockhart, T. P.; Manders, W. F. Inorg Chem 1986, 25, 892–895.
[29] Levy, G. C.; Lichter, R. L.; Nelson, G. L. Carbon-13 Nuclear Magnetic Resonance Spectroscopy; Wiley: New York, 1980.
[30] Holecek, J.; Handlir, K.; Lycka, A.; Chattopadhyay, T. K.; Majee, B.; Kumar, A. K. Collect Czech Chem Commun 1986, 15, 1100–1111.
[31] Holecek, J.; Lycka, A. Inorg Chim Acta 1986, 118, L15–L16.
[32] Holecek, J.; Nadvornik, M.; Handlir, K.; Lycka, A. J Organomet Chem 1986, 315, 299–308.
[33] Al-Allaf, T. A. K. J Organomet Chem 1986, 306 , 336–346.
[34] Al-Allaf, T. A. K.; Al-Jayy, J. M. J Organomet Chem 1990, 391, 37–46.
[35] Al-Allaf, T. A. K.; Al-Bayati, R. I. H.; Al-Botany, A. S. A. Asian J Chem 1996, 8, 489–499.
[36] Al-Allaf, T. A. K.; Kobs, U.; Neuman, W. P. J Organomet Chem 1989, 373, 29–35.
[37] Saraswat, B. S.; Mason, J. Polyhedron 1986, 5, 1449–1458.
[38] Adhikari, A.; Greenslade, D. L.; Ghosh, A. K. Indian J Chem 1993, 32A, 454–456.
[39] Gielen, M.; Joosen, E.; Mancilla, T.; Jurkschat, K.; Willem, R.; Roobol, C.; Bernheim, J.; Atassi, G.; Huber, F.; Hoffmann, E.; Prent, H.; Mahieu, B. Main Group Met Chem 1987, 10, 147–167.
[40] Allen, F. H.; Kennard, O.; Taylor, R. Acc Chem Res 1983, 16, 146–153.
[41] Tiekink, E. R. T. Appl Organomet Chem 1991, 5, 1.
[42] Danish, M.; Ali, S.; Mazhar, M.; Badshah, A.; Masood, T.; Tiekink, E. R. T. Main Group Met Chem 1995, 18, 27–34.
[43] Danish, M.; Ali, S.; Mazhar, M.; Badshah, A.; Teikink, E. R. T. Main Group Met Chem 1995, 18, 697–705.
[44] Nawaz, M.; Ulku, D.; Danish, M.; Ali, S.; Badshah, A.; Mazhar, M. Acta Crystallogr 1997, C53, 183–185.
[45] Parvez, M.; Bhatti, M. H.; Ali, S.; Mazhar, M.; Qureshi, S. I. Acta Crystallogr 2000, C56, 327–328.
[46] (a) Carron, R. A.; Maran, J. M.; Montero, L.; Fernandozalgo; Dominguez, A. Plantes Medicinales et Phytotherapic 1987, 21, 195–202; (b) Atta-ur-Rahman; Choudhary, M. I.; Thomsen, W. J. Bioassy Techniques for Drug Development; Harward Academic Press: Amsterdam, 2001; pp. 14–20.
[47] (a) Blank, H.; Rewbell, G. Arch Derm 1965, 92, 319–322; (b) Shaukat, S. S.; Khan, N. A.; Ahmed, F. Pakistan J Bot 1980, 12, 97–106.
[48] Molloy, K. C. Bio-Organotin Compounds. In The Chemistry of Metal-Carbon Bond; Hrtly, F. R. (Ed.); Wiley: New York, 1989; Vol. 5.
[49] Sisido, K.; Yakeda, Y.; Kingawa, Z. J Am Chem Soc 1961, 83, 538–541.
[50] Perrin, D. D.; Armarego, W. L. F. Purification of Labortary Chemicals, 4th ed.; Butterworth: Oxford, 1997.
[51] Walker, N.; Stuart, D. Acta Crystallogr 1983, A39, 158–166.
[52] Sheldrick, G. M. Shelx S86, Program for the Automatic solution of crystal structure; Göthingen: Germany, 1986.
[53] Texsan. Structure Analysis Package; Molecular Structure Cooperation: Texas, 1992.