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Synthesis, Characterization, and Biocidal Studies of the Newly Synthesized Di- and Triorganotin(IV) Complexes with *n*-Butylhydrogen Phthalate

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Di-(**1**, **3**, **8**) and triorganotin(IV) complexes (**2**, **5**, **7**) with the general formula R_nSnL_{4-n}, where R = Me, Et, *n*-Bu, *n*-Oct, Ph, and Bz, and L = the *n*-$C_4H_9OCOC_6H_4COO^-$ monoanionic ligand have been synthesized by the reaction of the silver salt of the *n*-butylhydrogen phthalate with di- and triorganotin chloride in dry chloroform. However, di-*n*-butyl- and di-*n*-octyltin(IV) derivatives (**4** and **6**, respectively) were synthesized by the reaction of the corresponding organotin(IV) oxide with *n*-butylhydrogen phthalate in dry toluene. All the synthesized complexes were characterized by elemental analysis, FT-IR, multinuclear (^{1}H, ^{13}C, ^{119}Sn) NMR, and mass spectrometric techniques to assess the binding mode of the *n*-butylphthalate (*n*-$C_4H_9OCOC_6H_4COO^-$) anion. The diorganotin(IV) derivatives were found to adopt distorted octahedral and triorganotin(IV) *n*-butylphthalates and to have linear, polymeric trigonal bipyramidal structures in which *n*-butylphthalate is a monoanionic bidentate coordinating through the C(O)O group. The biocidal activity and LD_{50} values of the synthesized compounds are also reported. Some complexes exhibited good activity comparable to that of standard drugs. Furthermore, triorganotin(IV) derivatives exhibited significantly better activity than the diorganotin(IV) derivatives.

Key Words: Organotin(IV) complexes, *n*-butylhydrogen phthalate, spectral characterization, biological activity.

Introduction

Tin(IV) is known to form stable complexes with oxygen, sulfur-, carbon-, and nitrogen-containing ligands.[1] Organotin(IV) compounds of oxygen and nitrogen donor ligands are well known for their biological activity.[2–4] Moreover, some tin complexes are also known to exhibit anti-bacterial and anti-tumor activity.[1,4,5] Recently, particular attention has again been given to triorganotin(IV) derivatives because of their strong in vitro anti-fungal activity against some medically important fungi.[6] In view of the well-known industrial

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applications[7−9]and biocidal properties of organotin(IV) compounds, we are continuously involved in the preparation and characterization of the organotin(IV) carboxylates.[10−13] In the present work, we report the synthesis, properties, and in vitro biological activity of the di- and triorganotin(IV) complexes of *n*-butylhydrogen phthalate (Figure 1).

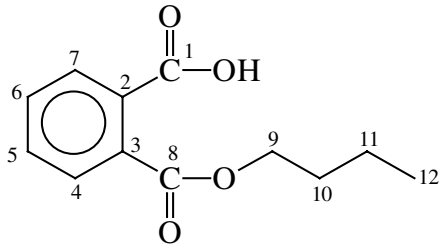


Figure 1. Numbering scheme of *n*-butylhydrogen phthalate.

Experimental

Materials and instrumentation

Di- and triorganotin(IV) chlorides/oxides were supplied by Aldrich, Fluka, or Alfa-Aesar chemical companies, and were used without further purification. Dibenzyltin dichloride[14] and the ligand acid *n*-butylhydrgenphthalate[15] were prepared by previously reported methods. Organic solvents were obtained from Merck (Germany) and dried in situ using standard procedures.[16] Melting points were determined in capillary tubes using a Mitamura Riken Kogyo MPD (Japan) electrothermal melting point apparatus. The elemental analyses were performed on a CE Instrument model EA 1110 (Italy) organic elemental analyzer. Infrared (IR) spectra in the range of 4000-400 cm^{-1} were recorded as neat liquids, using KBr cells or KBr pellets (for solid compounds), on a Bio-Rad Excalibur 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]. Mass spectral data were recorded on a Finnigan MAT 8500 mass spectrometer (Germany).

Synthesis

Organotin(IV) complexes

Methyl-, ethyl-, tri-*n*−butyl-, triphenyl, and dibenzyltin(IV) complexes (**1-3**, **5**, **7,** and **8**) were synthesized by heating at reflux for 6-8 h the corresponding diorganotin dichloride (3.04 mmol) or triorganotin chloride (6.08 mmol) with the silver salt of *n*-butylhydrogen phthalate (2.0 g, 6.08 mmol) in 1:2 and 1:1 molar ratios, respectively, in dry chloroform (60 mL), contained in a 250-mL 2-necked round-bottom flask fitted with a water condenser and a magnet bar (Eqs. (1) and (2)). It was placed overnight at room temperature. The silver chloride (AgCl) formed was then filtered off and the solvent was evaporated under reduced pressure.

Di-*n*−butyl- and di-*n*−octyltin(IV) derivatives (**4** and **6**) were prepared by the condensation of *n*-butylhydrogen phthalate (2.0 g, 9.01 mmol) in 2:1 molar ratio by heating at reflux temperature for 8-10 h

with di-*n*-butyl- (1.12 g, 4.51 mmol) and di-*n*-octyltin(IV) oxide (1.63 g, 4.51 mmol), respectively, in toluene (80 mL), using a Dean and Stark apparatus (Eq. (3)). The water formed was removed intervally and the solvent was rotary evaporated.

Results and Discussion

The reactions of R_2SnCl_2 and R_3SnCl with the silver salt of *n*-butylhydrogen phthalate (**AgL**) were carried out in 1:2 and 1:1 molar ratios in dry chloroform, respectively. Di-*n*-butyl- and di-*n*-octyltin(IV) derivatives (**4** and **6**) were synthesized by the reaction of (**HL**) with di-*n*-butyl- and di-*n*-octyltin(IV) oxide in 1:2 molar ratios, respectively, in dry toluene using a Dean and Stark apparatus. The ligand acid, *n*-butylhydrogen phthalate (**HL**), was prepared by refluxing a mixture of phthalic anhydride and 1-butanol (dry and in excess) for 4 h, as given in Scheme 1.[15] The composition of the complexes and nature of bonding were elucidated by spectroscopic methods.

$$R_2SnCl_2 + 2AgL \longrightarrow R_2SnL_2 + 2AgCl \quad \textbf{(1)}$$

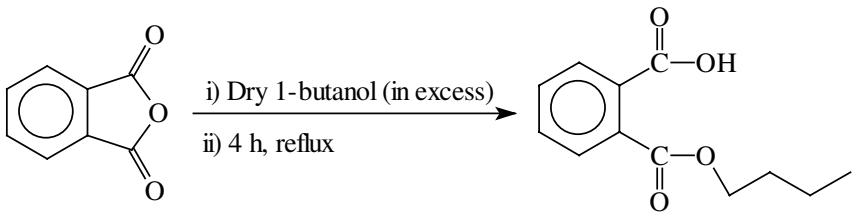
R = Me (**1**), Et (**3**), Bz (**8**)

$$R_3SnCl + AgL \longrightarrow R_3SnL + AgCl \quad \textbf{(2)}$$

R = Me (**2**), *n*-Bu (**5**), Ph (**7**)

$$R_2SnO + 2HL \longrightarrow R_2SnL_2 + H_2O \quad \textbf{(3)}$$

R = *n*-Bu (**4**), *n*-Oct (**6**)



Scheme 1

All the newly synthesized compounds are crystalline solids, excluding dimethyl-, diethyl-, tri-*n*-butyl-, di-*n*-octyl-, and dibenzyltin(IV)-di-*n*-butylphthalate. They are air stable and soluble in all common organic solvents. These compounds were characterized by elemental analysis, IR spectroscopy, multinuclear NMR (^{1}H, ^{13}C, and ^{119}Sn), and mass spectrometry in order to determine their structures and explore other properties. All the investigated complexes were additionally screened for their biological activity and cytotoxicity. The physical data are given in Table 1.

Table 1. Physical data of the synthesized organotin(IV) derivatives of *n*-butylhydrogen phthalate.[a]

Comp. No.	Compound (Formula Weight)	M.P. °C	Yield (%)	%C Calc. (Found)	%H Calc. (Found)
(**1**)	Me_2SnL_2 $C_{26}H_{32}O_8Sn$ (591)	Liquid	80.7	52.79 (52.77)	5.41 (5.47)
(**2**)	Me_3SnL $C_{15}H_{22}O_4Sn$ (385)	118-120	91.0	46.75 (46.77)	5.71 (5.80)
(**3**)	Et_2SnL_2 $C_{28}H_{36}O_8Sn$ (619)	Viscous Liquid	80.0	54.28 (54.30)	5.82 (5.77)
(**4**)	n-Bu_2SnL_2 $C_{32}H_{44}O_8Sn$ (675)	115-117	88.9	56.89 (56.91)	6.52 (6.60)
(**5**)	n-Bu_3SnL $C_{24}H_{40}O_4Sn$ (511)	Liquid	84.8	56.36 (56.29)	7.83 (7.88)
(**6**)	n-Oct_2SnL_2 $C_{40}H_{60}O_8Sn$ (787)	Liquid	78.9	60.99 (60.97)	7.62 (7.58)
(**7**)	Ph_3SnL $C_{30}H_{28}O_4Sn$ (571)	127-129	77.5	63.05 (63.10)	4.90 (4.87)
(**8**)	Bz_2SnL_2 $C_{38}H_{40}O_8Sn$ (743)	Viscous Liquid	70.6	61.37 (61.41)	5.38 (5.40)

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

Infrared Spectra

IR spectra of the investigated compounds, ligand acid, and its silver salt were recorded as KBr pellets or neat liquids in the range of 4000-400 cm^{-1}. Determining the coordinating behavior of the ligand (n-$C_4H_9OCOC_6H_4COO^-$) with the di- and triorganotin(IV) moieties can be facilitated by comparing the IR spectra of the free acid to its silver salt and the synthesized organotin(IV) compounds. The absorption frequencies assigned to ν_{asym}(COO), ν_{sym}(COO), and ν(C=O) for the free ligand acid, its silver salt, and the synthesized compounds are reported together with bands assigned to ν(Sn-C) and ν(Sn-O) in Table 2.[17] The absorption bands in the range of 1730-1719 cm^{-1} can most likely be attributed to the C=O stretching vibration of the ester group of the ligand moiety (n-$C_4H_9OCOC_6H_4COO^-$) and confirms the assessment that there is no participation of the ester group (C=O) in the bond formation with tin atoms. This evidence predicts the conclusion that the sharp absorption band at 1697 cm^{-1} is due to carboxyl, ν(COO), stretching and that the band at 1721 cm^{-1} is the absorption frequency of the ester group, ν(C=O), which contradicts an earlier report.[15] However, this approach is supported by the observation that the ν(C=O) band occurs almost at the same position in the investigated complexes. Moreover, absorption bands in the ranges of 481-456 cm^{-1} and 591-538 cm^{-1}, assigned to Sn-O and Sn-C bonds, respectively, also support the formation of the complexes.[17]

Table 2. Infrared data (cm^{-1}) of organotin(IV) derivatives of *n*-butylhydrogen phthalate.[a]

Comp. No.	ν(COO)		Δν	ν(C=O)	ν(Sn–C)	ν(Sn–O)
	Asym.	Sym.				
(**1**)	1599 s	1379 s	220	1726 s	531 w	474 w
(**2**)	1578 s	1404 s	174	1725 s	549 w	465 m
(**3**)	1593 s	1370 s	223	1723 s	586 w	468 w
(**4**)	1578 s	1377 s	201	1727 s	538 w	457 w
(**5**)	1598 s	1401 m	197	1726 s	591 w	470 w
(**6**)	1593 s	1382 s	211	1730 s	577 w	469 m
(**7**)	1582 s	1406 s	176	1727 s	–	481 w
(**8**)	1597 s	1411 s	186	1719 s	575 m	456 w
HL (**Acid**)	1697 s	1413 s	284	1721 s	–	–
AgL	1608 s	1383 s	225	1724 s	–	–

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

The IR stretching vibration frequencies of the carboxyl groups [(ν_{asym}(COO) and ν_{sym}(COO)] in organotin(IV) carboxylates are important and may help to elucidate the structures and the bonding mode of the ligands.[4–7] When the structure changes to a higher symmetric structure, the ν_{asym}(COO) frequencies shift to a lower and the ν_{sym}(COO) frequencies to a higher symmetric structure,$\nu\nu$ causing the $\Delta\nu$ value to decrease.[4,9,10] Thus, a marked decrease in the $\Delta\nu$ value [$\Delta\nu = \nu_{asym}$(COO-ν_{sym}(COO)] was observed in all the complexes compared to the corresponding free acid and its silver salt. These results suggest that the tin atom in each of the di- and triorganotin(IV) species approaches 6- and 5-coordination, respectively. Referring to the literature,[11] the geometry of the tin atom in the diorganotin(IV) carboxylates is based on skew-trapezoidal bipyramidal geometry (Figure 2 a, b), although triorganotin(IV) carboxylates are known to adopt a variety of motifs in the solid state (Figure 2 c-e).[11,12] However, in the same way,[11] it is likely that the triorganotin(IV) species can form linear polymers, as commonly found for triorganotin(IV) carboxylates, with bidentate ligands leading to *trans*-R_3SnO_2 geometry for tin (Figure 2 e). In conclusion, IR data ($\Delta\nu$) suggest a bidentate coordination of the COO group to tin atoms for carboxylate ligands in the solid state.

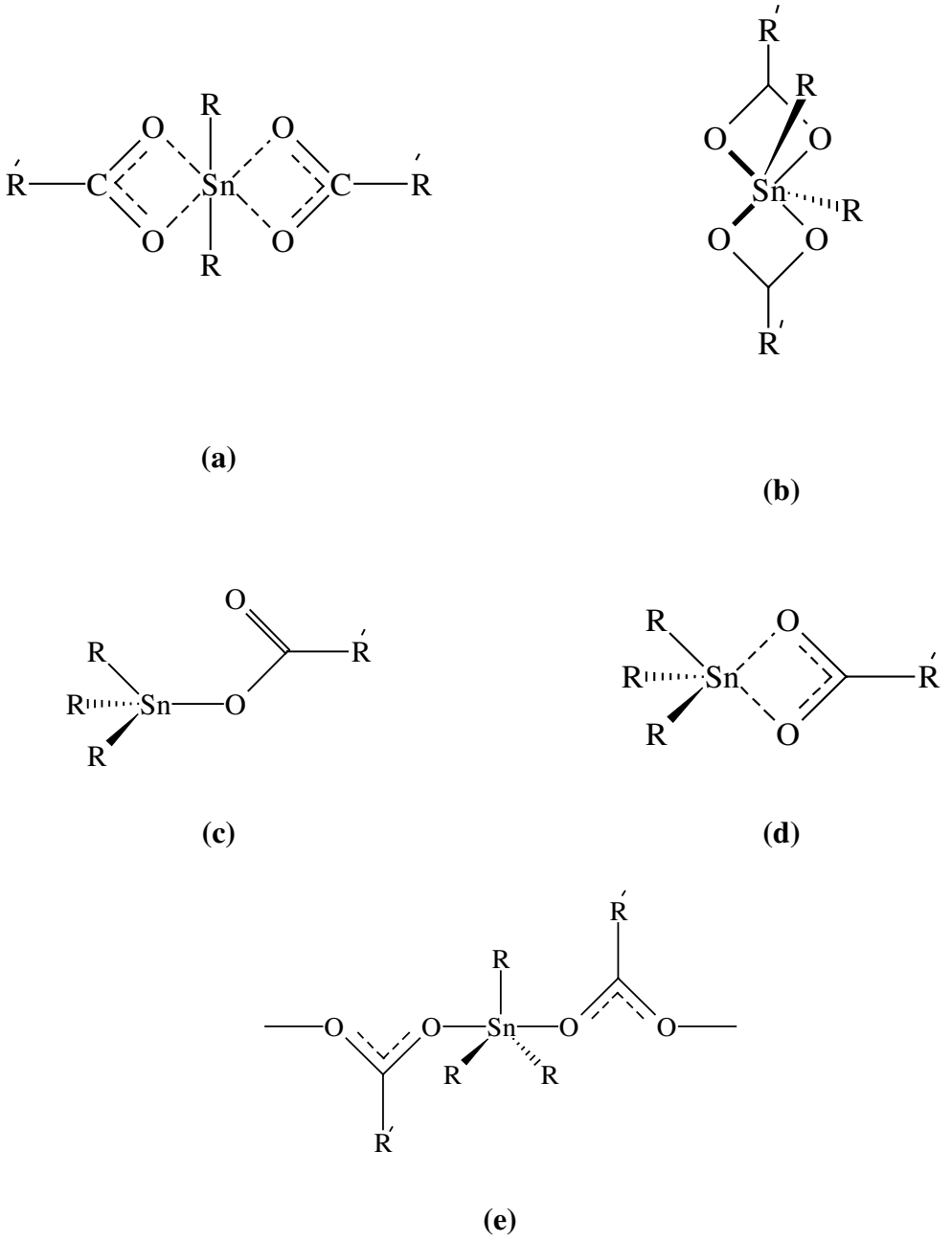


Figure 2. Proposed structures (a) for diorganotin(IV) derivatives (b) and for triorganotin(IV) carboxylates (c-e).

Multinuclear NMR

^{1}H-NMR data

^{1}H-NMR spectra for the synthesized compounds and free acids were recorded in $CDCl_3$ solution and the data are given in Table 3.

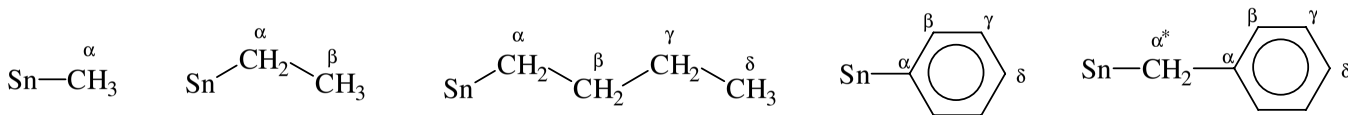
Table 3. ^{1}H NMR data of organotin(IV) derivatives of n-butylhydrogen phthalate.a[a,b,c]

^{1}H No.	(**HL**) Acid	(**1**) Me_2SnL_2	(**2**) Me_3SnL	(**3**) Et_2SnL_2	(**4**) *n*-Bu_2SnL_2	(**5**) *n*-Bu_3SnL	(**6**) *n*-Oct_2SnL_2	(**7**) Ph_3SnL	(**8**) Bz_2SnL_2
4	7.56-7.60 (m)	7.48-7.55 (m)	7.46-7.51 (m)	7.47-7.50 (d, 6.85	7.50-7.56 (m)	7.45-7.52 (m)	7.38-7.44 (m)	7.50-7.58 (m)	4.59-7.66 (m)
5	7.40-7.51 (m)	7.30-7.35 (m)	7.34-7.41 (m)	7.35-7.42 (m)	7.28-7.35 (m)	7.28-7.32 (m)	7.32-7.34 (m)	7.36-7.42 (m)	7.41-7.51 (m)
6	7.40-7.51 (m)	7.30-7.35 (m)	7.34-7.41 (m)	7.35-7.42 (m)	7.41-7.47 (m)	7.28-7.32 (m)	7.32-7.34 (m)	7.36-7.42 (m)	7.41-7.51 (m)
7	7.76-7.80 (m)	7.66-7.69 (m)	7.66-7.71 (m)	7.48 (d, 6.6)	7.67-7.72 (m)	7.65-7.71 (m)	7.74 (bs)	7.82-7.85 (m)	7.77 (d, 6.6)
9	4.23 (t, 6.6)	4.09 (t, 8.0)	4.18 (t, 6.7)	4.18 (t, 6.6)	4.15 (t, 6.6)	4.17 (t, 8.1)	4.20 (t, 6.5)	3.56 (t, 7.0)	4.26 (t, 6.5)
10	1.55-1.67 (m)	1.54-1.76 (m)	1.55-1.64 (m)	1.50-1.61 (m)	1.66-1.79 (m)	1.54-1.56 (m)	1.55-1.61 (m)	1.36-1.49 (m)	1.61-1.69 (m)
11	1.25-1.40 (m)	1.03-1.29 (m)	1.24-1.42 (m)	1.22-1.34 (m)	1.25-1.34 (m)	1.23-1.26 (m)	1.21-1.29 (m)	1.10-1.19 (m)	1.22-1.40 (m)
12	0.82 (t, 7.3)	0.77 (t, 7.2)	0.85 (t, 7.3)	0.77 (t, 7.3)	0.76 (t, 6.7)	0.78 (t, 7.9)	0.79 (t, 7.2)	0.95 (t, 7.6)	0.86 (t, 7.3)
α	–	1.13 (s, 74.1)	0.54 (s, 56.8, 58.6)	1.70 (q, 7.8)	1.53-1.60 (m)	1.54-1.56 (m)	1.75-1.91 (m)	–	–
β	–	–	–	1.26 (t, 7.8)	1.46-1.52 (m)	1.23-1.26 (m)	1.75-1.91 (m)	7.27-7.33 (m)	7.17-7.35 (m)
γ	–	–	–	–	1.12-1.22 (m)	1.23-1.26 (m)	–	7.27-7.33 (m)	7.17-7.35 (m)
δ	–	–	–	–	0.79 (t, 6.6)	0.83 (t, 8.7)	–	6.77-7.11 (m)	7.01-7.13 (m)
γ-γ′	–	–	–	–	–	–	1.10 (bs)	–	–
δ′	–	–	–	–	–	–	0.73 (t, 6.0)	–	–
α*	–	–	–	–	–	–	–	–	3.57 (s)

[a]Chemical shifts (δ) in ppm. $^{2}J[^{117/119}Sn,^{1}H]$, $^{2}J[^{119}Sn,^{1}H]$, and $^{3}J[^{1}H, ^{1}H]$, in Hz, are listed in parentheses. Multiplicity is given as s = singlet, bs = broad signal, d = doublet, t = triplet, q = quartet, and m = multiplet.

[b]Numbering is according to Figure 1.

[c]



^{1}H-NMR data of the *n*-butylhydrogen phthalate (**HL**) were assigned according to an earlier report.[18] The CH_2 (9) and CH_3 (12) protons of the ligand moiety resonate as a triplet at 4.23 and 0.82 ppm, with $^3J[^1H, ^1H]$ = 6.6 and 7.3 Hz, while CH_2 (10) and CH_2 (11) are multiplets in the range of 1.55-1.67 and 1.25-1.40 ppm, respectively. The analogous pattern of the ^{1}H signals at rather similar positions for the ligand was observed in almost all the investigated compounds.

The CH_3 protons of dimethyl- and trimethyltin(IV) derivatives (**1** and **2**) appear as sharp singlets at 1.13 and 0.54 ppm, both with well-defined satellites, $^2J[^{119}Sn, ^1H]$ = 74.1 and 58.6 Hz. The α-CH_2 protons of the diethyltin(IV) compound resonate as a quartet at 1.70 ppm and have a well-resolved coupling constant, $^3J[^1H, ^1H]$ = 7.8 Hz, whereas β-CH_3 protons resonate as a triplet at 1.26 ppm with $^3J[^1H,^1H]$ = 7.8 Hz. The protons of *n*-butyltin and of the phenyl moieties of the triphenyltin(IV) derivatives show a complex pattern and were assigned according to the literature;[18,19] however, δ-CH_3 protons of both di-*n*-butyl- and tri-*n*-butyltin(IV) moieties of compounds **4** and **5** appear as a triplet at 0.79 and 0.83 ppm, with $^3J[^1H,^1H]$ = 6.6 and 8.7 Hz, respectively, while the α-CH_2, β-CH_2 and γ-CH_2 protons appear as multiplets.

Similarly, the α-CH_2 and β-CH_2 protons of the *n*-octyltin(IV) derivative **6** give a multiplet at 1.75-1.91 ppm and γ-CH_2 to $\gamma\prime$-CH_2 protons appear as a broad signal at 1.10 ppm, which are consistent with those calculated by the incremental method.[20] However, the $\delta\prime$-CH_3 protons resonate as a triplet at 0.73 ppm with $^3J[^1H,^1H]$ = 6.0 Hz.

In the dibenzyltin(IV) complex a complex pattern is also observed due to the aromatic protons of the ligand and phenyl groups, whereas the α*-CH_2 protons of the benzyl moiety show a singlet at 3.57 ppm.

Various methods have been applied to calculate the C-Sn-C bond angles in solution based on $^2J[^{119}Sn,^1H]$ coupling constants as given in Table 5.[21−23] The coupling constants and the calculated C-Sn-C bond angles support a 5-coordinated geometry for the diorganotin and a 4-coordinated one for the triorganotin(IV) carboxylates in non-coordinating solvents.[22,23]

^{13}C-NMR data

^{13}C-NMR data taken from the $CDCl_3$ solution of the ligand acid (**HL**) and its di- and triorganotin(IV) derivatives are given in Table 4.

The ^{13}C-NMR spectral data for the R groups attached to the tin atom, where R = Me, Et, *n*-Bu, *n*-Oct, Ph, and Bz, were assigned by comparison to related analogues as model compounds.[18,5,24−26] The assignment of the ^{13}C resonances associated with the carboxylate ligand is based on comparison to the results obtained from the incremental methods[27] and earlier reports.[15]

The magnitudes for $^nJ[^{119}Sn,^{13}C]$ coupling were also observed and are given in Table 4. The coupling constants, $^nJ[^{119}Sn,^{13}C]$, are important parameters for the determination of C-Sn-C bond angles (Table 5) and structure characterization of organotin(IV) compounds. For triorganotin compounds, the magnitudes of $^1J[^{119}Sn,^{13}C]$ coupling suggest the typical tetrahedral geometry around the tin atom in solution,[18,28,29] while diorganotin dicarboxylates in non-coordinating solvents may acquire penta-coordinated geometry around the tin atom.[30,31]

Table 4. ^{13}C NMR data of organotin(IV) derivatives of n-butylhydrogen phthalate.[a,b,c]

^{13}C No.	(**HL**) Acid	(**1**) Me_2SnL_2	(**2**) Me_3SnL	(**3**) Et_2SnL_2	(**4**) *n*-Bu_2SnL_2	(**5**) *n*-Bu_3SnL	(**6**) *n*-Oct_2SnL_2	(**7**) Ph_3SnL	(**8**) Bz_2SnL_2
1	176.66	172.22	172.75	175.27	177.11	172.79	176.73	175.64	173.32
2	130.75	130.24	133.80	130.91	129.13	133.91	131.63	130.18	131.00
3	134.41	131.29	133.93	134.55	132.40	134.26	134.75	134.13	134.20
4	129.53	128.44	128.94	129.12	128.0	128.71	128.88	129.49	129.58
5	133.03	133.15	131.34	132.69	133.75	131.15	132.19	133.95	132.97
6	131.57	132.18	131.24	131.38	130.23	130.96	131.03	132.27	131.71
7	130.53	130.46	130.28	130.66	129.65	130.29	130.58	130.93	130.59
8	169.08	167.13	169.59	169.23	168.18	169.45	168.89	168.38	169.21
9	66.68	65.24	66.21	66.56	65.31	65.96	66.18	65.65	66.78
10	31.21	31.68	31.42	31.25	30.49	31.42	31.39	31.16	31.26
11	19.97	21.83	20.06	19.94	19.08	20.00	19.97	19.68	20.02
12	14.48	13.73	14.61	14.49	13.56	14.41	14.48	14.54	14.57
α	–	6.82 (536.6)	-1.41 (382.7, 394.4)	19.94 (517.6, 544.1)	25.53 (517.6, 543.7)	17.49 (345.5, 365.4)	26.69 (476.7)	138.07	136.12 (78.5)
β	–	–	–	9.90 (41.9)	26.64 (21.3)	28.62 (21.3)	25.42 (31.0)	136.72	131.88
γ	–		–	–	26.36 (69.9)	27.87 (65.4)	34.21 (92.9)	129.17	129.68
δ	–	–	–	–	13.48	14.41	29.97	128.43	126.00
α′	–	–	–	–	–	–	29.90	–	–
β′	–	–	–	–	–	–	32.61	–	–
γ′	–	–	–	–	–	–	23.40	–	–
δ′	–	–	–	–	–	–	14.82	–	–
α*	–	–	–	–	–	–	–	–	39.56 (604.3)
δ-^{119}Sn	–	-290.29	141.73	-135.79	-140.72	110.48	-141.50	-109.75	-227.72

[a]Chemical shifts (δ) in ppm. $^nJ[^{117/119}Sn,^{13}C]$ and $^nJ[^{119}Sn,^{13}C]$, in Hz, are listed in parentheses.

[b]Numbering is according to Figure 1.

[c]See footnotes of Table 3 for α, β, γ, δ, α′, β′, γ′, δ′, α*.

Table 5. C-Sn-C angles (°) based on NMR parameters of selected organotin(IV) derivatives of *n*-butylhydrogen phthalate.

Comp. No.	Compound	$^{1}J[^{119}Sn, ^{13}C]$ (Hz)	$^{2}J[^{119}Sn, ^{1}H]$ (Hz)	Angle (°)	
				^{1}J	^{2}J
(**1**)	Me_2SnL_2	536.6	74.1	123.8	124.0
(**2**)	Me_3SnL	394.4	58.6	111.4	111.3
(**3**)	Et_2SnL_2	544.1	–	129.1	–
(**5**)	*n*-Bu_3SnL	365.4	–	111.3	–
(**6**)	*n*-Oct_2SnL_2	476.7	–	122.4	–

^{119}Sn-NMR data

The ^{119}Sn-NMR spectra were recorded as $CDCl_3$ solution, a non-coordinating solvent, and the data obtained are reported in Table 4. The ^{119}Sn chemical shift values obtained for the triorganotin(IV) derivatives lie in the range expected for a tetrahedral geometry, whereas the diorganotin(IV) compounds indicate a higher coordination number.[31]

To obtain some more information about the possible coordination geometries in solution, the $^{1}J[^{119}Sn, ^{13}C]$ and $^{2}J[^{119}Sn,^{1}H]$ coupling constants were used for the enumeration of C-Sn-C bond angles, using methods described in the literature,[21−23] and are summarized in Table 5. For the tri-*n*-butyltin(IV) derivative, the $^{1}J[^{119}Sn,^{13}C]$ value was 365.4 Hz, and by the use of the Holeček and Lycka equation[32,33] established for tetra-, penta-, and hexa-coordinated butyltin(IV) compounds, the C-Sn-C bond angle –value of 111.3° was calculated, which corresponds to a quasi-tetrahedral geometry in $CDCl_3$ solution. The geometric data calculated, as just described, are consistent with tetrahedral geometries for the triorganotin(IV) species, i.e. monomers in solution. For the diorganotin(IV) species, for which earlier results indicate 5-coordination, the calculated C-Sn-C angles are consistent with skew-trapezoidal bipyramidal geometries, with the lower apparent coordination number arising from the asymmetric coordination mode of the carboxylate ligands.

Mass spectrometric data

The molecular ion peak was not observed for either the di- or triorganotin(IV) complexes. In all of the investigated compounds (**1**-**8**), the base peak is due to the ligand moiety, $[OCH(C_6H_4)COO]^+$ or $[C_4H_9OCH_2OH]^+$, with m/z = 149 and 104, respectively,.

In diorganotin(IV) derivatives, the primary fragmentation is due to the loss of the ligand (R″COO), while the secondary fragmentation occurs through elimination of hydrogen (H) or CO_2, or simply involves loss of the ligand (R″COO). Tertiary fragmentation occurs via cleavage of the ligand or the ligand moiety (R′) and gives the fragments $[RSnR'']^+$ and $[R_2Sn]^+$, respectively, which is followed by elimination of R or R″, ending at $[Sn]^+$ (m/z = 120).

In triorganotin(IV) carboxylates, the primary fragmentation is due to the loss of the R′COO group, followed by successive cleavage of R groups, ending at $[Sn]^+$. A second fragmentation pathway is characterized by the loss of the R group in primary fragmentation, followed by liberation of CO_2. The secondary and tertiary fragmentations involve the loss of R or R′, and end at $[Sn]^+$. This route is much more probable than the first one. The most common fragments, together with their m/z ratios and relative abundances, are given in Tables 6 and 7.

Table 6. Fragmentation pattern and relative abundance of diorganotin(IV) derivatives of *n*−butylhydrogen phthalate.

Fragment Ions	(**1**) [m/z(%)] R=CH_3	(**3**) [m/z(%)] R=C_2H_5	(**4**) [m/z(%)] R=*n*-C_4H_9	(**6**) [m/z(%)] R=*n*-C_8H_{17}	(**8**) [m/z(%)] R=$C_6H_5CH_2$
$[R_2Sn(OCO(C_6H_4)COOC_4H_9)_2]^+$	–	–	–	–	–
$[RSn(OCO(C_6H_4)COOC_4H_9)_2]^+$	–	591(6)	619(57)	675(4)	–
$[R_2SnOCO(C_6H_4)COOC_4H_9]^+$	–	–	399(30)	455(58)	567(5)
$[R(R')Sn(OCO(C_6H_4)COOC_4H_9]^+$	–	355(1)	411(2)	523(3)	–
$[SnC_6H_4COOC_4H_9]^+$	297(4)	297(5)	297(49)	297(4)	297(6)
$[R_2Sn]^+$	150(47)	178(3)	234(12)	346(11)	302(2)
$[RSnR']^+$	149(80)	177(13)	233(31)	345(8)	301(4)
$[RSn]^+$	135(13)	149(13)	177(53)	233(24)	211(6)
$[SnR']^+$	134(3)	148(16)	176(16)	232(8)	210(4)
$[Sn]^+$	120(6)	120(4)	120(22)	120(4)	120(5)
$[C_4H_9OOC(C_6H_4)COOH]^+$	222(2)	222(1)	222(5)	–	–
$[C_4H_9OOC(C_6H_4)COO]^+$	221(3)	221(7)	221(9)	–	221(2)
$[OCH(C_6H_4)COO]^+$	149(100)	149(13)	149(98)	149(39)	149(100)
$[C_4H_9OCH_2OH]^+$	104(40)	104(100)	104(100)	104(100)	104(84)
$[C_6H_5CH_2]^+$	–	–	–	–	91(89)
$[CH_3(CH_2)_2CH_2]^+$	57(83)	57(6)	57(95)	57(51)	57(88)
$[C_4H_2]^+$	50(11)	50(20)	50(85)	–	50(80)

[a]R′ = CH_2, C_2H_5, *n*-C_4H_9, *n*-C_8H_{17}, C_7H_7.

Table 7. Fragmentation pattern and relative abundance of triorganotin(IV) derivatives of $n-$butylhydrogen phthalate.

Fragment Ions	(**2**) [m/z(%)] R=CH_3	(**5**) [m/z(%)] R=n-C_4H_9	(**7**) [m/z(%)] R=C_6H_5
$[R_3SnOCO(C_6H_4)COOC_4H_9]^+$	386(n.o)	512(n.o)	572(n.o)
$[R_2SnOCO(C_6H_4)COOC_4H_9]^+$	371(67)	455(83)	495(1)
$[R_2SnC_6H_4COOC_4H_9]^+$	327(5)	–	451(5)
$[RSnC_6H_4COOC_4H_9]^+$	312(12)	–	–
$[SnC_6H_4COOC_4H_9]^+$	297(7)	297(6)	297(2)
$[R_3Sn]^+$	165(74)	291(3)	351(3)
$[R_2Sn]^+$	150(61)	234(18)	274(1)
$[RSn]^+$	135(63)	177(50)	197(15)
$[Sn]^+$	120(43)	120(7)	120(9)
$[C_4H_9OOC(C_6H_4)COOH]^+$	222(45)	222(3)	–
$[C_4H_9OOC(C_6H_4)COO]^+$	221(59)	221(4)	–
$[OCH(C_6H_4)COO]^+$	149(100)	149(100)	149(100)
$[C_6H_5]^+$	–	–	77(47)
$[CH_3(CH_2)_2CH_2]^+$	57(28)	57(43)	57(50)
$[C_4H_2]^+$	50(30)	–	50(60)

Biological activity

Biological screening tests for the synthesized complexes were carried out against various bacteria and fungi by the agar well diffusion and tube diffusion methods, respectively[34,35]. The results are given in Tables 8 and 9.

The results show that tri-n-butyltin(IV) is potent against *Bacillus subtilis* and *Staphlococcus aureus*, and that it exhibits moderate activity against *Pseudomonas aeruginosa*. The other investigated compounds showed either low or no activity, including the ligand acid (Table 8). It is well established that tri-n-butyltin compounds are significantly more biologically active than other classes of alkyltin species.[36]

Table 8. Antibacterial activity data of organotin(IV) derivatives of n-butylhydrogen phthalate.[a,b]

Name of Bacterium	Clinical Implication	Zone of Inhibition (mm)									Ref. Drug
		(**1**)	(**2**)	(**3**)	(**4**)	(**5**)	(**6**)	(**7**)	(**8**)	(**HL**)	
Escherichia coli	Infection of wounds, urinary tract and dysentery	–	–	–	–	–	–	–	–	–	30
Bacillus subtilis	Food poisoning	9	–	–	13	22	9	15	–	–	31
Shigella flexenari	Blood diarrhea with fever and severe prostration	–	–	10	–	–	–	–	–	–	33
Staphlococcus aureus	Food poisoning, scaled skin syndrome, endocarditis	–	–	–	15	20	–	9	–	–	43
Pseudomonas aeruginosa	Infection of wounds, eyes, septicemia	11	–	–	14	11	11	11	12	–	25
Salmonella typhi	Typhoid fever, localized infection	–	–	10	–	–	11	11	–	–	41

[a]In vitro, agar well diffusion method, concentration: 1 mg/mL of DMSO.

[b]Reference drug, imipenum.

Table 9. Antifungal activity data of organotin(IV) derivatives of n-butylhydrogen phthalate.[a,b]

Name of Fungus	Percent Inhibition									Standard Drug	Percent Inhibition	MIC µg/mL
	(**1**)	(**2**)	(**3**)	(**4**)	(**5**)	(**6**)	(**7**)	(**8**)	(**HL**)			
Trichophyton longifusus	25	80	20	–	85	–	70	–	–	Miconazole	100	70
Candida albicans	–	75	25	–	100	–	–	–	80	Miconazole	100	110.8
Aspergillus flavus	19	70	30	60	90	40	60	50	90	Amphotericin B	100	20
Microsporum canis	22	90	10	60	95	75	–	90	–	Miconazole	100	98.4
Fusarium solani	–	65	25	55	90	–	65	–	60	Miconazole	100	73.25
Candida glaberata	–	–	10	–	–	–	–	–	–	Miconazole	100	110.8

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

The antifungal activity of di- and triorganotin(IV) derivatives is given in Table 9, which shows that the triorganotin(IV) carboxylates are more active than the diorganotin(IV) derivatives.[18,36] Furthermore, tri−*n*−butyltin(IV) complex showed the same activity as the reference drug (miconazole) against *Candida albicans*. The ligand acid also exhibits good activity, though only against *Candida albicans*. Thus, activity of the compounds against various fungi was observed to decrease in the following order: **5** > **2** > **7** > **3** > **4** > **8** ∼ **6** > **1** (Table 9).

The synthesized compounds were also evaluated for their cytotoxicity to determine LD_{50} data using the brine-shrimp bioassay lethality method[37] (Table 10). It was observed that compounds **2**, **4**, and **7** showed positive lethality, with LD_{50} values of 0.7151, 129.7894, and 83.6901 μg/mL, respectively. Thus, compound **2** was the most toxic and compound **4** was the least toxic of all the synthesized organotin(IV) derivatives. The other compounds, **1**, **3**, **5**, **6**, **8**, and **HL**, did not exhibit cytotoxicity.

Table 10. Cytotoxicity data of organotin(IV) derivatives of *n*-butylhydrogen-phthalate.[a,b,c]

Comp.	(**1**)	(**2**)	(**3**)	(**4**)	(**5**)	(**6**)	(**7**)	(**8**)	(**HL**)
LD_{50}	–	0.7151	–	129.7894	–	–	83.6901	–	–

[a]Against brine-shrimp, *Artemia salina* (in vitro).
[b]No cytotoxicity for compounds **1**, **2**, **5**, **6**, **8**, and **HL**.
[c]Reference drug: etoposide.

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