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ORIGINAL PAPER

Synthesis, spectral characterization and X-ray crystal structure of biologically active organotin(IV) 3-[(3′,5′-dimethylphenylamido)]propanoates

F. A. Shah · S. Ali · S. Shahzadi · C. Rizzoli · S. Ahmad

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Abstract A new ligand was prepared by reacting 3,5-dimethylaniline with succinic anhydride in glacial acetic acid at room temperature. A series of organotin(IV) carboxylates were prepared by reacting the ligand with R_2SnCl_2/R_3SnCl (R = Me, Bu, Ph, Oct) in 1:2/1:1 molar ratio. The synthesized complexes were characterized by elemental analyses, FT-IR, multinuclear magnetic resonance (^1H and ^{13}C) and mass spectrometry. The structures of the ligand (**HL**) and complex (**5**) were determined by single crystal X-ray diffraction analysis. FT-IR data shows that the coordination takes place through both carboxylate oxygen atoms. NMR data confirm the tetrahedral geometry in solution. In the crystal structure of ligand (**HL**), centrosymmetrically related molecules are linked into dimers by N–H…O hydrogen bonding interactions, while in complex (**5**) coordination around the tin atom is trigonal bipyramidal, with the carbon atoms of the methyl groups occupying the equatorial plane and the O atoms of symmetry-related ligands at the apices. Organotin(IV) complexes were also screened for their antibacterial and antifungal activities, and the results suggested that the synthesized complexes are better antimicrobial agents as compared to the free ligand.

F. A. Shah · S. Ali (✉) · S. Ahmad
Department of Chemistry, Quaid-i-Azam University, Islamabad 45320, Pakistan
e-mail: drsa54@yahoo.com

S. Shahzadi (✉)
Department of Chemistry, GC University, Faisalabad, Pakistan
e-mail: sairashahzadi@hotmail.com

C. Rizzoli
Dipartimento di Chimica Generale ed Inorganica, Chimica Analitica, Chimica Fisica, Parco Area delle Scienze 17/A, 43124 Parma, Italy

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Introduction

Among organotin(IV) compounds, organotin carboxylates are highly important and have been receiving more attention in recent years. Organotin(IV) carboxylates form an important class of compounds which find many applications in chemistry and biology, such as catalysts, stabilizers, biocides, antifouling agents and wood preservatives [1]. Mostly, organotins are species specific and a general pattern revealed that their toxicity is a function of the organic group attached to the tin atom.

The biological investigations of organotin carboxylates have attracted considerable attention owing to their significant cytotoxic effect and relatively high antitumor activity [2, 3]. It may yield new leads for the development of antitumor drugs, which can display another spectrum of antitumor activity. For instance, they show non-cross resistance with platinum drugs and possess less toxicity than platinum compounds [4].

The structural diversity of organotin carboxylates is well recognized and a wide variety of coordination geometries have been reported [5, 6]. It is generally believed that a combination of steric and electronic factors determine the specific structure adopted by a particular organotin carboxylate [7]. This is supported by the observation of monomeric, dimeric, tetrameric, oligomeric ladder, cyclic and drum structure [5–7]. Therefore, synthesis of new organotin(IV) carboxylates with different structural features is beneficial in the development of pharmaceutical organotin and in other properties and applications. In view of the various applications of organotin carboxylates and as

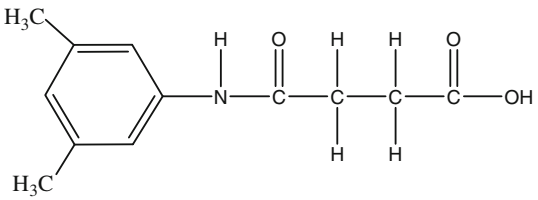


Fig. 1 3-[(3′,5′-Dimethylphenylamido)]propanoic acid (**HL**)

a continuation of our studies of biologically active organotin(IV) derivatives [8, 9], we synthesized some novel organotin(IV) derivatives of 3-[(3′,5′-dimethylphenylamido)] propanoic acid (Fig. 1). These complexes were characterized by elemental analysis, infrared, NMR (^{1}H, ^{13}C), mass spectrometry and X-ray diffraction studies. Their biological activity data has also been investigated.

Experimental

Materials and instrumentation

3,5-Dimethylaniline, succinic anhydride, organotin(IV) chlorides and dioctyltin(IV) oxide were purchased from Aldrich Chemical (USA). Glacial acetic acid, acetone, toluene, diethyl ether and chloroform were obtained from Merck (Germany). Acetone, toluene, diethyl ether and chloroform were purified before use by reported procedures [10, 11].

Melting points of the synthesized compounds were recorded by the electrothermal melting point apparatus MP-D Mitamura Riken Kogyo (Japan) and are uncorrected. Elemental analysis was carried out using a Leco CHNS-932 analyzer. The IR spectra of the synthesized complexes were obtained using KBr pallets on a Bio-Rad Excaliber FT-IR spectrophotometer. Mass spectral data was collected on a Finnigan MAT-311A spectrometer. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker ARX 300 MHz-X Spectrometer at room temperature operating at 300 and 75.3 MHz, respectively. X-ray single crystal diffraction data for the ligand (**HL**) was collected on a Siemens AED diffractometer using graphite monochromated Cu–Kα radiation, while that for complex (**5**) was collected on a Bruker APEX-II CCD diffractometer using graphite monochromated Mo–Kα radiation.

Synthesis

*Synthesis of 3-[(3′, 5′-dimethylphenylamido)]propanoic acid (**HL**)*

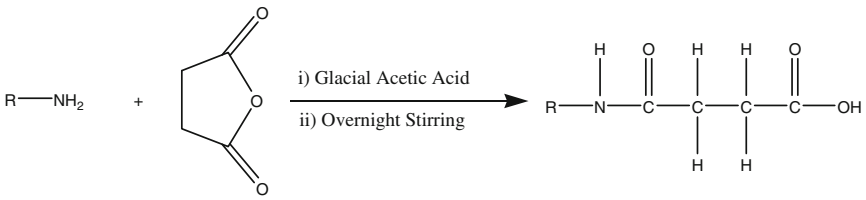
A solution of 3,5-dimethylaniline (1 mmol) in glacial acetic acid was added to a solution of succinic anhydride (1 mmol) in glacial acetic acid followed by continuous overnight stirring at room temperature. The resulting white solid product was subsequently filtered and washed with cold distilled water (400 mL). The product thus obtained was recrystallized from acetone (Scheme 1).

General procedure for the synthesis of complexes

Procedure (a)

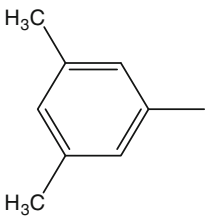
3-[(3′,5′-Dimethylphenylamido)]propanoic acid (4.6 mmol, 1 g) was suspended in dry toluene (100 mL) and treated with Et_3N (4.6 mmol, 0.63 mL). The mixture was refluxed for 2–3 h and to this solution diorganotin dichloride (2.3 mmol) or triorganotin chloride (4.6 mmol) was added as solid (or liquid in case of Bu_3SnCl) with constant stirring and then refluxed for 8 h. The reaction mixture

Scheme 1



Where

R =



$R_2SnCl_2 + 2Et_3NHL \xrightarrow[\text{ii) Reflux for 8-10 hrs}]{\text{i) Toluene}} R_2SnL_2 + 2Et_3NHCl$

$R_3SnCl + Et_3NHL \xrightarrow[\text{ii) Reflux for 8-10 hrs}]{\text{i) Toluene}} R_3SnL + Et_3NHCl$

$Oct_2SnO + 2HL \xrightarrow[\text{ii) Reflux for 8-10 hrs}]{\text{i) Toluene}} Oct_2SnL_2 + H_2O$

R	Me_2	Bu_2	Ph_2	Oct_2
Comp. No	(**1**)	(**2**)	(**3**)	(**4**)
R	Me_3	Bu_3	Ph_3	-
Comp. No	(**5**)	(**6**)	(**7**)	-

Scheme 2

containing Et_3NHCl was filtered off leaving the organotin(IV) derivative in the filtrate. Solvent was removed by rotary evaporator and the precipitate was recrystallized from a chloroform/methanol (4:1 v/v) mixture (Eqs. 2 and 3 in Scheme 2).

Procedure (b)

3-[(3′,5′-Dimethylphenylamido)]propanoic acid (4.6 mmol, 1 g) was suspended in dry toluene (100 mL). To this solution, Oct_2SnO (2.3 mmol, 0.8 g) was added as solid with constant stirring and the mixture refluxed for 8–10 h. Water formed during the reaction was removed via Dean and Stark trap. The solvent was evaporated through rotary apparatus and the product obtained was recrystallized by a chloroform:*n*-hexane (4:1 v/v) mixture (Eq. 4 in Scheme 2).

Results and discussion

All complexes (**1**)–(**7**) are solid, generally with sharp melting points, which are stable in light and dry air. They are soluble in polar solvents. Physical data are reported in Table 1.

IR spectra

Characteristic FT-IR vibrations ligand (**HL**) and its organotin(IV) complexes are summarized in Table 2. The complexation of tin with the ligand through the –COO group is confirmed by the absence of a broad –OH band in the region of 2,650 cm^{-1}. The values of different vibrational frequencies were assigned to different bonds by comparing the spectra of ligand and complexes. The –NH group does not participate via intra- or intermolecular modes of interactions, as confirmed by the presence of characteristic strong band at 3,300–3,340 cm^{-1}, which does not show any shift after complexation [12]. The description of the coordination modes was based on the difference between $(COO)_{sym}$ and $(COO)_{asym}$ and the corresponding band position [13].

In all the synthesized complexes, Δv is <200 cm^{-1} which confirms the bidentate nature of the ligand. In the spectra of the compounds, new bands confirming the complexation [14] appear in the region 465–423 cm^{-1} [for (**1**), (**2**), (**4**)–(**6**)] and 540–512 [for (**1**)–(**7**)] cm^{-1} and were assigned to Sn–O and Sn–C bonds, respectively. For the phenyl derivatives (**3**) and (**7**), the Sn–C band appears at 244 and 253 cm^{-1}, respectively.

Table 1 Physical data of 3-[(3′,5′-dimethylphenylamido)]propanoic acid and its organotin(IV) complexes

Comp. no.	Mol. formula	m.p. (°C)	% yield	Elemental analysis % calculated (found)		
				C	H	N
(**HL**)	$C_{12}H_{15}NO_3$	195–196	74	65.16	6.78	6.33
				(65.12)	(6.74)	(6.29)
(**1**)	$C_{26}H_{34}N_2O_6Sn$	163–165	70	52.97	5.77	4.75
				(52.93)	(5.74)	(4.73)
(**2**)	$C_{32}H_{46}N_2O_6Sn$	140–142	67	57.05	6.83	4.16
				(57.08)	(6.81)	(4.20)
(**3**)	$C_{36}H_{38}N_2O_6Sn$	128–129	60	60.58	5.32	3.92
				(60.55)	(5.29)	(2.95)
(**4**)	$C_{40}H_{62}N_2O_6Sn$	145–146	69	61.14	7.89	3.56
				(61.10)	(7.85)	(3.53)
(**5**)	$C_{15}H_{23}NO_3Sn$	98–100	71	46.87	5.89	3.64
				(46.84)	(5.92)	(3.67)
(**6**)	$C_{24}H_{41}NO_3Sn$	121–122	68	56.47	8.03	2.74
				(56.43)	(8.05)	(2.70)
(**7**)	$C_{30}H_{29}NO_3Sn$	210–211	66	63.15	5.08	2.45
				(63.14)	(5.03)	(2.47)

^{1}H NMR spectra

^{1}H NMR spectra for the investigated compounds were obtained in deuterated chloroform at room temperature. Different protons were assigned on the basis of their multiplicity and intensity patterns. The integration of spectra was in accordance with the number of protons proposed for each molecular fragment. The ^{1}H NMR spectra of the complexes exhibit the useful features and the observed chemical shifts are reported in Table 3. In the complexes, the COOH resonance of the ligand at 10.4 ppm is absent which suggests the deprotonation of the

Table 2 Assignment of characteristic FT-IR vibrations (cm^{-1}) of 3-[(3′,5′-dimethylphenylamido)]propanoic acid and its organotin(IV) complexes

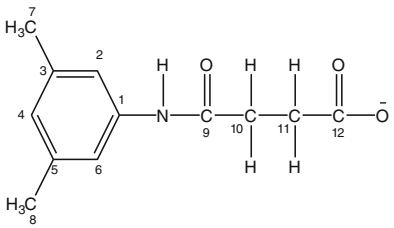
Comp. no.	IR peak (cm^{-1})							
	ν_{OH}	ν_{NH}	$\nu_{C=O}$	ν_{COO}		$\Delta\nu$	ν_{Sn-C}	ν_{Sn-O}
				Asymm	Symm			
(**HL**)	3,416	3,326	1,748	1,532	1,310	222	–	–
(**1**)	–	3,317	1,746	1,550	1,432	118	526	486
(**2**)	–	3,334	1,740	1,560	1,444	116	540	460
(**3**)	–	3,320	1,735	1,554	1,416	138	244	454
(**4**)	–	3,300	1,754	1,568	1,429	139	513	445
(**5**)	–	3,302	1,736	1,570	1,433	164	512	465
(**6**)	–	3,337	1,745	1,565	1,450	115	534	423
(**7**)	–	3,340	1,736	1,575	1,456	119	253	474

Table 3 ^{1}H NMR data of 3-[(3′,5′-dimethylphenylamido)]propanoic acid and its organotin(IV) complexes

Proton no.	Chemical shift (ppm)							
	(**HL**)	(**1**)	(**2**)	(**3**)	(**4**)	(**5**)	(**6**)	(**7**)
2/6	6.65s	6.65s	6.65s	6.68s	6.65s	6.64s	6.63s	6.66s
4	7.23s	7.20s	7.22s	7.25s	7.21s	7.2s	7.21s	7.21s
7/8	2.22s	2.21s	2.20s	2.25s	2.21s	2.21s	2.20s	2.22s
10	7.52–7.54d [6.0]	7.20–7.23d [6.0]	7.20–7.23d [6.0]	7.43–7.45d [6.0]	7.20–7.22d [6.0]	7.45–7.43d [6.0]	7.46–7.49d [6.0]	7.48–7.50d [6.0]
11	7.53–7.55d [6.0]	7.50–7.53d [6.0]	7.50–7.53d [6.0]	7.50–7.52d [6.0]	7.50–7.48d [6.0]	7.52–7.50d [6.0]	7.51–7.49d [6.0]	7.51–7.53d [6.0]
NH	9.8s	9.7s	9.7s	9.7s	9.7s	9.7s	9.6s	9.8s

[a] Compound (**1**) Sn–CH_3, 0.95s ^{2}J[96]; Compound (**2**) Sn–$CH_2CH_2CH_2CH_3$, 0.85–1.20m, 0.23t (7.2); Compound (**3**) Sn–C_6H_5, 7.40–7.92m; Compound (**4**) Sn–$CH_2CH_2CH_2CH_2$ $CH_2CH_2CH_2CH_3$, 0.82–1.18m; Compound (**5**) Sn–CH_3, 0.83s ^{2}J[82]; Compound (**6**) Sn–$CH_2CH_2CH_2CH_3$, 0.82–1.39m, 0.23t (7.2); Compound (**7**) Sn–C_6H_5, 6.84–7.08m

[b] Chemical shifts (δ) in ppm $^{2}J[^{119}Sn,^{1}H]$ and $^{3}J(^{1}H,^{1}H)$ in Hz are listed in square brackets and parenthesis, respectively. Multiplicity is given as: *s* singlet, *d* doublet, *t* triplet, *m* multiplet



carboxylic acid by the organotin(IV) moiety, as charge donation from the COO^{-} donor to the tin atom decreases the electron density and results in deshielding of the ligand protons. The NH group does not show any significant shift upon complexation indicating that the NH group does not contribute to the coordination of the tin metal atom.

In the case of dimethyl (**1**) and trimethyl (**5**) organotin(IV) derivatives, the methyl protons gave a characteristic singlet at 0.95 and 0.83 ppm, respectively. In the *n*-butyl derivatives, a triplet for the terminal methyl group of the butyl chain at 0.85 ppm for the dibutyltin (**2**) and at 0.82 ppm for the tributyl (**5**) derivatives. For other protons of the butyl chain in (**2**) and (**5**), the multiplets were observed (Table 3).

The $^{n}J(^{119}Sn,\ ^{1}H)$ for dimethyl and trimethyltin(IV) derivatives have approximately the same value, confirming

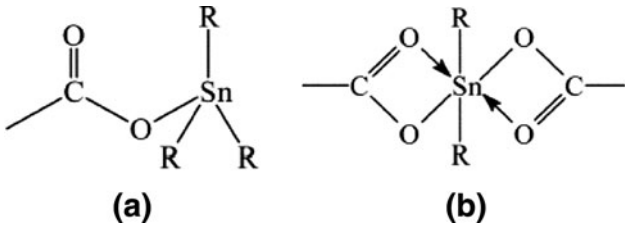


Fig. 2 Suggested structure of the complexes

the tetrahedral coordination environment in solution, i.e., carboxylate groups act as monodentate in solution. The aromatic proton resonances were assigned by comparing the experimental chemical shifts with those calculated by the incremental method [15]. In triorganotin carboxylates, $^{2}J[^{119}Sn–^{1}H]$ for triorganotin compounds suggest a tetrahedral geometry (Fig. 2a) of the tin atom.

Unlike the triorganotin carboxylates in solution, the geometry of diorganotin dicarboxylates cannot be defined with certainty because of dynamic processes involving different modes of carboxylate oxygen coordination to the tin atom [16]. However, in the solid state, the tin atom is mostly hexa-coordinated in such systems (Fig. 2b) [17].

^{13}C NMR spectra

According to ^{13}C NMR data, the involvement of the carboxylate group in bonding to Sn is confirmed by the resonance of the carboxylic carbon in all the compounds, which exhibits a lower shift after coordination as compared to the ligand, suggesting the coordination of the ligand through a carboxylic oxygen to the organotin(IV) moiety. The remaining carbons do not shift significantly after complexation. The spectral data is given in Table 4.

The carbon of phenyl and alkyl groups attached to tin are observed at almost similar positions in the experimental data with respect to that calculated from the incremental method [17] and reported in the literature [18, 19].

The tributyltin and trimethyltin complexes exhibit $^{n}J(^{13}C–^{117/119}Sn)$ coupling satellites in the range 349–396 Hz in $CDCl_3$ solution, suggesting that the tin atom is four-coordinated in solution [20, 21].

Mass spectrometry

Mass spectra for the investigated compounds were recorded at 70 eV for all di- and triorganotin(IV) derivatives. The molecular ion peaks of very low intensity are observed

Table 4 ^{13}C NMR data of 3-[(3′,5′-dimethylphenylamido)]propanoic acid and its organotin(IV) complexes

Carbon	(**HL**)	(**1**)	(**2**)	(**3**)	(**4**)	(**5**)	(**6**)	(**7**)
1	138.03	138.03	138.03	138.17	138.50	138.91	138.80	138.03
2/6	117.18	117.08	117.38	117.12	117.92	117.19	117.20	117.18
3/5	139.60	139.67	139.69	139.80	139.56	139.67	139.80	139.61
4	124.91	124.84	124.18	124.97	124.18	124.95	124.99	124.92
7/8	21.53	21.85	21.55	21.63	21.61	21.58	21.62	21.59
9	170.39	170.69	170.43	170.90	170.47	170.27	170.97	170.39
10	29.28	29.26	29.29	29.75	29.02	29.49	29.14	29.98
11	31.48	31.38	31.26	31.04	31.62	31.09	31.64	31.49
12	174.34	177.4	176.25	176.28	177.50	176.39	176.38	177.43

Chemical shifts (δ) in ppm: $^{n}J[^{119}Sn, ^{13}C]$ in hertz is listed in parenthesis

[a] Compound (**1**): Sn–CH_3, (C-α) 29.6; Compound (**2**): Sn–$CH_2CH_2CH_2CH_3$, (C-α) 29.5, (C-β) 27.4, (C-γ) 26.2, (C-δ) 13.9; Compound (**3**): Sn–C_6H_5, (C-α) 137.9 ^{1}J[635], (C-β) 135.0, (C-γ) 136.0, (C-δ) 129.2; Compound (**4**): Sn–$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$, (C-$\alpha$) 33.5, (C-$\beta$) 31.7, (C-$\gamma$) 30.1, (C-$\delta$) 29.3, (C-$\alpha$*) 29.1, (C-$\beta$*) 28.8, (C-$\gamma$*) 22.6, (C-$\delta$*) 14.40; Compound (**5**): Sn–CH_3, (C-α) 2.7 ^{1}J[396]; Compound (**6**): Sn–$CH_2CH_2CH_2CH_3$, (C-α) 31.3 [349], (C-β) 27.4 ^{2}J[21], (C-γ) 28.7 ^{3}J[63], (C-δ) 14.2; Compound (**7**): Sn–C_6H_5, (C-α) 138.0 ^{1}J[640], (C-β) 133.0 ^{2}J[49.0], (C-γ) 130.0, (C-δ) 125.1

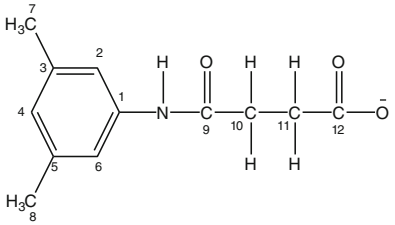


Table 5 Mass spectral data of 3-[(3′,5′-dimethylphenylamido)]propanoic acid and its organotin(IV) complexes

Fragment ion	(**1**) *m/z* (%)	(**2**) *m/z* (%)	(**3**) *m/z* (%)	(**4**) *m/z* (%)	(**5**) *m/z* (%)	(**6**) *m/z* (%)	(**7**) *m/z* (%)
[SnL]	340 (6)	340 (40)	340 (10)	340 (16)	340 (13)	340 (20)	340 (32)
$[C_{11}H_{14}ONSn]^+$	296 (8)	296 (12)	296 (18)	296 (18)	296 (11)	296 (19)	296 (13)
$[R_2Sn]^+$	150 (8)	234 (8)	274 (27)	345 (27)	150 (95)	234 (28)	274 (31)
$[Sn]^+$	120 (10)	120 (8)	120 (25)	120 (12)	120 (25)	120 (30)	120 (10)
$[C_8H_{10}N]^+$	120 (25)	120 (19)	120 (38)	120 (38)	120 (70)	120 (14)	120 (14)
$[C_{12}H_{14}O_2N]^+$	204 (100)	204 (100)	204 (100)	204 (100)	204 (100)	204 (59)	204 (59)
$[C_{10}H_{12}ON]^+$	162 (43)	162 (29)	162 (22)	162 (53)	162 (42)	162 (24)	162 (24)
$[C_8H_9]^+$	105 (12)	105 (13)	105 (12)	105 (6)	105 (28)	105 (30)	105 (30)
$[C_6H_5]^+$	77 (6)	77 (9)	77 (18)	77 (10)	77 (30)	77 (22)	77 (22)
$[C_4H_9]^+$	57 (6)	57 (33)	57 (6)	57 (19)	57 (19)	57 (98)	57 (98)

in few complexes [22]. In di- and triorganotin(IV) derivatives, a rather similar pattern of fragmentation is observed.

For the synthesized complexes, the fragmentation takes place by the loss of alkyl or aryl groups followed by the elimination of CO_2. The second route of fragmentation is the loss of CO_2 and other neutral species which ultimately gives $[C_6H_5^+]$ in the last step. Another possible route is disintegration of the ligand and stepwise elimination of R groups to Sn^+ or SnH^+ as a residue. Some common and different peaks (with *m/z* and % abundance) which were observed in di- and triorganotin(IV) derivatives are reported in Table 5.

Table 6 Crystal data and structure refinement parameters for (**HL**) and compound (**5**)

	(**HL**)	(**5**)
Emp. formula	$C_{12}H_{15}NO_3$	$C_{15}H_{23}NO_3Sn$
Formula weight	221.25	384.03
Crystal system	Monoclinic	Monoclinic
Space group	*P* 2_1/n	*P* 2_1/c
a (Å)	14.355 (2)	17.168 (8)
b (Å)	5.0170 (10)	10.925 (6)
c (Å)	17.858 (4)	9.623 (7)
α (°)	90.00	90.00
β (°)	111.980 (15)	101.48 (5)
γ (°)	90.00	90.00
V (Å^3)	1,192.6 (4)	1,768.8 (18)
Z	4	4
Crystal size (mm)	0.28 × 0.22 × 0.18	0.14 × 0.10 × 0.08
T (K)	295 (2)	295 (2)
λ (Å)	1.54178	0.71073
Total reflections	2,332	3,498
Independent reflections (all)	2,263	3,285
Final *R* indices [$I > 2\sigma(I)$]	$R1 = 0.039$	$R1 = 0.054$
	w$R2 = 0.089$	w$R2 = 0.125$
R indices (all data)	$R1 = 0.047$	$R1 = 0.092$
	w$R2 = 0.097$	w$R2 = 0.135$
Goodness-of-fit	1.038	1.004
θ range for data collection (°)	3.4–70.1	3.1–25.5

Crystal structures

Crystal data and structure refinement parameters for ligand (**HL**) and complex (**5**) are given in Table 6, and selected bond angles and lengths are listed in Table 7.

Table 7 Selected bond lengths (Å) and bond angles (°) for (**HL**) and compound (**5**)

(**HL**)			
N1–C4	1.340(12)	O3–C4	1.239(11)
N1–C5	1.411(14)	C9–C12	1.513(17)
C7–C11	1.508(18)	O2–C1	1.324(12)
C4–N1–C5	129.78(9)	O3–C4–N1	122.24(10)
C6–C7–C11	119.64(12)	O3–C4–C3	122.62(9)
(**5**)			
Sn1–C15	2.109(8)	Sn1–O2	2.358(5)
Sn1–C14	2.112(8)	O1–C1	1.274(8)
Sn1–C13	2.120(7)	O2–C1	1.246(8)
Sn1–O1	2.203(4)	O3–C4	1.209(8)
C15–Sn1–C14	126.3(3)	C15–Sn1–O2	86.2(3)
C15–Sn1–C13	116.1(3)	C14–Sn1–O2	88.1(3)
C14–Sn1–C13	116.9(3)	C13–Sn1–O2	87.4(2)
C15–Sn1–O1	97.0(3)	O1–Sn1–O2	176.1(18)
C14–Sn1–O1	91.8(3)	C1–O1–Sn1	115.2(4)
C13–Sn1–O1	89.2(2)	O2–C1–O1	121.8(6)

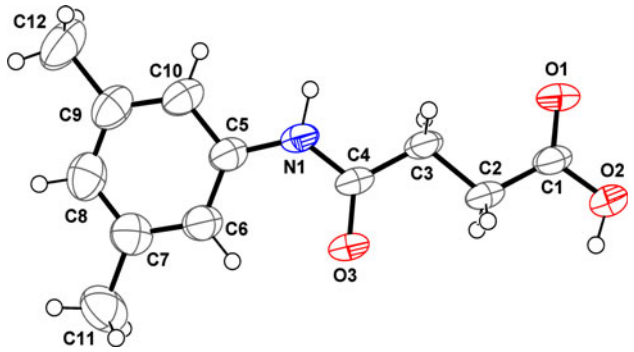


Fig. 3 ORTEP drawing of 3-[(3′,5′-dimethylphenylamido)]propanoic acid (**HL**) showing 50 % displacement ellipsoids

Crystal structures of ligand (**HL**)

In the crystal structure of the free ligand (**HL**), all bond lengths and angles are unexceptional and in agreement with those found in the literature for related compounds [23]. The carbonyl O1 and O3 oxygen atoms are in *trans* position with respect to the C1–C4 butyl group (Fig. 3). The $C(O_2)C_2C(O)N$ fragment is approximately planar (maximum deviation 0.0547(10) Å for atom C3) and is tilted by 8.12(4)° to the benzene ring. In the crystal structure, centrosymmetrically related molecules are linked into dimers by N–H…O hydrogen bonding interactions [N1–H1N, 0.946(15) Å; H1N…O1^{i}, 1.940(15) Å; N1…O1^{i}, 2.879(1) Å; N1–H1N…O1^{i}, 172.0(14)°; symmetry code: (i) $2 - x, -y, -z$]. The dimers are further connected into layers parallel to the (101) plane by intermolecular O–H…O hydrogen bonds [O2–H1O, 0.911(14) Å; H1O…O3^{ii}, 1.738(14) Å; O2…O3^{ii}, 2.628(1) Å; O2–H1O…O3^{ii}, 164.9(14)°; symmetry code: (ii) $5/2 - x, -1/2 + y, 1/2 - z$]. A packing diagram of (**HL**) approximately viewed along the *b* axis is given in Fig. 4.

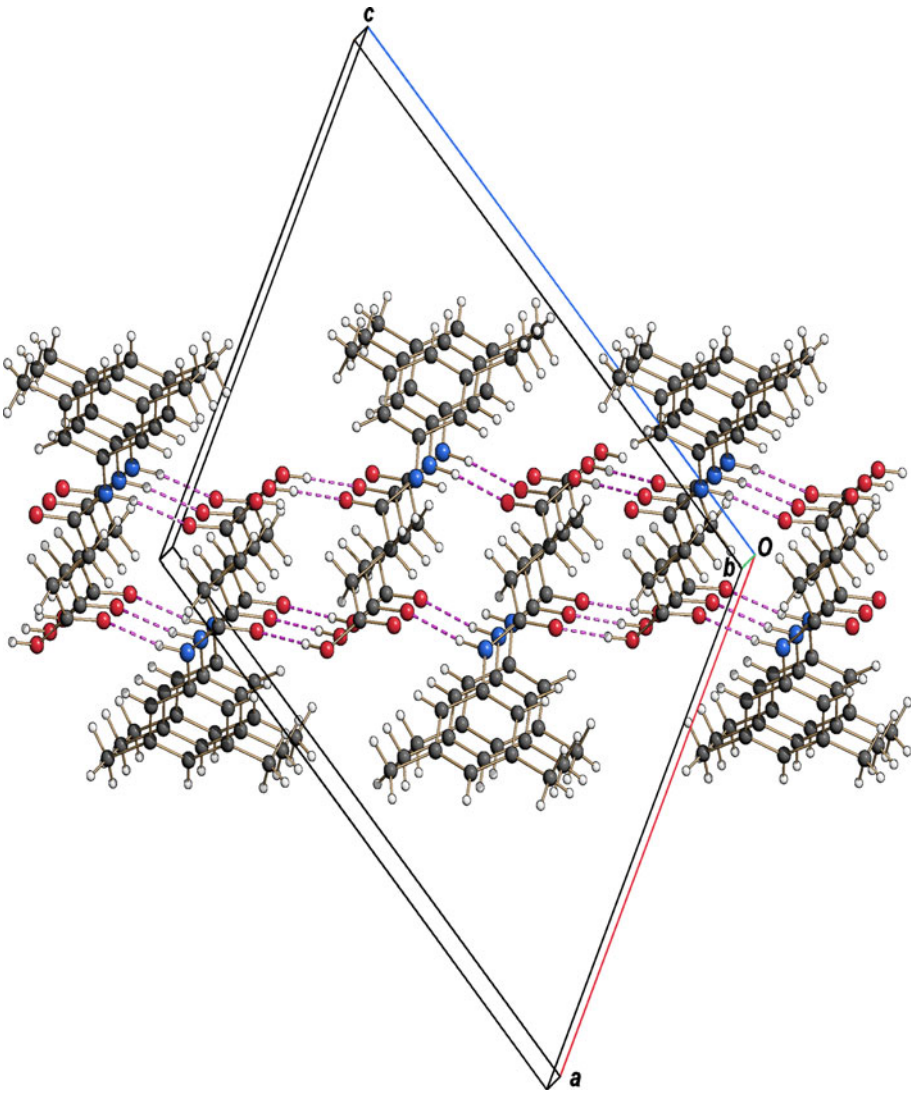


Fig. 4 Packing diagram of (**HL**) approximately viewed along the *b* axis. Intermolecular hydrogen bonds are shown as *dashed lines*

Crystal structure of complex (5)

Coordination around the metal is trigonal bipyramidal, with the carbon atoms of the methyl groups occupying the equatorial plane and the O1 and O2 atoms of symmetry-related ligands at the apices (Fig. 5). In complex (**5**), the carboxylic oxygen atoms of the ligand bridge adjacent tin metal atoms to form zigzag polymeric chains parallel to the crystallographic *c* axis (Fig. 6). According to the literature [24], trigonality around the Sn atom can be described by the index $\tau = (\beta - \alpha)/60$, where β is the largest of the basal angles and α is the second largest angle. The calculated τ value is 0.16, which indicates a slightly distorted trigonal bipyramidal arrangement. The sum of the equatorial C–Sn–C angles is 359.3°. The Sn–C [2.109(8) − 2.120(7) Å] and Sn–O bond lengths [2.109(8) − 2.358(5) Å] are in agreement with those reported for related triorganotin(IV) carboxylates [25, 26]. With respect to the free ligand (**HL**), the planarity of the $C(O_2)C_2C(O)N$ fragment is lost, as indicated by the dihedral angle of 23.6(6)° formed by the plane of the carboxylic group with the mean plane through the C2–C4/N1/O3 atoms. The dihedral angle between this plane and the benzene ring is 11.6(3)°. In the crystal structure (Fig. 6), interchain N–H…O hydrogen bonds link the polymers into layers parallel to the (100) plane [N1–H2N, 0.914(8) Å; H2N…O3^{iii}, 2.18(8) Å; N1…O3^{iii}, 3.088(8) Å; N1–H2 N…O3^{iii}, 170(6)°; symmetry code: (iii) *x*, −1/2 − *y*, −1/2 + *z*].

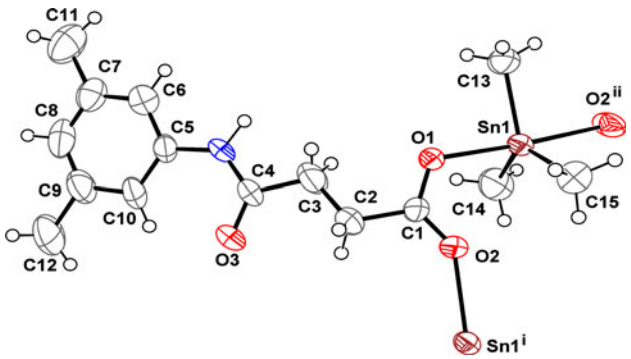


Fig. 5 ORTEP drawing of complex (**5**) showing 50 % displacement ellipsoids [symmetry codes: (i) *x*, 1/2 − *y*, 1/2 + *z*; (ii) *x*, ½ −*y*, −1/2 + *z*)]

Antibacterial activity

The antibacterial activity of the compounds was studied by using agar well diffusion method [27]. Bacterial strains, e.g., *E. coli*, *B. subtilis*, *S. flexneri* and *P. aeruginosa* were selected to study the antibacterial activity of the ligand (**HL**) and complexes (**1**)–(**7**) (concentration of 1 mg/mL of DMSO). Imipenem was used as a standard drug and the zone of inhibition was measured in millimeter. Antibacterial data obtained from the experiment are presented in Table 8. The data indicated that the ligand showed no activity against tested bacterial strains. Complex (**5**) showed significant activity against *E. coli*, *B. subtilis* and *S. flexneri* among the synthesized complexes, possibly due to its lipophilicity. This balance of hydrophobic and hydrophilic forces helped the complex (**2**) in the penetration through cell membrane and perturbation on growth, respiration and membrane physical properties [28]. The data obtained in this study, which are consistent with those reported in literature [29, 30], seems to suggest a strong link between the biological activity and the alkyl groups attached to the tin metal rather than ligand, whose role is merely to transport the organotin(IV) species to the site of the action where it is released by hydrolysis.

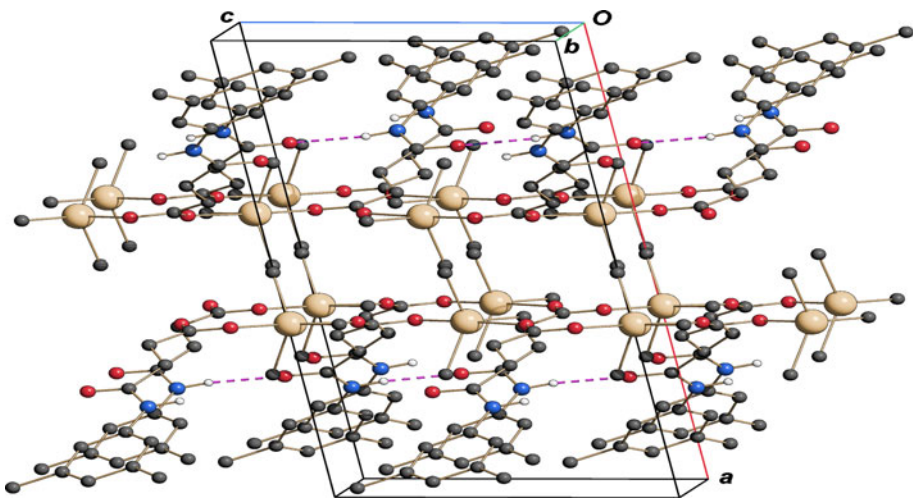


Fig. 6 Packing diagram of complex (**5**) approximately viewed along the *b* axis. Interchain hydrogen bonds are shown as *dashed lines*. Hydrogen atoms not involved in hydrogen bonding are omitted for clarity

Table 8 Antibacterial activity data of 3-[(3′,5′-dimethylphenylamido)]propanoic acid and its organotin(IV) complexes

Compound	Zone of inhibition (mm)			
	E. coli	*B. subtilis*	*S. flexneri*	*P. aeruginosa*
(**HL**)	0	0	0	0
(**1**)	10	11	0	0
(**2**)	17	19	17	12
(**3**)	0	16	0	10
(**4**)	11	14	10	14
(**5**)	12	0	12	14
(**6**)	0	11	9	16
(**7**)	15	10	13	0
Imipenem	30	37	36	32

Concentration: 1 mg/mL of DMSO

Antifungal activity

The in vitro antifungal properties of the (**HL**) and its synthesized complexes were evaluated against representative fungi using a literature method [27]. The percent growth inhibition (%) of the synthesized ligand and the compounds are listed in Table 9. The ligand showed no potency against the selected strains of fungus. The higher activity of tin(lV) complexes as compared to the ligand owed to the chelate formation, in which the ligand coordinated to the central tin atom through the carboxylate oxygen. The tin metal atom caused apoptosis which increased fungitoxic action. Data obtained showed that triorganotin(IV) carboxylates were more active than diorganotin(IV) carboxylates [31]. This situation is in sharp contrast to the earlier assessment that increase in the number of R groups on the tin(IV) atom enhances its biological activity. This anomalous behavior can be explained on the basis of the anionic ligand group that generally plays a secondary role. In some cases, however, it may also play important role to enhance the biocidal activity of organotin(IV) compounds [32].

Table 9 Antifungal activity data of 3-[(3′,5′-dimethylphenylamido)]propanoic acid and its organotin(IV) complexes

Compound	Inhibition (%)			
	T. longifusus	*A. flavus*	*C. glabrata*	*C. albicans*
(**HL**)	0	0	0	0
(**1**)	73	52	50	43
(**2**)	81	71	73	76
(**3**)	53	59	56	51
(**4**)	31	78	71	70
(**5**)	0	0	0	11
(**6**)	32	12	51	70
(**7**)	0	0	12	0
Standard drug	Miconazole	Amphotericin B	Miconazole	Miconazole
MIC (μg/ml)	70.0	20.0	110.8	110.8
DMSO	–	–	–	–

Concentration: 200 μg/mL of DMSO

Percent inhibition (standard drug) = 100

MIC minimum inhibitory concentration

Conclusion

Di- and triorganotin(IV) complexes of 3-[(3′,5′-dimethylphenylamido)]propanoic acid have been synthesized and characterized. Detailed studies of the reported complexes indicate that triorganotin compounds exhibit a trigonal bipyramidal geometry which is also confirmed by the crystal structure of complex (**5**), while a six-coordination geometry is preferred by diorganotin compounds in the solid state. The structure of ligand acid (**HL**) was also determined by XRD. Multinuclear NMR data shows that the synthesized complexes exhibit tetrahedral geometry in solution.

Supplementary material

CCDC nos. 859832 and 859833 contains the supplementary crystallographic data for (**HL**) complexes (**5**), respectively. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via http://www.ccdc.cam.ac.uk/data_request/cif.

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