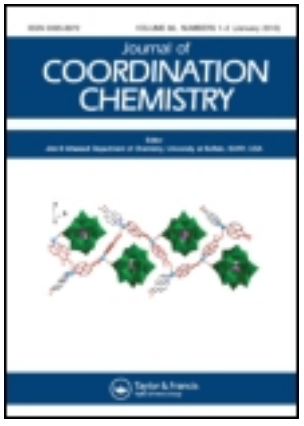

Journal of Coordination Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gcoo20

Structural and biological studies of new monomeric, tetrameric, and polymeric organotin(IV) esters of 3-(benzo[d][1,3]dioxol-4-yl)propanoic acid

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Accepted author version posted online: 29 Jan 2013.Published online: 15 Mar 2013.

To cite this article: Mukhtiar Hussain, Zia-Ur-Rehman, Muhammad Sheeraz Ahmad, Muhammad Altaf, Helen Stoeckli-Evans & Saqib Ali (2013) Structural and biological studies of new monomeric, tetrameric, and polymeric organotin(IV) esters of 3-(benzo[d][1,3]dioxol-4-yl)propanoic acid, Journal of Coordination Chemistry, 66:5, 868-860, DOI: 10.1080/00958972.2013.770845

To link to this article: http://dx.doi.org/10.1080/00958972.2013.770845

Journal of Coordination Chemistry
Vol. 66, No. 5, 10 March 2013, 868–880

Structural and biological studies of new monomeric, trameric, and polymeric organotin(IV) esters of 3-(benzo[d][1,3]dioxol-4-yl)propanoic acid

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(*Received 16 June 2012; in final form 29 November 2012*)

Six new monomeric, trameric, and polymeric organotin(IV) derivatives of sodium 3-(benzo[d][1,3]dioxol-4-yl)propanoate (NaL) have been synthesized and characterized by various analytical techniques. These compounds show different structural behavior in solution and solid state as confirmed by NMR and X-ray single-crystal analysis. Antimicrobial and antitumor activities are mainly governed by diffusion, lipophilicity, geometry, and steric factors. The high antitumor and antifungal activities of some of these organotin compounds demand further investigations to commercialize them as new tin-based drugs.

Keywords: Organotin(IV) carboxylates; Spectroscopic studies; X-ray crystallography; Biological screening

1. Introduction

Di- and triorganotin(IV) derivatives of substituted carboxylic acids have been an active area of research [1–6] because of their interesting structural motifs ranging from discrete monomeric structures to supramolecular assemblies [7] and antimicrobial [8] and antitumor activities [9–11]. The diverse structural motifs can be attributed to the ambidentate character of carboxylates. Steric and electronic features of organic substituents on tin and/or the carboxylate impart significant influence on the structures of tin carboxylates [12]. Among organotin(IV) carboxylates, bis[dicarboxylatotetraorgano-distannoxanes] with dimeric ladder-type structures $[R'OO(R_2Sn)–O–(SnR_2)OOCR']_2$ [13] have good efficacy in biological and catalytic applications [14–16]. Structural data of distannoxanes reveal varying intramolecular or intermolecular Sn–O coordinate bond distances. Although these linkages

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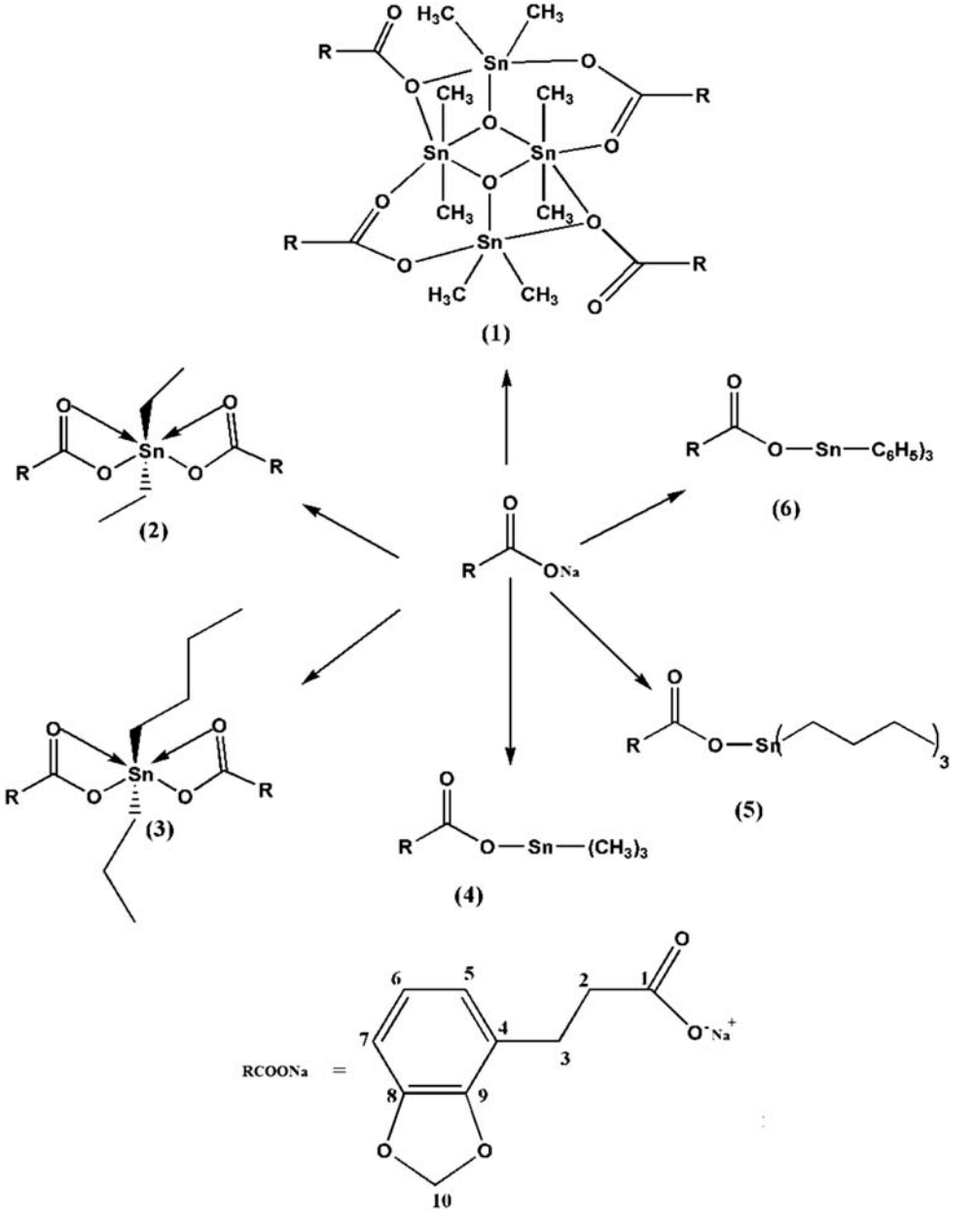
Journal of Coordination Chemistry
ISSN 0095-8972 print/ISSN 1029-0389 online
http://dx.doi.org/10.1080/00958972.2013.770845

have been regarded as weak or even non-bonding interactions [17], it is difficult to ignore their contribution to geometry of Sn (endocyclic) and Sn (exocyclic) atoms.

In connection with exploring the structural and biological properties of organotin(IV) derivatives and our interest in structural chemistry of these complexes [18], we report new organotin(IV) derivatives of 3-(benzo[d][1,3]dioxol-4-yl)propanoic acid (HL) (scheme 1). The acid has been selected due to the presence of methylenedioxy moiety, which it is



Scheme 1. Schematic diagram for synthesis of **1**–**6** along with ligand numbering scheme.

reported to have the potential to form stronger intermolecular interactions with DNA. Complex 3 has been prepared by azeotropic removal of H_2O from the reaction (in toluene) of di-*n*-butyltin oxide with HL in a molar ratio of 1 : 2. For other complexes, NaL has been used with organotin(IV) chlorides as discussed in the experimental section. All complexes have been investigated by elemental analysis, vibrational, ^1H, ^{13}C, and ^{119}Sn NMR spectroscopies. Solid-state structures of 1 and 4 have been elucidated by X-ray crystallography.

2. Experimental

Reagents were purchased from commercial sources (Aldrich, USA) and used without purification. Solvents were dried prior to use by standard procedures. Melting points were determined with a Gallenkemp (UK) apparatus and were uncorrected. Elemental analyses were carried out using a Leco CHNS-932 analyzer USA. Infrared spectra were recorded as KBr pellets on a Bio-Rad Excalibur FT-IR, model FTS 300 MX spectrophotometer, from 4000 to 400 cm^{-1}. ^1H, ^{13}C, and ^{119}Sn NMR spectra in solution were recorded on Bruker ARX 300, 400 and 500 MHz FT-NMR spectrometers, respectively. Chemical shifts are reported in ppm relative to external references, tetramethylsilane for ^1H, ^{13}C NMR, and tetramethyltin for ^{119}Sn chemical shifts. All X-ray crystallographic data were collected on a Stoe Imaging Plate Diffractometer System. The structures were solved by direct methods and refined by full-matrix least squares based on F^2 using SHELXS-97 and SHELXL-97 [19]. All data were collected with graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å) at 173 K. A semi-empirical multi-scan absorption correction was applied for **1** using the MULscanABS routine in PLATON [20]. For **4**, an empirical absorption correction was used from the DIFscanABS routine in PLATON. The C-bound hydrogens were included in calculated positions using SHELXL default parameters and refined as riding. Crystallographic data and refinement details are given in table 1. Selected bond distances and angles are given in table 2.

2.1. *Sodium salt of 3-(benzo[d][1,3]dioxol-4-yl)propanoic acid (NaL)*

NaL was freshly prepared with 2% sodium amalgam and 3-(2,3-methylenedioxyphenyl) acrylic acid (prepared in lab) in 2.5 N sodium hydroxide solution as reported earlier [21,22]. M.p. 80–82 °C. Yield: 81%.

IR (cm^{-1}): $\nu_{O\text{-}H}$ 3120–2628, $\nu_{asym(COO)}$ 1669, $\nu_{sym(COO)}$ 1422, $\Delta\nu$ ($\nu_{asym(COO)} - \nu_{sym(COO)}$) 247, O–$CH_2$–O 929. ^1H NMR δ (ppm): 10.48 (s, H_1), 6.79 (d8.0, H_7), 6.67 (t7.8, H_6), 6.31 (d8.0, H_5), 5.95 (s, H_{10}), 2.94 (t8.0, H_3), 2.60 (t8.0, H_2). ^{13}C NMR δ (ppm): 168.1 (C_1), 148.2 (C_8), 147.4 (C_9), 122.8 (C_4), 121.5 (C_5), 121.0 (C_6), 108.0 (C_7), 102.2 (C_{10}), 29.4 (C_2), 26.2 (C_3).

2.2. *Bis[3-(benzo[d][1,3]dioxol-4-yl)propanato] tetramethyldistannoxane] (1)*

Mixture of dimethyltin(IV) chloride (0.26 g, 1.16 mmol) and NaL (0.5 g, 2.3 mmol) was refluxed in dry tolouene (100 mL) for 6–7 h with constant stirring. The by-product, NaCl, was removed by filtration, and clear filtrate was evaporated under reduced pressure to obtain a solid product (scheme 1). Yield: (83%), M.p. 178–180 °C, Elemental Anal. Calcd (Found) for $C_{48}H_{60}O_{18}Sn_4$: C, 41.2(40.7); H, 4.3(3.9). IR (cm^{-1}): $\nu_{asym(COO)}$ 1638, 1610,

Table 1. Crystal data and structure refinement parameters for **1** and **4**.

Empirical formula	$C_{48}H_{60}O_{18}Sn_4$ (**1**)	$C_{13}H_{18}O_4Sn$ (**4**)
Formula weight	1399.72	356.96
Crystal system	Triclinic	Monoclinic
Space group	*P*-1	$P2_1/c$
a (Å)	10.0998(9)	11.7664(13)
b (Å)	11.4676(10)	9.8220(7)
c (Å)	13.1851(12)	12.6797(14)
α (°)	89.221(11)	90.00
β (°)	69.558(10)	91.945(9)
γ (°)	70.020(10)	90.00
V (Å^3)	135.1(2)	1464.5(3)
Z	1	4
Meausure. temp.	173 K	173 K
Density calc. mg m^{-3}	1.741	1.619
Crystal size (mm^3)	0.30 × 0.30 × 0.12	0.40 × 0.25 × 0.25
F(000)	692	712
Theta range for data collection (°)	2.31–25.91	1.73–29.19
μ (MoKα, mm^{-1})	1.919	1.748
Absorption T_{min}, T_{max}	0.439, 0.755	0.243, 0.702
Measured reflections	10,505	12,328
Unique reflections, R_{int}	4841, 0.053	3935, 0.047
Observed reflections [$I > 2\sigma(I)$]	4079	3518
R_1, wR_2 (obs. data)	0.0428, 0.1151	0.0276, 0.0736
R_1, wR_2 (all data)	0.0533, 0.1658	0.0320, 0.0758
Goodness-of-fit	1.216	1.043
$\Delta\rho$ max., min. (e Å^{-3})	1.542, −3.366 Near Sn atoms	0.519, −1.483

$\nu_{sym(COO)}$ 1456, 1390, $\Delta\nu$ ($\nu_{asym(COO)} - \nu_{sym(COO)}$) 182, 220, Sn–C 544, (Sn-O)$_2$ 476, 454, Sn–O 273, 254, O_2–CH_2 929. ^{1}H NMR δ (ppm): 6.77 (d7.6, H_7), 6.61 (t7.5, H_6), 6.23 (d7.8, H_5), 5.95 (s, H_{10}), 2.88 (t7.4, H_3), 2.53 (t7.5, H_2), 0.70/0.68 (s, H_α) ^2J[^{119}Sn, ^{1}H] 71, 86 Hz. ^{13}C NMR δ (ppm): 180.7 (C_1), (147.9 (C_8), 147.1 (C_9), 122.4 (C_4), 121.8 (C_5), 121.5 (C_6), 106.9 (C_7), 101.4 (C_{10}), 29.7 (C_2), 25.6 (C_3), 4.4/6.4 (C_α) ^1J[^{119}Sn, ^{13}C] 742, 778 Hz. ^{119}Sn NMR δ (ppm): −216.4, −160.2.

2.3. *Diethylstannyl bis[3-(benzo[d][1,3]dioxol-4-yl)propanoate] (2)*

Diethyltin(IV) chloride (0.29 g, 1.16 mmol), L-salt (0.5 g, 2.3 mmol). Yield: (80%), M.p. 198–200 °C, Elemental Anal. Calcd (Found) for $C_{24}H_{28}O_8Sn$: C, 51.2(51.0); H, 5.0(4.8). IR (cm^{-1}): $\nu_{asym(COO)}$ 1614, $\nu_{sym(COO)}$ 1436, $\Delta\nu$ ($\nu_{asym(COO)} - \nu_{sym(COO)}$) 178, Sn–C 545, Sn–O 475, O_2–CH_2 931. ^{1}H NMR δ (ppm), ^nJ[^{119}Sn–^{1}H]: 6.71 (d7.5, H_7), 6.52 (t8.1, H_6), 6.28 (d8.1, H_5), 5.99 (s, H_{10}), 2.91 (t7.5, H_3), 2.65 (t8.0, H_2), 1.80 (q8.0, H_β), 1.35[76] (t7.6, H_α). ^{13}C NMR δ (ppm), ^nJ[^{119}Sn-^{13}C]: 175.7 (C_1), 148.2 (C_8), 147.6 (C_9), 125.6 (C_4), 124.4 (C_5), 123.3 (C_6), 109.6 (C_7), 101.6 (C_{10}), 35.8 (C_2), 28.6 (C_3), 17.6 [579] (C_α), 8.7[45] (C_β). ^{119}Sn NMR δ (ppm): −161.8.

2.4. *Di-n-butylstannyl bis[3-(benzo[d][1,3]dioxol-4-yl)propanoate] (3)*

Di-*n*-butyltin(IV) oxide (0.32 g, 1.3 mmol), HL (0.5 g, 2.6 mmol). Yield: (80%), M.p. 176–178 °C, Elemental Anal. Calcd (Found) for $C_{28}H_{36}O_8Sn$: C, 54.3(53.9); H, 5.9(5.7). IR (cm^{-1}): $\nu_{asym(COO)}$ 1610, $\nu_{sym(COO)}$ 1427, $\Delta\nu$ ($\nu_{asym(COO)} - \nu_{sym(COO)}$) 183, Sn–C 545,

Table 2. Selected bond lengths and angles of **1** and **4**.

1		**4**	
Sn(1)–O(9)	2.024(4)	Sn(1)–C(1)	2.118(2)
Sn(1)–C(22)	2.105(6)	Sn(1)–C(3)	2.118(3)
Sn(1)–C(21)	2.118(6)	Sn(1)–C(2)	2.121(3)
Sn(1)–O(9^{i})	2.140(4)	Sn(1)–O(1)	2.2084(16)
Sn(1)–O(2)	2.294(4)	Sn(1)–O(2^{ii})	2.3279(18)
Sn(1)–Sn(1^{i})	3.291(8)	O(2)–C(4)	1.261(3)
Sn(2)–O(9)	2.045(4)	O(1)–C(4)	1.266(3)
Sn(2)–C(23)	2.103(4)	O(3A)–C(12A)	1.339(14)
Sn(2)–C(24)	2.106(6)	O(3A)–C(13A)	1.574(12)
Sn(2)–O(6)	2.177(4)	O(4A)–C(11A)	1.363(8)
Sn(2)–O(1)	2.257(4)	O(4A)–C(13A)	1.419(10)
O(9)–Sn(1)–C(22)	106.2(2)	C(1)–Sn(1)–C(3)	126.44(12)
O(9)–Sn(1)–C(21)	111.8(2)	C(1)–Sn(1)–C(2)	117.10(12)
O(9)–Sn(1)–O(9^{i})	75.57(17)	C(3)–Sn(1)–C(2)	116.08(13)
C(22)–Sn(1)–O(9^{i})	101.2(2)	C(1)–Sn(1)–O(1)	92.66(9)
C(21)–Sn(1)–O(9^{i})	98.4(2)	C(3)–Sn(1)–O(1)	92.88(10)
O(9)–Sn(1)–O(2)	88.32(16)	C(2)–Sn(1)–O(1)	90.45(9)
C(22)–Sn(1)–O(2)	89.5(2)	C(1)–Sn(1)–O(2^{ii})	89.10(9)
C(21)–Sn(1)–O(2)	81.3(2)	C(3)–Sn(1)–O(2^{ii})	87.66(10)
O(9^{i})–Sn(1)–O(2)	162.60(18)	C(2)–Sn(1)–O(2^{ii})	86.99(9)
O(9)–Sn(1)–Sn(1^{i})	39.02(10)	O(1)–Sn(1)–O(2^{ii})	177.35(5)
O(9)–Sn(2)–C(23)	105.5(2)	C(4)–O(1)–Sn(1)	116.08(13)
O(9)–Sn(2)–C(24)	1107(3)	C(4)–O(2)–Sn(1^{iii})	135.79(15)
C(23)–Sn(2)–C(24)	143.5(3)		
O(9)–Sn(2)–O(6)	76.86(16)		
C(23)–Sn(2)–O(6)	97.3(3)		

Note: Symmetry codes: (i) $-x, -y+1, -z+1$; (ii) $-x-2, y+1/2, -z-1/2$; and (iii) $-x-2, y-1/2, -z-1/2$.

Sn–O 475, O_2–CH_2 931. ^{1}H NMR δ (ppm), $^nJ[^{119}Sn–^1H]$: 6.68 (d7.1, H_7), 6.54 (t7.6, H_6), 6.24 (d8.0, H_5), 5.98 (s, H_{10}), 2.88 (t7.0, H_3), 2.59 (t7.6, H_2), 1.60 (bs, H_α), 1.17–1.37 (m, Hβ, H_γ), 0.83 (t7.3, Hδ). ^{13}C NMR δ (ppm) $^nJ[^{119}Sn–^{13}C]$: 172.7 (C_1), 148.4 (C_8), 147.1 (C_9), 129.4 (C_4), 122.6 (C_5), 121.3 (C_6), 108.4 (C_7), 101.1 (C_{10}), 34.6 (C_2), 29.7 (C_3), 25.6[584] Cα, 28.4[36] Cβ, 26.6[97] Cγ, 13.5 Cδ. ^{119}Sn NMR δ (ppm): −140.3.

2.5. *Trimethylstannyl [3-(benzo[d][1,3]dioxol-4-yl)propanoate] (4)*

Me_3SnCl (0.5 g, 2.5 mmol), L-salt (0.5 g, 2.5 mmol). Yield: (64%), M.p. 137–139 °C, Elemental Anal. Calcd (Found) for $C_{13}H_{18}O_4Sn$: C, 43.7(43.4); H, 5.1(4.8). IR (cm^{-1}): $\nu_{asym(COO)}$ 1634, $\nu_{sym(COO)}$ 1456, $\Delta\nu$ ($\nu_{asym(COO)} - \nu_{sym(COO)}$) 178, Sn–C 544, Sn–O 454, O_2–CH_2 929. ^{1}H NMR δ (ppm), $^nJ[^{119}Sn–^1H]$: 6.70 (d7.3, H_7), 6.52 (t7.4, H_6), 6.26 (d7.8, H_5), 5.99 (s, H_{10}), 2.92 (t8.0, H_3), 2.65 (t7.8, H_2), 0.55[55/58] (s, H_α). ^{13}C NMR δ (ppm), $^nJ[^{119}Sn–^{13}C]$: 180.7 (C_1), 149.2 (C_8), 147.8 (C_9), 125.0 (C_4), 124.8 (C_5), 123.8 (C_6), 109.1 (C_7), 102.9 (C_{10}), 36.9 (C_2), 28.3 (C_3), 0.04[374/399] (C_α). ^{119}Sn NMR δ (ppm): 132.7.

2.6. *Tri-n-butylstannyl [3-(benzo[d][1,3]dioxol-4-yl)propanoate] (5)*

n-But_3SnCl (0.75 g, 2.31 mmol), L-salt (0.5 g, 2.31 mmol). Yield: (80%), M.p. 188–191 °C, Elemental Anal. Calcd (Found) for $C_{22}H_{36}O_4Sn$: C, 54.7(54.5); H, 7.5(7.3). IR (cm^{-1}): $\nu_{asym(COO)}$ 1639, $\nu_{sym(COO)}$ 1456, $\Delta\nu$ ($\nu_{asym(COO)} - \nu_{sym(COO)}$) 183, Sn–C 560, Sn–O 456, O_2–CH_2 934. ^{1}H NMR δ (ppm), $^nJ[^{119}Sn–^1H]$: 6.67 (d7.6, H_7), 6.55 (t7.2, H_6), 6.22 (d7.4,

H_5), 5.99 (s, H_{10}), 2.91 (t8.1, H_3), 2.66 (t8.0, H_2), 1.56 (bs, H_α), 1.13–1.32 (m, Hβ, H_γ), 0.85 (t7.3, Hδ). ^{13}C NMR δ (ppm), $^{n}J[^{119}Sn–^{13}C]$: 180.3 (C_1), 148.8 (C_8), 147.3 (C_9), 125.9 (C_4), 124.1 (C_5), 122.9 (C_6), 108.7 (C_7), 101.3 (C_{10}), 36.4 (C_2), 29.1 (C_3), 16.6 [380/396] (Cα), 28.0[34] (Cβ), 27.1 [96] (Cγ), 13.7 (Cδ). ^{119}Sn NMR δ (ppm): 123.7.

2.7. *Triphenylstannyl [3-(benzo[d][1,3]dioxol-4-yl)propanoate] (6)*

Ph_3SnCl (0.5 g, 2.3 mmol), L-salt (1.0 g, 2.3 mmol). Yield: (63%), M.p. 290–295 °C, Elemental Anal. Calcd (Found) for $C_{28}H_{24}O_4Sn$: C, 61.9(61.6); H, 4.4(4.3). IR (cm^{-1}): ν_{asym}(COO) 1634, ν_{sym}(COO) 1453, $\Delta\nu$ (ν_{asym}(COO) − ν_{sym}(COO)) 181, Sn–C 234, Sn–O 455, O_2–CH_2 926. ^{1}H NMR δ (ppm), $^{n}J[^{119}Sn–^{1}H]$: 7.39–7.75 (m, Ar–H), 6.71 (d8.0, H_7), 6.51 (t7.6, H_6), 6.20 (d7.1, H_5), 5.97 (s, H_{10}), 2.89 (t8.0, H_3), 2.63 (t7.9, H_2). ^{13}C NMR δ (ppm), $^{n}J[^{119}Sn–^{13}C]$: 174.3 (C_1), 147.2 (C_8), 145.4 (C_9), 138.2[640/663] (C_α), 136.9[40] (C_β), 130.1[69] (C_γ), 128.9 (C_δ), 125.0 (C4), 122.4 (C_5), 121.4 (C_6), 106.7 (C_7), 102.9 (C_{10}), 33.8 (C_2), 29.7 (C_3). ^{119}Sn NMR δ (ppm): 111.4.

3. Results and discussion

3.1. *Vibrational spectroscopy*

Weak, medium and intense absorptions due to "breathing" vibrations of different functional groups were observed in 1–6. The vibration frequencies of COO were identified by intense asymmetric (1669–1610 cm^{-1}) and symmetric stretches (1456–1390 cm^{-1}). The difference $\Delta\upsilon[\upsilon_{asym(COO)} - \upsilon_{sym(COO)}]$ in 2–6 is 178–183 cm^{-1}, indicating skew trapezoidal environment around tin with bridging bidentate L.

In **1**, two bands of asymmetric (1638, 1610 cm^{-1}) and symmetric frequencies (1456, 1390 cm^{-1}) were observed. The $\Delta\upsilon$ values for this compound (220, 180 cm^{-1}) are close to that found for anisobidentate chelate mode (220 cm^{-1}) and bridging bidentate carboxylate (180 cm^{-1}), consistent with the X-ray structure of distannoxane [23]. Bands at 476 and 454 cm^{-1} for **1** were assigned to non-linear O–Sn–O, while bands at 274–253 cm^{-1} were allocated to tin-oxygen (COO) stretches [24]. A sharp absorption at 934–926 cm^{-1} due to O–CH_2–O stretch was found in all complexes and also in ligand (929 cm^{-1}).

3.2. *NMR spectroscopy*

The ^{1}H and ^{13}C NMR resonances for **1**–**6** and free acids have been assigned (presented in experimental section). The single resonance of OH in ligand acid disappeared on coordination with tin. Two signals having similar intensity with satellites are assigned in bis[(2,3-methylenedioxypropanoate)dimethyltin(IV)] oxide (1). These resonances are similar to that observed for pairwise heterotopic non-equivalent exo- and endocyclic Me_2Sn moieties [25]. $^{2}J[^{119}Sn, ^{1}H]$ coupling values calculated for **1** are 71 and 86 Hz which suggest sp^3d hybridization around tin. The values calculated for diethyltin(IV) (**2**) [76] and trimethyltin(IV) (**4**) [55/58] identify highly distorted five-coordinate environment for diorganotins while tetrahedral for triorganotin derivatives [26]. Methylene protons of the three member heterocyclic ring appear downfield (5.95–5.99 ppm) due to intermolecu-

lar interactions and electron withdrawing nature of oxygen. The proton signals for butyl in **3** and **5** show a complex pattern due to $-CH_2-CH_2-CH_3$, however, methyl protons are clear triplets in the normal range. Signals for triphenyltin(IV) derivative (**6**) are multiplets due to overlapping signals.

In ^{13}C NMR spectra, σ-charge donation from COO-donor to tin removes electron density from the ligand and produces deshielding [27]. In **1**, non-equivalence of endocyclic and exocyclic Me_2Sn moieties was preserved on ^{1}H and ^{13}C NMR timescales, while carboxylates undergo site-exchange averaging. Obviously, carboxylates (bidentate and monodentate) and aromatic moieties should display pairwise different chemicals shifts. However, ligand protons and carbon signals remain similar in spite of their different bonding patterns within the stannoxane framework in the solid state. A fluxional mechanism is responsible for exchanging the chemical environment of monodentate and bidentate carboxylates. Satellites have importance for structure assessment and to correlate it with already reported complexes. In diorganotin(IV) compounds, $^{n}J[^{119}Sn, ^{13}C]$ values calculated for **1** ^{1}J[742(exo), 778(endo)], **2** ^{1}J[579], ^{2}J[45], and **3** ^{1}J[584], ^{2}J [36], ^{3}J[97] indicate five-coordinate tin [28–30].

Similarly, ^{n}J values calculated for **4** ^{1}J[374/399], **5** ^{1}J[380/396], and **6** ^{1}J[640/663], ^{2}J [40], ^{3}J[69] suggest bridging bidentate nature is lost in solution to generate a monomeric four coordinate, tetrahedral structure [31].

^{119}Sn NMR spectra of **1**–**6** were taken to validate the information. R groups bonded to tin and donor ligand influence the Sn resonances, but it can be used to infer the geometry around Sn [31]. Two ^{119}Sn isotropous resonances (−214.4, −160.2 ppm) in **1** can be assigned to the endocyclic and exocyclic tin, respectively. The broadness of endo ^{119}Sn resonances is due to the wagging motion of endocyclic Sn and the shift of frequency is an indication of dynamic behavior of this tin, but the difference (54 ppm) is much smaller and hence five-coordinate tin can be confidently suggested. Pairs of ^{1}H, ^{13}C, and ^{119}Sn resonances indicate dynamic behavior as previously discussed [32–34]. Compound **2** and **3** have shift values ranging between −140.3 and −161.8 ppm, thus confirming penta-coordination [35]. The δ(Sn) resonances for **4**, **5**, and **6** are for four-coordinate compounds [36].

3.3. *X-ray crystallography*

The molecular structure of **1** is shown in figure 1 and selected interatomic parameters are presented in table 1 and shown in figure 2. It is a tetranuclear centrosymmetric dimeric structure composed of oxoditin unit with central four-membered ring [Sn(1)–O(9)–Sn(1)–O(9)]. However, the Sn(1)–O(9) distances are different by 0.116 Å. Two four-membered and two six-membered rings in **1** encompass the central Sn_2O_2 core. The outer four-membered rings [Sn_2O_2, i.e. O(9)–Sn(2)–O(6)–Sn(1)] are formed by a bridging monodentate ligand that connects Sn1 and Sn2 via O6 giving longer Sn1–O6 (2.685 Å) and shorter Sn2–O6 (2.117 Å) bonds. A skew trapezoidal geometry is observed around endocyclic tin having three Sn–O bonds and two Sn–C covalent interactions, while the sixth position is occupied by weaker Sn–O interaction 2.68 Å, longer than sum of the covalent radii of tin-oxygen (2.13 Å) but significantly shorter than sum of the van der Waal's radii of Sn–O (3.68 Å) [37]. The axial C–Sn–C angle of endocyclic tin C(25)–Sn(2)–C(29) = 140.5(4)° is lower than the ideal value (180°), providing enough space for other donors to develop inter- and intramolecular interactions with tin [38]. Oxoditin is also a part of two six-membered [Sn_2O_3C, i.e. Sn(1)–O(2)–C(1)–O(1)–Sn(2)–O(9)] rings. The bridging ligand at the periph-

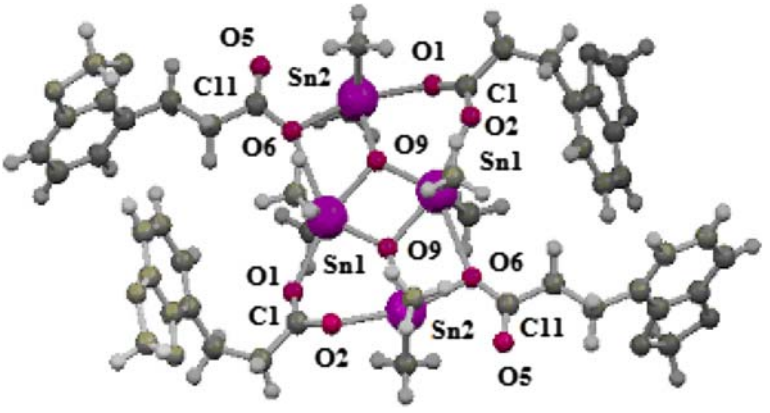


Figure 1. Molecular structure of 1 with atomic numbering scheme.

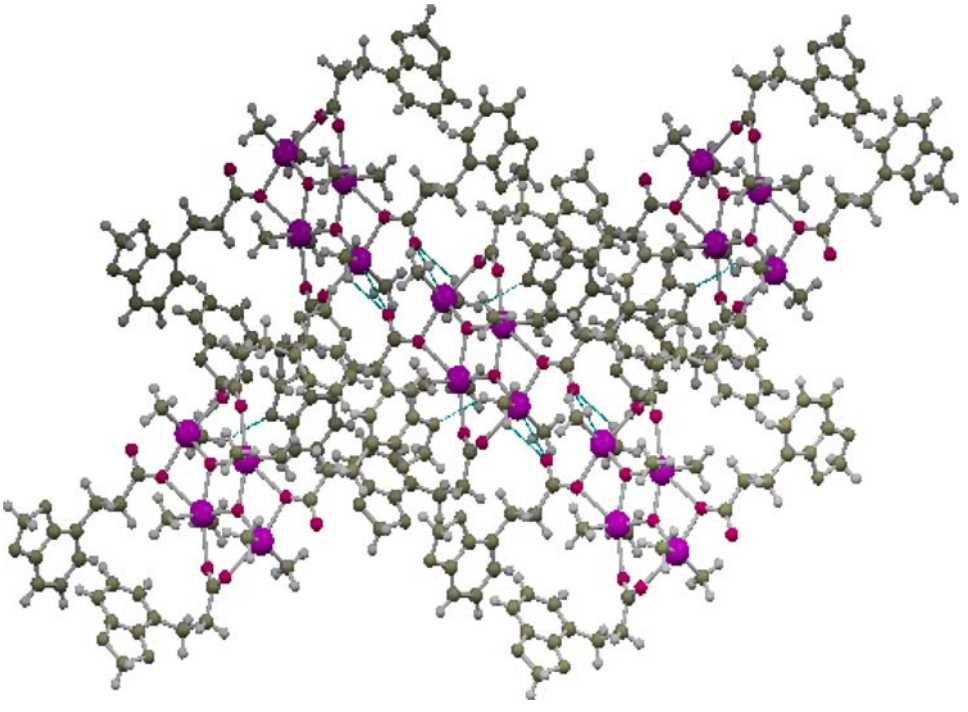


Figure 2. Supramolecular structure of 1 mediated by Sn–O = 3.106 Å, O–H = 2.574–2.499 and π–H = 2.613 Å intermolecular non-covalent interactions.

ery of the oxoditin unit connects Sn(1) and Sn(2), resulting in one longer and one shorter Sn–O bond [Sn(1)–O(2) = 2.294 and Sn(2)–O(1) = 2.257 Å]. The weaker interaction between neighboring endocyclic tins is also observed with distance 2.55 Å which is smaller than the sum of van der Waal's radii. The $\tau = (\beta - \alpha)/60$ can be used to assess geometry of five-coordinate exocyclic Sn. Here, β and α are consecutive largest basal angles around Sn. The angle $\alpha = \beta = 180°$ corresponds to a square-pyramidal geometry with τ value zero, while the value of $\alpha = 120°$ ($\tau = 1$) corresponds to perfectly trigonal-bipyrami-

dal geometry [39,40]. For the given structure, β and α angles are 164.93° and 143.48°, respectively, that correspond to τ value of 0.36. Based on this value, the geometry around exocyclic Sn is distorted square-pyramidal. The inclination of the geometry from trigonal-bipyramidal toward square-pyramidal can be attributed to the secondary non-covalent interaction of O5 with the exocyclic Sn of neighboring molecules. This interaction may be due to a wide C–Sn–C equatorial angle that provides enough space for O5 to interact with exocyclic Sn. The smaller methyl presumably also facilitates these interactions. The structure of **1** is a supramolecular cage, mediated by Sn–O = 3.106 Å, O–H = 2.574–2.499, and π–H = 2.613 Å non-covalent interactions.

Compound **4** is a polymeric structure (figures 3 and 4) in which each Sn is five-coordinate. Carboxylate bridges two symmetry related tins with unequal Sn–O bond lengths. The Sn–O distances vary from 2.208(16) to 2.328(18) Å with a mean value of 2.268 Å, while Sn–C distances are 2.118(2)–2.121 (3) Å. The inequality in the Sn–O bonds is reflected in associated C-O distances, the longer C–O bond is associated with shorter Sn–O bond and vice versa. Intermolecular C=O–Sn coordination results in an infinite zig-zag chain polymer containing Sn and bridging carboxylates. The O–Sn–O angle is 177.3°, mean O–Sn–C angle is 90.5°, and mean C–Sn–C angle is 119.9°. The largest basal angle (β) [O(1)–Sn(1)–O(2)] for trimethyltin (**4**) is 177.3° and the second largest (α) [C(1)–Sn(1)–C(3)] is = 126.43°. The τ value (0.85) calculated for 4 confirms distorted trigonal bipyramidal geometry in which the equatorial plane is defined by three methyls and axial positions are occupied by two oxygens (figure 3). The supramolecular layer structure of **4** is formed by Sn–O = 3.072 Å and π–H = 2.248 Å intermolecular interactions. These molecular dimensions are in agreement with values reported in the Cambridge Structural Database (CSD); a search of the CSD [41] for five-coordinate Sn with similar coordination environments gave many hits.

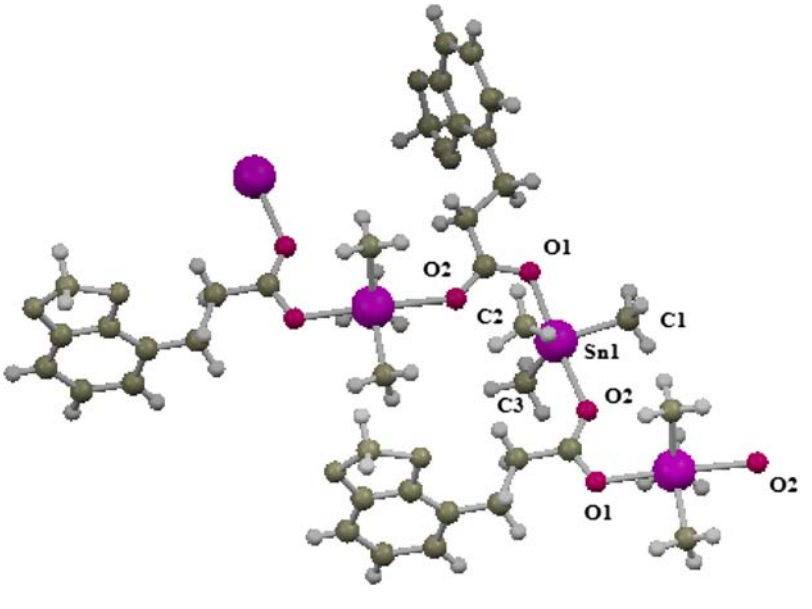


Figure 3. Polymeric structure of 4 with selected atomic numbering scheme.

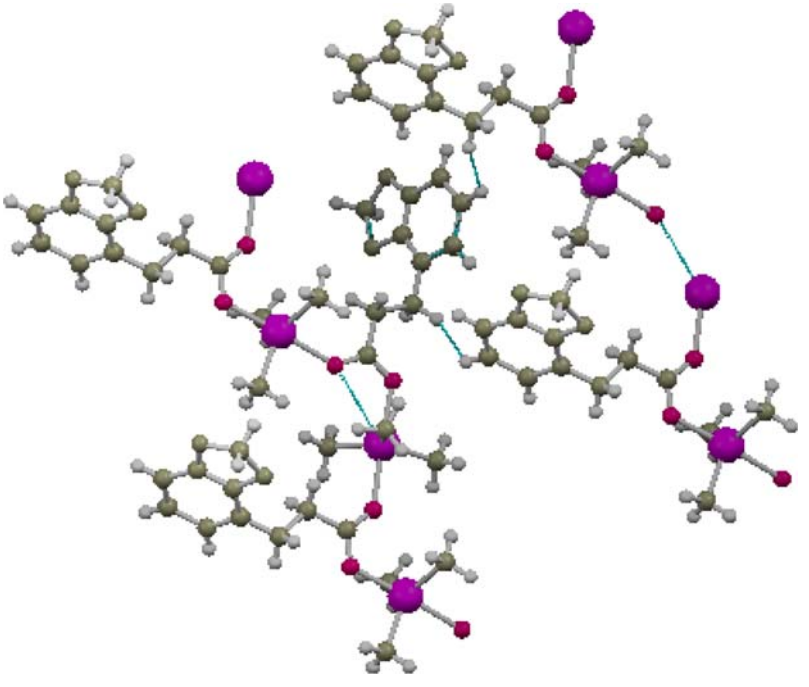


Figure 4. Supramolecular structure of 4 formed by Sn–O = 3.072 Å and π–H = 2.248 Å (Sn–O–Sn = 149.44°).

3.4. *Biological studies*

Compounds **1**–**6** were also tested for their *in vitro* antibacterial, antifungal, cytotoxicity, and antitumor activity and results are given in tables 3–5. The antibacterial activity was performed against six bacterial strains [*Escherichia coli, Bacillus subtilis, Shigella flexenari, Pseudomonas aeruginosa, Staphylococcus aureus, Salmonella typhi*] by agar well-diffusion method [42] using Imipenum standard drug. All compounds are moderately active against these strains, and the activity is highly strain-dependent. Inhibition of *E. coli*, *P. aeruginosa*, *S. aureus,* and *S. typhi* was remarkable for these compounds. The *S. Flexenari* showed more resistivity toward these organotins, especially **1**, **2**, **4**, and **6**. The trend for the activity against *B. subtilis* is not very different than *S. Flexenari*. The difference may be due to different structure of cell membranes that ultimately facilitate or

Table 3. Antibacterial activities[a,b] of di- and triorganotin(IV) derivatives (**1**–**6**).

	Zone of Inhibition (mm)						
Name of bacterium	**1**	**2**	**3**	**4**	**5**	**6**	Ref. drug
E. coli	13	14	16	19	12	09	35
B. subtilis	05	08	09	04	06	07	38
S. flexenari	–	–	07	–	04	–	32
P. aeruginosa	12	09	17	14	11	12	38
S. aureus	16	12	14	10	11	14	29
S. typhi	13	11	14	15	13	07	28

[a]*In vitro*, agar well diffusion method, conc. 3 mg mL^{-1} of DMSO.
[b]Reference drug = imipenum.

Table 4. Antifungal activities[a–c] of **1**–**6**.

	Zone of Inhibition (mm)								
Name of fungus	**1**	**2**	**3**	**4**	**5**	**6**	Std. drug	% Inhibition	MIC ($\mu g\,mL^{-1}$)
T. longifusus	44	56	67	84	90	97	Miconazole	100	70
C. albicans	59	61	70	79	81	83	Miconazole	100	110.8
A. flavus	52	43	59	74	100	78	Amphotericin-B	100	20
M. canis	63	54	64	72	71	67	Miconazole	100	98.4
F. solani	33	56	68	74	68	88	Miconazole	100	73.25
C. glabrata	55	46	62	94	73	67	Miconazole	100	110.8

[a]Concentration: 100 $\mu g\,mL^{-1}$ of DMSO.
[b]MIC: Minimum inhibitory concentration.
[c]Percent inhibition (standard drug) = 100.

Table 5. Cytotoxic and antitumor activities[a–c] of **1**–**6**.

Compound no.	**1**	**2**	**3**	**4**	**5**	**6**
LD_{50} ($\mu g\,mL^{-1}$)	0.65	35.40	10.81	1.02	6.25	5.87
% Inhibition of tumors	88.88	48.14	69.41	96.29	83. 45	40.74

[a]Against brine-shrimps (*in vitro*).
[b]Standard drug Etoposide LD_{50} 7.46 $\mu g\,mL^{-1}$ (cytotoxicity).
[c]Standard drug Vincristine (100% Inhibition) (antitumor).

interrupt the passage of these compounds into the cell. Antibacterial activities of our compounds supersedes the activity of previously reported organotin(IV) Schiff bases [43], affirming ligand role in the biological action.

The antifungal activities of **1**–**6** were examined against six fungal strains (*Trichophyton longifusus*, *Candida albicans*, *Aspergillus Flavus*, *Microsporum Canis*, *Fusarium Solani*, and *Candida glabrata*) by Agar tube dilution method [42] (table 4). Miconazole and Amphotericin-B were used as standard drugs in this assay. Criteria for activity are based on percent growth inhibition; more than 70% growth inhibition shows significant activity, 60–70% inhibition activity is good, 50–60% inhibition activity is moderate and below 50% inhibition activity is not significant. In general, the triorganotin(IV) derivatives are better antifungal agents than their corresponding diorganotin(IV) compounds. In addition, these compounds are less lethal to the organism as shown in table 4 and thus have potential to be commercialized as new antifungal drugs.

In vitro cytotoxicity was performed by the brine-shrimp bioassay method [44], and results are summarized in table 5. The LD_{50} data showed that all tested compounds were toxic with LD_{50} values of 0.65–35.40 $\mu g\,mL^{-1}$ in comparison with reference drug Etoposide with LD_{50} value 7.46 $\mu g\,mL^{-1}$. Triorganotin(IV) compounds are significantly more toxic than reference drug. Dimethyltin and di-*n*-butyltin(IV) compounds exhibit good activity, whereas diethyltin(IV) derivatives require higher concentrations.

Potato Disc Antitumor assay was performed for all these synthesized compounds using *Agrobacterium tumefaciens* (At10) [45] (table 5). All complexes significantly blocked the tumor growth in comparison with the reference drug (Vincristine) with 100% tumor inhibition, as shown in table 5. For organotin(IV) derivatives of 3-(benzo[d][1,3] dioxol-4-yl)propanoate, the antitumor activity fall in the sequence $Me_3Sn > Me_2Sn >$ n-$Bu_3Sn >$n-$Bu_2Sn > Et_2Sn > Ph_3Sn$. In the biological system, these compounds presumably

insert into DNA double-helix and intercalate with DNA-bases (intercalation), thus altering its structure and ultimately its functional machinery. The above trend of antitumor action suggests that the activity is mainly governed by diffusion, geometry, lipophilic, and steric factors. The highest activity of methyltin derivatives can be explained on the basis of their high diffusion (low molecular weights). The better antitumor action of butyltin analogues than low-molecular-weight ethyltin and one can be attributed to the high lipophilic character of the former. The lowest activity of triphenyltin derivative may be because of its high molecular weight, due to which the compounds took longer to get into the DNA helix. The higher activity of triorganotin(IV) than diorganotin(IV) derivatives is presumably due to the low coordination environment of Sn in solution, creating the possibility for them to expand their coordination by making new bonds with nitrogens of DNA bases. Organotin (IV) derivatives of different ligand show almost the same trend, pointing toward the significance of ligand in alteration and modulation of activity of specific organotin(IV) complexes.

4. Conclusions

New organotin(IV) carboxylates have been synthesized and characterized as solids and in solution by various techniques. These compounds have diverse structural motifs in solid state that depend on the number of organic groups around Sn and on the mode of coordination of the ligand. Non-covalent intermolecular interactions also play a role in packing diagrams. Solution structures in some compounds are different than the solid-state structures, attributed to fluxional behavior of the ligand. These compounds have significant antimicrobial and anticancer activities with potential to be marketed as drugs. The biological activity may arise because of their intermolecular capabilities with the cell constituents as shown from packing diagrams. The data show that activities of the compounds are governed by diffusion, geometry, lipophilic, and steric factors.

Supplementary material

Single crystal X-ray diffraction data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 787511 (1) and CCDC No. 787512 (4). The copy of this information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge, CBZ 1EZ, UK (Fax: +44 1223 336033; Email: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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