

## ***In vitro* Antitumor and Antibacterial Assay of Organotin(IV) Complexes of 2,3-Methylenedioxybenzoic Acid; X-Ray Crystal Structure of $[(C_2H_5)_2Sn(C_8H_5O_4)_2]$**

M. Hussain<sup>a</sup>, M. Hanif<sup>a</sup>, S. Ali<sup>a,\*</sup>, S. Shahzadi<sup>b,\*</sup>, M.S. Ahmad<sup>c</sup>, B. Mirza<sup>c</sup> and H.S. Evans<sup>d</sup>

<sup>a</sup>Department of Chemistry, Quaid-i-Azam University, Islamabad-45320, Pakistan

<sup>b</sup>Department of Chemistry, GC University, Faisalabad, Pakistan

<sup>c</sup>Department of Biochemistry, Quaid-i-Azam University, Islamabad-45320, Pakistan

<sup>d</sup>Institute of Microtechnology, University of Neuchatel, Rue Emile-Argand 11, CH-2009 Neuchatel, Switzerland

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New organotin(IV) compounds containing the carboxylate ligand 2,3-methylenedioxybenzoic acid (**HL**) have been synthesized with the general formula  $R_2SnL_2$  (R = Me, Et, *n*-Bu, Ph and *n*-Oct) and  $R_3SnL$  (R = *n*-Bu). All compounds have been studied in the solution state by multinuclear NMR (<sup>1</sup>H, <sup>13</sup>C and <sup>119</sup>Sn) by using the non-coordinating solvent and also in solid state by FTIR, mass spectrometry and X-ray crystallography. Spectroscopic data have shown that methylenedioxy moiety does not coordinate with tin atom and the coordination site is actually -COO group, as is proved by X-ray structure determination. The solid state structure of compound (**2**) has been determined by X-ray crystallography which shows that the complex (**2**) has distorted octahedral geometry. These complexes have been evaluated *in vitro* against crown gall tumor and antibacterial activity. Interesting results were noticed during the bio-activity screenings, which proved their *in vitro* biological potential and possible use as drugs.

**Keywords:** Organotin(IV) 2,3-methylenedioxy benzoates, Spectroscopy, X-ray structure, Antitumor activity, Antibacterial activity

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### **INTRODUCTION**

The increasing interest in organotin(IV) carboxylates of substituted benzoic acids in recent years has, to a large extent, been prompted by their new structural diversity [1] and broad therapeutic activity [2]. Research on the structure of organotin(IV) carboxylates continues and, at the same time, some new applications of high importance are being discovered which are relevant to ecological medicinal applications. The increasing interest in the chemistry of

organotin(IV) compounds has led to the extended studies on their reactions with different biomolecules *e.g.*, carbohydrates [3-5], nucleic acid derivatives [6-8], amino acids [9-11] and peptides [12-14].

In general, triorganotin(IV) compounds display a vast array of biological activity compared with their diorganotin and monoorganotin analogues. This has been attributed to their ability to bind proteins [15-17]. Furthermore, many organotin(IV) carboxylates have been found to possess anticancer activity in a variety of tumor cells and the structure of these organotin(IV) compounds have been characterized both in solid and solution forms [18]. Dialkytin(IV)

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\*Corresponding author. E-mail: drsa54@yahoo.com

compounds have selective effect on lymphocytes [19] which can be used in cancer chemotherapy. Among diorganotin(IV) compounds tetra-organodistannoxanes are an important class of compounds owing to their applications in catalysts [20] and their interesting biological activity [21].

Having these applications in view, and our interest in the synthesis, characterization and biological studies of organotin(IV) carboxylates [22-24], we synthesized organotin(IV) carboxylates of 2,3-methylenedioxybenzoic acid (Fig. 1) and characterized them by multinuclear NMR ( $^1\text{H}$ ,  $^{13}\text{C}$  and  $^{119}\text{Sn}$ ), FTIR, mass spectrometry and X-ray crystallography. These compounds were tested for their *in vitro* antitumor and antibacterial activity.

## EXPERIMENTAL

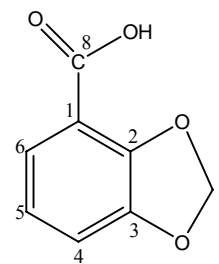
### Materials and Instrumentation

Melting points were determined in a capillary tube using an MPD Mitamura Riken Kogyo (Japan) electrothermal melting point apparatus. The infrared spectra were recorded as KBr pellets on a Bio-Rad Excaliber FT-IR, model FTS 300 MX spectrophotometer (USA), in the frequency range 4000-400  $\text{cm}^{-1}$ . Multinuclear NMR ( $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{119}\text{Sn}$ ) spectra were recorded on a Bruker ARX 300 MHz, FT-NMR spectrometer using  $\text{CDCl}_3$  as an internal reference for [ $\delta$   $^1\text{H}$  ( $\text{CDCl}_3$ ) = 7.25 and  $\delta$   $^{13}\text{C}$  ( $\text{CDCl}_3$ ) = 77.0]. Elemental analyses were carried out with a Perkin-Elmer 2400 Series II instrument. Mass spectral data were taken on a MAT-312 Mass spectrometer. X-ray single crystal analysis was made on a Nonius Kappa CCD diffractometer with graphite monochromated  $\text{MoK}_\alpha$  radiation.

All the reactions were carried out under an anhydrous atmosphere. Solvents were purified and dried before use [25]. All the chemicals were of analytical grade and used without further purification.

### Syntheses

**Synthesis of 2,3-methylenedioxybenzoic acid (HL).** 5.0 g (3.3 mmol) of finely powdered *o*-piperonal was added to 300 ml of water and the mixture was heated up to 40-50  $^\circ\text{C}$  and stirred mechanically in 500 ml round bottom flask. To this, potassium permanganate solution (12.5 g) run slowly until the odour of piperonal is no longer perceptible. Excess of the later was destroyed by the addition of a little alcohol, the mixture



**Fig. 1.** The structure and numbering Scheme of 2,3-methylenedioxybenzoic acid (HL).

was filtered hot and the filtrate was acidified with dilute hydrochloric acid. The piperonylic acid, which was separated as the solution, when cooled was practically pure. After the preparation of acid, it was converted to its sodium salt by dissolving the acid (3.5 g, 2.1 mmol) in the absolute ethanol and treating it with sodium bicarbonate (1.77 g, 2.1 mmol). After one hour stirring, the mixture of water and ethanol was evaporated by using rotary evaporator. The solid product was obtained which was dried over  $\text{CaO/P}_2\text{O}_5$ . Yield 95%, m.p.: 300  $^\circ\text{C}$ . Analysis: Calcd. for  $\text{C}_8\text{H}_5\text{O}_4\text{Na}$ : C, 51.06; H, 2.65. Found: C, 51.12; H, 2.70.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , ppm),  $^nJ(^1\text{H}, ^1\text{H})$ , 7.00 (H-4, d, (8.1)), 6.90 (H-5, d, (7.5)), 7.40 (H-6, d, (8.2)), 6.01 (H-7, s).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , ppm), 112 (C-1), 148 (C-2), 149 (C-3), 112 (C-4), 121 (C-5), 123 (C-6), 102 (C-7), 173 (C-8). IR (KBr,  $\text{cm}^{-1}$ ), 1679 ( $\nu_{\text{asym}}\text{COO}$ ), 1400 ( $\nu_{\text{sym}}\text{COO}$ ), 279 ( $\Delta\nu$ ).

**Synthesis of  $\text{Me}_2\text{Sn}[\text{C}_8\text{H}_5\text{O}_4]_2$  (1).**  $\text{C}_8\text{H}_5\text{O}_4\text{Na}$  (1.0 g, 5.35 mmol) and  $\text{Me}_2\text{SnCl}_2$  (0.6 g, 2.74 mmol) were added to 100  $\text{cm}^3$  of dry toluene in 1:2 ratio in round bottom two necked flask (250 ml). The mixture was refluxed for 5-6 h. After cooling, sodium chloride was filtered off and filtrate was evaporated by rotary evaporator under reduced pressure. The solid product obtained was recrystallized from chloroform and *n*-hexane (4:1). Yield 96%, m.p.: 277  $^\circ\text{C}$ . Analysis Calculated for  $\text{C}_{18}\text{H}_{16}\text{O}_8\text{Sn}$ : C, 45.09; H, 3.34. Found: C, 45.13; H, 3.41.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , ppm),  $^nJ(^1\text{H}, ^1\text{H})$ ,  $^nJ(^{119}\text{Sn}, ^1\text{H})$ , 7.00 (H-4, d (8.1)), 6.88 (H-5, d (7.5)), 7.52 (H-6, d (8.3)), 6.13 (H-7, s), 1.17 [78.5] (s, H- $\alpha$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , ppm), 112.8 (C-1), 148.7 (C-2), 149.1 (C-3), 112.3 (C-4), 121.1 (C-5), 123.8 (C-6), 102.0 (C-7), 177.9 (C-8), 14.9 (C- $\alpha$ ). IR (KBr,  $\text{cm}^{-1}$ ), 1567 ( $\nu_{\text{asym}}\text{COO}$ ), 1400 ( $\nu_{\text{sym}}\text{COO}$ ), 167 ( $\Delta\nu$ ), 523 ( $\nu_{\text{Sn-C}}$ ), 453 ( $\nu_{\text{Sn-O}}$ ). EIMS major positive ions  $m/z$ (%),

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$[\text{CH}_3\text{Sn}(\text{C}_7\text{H}_5\text{O}_2\text{COO})_2]^+$  465(19.84),  $[(\text{Sn}(\text{C}_5\text{H}_3\text{COO})-(\text{C}_6\text{H}_3\text{O}_2\text{COO}))^+]$  378(23.49),  $[(\text{CH}_3)_2\text{Sn}(\text{C}_7\text{H}_6\text{O}_2\text{COO})]^+$  316(21.03),  $[\text{Sn}(\text{C}_6\text{H}_6\text{COO})]^+$  242(69.85),  $[(\text{CH}_3)_2\text{Sn}]^+$  150(86.35),  $[\text{C}_5\text{H}_3\text{CO}]^+$  91(45.86),  $[\text{C}_5\text{H}_5]^+$  65(100),  $[\text{CH}_3\text{Sn}]^+$  135(4.95),  $[\text{Sn}]^+$  120(31.53),  $[\text{SnH}]^+$  121(18.93).  $\delta(^{119}\text{Sn})$  NMR ( $\text{CDCl}_3$ , ppm): -99.80.

**Synthesis of  $\text{Et}_2\text{Sn}[\text{C}_8\text{H}_5\text{O}_4]_2$  (2).** Compound (2) was prepared similarly as compound (1) by using  $\text{C}_8\text{H}_5\text{O}_4\text{Na}$  (1.0 g, 5.35 mmol) and  $\text{Et}_2\text{SnCl}_2$  (0.6 g, 2.66 mmol) in 100  $\text{cm}^3$  of dry toluene in 1:2 molar ratio. The solid product was recrystallized from chloroform and *n*-hexane (4:1). Yield: 80%. m.p.: 210-215 °C. Anal. Calcd. for  $\text{C}_{20}\text{H}_{20}\text{O}_8\text{Sn}$ : C, 47.33; H, 3.94. Found: C, 47.23; H, 3.81.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , ppm),  $^nJ(^1\text{H}, ^1\text{H})$ ,  $^nJ(^{119}\text{Sn}, ^1\text{H})$ , 7.09 (H-4, d (8.1)), 6.88 (H-5, d (7.5)), 7.53 (H-6, d (8.3)), 6.13 (H-7, s), 1.77 (H- $\alpha$  (q (8.0)), 1.38 [74.5] (H- $\beta$ , t (7.9)).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , ppm), 112.9 (C-1), 149.0 (C-2), 149.3 (C-3), 112.7 (C-4), 121.3 (C-5), 124.2 (C-6), 102.3 (C-7), 178.1 (C-8), 18.2 [545.8] (C- $\alpha$ ), 9.3 (C- $\beta$ ). IR (KBr,  $\text{cm}^{-1}$ ), 1567 ( $\nu_{\text{asym}}\text{COO}$ ), 1378 ( $\nu_{\text{sym}}\text{COO}$ ), 189 ( $\Delta\nu$ ), 550 ( $\nu_{\text{Sn-C}}$ ), 450 ( $\nu_{\text{Sn-O}}$ ). EIMS major positive ions  $m/z$ ,  $[(\text{C}_2\text{H}_5)\text{Sn}(\text{C}_7\text{H}_5\text{O}_2\text{COO})_2]^+$  479(16.88),  $[(\text{C}_2\text{H}_5)_2\text{Sn}(\text{C}_7\text{H}_5\text{O}_2\text{COO})_2\text{C}_6\text{H}_5\text{COO}]^+$ , 435(2.65),  $[(\text{C}_2\text{H}_5)\text{Sn}(\text{C}_7\text{H}_5\text{O}_2\text{COO})]^+$  343.0(2.04),  $[\text{Sn}(\text{C}_6\text{H}_5\text{COO})]^+$  242(100),  $[(\text{C}_2\text{H}_5)\text{Sn}]^+$ , 148(32.90),  $[(\text{C}_7\text{H}_6\text{O}_2\text{COO})]^+$  166.0(17.70),  $[(\text{C}_7\text{H}_5\text{O}_2\text{CO})]^+$  150(32.90),  $[\text{C}_5\text{H}_3]^+$  63(17.58),  $[(\text{C}_2\text{H}_5)_2\text{Sn}]^+$  178(1.30),  $[\text{Sn}]^+$  120(9.86),  $[\text{SnH}]^+$  121(4.65).  $\delta(^{119}\text{Sn})$  NMR ( $\text{CDCl}_3$ , ppm): -123.33.

**Synthesis of  $n\text{-Bu}_2\text{Sn}[\text{C}_8\text{H}_5\text{O}_4]_2$  (3).** Synthesized carboxylic acid  $[\text{C}_8\text{H}_5\text{O}_4]$  (1.0 g, 6.01 mmol) was suspended in dry toluene (100 ml) and treated with *n*-But $_2$ SnO (0.4 g, 1.89 mmol) in a reaction flask with constant stirring and mixture was refluxed for 6 h. Water formed was removed *via* Dean and Stark trap. After completion and cooling the reaction mixture to room temperature, solvent was removed through rotary apparatus under reduced pressured. The mass left behind was recrystallized from  $\text{CHCl}_3$  and *n*-hexane (4:1). Yield: 78%. m.p.: 180-184 °C. Anal. Calcd. for  $\text{C}_{24}\text{H}_{28}\text{O}_8\text{Sn}$ : C, 51.15; H, 4.97. Found: C, 51.20; H, 5.01.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , ppm),  $^nJ(^1\text{H}, ^1\text{H})$ ,  $^nJ(^{119}\text{Sn}, ^1\text{H})$ , 7.01 (H-4, d (8.1)), 6.89 (H-5, d (7.5)), 7.55 (H-6, d (8.3)), 6.15 (H-7, s), 1.78-1.82 (H- $\alpha$ , m), 1.26-1.37 (H- $\beta$ , m), 1.12-1.22 (H- $\gamma$ , m), 0.90 [72.9] (H- $\delta$ , t (7.2)),  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , ppm), 112.8 (C-1), 149.0 (C-2), 149.2 (C-3), 112.8 (C-4), 121.3 (C-5), 124.2 (C-6), 102.3 (C-

7), 178.9 (C-8), 25.7 (C- $\alpha$ ), 29.9 (C- $\beta$ ), 31.5 (C- $\gamma$ ), 13.8 (C- $\delta$ ). IR (KBr,  $\text{cm}^{-1}$ ), 1588 ( $\nu_{\text{asym}}\text{COO}$ ), 1400 ( $\nu_{\text{sym}}\text{COO}$ ), 188 ( $\Delta\nu$ ), 520 ( $\nu_{\text{Sn-C}}$ ), 457 ( $\nu_{\text{Sn-O}}$ ). EIMS major positive ions  $m/z$ ,  $[(\text{C}_4\text{H}_9)\text{Sn}(\text{C}_7\text{H}_5\text{O}_2\text{COO})_2]^+$  508(16.88),  $[(\text{C}_4\text{H}_9)_2\text{Sn}(\text{C}_7\text{H}_5\text{O}_2\text{COO})]^+$  400(5.90),  $[\text{Sn}(\text{C}_7\text{H}_5\text{O}_2\text{COO})]^+$  286(87.97),  $[\text{Sn}(\text{C}_6\text{H}_5\text{COO})]^+$  242(53.56),  $[(\text{C}_7\text{H}_6\text{O}_2\text{COO})]^+$  166(77.06),  $[\text{C}_4\text{H}_9]^+$  57(100),  $[(\text{C}_4\text{H}_9)_2\text{Sn}]^+$  234(2.28),  $[(\text{C}_4\text{H}_9)\text{Sn}]^+$  177(2.50),  $[\text{Sn}]^+$  120(27.12),  $[\text{SnH}]^+$  121(10.29).  $\delta(^{119}\text{Sn})$  NMR ( $\text{CDCl}_3$ , ppm): -127.30.

**Synthesis of  $n\text{-Oct}_2\text{Sn}[\text{C}_8\text{H}_5\text{O}_4]_2$  (4).** Compound (4) was prepared similarly as compound (3) by using  $[\text{C}_8\text{H}_5\text{O}_4]$  (1.0 g, 6.0 mmol) and *n*-Oct $_2$ SnO (1.12 g, 3.1 mmol) in 100  $\text{cm}^3$  of dry toluene in 1:2 molar ratio. The solid product was recrystallized from chloroform and *n*-hexane (4:1). Yield: 83%. m.p.: 126-128 °C. Anal. Calcd. for  $\text{C}_{32}\text{H}_{44}\text{O}_8\text{Sn}$ : C, 56.88; H, 6.51. Found: C, 56.79; H, 6.31.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , ppm),  $^nJ(^1\text{H}, ^1\text{H})$ ,  $^nJ(^{119}\text{Sn}, ^1\text{H})$ , 6.96 (H-4, d (8.1)), 6.85 (H-5, d (7.5)), 7.45 (H-6, d (8.3)), 6.09 (H-7, s), 1.26-1.36 (H- $\alpha$ , m), 1.61-1.62 (H- $\beta$ , m).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , ppm), 112.0 (C-1), 148.6 (C-2), 148.8 (C-3), 112.2 (C-4), 121.2 (C-5), 124.4 (C-6), 102.1 (C-7), 178.7 (C-8), 22.9 (C- $\alpha$ ), 25.0 (C- $\beta$ ), 25.8 [462.8] (C- $\gamma$ ), 29.6 (C- $\delta$ ), 30.0 (C- $\alpha'$ ), 32.2 (C- $\beta'$ ), 34.2 (C- $\gamma'$ ), 14.5 (C- $\delta'$ ). IR (KBr,  $\text{cm}^{-1}$ ), 1580 ( $\nu_{\text{asym}}\text{COO}$ ), 1430 ( $\nu_{\text{sym}}\text{COO}$ ), 150 ( $\Delta\nu$ ), 548 ( $\nu_{\text{Sn-C}}$ ), 446 ( $\nu_{\text{Sn-O}}$ ). EIMS major positive ions  $m/z$ ,  $[(\text{C}_7\text{H}_6\text{O}_2\text{COO})]^+$  166(34.58),  $[(\text{C}_7\text{H}_5\text{O}_2\text{COO})]^+$  165(18.22)  $[(\text{C}_7\text{H}_5\text{O}_2\text{CO})]^+$  149(13.65),  $[(\text{C}_5\text{H}_4\text{COO})]^+$  108(14.75),  $[\text{C}_5\text{H}_{11}]^+$  71(56.81),  $[\text{C}_6\text{H}_{13}]^+$  85(37.20),  $[\text{C}_4\text{H}_9]^+$  57(100),  $[\text{C}_8\text{H}_{17}\text{Sn}]^+$  233(2.25),  $[\text{Sn}]^+$  120(10.38),  $[\text{SnH}]^+$  121(8.14).  $\delta(^{119}\text{Sn})$  NMR ( $\text{CDCl}_3$ , ppm): -91.50.

**Synthesis of  $\text{Ph}_2\text{Sn}[\text{C}_8\text{H}_5\text{O}_4]_2$  (5).** Compound (5) was prepared similarly as compound (1) by using  $\text{C}_8\text{H}_5\text{O}_4\text{Na}$  (1.0 g, 5.35 mmol) and  $\text{Ph}_2\text{SnCl}_2$  (0.9 g, 2.67 mmol) in 100  $\text{cm}^3$  of dry toluene in 1:2 molar ratio. The solid product was recrystallized from chloroform and *n*-hexane (4:1). Yield: 80%. m.p.: 180-185 °C. Anal. Calcd. for  $\text{C}_{28}\text{H}_{20}\text{O}_8\text{Sn}$ : C, 55.72; H, 3.31. Found: C, 55.79; H, 3.37.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , ppm),  $^nJ(^1\text{H}, ^1\text{H})$ ,  $^nJ(^{119}\text{Sn}, ^1\text{H})$ , 7.48 (H-4, d (8.1)), 6.88 (H-5, d (7.5)), 7.81 (H-6, d (8.3)), 6.04 (H-7, s), 7.12-7.17 (m, H- $\beta$ ), 7.67-7.70 (m, H- $\gamma$ ), 7.67-7.70 (m, H- $\delta$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , ppm), 110.6 (C-1), 147.9 (C-2), 148.0 (C-3), 107.9 (C-4), 127.0 (C-5), 129.1 (C-6), 101.8 (C-7), 178.9 (C-8), 130.8 [462.8] (C- $\alpha$ ), 135.8 (C- $\beta$ ), 136.9 (C- $\gamma$ ), 128.5 (C- $\delta$ ). IR (KBr,  $\text{cm}^{-1}$ ), 1580 ( $\nu_{\text{asym}}\text{COO}$ ), 1430 ( $\nu_{\text{sym}}\text{COO}$ ), 150 ( $\Delta\nu$ ), 548 ( $\nu_{\text{Sn-}}$

C), 446 ( $\nu_{\text{Sn-O}}$ ). EIMS major positive ions  $m/z$ ,  $[(\text{C}_7\text{H}_6\text{O}_2\text{COO})]^+$  166(79.61),  $[(\text{C}_7\text{H}_5\text{O}_2\text{COO})]^+$  165(36.14),  $[(\text{C}_7\text{H}_5\text{O}_2\text{CO})]^+$ , 149(11.29),  $[\text{SnO}]^+$  136(100),  $[(\text{C}_5\text{H}_4\text{O})]^+$  80(20.18),  $[\text{C}_5\text{H}_5]^+$  65(47.77),  $[\text{Sn}]^+$  120(17.38).  $\delta(^{119}\text{Sn})$  NMR ( $\text{CDCl}_3$ , ppm): -298.60.

**Synthesis of *n*-Bu<sub>3</sub>Sn[C<sub>8</sub>H<sub>5</sub>O<sub>4</sub>] (6).** Compound (6) was prepared similarly as compound (1) by using C<sub>8</sub>H<sub>5</sub>O<sub>4</sub>Na (1.0 g, 5.35 mmol) and *n*-Bu<sub>3</sub>SnCl (1.7 g, 5.35 mmol) were added to 100 cm<sup>3</sup> of dry toluene in 1:1 ratio in round bottom two necked flask (250 ml). The mixture was refluxed for 5-6 h. After cooling, sodium chloride was filtered off and filtrate was evaporated by rotary evaporator under reduced pressure. The solid product obtained was recrystallized from chloroform and *n*-hexane (4:1). Yield 73%, m.p.: 160-161 °C. Anal. Calcd. for C<sub>20</sub>H<sub>32</sub>O<sub>4</sub>Sn: C, 52.74; H, 7.03. Found: C, 52.88; H, 7.19. <sup>1</sup>H NMR ( $\text{CDCl}_3$ , ppm), <sup>n</sup>J(<sup>1</sup>H, <sup>1</sup>H), <sup>n</sup>J(<sup>119</sup>Sn, <sup>1</sup>H)], 6.99 (H-4, d (8.7)), 6.87 (H-5, d (8.1)), 7.53 (H-6, d (8.7)), 6.12 (H-7, s), 1.20-1.25 (m, H- $\alpha$ ), 1.80-1.84 (m, H- $\beta$ ), 1.23-1.26 H (m, H- $\gamma$ ), 0.83 (H- $\delta$ , t (7.5)). <sup>13</sup>C NMR ( $\text{CDCl}_3$ , ppm), 112.7 (C-1), 148.6 (C-2), 149.0 (C-3), 111.6 (C-4), 120.9 (C-5), 124.1 (C-6), 101.9 (C-7), 179.10 (C-8), 13.8 (C- $\alpha$ ), 27.0 (C- $\beta$ ), 28.7 [20.3] (C- $\gamma$ ), 29.9 [350.6] (C- $\delta$ ). IR (KBr, cm<sup>-1</sup>), 1584 ( $\nu_{\text{asymCOO}}$ ), 1459 ( $\nu_{\text{symCOO}}$ ), 125 ( $\Delta\nu$ ), 532 ( $\nu_{\text{Sn-C}}$ ), 480 ( $\nu_{\text{Sn-O}}$ ).  $\delta(^{119}\text{Sn})$  NMR ( $\text{CDCl}_3$ , ppm): -189.17.

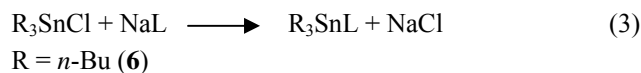
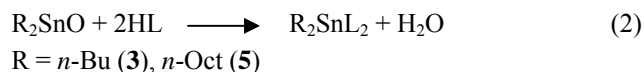
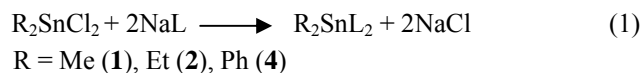
### X-Ray Crystallography

X-Ray crystallographic data were collected on a Nonius Kappa CCD AXS diffractometer. Correction for semi-empirical from equivalents was applied, and the structure was solved by direct methods and refined by a full-matrix least squares procedure based on  $F^2$  using the SHELXL-97 Program System. All data were collected with graphite-monochromated  $\text{M}_\alpha\text{K}_\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ) at 173K.

## RESULTS AND DISCUSSION

### Synthesis

The organotin derivatives (1)-(6) were obtained by heating at reflux, the stoichiometric amount of 2,3-methylene-dioxybenzoic acid or its sodium salt with the corresponding organotin oxide or organotin chloride in anhydrous toluene (Eqs. (1)-(3)).



### Infrared Spectroscopy

The infrared spectra of compounds (1)-(6) were recorded in the range 4000-400 cm<sup>-1</sup> using KBr optics. Tentative assignments were made on the basis of earlier work and important data are listed in Experimental section. The absorptions of interest were those of carbonyl  $\nu(\text{C=O})$ ,  $\nu(\text{Sn-C})$  and  $\nu(\text{Sn-O})$ . In spectra of the complexes, medium to weak bands in the region 480-430 cm<sup>-1</sup> were assigned to Sn-O [26] and those in the region of 552-520 cm<sup>-1</sup> were assigned to Sn-C bonds [27].

The carbonyl absorption of diorganotin dicarboxylates was apparently more complicated than that 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 absorption in the IR spectra, but if there are two carbonyl absorptions in the IR spectra, the two carbonyl groups have different coordination environments [28]. In all organotin compounds, the  $\Delta\nu$  is less than 200 cm<sup>-1</sup>, which indicates a bidentate coordination mode for the carboxylate ligand. These indications suggest that the tin atom in di- and triorganotin species approaches six or five coordination, respectively.

### NMR Spectroscopy

**<sup>1</sup>H NMR.** The <sup>1</sup>H NMR data of the sodium salt of ligand acid and its organotin derivatives in  $\text{CDCl}_3$  solution are given in Experimental section. The methyl protons of (1) appear as sharp singlets at 1.17 ppm. The CH<sub>2</sub> protons of (2) resonate as a quartet at 1.81 ppm and CH<sub>3</sub> protons resonate as a triplet at 1.38 ppm with <sup>3</sup>J(<sup>1</sup>H,<sup>1</sup>H) = 8.0 and 7.9 Hz, respectively. Similarly, the CH<sub>2</sub> protons of (3) appear as triplet in the range 1.78-1.82 ppm with <sup>2</sup>J(<sup>119</sup>Sn,<sup>1</sup>H) = 72.9 and <sup>3</sup>J(<sup>1</sup>H,<sup>1</sup>H) = 8.0 Hz; CH<sub>2</sub> protons appear as a triplet with <sup>3</sup>J(<sup>1</sup>H,<sup>1</sup>H) = 7.2 Hz. In compound (6), CH<sub>3</sub> resonates as a triplet at 0.83 ppm with

$$^3J(^1\text{H}, ^1\text{H}) = 7.5 \text{ Hz.}$$

**$^{13}\text{C}$  NMR.** The  $^{13}\text{C}$  NMR spectral data in  $\text{CDCl}_3$  solution of the ligand acid and its di- and triorganotin(IV) derivatives (1)-(6) are given in the Experimental section. The number of signals found correspond with the presence of magnetically nonequivalent carbon atoms which were assigned analogues as model compounds [29,30]. The position of carboxylate carbon moves to lower field in all the complexes as compared with the ligand acid, indicating the participation of the carboxylic group in coordination with tin(IV) [31]. The C-7 of methylene group does not show any shift in the complexes, which means that this site is not involved in bonding to tin but rather the bonding is through -COO group.

The identification of alkyl/phenyl carbons in all the complexes confirms the complexation, and the complete assignment of the signals confirms the identity of the compounds. The coupling constant  $^nJ[^{119}\text{Sn}, ^{13}\text{C}]$  and the values of the inter-bond angles C-Sn-C are most important indicators for the structural elucidation of organotin(IV) carboxylates [32-34]. In order to gain further information about the possible coordination geometries in the solution, a close examination of the  $^1J[^{119}\text{Sn}-^{13}\text{C}]$  and  $^2J[^{119}\text{Sn}-^1\text{H}]$  coupling constants was undertaken, as structural details such as the determination of C-Sn-C bond angles can be enumerated by the use of the literature methods [35,36]. Data are summarized in Table 1. As indicated by Nadvornik and co-workers [30,36] and  $^1J[^{119}\text{Sn}-^{13}\text{C}]$  coupling constant is, instead, quite amenable for making predictions about the geometry around the tin atom. For the *n*-tributyltin(IV) derivative, with the  $^1J[^{119}\text{Sn}-^{13}\text{C}]$  value being 350.6 Hz and by the use of the Holecek and Lycka equation [31], a C-Sn-C value of  $111.6^\circ$  was calculated, which corresponded to a

quasi-tetrahedral geometry in  $\text{CDCl}_3$  solution. The geometric data just described, are consistent with tetrahedral geometries for the triorganotin(IV) species, *i.e.* monomer in solution. For the diorganotin(IV) species, for which earlier results indicate five coordination, the calculated C-Sn-C angles are consistent with the skew-trapezoidal bipyramidal geometries, with the apparent lower coordination number arising from the asymmetric coordination mode of the carboxylate ligands.

**$^{119}\text{Sn}$  NMR.** The  $^{119}\text{Sn}$  NMR spectra were recorded where the chemical shifts for the triorganotin(IV) derivatives lie in the range of tetrahedral geometry, whereas the diorganotin(IV) derivatives show the higher coordination. Data are given in the Experimental section. These values are strongly dependent upon the nature and the orientation of 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 [37].

### Mass Spectrometry

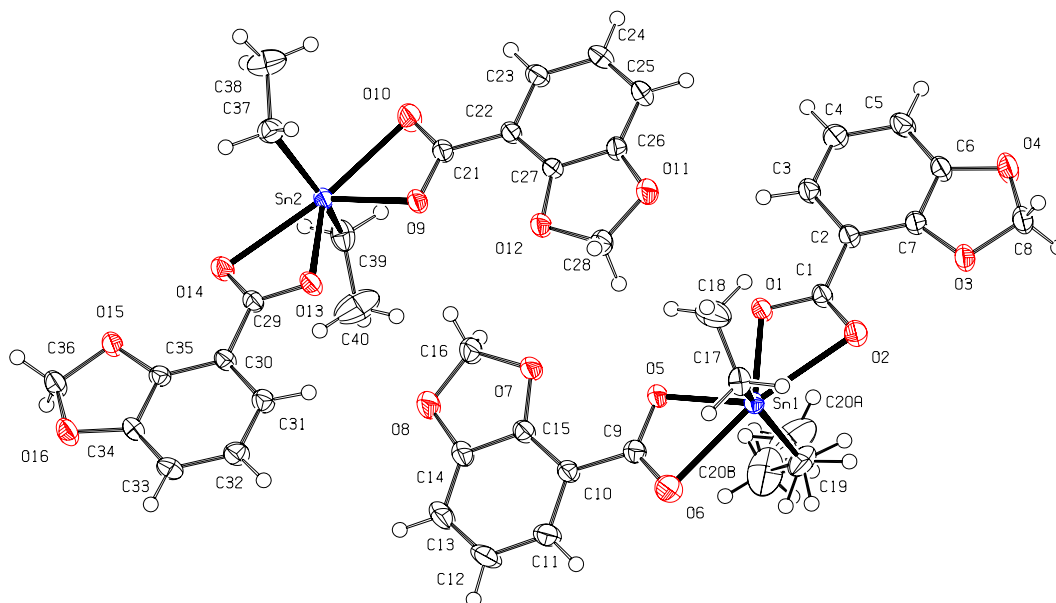
The 70 eV mass spectral data using Electron Impact (EI) method for the reported compounds are given in Experimental section. The molecular ion peak is not observed in all the organotin(IV) carboxylates. The fragment ions are in good agreement with the expected structures of the compounds. Base peak for compounds (1) and (2) is due to  $[\text{C}_5\text{H}_5]^+$  and  $[\text{Sn}(\text{C}_6\text{H}_5\text{COO})]^+$ , respectively, while in compound (3), it is due to  $[\text{C}_4\text{H}_9]^+$ . Other fragments observed are quite intense as given in the Experimental section.

### Crystal Structure

Figure 2 shows the molecular structure and atomic numbering scheme of complex (2). The crystal data and

**Table 1.** C-Sn-C Angles ( $^\circ$ ) Calculated from NMR

Compound No.	$^1J[^{119}\text{Sn}-^{13}\text{C}]$ (Hz)	$^2J[^{119}\text{Sn}-^1\text{H}]$ (Hz)	C-Sn-C Angles ( $^\circ$ ) calculated from	
			$^1J$	$^2J$
(1)	-	78.5	-	129.0
(2)	545.8	74.5	124.6	124.4
(3)	-	72.9	-	122.7
(5)	462.8	-	122.1	-
(6)	350.6	-	111.6	-



**Fig. 2.** ORTEP drawing of the X-ray structure of complex (2).

intermolecular bond distances and angles are given in Tables 2 and 3, respectively. The unit cell of compound (2) contains two crystallographically independent molecules A and B. Conformations of two independent molecules are almost the same, with only minor differences in bond lengths and bond angles.

The coordination geometry of Sn(IV) is an octahedral in which two ethyl groups are in trans position while the ligand oxygen atoms occupy the apical plane. In this way the ligand behaves as a bidentate specie and chelates the tin atom by means of carboxylate oxygens. The consequence is the formation of six member ring. The O(1)-Sn(1)-O(6) bond angle in molecule A is  $136.52(5)^\circ$  and O(6)-Sn(1)-O(2) bond angle is  $167.89(5)^\circ$ . The Sn-C bond distances are [2.116(18) and 2.118(2) Å]. In molecule B, as seen in Fig. 2, O(13)-Sn(2)-O(10) bond angle is  $136.69(4)^\circ$  and O(10)-Sn(2)-O(14) bond angle is  $167.50(5)^\circ$  which suggests octahedral structure [38-40] for complex (2).

### Microbial Assay

**Antibacterial activity.** The organotin(IV) complexes were tested against the three Gram-positive bacterial strains, *Bacillus subtilis* (ATCC 6633), *Micrococcus leuteus* (ATCC 10240) and *Staphylococcus aureus* (ATCC 6538) and three

Gram-negative bacterial strains, *Escherichia coli* (ATCC 15224), *Enterobacter aerogenes* (ATCC 13048) and *Bordetella bronchiseptica* (ATCC 4617). The agar well-diffusion method [41] was used and each experiment was done in triplicate. The results are shown in Table 4.

The antibacterial studies show that complexes (1) and (6) do not show any activity towards bacterial strain, while complex (3) exhibits some non-significant activity against all the bacterial strains; however, a lower activity was shown by them as compared to standard drugs. Complex (5) has shown a significant activity against the *Staphylococcus aureus* (ATCC 6538) and *Enterobacter aerogenes* (ATCC 13048), while no activity was shown against *Bacillus subtilis* (ATCC 6633) and *Micrococcus leuteus* (ATCC 10240).

**Antitumor potato disc assay.** The organotin(IV) complexes (1-5) were screened against *Agrobacterium tumefaciens* (At10) mediated tumor by crown gall tumor inhibition assay with the concentration of 1000 ppm for the incubation period of 21 days to check their antitumor activity [41] by using the formula:

$$\% \text{Inhibition of tumors} = 100 - \frac{ns}{nc} \times 100$$

ns = Average number of tumors in sample  
nc = Average number of tumors in control

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**Table 2.** Crystal Data and Structure Refinement Parameters for Complex (2)

Empirical formula	C <sub>20</sub> H <sub>20</sub> O <sub>8</sub> Sn
Formula weight	507.05
Crystal system	Triclinic
Space group	P-1
Unit cell dimension	
a (Å)	10.709(6)
b (Å)	12.613(8)
c (Å)	16.574(13)
α (°)	111.813(5)
β (°)	106.234(6)
γ (°)	93.944(5)
V (Å <sup>3</sup> )	1958.0(2)
Z	4
D <sub>c</sub> (g cm <sup>-3</sup> )	1.720
Crystal size (mm)	0.40 × 0.25 × 0.20
F(000)	1016
Total reflections	10548
Independent reflections	8765
All indices (all data)	R <sub>1</sub> = 0.0326, WR <sub>2</sub> = 0.0562
Final R indices [I > 2σ(I)]	R <sub>1</sub> = 0.0230, WR <sub>2</sub> = 0.0538
Goodness of fit	1.027
θ Range for data collection (°)	1.75-29.21
Date/restraints/parameters	10548/0/537

**Table 3.** Selected Bond Lengths (Å) and Bond Angles (°) for Complex (2)

Bond lengths	
Sn(1)-C(17)	2.116(18)
Sn(1)-C(19)	2.118 (2)
Sn(1)-O(5)	2.158(13)
Sn(1)-O(6)	2.490(16)
Sn(1)-O(2)	2.530(14)
Sn(2)-C(39)	2.119(19)
Sn(2)-C(37)	2.120(19)
Sn(2)-O(13)	2.129(13)
Sn(2)-O(9)	2.155(13)
Sn(2)-O(10)	2.457(15)
Bond angles	
C(17)-Sn(1)-C(19)	147.31(8)
C(17)-Sn(1)-O(1)	102.93(6)
C(19)-Sn(1)-O(1)	101.25(8)
C(17)-Sn(1)-O(5)	104.81(6)
C(17)-Sn(1)-O(6)	89.43(7)
O(1)-Sn(1)-O(6)	136.52(5)
O(6)-Sn(1)-O(2)	167.89(5)
C(37)-Sn(2)-O(9)	102.66(7)
O(13)-Sn(2)-O(10)	136.69(5)
O(10)-Sn(2)-O(14)	167.50(4)
O(13)-Sn(2)-O(14)	55.71(4)

**Table 4.** Antibacterial Bioassay of Organotin(IV) Carboxylates

Comp. No.	Zone of inhibition (mm)					
	<i>S. aureus</i>	<i>B. subtilis</i>	<i>M. luteus</i>	<i>Ent. aerog</i>	<i>E. coli</i>	<i>Bor. bron</i>
(1)	-	-	-	-	-	-
(3)	5.76 ± 0.11	4.7 ± 0.43	2.1 ± 0.30	3.0 ± 0.20	4.26 ± 0.11	5.7 ± 0.4
(5)	19.9 ± 0.00	-	-	12.53 ± 0.1	5.4 ± 0.20	8.2 ± 0.20
(6)	-	-	-	-	-	-
Rox.	13.3 ± 0.2	4.3 ± 0.17	9.16 ± 0.15	19.3 ± 0.20	15.93 ± 0.45	5.12 ± 0.40
Cef.	17.73 ± 0.5	29.56 ± 0.7	26.73 ± 0.75	4.83 ± 0.05	33.13 ± 0.05	28.5 ± 0.2

**Table 5.** Antitumor Activity<sup>a,b</sup> of Organotin(IV) Carboxylates

Comp. No.	Average number of tumors + SE	%Inhibition of tumors
(1)	3.5 ± 0.67	53.94
(2)	0.0 ± 0.00	100
(3)	0.0 ± 0.00	100
(4)	4.2 ± 1.01	44.73
(5)	0.0 ± 0.00	100
Cis-Cristine <sup>b</sup>	0.0 ± 0.00	100.00
-ive Control	7.6 ± 0.68	

<sup>a</sup>Concentration: 1000 ppm of DMSO. <sup>b</sup>Reference drug; cis-Cristine.

For each test sample 15 replicates were used to study this activity and their average value was used to determine % tumor inhibition and more than 20% tumor inhibition was considered as significant activity [42,43]. All the reported complexes show the significant antitumor activity. The data are given in Table 5.

## CONCLUSIONS

Organotin(IV) complexes of 2,3-methylenedioxybenzoic acid were synthesized in anhydrous toluene and characterized by various analytical and spectroscopic techniques. Detailed studies of the reported complexes indicate tetrahedral geometry for triorganotin(IV) complexes, but skew-trapezoidal geometry by diorganotin(IV) complexes in the solution state. In solid state, the diorganotin complexes show the distorted octahedral geometry, which is also confirmed by X-ray structure of complex (2). These complexes were checked for their antibacterial activity against different bacteria by agar well diffusion which showed significant activity with few exceptions. Antitumor activity data show that the reported complexes have a significant antitumor effect against the tested bacterial strain At10.

## SUPPLEMENTARY MATERIAL

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 624059 for complexes (2). 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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