

Synthesis, Spectroscopic Studies and Biological Applications of Organotin(IV) Derivatives of 3-[N-(4-Nitrophenyl)-amido]propenoic Acid and 3-[N-(4-Nitrophenyl)-amido]propanoic Acid

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New organotin(IV) derivatives with general formulae R_2SnL_2 and R_3SnL , where R = methyl, n-butyl, n-octyl and phenyl and HL is either 3-[N-(4-nitrophenyl)amido]-propenoic acid or 3-[N-(4-nitrophenyl)amido]propanoic acid have been synthesized in 1 : 2 and 1 : 1 molar ratio by different methods. The FTIR spectra clearly demonstrated that the organotin(IV) moieties react with [O,O] atoms of the ligands. The bonding and coordination behavior in these complexes are discussed on the basis of multinuclear (1H , ^{13}C , ^{119}Sn) NMR and mass spectrometric studies. Antibacterial, and antifungal screening tests were performed for these compounds and reported here. These values were compared to those of the precursors and it was found that diorganotin(IV) complexes exhibit less activity as compared to triorganotin(IV) complexes. LD₅₀ data were obtained by Brine Shrimp assay method. Insecticidal activity was performed for selective compounds by contact toxicity method.

Key Words : Organotin(IV) carboxylates, Spectroscopic characterization, Biological activity

Introduction

The synthesis of organotin(IV) carboxylates has received considerable attention during the last three decades.¹⁻¹⁰ Increasing interest in generating these complexes lies in the possibility to enhance biological activities associated with the respective organotin(IV) and unreacted carboxylate compounds.

The biological importance of organotin(IV) has been supported by studies concentrating on structure-activity correlations¹¹⁻¹⁸ that dealt mainly with structural aspects and antitumour activity, and also linked with possible tumorigenic activity. Indeed, butyltins present genotoxic effects,^{19,20} and may predispose animals to malignancy. Several studies have reported that ligands containing oxygen and nitrogen atoms as donor sites are often involved in compounds with potential antitumour activity.²¹⁻²⁷

In order to obtain better insight into how the metallic species behave inside biological systems, it is necessary to study their coordination behaviour with ligands that can occur in the biological medium, and hence to formulate the structure-activity correlations to devise new derivatives with potential antitumour activity. This explains why attention has shifted towards metal derivatives of amino acids and peptides.

Our current interest in the synthesis of organotin(IV) carboxylates²⁸⁻³² prompted us to extend our investigation in the synthesis of new organotin(IV) carboxylates, which could have biological properties. This paper describes the synthesis of new organotin(IV) carboxylates of 3-[N-(4-nitrophenyl)amido]propenoic acid and 3-[N-(4-nitrophenyl)amido]propanoic acid.

All compounds were characterized by IR, 1H , ^{13}C , ^{119}Sn NMR and mass spectrometry. These complexes were

screened against various bacteria, fungi and insects to investigate their possible as antibacterial and antifungal agents. LD₅₀ values were obtained for these compounds by using Brine Shrimp assay method and the data are reported in this paper.

Experimental Section

Materials and Instrumentation. All the glass apparatus with standard quick fit joints was used throughout the work after cleaning and drying at 120 °C. Maleic anhydride, succinic anhydride, *p*-nitroaniline, chloroform and petroleum ether from Aldrich, glacial acetic acid from Merck and toluene from Fluka were purchased. Solvents were purified by standard methods³³ while other chemicals were used as supplied. Melting points were determined with a Mitamura Rikero Kogyo (Japan) and are uncorrected. Mass spectra were recorded on a MAT 8500 Finnigan (Germany). The 1H and ^{13}C NMR spectra were recorded on a Bruker AM-250 MHz spectrometer using $CDCl_3$ as internal reference. ^{119}Sn NMR spectra were obtained on a Bruker 250 ARX instrument with Me_4Sn as external reference.

Preparation of 3-[N-(4-Nitrophenyl)-amido]propenoic Acid (HL¹). A solution of maleic anhydride (10 g, 0.1 mol) in acetic acid (300 mL) was added to a solution of *p*-nitroaniline (13.8 g, 0.1 mol) in acetic acid (150 mL) and the mixture was stirred at room temperature overnight. The light yellow precipitates were filtered, washed with cold distilled H_2O (200 mL) and air dried. Yield 85%, m.p. °C. Analysis: Calculated for $C_{10}H_8N_2O_5$: C, 50.85; H, 3.41; N, 11.86. Found: C, 50.80; H, 3.45; N, 11.80. 1H NMR ($CDCl_3$, ppm), 8.03-8.06 δ (9.17); 8.14-8.18d (9.17) (-CH=CH-), 7.64-7.68m ($NO_2-C_6H_4$), 6.9s (-NH). ^{13}C NMR ($CDCl_3$, ppm), 137.8 (C-1), 132.3 (C-2/6), 134.6 (C-3/5), 126.3 (C-4),

166.0 (C-7), 124.4 (C-8), 114.1 (C-9), 196.6 (C-10).

3-[N-(4-Nitrophenyl)amido]propanoic Acid (HL²). A solution of succinic anhydride (9.8 g, 0.1 mol) in acetic acid (300 mL) was added to a solution of *p*-nitroaniline (13.80 g, 0.099 mol) in acetic acid (150 mL) and the mixture was stirred at room temperature overnight. The light yellow precipitates were filtered, washed with cold distilled H₂O (200 mL) and air dried. Yield 85%, m.p. °C. Analysis: Calculated for C₁₀H₁₀N₂O₅: C, 50.42; H, 4.23; N, 11.76. Found: C, 50.45; H, 4.19; N, 11.71. ¹H NMR (CDCl₃, ppm), 8.07-8.11d (9.2); 8.34-8.36d (9.2) (-CH₂-CH₂-), 7.60-7.63m (NO₂-C₆H₄), 7.28s (-NH). ¹³C NMR (CDCl₃, ppm), 136.9 (C-1), 132.0 (C-2/6), 134.4 (C-3/5), 126.8 (C-4), 167.0 (C-7), 124.3 (C-8), 118.2 (C-9), 192.1 (C-10).

Preparation of Complexes. Me₂Sn(L¹)₂ (1): 3-[N-(4-Nitrophenyl)amido]propenoic acid (1 g, 4.23 mmol) was suspended in dry toluene (100 mL) and treated with triethylamine (0.59 mL, 4.23 mmol). The mixture was refluxed for 2-3 hours. To a solution of triethylammonium 3-[N-(4-nitrophenyl)amido]propenoate in dry toluene, dimethyltin dichloride (2.11 mmol) was added as a solid to a reaction flask with constant stirring and reaction mixture was refluxed for 8-10 hours. The reaction mixture contained Et₃NHCl was filtered off such that filtrate had the organotin(IV) derivative. The solvent was removed through rotary apparatus under reduced pressure. The mass left behind was recrystallized from CHCl₃ and pet.ether (1 : 1). Yield 85%, m.p. 105 °C. Analysis: Calculated for C₂₀H₂₀N₄O₁₀Sn: C, 38.77; H, 3.23; N, 9.04. Found: C, 38.65; H, 3.20; N, 9.12. ¹H NMR (CDCl₃, ppm), 8.02-8.06d (8.98); 8.14-8.32d (8.98) (-CH=CH-), 7.63-7.67m (NO₂-C₆H₄), 6.9s (-NH), 1.2s [78.5] (Sn-CH₃). ¹³C NMR (CDCl₃, ppm), 138.0 (C-1), 132.6 (C-2/6), 134.6 (C-3/5), 126.3 (C-4), 168.4 (C-7), 124.4 (C-8), 113.3 (C-9), 178.4 (C-10), 29.68 (C-11).

IR (KBr, cm⁻¹), 3392s ν(NH), 1720s ν(C=O), 1555s ν(COO_{asym}), 1402s ν(COO_{sym}), Δν 155, 580m ν(Sn-C), 405m ν(Sn-O). Mass data m/z(%); RSnOOCR' 368 (n.o), SnOOCR' 353 (n.o), R₂Sn⁺ 149 (n.o), C₆H₅⁺ 76 (8), [Sn]⁺ 120 (22), C₇H₅O₃N⁺ 165 (6), CNHO⁺ 43 (6), [C₆H₅]⁺ 77 (2), C₆H₅N₂O₂⁺ 138 (100). δ(¹¹⁹Sn) ppm; -98.3.

Ph₂Sn(L¹)₂ (2): 3-[N-(4-Nitrophenyl)amido]propenoic acid (1 g, 4.23 mmol) was suspended in dry toluene (100 mL) and treated with triethylamine (0.59 mL, 4.23 mmol). The mixture was refluxed for 2-3 hours. To a solution of triethylammonium 3-[N-(4-nitrophenyl)amido]propenoate in dry toluene, diphenyltin dichloride (2.11 mmol) was added as a solid to a reaction flask with constant stirring and reaction mixture was refluxed for 8-10 hours. The reaction mixture contained Et₃NHCl was filtered off such that filtrate had the organotin(IV) derivative. The solvent was removed through rotary apparatus under reduced pressure. The mass left behind was recrystallized from CHCl₃ and pet.ether (1 : 1). Yield 70%, m.p. 121-122 °C. Analysis: Calculated for C₃₂H₂₄N₄O₁₀Sn: C, 51.68; H, 3.23; N, 7.53. Found: C, 51.32; H, 3.30; N, 7.49.

¹H NMR (CDCl₃, ppm), 8.05-8.06d (9.08); 8.35-8.36d (9.08) (-CH=CH-), 7.68-7.71m (NO₂-C₆H₄), 6.9s (-NH),

7.28m (Sn-C₆H₅). ¹³C NMR (CDCl₃, ppm), 137.1 (C-1), 132.4 (C-2/6), 134.6 (C-3/5), 126.7 (C-4), 168.5 (C-7), 124.4 (C-8), 113.3 (C-9), 176.8 (C-10), 137.1 (C-11), 136.1 (C-12), 129.1 (C-13), 128.4 (C-14).

IR (KBr, cm⁻¹), 3378s ν(NH), 1725s ν(C=O), 1599s ν(COO_{asym}), 1424s ν(COO_{sym}), Δν 175, 440s ν(Sn-O). Mass data m/z(%); RSnOOCR' 429 (5), SnOOCR' 353 (4), R₂Sn⁺ 271 (7), C₆H₅⁺ 76 (n.o), [Sn]⁺ 120 (2), C₇H₅O₃N⁺ 165 (2), CNHO⁺ 43 (9), [C₆H₅]⁺ 77 (6), C₆H₅N₂O₂⁺ 138 (100). δ(¹¹⁹Sn) ppm; -98.4.

Oct₂Sn(L¹)₂ (3): 3-[N-(4-Nitrophenyl)amido]propenoic acid (1 g, 4.23 mmol) was suspended in dry toluene (100 mL) and treated with equimolar in a reaction flask with constant stirring and mixture was refluxed for 8-10 hours. Water formed was removed via Dean and Stark trap. The solvent was removed through rotary apparatus under reduced pressure. The mass left behind was recrystallized from CHCl₃ and pet.ether (1 : 1). Yield 86%, m.p. 98 °C. Analysis: Calculated for C₃₆H₄₈N₄O₁₀Sn: C, 53.00; H, 5.88; N, 6.87. Found: C, 53.20; H, 5.77; N, 6.84.

¹H NMR (CDCl₃, ppm), 8.02-8.05d (9.08) 8.32-8.36d (9.08) (-CH=CH-), 7.60-7.68m (NO₂-C₆H₄), 6.9s (-NH), 0.83-1.9m (Sn-C₈H₁₃). ¹³C NMR (CDCl₃, ppm), 138.2 (C-1), 132.5 (C-2/6), 134.6 (C-3/5), 126.3 (C-4), 168.4 (C-7), 124.4 (C-8), 114.5 (C-9), 175.0 (C-10), 34.1 (C-11), 31.9 (C-12), 29.5 (C-13), 26.3 (C-14), 26.3 (C-15), 25.8 (C-16), 23.4 (C-17), 14.9 (C-18).

IR (KBr, cm⁻¹), 3349s ν(NH), 1701m ν(C=O), 1560s ν(COO_{asym}), 1412s ν(COO_{sym}), Δν 148, 520m ν(Sn-C), 410m ν(Sn-O). Mass data m/z(%); RSnOOCR' 465 (n.o), SnOOCR' 353 (2), R₂Sn⁺ 345 (10), C₆H₅⁺ 76 (n.o), [Sn]⁺ 120 (n.o), C₇H₅O₃N⁺ 165 (n.o), CNHO⁺ 43 (12), [C₆H₅]⁺ 77 (n.o), C₆H₅N₂O₂⁺ 138 (100).

Me₂Sn(L²)₂ (4): 3-[N-(4-nitro-phenylamido)propanoic acid (1 g, 4.20 mmol) was suspended in dry toluene (100 mL) and treated with triethylamine (0.58 mL, 4.20 mmol). The mixture was refluxed for 2-3 hours. To a solution of triethylammonium 3-[N-(4-nitrophenyl)amido]propanoate in dry toluene, dimethyltin dichloride (2.10 mmol) was added as a solid to a reaction flask with constant stirring and reaction mixture was refluxed for 8-10 hours. The reaction mixture contained Et₃NHCl was filtered off such that filtrate had the organotin(IV) derivative. The solvent was removed through rotary apparatus under reduced pressure. The mass left behind was recrystallized from CHCl₃ and pet.ether (1 : 1). Yield 86%, m.p. 92 °C. Analysis: Calculated for C₂₂H₂₄N₄O₁₀Sn: C, 42.37; H, 3.85; N, 8.98. Found: C, 41.98; H, 3.79; N, 9.10.

¹H NMR (CDCl₃, ppm), 8.11-8.15d (9.0); 8.38-8.42d (9.0) (-CH₂-CH₂-), 7.64-7.67m (NO₂-C₆H₄), 7.32s (-NH), 1.31s [79.1] (Sn-CH₃). ¹³C NMR (CDCl₃, ppm), 137.8 (C-1), 132.6 (C-2/6), 134.5 (C-3/5), 126.3 (C-4), 167.6 (C-7), 124.4 (C-8), 118.3 (C-9), 175.3 (C-10), 29.7 (C-11).

IR (KBr, cm⁻¹), 3362s ν(NH), 1752s ν(C=O), 1586s ν(COO_{asym}), 1440s ν(COO_{sym}), Δν 146, 542m ν(Sn-C), 452m ν(Sn-O). Mass data m/z(%); RSnOOCR' 608 (n.o), SnOOCR' 593 (n.o), R₂Sn⁺ 149 (6), C₆H₅⁺ 76 (5), [Sn]⁺ 120

(6), $\text{C}_3\text{H}_4\text{O}^+$ 55 (68), $[\text{R}_2\text{SnOOCCH}_2\text{CH}_2]^+$ 220 (100), $\text{C}_7\text{H}_5\text{O}_3\text{N}^+$ 165 (10), CNHO^+ 43 (18), $\text{C}_3\text{H}_5\text{NO}^+$ 71 (19), $[\text{C}_6\text{H}_5]^+$ 77 (1), $\text{C}_6\text{H}_5\text{N}_2\text{O}_2^+$ 138 (5).

Bu₂Sn(L²)₂ (5): 3-[N-(4-nitro-phenylamido)]propanoic acid (1 g, 4.20 mmol) was suspended in dry toluene (100 mL) and treated with triethylamine (0.58 mL, 4.20 mmol). The mixture was refluxed for 2-3 hours. To a solution of triethylammonium 3-[N-(4-nitrophenyl)amido]propanoate in dry toluene, dibutyltin dichloride (2.10 mmol) was added as a solid to a reaction flask with constant stirring and reaction mixture was refluxed for 8-10 hours. The reaction mixture contained Et₃NHCl was filtered off such that filtrate had the organotin(IV) derivative. The solvent was removed through rotary apparatus under reduced pressure. The mass left behind was recrystallized from CHCl₃ and pet.ether (1 : 1). Yield 90%, m.p. 62 °C. Analysis: Calculated for C₂₈H₃₆N₄O₁₀Sn: C, 47.52; H, 5.09; N, 7.92. Found: C, 47.45; H, 5.11; N, 8.01.

¹H NMR (CDCl₃, ppm), 8.10-8.13d (9.0); 8.37-8.41d (9.0) (-CH₂-CH₂-), 7.63-7.71m (NO₂-C₆H₄), 7.32s (-NH), 0.8t, 1.30-1.55m (Sn-C₄H₉). ¹³C NMR (CDCl₃, ppm), 137.6 (C-1), 132.8 (C-2/6), 134.2 (C-3/5), 126.3 (C-4), 167.8 (C-7), 124.4 (C-8), 113.3 (C-9), 175.3 (C-10), 29.7 (C-11), 27.3 (C-12), 26.7 (C-13), 13.6 (C-14).

IR (KBr, cm⁻¹), 3351s ν(NH), 1742s ν(C=O), 1578s ν(COO_{asym}), 1420s ν(COO_{sym}), Δν 158, 552w ν(Sn-C), 480m ν(Sn-O). Mass data m/z(%); R₂SnOOCR' 650 (n.o), SnOOCR' 593 (n.o), R₂Sn⁺ 233 (n.o), C₆H₅⁺ 76 (n.o), [Sn]⁺ 120 (8), C₃H₄O⁺ 55 (3), [R₂SnOOCCH₂CH₂]⁺ 220 (8), C₇H₅O₃N⁺ 165 (2), CNHO⁺ 43 (8), C₃H₅NO⁺ 71 (13), [C₆H₅]⁺ 77 (9), C₆H₅N₂O₂⁺ 138 (9), C₄H₉⁺ 57 (100). δ(¹¹⁹Sn) ppm; -88.3.

Oct₂Sn(L²)₂ (6): 3-[N-(4-Nitrophenyl)amido]propanoic acid (1 g, 4.20 mmol) was suspended in dry toluene (100 mL) and treated with equimolar in a reaction flask with constant stirring and mixture was refluxed for 8-10 hours. Water formed was removed via Dean and Stark trap. The solvent was removed through rotary apparatus under reduced pressure. The mass left behind was recrystallized from CHCl₃ and pet.ether (1 : 1).

Yield 78%, m.p. 170 °C. Analysis: Calculated for C₃₆H₅₂N₄O₁₀Sn: C, 52.74; H, 6.34; N, 6.83. Found: C, 52.63; H, 6.39; N, 6.81.

¹H NMR (CDCl₃, ppm), 8.07-8.10d (9.0); 8.34-8.37d (9.0) (-CH₂-CH₂-), 7.60-7.69m (NO₂-C₆H₄), 7.28s (-NH), 0.89-1.73m (Sn-C₆H₅). ¹³C NMR (CDCl₃, ppm), 137.2 (C-1), 132.4 (C-2/6), 134.9 (C-3/5), 126.9 (C-4), 167.2 (C-7), 124.4 (C-8), 118.6 (C-9), 175.8 (C-10), 33.9 (C-11), 31.9 (C-12), 29.6 (C-13), 29.3 (C-14), 26.3 (C-15), 25.3 (C-16), 24.2 (C-17), 12.3 (C-18).

IR (KBr, cm⁻¹), 3395s ν(NH), 1732s ν(C=O), 1580s ν(COO_{asym}), 1400s ν(COO_{sym}), Δν 180, 532m ν(Sn-C), 472m ν(Sn-O). Mass data m/z(%); R₂SnOOCR' 706 (n.o), SnOOCR' 356 (100), R₂Sn⁺ 345 (n.o), C₆H₅⁺ 76 (6), [Sn]⁺ 120 (5), C₃H₄O⁺ 55 (100), [R₂SnOOCCH₂CH₂]⁺ 220 (97), C₇H₅O₃N⁺ 165 (16), CNHO⁺ 43 (11), C₃H₅NO⁺ 71 (18), [C₆H₅]⁺ 77 (6), C₆H₅N₂O₂⁺ 138 (12). δ(¹¹⁹Sn) ppm; -148.7.

Me₃Sn(L¹) (7): 3-[N-(4-Nitrophenyl)amido]propanoic acid (1 g, 4.23 mmol) was suspended in dry toluene (100 mL) and treated with triethylamine (0.59 mL, 4.23 mmol). The mixture was refluxed for 2-3 hours. To a solution of triethylammonium 3-[N-(4-nitrophenyl)amido]propanoate in dry toluene, trimethyltin chloride (4.23 mmol) was added as a solid to a reaction flask with constant stirring and reaction mixture was refluxed for 8-10 hours. The reaction mixture contained Et₃NHCl was filtered off such that filtrate had the organotin(IV) derivative. The solvent was removed through rotary apparatus under reduced pressure. The mass left behind was recrystallized from CHCl₃ and pet.ether (1 : 1). Yield 77%, m.p. 45-46 °C. Analysis: Calculated for C₁₃H₁₇N₂O₅Sn: C, 39.00; H, 4.25; N, 7.00. Found: C, 39.22; H, 4.19; N, 7.11.

¹H NMR (CDCl₃, ppm), 8.00-8.03d (9.08); 8.09-8.13d (9.08) (-CH=CH-), 7.63-7.66m (NO₂-C₆H₄), 6.9s (-NH), 0.74s [57.17] (Sn-CH₃). ¹³C NMR (CDCl₃, ppm), 137.9 (C-1), 132.5 (C-2/6), 134.2 (C-3/5), 126.3 (C-4), 168.5 (C-7), 124.4 (C-8), 113.3 (C-9), 181.6 (C-10), 29.68 (C-11). IR (KBr, cm⁻¹), 3334s ν(NH), 1724s ν(C=O), 1597s ν(COO_{asym}), 1415s ν(COO_{sym}), Δν 182, 550m ν(Sn-C), 420m ν(Sn-O). Mass data m/z(%); R₂SnOOCR' 385 (43), R₂SnOOCR' 370 (35), SnOOCR' 354 (2), R₃Sn⁺ 164 (5), R₂Sn⁺ 149 (12), C₆H₅⁺ 76 (9), [Sn]⁺ 120 (4), C₇H₅O₃N⁺ 165 (n.o), CNHO⁺ 43 (20), [C₆H₅]⁺ 77 (n.o), C₆H₅N₂O₂⁺ 138 (100). δ(¹¹⁹Sn) ppm; 113.14.

Bu₃Sn(L¹) (8): 3-[N-(4-Nitrophenyl)amido]propanoic acid (1 g, 4.23 mmol) was suspended in dry toluene (100 mL) and treated with triethylamine (0.59 mL, 4.23 mmol). The mixture was refluxed for 2-3 hours. To a solution of triethylammonium 3-[N-(4-nitrophenyl)amido]propanoate in dry toluene, trimethyltin chloride (4.23 mmol) was added as a solid to a reaction flask with constant stirring and reaction mixture was refluxed for 8-10 hours. The reaction mixture contained Et₃NHCl was filtered off such that filtrate had the organotin(IV) derivative. The solvent was removed through rotary apparatus under reduced pressure. The mass left behind was recrystallized from CHCl₃ and pet.ether (1 : 1). Yield 89%, m.p. 79-80 °C. Analysis: Calculated for C₃₂H₃₄N₂O₅Sn: C, 50.28; H, 6.47; N, 5.33. Found: C, 50.31; H, 6.38; N, 5.40.

¹H NMR (CDCl₃, ppm), 8.06-8.10d (9.08); 8.20-8.24d (9.08) (-CH=CH-), 7.79-7.85m (NO₂-C₆H₄), 6.79s (-NH), 0.89t, 1.27-1.69m (Sn-C₄H₉). ¹³C NMR (CDCl₃, ppm), 136.9 (C-1), 130.3 (C-2/6), 134.7 (C-3/5), 126.4 (C-4), 167.2 (C-7), 124.9 (C-8), 113.6 (C-9), 176.8 (C-10), 29.6 (C-11), 27.9 (C-12), 16.8 (C-13), 13.6 (C-14). IR (KBr, cm⁻¹), 3366s ν(NH), 1710s ν(C=O), 1587s ν(COO_{asym}), 1430s ν(COO_{sym}), Δν 142, 575m ν(Sn-C), 430w ν(Sn-O). Mass data m/z(%); R₂SnOOCR' 469 (100), R₂SnOOCR' 411 (n.o), SnOOCR' 351 (2), R₃Sn⁺ 291 (4), R₂Sn⁺ 233 (7), C₆H₅⁺ 76 (9), [Sn]⁺ 120 (3), C₇H₅O₃N⁺ 165 (n.o), CNHO⁺ 43 (22), [C₆H₅]⁺ 77 (9), C₆H₅N₂O₂⁺ 138 (13), [C₄H₉]⁺ 57 (4). δ(¹¹⁹Sn) ppm; 59.5.

Ph₃Sn(L¹) (9): 3-[N-(4-Nitrophenyl)amido]propanoic acid (1 g, 4.23 mmol) was suspended in dry toluene (100

mL) and treated with triethylamine (0.59 mL, 4.23 mmol). The mixture was refluxed for 2-3 hours. To a solution of triethylammonium 3-[N-(4-nitrophenyl)amido]propanoate in dry toluene, trimethyltin chloride (4.23 mmol) was added as a solid to a reaction flask with constant stirring and reaction mixture was refluxed for 8-10 hours. The reaction mixture contained Et₃NHCl was filtered off such that filtrate had the organotin(IV) derivative. The solvent was removed through rotary apparatus under reduced pressure. The mass left behind was recrystallized from CHCl₃ and pet.ether (1 : 1). Yield 87%, m.p. 63 °C. Analysis: Calculated for C₂₈H₂₃N₂O₅Sn: C, 57.33; H, 3.92; N, 4.77. Found: C, 57.41; H, 3.96; N, 4.71.

¹H NMR (CDCl₃, ppm), 8.02-8.05d (8.98); 8.29-8.33d (8.98) (-CH=CH-), 7.65-7.66m (NO₂-C₆H₄), 6.88s (-NH), 7.44-7.45m (C₆H₅). ¹³C NMR (CDCl₃, ppm), 137.2 (C-1), 130.5 (C-2/6), 134.5 (C-3/5), 126.3 (C-4), 167.2 (C-7), 124.9 (C-8), 114.3 (C-9), 174.4 (C-10), 136.5 (C-11), 135.7 (C-12), 129.1 (C-13), 125.4 (C-14). IR (KBr, cm⁻¹), 3382s ν (NH), 1729s ν (C=O), 1587s ν (COO_{asym}), 1430s ν (COO_{sym}), Δν 157, 425m ν (Sn-O). Mass data m/z(%); R₂SnOOCR' 505 (2), RSnOOCR' 429 (3), SnOOCR' 351 (n.o), R₃Sn⁺ 347 (26), R₂Sn⁺ 271 (n.o), C₆H₅⁺ 76 (3), [Sn]⁺ 120 (4), C₇H₅O₃N⁺ 165 (n.o), CNHO⁺ 43 (9), [C₆H₅]⁺ 77 (4), C₆H₅N₂O₂⁺ 138 (100). δ (¹¹⁹Sn) ppm; -98.2.

Me₃Sn(L²) (10): 3-[N-(4-nitro-phenylamido)]propanoic acid (1 g, 4.20 mmol) was suspended in dry toluene (100 mL) and treated with triethylamine (0.58 mL, 4.20 mmol). The mixture was refluxed for 2-3 hours. To a solution of triethylammonium 3-[N-(4-nitrophenyl)amido]propanoate in dry toluene, trimethyltin chloride (4.20 mmol) was added as a solid to a reaction flask with constant stirring and reaction mixture was refluxed for 8-10 hours. The reaction mixture contained Et₃NHCl was filtered off such that filtrate had the organotin(IV) derivative. The solvent was removed through rotary apparatus under reduced pressure. The mass left behind was recrystallized from CHCl₃ and pet.ether (1 : 1). Yield 80%, m.p. 75 °C. Analysis: Calculated for C₁₃H₁₈N₂O₅Sn: C, 38.90; H, 4.48; N, 6.98. Found: C, 39.11; H, 4.45; N, 6.88.

¹H NMR (CDCl₃, ppm), 8.07-8.10d (9.0); 8.34-8.38d (9.0) (-CH₂-CH₂-), 7.59-7.63m (NO₂-C₆H₄), 7.28s (-NH), 0.73s [58.2] (Sn-CH₃). ¹³C NMR (CDCl₃, ppm), 137.8 (C-1), 132.5 (C-2/6), 134.6 (C-3/5), 126.3 (C-4), 167.5 (C-7), 124.3 (C-8), 118.6 (C-9), 175.3 (C-10), -1.3 (C-11).

IR (KBr, cm⁻¹), 3345s ν (NH), 1760s ν (C=O), 1590s ν (COO_{asym}), 1425s ν (COO_{sym}), Δν 165, 562w ν (Sn-C), 428m ν (Sn-O). Mass data m/z(%); R₂SnOOCR' 386 (2), RSnOOCR' 371 (n.o), SnOOCR' 356 (n.o), R₃Sn⁺ 164 (8), R₂Sn⁺ 149 (n.o), C₆H₅⁺ 76 (n.o), [Sn]⁺ 120 (4), C₃H₄O⁺ 55 (7), [R₂SnOOCCH₂CH₂]⁺ 220 (11), C₇H₅O₃N⁺ 165 (72), CNHO⁺ 43 (7), C₃H₅NO⁺ 71 (18), [C₆H₅]⁺ 77 (3), C₆H₅N₂O₂⁺ 138 (100). δ (¹¹⁹Sn) ppm; 170.7.

Bu₃Sn(L²) (11): 3-[N-(4-nitro-phenylamido)]propanoic acid (1 g, 4.20 mmol) was suspended in dry toluene (100 mL) and treated with triethylamine (0.58 mL, 4.20 mmol). The mixture was refluxed for 2-3 hours. To a solution of

triethylammonium 3-[N-(4-nitrophenyl)amido]propanoate in dry toluene, tributyltin chloride (4.20 mmol) was added as a solid to a reaction flask with constant stirring and reaction mixture was refluxed for 8-10 hours. The reaction mixture contained Et₃NHCl was filtered off such that filtrate had the organotin(IV) derivative. The solvent was removed through rotary apparatus under reduced pressure. The mass left behind was recrystallized from CHCl₃ and pet.ether (1 : 1). Yield 60%, m.p. 132-133 °C. Analysis: Calculated for C₂₂H₃₆N₂O₅Sn: C, 50.09; H, 6.83; N, 5.31. Found: C, 50.21; H, 6.91; N, 5.28.

¹H NMR (CDCl₃, ppm), 8.05-8.09d (9.0); 8.33-8.36d (9.0) (-CH₂-CH₂-), 7.59-7.71m (NO₂-C₆H₄), 7.28s (-NH), 0.89t, 1.26-1.67m (Sn-C₄H₉). ¹³C NMR (CDCl₃, ppm), 137.5 (C-1), 132.9 (C-2/6), 134.7 (C-3/5), 126.5 (C-4), 167.9 (C-7), 124.9 (C-8), 118.7 (C-9), 175.6 (C-10), 29.6 (C-11), 27.7 (C-12), 26.8 (C-13), 13.5 (C-14).

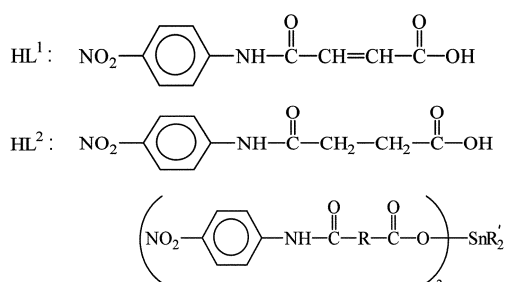
IR (KBr, cm⁻¹), 3356s ν (NH), 1701s ν (C=O), 1558s ν (COO_{asym}), 1379s ν (COO_{sym}), Δν 179, 520m ν (Sn-C), 433w ν (Sn-O). Mass data m/z(%); R₂SnOOCR' 470 (17), RSnOOCR' 413 (2), SnOOCR' 356 (6), R₃Sn⁺ 290 (14), R₂Sn⁺ 233 (41), C₆H₅⁺ 76 (2), [Sn]⁺ 120 (13), C₃H₄O⁺ 55 (49), [R₂SnOOCCH₂CH₂]⁺ 220 (14), C₇H₅O₃N⁺ 165 (18), CNHO⁺ 43 (47), C₃H₅NO⁺ 71 (19), [C₆H₅]⁺ 77 (11), C₆H₅N₂O₂⁺ 138 (17), C₄H₉⁺ 57 (100). δ (¹¹⁹Sn) ppm; 157.2.

Ph₃Sn(L²) (12): 3-[N-(4-nitro-phenylamido)]propanoic acid (1 g, 4.20 mmol) was suspended in dry toluene (100 mL) and treated with triethylamine (0.58 mL, 4.20 mmol). The mixture was refluxed for 2-3 hours. To a solution of triethylammonium 3-[N-(4-nitrophenyl)amido]propanoate in dry toluene, triphenyltin chloride (4.20 mmol) was added as a solid to a reaction flask with constant stirring and reaction mixture was refluxed for 8-10 hours. The reaction mixture contained Et₃NHCl was filtered off such that filtrate had the organotin(IV) derivative. The solvent was removed through rotary apparatus under reduced pressure. The mass left behind was recrystallized from CHCl₃ and pet.ether (1 : 1). Yield 88%, m.p. 105 °C. Analysis: Calculated for C₂₈H₂₄N₂O₅Sn: C, 57.24; H, 4.08; N, 4.77. Found: C, 57.29; H, 4.02; N, 4.73.

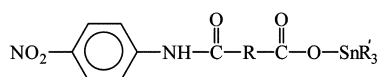
¹H NMR (CDCl₃, ppm), (8.07-8.10d (9.0); 8.32-8.34d (9.0) (-CH₂-CH₂-), 7.61-7.65m (NO₂-C₆H₄), 7.27s (-NH), 7.43-7.44m (Sn-C₆H₅). ¹³C NMR (CDCl₃, ppm), 137.3 (C-1), 132.2 (C-2/6), 134.8 (C-3/5), 126.3 (C-4), 167.4 (C-7), 124.6 (C-8), 118.9 (C-9), 177.6 (C-10), 136.1 (C-11), 135.8 (C-12), 129.1 (C-13), 125.4 (C-14).

IR (KBr, cm⁻¹), 3386s ν (NH), 1720s ν (C=O), 1599s ν (COO_{asym}), 1429s ν (COO_{sym}), Δν 170, 446m ν (Sn-O). Mass data m/z(%); R₂SnOOCR' 510 (n.o), RSnOOCR' 433 (n.o), SnOOCR' 356 (20), R₃Sn⁺ 347 (53), R₂Sn⁺ 271 (12), C₆H₅⁺ 76 (3), [Sn]⁺ 120 (24), C₃H₄O⁺ 55 (n.o), [R₂SnOOCCH₂CH₂]⁺ 220 (n.o), C₇H₅O₃N⁺ 165 (n.o), CNHO⁺ 43 (3), C₃H₅NO⁺ 71 (5), [C₆H₅]⁺ 77 (100), C₆H₅N₂O₂⁺ 138 (21). δ (¹¹⁹Sn) ppm; -46.7.

General chemical reactions are given in Scheme 1 and numbering for NMR is given in Scheme 2.

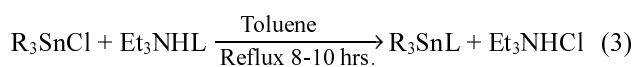
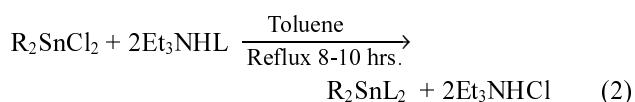
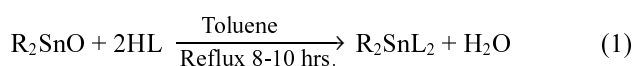


Comp. No.	R	R'
(1)	—CH=CH—	Me(CH ₃)
(2)	—CH=CH—	Ph(C ₆ H ₅)
(3)	—CH=CH—	Oct(C ₈ H ₁₇)
(4)	—CH ₂ —CH ₂ —	Me(CH ₃)
(5)	—CH ₂ —CH ₂ —	Bu(C ₄ H ₉)
(6)	—CH ₂ —CH ₂ —	Oct(C ₈ H ₁₇)



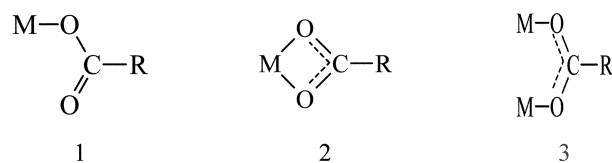
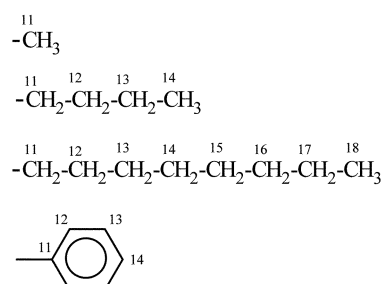
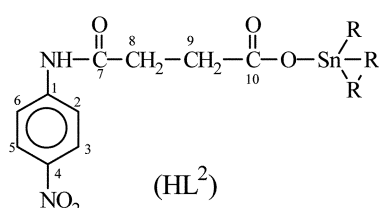
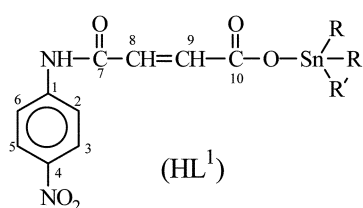
Comp. No.	R	R'
(7)	$-\text{CH}=\text{CH}-$	$\text{Me}(\text{CH}_3)$
(8)	$-\text{CH}=\text{CH}-$	$\text{Bu}(\text{C}_4\text{H}_9)$
(9)	$-\text{CH}=\text{CH}-$	$\text{Ph}(\text{C}_6\text{H}_5)$
(10)	$-\text{CH}_2-\text{CH}_2-$	$\text{Me}(\text{CH}_3)$
(11)	$-\text{CH}_2-\text{CH}_2-$	$\text{Bu}(\text{C}_4\text{H}_9)$
(12)	$-\text{CH}_2-\text{CH}_2-$	$\text{Ph}(\text{C}_6\text{H}_5)$

Scheme 1



Results and Discussion

With few exceptions all the complexes are coloured solids.



Scheme 3. Possible coordination modes of carboxylate group to metal.

They are slightly soluble in cold methanol and *n*-hexane but freely soluble in DMSO and CHCl_3 . The complexes have sharp melting points. The metal derivatives are stable at room temperature and are non-hygroscopic.

Infrared Spectra. The FTIR data are consistent with the formation of compounds with the composition R_2SnL_2 and R_3SnL . The carboxylate group ligands coordinate to metal ions by different modes as shown in Scheme 3.³⁴

Disappearance of a broad band in the spectra of the complexes in the region 2800-2200 cm^{-1} , which was present in free ligands as a weak intensity band, suggests the deprotonation of the free COOH group upon complexation.

The presence of Sn-C absorption bands in all complexes in the region 520-580 cm^{-1} confirms the formation of Sn-C bond in all complexes.

The appearance of very weak and wide band in the region of 405-480 cm^{-1} assigned to $\nu_{\text{asym}}(\text{Sn-O})$, indicate the formation of Sn-O bond.

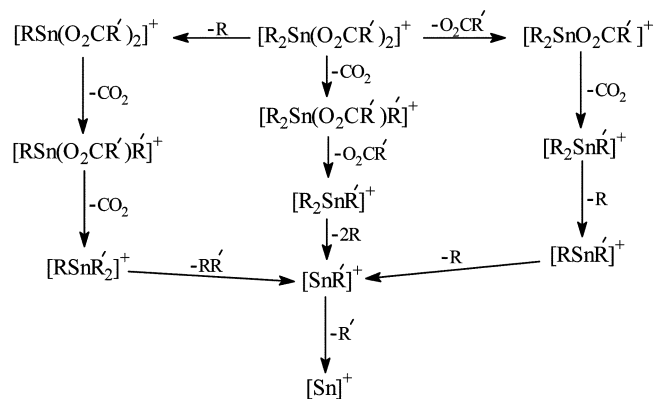
The carboxylate group generally adopts a bridged structure in the solid state unless the organic substituents at the tin atom are bulky or the carboxylate group is branched at α -carbon.³⁵ The IR absorption spectra indicate that $\nu_{\text{asym}}(\text{COO})$ values ($1520\text{--}1599\text{ cm}^{-1}$) and $\nu_{\text{sym}}(\text{COO})$ values ($1379\text{--}1465\text{ cm}^{-1}$) reveal the strong interaction between the oxygens and the tin atom. The magnitude of the $(\nu_{\text{asym}} - \nu_{\text{sym}})\text{COO} = (\Delta\nu)$ separation, which has been shown to be useful in identifying structural features, lies in the range $142\text{--}182\text{ cm}^{-1}$ which confirm the bidentate nature of the ligand.³⁶

Mass Spectrometry. Molecular ion peak was exceptionally observed in some of the complexes. All compounds lose an alkyl or aryl group first, followed by elimination of CO₂ and other neutral species which ultimately gives C₆H₅⁺. Another possible route is disintegration of the ligand and stepwise elimination of R groups to give Sn⁺ as the end product.

Base peak in the compounds (1)-(3) is due to fragment $[C_6H_5O_2N_2]^+$ at m/z 138 (100), while in compounds (4), (5)

Scheme 2

In studied complexes, the CO(OH) resonance of the ligands is absent which suggests the replacement of the carboxylic proton by the organotin(IV) moiety. $^3J(^1\text{H}, ^1\text{H})$ values for HL¹ compounds (1)–(3) and (7)–(9) suggests that protons of acetylene group (HC=HC) are in the cis position. In all diorganotin(IV) and triorganotin(IV) derivatives, the –NH resonance observed as a broad or a sharp weak signal. The aromatic carbon resonances were assigned by comparing experimental chemical shifts with those calculated by the incremental method.³⁷ In triorganotin carboxylates $^2J[^{119}\text{Sn}-^1\text{H}]$ for compounds (7) and (8) suggests tetrahedral geometry (Fig. 1(a)) around the tin atom. Unlike the triorganotin carboxylates in solution, the geometry of diorganotin dicarboxylates cannot be defined with certainty because of dynamic process involving in carboxylate oxygens due to competition in their coordination behaviour with the tin atom.³⁸ However, in the solid state the tin atom is mostly


$$\begin{array}{ccccc}
 [\text{R}_3\text{Sn}]^+ & \xleftarrow{-\text{O}_2\text{CR}'} & [\text{R}_3\text{SnO}_2\text{CR}']^+ & \xrightarrow{-\text{R}} & [\text{R}_2\text{SnO}_2\text{CR}']^+ \\
 \downarrow -\text{R} & & & & \downarrow -\text{CO}_2 \\
 [\text{R}_2\text{Sn}]^+ & & & & [\text{R}_2\text{SnR}']^+ \\
 \downarrow -\text{R} & & & & \downarrow -\text{R} \\
 [\text{RSn}]^+ & \xrightarrow{-\text{R}} & [\text{Sn}]^+ & \xleftarrow{-\text{RR}'} & [\text{RSnR}']^+
 \end{array}$$

Chemical structures (a) and (b) are shown. Structure (a) depicts a tin atom (Sn) coordinated by a carbonyl group (C=O) and three R groups. Structure (b) depicts a tin atom (Sn) coordinated by two oxygen atoms (O) and two R groups, with additional bonds to carbon atoms (C) and oxygen atoms (O) forming a cyclic structure.

In all complexes, ^{119}Sn spectra show only a sharp singlet indicating the formation of single species. In general ^{119}Sn chemical shifts move to lower frequency with increasing coordination number. Although the shift ranges are somewhat dependent on the nature of the substituents at the tin

Comp. No.	Dose (µg/mL)	No. of Shrimps	No. of Survivors	LD ₅₀ (µg/mL)
HL ¹	100	30	5	74.16
	10	30	9	
	1	30	10	
(1)	100	30	0	< 1
	10	30	0	
	1	30	0	
(2)	100	30	0	7.14
	10	30	10	
	1	30	30	
(3)	100	30	10	—
	10	30	10	
	1	30	10	
(7)	100	30	10	—
	10	30	10	
	1	30	10	
(8)	100	30	0	25.94
	10	30	8	
	1	30	10	
(9)	100	30	0	1.90
	10	30	1	
	1	30	9	

Standard drug; Etoposide
LD₅₀ (μg/mL); 7.4625.

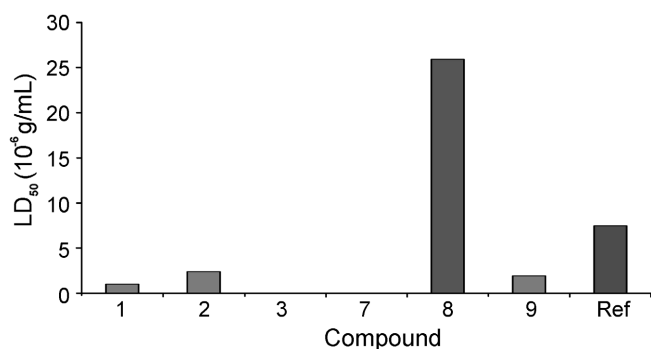


Figure 2. Cytotoxic study of organotin(IV) derivatives.

atom. In all the complexes, ¹¹⁹Sn chemical shifts values lie in the tetrahedral environment around the tin atom in non-coordinated solvents.

Biological Activity: LD₅₀ data of the compound (1)-(3) and (7)-(9) have been determined by the Brine-Shrimp assay method⁴⁰ and the results are summarized in Table 1 and Figure 2. Previous reports^{41,42} show that the nature of organic group is responsible for the toxicity of organotin compounds. The highest toxicity being shown by the ligand with LD₅₀ value 74.16 μg/mL while the compounds (3) and (7) do not show any toxicity at all. Antibacterial activity tests of compounds (1)-(3) and (7)-(9) were carried out against various bacteria by the “agar diffusion technique”.⁴³ The screening tests show that phenyltin carboxylates are the most potent candidates against the tested bacteria. The activity of the other derivatives varies according to their R groups. However, all of these compounds are active against *Bacillus subtilis*. The results are given in Table 2 and Figure 3.

Compounds (1)-(11) were also tested for their antifungal

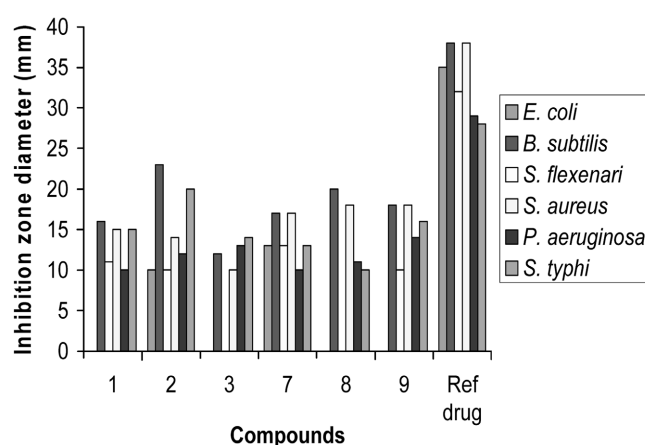


Figure 3. Antibacterial activity of organotin(IV) derivatives against various bacteria.

activity by the tube diffusion method.⁴⁴ The results of antifungal assay are given in Table 3 and Figure 4. It has been shown that the ligand along with its organotin carboxylates are significantly active against all of the tested fungal strains. It has been reported that, within the given series, the triorganotin(IV) derivatives are more active against fungi⁴⁵ as compared to diorganotin(IV) derivatives. The insecticidal activity data of the compounds (4)-(6) and (10)-(12) are given in Table 4 and Figure 5. It shows that diorganotin(IV) dicarboxylates are found to be inactive against the tested insects while the triorganotin(IV) carboxylates shows the activity. It can be explained as the length or number of R group increases, activity also increases. That's why triorganotin(IV) derivatives show more activity as compared to diorganotin derivatives and butyl derivatives show more activity than methyl derivatives.

Table 2. Antibacterial Activity for R₂SnL₂¹/R₂SnL₂² and R₃SnL¹/R₃SnL²

Name of Bacteria	Compound No.							Standard Drug
	HL ¹	(1)	(2)	(3)	(7)	(8)	(9)	
<i>Escherichia coli</i>	11	—	10	—	13	—	—	Ampicilline (H ₂ O) ₃ Cephalixin Na
<i>Bacillus subtilis</i>	17	16	23	12	17	20	18	"
<i>Shigella flexenari</i>	11	11	10	—	13	—	10	"
<i>Staphylococcus aureus</i>	14	15	14	10	17	18	18	"
<i>Pseudomonas aeruginosa</i>	10	10	12	13	10	11	14	"
<i>Salmonella typhi</i>	11	15	20	14	13	10	16	"

Table 3. Antifungal Activity for R₂SnL₂¹/R₂SnL₂² and R₃SnL¹/R₃SnL²

Name of Fungi	Compound No.													Standard Drug
	HL ¹	HL ²	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	
<i>Trichophyton longifusus</i>	57.8	70	78.9	45	47.3	75	75	75	78.9	100	84.2	70	70	Miconazole, Ketoconazole
<i>Candida albicans</i>	63.1	10	0	0	0	10	0	10	68.4	100	100	25	0	Miconazole, Ketoconazole
<i>Aspergillus flavies</i>	0	60	0	0	10	60	60	70	0	100	100	70	60	Amphotericin B, Flucytosine
<i>Microsporium canis</i>	40	30	0	40	47.3	30	35	40	73	90	88	30	30	Miconazole, Ketoconazole
<i>Fusarium solani</i>	15	30	50	70	0	30	0	10	70	90	80	0	0	Ketoconazole
<i>Candida glabrata</i>	0	10	0	0	0	10	10	10	0	100	94.7	0	0	Ketoconazole

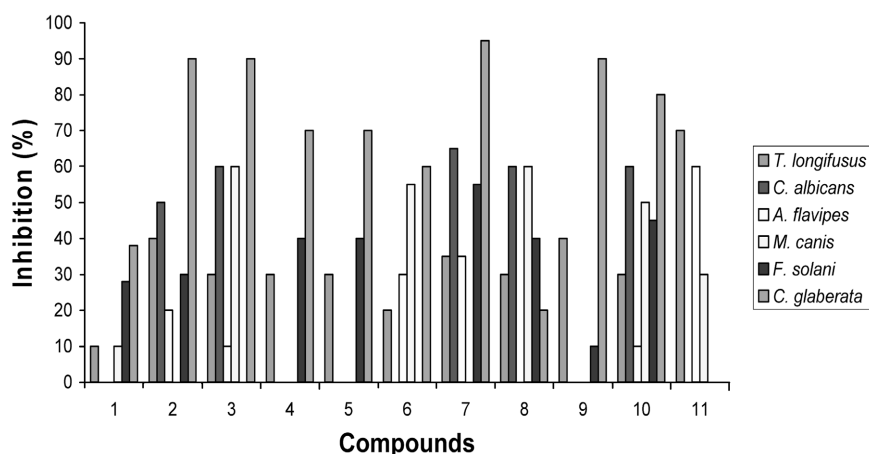


Figure 4. Antifungal activity of organotin(IV) derivatives against various fungi.

Table 4. Insecticidal activity data for R_2SnL_2 and R_3SnL_2

Name of Insect	% Mortality (–ve Control)							+ve Control	Standard Drug
	HL ²	(4)	(5)	(6)	(10)	(11)	(12)		
<i>Tribolium castaneum</i>	0	0	0	0	20	25	0	100	Premethrin
<i>Sitophilus oryzae</i>	25	0	0	0	0	25	25	100	Premethrin
<i>Rhyzopertha dominica</i>	0	0	0	0	25	0	0	100	Premethrin
<i>Callosobruchus analis</i>	0	0	0	0	20	25	0	100	Premethrin

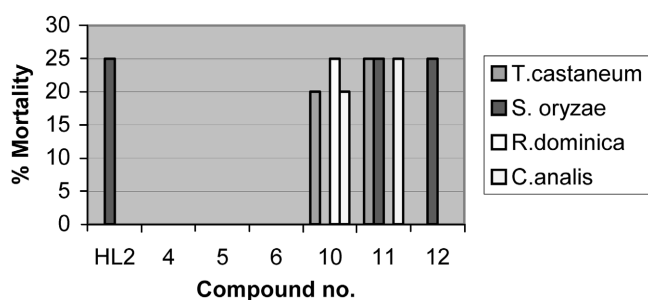


Figure 5. Insecticidal activity of organotin(IV) derivatives.

Conclusion

It was concluded that in solid state organotin(IV) carboxylates have five or six coordination around tin, due to bidentate nature of carboxylates group, while in solution the bidentate carboxylate group is cleaved and the resulting monomer contains four coordinated tin with a tetrahedral arrangement. All complexes show the primary fragmentation due to the loss of the alkyl group followed by elimination of CO_2 and the remaining part of the ligand, which leaves Sn^+ as the end product. Organotin(IV) carboxylates are found to be active against tested Brine Shrimp larvae, bacteria, fungi and the insects.

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