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New tetrahedral, square-pyramidal, trigonal-bipyramidal and octahedral organotin(IV) 4-ethoxycarbonylpiperazine-1-carbodithioates: Synthesis, structural properties and biological applications

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ABSTRACT

This article describes the synthesis of triorganotin(IV)-, chlorodiorganotin(IV)- and diorganotin(IV) 4-ethoxycarbonylpiperazine-1-carbodithioates with general R_3SnL {where R = CH_3 (**1**), *n*-C_4H_9 (**2**) and C_6H_5 (**3**)}, R_2SnClL {where R = CH_3 (**4**), *n*-C_4H_9 (**5**) and C_6H_5 (**6**)} and R_2SnL_2 {where R = CH_3 (**7**), *n*-C_4H_9 (**8**) and C_6H_5 (**9**)}, respectively. The coordination behavior of ligand (L) in all compounds was investigated by different analytical techniques such as FT-IR and multinuclear NMR. X-ray single crystal analysis confirmed supramolecular structure for compounds (**3**) and (**4**) with distorted trigonal-bipyramidal and distorted square-pyramidal geometries, respectively. The compounds have pronounced antimicrobial (antibacterial and antifungal) potency and moderate insecticidal activity. These compounds also inhibit effectively the activity of urease enzyme.

1. Introduction

Dithiocarboxylate anions are distinguished coordinating agents for metals. The resonance due to these anions is the significant contribution from dithiocarboxylates anions to stabilize the overall electronic structure. These ions play a notable role in medicine also. For example, the diethyldithiocarbamate anion, Et2CNS2 has been used for clinical use as antidote for copper poisoning, i.e., Wilson's disease [1]. Alkyltin(IV) or aryltin(IV) derivatives of dithiocarboxylate ligands have been extensively studied owing to their enormous biological [2,3] and industrial applications [4] with a view to establish structure–biological activity relationship [5–8]. Organotins especially, organotin(IV) dithiocarboxylates have potential apoptotic inducing character and have also high therapeutic index [9–11]. They are good DNA binders and can interact with DNA in two different ways: electrostatic interaction with phosphate group of DNA and intercalative mode in which organotins establish secondary interactions with the nitrogenous bases [6,12]. This alteration of structure hinders DNA replication and the ultimate result is the death of the cancerous cells.

The activity of organotin compounds depends upon the number and nature of R group linked to metal ion as well as on the anionic ligand. In addition to the biological applications, organotin dithiocarboxylates exhibit diverse structural motifs. Depending on the number of R groups present, the mode of coordination of CS_2 moiety and the number of ligands attached to Sn atom, organotin may be tetrahedral, trigonal-bipyramidal, square-pyramidal, octahedral and pentagonal bipyramidal [6,7,12]. The structure of organotins may be monomeric, dimeric, trimeric or supramolecular based on the absence and presence of secondary non-covalent interactions between the ligand molecules [13]. These interactions play also a vital role in the biological applications of organotins. In nutshell, in order to get a good antimicrobial response for the organotins, the attached ligand must have substituents capable of making secondary interactions. Keeping all these factors in mind, we synthesized, characterized organotin(IV) derivatives of a new ligand (4-ethoxycarbonylpiperazine-1-carbodithioate) and screened them for their antimicrobial applications.

2. Experimental

2.1. Materials and methods

The reagents, di- and triorganotin(IV) chlorides, 4-ethoxycarbonylpiperazine and CS_2 were purchased from commercial sources (Aldrich, USA) and were used without further purification.

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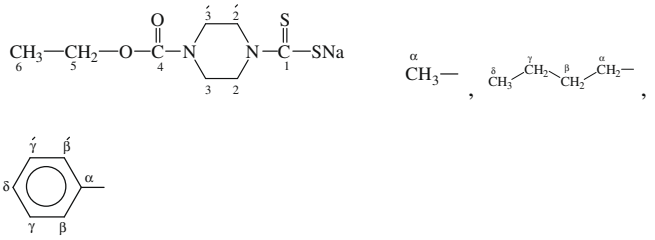
Methanol was dried before use by the literature procedure [14]. The infrared (IR) measurements were taken as KBr pellets on a Bio-Rad Excalibur FT-IR, model FTS 4800 MX spectrophotometer (USA) in the frequency range of 4000–200 cm^{-1}. ^{1}H, ^{13}C, and ^{119}Sn NMR spectra in solution were undertaken using Bruker ARX 300, 400 MHz and Bruker 500 MHz-FT-NMR spectrometers, respectively. The chemical shifts are reported in ppm relative to the external references, tetramethylsilane (TMS) for ^{1}H, ^{13}C and tetramethyltin for ^{119}Sn shifts. The crystallographic studies were carried out on a Nonius Kappa CCD diffractometer with graphite monochromated Mo Kα radiation.



Scheme 2. Numbering of ligand and Sn moieties for ^{1}H and ^{13}C NMR data.

2.2. Synthesis

2.2.1. Sodium 4-ethoxycarbonylpiperazine-1-carbodithioate [NaL]

A stoichiometric amount of 4-ethoxylcarbonylpiperazine (0.72 g, 3.0 mmol) and sodium hydroxide (0.12 g, 3.0 mmol) in methanol (50 mL) was stirred at room temperature for 1 h. To this solution, carbon disulfide (3.0 mmol) was added dropwise and the mixture was stirred for 6 h [13,15]. The solid product (Scheme 1) was washed with diethyl ether and it was air dried (Yield: 1.4 g, 87%). M.p. 158–163 °C. Anal. Calc. for: C, 37.5; H, 5.1; N, 10.9. Found: C, 36.8; H, 4.9; N, 10.4%. IR ν(C–N) 1471, ν(C–S) 1107, ν(C=S) 945. ^{1}H NMR δ (ppm): 2.58–2.63 (4H, m, $H_{2,2'}$), 3.20–3.48 (4H, m, $H_{3,3'}$), 4.49 (2H, q, H_5) ^{3}J[H, H] 7.4 Hz, 1.09 (3H, t, H_6) ^{3}J[H, H] 7.4 Hz. ^{13}C NMR δ (ppm): 203.1 (C_1), 42.9 ($C_{2,2'}$), 51.7 ($C_{3,3'}$), 156.1 (C_4), 61.8 (C_5), 14.4 (C_6).

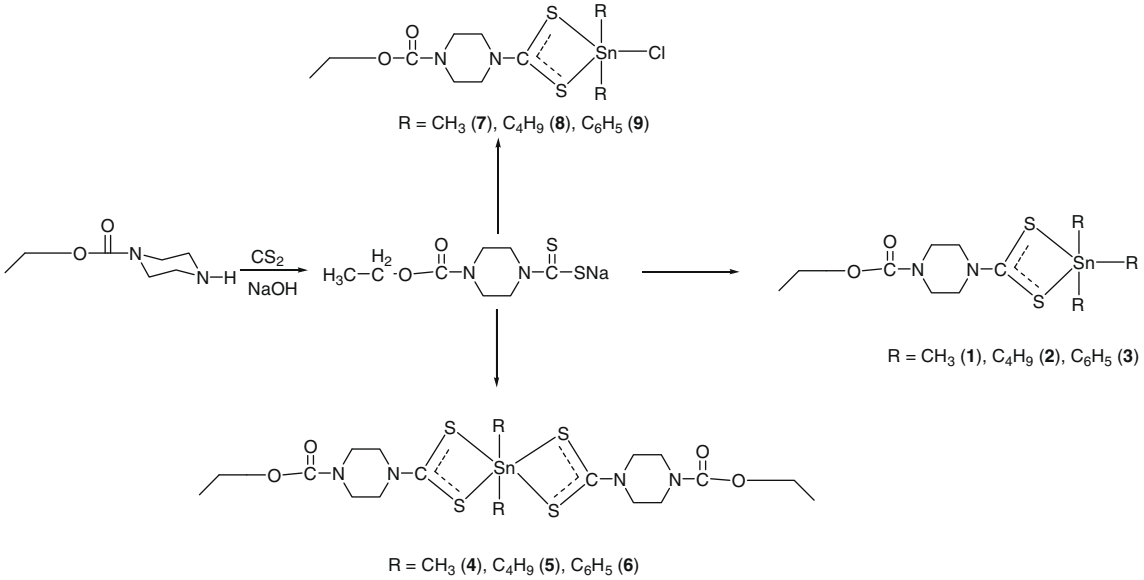
2.2.2. General synthetic procedure for compounds (**1–9**)

Stoichiometric amounts of organotin(IV) chlorides in methanol (30 mL) were added dropwise to the methanolic solution of sodium salt of ligand (NaL) as shown in Scheme 1. The mixture was refluxed for 4 h with constant stirring. The solid product obtained in each case after filtration was recrystallized from chloroform/ethanol mixture. The slow evaporation of the mixture gave crystalline products for compound (**3**) and (**4**). The NMR data for compounds (**1–9**) given below is in accordance with Scheme 2.

*2.2.2.1. Trimethyltin(IV) [4-ethoxylcarbonylpiperazine-1-carbodithioate] (**1**). Stoichiometric amounts:* Trimethyltin(IV) chloride (0.4 g, 1.86 mmol) and sodium salt of 4-ethoxycarbonylpiperazine-1-carbodithioate (0.5 g, 1.86 mmol). (Yield: 83%). M.p. 138–140 °C. Anal. Calc. for: C, 39.0; H, 6.5; N, 8.3. Found: C, 38.7; H, 6.1; N, 7.8%. IR (cm^{-1}) ν(C–N) 1471, ν(C–S) 945, ν(Sn–C) 524, ν(Sn–S) 409. ^{1}H NMR δ (ppm): 2.63–2.68 (4H, m, $H_{2,2'}$), 3.24–3.51 (4H, m, $H_{3,3'}$), 4.56 (2H, q, H_5) ^{3}J[H, H] 7.4 Hz, 1.14 (3H, t, H_6) ^{3}J[H, H] 7.4 Hz, 0.72 (9H, s, H_β) $^{2}J[^{119}Sn,^{1}H]$ = 57 Hz, C–Sn–C 110°. ^{13}C NMR δ (ppm): 192.1 (C_1), 42.9 ($C_{2,2'}$), 51.6 ($C_{3,3'}$), 156.0 (C_4), 61.8 (C_5), 14.6 (C_6) −1.72 (C_α) $^{1}J[^{119}Sn,^{13}C]$ = 386 Hz, C–Sn–C 110°. ^{119}Sn δ (ppm): 138.3.

*2.2.2.2. Tri-n-butyltin(IV) [4-ethoxylcarbonylpiperazine-1-carbodithioate] (**2**). Stoichiometric amounts:* Tri-*n*-butyltin(IV) chloride (0.5 g, 1.53 mmol) and sodium salt of 4-ethoxycarbonylpiperazine-1-carbodithioate (0.4 g, 1.53 mmol). (Yield: 88%). M.p. 118–121 °C. Anal. Calc. for: C, 45.8; H, 7.6; N, 5.3. Found: C, 45.2; H, 7.4; N, 4.0%. IR (cm^{-1}): ν(C–N) 1424, ν(C–S) 957, ν(Sn–C) 518, ν(Sn–S) 422. ^{1}H NMR δ (ppm): 1.59–1.64 (6H, m, H_α), 1.31–1.34 (6H, m, H_β), 1.21–1.31 (6H, m, H_γ), 0.83 (9H, t, H_δ) $^{3}J[^{1}H,^{1}H]$ = 7.4 Hz, 2.38–2.57 (4H, m, $H_{2,2'}$), 3.42–3.52 (4H, m, $H_{3,3'}$), 4.13 (2H, q, H_5) ^{3}J[H, H] = 7.2 Hz, 1.31 (3H, t, H_6) ^{3}J[H, H] 7.2 Hz. ^{13}C NMR δ (ppm): 194.0 (C_1), 44.3 ($C_{2,2'}$), 52.7 ($C_{3,3'}$), 155.4 (C_4), 63.0 (C_5), 14.2 (C_6), 16.1 (C_α) $^{1}J[^{119}Sn,^{13}C]$ = 353 Hz, C–Sn–C, 107°, 26.5 (C_β), 26.1 (C_γ), 14.0 (C_δ). ^{119}Sn NMR δ (ppm): 117.4.

*2.2.2.3. Triphenyltin(IV) [4-ethoxylcarbonylpiperazine-1-carbodithioate] (**3**). Stoichiometric amounts:* Triphenyltin(IV) chloride (0.6 g 1.53 mmol) and sodium salt of 4-ethoxycarbonylpiperazine-1-carbodithioate of ligand (0.4 g, 1.53 mmol) (Yield: 84%). M.p. 178–181 °C. Anal. Calc. for: C, 53.4; H, 4.8; N, 4.8. Found: C, 52.9; H, 4.5; N, 4.3%. IR (cm^{-1}) ν(C–N) 1461, ν(C–S) 943, ν(Sn–C) 241, ν(Sn–S) 415.^{1}H NMR δ (ppm): 2.41–2.56 (4H, m, $H_{2,2'}$), 3.12–3.28



Scheme 1. Schematic diagram for synthesis of NaL and for organotin(IV) compounds (**1–9**).

(4H, m, $H_{3,3'}$), 3.96 (2H, q, H_5) ^3J[H, H] = 7.4 Hz, 1.21 (3H, t, H_6) ^3J[H, H] = 7.4 Hz, 7.71–7.74 (12H, m, H_β, H_γ), 7.12–7.17 (3H, m, H_δ). ^{13}C NMR δ (ppm): 193.6 (C_1), 43.3 ($C_{2,2'}$), 52.2 ($C_{3,3'}$), 155.6 (C_4), 62.3 (C_5), 15.0 (C_6), 128.6, 129.5, 137.0 142.3 (C_α, C_β, C_γ, C_δ). ^{119}Sn NMR δ (ppm): −175.5.

*2.2.2.4. Chlorodimethyltin(IV) [4-ethoxylcarbonylpiperazine-1-carbodithioate] (**4**). Stoichiometric amounts:* Dimethyltin(IV) dichloride (0.50 g, 2.27 mmol) and sodium salt of 4-ethoxycarbonylpiperazine-1-carbodithioate (0.58 g, 2.27 mmol). (Yield: 69%). M.p. 143–146 °C. Anal. Calc. for: C, 28.7; H, 4.5; N, 6.6. Found: C, 28.4; H, 4.3; N, 6.2%. IR (cm^{-1}) ν(C–N) 1476, ν(C–S) 917, ν(Sn–C) 538, ν(Sn–Cl) 312. ^{1}H NMR δ (ppm): 2.46–2.58 (4H, m, $H_{2,2'}$), 3.28–3.43 (4H, m, $H_{3,3'}$), 4.37 (2H, q, H_5) ^3J[H, H] = 7.5 Hz, 1.14 (6H, t, H_6) ^3J[H, H] = 7.5 Hz, 1.06 (6H, s, H_α) ^2J[^{119}Sn,^{1}H] = 75 Hz, C–Sn–C 125°. ^{13}C NMR δ (ppm): 198.0 (C_1), 43.1 ($C_{2,2'}$), 51.5 ($C_{3,3'}$), 155.5 (C_4), 62.5 (C_5), 14.3 (C_6), 7.5 (C_α) ^1J[^{119}Sn,^{13}C] = 607 Hz, C–Sn–C 130°. ^{119}Sn NMR δ (ppm): −185.8.

*2.2.2.5. Chlorodi-n-butyltin(IV) [4-ethoxylcarbonylpiperazine-1-carbodithioate] (**5**). Stoichiometric amounts:* Di-*n*-butyltin(IV) dichloride (0.5 g, 1.64 mmol) and sodium salt of 4-ethoxycarbonylpiperazine-1-carbodithioate (0.42 g, 1.64 mmol). (Yield: 67%). M.p. 110–113 °C. Anal. Calc. for: C, 38.2; H, 6.2; N, 5.6. Found: C, 37.9; H, 5.7; N, 5.4%. IR (cm^{-1}) ν(C–N) 1433, ν(C–S) 941, ν(Sn–C) 541, ν(Sn–S) 457, ν(Sn–Cl) 323. ^{1}H NMR δ (ppm): 2.42–2.51 (4H, m, $H_{2,2'}$), 3.36–3.47 (4H, m, $H_{3,3'}$), 4.07 (2H, q, H_5) ^3J[H, H] 7.4, 1.16 (3H, t, H_6), ^3J[H, H] 7.4 Hz, 1.63–1.66 (4H, m, H_α), 1.53–1.63 (4H, m, H_β), 1.53–1.63 (4H, m, H_γ), 0.89 (6H, t, H_δ) ^3J[H, H] 7.3 Hz. ^{13}C NMR δ (ppm): 195.7 (C_1), 42.4 ($C_{2,2'}$), 53.1 ($C_{3,3'}$), 155.7 (C_4), 61.4 (C_5), 13.8 (C_6), 25.3 (C_α) ^1J[^{119}Sn, ^{13}C] = 604 Hz, C–Sn–C 129°, 27.4 (C_β), 26.2 (C_γ), 13.8 (C_δ). ^{119}Sn NMR δ (ppm): −228.3.

*2.2.2.6. Chlorodiphenyltin(IV) [4-ethoxylcarbonylpiperazine-1-carbodithioate] (**6**). Stoichiometric amounts:* Diphenyltin(IV) chloride (0.40 g, 1.56 mmol) and sodium salt of 4-ethoxycarbonylpiperazine-1-carbodithioate (0.54 g, 1.56 mmol). (Yield: 70%). M.p. 104–108 °C. Anal. Calc. for: C, 44.3; H, 4.2; N, 5.2. Found: C, 44.0; H, 3.7; N, 4.6%. IR (cm^{-1}) ν(C–N) 1463, ν(C–S) 976, ν(Sn–C) 248, ν(Sn–S) 429, ν(Sn–Cl) 361. ^{1}H NMR δ (ppm): 2.46–2.52 (4H, m, $H_{2,2'}$), 3.09–3.16 (4H, m, $H_{3,3'}$), 3.84 (2H, q, H_5) ^3J[H, H] = 7.5 Hz, 1.19 (3H, t, H_6) ^3J[H, H] = 7.5 Hz, 7.59–7.70 (8H, m, H_β, H_γ), 7.42–7.48 (2H, m, H_δ). ^{13}C NMR δ (ppm): 195.4 (C_1), 42.8 ($C_{2,2'}$), 52.1 ($C_{3,3'}$), 154.8 (C_4), 61.5 (C_5), 14.9 (C_6), 129.4 (C_α) ^1J[^{119}Sn, ^{13}C] = 594 Hz, C–Sn–C 129°, 128.6, 135.5, 142.6 (C_β, C_γ, C_δ). ^{119}Sn NMR δ (ppm): −337.2.

*2.2.2.7. Dimethyltin(IV)bis[4-ethoxycarbonylpiperazine-1-carbodithioate] (**7**). Stoichiometric amounts:* Dimethyltin(IV) chloride (0.40 g, 1.56 mmol), sodium salt of 4-ethoxycarbonylpiperazine-1-carbodithioate (0.69 g, 3.1 mmol). (Yield: 75%). M.p. 140–142 °C. Anal. Calc. for: C, 35.0; H, 5.2; N, 9.1. Found: C, 34.6; H, 4.8; N, 8.6%. IR (cm^{-1}) ν(C–N) 1471, ν(C–S) 945, ν(Sn–C) 524, ν(Sn–S) 409. ^{1}H NMR δ (ppm): 2.59–2.62 (8H, m, $H_{2,2'}$), 3.31–3.45 (8H, m, $H_{3,3'}$), 4.62 (4H, q, H_5) ^3J[H, H] = 7.2 Hz, 1.08 (6H, t, H_6) ^3J[H, H] = 7.2 Hz, 1.13 (6H, s, H_α) ^2J[^{119}Sn,^{1}H] = 79 Hz, C–Sn–C 130°. ^{13}C NMR δ (ppm): 196.3 (C_1), 43.7 ($C_{2,2'}$), 52.4 ($C_{3,3'}$), 156.0 (C_4), 62.5 (C_5), 15.3 (C_6), 6.5 (C_α) ^1J[^{119}Sn, ^{13}C] = 593 Hz, C–Sn–C 129°. ^{119}Sn NMR δ (ppm): −197.3.

*2.2.2.8. Di-n-butyltin(IV) bis[4-ethoxylcarbonylpiperazine-1-carbodithioate] (**8**). Stoichiometric amounts:* Di-*n*-butyltin(IV) chloride (0.5 g, 1.64 mmol) and sodium salt of 4-ethoxycarbonylpiperazine-1-carbodithioate (0.84 g, 3.28 mmol). (Yield: 71%). M.p. 110–113 °C. Anal. Calc. for: C, 38.2; H, 6.2; N, 5.6. Found: C, 37.9; H, 5.7; N, 5.4%. IR (cm^{-1}) ν(C–N) 1424, ν(C–S) 957, ν(Sn–C) 518, ν(Sn–S) 422. ^{1}H NMR δ (ppm): 2.94–3.04 (8H, m, $H_{2,2'}$), 3.24–3.47 (8H, m, $H_{3,3'}$), 4.43 (4H, q, H_5) ^3J[H, H] 7.3 Hz, 1.18 (6H, t H_6) ^3J[H, H] 7.3 Hz, 1.66–1.73 (4H, m, H_α), 1.67–1.73 (4H, m, H_β), 1.32–1.52 (4H, m, H_γ), 0.84 (6H, t, H_δ) ^3J[H, H] 7.6 Hz. ^{13}C NMR δ (ppm): 195.5 (C_1), 42.8 ($C_{2,2'}$), 51.6 ($C_{3,3'}$), 154.8 (C_4), 60.8 (C_5), 14.8 (C_6), 24.4 (C_α) ^1J[^{119}Sn, ^{13}C] = 585 Hz, C–Sn–C 128° 27.3 (C_β), 26.4 (C_γ), 14.1 (C_δ). ^{119}Sn NMR δ (ppm): −153.6.

*2.2.2.9. Diphenyltin(IV) bis[4-ethoxylcarbonylpiperazine-1-carbodithioate] (**9**). Stoichiometric amounts:* Diphenyltin(IV) chloride (0.40 g, 1.56 mmol) and sodium salt of 4-ethoxycarbonylpiperazine-1-carbodithioate (1.06 g, 3.12 mmol). (Yield: 74%). M.p. 93–96 °C. Anal. Calc. for: C, 45.4; H, 4.8; N, 7.3. Found: C, 44.8; H, 4.5; N, 7.3%. IR (cm^{-1}): ν(C=N) 1483, ν(C–S) 968, ν(Sn–C) 262, ν(Sn–S) 421. ^{1}H NMR δ (ppm): 2.73–2.85 (8H, m, $H_{2,2'}$), 3.06–3.47 (8H, m, $H_{3,3'}$), 4.26 (4H, q, H_5) ^3J[H, H] = 7.3 Hz, 1.16 (6H, t, H_6) ^3J[H, H] = 7.3 Hz, 7.57–7.64 (8H, m, H_β, H_γ), 7.42–7.48 (2H, m, H_δ). ^{13}C NMR δ (ppm): 197.5 (C_1), 43.3 ($C_{2,2'}$), 52.3 ($C_{3,3'}$), 155.4 (C_4), 62.6 (C_5), 15.0 (C_6), 129.5 (C_α) ^1J[^{119}Sn, ^{13}C] = 589 Hz, C–Sn–C 128°, 128.7, 136.3, 142.2, (C_β, C_γ, C_δ). ^{119}Sn NMR δ (ppm): −314.2.

3. Results and discussion

3.1. IR spectroscopy

In the IR spectra of compounds (**1**–**9**), the vibration modes C–N and CS_2 are of prime interest to differentiate between mono and bidentate coordination of 1,1-dithiolate moiety. The single band appears at 917–976 cm^{-1} is assignable to the CS_2 absorption frequency which indicates the bidentate coordination of 1,1-dithiolate moiety of the ligand to the Sn atom [16,17]. The stretching of the C–N was positioned at frequency (1424–1483 cm^{-1}) that corresponds to a partial double bond character in C–N moiety [6,7]. The presence of delocalized double bond in NCS_2 moiety was further confirmed by X-ray single crystal analysis for complexes **3** and **4**. The observed Sn–C peak, in compounds **1–9**, matched-well with early reports [12,13].

3.2. NMR spectroscopy

The ^{1}H NMR spectra were recorded for the compounds (**1–9**) in DMSO-d_6. The chemical shifts were identified by their intensity and multiplicity patterns. The total numbers of protons, calculated from the integration curves, are in agreement with the expected molecular composition of the compounds. The piperazine protons display two multiplets at chemical shift value of 2.63–2.68 and 3.24–3.31 ppm in the aliphatic region. The ^2J[^{119}Sn, ^{1}H] of the organic groups attached to Sn atom is of special significance for structure elucidation of organotins in solution. In methyl derivatives (**1**), (**4**) and (**7**) small satellites are clearly visible along with the chemical shift value of the methyl moiety, providing ^2J[^{119}Sn, ^{1}H] coupling values of 57, 75 and 79 Hz, respectively. These values correspond to C–Sn–C bond angle of 110°, 125° and 130° thus suggested four (**1**) and penta-coordinated (**4** and **7**) Sn [4,18–20]. Chemical shifts of *n*-butyl and aromatic protons are difficult to assign because of their peaks multiplicity and consequently overlapping of signals. In compounds (**4**), (**5**) and (**6**) integration values demonstrate the attachment of only one ligand to Sn atom.

The ^{13}C NMR chemical shifts due to methyl, *n*-butyl and phenyl groups, attached to Sn atom, were observed at positions comparable to the other similar compounds [21,22]. All the chemical shifts of carbon atoms due to ligand moiety remain unchanged in compounds **1–9** except the CS_2 carbon, that shift upfield, thus confirmed the coordination of ligand via S, S atoms. The unchanged

chemical shift value for carbonyl carbon in all compounds confirmed no coordination through this site. The most distinct feature of ^{13}C NMR is $^{1}J[^{119}Sn, ^{13}C]$ values that can be used to assess mono or bidentate coordination of ligand to the Sn atom. On the basis of $^{1}J[^{119}Sn,^{13}C]$ values, trimethyltin(IV) and tri-*n*-butyltin(IV) derivatives [386 and 353 Hz, respectively] are tetrahedral [23,24]. In case of diorganotin(IV) compounds (**4–9**) the $^{1}J[^{119}Sn,^{13}C]$ coupling constant values in the range 585–607 Hz are in agreement with the analogous five- and six-coordinated organotins [25,26]. It has been suggested that the coupling constants values are associated with the hybridization of the tin atom in organotin compounds and are measured of the percentage of the s orbital character in the Sn–C bond [27]. The Sn–C bond in tetrahedral, trigonal-bipyramidal and octahedral arrangements at the tin atom proceed *via* sp^3, sp^2 and sp hybridization. An increase of the s orbital character (s-orbital electron participation) in the Sn–C bond causes an increase in values of the coupling constants [28]. The coupling constants, $^{2}J[^{119}Sn, ^{1}H]$ provide an effectively informative probe for the assessment of the coordination of tin [27].

^{119}Sn NMR spectroscopy has also been very supportive for the revelation of environment around Sn atom in the organotin(IV) dithiocarboxylates. The presence of single ^{119}Sn peak in the spectra of all compounds indicates the formation of single species. On the basis of $\delta(^{119}Sn)$ value, Sn atom in these organotin is four- (**1** and **2**), five- (**3–6**) and six-coordinated (**7–9**).

3.3. Crystallographic studies

In compound **3**, the geometry around Sn atom can be described as distorted trigonal-bipyramidal with the equatorial plane comprising the C9 and C15 of the phenyl moiety and a sulfur atom, S2, of the ligand. The second sulfur (S1) and a C21 of phenyl group occupied the apical positions (Fig. 1). The $Sn–S_{ax}$ bond length [2.7099(9) Å] is greater than $Sn–S_{eq}$ bond distance indicating asymmetric coordination of ligand. The bond length, $Sn–S_{eq}$ is close to the covalent radii of Sn–S [2.4841(9) Å] and the axial Sn–S bond distance is much shorter than the van der Waals radii of the two atoms (4.0 Å). The asymmetric coordination of ligand is also reflected in C–S bonds, the longer C–S bond is connected with shorter Sn–S bond and vice versa. For a five-coordinated metal, a structural index τ, can be calculated by equation, $\tau = (\beta - \alpha)/60$, where β and α are the consecutive largest angles around the metal center. For perfect square-pyramidal and trigonal-bipyramidal geometry, the τ value is zero and one, respectively [29]. The calculated τ value (0.55) confirmed distorted trigonal-bipyramidal geometry around Sn. Furthermore, the angle of axial S1–Sn–C21 is 156.19° that showed a marked deviation from 180°. These bond distances and angles are in agreement with the corresponding values found for similar Sn complexes [30]. The packing diagram shows (Fig. 2) supramolecular structure mediated by OCO···H–phenyl intermolecular interactions. No secondary intermolecular Sn···S interaction is evident in structure of **3**.

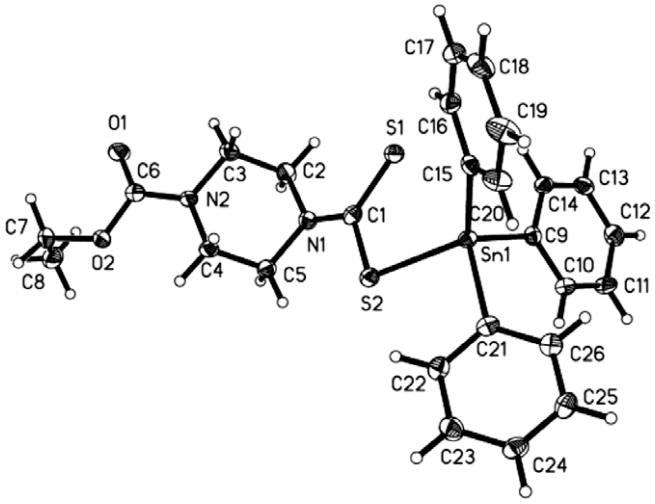


Fig. 1. ORTEP drawing of compound (**3**) with atom numbering scheme.

The crystal data and structure refinement parameters of compound **4** are given in Table 1. The selected bond lengths and angles are shown in Table 2. The crystal structure is shown in Fig. 3. The tin atom is five-coordinated, being chelated by an asymmetrically coordinating dithiocarboxylate ligand, a chloride and two methyl substituents. The Sn1–S1 bond distance (2.70 Å) approximately *trans*- to the chloride atom is longer than the other Sn1–S2 bond distance (2.48 Å) and is an indicative of asymmetric coordination of the ligand. The $Sn–S_{shorter}$ and $Sn–S_{longer}$ distances are comparable with our early reported methyltin(IV) analogue [12]. The coordination geometry is almost intermediate between square-pyramidal and trigonal-bipyramidal having a small bias towards the former, at least based on the values of τ (0.38). The deviation of coordination geometry towards square-pyramidal is presumably

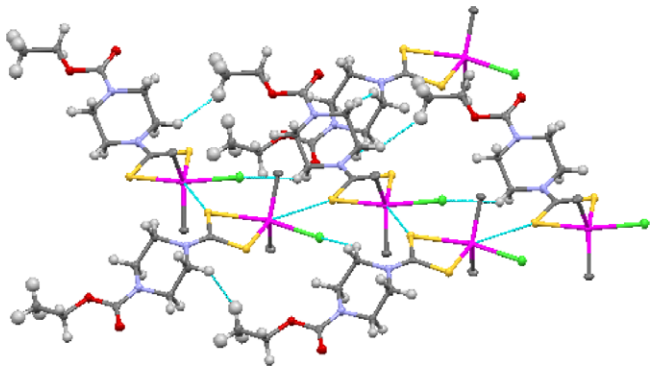


Fig. 2. Packing diagram of compound (**3**).

Table 1
Crystal data and structure refinement parameters for complexes **3** and **4**.

Empirical formula	$C_{26}H_{28}N_2O_2S_2Sn$ (**3**)	$C_{10}H_{13}ClN_2O_2S_2Sn$ (**4**)
Formula weight	583.31	411.48
Crystal system	Triclinic	Monoclinic
Space group	$P\bar{1}$	$C2/c$
A (Å)	9.0433(8)	27.718(2)
B (Å)	11.1221(10)	9.2064(7)
C (Å)	13.0875(11)	12.5099(9)
α (°)	100.4480(10)	90.00
β (°)	94.1200(10)	105.5020(10)
γ (°)	1264.54(19)	90.00
V (Å^3)	1264.54(19)	3076.1(4)
Z	2	8
Density (calculated) (mg/m^3)	1.532	1.777
Crystal size (mm^3)	0.40 × 0.20 × 0.20	0.25 × 0.20 × 0.20
F(0 0 0)	592	1616
Total reflections	5080	4117
Independent reflections	7855 [R_{int} = 0.0176]	3153 [R_{int} = 0.0314]
R indices (all data)	R_1 = 0.0263, wR_2 = 0.0628	R_1 = 0.0338, wR_2 = 0.0720
Final R indices [$I > 2\alpha(I)$]	R_1 = 0.0239, wR_2 = 0.0613	R_1 = 0.0288, wR_2 = 0.0700
Goodness-of-fit (GOF)	1.030	1.054
θ Range for data collection (°)	2.22–26.32	2.34–26.26
Data/restraints/parameters	7855/0/298	3153/0/164

Table 2
Selected bond lengths (Å) and angles (°) for complexes **3** and **4**.

Ph_3SnL (**3**)		Me_2SnClL (**4**)	
Sn1C9	2.134(3)	Sn1S2	2.4841(9)
Sn1C21	2.164(3)	Sn1S1	2.7099(9)
Sn1C15	2.144(3)	Sn1C10	2.131(3)
Sn1S2	2.4683(8)	Sn1C9	2.122(3)
S1C1	1.687(3)	Sn1Cl1	2.4957(9)
S2C1	1.748(3)	S2C1	1.746(3)
C9–Sn1–C15	117.80(11)	C9–Sn1–C10	131.88(14)
C15–Sn1–C21	105.12(11)	C10–Sn1–S2	109.85(10)
C15–Sn1–S2	119.87(8)	C10–Sn1–Cl1	95.94(10)
C1–S2–Sn1	97.18(10)	C9–Sn1–S1	93.17(10)
C9–Sn1–C21	104.79(11)	S2–Sn1–S1	68.86(3)
C9–Sn1–S2	111.85(8)	C9–Sn1–S2	117.64(10)
C21–Sn1–S2	92.36(8)	C9–Sn1–Cl1	94.47(10)
C6–N2–C4	124.5(3)	S2–Sn1–Cl1	86.14(3)
N1–C1–S1	123.3(2)	C10–Sn1–S1	96.88(10)
S1–Sn–C21	156.19	Cl1–Sn1–S1	154.57(3)

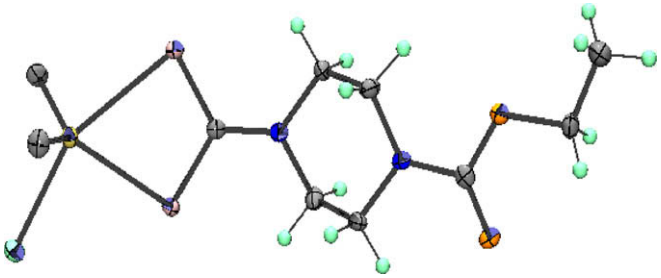


Fig. 3. ORTEP drawing of compound (**4**) with atom numbering scheme.

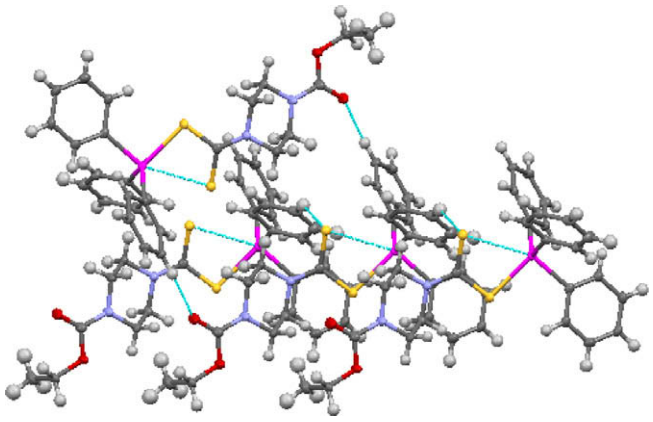


Fig. 4. Packing diagram for compound (**4**).

due to the presence of intermolecular secondary Sn···S interactions that lead to the formation of a supramolecular zig-zag chain (Fig. 4). The atoms, S2, Cl1, C9 and C10 are at the plane positions. Being a part of chelate S1 cannot occupy the exact axial position of the plan and the S(1)–Sn–S(2) angle is not 90° but only 69°. Due to steric and electronic reasons, Cl1 is bent towards S2 atom of the plan as can be seen from S2–Sn–Cl1 [86.14°]. The angle between the pseudo axial sulfur and chlorine atoms is 154.57° and is comparable with similar square-pyramidal complexes [31]. The sum of equatorial angles formed in the complex is 359°, showing a little distortion from the ideal value of 360°. The Sn–C bond lengths [Sn(1)–C(9) 2.12, Sn(1)–C(10) 2.13 Å] are similar with those reported in the literature [31]. The Sn–Cl bond length [Sn(1) Cl(1) 2.49 Å] lies in a range of the covalent radii of Sn–Cl, 2.37–2.60 Å [32].

By comparing the two structures it is obvious that the complex **3** and **4** exist in distorted trigonal-bipyramidal and distorted square-pyramidal geometry, respectively. This difference can be attributed to the presence of secondary intermolecular Sn···S interactions in the later. The occurrence of such kind of interactions in complex **4** only, is due to less steric methyl groups that allow close packing of the molecules and owing to the electron withdrawing chloro group that makes the Sn center electron deficient. These two factors allow the neighboring sulfur to interact with Sn atom of the adjacent molecule. The absence of intermolecular Sn···S interactions, in complex **3**, can be explained on the basis of steric reasons of the bulky phenyl groups. In addition to this, the back-donation capability of the phenyl groups stabilize Sn atom d-orbitals, rendering its interaction with S atom of the adjacent molecule.

4. Biological studies

4.1. Antibacterial activity

The compounds **1–9** have been tested against six different strains of bacteria by agar well diffusion method and the results are listed in the Table 3. The data revealed the following sequence of activity against different strains: *Pseudomonas aeruginosa* > *Shigella flexenari* > *Bacillus subtilis* ~ *Escherichia coli* > *Salmonella typhi* > *Staphylococcus aureus*. In general, triorganotin(IV) derivatives are more active than the diorganotin(IV) compounds and their activity vary in the sequence: Me (Mr = 398) > Bu (Mr = 524) > Ph (Mr = 584). This trend can be explained on the basis of ease of diffusion of lighter molecules (low molecular weight) through the bacterium cell membrane than the heavier ones. The high activity of tributyltin(IV) compounds than trimethyltin(IV) derivatives, in some cases, can be attributed to the high lipophilic character of the large butyl groups. The high activity of chlorodiorganotin(IV) derivatives than the corresponding diorganotin(IV) compounds may be described on the basis of labile nature of the chloro group and may be due to their low molecular weight that facilitate diffusion.

4.2. Antifungal activity

The fungicidal test for compounds **1–9** against six fungi; *Trichophyton longifusus, Candida albicans, Aspergillus flavus, Microsporum canis, Fusarium solani* and *Candida glaberata* were carried out using Miconazole and Amphotericin-B as standard drugs. These compounds showed (Table 4) pronounced activity against different fungi, especially the complexes **2**, **3**, **5**, **6** and **9**, for which the percent inhibition is almost comparable with standard drugs against some fungi (Table 4). The remaining derivatives exhibited moderate activity.

4.3. Insecticidal activity

The insecticidal activity of the compounds (**1–9**) was determined by direct contact application using filter paper [33]. The compounds were tested against *Tribolium castaneum*, *Callosobruchus analis*, *Sitophilus oryzae*, and *Rhyzopartha dominica*. Permethrin (235.71 μg/cm^2) was used as a reference insecticide (Table 5). All compounds were found active but the mortality rate is less than reference insecticidal drug.

4.4. Cytotoxic activity

The cytotoxic studies were taken by brine-shrimp bioassay lethality method [34,35] and the results are summarized in Table 6. The LD_{50} data depicts the toxicity of all the tested compounds

Table 3
Antibacterial activity[a,b] of organotin(IV) derivatives (**1–9**) of "S" donor ligands.

Name of bacterium	Clinical implication	Zone of inhibition (mm)									Ref. drug
		(**1**)	(**2**)	(**3**)	(**4**)	(**5**)	(**6**)	(**7**)	(**8**)	(**9**)	
Escherichia coli	Infection of wounds, urinary tract and dysentery	**37**	**57**	17	22	30	26	20	23	18	35
Bacillus subtilis	Food poisoning	**48**	**44**	12	24	24	28	23	21	24	38
Shigella flexenari	Blood diarrhea with fever and severe prostration	**54**	**34**	24	23	25	22	21	18	21	32
Pseudomonas aeruginosa	Infection of wounds, eyes, septicemia	**47**	**68**	20	20	25	26	22	19	–	38
Staphylococcus aureus	Food poisoning, scaled skin syndrome, endocarditis	–	–	–	20	22	20	20	17	16	29
Salmonella typhi	Typhoid fever, food poisoning, localized infection	**42**	12	21	18	24	14	20	21	–	28

[a] In vitro, agar well diffusion method, conc. 3 mg/mL of DMSO.
[b] Reference drug = Imipenum.

Table 4
Antifungal activity[a,b,c] data of organotin(IV) derivatives (**1–9**) of "S" donor ligand.

Name of Fungus	Percent inhibition									Standard drug	Percentage inhibition	MIC (μg/mL)
	(**1**)	(**2**)	(**3**)	(**4**)	(**5**)	(**6**)	(**7**)	(**8**)	(**9**)			
Trichophyton longifusus	21	24	35	–	64	90	–	20	80	Miconazole	100	70
Candida albicans	29	36	47	–	80	62	–	38	80	Miconazole	100	110.8
Aspergillus flavus	73	80	90	–	45	36	43	50	80	Amphotericin-B	100	20
Microsporum canis	64	80	90	40	50	56	–	50	75	Miconazole	100	98.4
Fusarium solani	34	41	46	–	–	80	65	44	30	Miconazole	100	73.25
Candida glaberata	18	20	38	–	–	–	44	59	80	Miconazole	100	110.8

[a] Concentration: 100 μg/cm^3 of DMSO.
[b] MIC: minimum inhibitory concentration.
[c] Percent inhibition (standard drug) = 100.

Table 5
Insecticidal bioassay[a–c] of organotin(IV) derivatives (**1–9**) of "S" donor ligand.

Insects	% Mortality								
	(**1**)	(**2**)	(**3**)	(**4**)	(**5**)	(**6**)	(**7**)	(**8**)	(**9**)
Tribolium castaneum	3	12	10	5	2	3	2	6	7
Sitophilus oryzae	4	5	5	–	7	4	3	–	3
Rhyzopertha dominica	5	2	3	8	4	6	7	4	7
Callosbruchus analis	–	8	7	5	7	7	9	6	8

[a] +ve control = 100%.
[b] +ve control = 0%.
[c] Reference drug = Permethrin.

Table 6
Brine shrimp lethality bioassay of organotin(IV) derivatives (**1–9**) of "S" donor ligand.

Compound no.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
LD_{50} (μg/mL)	1.10	0.75	1.25	0.25	0.62	–	0.75	2.45	4.6

Against brine-shrimps (in vitro).
Standard drug Etoposide LD50 7.46 μg/mL.

with LD_{50} values in the range 0–4.6 μg/mL in comparison to LD_{50} value (7.46 μg/mL) of the reference drug, Etoposide. Among these organotins, di-*n*-butyltin(IV)- and diphenyltin(IV) derivatives (**8** and **9**) emerged as most toxic compounds.

4.5. Urease inhibition activity

All compounds (**1–9**) were tested for their antiurease activity according to literature protocol [36]. Thiourea was used as standard inhibitor and results are given in Table 7. All the tested compounds demonstrated fairly good inhibition even at micromolar level. Methyltin(IV) derivatives (**1**, **4** and **7**) and phenyl derivatives (**3**, **6** and **9**) demonstrated interesting activity. This can be attributed to the ability of these compounds to establish secondary interactions with the active site of enzyme i.e. nickel. The reduction in activity in case of tri-*n*-butyltin (**2**), chlorodi-*n*-butyltin (**5**) and di-*n*-butyltin (**6**) derivatives is presumably due to the presence of bulky butyl group that hinder such kind of interaction of the ligand moiety with enzyme.

Table 7
Insecticidal bioassay[a–c] of organotin(IV) derivatives (**1–9**) of "S" donor ligand.

Compound	% Age inhibition ± S.E.M[a]
1	65.8% ± 0.43
2	45.02% ± 0.35
3	87.15% ± 0.26
4	71.46% ± 0.14
5	45.23% ± 0.16
6	81.54% ± 0.24
7	84.34% ± 0.41
8	48.32% ± 0.12
9	75.43% ± 0.16

[a] Standard error of mean.
[b] Standard drug Thiourea.
[c] % Inhibition 100.

The triphenyltin (**3**), chlorodiphenyltin(**6**) and diphenyltin (**9**) derivatives were also found very good inhibitor against this enzyme.

5. Conclusions

A series of organotin(IV) derivatives (**1–9**) of 4-ethoxycarbonyl-piperazine-1-carbodithioate ligand has been synthesized and fully characterized by different analytical techniques. The results indicate the diverse structural motifs for these compounds (tetrahedral, square-pyramidal, trigonal-bipyramidal and octahedral geometries) depending upon the mode of coordination of ligand as well as the presence or absence of intermolecular S···Sn interactions (in case of five-coordinated Sn). The X-ray structure confirmed supramolecular design for compounds **3** and **4** owing to the presence of non-covalent secondary interactions between the neighboring molecules. The good antimicrobial, insecticidal and antiurease activity of these compounds can be attributed to their

ease of diffusion and the ability to establish secondary interactions with the cell constituents (as evident in Figs. 2 and 3, packing diagrams). In nutshell, the biological action of organotin(IV) compounds can be monitored by two factors: its ease of diffuse (low molecular weight or lipophilicity) and the ability to interact strongly with the cell constituents.

Acknowledgements

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Appendix A. Supplementary material

CCDC 760013 and 760014 contain the supplementary crystallographic data for compounds **3** and **4**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2010.03.008.

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