Potentiometric and multinuclear NMR investigations of di-/trimethyltin(IV) cations with some heterocyclic thiones in aqueous media

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Equilibrium (pH-metric) studies of the interaction of $Me_2Sn(IV)^{2+}$ and $Me_3Sn(IV)^+$ with heterocyclic thiones, *viz*. 5-amino-3*H*-1,3,4-thiadiazole-2-thione (HL-**1**), 3-amino-1,2,4-triazole-5-thione (HL-**2**) and 4-amino-3*R*-1,2,4-triazole-5-thione (where R = CH_3 (HL-**3**) and C_2H_5 (HL-**4**)), in aqueous solution (I = 0.1 M KNO_3, 298 K) were performed. The concentration distribution of the various complex species in solution was evaluated as a function of pH. It was found that these thione ligands (HL) with potential sulfur donor groups interact strongly with $Me_2Sn(IV)^{2+}$ and $Me_3Sn(IV)^+$, even at rather acidic pHs < 4.0. The species that exist at physiological pH (7.0) are $Me_2SnL(OH)$ (~70–85%) and $Me_2Sn(OH)_2$ (~15–30%) for dimethyltin(IV) systems, whereas $Me_3SnL(OH)$ (~73–95%), Me_3SnL (8–24%) and $Me_3Sn(OH)$ (~1–3%) exist for $Me_3Sn(IV)^+$ systems. The complex species formed are water soluble in the pH range 2–10.5. In all of the studied systems, no polymeric species were detected in the experimental pH range. Beyond pH 8.0, significant amounts of hydroxo species, *viz*. Me_3SnOH and $Me_2Sn(OH)_2$, were formed. Multinuclear (^1H, ^{13}C and ^{119}Sn) NMR studies were also carried out at different pHs in order to characterize the possible geometry of the proposed complex species in aqueous solution.

Introduction

Organotin compounds are widely used as PVC stabilizers, fungicides, wood and stone preservatives, surface disinfectants, antifouling agents in paints for ships and in glass coating operations, *etc*.[1–4] As a result of this, they may enter the environment directly, through their biocidal uses, and indirectly, through leaching/weathering, land burial and incineration of waste materials in water. In the natural environment, organotin compounds can also originate from chemical and biological processes,[5,6] *viz*. methylation and biomethylation. Therefore, methyltin derivatives are the most encountered organotin compounds and are often present in the marine environment. Di- and trimethyltin compounds have high mammalian toxicity,[6,7] and their solubility in water makes them very dangerous for aquatic living organisms. Since water is a crucial part of the cellular organization of all terrestrial and aquatic species, *in vitro* speciation of organotin(IV) compounds is highly desirable. Their solution equilibrium studies could provide essential information on the biospeciation of organotins and thus on their bioavailability. Although it is known[8,9] that Me_2SnCl_2 and Me_3SnCl form stable hydrolyzed organotin cations of the type $Me_2Sn(H_2O)_4^{2+}$ and $Me_3Sn(H_2O)^+$, respectively, very few quantitative studies have been performed during the last decade[10–16] to determine the formation constants, stabilities and structures of these species in solution.

Organotin(IV) compounds have emerged as potential metallopharmaceuticals, exhibiting antitumor activity among non-platinum chemotherapeutics.[10,17–23] Furthermore, the speciation of organotin(IV) compounds in biological systems has revealed that their biological activity may be due to the presence of hydrolysed intermediates such as $R_nSn^{(4-n)+}$ (n = 2 or 3) moieties, which may bind with DNA or certain proteins.[17] Although the exact nature of the binding sites is not known, it has been reported that in cat haemoglobin, the cysteine and histidine residues are associated with the trialkyltin moiety,[24] indicating the strong affinity of organotin cations towards thiol S/histidyl N. Therefore, the *in vitro* speciation of organotin compounds with S-containing heterocyclic ligands is indispensable and important due to the implication of organotin compounds in cancer prophylaxis and other physiological processes, and it may also be useful for the further modelling of organotin binding to macromolecular compounds.

Organotin derivatives with heterocyclic thiones are reported to possess good antifungal activity,[25,26] and the sulfur binding in these compounds can mimic cystine bonding in metalloenzymes. Furthermore, the structure of organotin derivatives of several heterocyclic thiones have been fully characterized in the solid state.[25–31] However, investigations directed at exploring the structure of possible complex species existing in solution for such systems have not been reported. To add to the results on solid diorganotin(IV) or triorganotin(IV) complexes with heterocyclic S-ligands,[30,31] we have now extended our studies to the interaction of $Me_nSn^{(4-n)+}$ (where n = 2 or 3) with heterocyclic thiones, *viz*. 5-amino-3*H*-1,3,4-thiadiazole-2-thione (HL-**1**), 3-amino-1,2,4-triazole-5-thione (HL-**2**) and

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4-amino-3*R*-1,2,4-triazole-5-thione (where R = CH_3 (HL-**3**) and C_2H_5 (HL-**4**)), in aqueous solution at 298 ± 0.1 K and at an ionic strength (*I*) of 0.1 M of KNO_3 in the pH range 2.0–10.5. In this paper, the equilibrium behavior and possible structures of the complex species formed under experimental conditions will be discussed on the basis of pH-metric titrations, and ^1H, ^{13}C and ^{119}Sn NMR spectroscopic results.

Experimental

Chemicals

5-Amino-3*H*-1,3,4-thiadiazole-2-thione (HL-**1**) and 3-amino-1,2,4-triazole-5-thione (HL-**2**) (Sigma-Aldrich), and dimethyltin(IV) dichloride and trimethyltin(IV) chloride (Merck-Schudardt) were used as received. 4-Amino-3*R*-1,2,4-triazole-5-thione (where R = CH_3 (HL-**3**) and C_2H_5 (HL-**4**)) were synthesized by a previously reported method.[32] Potentiometric titrations were performed under a nitrogen atmosphere and precautions to avoid the presence of oxygen were taken at every stage. All solutions were prepared using de-ionized water.

Potentiometric measurements

pH measurements were carried out with an Orion 960 plus autotitroprocessor equipped with a combined glass Orion Ross flow electrode in an aqueous medium at 298 ± 0.1 K. The ionic strength of the solutions was adjusted to 0.1 M with KNO_3 (Merck) solution. The electrode and autotitroprocessor were calibrated with standard buffer solutions (Merck) of pH 4.0 ± 0.05, 7.0 ± 0.05 and 9.2 ± 0.05. Atmospheric CO_2 was excluded from the titration cell with a purging steam of purified nitrogen gas.

The following sets of solution (total volume 50 mL) (A)–(C) were titrated potentiometrically with standardized NaOH solution (0.2 M) in aqueous media:

(A) 4.0×10^{-3} M ligand and 0.1 M KNO_3.

(B) 4.0×10^{-3} M Me_3SnCl/Me_2SnCl_2 and 0.1 M KNO_3.

(C) 4.0×10^{-3} M ligand, 4.0×10^{-3} M Me_3SnCl/Me_2SnCl_2 and 0.1 M KNO_3.

In the applied concentration range, no precipitation was observed in the presence of $Me_2Sn(IV)^{2+}/Me_3Sn(IV)^{+}$ up to pH 10.5, and the solution became turbid beyond pH 10.5. Each of the above set of solutions was titrated twice in order to check for reproducibility. Furthermore, these parallel experiments were performed at different time intervals to confirm that there were no kinetic problems. The pH-metric data obtained from titrating mixtures (A) and (B) were used to calculate the acid dissociation constants of the ligands and the formation constants of the hydroxo-organotin(IV) species, respectively, whereas the formation constants of the trimethyltin(IV)/dimethyltin(IV) complexes were calculated by utilizing the data from titrating mixture (C). Furthermore, the metal-to-ligand ratios in mixture (C) varied between 1 : 1 and 1 : 3, and the metal ion concentration ranged from 1.0–4.0 × 10^{-3} M. The species formed in these systems were characterized by using the following general equilibrium (1):

$$pM + qL + rH \rightleftharpoons M_pL_qH_r \qquad (1)$$

(where M = $Me_3Sn(IV)$ or $Me_2Sn(IV)$ cation, L = non-protonated ligand or deprotonated ligand on the thiol group and the charge on L is −1; *p* and *q* are positive integers or zero; *r* is positive for a protonated species and negative for hydroxo species). Charges are omitted for the sake of simplicity, but can be easily calculated by considering the notation HL for the fully protonated ligands.

pH-metric data between pH 2.0 and 10.5 were used for the evaluation. The calculations concerning the protonation constants of the ligands and the formation constants of the complex species in solution at different pHs were performed using the SCOGS program.[33,34] Tentative values of the constants, along with ionic product of water and activity coefficient of hydrogen ion at experimental temperature and ionic strength,[35] were supplied as inputs. The values of the constants were refined by several cycles of the operation, and values corresponding to the minimum standard deviations were accepted. The output files obtained from the SCOGS program for a given system were used to draw speciation curves using Origin 6.0 software. The complex formation equilibria were elucidated with the help of the speciation curves.

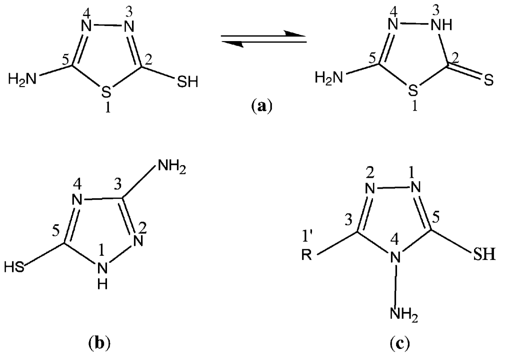
NMR measurements

^1H, ^{13}C and ^{119}Sn NMR experiments were performed at 500.13, 125.75 and 186.50 MHz, respectively, on a Bruker Avance 500 MHz NMR spectrometer (at 296.3 K) at the Indian Institute of Technology Roorkee, Roorkee, using TMS as an internal reference for ^1H and ^{13}C NMR experiments, and tetraphenyltin(IV) as an external reference for ^{119}Sn NMR experiments. The ligands used (HL-**1** to HL-**4**) have limited solubility in water. Therefore, for ^1H, ^{13}C and ^{119}Sn NMR experiments, the ligand concentration was 1.50×10^{-2} M for HL-**1** and HL-**2**, and 3.50×10^{-2} M for HL-**3** and HL-**4** with 1.50×10^{-2} M of dimethyltin(IV) dichloride/trimethyltin(IV) chloride. The experiments were performed in a $H_2O : D_2O$ (9 : 1) mixture. A suitable signal-to-noise ratio was obtained after the collection of ~64 transients. During the recycling delay, the water resonance was suppressed as much as possible.

Results and discussion

Potentiometric studies

The heterocyclic thiones, *viz*. 5-amino-3*H*-1,3,4-thiadiazole-2-thione (HL-**1**), 3-amino-1,2,4-triazole-5-thione (HL-**2**) and 4-amino-3*R*-1,2,4-triazole-5-thione (where R = CH_3 (HL-**3**) and C_2H_5 (HL-**4**)) (Scheme 1), titrated as weak monoprotic acids (HL) due to deprotonation of the S_{exo} proton (or –SH group)[36] with a pK_a of 8.23–8.63, as presented in Table 1. All of the ligands have a very low acidic character and exhibit a thione–thiolic tautometric equilibrium (Scheme 1). It has been reported[36] that in an alkaline environment, the tautomer equilibrium in 2-mercapto-5*R*-amino-1,3,4-thiadiazole derivatives moves towards the thiolic form, in which the ligands participate in the formation of complexes with different metal ions. The observed protonation constants of the ligands and formation constants of the complex species, calculated from the pH-metric titrations, together with some derived data, are listed in Table 1. The speciation curves are depicted in Fig. 1, Fig. 2, Fig. 3 and Fig. 4.



Scheme 1 (a) Thiol–thione tautomers of 5-amino-3*H*-1,3,4-thiadiazole-2-thione (HL-**1**) (ref. 36), (b) 3-amino-1,2,4-triazole-5-thione (HL-**2**) and (c) 4-amino-3*R*-1,2,4-triazole-5-thione (R = $C^{1'}H_3$ (HL-**3**) and $C^{1'}H_2C^{2'}H_3$ (HL-**4**)).

Dimethyltin(IV)–thione systems

It has been reported[13] that dimethyltin(IV) cation hydrolyses to form a series of mono- and polynuclear hydroxo species according to general equilibrium (2)

$$x\mathrm{Me_2Sn^{2+}} + y\mathrm{H_2O} \rightleftharpoons (\mathrm{Me_2Sn})_x(\mathrm{OH})_y^{(2x-y)+} + y\mathrm{H^+} \quad (2)$$

(where $x = 1, y = 1, 2, 3$; $x = 2, y = 2, 3$; $x = 3, y = 4$; $x = 4, y = 6$). The results of the hydrolysis of $\mathrm{Me_2Sn(IV)^{2+}}$ in different media have been compiled in ref. 10.

The formation constants of $[\mathrm{Me_2Sn(OH)}]^+$, $[\mathrm{Me_2Sn(OH)_2}]$, $[\mathrm{Me_2Sn(OH)_3}]^-$, $[(\mathrm{Me_2Sn})_2(\mathrm{OH})_2]^{2+}$ and $[(\mathrm{Me_2Sn})_2(\mathrm{OH})_3]^+$ have been reported by Arena *et al.*[13] These hydroxo species have also been considered in the present study, and the observed values of their formation constants in the pH range (2–10) at 25 °C and $I = 0.1$ M ($\mathrm{KNO_3}$) are given in Table 1 along with the previously reported values. The observed log β values are in close agreement with the reported values.

Since the heterocyclic thione ligands used in the present study have the same set of coordinating atoms, the same species were considered for all the binary dimethyltin(IV) systems, namely: $[\mathrm{SnMe_2L}]^+$, $[\mathrm{SnMe_2L(OH)}]$, $[\mathrm{SnMe_2(OH)}]^+$, $[\mathrm{SnMe_2(OH)_2}]$, $[\mathrm{SnMe_2(OH)_3}]^-$, $[\mathrm{SnMe_2L(OH)_2}]^-$, $[\mathrm{SnMe_2L_2}]$, $[\mathrm{SnMe_2L_2(OH)}]^-$ and $[\mathrm{SnMe_2L_2(OH)_2}]^{2-}$ (where HL = HL-**1**, HL-**2**, HL-**3** and HL-**4**). Introduction of $[\mathrm{SnMe_2L(OH)_2}]^-$ species into the species matrix resulted in a high standard deviation value and hence it was ruled out. Furthermore, for all four systems, the last three were rejected by SCOGS as negative. This confirms that in all the dimethyltin(IV) systems, 1 : 1 metal : ligand complex species are formed in the studied pH range, regardless of metal-to-ligand ratio, which was varied from 1 : 1 to 1 : 3 in the different titration sets.

The complex formation process of $\mathrm{Me_2SnCl_2}$ with these heterocyclic thione ligands (HL-**1** to HL-**4**) starts at pH 2.8 ± 0.2 with the formation of 35–73% $\mathrm{Me_2SnL}$ complex, *i.e.* the 110 species. This species is formed by the coordination of a deprotonated ligand, most likely on its –SH group. In the ^{1}H NMR spectra, the absence of an SH resonance at $\delta \sim 2.50$–1.30 ppm in the equilibrium mixtures at this pH confirms the coordination of the ligands *via* the deprotonated $\mathrm{S_{exo}}$ atom to tin. Furthermore, similar values of the formation constants (log $\beta_{110} \approx 8.01$–8.85) observed for this complex 110 species (*i.e.* $\mathrm{Me_2SnL}$ for the reactions M + HL $\rightleftharpoons$ ML + H) (Table 1)) and the similar values of the stability constants of these species (*i.e.* when the formation of 110 species is represented as HL $\rightleftharpoons$ H + L; dissociation of the ligand *i.e.*, log β_{011}, and M + L $\rightleftharpoons$ ML; log K = log β_{110} − log $\beta_{011} \approx 0.20$, see Table 1) in all the studied dimethyltin(IV) systems are in favor of the thiolate ($\mathrm{S_{exo}}$) coordination in these complex species in the acidic pH range 2.6–4.5 according to equilibrium (3). Furthermore, $\mathrm{Me_2SnL}$ is

Table 1 Protonation constants (log K) of the ligands, formation constants (log β) of the organotin(IV) complexes and hydrolysis constants of the dimethyltin(IV) and trimethyltin(IV) cations at 298 ± 0.1 K, $I = 0.1$ M $\mathrm{KNO_3}$; $\beta_{pqr} = \mathrm{M}_p\mathrm{L}_q\mathrm{H}_r/[\mathrm{M}]^p[\mathrm{L}]^q[\mathrm{H}]^r$; p$K_1$ = log β_{110} − log β_{11-1}; log K = log β_{110} − log β_{011}; standard deviations shown in parentheses. Neg. = negligible

log β_{pqr}	HL-1	HL-2	HL-3	HL-4
For $\mathrm{Me_2Sn}$(IV) systems				
110	8.01(2)	8.51(1)	8.75(3)	8.85(2)
11−1	2.75(3)	3.60(2)	3.87(1)	3.91(2)
pK_1	5.26	4.91	4.88	4.94
log K	−0.24	0.28	0.16	0.22
For $\mathrm{Me_3Sn}$(IV) systems				
110	8.05(1)	7.55(2)	7.55(2)	7.60(1)
11−1	2.07(1)	1.57(1)	1.50(1)	1.78(2)
pK_1	5.98	5.98	6.05	5.82
Proton-ligand constants				
011	8.25(2)[a] 8.79[b]	8.23(2)	8.59(1)	8.63(1)
Hydrolysis constants				
	$\mathrm{Me_2Sn(IV)^{2+}}$		$\mathrm{Me_3Sn(IV)^+}$	
	[a]	[c]	[a]	[d]
10−1	−3.16(1)	−3.12	−6.18(1)	−6.26
10−2	−8.42(2)	−8.43	−17.80(2)	—
10−3	−19.46(1)	−19.45	—	—
20−2	−4.95(2)	−5.05	—	—
20−3	−9.79(2)	−9.74	—	—
30−4	—	Neg.	—	—
40−6	—	Neg.	—	—

[a] This work. [b] Ref. 36. [c] Ref. 11, at 25 °C and $I = 0.1$ M ($\mathrm{KNO_3}$). [d] Ref. 37, at 25 °C and $I = 0.3$ M ($\mathrm{NaClO_4}$).

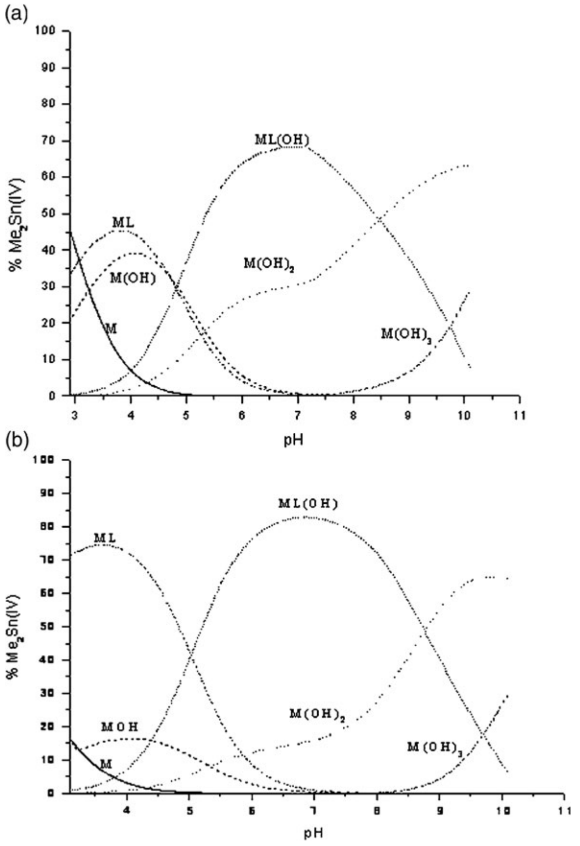


Fig. 1 Speciation curves for 1 : 1 (a) dimethyltin–HL-**1** and (b) dimethyltin–HL-**2** systems.

the main complex species formed in the pH range 2.6–4.5, and approximately 5–38% monohydroxo species of the parent dimethyltin(IV) compound is also formed in this pH range (Fig. 1 and Fig. 2) according to equilibrium (4).

$$Me_2Sn + HL \rightleftharpoons Me_2SnL + H_3O \qquad (3)$$

$$Me_2Sn + H_2O \rightleftharpoons Me_2Sn(OH) + H_3O \qquad (4)$$

The formation of the 110 species, as defined by equilibrium (1), might truly refer to Me_2SnL (*i.e.*, with the deprotonated ligand or thiol form) or $[Me_2Sn(HL)(OH)]$ (*i.e.*, with the thione form of the ligand), and that EMF (electromotive force) are of little help in this direction. It has been reported[8] that the formation of a complex by the inner sphere mechanism usually involves the substitution of a water of hydration in $[Me_2Sn(H_2O)_4]^{2+}$ with a ligand. This means breaking bonds between the metal ion and the oxygen of water molecules, and the formation of bonds between the metal ion and the S^- of the ligand. The formation of hydroxo complexes in acidic solution is best described as a transfer of protons from water molecules outside of this shell. In such a process, metal-to-oxygen bonds are neither broken nor formed. Consequently, the formation of hydroxo species represents the detachment of a proton rather than the substitution of water molecules by OH^- ions. The determination of enthalpy (ΔH°) and entropy (ΔS°) would give useful information in this regard, but their determination could not be possible due to the relatively low percentage of these species. However, the considerations that follow seem to support the notion that all the thione ligands in aqueous solution are coordinated in a monodentate fashion through a thiol S^- in 110 species. All the ligands have a proton dissociation constant (pK_a) in the same range (8.23–8.63) as the log β values of 110 complex species (Table 1). Furthermore, in ^1H NMR, δ_{NH} and δ_{SH} are not observed in all the systems in this pH range. Therefore, it has been concluded that in the Me_2SnL species, the thione ligands are monodentate, giving a highly distorted octahedral geometry (Fig. 5 (b1/b2)). This is supported by NMR studies (discussed later). The Me_2SnL complexes suffered deprotonation of a metal bound water molecule[11] in the pH range 4.5–7.5, with the addition of base leading to $Me_2SnL(OH)$ (*i.e.* MLH_{-1} according to equilibrium (1)) species (~80%) (equilibrium (5)). In the case of ligand HL-**2**, the metal promoted deprotonation of N(1) hydrogen (equilibrium (6)) can also be considered.

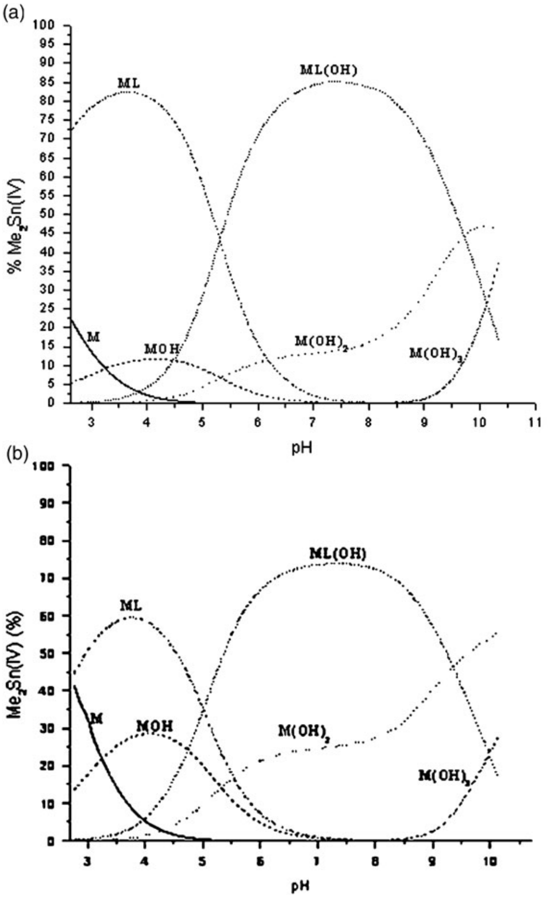


Fig. 2 Speciation curves for 1 : 1 (a) dimethyltin–HL-**3** and (b) dimethyltin–HL-**4** systems.

$$Me_2SnL + H_2O \rightleftharpoons Me_2SnL(OH) + H_3O \qquad (5)$$

$$Me_2SnL \rightleftharpoons Me_2SnLH_{-1} + H_3O \qquad (6)$$

However, log β_{012} for HL-**2** is not reported in the literature and is also not observed in the studied pH range (2–10.5). Furthermore, the observed log β_{11-1} value of the complex

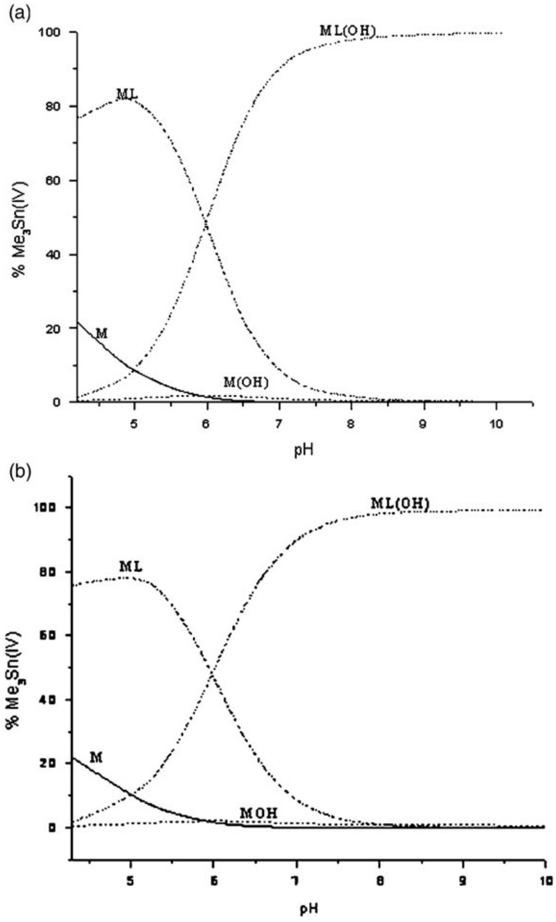


Fig. 3 Speciation curves for 1 : 1 (a) trimethyltin–HL-**1** and (b) trimethyltin–HL-**2** systems.

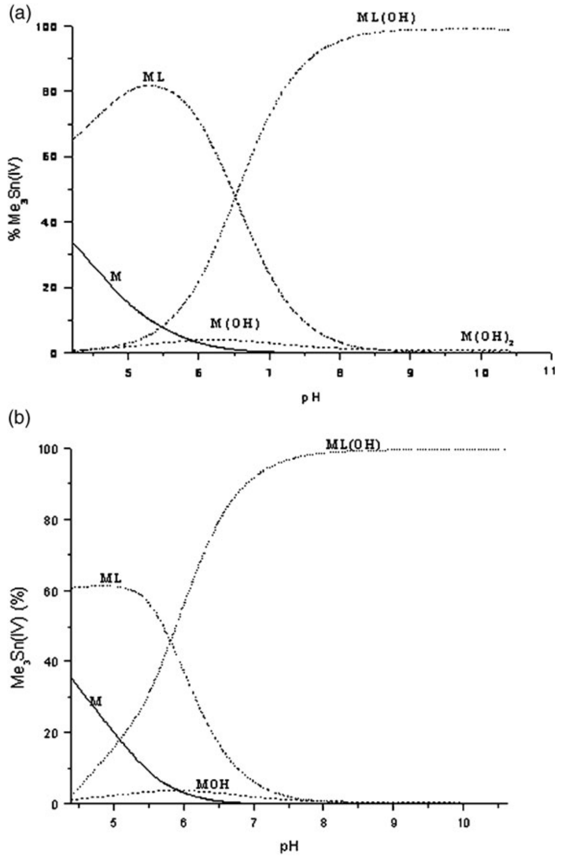


Fig. 4 Speciation curves for 1 : 1 (a) trimethyltin–HL-**3** and (b) trimethyltin–HL-**4** systems.

species with HL-**2** in the pH range 4.5–7.5 is similar to those obtained for the corresponding complex species of HL-**1**, HL-**3** and HL-**4** (Table 1). These observations rule out the deprotonation of N(1) of the HL-**2** ligand for the formation of Me_2SnLH_{-1} species, and the results can be easily rationalized by the formation of a similar type of complex species, *i.e.* a mixed hydroxo-ligand complex $Me_2SnL(OH)$, in all the systems. Furthermore, with regard to the formation of $[Me_2SnL(OH)]$, the pK value corresponding to the process is close to ≈ 5 (5.085 ± 0.175) and similar in all the systems investigated in the present study (Table 1). It may be attributed to the deprotonation of a coordinated metal-bound water molecule, forming mixed hydroxo-ligand $Me_2SnL(OH)$ complexes. Quite similar pK values have been reported for the analogous equilibria pertinent to dimethyltin(IV)–amino acid systems.[12] On further addition of base, $Me_2SnL(OH)$ complexes produce the dihydroxo $Me_2Sn(OH)_2$ species (equilibrium (7)). The dihydroxo species also results from the hydrolysis of the monohydroxo species in the pH range 4.0–10.0 (equilibrium (8)), which forms a small amount of the trihydroxo species $Me_2Sn(OH)_3$ (equilibrium (9)) above pH 8.5, as indicated from the speciation curves (Fig. 1 and Fig. 2). However, no polymeric species, even in negligible amounts (<1–2%), are observed. Only the hydroxo species of the dimethyltin(IV) cation is present above pH 10 in all the systems.

$$Me_2SnL(OH) + H_2O \rightleftharpoons Me_2Sn(OH)_2 + L + H_3O \quad (7)$$

$$Me_2Sn(OH) + H_2O \rightleftharpoons Me_2Sn(OH)_2 + H_3O \quad (8)$$

$$Me_2Sn(OH)_2 + H_2O \rightleftharpoons Me_2Sn(OH)_3 + H_3O \quad (9)$$

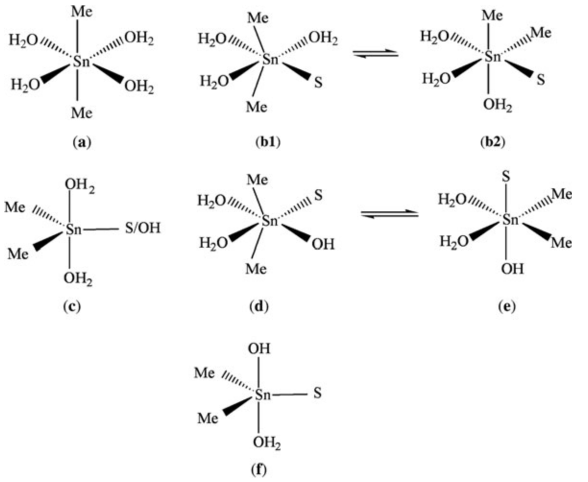


Fig. 5 Possible geometrical structures of the complex species (a) M or $Me_2Sn(H_2O)_4^{2+}$, (b1/b2) isomers of ML, (c) ML or M(OH), (d/e) isomers of ML(OH) and (f) ML(OH).

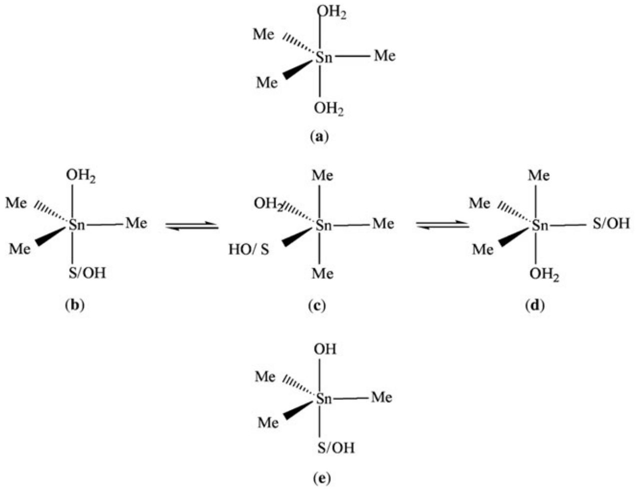


Fig. 6 Possible geometrical structures of the complex species: (a) M or $Me_3Sn(H_2O)_2{}^+$, (b–d) isomers of ML/M(OH) and (e) ML(OH) or $M(OH)_2$.

Trimethyltin(IV)–thione systems

It has been reported[37] that in aqueous solution, $(CH_3)_3SnCl$ dissociates and hydrolyses to form $[Sn(CH_3)_3(H_2O)_2]^+$, having a trigonal bipyramidal structure (Fig. 6(a)) with the three methyl groups in equatorial positions and the two water molecules in axial positions. Furthermore, $[Sn(CH_3)_3(H_2O)_2]^+$ undergoes hydrolysis in aqueous solution according to equilibrium (10)

$$[Sn(CH_3)_3(H_2O)_2]^+ + H_2O \rightleftharpoons [Sn(CH)_3(H_2O)(OH)] + H_3O^+ \qquad (10)$$

The hydrolysis of trimethyltin(IV) chloride has been investigated in the present study in the pH range 2.0–11.0 at 25 °C and I = 0.1 M (KNO_3), and the observed log β_{10-1} value (−6.18) is in fair agreement with the previously reported value (−6.26)[37] obtained in 0.3 M $NaClO_4$. The formation constant of $[Sn(CH_3)_3(OH)_2]^-$ (log β_{10-2} = −17.80) has also been determined and given in the Table 1, but no polymeric species have been observed. Furthermore, it has been observed that the degree of hydrolysis of trimethyltin chloride is considerably less than that of its dimethyltin counterpart (log β_{10-1} = −3.16/−3.12[11] (Table 1); log β_{10-2} = −8.42/−8.43[11] (Table 1)).

In all of the ligand–trimethyltin systems, only one species, having a ligand-to-metal ratio of 1 : 1, has been found, irrespective of the ligand-to-metal ratio at which the titration was carried out. There was no evidence for the formation of polymeric species in the present study. For the trimethyltin systems, complex formation started at pH 4.2 ± 0.2 (Fig. 3 and Fig. 4) to form 62–76% Me_3SnL species (equilibrium (11)). Furthermore, complex formation (equilibrium (11)) predominates over hydroxide formation (equilibria (12a) and (12b)) at the early stages of the reaction (pH < 7.0). The extent of the mono- and dihydroxo species formed (equilibria (12a) and (12b)) is very low (1–3%) for all the studied trimethyltin(IV) systems, as indicated from the speciation curves (Fig. 3 and Fig. 4). In the pH range 7.0–10.0, the Me_3SnL complexes result in $Me_3SnL(OH)$ (*via* deprotonation of a metal-bound water molecule) (equilibrium (13)), which is the predominant species (73–99%) in this pH range. Some $Me_3SnL(OH)$ is also produced from the monohydroxo species $Me_3Sn(OH)$ in this pH range (equilibrium (14)).

$$Me_3Sn + HL \rightleftharpoons Me_3SnL + H_3O \qquad (11)$$

$$Me_3Sn + H_2O \rightleftharpoons Me_3Sn(OH) + H_3O \qquad (12a)$$

$$Me_3Sn(OH) + H_2O \rightleftharpoons Me_3Sn(OH)_2 + H_3O \qquad (12b)$$

$$Me_3SnL + H_2O \rightleftharpoons Me_3SnL(OH) + H_3O \qquad (13)$$

$$Me_3Sn(OH) + HL \rightleftharpoons Me_3SnL(OH) + H_3O \qquad (14)$$

NMR studies

Multinuclear (^1H, ^{13}C and ^{119}Sn) NMR experiments of the reaction mixtures were performed to provide further supporting evidence for the possible existing complex species at different pHs in aqueous solution. The ^1H NMR data, *i.e.* chemical shifts and two-bond coupling constants $^2J_{^1H-^{117/119}Sn}$ for the $(Me_2Sn(IV))^{2+}/Me_3Sn(IV)^+$ + HL) systems, together with the calculated $\angle_{C-Sn-C}$ bond angles using the Lockhart and Manders equation,[38] are collected in Table 2. The ^{13}C and ^{119}Sn NMR data are presented in Table 3 and Table 4, respectively. The representative ^1H, ^{13}C and ^{119}Sn NMR spectra of the mixtures ($Me_2Sn(IV)$ + HL-**2**) at pH 7.2, ($Me_2Sn(IV)$ + HL-**3**) at pH 7.1 and ($Me_2Sn(IV)$ + HL-**4**) at pH 2.7 are shown in Fig. 7(a–c), respectively. Spectra of the mixtures ($Me_3Sn(IV)$ + HL-**1**) at pH 7.2, ($Me_3Sn(IV)$ + HL-**4**) at pH 7.2 and ($Me_2Sn(IV)$ + HL-**3**) at pH 6.9 are shown in Fig. 8(a–c), respectively. The individual chemical shifts and coupling constants $^2J_{^1H-^{117/119}Sn}$ of the different hydrolyzed species existing for the dimethyltin cation, as well as their geometry (Fig. 5(a) and (c)), were earlier reported in detail by Surdy *et al.*[11]

In order to obtain high quality spectra within a normal detection time interval, the NMR measurements were performed with [M] = 1.50 × 10^{-2} M, and [L] = 1.50 × 10^{-2} M for HL-**l**/HL-**2** and [L] = 3.50 × 10^{-2} M for HL-**3**/HL-**4**. These concentration limits of the metals and ligands were optimized in order to avoid their precipitation during and after the NMR experiments.

NMR of dimethyltin(IV)–thione ligand systems

The ^1H NMR spectra of all the studied dimethyltin(IV)–ligand systems, except that with HL-**3**, in D_2O : H_2O solution exhibited only one sharp methyl proton (bound to tin) resonance, with well resolved satellites at different pHs from 2.6 to 9.2 (Table 2). This indicates that the complex species formed at a given pH are in fast mutual exchange relative to the NMR timescale. Similarly, in the ^{13}C NMR spectra, only one set of resonances of methyl carbon bound to tin and those of the bound ligand (in the case of HL-**3**/HL-**4**) were observed, except $Me_2Sn(IV)$–HL-**3** at pH 2.6, 4.0 and 9.2, and $Me_2Sn(IV)$–HL-**4** at pH 7.0. Unfortunately the $^1J_{^{13}C-^{119}Sn}$ coupling constant could not be determined in most of the systems, except the few presented in Table 3. Due to ligand-

Table 2 ^{1}H NMR spectral data[a] of dimethyltin(IV)/trimethyltin(IV)–thione ligand mixtures at different pHs

		δ/ppm[c] [$^{2}J_{^{1}H-^{117/119}Sn}$/Hz]				
M + ligand (pH)	Species (%)[b]	H_α	Line width[e]	$H_{1'}$	$H_{2'}$	$\angle_{C-Sn-C}$/°[d]
For (M + HL) (M = $Me_2Sn(IV)^{2+}$) mixture						
M (2.0)	$Me_2Sn(H_2O)_4{}^{2+}$	0.78s [105]	2.89			171
M + HL-**1** (2.9)	M (45), ML (35), M(OH) (20)	0.79s [103]	4.0			168
(3.7)	M (7), ML (45), M(OH) (38), ML(OH) (7)	0.73s [91]	3.75			147
(7.4)	ML(OH) (70), $M(OH)_2$ (30)	0.68s [87]	2.54			140
(9.1)	ML(OH) (35), $M(OH)_2$ (60), $M(OH)_3$ (5)	0.47s [81]	3.22			132
M + HL-**2** (3.1)	M (15), ML (70), M(OH) (14)	0.82s [101/103]	1.93			166
(3.9)	M (5), ML (75), M(OH) (15)	0.79s [95]	2.57			153
(7.2)	ML(OH) (82), $M(OH)_2$ (18)	0.61s [81]	3.36			132
(9.3)	ML(OH) (60), $M(OH)_2$ (33), $M(OH)_3$ (7)	0.59s [82/80]	2.79			133
M + HL-**3** (2.6)	M (22), ML (73), M(OH) (5)	0.73s [119], 0.74s [102]	8.52	1.88s, 2.19s		166
(4.0)	ML (82), M(OH) (12), ML(OH) (5)	0.83s [88], 0.84s	6.19	2.03s, 2.33s		142
(7.1)	ML(OH) (85), $M(OH)_2$ (15)	0.73s [84]	3.87	2.31s, 1.99s		136
(9.2)	ML(OH) (65), $M(OH)_2$ (32)	0.51s [80]	2.71	2.03s		131
M + HL-**4** (2.7)	M (42), ML (45), M(OH) (13)	0.78s [104]	3.07	2.65–2.60q[f]	1.11t[f]	170
(3.8)	M (5), ML (60), M(OH) (28), ML(OH) (5)	0.73s [91]	3.37	2.65–2.60q[f]	1.11t[f]	147
(7.2)	ML(OH) (72), $M(OH)_2$ (25)	0.59s [82]	4.33	3.53–3.49q[g]	1.03t[g]	133
(9.2)	ML(OH) (58), $M(OH)_2$ (40)	0.56s [81]	3.52	2.64–2.60q[f]	1.11t[f]	132
For (M + HL) (M = $Me_3Sn(IV)^{+}$) mixture						
M (2.2)	$Me_3Sn(H_2O)_2{}^{+}$	0.50 [68]	2.33	—	—	118
Me_3Sn(L-**1**)[h]		−1.04 [63], −0.80, 1.80	3.70, 4.46, 6.21	—	—	116
M + HL-**1** (4.1)	M (21), ML (76), ML(OH) (2)	0.41s [67], 0.80s, 1.95s	4.77, 5.04, 4.64	—	—	117
(7.2)	ML (10), ML(OH) (89)	0.38s [66], 0.59s [83], 1.93s	5.34, 5.25, 5.10	—	—	116, 135
(8.8)	ML(OH) (99)	0.33s [64], 0.61s [81]	4.10, 4.20, 4.0	—	—	115, 132
M + HL-**2** (4.0)	M (22), ML (76), ML(OH) (2)	0.49s [68], 0.78s, 1.97s	4.24, 6.55, 3.93	—	—	118
(7.1)	ML (7), ML(OH) (95), M(OH) (3)	0.33s [64], 0.59s [81], 1.95s	4.65, 4.57, 4.91	—	—	115, 132
(9.1)	ML(OH) (99)	0.32s [64], 0.60 [81], 1.97s	4.69, 4.33, 4.19	—	—	115, 132
M + HL-**3** (4.2)	M (33), ML (66), ML(OH) (1)	0.47s [68], 0.74s [90], 1.95s	4.73, 4.85, 4.47	2.27s	—	118, 145
(6.9)	ML (24), ML(OH) (73), M(OH) (1)	0.38s [65], 0.63s [81], 1.99s	4.47, 4.49, 4.19	2.31s	—	116, 132
(9.2)	ML(OH) (99)	0.29s [64], 0.57s [81], 1.94s	5.18, 4.82, 5.31	2.30s	—	115, 132
M + HL-**4** (4.4)	M (35), ML (62), ML(OH) (3)	0.48s [69/67], 0.78s[i]	2.04	2.66–2.53q[f]	1.15t[f]	119
(7.2)	ML 8), ML(OH) (91)	0.32s [65/63], 0.60s[i]	2.01	2.68–2.64q[f]	1.15t[f]	116
(8.9)	ML(OH) (99)	0.30s [065/63], 0.60s[i]	1.96	2.65–2.60q[f]	1.14t[f]	116

[a] Solvent: $H_2O : D_2O$ (9 : 1). Atom numbers as mentioned in Scheme 1; $C^{\alpha}H_3$–Sn. [b] Percentage of species from speciation diagram. [c] s = singlet, t = triplet, q = quartet. [d] Eqn.: θ ($\angle$C–Sn–C) = $0.0161|^{2}J(^{1}H-^{119}Sn)|^{2}-1.32\ |^{2}J(^{1}H-^{119}Sn)| + 133.4$.[38] [e] Line width = the half line-width of the methyl protons. [f] $^{3}J_{H-H}$ = 7.5 Hz. [g] $^{3}J_{H-H}$ = 7.0 Hz. [h] Solid complex [Me_3Sn(L-**1**)] in solvent: MeOH-d_4 + D_2O (1 : 9). [i] Half line-width not determined.

bound OH^- and H_2O exchange on $Me_2Sn(IV)^{2+}$, the CH_3–Sn resonance was broadened and $^{1}J_{^{13}C-^{119}Sn}$ coupling constants could not be determined with sufficient certainty from the spectra at different pHs. Furthermore, a resonance (in the ^{13}C NMR) observed around ≈9.0 ppm, along with its coupling constant value at pH 2.6 ± 0.3, may be assigned to the octahedral $[Me_2Sn(H_2O)_4]^{2+}$ (Fig. 5(a)), together with ML (octahedral) (Fig. 5(b)), because Me_2SnCl_2 in D_2O at pH 2.0 gave a methyl resonance at 10.43 ppm (Table 3) due to the octahedral tetraaquadimethyltin(IV) species (Fig. 5(a)). At pH 3.0, the ^{1}H NMR methyl proton resonance in the case of dimethyltin–HL-**2** system is narrow, suggesting one tin-containing species is present in solution. According to the speciation diagram (Fig. 1(b)), 70% of ML is formed at this pH, and this species may be stable enough to dominate over other species formed in small amounts (<15%) (Table 2). The half line-width of the methyl proton (bound to tin) resonance in all the studied systems is in the range 2.54–8.52 Hz, indicating that more than one tin-containing species is present in the solution and are under fast mutual exchange. Furthermore, in the $Me_2Sn(IV)$–HL-**3** system at pH 2.6 and 4.0, the methyl proton resonance splits into two, with linewidths of 8.52 and 6.19 Hz, respectively, clearly indicating the presence of more than one tin-containing species in equilibrium and under relatively slow mutual exchange. Taking into account the speciation diagram (Fig. 2(a)), the resonances at 0.73 and 0.74 ppm may be attributed to ML (73%) and free metal ion (22%), respectively, at pH 2.6, and those at 0.83 and 0.84 ppm to ML (82%) and M(OH) (12%), respectively, at pH 4.0. The measured values of $^{1}J_{^{13}C-^{119}Sn}$ coupling constants (Table 3, wherever it was possible to determine) also suggest the existence of 6- or 5-coordinated species, and may be attributed to the distorted octahedral geometry (Fig. 5(b) or (d) or (e)) with axial or *cis*-methyl groups, or trigonal bipyramidal geometry assigned to the major possible species, especially ML or ML(OH), *viz.* for $Me_2Sn(IV)$–HL-**1** at pH 3.7, $Me_2Sn(IV)$–HL-**2** at pH 3.9, $Me_2Sn(IV)$–HL-**3** at pH 4.0 and 7.1, and $Me_2Sn(IV)$–HL-**4** at pH 3.8 (Table 3).

In all the studied systems, it has been observed that the methyl proton (bound to tin) resonance shifts to higher fields and the $^{2}J_{^{1}H-^{119}Sn}$ coupling constant value decreases on increasing the pH of the solution, similar to that found for a solution of $Me_2Sn(IV)$[39] and Me_2Sn–captopril/-dipeptide systems.[11,15] Furthermore, the measured $^{2}J_{^{1}H-^{117/119}Sn}$ values

Table 3 ^{13}C NMR spectral data^a of dimethyltin(IV)/trimethyltin(IV)–thione ligand mixtures at different pHs

	^{13}C δ/ppm ($^1J_{^{13}C-^{119}Sn}$/Hz)					
M + ligand (pH)	C_α	Possible species	C1′	C2′	C2/C3^b	C5
For (M + HL) (M = Me$_2$Sn(IV)$^{2+}$) mixture						
M	10.43	Me$_2$Sn(H$_2$O)$_4$$^{2+}$	—	—	—	—
M + HL-**1** (2.9)	9.21 (605)	M/ML	—	—	168.40	154.29
(3.7)	5.76 (596)	ML/M(OH)	—	—	168.74	154.29
(7.4)	4.69^c	ML(OH)/M(OH)$_2$	—	—	168.89	154.64
(9.1)	1.96^c	M(OH)$_2$/ML(OH)	—	—	168.70	154.90
M + HL-**2** (3.9)	6.88 (515)	ML/M(OH)	—	—	158.26	164.15
(7.2)	1.56^c	ML(OH)/M(OH)$_2$	—	—	158.72	163.86
M + HL-**3** (2.6)	0.80 (598)	ML/M	9.76	—	151.90	164.29
(4.0)	0.98 (627), 5.55^c	ML, M(OH)	9.94	—	151.90	164.80
(7.1)	0.93 (583)	ML(OH)/M(OH)$_2$	9.89	—	151.67	164.40
(9.2)	0.95^c, 1.53^c, 2.01^c	ML(OH)/M(OH)$_2$	10.08	—	151.70	164.10
M + HL-**4** (2.7)	9.23 (626)	M/ML	17.98	9.40	155.71	165.10
(3.8)	5.76 (540)	ML/M(OH)	17.97	9.40	155.77	165.25
(7.0)	−5.10^c, 5.73^c	ML(OH)/M(OH)$_2$	16.80	9.47	155.60	165.20
(9.2)	2.40^c	ML(OH)/M(OH)$_2$	18.01	9.55	155.80	164.90
For (M + HL) (M = Me$_3$Sn(IV)$^+$) mixture						
M	−1.57 (475)	Me$_3$Sn(H$_2$O)$_2$$^+$	—	—	—	—
M(L-**1**)^d	−4.11 (490)		—	—	157.05	166.79
M+ HL-**1** (4.1)	−1.63 (550), 0.87 (530)	M, ML	—	—	168.32	155.04
(7.2)	−0.60 (535), 0.86 (431)	M, ML	—	—	168.38	155.36
(8.8)	−2.84 (532)	ML(OH)	—	—	168.36	155.98
M+ HL-**2** (4.0)	−1.65 (510)	ML/M	—	—	158.74	164.27
(7.1)	−2.63 (474), 0.88^c	ML(OH), ML	—	—	159.02	163.28
(9.1)	−2.80 (522)	ML(OH)	—	—	158.69	164.34
M+ HL-**3** (4.2)	−1.68 (584)	ML/M	9.84	—	155.46	164.82
(6.9)	−2.47 (437)	ML(OH)/ML	9.87	—	154.47	164.69
(9.2)	−2.90 (481), 0.87 (518)	ML(OH), ML	9.86	—	154.29	164.91
M+ HL-**4** (4.4)	−1.67 (555)	ML/M	18.02	9.46	155.78	164.55
(7.2)	−2.85 (530)	ML(OH)	18.06	9.66	155.88	164.21
(8.9)	−2.94 (547)	ML(OH)	18.15	10.07	155.99	164.60

[a] Solvent: H$_2$O : D$_2$O (9 : 1). Atom numbers as mentioned in Scheme 1; C$^\alpha$H$_3$–Sn. [b] C2 for HL-**1** and C3 for HL-**2** to HL-**4**. [c] [$^1J_{^{13}C-^{119}Sn}$] not resolved. [d] Solid complex [Me$_3$Sn(L-**1**)] in solvent: MeOH-d_4 + D$_2$O (1 : 9).

provide information on the average C–Sn–C bond angle ($\angle_{C-Sn-C}$) of all the possible complex species (because they are under fast mutual exchange) at a given pH, and thereby indicate the possible coordination number and geometry around the Sn atom. The calculated average $\angle_{C-Sn-C}$ at pH 2.8 ± 0.2 is 168 ± 2°, which indicates a distorted octahedral geometry with axial methyl groups (Fig. 5(a)/(b1)) for the existing species (M/ML) in significant amounts, together with distorted trigonal bipyramidal MOH, formed in a small amount. A distorted octahedral geometry with *cis*-methyl groups (Fig. 5(b2)) in equilibrium with its *trans* counterpart (Fig. 5(b1)) cannot be ignored. However, at pH 3.8 ± 0.2, 7.2 ± 0.2 and 9.2 ± 0.1, the calculated average $\angle_{C-Sn-C}$ are 148 ± 6, 136 ± 4 and 132 ± 1°, respectively, which cannot be interpreted in terms of *trans*-octahedral or trigonal bipyramidal geometry with equatorial methyl groups. These intermediate values are probably as a result of (i) the coexistence of both distorted octahedral (Fig. 5(b), (d) and (e)) and trigonal bipyramidal (Fig. 5(c) and (f)) structures in fast mutual exchange, or (ii) a very distorted structure, similar to that found for the hydrolysis of Me$_2$Sn(IV)$^{2+}$ [39] and Me$_2$Sn(IV)$^{2+}$–captopril/dipeptide systems.[11,15] A $\angle_{C-Sn-C}$ of ≈132° has been reported for Me$_2$Sn(OH)$_2$/Me$_2$Sn(OH)$_3$/(Me$_2$Sn)$_2$(OH)$_2$/(Me$_2$Sn)$_2$(OH)$_3$ species, having trigonal bipyramidal structures[11] with equatorial methyl groups. Furthermore, ^{119}Sn chemical shifts are more diagnostic compared to those of ^{1}H and ^{13}C, and provide very useful information regarding the coordination number around tin, as well as the existence of more than one tin-containing species. The ^{119}Sn chemical shifts observed at physiological pH in all of the studied systems are given in Table 4. It has been reported in the literature[40] that ^{119}Sn chemical shifts in the ranges δ 200 to −60, −90 to −190 and −210 to −400 ppm are associated with four-, five- and six-coordinate tin centers, respectively. Two ^{119}Sn resonances are observed, at −204 and −252 ppm in the case of the Me$_2$Sn(IV)–HL-**1** system at pH 7.4, which may be

Table 4 ^{119}Sn NMR spectral data^a of dimethyltin(IV)/trimethyltin(IV)–thione ligand mixtures at different pHs

M + ligand (pH)	^{119}Sn δ/ppm
For (M + HL) (M = Me$_2$Sn(IV)$^{2+}$) mixture	
M + HL-**1** (7.4)	−204, −252
M + HL-**2** (7.2)	−279
M + HL-**3** (7.1)	−89, −196, −268
M + HL-**4** (2.7)	−195, −262, −297
M + HL-**4** (7.0)	−65, −273
For (M + HL) (M = Me$_3$Sn(IV)$^{2+}$) mixture	
M + HL-**3** (6.9)	−90, −197
M + HL-**4** (7.2)	−107, −204

[a] Solvent: H$_2$O : D$_2$O (9 : 1).

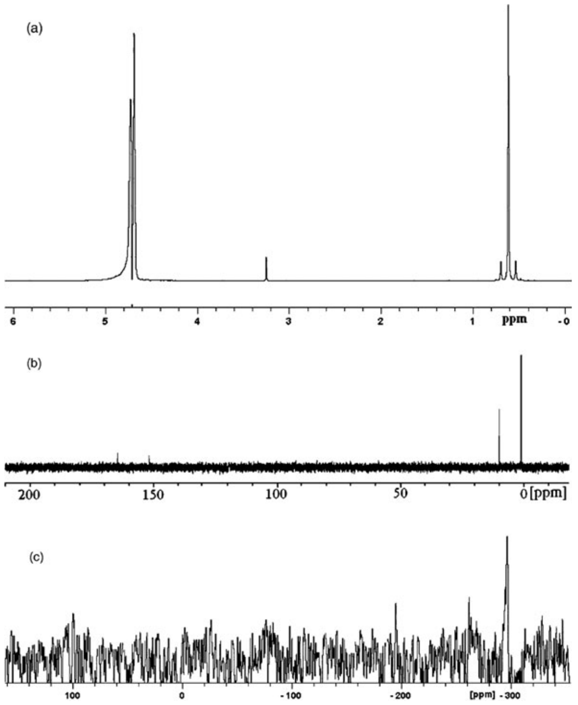


Fig. 7 NMR spectra of dimethyltin(IV)–ligand system in a $H_2O : D_2O$ (9 : 1) mixture: (a) ^1H NMR spectrum of (Me_2Sn(IV) + HL-**2**) at pH 7.2, (b) ^{13}C NMR spectrum of (Me_2Sn(IV) + HL-**3**) at pH 7.1 and (c) ^{119}Sn NMR spectrum of (Me_2Sn(IV) + HL-**4**) at pH 2.7.

assigned to five- and six-coordinated species, respectively. The intensity of these signals, together with the percentage of tin-containing species from the speciation diagrams, suggest the presence of a distorted trigonal bipyramidal $M(OH)_2$ and a distorted octahedral ML(OH) (Fig. 5(d) and (e)) complex species at this pH. However, in the case of the Me_2Sn(IV)–HL-**2** system, only one resonance at −279 ppm has been observed, which also suggests a six-coordinated tin species that may be assigned to the major species ML(OH) (82%) existing at pH 7.2. Furthermore, in the case of the Me_2Sn(IV)–HL-**3** system, three resonances at −89, −196 and −268 ppm are obtained, which indicates the presence of five- and six-coordinated species. On the basis of the intensity of these signals, in conjugation with the speciation diagrams, the resonance at −89 ppm may be attributed to $M(OH)_2$, and those at −196 and −268 ppm to ML/ML(OH) (in traces) (Fig. 5(b), (d) or (e)).

Three resonances at −195, −262 and −297 ppm have been observed in the Me_2Sn(IV)–HL-**4** system at pH 2.7, which suggests the presence of 5- and 6-coordinated species. The resonances at −262 and −297 ppm have been assigned to 6-coordinated M and ML (Fig. 5(a) and (b)), respectively, whereas that at −195 ppm has been assigned to 5-coordinated MOH (Fig. 5(c)). On the other hand, only two resonances at −65 and −273 ppm have been observed at pH 7.0, which are indicative of four- and six-coordinated tin species, and may be assigned as $M(OH)_2$ and ML(OH), respectively. It has been reported that $M(OH)_2$ may have a tetrahedral (most likely) or trigonal bipyramidal structure, with a $\angle_{C-Sn-C}$ of ≈132°.[11]

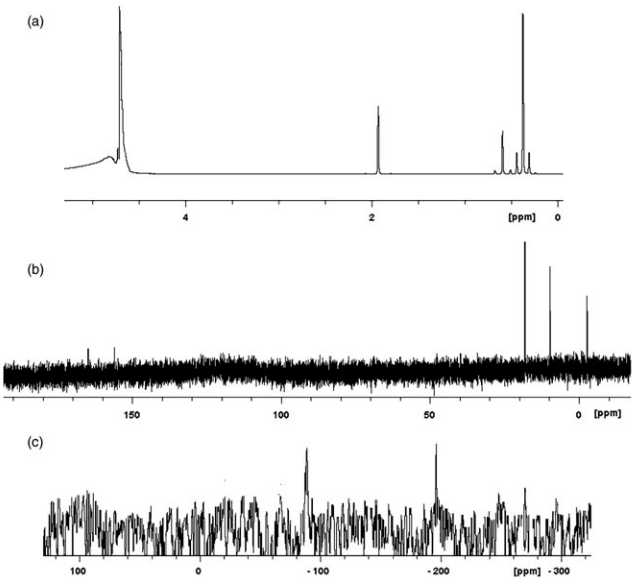


Fig. 8 NMR spectra of trimethyltin(IV)–ligand system in a $H_2O : D_2O$ (9 : 1) mixture: (a) ^1H NMR spectrum of (Me_3Sn(IV) + HL-**1**) at pH 7.2, (b) ^{13}C NMR spectrum of (Me_3Sn(IV) + HL-**4**) at pH 7.2 and (c) ^{119}Sn NMR spectrum of (Me_3Sn(IV) + HL-**3**) at pH 6.9.

NMR of trimethyltin(IV)–thione systems

It has been reported[37] that the coordination geometry around the tin of $(CH_3)_3Sn(IV)^+$ in aqueous solution is believed to be trigonal bipyramidal, with the three methyl groups in equatorial positions and two water molecules in axial positions (Fig. 6(a)). Complex formation would then be procured by ligand substitution of one water molecule (Fig. 6(b)). However, the equilibration of different methyl sites in penta-coordinated trimethyltin compounds (as shown in Fig. 6(b), (c) and (d)) is expected to be fast on the NMR time scale, and measured ^1J and ^2J values should correspond to an average of the different Me–Sn–Me angles in the molecule.

In the ^1H NMR spectra of all four trimethyltin(IV)–thione ligand systems at different pHs (Table 2), multiple methyl proton (bound to tin) resonances of varying intensity were obtained, indicating the presence of more than one trimethyltin(IV)-containing species. At pH 4.2 ± 0.2, a very sharp methyl proton resonance, observed at 0.45 ± 0.05 ppm, has been assigned to the trigonal bipyramidal $[(CH_3)_3Sn(OH_2)_2]^+$ species (Fig. 6(a)) on the basis of the observed $^2J_{^1H-^{119}Sn}$ coupling constant (68 ± 1 Hz) and calculated $\angle_{C-Sn-C}$ (118 ± 1°) in all the studied trimethyltin(IV) systems. The corresponding ^{13}C NMR chemical shift of this aqua species at pH 4.2 ± 0.2 was obtained at −1.67 to −1.68 ppm, with $^1J_{^{13}C-^{119}Sn}$ coupling constant values of 510–555 Hz, which also supports a trigonal bipyramidal structure (Fig. 6(a)). Furthermore, on increasing the pH, the chemical shifts of the methyl protons decreased, and the observed values of $^2J_{^1H-^{119}Sn}$ coupling constants and calculated $\angle_{C-Sn-C}$ in all the systems at all pHs suggested the presence of 5-coordinated $Me_3SnL/Me_3SnL(OH)/Me_3SnOH/Me_3Sn(OH)_2$ complex species, having a distorted trigonal bipyramidal geometry (Fig. 6(b–e)). In the ^{13}C NMR spectra of most of the cases, two methyl carbon resonances were observed (Table 3), but the ${}^1J_{^{13}\mathrm{C}-^{119}\mathrm{Sn}}$ coupling constants in some cases were not determined with certainty due to the presence of broad resonances. The observed values of ${}^1J_{^{13}\mathrm{C}-^{119}\mathrm{Sn}}$ also confirmed the existence of five-coordinated tin species. Only one set of ligand bound proton/carbon resonances were observed, which indicates that the exchange between bound and free ligand is very fast or no appreciable shifts occur due to the coordination of ligands. Furthermore, the existence of only 5-coordinated species in the Me_3Sn(IV)–HL-**3** and Me_3Sn(IV)–HL-**4** systems at physiological pH is also confirmed by the observed ^{119}Sn chemical shifts at −90 and −197 ppm, and −107 and −204 ppm, respectively. On the basis of the intensity of these resonances, in conjunction with the percentage of species from the speciation diagram, the resonances at −90/−107 and −197/−204 ppm have been assigned to ML and ML(OH), respectively (Fig. 6(b) and (e)).

Conclusions

The order of the extent of interaction of heterocyclic thione ligands with the dimethyltin(IV) cation, in terms of the percentage of ML/ML(OH), is: HL-**1** < HL-**4** < HL-**2** < HL-**3**; however, for the trimethyltin cation, it is: HL-**4** < HL-**2** < HL-**1** < HL-**3**. The extent of interaction of these S-ligands with $Me_3Sn(IV)^+$ is greater (in terms of partially hydrolysed species, $Me_3SnL(OH)$ ∼99%) compared to $Me_2Sn(IV)^{2+}$ ($Me_2SnL(OH)$ ∼78 ± 8%) in the pH range 7.5–8.0. The possible existing complex species at physiological pH 7.0 are $Me_2SnL(OH)$ (∼70–85%) and $Me_2Sn(OH)_2$ (∼15–30%) for dimethyltin(IV) systems, whereas $Me_3SnL(OH)$ (∼73–95%) exists, along with Me_3SnL (8–24%) and traces of $Me_3Sn(OH)$ (∼1–3%), for Me_3Sn(IV) systems. From the observed data, it has been inferred that the studied heterocyclic thione ligands are not able to suppress the formation of hydroxo species completely due to appreciable competition between the ligand and the hydroxide ion. The dihydroxo species, $Me_2Sn(OH)_2$, becomes predominant at higher pH (above pH > 10) in all the studied dimethyltin(IV) systems (Fig. 1 and Fig. 2), whereas for trimethyltin systems, the $Me_3SnL(OH)$ species is the predominant one in the pH range 6.5–10. In general, it appears that in aqueous solutions, only one of the two coordinated water molecules at the trimethyltin(IV) cation, or only one of the four coordinated water molecules at the dimethyltin(IV) cation, is replaced by other ligands, irrespective of the other donor atoms involved. Furthermore, it is observed that heterocyclic thione ligands with a potential sulfur donor group interact much more strongly with R_nSn cations at physiological pH (7.0) than do ligands with potential nitrogen donor groups, such as uracil, thymine and 5-fluorouracil ($Me_2SnL(OH)$/Me_3SnL 10–20%), and oxygen donor groups, *viz*. thiamidine and L-ascorbic acid (∼28% Me_2Sn(thiamidine), 60% Me_2Sn(L-ascorbic acid)(OH))/60% Me_3Sn(thiamidine)H, 60% Me_3Sn(L-ascorbic acid)), which were investigated previously by our research group,[16] in which metal–hydroxo complex formation was always preferred. Therefore, it can be concluded that $R_nSn^{(4-n)+}$ (n = 2 and 3) species may interact strongly with the thiol group of the protein and can effectively disturb the DNA duplication process.

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