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Coordination Chemistry Reviews
215 (2001) 99–149

COORDINATION
CHEMISTRY
REVIEWS

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Organotin(IV) complexes of amino acids and peptides

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Received 16 March 2000; accepted 22 August 2000

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PII: S0010-8545(00)00404-5

Abstract

A comprehensive review, > 120 references, on organotin(IV) complexes of the amino acids and peptides is presented with special reference to their methods of synthesis, structural and thermal properties as well as their solution studies and biological activity. The structures of these complexes are discussed on the basis of IR, electronic, multinuclear (^{1}H-, ^{13}C- and ^{119}Sn-) NMR, X-ray and ^{119}Sn Mössbauer spectral studies.

Keywords: Amino acids; Peptides; Organotin(IV); Spectroscopic studies; Biological activity

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1. Introduction

The exponential increase of the industrial, agricultural and biological applications of organotin(IV) compounds during the last 50 years has led to their accumulation in the environment and finally in biological systems. In this way, their interaction with living organisms and, finally, with man will surely increase within the next few years giving rise to pollution and toxicological problems. The solution to these problems will require an in-depth knowledge of the mechanisms of cell detoxification, a process that probably involves a reaction with biologically important ligands such as glutathione reduced, amino acids and peptides, etc. Knowledge on specific or selective bonding of metal and organometal species to donor sites in biological structures and even in simple biologically relevant oligofunctional molecules is rather scarce. To obtain better insight into the biological action of organotin chemicals, first their speciation in biological systems must be known. The interaction of the organotin moieties with different biologically important compounds has received considerable importance only in the last decade [1–25]. The study of binding the triethyltin moiety to rat-liver mitochondria has led to the assignment of two binding sites in the membrane: one of high-affinity, the other of low-affinity [26]. These binding sites are considered to involve histidine and thiol groups, respectively [26,27]. Most notable amongst the protein systems to which triorganotin or $Me_2Sn(IV)$ fragments are known to bind are the haemoglobins [28–31] and ATP-ase system [27,32–35]. Both histidine (via the imidazole ring nitrogen) and cysteine (via the sulphydryl group) residues have been implicated in the binding of trialkyltin moieties to cat and rat haemoglobins, with two triorganotin residues bound at identical sites on the alpha-chain sub-unit of the haemoglobin tetramer, and also in the low-affinity site of the ATP-ase system. In both cases the coordination number of tin was considered from ^{119}Sn Mössbauer data to be five in a distorted trigonal bipyramidal arrangement with equatorial alkyl carbon and axial nitrogen and sulfur atoms $SnR_3(S_{thiol})(N_{het})$ [27,29–31,34]. However, the binding at the high-affinity ATP-ase site appears to involve only a histidyl imidazole residue resulting in four-coordination for tin, although a *cis*-trigonal bipyramidal geometry, could not be unequivocally excluded [27,34]. Such studies, however, concerning organotin binding to biological macromolecules are still very rare in the literature and they are far from the quantitative description. Low molecular weight compounds present in biological fluids may also bind to organotin moieties, significantly altering their speciation. The characterization of these interactions can be also used for modeling the organotin binding to macromolecular compounds. The solution equilibrium studies of the organotin and biologically important ligands have gained importance due to the potential pharmaceutical application of organotin compounds. Today, a number of dialkyltin derivatives are known to have an efficient anticancer activity and their structure are well characterized in the solid state [1–3,5,7,14,15,17,18]. In view of the rapid progress including salient observations made in the relevant tin(IV) chemistry, an attempt is being made in this article to present a brief up to date review on the organotin(IV) complexes of the amino acids and peptides with special reference to their synthetic methods, structural and thermal behavior, and biological applications.

2. Synthesis

Most of the organotin(IV) derivatives of the amino acids and peptides have been prepared either, (i) by the condensation reactions of the organotin oxides or hydroxides and the amino acids or peptides, or (ii) by the replacement reactions of the organotin chlorides and the sodium salts of the amino acids and peptides.

2.1. From organotin(IV) oxides or hydroxides and ligands

Several compounds of the type R_3SnAA, where R = alkyl or aryl, and AA is the anion of the amino acids or glycylglycine (Gly-Gly), have been prepared by an azeotropic distillation of water from benzene or toluene solutions of the corresponding stannol or bis(triorganyltin)oxide and the amino acids or Gly-Gly (Eqs. (1) and (2)):

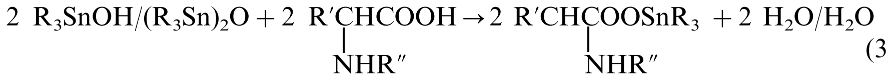
$$(n\text{-Bu}_3\text{Sn})_2\text{O} + 2\text{HOOCCH(R)NH}_2 \rightarrow 2n\text{-Bu}_3\text{Sn[OOCCH(R)NH}_2] + \text{H}_2\text{O} \tag{1}$$

(R = H (Gly) [36,37], DMF is used as catalyst [36]; RCH = CH_2CH_2 (β-Ala), solvent, toluene [38]).

$$\text{R}_3\text{SnOH} + \text{HOOCCH(R}')\text{NH}_2 \rightarrow \text{R}_3\text{Sn[OOCCH(R}')\text{NH}_2] + \text{H}_2\text{O} \tag{2}$$

(R = Et, R′CH = CH_2CH_2 (β-Ala) [36,39]; R = Me, R′ = CH_3 (DL-α-Ala) [39,40]; R = Me and Cy, R′ = H (Gly), CH_3 (DL-α-Ala), CH_2CH_3 (DL-α-Aminobut), $CH(CH_3{=})_2$ (DL-α-Val), $CH_2CH(CH_3)_2$ (DL-α-Leu), $CH(CH_3)C_2H_5$ (L-α-Ile), $HNHCOCH_2$ (Gly-Gly) and R′CH = CH_2CH_2; DMF is used as catalyst for R = Me and R′ = H and CH_3 [36]).

Frankel et al. [41] have synthesized the organotin esters of both amino and *N*-protected amino acids by using benzene or toluene as a solvent (Eq. (3)). Tri-*n*-butyltin-*N*-acetyl-valinate has also been synthesized from $(Bu_3Sn)_2O$, Et_3N, acetic anhydride and valine [38]:



$$2\ R_3SnOH/(R_3Sn)_2O + 2\ R'\underset{NHR''}{CH}COOH \rightarrow 2\ R'\underset{NHR''}{CH}COOSnR_3 + 2\ H_2O/H_2O \qquad (3)$$

($R = n$-Bu, $R' = CH_3$ (DL-α-Ala), CH_2CH_3 (DL-α-Aminobut), $CH(CH_3)_2$ (DL-α-Val), $CH_2CH(CH_3)_2$ (DL-α-Leu) and CH_2COOH (Asp), $R'' = H$; $R = Et$, $R'CH = CH_2CH_2$, $R'' = H$; $R = Et$ and n-Bu, $R' = H$ (Gly) and $CH(CH_3)_2$, $R'' = COCH_3$; $R = Et$ and n-Bu, $R' = H$ and $CH_2C_6H_5$ (DL-α-Phe), $R'' = COC_6H_5$; $R = Et$ and n-Bu, $R' = H$, $R'' = COOCH_2C_6H_5$; $R = n$-Bu, $R' = CH_2CH_2SCH_3$ (DL-Met) and $CH_2CH(CH_3)_2$, $R'' = COCH_3$ [41]).

A series of air stable triorganostannyl derivatives of L-cysteine and DL-homocysteine have been prepared by reacting the appropriate bis(triorganotin)oxide or triorganotin hydroxide with the sulphydryl-containing amino acids in methanol/water at room temperature (Eqs. (4) and (5)) [42]. Similarly, tri-n-butyltin(IV) 3-ureidopropionate has been synthesized by the interaction of bis(tri-n-butyltin)oxide and 3-ureidopropionic acid in 1:2 molar ratio in ethanol (Eq. (6)) [43].

$$(R_3Sn)_2O + 2HS(CH_2)_nCH(NH_2)COOH$$
$$\rightarrow 2R_3SnS(CH_2)_nCH(NH_2)COOH + H_2O \qquad (4)$$

($n = 1$ (L-Cys), $R = Np$; $n = 2$ (DL-Homocys), $R = n$-Bu and Np [42]).

$$R_3SnOH + HS(CH_2)_nCH(NH_2)COOH$$
$$\rightarrow R_3SnS(CH_2)_nCH(NH_2)COOH + H_2O \qquad (5)$$

($n = 1$ and 2, $R = Ph$ and Cy [42]).

$$(n\text{-}Bu_3Sn)_2O + 2HOOC(CH_2)_2NHCONH_2$$
$$\rightarrow 2n\text{-}Bu_3SnOCO(CH_2)_2NHCONH_2 + H_2O \qquad (6)$$

The triorganotin(IV) derivatives of L-cysteic acid and glutathione reduced have been prepared according to Eq. (7) [44,45]:

$$(R_3Sn)_2O + H_2L \rightarrow (R_3Sn)_2L{\cdot}xH_2O + H_2O \qquad (7)$$

($R = n$-Bu, $x = 2$, solvent, ethanol; $R = Ph$, $x = 0$, solvent, chloroform, $H_2L = HO_3SCH_2CH(NH_2)COOH$ (L-Cys acid); $R = Ph$, $x = 1$, $H_2L = HOOCCH(NH_2)CH_2CH_2CONHCH(CH_2SH)CONHCH_2COOH$) (GSH), solvent, water/ethanol [45]; $R = n$-Bu, $x = 1$, $H_2L = GSH$, solvent, water/ethanol, and pH 7.0 was adjusted with aqueous NaOH [44]).

It has been reported that the interaction of cysteine with $(Ph_3Sn)_2O$ resulted in the formation of $(Ph_3Sn)_2S$ [46], whereas the reaction of L-cysteine ethyl ester hydrochloride with $(Ph_3Sn)_2O$ or $(Bu_3Sn)_2O$ led to the formation of $R_3SnCysEt$ (where, $R = n$-Bu and Ph) at pH 10.5, adjusted by aqueous NaOH in ethanol (Eq. (8)) [44,46,47]. The reactions of N-acetyl-L-cysteine and glutathione reduced with bis(tri-n-butyltin)oxide in $CHCl_3$ and water/ethanol system, respectively, yielded stable N-acetyl-L-cysteinato(S-,O-)bis(tri-n-butylstannane)(IV), and α-glutamylcysteinatoglycinato(S-,O-)bis(tri-n-butylstannane)(IV), respectively (Eq. (9)) [44,46,47]:

$$(R_3Sn)_2O + 2HLEt{\cdot}HCl \rightarrow 2R_3SnLEt + H_2O + 2HCl \tag{8}$$

($R = n$-Bu and Ph, $HLEt{\cdot}HCl = HSCH_2CH(NH_2)COOC_2H_5{\cdot}HCl$(L-Cys.eth.est. hydro.) [44,46,47]).

$$(Bu_3Sn)_2O + H_2L \rightarrow (Bu_3Sn)_2L + H_2O \tag{9}$$

($H_2L = HSCH_2CH(NHCOCH_3)COOH$ (N-Ac-L-Cys) and GSH [44,46,47]).

Roge and his co-workers have also synthesized triorganotin(IV) derivatives of *N*-formyl- and -benzoylglycine according to Eq. (10) [48]. They have also reported triorganotin(IV) derivatives of *N*-acetylglycine, -α-alanine and -methionine (Eqs. (10) and (11)) [49]. Triphenyltin(IV) complex of *N*-acetylserine (Eq. (10)) [50], and triorganotin(IV) derivatives of mercaptoamino acids (Eq. (12)) [51], 3-ureidopropionic acid (Eq. (13)) [43] and *N*-protected dipeptides (Eq. (14)) [52] have also been reported:

$$R_3SnOH + HOOCCH(R'')NHCOR' \rightarrow R_3Sn[OOCCH(R'')NHCOR'] + H_2O \tag{10}$$

($R = Me$ and Ph, $R' = H$ and C_6H_5, $R'' = H$ [48]; $R = Me$ and Ph, $R' = CH_3$, $R'' = H$, CH_3 and $CH_2CH_2SCH_3$ [49]; $R = Ph$, $R' = CH_3$, $R'' = CH_2(OH)$ [50]).

$$(n\text{-}Bu_3Sn)_2O + 2HOOCCH(R')NHCOR$$
$$\rightarrow 2n\text{-}Bu_3Sn[OOCCH(R')NHCOR] + H_2O \tag{11}$$

($R = CH_3$, $R' = H$ and CH_3 [49])

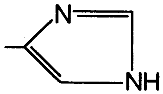
$$nR_3SnOH + HSCR'_2CH(NH_2)COOH$$
$$\rightarrow (R_3Sn)_nSCR'_2CH(NH_2)COOH_{(2-n)} + nH_2O \tag{12}$$

($R = Me$ and Ph, $R' = H$, $n = 1$; $R = Me$, $R' = CH_3$, $n = 1$; $R = Ph$, $R' = CH_3$, $n = 2$ [51]).

$$R_2R'SnOH + HOCO(CH_2)_2NHCONH_2$$
$$\rightarrow R_2R'SnOCO(CH_2)_2NHCONH_2 + H_2O \tag{13}$$

($R = R' = Ph$, c-C_6H_{11} (cyclohexyl) and p-$CH_3C_6H_4$ (p-tolyl); $R = Ph$, $R' = n$-Bu, p-ClC_6H_4 and c-C_5H_9 (cyclopentyl); solvent, ethanol [43]).

$$Me_3SnOH + HL(Me) \rightarrow Me_3Sn[L(Me)] + H_2O \tag{14}$$

($HL(Me) = C_6H_5CONHCH[CH_2CH(CH_3)_2]CONHCH(CH_2(R))COOCH_3$ (methyl *N*-Bz-L-Leu-L-His) and $((R)CH_2)CH(NHCOC_6H_5)CONHCH(CH_2SH)COOCH_3$ (methyl *N*-Bz-L-His-L-Cys), R =  [52]).

Zuckerman and Hall have reported synthesis of dimethyltindiglycinate and -di-β-alaninate (Eq. (15)) [53]. Chlorodimethyl- and chlorodi-*n*-butyltin(IV) derivatives of L-Cys, L-Cys.eth.est. and DL-penicillamine have been synthesized by Domazetis and his co-workers (Eqs. (16)–(18)) [44,54]:

$$Me_2SnO + 2HOOCCH(R)NH_2 \rightarrow Me_2Sn[OOCCH(R)NH_2]_2 + H_2O \quad (15)$$

($R = H$ and CH_3 [53]).

$$R_2SnO + HL \cdot HCl \cdot H_2O \rightarrow R_2SnClL \cdot H_2O + H_2O \quad (16)$$

$$R_2SnO + HLEt \cdot HCl \rightarrow R_2SnClLEt + H_2O \quad (17)$$

$$R_2SnO + HL + HCl \rightarrow R_2SnClL \cdot nH_2O + H_2O \quad (18)$$

($R = Me$ and n-Bu, $HL \cdot HCl \cdot H_2O = HSCH_2CH(NH_2)COOH \cdot HCl \cdot H_2O$ (L-Cys.hydro.hyd.), solvent, ethanol/water; $HLEt \cdot HCl$ = L-Cys.eth.est.hydro., solvent, ethanol; when $R = Me$, $n = 0$; $R = n$-Bu, $n = 1$, $HL = (CH_3)_2C(SH)CH(NH_2)COOH$ (DL-Pen), solvent, ethanol/H_2O (70:30) [44,54]).

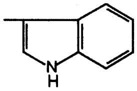
Sandhu and his co-workers have synthesized the diorganotin(IV) complexes of the *N*-protected amino acids and dipeptides in benzene/absolute ethanol (Eqs. (19) and (20)) [55–59]. The diorganotin(IV) complexes of the dipeptides in methanol/2,2-dimethoxypropane have also been synthesized with an azeotropic removal of water (Eq. (21)) [60–65]:

$$2R_2SnO/R_2SnO + 2HL \xrightarrow{2:2/1:2} R_2(L)SnOSn(L)R_2/R_2SnL_2 + H_2O \quad (19)$$

$$4R_2SnO + 4HL \rightarrow [[R_2Sn(L)]_2O]_2 + 2H_2O \quad (20)$$

($R = Me$, Et, n-Bu and n-Oct, $HL = [C_6H_4(CO)_2]NCH(X)COOH$, where, $X = CH_3$(N–Pht–DL-Ala), $CH_2CH(CH_3)_2$ (*N*-Pht-L-Leu) and $CH_2C_6H_5$ (*N*-Pht-L-Phe) [55], $HL = C_6H_5CONHCH(CH_3)CONHCH_2COOH$ (*N*-Bz-DL-Ala-Gly) [58], $HL = (CH_3)_2CHCH_2CH(NHCOCH_3)COOH$ (*N*-Ac-L-Leu) and $C_6H_5CH_2CH(NHCOCH_3)COOH$ (*N*-Ac-L-Phe) [56]; $R = Me$, n-Pr, n-Bu and n-Oct, $HL = C_6H_5CH_2CH(NHCOCH_2Cl)COOH$ (monochloro-Ac-L-Phe) [57]; $R = Me$, n-Bu and n-Oct, $HL = HOOCCH(CH(CH_3)_2)C_8H_4NO_2$(*N*-Pht-DL-Val) (Eq. (20))] [59].

$$R_2SnO + H_2L \xrightarrow{1:1} R_2SnL \cdot xH_2O/R_2SnL \cdot yCH_3OH + H_2O \quad (21)$$

($R = n$-Bu, n-Oct [60] and Ph [61], $H_2L = H_2NCH_2CONHCH_2COOH$ (Gly-Gly), $x = 0$; $R = Et$, H_2L = Gly-Gly, $H_2NCH_2CONHCH[CH(CH_3)_2]COOH$ (Gly-Val), $H_2NCH_2CONHCH(CH_2CH_2SCH_3)COOH$ (Gly-Met) and $H_2NCH_2CONHCH(CH_2C_6H_4OH)COOH$ (Gly-Tyr), $x = 0$ [62]; $R = n$-Bu, $H_2L = H_2NCH_2CONHCH(CH_3)COOH$ (Gly-Ala) and Gly-Val, and $R = Ph$, H_2L = Gly-Met, $x = 0$; $R = n$-Bu, H_2L = Gly-Gly and Gly-Ala, $x = 1$ [63]; $R = Me$ and Ph, $x = 0$, $H_2L = H_2NCH(R')CONHCH_2CH_2COOH$ (L-Trp-L-Ala), $H_2NCH(R')CONHCH(CH_2C_6H_4OH)COOH$ (L-Trp-L-Tyr), $H_2NCH(R')CONHCH(R')COOH$ (L-Trp-L-Trp), where $R' = CH_2$ , and $H_2L = H_2NCH(R')CONH(CH_2C_6H_4OH)COOH$ (L-His-L-Tyr), where $R' = CH_2$  [64]; $x = 1$, $R = Ph$, H_2L = L-Trp-L-Ala [65]; $y = 1$, $R = Me$, H_2L = L-Trp-L-Ala and L-Trp-L-Tyr [65];$R = Me$, n-Bu and Ph, $y = 0.5$, H_2L = L-Met-L-His [22]).

Similarly, dibutyltin(IV) derivatives of the amino acids having acidic or basic groups or nitrogen containing heterocyclic rings and of some dipeptides have also been reported from our laboratory (Eq. (22)) [66–69].

$$n\text{-Bu}_2\text{SnO} + 2\text{HL}/\text{H}_2\text{L} \rightarrow n\text{-Bu}_2\text{SnL}_2/n\text{-Bu}_2\text{SnL} + \text{H}_2\text{O} \quad (22)$$

(HL = DL-Met and $H_2NCOCH_2CH(NH_2)COOH$ (L-Asn) [66]; L-Tyr [67]; L-His and DL-Trp [68]; $H_2L = HOOCCH_2CH(NH_2)COOH$ (DL-Asp) and $HOOCCH_2CH_2CH(NH_2)COOH$ (L-Glu) [67]; $H_2NCH(CH_3)CONHCH(CH_2C_6H_5)COOH$ (Ala-Phe), $H_2NCH(CH_2C_6H_5)CONHCH(CH_2CH(CH_3)_2)COOH$ (Phe-Leu), $H_2NCH(CH_2C_6H_5)CONHCH(CH_2C_6H_5)COOH$ (Phe-Phe), $H_2NCH_2CONHCH(CH_2CH(CH_3)_2)COOH$ (Gly-Leu) and $H_2NCH_2CONHCH(CH(CH_3)CH_2CH_3)COOH$ (Gly-Ile) [69], solvent used, benzene-methanol 3:1 v/v).

The diorganotin(IV) derivatives of mercaptoamino acids have been synthesized from the condensation reaction of R_2SnO and mercaptoamino acids in $CHCl_3$ or water/chloroform system in 1:1 and 1:2 molar ratio [51]:

$$\text{R}_2\text{SnO} + \text{HSCR}'_2\text{CH(NH}_2\text{)COOH} \xrightarrow{1:1/1:2} \text{R}_2\text{Sn[SCR}'_2\text{CH(NH}_2\text{)COO]}/$$

$$\text{R}_2\text{Sn[SCR}'_2\text{CH(NH}_2\text{)COOH]}_2 + \text{H}_2\text{O} \quad (23)$$

(R = Me and Ph, R′ = H and CH_3 [51]).

2.2. From organotin(IV) chlorides and ligands

The interaction of trimethyltin(IV) chloride with L-Cys.eth.est.hydro. and N-Ac-L-Cys has been investigated using a water/chloroform two phase solvent system at pH 7.0, which was adjusted with NaOH (Eq. (24)) [44,46]. Whereas the interaction of the organotin(IV) chlorides with Gly-Gly in methanol yielded the adducts, $R_nSnCl_{4-n}.H_2L$ (Eq. (25)) [70]:

$$\text{Me}_3\text{SnCl}/2\text{Me}_3\text{SnCl} + \text{HLEt}\cdot\text{HCl}/\text{H}_2\text{L} \rightarrow \text{Me}_3\text{SnLEt}/(\text{Me}_3\text{Sn})_2\text{L} + 2\text{HCl} \quad (24)$$

(HLEt·HCl = L-Cys.eth.est.hydro. [46], H_2L = N-Ac-L-Cys [44]).

$$\text{R}_n\text{SnCl}_{4-n} + \text{H}_2\text{L} \rightarrow \text{R}_n\text{SnCl}_{4-n}\cdot\text{H}_2\text{L} \quad (25)$$

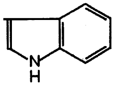
(R = n-Bu, n-Oct and Ph, $n = 1$ and 2; R = Me, $n = 2$; H_2L = Gly-Gly [70]).

2.3. From organotin(IV) chlorides and sodium salts of ligands

The organotin(IV) complexes of the types R_3SnL and R_2SnL have been synthesized by the replacement reactions of R_3SnCl and R_2SnCl_2, respectively, with the sodium salts of the amino acids, N-protected amino acids/dipeptides, and dipeptides:

$$\text{R}_3\text{SnCl}/\text{R}'_2\text{SnCl}_2 + \text{NaL}/\text{Na}_2\text{L} \rightarrow \text{R}_3\text{SnL}/\text{R}'_2\text{SnL} + \text{NaCl}/2\text{NaCl} \quad (26)$$

(R = Me, n-Bu and Ph, HL = DL-Met and L-Asn [66], L-Tyr [67], L-His and DL-Trp [68]; R′ = n-Bu, $HL = C_6H_5CONHCH(CH_2C_6H_5)COOH$ (N-Bz-DL-Phe) [41]; R = Me, n-Pr, n-Bu, Ph and Cy, $HL = C_6H_5CONHCH(CH_3)COOH$ (N-Bz-DL-Ala), $C_6H_5CONHCH(CH_3)CONHCH_2COOH$ (N-Bz-DL-Ala-Gly) [71],

$CH_3CONHCH(CH_2C_6H_5)COOH$ (*N*-Ac-L-Phe), $CH_3CONHCH(CH_2C_6H_5)$-$CONHCH_2COOH$ (*N*-Ac-L-Phe-Gly) [72], $C_6H_5CONHCH_2COOH$ (*N*-Bz-Gly), $C_6H_5CONHCH_2CONHCH_2COOH$ (*N*-Bz-Gly-Gly) [73], $HCONHCH(CH_2C_6H_5)$-$COOH$ (*N*-Fm-L-Phe) and $HCONHCH(CH_2C_6H_5)CONHCH_2COOH$ (*N*-Fm-L-Phe-Gly) [74]; $R' = Ph$, $H_2L =$ DL-Asp and L-Glu [67], Ala-Phe, Phe-Leu, Phe-Phe, Gly-Leu and Gly-Ile [69]; $R' = Et$, $H_2L =$ Gly-Gly, H_2NCH_2CONH–$CH(CH_3)COOH$ (Gly-Ala), $H_2NCH(CH_3)CONHCH(CH_3)COOH$ (Ala-Ala), Gly-Val and $H_2NCH[CH(CH_3)_2]CONHCH[CH(CH_3)_2]COOH$ (Val-Val) [62]; $R' = Me$ and *t*-Bu, $H_2L =$ Gly-Val; $R' = Me$ and Ph, $H_2L = H_2NCH_2CONHCH$-(CH_2 )COOH (Gly-Trp); $R' = t$-Bu and Ph, $H_2L =$ Gly-Ala; $R' = Ph$, $H_2L =$ Gly-Tyr; $R' = t$-Bu, $H_2L =$ Gly-Gly, containing one molecule of water [63]).

$$\mathrm{Ph_2SnCl_2 + 2(NaHL) \xrightarrow{1:2} Ph_2Sn(HL)_2 + 2NaCl} \tag{27}$$

($H_2L =$ Gly-Val [63]).

$$\mathrm{Ph_2SnCl_2 + 2NaL \rightarrow Ph_2SnL_2 + 2NaCl} \tag{28}$$

(HL = DL-Met and L-Asn [66], L-Tyr [67], L-His and DL-Trp [68]).

2.4. From organotin(IV) alkoxides and ligands

The alkoxides, $R_2Sn(OMe)_2$, have been synthesized under nitrogen from sodium methoxide and R_2SnCl_2 in methanol, and the complexes have been prepared by adding dipeptides in $R_2Sn(OMe)_2$ solution [63]:

$$\mathrm{R_2Sn(OMe)_2 + H_2L \rightarrow R_2SnL + 2MeOH} \tag{29}$$

($R = Me$, $H_2L =$ Gly-Ala, Gly-Met and Gly-Tyr; $R = Ph$, $H_2L =$ Gly-Val [63]).

3. Properties

3.1. Physical state and thermal stability

Most of the organotin(IV) derivatives of the amino acids and peptides are non-volatile, crystalline solids, which possess sharp melting points [37–43,45,47,48,52,54–63,65–74], but a few of them decompose on heating [36,49,53,57–68]. However, ethyl-L-cysteinatoS-(tri-n-butylstannane)(IV) [47], DL-penicillaminoS-(chlorodi-*n*-butyl)stannane hydrate [54], $[(n\text{-Oct})_2SnL_2]$ and $[\{(n\text{-Oct})_2SnL\}_2O]_2$ (where HL = *N*-pht-DL-Val) [59] and trialkyltin(IV) derivatives of *N*-Bz-Gly are viscous liquids [73]. Generally, the triorganotin(IV) complexes of the *N*-protected amino acids and di- and triorganotin(IV) complexes of the *N*-protected dipeptides solidify after standing 3–6 months in a vacuum desiccator [58,71–74]. A few tributyltin(IV) derivatives of the amino acids are semi-solids [66–68].

3.2. Hydrolysis and solubility

The organotin(IV) complexes of the amino acids are mostly stable towards air and have very low solubility in common organic solvents [36,41,42,45,47,49,54–57,66–68,71–74], whereas the corresponding compounds of the peptides are soluble in methanol, ethanol, chloroform and dimethyl sulfoxide [47,52,58,62,63,69–74]. Some diphenyltin derivatives of dipeptides are sparingly soluble in common organic solvents [69]. Dimethyltin diglycinate and dialaninate are insoluble in common organic solvents, and are readily hydrolyzed by atmospheric moisture [53]. Tributyltin *N*-acetylvalinate also undergoes hydrolysis in dilute acid [36]. Owing to the high electropositivity of the tin atom, the trialkyltin derivatives of the amino acids were attacked readily by strong electrophilic and nucleophilic reagents [41]. Heating the *N*-acetylamino tin esters with benzylamine or ammonia under anhydrous conditions in toluene did not lead to cleavage of the ester group or to amidation, while in the presence of water or alcohol these esters were readily split to give the benzylamine or ammonium salt of the *N*-acetylamino acids. This behavior prevents the use of the organotin esters as acetylating agents, indicating the weak electrophilic character of their carbonyl group. Acetic acid was found to cleave the organotin esters immediately, giving the trialkyltin acetate besides the free *N*-acetylamino acids. The trialkyltin esters of the amino acids behaved differently from those of the *N*-acetylamino acids. On contact with reagents such as water, ethanol, benzyl alcohol, benzoic acids, and *m*-cresol the former decomposed readily and quantitatively to the free amino acids. Under anhydrous conditions, they were stable to amines such as benzylamine [41].

4. Solution studies and formation constant

Determination of the formation constants potentiometrically for L-Cys, DL-Ala and L-His with trimethyltin chloride indicates that L-Cys binds far more readily than the other two amino acids. It has been reported that the equilibria concerned are complex and appear to involve polynuclear species in the pH range 7.0–9.0. If it is assumed that mononuclear species are formed in the pH range 5.5–6.5, then the formation constant values (pK_1) obtained under identical conditions are of the order: L-Cys, ca.10; DL-Ala, ca. 6; L-His, ca. 5 [44]. The proton formation constants of the ligands and formation constants as well as thermodynamic parameters of the dimethyltin(IV) complexes of Gly, DL-Ala and DL-Met have been determined potentiometrically at 20, 30 and 40°C and constant ionic strength (0.1 N NaCl) in the pH range 3.5–5.5 [75]. The interaction of tributyltin(IV) moiety with some amino acids and related compounds yielding 1:1 complexes has been investigated at 25°C in 0.1 M $NaNO_3$ using potentiometric film [76]. Domazetis et al. have reported that the behavior of the $Me_2Sn(Cl)L\cdot H_2O$ ($HL = Cys\cdot HCl\cdot H_2O$] in solution appears complicated. Two end points have been observed on titrating it with NaOH, corresponding to the protons on the carboxylate and amino groups [54]. Rose has observed that one molecule of rat haemoglobin binds two triethyltin fragments [26]. The binding sites are located on the globin and there is co-operativity between the sites such that the intrinsic affinity constant at pH 8.0 increases from 3.5×10^{-5} M^{-1} for the binding of the first triethyltin moiety to 5.0×10^{-5} M^{-1} for the binding of the second. Evidence is presented, from pH studies and the kinetics of inhibition due to photo-oxidation, that each binding site contains two histidine residues [26]. The proton formation constants of the ligands (log $K =$ 1.55–4.67) and log β values (9.34 ± 0.02–18.97 ± 0.01) of the monomeric complexes of diaquotrimethyltin(IV) cation $[Sn(CH_3)_2(H_2O)_2]^+$ with Gly, Asp, His, Cys, GS(glutathione) and Pen have been determined potentiometrically at 25°C and ionic strength (0.3 mol dm^{-3} $NaClO_4$) [77]. There is little or no interaction with glycine. Glutathione appears to coordinate through the S_{thiol} atom. The low stability of the penicillamine complex is rather surprising and may be due to steric factor [77].

Stoicheiometries and stability constants for the complexes formed between $R_3Sn(IV)$ species and selected amino acids (HL) (R = Me and Ph, HL = Gly, proline (Pro), threonine (Thr), serine (Ser), His and histamine (Hista); R = Me, HL = NorVal, Met, Leu; R = Ph, HL = Val, β-PhVal, S-MeCys, Isoleu (Ile), Pen, lysine (Lys); reaction medium, water [78] and 75% dioxane–water [79]) have been determined potentiometrically. The hydrolysis of the triorganotin(IV) moiety has been found to be consistent with $[R_3Sn(OH)]$ species (log $\beta_{10-1} = -5.79$ and -5.71 for $Me_3Sn(IV)$ and $Ph_3Sn(IV)$ moieties, respectively). The 1:1 complexes are formed irrespective of the ligand to metal ratio and most of the amino acids coordinate to the $R_3Sn(IV)$ moiety as a monodentate ligand (log $\beta_{110} = 5.71$–7.45), most likely via the amino group. Histidine and histamine have been found to form with the $R_3Sn(IV)$ moiety both the protonated and deprotonated complexes. The acid dissociation constants (pK^H) of the protonated complexes ($pK^H = 5.75$ (R = Me), 5.71 (R = Ph), HL = His; $pK^H = 5.70$ (R = Me), 5.29 (R = Ph), HL = Hista) indicate that His and Hista bind to the $R_3Sn(IV)$ moiety through their amino groups and the proton is located at the imidazole nitrogen in the protonated complex [78,79]. Penicillamine may coordinate either as *S*- or *N*-donor. Stability constant of its triphenyltin(IV) complex indicates that it coordinates through the *S*-atom ($pK^H = 7.80$) [79]. It has been reported that in all the species, distribution of the concentration of the complex increases with increasing pH, thus favoring complex formation with $R_3Sn(IV)$ moiety in the physiological pH range [78,79]. The coordination geometry of $R_3Sn(IV)$ moiety in solution is believed to be trigonal bipyramidal with three R groups equatorial and two solvent molecules in axial positions, complex formation would then involve ligand substitution of one solvent molecule. The location of the two *trans* solvent molecules prevents chelation of the ligands which is also evidenced by the experimental results. This is in marked contrast to the situation in the solid state, where extensive bridging frequently occurs [77–79].

Recently, Arena et al. have studied the complex formation of dimethyltin(IV) hydroxo species with Ala, Phe, Trp and Val potentiometrically at ionic concentration of 0.1 mol dm^{-3} of KNO_3. The stability constants of the complexes have been reported by selecting the models and using three different computer programs [80].

It has been reported that in the presence of threefold excess of the ligand, dimethyltin hydroxo species still form in high percentages. The species forming in low percentages have also been detected. At pH 2.5 dimethyltin moiety forms protonated species $[SnMe_2(L)H]$ in low percentage in which the amino acid behaves as monodentate and coordinates through carboxylic oxygen, whereas in the pH range 3.0–5.0, $[SnMe_2(L)]^+$ is the main species formed in which the amino acid may behave as a bidentate ligand. In the pH range 5.0–7.0 and above pH 8.0, the deprotonation of one and two coordinated water molecules leads to the formation of $[SnMe_2(L)H_{-1}]$ ($pK \sim 5$) and $[SnMe_2(L)H_{-2}]$, respectively [80]. Nevertheless, the similarity of the reported log β values, regardless of the nature (aromatic or aliphatic) and of the presence of the bulky side groups (Phe versus Ala) makes one think that solvophobic forces do not play any significant role on the stability of these systems [80].

Shoukry has also studied the interaction of hydroxo species of dimethyltin(IV) and diethyltin(IV) with Gly, Pro, Ala, Val, Leu, Ser, hydroxyproline, Phe, His and Hista potentiometrically at ionic strength of 0.1 M $NaNO_3$ using computer program MINIQUAD [81]. The hydrolysis of dialkyltin moieties results in mono- and dihydroxo-organotin(IV), $[R_2Sn(OH)_n$, where $n = 1$ or 2]. The formation of 1:1 and 1:2 (organotin: ligand) complexes with log β values in the range 8.18–10.38 and 14.43–18.52, respectively, has been reported in which the amino acids coordinate through amino and carboxylate groups. Histidine and histamine also form protonated complexes. It has been found that a linear relationship between the stability constant of the complex and acid dissociation constant of the ligand occurs. The dimethyltin complexes have been found to be more stable than the diethyltin complexes due to steric factor [81].

Very recently, Peter Surdy et al. have studied the interaction of the dimethyltin hydroxo species with Gly, Gly-Gly, Hista, His, Gly-Hista, Gly-His and β-Ala-His (carnosine) potentiometrically in aqueous media (0.1 mol dm^{-3} $NaClO_4$) [82]. For Hista and Gly-Hista (having only nitrogen donor atoms) no complex formation takes place showing the low coordination affinity in aqueous solution of this metal ion towards imidazole or amino groups, in the absence of other donor atoms. In the case of the other ligands, the complex formation process starts at pH 2.0 and two complexes MLH and MLH_2 are formed with the ligands having two and three labile protons, respectively. The hydroxo species of the dimethyltin cation have always been found to be dominant over the complexes formed with other ligands except with Gly-Gly and Gly-His. For these two ligands, [COO, $N_{peptide}$, NH_2] coordinated complexes are dominant in the neutral pH range with a trigonal bipyramidal structure, providing the first example that alkyltin(IV) moieties are able to promote the deprotonation of the peptide-nitrogen in aqueous solutions, at unexpectedly low pH. In this process, the carboxylate is the anchoring group (assisting by chelate formation), in contrast with any other metal ions, which are known to coordinate to amide nitrogen. The metal coordination of the imidazole ring, which is suggested as the binding site toward alkyltin(IV) species in several proteins, has not been observed for Gly-His under the conditions used and it is probably the case for the other ligands too [82]. Above pH 10.0, in all the systems, only the hydrolytic species of dimethyltin cation are present [82].

5. Molecular association

Molecular weight measurements for a number of trialkyltin(IV) esters of both amino and *N*-protected amino acids by titrating with 0.1 N NaOH, 0.1 N $HClO_4$ in dioxane, 0.1 N HCl and $NaOCH_3$ indicate the monomeric nature of the complexes in solution [41]. Osmometric measurements (in $CHCl_3$, C_6H_6 and CH_3COCH_3 at 37°C, in tetrahydrofuran at 45°C, and in pyridine at 60°C) of the R_3SnL (HL = *N*-protected amino acids [49]) and R_2SnL/R_2SnL_2 (H_2L = dipeptides [62,63], in methanol) complexes also indicate their monomeric nature in solution. Similar monomeric behavior of the compounds of the general formulae R_3SnL, R_2SnL_2 and $R_2(L)SnOSn(L)R_2$ (HL = *N*-protected amino acids and dipeptides) determined by Rast and Sandhu et al. has been reported [56,58,71,74]. On the other hand, molecular weight determination of the diorganotin(IV) complexes of *N*-Pht-L-Leu, *N*-Pht-DL-Ala and *N*-Pht-L-Phe in benzene shows various degrees of polymerization ($n = 1$, 2, 3 or 4 for different complexes), while all the complexes exist as monomers in molten camphor (175°C) [55]. $(n\text{-}Bu_3Sn)_2SG$ is strongly associated in solution probably via $N \rightarrow Sn$ coordination [47].

6. Spectroscopic and structural studies

Structural aspects of the organotin(IV) complexes of the amino acids and peptides have received much attention. Ultraviolet and multinuclear (^1H, ^{13}C and ^{119}Sn) magnetic resonance spectral studies along with molecular weight and potentiometric studies have been carried out to throw light on the structures of the complexes in solution. On the other hand, infrared and ^{119}Sn Mössbauer spectral studies, and X-ray crystallographic studies of a few representative complexes, have of course, been made to elucidate the structures of these compounds in the solid state. Conclusions drawn based on these studies are summarized below.

6.1. Ultraviolet spectra

The ultraviolet spectral studies of only one compound, L-cysteinato-*S*-(chlorodimethyl)stannane(IV) have been made at different pH. Its UV spectrum at pH 3.8 contains two maxima, whereas at pH 1.3 and > 12.0 only one peak is present. The pH dependence of the spectrum indicates that ionic species are formed in solution: protonation of the ligand and coordination at the tin atom being the likely possibilities. It is not possible to postulate from the UV spectrum which species are present but it is clear from the absence of a peak at 236 nm that the cysteinate anion is not present at pH > 12.0. Likewise, the absence of a peak at 256 nm (pH 1.3) indicates that a chlorodimethyltin ion is not present. Thus, a simple dissociation into dimethyltin and cysteinate ions is not indicated by the UV spectrum [54].

The electronic spectra of L-Tyr, DL-Asp, L-Glu, DL-Met and L-Asn exhibit a very intense band at 202 ± 3 nm, which may be due to the $n\text{–}\pi^*$ transition of COO^-

chromophore. The corresponding absorption band in the spectra of the tri- and diorganotin(IV) complexes has been observed at 223 ± 15 nm [66,67].

6.2. Infrared spectra

Infrared spectra of the complexes of organotin(IV) moieties provide valuable information regarding the structures of the compounds in the solid state. The structures of the organotin(IV) complexes of the amino acids and dipeptides raise several questions: whether there is a coordination to tin by the amino group nitrogen or carbonyl oxygen atoms, which coordination numbers result from these interactions, and the detailed coordination geometry about the tin atom in cases in which the possibility for isomerism exists. In addition, owing to the potentially polydentate nature of the amino acid and dipeptide ligands, it is necessary to distinguish chelated (intramolecular) monomeric structures from bridged (intermolecular) polymeric structures where the latter can adopt either one- or two-dimensional or cyclic oligomeric forms [36].

The position of ν(N–H) bands is influenced by hydrogen bonding and by coordination of the nitrogen to tin. Coordinated amino groups show a substantial lowering of the N–H stretching frequencies accompanied by an enhancement of their intensities. Infrared $\nu(NH_2)$ values for the triorganotin (IV) derivatives, R_3SnL (R = Me, HL = Gly, α-Ala, β-Ala, α-Aminobut, Val, Leu, Ile and Gly-Gly; R = *n*-Bu, HL = Gly; R = Cy, HL = Gly, β-Ala and Gly-Gly [36,83]; R = Me, *n*-Bu and Ph, HL = DL-Met, L-Asn [66], HL = L-Tyr, DL-Asp, L-Glu [67], HL = L-His and DL-Trp [68]), and the R_2SnL_2 (R = Me, HL = Gly and Ala [53]; R = *n*-Bu and Ph, HL = DL-Met, L-Asn [66], HL = L-Tyr [67], HL = L-His and DL-Trp [68]) and R_2SnL complexes (where R = Me, Et, *n*-Bu, *t*-Bu and Ph, H_2L = dipeptides [62,63]; R = *n*-Bu and Ph, H_2L = DL-Asp and L-Glu [67]; H_2L = Ala-Phe, Phe-Leu, Phe-Phe, Gly-Leu and Glu-Ile [69]) are markedly lower (2920–3400 cm^{-1}) than in the Cy_3SnL (HL = α-Ala, α-Aminobut, Val, Leu and Ile, 3396–3400 cm^{-1}) or in the alkali metal salts (e.g. 3380 cm^{-1} for NaGly, 3086 cm^{-1} for NaMet, 3400 cm^{-1} for NaAsn [66], 3168 cm^{-1} for NaTyr, 2999 cm^{-1} for NaAsp, 3018 cm^{-1} for NaGlu [67], 3500 cm^{-1} for NaHis and 3422 cm^{-1} for NaTrp [68]) or in the matrix-isolated amino acids (e.g. 3414 cm^{-1} for Gly [84,85] or in the free dipeptides (3029–3342 cm^{-1}) [69]). Protonation, as in the zwitterionic solid e.g. $H_3N^+CH_2COO^-$ (3170 cm^{-1}) or coordination to Co, Ni, Cu and Pt in several chelated complexes of known structure also produces a substantial lowering of $\nu(NH_2)$ (3207–3379 cm^{-1}) [86]. In addition, all the tin compounds which show lowered $\nu(NH_2)$ also exhibit intense absorptions, while the bands at ca. 3400 cm^{-1} in the other compounds are relatively weak. The intense $\nu(NH_2)$ absorptions observed are relatively narrow, suggesting that hydrogen bonding, usually prominent in the amino acids and their derivatives, is not pronounced in the tin compounds [36,66–69,83]. A band at 3418 ± 18 cm^{-1} in the IR spectra of asparagine and its sodium salt has been assigned to the stretching mode of the amido (–$CONH_2$) group which remains unaltered in the organotin(IV) complexes, indicating its non-involvement in coordination [66]. The $\nu(NH_2)$ frequencies in the R_3SnGly-Gly

[36,83], and $R_2SnCl_2(H_2Gly\text{-}Gly)$ and $RSnCl_3(H_2Gly\text{-}Gly)$ [70] are compared to a copper complex [87], whose structure is chelated through the amino group. Hardly any significant shift is observed for the $\sim 3300\ cm^{-1}$ band in the spectra of the adducts. However, the broad absorptions are observed for these adducts indicating the presence of inter and/or intramolecular hydrogen bonding [70]. The spectra of the $R_2Sn(Cl)L$ (HL = Cys and Pen) and n-Bu_3Sn(L-Cys. eth. est.) contain broad peaks centered at 3000 (νNH_2) and 3450 cm^{-1} (νH_2O) [54], and at 3375 cm^{-1} (νNH_2) [47], respectively, which are characteristic of H_2O and NH_2 groups involved in hydrogen bonding [54].

However, in the organotin(IV) complexes of the *N*-protected amino acids information on the occurrence of metal coordination by the basic atoms of the amide group may be obtained from the infrared frequencies of the modes, amide I [essentially $\nu(C{=}O)$] and amide II [$\nu(CN) + \delta(NH)$] as well as $\nu(NH)$ [88,89]. The following general pattern is observed upon coordination by oxygen (nitrogen) of the amido group to metal atom: (i) the frequency of the amide I absorption band decreases (increases), and (ii) that of amide II increases (decreases), with respect to values observed for the free groups; furthermore, (iii) eventual $\nu(NH)$ bands are nearly unchanged (in the absence of hydrogen bonding). For the solid complexes of the general formula R_3SnL (HL = *N*-Ac-Gly, *N*-Ac-Ala and *N*-Ac-Met [49]) the frequencies of amide I decreased and of amide II [with the exception of amide II of Ph_3Sn(*N*-Ac-MetO)] increased with respect to those found in *N*-Ac-GlyOEt (amide I at 1665, amide II at 1545 cm^{-1} [90]) and Me_3Si(*N*-Ac-GlyO) (amide I at 1666, amide II at 1549 cm^{-1} [91]), indicating the coordination through the carbonyl oxygen of the amide group ($CO \rightarrow Sn$) [49]. But for the triorganotin(IV) complexes of *N*-Bz-Gly, the amide I frequencies increase or remain the same; and those of amide II behave similarly or increase compared with those found in the amino acid ester (amide I at 1640, amide II at 1330 cm^{-1}), which indicates the non-participation of the C=O and NH groups in the coordination to tin(IV) and in addition indicates the presence of hydrogen bonding of the NH with the C=O group of the neighboring molecules in the solid state [73]. However, in the triorganotin(IV) complexes of *N*-Bz-Gly-Gly, amide I band frequencies decreased and amide II increased with respect to the ligand ester indicating the NHCO coordination to tin(IV). A marked shift of the [$\nu(CN) + \delta(NH)$] band towards higher frequencies and simultaneous shift of the $\nu(CO)$ amide band towards lower frequencies with change of state solid to one in solution are consistent with participation of the CONH group in the coordinate bonding with tin atom via donor oxygen atom in the solid state to form a NHCO–Sn donor–acceptor bond. It has been suggested that in solutions these complexes are present as simple molecules having a tetrahedrally coordinated tin atom, whereas in the solid state tin becomes penta-coordinated owing to the formation of a NHCO–Sn donor–acceptor bond [73].

The N–H stretching frequencies of the solid complexes of the general formulae R_3SnL [71,72,74], and R_2SnL_2 and $(R_2SnL)_2O$ [56,57] (HL = *N*-protected amino acids) are higher than those of the ethyl esters, suggesting that the amido nitrogen is not coordinating, which would be consistent with its low basicity. In addition to this, the intermolecular hydrogen bonding has been observed for R_2SnL_2 and

$(R_2SnL)_2O$ as the ν(N–H) bands are considerably broadened [56]. An upward shift of the ν(N–H) (3300–3420 cm^{-1}) in the solution spectra ($CHCl_3$) of the R_3SnL complexes is consistent with the loss of hydrogen bonding in solution. The stretching frequencies of the amido C=O in these solid compounds are shifted to lower values (while those of [ν(CN) + δ(NH)] are shifted to higher values) than those in $CHCl_3$ solution. This fact indicates that the CONH group is coordinated to the central tin atom in the solid state via an inter or intramolecular NHCO…Sn interaction [71,72,74]. The solution spectra ($CHCl_3$) of the R_3SnL [71,72,74], and R_2SnL_2 and $(R_2SnL)_2O$ [58] complexes (where HL = *N*-protected dipeptides) showed two broad medium-intensity N–H stretching bands at 3430 ± 30 and 3290 ± 10 cm^{-1}. The former band is assigned to a free amido group, while the latter is assigned to the N–H band of the peptide group. In the solid state, the N–H stretching frequency in the R_2SnL_2 and $(R_2SnL)_2O$ generally shifts slightly to higher frequency, suggesting that neither the amide nor peptide nitrogen atoms are coordinated, and bonding occurs between the NH groups and C=O groups of neighboring molecules [58]. Whereas the presence of doublets for ν(CO) amide and [ν(CN) + δ(NH)] or broad bands in the region 1500–1550 cm^{-1} in the R_3SnL complexes give an evidence for participation of only one CONH group in the NHCO…Sn donor–acceptor interaction. The above results showed that these compounds have tetrahedrally coordinated tin atom in solution. However, in the solid state the tin atom is five-coordinated [71,72,74].

The infrared spectrum of $(n\text{-}Bu_3Sn)_2$(*N*-Ac-L-Cys) over a wide concentration range indicates that the intensity of hydrogen bonded NH stretching band decreases on dilution. A dimeric hydrogen bonded structure has been proposed on the basis of steric requirements of the bulky organotin moieties (Fig. 1) [47]. Whereas the ν(N–H) peaks do not show appreciable concentration dependence in $(n\text{-}Bu_3Sn)_2SG$, which rules out the presence of intermolecular hydrogen bonding, but its molecular weight determinations show that the complex is associated in solution [47]. In the spectrum of *N*-Pht-DL-Val the stretching modes of imido CO are observed at 1770 cm^{-1}, which shift little after complexation indicating non-participation of the imido C=O group in significant coordination to Sn [59]. The asymmetric and

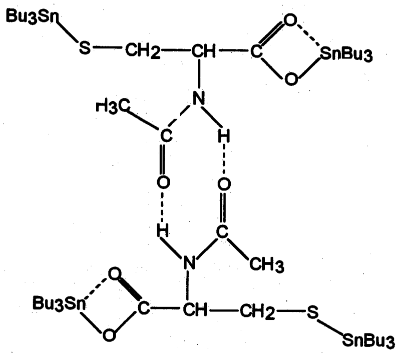


Fig. 1. Structure of $(n\text{-}Bu_3Sn)_2$(*N*-Ac-L-Cys).

symmetric stretching modes of the imido (C=O) are observed around 1720 and 1770–1780 cm^{-1}, respectively, in the R_2SnL_2 and $(R_2SnL)_2O$ (HL = *N*-Pht-amino acids derivatives [55]), and slightly higher ν(C=O) is observed for the R_2SnL_2 and $(R_2SnL)_2O$ (HL = monochloro-Ac-L-Phe [57]) complexes, indicating non-participation of the imido (C=O) in complex formation.

The N–H asymmetric stretching frequencies ($\sim 3475 \pm 20$ cm^{-1}) associated with the primary amide fragment in the organotin compounds of 3-ureidopropionic acid are practically unshifted from the value for the free ligand; this is not the case, however, for the N–H asymmetric stretching frequencies associated with the secondary amide fragment, which are about 45–108 cm^{-1} higher in the organotin compounds [43]. The latter values are further shifted by 100–120 cm^{-1} to higher wave numbers upon going from solid to solution (in $CHCl_3$) states. These features have been interpreted in terms of hydrogen-bonding interactions in the crystals of the compounds involving N–H and (presumably) an oxygen of the carboxylate group [43]. The amido C=O frequency which occurs at 1682 cm^{-1} in the free ligand is shifted to lower wave number ($\Delta\nu$ in the range 26–65 cm^{-1}) in the organotin compounds, and this is taken as evidence for coordinative attachment of this group to tin. It has been reported that this coordination is more likely to be inter than intramolecular since the latter would imply an eight membered chelate ring of doubtful stability [43].

Carboxylate groups in the organotin derivatives generally adopt a bridged structure in the solid state unless the organic substituents at tin are bulky or unless the carboxylate group is branched at the α carbon [92]. The zwitterionic forms of the amino acids in the solid state have symmetric anionic carboxylate groups as do their salts. The anionic sodium glycinate, the zwitterionic solid glycine itself, and the matrix-isolated molecular glycine have carbonyl absorptions at 1588, 1605 and 1781 cm^{-1}, respectively, taking ν_{as}(O–C=O) the feature which is most sensitive to structural changes [84,85]. The carboxylate groups in the first two forms of glycine are in a situation similar to that of a coordinated (bridged) carbonyl, while the matrix-isolated species is like a normal ester. The magnitude of the $\nu_{as}COO - \nu_{s}COO$ ($\Delta\nu$) separation, which has been shown to be useful in drawing structural inferences [93], is larger ($\Delta\nu = 243 \pm 38$ cm^{-1}) in the amino coordinated organotin(IV) complexes than in the amino acids and dipeptides themselves ($\Delta\nu = \sim 200$ cm^{-1}). The ν_{as}(O–C=O) values in the complexes are substantially higher (~ 1650 cm^{-1}) than for the corresponding zwitterionic compounds (~ 1600 cm^{-1}). Whereas the corresponding ν_{s}(O–C=O) absorptions either remain at the same value or move to lower frequencies than in the amino acids and dipeptides themselves. Strong interactions between the carboxylate carbonyl and the tin atom can thus be ruled out on this basis [36]. In the IR spectra of the complexes of the general formulae, Cy_3SnL (HL = amino acids [36,83]), R_3SnL (HL = amino acids [66–68], 3-ureidopropionic acid [43], *N*-protected amino acids and -dipeptides [49,57,71,72,74]), $R_2Sn(Cl)L$ (HL = amino acids [54]) and R_2SnL (H_2L = dipeptides [62,69]), the $\Delta\nu$ value is higher ($\Delta\nu = 245 \pm 45$ cm^{-1}) than in the alkali metal complexes ($\Delta\nu = < 200$ cm^{-1}). Ionic bonding and also bridging or chelation can therefore be excluded, and carboxylic groups bonding to tin unidentately must be assumed. However, some R_3SnL, and R_2SnL_2 and $R_2(L)SnOSn(L)R_2$ complexes (where HL = *N*-protected amino acids and -dipeptides [50,55,56,59,73,83]) have $\Delta\nu$ values of 200 ± 10 cm^{-1}, which indicate the chelated carboxyl groups, but in R_2SnL_2, where HL = *N*-Pht-amino acids, a strong band present in the free carboxylate region (1705–1710 cm^{-}$^{-}$) shows that the second carboxylate group is bonded to tin(IV) in a unidentate manner [55].

The ν_{as}(O–C=O) stretch has been assigned in the range 1630–1645 cm^{-1} in the complexes of the general formulae R_3SnL (HL = Cys, Homocys, *N*-Ac-Cys and L-Cys.eth.est. [42,47]) and Me_2SnL_2 (HL = Gly and Ala [53]), which indicates the non-coordinated carboxylate groups. A broad band in the range 2500–2800 cm^{-1} in the spectrum of *N*-Bz-DL-Ala-Gly is absent for its organotin(IV) complexes, R_2SnL_2 and $(R_2SnL)_2O$ [58], indicating deprotonation of the carboxyl group. The complexes show a broad band in the range 1630–1640 cm^{-1}, which is assigned to the ν(CO) of the amide and peptide groups together. Complex formation results in an increase in $\nu(CO)_{amide}$ and a decrease in $\nu(CO)_{pept}$, indicating that the peptide group is coordinated to tin and the amide group is not. The ν_{as}(O–C=O) is observed as a strong band at 1742 ± 3 cm^{-1} in the R_2SnL_2 (R = Me, Et, *n*-Bu and *n*-Oct) and $(R_2SnL)_2O$ (R = Me and *n*-Oct) complexes indicating unidentate carboxyl group. While the $(R_2SnL)_2O$ (R = Et and *n*-Bu) complexes show ν_{as}(O–C=O) frequencies at 1580 cm^{-1} indicating the bidentate coordination of carboxyl group [58]. In the diorganotin(IV) complexes of the dipeptides, R_2SnL (R = Me and *n*-Bu, H_2L = Gly-Gly; R = Me, H_2L = Gly-Ala) and *n*-$Bu_2SnL\cdot H_2O$ (H_2L = Gly-Gly and Gly-Ala), the carboxylate groups are also bidentate and bridging (ν_{as}(O–C=O) = 1595–1610 cm^{-1}; $\Delta\nu$ = 185–200 cm^{-1}), but for other complexes (as mentioned in synthesis in Eqs. (21), (26), (27) and (29) [62,63]) the carboxylate groups are monodentate (ν_{as}(O–C=O) = 1615–1635 cm^{-1}; $\Delta\nu$ = 210–240 cm^{-1}). Further, the presence of the $\nu(CO)_{pept}$ at < 1630 cm^{-1} in the above five complexes and at $\geqslant 1655$ cm^{-1} in other compounds is indicative of the involvement of $(CO)_{pept}$ in bonding in the above five complexes. From these observations it may be inferred that bulky substituent groups bound to tin, as well as to the carbon atom of $(CO)_{pept}$ of the ligand, favor the formation of monomeric complexes, with monodentate carboxyls and non-coordinating peptide carbonyl, whilst the reverse would occur with sterically less hindering substituents [63].

The IR spectra of *n*-Bu_2SnGly-$Gly\cdot H_2O$ and *n*-Bu_2SnGly-$Ala\cdot H_2O$ show one broad ν(OH) band at 3430 and 3420 cm^{-1}, respectively. In the case of *t*-Bu_2SnGly-$Gly\cdot H_2O$ this ν(OH) absorption is split into two bands, at 3490 and 3370 cm^{-1}. This should indicate differences in the mode of interaction of the water molecules and the Bu_2SnL moieties. The IR spectrum of $Ph_2Sn(Hgly\text{-}Val)_2$ is characterized by a low value of ν_{as}(O–C=O) as well as $\Delta\nu$, which strongly suggests the occurrence of bidentate carboxyl. Moreover, $\nu(NH_2)$ does not differ substantially from the value of the alkali-metal salts of dipeptides (3410, 3350 cm^{-1}), and $\nu(CO)_{pept}$ would indicate the O_{pept} is not coordinating. A polymeric structure, with bridging carboxyl groups has been proposed [63]. However, in case of $(n\text{-}Bu_3Sn)_2SG$ complex, ν(C=O) region is complicated by the presence of two carboxylate and two amide carbonyl groups. The disappearance of the 1715 cm^{-1} band, which occurs in the free ligand, due to the glycine residue, shows that bonding has occurred at this carboxylate group. A broad band that is observed in the complex (1645 cm^{-1}) shows a small upward shift in solution. The ν_s(O–C=O) band observed at 1390 cm^{-1} does not show any appreciable shift in solution, thus eliminating the possibility of carboxylate bridging [47].

The presence of both Sn–C stretching vibrations, ν_{as}(Sn–C) and ν_s(Sn–C), in the IR spectra of the R_3SnL (HL = various amino acids or dipeptides [36,47,49,52,66–68,71–74,83]) in the ranges 490–600 and 400–500 cm^{-1} for alkyl, and 250–280 and 200–230 cm^{-1} for phenyl, respectively, excludes an exactly planar arrangement of the three Sn–C bonds and thus a precisely symmetrical shape of the *trans*-trigonal bipyramidal arrangement of bonds around the central tin atom in these complexes in the solid state. In the IR spectra of $R_2Sn(Cl)L$, and $R_2SnL'(H_2L' =$ amino acids and dipeptides) the observation of two Sn–C absorption bands in the 500–600 cm^{-1} region for alkyl and 200–280 cm^{-1} region for aryl reveals a non-linear *trans*-configuration of the R_2Sn moiety [54,57,59,66–69]. Whereas, only one ν(Sn–C) band has been reported in the complexes of the types R_2SnL_2 and $(R_2SnL)_2O$ (HL = amino acids), which indicates a linear configuration of the C–Sn–C moiety [53,55–57]. For the 1:1 complexes of the type, $R_2(L)SnOSn(L)R_2$, a broad strong band at 630 ± 20 cm^{-1} has been assigned to an Sn–O–Sn stretching vibration [55–59].

6.3. Nuclear (^1H, ^{13}C and ^{119}Sn) magnetic resonance spectral studies

The ^{1}H-NMR spectra of the R_3Sn(L-Cys. eth.), where R = Me and *n*-Bu, and $(n\text{-}Bu_3Sn)_2$(*N*-Ac-L-Cys) have been studied by Domazetis et al. at various concentrations in $CDCl_3$ [47] (Table 1). The three spin systems and the four spin systems (at 15% w/w concentration) have been analyzed with the LAOCOON III program. Peaks due to the butyl groups tended to obscure peaks of low intensity arising from the ligand protons. The residence times of the rotational isomers (Fig. 2) have also been calculated by using Pachler's method. The larger proportion of isomer type I for the ligand anion may be due partly to electrostatic interactions. The compounds exist largely as isomers of type I, with isomer III also somewhat favored. These configurations permit closer approach of nitrogen to the tin atom and, as a result, the isomers may be stabilized by a Sn…N interaction. The spectrum of $(n\text{-}Bu_3Sn)_2$(*N*-Ac-L-Cys) changes on dilution, probably due to disruption of hydrogen bonding. At 15% w/w concentration hydrogen bonding is still present, and the results indicate that the isomer of type III predominates. The species present at this concentration are postulated to be cyclic dimers and it is possible that the presence of the species IV accounts for the large residence time obtained. From the ^3J(NH–CH) value of 7.2 Hz, a dihedral angle of ca. 30° has been estimated for the CH–NH fragment [47].

Several workers have reported that the CO(OH) resonance of the ligand is missing in the ^{1}H-NMR spectra of the complexes of the types R_3SnL, R_2SnL_2 and $(R_2SnL)_2O$ (HL = *N*-protected amino acids and dipeptides) and the NH (amide/

Table 1

^{1}H-NMR and ^{13}C-NMR data of triorganotin complexes and ^{13}C-NMR data of *n*-Bu$_2$Sn(L-Cys.eth.) in CDCl$_3$

Compound	J_{AB} (Hz)	J_{AC} (Hz)	J_{BC} (Hz)	*a* (I)	*b* (II)	*c* (III)	Reference
^{1}H-NMR							
L-Cys.eth. (pH 12)	−12.6	3.8	8.6	0.76	0.14	0.10	[47]
Me$_3$Sn(L-Cys.eth)	−13.1	3.5	7.7	0.64	0.10	0.26	[47]
n-Bu$_3$Sn(L-Cys.eth)	−12.4	3.8	7.7	0.64	0.14	0.22	[47]
(*n*-Bu$_3$Sn)$_2$(*N*-Ac-L-Cys.) (15% w/w)	−11.6	3.6	3.5	0.11	0.11	0.79	[47]

Compound	Chemical shifts (ppm)				Coupling constant (Hz)			Ligand shifts δ (ppm)	Reference
	αC	βC	γC	δC	$^1J(^{119/117}$Sn)	^2J	^3J		
^{13}C-NMR									
n-Bu$_2$Sn(L-Cys.Eth.)	13.9	28.8	27.2	13.7	332.1/317.4		61	173.6; 60.9; 57.1; 31.9; 16.8.	[47]
(*n*-Bu$_3$Sn)$_2$(*N*-Ac-L-Cys.)	17.1	28.0	27.2	13.7	358.9/344.3			169.4; 174.7; 54.7; 28.7; 23.4	[47]
	13.7				332.0/317.4				
(*n*-Bu$_3$Sn)$_2$SG	17.1	28.0	27.2	13.8	366.1/349.1		63	170.6; 174.3; 173.0; 56.0; 54.4; 42.7; 33.0; (28.8); (27.2)	[47]
	13.8				329.1/315.0				
(Me$_3$Sn)$_2$(*N*-Ac-L-Cys.)	−1.3				443.0			174.2; 169.6; 54.8; 29.2; 23.2	[46]
	−5.3				416.0				
(Me$_3$Sn)$_2$SG(D$_2$O)	−1.5				439.0/418.0			177.2; 175.8; 175.1; 172.9; 57.5; 55.3; 44.7; 32.8; 29.0	[46]
(*n*-Bu$_3$Sn)$_2$SG	17.1	28.0	27.2	13.8	366.0/349.0			170.6; 173.0; 174.3; 56.0; 54.4; 42.7; 33.0; 28.8 (28.4)	[46]
	13.8				329.0/315.0				

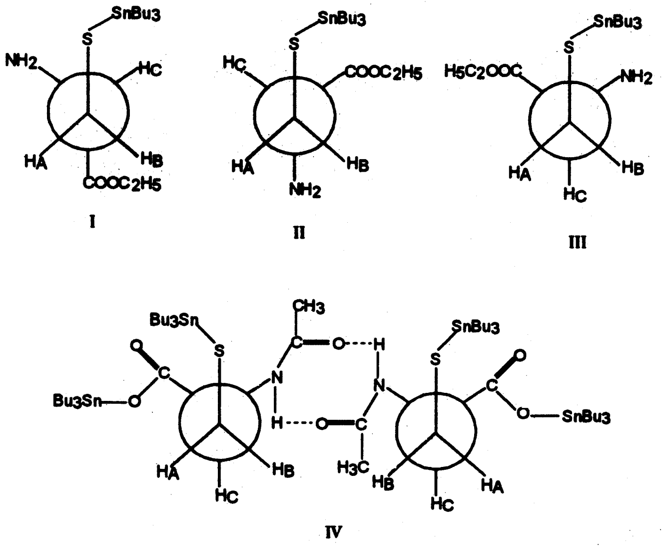


Fig. 2. Rotational isomers for n-Bu_3Sn(L-Cys.eth.) (I, II and III) and (n-$Bu_3Sn)_2$(N-Ac-L-Cys) (IV).

peptide) observed as a broad and weak signal is either absent or shifted towards lower δ value (if not obscured by superposition by phenyl protons attached to tin) in the complexes [47,49,55,56,58,59,66–69,71,73,74]. The extent of the shift depends on the solvent and the concentration. In $CDCl_3$ solutions of Me_3Sn(N-Ac-Gly) and (n-$Bu_3Sn)_2$(N-Ac-L-Cys) at lower concentration the NH signal is markedly shifted to lower δ value, while the NCH_2 signal is shifted a little to higher δ value. This effect can be correlated with an increase of breaking of the hydrogen bonds present in the solid state [47,49]. The resonances of the Me_3Sn protons in different solvents have been reported and the shift to lower δ values increases with increasing donor strength of the solvents in the series $CDCl_3$, CD_3OD and DMSO-d_6, as does $J(^{119}Sn–^{1}H)$. The values of coupling constant $[J(^{119}Sn–^{1}H)]$ of (60–63 Hz) for the Me_3Sn derivatives in $CDCl_3$, indicate four-coordination. The values of 70–71 Hz measured in DMSO-d_6 solutions are in the range for five-coordinate compounds, due to adduct formation with the donor solvent [49] (Table 2). In the dimethyl- and diethyltin(IV) derivatives of the N-protected amino acids, the presence of single methyl and ethyl resonances shows *trans*-configuration of the two alkyl groups [55,56,59]. The $J(^{119}Sn–^{1}H)$ values for the dimethyltin(IV) complexes of N-Pht-DL-Ala and -L-Leu in 1:2 ratio are 67 and 90 Hz, respectively, which are consistent with a higher than four-coordinated structure in solution. Whereas, the di-n-butyl- and di-n-octyltin(IV) complexes show two very broad signals due to the alkyl groups [55]. The $^{1}J(^{119/117}Sn–^{13}C)$ and $^{2}J(^{119/117}Sn–^{1}H)$ values at 475 and 62.6 ± 1.4 Hz, respectively for PhCO·Leu·His·OMe($SnMe_3$), suggest five-coordination to tin in CD_3OD. While $^{1}J(^{119/117}Sn–^{13}C)$ at 520 Hz and $^{2}J(^{119/117}Sn–^{1}H)$ at 96 Hz for PhCO.His.Cys.OMe($SnMe_3$), suggest six-coordination to tin in DMSO-d_6 [52]. The $^{2}J(^{119}Sn–^{1}H)$ for the R_2SnL_2 (HL = N-Bz-DL-Ala-Gly [58]) and R_2SnL (H_2L =

Table 2
^{1}H-NMR data of R_3Sn(*N*-Proc.A.A.) and diorganotin dipeptides

Compound	δ(MR_3/MR_2) ppm	Coupling constant $^2J(^{119}Sn, ^1H)$.(Hz)	Solvent (conc./mol dm^{-3})	Ligand proton shifts, δ (ppm)	Reference
Me_3Sn(*N*-Ac-Gly)	0.58	60	$CDCl_3$(0.43)	2.05(CH_3); 3.89(d, CH_2); 6.69(br, NH)	[49]
	0.58	60	$CDCl_3$(0.07)	2.05; 3.97(d); 6.23(br)	[49]
	0.45	67	CD_3OD(0.45)	1.91; 3.68	[49]
	0.36	70	DMSO-d_6(0.36)	1.74; 3.48(d); 7.76(br)	[49]
Ph_3Sn(N-Ac-Gly)	7.3 − 8.2		$CDCl_3$	1.97; 4.10(d); 6.03(br)	[49]
	7.3 − 8.4		DMSO-d_6	1.79; 3.60(d)	[49]
Me_3Sn(*N*-Ac-Ala)	0.58	62	$CDCl_3$	1.40(d, CH_3); 1.98($COCH_3$); 4.40(qnt, CH); 6.36(d, br, NH)	[49]
	0.41	70	DMSO-d_6	1.17(d); 1.79; 4.06(qnt); 7.79(d, br)	[49]
Ph_3Sn(N-Ac-Ala)	7.3–8.3		$CDCl_3$	1.39(d); 1.95; 4.69(qnt); 6.29(d)	[49]
Me_3Sn(*N*-Ac-Met)	0.59	63	$CDCl_3$	2.00(s, CH_3, CH_2); 2.12($COCH_3$), 2.55(br, –CH_2S); 4.58(q, –CHNH); 6.47(d,OOCCH)	[49]
	0.39	71	DMSO-d_6	1.81; 2.01; 2.39(br); 4.15(q); 7.79(d)	[49]
Ph_3Sn(*N*-Ac-Met)	7.3–8.2		$CDCl_3$	1.91; 1.94; 2.30(br); 4.70(br); 6.24(d)	[49]
	7.2-8.5		DMSO-d_6	1.78; 1.92; 2.17(br); 4.20(br)	[49]
Me_3Sn(Cys.eth.)	0.44	56.1	$CDCl_3$	4.19; 1.29(C_2H_5); 3.54(–CHN); 2.86(–SCH_2)	[46]
$(Me_3Sn)_2$(NAc-L-Cys)	0.44	56.2	$CDCl_3$	3.02(d, –SCH_2); 4.70(q, –CHN); 6.56(d, NH); 2.02(CH_3)	[46]
	0.61	59.0			
$(Me_3Sn)_2$SG	1.03	64.0	D_2O	2.74(t); 3.09(t); 3.49(q); 4.29(s); 4.96(t)	[46]
Me_3Sn(*N*-Bz-DL-Ala)	0.59	59.1	$CDCl_3$	7.36–7.78(C_6H_5); 7.00(NH); 4.46(CH(CH_3)); 1.50((CH)CH_2)	[71]
Me_3Sn(*N*-Bz-Ala-Gly)	0.60	59.3	$CDCl_3$	7.28–7.85(C_6H_5); 6.95; 7.10(NH); 4.75(CH(CH_3)); 3.96(NHCH_2); 1.52((CH)CH_2)	[71]
n-Bu_2Sn(*N*-Bz-Ala-Gly)$_2$	1.54–1.00(CH_2) 1.00–0.68(CH_3)	74	$CDCl_3$	7.90(m, –C_6H_4); 4.75(m, CH); 4.05(bm, CH_2); 1.00–0.50(m, CH_3)	[58]
n-Oct_2Sn(*N*-Bz-Ala-Gly)$_2$	1.25(CH_2) 0.88(CH_3)	64	$CDCl_3$	7.75(m); 4.75(m); 3.92(m) 1.43(bm)	[58]

Table 2 (*Continued*)

Compound	δ(MR_3/MR_2) ppm	Coupling constant $^2J(^{119}Sn, ^1H)$.(Hz)	Solvent (conc./mol dm^{-3})	Ligand proton shifts, δ (ppm)	Reference
n-Bu_2Sn(Gly-Gly)	0.77–1.67		CD_3OD	3.42(CH_2); 3.80(CH_2)	[63]
t-Bu_2Sn(Gly-Gly)	1.37	102	CD_3OD	3.51; 3.84	[63]
Me_2Sn(Gly-Ala)	0.59	82	DMSO-d_6	3.80(CH–); 1.09(CH_3)	[63]
	0.66	84			
	0.71	84	D_2O	3.33(CH_2); 4.11(CH–); 1.24(CH_3)	[63]
	0.78	82			
t-Bu_2Sn(Gly-Ala)	1.37	102	CD_3OD	3.41; 4.18; 1.35	[63]
	1.30	101			
Me_2Sn(Gly-Val)	0.51	78	DMSO-d_6	3.84(NCH–); 1.98(CH–); 0.91, 0.73[$(CH_3)_2$]	[63]
	0.67	80			
	0.71	78	CD_3OD	3.51(CH_2); 4.23(NCH–); 2.22(CH–); 1.07, 0.88[$(CH_3)_2$)]	[63]
	0.84	78			
	0.78	80	D_2O	3.39; 3.59; 2.21; 1.05; 0.90	[63]
	0.95	82			
n-Bu_2Sn(Gly-Val)	0.71–1.69		CD_3OD	3.34; 4.14; 2.13; 1.02; 0.84	[63]
t-Bu_2Sn(Gly-Val)	1.36	105	CD_3OD	3.27; 4.22; 2.22; 1.17; 1.03	[63]
	1.51	98			

dipeptides [63]) complexes are in the range 64–74 and 78–105 Hz (Table 2), respectively, indicating a coordination number greater than four for tin. The C–Sn–C angles have also been reported for the R_2SnL type of complexes ($\angle$C–Sn–C = 128–136° for R = Me and 166–172° for R = *t*-Bu) [63].

The values of ^{13}C chemical shift for the carboxylic and amide carbonyl carbon atoms in the R_3SnL and R_2SnL complexes (HL/H_2L = *N*-protected amino acids and dipeptides) unshifted relative to the ethyl esters of the ligands. This is consistent with the absence of interaction of the carbonyl groups with the central tin atoms (C=O…SnR_3) [69,71,72,74]. Whereas the signals of the carboxylic carbon of the amino acids have been reported at lower δ upon complexation, compared to those of free amino acids [66,67]. In the trialkyltin(IV) derivatives of the *N*-protected amino acids and dipeptides the values of $^1J(^{119}Sn–^{13}C)$ are in the range 330–405 Hz in $CDCl_3$, which are typical of the pseudo-tetrahedral arrangement of R_3SnO configuration with four coordinating tin(IV) atom [47,49,71,72,74] (Table 3). But in DMSO-d_6 solution, the ^1J values of Bu_3Sn(*N*-Ac-Gly) and Ph_3Sn(*N*-Bz-DL-Ala-Gly) are higher (444–466 and 833 Hz, respectively) which indicate that coordination number increases from four to five around the central tin atom due to the coordination of one molecule of coordinating solvent [49,71] (Table 3). Since the ^1J values of 330–390 and 450–480 Hz have been reported for four-coordinate and five-coordinate trialkyltin compounds, respectively [94]. The ^1J values are normally higher with phenyl compared to that of alkyl substituent [95]. The *n*-Bu_3Sn-S and *n*-Bu_3Sn-O moieties in (*n*-$Bu_3Sn)_2$(*N*-Ac-L-Cys) and (*n*-$Bu_3Sn)_2$SG have been identified from the αC shift [in $SnCH_2(\alpha)$-$CH_2CH_2CH_3$] values at 13.8 ± 0.1 and 17.1 ppm, respectively [47] (Table 1). The ^1J and $^2J(^{119/117}Sn–^{13}C)$ values in the R_2Sn(Cl)Cys.eth. are in the range 510–600 and 72–82 Hz, respectively, [54] and $^1J(^{119}Sn–^{13}C)$ values in the diethyltin dipeptides are in the range 608–633 Hz [62], which are indicative of five-coordinate tin in these complexes in $CDCl_3$ (Table 3).

The triorganotin complexes of the *N*-protected amino acids and dipeptides give sharp signals at 125 ± 25 ppm in ^{119}Sn-NMR spectra (in $CDCl_3$) which are typical of quasi-tetrahedral arrangement of simple trialkyltin(IV) compounds with a four-coordinate central tin atom. The value of $\delta(^{119}Sn)$ for [(c-$C_6H_{11})_3$Sn(*N*-Bz-DL-Ala)] (31.4 ppm) corresponds well to the tetrahedral configuration of $(C_6H_{11})_3SnOCO$ [71], whereas the $\delta(^{119}Sn)$ values of [(*n*-$C_4H_9)_3$Sn(*N*-Bz-DL-Ala-Gly] in hexamethylphosphortriamide (− 58.6 ppm) and those of the compounds $(C_6H_5)_3$Sn(*N*-Bz-DL-Ala) and $(C_6H_5)_3$Sn(*N*-Bz-DL-Ala-Gly) in DMSO-d_6 (− 269.0 and 263.0 ppm, respectively) are typical of tri-*n*-butyl- and triphenyltin(IV) complexes with one molecule of coordinating solvent bonded through the donor atom to the central tin atom (Table 3). The tin atom assumes coordination number of five [71]. The values of $\delta(^{119}Sn)$ of $(C_6H_5)_3$Sn(*N*-Ac-L-Phe) and $(C_6H_5)_3$Sn(*N*-Ac-L-Phe-Gly) (− 114.8 and − 99.7 ppm, respectively) also correspond to the pseudo-tetrahedral configuration of Ph_3SnO group [72].The values of $^1J(^{119}Sn–^{13}C)$ have also been used to calculate C–Sn–C angle, which is at 111 ± 1° in these complexes [71,72,74] (Table 3).The deformation of tetrahedral geometry of groups R_3SnO (R = Me, *n*-Bu, Ph, c-C_6H_{11}) in these compounds is negligible. The almost ideal shape of R_3SnO excludes even a more obvious interaction with nitrogen atom of the amide group

Table 3
^{13}C- and ^{119}Sn-NMR data of di- and triorganotin derivatives of the amino acids and dipeptides

Compound	δ (^{119}Sn) (ppm)	δ (^{13}C) (ppm) ($^{n}J(^{119}$Sn, ^{13}C) (Hz))				C–Sn–C (°)	Reference
		C(1)	C(2)	C(3)	C(4)		
Me$_3$Sn(*N*-Bz-DL-Ala)	142.4	−2.04 (405.9)				112.0	[71]
n-Pr$_3$Sn(*N*-Bz-DL-Ala)	129.8	19.61 (351.6)	19.14 (22.0)	18.44 (64.4)			[71]
n-Bu$_3$Sn(*N*-Bz-DL-Ala)	129.3	16.68 (353.5)	27.74 (22.0)	26.92 (64.0)	13.58	110.0	[71]
Ph$_3$Sn(*N*-Bz-DL-Ala) [a]	−263.0	143.15 ([b])	136.36 (47.0)	128.23 (70.4)	128.87 ([b])		[71]
n-Hex$_3$Sn(*N*-Bz-DL-Ala)	31.4	34.06 (331.2)	30.96 ([b])	28.79 ([b])	26.80 ([b])		[71]
Me$_3$Sn(*N*-Bz-Ala-Gly)	147.4	−2.10 (401.5)				112.0	[71]
n-Pr$_3$Sn(*N*-Bz-Ala-Gly)	127.4	19.59 (351.6)	19.00 ([b])	18.27 (64.6)			[71]
n-Bu$_3$Sn(*N*-Bz-Ala-Gly)	129.0	16.80 (349.4)	27.62 (21.50)	26.56 (64.5)	13.52 ([b])	109.5	[71]
Ph$_3$Sn(*N*-Bz-Ala-Gly) [a]	−269.0	144.20 (832.4)	136.25 (47.0)	128.59 (70.4)	128.69 ([b])		[71]
n-Pr$_3$Sn(*N*-Ac-Phe)	102.4	18.9 (372.2)	19.8	18.2			[72]
n-Bu$_3$Sn(*N*-Ac-Phe)	116.7	16.8 (362.5)	27.6 (22.0)	26.8 (66.0)	13.4 (< 10.0)	111.0	[72]
n-Bu$_3$Sn(*N*-Ac-Phe-Gly)	121.6	16.8 (354.0)	27.6 (22.0)	28.8 (66.0)	13.5 (< 10.0)	110.0	[72]
n-Bu$_3$Sn(*N*-Fm-L-Phe)	117.1	17.56 (367.8)	27.62 ([b])	26.63 ([b])	13.82 ([b])	110.0	[74]
n-Bu$_2$Sn(*N*-Bz-Ala-Gly)$_2$		26.50 (840.0)	27.44	27.19	21.05		[58]
n-Oct$_2$Sn(*N*-Bz-Ala-Gly)$_2$		25.24 (870.0)	25.72	29.38	22.70		[58]
Et$_2$Sn(Gly-Gly) [c]	−128.1	14.07 (632.8)	9.61, 9.69			132.4	[62]
Et$_2$Sn(Gly-Ala)	−126.2	13.38, 13.44 (623.0)	9.87, 9.66			126.2	[62]
Et$_2$Sn(Ala-Ala)	(d)	9.89, 9.69 (605.0)	12.89, 12.76			129.8	[62]
Et$_2$Sn(Gly-Val)	−126.7	12.05, 13.34 (607.8)	9.69, 9.80			130.2	[62]
Et$_2$Sn(Val-Val)	([d])	11.83, 13.02	9.94, 9.69 ([b])			(d)	[62]
Et$_2$Sn(Gly-Met)	−123.4	12.71, 13.66 (612.3)	9.65, 9.87			130.5	[62]
Et$_2$Sn(Gly-Tyr)	−122.2	12.33, 12.38 (616.3)	9.60, 9.69			130.9	[62]
Me$_2$Sn(Gly-Ala) [e]	−93.8	3.72, −3.15 ([d])					[63]
Me$_2$Sn(Gly-Val) [c]	−89.4	0.08, −0.74 ([d])					[63]
	−94.4 [e]	3.07, −2.08 ([d])					[63]
n-Bu$_2$Sn(Ala-Phe)	−197.8	26.54 ([d])	27.82	26.58	14.45	([d])	[69]
n-Bu$_2$Sn(Phe-Leu)	−201.8	([d])	([d])	([d])	([d])	([d])	[69]
n-Bu$_2$Sn(Phe-Phe)	−195.6	26.55 ([d])	27.12	26.82	13.47	([d])	[69]
Bu$_2$Sn(Cl)Cys.eth.		26.00 (539.6)	28.10	26.50 (68.4)	13.70	([d])	[54]
Me$_2$Sn(Cl)Cys.eth.		7.10 (581.1)				([d])	[54]
Me$_2$Sn(Cl)Pen		5.20 (600.6)				([d])	[54]

[a] Solvent DMSO-d$_6$.

[b] Not found.

[c] Solvent CD$_3$OD.

[d] Not measured.

[e] Solvent D$_2$O.

and/or oxygen atoms of carbonyl groups (if any such interactions exist, they must be very weak) [71,72,74]. The $^{117/119}$Sn chemical shift values of the diorganotin dipeptides are in the range -122.21 to -128.06 for the diethyltin compounds [62], -93.80 to -97.10 ppm for the dimethyltin compounds [63], and -195.6 to -201.8 ppm for the dibutyltin compounds [69], which are characteristic of penta-coordinated tin (Table 3).

^{1}H-NMR measurements on aqueous solutions of GSH and mono-, di-, and tri-methyltin(IV) derivatives in HEPES or TRIS buffers at room temperature have been done by Capolongo and his coworkers [96]. In the case of the monomethyl derivative an equilibrium between the starting material and another not identified species is obtained, while with the two other organotin derivatives, stable and well defined complexes are formed. In absence of GSH several methyl proton resonances are observed for monomethyltin(IV) moiety, confirming the presence of several hydrolyzed species in solution. Upon the gradual addition of GSH (ligand to metal molar ratio increasing to 8), a new resonance grows at lower fields ($\delta = 1.19$ ppm), while the others progressively decrease in intensity. At GSH to tin ratio 8:1 only this new resonance is observed together with a weak, narrow one at 0.89 ppm, that is probably due to a monomeric species. The $^2J(^{119}\mathrm{Sn}, {}^1\mathrm{H})$ value for this resonance is constant for all the ligand to metal ratios and equal to 81.0 ± 1.0 Hz.

A plots of δ versus the GSH to tin molar ratio, in Me_2SnCl_2-GSH and Me_3SnCl-GSH systems in TRIS buffer indicated 1:2 and 1:1 metal to ligand stoicheiometry, respectively. The $^2J(^{119}\mathrm{Sn}, {}^1\mathrm{H})$ value gradually decreases with increase in GSH concentration and is found in the range 83.3–67.7 Hz for Me_2SnCl_2-GSH system, whereas it shows minor variation (65.2–61.4 Hz) for Me_3SnCl-GSH. The C–Sn–C angle, θ, has also been calculated and it is 129° for Me_2SnCl_2 in TRIS buffer. This suggests that the TRIS molecule may occupy a coordination position around the tin, giving rise to trigonal bipyramidal geometry, with equatorial methyl groups and distorted toward a *trans*-octahedron. The addition of GSH shifts θ to 117° (GSH to tin ratio = 8) and also shifts the geometry towards a regular trigonal bipyramidal structure. The θ values in the range 115.8–113.1° for Me_3SnCl-GSH system correspond to the geometry of a highly distorted trigonal bipyramid, which remains practically unchanged when GSH to tin ratio is changed from 0 to 8 [96] (Table 4).

Recently, Peter Surdy et al. have investigated spectroscopically (^{1}H-, ^{13}C- and ^{119}Sn-NMR) the interaction of dimethyltin hydroxo species with Gly-Gly and Gly-His in aqueous solution [82]. The chemical shifts and coupling constants of the MLH_{-1} complexes [$^2J(^{119}\mathrm{Sn}–{}^1\mathrm{H})$, 82.2 Hz for Me_2SnGly-Gly and 80.2, 80.7 Hz (due to two different methyl signals) for Me_2SnGly-His; $^1J(^{119}\mathrm{Sn}–{}^{13}\mathrm{C})$, 656.9 Hz for Me_2SnGly-Gly and 646.6, 663.4 Hz for Me_2SnGly-His], which are nearly coincident with those reported for the corresponding crystalline complexes dissolved in aqueous solution, strongly support the trigonal bipyramidal structure for MLH_{-1} species with (COO, $N_{peptide}$, NH_2) coordination. In case of Me_2SnGly-His, the ML species is also formed [$^2J(^{119}\mathrm{Sn}–{}^1\mathrm{H}$, 82.2, 79.7 Hz) and the $ML = MLH_{-1} + H^+$ deprotonation is characterized by fast NMR site exchange; e.g. the imidazole protons continuously shifted to the upper field during this process and, also, only one set of peaks is detected for ML and MLH_{-1}. This indicates a deprotonation on a distant group from the metal ion, which is not involved in the coordination. Several NMR evidences may also support the proposed (COO, $N_{peptide}$, NH_2) coordination: (a) the slow NMR site exchange of the ML and MLH_{-1} complexes with the free ligands, prevents the fast proton-exchange between water molecules and the coordinated terminal amino group in the complex. This results in a detectable coupling between these amino protons and those of the next methylene group in the complexes of Gly-Gly and Gly-His. This is proof for the coordination of the amino group; (b) on the ^{13}C-NMR spectra of both systems, couplings of the amide ($J \sim 35$–36 Hz) and the carboxylate carbon ($J \sim 10$–11 Hz), and also for the methylene carbon in the case of Gly-Gly and for the CH carbon in Gly-His system are observed; (c) on ^{1}H-NMR spectra, couplings are observed between the hydrogens of the CH_2–COO^- group and tin for the Gly-Gly system ($J \sim 22$ Hz) and between the CH hydrogen and tin for the Gly-His system ($J \sim 28$ Hz). For this later system a weak coupling is also observed for one of the two H of the CH_2- amino group with tin ($J \sim 9$–10 Hz); the corresponding coupling for Gly-Gly is not observed probably as the consequence of broader peaks for this system than for the other. Thus, the MLH_{-1} species of Gly-Gly can be formulated as $M(LH)(OH) = MLH_{-1} + H^+ + H_2O$. Thus, the deprotonation of the amide and amine nitrogens takes place in a cooperative manner with the removing of the coordinated hydroxy group [82]. Two important features of hydroxo species of dimethyltin(IV) cation which promote ionization of amide nitrogen are: (i) the metal-promoted deprotonation of amide nitrogen is observed at low pH (4.0–5.0), indicating the 'soft'

Table 4
^{1}H-NMR parameters for the GSH/Me_2SnCl_2 and GSH/Me_3SnCl systems in 200 mM deuterated TRIS buffer ($B_o = 9.4T$, $T = 300$ K, [Sn] = 10 or 5 mM, pH = 7.30 ± 0.2 for Me_2SnCl_2; 7.4 ± 0.1 for Me_3SnCl) (Ref. [96])

GSH/Me_nSn-Cl_{4-n} ratio	GSH/Me_2SnCl_2			GSH/Me_3SnCl		
	δ CH_3Sn (ppm)	^2J (^{119}Sn, ^{1}H) (Hz)	θ (°)	δ CH_3Sn (ppm)	^2J (^{119}Sn, ^{1}H) (Hz)	θ (°)
0.0	0.760 [a]	83.3	129	0.427	65.2	115.8
0.2	0.734	79.6 [b]	125	0.444	63.2 [b]	114.3
0.5	0.751	77.1 [b]	123	0.465	62.3 [b]	113.7
0.8	0.775	74.4 [b]	121	0.482	62.8	114.0
1.0	0.788	74.0 [b]	121	0.493	62.3	113.7
1.5	0.829	70.7 [b]	118	0.504	62.0	113.4
2.0	0.856	69.9	118	0.510	61.7	113.2
3.0	0.876	68.2	117	0.517	61.5	113.1
4.0	0.881	67.9	117	0.515	61.5	113.1
5.3	0.882	67.7	116	0.511	61.4	112.7
8.0	0.880	67.9	117	0.511	61.5	113.1

[a] pH = 6.53.

[b] Average of ^{119}Sn and ^{117}Sn couplings.

character of dimethyltin moiety, which is generally considered as a ‘hard’ acceptor. In this context it is a unique example; (ii) the metal ion-promoted deprotonation of amide nitrogen in peptides is always preceded by a coordination of the metal ion to another donor group(s) of the ligand (anchoring group), which assists through the formation of a chelate ring. In case of the metal ions featuring a strong ability to bind amide nitrogen, the anchoring group is always the *N*-terminal amino group (completed with the coordination of the carbonyl oxygen), as the consequence of their ‘soft’ character. This picture does not hold, however, for the dimethyltin(IV) species, as it was supported by the NMR results and by the characteristic differences between the dimethyltin(IV) binding of glycyl-histamine and glycyl-histidine. In this case, the carboxylate oxygen plays the role of anchoring group, which is again a unique behavior of this moiety [82].

6.4. ^{119}Sn Mössbauer and X-ray crystallographic studies

The ^{119}Sn Mössbauer spectroscopy has been frequently employed to throw light on the structures of the organotin(IV) compounds. Whether the coordination of the amino group nitrogen atom leads to chelation or polymerization can be discussed with reference to the ^{119}Sn Mössbauer data. The structural inferences have been based mainly upon the magnitude of the quadrupole splitting (*Q.S.*) and upon the temperature dependence of Mössbauer effect.

The complexes such as Me_3SnL, where, HL = amino acids and Gly-Gly, and *n*-Bu_3SnGly, Cy_3SnGly and $Cy_3Sn\beta$-Ala, exhibit *Q.S.* values in the range 3.2 ± 0.1 mm s^{-1}, and ρ values greater than 2.1, consistent with higher than four-coordination, and possess a distorted trigonal bipyramidal arrangement with axially most electronegative atoms. In addition, the doublets of all the compounds exhibit pronounced line intensity asymmetry (Goldanskii-Karyagin effect), and four R_3SnL compounds (R = Me, HL = Gly, α-Ala and Gly-Gly; R = *n*-Bu, HL = Gly) give spectra at ambient temperature indicative of a polymeric structure through intermolecular coordination. On the basis of low ρ values (1.50–1.58), a tetrahedral structure has been proposed for Cy_3Sn-α-Aminobut and Cy_3SnVal owing to the lack of carboxylate coordination. Cy_3SnIle is, on the other hand, clearly higher than four-coordinated from Mössbauer data (*Q.S.* = 3.20 mm s^{-1} and $\rho = 2.1$) owing to the carboxylate coordination. It has trigonal bipyramidal structure with both the donor atoms of the ligand in the equatorial position. Whereas the ligand atoms in $Cy_3Sn\alpha$-Ala and Cy_3SnLeu are likely equatorial–axial, and equatorial–equatorial, respectively, on the basis of their *Q.S.* values (1.44 and 1.78 mm s^{-1}). The *Q.S.* value (3.45 mm s^{-1}) for Cy_3SnGly-Gly is distinctly outside the range of the values for other compounds and is consistent with hexa-coordination at tin involving both amide carboxyl oxygen and terminal amino group nitrogen association (either intra or intermolecular) [36,83] (Table 5).

Trimethyltin glycinate is shown by X-ray crystallography to be linear polymer having tetragonal crystals with $a = b = 7.839$, $c = 14.659$ Å, space group $P4_1$ or $P4_3$, $Z = 4$, and $\angle$N–Sn–O(1) = 159.8°, mean Sn–C, 2.14 Å, Sn–N, 2.53 Å and Sn–O(1), 2.27 Å (Fig. 3). The Me_3Sn unit is distinctly non-planar (C_{3v} local symmetry with Sn atom displaced towards the carboxylate oxygen) in trigonal bipyramidal geometry. The tin carboxylate carbonyl [Sn–O(2)] contact distance is 3.22(3) Å indicating some weak interaction. The hydrogen atoms of the amino group are apparently used in hydrogen bonding, as illustrated by the intramolecular N–O(2) distance of 2.94(3) Å and an intermolecular contact distance of 2.67(3) Å with the adjacent symmetry related to carboxylate carbonyl O(2) [97,98]. In the R_3SnL (HL = *N*-protected amino acids) the consistency of $Q.S._{\text{expt}}$ values (3.12–3.65 mm s^{-1}) with the structure as shown in Fig. 4, has been checked through calculation of *Q.S.* by the point-charge model formalism using a suitable computer program. The Ph_3Sn(*N*-Ac-Gly) crystallizes in the space group $P2_12_12_1$ with the lattice parameters, $a = 2172.5(8)$, $b = 1173.0(5)$, $c = 954.7(5)$ pm and $Z = 4$ [49].

Several workers have reported the Mössbauer parameters for the R_3SnL and $R_2Sn(Cl)L$ [HL = amino acids and their ethyl esters], and $(n\text{-}Bu_3Sn)_2SG$ [45,47,99]. The five-coordinate structural types for which *Q.S.* values (I, 3.0–3.3; II, ~ 3.8; III, 2.0–2.3 and IV, ~ 3.5 mm s^{-1}) have been calculated, are depicted in Fig. 5.

The compounds, $R_2Sn(Cl)L$ [45] and R_2SnL [67] have been proposed to have the structure as shown in I (Table 5). The ^{119}Sn Mössbauer studies (in frozen solution) of Me_2Sn-L-Cys at pH > 2.0 indicate the complexation of dimethyltin aquocation with ionized SH group of L-Cys to form a five-coordinate species. At high pH, a chelate is formed involving both the SH and the NH_2 groups bonded to Sn and one water molecule (or OH^- at still higher pH) occupying the fifth coordination site. Finally at pH > 10.0, the NH_2 group is also replaced by OH^- [100]. The inner doublets of both $(n\text{-}Bu_3Sn)_2$(*N*-Ac-Cys) and $(n\text{-}Bu_3Sn)_2SG$ complexes, have been assigned to the *n*-Bu_3Sn-S moiety and the outer doublets to *n*-Bu_3Sn-O. The associated nature of $(n\text{-}Bu_3Sn)_2SG$ indicates that the outer doublet is likely to have originated from a structure of type IV. The monomeric nature of $(n\text{-}Bu_3Sn)_2$(*N*-Ac-Cys) would suggest a structure of type II [45,47] (Table 5). $(Ph_3Sn)_2SG{\cdot}H_2O$, however, shows an intriguing spectrum, with a very low *I.S.*(0.78 mm s^{-1}) for one moiety, while the other (*I.S.* = 1.61 and *Q.S.* = 2.20 mm s^{-1}) compares favourably with the values reported (*I.S.* = 1.34 and *Q.S.* = 2.35 mm s^{-1} [101]) for triphenyltin thioacetate in pyridine. The structure of this compound has been proposed to be of type IV. On the other hand, the calculated *Q.S.* value (2.0 mm s^{-1}) suggests structure III. The higher *Q.S.* value for the Ph_3Sn–S moiety may then be due to water coordinating to that tin atom. The other moiety, Ph_3Sn–O may be type III (X = N) via inter or intramolecular association [45]. The structure III has been proposed for R_3SnL complexes (where, R = Me, *n*-Bu and Ph, HL = L-Tyr [67], DL-Met and L-Asn [66]) with some intermolecular interactions. Whereas, the isomer shifts for R_3SnL (where, R = Me, *n*-Bu and Ph; HL = DL-Trp and L-His) [68] (Table 5) and for Me_3Sn and Ph_3Sn derivatives of *N*-Bz-DL-Ala-Gly [71] lie in the range typical of the triorganotin(IV) carboxylates, while *Q.S.* values (2.79 ± 0.27 mm s^{-1}) are slightly lower than those typical for *trans*-trigonal bipyramidal coordination of tin in R_3SnO_2 fragment (3.00–4.00 mm s^{-1}), but substantially higher than that for *cis*-trigonal bipyramid (1.70–2.40 mm s^{-1}). Polymer like structure in the solid state and intermolecular O…Sn coupling [68,71] and thus a *trans*-trigonal bipyramid coordination of tin atom are also supported by the fact that mössbauer spectra were obtained at room temperature [71].

The *I.S.* (1.20–1.51 mm s^{-1}) and *Q.S.* values (3.06–3.62 mm s^{-1}) of $R_2R'Sn–(OCO(CH_2)_2NHCONH_2)$ (R = R′ = Ph, *n*-Bu, cyclohexyl and *p*-ClC_6H_4; R = Ph, R′ = *n*-Bu, *p*-ClC_6H_4 and cyclopentyl) indicate structure IV [43]. It has been proposed that the compounds adopt ureido–carbonyl bridged polymeric structure with the most electronegative *trans*-O_2SnC_3 axially in trigonal bipyramidal geometries about the tin atom with some reinforcement of the associated lattice as a result of intermolecular hydrogen bonding interactions between NH and presumably C(O)O. It was also confirmed by the X-ray structure of triphenyltin 3-ureidopropionate (Fig. 6[A]). The tin is five coordinate, with the axial positions of the trigonal bipyramid being occupied by the ester oxygen and the ureido oxygen of an adjacent molecule. The structure is orthogonal, space group $P2_1/n$ with $a = 11.150(1)$, $b = 12.719(3)$ and $c = 15.164(2)$ Å, $\beta = 94.05(1)°$, and $Z = 4$. The C–O bond distances in the carboxylate group are 1.289(4) and 1.224(4) Å, and the amide C=O in the ureido fragment is 1.253(4) Å. The sum of C–Sn–C angles in the trigonal plane is 359.0(1)° and the three phenyl groups are tilted at 156.30, 127.17 and 145.12° with respect to this plane. The tin-oxygen distances are 2.143(2) and 2.352(2) Å [43]. The molecular packing (Fig. 6[B]) shows that the polymer units are held together in the lattice by relatively strong hydrogen bonding interactions between the amide hydrogen and the carboxylate carbonyl oxygen [HN–OCO = 2.882(4) Å] of an adjacent molecule [43].

The crystal structure of chloro(ethyl-L-cysteinato-*N*,*S*)dimethyltin(IV) is orthorhombic, space group $P2_12_12_1$ with $a = 6.658(5)$, $b = 10.974(3)$, and $c = 17.144(5)$ Å, and $Z = 4$. The geometry about the Sn is distorted trigonal bipyramidal; the N and Cl atoms are in the axial positions, and the Sn lies at 0.107(1) Å from the equatorial plane. The Sn–Cl, Sn–S, and Sn–N bonds are 2.523(4), 2.413(3), and 2.434(12) Å, respectively; and the N–Sn–Cl angle is 166.9(3)° [102].

The observed *Q.S.* values ($\sim 3.75 \pm 0.35$ mm s^{-1}) and *I.S.* (1.31 ± 0.52 mm s^{-1}) in the R_2SnL_2 complexes indicate a distorted *trans*-octahedral configuration [53,55,56,58] (Table 5). But in the dimethyltin(IV) complexes of the *N*-phthaloyl amino acids [55], the *I.S.* values (~ 1.05 mm s^{-1}), and in the R_3SnL(HL = L-Cys and DL-Homocys) [42], the *Q.S.* values (≤ 1.79 mm s^{-1}) are comparatively lower, than the other complexes, indicating four coordinate tin atom (Table 5). The distorted octahedral structure with *cis*-organic groups has been proposed for the complexes R_2SnL_2 (where, R = *n*-Bu and Ph; HL = L-Tyr, DL-Met, L-Asn, L-His and DL-Trp [66–68]) as the observed *I.S.* (1.02–1.15 mm s^{-1}) and *Q.S.* (2.35–2.94 mm s^{-1}) values lie well within the range (Table 5). The 1:1 complexes, $(R_2SnL)_2O$ (HL = *N*-Ac-amino acids), have *Q.S.* values (3.24 ± 0.14 mm s^{-1}), corresponding to five coordination [56]. However, in the adducts, $R_2SnCl_2{\cdot}H_2$Gly-Gly and $RSnCl_3{\cdot}H_2$Gly-Gly, the *I.S.* and *Q.S.* values (0.76–1.48 and 2.01–3.82 mm s^{-1}, respectively) suggest the bonding is relatively weak between the tin(IV) moiety and the ligand. The slope $d\ln A/dt = -1.41 \times 10^{-2}$ K^{-1} has been determined by variable temperature ^{119}Sn Mössbauer, which is lower than the slope (-1.8×10^{-2} K^{-1}) found for the compounds having non-interacting monomeric molecules [70]. The ^{119}Sn Mössbauer data of solid-state R_2SnL(H_2L = dipeptides) complexes have fallen into two different classes: (i) by employing the partial nuclear quadrupole

Table 5
^{119}Sn Mössbauer parameters of some selected organotin compounds of amino acids and dipeptides

Complex	I.S. (mm s^{-1})	*Q.S.* (mm s^{-1})	τ_1 (mm s^{-1})	τ_2 (mm s^{-1})	Reference
Me$_3$Sn(Gly) [a]	1.26	3.14	1.16	1.07	[36,83]
Me$_3$Sn(α-Ala) [a]	1.30	3.21	1.50	1.03	[36,83]
Me$_3$Sn(Ile)	1.29	3.23	1.85	1.08	[36,83]
Me$_3$Sn(Gly-Gly) [a]	1.31	3.26	1.13	1.12	[36,83]
Cy$_3$Sn(Gly)	1.56	3.14	1.48	1.13	[36,83]
Cy$_3$Sn(β-Ala)	1.52	3.21	1.06	1.12	[36,83]
Bu$_3$Sn(Gly) [a]	1.42	3.21	1.02	1.19	[36,83]
Cy$_3$Sn(α-Ala)	1.45	2.09	1.59	1.78	[36,83]
Cy$_3$Sn(α-Aminobut)	1.53	2.41	1.61	1.60	[36,83]
Cy$_3$Sn(Val)	1.54	2.78	1.31	1.21	[36,83]
Cy$_3$Sn(Leu)	1.54	2.75	1.34	1.85	[36,83]
Cy$_3$Sn(Ile)	1.54	3.20	1.18	1.13	[36,83]
Ph$_3$Sn(L-His)	1.18	2.74	1.21	1.18	[68]
Me$_3$Sn(DL-Trp)	1.27	3.06	0.58	0.63	[68]
Me$_3$Sn(L-Asn)	1.26	3.05			[66]
Ph$_3$Sn(DL-Met)	1.13	2.40			[66]
Me$_3$Sn(L-Tyr)	1.20	2.98			[67]
n-Bu$_3$Sn(uried)	1.51	3.41	0.90	0.92	[43]
Ph$_2$(*p*-ClPh) Sn(uried)	1.23	3.38	0.88	0.88	[43]
Ph$_2$(c-C$_5$H$_9$) Sn(uried)	1.26	3.17	0.91	0.93	[43]
Cy$_3$Sn(uried)	1.43	3.62	0.87	0.88	[43]
(*p*-tolyl)$_3$ Sn(uried)	1.21	3.06	0.88	0.86	[43]
Ph$_2$Sn(L-His)$_2$	1.07	2.35	0.89	1.06	[68]
n-Bu$_2$Sn-(DL-Trp)$_2$	1.15	2.46	0.84	0.95	[68]
Ph$_2$Sn(L-Tyr)$_2$	1.10	2.79			[67]
n-Bu$_2$Sn(L-Glu)	0.88	2.40			[67]
Ph$_2$Sn(DL-Asp)	0.90	2.66			[67]
n-Bu$_2$Sn(DL-Met)$_2$	1.14	2.49			[66]
Ph$_2$Sn(L-Asn)$_2$	1.08	2.40			[66]
Me$_2$Sn(Cl)(L-Cys)·H$_2$O	1.33	3.26			[45,47]
Me$_2$Sn(Cl)(DL-Pen)	1.28	3.16			[45,47]
n-Bu$_2$Sn(Cl)(L-Cys)	1.44	3.15			[45,47]
Me$_2$Sn(Cl)(L-Cys.eth.)	1.27	2.84			[45,47]
(*n*-Bu$_3$Sn)$_2$ (*N*-Ac-L-Cys)	1.41, 1.37	3.59, 1.62			[45,47]
(*n*-Bu$_3$Sn)$_2$SG	1.40, 1.39	3.43, 1.76			[45,47]
Et$_2$Sn(*N*-Pht-L-Leu)·3H$_2$O	1.67	4.09	0.84	0.91	[55]
Et$_2$Sn(*N*-Pht-DL-Ala)	1.57	3.91	0.90	1.00	[55]
Bu$_2$Sn(*N*-Pht-L-Phe)·4H$_2$O	1.33	3.45	1.02	1.00	[55]
n-Oct$_2$Sn(*N*-Pht-L-Leu)·3H$_2$O	1.38	3.43	0.88	0.89	[55]
n-Oct$_2$Sn(*N*-Pht-DL-Ala)	1.46	3.63	0.84	1.10	[55]
Me$_2$Sn(*N*-Pht-DL-Ala)	1.06	3.41	1.02	1.09	[55]
Me$_2$Sn(*N*-Pht-L-Phe)	1.03	3.56	1.04	1.24	[55]
Me$_2$Sn(Gly)$_2$ [a]	1.14	3.73	1.50	1.71	[53]
Me$_2$Sn(β-Ala)$_2$ [a]	1.28	3.77	1.30	1.36	[53]
Me$_2$Sn(*N*-Ac-L-Leu)$_2$	1.32	3.63	1.14	1.32	[56]
Me$_2$Sn(*N*-Ac-L-Phe)$_2$	1.26	3.44	0.93	1.11	[56]
Et$_2$Sn(*N*-Ac-L-Leu)$_2$	1.34	3.35	0.86	0.90	[56]
Et$_2$Sn(*N*-Ac-L-Phe)$_2$	1.34	3.35	0.91	0.97	[56]
Bu$_2$Sn(*N*-Ac-L-Leu)$_2$	1.42	3.46	0.97	0.94	[56]

Table 5 (*Continued*)

Complex	I.S. (mm s^{-1})	*Q.S.* (mm s^{-1})	τ_1 (mm s^{-1})	τ_2 (mm s^{-1})	Reference
n-Oct$_2$Sn(N-Ac-L-Phe)$_2$	1.44	3.60	0.93	1.03	[56]
Bu$_2$Sn(DL-Homocys)	1.35	1.54			[42]
Ph$_3$Sn(L-Cys)	1.24	1.34			[42]
Ph$_3$Sn(DL-Homocys)	1.28	1.48			[42]
Cy$_3$Sn(L-Cys)	1.44	1.68			[42]
Cy$_3$Sn(DL-Homocys)	1.45	1.63			[42]
Np$_3$Sn(L-Cys)	1.36	1.79			[42]
Np$_3$Sn(DL-Homocys)	1.35	1.70			[42]
[n-Bu$_2$Sn(N-Ac-L-Leu)]$_2$O	1.30	3.17	0.91	1.13	[56]
[n-Bu$_2$Sn(N-Ac-L-Phe)]$_2$O	1.28	3.10	0.86	1.23	[56]
[n-Oct$_2$Sn(N-Ac-L-Leu)]$_2$O	1.36	3.37	0.87	1.26	[56]
Me$_2$SnCl$_2$·H$_2$Gly-Gly [e]	1.36	3.58			[70]
Bu$_2$SnCl$_2$·H$_2$Gly-Gly [e]	1.40	3.71			[70]
Oct$_2$SnCl$_2$·H$_2$Gly-Gly [e]	1.48	3.82			[70]
Ph$_2$SnCl$_2$·H$_2$Gly-Gly [e]	0.76	1.80			[70]
BuSnCl$_3$·H$_2$Gly-Gly [e]	1.04	2.06			[70]
OctSnCl$_3$·H$_2$Gly-Gly [e]	1.09	2.01			[70]
PhSnCl$_3$·H$_2$Gly-Gly [e]	1.02	2.18			[70]
Et$_2$Sn Gly-Gly (in frozen CH$_3$OH)	1.18 (1.33)	2.69 (3.49)	0.88 (0.87)	0.88 (0.84)	[62]
Et$_2$Sn Gly-Ala	1.32	3.14	0.87	0.86	[62]
Et$_2$Sn Ala-Ala	1.29	2.96	0.93	0.83	[62]
Et$_2$Sn Gly-Val	1.17	2.46	0.85	0.84	[62]
Et$_2$Sn Gly-Met	1.20	2.58	0.88	0.85	[62]
Et$_2$Sn Gly-Tyr	1.26	2.87	0.83	0.80	[62]
Me$_2$Sn Gly-Ala	1.20	3.27 [f]	0.81	0.83	[63]
n-Bu$_2$Sn Gly-Gly·H$_2$O	1.37	3.23 [f]	0.83	0.82	[63]
n-Bu$_2$Sn Gly-Ala	1.34	3.27 [f]	0.90	0.81	[63]
n-Bu$_2$Sn Gly-Ala·H$_2$O	1.29	3.00 [f]	0.96	0.85	[63]
Me$_2$Sn Gly-Val (in frozen CH$_3$OH)	1.12 (1.21)	2.59 [f] (3.09)	0.85 (0.90)	0.87 (0.81)	[63]
Me$_2$Sn Gly-Met (in frozen CH$_3$OH)	1.11 (1.22)	2.53 [f] (3.13)	0.83 (0.93)	0.82 (0.80)	[63]
n-Bu$_2$Sn Gly-Val	1.23	2.65 [f]	0.83	0.82	[63]
t-Bu$_2$Sn Gly-Gly·H$_2$O	1.37	2.65 [f]	0.87	0.91	[63]
t-Bu$_2$Sn Gly-Ala	1.39	2.70 [f]	0.86	0.87	[63]
Ph$_2$Sn Gly-Ala	1.05	2.21 [f]	0.82	0.88	[63]
Ph$_2$Sn Gly-Trp	1.03	2.30 [f]	0.99	0.86	[63]
Me$_2$Sn Gly-Gly	1.26	3.29 [f]			[60]
n-Bu$_2$Sn Gly-Gly	1.35	3.19 [f]			[60]
n-Oct$_2$Sn Gly-Gly	1.37	3.43 [f]			[60]
Sn Me$_2$ (Trp-Ala) [b]	1.11	2.73			[65]
Sn Ph$_2$ (Trp-Ala) [c]	1.03	2.46			[65]
Sn Me$_2$ (Trp-Tyr) [d]	1.12	2.78			[65]
Bu$_2$Sn (Phe-Leu)	1.31	3.08	0.91	1.17	[69]
Ph$_2$Sn (Phe-Leu)	1.19	2.76	0.92	0.95	[69]
Bu$_2$Sn (Phe-Phe)	1.20	2.57	0.86	1.03	[69]
Ph$_2$Sn (Gly-Leu)	1.19	2.78	0.92	0.95	[69]
Bu$_2$Sn (Phe-Ile)	1.22	2.59	0.91	0.96	[69]

[a] Exhibit room temperature spectra, remaining spectra at 77°K.

[b] Temperature range/K 77.3–185.0.

[c] Temperature range/K 77.3–160.5.

[d] Temperature range /K 77.3–125.3.

[e] I.S. w.r.t. CaSnO$_3$ (room temperature), *Q.S.*, Nuclear quadrupole splitting at liquid N$_2$ temperature.

[f] Nuclear quadrupole splitting.

splitting (pqs) value $\{COO\}^{tba} = +0.075$ mm s^{-1}, indicative of bridging (bidentate) behavior, the value $Q.S._{calcd} = -3.09$ mm s^{-1} is obtained, which would correspond to $Q.S._{exp} = 3.14 \pm 0.29$ mm s^{-1} in some complexes, (ii) by employing the pqs value $\{O{=}C{-}O\}^{tbe} = -0.10$ mm s^{-1}, corresponding to the value for monodentate carboxyl, $Q.S._{calcd} = +2.78$ mm s^{-1} (-2.39 mm s^{-1} for Ph_2SnL complexes) results, which would agree with $Q.S._{exp} = 2.80 \pm 0.28$ mm s^{-1} (2.25 ± 0.05 for Ph_2SnL) in other complexes [60,62,63,69] (Table 5).

The crystal structural data of n-$Bu_2Sn[O_2C(CH_2C_6H_5)C(H)N(H)C(O)CH_2Cl]_2$ indicate that the Sn atom is chelated by two symmetry-related, asymmetrically coordinating carboxylate ligands with Sn–O(41) 2.140(4) Å and Sn–O(42) 2.506(5) Å; this asymmetry is reflected in the disparate C(4)–O(41) and C(4)–O(42) bond distances, with the longer C–O bond being associated with the O atom involved in shorter Sn–O bond. The remaining sites about the six coordinate Sn atom are occupied by two n-butyl groups, which lie over the weaker Sn–O(42) bonds and

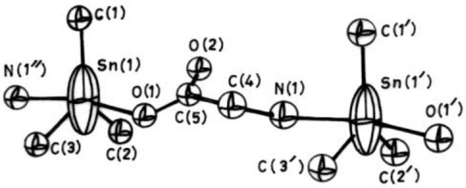


Fig. 3. The asymmetric unit of trimethyltin glycinate (primed atoms are related to those in the asymmetric unit by x, $y+1$, z; double primed atoms are related by x, $y-1$, z).

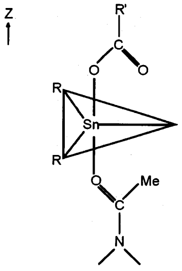


Fig. 4. Structure of R_3Sn (N-Ac-Amino acid).

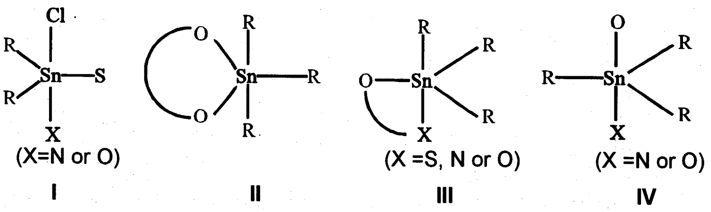


Fig. 5. Possible structures of five-coordinated organotin(IV) complexes.

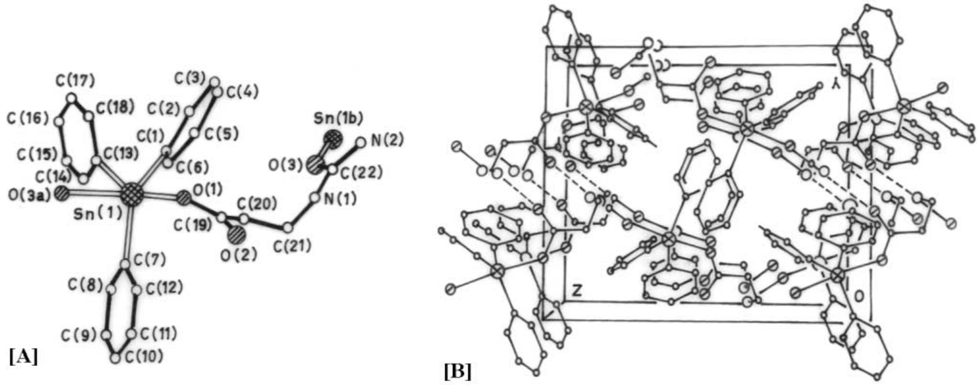


Fig. 6. Molecular structure of triphenyltin 3-ureidopropionate [A]; Perspective view of the molecular packing (hydrogen bonds are shown as broken lines) [B].

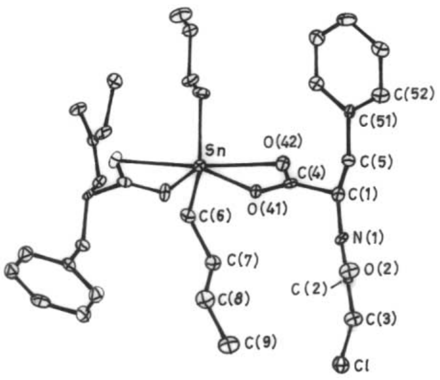


Fig. 7. Structure of n-$Bu_2Sn(O_2C(CH_2C_6H_5)C(H)N(H)C(O)CH_2Cl)_2$.

define a C–Sn–C angle of 138.3(2)°. Therefore, a skew-trapezoidal planar geometry for the tin atom has been suggested (Fig. 7) [57]. The crystal structure of $[Me_2Sn(O_2CCH(CHMe_2)C_8H_4NO_2)_2O]_2 \cdot 2H_2O$ shows both the endocyclic and exocyclic Sn atoms to be five coordinate, trigonal bipyramidal. The crystal system is orthorhombic with space group P_{ccn}, $a = 13.524(2)$, $b = 34.658(5)$, $c = 15.305$ (2) Å, and $Z = 4$. The structure features a centrosymmetric Sn_2O_2 moiety that is connected to two exocyclic Me_2Sn groups. A bridge between the Sn(1) and Sn(2) atoms is provided by bidentate carboxylate group; Sn(1)–O(2) 2.261(8) and Sn(2)–O(3) 2.275(9) Å. The second carboxylate ligand functions essentially in the monodentate mode [Sn(2)–O(6) 2.197(9) Å]. This ligand coordinates the exocyclic Sn atom exclusively such that the pendant O(7) atom is orientated away from the rest of the molecule and is 2.901(9) Å from the Sn(2) atom. The O(6) atom simultaneously forms a close intramolecular contact with the Sn(1) atom such that Sn(1)...O(6) is 2.939 Å. The Sn(1) atom also forms a close intramolecular contact with the imido

C=O(9) atom at 3.15(1) Å. On the basis of the Sn atom geometries, it is proposed that the weaker Sn…O interaction are not indicative of significant bonding interactions [59]. Ph_2SnGly-Gly, Et_2SnGly-Tyr, n-Bu_2SnGly-Val and Me_2SnGly-Met crystallize in the orthorhombic space group $P2_12_12_1$ with $a = 9.860(5)$, $b = 11.787(8)$, $c = 13.962(2)$ Å, $Z = 4$ [61]; $a = 11.492(6)$, $b = 11.618(6)$, $c = 12.786(10)$ Å, $Z = 4$ [62]; $a = 980.4(9)$, $b = 1360.2(12)$, $c = 1413.6(14)$ pm, $Z = 4$ [63] and $a = 9.662(5)$, $b = 11.503(4)$, $c = 12.349(4)$ Å, $Z = 4$ [103], respectively. It has been observed that the tin atom has a considerably distorted trigonal bipyramidal environment. The dipeptides act as tridentate ligands bonding the tin of the C_2Sn fragment (equatorial carbon atoms) with the peptide nitrogen atom (equatorial) and axial (monodentate) carboxyl oxygen and amino nitrogen atoms, into a monomeric unit (Fig. 8) [61–63]. Di-tert-butyl(glycylglycinato)tin(IV) monohydrate and bis [diethyl(glycylhistidinato)tin]methanol (1/1) are monoclinic, space group $P2_1/n$ and $P2_1$ with $a = 8.895(6)$, $b = 14.092(7)$, $c = 13.653(8)$ Å, $\beta = 93.17(5)°$, $Z = 4$ and $a = 8.711(4)$, $b = 13.009(5)$, $c = 15.020(6)$ Å, $\beta = 102.91(3)°$, $Z = 2$, respectively. It has been observed that the polyhedron around Sn is a distorted trigonal bipyramid [104,105]. A Mössbauer–Zeeman spectroscopic study of glycylglycinato-*O*,*N*,*N*(2-)-diphenyltin(IV), and the point-charge model rationalization of the quadrupole splittings of some glycylglycinato-*O*,*N*,*N*(2-)diorganotin(IV) complexes have been reported by Barbieri et al. [106].

The crystal and molecular structure of dimethyl(L-tryptophyl-L-alaninato)tin(IV)-methanol(1/1) has been determined by Girasola et al. (Figs. 9 and 10). The tin atom, bonding to two methyl carbons [Sn–C(1) 2.107(6), Sn–C(2) 2.121 (8) Å; C(1)–Sn–C(2) 123.8(3)°], terminal amino nitrogen [$Sn–N_{amino}$ 2.272(5) Å], deprotonated peptide nitrogen [$Sn–N_{peptide}$ 2.064(5) Å], and terminal carboxylate [$Sn–O_{carboxylate}$ 2.174(5)Å], has a five-coordinated trigonal-bipyramidal environment. An extended hydrogen-bond network gives rise to one-dimensional polymeric chain [65]. The molecular dynamics of three tryptophan-containing dipeptide complexes with $R_2Sn(IV)$ (dipeptide dianion = Trp-Ala, for R = Me or Ph; dipeptide dianion = Trp-Tyr for R = Me) have been investigated by variable-temperature ^{119}Sn

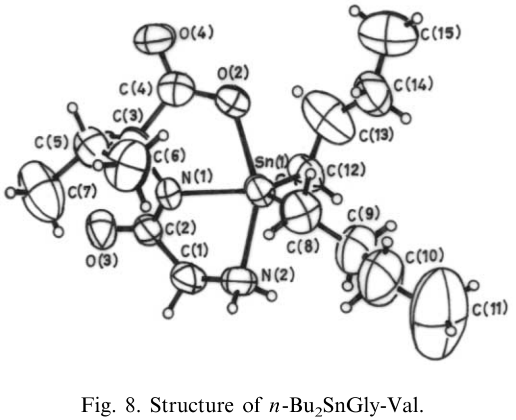


Fig. 8. Structure of n-Bu_2SnGly-Val.

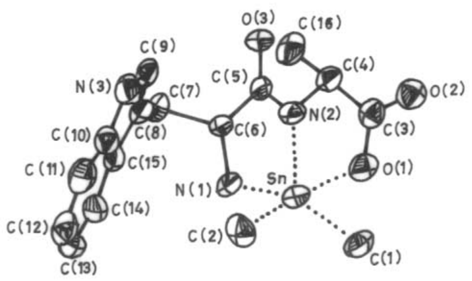


Fig. 9. Structure of $SnMe_2$(Trp-AlaO).

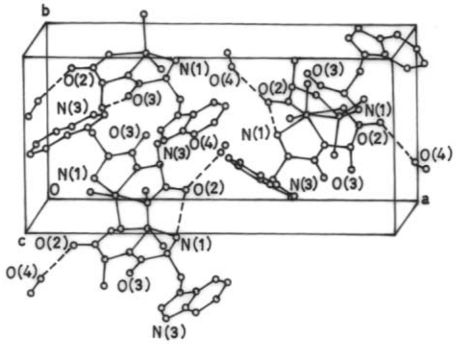


Fig. 10. The unit cell of $SnMe_2$(Trp-AlaO)MeOH. Dashed lines indicate hydrogen bonds.

Mössbauer spectroscopy. The complexes behave as Debye solids and in particular, the calculated mean-square displacements of the tin atoms confirm the occurrence of monomeric structure in such complexes interconnected through hydrogen bonds, which appear to be much stronger in $SnMe_2$ (Trp-Ala) and $SnMe_2$(Trp-Tyr) than in $SnPh_2$ (Trp-Ala) [65].

Recently Parvej et al. have reported that crystals of tri-*n*-butyl-(*N*-malcoyl-β-alaninato)tin(IV) and (*N*-malcoylmethioninato)trimethyltin(IV) are monoclinic with space group $P2_1/a$ ($a = 10.574(3)$, $b = 16.812(2)$, $c = 12.882(2)$ Å, and $\beta = 102.15(2)°$, $Z = 4$, $D_{calc} = 1.359$, $R = 0.039$, $R_w(F^2) = 0.141$) and $P2_1/n$ ($a = 6.507(5)$, $b = 9.640(3)$, $c = 26.376(3)$ Å, and $\beta = 91.51(3)°$, $Z = 4$, $D_{calc} = 1.574$, $R = 0.059$, $R_w(F^2) = 0.159$), respectively [107,108].The structure of both compounds contains polymeric chains wherein each trialkyltin moiety bridges two neighboring *N*-malcoylamino acid ligands via carboxyl moieties. The Sn atom has a distorted trigonal bipyramidal geometry, with three alkyl groups in the equatorial plane. The carboxyl O atoms bonded to the Sn atom in the axial positions have significantly different Sn–O bond lengths (2.215(5) and 2.424(5) Å for tri-*n*-butyltin derivative and 2.152(6) and 2.484(6) Å for trimethyltin derivative) [107,108].

The ^{119}Sn Mössbauer spectroscopic measurements have recently been performed at selected pH values for the quick frozen solution of the dimethyltin (IV)-glycine,

-Gly-Gly and -Gly-His systems [82]. The spectra for the three systems in the strong acidic region contain two overlapping doublets which have been assigned, on the basis of the concentration distribution curves to the hydrated metal ion (100), and to the MLH (111) complex for Gly and Gly-Gly or to MLH_2 (112) for Gly-His. The comparison of the experimental (3.54–3.73 mm s^{-1}) and calculated (3.57 mm s^{-1}) *Q.S.* values indicates that the other species formed contains the coordinating carboxylate group as well as alkyl groups in the equatorial and slightly bounded water molecules in axial positions (Fig. 11(a)). On increasing pH the MOH, ML(Gly-Gly), and MLH(Gly-His) complexes are the major species. The structure of MOH complex is similar to the carboxylato mono-coordinated one, but the third equatorial position is occupied by a hydroxide ion instead of a carboxylate group. The experimental *Q.S.* values for ML (4.37 ± 0.01 mm s^{-1}) and MLH(4.09 mm s^{-1}) [in case of Gly-His] complex species are in good agreement with that calculated (4.27 mm s^{-1}) for the octahedral mixed hydroxo complex confirming the previous assumption that these complexes are formed from the MLH (MLH_2 in the case of Gly-His) by the additional coordination of the OH^-, while the amino nitrogens remain protonated (Fig. 11(b)). Above pH 5.0, the mössbauer spectrum of the dimethyltin-dipeptide systems has two doublets representing the $M(OH)_2$ hydrolysis product and the corresponding complex species MLH_{-1} (ML for Gly-His), respectively. The experimental *Q.S.* values for MLH_{-1} (3.35 mm s^{-1} for Gly-Gly) and ML (3.07 mm s^{-1} for Gly-His) indicate that these species are penta-coordinated complexes in which the alkyl groups and peptide-nitrogen are in equatorial, while the carboxylate and amino donor groups are in axial positions (Fig. 11(c)). Further, it has been observed that there are no significant differences between the ML and MLH_{-1} complexes formed in dimethyltin(IV) Gly- His system (*Q.S.* for $MLH_{-1} = 3.02$ mm s^{-1}). This fact confirms that the process ML MLH_{-1} belongs to the deprotonation of the histidine side-chain of the ligand without the metal assistance as suggested based on potentiometric and NMR experiments [82].

The Mössbauer parameters have been used to propose a structure for each species eventually formed in aqueous solutions of $MeSnCl_3/Me_2SnCl_2/Me_3SnCl$ and glutathione reduced (GSH) [96]. The dissolution of $MeSnCl_3$ in water produces a strongly acidic solution ($pH = 1.72$) and point charge calculations indicate $[MeSn(H_2O)_2(OH)_2]^+$ species ($Q.S. = 1.83$ mm s^{-1}) as the most probable compound present in solution. On increasing the pH to physiological values, a small decrease of both the *I.S.* and the *Q.S.* indicates the loss of protons from the

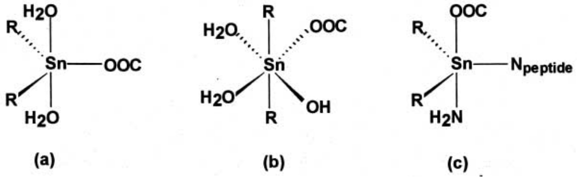


Fig. 11. Schematic structure of the complex species.

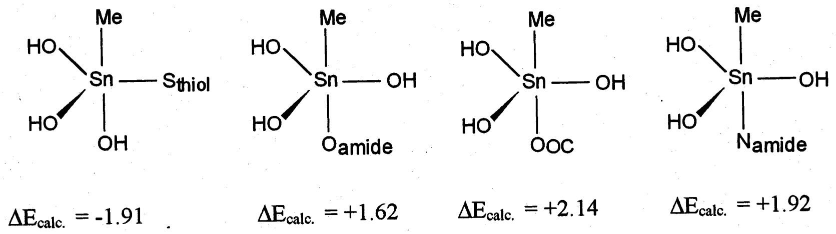


Fig. 12. Some possible tin coordination spheres in the HEPES buffer solution for the 1:1 GSH/$MeSnCl_3$ system.

coordinated water molecules. If the pH is fixed to 7.4 by means of HEPES, one molecule of the buffer substitutes the water in the coordination sphere of the tin. The addition of GSH to this solution results in the formation of a second species in an amount that is related to the ligand to metal molar ratio and its amount increases until the ligand to tin molar ratio is ~ 12. From this point on, the two tin compounds are present in the solution approximately in the same amount (Table 6). The hyperfine parameters of the first species are virtually identical with those of the starting material, the new component presents values which indicate that large variations in the coordination geometry has not taken place. The point charge calculations are not able to distinguish among the many different possibilities (Fig. 12) [96].

The addition of GSH to a HEPES solution of Me_2SnCl_2 gives rise to a continuous decrease of *Q.S.* (3.13–2.21 mm s^{-1}) and a simultaneous increase of the *I.S.* (1.09–1.33 mm s^{-1})(Table 6). The plot of these values against the ligand to metal ratio is linear up to a value of two, after which the *Q.S.* and the *I.S.* remain virtually constant. This indicates a well defined complex with a 2:1 stoicheiometry having trigonal bipyramidal geometry with the three equatorial positions should be occupied by the two methyl and an S_{thiol} groups, while a second S_{thiol} and an N_{amino} should occupy the two axial positions (observed *Q.S.* 2.21–2.27 mm s^{-1}; calculated 1.92 mm s^{-1}). At pH values lower than 2.0, no reaction takes place as *Q.S.* value remains identical with that of pure aqueous solution of the hydrated Me_2Sn^{2+} ion. As the pH value increases up to 6.0, GSH loses the two carboxylic protons and becomes negatively charged and leads to the formation of the bis adduct. The hyperfine parameters are virtually identical with those obtained in the HEPES solution indicating the same tin environment in the two solutions (Table 7). The complexation takes place when the thiolic sulfur is still protonated and the aminic nitrogen belongs to a chelating GSH rather than to a HEPES molecule. The aqueous solution of Me_3SnCl is slightly acidic (pH = 4.1) and its Mössbauer spectrum has been fitted to a single doublet with *Q.S.* value of 3.80 mm s^{-1}, which suggests trigonal bipyramidal geometry with the three methyl groups in the equatorial plane and two water molecules (or one water and one OH^- ion) in the axial positions. On increasing pH to ~ 7.0, the *Q.S.* decreases to a value of 2.87 mm s^{-1} indicating *trans*-$Me_3Sn(OH)_2^-$ species. But at pH = 7.4, the *Q.S.* is 3.31

Table 6
^{119}Sn Mössbauer effect [a] parameters for the GSH/R_nSnCl_{4-n} systems in aqueous HEPES buffer at pH 7.40 recorded at 80.0 K (Ref. [96])

GSH/R_nSnCl_{4-n} ratio	GSH/$MeSnCl_3$		GSH/Me_2SnCl_2		GSH/Me_3SnCl	
	I.S. (mm s^{-1})	*Q.S.* (mm s^{-1})	I.S. (mm s^{-1})	*Q.S.* (mm s^{-1})	I.S. (mm s^{-1})	*Q.S.* (mm s^{-1})
0.0	0.51	1.83	1.09	3.13	1.28	3.31
0.2					1.31	3.12
0.5			1.10	2.97	1.33	2.80
1.0			1.17	2.75	1.34	2.41
2.0			1.31	2.31	1.31	2.37
3.0			1.33	2.25		
4.0			1.38	2.27		
5.0	1.04, 0.45	1.69, 1.82			1.34	2.38
6.0			1.35	2.26		
8.0	1.28, 0.48	1.81, 1.88	1.33	2.25		
12.0	1.25, 0.46	1.84, 1.87				
23.0	1.33, 0.51	1.79, 1.85				

[a] Referred to room temperature $CaSnO_3$.

mm s^{-1}, which may be due to the substitution of an OH^- ion with a HEPES molecule bonded to the tin center by an aminic nitrogen (Table 7). The *Q.S.* decreases on the addition of GSH almost linearly with the GSH/Me_3SnCl ratio down to 2.4 mm s^{-1} when the ratio is 1:1 and there after it remains constant indicating that a stable 1:1 adduct has been formed in solution (Table 6). A trigonal bipyramidal structure has been assigned in which the organic groups occupy the equatorial plane, a thiolic sulfur from a GSH one of the axial positions, while the other is occupied by a water molecule or by an aminic nitrogen of either a GSH or a HEPES molecule [96].

6.5. Mass spectral studies

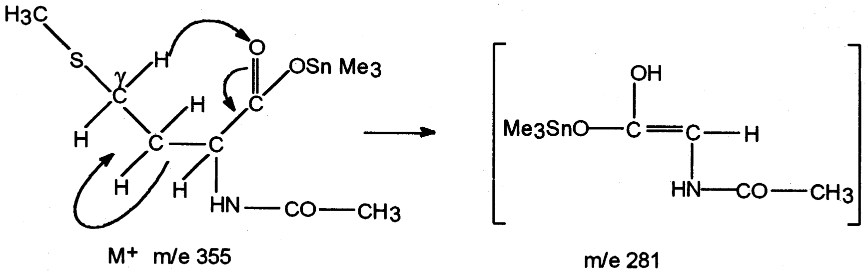
The mass spectral data of the $R_2Sn(Cl)SCH_2CH(NH_2)COOH{\cdot}H_2O$ and $R_2Sn(Cl)SCH_2CH(NH_2)COOC_2H_5$ (where R = Me and *n*-Bu) have been reported by Domazetis et al. [54]. The spectrum of *n*-$Bu_2Sn(Cl)SCH_2CH(NH_2)COOH$ shows the presence of ditin-species, while that of $Me_2Sn(Cl)SCH_2CH(NH_2)COOH$ shows a number of peaks which arise from the $[Me_2Sn(Cl)SCH_2COO]_2^+$ dimer. At the temperatures (100–260°C) employed to obtain the mass spectra, decomposition of the complexes occurs, and this may make structural assignments less straight forward [54]. Mass spectra showed, as peaks of maximum mass, the following molecule ions: *n*-Bu_3Sn(*N*-Ac-GlyO), 407; Ph_3Sn(*N*-Ac-GlyO), 467 and Me_3Sn(*N*-Ac-MetO), 335. This is an indication that monomers exist under the conditions in the mass spectrometer (16, 180; 70, 170; and 70 eV, 190°C). In the mass spectrum of Me_3Sn(*N*-Ac-MetO) a peak at m/e 281 can be interpreted as caused by a fragment ion resulting from a McLafferty rearrangement. As shown in the following scheme (Eq. (30)), this arrangement can only proceed when a unidentate

Table 7
^{119}Sn Mössbauer effect parameters for the GSH/R_2SnCl_2 system in 2:1 ratio and the GSH/Me_3SnCl in 1:1 ratio in water as a function of pH recorded at 80.0 K (Ref. [96]) [a]

GSH/Me_2SnCl_2			GSH/Me_3SnCl		
pH	I.S. (mm s^{-1})	*Q.S.* (mm s^{-1})	pH	I.S. (mm s^{-1})	*Q.S.* (mm s^{-1})
1.31	1.52	4.15	2.87	1.33	3.73
2.00	1.51	4.16	3.87	1.36	3.63
2.55	1.33	3.31	5.17	1.37, 1.39	3.81, 2.43
3.50	1.32	2.95	5.45	1.34, 1.30	3.59, 2.15
4.50	1.32	2.62	6.10	1.41, 1.30	3.39, 2.04
5.66	1.33	2.36	6.62	1.36, 1.32	2.82, 1.90
6.66	1.35	2.19	7.26	1.33, 1.29	2.64, 1.83
8.02	1.34	2.25	7.51	1.33	2.11
9.37	1.30	2.26	9.24	1.33	2.15
10.20	1.19	2.40			
12.12	0.19	2.30			

[a] Referred to room temperature $CaSnO_3$.

O=C–O$^-$ group is available. Since *N*-Ac-Gly and -Ala derivatives do not contain γC atom, an analogous rearrangement can not occur [49].

 (30)

7. Thermal studies

Only a few references are available on the thermal studies of the organotin(IV) derivatives of the amino acids and peptides. It has been reported that the diorganotin(IV) complexes of the *N*-phthaloyl amino acids underwent a weight loss between 25–120°C corresponding to the water molecule present in the crystal lattice. No definite conclusion could be drawn about the nature of the other decomposition products [55]. The *n*-Bu_3SnL compounds (where, HL = *N*-Ac-Cys and L-Cys.eth.est.) and (*n*-$Bu_3Sn)_2SG$ decomposed rapidly under nitrogen between 200–300°C and 172–350°C, to loose over 90 and 60%, respectively, of the original sample mass [47]. Thermal decomposition studies of $R_2SnCl_2 \cdot H_2$Gly-Gly have been compared with those of R_2SnCl_2, H_2Gly-Gly and of mixtures of R_2SnCl_2 and H_2Gly-Gly [70]. The decomposition data of the mixtures indicate that R_2SnCl_2 moieties volatilize off from molten mixtures at temperature similar to their boiling point followed by the decomposition of H_2Gly-Gly. Whereas the decomposition of the adducts falls into two classes, (i) in which the decomposition of the adduct follows a process similar to that of the mixture, e.g. $R_2SnCl_2 \cdot H_2$Gly-Gly, where R = *n*-Bu and *n*-Oct, (ii) in which the decomposition involves a reaction within the lattice which does not occur in the mixture, e.g. dimethyl- and diphenyltin(IV) compounds. On the other hand, the $RSnCl_3 \cdot H_2$Gly-Gly decompose at temperature lower than the boiling point of their parent organotin compounds ($RSnCl_3$), but in a similar manner to the mixture of $RSnCl_3$ and H_2Gly-Gly in multistage decomposition steps [70].

Recently, Nath et al. have reported thermal decomposition of some complexes viz., R_3SnL and $R'_2Sn(L')_2$ (where, R = Me and Ph, HL = DL-Met [66], DL-Trp; R = Ph, HL = L-Asn [66], L-His; R′ = *n*-Bu, HL = L-Asn [66], DL-Trp). All of the complexes except Bu_2Sn(DL-Trp)$_2$ gradually decomposed along with the formation of SnO as residue under a dry nitrogen atmosphere. All of the complexes except Ph_3Sn(L-Met) and Ph_3Sn(L-His) decomposed in two or three steps, in the temperature range 40–1000°C, corresponding to the loss of organic groups attached to tin in the first step, followed by the loss of an amino acid anion. The complexes, Ph_3Sn(L-His) and Ph_3Sn(L-Met) decomposed in a single step in the temperature range 58–870°C and 80–512°C with inflection point at 309 and 310°C, respectively [66]. The order of the thermal decomposition reaction of the Ph_3Sn(L-His) complex has been found to be one because Cs = 0.3571, which corresponds to the value for the first order reaction. Three different methods, viz. Coats–Redfern, Horowitz and Metzger, and Fuoss method have been used to evaluate the kinetic data ($E^* = 118 \pm 5$ kJ mol^{-1}, $A = 1–7 \times 10^8$, $S^* = -92 \pm 10$ kJ mol^{-1}, $H^* = 110 \pm 6$ kJ mol^{-1} and $G^* = 167 \pm 3$ kJ mol^{-1}) from the TG curve.

8. Biological activity: antimicrobial and anticancer activities

The organotin(IV) derivatives of the amino acids have been of interest as possible biocides [37,39,40] and as an intermediate in peptide synthesis [38,41]. Tricyclohexyltin alaninate has been found active as a fungicide and bactericide for seeds and plants [109]. The complexes, R_3SnL, $R'_2Sn(L)_2$ (R = Me, Ph and *n*-Bu and R′ = *n*-Bu and Ph, HL = various amino acids [66–68]) were active against a wide spectrum of bacteria and fungi. The order of the fungicidal and bactericidal activities of these compounds is as: triphenyl- > diphenyl- > dibutyl- > trimethyltin complex. Because of the high antifungal activities of Ph_3Sn derivatives of a few amino acids, and Bu_2Sn(L-tyr) and Ph_2Sn(DL-Asp) have been screened in vivo against a multi-infection fungal model in mice (Table 8) [66–68]. The compounds were tested at 100 and 50 mg kg^{-1}, p.o., for 4 days for antifungal efficacy. The compounds were toxic at 100 mg kg^{-1} as most of the animals died during experimental period and they did not show promising activity, but they were active at a dose of 50 mg kg^{-1} [66–68].

Organotin compounds show a spectrum of biological effects and have been extensively studied as fungicides, bactericides, acaricides and wood preservatives [110–114]. However, only scantly and scattered information is available on their activity against cancer [1–3,5,7,8,15–18,115–118]. More recent results on the tumor cell lines seem to point to a necessary balance between solubility and lipophilicity in order to optimize their efficacy [15,119–123]. The L-cysteinates, R_2Sn(L-Cys) have been found to be active against murine leukemia P-388 for R = Et and Ph, while inactive for R = Me and *n*-Bu [100,111]; DL-penicillaminates, R_2Sn (DL-Pen), were instead moderately active for R = Me and *n*-Bu, at very large and low doses, respectively, while Ph_2Sn(DL-Pen) was inactive [124](Table 9). The chirality of the ligands may possibly contribute towards the antitumor effect of the complexes [124]. The *N*-substituted glycinates, $Me_2Sn(N\text{-Bz-Gly})_2$ and R_3SnL (where, R = Me, HL = *N*-Bz-Gly, *N*-(2,4-dinitrophenyl)glycine (Dnp-Gly); R = *n*-Bu, HL = *N*-Ac-Gly) have been reported to be inactive [124]. The water soluble penicillaminates, Me_2Sn(L-Pen), Me_2Sn(D-Pen), $Me_2Sn(\text{D-PenH})_2$ and $Me_2Sn(\text{L-PenH})_2$ are essentially inactive against P-388 lymphocytic leukemia in mice and do not show any dependence of the antitumor activity from the configuration about the chiral center [125] (Table 9). A comparison of the structures of the active and inactive compounds suggests that in all active compounds there is (i) the availability of coordination positions at Sn, (ii) the occurrence of relatively stable ligand–Sn

Table 8
In vivo evaluation of the selected organotin (IV) complexes of amino acids against multiinfection fungal model

Complex	Number of animals used/survival	Dose (mg/kg)	A.V. cfu/gram tissue		Vaginal culture cfu	Skin culture positive/total number animals	Reference
			Kidney	Lungs			
Ph_3Sn (L-His)	5/0	100					[68]
	5/3	50	60×10^5	7.0×10^6	5.0×10^3	1/1	
Ph_3Sn(DL-Trp)	5/0	100					[68]
	5/5	50	5.0×10^5	9.0×10^6	8.0×10^3	5/5	
Ph_3Sn(DL-Met)	5/0	100					[66]
	5/2	50	0.1	0.0	2.4×10^4	1/1	
Ph_3Sn(L-Asn)	5/0	100					[66]
	5/1	50	0.0	0.0	2.0×10^4	1/1	
$Bu_2Sn(L\text{-}Tyr)_2$	5/0	100					[67]
	5/1	50	0.1	0.0	1.0×10^3	1/1	
Ph_2Sn(DL-Asp)	5/1	100	1.2×10^7	1.0×10^7	1.0×10^4	1/1	[67]
	5/4	50	2.1×10^3	1.7×10^6	5.2×10^3	4/4	
Control	5/5	(PEG)	6.0×10^4	2.0×10^7	3.5×10^4	3/5	[66–68]

Table 9
The activity of some organotin compounds against P388 lymphocyte leukemia

Compound	Dose (mg kg^{-1})	T/C (%)	Reference
Me_2Sn[Gly-Gly] [a]	25.0	139	[127]
n-Bu_2Sn[Gly-Gly] [a]	3.12	150	[127]
n-Oct_2Sn[Gly-Gly] [a]	1.56	132	[127]
Ph_2Sn[Gly-Gly] [b]	3.12; 1.56	141; 128	[127]
Ph_2Sn[Cys]	50	181	[124]
Me_2Sn(DL-Pen)	400	148	[124]
n-Bu_2Sn(DL-Pen)	3.12	120, 130	[124]
Ph_2Sn(DL-Pen)		Inactive	[124]
Me_2Sn(*N*-Bz-Gly)$_2$		Inactive	[124]
Me_3Sn(*N*-Bz-Gly)		Inactive	[124]
n-Bu_3Sn(*N*-Ac-Gly)		Inactive	[124]
Me_3Sn(Dnp-Gly)		Inactive	[124]
Me_2Sn(D-Pen)	50	95, Inactive	[125]
	25; 12.5	118, Inactive	
Me_2Sn(L-Pen)	50; 12.5	114; 118 Inactive	[125]
	25	136	
Me_2Sn(D-PenH)$_2$	50–12.5	100–104 Inactive	[125]
Me_2Sn(L-PenH)$_2$	50–12.5	109–100 Inactive	[125]

[a] Suspension or solution in saline with Tween-80.

[b] Suspension or solution in Klucel. Reproducible T/C $\geqslant$ 120% is required to demonstrate activity.

bonds, Sn–N and Sn–S, (iii) low hydrolytic decomposition of these bonds. The dibutyltin histidinate was reported to be given to cancerous mice in drinking water and tumor growth rates were significantly reduced [126]. A number of diorganotin compounds of the mercaptoamino acids and dipeptides have been reported to possess considerable antitumor and antileukaemic activities against P-388 lymphocytic leukemia cells [3,127–129]. The dipeptide complexes hydrolyze slowly and precipitate diorganotin oxides [3]. The complexes of the type R_2SnL (R = Me, *n*-Bu, *n*-Oct and Ph, H_2L = Gly-Gly) are found to be active in small doses against P-388 Lymphocyte leukemia in mice [127]. The derivatives of *n*-Bu_2Sn(IV), *n*-Oct_2Sn(IV) and Ph_2Sn(IV), practically insoluble in aqueous systems, are the most active (Table 9). It has been proposed that the antileukaemic activity of trigonal bipyramidal R_2SnL depends on the peculiar structure and bonding of the solids, which presumably suffers gradual alteration when attacked by water. Consequently, it seems either probable that: (i) Gly-Gly^{-2}, as coordinated to R_2Sn(IV) is quite effective in bringing the complexes into the cells; (ii) the R_2SnL complexes behave as anti-metabolites [127].

Ruisi et al. have tried to interpret the action of R_2Sn(IV) glycylglycinates (R = Me, *n*-Bu, *n*-Oct and Ph) on a molecular basis [128]. Of the various tumors studied the Bu_2Sn(Gly-Gly) was active only against leukemia P-388. On the basis of solution studies using various spectroscopic techniques, it is likely that solvated species in aqueous solution or a mixture of H_2O and organic solvent and unsolvated species (mainly organic solvent) are present in equilibrium and contribute to

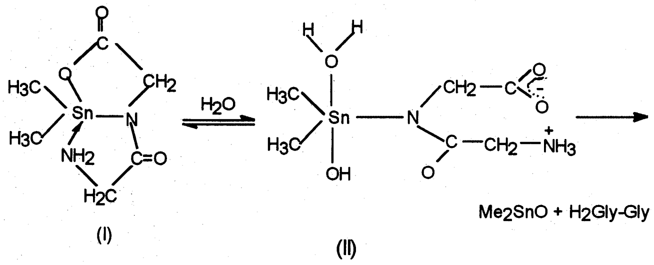
Table 10
Results of antimicrobial activity, and antiinflammatory activity of diorganotin complexes of dipeptides (Ref. [69])

Complexes	MIC in μg ml^{-1} against [a]								% inhibition (50mg kg^{-1} oral dose)
	Bacteria [b]				Fungi [c]				
	1	2	3	4	5	6	7	8	
Ph_2SnCl_2	12.5	50	12.5	12.5	12.5	12.5	25	25	-
Bu_2SnO	50	50	12.5	50	25	25	25	25	-
Bu_2Sn-(Ala-Phe)	25	50	12.5	12.5	50	12.5	12.5	25	22.0
Bu_2Sn-(Phe-Leu)	25	50	12.5	12.5	25	12.5	12.5	12.5	23.9
Ph_2Sn-(Phe-Leu)	50	50	12.5	50	50	25	12.5	25	24.5
Bu_2Sn-(Phe-Phe)	25	25	6.25	12.5	25	12.5	6.25	12.5	14.3
Bu_2Sn-(Gly-Leu)									21.5
Bu_2Sn-(Gly-Ile)	12.5	25	6.25	12.5	25	12.5	6.25	25	12.0
Ph_2Sn-(Gly-Ile)	50	50	6.25	25	25	12.5	25	12.5	29.3
Phenylbuta-zone									38.4

[a] Solvent used, DMSO. LD_{50} values of all the complexes is >500 mg kg^{-1}.

[b] 1. *Escherichia coli*; 2. *Rhizobium meliloti*; 3. *Pseudomonas putida*; 4. *Aeromonas formicans*.

[c] 5. *Aspergillus niger*; 6. *Penicillum chrysogenum*; 7. *Auerobasidium pullulans*; 8. *Verticillium dahliae*.



Scheme 1.

the passage of the alkyltin complexes across the cell membrane which in turn produces the biological activity [128]. The reaction of Me_2Sn(Gly-Gly) in aqueous solution seems to consist of a hydrolytic process occurring via the mechanism given in Scheme 1. The species I would structurally correspond to the solid state structure or the structure in organic solvents (in some way mimicking the cell membrane phase). The species II slowly releases $R_2Sn(IV)$ moieties in aqueous media, which are responsible for the antitumor activity [128].

Recently, antimicrobial and antiinflammatory activity of R_2SnL (R = *n*-Bu and Ph; HL = Ala-Phe, Phe-Leu, Phe-Phe, Gly-Leu and Gly-Ile) have been reported by Nath et al. [69]. The MIC (in $\mu g\ ml^{-1}$) values indicate that the dibutyltin complexes are found to be more active than Bu_2SnO whereas diphenyltin derivatives are less active than Ph_2SnCl_2 except Ph_2Sn(Gly-Ile) against *P. putida* and *V. dahliae* and Ph_2Sn(Phe-Leu) against *A. pullulans* (Table 10). The relationship between the activity and the nature of the substituents (electron-withdrawing or electron-donating) present in the dipeptide chain has also been discussed [69]. The anti-inflammatory activity (% inhibition) of these compounds on adult albino rats (body weight 80–100 g) of Foster Charles species against carrageenin induced oedema in the doses of 50 mg kg^{-1} given orally and the toxicity (LD_{50}) on the mice (body weight 20–25 g) of either sex have been reported [69]. The dibutyltin complexes are found to be more active than diphenyltin complexes (Table 10). The compound Ph_2Sn(Gly-Ile), which possesses methylene group close to NH_2 group and 1-methylpropyl group at positon-2, has exhibited the most potent anti-inflammatory activity, and it was compared with the standard drug, phenyl butazone, and was found to be nearly equipotent. The correlation between the observed activity and chirality of the ligands is also discussed [69].

9. List of abbreviations

DL-Ala	DL-alanine
DL-α-Ala	DL-α-alanine
α-Ala	α-alanine

β-Ala	β-alanine
DL-α-Aminobut	DL-α-aminobutyric acid
Ala-Ala	alanylalanine
N-Ac-Ala	*N*-acetyl-L-alanine
N-Ac-L-Cys	*N*-acetyl-L-cysteine
N-Ac-Gly	*N*-acetyl-L-glycine
N-Ac-L-Leu	*N*-acetyl-L-leucine
N-Ac-Met	*N*-acetyl-L-methionine
N-Ac-L-Phe	*N*-acetyl-L-phenylalanine
N-Ac-L-Phe-Gly	*N*-acetyl-L-phenylalanylglycine
β-Ala-His	β-alanylhistidine
Ala-Phe	alanylphenylalanine
L-Asn	L-asparagine
Asp	aspartic Acid
DL-Asp	DL-aspartic acid
N-Bz-DL-Ala	*N*-benzoyl-DL-alanine
N-Bz-DL-Ala-Gly	*N*-benzoyl-DL-alanylglycine
N-Bz-Gly	*N*-benzoyl-glycine
N-Bz-Gly-Gly	*N*-benzoyl-glycylglycine
N-Bz-L-His-L-Cys	*N*-benzoyl-L-histidyl-L-cysteine
N-Bz-L-Leu-L-His	*N*-benzoyl-L-leucyl-L-histidine
N-Bz-DL-Phe	*N*-benzoyl-DL-phenylalanine
L-Cys	L-cysteine
L-Cys.acid	L-cysteic acid
L-Cys.eth.est.	L-cysteine ethyl ester
L-Cys.eth.est.hydro.	L-cysteine ethyl ester hydrochloride
L-Cys.hydro.hyd.	L-cysteine hydrochloride hydrate
DnpGly	*N*-(2,4-dinitrophenyl)glycine
N-Fm-L-Phe	*N*-formyl-L-phenylalanine
N-Fm-L-Phe-Gly	*N*-formyl-L-phenylalanylglycine
GSH	glutathione reduced
SG	glutathione anion
L-Glu	L-glutamic acid
Gly	glycine
Gly-Ala	glycylalanine
Gly-Gly	glycylglycine
Gly-His	glycylhistidine
Gly-Hista	glycylhistamine
Gly-Ile	glycylisoleucine
Gly-Leu	glycylleucine
Gly-Met	glycylmethionine
Gly-Trp	glycyltryptophane
Gly-Tyr	glycyltyrosine
Gly-Val	glycylvaline

His	histidine
L-His	L-histidine
L-His-L-Tyr	L-histidyl-L-tyrosine
DL-Homocys	DL-homocysteine
L-α-Ile	L-α-isoleucine
DL-α-Leu	DL-α-leucine
DL-Met	DL-methionine
L-Met-L-His	L-methionyl-L-histidine
S-MeCys	S-methylcysteine
Monochloro-Ac-L-Phe	monochloro-acetyl-L-phenylalanine
NorVal	norvaline
DL-α-Phe	DL-α-phenylalanine
Phe-Leu	phenylalanylleucine
Phe-Phe	phenylalanylalanine
DL-Pen	DL-penicillamine
TRIS	tris(hydroxymethyl)aminomethane
HEPES	2-[4-(2-hydroxyethyl)piperazin-1-yl]ethane-sulfonic acid
N-Pht-DL-Ala	*N*-phthaloyl-DL-alanine
N-Pht-L-Leu	*N*-phthaloyl-L-leucine
N-Pht-L-Phe	*N*-phthaloyl-L-phenylalanine
N-Pht-DL-Val	*N*-phthaloyl-DL-valine
DL-Trp	DL-tryptophane
L-Trp-L-Ala	L-tryptophyl-L-alanine
L-Trp-L-Trp	L-tryptophyl-L-tryptophane
L-Trp-L-Tyr	L-tryptophyl-L-tyrosine
L-Tyr	L-tyrosine
Val	valine
DL-α-Val	DL-α-valine
β-PhVal	β-phenylvaline
Val-Val	valanylvaline
Uried	3-ureidopropionic acid

Miscellaneous

Bu	butyl (Prefix *n*, *i* or *t*, normal, *iso* or tertiary butyl)
Cy	cyclohexyl
Et	ethyl
Me	methyl
Oct	octyl (Prefix *n* or *i*, normal or *iso* octyl)
Ph	phenyl
Pr	propyl (Prefix *n* or *i*, normal or *iso* propyl)
Np	neophyl
IR	infrared
I.S.	isomer shift
MIC	minimum inhibitory concentration

NMR	nuclear magnetic resonance
Q.S.	quadrupole splitting
TG	thermogravimetry
$CDCl_3$	deuteriochloroform
CD_3OD	deuteriomethanol
DMSO-d_6	deuteriodimethyl sulphoxide

Acknowledgements

The authors are thankful to CST, Lucknow, India, for providing financial support to the project.

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