Applied Organometallic Chemistry (1988) 2 525–531

0268–2605/88/02604525/$03.50

^{119}Sn Mössbauer studies of bis[cysteinato(1$^-$)-*S*]- and of bis[penicillaminato(1$^-$)-*S*]-diorganotin(IV) species in the crystalline state and in frozen aqueous solution

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Received 23 June 1988 *Accepted 4 August 1988*

The bonding and the configuration of the tin environment in the title compounds {$R_2Sn[SCH_2CH(NH_3^+)COO^-]_2$ and $R_2Sn[SC(CH_3)_2CH(NH_3^+)COO^-]_2$, indicated in the following as $R_2Sn(cysH)_2$ and $R_2Sn(penH)_2$ respectively} has been investigated through the determination of the Mössbauer–Zeeman spectra of $Ph_2Sn(cysH)_2$ and $Ph_2Sn(penH)_2$ in the solid state, and through conventional Mössbauer spectroscopy of $Me_2Sn(penH)_2$ in the solid state as well as of $Me_2Sn(cysH)_2$ and $Me_2Sn(penH)_2$ in aqueous solution (frozen). The treatment of the data by the point-charge model approach suggested the general occurrence of a tetrahedral C_2SnS_2 core. In aqueous Hepes buffer, a tertiary amino nitrogen atom has been observed to coordinate tin in $Me_2Sn(cysH)_2$ and $Me_2Sn(penH)_2$, with formation of trigonal bipyramidal tin environments. The latter solutions undergo slow decomposition reactions at room temperature. From $Me_2Sn(cysH)_2$, the formation of solid $(Me_2SnS)_3$ occurs, as well as formation of soluble complex species in the presence of glycylglycine; $Me_2Sn(penH)_2$ appears to undergo a slow desulfuration reaction.

Keywords: organotin, amino-acid, cysteine, penicillamine, Mössbauer

INTRODUCTION

The present investigation has been planned in the context of our studies on the anti-leukemia P-388 activity in mice of diorganotin(IV) compounds characterized by Sn–S bonds,[1] i.e., complexes of R_2Sn^{IV} (R = Alk, Ph) with cysteine ($cysH_2$) and penicillamine ($penH_2$) of formula R_2Sncys and R_2Snpen, as well as with 2-mercaptoethanesulfonates (i.e. MesH; sodium and guanidinium salts; $[R_2Sn(Mes)_2]^{2-}$ [1,2]). These studies have been recently extended to R_2Sn^{IV} complexes of 3-mercaptopropionic acid, as well as to Me_2Snpen and $Me_2Sn(penH)_2$, employing the *R* and *S* enantiomers of this ligand.[3] The largest activity has generally been detected for the Ph_2Sn^{IV} complexes, irrespective of the nature of the ligands.[1–3]

In order to investigate the role of the ligand in the structure–antitumor activity relationship for this class of compounds, the nature of the species Me_2Sncys and $[Me_2Sn(Mes)_2]^{2-}$ in aqueous solution (the pH being adjusted at about the physiological value) has been studied, and evidence has been obtained for the formation of the trigonal bipyramidal (tbp) complex[2] $Me_2Sn(S_{thiol})(N_{am})(OH)$, and of the tetrahedral species[4] $Me_2Sn(S_{thiol})_2$ respectively (N_{am} indicates amino nitrogen). Moreover, $Me_2Sn(cys)$ binds to rat hemoglobin (as do other Me_2Sn^{IV} derivatives), forming a second Sn–S bond with a cysteine side chain of the globin and possibly a coordinative nitrogen–tin bond by imidazole histidine to form a tbp-type structure.[5]

The work reported in the present paper continues this line of research. The configuration at the tin sites in $R_2Sn(cysH)_2$ and $R_2Sn(penH)_2$ (R = Ph and Me) has

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been investigated by ^{119}Sn Mössbauer spectroscopy in the solid state as well as in frozen solution (R=Me), in water at pH ≃ 7.4 and in Hepes buffer at the same pH, the latter compound potentially behaving as a ligand through its tertiary amino nitrogen atoms.[4,5] The Mössbauer–Zeeman spectra of solid $Ph_2Sn(cysH)_2$ and $Ph_2Sn(penH)_2$ have been measured, and the sign of the nuclear quadrupole splitting ΔE, as well as the value of the asymmetry parameter ($\eta=(V_{xx} - V_{yy})/V_{zz}$, where V are the diagonal components of the electric field gradient tensor)[6,7] have been determined. Configurational assignments have been extracted from the experimental data in the various physical states and from point-charge model calculations[6] of ΔE and η for possible structures. Lastly, the reactivity of the aqueous systems, and the nature of the products formed on standing at room temperature, have been subject to preliminary investigation.

Information on the nature of aqueous solutions of $Me_2Sn(cysH)_2$ and $Me_2Sn(penH)_2$ has been essential for the interpretation of the bonding of these compounds to rat hemoglobin (taken as a model protein) which has been very recently studied in our laboratories.[8]

EXPERIMENTAL

The diorganotin(IV) compounds were a gift from Schering AG, Bergkamen, FRG. L-cysteine ($HSCH_2CH(NH_2)COOH$) and L-, D- and DL-penicillamine ($HSC(CH_3)_2CH(NH_2)COOH$) were from Fluka AG, Buchs, Switzerland, and Hepes (*N*-2-hydroxyethylpiperazine-*N'*-2-ethanesulfonic acid) was from Calbiochem, La Jolla, CA, USA. Other reagents and solvents were C.Erba products, Milan, Italy.

The solid samples of bis[cysteinato(1$^-$)-*S*]- and bis[penicillaminato(1$^-$)-*S*]-diphenyl- and dimethyltin(IV) {$R_2Sn[SCH_2CH(NH_3^+)COO^-]_2$ and $R_2Sn[SC(CH_3)_2CH(NH_3^+)COO^-]_2$} were prepared according to the literature.[9]

The Mössbauer spectra at 77.3 K for solid and frozen-solution samples were obtained and treated as previously[5] (see also footnotes to Table 1). The sources ($Ca^{119}SnO_3$ and ^{57}Fe, the latter employed for velocity calibration) were moving at room temperature with linear velocity, constant acceleration, in a

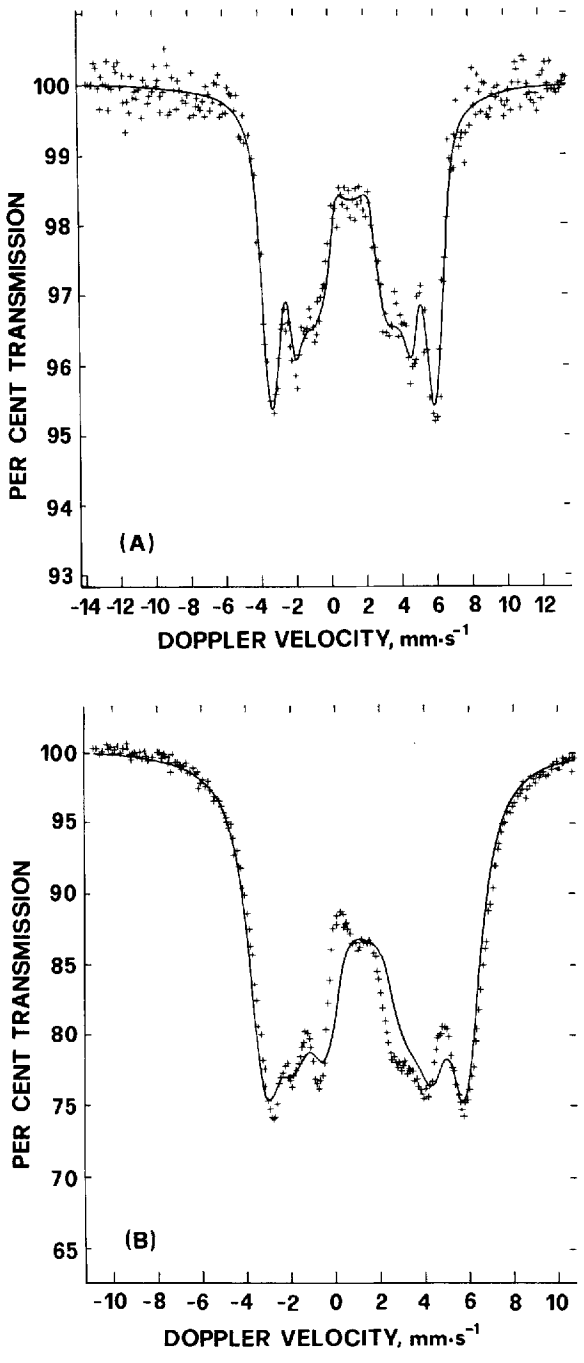

Figure 1 The Mössbauer–Zeeman spectra of $Ph_2Sn(cysH)_2$ (A) and $Ph_2Sn(penH)_2$ (B) measured at 4.2 K in a transverse magnetic field of 6 Tesla. The experimental data points (+) are fitted by computed spectra (full lines) with δ, ΔE and η values reported in Table 1. The uncertainty of the fitting of (B) originates from the unequal areas of the quadrupole doublet in the zero-field spectrum which has been detected for the sample employed here. See Experimental.

Table 1 ^{119}Sn Mössbauer parameters of bis[cysteinato(1$^-$)-*S*]- and bis[penicillaminato(1$^-$)-*S*]-diorganotin(IV) in the crystalline state and in frozen aqueous solution[a]

Number	Absorber sample[b]	δ[c] (mm s^{-1})	ΔE[d] (mm s^{-1})	Γ_1[e] (mm s^{-1})	Γ_2[e] (mm s^{-1})
(1)	$Ph_2Sn(cysH)_2$ (solid)	1.27 1.31[f]	2.21 ±2.32[f] (η=0.98)[f]	0.85 —	0.85 —
(2)	$Ph_2Sn(penH)_2$ (solid)	1.18 1.29[f]	2.43 −2.36[f] (η=0.75)[f]	1.01 —	0.93 —
(3)	$Me_2Sn(penH)_2$ (solid)	1.22	2.57	0.85	0.89
(4)	$Me_2Sn(cysH)_2$ (solution in H_2O; pH=7.27–7.50)	1.32	2.40	0.88	0.89
(5)	$Me_2Sn(penH)_2$ (solution in H_2O; pH=5.80–7.30)	1.29	2.59	0.83	0.86
(6)	$Me_2Sn(cysH)_2$ (solution in Hepes; pH=7.40)[g]	1.28	2.32	0.79	0.81
(7)	$Me_2Sn(penH)_2$ (solution in Hepes; pH=7.40)[h]	1.28	2.38	0.77	0.88
(8)	Solid products from $Me_2Sn(cysH)_2$in Hepes, pH=7.40, formed upon standing at room temp.[i]	1.35	1.85[j]	0.90	0.88
(9)	$Me_2Sn(cysH)_2$ + $H_2GlyGly$ (solution in Hepes, pH=7.40; measured after storage at room temp. for 8 months).	1.19	3.00	0.86	0.94
(10)	$Me_2Sn(penH)_2$ (solution in Hepes pH=7.40)[h]. Measured after storage at room temp. for:				
	(a) 2 months	1.24	2.77	0.93	0.83
	(b) 5 months	1.10	2.98	1.22	0.75

[a] T=77.3 K unless otherwise stated. See text (Discussion) for the structural assignments.
[b] Abbreviations: cysH, $SCH_2CH(NH_3)^+COO^-$; penH, $SC(CH_3)_2CH(NH_3)^+COO^-$; Hepes, *N*-2-hydroxyethylpiperazine-*N'*-2-ethanesulfonic acid; $H_2GlyGly$,glycylglycine. The chirality of $cysH_2$ and $penH_2$, as employed in the synthesis of the various samples of solid and/or of the solutions here investigated, were as follows. L-: (1), (4), (6), (8), (9); DL-: (2); L- and D-: (3); L-, D- and DL-: (5); L- and DL-: (7), (10). Further details are reported under Experimental. The concentration of aqueous Hepes buffer was 0.2 mol dm^{-3}.
[c] Isomer shift with respect to $Ca^{119}SnO_3$ at room temperature, average values.
[d] Nuclear quadrupole splitting, ±0.02 mm s^{-1},[5] average values.
[e] Full width at half height of the resonant peaks, at lower and higher velocity than the spectrum centroid, respectively, average values.
[f] Data from Mössbauer–Zeeman spectra, 4.2 K; $\eta=(V_{xx}-V_{yy})/V_{zz}$ is the asymmetry parameter.[6,7] See Fig. 1 and legend.
[g] Average of data reported in Ref. 5, Table 3, nos (8)–(11).
[h] Solutions containing 10 mmol dm^{-3} Me_2SnCl_2 and 30–40 mmol dm^{-3} $penH_2$ (1:3 and 1:4 respectively) were also measured, analogously to the systems (6); see Experimental, this paper, and Ref. 5.
[i] Obtained from the solutions described under Experimental, average values.
[j] Standard error = ±0.03 mm s^{-1}.

triangular waveform. The results obtained are reported in Table 1.

The Mössbauer–Zeeman spectra were measured by the Physicochemical Measurements Unit, AERE, Harwell, UK; the quality of the spectra is shown in Fig. 1, while the results are reported in Table 1.

Point-charge model calculation of ΔE and of η have been performed according to the literature,[5,6] employing tabulated values of the parameters for partial nuclear quadrupole splitting (pqs).[5,6,10–13] The pqs value for octahedral monodentate carboxyl (−0.11 mm s^{-1}), which has been employed in the present work and not reported previously, has been calculated from the tetrahedral value, −0.15 mm s^{-1}, according to the literature.[6,10] Calculated values of ΔE and η concerning possible structures of the systems investigated here are reported in Fig. 2 and in the text (Discussion).

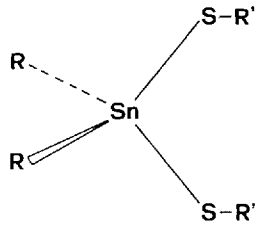

Figure 2 The tetrahedral structure assumed for $R_2Sn(cysH)_2$ and $R_2Sn(penH)_2$, in the solid state (R=Ph,Me) and in aqueous solution at physiological pH (R=Me). S—R′ = $SCH_2CH(NH_3^+)COO^-$; $SC(CH_3)_2CH(NH_3^+)COO^-$.

The point-charge model calculation of the nuclear quadrupole splitting ΔE and of the asymmetry parameter η gives the following values for the regular tetrahedral geometry:

R=Alk: $\Delta E_{calcd}=(\pm)2.03$, $\eta=1.00$; R=Ph: $\Delta E_{calcd}=(\pm)1.78$, $\eta=1.00$. See text, Experimental and Discussion.

The absorber thickness of the crystalline samples, (1) to (3) in Table 1, was in the range 0.35–0.58 mg $^{119}Sn\ cm^{-2}$. The solution samples consisted of about 2 cm^3 of 10–15 mmol dm^{-3} solutions.[5] Solutions were also prepared with 10 mmol dm^{-3} Me_2SnCl_2 and 20–40 mmol dm^{-3} ligand; if required the pH was adjusted by addition of sodium hydroxide. The absorber samples of the solutions were obtained by rapidly freezing them through immersion of the holder in liquid nitrogen which yields a glassy metal environment.[5] The resonant absorption of (4)–(7), (9) and (10), Table 1, was in the range $\epsilon=0.4-1.6\%$. For any system or compound [except (9)] three to four spectra were measured on distinct samples obtained by different syntheses of solid or preparation of solutions.

The parameters of the sample (8), Table 1, are average values obtained from the products which had precipitated from the following solutions (all with $[Me_2Sn^{IV}]$ = 10 mmol dm^{-3}) on standing at room temperature during the time indicated: (I), Me_2Sncys + $cysH_2$ (seven months); (II), $Me_2SnGlyGly$ + 2 $cysH_2$ (eight months) (GlyGly=glycylglycinate); (III), Me_2SnCl_2 + 3 $cysH_2$ (six months); (IV), Me_2SnCl_2 + 4 $cysH_2$ (seven months). The solid samples (7–22 mg from about 10 cm^3 of solution) were recovered by centrifugation and dried. Elemental analyses gave the following results (Found, av.): (I), C 14.3, H 3.2, N 0.9; (III), C 21.0, H 4.4, N 4.9; (IV), C 20.3, H 4.5, N 4.7%. The product from (I) could consist of $(Me_2SnS)_3$ (Calcd: C 13.29, H 3.34%) in the presence of small amounts of amino-acid derivatives; the samples from (III) and (IV) may contain also cystine (Calcd: C 29.99, H 5.03, N 11.66%).

DISCUSSION

The Mössbauer isomer shift parameters, δ, of compounds (1)–(8) in Table 1 are typically in the range shown by R_2Sn^{IV} moieties,[6] while the narrowness of the Γ data of (1)–(9) is consistent with the general occurrence of single tin sites (i.e. the resonant lines in each compound are doublets, due to unique values of the electric field gradient tensor at the given tin atom).[6]

Detailed information on the solid-state structure of the complexes (1)–(3), Table 1, is primarily extracted from the Mössbauer–Zeeman spectra of $Ph_2Sn(cysH)_2$ and $Ph_2Sn(penH)_2$ (Table 1, (1) and (2), and Fig. 1). These are characterized by large values of asymmetry parameter η, being possibly equal to unity, and by the consequent uncertainty on the sign of ΔE. According to point-charge model calculation, these data are consistent with the regular tetrahedral structure of Fig 2, although the absolute values of $\Delta E_{exp.calcd}$ for (1), (2) and (3) (Table 1 and Fig. 2) differ by more than the limiting value ± 0.4 mm s^{-1}. Moreover, for the same reasons, the structures described in the following would also be acceptable, in the context of octahedral and tbp species (including also polymers with C_2SnS_3 skeletons and axially bridging sulfur atoms): (i) octahedral $(R_2Sn(S_{thiol})_2(R'COO)_2$, with *trans*-$R_2$, *trans*-$(S_{thiol})_2$, *trans*-$(R'COO)_2$) where the ligand would chelate through S,O atoms, the latter from monodentate carboxyl (R=Alk: ΔE_{calcd} = +3.19, $\eta=0.97$; R=Ph: ΔE_{calcd} = −2.91, η = 0.91); and (ii) tbp $[R_2Sn(S_{thiol})_2(N_{am})$, with axial N_{am} (an amino nitrogen atom from —cysH and —penH, *vide supra*) and one S_{thiol} atom] where only one ligand would chelate through S,N atoms (R=Alk: ΔE_{calcd} = −1.92, η = 0.94; R=Ph: ΔE_{calcd} = −1.54, η = 0.82).

The possible configurations of $R_2Sn(penH)_2$ and $Ph_2Sn(cysH)_2$ discussed above are all in line with the coordinating properties of the ligands. Cysteine and penicillamine have been demonstrated to act as monodentate ligands through thiol sulfur in a number of complexes; *inter alia*, in R_3Sn^{IV} derivatives in the

solid state,[14] in $Alk_3Sn(cysH)$ in aqueous solution at pH=7.4,[15] and in Me_3Pb^{IV} and RHg^{II} complexes in aqueous solution.[16,17] Moreover, the coordination number of the tin center may in principle expand to five and/or six due to coordination by carboxyl oxygen and/or amino nitrogen atoms of the amino-acid tails, e.g. according to the X-ray molecular structures of $Me_2SnCl[SCH_2CH(NH_2)COOC_2H_5]$[18] and of $(Me_3SnOOCCH_2NH_2)_n$,[19] as well as to Mössbauer studies, including lattice dynamics, carried out on the latter compound and on $Me_2Sn[SC(CH_3)_2CH(NH_2)COO]$;[13] it may also be mentioned that in $Me_2Sn(cys)$ in aqueous solution, in the pH range 5.0–9.5, tin seems to be chelated by N,S atoms.[2] In the great majority of their metal complexes, cysteine and penicillamine act as multidentate ligands.[20,21]

In the context of the structure of $Ph_2Sn(cysH)_2$ and $R_2Sn(penH)_2$, (1)–(3) of Table 1, we are inclined to assume the presence of a tetrahedral structure, as shown in Fig. 2, for the following reasons.

(1) The near-coincidence of the value and the sign of ΔE and the value of η for the Mössbauer–Zeeman spectrum of $Ph_2Sn(cysH)_2$, (1) of Table 1, and the corresponding point-charge model data for the regular tetrahedral structure.

(2) The infrared spectra of compounds (1)–(3) are consistent with the presence of $-NH_3^+$ and $-COO^-$ groups in the amino-acid tails, and exclude the coordination of the metal by these groups.[9]

(3) The species (3) cannot consist of a linear carbon–tin–carbon (CSnC) skeleton, since both ν_s and ν_{as} (SnC_2) vibrational modes are observed to occur,[9] and this excludes the all-*trans* octahedral structure mentioned above.

(4) Four-coordination of tin in skeletons C_2SnS_2would be consistent with a large electron density induced on tin by two sulfur atoms, which would sensibly reduce the Lewis acidity of Sn with respect for example to the mono-derivatives, such as $Me_2Sn(cys)$ and related compounds.

On the other hand, it must be recalled here that the ΔE_{exp} values of (1)–(3), Table 1, are consistently larger than the data for the 2-mercaptoethanesulfonate complexes $[R_2Sn(Mes)_2]^{2-}$, both in the solid state (R=Me,Ph) and in aqueous solution (R=Me), which have been assumed as tetrahedral species $R_2Sn(S_{thiol})_2$,[4] as well as being larger than the majority of ΔE data for a series of tetrahedral $R_2Sn(S_{thiol})_2$ compounds;[22–24] they are also too large with respect to point-charge ΔE_{calcd} for the structure in Fig. 2 as mentioned earlier. These circumstances cannot apparently be attributed to the distortion of (1)–(3) from the ideal tetrahedral structure, resulting for example in changes of the C–Sn–C and/or S–Sn–S angles in Fig. 2 and preserving the C_{2v} symmetry. Such distortions would yield η values consistently smaller than unity,[10] inconsistent with the data of the Mössbauer–Zeeman spectra (particularly for (1), Table 1), when providing ΔE_{calcd} data for agreement with ΔE_{exp} of (1)–(3), Table 1. For example, distortion of the C–Sn–C angle to 120° yields $\Delta E_{calcd}=+2.52$, $\eta=0.44$ for $Alk_2Sn(S_{thiol})_2$, and $\Delta E_{calcd}=+2.23$, $\eta=0.42$ for $Ph_2Sn(S_{thiol})_2$, using the pqs values pertaining to regular configurations. In turn, such calculations have a limited significance; in fact, the literal point-charge model refers always to regular structures, ignoring small deviations from ideality and employing invariant values of the pqs parameters,[10] while the treatment of severe distortions instead requires, in principle, the variability of pqs parameters and their estimation in each individual distorted configuration.[25] No attempts are made here to employ the latter approach, and to try further to correlate our ΔE_{exp} data with structural distortions in tetrahedral type $R_2Sn(S_{thiol})_2$ compounds.

The ΔE values of $Me_2Sn(cysH)_2$ and $Me_2Sn(penH)_2$ in frozen aqueous solutions, (4) and (5) in Table 1, correspond to ΔE of $Me_2Sn(penH)_2$ in the solid state, (3), as well as to the data for the diphenyltin(IV) complexes (1) and (2). This agrees with findings for 2-mercapto-ethanesulfonato complexes $[Me_2Sn(Mes)_2]^{2-}$ in the two physical states[4] [although ΔE values in these complexes are noticeably less than those of our compounds (3)–(5)[4]], and strongly suggests that the tetrahedral configuration assumed in the solid state (Fig. 2) persists in aqueous solution.[4] The reluctance of tin in these complexes towards coordination by water in these aqueous solutions is in accord with the analogous behavior detected for $Me_2Sn(OH)_2$,[26] which has been ascribed to the low Lewis acidity of the metal ion with respect to coordination by water.[27]

Hepes coordinates tin centers in $Me_2Sn(cysH)_2$ and other Me_2Sn^{IV} derivatives,[5] as well as in $[Me_2Sn(Mes)_2]^{2-}$,[4] forming the tbp complexes

$Me_2Sn(S_{thiol})_2(N_{am})$ referred to in the preceding discussion (N_{am} now being a tertiary amino nitrogen from Hepes[4,5]), ΔE_{calcd} being -1.92 and ΔE_{exp} ranging from 2.16 to 2.35.[4,5] Moreover, the composition of these complexes is invariable in excess of both the thiol-bearing ligand and Hepes.[4,5] The same holds for $Me_2Sn(penH)_2$, (7) of Table 1, which is shown to correspond strictly to the related $Me_2Sn(cysH)_2$ system, (6) in Table 1. This information is essential for studies on the interaction of diorganotin(IV) derivatives with proteins,[5,8] where, *inter alia*, the *in vitro* reaction is effected in aqueous Hepes buffer.[5,8]

The complexes $Me_2Sn(cysH)_2 \cdot$Hepes and $Me_2Sn(penH)_2 \cdot$Hepes undergo the following reactions on standing at room temperature in aqueous Hepes buffer.

(1) $Me_2Sn(cysH)_2 \cdot$Hepes slowly yields the solid organotin(IV)-containing species (8), Table 1; these are the only tin-containing products (no ^{119}Sn γ-resonance absorption being detectable in solution phase), unless an additional ligand, such as glycylglycinate, is present in solution [(9), Table 1]. Moreover, further solid products are obtained, other than (8), from solutions containing excess cysteine with respect to the stoichiometry Me_2Sn^{IV}:cysteine = 1:2 (as demonstrated by the elemental analyses reported under Experimental).

(2) $Me_2Sn(penH)_2 \cdot$Hepes very slowly gives soluble products, (10) of Table 1.

The organotin(IV)-containing solids (8) seem to consist of $(Me_2SnS)_3$ according to elemental compositions (see Experimental). Their Mössbauer parameters closely correspond to literature values for $(Me_2SnS)_3$ ($\delta = 1.23-1.24$; $\Delta E = 1.51-1.85$ mm s^{-1}).[28] The latter compound in the crystalline state consists of the cyclic trimer $(Me_2SnS)_3$ where the environment of tin is tetrahedral,[29] and the ΔE_{exp} data referred to above essentially agree with $\Delta E_{calcd} = (\pm)2.03$ mm s^{-1} for the regular tetrahedral structure of C_2SnS_2 skeletons (Fig. 2 and legend). According to the literal point-charge model,[10] the magnitude of ΔE_{exp} for $(Me_2SnS)_3$ would imply that the pqs value for $([Me_2SnS]-[hal])^{tet}$ corresponds[22] to $([R-S]-[hal])^{tet} = -0.49$ mm s^{-1} (employed in the calculation in the legend to Fig. 2), which seems reasonable on the basis of the similarity of carbon and tin electronegativities (hal = halogen).

It seems worthwhile to note that the formation of $(Me_2SnS)_3$ from $Me_2Sn(cysH)_2$, under the very mild conditions described above, seems to us to be a unique reaction in the context of metal ion–mercaptoacid complexes in solution. To our knowledge, an analogous decomposition of the thiol ligand occurs only for $R_3Sn(cysH)$, where $(R_3Sn)_2S$ species are formed in the context of synthetic reactions.[14,30,31] Other examples apparently have not been reported in the field of metal ion–mercaptoacid derivatives.

The occurrence of Me_2Sn^{IV} moieties in the solution phase in the presence of glycylglycine, (9) of Table 1 (besides crystalline $(Me_2SnS)_3$), may be ascribed to the partial formation of the tbp complex $Me_2Sn(OH)(GlyGly)(Hepes)$[5] upon desulfuration of $Me_2Sn(cysH)_2$, the related parameters being[5] $\delta = 1.16-1.17$, $\Delta E = 3.02-3.08$ mm s^{-1}. The magnitude of δ in (9) agrees well with lysis of Sn–S bonds and their replacement by bonding of tin to more electroegative atoms than sulfur.

The solid product obtained from solutions containing excess ligand could consist, besides $(Me_2SnS)_3$, of cystine $[-(SCH_2CH(NH_2)COOH)_2]$ formed by oxidation of cysteine;[32] the elemental analyses (see Experimental) are consistent with the presence of solid amino-acid derivatives. In fact, the solubility of cystine in H_2O at 25°C is quite low (0.109 g dm^{-3});[33] moreover, the formation of a Me_2Sn^{IV}–cystine complex seems to be excluded, since metal ion coordination by a disulfide group does not seem to occur.[20,21,34]

In the aqueous solutions of $Me_2Sn(penH)_2$ in Hepes buffer, very slow reactions occur which yield species (10), Table 1, showing smaller δ values, and larger ΔE, than the parent solutions (7). The data of (10) do indeed correspond to those analogously obtained for the mercaptoethanesulfonate complexes[4] $[Me_2Sn(Mes)_2]^{2-}$, the species formed being the desulfurated tbp complex $Me_2Sn(OH)_2(N_{am})$, with axial N_{am} (from Hepes) and one OH group, ΔE_{calcd} being $+2.82$ mm s^{-1} for this structure.[4,5] Moreover, it is noted that the rate of decomposition of $Me_2Sn(penH)_2$ appears to be consistently slower than that of the corresponding cysteinate. In fact, no Mössbauer spectral changes are detectable for $Me_2Sn(penH)_2$ solutions stored at room temperature for about one week; moreover, no solid products are formed, irrespective of the storage time and of the eventual excess ligand, contrary to the analogous cysteine systems. The gradual formation of water-soluble penicillamine disulfide seems to take place.

The greater reactivity of $Me_2Sn(cysH)_2$ with respect to $Me_2Sn(penH)_2$ may be related to known properties of the ligands. For example, it may be recalled that the metabolism of cysteine involves facile desulfuration while penicillamine is not metabolized and is excreted as the disulfide.[32] Moreover, the stability constant of a given metal ion–penicillamine complex is usually larger than that of the corresponding complex with cysteine,[17,35] following the trend of the Brønsted basicity of the ligands, penicillamine > cysteine.[17]

CONCLUSIONS

(1) The complexes $R_2Sn(cysH)_2$ and $R_2Sn(penH)_2$ are characterized by tetrahedral C_2SnS_2 tin sites, both in the solid state (R=Ph, Me) and in aqueous solution (R=Me), the ligands acting as monodentate donors through the thiol sulfur atom. The nature of the environment of tin is independent of the chirality of the ligands. The compounds are then correctly indicated as bis[cysteinato(1^-)-*S*]- and bis[penicillaminato(1^-)-*S*]-diorganotin(IV).

(2) Amino nitrogen atoms may coordinate tin in $Me_2Sn(cysH)_2$ and $Me_2Sn(penH)_2$, in aqueous solution, in the presence of excess ligand (e.g. Hepes buffer), which is in line with recent findings on the respective extent of the interaction of sulfur and nitrogen donors with Me_3Sn^{IV} in aqueous media.[36]

(3) The *in vitro* degradation of $Me_2Sn(cysH)_2$ and $Me_2Sn(penH)_2$ in aqueous solution at pH=7.4 does not seem to have any *in vivo* significance, unless the reaction rates are much larger in living organisms. In particular, the formation of solid $(Me_2SnS)_3$ would not occur in the latter context, the Me_2Sn^{IV} moiety being possibly involved in complex formation with ligands present in biological media.

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