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Synthesis and spectroscopic characterization of R_3Sn^{IV} derivatives of *N*-acetyldipeptides

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Triorganotin(IV) derivatives of *N*-acetyldipeptides $R_3SnAcDip$; R = Me, Et, n-Bu, n-Oct, Cy or Ph (HAcDip = *N*-acetylglycylglycine and *N*-acetylglycylvaline; R = Me, n-Bu, Cy, HAcDip = *N*-acetylglycylalanine) were obtained by neutralization of R_3SnOH and HAcDip. The complexes were studied by means of ^{119}Sn Mössbauer, IR and ^{1}H, ^{13}C and ^{119}Sn NMR spectroscopy. The C–Sn–C bond angles have been inferred by rationalization of Mössbauer nuclear quadrupole splittings as well as from NMR coupling constants. Correlations of Mössbauer isomer shifts with partial atomic charges on tin atoms have been determined. Polymeric trigonal bipyramidal structures, with near-planar R_3Sn units and axial carboxylate (unidentate) and C=O amide donor groups are inferred for all the compounds in the solid state, except for $Cy_3SnAcGlyVal$ for which a tetrahedral structure is proposed. In solution the complexes are monomeric; in methanol a solvent molecule is coordinated to tin which then is still in a trigonal bipyramidal environment.

Keywords: Organotin, biocidal, biological, Mössbauer, NMR, IR, peptide, protein

INTRODUCTION

Triorganotin(IV) compounds exhibit considerable biological activity, and their biocidal potential and problems of toxicity, in connection with their applications, have found broad interest.[1] In contrast, detailed investigations on the binding of organotin species to proteins or protein constituents are not very numerous. The binding of triorganotin(IV) species to rat hemoglobin has been amply studied as a triorganotin–protein model system,[2,3] and we ourselves and other groups have studied triorganotin(IV) derivatives of amino acids and dipeptides.[4–7] We have continued our research in this field and we report in this paper results of work on the interaction of R_3Sn^{IV} moieties with *N*-acetyldipeptides (HAcDip) which can be considered to be simple protein models.

EXPERIMENTAL

N-Acetyldipeptides were prepared by a procedure described in Ref. 8. Ph_3SnOH was obtained by hydrolysis of Ph_3SnCl;[9] the other triorganotin hydroxides were prepared analogously. Other reagents and solvents were commercial products.

The complexes in Table 1 were synthesized as follows.

Method A

R_3SnOH (5 mmol) and *N*-acetyldipeptide (5 mmol) in 50 cm^3 methanol were refluxed for 3 h. The volume of the clear solution was then reduced *in vacuo* to about 5 cm^3. Addition of diethyl ether caused the precipitation of white solids. These were separated by filtration, washed with diethyl ether, and dried *in vacuo*.

Method B1

The procedure was analogous to that of method A, but the reaction mixture was stirred for 3 h at room temperature.

Method B2

The procedure was analogous to that of method A, but *n*-pentane was added instead of diethyl ether. The solution was subsequently refluxed for *ca* 20 min more. The solvent was then removed *in vacuo*.

Crystalline products were obtained in all cases. $Et_3SnAcGlyGly$ first separated as an oil which crystallized slowly at −6 °C.

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Table 1 Analytical data for triorganotin derivatives of *N*-acetyldipeptides[a]

Compound		Method	Yield (%)	M.p. (°C)	Analysis: Found (calcd) (%) C	H	N
1	$Me_3SnAcGlyGly$	A	59.5	158 dec.	32.3 (32.08)	5.3 (5.38)	8.4 (8.31)
		B1	45.0	158 dec.			
2	$Et_3SnAcGlyGly$	B2	55.3		38.8 (38.03)	6.8 (6.38)	6.9 (7.39)
3	$(n\text{-}Bu)_3SnAcGlyGly$	A	71.2	105 dec.	46.3 (46.67)	7.6 (8.83)	5.7 (6.05)
4	$(n\text{-}Oct)_3SnAcGlyGly$	B2	47.5	74 dec.	57.8 (57.06)	9.7 (9.58)	4.7 (4.44)
5	$Cy_3SnAcGlyGly$	B2	72.3	119 dec.	—[b]	8.1 (7.82)	4.8 (5.18)
6	$Ph_3SnAcGlyGly$	A	61.2	96 dec.	52.8 (55.10)	4.6 (4.62)	5.2 (5.35)
7	$Me_3SnAcGlyAla$	A	65.5	52 dec.	35.2 (34.22)	6.1 (5.74)	7.4 (7.98)
8	$(n\text{-}Bu)_3SnAcGlyAla$	A	75.6	111 dec.	47.2 (47.82)	7.9 (8.03)	5.7 (5.87)
9	$Cy_3SnAcGlyAla$	B2	85.0	122 dec.	54.2 (54.07)	7.9 (7.99)	5.1 (5.04)
10	$Me_3SnAcGlyVal$	A	55.4	80 dec.	37.6 (38.03)	6.2 (6.38)	6.8 (7.39)
11	$Et_3SnAcGlyVal$	B2	83.1	149 dec.	43.4 (42.78)	7.5 (7.18)	6.2 (6.65)
12	$(n\text{-}Bu)_3SnAcGlyVal$	A	61.4	128 dec.	49.8 (49.92)	8.3 (8.38)	5.5 (5.54)
13	$(n\text{-}Oct)_3SnAcGlyVal$	B2	52.0	40 dec.	60.4 (58.84)	10.4 (9.88)	4.6 (4.16)
14	$Cy_3SnAcGlyVal$	A	49.0	97 dec.	56.3 (55.59)	8.4 (8.29)	4.9 (4.80)
15	$Ph_3SnAcGlyVal$	A	51.2	68 dec.	56.8 (57.37)	5.0 (5.35)	4.4 (4.96)

[a] Ac, *N*-acetyl; GlyGly, glycylglycine; GlyVal, glycylvaline; GlyAla, glycylalanine. [b] No satisfactory analysis for C obtained.

All derivatives are very soluble in dimethyl sulfoxide, hexamethylphosphoramide, methanol, ethanol and, with the exception of the Me_3Sn and $(n\text{-}Oct)_3Sn$ compounds, in acetone, chloroform and water. In non-polar solvents such as *n*-pentane, diethyl ether or petroleum ether (40–60 °C), all compounds are sparingly soluble.

Elemental analyses were carried out with an Elemental Analyzer 1106 (Carlo Erba, Milan, Italy). Melting points were measured in open capillaries and are uncorrected. Analytical data are collected in Table 1. Molecular weights (in $g\,mol^{-1}$) were determined osmometrically in anhydrous methanol [$Me_3SnAcGlyGly$ 298 (calcd 337)] and in chloroform [$Et_3SnAcGlyVal$ 432 (421); $(n\text{-}Bu)_3SnAcGlyGly$ 473 (463); $(n\text{-}Bu)_3SnAcGlyVal$ 501 (505); $(n\text{-}Oct)_3SnAcGlyVal$ 661 (673); $Ph_3SnAcGlyVal$ 558 (565)]. ^{119}Sn Mössbauer spectra (Table 2) were measured with a Mössbauer spectrometer consisting of a Master 4000 multichannel analyzer (Laben, Milan), equipped with function generator, driving unit, scintillation and proportional counters, and related instrumental units. The velocity transducer (Halder, Munich, Germany) moved with linear velocity and constant acceleration, in a triangular waveform. The Mössbauer source was $Ca^{119}SnO_3$ and ^{57}Fe (5 mCi) from the Radiochemical Centre, Amersham, UK. The latter was employed for the velocity calibration of the spectrometer using natural-iron foil absorbers. The absorber samples were held at 77.3 K in a liquid-nitrogen cryostat (AERE Harwell, UK). The IR spectra (Tables 3 and 4) were recorded on a Perkin–Elmer grating spectrometer PE 580B (KBr, or in solution, solvent indicated in Table 3). Raman spectra were measured on a Coderg Laser Raman Spectrometer PHO (glass capillaries; $\lambda = 514.5$ and 647.1 nm, respectively). ^1H, ^{13}C and ^{119}Sn NMR spectra (Tables 5–10) were recorded on a Bruker AM300 spectrometer and chemical shifts were measured in ppm downfield from internal TMS or DSS and external Me_4Sn references.

RESULTS AND DISCUSSION

The structural proposals for the solid-state complexes are based on ^{119}Sn Mössbauer and infrared spectroscopic data. The values of the quadrupole splitting parameter of the triorganotin derivatives of *N*-acetyldipeptides (Table 2) strongly suggest, except for $Cy_3SnAcGlyVal$, a trigonal bipyramidal arrangement around tin with alkyl or phenyl groups in the trigonal plane and electronegative atoms in apical positions.[10,11] (Fig. 1). In comparable triorganotin derivatives of amino acids and dipeptides the presence of an essentially uniden-

Table 2 ^{119}Sn Mössbauer parameters of triorganotin derivatives of *N*-acetyldipeptides

Compound[a]		δ^b (mm s^{-1})	ΔE^c (mm s^{-1})	Γ_1^d (mm s^{-1})	Γ_2^d (mm s^{-1})
1	$Me_3SnAcGlyGly$	1.39	3.66	0.85	0.83
	solution in MeOH[e]	1.30	3.43	0.79	0.85
2	$Et_3SnAcGlyGly$	1.48	3.55	1.13	1.04
3	$(n\text{-}Bu)_3SnAcGlyGly$	1.47	3.54	0.83	0.82
4	$(n\text{-}Oct)_3SnAcGlyGly$	1.44	3.46	0.76	0.86
5	$Cy_3SnAcGlyGly$	1.53	3.28	1.01	1.08
6	$Ph_3SnAcGlyGly$	1.29	3.14	0.88	0.86
7	$Me_3SnAcGlyAla$	1.32	3.48	1.01	1.02
	Solution in MeOH[e]	1.29	3.43	0.80	0.87
8	$(n\text{-}Bu)_3SnAcGlyAla$	1.43	3.43	0.80	0.80
9	$Cy_3SnAcGlyAla$	1.53	3.32	0.83	0.87
10	$Me_3SnAcGlyVal$	1.37	3.49	0.83	0.80
	Solution in MeOH[e]	1.28	3.37	0.82	0.86
11	$Et_3SnAcGlyVal$	1.42	3.51	0.83	0.91
12	$(n\text{-}Bu)_3SnAcGlyVal$	1.44	3.47	0.85	0.83
13	$(n\text{-}Oct)_3SnAcGlyVal$	1.42	3.39	0.79	0.86
14	$Cy_3SnAcGlyVal$	1.51	2.71	0.94	0.95
	Solution in MeOH[f]	1.53	3.29	1.01	1.08
15	$Ph_3SnAcGlyVal$	1.29	3.12	0.84	0.88

[a] Sample thickness was about 0.50 mg ^{119}Sn cm^{-2}. [b] isomer shift with respect to $Ca^{119}SnO_3$. [c] Nuclear quadrupole splitting. [d] Full width at half-height of the resonant peaks, at greater and lesser velocity than the spectrum centroid respectively. [e] 0.1 M solution. [f] Approx. 0.1 M solution.

tate carboxylate group was proposed on the basis of vibrational and Mössbauer data;[5] for trimethyltin glycinate this structure was established by X-ray diffraction.[4] The coordination number five is attained by means of the coordination of the amino group to another R_3Sn unit, resulting in a polymeric structure. In triorganotin derivatives of *N*-acylated amino acids the R_3Sn moieties are coordinated by unidentate carboxylic groups and oxygen of $C{=}O_{amide}$ as evidenced for derivatives of *N*-formylglycine, *N*-acetylglycine, *N*-acetylalanine and *N*-acetylmethionine.[12,13] A second type of coordination with planar R_3Sn moieties, linked by bidentate bridging carboxylate groups, was inferred from vibrational data for *N*-benzoylglycinates[12,13] (an analogous coordination was found in *N*-benzoylglycylglycinates[14]). The second type of structure, with bridging carboxylate groups, has been found hitherto only in *N*-benzoyl derivatives, and it was argued that the inductive (−I) effect of the phenyl group would favor the mesomeric form A (R = Ph), decreasing the Lewis basicity of the $C{=}O_{amide}$ group with the effect that tin reaches pentacoordination by bonding to bidentate bridging carboxylate groups.

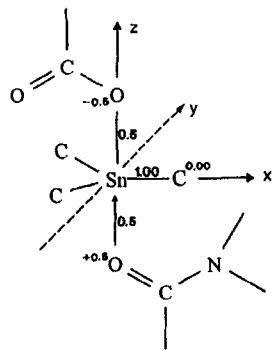
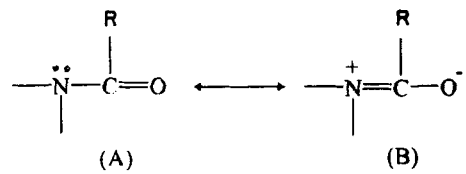


Figure 1 The configuration of the tin environment assumed for the rationalization of the ^{119}Sn Mössbauer nuclear quadrupole splitting parameters, ΔE, and isomer shift, δ. The direction of the principal components of the electric field gradient tensor[10] (x, y, z) from point-charge model calculations[10] are indicated. Numbers refer to input data for bond orders and formal charges employed in the calculation of CHELEQ partial atomic charges;[21-24] see text.



Form **B** would be promoted in cases where R = H or alkyl, and the competitive tendency of the carboxylate group to enter into monodentate or bidentate coordination would be influenced in favor of unidentate coordination. In both cases the molecules form polymeric chains.[12-14] Point-charge model calculations for regular structures of triorganotin *N*-acetyldipeptides (Fig. 1, and related configurations) do not allow us to distinguish between the two coordination types established for the analogous triorganotin derivatives of *N*-acylated amino acids. For a structure of the first type, in which R_3Sn units are coordinated by unidentate carboxylate groups and $C{=}O_{amide}$, ΔE_{calcd} is (−)3.51 mm s^{-1} when R = alkyl, and (−)3.06 mm s^{-1} when R = phenyl (pqs used, in mm s^{-1}: $[Alk]^{tbe}$, −1.13;[11] $[Ph]^{tbe}$, −0.98;[11] $[COO_{unid}]^{tba}$, −0.10;[15] $[C{=}O_{amide}]^{tba}$, 0.16[11]). For the second type of structure in which bridging carboxylate groups are present, ΔE_{calc} = (−)3.69 mm s^{-1} for R = alkyl and (−)3.24 for R = phenyl ($[COO_{bridg}]^{tba}$, 0.075 mm s^{-1}).[11] Thus, the difference between point-charge estimates and the experimental quadrupole splittings (Table 2) do not exceed 0.4 mm s^{-1} and both structures are possible on the basis of the Mössbauer parameters.[16] However, on the basis of IR data (see below), we suppose that *N*-acetyldipeptide ligands coordinate the R_3Sn moieties through unidentate carboxylate and $C{=}O_{amide}$. It should be pointed out that coordination of the amide (or peptide) group through nitrogen cannot be excluded on the basis of the Mössbauer spectra. ΔE_{calc} is in fact −3.21 mm s^{-1} for R = alkyl and −2.76 mm s^{-1} for R = phenyl (pqs used: $[N\text{-(COMe)}]^{tba}$[piperidine]^{tba} = +0.01 mm s^{-1}).[11] This type of coordination is however ruled out by the infrared spectra.

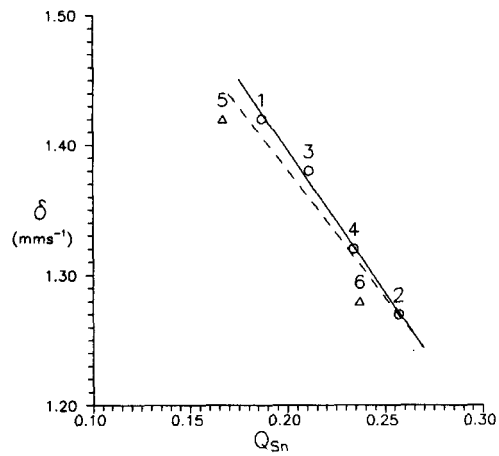


Figure 2 The correlation of ^{119}Sn Mössbauer isomer shifts, δ (mm s^{-1}), with partial atomic charges on tin, Q_{Sn}, for complexes of R_3Sn^{IV} moieties with carboxylic acids, acetylamino acids and acetyldipeptides. 1, $Alk_3SnOCOR$ ($\delta_{av.}$ = 1.43, Nos 1–22 in Table XXIX, p. 136, of Ref. 10; Q_{Sn}(av.) = 0.187[35]); 2, $Ph_3SnOCOR$ ($\delta_{av.}$ = 1.27, Nos 23–35 in Table XXIX, Ref. 10; Q_{Sn} = 0.257[35]); 3, 4, $Ph(n\text{-}Bu)_2SnOCOCH_3$ and $Ph_2(n\text{-}Bu)SnOCOCH_3$ (δ = 1.38, 1.32;[36] Q_{Sn} = 0.211, 0.234[35]); 5, Alk_3Sn-acetylamino acids and -acetyldipeptides ($\delta_{av.}$ = 1.42, Refs 12 and 13 and Table 2, this work; Q_{Sn}(av.) = 0.167, this work); 6, Ph_3Sn-acetylamino acids and -acetyldipeptides ($\delta_{av.}$ = 1.28, Ref. 12 and Table 2, this work; Q_{Sn}(av.) = 0.237, this work). The input structure and parameters for the calculation of Q_{Sn} for 5 and 6 are in Fig. 1; for 1–4, in Ref. 35 (trigonal bipyramidal, axial bridging carboxylate, formal charges 0.00, bond orders 0.5 for Sn–O and 1.5 for C–O[35]). Least squares fit equations: Nos 1–4: $\delta = 1.834 - 2.187Q_{Sn}$ (r = 0.997), full line; Nos 1–6: $\delta = 1.760 - 1.909Q_{Sn}$ (r = 0.954), broken line.

The only exception to the proposed pattern is $Cy_3SnAcGlyVal$ (**14**, Table 2), the quadrupole splitting of which, 2.71 mm s^{-1}, is at variance with point-charge estimates for trigonal bipyramidal structures with two oxygen atoms in *trans* positions. In contrast, a tetrahedral structure is suggested in which the acetyldipeptide ligand is bound to the Cy_3Sn moiety through the carboxylate, which obviously acts as a unidentate ligand. For such a structure, ΔE_{calcd} = 2.44 mm s^{-1} ($[COO_{unid}]^{tet}$ = −0.15 mm s^{-1}).[10] The value of ΔE_{exp} (larger than the calculated one) is indicative of some distortion from the regular structure, as could be foreseen on the basis of the steric hindrance of cyclohexyl groups. In effect, the treatment suggested by Parish[17] for tetrahedral R_3SnX compounds (Eqn [1]):

$$\Delta E = 2[X]^{tet} - 3[R]^{tet}(1 - 3\cos^2\theta) \qquad [1]$$

where θ is the C—Sn—X bond angle, gives θ = 107.4°, very similar to the C–Sn–X angle observed in $Cy_3SnO_2CCF_3$ (106.3°).[18] On the other hand, a long-range interaction of $C{=}O_{amide}$ with the C_3Sn unit is also possible; in fact the ΔE calculated for such a structure, assuming COO–Sn–C angles of 106°, is −2.74 mm s^{-1}. Obviously, a structure of this type is very close to a tetrahedral one.

The parameter δ, the ^{119}Sn Mössbauer isomer shift, is rationalized through correlation with the electronegativities of bonded atoms,[19] the latter being reflected in the partial atomic charges[20] on tin, Q_{Sn}. Values of Q_{Sn} may be estimated through a procedure based upon orbital electronegativity equalization on bond formation, employing the

program CHELEQ.[21-24] In this way, series of strictly congeneric compounds are identified, as far as the nature of the metal environment is concerned.[25-28] The Q_{Sn} data obtained here, related to the input structure in Fig. 1 for R_3Sn complexes with acetylamino acids and acetyldipeptides, are shown in Fig. 2 to correlate well with the function inherent for R_3Sn carboxylate complexes. As a consequence, the corresponding structure shown in Fig. 1 is likely to be attributed to our compounds, in analogy to previous assumptions for R_3Sn complexes with *N*-acetylamino acids.[12,13] It is then concluded that the present rationalization of δ parameters essentially confirms the structural findings obtained from the point-charge model treatment of the parameters ΔE (*vide supra*).

In the infrared spectra of the complexes (Table 3), vibrations associated with CO(OH) of free *N*-acetyldipeptides (Table 4) have disappeared, so that it can be concluded that the SnR_3 groups are bound through the carboxylic group to the acetyldipeptide moiety. The frequencies $\nu_{asym}(COO)$ and $\nu_{sym}(COO)$ and $\Delta\nu$ values ($\nu_{asym} - \nu_{sym}$) are distinctly different from those of the appropriate alkali-metal compound. Ionic bonding or chelation and also bridging may therefore be excluded, and carboxylic groups bonding tin in unidentate fashion can be assumed.[29,30] As far as the amide/peptide group is concerned,

Table 3 Infrared spectral data for triorganotin derivatives of *N*-acetyldipeptides

	Compound	ν(NH) (cm^{-1})	$\nu(CO_{am})/\nu(CO_{pept})/\nu_{asym}(COO)$ (cm^{-1})	$\nu(CN) + \delta(NH)$ (cm^{-1})	$\nu_{sym}(COO)$ (cm^{-1})	$\Delta\nu$[a] (cm^{-1})
1	$Me_3SnAcGlyGly$	3280 s, br	1645	1540 m, br 1565 sh	1403 m, s	242
	(CD_3OD)		1653 vs, br		1398 m, s	255
2	$Et_3SnAcGlyGly$	3290 m, br	1642 vs, br	1550 m, br	1397 m, s	245
3	$(nBu)_3SnAcGlyGly$	3294 s, br	1655 s/1632 vs	1570 m, br	1400 s	>232
	(CD_3OD)		1655 vs, br		1397 s	258
4	$(n\text{-}Oct)_3SnAcGlyGly$	3295 s, br	1652 vs, br	1565 m, br	1397 s	255
	(CD_3OD)		1668 vs, br		1398 s	256
5	$Cy_3SnAcGlyGly$	3305 s	1650 vs, br	1555 s, br	1398 s	252
	($CHCl_3$)	3320 s, br 3420 m, br	1665 vs, br	1525 s, br	1398 vs	267
6	$Ph_3SnAcGlyGly$	3285 s, br	1650 vs, br	1545 s, br	1397 s	253
7	$Me_3SnAcGlyAla$	3280 s, br	1650 vs, br	1555 m, br	1398 s	252
8	$(n\text{-}Bu)_3SnAcGlyAla$	3285 s, br	1670 s/1630 vs, br	1557 s, br	1400 s	>230
	($CHCl_3$)	3420 m, br 3320 s, br	1655 vs, br	1522 s, br	1397 s, br	257
9	$Cy_3SnAcGlyAla$	3320 s, br	1672 s/1630 s, br	1540 s, br	1402 s	>228
	($CHCl_3$)	3420 m, br 3330 s, br	1660 vs, br	1522 s, br	1398 s	262
10	$Me_3SnAcGlyVal$	3280 m, br 3343 m, s	1685m/1660s/1640s/1625s	1577 s 1530 sh, br	1397 s 1392 s	>228
	(CD_3OD)		1650 vs, br		1400 br	250
11	$Et_3SnAcGlyVal$	3290 s, br	1672 m/1630 vs, br	1550 m, br	1398 s	>232
	($CHCl_3$)	3430 m, br 3320 m, br	1660 vs, br	1520 s, br	1400 m, br	260
12	$(n\text{-}Bu)_3SnAcGlyVal$	3300 s, br	1675 s/1630 vs, br	1560 s, br	1405 m, br	>225
	($CHCl_3$)	3425 s 3330 m, br	1662 vs, br	1520 vs, br	1390 s	262
13	$(n\text{-}Oct)_3SnAcGlyVal$	3280 s, br	1674 s/1630 vs, br	1540 s, br	1396 s	>234
14	$Cy_3SnAcGlyVal$	3310 s, br	1665 vs, br	1554 s, br	1398 s	267
	($CHCl_3$)	3320 s, br 3425 m, br	1665 s, br	1530 s, br	1398 s	267
15	$Ph_3SnAcGlyVal$	3280 s, br	1635 vs, br	1550 s, br	1395 s	240
	($CHCl_3$)	3425 m, br 3335 m, br	1660 vs, br	1520 s, br	1400 m, br	260

[a] $\nu_{asym}(COO) - \nu_{sym}(COO)$.

Table 4 Infrared data for *N*-acetyldipeptides and their sodium or ethoxide salts

Compound	ν(NH) (cm^{-1})	$\nu(CO_{am})/(CO_{pept})$ (cm^{-1})	ν_{asym}(COO) (cm^{-1})	ν_{sym}(COO) (cm^{-1})	ν(CN) + δ(NH) (cm^{-1})	$\Delta\nu^a$ (cm^{-1})
HAcGlyGly	3318 s, br 3348 s, br	1655 s, br/1620 s, br	1713 s	1250 vs	1560 s, br	463
NaAcGlyGly	3270 s, br 3385 s, br	1635 s, br/1618 s, br	1600 s, br	1400 s, br	1535 s, br	200
EtAcGlyGly	3280 s	1675 s, br/1640 s, br	1742 vs	1374 vs	1540 s, br	368
HAcGlyAla	3320 vs 3355 vs	1663 vs/1620 s, br	1713 vs	1240 vs	1549 vs 1569 vs	473
HAcGlyVal	3290 vs 3338 vs	1650 s, br/1635 s, br	1712 vs	1365 vs	1555 s, br	347
NaAcGlyVal	3275 s, br 3365 s, br	1640 s, br/1622 s, br	1600 s, br	1405 s, br	1530 s, br	195

[a] $\nu_{asym} - \nu_{sym}$.

Table 5 ^{13}C NMR data for triorganotin derivatives of *N*-acetylglycylglycine

CH_3—(CO)—NH—CH_2—(CO)—NH—CH_2—$COOSnR_3$

A D B D C D E

Compound	A	B	C	D	E	Solvent	$^1J^a$ (Hz)	$^2J^b$ (Hz)	$^3J^c$ (Hz)
1 $Me_3SnAcGlyGly$	22.44	42.58	42.17	173.61 171.35 168.99	−2.00	$CD_3OD/CDCl_3$	478.1		
	22.51	43.51	43.26	175.57 173.65 171.62	−1.73	CD_3OD	511.2		
	22.71	42.19	42.13	172.77 169.69 168.88	0.48	DMSO	527.4		
2 $Et_3SnAcGlyGly$	22.90	42.92	41.89	173.85 170.61 168.65	8.26 9.73	$CDCl_3$	366.2	25.4	
3 $(n\text{-}Bu)_3SnAcGlyGly$	22.89	42.87	41.94	173.62 170.48 168.56	16.68 27.65 26.89 13.57	$CDCl_3$	353.5	66.1	20.3
4 $(n\text{-}Oct)_3SnAcGlyGly$	22.22	42.45	41.62	173.74 174.46 169.12	17.12 33.86 25.38 31.64 28.93 25.36 13.78	$CD_3OD/CDCl_3$	373.8	63.6	21.6
5 $Cy_3SnAcGlyGly$	22.95	42.84	42.04	173.44 170.43 168.43	34.18 31.08 30.98 26.78	$CDCl_3$	330.6	63.8	12.8
6 $Ph_3SnAcGlyGly$	22.57	42.69	42.68	174.49 170.90 168.86	128.84[d] 137.83[d]	$CDCl_3$	658		

[a] $|^1J(^{13}C-^{119}Sn)|$. [b] $|^2J(^{13}C-^{119}Sn)|$. [c] $|^3J(^{13}C-^{119}Sn)|$. [d] Only two resonomers observed.

Table 6 ^{13}C NMR data for triorganotin derivatives of *N*-acetylglycylalanine

CH_3—(CO)—NH—CH_2—(CO)—NH—$CH(CH_3)$—$COOSnR_3$

A E B E C D E F

Compound	A	B	C	D	E	F	Solvent	$^1J^a$ (Hz)	$^2J^b$ (Hz)	$^3J^c$ (Hz)
7 $Me_3SnAcGlyAla$	22.28	42.61	48.69	18.32	176.76 173.55 168.30	−2.06	$CD_3OD/CDCl_3$	448.0		
9 $Cy_3SnAcGlyAla$	22.92	42.82	49.12	19.22	176.72 170.29 168.78	28.36 27.79 31.02 34.05	$CDCl_3$	330.6	15.26	63.6

[a] $|^1J(^{13}C-^{119}Sn)|$. [b] $|^2J(^{13}C-^{119}Sn)|$. [c] $|^3J(^{13}C-^{119}Sn)|$.

coordination through nitrogen is ruled out on the basis of the frequency of the amide II band [ν(C–N) + δ(NH)], which is generally higher than values observed for the free groups (Table 4). Coordination by nitrogen would imply in fact a decrease in the frequency of the amide II band and an increase of the amide I with respect to values for the free groups. An opposite behavior is observed upon coordination by oxygen.[6] Owing to poor resolution in the region 1600–1700 cm^{-1}, absorptions due to carbonyl groups overlap and it is not then a simple matter to observe the shift of the amide I band. Sn–C frequencies in trimethyltin derivatives give information on the symmetry of the SnC_3 group. A trigonal–planar SnC_3 structure (local D_{3h} symmetry) will give rise to the infrared active ν_{asym}(Sn–C) mode; the ν_{sym}(Sn–C) mode (Raman-active) will appear in the infrared spectrum if there is significant deviation from planarity (local C_{3v} symmetry). In the Raman spectra of $Me_3SnAcGlyGly$ and $Me_3SnAcGlyVal$ strong bands, at 528 and 520 cm^{-1} respectively, can be assigned to ν_{sym}(Sn–C) and a weak band (at 550 cm^{-1}) to ν_{asym}(Sn–C). In the IR spectrum these bands are observed at 523, 520 cm^{-1} and at 552, 555 cm^{-1} respectively, with reversed intensit-

Table 7 ^{13}C NMR data for triorganotin derivatives of *N*-acetylglycylvaline

CH_3—(CO)—NH—CH_2—(CO)—NH—CH(C$H(CH_3)_2$)—$COOSnR_3$

A F B F C F G D E

Compound	A	B	C	D	E	F	G	Solvent	$^1J^a$ (Hz)	$^2J^b$ (Hz)	$^3J^c$ (Hz)
10 $Me_3SnAcGlyVal$	22.38	42.79	58.14	31.15	17.43 18.87	175.77 171.39 168.81	−2.06	$CD_3OD/CDCl_3$	473.2		
11 $Et_3SnAcGlyVal$	22.82	43.03	57.85	31.36	18.97 17.71	175.85 170.60 168.64	9.75 8.20	$CDCl_3$	368.1	26.98	
12 $(n\text{-}Bu)_3SnAcGlyVal$	22.90	43.03	57.73	31.49	18.98 17.70	175.75 170.36 168.42	13.58 26.76 27.81 16.68	$CDCl_3$	355.2	20.34	66.12
15 $Ph_3SnAcGlyVal$	22.72	42.95	57.41	31.69	18.84 17.50	176.65 170.51 168.55	128.89 136.63 137.76 128.40	$CDCl_3$	628.3	—[d]	63.8

[a] $|^1J(^{13}C-^{119}Sn)|$. [b] $|^2J(^{13}C-^{119}Sn)|$. [c] $|^3J(^{13}C-^{119}Sn)|$. [d] Not observed.

Table 8 ^{1}H NMR spectral data for triorganotin derivatives of *N*-acetylglycylglycine

$$\underset{A}{CH_3}—C(O)—\underset{E}{NH}—\underset{B}{CH_2}—C(O)—\underset{E}{NH}—\underset{C}{CH_2}—\underset{D}{COOSnR_3}$$

Compound	A	B	C	D	E	Solvent	$\lvert^2J(^{119}Sn-^1H)\rvert$ (Hz)
1 $Me_3SnAcGlyGly$	2.02 s	3.68 s	3.91 s	0.53 s	—	D_2O	64
	1.96 s	3.89 s	3.69 s	0.47 s	—	CD_3OD	66
	1.78 s	3.60 d	3.44 d	0.36 s	7.64 br 7.94 br	DMSO-d_6	72
2 $Et_3SnAcGlyGly$	1.93 s	3.93 d	3.91 d	1.18 br, s	—[a]	$CDCl_3$	—[a]
3 $(n\text{-}Bu)_3SnAcGlyGly$	2.05 s	4.06 d	4.02 d	0.80 q 0.85–1.9 m	6.8 br	$CDCl_3$	—[a]
4 $(n\text{-}Oct)_3SnAcGlyGly$	1.92 s	3.91 s	3.74 s	0.82 q 0.9–1.8 m	—	CD_3OD	—[a]
6 $Ph_3SnAcGlyGly$	1.90 s	4.05 d	3.85 d	7.4–8.0 m	—[a]	$CDCl_3$	—[a]

[a] Unassigned.

ies., Local C_{3v} symmetry of the SnC_3 skeleton is therefore suggested, the deviation from planarity being not very serious.

As far as structures in the solution phase are concerned, all the complexes dissolve in polar solvents giving monomers, as indicated by the experimental molecular weights. In methanol, the SnC_3 unit presumably maintains planar configuration, five-coordination being attained by means of coordination of a molecule of solvent. This is evidenced by the quadrupole splitting values of trimethyltin derivatives (Table 2), which are very similar to those of the solid compounds. It is noteworthy that $Cy_3SnAcGlyVal$, which in the solid state is characterized by a ΔE value typical of tetrahedral structures, in methanol also assumes a trigonal–bipyramidal configuration. It is evident that the steric hindrance of the substituent on the valine fragment of *N*-acetyldipeptide, together with the bulkiness of the cyclohexyl groups, prevent the coordination of tin by $C{=}O_{amide}$, while methanol is able to coordinate. The same effect is not observed in the case of $Ph_3SnAcGlyVal$, probably due to the greater acidity of tin in the Ph_3Sn unit. These findings are supported by NMR spectra; the coupling constants $|^1J(^{13}C-^{119}Sn)|$ (Tables 5–7) are in fact indicative of a planar C_3Sn unit in these compounds. Applying Lockhart's relation between $|^1J(^{13}C-^{119}Sn)|$ and the C–Sn–C bond angle,[31] we found an average value of 121° (in $CDCl_3/CD_3OD$ and in DMSO coupling constants

Table 9 ^{1}H NMR spectral data for triorganotin derivatives of *N*-acetylglycylvaline

$$\underset{A}{CH_3}—C(O)—\underset{F}{NH}—\underset{B}{CH_2}—C(O)—\underset{F}{NH}—\underset{\substack{D\\ \vert\\ CH—(CH_3)_2\\ E}}{\overset{\overset{C}{\vert}}{CH}}—\underset{G}{COOSnR_3}$$

Compound	A	B	C	D	E	F	G	Solvent	$\lvert^2J(^{119}Sn-^1H)\rvert$ (Hz)
10 $Me_3SnAcGlyVal$	2.14 s	3.95 s	4.20 d	2.20 m	1.05 d 1.11 d	—	0.58	CD_3OD	66
11 $Et_3SnAcGlyVal$	2.00 s	3.93 d	4.50 q	2.20 m	0.96 d 0.88 d	6.8 br	1.25 s, br	$CDCl_3$	—[a]
12 $(n\text{-}Bu)_3SnAcGlyVal$	2.05 s	4.00 d	4.53 q	2.20 m	0.98 d 0.89 d	6.8 br	1.1 q 1.2–1.8 m	$CDCl_3$	—[a]
15 $Ph_3SnAcGlyVal$	1.95 s	3.92 d	4.65 q	2.20 m	0.91 d 0.86 d	6.7 m	7.4–7.9 m	$CDCl_3$	—[a]

[a] Unassigned.

Table 10 ^{119}Sn NMR spectra of some triorganotin derivatives of *N*-acetyldipeptides

Compound		Solvent	$\delta(^{119}Sn)$
1	$Me_3SnAcGlyGly$	$CD_3OD/CDCl_3$	54.42
		CD_3OD	25.67
		DMSO	−8.29
2	$Et_3SnAcGlyGly$	$CDCl_3$	122.39
3	$(n\text{-}Bu)_3SnAcGlyGly$	$CDCl_3$	129.25
4	$(n\text{-}Oct)_3SnAcGlyGly$	$CD_3OD/CDCl_3$	101.10
5	$Cy_3SnAcGlyGly$	$CDCl_3$	33.18
6	$Ph_3SnAcGlyGly$	$CDCl_3$	−117.8
7	$Me_3SnAcGlyAla$	$CD_3OD/CDCl_3$	45.55
9	$Cy_3SnAcGlyAla$	$CDCl_3$	30.46
10	$Me_3SnAcGlyVal$	$CD_3OD/CDCl_3$	56.66
11	$Et_3SnAcGlyVal$	$CDCl_3$	118.45
12	$(n\text{-}Bu)_3SnAcGlyVal$	$CDCl_3$	125.89
15	$Ph_3SnAcGlyVal$	$CDCl_3$	−107.90

give 119 and 123° respectively) for $Me_3SnAcGlyGly$, 116° for $Me_3SnAcGlyAla$ (solvent $CDCl_3/CD_3OD$) and 118° for $Me_3SnAcGlyVal$. The $|^1J(^{13}C-^{119}Sn)|$ coupling constants of the other trialkyltin derivatives, whose spectra were recorded in $CDCl_3$ and, in the case of $n\text{-}Oct_3SnAcGlyGly$, in $CDCl_3/CD_3OD$, are consistent with tetrahedral species. In particular, Holecek's relation for n-butyltin compounds,[32] very similar to Lockhart's relation, gives C–Sn–C bond angles of 110° for both $n\text{-}Bu_3SnAcGlyGly$ and $n\text{-}Bu_3SnAcGlyVal$. $|^2J(^1H-^{119}Sn)|$ coupling constants (Tables 8 and 9) give, of course, the same information on the geometry of the R_3Sn group. According to Holmes and Kaesz,[33] the *s*-character of the Sn atomic orbital in the Sn–C bonds of the $Me_3SnAcDip$ complexes ranges from 29 to 33%, as expected for a planar C_3Sn group. The ^{119}Sn NMR spectra (Table 10) do not give further information. It is generally observed that the $\delta(^{119}Sn)$ values in the five-coordinate compounds appear *ca* 60–150 ppm upfield of the corresponding four-coordinate analogs.[34] This trend is not always observed in the data of Table 10, where the chemical shifts of trimethyltin derivatives which are five-coordinated would be upfield from those of the other derivatives, which are supposed to be tetrahedral in $CDCl_3$ solution.

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