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Preparation, infrared and ^{13}C and ^{119}Sn NMR spectral studies of triorganotin(IV) derivatives of *N*-acetyl-L-phenylalanine and *N*-acetyl-L-phenylalanylglycine

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Abstract

Triorganotin(IV) derivatives of *N*-acetyl-L-phenylalanine (HAA) and *N*-acetyl-L-phenylalanylglycine (HDP), R_3SnAA and R_3SnDP (where R = methyl, n-propyl, n-butyl, phenyl and cyclohexyl, respectively), have been prepared from triorganotin(IV) chlorides (R_3SnCl) and the sodium salt of the appropriate *N*-acetylamino acids. All the compounds in the solid state have a polymeric structure with a unidentate carboxylic group. The molecules are linked together via the weak intermolecular donor–acceptor bond $NHCO \ldots Sn(R_3)O$. The fragment of $O \ldots Sn(R_3)O$ has slightly deformed *trans*-trigonal bipyramidal geometry around the central tin atom. In chloroform solution, all the compounds are present in the form of simple molecules with a nearly tetrahedral configuration of the R_3SnOCO group.

Introduction

The organotin(IV) derivatives of *N*-acetylamino acids are of interest as potential biocides [1,2]. Tri-n-butyltin(IV) and triethyltin(IV) esters of *N*-acetyl derivatives of

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glycine, DL-valine, DL-leucine and DL-methionine were found to be suitable as intermediates in peptide synthesis [3,4]. A number of di- and tri-organotin(IV) derivatives of *N*-acetylamino acids have recently been reported [5,6], while derivatives of *N*-acetyldipeptides are not known. In this paper we report the synthesis, infrared and ^{13}C and ^{119}Sn NMR spectra of a series of triorganotin(IV) derivatives of *N*-acetyl-L-phenylalanine (HAA) and *N*-acetyl-L-phenylalanylglycine (HDP) as a continuation of our interest in organotin(IV) derivatives of amino acids and peptides [7–9].

Experimental

Melting points were determined in open capillaries and are uncorrected. Elemental analyses were carried out by the Regional Sophisticated Instrumentation Centre, Panjab University, Chandigarh. The tin content was determined gravimetrically as SnO_2. Molecular weights were determined cryoscopically in benzene and nitrobenzene. IR spectra were recorded on a Pye-Unicam P321 Spectrometer in KBr discs and chloroform solutions. ^{13}C and ^{119}Sn NMR spectra were measured on a JNM-FX 100 spectrometer (JEOL, Japan) at 25.047 and 37.14 MHz, respectively, at 300 K in the pulse mode with Fourier transform. Saturated solutions of the compounds ($\leq$ 150 mg/ml) were measured in deuteriochloroform. Chemical shifts $\delta(^{119}Sn)$ are related to external neat tetramethylstannane. Chemical shifts $\delta(^{13}C)$ were referred to a solvent signal (δ 77.00 ppm) and converted to the δ-scale. Positive values of the chemical shifts denote downfield shifts. Signals of carbon atoms were assigned on the basis of relative integral intensities, values of coupling constants, $^{n}J(^{119}Sn,^{13}C)$, and multiplicity in proton-coupled spectra.

Literature procedures were used to prepare tripropyltin(IV) chloride [10], triphenyltin(IV) chloride [11], *N*-acetyl-L-phenylalanine [12] and *N*-acetyl-L-phenylalanylglycine [13,14]. Trimethyltin(IV), tri-n-butyltin(IV) and tricyclohexyltin(IV) chlorides were obtained from Alfa Products, U.S.A., and were used without further purification.

Preparation of compounds

To a solution of the sodium salt of *N*-acetyl-L-phenylalanine (5 mmol) or *N*-acetyl-L-phenylalanylglycine (5 mmol) in a dry solvent mixture of benzene (30 ml) and absolute ethyl alcohol (10 ml) was added triorganotin(IV) chloride (5 mmol). The reaction mixtures were refluxed over a water bath for 6–8 h during which a solid (sodium chloride) separated. The contents were cooled and filtered through a filter unit under reduced pressure. Benzene (30 ml) was added to the filtrate and the mixture was refluxed azeotropically using a Dean Stark trap; this process of refluxing and filtration was repeated two or three times until all of the sodium chloride was separated. Then the solvent was removed by distillation under reduced pressure to leave behind a solid or a syrup. Trimethyl-, tri-n-butyl-, tri-n-propyl- and triphenyl-tin(IV) derivatives were syrups; they were washed with petroleum ether (40–60 °C), in which trialkyl- and triphenyl-tin(IV) chlorides are soluble. These compounds solidify after being kept over concentrated sulphuric acid in a desiccator for 3 to 6 months. (cyclo-$C_6H_{11})_3SnDP$ was recrystallized from absolute ethyl alcohol, while (cyclo-$C_6H_{11})_3SnAA$ and $(C_6H_5)_3SnAA$ were recrystallized

Table 1

Physical and analytical data of triorganotin(IV) derivatives of *N*-acetyl-L-phenylalanine and *N*-acetyl-L-phenylalanylglycine

Compound [a]	Yield (%)	M.p. (°C)	Analysis (Found(Calcd.)(%))				Mol.wt.
			C	H	N	Sn	Found(Calcd.)
$(CH_3)_3SnAA$	72	180–184	44.93	5.23	3.52	32.28	517 [b]
(1)			(45.45)	(5.68)	(3.78)	(32.08)	(369.6)
$(n\text{-}C_3H_7)_3SnAA$	76	85– 95	43.11	5.75	2.35	21.05	550 [c]
(2)			(43.35)	(5.96)	(2.52)	(21.42)	(453.6)
$(n\text{-}C_4H_9)_3SnAA$	89	111–115	55.41	7.87	2.52	23.72	517 [b]
(3)			(55.69)	(7.86)	(2.82)	(23.93)	(495.6)
$(C_6H_5)_3SnAA$	75	190–193	61.89	4.77	2.39	20.80	[d]
(4)			(62.63)	(4.85)	(2.51)	(21.34)	
$(cyclo\text{-}C_6H_{11})_3SnAA$	56	134–139	60.47	7.39	3.07	20.64	588 [c]
(5)			(60.66)	(7.84)	(2.44)	(20.67)	(573.6)
$(CH_3)_3SnDP$	60	92–103	44.76	5.23	6.27	27.80	450 [c]
(6)			(45.00)	(5.62)	(6.57)	(27.50)	(426.6)
$(n\text{-}C_3H_7)_3SnDP$	67	75– 85	50.67	6.98	5.22	23.18	480 [c]
(7)			(51.74)	(7.05)	(5.48)	(23.22)	(510.6)
$(n\text{-}C_4H_9)_3SnDP$	73	73– 80	53.81	7.12	4.96	20.92	493 [c]
(8)			(54.28)	(7.60)	(5.06)	(21.46)	(552.6)
$(C_6H_5)_3SnDP$	85	78– 88	59.59	5.03	3.54	21.34	650 [c]
(9)			(60.72)	(4.57)	(4.89)	(21.56)	(612.6)
$(cyclo\text{-}C_6H_{11})_3SnDP$	65	125–127	58.61	7.12	–	18.67	678 [c]
(10)			(58.99)	(7.61)		(18.80)	(630.6)

[a] Abbreviations: HAA = $CH_3CONHCH(CH_2C_6H_5)COOH$, HDP = $CH_3CONHCH(CH_2C_6H_5)CONHCH_2COOH$. [b] Benzene. [c] Nitrobenzene. [d] Separates at low temperature in nitrobenzene.

from dry benzene. Analytical data, melting points and molecular weights of compounds are listed in Table 1.

Results and discussion

The triorganotin(IV) derivatives of *N*-acetyl-L-phenylalanine and *N*-acetyl-L-phenylalanylglycine listed in Table 1 were prepared by reaction of the appropriate organotin(IV) chloride and the sodium salt of the HAA and HDP, respectively, in 1/1 molar ratio. R_3SnAA and R_3SnDP are soluble in chloroform. Molecular weight determination showed (Table 1) that all the compounds are monomers at low temperature (cryoscopically) in benzene and nitrobenzene. Bromoform reacts with all these compounds.

Structural determination was based on vibrational data, collected in Table 2, and ^{13}C and ^{119}Sn NMR data (Tables 3 and 4).

Infrared data

Infrared spectra of the sodium salts and ethyl- and triorgano-tin(IV) esters of both the amino acid and dipeptide studied were recorded in KBr discs and chloroform solutions (4000–200 cm^{-1}). In the spectra of the triorganotin(IV) compounds, vibration associated with the COOH group of the free HAA and HDP has disappeared, so that it can be concluded that the R_3Sn groups are bound through the carboxylic group to the *N*-acetylamino acid and dipeptide moiety,

Table 2

Infrared spectral data (cm^{-1})

Compound [a]		ν(NH)	$\nu(CO_{amide})$	ν(CN) + ν(NH)	ν_{as}(COO)	ν_s(COO)	$\Delta\nu$	ν_{as}(SnC)	ν_s(SnC)
EtAA	*b*	3315 s	1640 s	1525 s,b	1730 s	1373 s	357	–	–
	c	3420 m	1660 s	1510 s	1735 s	1380 m	355	–	–
NaAA	*b*	3280 s,b	1640 m	1570 s,b	1595 s,b	1405 s,b	190	–	–
1	*b*	3300 s	1615 m	1560 m	1625 s,b	1390 s	235	560 s	510 vw
2	*c*	3420 m,b	1645 s,b	1505 s,b	1652 s,b	1373 m,b	279	–	–
3	*b*	3260 m,b	1620 s,b	1570 m,b	1645 s,b	1375 s,b	270	595 m	515 m
3	*c*	3420 m	1645 s,b	1505 s,b	1645 s,b	1375 s,b	270	–	–
4	*b*	3370 m,b	1620 s	1505 m,b	1620 s	1375 s	245	270 m	225 w,sh
5	*b*	3360 m,b	1610 s,b	1555 m,b	1643 s,b	1378 s	265	493	415 w
5	*c*	3420 m,b	1648 s,b	1505 m,b	1648 s,b	1375 s	273	–	–
EtDP	*b*	3285 s	1675 m,b 1640 s	1540 s	1743 s	1372 m	371	–	–
	c	3420 m,b 3310 m,b	1660 s,b 1650 s,b	1520 m,b	1740 s	1378 m,b	362	–	–
NaDP	*b*	3390 m,b 3280 m,b	1633 s,b 1612 s,b	1540 m,b	1600 m,b	1400 m,b	200	–	–
6	*b*	3280 m,b	1630 s,b	1535–40 m,b	1630 s,b	1390 s,b	240	570 m	530 w
6	*c*	3420 m,b 3300 m,b	1655 s,b	1505 m,b	1660 s,b	1390 m	270	–	–
7	*c*	3420 m 3300 m,b	1656 s,b	1508 s,b	1656 s,b	1380 m,b	276	595 w	530 m
8	*c*	3420 m 3300 m,b	1658 s,b	1500 m,b	1658 s,b	1390 m,b	268	–	–
9	*b*	3280 m,b 3400 w,b	1640 s,b 1630 s,b	1552 m,b 1530 m,b	1660 s,b	1380 m,b	280	270 m	230 m
9	*c*	3420 m 3300 m,b	1655 s,b	1510 m,b	1665 s,b	1390 m,b	275	–	–
10	*b*	3360 m,b	1630–45 m,b	1545 m,b 1535 m,b	1655 s,b	1380 w,b	275	490 m	418 m
10	*c*	3420 m,b 3300 m,b	1657 s,b	1500 m,b	1657 s,b	1390 m	267	–	–

[a] See Table 1. [b] KBr disc. [c] Chloroform solution.

respectively. The type of bonding of the carboxylic groups follows, taking $(CH_3)_3SnAA$ (compound **1**) as an example, from the frequencies of ν_{as}(COO) and ν_s(COO), which appear at 1625 and 1390 cm^{-1} in the solid state (difference $\Delta\nu$ 235 cm^{-1}). The band positions and also $\Delta\nu$ are distinctly different from those of the alkali metal compounds (NaAA 1595 and 1405 cm^{-1}, $\Delta\nu$ 190 cm^{-1}). Similar behaviour was found in all the other compounds studied. So bridging or chelation can therefore be excluded, and carboxylic groups bonding the tin atom unidentatively must be assumed [15].

The N–H stretching frequencies of the solid complexes are higher than those of the ethyl esters, suggesting that the amido nitrogen is not coordinating, which would be consistent with its low basicity. For some solid samples (compounds **1** and **4**) and for chloroform solutions, the bands are sharp. Those of the other solids are considerably broadened, indicating intermolecular hydrogen bonding, presumably to an amido carbonyl group of an adjacent molecule [9,16–18]. The solution spectra

Table 3

^{13}C and ^{119}Sn NMR parameters of ethyl- and triorganotin(IV) derivatives of *N*-acetyl-L-phenylalanine

NMR Parameter	Compound [a]				
	EtAA	**1**	**2** [b]	**3** [c]	**4**
$\delta(^{119}Sn)$	–	101.0	102.4	116.7	−99.7
$\delta(^{13}C)$(AA)					
CH_3	23.1	23.0	22.7	23.0	23.2
CH	53.1	54.1	53.8	53.8	53.5
$CH_2C_6H_5$	37.9	37.7	37.6	37.7	37.9
$C_6H_5(i)$	135.9	136.8	136.7	136.8	136.1
$C_6H_5(o)$	129.3	129.4	129.1	129.3	129.5
$C_6H_5(m)$	128.5	128.1	127.8	127.9	128.1
$C_6H_5(p)$	127.1	126.6	126.3	126.5	126.6
CONH	169.7	169.6	169.2	169.2	169.3
COO	171.7	175.3	175.6	175.5	176.6
$\delta(^{13}C)$(Et or R_3Sn)					
C(1)	61.5	−1.4	18.9	16.8	137.7
C(2)	14.1		19.8	27.6	136.8
C(3)			18.2	26.8	129.0
C(4)				13.4	130.4

[a] See Table 1. [b] $^1J(^{119}Sn,^{13}C)$ 372.2 Hz. [c] $^nJ(^{119}Sn,^{13}C)$ (Hz): 362.5 ($n=1$), 22.0 ($n=2$), 66.0 ($n=3$), <10 ($n=4$).

Table 4

^{13}C and ^{119}Sn NMR parameters of ethyl- and triorgano-tin(IV) derivatives of *N*-acetyl-L-phenylalanylglycine

NMR Parameter	Compound [a]				
	EtDP	**6**	**7**	**8** [b]	**9**
$\delta(^{119}Sn)$	–	126.9	125.0	121.6	−114.8
$\delta(^{13}C)$(DP)					
CH_3	22.9	22.9	23.1	22.9	22.7
CH	54.2	54.4	54.3	54.2	54.1
$CH_2C_6H_5$	38.2	38.4	38.1	38.4	38.3
$C_6H_5(i)$	136.5	136.4	136.5	136.6	136.4
$C_6H_5(o)$	129.2	129.2	129.2	129.1	129.1
$C_6H_5(m)$	128.5	128.5	128.5	128.3	128.3
$C_6H_5(p)$	126.8	126.9	126.9	126.7	126.7
CH_2COO	41.3	42.2	41.3	41.9	41.8
CH_3CONH	169.3	170.2	170.0	169.9	170.2
CHCONH	170.3	170.7	170.6	170.8	170.7
COO	171.5	173.5	173.5	173.3	174.0
($\delta(^{13}C)$(Et or R_3Sn)					
C(1)	61.4	−1.7	18.4	16.8	138.4
C(2)	14.1		19.2	27.6	136.4
C(3)			18.4	28.8	128.8
C(4)				13.5	130.6

[a] See Table 1. [b] $^nJ(^{119}Sn,^{13}C)$ (Hz): 354.0 ($n=1$), 22.0 ($n=2$), 66.0 ($n=3$), <10 ($n=4$).

($CHCl_3$) of the compounds **1–10** show broad N–H stretching bands of medium intensity at 3420 and 3300 cm^{-1}. The former band is assigned to a free amido group, while the latter corresponds to the formation of a hydrogen bond, NHCO...H, in the solid state. The shift of ν(N–H) is consistent with the loss of hydrogen bonding in the solution state. Hydrogen bonding is an essential structure parameter in *N*-acetylamino acids [6].

For the compounds in the solid state studied here, the frequencies of the amido C=O are shifted to lower frequencies than those in the chloroform solution. This fact is indicative of participation of the CONH group in the coordination bonding with the tin atom via the donor oxygen atom in the solid state [9]. The presence of doublets for $\nu(CO_{amide})$ and (ν(CN) + δ(NH)) in compounds **9** and **10** and broad bands in the same region in compound **6** is evidence for the participation of only one CONH group in the NHCO...Sn donor–acceptor coordination [9]. Thus, the tin atom in all the compounds under study is five-coordinated in the solid state (*trans*-trigonal bipyramid geometry of the tin neighbourhood). But in chloroform solutions compounds **1–10** are present in the form of simple molecules having tetrahedral coordination of the tin atom.

The medium intensity bands at 560 and 510 cm^{-1} (compound **1**) and 595 and 515 cm^{-1} (compound **3**) can be assigned to ν_{as}(SnC) and ν_s(SnC). The bands at 270 and 225 cm^{-1} for compound **4** [19] and at 493 and 415 cm^{-1} for compound **5** also show the same behaviour. A similar situation was found in the spectra of the dipeptide compounds: 570 and 530 cm^{-1} (compound **6**) [20], 270 and 230 cm^{-1} (compound **9**) and 490 and 418 cm^{-1} (compound **10**). Thus, the presence of both stretching vibrations ν_{as}(SnC) and ν_s(SnC) in the infrared spectra of all the compounds in the solid state excludes an exactly planar arrangement of the three Sn–C bonds and thus a precisely symmetrical shape of the *trans*-trigonal bipyramide arrangement of bonds around the central tin atom in compounds **1–10** in the solid state.

^{13}C and ^{119}Sn NMR spectra

In the ^{119}Sn NMR spectra of all the compounds studied (Tables 3 and 4) only one signal was found. The number of signals in the ^{13}C NMR spectra corresponds to the number of magnetically non-equivalent carbon atoms in the ethyl- and triorgano-tin(IV) derivatives of *N*-acetyl-L-phenylalanine (Table 3) and *N*-acetyl-L-phenylalanylglycine (Table 4). This fact, together with the analysis of the ^{13}C and ^{119}Sn NMR spectra (see later), confirms the identity of the compounds.

The chemical shifts $\delta(^{119}Sn)$ of trialkyltin(IV) derivatives **1–3** and **6–8** ranging from 101.0 to 126.9 ppm are typical of the four-coordinate central tin atom in simple trialkyltin(IV) compounds [21,22], and the values of $\delta(^{119}Sn)$ of triphenyltin(IV) derivatives **4** and **9** (−114.8 and −99.7 ppm, respectively) also correspond to the pseudo-tetrahedral configuration of $(C_6H_5)_3SnO$ groups [23]. The values of $\delta(^{13}C)$ for the carboxylic and amide carbonyl carbon atoms are practically unshifted relative to the ethyl esters of *N*-acetyl-L-phenylalanine and *N*-acetyl-L-phenylalanylglycine. This is consistent with the absence of interaction of the carbonyl groups with the central tin atoms (C=O...SnR_3). The values of $^1J(^{119}Sn,^{13}C)$, which were measured in some cases (compounds **2**, **3** and **8**), are in range from 354.0 to 372.2 Hz, which are typical of the pseudo-tetrahedral arrangement of R_3SnO groups. The mean values of the angles C–Sn–C calculated accord-

ing to ref. 24 are ca. 110 and 111° for compounds **8** and **3**, respectively. Deformation of the tetrahedral geometry of the Bu_3SnO groups in these compounds is insignificant, and the almost ideal tetrahedral shape of the R_3SnO groups thus excludes a more obvious interaction of the central tin atom with the nitrogen atoms of the amide groups and/or the oxygen atoms of the carbonyl groups. If some interaction of this type exists, it must be very weak.

Conclusion

Triorganotin(IV) derivatives of *N*-acetyl-L-phenylalanine (R_3SnAA) and *N*-acetyl-L-phenylalanylglycine (R_3SnDP) (**1**–**10**) in the solid state have a polymeric structure with a unidentate carboxylate group. The molecules are linked together via weak donor–acceptor interactions, $NHCO\ldots SnR_3$. The fragment $O\ldots Sn(R_3)O$ has a deformed *trans*-trigonal bipyramidal geometry around the central tin atom. In chloroform solutions, compounds **1**–**10** are present in the form of simple molecules with a nearly ideal tetrahedral configuration of the R_3SnOCO group.

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