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Preparation and infrared and ^{1}H, ^{13}C and ^{119}Sn NMR spectra of triorganotin(IV) derivatives of *N*-formyl-L-phenylalanine and *N*-formyl-L-phenylalanylglycine

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Abstract

The triorganotin(IV) derivatives of *N*-formyl-L-phenylalanine (HAA) R_3SnAA and *N*-formyl-L-phenylalanylglycine (HDP) R_3SnDP (R methyl, n-propyl, n-butyl, phenyl and cyclohexyl, respectively) have been prepared from the triorganotin(IV) chlorides R_3SnCl and the appropriate amino acids or their sodium salts in 1/1 molar ratio. The compounds are characterized by infrared and ^{1}H, ^{13}C and ^{119}Sn NMR spectroscopy. The tin atoms in triorganotin(IV) groups are coordinated by the unidentate carboxylic group and by the oxygen atom of the amidocarbonyl group in the solid state (five-coordinate central tin atom). The weak donor–acceptor $NHCO \ldots Sn(R_3)O$ bonds break in the chloroform solution and all compounds studied are present in the form of simple molecules with pseudotetrahedral configuration of R_3SnOCO groups (four-coordinate tin atom).

Introduction

In continuation of our earlier studies on triorganotin(IV) derivatives of *N*-protected amino acids and *N*-protected dipeptides [1,2], we report here the synthesis and characterization of a series of triorganotin(IV) derivatives of *N*-formyl-L-phen-

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ylalanine, $HCONHCH(CH_2C_6H_5)COOH$ (HAA), and *N*-formyl-L-phenylalanylglycine, $HCONHCH(CH_2C_6H_5)CONHCH_2COOH$ (HDP).

Experimental

Melting points were determined on open capillaries and are uncorrected. Elemental analyses were carried out by the Regional Sophisticated Instrumentation Centre, Punjab University, Chandigarh. Tin was estimated gravimetrically as SnO_2. Molecular weights were determined cryoscopically in nitrobenzene. IR spectra were recorded on a Pye-Unicam P 321 Spectrometer in KBr discs and in chloroform solutions. ^1H NMR spectra were recorded on a Jeol PMX 60 SI spectrometer using tetramethylsilane as internal standard. ^{13}C and ^{119}Sn were measured on a Jeol JNM-FX 100 spectrometer at 25.047 or 37.14 MHz, respectively, at 300 K in pulse mode with Fourier transform. The saturated solutions of compounds ($\leqslant$ 150 mg/ml) were measured in deuteriochloroform ($CDCl_3$). Chemical shifts $\delta(^{119}Sn)$ are related to external neat tetramethylstannane. Chemical shifts $\delta(^{13}C)$ were related to a solvent signal and converted to the δ-scale ($CDCl_3$ (δ 77.00 ppm)). Positive values of chemical shifts denote downfield shifts. Signals of carbon atoms were assigned on the basis of relative integral intensities, values of coupling constants $^nJ(^{119}Sn, ^{13}C)$ and multiplicity in proton-coupled spectra.

Literature procedures were used to prepare tri-n-propyltin(IV) and triphenyltin (IV) chlorides [3,4], *N*-formyl-L-phenylalanine [5] and *N*-formyl-L-phenylalanylglycine [5,6]. Trimethyltin(IV), tri-n-butyltin(IV) and tricyclohexyltin(IV) chlorides were obtained from Alfa Products, USA.

Preparation of compounds

N-Formyl-L-phenylalanine derivatives. *N*-formyl-L-phenylalanine (5 mmol) dissolved in absolute ethyl alcohol (50 cm^3) was added to triorganotin(IV) chlorides (5 mmol) and refluxed on a water bath for 2 h, followed by the addition of anhydrous triethylamine (5 mmol). The reaction mixture was again refluxed for 2–4 h. A white solid product was separated when triphenyltin(IV) or tricyclohexyltin(IV) chlorides were used. The products were cooled, filtered and washed three times with absolute ethyl alcohol and dried under vacuum. Trimethyltin(IV), tri-n-propyltin(IV) and tri-n-butyltin(IV) derivatives of *N*-formyl-L-phenylalanine were soluble in absolute ethyl alcohol, along with triethylamine hydrochloride. The derivatives were obtained by removing ethanol by distillation and adding excess of dry benzene, when all of the triethylamine hydrochloride separated out leaving behind the derivatives in benzene. Complete removal of benzene by distillation under reduced pressure gave a solid/syrupy product.

Triphenyltin(IV) compound is recrystallized from hot $CHCl_3$, and tricyclohexyltin(IV) compound from absolute ethyl alcohol. Trimethyltin(IV), tri-n-propyltin(IV) and tri-n-butyltin(IV) compounds were syrups, and thus were washed with petroleum ether (40–60 °C) in which triorganotin(IV) chlorides are soluble. These compounds solidify after 3–6 months in a vacuum desiccator.

N-Formyl-L-phenylalanylglycine derivatives. Triorganotin(IV) chloride (5 mmol) was added to a solution of the sodium salt of *N*-formyl-L-phenylalanylglycine (5 mmol) in a dry solvent mixture of benzene (30 cm^3) and absolute ethyl alcohol (10 cm^3). The reaction mixture was refluxed over a water bath for 6–8 h, during which

time a solid (sodium chloride) separated out. The contents were cooled and filtered through a filter unit under reduced pressure. Benzene (30 cm^3) was added to the filtrate and the solution was refluxed. This process of refluxing and filtration was repeated two or three times until all of the sodium chloride was separated out. Then, all of the solvent was removed by distillation under reduced pressure to leave behind a solid/syrup. Trimethyl, tri-n-butyl, triphenyl and tri-n-propyltin(IV) derivatives were syrups, washed with petroleum ether (40–60 °C) in which the triorganotin(IV) chlorides are soluble. These compounds solidify after 3–6 months in a vacuum desiccator. Tricyclohexyltin(IV) *N*-formyl-L-phenylalanylglycinate was recrystallized from absolute ethyl alcohol.

Results and discussion

Triorganotin(IV) derivatives of *N*-formyl-L-phenylalanine and *N*-formyl-L-phenylalanylglycine listed in Table 1 have been prepared by conversion of the appropriate triorganotin(IV) chloride and *N*-formyl-L-phenylalanine in the presence of a base (triethylamine) or the sodium salt of *N*-formyl-L-phenylalanylglycine. Compounds **1**–**4** and **6**–**9** (Table 1) are soluble in chloroform, and compounds **5** and **10** are soluble in hot chloroform. Molecular weight measurements (Table 1) showed

Table 1

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

No	Compound [a]	Yield (%)	m.p. (°C)	Analysis (Found(calcd.)(%))				Mol.wt
				C	H	N	Sn	Found [b] (calcd.)
1	$(CH_3)_3SnAA$	47	42– 47	44.50 (43.87)	5.50 (5.34)	4.20 (3.94)	33.98 (33.35)	370 (356)
2	$(n\text{-}C_3H_7)_3SnAA$	50	96–103	52.06 (51.86)	7.25 (7.05)	3.37 (3.18)	27.12 (26.98)	380 (440)
3	$(n\text{-}C_4H_9)_3SnAA$	65	68– 80	54.16 (54.81)	7.49 (7.68)	2.78 (2.90)	24.81 (24.62)	460 (481)
4	$(C_6H_5)_3SnAA$	78	215–216	61.58 (62.03)	4.54 (4.61)	2.01 (2.58)	22.13 (21.89)	[c]
5	$(cyclo\text{-}C_6H_{11})_3SnAA$	67	180 [d]	59.13 (60.04)	7.43 (7.68)	2.11 (2.50)	21.74 (21.19)	520 (560)
6	$(CH_3)_3SnDP$	50	159 [d]	43.28 (43.62)	4.98 (5.33)	5.85 (6.78)	28.88 (28.74)	380 (413)
7	$(n\text{-}C_3H_7)_3SnDP$	55	45– 55	50.46 (50.74)	6.21 (6.84)	5.42 (5.64)	23.68 (23.88)	470 (497)
8	$(n\text{-}C_4H_9)_3SnDP$	77	80– 87	53.86 (53.47)	7.63 (7.43)	5.37 (5.20)	22.28 (22.02)	508 (538)
9	$(n\text{-}C_6H_5)_3SnDP$	75	85– 89	60.85 (60.14)	4.79 (4.67)	3.47 (4.60)	19.25 (19.81)	550 (599)
10	$(cyclo\text{-}C_6H_{11})_3SnDP$	60	125–130	58.92 (58.38)	8.54 (7.46)	5.23 (4.54)	19.76 (19.23)	590 (617)

[a] Abbreviations: HAA = $HCONHCH(CH_2C_6H_5)COOH$, HDP = $HCONHCH(CH_2C_6H_5)CONHCH_2COOH$. [b] Cryoscopically in nitrobenzene. [c] Separate at low temperature in nitrobenzene. [d] Decomposition.

that all compounds studied are monomers at low temperature in nitrobenzene solution. Bromoform reacts with these compounds.

The identity of the compounds is confirmed by elemental analysis (Table 1) and by infrared and ^{1}H, ^{13}C and ^{119}Sn NMR spectral analysis (see later). Structural proposals are based on vibrational and ^{13}C and ^{119}Sn NMR data.

Infrared spectra

In the infrared spectra (Table 2) of all the compounds studied, vibrations associated with the COOH group of the free HAA and HDP acids have disappeared, so it can be concluded that the MR_3 groups are bonded through the carboxylic group to the *N*-formylamino acid and dipeptide moieties. This type of bonding of carboxylic groups, taking compound **4** as an example, follows from the frequencies of $\nu_{as}(COO)$ and $\nu_{s}(COO)$, which appear at 1645 and 1365 cm^{-1} in the solid state and at 1650 and 1365 cm^{-1} in chloroform solution, respectively. Band positions and values of differences in frequencies $\Delta\nu$ 280 and 285 cm^{-1}, respectively, are distinctly different from those of the corresponding sodium compounds NaAA (1592 and 1400 cm^{-1}, $\Delta\nu$ 192 cm^{-1}). Similar trends are found in other

Table 2

Infrared spectral data (cm^{-1})

Compound [a]	ν(NH)	$\nu(CO_{amide})$	[ν(CN)+δ(NH)]	ν_{as}(COO)	ν_{s}(COO)	$\Delta\nu$ [b]	ν_{as}(SnC)	ν_{s}(SnC)
NaAA [c]	3370m,b	1660s,b	1510m	1592s	1400s	192		
EtAA [c]	3300s	1660s,b	1515m,b	1740s,b	1390s	350		
1 [d]	3395m,b 3300m,b	1647s	1490s	1670m,b	1380s,b	290	540m	515w
2 [d]	3410m	1650s	1492m	1680m	1370m,b	310	555w	520w
3 [d]	3410m	1655s	1490m	1675s	1385m,b	290	570w	520w
4 [c,e]	3310m	1620s	1500m	1645s	1365s,b	280	270m	225w
4 [d]	3410m	1650s	1490m	1650s	1365m	285		
5 [c]	3310m,b	1630m	1500m	1648m	1340m,b	308	485m	410w
5 [d]	3410m,b	1645m	1490m	1675m	1370m,b	305		
NaDP [c]	3320m,b	1648m,b	1530m,b	1593m,b	1385s,b	208		
EtDP [c]	3280s	1655s	1535s	1730s	1390s	340		
EtDP [d]	3410m 3310m,b	1655s,b	1535s,b	1740s	1380s	360		
6 [c,f]	3350m,b	1630s,b	1520m,b	1658m,b	1393m,b	265	550m	505w
6 [d]	3410m,b	1660s,b	1505m,b	1660m,b	1385m	275		
7 [d]	3410m,b 3310m,b	1650s,b	1496m,b	1670s,b	1382s	288	595m	520m
8 [d]	3410m 3300m,b	1655s,b	1515m,b	1668s,b	1385m	283	602m	540m
9 [c,g]	3280m,b	1630s,b	1555m,b	1650s,b	1375m	275	255w	225w
9 [d]	3400m,b 3300m,b	1655s,b	1560w	1663m	1380s	283		
10 [c,h]	3300m,b	1645s 1615s	1555w 1510w	1645s,b	1390m	255	490m	420w
10 [d]	3410m,b	1655s,b	1510w,b	1655s,b	1385m,b	270		

[a] See Table 1. [b] $\Delta\nu = \nu_{as}(COO) - \nu_{s}(COO)$. [c] KBr disc. [d] Chloroform solution. [e–h] ν(SnO), cm^{-1}: [e] 485m, [f] 473w, [g] 495m, [h] 490m.

R_3SnAA compounds. Bridging and chelation can therefore be excluded, and carboxylic groups in the solid state and also in solution mono-dentately bonded to tin(IV) must be assumed. Values of the frequencies $\nu_{as}(COO)$ and $\nu_s(COO)$ for compound **9** appear at 1650 and 1375 cm^{-1} (solid state) and 1663 and 1380 cm^{-1} (chloroform solution), respectively. Band positions and $\Delta\nu$ (275 and 283 cm^{-1}, respectively) are significantly different from the sodium salt NaDP (1593 and 1385 cm^{-1}, $\Delta\nu$ 208 cm^{-1}). Similarly, in other R_3SnDP compounds having $\Delta\nu$ in the range 255–288 cm^{-1} the carboxylic groups are monodentately bonded to tin(IV), both in the solid state and also in chloroform solution.

The N–H stretching frequencies of the solid compounds are higher than those of the ethyl esters, suggesting that the amido and peptide nitrogens are not coordinating, which would be consistent with its low basicity. The solution spectra ($CHCl_3$) of compounds **1–10** showed an upward shift of ν(N–H), consistent with the loss of hydrogen bonding in solution [7,8]. The solution spectra ($CHCl_3$) of compounds **7–9** showed two broad medium-intensity N–H stretching bands at 3400–3410 and 3300–3310 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 [9].

The stretching frequencies $\nu(CO)_{amide}$ in solid compounds **1–10** are shifted to lower values (while those of $[\nu(CN) + \delta(NH)]$ are shifted to higher values) than the frequencies in chloroform solution. This fact indicates that the CONH group is coordinated to the central tin atom in the solid state via an inter- or intra-molecular NHCO...Sn interaction (coordination number of the tin atom is five). The presence of doublets for $\nu(CO)_{amide}$ and $[\nu(CN) + \delta(NH)]$ in compound **10** and broad bands in the same region for compounds **6–9** give evidence for participation of only one CONH group in the NHCO...Sn donor–acceptor connection. In chloroform solution, a similar connection was not detected and the compounds present in the form of simple molecules having pseudotetrahedral coordination of the tin atom (coordination number of the tin atom is five).

Medium-intensity bands at 270 and 225 cm^{-1} for compound **4** and 485 and 410 cm^{-1} for compound **5** (both in the solid state) can be assigned to $\nu_{as}(SnC)$ and $\nu_s(SnC)$. Bands at 550 and 505 cm^{-1} for compound **6**, 255 and 225 cm^{-1} for compound **9** and 490 and 420 cm^{-1} for compound **10** also show the same behaviour [10,11]. This observation excludes a planar arrangement of the three Sn–C bonds of the organyl group in the coordination sphere of the central five-coordinate tin atom. A weak- or medium-intensity band in the region 480–490 cm^{-1} has been assigned to Sn–O stretching vibrations [12].

NMR spectra

The ^1H NMR spectra of compounds **1–4** and **6–9** were recorded in deuteriochloroform and are given (together with NMR spectra of HAA and HDP acids in trifluoracetic acid) in Table 3. The number of protons calculated from integration curves is equal to that calculated from the molecular formula of each compound. Thus, the compounds studied have been fully identified by analysis of ^1H NMR spectra.

Four-coordinate pseudotetrahedral geometry around the central tin atom has been confirmed in four of the compounds studied (compounds **2**, **3**, **6** and **8**) by means of ^{13}C and ^{119}Sn NMR spectroscopy in deuteriochloroform. The ^{13}C and ^{119}Sn NMR parameters relevant to the identification and determination of the structure of the compounds are given in Table 4.

Table 3

^{1}H NMR data [a] (in $CDCl_3$, δ(ppm))

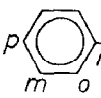
Compound [b]	C_6H_5	NH	CH	$C\underline{H}_2C_6H_5$	CH_2COO	Sn-R	
						CH_2-	-CH_3
HAA [c]	7.13m, 5H	8.13bs, 1H	5.07q, 1H	3.23bd, 2H			
1	6.63bm, 5H	7.43bs, 1H	4.13q, 1H	3.06m, 2H			0.40–2.70bm, 9H
2	7.23bm, 5H	8.20bs, 1H	4.90q, 1H	3.13bm, 2H			0.43–2.33bm, [d] 21H
3	7.07bm, 5H	7.93bs, 1H	4.76q, 1H	3.00bm, 2H		1.00–1.73bm, 18H	0.66–1.73bm, 9H
4	7.80–6.56bm, 20H	8.10bm, 1H	3.26m, 1H	1.60bd, 2H			
HDP [c]	7.20m, 5H	8.10bm, 2H	5.06q, 1H	3.16bd, 2H	4.20bd, 2H		
6	7.40m, 5H	8.30bs, 2H	4.90q, 1H	3.16bd, 2H	4.33bd, 2H		0.43–1.93bm, 9H
7	7.20m, 5H	8.13bs, 2H	4.93bm, 1H	3.13bd, 2H	4.06bm, 2H	1.40–2.10bm, 12H	0.56–1.40bm, 9H
8	7.23m, 5H	8.13bs, 2H	4.86m, 1H	3.13bd, 2H	3.97m, 2H	1.33–1.80bm, 18H	0.63–1.13bm, 9H
9	6.90–8.16bm, [e] 22H		4.70m, 1H	2.96bd, 2H	3.93m, 2H		

[a] Abbreviation: s = singlet, d = doublet, q = guadruplet, m = multiplet, b = broad. [b] See Table 1. [c] In trifluoracetic acid. [d] Hydrogen atoms of CH_2 and CH_3 groups. [e] Hydrogen atoms of C_6H_5 and NH groups.

Table 4

^{13}C and ^{119}Sn NMR parameters of compounds **2**, **3**, **6** and **8**

NMR parameter	Compound [a]				
	2	**3**	**6**	**8**	EtDP
δ(^{13}C) (AA or DP):					
HCO	160.78	160.48	160.78	161.00	161.13
CH	52.90	52.90	52.96	52.78	52.90
$C\underline{H}_2Ph$	37.45	37.57	38.45	38.27	38.21
C_i [b]	136.38	136.56	136.09	136.09	136.20
C_o	129.24	129.30	129.24	129.00	129.24
C_m	127.96	127.96	128.66	128.13	128.60
C_p	126.43	126.43	127.08	126.55	127.02
COO	175.92	174.99	173.41	173.24	170.90
$CH\underline{C}ONH$			169.96	167.19	169.32
$C\underline{H}_2COO$			42.62	41.90	41.37
δ(^{13}C) (R_3Sn or Et):					
C_α	18.97	17.56		17.03	61.56
C_β	20.72	27.62		27.51	
C_γ		26.63		26.63	
CH_3	18.09	13.82	−2.04	13.35	14.11
δ(^{119}Sn)	115.4	117.1 [c]	153.4	112.0	

[a] See Table 1. [b] 

. [c] ^1J(^{119}Sn, ^{13}C) 367.8 Hz.

In the ^{119}Sn NMR spectra of all the compounds studied, only one signal was found. The number of signals in ^{13}C NMR spectra corresponds to the number of magnetically non-equivalent carbon atoms in triorganotin(IV) derivatives of *N*-formyl-L-phenylalanine and *N*-formyl-L-phenylalanylglycine. This fact, together with analysis of ^{13}C and ^{119}Sn NMR spectra (see later), is further confirmation of the identity of compounds **2**, **3**, **6** and **8**.

The chemical shifts $\delta(^{119}Sn)$ of trialkyltin(IV) derivatives **2**, **3**, **6** and **8**, ranging from 112.0 to 153.4 ppm, are typical of a four-coordinate central tin atom in simple pseudotetrahedral trialkyltin(IV) compounds [13]. The value of $^{1}J(^{119}Sn, ^{13}C)$ of compound **3** (367.8 Hz) corresponds to a C–Sn–C angle of ~ 111° [14]. The values of $\delta(^{13}C)$ for carboxylic and amide carbonyl carbon atoms are practically unshifted relative to the ethyl esters of *N*-formyl-L-phenylalanylglycine. All these facts are consistent with the absence of the interaction of carbonyl group oxygen atoms or amide nitrogen atoms with the central tin atom in solution.

Conclusion

In triorganotin(IV) derivatives of *N*-formyl-L-phenylalanine and *N*-formyl-L-phenylalanylglycine (**1**–**10**) in the solid state a weak donor–acceptor interaction NHCO...Sn was detected. We assume that this interaction is of intermolecular type, such as in similar compounds with *N*-benzoyl- and *N*-acetyl-protected derivatives of alanine and alanylglycine [1,2]. In chloroform solution, this interaction is broken and molecules of compounds **1**–**10** show a virtually ideal tetrahedral configuration of the R_3SnOCO group.

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