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DIORGANOTIN(IV) COMPLEXES OF *N*-PROTECTED DIPEPTIDES

G.K. SANDHU*, R. GUPTA, S.S. SANDHU,

Chemistry Department, Guru Nanak Dev University, Amritsar-143005 (India)

L.S. MOORE and R.V. PARISH

Department of Chemistry, The University of Manchester Institute of Science and Technology, PO Box 88, Manchester M60 1QD (Great Britain)

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Summary

Eight new diorganotin(IV) complexes of general formula $R_2Sn(DP)_2$ and $[R_2Sn(DP)]_2O$ (DP = anion of *N*-benzoyl-DL-alanylglycine; R = CH_3, C_2H_5, n-C_4H_9, n-C_8H_{17}) have been prepared and characterised by IR, and ^{119m}Sn Mössbauer spectroscopy. However, only two complexes, $(DP)_2Sn(n\text{-}C_4H_9)_2$ and $(DP)_2Sn(n\text{-}C_8H_{17})_2$ were sufficiently soluble for NMR (^{1}H and ^{13}C) studies. The 2:1 complexes are monomeric with distorted *trans*-octahedral structures. The 1:1 complexes are dinuclear with Sn–O–Sn bridges and trigonal bipyramidal geometry about tin. In both cases the dipeptide acts as an *O,O*-bidentate ligand.

Introduction

Very few organotin complexes of peptides are known. Diorganotin(IV) derivatives have been prepared only with glycylglycine, which acts as a dinegative tridentate, giving trigonal-bipyramidal complexes [1–3]. Studies have also been made of the trimethyl- and tricyclohexyltin(IV) derivatives of glycylglycine [4] and of tributyltin with glutathione [5,6]. This paper reports diorganotin(IV) complexes of *N*-benzoyl-DL-alanylglycine (HDP).

Experimental

N-benzoyl-DL-alanylglycine was obtained [7] by alkaline hydrolysis of the ethyl ester, which was prepared [8] using 1-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline [9] as coupling agent. Diethyltin(IV) oxide was precipitated from a methanolic solution of diethyltin dichloride by addition of sodium hydroxide solution [10] and was washed with water and dried at 120°C.

Melting points were determined in open capillaries, and are uncorrected. Elemental analyses were carried out by the Microanalytical Service of Calcutta University. Molecular weights were determined by cryoscopy in nitrobenzene or bromoform,

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and by the Rast method (camphor, 175°C). Infrared spectra were recorded on a Pye Unicam P321 spectrophotometer in KBr or $CHCl_3$. ^1H and ^{13}C NMR spectra were obtained with Tesla B487 (80 MHz) and JEOL FX100 spectrometers, respectively. ^{119m}Sn Mössbauer spectra were recorded with a Harwell 6000 Series Spectrometer using a Pd-Sn source at room temperature and samples cooled to 80 K. Isomer shifts are given relative to SnO_2 at room temperature.

Preparation of complexes

N-benzoyl-DL-alanylglycine (2 mmol) was dissolved in a mixture of dry benzene (30 ml) and absolute ethanol (10 ml), and the dialkyltin oxide (1 or 2 mmol, as required) was added. The mixture was refluxed using a Dean and Stark apparatus, giving clear solutions in 10–30 min. Refluxing was continued for 3–4 h, after which the clear solution was filtered and the solvent was removed under reduced pressure. The resulting solid was washed with chloroform and then carbon tetrachloride. Although the compounds redissolved readily, they could not be satisfactorily recrystallized. Only pasty products were obtained which presumably contained some solvent: solidification occurred after prolonged evacuation.

Results and discussion

Dialkyltin(IV) oxides react with *N*-benzoyl-DL-alanylglycine (C_6H_5CONH-$CH(CH_3)CONHCH_2CO_2H$, (HDP)) in 1/2 and 1/1 molar ratios, giving the complexes $R_2Sn(DP)_2$ and $[(R_2Sn(DP)]_2O$, for which analytical data are presented in Table 1. The complexes are monomeric both in freezing nitrobenzene or bromoform and in molten camphor. However, the infrared data suggest that, in the solid state, there may be some association by intermolecular hydrogen bonding (see below).

Infrared spectra

Infrared data for the free dipeptide and the complexes are given in Table 2. A broad band at 2500–2800 cm^{-1} in the ligand spectrum is absent for the complexes, indicating deprotonation of the carboxyl group. The N–H stretching frequency generally shifts slightly to higher frequency, suggesting that neither the amide nor peptide nitrogen atoms are coordinated and that, in the solid state, hydrogen bonding occurs between the NH groups and C=O groups of neighbouring molecules [4]. In the solution spectra, the ν(N–H) band is split into two well resolved bands: that a higher frequency (3420–3440 cm^{-1}) is assigned to the amide group and the lower (3300–3320 cm^{-1}) to the peptide NH group.

The solids show a broad band in the range 1630–1640 cm^{-1}, assigned as ν(CO) of the amide and peptide groups together. Complex formation results in an increase in $\nu(CO)_{amide}$ and a decrease in $\nu(CO)_{peptide}$, indicating that the peptide group is coordinated to tin and the amide group is not: the amide may be involved in hydrogen bonding, however [4]. For the soluble complexes, two bands are observed of which the higher frequency band is assigned as $\nu(CO)_{amide}$ (1650–1680 cm^{-1}); the shift of this band to higher frequency is consistent with the breaking down of the hydrogen bonding [6].

Organotin carboxylates with bridged structures show $\nu(COO)_{asym}$ at 1540–1560 cm^{-1} while chelated carboxyl groups are expected to absorb at 1580–1600 cm^{-1} [11]. The presence of a medium-strong band at 1720–1740 cm^{-1} indicates uniden-

TABLE 1

PHYSICAL AND ANALYTICAL DATA OF DIALKYLTIN(IV) COMPLEXES WITH *N*-BENZOYL-DL-ALANYLGLYCINE

Complex [e]	M.p. [d] (°C)	Yield (%)	Analysis (Found (calcd.) (%))			Mol. Wt.		
			C	H	N	A	B	Calcd.
HDP [a]	160–161	95	57.27 (57.60)	6.04 (5.60)	11.24 (11.20)	–	–	–
$(DP)_2Sn(CH_3)_2$ (1)	130–132	77	48.29 (48.24)	4.72 (4.94)	–	574 [b]	560	646.7
$(DP)_2Sn(C_2H_5)_2$ (2)	109–111	80	49.02 (49.79)	5.39 (5.33)	7.72 (8.29)	772 [b]	570	674.7
$(DP)_2Sn(n\text{-}C_4H_9)_2$ (3)	208–212	85	52.71 (52.55)	6.02 (6.02)	7.50 (7.66)	717 [c]	680	730.7
$(DP)_2Sn(n\text{-}C_8H_{17})_2$ (4)	150–152	70	56.56 (56.95)	7.12 (7.11)	6.65 (6.64)	990 [c]	880	842.7
$[(DP)Sn(CH_3)_2]_2O$ (5)	155–156	96	42.21 (41.40)	4.69 (4.68)	–	957 [b]	710	811.4
$[(DP)Sn(C_2H_5)_2]_2O$ (6)	105–107	70	44.70 (44.24)	5.00 (5.30)	6.65 (6.45)	750 [b]	790	867.4
$[(DP)Sn(n\text{-}C_4H_9)_2]_2O$ (7)	180–183	65	48.52 (49.00)	6.85 (6.33)	–	864 [b]	810	979.4
$[(DP)Sn(n\text{-}C_8H_{17})_2]_2O$ (8)	90– 92	60	55.98 (55.84)	8.29 (7.81)	3.96 (4.65)	1150 [b]	1100	1203.4

[a] HDP = *N*-benzoyl-DL-alanylglycine. [b] In nitrobenzene. [c] In bromoform. A = Cryoscopy, B = Rast method. DP = anion of HDP. [d] Melting point in open capillary tube. [e] All complexes are white in colour.

TABLE 2

INFRARED SPECTRAL DATA (KBr/$CHCl_3$; cm^{-1})

Complex [a]	ν(N–H) (Solid/ solution)	ν(C=O) (amide I band) solid/solution	ν(COO) *asym*	ν(COO) *sym*	Δν [b]	ν(Sn–O–Sn)	ν(Sn–C)	ν(Sn–O)
HDP [c]	3300(s,sh)	1660(s,sh) 1615(s,sh)	1750 (s,sh)	1285 (m,sh)	460	–	–	–
DP-ethyl ester	3300(m,b)	1660(s,sh) 1615(s,sh)	1740 (s,b)	1385 (m,b)	355	–	–	–
1	3300(s,b)	1630(m,b)	1740 (m,b)	1380 (s,sh)	360	–	530, 550 (w,b)	480 (w,b)
2	3320/3440, 3300 (s,b) (s) (m)	1640(s,b)/ 1680–1650(s)	1750 (m,b)	1395 (s,b)	355	–	540 (m,b)	500 (w,b)
3	3320, 3420 (m,b) (s) 3300, 3320 (m,b) (m)	1635/1600–1640 (s,b) (s,b)	1740 (m,sh)	1380 (s,b)	360	–	610, 535 (m)	490 (w,b)
4	3300/3440, 3330 (m,b) (s) (m)	1640/1660–1640 (b) (s,b)	1740 (m,sh)	1405 (s,b)	355	–	605, 560 (m,sh)	490 (s,sh)
5	3450 (m,b)	1640 (m,b)	1740 (m,b)	1390 (m,b)	350	580 (m,b)	530,565 (m,b)	480 (w,b)
6	3310 (m,b)	1640 (s,b)	1580 (m,sh)	1390 (m,b)	190	600 (m,sh)	540 (w,b)	500 (w,b)
7	3320 (m,b)	1635 (s,b)	1580 (m,sh)	1390 (m,b)	190	578 (m,b)	615, 535 (w,b)	480 (w,b)
8	3330 (m,b)	1635 (s,b)	1740 (m,b)	1380 (w,b)	300	560 (m,b)	600, 560 (w,b)	475 (w,b)

[a] Complex number as listed in Table 1. [b] $\Delta\nu = \nu(COO)_{asym} - \nu(COO)_{sym}$. [c] HDP = *N*-benzoyl-DL-alanylglycine.

TABLE 3

^{1}H NMR DATA ($CDCl_3$ [c], δ(ppm))

Complex [a]	C_6H_4	CH	CH_2	CH_3	Sn-R		$[^2J(^{119}Sn-C-^1H)]$ (Hz)
					CH_2	CH_3	
HDP [b]	7.97 7.47 m,5H)	4.82 (m,1H)	4.32 (d,2H)	1.70 (d,3H)	–	–	–
DP-ethyl ester	8.00 7.00 (m,5H)	4.88 (q,1H)	4.25–3.75 (m,4H)	1.00–0.50 (m,6H)	–	–	–
3	7.90 (7.22 (m,10H)	4.75 (bm,2H)	4.05 (bm,4H)	1.45 (d,6H)	1.54–1.00 (bs,12H)	1.00–0.68 (bm,6H)	74
4	7.75 7.25	4.75 (bm,2H)	3.92 (bm,4H)	1.43 (bm,6H)	1.25 (b,28H)	0.88 (bs,H)	64

[a] Complex number as listed in Table 1. HDP = *N*-benzoyl-DL-alanylglycine. [b] In trifluoroacetic acid. All other complexes are insoluble in $CHCl_3$ and CCl_4. [c] 5% solution.

tate bonding [12]. In the complexes **1–5** and **8** of Table 2, the carboxylate is unidentate, while complexes **6** and **7** involve bidentate coordination.

The low-frequency region is complex, but bands attributable to ν(Sn–C), ν(Sn–O) and ν(Sn–O–Sn) can be seen [13–17].

NMR spectra

Only two compounds, $R_2Sn(DP)_2$ ($R = C_4H_9$ and C_8H_{17}), were sufficiently soluble in chloroform to permit NMR spectra to be obtained. The data are given in Tables 3 and 4. A broad signal at δ 8.07 in the ^{1}H spectrum of the ligand ethyl ester, due to the amide and peptide NH groups, is not present for the complexes. The coupling constants $[^2J(^{119}Sn-^1H)]$ for the $(DP)_2Sn(n\text{-}C_4H_9)_2$ and $(DP)_2Sn(n\text{-}C_8H_7)_2$ complexes (74 and 64 Hz) suggest a coordination number greater than four for tin [18], and are consistent with the distorted octahedral structures indicated by the Mössbauer data (see below).

In the ^{13}C spectra, the chemical-shift values of the α-carbon atoms of the alkyl groups (25–27 ppm) are similar to those reported for $Bu_2Sn(OAc)_2$ and $Bu_2SnCl(ET)$ (ET = ethylcysteinate) [19,20]. The signal for the carboxyl carbon atom is unshifted relative to the ethyl ester of the ligand, consistent with unidentate coordination to tin [4]. The shift of the amide carbonyl carbon atom is also unshifted by coordination, while that of the peptide group moves downfield showing, in agreement with the IR data, that the peptide carbonyl is coordinated while the amide is not [4].

Mössbauer spectra

^{119m}Sn Mössbauer data are given in Table 5. The 2 : 1 complexes (numbers **1–4**) have large quadrupole splitting (*QS*) values (3.2–3.5 mm s^{-1}) and isomer shifts (*IS*) greater than 1.2 mm s^{-1}, suggesting slightly distorted *trans*-octahedral coordination (21–24). The *QS* values are less than expected for linear C–Sn–C arrangements (ca. 4 mm s^{-1}); calculations based on the point-charge treatment, assuming the splitting to be due predominantly to the disposition of the Sn–C bonds [24], indicated bond angles of 140–145°.

TABLE 4

^{13}C NMR DATA ($CDCl_3$, δ (ppm))

Complex [a]	(C=O) amide	(C=O) peptide	(COO) acid	CH_3	CH_2	CH	C_6H_5	R-Sn-R				$[^2J(^{13}C-^{119}Sn)]$ (Hz)
								C_α	C_β	C_γ	C_δ	
DP-ethyl ester [b]	167.23	169.53	172.74	18.36	41.37	48.13	127.12 128.53 131.75 133.65	–	–	–	–	–
3	167.14	176.25	172.74	18.26	41.27	49.17	127.07 128.53 131.79 133.65	26.50	27.44	27.19	21.05	840
4	167.23	over-lapping with COO	172.74	18.96	41.92	49.22	127.02 128.53 131.79 133.65	25.24	25.72	29.38	22.70	870

[a] Complex number as listed in Table 1. [b] DP = *N*-benzoyl-DL-alanylglycine ester.

TABLE 5

^{119m}Sn MÖSSBAUER DATA (mm s^{-1}, 80 K)

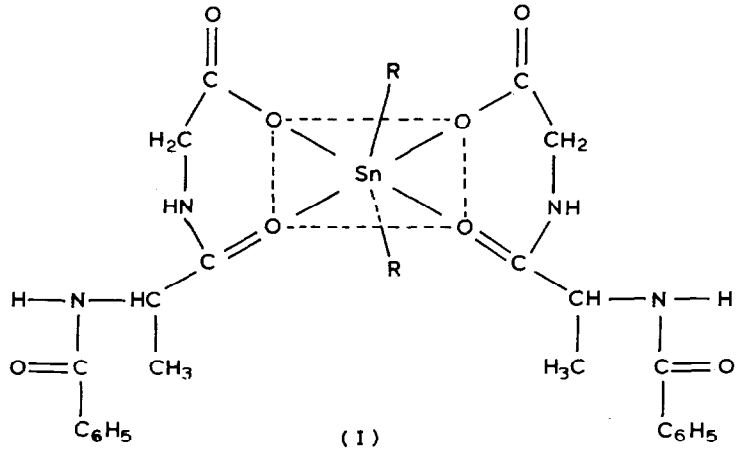
Complex [a]	*IS* [d] (SnO_2)	*QS* [d]	Line widths	∠C–Sn–C (°) [b]	*P* = *QS*/*IS*
1	1.16	3.21	0.91, 1.05	134	2.75
2	1.38	3.60	0.97, 1.13	146	2.60
3	1.47	3.56	0.89, 0.98	144	2.42
4	1.36	3.49	0.94, 0.99	142	2.56
5	1.14	2.96	0.97, 1.08	134	2.58
6	1.32	3.25	0.87, 1.06	143	2.46
7	1.28	3.12	0.92, 1.02	139	2.46
8	1.19 (65%)	2.55	0.88, 1.26	121 [c]	2.14
	1.32 (35%)	3.46	0.74, 0.78		2.68

[a] Complex number as in Table 1. [b] The C–Sn–C angle for each compound calculated using method given by Sham et al. (T.K. Sham and M.G. Bancroft, Inorg. Chem., 14 (1982) 2281. Taking the C–Sn–C angle as θ, the relationship is $QS = -4[R][1 - \frac{3}{4}\sin^2\theta]^{1/2}$. ($QS$ = quadrupole splitting). In six-coordinated complexes, $R = -1.03$ mm s^{-1}; in five-coordinated. $R = 0.95$ mm s^{-1}. [c] For octahedral tin(IV). [d] *IS*, ±0.5; *QS*, ±0.05.

For a given alkyl group, the 1 : 1 complexes (**5–8**) have rather smaller *QS* values than the corresponding 2 : 1 complexes, indicating a different structure. This is well illustrated by complex, $[DPSn(n\text{-}C_8H_{17})_2]_2O$ the sample of which adventitiously contained a little of the 2 : 1 complex. The parameters of the 1 : 1 complexes are consistent with trigonal-bipyramidal structures [13,24–27], with C–Sn–C bond angles of 130–140°. The ratio *QS*/*IS* = *P*, in all the complexes indicates a coordination number more than four [28].

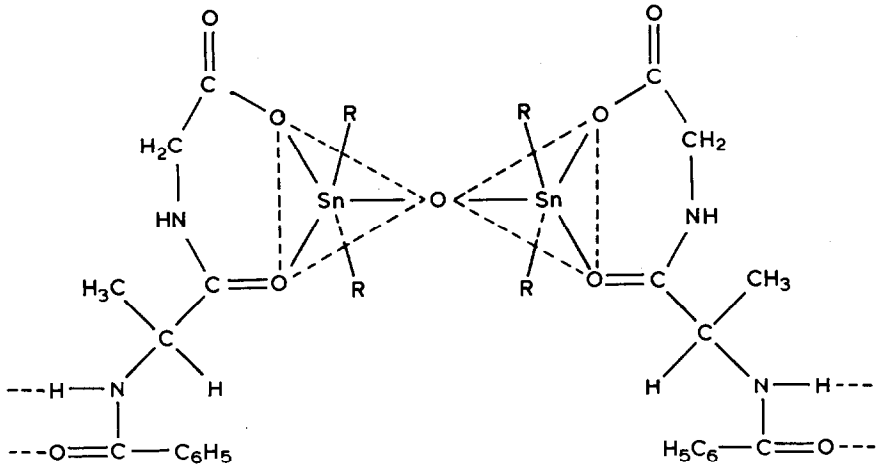
Conclusions

The four [2 : 1] complexes have monomeric octahedral structures involving coordination of the peptide carbonyl group and a unidentate carboxyl group, as shown by the IR and ^{13}C NMR data (structure I). In the solid state, the IR data suggest weak association by hydrogen bonding between the amide C=O and NH groups of neighbouring molecules, while the Mössbauer *QS* indicates that, as frequently happens, the R_2Sn group is distorted from exactly linear *trans* geometry.



(I)

The four [1 : 1] complexes have monomeric dinuclear oxygen-bridged structures, and the Mössbauer parameters are consistent with trigonal-bipyramidal geometry. The IR data, however, show that the dimethyl- and di-octyl-tin derivatives have unidentate binding of carboxyl group, while the diethyl and dibutyl complexes involve bidentate bonding. These complexes are, therefore, assigned structures II and III, respectively. In all cases, the dipeptide acts as an *O,O*-bidentate chelating ligand, binding through the carboxyl group and the peptide carbonyl group.



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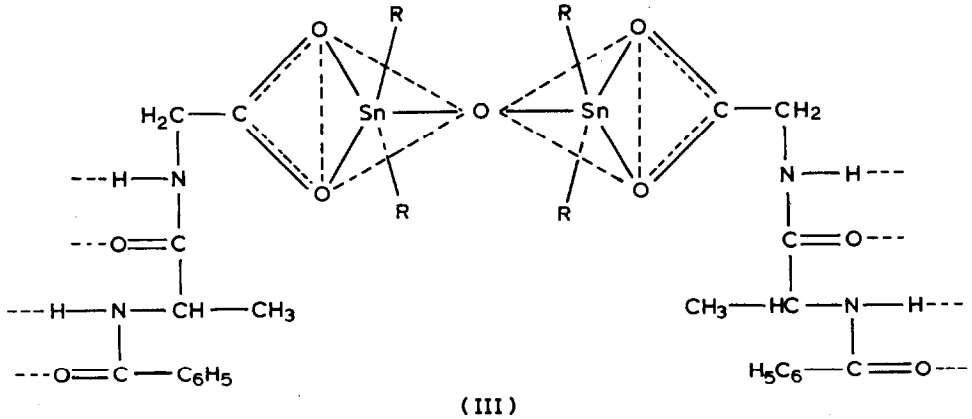

(III)

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