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Stannacycloalkyl and Stannepinyl Derivatives of Dipeptides

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Stannacyclohexyl and stannacycloheptyl derivatives of dipeptides $(CH_2)_nSnAA \cdot xH_2O$ (H_2AA = $H_2GlyGly$, with $n=5$, $x=2$ or $n=6$, $x=1$; $H_2AA = H_2GlyAla$, $H_2GlyVal$, $H_2GlyMet$, with $n=5$, 6, $x=1$) and stannepinyl glycylglycinate monohydrate have been obtained by the reaction of $(CH_2)_nSnCl_2$ or stannepinyl dichloride with Na_2AA. According to infrared and ^{119}Sn Mössbauer data of the solid compounds, AA acts as a tridentate ONN ligand and tin has a trigonal-bipyramidal environment. An analogous structure has been inferred from ^1H, ^{13}C, and ^{119}Sn NMR data for the undissociated molecules in methanol solution.

Keywords: Organotin, stannacycloalkyl compounds, dipeptides, Mössbauer, NMR, IR

INTRODUCTION

In the context of our studies on organotin derivatives of biologically relevant compounds such as amino-acids, dipeptides, nucleic acids, etc.,[1,2] and on the interaction of organotin compounds with biological systems,[3] we prepared and characterized stannacycloalkyl and stannepinyl derivatives of dipeptides. In these compounds tin is a member of a ring system. Its ability to extend its coordination sphere would possibly be restricted, since addition of ligands could cause additional constraints in the ring and could affect the acceptor properties of tin. The coordination behavior of organotin compounds is an important factor in determining their reactivity and consequently also their biological activity. It therefore appeared interesting to determine firstly whether there are really decisive sterical restraints at the central atom of the title compounds, and secondly whether there are limitations regarding the extension of the coordination sphere around tin and if there are effects on the coordination geometry.

EXPERIMENTAL

$(CH_2)_5SnCl_2$ and $(CH_2)_6SnCl_2$ were prepared according to Refs 4 and 5, and according to Ref. 6, respectively. The dipeptides were a gift from Degussa. The other reactants as well as solvents were commercial products; the solvents were dried as usual.

IR spectra (solids—KBr pellets; solutions—cell with KBr plates, 25 μm) were recorded on a Perkin–Elmer grating spectrometer PE 580 B, ^1H NMR spectra on a Perkin–Elmer R-32 90 MHz instrument at 37 °C, and ^{13}C and ^{119}Sn NMR spectra on a Bruker AM 300 spectrometer. Melting points (uncorrected) and decomposition temperatures were determined in the usual way. Molecular weights were determined osmometrically. The Mössbauer spectra were measured with the aparatus and techniques described in previous papers.[7,8]

The stannacycloalkyl derivatives of dipeptides were prepared as follows. A 1 M solution of sodium methoxide in methanol was added to a suspension of the appropriate dipeptide H_2AA (1 mmol/40 ml; 2:1 mole ratio) in MeOH. The mixture was stirred until it was clear. Then, a solution of $(CH_2)_5SnCl_2$, $(CH_2)_6SnCl_2$ or 1,1-dichlorostannepine ($StanepCl_2$) (1 mmol/15 ml; equimolar with H_2AA) in a small amount of methanol was added and the solution was stirred at 40 °C for 12 h. After reduction of the volume of the solution and removal of NaCl by filtration, diethyl ether was added as long as a precipitate formed. This was filtered off and was recrystallized from $EtOH/CHCl_3$ (5:4, v/v).

The new compounds obtained are listed together with the elemental analyses, the yields, melting points and decomposition temperatures in Table 1.

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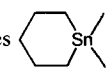
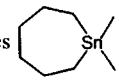
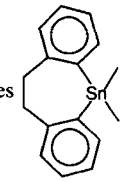
Table 1 Analytical data for stannacycloalkyl and stannepin derivatives of dipeptides

	Compound[a]	Yield (%)	M.p. (dec.) (°C)	Analysis (%) Found (Calcd.) C	H	N
1	$(CH_2)_5SnGlyGly \cdot 2H_2O$	58	222	29.8	5.2	7.7
	$C_9H_{20}N_2O_5Sn$			(30.4)	(5.6)	(7.9)
5	$(CH_2)_6SnGlyGly \cdot H_2O$	55	>200	34.6	5.8	8.0
	$C_{10}H_{20}N_2O_4Sn$			(34.2)	(5.7)	(8.0)
9	$StanepGlyGly \cdot H_2O$	60	>200	48.5	4.4	6.1
	$C_{18}H_{18}N_2O_4Sn$			(48.4)	(4.5)	(6.2)
2	$(CH_2)_5SnGlyAla \cdot H_2O$	45	226	33.6	5.6	7.8
	$C_{10}H_{20}N_2O_4Sn$			(34.2)	(5.7)	(8.0)
6	$(CH_2)_6SnGlyAla \cdot H_2O$	40	>200	35.3	5.5	7.7
	$C_{11}H_{22}N_2O_4Sn$			(36.2)	(6.0)	(7.7)
3	$(CH_2)_5SnGlyVal \cdot H_2O$	42	215	38.0	6.2	7.3
	$C_{12}H_{24}N_2O_4Sn$			(38.0)	(6.3)	(7.4)
7	$(CH_2)_6SnGlyVal \cdot H_2O$	48	>200	40.0	6.4	7.1
	$C_{13}H_{26}N_2O_4Sn$			(39.7)	(6.6)	(7.1)
4	$(CH_2)_5SnGlyMet \cdot H_2O$	52	228	36.2	6.0	6.5
	$C_{12}H_{24}N_2O_4SSn$			(35.1)	(5.8)	(6.8)
8	$(CH_2)_6SnGlyMet \cdot H_2O$	50	>200	36.3	5.9	6.5
	$C_{13}H_{26}N_2O_4SSn$			(36.7)	(6.1)	(6.6)

[a] Abbreviations: $H_2GlyGly$, glycylglycine; $H_2GlyAla$, glycylalanine; $H_2GlyVal$, glycylvaline; $H_2GlyMet$, glycylmethionine. Cyclic structures are indicated as follows:

$(CH_2)_5Sn$ denotes  $(CH_2)_6Sn$ denotes  Stanep denotes 

RESULTS AND DISCUSSION

The stannacycloalkyl derivatives of the dipeptides, $(CH_2)_5SnGlyGly \cdot 2H_2O$ (**1**), $(CH_2)_5SnAA \cdot H_2O$ (**2–4**), $(CH_2)_6SnAA \cdot H_2O$ (**5–8**) and $StanepGlyGly \cdot H_2O$ (**9**), listed in Table 1 were prepared by the reaction of $(CH_2)_5SnCl_2$, $(CH_2)_6SnCl_2$, and $StanepCl_2$, respectively, with the appropriate Na_2AA in methanol. The products are colorless crystalline solids, insensitive to light and dry air, but sensitive to moisture, and take up water to form hydrates. The water is liberated again on heating (beginning of liberation of H_2O, as determined by thermogravimetry **1**, 108 °C; **2**, 114 °C; **3**, 48 °C; **4**, 70 °C). Compounds **1–4** are solvated also by alcohol, but not **5–9**. The compounds are soluble in methanol and ethanol, but they are not soluble in $CHCl_3$ and non-polar solvents. Molecular weight measurements showed **1–4** to be monomeric in solution: **1** in MeOH, 311 (calcd 318.7, for the anhydrous compound); **2**, **3**, **4** in DMSO, 344 (332.7), 337 (360.7), 368 (392.7). We assume that they retain (like the dialkyltin derivatives of dipeptides[7,9,10]) in methanol their solid-state molecular structure in solution (*vide infra*).

A comparison of the IR spectra of H_2AA and of the appropriate solid compounds **1–9** (Table 2) showed that $\nu(NH_{pep})$ disappeared in the spectra, indicating that the organotin moiety is bonded to the dipeptide via N_{pep}. Such Sn–N bonds have been shown by X-ray structure analysis to be rather short and to exist in all compounds Alk_2SnAA.[7,10–15] Also, other structural features are evidently the same as in Alk_2SnAA; thus, from the values of $\Delta\nu = 220$ to $240\,cm^{-1}$ $[\Delta\nu = \nu_{as}(COO) - \nu_s(COO)]$ (Table 2) unidentate bonding of the carboxylate group to tin can be inferred.[16] Further, instead of the broad NH_3^+ band found in the spectra of free H_2AA, an

Table 2 Characteristic IR vibrations of stannacycloalkyl and stannepin derivatives of dipeptides[a] (cm^{-1})

Compound		$\nu(NH_2)$	$\nu(CO_{pep})$	$\nu_{as}(COO)$	$\nu_s(COO)$	$\Delta\nu$[b]
1	$(CH_2)_5SnGlyGly \cdot 2H_2O$	3200 s 3100 s	1655 vs	1635 vs	1400 vs	235
2	$(CH_2)_5SnGlyAla \cdot H_2O$	3210 s 3120 s	1660 vs	1625 vs	1400 vs	225
3	$(CH_2)_5SnGlyVal \cdot H_2O$	3190 s 3100 s	1670 vs	1625 vs	1405 vs	220
4	$(CH_2)_5SnGlyMet \cdot H_2O$	3210 s 3120 s	1655 vs	1620 vs	1400 vs	220
5	$(CH_2)_6SnGlyGly \cdot H_2O$	3220 s 3110 s	1660 vs	1635 vs	1405 vs	230
6	$(CH_2)_6SnGlyAla \cdot H_2O$	3210 a 3080 s	1650 vs	1620 vs	1395 vs	225
7	$(CH_2)_6SnGlyVal \cdot H_2O$	3220 s 3130 s	1655 vs	1620 vs	1400 vs	220
8	$(CH_2)_6SnGlyMet \cdot H_2O$	3210 s 3080 s	1645 vs	1620 vs	1400 vs	220
9	$StanepGlyGly \cdot H_2O$	3280 s 3180 s	1660 vs	1645 vs	1405 vs	240

[a] In the solid state. [b] $\Delta\nu = \nu_{as}(COO) - \nu_s(COO)$.

intensive $\nu(NH_2)$ band is found in the range 3280–3100 cm^{-1} (Table 2). These are lower than $\nu(NH_2)$ in alkali-metal salts (e.g. 3380 cm^{-1} in sodium glycinate)[17] or with matrix-isolated amino acids (e.g. 3380 cm^{-1}).[17] This shifting can be correlated with $Sn \leftarrow NH_2$ coordination and would be fully consistent with the observation that this type of coordination was found in all Alk_2SnAA compounds for which single-crystal X-ray structure determinations have been carried out.[7, 10–15]

The $\nu(CO_{pep})$ values (Table 2) are shifted to wavenumbers about 20–40 cm^{-1} lower than in the appropriate H_2AA. This would correspond with a weakening of the (CO_{pep}) bond in relation to the formation of a strong SnN_{pep} bond (*vide supra*), but also with the existence of hydrogen bonds involving CO_{pep}. The relative broadness of the $\nu(NH_2)$ bands would also be consistent with their participation in hydrogen bonding.

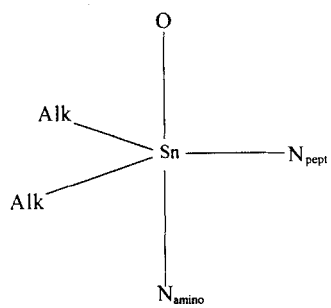


Figure 1 The skeletal structure of Alk_2SnAA complexes. N_{pept}, peptide nitrogen (equatorial); N_{amino}, amino nitrogen (apical).

In conclusion, the IR data allow us to propose that **1** to **9** in the solid state follow the structural pattern found in all other Alk_2SnAA compounds hitherto investigated: tin is in the centre of a trigonal-bipyramidal coordination polyhedron, AA acts as a tridentate ONN ligand, N_{amino} and $O_{carboxylate}$ are in apical positions, and two C and N_{pep} are in equatorial positions (Fig. 1).

The Mössbauer parameters of the compounds **1**, **4** and **5** have been measured. The data corroborate the proposal advanced from the IR data. The isomer shifts δ and the quadrupole splittings ΔE (Table 3) correspond to values found in a series of Alk_2SnAA compounds (*vide infra*) for which the above structure was established by X-ray structure analysis (e.g. n-$Bu_2SnGlyVal$: $\delta = 1.23$ mm s^{-1}, $\Delta E = 2.65$ mm s^{-1}).[10]

It therefore seems clearly demonstrated that there are no basic restrictions for tin to extend its coordination sphere (at least to attain pentacoordination) when it is an integral part of a cycloalkyl system. This result is verified by an X-ray structure determination of the Schiff-base complex StanepSAT (H_2SAT = 2-(*o*-hydroxyphenyl)benzothiazoline) in which tin is pentacoordinated.[18]

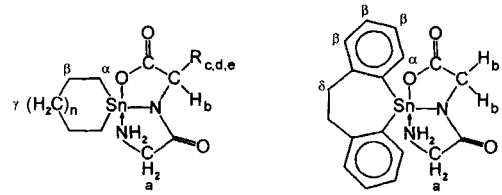
^1H NMR data are listed in Table 4. The chemi-

Table 3 ^{119}Sn Mössbauer parameters[a] of stannacycloalkyl and stannepinyl derivatives of dipeptides

Compound		δ[b] (mm s^{-1})	ΔE[c] (mm s^{-1})	Γ_1[d] (mm s^{-1})	Γ_2[d] (mm s^{-1})
$(CH_2)_5SnGlyGly \cdot 2H_2O$	**1**	1.18	2.58	0.86	0.86
$(CH_2)_5SnGlyMet \cdot H_2O$	**4**	1.15	2.44	0.82	0.81
$(CH_2)_6SnGlyGly \cdot H_2O$	**5**	1.24	2.62	0.88	0.78

[a] Solid samples, *ca* 0.5 mg ^{119}Sn cm^{-2}, measured at 77.3 K. [b] Isomer shift with respect to room-temperature $CaSnO_3$. [c] Nuclear quadrupole splitting. [d] Full width at half height of the resonant peaks.

Table 4 ^{1}H NMR data of stannacycloalkyl and stannepinyl derivatives of dipeptides, and of free dipeptides; δ (ppm)



Compound	Solvent	a	b	c	d	e	α	$\beta+\gamma$	δ
$H_2GlyGly$[10] (R = H)	D_2O	3.84	3.90	—	—	—	—	—	—
1 (R = H)	CD_3OD	3.47	3.78	—	—	—	1.89–2.22	1.48–1.71	—
5 (R = H)	CD_3OD	3.50	3.85	—	—	—	1.85–2.14	1.41–1.83	—
9 (R = H)	CD_3OD	3.36	3.76	—	—	—	7.61–7.64	7.30–7.39	3.19
$H_2GlyAla$[10] ($R = CH_3$)	D_2O	3.76	4.08	1.29	—	—	—	—	—
2 ($R = CH_3$)	CD_3OD	3.38	4.16	1.33	—	—	1.84–2.18	1.42–1.67	—
6 ($R = CH_3$)	CD_3OD	3.48	4.25	1.40	—	—	1.86–2.10	1.46–1.83	—
$H_2GlyVal$[10] ($R = CH(CH_3)_2$) c d	D_2O	3.78	4.00	2.20	0.83 0.99	—	—	—	—
3 ($R = CH(CH_3)_2$) c d	CD_3OD	3.39	4.17	f	0.83 0.99	—	1.79–2.32[f]	1.33–1.73	—
7 ($R = CH(CH_3)_2$) c d	CD_3OD	3.37	4.11	f	0.75 0.93	—	1.80–2.10[f]	1.48–1.68	—
$H_2GlyMet$[10] ($R = CH_2CH_2SCH_3$) c d e	D_2O	3.85	4.20	2.50	1.96	2.03	—	—	—
4 ($R = CH_2CH_2SCH_3$)	CD_3OD	3.44	4.42	g	g	2.03	g	1.37–1.82	—
8 ($R = CH_2CH_2SCH_3$)	CD_3OD	3.35	4.18	g	g	1.93	g	1.34–1.88	—

[f] α and c overlap. [g] α, c and d overlap.

cal shifts $\delta(^1H)$ of the ring protons, α, β and γ appear as very broad multiplets; $^2J(Sn, H)$ coupling constants therefore could not be determined. The $\delta(^1H)$ values of the AA ligands of **1–9** lie in the same range as in other Alk_2SnAA compounds.[10] The ^{13}C and ^{119}Sn NMR data were measured for **1** and **5** (Table 5). The $\delta(^{13}C)$ values of the ring C atoms in **1** and **5** are shifted to low field compared with the appropriate values of $(CH_2)_5Sn(CH_3)_2$ (**10**) (Table 5).[19] This low-field shift can be correlated with an increase of the coordination number of the metal ring atom.

Table 5 ^{13}C and ^{119}Sn NMR data of compounds **1**, **5** and **10**: δ (ppm), $^{1}J(Sn, C)$ (Hz)[a]

	^{13}C				^{119}Sn
	$\delta(C-\alpha)$	$\delta(C-\beta)$	$\delta(C-\gamma)$	$^{1}J(Sn, C)$	δ
1	22.12	28.73	31.51	536.0	−112.5
5	21.50	24.37	31.74	559.0	−85.3
10[19]	8.53	23.07	26.51	321.5	−42.5

[a] Compounds **1** and **5** were in CD_3OD and **10** was neat. For the numbering of the C atoms, see Table 4.

Similar effects have been observed on increasing the coordination number, e.g. in di-n-butyltin compounds.[20] More conclusive for inferring a proposal for the solution-state structure are values of $\delta(^{119}Sn)$ and of coupling constants $^{1}J(Sn, C)$. the ^{119}Sn chemical shifts of pentacoordinated tin compounds are expected to lie between 0 and −200 ppm.[21–24] The $\delta(^{119}Sn)$ values lie in this range like those of other Alk_2SnAA compounds[10] and below the value of −125 ppm which is considered as the lower limit for hexacoordinated tin compounds.[21–24] Also, $^{1}J(Sn, C)$ values favor the assumption of pentacoordinated tin in **1** and **5**, since they actually have increased from 321.5 Hz in $(CH_2)_5Sn(CH_3)_2$[19] to values of 536.0 and 559.0 in **1** and **5**, respectively, and lie in a range characteristic of pentacoordinate diorganotin compounds.[25]

From all these observations we conclude that **1** and **5**, and for reasons of analogy, presumably also **2–4** and **6–9**, retain their solid-state molecular structure also in solution in methanol.

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