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Preliminary communication

SYNTHESIS OF AIR STABLE TRIORGANOTIN DERIVATIVES OF AMINO ACIDS

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SUMMARY

A series of air stable S-triorganostannyl derivatives of L-cysteine and DL-homocysteine has been prepared by reacting the appropriate triorganotin hydroxide or bis(triorganotin) oxide with the sulphydryl-containing amino acids in methanol/water at room temperature.

Triorganotin compounds, R_3SnX, where R = ^{n}Bu, Ph, cyclo-C_6H_{11} (Cy) and Neophyl (Np), are widely used in industry as biocides [1] and their biological activity is due to an interaction of the triorganotin moiety with certain proteins [2]. It has been suggested that both thiol [3] and histidine [4] residues are involved in binding the organotin compound and the recent interest [5,6,7] in organotin derivatives of the former type has prompted us to report our own preliminary results in this area. At physiological pH, the triorganotin derivative, R_3SnX, is likely to be present in the cell essentially as [8] the hydroxide, R_3SnOH, or the bis(oxide), $R_3SnOSnR_3$, and we have therefore studied the reactions of these compounds with the sulphydryl-containing amino acids, L-cysteine and DL-homocysteine, in polar media at room temperature.

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TABLE 1

Physical, Analytical and Mössbauer Data for S-Triorganostannyl Derivatives

	M Pt (°C)	Analysis Calculated (Observed)				^{119m}Sn Mössbauer data	
		C	H	N	S	δ^{a} (mm.s^{-1})	ΔE_Q (mm.s^{-1})
$Bu_3SnSCH_2CH_2CHNH_2COOH$	210 (d)	45.28(44.59)	8.25(8.34)	3.30(3.60)	7.55(6.93)	1.35	1.54
$Ph_3SnSCH_2CHNH_2COOH$	152 (d)	53.61(53.10)	4.47(4.40)	2.98(3.05)	6.81(6.98)	1.24	1.34
$Ph_3SnSCH_2CH_2CHNH_2COOH$	159-164	54.54(54.57)	4.75(4.66)	2.89(2.20)	6.61(5.72)	1.28	1.48
$Cy_3SnSCH_2CHNH_2COOH$	185-187	51.64(50.87)	7.99(8.05)	2.87(2.62)	6.56(6.25)	1.44	1.68
$Cy_3SnSCH_2CH_2CHNH_2COOH$	198-201	52.59(52.40)	8.17(8.06)	2.79(2.14)	6.37(5.66)	1.45	1.63
$Np_3SnSCH_2CHNH_2COOH$	200-203	62.07(61.55)	7.05(7.00)	2.19(2.08)	5.02(4.54)	1.36	1.79
$Np_3SnSCH_2CH_2CHNH_2COOH, H_2O$	154-220	60.89(60.99)	7.31(7.20)	2.09(1.84)	4.78(4.39)	1.35	1.70
$Ph_3Sn\text{-}SCH_2CHOH$ | $Ph_3Sn\text{-}SCH_2CHOH$	113-114	55.82(56.34)	4.46(4.63)	-	7.51(6.88)	b	b

[a] Relative to $CaSnO_3$. [b] Not determined.

On adding a methanol or methanol/ether solution of the bis(triorganotin) oxide (0.5 mol) or the triorganotin hydroxide (1 mol) to a solution of the amino acid (1 mol) in water at room temperature, a voluminous white precipitate of the S-triorganostannyl derivative is formed immediately (equations 1 and 2):

$$(R_3Sn)_2O + 2\ HS(CH_2)_nCHNH_2COOH \rightarrow 2R_3SnS(CH_2)_nCHNH_2COOH + H_2O \quad (1)$$

(n=1, R=Np; n=2, R= Bu or Np)

$$R_3SnOH + HS(CH_2)_nCHNH_2COOH \longrightarrow R_3SnS(CH_2)_nCHNH_2COOH + H_2O \quad (2)$$

(n= 1 or 2, R= Ph or Cy)

A slight warming of the solutions was found to be necessary to form the two trineophyltin derivatives. After filtration and drying at room temperature, the products were obtained analytically pure as air stable white powders, which could be recrystallised from aqueous methanol. Under the same conditions, however, we were unable to isolate pure derivatives using trimethyl- or triethyltin hydroxides and, in line with this, it has recently been found [6] that the ethyl ester of S-trimethylstannyl-cysteine is rather unstable on standing. The analytical and Mössbauer data for the new compounds are shown in Table 1. Mössbauer spectra were recorded at 80°K using a constant acceleration spectrometer which has been described previously [9].

All the compounds showed a strong band in their far infrared spectra at 327-338 cm^{-1}, confirming the presence of an Sn-S bond. The low values of the Mössbauer quadrupole splitting parameter, ΔE_Q (≤ 1.79 mm. s^{-1}) are characteristic [9] of a tetrahedral R_3SnX tin atom geometry, as found in the corresponding bis(triorganostannyl) sulphides, *e.g.* $Ph_3SnSSnPh_3$, which shows [10] $\delta = 1.20$ mm. s^{-1}, $\Delta E_Q = 1.46$ mm. s^{-1}, and is known [11] by X-ray crystallography to contain four-coordinate tin. The ν(CO) values found in the infrared spectra of the compounds (*ca.* 1630 cm^{-1}) are indicative of non-coordinating carbonyl groups, as in trimethyltin glycinate, where ν(CO) = 1630 cm^{-1} [12].

Although trialkylstannyl esters of amino acids, which are relatively sensitive to hydrolysis, have been known for some time [2,12], there are very few examples of stable organotin-amino acid derivatives [5,6,7] and these all contain the organometallic moiety bond *via* sulphur. An interesting comparison may be drawn here with mercaptoacetic acid, $HSCH_2COOH$, where reaction with 0.5 moles of a bis(triorganotin) oxide leads to substitution at the carboxyl group and not at sulphur [13].

We have also found that, under identical conditions, triphenyltin hydroxide (2 mol.) will react rapidly with dithiothreitol (1 mol.) to form the bis(S-triphenylstannyl) derivative (Table 1). This dithiol has recently been shown by Gould [14] to be capable of reversing the inhibition of the ATP synthases in chloroplasts by triphenyltin chloride. A similar derivative of 1,2-ethanedithiol has been reported by Poller [15].

Our work indicates that a facile reaction occurs between certain triorganotin hydroxides or oxides and biologically important mono- and di-thiols in polar media at room temperature. Reactions of this type are likely to be of considerable importance in understanding the mode of action of the triorganotin compounds. Further studies are under way to prepare stable triorganotin derivatives of histidine and these will be reported at a later date.

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