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Interaction of Organotin Compounds with Biological Ligands and the Molecular Structure of Ethyl L-Cysteinato S,N-(chlorodimethyl)stannate(IV)

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Although organotin compounds find many practical applications, their co-ordination by biological molecules is poorly understood [1]. We have investigated the binding of organotins by some biologically relevant thiol ligands and have found that reactions occur in aqueous medium and under mild conditions [2, 3].

The interaction of organotin chlorides with a number of ligands was investigated using a water/chloroform two phase solvent system. When equimolar quantities of reagents had been added together, the mixture was stirred thoroughly and adjusted to pH 7 with aqueous sodium hydroxide. The products in the chloroform layer were isolated and identified. A water/ethanol mixture was found to be a more convenient solvent for investigating reactions of organotin oxides with the ligands. Results of some reactions of trimethyltin chloride, tri-n-butyltin chloride, dimethyltin oxide and bis(tri-n-butyltin) oxide are summarized in the Table.

Details of the L-cysteine derivatives have already been published [2] and details of the other products will be published shortly.

Ligands which failed to form identifiable products under these conditions were 2-thiouracil, 2-amino 6-mercaptopurine, L-cystine, L-histidine, L-histidine methyl ester, DL-alanine, N-acetylglycine, 1-(2-mercaptoethyl), N^1-phenyl thiourea (in the last two cases it appeared that some reaction had occurred, but the products could not be identified).

These results may, in part, be contrasted with those of Aldridge *et al.*, who reported that under the conditions which they employed, Glutathione and B.A.L. were amongst the ligands which did not bind triorganotins [4]. It is interesting to note that the products formed in all cases (except that with L-cysteic acid) have Sn–S bonds.

Further, formation constants (obtained via potentiometric titrations) for L-cysteine, DL-alanine and L-histidine with trimethyltin chloride, indicate that L-cysteine binds far more readily than the other two amino acids. The equilibria concerned are complex and appear to involve polynuclear species in the range pH 7 to 9. If it is assumed that mononuclear species are formed in the range pH 5.5–6.5, then the formation constant values (pK_1) obtained under identical conditions are of the order: L-cysteine, *ca.* 10; DL-alanine, *ca.* 6; L-histidine, *ca.* 5.

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TABLE. Reaction Products from Ligand–Organotin Interaction.

Ligand (H_xL)	Products[a]	Characterization Methods
2-thiolethanol	Me_3SnL; Bu_3SnL	^1H, ^{13}C, N.M.R.
2-thiolaminoethane	Me_3SnL, $Me_2Sn(Cl)L$	^1H N.M.R., M.S.
B.A.L.[b]	$(Me_3Sn)_2L$, Me_2SnL[c]	^1H, ^{13}C N.M.R.
L-cysteine	Me_2SnClL, Bu_2SnClL	see ref. 2
DL-penicillamine	Me_2SnClL, Bu_2SnClL	see ref. 2
L-cysteine ethyl ester	Me_2SnClL, Me_3SnL Bu_2SnClL, Bu_3SnL	see refs. 2, 3
N-acetyl L-cysteine	$(Me_3Sn)_2L$, $(Bu_3Sn)_2L$	see ref. 3
L-cysteic acid	$(Bu_3Sn)_2L \cdot H_2O$	Microanalysis
Glutathione (reduced)	$(Bu_3Sn)_2L$	Microanalysis, ^{13}C N.M.R., I.R.
2-thiol 5-acetaminopyridine	Me_3SnL, Me_2SnL_2	^{13}C N.M.R., Microanalysis
4,6-dihydroxy 2-mercapto pyrimidine	Bu_3SnL	^{13}C N.M.R., Microanalysis
2′,3′-isopropylidene 6-mercapto riboside	Bu_3SnL	^1H N.M.R., ^{13}C N.M.R.

[a] Abbreviations employed in this Table are: methyl, Me; n-butyl, Bu; mass spectrometry, MS; infra-red spectroscopy, I.R. [b] 2,3-Dimercapto-1-propanol. [c] An insoluble white solid was obtained.

The crystal and molecular structure of the previously reported [2] compound ethyl L-cysteinato S,N-(chlorodimethyl)stannate(IV) has also been determined.

Crystal data: $C_7H_{16}O_2NClSSn$, M = 333.6, orthorhombic, space group $P2_12_12_1$, a = 6.658(5), b = 10.974(3), c = 17.144(5) Å, Z = 4, μ(CuKα) = 190.4 cm^{-1}. Intensities ($2\theta_{max}$ = 128°) were measured with CuKα radiation on a Rigaku-AFC four-circle diffractometer (graphite monochromator) with a θ–2θ scan. The structure was solved by the heavy-atom method and refined by full-matrix anisotropic least-squares with 1110 terms ($F_{obs} > 3\sigma F_{obs}$), absorption corrected to R = 0.057, H-atom parameters were not included.

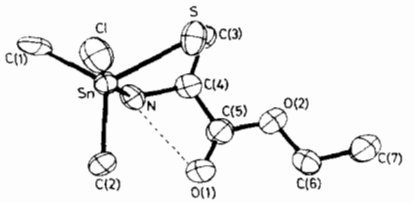

Figure. ORTEP plot of the structure of $(CH_3)_2Sn(Cl)SCH_2$-$CH(NH_2)COOC_2H_5$. Bonds about the tin atom: Sn–C(1) = 2.116(12); Sn–C(2) = 2.158(13); Sn–S = 2.413(2); Sn–Cl = 2.523(4); Sn–N = 2.434(12). Angles about the tin atom: C(1)–Sn–C(2) = 119.5(7)°; Cl–Sn–S = 86.8(1); N–Sn–S = 80.1(3); N–Sn–Cl = 166.9(3); C(1)–Sn–S = 119.3(4); C(1)–Sn–Cl = 94.4(5); C(1)–Sn–N = 92.3(5); C(2)–Sn–S = 120.5(5); C(2)–Sn–Cl = 96.9(6); C(2)–Sn–N = 89.6(7).

The stereochemistry of the complex is illustrated in the Figure. The ligand is S,N chelating with the tin atom in a distorted trigonal bipyramidal configuration. The tin lies 0.107(1) Å towards Cl from the plane of the C(1), C(2) and S atoms, while the more electronegative Cl and N atoms occupy the apical positions [5], giving a N–Sn–Cl angle of 166.9(3)°. The dimensions of the organic group do not differ significantly from those reported for similar ligands. The Sn–Cl bond distance is significantly longer than values reported for methyltin chloride [6], and dimethyltin chloride N,N,-dimethyldithiocarbamate [7]. The Sn–N bond distance is similar to that reported for trimethyltinglycinate [8], and other bond distances and angles agree well with values found for organotin complexes [9]. The five-membered chelate ring is characteristic of amino acid complexes [10] and has a 'bite' angle of 80.1(3)°.

For the organotin compounds with Sn–S bonds which have so far been studied, the structures appear to contain either four co-ordinate or five co-ordinate tin atoms. The diorganotin complexes appear to have structures similar to that of the title compound [2]. The triorganotin series can be assigned four co-ordinate tin structures on the basis of ^{13}C N.M.R. data [11], although higher co-ordination numbers are indicated for some complexes. For example, ligands which contain a favourably situated heterocyclic nitrogen atom (as in 2-thiol 5-nitropyridine [12]) are able to increase the co-ordination number.

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