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The X-ray Crystal Structure of Dichloro-S,S′-Bis(O-methylcysteinato)tin(IV): The First Determination of an Inorganic Tin–Amino Acid Derivative

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The crystal structure of dichloro-S,S′-bis(O-methylcysteinato)tin(IV), $Cl_2Sn\{SCH_2CH(NH_2)COOMe\}_2$*, has been solved by a three-dimensional Patterson synthesis: the crystals are orthorhombic, space group* $P2_12_12_1$*, with cell parameters* $a = 16.621(9)$, $b = 9.843(5)$, $c = 10.323(5)$ Å, $Z = 4$, *refined to* $R = 0.0356$ *for 1715 observable reflections. The tin is coordinated to two* cis- *nitrogen and two* trans- *sulphur atoms from the O-methylcysteinato ligands, and to two* cis- *chlorine atoms, in an approximately octahedral arrangement. The bond distances in the tin coordination sphere are: Sn–Cl 2.445 Å, Sn–S 2.434 Å and 2.446 Å, and Sn–N 2.264 Å and 2.309 Å. This structure is compared with those of other octahedral* cis-$Cl_2Sn(L_2)_2$ *complexes and the results of anti-tumour tests on these derivatives are reported. The lack of anti-tumour activity exhibited by the title compound may be associated with the large (99.4°)* cis-*Cl–Sn–Cl bond angle.*

Introduction

Although there have been several X-ray structural determinations of organotin derivatives of amino acids [1–3], there have been no such studies on the corresponding inorganic tin compounds. The organotin complexes of known structure have either inter- [1] or intra- [2, 3] molecular coordination of the amino acid ligands to the tin, *via* the amino N atoms (in preference to the carbonyl groups). Recent work on the vibrational spectra of a series of inorganic tin(II) and tin(IV) derivatives of both sulphur-containing and hydrocarbon chain amino acids [4, 5], including the title compound, is also consistent with the presence of tin-amino N bonds. We now report the determination of the crystal structure of dichloro-S,S′-bis(O-methylcysteinato)tin(IV), to establish the coordination preference of the amino acid ligands in inorganic tin(IV) complexes. Additional interest in the structures of this type of complex arises from the recent discovery that both organotin(IV) [6] and inorganic tin(IV) [7] halide adducts show anti-tumour activity. Moreover, since it has been suggested [8] that the magnitude of the Cl–M–Cl bond angle in metallocene dichlorides, $(\eta^5\text{-}C_5H_5)_2MCl_2$, may influence their antitumour properties, a knowledge of this angle in the title compound would be of considerable value.

Experimental

Preparation

Dichloro-S,S′-bis(O-methylcysteinato)tin(IV) was obtained as colourless crystals by allowing a methanolic mixture of tin(II) chloride (1 mol) and L-cysteine methyl ester hydrochloride (2 mol) to stand for 2 days [4, 5].

TABLE I. Final Fractional Atomic Co-ordinates (with standard deviations in parentheses).

Atom	x/a	y/b	z/c
Sn	0.3703(1)	−0.0260(1)	0.7236(1)
Cl(1)	0.2642(2)	−0.1940(3)	0.7592(3)
Cl(2)	0.4500(2)	−0.0639(3)	0.9194(3)
S(1)	0.2986(2)	0.1548(3)	0.8380(3)
S(2)	0.4455(2)	−0.1922(3)	0.5978(3)
N(1)	0.2969(7)	0.0526(10)	0.5547(10)
N(2)	0.4695(6)	0.1170(10)	0.6468(9)
O(1)	0.3499(5)	0.3141(8)	0.5381(9)
O(2)	0.2254(6)	0.3984(10)	0.5646(14)
O(3)	0.5575(5)	−0.0048(13)	0.3481(8)
O(4)	0.4402(5)	0.0990(10)	0.3851(8)
C(1)	0.2132(7)	0.1524(14)	0.7282(14)
C(2)	0.2391(7)	0.1634(12)	0.5867(14)
C(3)	0.2802(7)	0.2978(11)	0.5632(12)
C(4)	0.2575(13)	0.5383(15)	0.5447(28)
C(5)	0.5400(8)	−0.1001(16)	0.6067(13)
C(6)	0.5296(7)	0.0481(13)	0.5618(11)
C(7)	0.5029(7)	0.0542(14)	0.4240(11)
C(8)	0.5402(13)	−0.0187(28)	0.2138(18)
H(N11)	0.317(5)	0.074(9)	0.479(9)
H(N12)	0.280(8)	−0.019(16)	0.521(14)
H(N21)	0.492(6)	0.157(10)	0.710(12)
H(N22)	0.438(9)	0.156(16)	0.580(16)
H(C11)	0.175(8)	0.080(14)	0.756(15)
H(C12)	0.184(5)	0.219(9)	0.750(9)
H(C2)	0.188(7)	0.164(13)	0.550(12)
H(C41)	0.242(12)	0.533(22)	0.473(17)
H(C42)	0.305(14)	0.555(29)	0.563(26)
H(C43)	0.236(15)	0.420(29)	0.665(23)
H(C51)	0.560(5)	−0.107(8)	0.692(8)
H(C52)	0.575(8)	−0.133(13)	0.545(13)
H(C6)	0.580(6)	0.096(10)	0.568(10)
H(C81)	0.538(6)	0.073(10)	0.181(9)
H(C82)	0.494(10)	−0.007(21)	0.188(17)
H(C83)	0.589(9)	−0.053(17)	0.176(15)

Crystal Data

$C_8H_{16}N_2O_4S_2Cl_2Sn$, $M = 457.98$, Orthorhombic, $a = 16.621(9)$, $b = 9.843(5)$, $c = 10.323(5)$ Å, $U = 1688.8$ Å^3, $Z = 4$, $D_m = 1.70$, $D_c = 1.67$ g cm^{-3}, F(000) = 904; Space group $P2_12_12_1$ (No. 19), crystal dimensions 0.30 X 0.25 X 0.60 mm; $\mu = 19.4$ cm^{-1}.

Data Collection

Intensity data were collected using a Philips PW 1100 four-circle diffractometer in the range $4 \leqslant 2\theta \leqslant 50°$, with Mo-K$\alpha$ radiation. Using the criterion $I \geqslant 3\sigma(I)$, 1715 of the 1735 recorded intensities were independent and observable. The data were corrected for Lorentz and polarisation effects, but not for absorption.

TABLE II. Bond Distnces (Å) and Bond Angles (°) (with standard deviations in parentheses).

Bond Distances		Bond Angles	
Sn–Cl(1)	2.445(3)	Cl(1)–Sn–Cl(2)	99.4(1)
Sn–Cl(2)	2.445(3)	Cl(1)–Sn–S(2)	89.7(1)
Sn–N(1)	2.264(10)	Cl(1)–Sn–N(1)	87.6(3)
Sn–N(2)	2.309(10)	Cl(1)–Sn–S(1)	93.9(1)
Sn–S(1)	2.446(3)	Cl(1)–Sn–N(2)	168.2(2)
Sn–S(2)	2.434(3)	Cl(2)–Sn–S(2)	93.5(1)
S(1)–C(1)	1.816(12)	Cl(2)–Sn–N(1)	168.7(3)
C(1)–C(2)	1.527(19)	Cl(2)–Sn–S(1)	88.6(1)
C(2)–N(1)	1.490(15)	Cl(2)–Sn–N(2)	89.4(2)
C(3)–C(2)	1.509(16)	S(2)–Sn–N(1)	95.5(3)
O(1)–C(3)	1.198(13)	S(2)–Sn–S(1)	175.4(1)
O(2)–C(3)	1.345(14)	S(2)–Sn–N(2)	81.9(2)
C(4)–O(2)	1.491(19)	N(1)–Sn–S(1)	82.0(3)
C(5)–S(2)	1.816(14)	N(1)–Sn–N(2)	85.0(4)
C(6)–C(5)	1.540(18)	S(1)–Sn–N(2)	94.0(2)
C(6)–N(2)	1.492(14)		
C(7)–C(6)	1.492(16)		
O(4)–C(7)	1.201(14)		
O(3)–C(7)	1.332(14)		
C(8)–O(3)	1.422(19)		

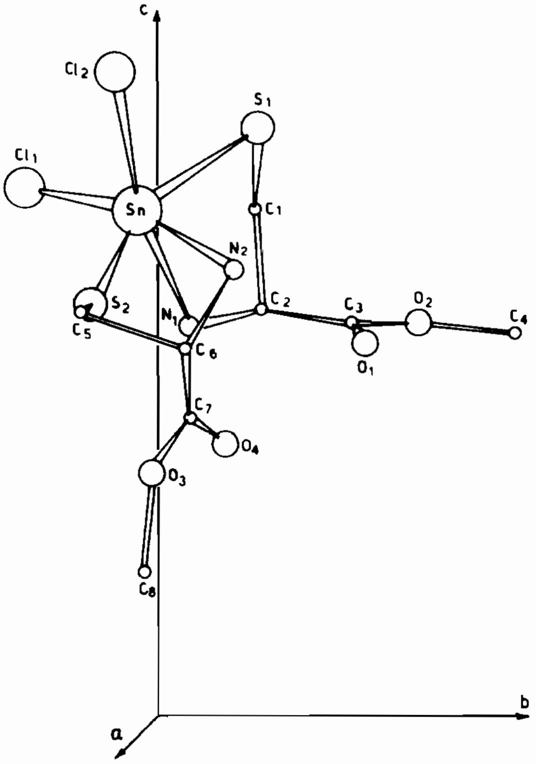

Fig. 1. Molecular structure and atomic labelling for dichloro-S,S'-bis(O-methylcysteinato)tin(IV).

TABLE III. Chelating Ring Size, Cl–Sn–Cl Bond Angle (with standard deviations in brackets), and Anti-tumour Activity of *cis*-$Cl_2Sn(L_2)_2$ Complexes.

Complex	Chelate ring size	ClSnCl	T/C (%)[a]	Ref.[b]
$Cl_2Sn\{SCH_2CH(NH_2)COOMe\}_2$	5-membered	99.4(1)°	91–98	[c]
$Cl_2Sn\{SCH_2CH(NH_2)COOEt\}_2$	5-membered	[d]	99–102	–
$Cl_2Sn(ONPhCOPh)_2$	5-membered	99.0(2)°	[d]	11
$Cl_2Sn(OCMe.CHCOOEt)_2$	6-membered	98.1(1)°	[d]	12
$Cl_2Sn(acac)_2$	6-membered	96.9(1)°	[e]	14
$Cl_2Sn(SC_5H_4N\text{-}2)_2$	4-membered	94.8(1)°	86–105	15

[a] Ratio of survival times (days) of treated mice and untreated animals; a compound is active if the maximum T/C ⩾ 120%. The values refer to all tests performed (up to 400 mg/kg dosage). [b] X-ray structure. [c] This work. [d] Not determined. [e] Inactive [13].

Structure Determination and Refinement

The molecular structure was solved by different electron-density syntheses from a three-dimensional Patterson. A full-matrix least-squares refinement of F was computed, minimising the function $\Sigma_w (|F_o| - |F_c|)^2$, where w = 1. Scattering factors given in ref. [9] were used. The Sn, Cl, C, N, S and O atoms were refined anisotropically; all the H atoms were found and refined isotropically. For the 1715 observed reflections, the final conventional R value was 0.0356. The atoms of the terminal OMe groups are affected by relatively high thermal parameters. The usual crystallographic programs [10] were used.

The molecular structure of the complex is shown in Fig. 1. The final atomic coordinates are listed in Table I and intramolecular bond distances and angles are given in Table II. Observed and calculated structure factors, together with their thermal parameters, may be obtained from the Editor on request.

Discussion

The crystal structure of dichloro-S,S′-bis(O-methylcysteinato)tin(IV) consists of discrete covalent units containing two *cis-* chlorine atoms and two bidentate O-methylcysteinato ligands. Figure 1 shows that the two nitrogen and two sulphur atoms are *cis-* and *trans-* respectively. The observed coordination to tin through the nitrogens of the NH_2 groups and the absence of tin–carbonyl oxygen bonds, is in accord with our infrared studies [4, 5].

The bond lengths and bond angles (Table II) indicate a distorted octahedral arrangement about the tin atom. The Sn–Cl bond lengths are equal, but the differences between the two Sn–N and two Sn–S bond distances (0.045 Å and 0.012 Å respectively), are greater than the standard deviations in the measurement of the bond lengths. The bond angles in the tin coordination sphere deviate from regular octahedral angles by differing amounts, depending upon the ligand. A least-squares analysis of the coordination planes shows that the maximum deviation of the tin atom from the centre of an octahedron is 0.11 Å.

It is of interest to compare the structure of dichloro-S,S′-bis(O-methylcysteinato)tin(IV) with those of other octahedral *cis*-$Cl_2Sn(L_2)_2$ complexes (Table III). In all cases, the atoms in the chelate ring are essentially co-planar with the tin, except in $Cl_2Sn(ONPhCOPh)_2$, where the metal atom lies substantially out of the ligand plane [11].

The only other tin(IV) complex of known structure that contains two Cl, two N and two S atoms bonded to the metal is dichlorobis(2-pyridinethiolato)tin(IV), $Cl_2Sn(SC_5H_4N\text{-}2)_2$ [15]. Interestingly, the ^{119m}Sn Mössbauer isomer shift, δ of this compound (0.80 mm s^{-1}), is similar to that of the title compound (0.85 mm s^{-1}), but a difference arises in the quadrupole splitting, ΔE_Q, which, for $Cl_2Sn(SC_5H_4N\text{-}2)_2$, is 0.68 mm s^{-1}, and, for $Cl_2Sn\{SCH_2CH(NH_2)COOMe\}_2$, is 1.34 mm s^{-1} [5]. The comparable values of δ for the two complexes suggest that the total use of *s*-electron density in the bonding of the tin to the organic ligands is similar, and the large difference in ΔE_Q is indicative of an electric field gradient which is very sensitive to slight changes in the tin atom environment. The main difference between the structures of the two compounds is the presence of two four-membered rings condensed with pyridine units in $Cl_2Sn(SC_5H_4N\text{-}2)_2$. The depletion of π-electron density from the pyridine ring appears to be responsible for the decrease in the C–C, C–N, C–S, and Sn–N bond distances in this compound [15] with respect to those in the O-methylcysteine derivative. Hence, the N → Sn interactions in the title compound are weaker than those in $Cl_2Sn(SC_5H_4N\text{-}2)_2$, resulting in a larger crystal field, and, consequently, a larger value of ΔE_Q.

Köpf-Maier *et al.* [8] have recently suggested that the magnitude of the Cl–M–Cl angle in metallocene dichlorides, $(\eta^5\text{-}C_5H_5)_2MCl_2$, where M = Ti, Zr, Hf, V or Mo, may be an important factor in determining their anti-tumour properties, and, more specifically, that, for antitumour activity to occur, the Cl–M–Cl angle must be in the range *ca.* 82.0–94.5°. Since two inorganic tin(IV) halide adducts, *viz.* $SnCl_4$·phen (T/C = 98–123%) and $SnCl_4$·bipy (T/C = 115–130%), are known to exhibit mild anti-tumour activity [7], some of the compounds in Table III were tested for activity *in vivo* towards P388 lymphocytic leukaemia in mice, in accordance with U.S. National Cancer Institute Standard protocols for primary screening [16]. It can be seen from Table III that none of the complexes screened in this study exhibit anti-tumour activity, and, in accordance with the suggestion of Köpf-Maier *et al.*, none of the Cl–Sn–Cl bond angles are less than 94.5°. Additionally, recent studies by Denechaud *et al.* [17], using mice implanted with solid tumours, has shown that the octahedral complex, dichlorotin(IV)-tetraammonium-*meso*-tetra-*p*-sulphophenylporphyrin, $Cl_2Sn\cdot TPP(SO_3^-NH_4^+)_4$, in which the chlorine atoms, by necessity, are occupying *trans*- positions, exhibits no anti-tumour activity.

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