PHENYLTIN DIETHYLDITHIOCARBAMATES: SOLID STATE AND SOLUTION STRUCTURES AND *IN VITRO* ANTI-TUMOUR ACTIVITY

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Abstract.

Solution and cross-polarized magic-angle spinning (CP-MAS) solid state NMR data (¹³C and ¹¹⁹Sn) for a series of phenyltin diethyldithiocarbamate compounds and the crystal structures of a *tetragonal* modification of [Ph₂Sn(dedtc)₂] and of [Ph₃Sn(dedtc)] are reported. A strong correspondence between the solution and solid state structures of these compounds has been discovered. The phenyltin diethyldithiocarbamate compounds have been evaluated for activity against the L1210 mouse leukemia cell line. They have been found to be as least as active as cisplatin, but there is no obvious structure-activity correlation.

Introduction.

A recent review of the structural chemistry of the tin 1,1-dithiolates has shown that there exists a large diversity among even closely related compounds [1]. Of the tin 1,1-dithiolates, the best studied compounds are those containing the dialkyl- or diaryl-dithiocarbamate ligands (⁻S₂CNR'₂) and some of the more interesting structural motifs are found in this category. It is likely that the different structures arise as a result of a subtle combination of steric and electronic factors, related to both the tin centre and to the ligand. Crystal structure determinations for the following complexes: [PhSn(dedtc)₃] [2], [PhSn(dedtc)₂Cl] [3, 4], [Ph₂Sn(dedtc)₂] [5, 6] and [Ph₂Sn(dedtc)Cl] [7], where

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dedtc is diethyldithiocarbamate, are available in the literature. Multinuclear magnetic resonance studies are invaluable in structure assignment in such systems as shown recently [7] and solid state NMR techniques, in particular, have proven useful in assigning structure for dimethyltin dithiocarbamates [8, 9]. Whereas solution NMR studies provide information on the average structure owing to rapid intramolecular processes, the solid state NMR data should mirror more closely the structure deduced from X-ray crystal structure analysis as the molecules are effectively 'locked' into place by intermolecular forces.

The focus of the present report is to correlate the solution and solid state structures for a series of phenyltin diethyldithiocarbamate compounds. The diethyldithiocarbamate ligand is known to adopt different modes of coordination [1] and it is of interest to determine precisely which factors are responsible for this behaviour as the Lewis acidity of the tin atom is altered. Hence, this contribution describes the crystal structure determinations of *tetragonal*-[Ph₂Sn(dedtc)₂] and [Ph₃Sn(dedtc)] as well as solution and solid state ¹³C and ¹¹⁹Sn NMR data for these and related derivatives.

The investigation of the anti-tumour activity of organotin compounds is an area of current interest [10-12]. Previous studies of the anti-tumour activity of tin dithiocarbamate compounds have suggested that Sn(IV) compounds are more active than Sn(II) derivatives [13, 14] but nothing is known, however, about the activity of analogous organotin(IV) dithiocarbamates, although a series of related organotin xanthates (where the xanthate anion is 'S₂COR') shows promising *in vitro* anti-tumour activity [15]. Hence, it was thought worthwhile to examine the anti-tumour activity of the compounds employed in this study to ascertain whether there existed any relationship between the number of tin-bound phenyl substituents and anti-tumour activity as measured against a murine L1210 cell line.

Experimental.

Preparations. The following compounds were prepared employing standard literature procedures: [PhSn(dedtc)₃] [16], [PhSn(dedtc)₂Cl] [16], [Ph₂Sn(dedtc)₂] [6], [Ph₂Sn(dedtc)Cl] [17] and [Ph₃Sn(dedtc)] [18]. Crystal structure determinations have also been performed on the tetragonal modification of [Ph₂Sn(dedtc)₂] and on [Ph₃Sn(dedtc)].

Solution NMR. ^{13}C and ^{119}Sn NMR spectra were measured in CDCl_3 solution (100 - 250 mg/3 ml) on Bruker ACP-300 spectrometers operating at 75.47 and 111.922 MHz, respectively. Carbon chemical shifts, δ_{C} , are reported with respect to tetramethylsilane as an internal standard. Tin chemical shifts, δ_{Sn} , are reported with respect to tetramethyltin as an external standard. Composite pulse decoupling was used to remove any ^1H -X coupling. In particular, ^{119}Sn spectra were acquired with spectral widths of 15 kHz and an acquisition time of 1.45 s. A relaxation delay of 1.5 s was used together with a pulse width of 24 μs (90°). These conditions were more than adequate to prevent saturation since the ^{119}Sn T_1 values were less than 2 s in solution (see Table 6). Free induction decays (FID's) were multiplied by an exponential line broadening function (1-2 Hz), zero-filled to 32 K data points prior to Fourier transformation. T_1 data were acquired using an inversion-recovery sequence (-180-t-90-acquire), and processed using standard Bruker software.

Solid state NMR. Solid state ^{119}Sn and ^{13}C NMR spectra were recorded on a Bruker MSL 300S spectrometer operating at 111.922 and 75.47 MHz, respectively. Samples of approximately 100 mg were packed into 4 mm o.d. zirconia double-bearing rotors and subjected to 'magic angle spinning' (MAS) at speeds ranging from 3 - 11 kHz. Conditions for cross-polarization (CP) were determined as follows: pulse times for ^{119}Sn NMR were 3.5 - 4.0 μs (90°) with 1 - 2 ms contact times and 8 - 20 s recycle times using tetracyclohexyltin as a secondary external standard, $\delta_{\text{Sn}} = -97.4$ ppm [19]. Power levels for optimum CP had to be readjusted for ^{119}Sn NMR spectra acquired at higher speeds. The isotropic peak, σ_{iso} , in each spectrum was identified by comparing spectra acquired at various speeds. The spectral width was varied from 125 - 172 kHz over 2 K data points to accommodate the chemical shift anisotropy of the tin samples which ranged from 400 - 900 ppm. The FID's were multiplied by an exponential line broadening function of 50 - 300 Hz zero filled to 4 K data points prior to Fourier transformation. Acquisition of between 3000 - 6000 scans was necessary to give spectra of adequate signal to noise (S/N). For ^{13}C NMR spectra, pulse times of between 3.5 - 4.0 μs (90°) were determined using adamantane as a standard, with chemical shifts relative to the resonance of the methylene carbon of this compound, $\delta_{\text{C}} = 37.8$ ppm. Contact times of 2 ms and recycle times of 5 s were used. Spinning the samples at 10 kHz was usually sufficient to remove the spinning side bands. The spectral width was 20 - 30 kHz with a time domain of 2 K data points. Between 1000 - 4000 scans were accumulated before multiplying the FID by an exponential line broadening function (1 - 5 Hz), zero filling to 8 K data points and Fourier transformation.

Crystallography. Crystal data and refinement details for both determinations are collected in Table 1. In each case intensity data for a colourless crystal were measured at room temperature on a Rigaku AFC6R four-circle diffractometer fitted with graphite monochromatized MoK α radiation, $\lambda = 0.71073$ Å employing the $\omega:2\theta$ scan technique to $\theta_{\max}$ 27.5°. Each data set was corrected for Lorentz and polarization effects [20] and for absorption employing the DIFABS program [21].

Table 1. Crystal data for *tetragonal*-[Ph₂Sn(dedtc)₂] and for [Ph₃Sn(dedtc)]

	[Ph ₂ Sn(dedtc) ₂]	[Ph ₃ Sn(dedtc)]
Formula	C ₂₂ H ₃₀ N ₂ S ₄ Sn	C ₂₃ H ₂₅ NS ₂ Sn
Mol. wt.	569.4	498.3
Crystal system	tetragonal	orthorhombic
Space group	<i>P</i> 4 ₁ 2 ₁ 2 (D ₄ ⁴ , No. 92)	<i>Pbca</i> (D _{2h} ¹⁵ , No. 61)
<i>a</i> , Å	9.866(3)	16.863(2)
<i>b</i> , Å	9.866(3)	23.444(3)
<i>c</i> , Å	26.679(3)	10.946(3)
<i>V</i> , Å ³	2597(1)	4327(1)
<i>Z</i>	4	8
<i>D</i> _C , g cm ⁻³	1.456	1.530
Crystal size, mm	0.35 dia.	0.05 x 0.10 x 0.17
<i>F</i> (000)	1160	2016
μ , cm ⁻¹	13.17	12.64
No. of data collected	1900	5746
No. of unique reflections used with <i>I</i> > 3.0 σ (<i>I</i>)	1654	2348
<i>R</i>	0.033	0.038
<i>R</i> _w	0.048	0.054
Residual $\rho_{\max}$, e Å ⁻³	0.46	0.60

Each structure was solved by direct methods [22] and refined by a full-matrix least-squares procedure based on F [20]. Non-H atoms were refined with anisotropic thermal parameters and H-atoms were included in the model at their calculated positions (C-H 0.97 Å). At convergence $R = 0.033$ and $R_w = 0.048$ (sigma weights [20]) for *tetragonal*-[Ph₂Sn(dedtc)₂] and $R = 0.038$ and $R_w = 0.054$ (sigma weights) for [Ph₃Sn(dedtc)]. The analysis of variance showed no special features in either case. The final fractional atomic coordinates are listed in Table 2 and the crystallographic numbering schemes used are shown in Figures 2 and 4, which were drawn with ORTEP [23] at 15% and 30% probability ellipsoids, respectively. Data manipulation was performed with the teXsan package [20] installed on an Iris Indigo workstation.

In vitro anti-tumour testing. L1210 mouse leukaemia cells were grown as suspension cultures in MEM (Eagle's Minimum Essential Medium) plus 1% glutamine and 10% foetal calf serum (Flow Laboratories). The compounds were dissolved in DMSO at 10 concentrations over a 3-log range, with a final maximum DMSO concentration in the medium of 0.5%. Growth inhibition was tested by incubation of log-phase cells at 37°C in a humidified incubator gassed with 10% CO₂/90% air for 48 h in the presence of the compound. Cells were then counted using a Coulter counter, and the ID₅₀ in $\mu\text{mol dm}^{-3}$, or dose causing 50% inhibition of cell growth, was determined from the curve of percentage growth versus dose. All assays were performed in duplicate. Control cultures exposed only to the vehicle were included with each test.

Results and Discussion.

Crystallography and ¹³C CP-MAS NMR Correlations

The ¹³C CP-MAS NMR spectra for the five phenyltin dithiocarbamate compounds have been recorded for samples recrystallized from acetone solution; the spectra are reproduced in Figure 1 and chemical shift values are listed in Table 3. In the following discussion, the spectra are correlated in turn with known and new results of crystal structure determinations for these compounds.

[PhSn(dedtc)₃] The crystal structure of [PhSn(dedtc)₃] has been reported recently [2]. The Sn atom exists in a distorted pentagonal bipyramidal geometry with the three dedtc ligands chelating the Sn centre. Two of the dedtc ligands occupy equatorial positions exclusively whereas the third spans both an axial and an equatorial site; the remaining axial site is occupied by the phenyl substituent. More significantly, one of dedtc ligands

Table 2. Fractional atomic coordinates

<i>tetragonal-[Ph₂Sn(dedtc)₂]</i>			
Atom	x	y	z
Sn	0.94059(5)	0.94059(5)	0.0(-)*
S(1)	0.9116(2)	1.0641(2)	0.08352(7)
S(2)	1.1774(2)	0.9985(2)	0.04251(7)
N(1)	1.1426(7)	1.1580(7)	0.1200(2)
C(1)	1.0859(7)	1.0833(7)	0.0859(2)
C(2)	1.0674(10)	1.2288(9)	0.1577(3)
C(3)	1.0510(12)	1.1496(11)	0.2043(3)
C(4)	1.2876(8)	1.1782(10)	0.1216(3)
C(5)	1.3271(10)	1.2971(10)	0.0877(3)
C(11)	0.7313(7)	0.9543(8)	-0.0215(2)
C(12)	0.6444(8)	1.0458(9)	0.0018(3)
C(13)	0.5102(9)	1.0500(11)	-0.0114(3)
C(14)	0.4614(9)	0.9645(12)	-0.0481(3)
C(15)	0.5512(11)	0.8802(10)	-0.0714(3)
C(16)	0.6804(9)	0.8743(9)	-0.0581(3)
* site occupancy factor 0.5			
<i>[Ph₃Sn(dedtc)]</i>			
Atom	x	y	z
Sn	0.39859(4)	0.34423(3)	0.10152(7)
S(1)	0.3306(2)	0.4210(1)	0.2075(3)
S(2)	0.2540(2)	0.3984(1)	-0.0286(3)
N(1)	0.1913(5)	0.4603(4)	0.1486(8)
C(1)	0.2511(6)	0.4297(4)	0.1081(10)
C(2)	0.1184(6)	0.4678(5)	0.0779(11)
C(3)	0.1146(7)	0.5220(5)	0.0149(13)
C(4)	0.1914(7)	0.4884(4)	0.2665(11)
C(5)	0.1623(8)	0.4512(5)	0.3671(11)
C(11)	0.3363(6)	0.2658(4)	0.0903(11)
C(12)	0.2860(6)	0.2505(6)	-0.0030(11)
C(13)	0.2511(7)	0.1964(5)	-0.0031(13)
C(14)	0.2648(8)	0.1576(6)	0.0857(13)
C(15)	0.3152(9)	0.1709(5)	0.1744(13)
C(16)	0.3510(7)	0.2249(5)	0.1772(11)
C(21)	0.4669(6)	0.3740(5)	-0.0499(9)
C(22)	0.5116(7)	0.3355(5)	-0.1155(11)
C(23)	0.5623(8)	0.3584(7)	-0.2072(11)
C(24)	0.5662(9)	0.4140(6)	-0.2283(14)
C(25)	0.5220(8)	0.4493(6)	-0.1648(13)
C(26)	0.4726(7)	0.4298(4)	-0.0754(11)
C(31)	0.4796(6)	0.3321(4)	0.2475(11)
C(32)	0.4579(6)	0.3386(5)	0.3682(10)
C(33)	0.5082(8)	0.3288(5)	0.4613(11)
C(34)	0.5849(8)	0.3136(6)	0.4388(12)
C(35)	0.6095(7)	0.3079(5)	0.3206(13)
C(36)	0.5574(6)	0.3166(5)	0.2260(10)

Figure 1. 75.47 MHz ^{13}C solid state CP MAS NMR spectra of phenyltin diethyldithiocarbamates at 10 kHz running speed: (a) $[\text{PhSn}(\text{dedtc})_3]$, (b) $[\text{PhSn}(\text{dedtc})_2\text{Cl}]$, (c) $[\text{Ph}_2\text{Sn}(\text{dedtc})_2]$, (d) $[\text{Ph}_2\text{Sn}(\text{dedtc})\text{Cl}]$, and (e) $[\text{Ph}_3\text{Sn}(\text{dedtc})]$.

Table 3. Carbon-13 CP-MAS NMR (and CDCl₃ solution) spectroscopic data (ppm)^a

Compound	S ₂ C	Ph	CH ₂	CH ₃
[PhSn(dedtc) ₃]	199.6, 197.7 (197.6)	156.9, 129.8, 129.0, 127.8 (142.7, 136.7, 128.5, 129.0) ^b	50.6, 50.1 (50.5)	13.4, 12.0, 11.3 (12.1)
[PhSn(dedtc) ₂ Cl]	195.7, 193.7 (197.1)	157.5, 131.7, 130.2, 127.6 (n.o., 131.5, 128.3, 128.9)	55.1, 54.6, 50.5 (51.2)	15.7, 13.5, 11.4, 8.0 (12.0)
[Ph ₂ Sn(dedtc) ₂]	195.2, 194.4 (198.1)	156.5, 154.6, 131.7, 126.9 (151.8, 134.2, 128.0, 128.2)	52.0, 50.3, 49.2, 48.2 (50.2)	12.0, 11.5, 9.5 (12.1)
[Ph ₂ Sn(dedtc)Cl]	193.0 (189.9)	144.0, 137.7, 135.7, 133.6, 130.4 (142.0, 135.7, 128.8, 130.1)	52.0, 49.9 (50.8)	9.2 (12.1)
[Ph ₃ Sn(dedtc)]	193.3, 192.6 (197.6)	141.6 - 127.7 ^c (142.7, 136.7, 128.5, 129.0)	50.1, 49.7, 47.6, 47.1 (50.5)	12.1, 10.6 (12.1)

^a solution data are listed in parentheses; ^b assigned to C α , C β , C γ and C δ , respectively; ^c nine signals in this region

chelates the Sn centre quite symmetrically ($\Delta\text{Sn-S}$ is 0.068 Å) compared with the other two ($\Delta\text{Sn-S}$ 0.299 and 0.195 Å). Two resonances are observed, in the ratio 1:2, in the ^{13}C CP-MAS NMR spectrum in the S_2C region. The downfield resonance is assigned to the thiocarbonyl atom of the more symmetrically chelating ligand on the basis of the integration of the two peaks in this region. Moreover, symmetrically coordinated dithiolate ligands would give rise to downfield shifts for the thiocarbonyl carbon atom relative to asymmetrically coordinating ligands [24]. In solution only one resonance is observed in this region indicating magnetic equivalence of the dedtc ligands. Resonances in the region 156.9 to 127.8 ppm are assigned to the Sn-bound phenyl groups and, as in the subsequent spectra, are not particularly informative for structure assignment/correlation. From the lack of crystallographic symmetry in $[\text{PhSn}(\text{dedtc})_3]$, a total of six non-equivalent methylene C resonances may be anticipated and similarly six resonances are expected for the methyl C atoms. In the solid state NMR spectrum, however, only two and three resonances are resolved, respectively; in CDCl_3 solution only one resonance is found in each region.

$[\text{PhSn}(\text{dedtc})_2\text{Cl}]$ The Sn atom in this compound is in a six coordinate, distorted octahedral geometry defined by two chelating dedtc ligands, the phenyl substituent and a Cl atom. Accordingly, in the ^{13}C CP-MAS NMR spectrum there are two resonances in the S_2C region with the downfield resonance being assigned to the S_2C atom associated with the more symmetrically chelating dedtc ligand ($\Delta\text{Sn-S}$ 0.046 cf. 0.137 Å); see above. In the CH_2 region there are two distinct resonances of equal intensity, one of which is resolved into two peaks; four peaks would be anticipated on the basis of the crystallographic result. In the CH_3 region, four peaks of equal intensity are observed in accord with expectation.

$[\text{Ph}_2\text{Sn}(\text{dedtc})_2]$ The crystal structure of $[\text{Ph}_2\text{Sn}(\text{dedtc})_2]$ [5, 6] is unusual when compared with other $[\text{R}_2\text{Sn}(\text{S}_2\text{Y})_2]$ (where $\text{Y} = \text{NR}'_2$ and OR) compounds [1]. The majority of structures with this general formula have the Sn atom in skew-trapezoidal bipyramidal geometries in which the dithiolate ligands chelate the Sn centre with asymmetric Sn-S distances (ca 2.5 and 3.0 Å); the organic substituents are disposed as to lie over the weaker Sn-S interactions. By contrast, the structure of $[\text{Ph}_2\text{Sn}(\text{dedtc})_2]$, which has been the subject of two independent investigations [5, 6], shows the Sn atom to exist in a distorted octahedral geometry in which the two dedtc ligands chelate the Sn atom, one forming symmetrical Sn-S bonds ($\Delta\text{Sn-S}$ 0.024 Å) and the other coordinating more asymmetrically ($\Delta\text{Sn-S}$ 0.242 Å). Given the interesting structure for this

derivative it was thought worthwhile to investigate further the crystal structure of this compound.

The reported crystal structure determinations of $[\text{Ph}_2\text{Sn}(\text{dedtc})_2]$ used methylethylketone [5] and ethanol/dichloromethane [6] as the recrystallization solvents. Similar unit cell data to that reported was also obtained from the recrystallization of $[\text{Ph}_2\text{Sn}(\text{dedtc})_2]$ from both acetone and CHCl_3 solutions of the compound. However, from the slow evaporation of an acetone solution of the compound, a second polymorph was also obtained, i.e. *tetragonal*- $[\text{Ph}_2\text{Sn}(\text{dedtc})_2]$; this polymorph was also isolated from a acetonitrile/dichloromethane (1/1) solution of the compound. The molecular structure of *tetragonal*- $[\text{Ph}_2\text{Sn}(\text{dedtc})_2]$ is shown in Figure 2 and selected interatomic parameters are listed in Table 4.

Figure 2. Molecular structure of *tetragonal*- $[\text{Ph}_2\text{Sn}(\text{dedtc})_2]$.

Table 4. Selected bond distances (Å) and angles (°) for *tetragonal*-[Ph₂Sn(dedtc)₂]

Sn-S(1)	2.556(2)	Sn-S(2)	2.659(2)
Sn-C(11)	2.148(7)	S(1)-C(1)	1.731(7)
S(2)-C(1)	1.690(7)	C(1)-N(1)	1.297(8)
N(1)-C(2)	1.43(1)	N(1)-C(4)	1.45(1)
S(1)-Sn-S(2)	67.91(6)	S(1)-Sn-C(11)	95.4(2)
S(1)-Sn-S(1')*	150.1(1)	S(1)-Sn-S(2')	88.67(7)
S(1)-Sn-C(11')	103.5(2)	S(2)-Sn-S(2')	78.72(9)
S(2)-Sn-C(11)	160.9(2)	S(2)-Sn-C(11')	92.2(2)
C(11)-Sn-C(11')	101.1(4)	Sn-S(1)-C(1)	88.5(2)
Sn-S(2)-C(1)	85.9(2)	C(1)-N(1)-C(2)	123.1(7)
C(1)-N(1)-C(4)	121.8(7)	C(2)-N(1)-C(4)	115.1(7)
S(1)-C(1)-S(2)	116.8(4)	S(1)-C(1)-N(1)	121.1(6)
S(2)-C(1)-N(1)	122.1(6)		

* Primed atoms are related by the symmetry operation: $y, x, -z$.

Figure 3. Unit cell contents for *tetragonal*-[Ph₂Sn(dedtc)₂].

The structure of *tetragonal*-[Ph₂Sn(dedtc)₂] has crystallographic two-fold symmetry such that half the molecule defines the asymmetric unit. The structure is molecular there being no significant intermolecular contacts in the crystal lattice; the closest non-hydrogen contact occurs between the C(1) and C(5)^a atoms of 3.59(1) Å (symmetry operation a: 2.5-x, -0.5+y, 0.25-z). A view of the crystal structure is shown in Figure 3. The molecular structure is in essential agreement with the original, i.e. *monoclinic*-form, in that the Sn atom exists in a distorted octahedral geometry defined by two symmetry related, chelating dedtc ligands and two phenyl groups; the C-Sn-C angle is 101.1(4)°. It is interesting to note that the degree of asymmetry in the mode of coordination of the dedtc ligand is intermediate, i.e. ΔSn-S is 0.103 Å, between the two Sn-S values found in the *monoclinic* form (see above). The two C-S bond distances reflect the disparate Sn-S bonds with the longer C-S bond being associated with the shorter Sn-S bond distance. The relatively short C-N bond distance of 1.297(8) Å indicates a substantial localization of π-electron density in this bond. Consistent with this observation is the planarity of the S₂CN moiety with deviations from the least-squares plane of 0.000(2), 0.000(2), 0.003(7) and -0.006(6) Å for the S(1), S(2), N(1) and C(1) atoms, respectively; the Sn atom lies -0.384(1) Å out of this plane. The phenyl ring is planar to ± 0.02(1) Å with the Sn atom -0.060(1) Å out of the plane. In summary, the structure of the *tetragonal*-polymorph is a more symmetric form of the two polymorphs with the molecular geometries about the Sn atoms in each being in essential agreement with each other.

The ¹³C CP-MAS NMR spectrum was recorded for [Ph₂Sn(dedtc)₂] recrystallized from acetone solution, i.e. a sample containing both the *monoclinic*- and *tetragonal*-polymorphs. Assuming that the sample was a 50:50 mixture, (it was not possible to determine precisely the relative proportions of the polymorphs present in the sample) three, six and six distinct S₂C, CH₂ and CH₃ resonances would be expected, not allowing for accidental magnetic equivalence. Two resonances are discernable in the S₂C region, one being a shoulder of the other, four peaks are resolved from a complex multiplet in the CH₂ region and similarly three peaks are observed in the CH₃ region; see Table 3.

[Ph₂Sn(dedtc)Cl] The Sn atom in this structure exists in an distorted trigonal bipyramidal geometry in which the dedtc ligand is considered to be chelating; Sn-S: 2.445(1) and 2.716(1) Å. The Cl atom and the S atom forming the weaker Sn-S interaction occupying the axial positions. As there is only one dedtc ligand in this molecule a relatively simple ¹³C CP-MAS NMR spectrum may be anticipated. This is the

case with one, two and one resonances being observed in the S_2C , CH_2 and CH_3 regions, respectively.

[$Ph_3Sn(dedtc)$] The crystal structure of this compound has been determined in the present study and the molecular structure is illustrated in Figure 4 with selected interatomic parameters listed in Table 5. The structure is molecular with the closest intermolecular contact between non-hydrogen atoms being 3.60(1) Å for $S(2)...C(4)^b$

Figure 4. Molecular structure of [$Ph_3Sn(dedtc)$].

(symmetry operation b: 0.5-x, 1-y, -0.5+z); a view of the unit cell contents is shown in Figure 5. The Sn atom in this structure may be considered as existing in a distorted

tetrahedral geometry defined by the three phenyl substituents and a S atom derived from a monodentate dedtc ligand (Sn-S 2.428(3) Å). An alternate description is one based on a distorted trigonal bipyramidal geometry where the weakly associated S atom (Sn-S(2) 3.095(3) Å) occupies an axial position approximately *trans*- to the C(31) atom; S(2)-Sn-C(31) 155.3(3)°. In consideration of the sum of the van der Waals radii for the Sn and S atoms of 4.0 Å [25], it is reasonable to regard the structure as being five-coordinate. In this description the Sn atom lies 0.4316(5) Å out of the trigonal plane in the direction of the C(31) atom. The ^{13}C CP-MAS NMR spectrum is more complicated than that suggested by the crystal structure analysis.

Table 4. Selected bond distances (Å) and angles (°) for $[\text{Ph}_3\text{Sn}(\text{dedtc})]$

Sn-S(1)	2.428(3)	Sn-S(2)	3.095(3)
Sn-C(11)	2.12(1)	Sn-C(21)	2.13(1)
Sn-C(31)	2.12(1)	S(1)-C(1)	1.74(1)
S(2)-C(1)	1.67(1)	C(1)-N(1)	1.32(1)
N(1)-C(2)	1.46(1)	N(1)-C(4)	1.45(1)
S(1)-Sn-S(2)	62.87(9)	S(1)-Sn-C(11)	115.9(3)
S(1)-Sn-C(21)	112.5(3)	S(1)-Sn-C(31)	92.5(3)
S(2)-Sn-C(11)	86.5(3)	S(2)-Sn-C(21)	86.3(3)
S(2)-Sn-C(31)	155.3(3)	C(11)-Sn-C(21)	120.5(4)
C(11)-Sn-C(31)	104.3(4)	C(21)-Sn-C(31)	106.2(4)
Sn-S(1)-C(1)	98.8(4)	Sn-S(2)-C(1)	77.9(4)
C(1)-N(1)-C(2)	122(1)	C(1)-N(1)-C(4)	123.2(9)
C(2)-N(1)-C(4)	114.8(9)	S(1)-C(1)-S(2)	119.1(6)
S(1)-C(1)-N(1)	116.4(8)	S(2)-C(1)-N(1)	124.4(8)

As can be seen from Table 3 there are two resonances in the S_2C region and four resonances in the CH_2 region whereas if the crystal structure reported above was truly representative of the bulk material only one and two resonances, respectively would be expected in the solid state spectrum; two resonances are found in the CH_3 region. The most plausible explanation for the multiplicity in the spectrum is the existence of a second polymorph of $[\text{Ph}_3\text{Sn}(\text{dedtc})]$. The relative intensities of the peaks in the S_2C and

CH₂ regions suggest an equal population of each polymorph. In this context it is noteworthy that the analogous compound [Me₃Sn(dedtc)] exists in two crystalline forms with a total of three different conformations [26, 27].

In conclusion, it can be seen that whereas the ¹³C CP-MAS NMR results are consistent with the crystal structure determinations, the only valuable insight gained concerning the nature of the solid materials was the presence of polymorphs in two cases. The poor chemical shift dispersion in the spectra, in particular in the CH₂ and CH₃ regions, was disappointing and contrasted previous observations for the closely related As, Sb, Bi [24] and Hg [28] xanthate (–S₂COR) compounds, and suggests that under the conditions of the ¹³C CP-MAS NMR experiment that the methylene and methyl C atoms are still mobile and hence appear to be magnetically equivalent.

Figure 5. A [001] projection of the unit cell contents for [Ph₃Sn(dedtc)].

The chemical shifts associated with the S_2C atoms proved to be the most informative. There was a general shift upfield in the shifts changing from $CDCl_3$ solution to the solid state consistent with the reduced atomic motion in the solid. The notable exception to this trend was found for the $[Ph_2Sn(dedtc)Cl]$ compound suggesting that a tetrahedral geometry may be preferred in $CDCl_3$ solution. Generally, there was a shift upfield for S_2C as the number of phenyl groups were increased at the Sn centre indicating a more asymmetric mode of coordination for the dedtc ligands consistent with the decreased Lewis acidity at the Sn atom.

Tin-119 NMR

^{119}Sn data were obtained for all compounds in $CDCl_3$ solution and in the solid state; this data is summarized in Table 6. A representative spectrum, namely that of $[Ph_3Sn(dedtc)]$, is shown in Figure 6. The solution data show a downfield shift as the number of phenyl substituents at the Sn centre increases which correlates with a smaller coordination number owing to the diminished Lewis acidity at the Sn atom. This trend is mirrored closely in the solid state with only small differences in the values of the chemical shifts. This information suggests that similar coordination numbers persist in solution as observed in the solid state. A curious feature of the spectra is the appearance of two resonances, which are separated by 15 ppm, in the ^{119}Sn NMR spectrum of $[Ph_2Sn(dedtc)Cl]$. No explanation is offered for this observation at this stage and it is noted that in a recent study only one resonance was reported for this compound [7].

Figure 6. 111.922 MHz ^{119}Sn solid state CP MAS NMR spectrum of $[Ph_3Sn(dedtc)]$ run at 3 kHz; * indicates isotropic peak.

Table 6. ^{119}Sn NMR spectroscopic data (ppm)^a

Compound	$\delta(\text{solution})$	$T_1(\text{solution})$	$\delta(\text{solid})$
$[\text{PhSn}(\text{dedtc})_3]$	-807	0.220	b
$[\text{PhSn}(\text{dedtc})_2\text{Cl}]$	-649.9	0.79	-643
$[\text{Ph}_2\text{Sn}(\text{dedtc})_2]$	-502 (-499) ^c	0.37	-516
$[\text{Ph}_2\text{Sn}(\text{dedtc})\text{Cl}]$	-325/-340 (-327) ^c	0.411/0.383	-311
$[\text{Ph}_3\text{Sn}(\text{dedtc})]$	-192 (-192) ^c	1.95	-165

a Solution data recorded in CDCl_3 solution; b no signal observed after 48 h; c literature values recorded in dichloromethane solution [7].

In vitro anti-tumour results

The availability of the series of phenyltin dithiocarbamate compounds described above prompted an investigation of their potential anti-tumour activity as an extension of previous studies in the area [15]. The phenyltin dithiocarbamates were evaluated for their *in vitro* anti-tumour activity against L1210 mouse leukaemia cells and the results are listed in Table 7. All compounds show good activity against this model and it is

Table 7. Biological activity of phenyltin dithiocarbamates ^a

Compound	ID_{50} (μM)
$[\text{PhSn}(\text{dedtc})_3]$	0.03
$[\text{PhSn}(\text{dedtc})_2\text{Cl}]$	0.04
$[\text{Ph}_2\text{Sn}(\text{dedtc})_2]$	0.03
$[\text{Ph}_2\text{Sn}(\text{dedtc})\text{Cl}]$	0.08
$[\text{Ph}_3\text{Sn}(\text{dedtc})]$	0.03

a Dose of compound causing 50% growth inhibition of L1210 mouse leukaemia cells in culture after 48 h exposure to the compound.

noteworthy that the ID_{50} values for cisplatin and carboplatin are 0.6 and 1.2, respectively. Replacement of a dedtc ligand by a Cl atom in the mono- and diphenyl- tin

compounds results in a lower ID₅₀ value, however, the three Ph_xSn(dedtc)_{4-x} compounds, display the same level of activity. The results summarized in Table 7 confirm previous findings that suggest that organotin thiolates may possess significant antitumour activity and warrant further study [15].

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