Inorganica Chimica Acta, *162* (1989) 143–149

Structural, Infrared and Mössbauer Studies of Octahedral *cis*-Dichlorobis(diketonate)tin(IV) Complexes Having Anti-tumour Activity

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(Received February 1, 1989)

Abstract

Two complexes, $SnCl_2(bzac)_2$ [Hbzac = benzoylacetone] and $SnCl_2(bzbz)_2$ [Hbzbz = dibenzoylmethane], have been prepared and characterised by analytical, infrared and Mössbauer studies. In addition, the X-ray crystal structure of $SnCl_2(bzbz)_2$ has been determined. The crystals are orthorhombic, space group *Pbca* with cell parameters $a = 18.767(9)$, $b = 17.611(8)$, $c = 16.563(8)$ Å. A total of 2116 reflections with $I/\sigma(I) \geq 3$ gave $R = 3.0\%$. The tin is coordinated to two *cis*-chlorine and four oxygen atoms from the dibenzoylmethanato ligands in an approximately octahedral arrangement. The bond distances in the tin coordination sphere are Sn–Cl 2.335(2) and 2.344(2) Å and Sn–O 2.062(4), 2.074(4), 2.063(4) and 2.063(4) Å and the Cl–Sn–Cl angle is 95.1(1)°. The results of anti-tumour tests on these complexes are given and attempts are made to correlate the anti-tumour activity of $SnCl_2(bzbz)_2$ with its structure.

Introduction

Recent investigations [1,2] have shown that certain organotin compounds, e.g. $(Et_2SnO)_n$ and $ClMe_2SnOSnMe_2Cl$, are marginally active against P388 lymphocytic leukaemia. In addition, octahedral complexes of the type, $R_2SnX_2 \cdot L_2$ (R = alkyl or aryl group; X = F, Cl, Br, I or NCS; L = N- or O-donor ligand), have been shown to be active against the same tumour [1,3,4]. It is usual for L to be a bidentate ligand which frequently gives rise to a *cis* configuration of the halogen atoms and this has been found for Pt(II) complexes to be an essential requirement for activity [5]. To date, only four inorganic tin(IV) compounds have shown anti-tumour activity *in vivo* and these are summarised in Table 1. A knowledge of the structural factors which influence anti-tumour properties of inorganic tin(IV) complexes is of considerable importance, as their toxicity is expected to be significantly lower than that of their organotin counterparts. Since $SnCl_2(bzac)_2$ had been shown, by Keller *et al.* [6], to be active against the Sarcoma 180 tumour, it was decided to synthesise this compound and the analogous $SnCl_2(bzbz)_2$ for *in vivo* testing against P388 leukaemia. In addition, both compounds were tested *in vitro* against B16 murine melanoma. The crystal structure of $SnCl_2(bzbz)_2$ was determined and particular attention was paid to the Cl–M–Cl angle which, in metallocene dichlorides, $(\eta^5\text{-}C_5H_5)_2MCl_2$ (M = Ti, Zr, Hf, V or Mo), is believed to influence their anti-tumour properties [8,9].

Experimental

Care was taken to exclude moisture and $SnCl_4$ was distilled prior to usage. The ligands were commercially available and were not purified before use. C, H and Cl microanalyses were carried out by the Microanalytical Laboratory, University College, London and Sn by the Analytical Laboratory I.T.R.I.

Preparation

Bis(benzoylacetonato-*O,O*)dichlorotin(IV) was prepared by the method of Dilthey [10] and recrys-

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0020-1693/89/$3.50

TABLE 1. Anti-tumour activity of inorganic tin(IV) complexes

Complex	Tumour	Dose (mg/kg)	*T*/*C* [a] (%)	Reference
$SnCl_4$·bipy [b]	P388 Leukaemia	400	130	4
$SnCl_4$·phen [c]	P388 Leukaemia	100	123	4
$SnCl_2(bzac)_2$	Sarcoma 180	52	230	6
$SnBr_2(bzac)_2$	Sarcoma 180	84	141	6
$SnCl_2(DDTC)_2$ [d]	B16 Murine Melanoma	[e]	Significant inhibition of cell growth	7

[a] *T*/*C* is the ratio of survival time (in days) of treated (*T*) and untreated (*C*) mice. A compound is considered to be active at *T*/*C* values ⩾120%. [b] bipy = 2,2′-bipyridyl. [c] phen = 1,10-phenanthroline. [d] DDTC = diethyldithiocarbamate. [e] *In vitro* test.

tallised from toluene and then from dichloromethane as cream-coloured crystals, melting point (m.p.) 224–225 °C (lit. [11] 221–223 °C). *Anal.* Found: C, 46.48; H, 3.57; Cl, 14.01. Calc. for $C_{20}H_{18}Cl_2O_4Sn$: C, 46.92; H, 3.54; Cl, 13.85%.

Bis(dibenzoylmethanato-*O,O*)dichlorotin(IV) was prepared similarly, using tin(IV) chloride (6.78 g, 0.026 mol) and dibenzoylmethane (11.67 g, 0.052 mol). The yellow solid which precipitated on cooling was recrystallised from ethyl acetate/toluene, m.p. 260–262 °C (lit. [12] 263–264 °C). *Anal.* Found: C, 56.39; H, 3.44; Cl, 11.30; Sn, 18.4. Calc. for $C_{30}H_{22}Cl_2O_4Sn$: C, 56.65; H, 3.49; Cl, 11.15; Sn, 18.66%.

Spectroscopic Methods

^{119m}Sn Mössbauer spectra were recorded at 80 K using a constant acceleration microprocessor spectrometer described previously [13]. The experimental error in the measured values of isomer shift (δ) and quadrupole splitting (ΔE_q) parameters is ±0.05 mm s^{-1}. Isomer shifts are relative to $CaSnO_3$.

Infrared spectra were obtained as Nujol mulls on a Perkin-Elmer 1330 spectrophotometer and the error in ν is ±2 cm^{-1}.

Crystallographic Studies

$SnCl_2(bzbz)_2$ was recrystallised from dichloromethane as yellow needles. A crystal of approximate dimensions 0.04 × 0.20 × 0.60 mm was mounted with its *c* axis coincident with the ω axis of a Stöe-Stadi 2 two-circle diffractometer. Data were collected using the background–ω scan-background technique and with graphite monochromated Mo Kα radiation. A total of 3224 unique reflections were measured of which 2116 had $I/\sigma(I) \geqslant 3.0$ and were used for subsequent analysis. Data were corrected for Lorentz and polarisation effects, but not for absorption.

Crystal Data

$C_{30}H_{22}Cl_2O_4Sn$, $M_r = 636.1$, orthorhombic, $a = 18.767(9)$, $b = 17.611(8)$, $c = 16.563(8)$ Å, $U = 5474.5$ Å^3, $F(000) = 2544$, space group *Pbca*, $Z = 8$, $D_m = 1.52$, $D_c = 1.54$ g cm^{-3}, Mo Kα radiation, $\lambda = 0.71069$, μ(Mo Kα) = 10.6 cm^{-1}.

Structure Determination and Refinement

The position of the tin atom was located from the three-dimensional Patterson function while the remaining atoms were located from successive difference electron-density maps. All atoms except those of hydrogen were assigned anisotropic thermal parameters. Hydrogen atoms were included in the F_c calculations with an idealised geometry (C–H, 1.08 Å) and were given common isotropic temperature factors which refined to final values of $U = 0.1061(199)$ for H12 and H30 and 0.0724(74) Å for all other hydrogen atoms. Complex neutral atom scattering factors [14] were employed throughout and in the final cycles of refinement the weighting scheme $w = 0.3554/[\sigma^2(F_o) + 0.0041(F_o)^2]$ was adopted. Full matrix refinement gave a final *R* value of 0.030 and *R′* of 0.036. Final positional parameters are given in Table 2; bond distances and angles in Table 3. See also 'Supplementary Material'.

Anti-tumour Testing

In vivo testing of $SnCl_2(bzac)_2$ and $SnCl_2(bzbz)_2$ against P388 leukaemia in mice was carried out by Dr G. Atassi at the Institut Jules Bordet, Brussels. The activities of the tin compounds were evaluated by computing the *T*/*C* values, i.e. the median survival time of the treated group of animals (*T*) divided by that of the control group (*C*) expressed as a percentage. A compound is termed active if $T/C \geqslant 120\%$.

In vitro testing [7] of the same compounds against F10 metastatic cells of B16 murine melanoma was carried out by Professor L. Cima and Dr M. Carrara at the University of Padua. The cell growths were tested at 10^{-4}, 10^{-5} and 10^{-6} M, after 24 and 48 h exposure.

Results and Discussion

IR and ^{119m}Sn Mössbauer Studies

Selected infrared and far infrared bands for both $SnCl_2(bzac)_2$ and $SnCl_2(bzbz)_2$ are shown in Table 4.

TABLE 2. Non-hydrogen atomic coordinates (Sn × 10^5, other atoms × 10^4) for $(PhCOCHCOPh)_2SnCl_2$ with e.s.d.s in parentheses

Atom	*x*	*y*	*z*
Sn	50665(2)	76826(2)	80183(2)
Cl(1)	4062(1)	7770(1)	7192(1)
Cl(2)	5737(1)	8575(1)	7293(1)
O(1)	5548(2)	6779(2)	7445(2)
O(2)	4518(2)	6876(2)	8685(3)
C(11)	5645(3)	6110(3)	7772(3)
C(12)	5232(3)	5799(3)	8386(3)
C(13)	4667(3)	6170(3)	8784(3)
C(14)	4217(3)	5767(3)	9362(3)
C(15)	4156(3)	4978(4)	9353(4)
C(16)	3695(4)	4617(4)	9873(5)
C(17)	3308(4)	5031(5)	10435(5)
C(18)	3370(4)	5811(5)	10453(5)
C(19)	3830(4)	6170(4)	9928(4)
C(1)	6277(3)	5691(3)	7486(3)
C(2)	6318(3)	4900(4)	7508(3)
C(3)	6937(4)	4533(4)	7266(4)
C(4)	7515(4)	4953(5)	7024(4)
C(5)	7493(4)	5727(5)	6999(5)
C(6)	6870(4)	6106(4)	7234(4)
O(4)	4685(2)	8448(2)	8856(2)
C(41)	4898(3)	8541(3)	9593(3)
C(42)	4479(3)	9080(3)	10076(3)
C(43)	4028(3)	9594(3)	9679(3)
C(44)	3623(3)	10104(4)	10114(4)
C(45)	3663(3)	10109(4)	10941(4)
C(46)	4096(4)	9621(4)	11332(4)
C(47)	4506(3)	9097(4)	10913(4)
O(3)	5915(2)	7527(3)	8793(3)
C(31)	5976(3)	7734(3)	9538(3)
C(32)	6650(3)	7488(3)	9914(3)
C(33)	7210(3)	7244(4)	9436(4)
C(34)	7830(3)	7003(4)	9771(4)
C(35)	7909(4)	6987(4)	10585(5)
C(36)	7365(3)	7211(4)	11078(4)
C(37)	6731(3)	7469(4)	10728(4)
C(30)	5494(3)	8187(3)	9926(4)

The differences between the spectra of benzoylacetone and dibenzoylmethane and their respective dichlorotin(IV) derivatives are consistent with complex formation. A splitting of many bands on complexation was observed, indicating a lowering of symmetry. In general, the spectra of $SnCl_2(bzac)_2$ and $SnCl_2(bzbz)_2$ were similar to those reported by Nelson and Martin [15] for the same complexes and to those of $Pd(acac)_2$ [16] and $SnCl_2(acac)_2$ [11] for which assignments have been made.

Many β-diketones are known to exist in the mono-keto enol form and they do not show the normal carbonyl stretching band. The spectra of benzoylacetone and dibenzoylmethane contained resonances at 1595 and 1593 cm^{-1} respectively. This low carbonyl stretching frequency is due to a reduction in double bond character because of the existence of resonance forms. On complexation with tin, the $C\overset{\cdots}{-}O$ stretching frequency is further reduced to 1545 cm^{-1} for $SnCl_2(bzac)_2$. This band was assigned to $\nu(C\overset{\cdots}{-}O)$ following the conclusions of Nelson and Martin [15]. However, the band at 1510 cm^{-1} was in fact the strongest band. In the case of $SnCl_2(bzbz)_2$, $\nu(C\overset{\cdots}{-}O)$ has been split into a doublet with wave numbers 1535 and 1510 cm^{-1}. Splitting of the carbonyl resonance has been observed previously for the complex, $SnCl_2(acac)_2$, by Jones and Fay [11], who believe that this is caused by coupling through the metal atom of the $\nu_s(C\overset{\cdots}{-}O)$ vibrations of the two chelate rings. The carbonyl bands of other similar complexes, such as $SnCl_2(acac)_2$ [11, 15] and $SnCl_2(tacac)_2$ [Htacac = monothioacetylacetone] [17], have wave numbers which are slightly higher than those of $SnCl_2(bzac)_2$ and $SnCl_2(bzbz)_2$.

Bands at 450 and 455 cm^{-1} were assigned to $\nu(Sn-O)$ for $SnCl_2(bzac)_2$ and $SnCl_2(bzbz)_2$ respectively. These are comparable to the values obtained for $SnCl_2(acac)_2$ [11] and lower than those of $SnCl_2(tacac)_2$ and $SnCl_2(btbm)_2$ [Hbtbm = benzoyl(thiobenzoyl)methane] [17].

TABLE 3. Bond distances (Å) and angles (°) for $(PhCOCHCOPh)_2SnCl_2$ with e.s.d.s in parentheses

Bond distances (Å)					
Sn–Cl(1)	2.335(2)	C(1)–C(2)	1.396(9)	C(36)–C(37)	1.398(9)
Sn–Cl(2)	2.344(2)	C(1)–C(6)	1.395(9)	C(41)–C(42)	1.470(7)
Sn–O(1)	2.062(4)	C(2)–C(3)	1.387(10)	C(42)–C(43)	1.402(8)
Sn–O(2)	2.074(4)	C(3)–C(4)	1.373(11)	C(42)–C(47)	1.387(8)
Sn–O(3)	2.063(4)	C(4)–C(5)	1.364(12)	C(43)–C(44)	1.380(8)
Sn–O(4)	2.063(4)	C(5)–C(6)	1.402(10)	C(44)–C(45)	1.371(10)
O(1)–C(11)	1.309(7)	C(14)–C(15)	1.393(9)	C(45)–C(46)	1.350(10)
O(2)–C(13)	1.284(7)	C(14)–C(19)	1.382(9)	C(46)–C(47)	1.387(10)
O(3)–C(31)	1.292(7)	C(15)–C(16)	1.378(10)		
O(4)–C(41)	1.295(7)	C(16)–C(17)	1.387(11)		
C(11)–C(12)	1.391(8)	C(17)–C(18)	1.379(13)		
C(11)–C(1)	1.476(8)	C(18)–C(19)	1.379(11)		

(continued)

TABLE 3. *(continued)*

C(12)–C(13)	1.409(8)	C(32)–C(33)	1.383(8)
C(13)–C(14)	1.461(8)	C(32)–C(37)	1.358(8)
C(31)–C(30)	1.366(8)	C(33)–C(34)	1.357(9)
C(31)–C(32)	1.475(7)	C(34)–C(35)	1.356(11)
C(30)–C(41)	1.395(7)	C(35)–C(36)	1.366(10)
Bond angles (°)			
Cl(2)–Sn–Cl(1)	95.1(1)	C(1)–C(2)–C(3)	120.3(6)
Cl(1)–Sn–O(1)	97.7(1)	C(2)–C(3)–C(4)	119.6(7)
Cl(1)–Sn–O(2)	87.5(1)	C(3)–C(4)–C(5)	121.6(7)
Cl(1)–Sn–O(3)	175.2(1)	C(4)–C(5)–C(6)	119.5(7)
Cl(1)–Sn–O(4)	94.1(1)	C(5)–C(6)–C(1)	120.0(7)
Cl(2)–Sn–O(1)	92.7(1)	C(6)–C(1)–C(11)	118.4(5)
Cl(2)–Sn–O(2)	177.3(1)	C(6)–C(1)–C(2)	119.1(6)
Cl(2)–Sn–O(3)	89.6(1)	C(1)–C(11)–C(12)	119.0(5)
Cl(2)–Sn–O(4)	95.4(1)	C(11)–C(12)–C(13)	125.2(5)
O(1)–Sn–O(2)	86.2(2)	C(12)–C(13)–C(14)	121.0(5)
O(1)–Sn–O(4)	165.1(1)	C(13)–C(14)–C(15)	121.7(5)
O(1)–Sn–O(3)	81.1(2)	C(14)–C(15)–C(16)	120.4(6)
O(2)–Sn–O(3)	87.8(2)	C(15)–C(16)–C(17)	120.4(7)
O(2)–Sn–O(4)	85.2(2)	C(16)–C(17)–C(18)	119.5(7)
O(3)–Sn–O(4)	86.4(2)	C(17)–C(18)–C(19)	119.8(7)
Sn–O(1)–C(11)	124.4(3)	C(18)–C(19)–C(14)	121.4(7)
Sn–O(2)–C(13)	128.5(4)	C(19)–C(14)–C(15)	118.4(6)
Sn–O(3)–C(31)	128.7(3)	C(19)–C(14)–C(13)	119.9(5)
Sn–O(4)–C(41)	127.6(3)	C(14)–C(13)–O(2)	115.3(5)
O(1)–C(11)–C(1)	115.4(5)	C(12)–C(13)–O(2)	123.7(5)
O(1)–C(11)–C(12)	125.5(5)	O(3)–C(31)–C(32)	113.3(5)
C(11)–C(1)–C(2)	122.4(5)	O(3)–C(31)–C(30)	123.7(5)
C(30)–C(41)–C(42)	120.2(5)	C(31)–C(32)–C(33)	120.1(5)
C(41)–C(42)–C(43)	118.9(5)	C(32)–C(33)–C(34)	121.0(6)
C(42)–C(43)–C(44)	120.5(5)	C(33)–C(34)–C(35)	120.5(6)
C(43)–C(44)–C(45)	119.7(6)	C(34)–C(35)–C(36)	120.4(6)
C(44)–C(45)–C(46)	120.6(6)	C(35)–C(36)–C(37)	118.8(6)
C(45)–C(46)–C(47)	121.2(6)	C(36)–C(37)–C(32)	121.0(6)
C(46)–C(47)–C(42)	119.6(6)	C(37)–C(32)–C(33)	118.3(5)
C(47)–C(42)–C(43)	118.5(5)	C(37)–C(32)–C(31)	121.5(5)
C(47)–C(42)–C(41)	122.5(5)	C(32)–C(31)–C(30)	122.8(5)
C(42)–C(41)–O(4)	115.5(4)	C(31)–C(30)–C(41)	127.3(5)
C(30)–C(41)–O(4)	124.3(5)		

TABLE 4. Infrared assignments (cm^{-1}) for $SnCl_2(bzac)_2$ and $SnCl_2(bzbz)_2$

$SnCl_2(bzac)_2$	$SnCl_2(bzbz)_2$	Assignment
1595	1595	$\nu_{as}(\mathrm{C}\overset{\dots}{-}\mathrm{C})$
1545	1535	$\nu_s(\mathrm{C}\overset{\dots}{-}\mathrm{O})$
1510	1510	
1340	1345	$\nu_{as}(\mathrm{C}\overset{\dots}{-}\mathrm{O})$
450	455	ν(Sn–O)
336	347	ν_{as}(Sn–Cl)
314	334	ν_s(Sn–Cl)

Two bands were observed at 336 and 314 cm^{-1} in the far infrared region of the $SnCl_2(bzac)_2$ spectrum and at 347 and 334 cm^{-1} for $SnCl_2(bzbz)_2$ and these are assigned to ν_a(Sn–Cl) and ν_s(Sn–Cl). The fact that two resonances are observed indicated the non-linearity of the Cl–Sn–Cl group, implying that the chlorine atoms are *cis* to each other, a result confirmed by our X-ray studies. Nelson and Martin [15] observed only one band in their spectra in this region. The difference between the spectra reported by them and those herein may be due to higher resolution of the spectra in this case. The Sn–Cl bands observed for the $SnCl_2(bzbz)_2$ complex are similar to those observed by Douek *et al.* [18] for $SnCl_2(acac)_2$ and have higher wave numbers than those recorded for $SnCl_2(tacac)_2$ [17]. This implies Sn–Cl bond strengths for $SnCl_2(bzbz)_2$ comparable to those of $SnCl_2(acac)_2$, but greater than those in $SnCl_2(tacac)_2$.

TABLE 5. ^{119m}Mössbauer data for dihalobis(diketonate) complexes of tin

Complex	δ [a]	ΔE_q [a]	Reference
$SnCl_2(acac)_2$	0.25	0	19
$SnCl_2(acac)_2$	0.28	0.50	20
$SnCl_2(bzac)_2$	0.23	0.39	this work
$SnCl_2(bzac)_2$	0.18	0	19
$SnCl_2(bzbz)_2$	0.21	0	this work
$SnCl_2(bzbz)_2$	0.21	0.45	20

[a] mm s^{-1}.

The Mössbauer parameters of the two compounds under investigation are given in Table 5, along with values for $SnCl_2(acac)_2$.

The isomer shifts are similar for all three compounds, indicating an approximately equal degree of s electron density at the ^{119}Sn nucleus. No trend in δ was observed for the β-diketones, R.CO.CH$_2$.CO.R$'$, in the series, $R = R' = CH_3$, $R = CH_3$, $R' = Ph$ and $R = R' = Ph$, and, thus, the R (or R$'$) group does not appear to be exerting an effect. This is in contrast to the results obtained by Greenwood and Ruddick [19], who found that, for compounds of the type, $SnCl_2L_2$ [L = ox (Hox = 8-hydroxyquinoline), acac or bzac], there was a considerable variation in the isomer shift.

X-ray Crystal Structure Determination

The structure of $SnCl_2(bzbz)_2$ (Fig. 1) consists of discrete monomeric units. As for $SnCl_2(acac)_2$ [21] $SnCl_2(btbm)_2$ [17], $SnCl_2(tacac)_2$ [17], $SnCl_2(etac)_2$ [24] [Hetac = ethylacetoacetate] and other bis-chelate tin(IV) compounds [22–28], the halogen atoms occupy *cis* positions, confirming the far infrared results. The fact that *cis* complexes have formed, even when using bulky ligands, has been observed for the analogous β-diketonate-alkoxide derivatives, $Sn(OR)_2(acac)_2$, where $R = Pr^i$ or Bu^t, synthesised by Chandler *et al.* [29]. The tin atom in $SnCl_2(bzbz)_2$ is octahedrally coordinated, the other four positions being occupied by the oxygen atoms of the bidentate β-diketonate ligands. The geometry is distorted from an ideal octahedron, the angles subtended at the tin atom varying from 87.5(1)° [(Cl(1)–Sn–O(2)] to 97.7(1)° [Cl(1)–Sn–O(1)].

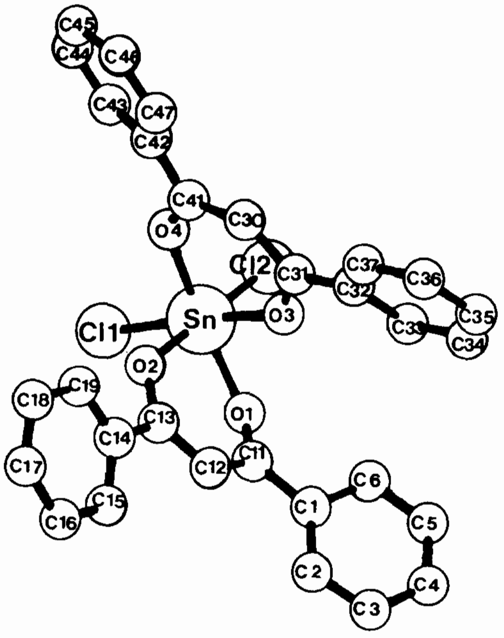

Fig. 1. Structure of $(PhCOCHCOPh)_2Cl_2Sn$ (hydrogen atoms omitted for clarity).

TABLE 6. Sn–O bond distances (Å) in tin(IV) β-diketonate and related complexes

Complex	Sn–O	Reference
$SnCl_2(bzbz)_2$	2.074(4), 2.062(4), 2.063(4)	this work
$SnCl_2(acac)_2$	2.051(2), 2.064(2)	21
$SnCl_2(ONPh{\cdot}COPh)_2$	2.05(2), 2.04(2)	23
$SnCl_2(etac)_2$	2.101(15), 2.066(15)	24
$SnCl_2(btbm)_2$	2.117(9), 2.120(7)	17
$SnCl_2(tacac)_2$	2.149(3)	17
$[Sn(O^iPr)_3(acac)]_2$	2.112(7), 2.106(5)	29
$Et_3NH[SnCl_4(acac)]$	2.094(4)	31

The geometry of the phenyl groups is unexceptional. Sn–O bond lengths usually fall within the range 2.11–2.45 Å in octahedral tin(IV) complexes [30], but the Sn–O bond lengths in $SnCl_2(bzbz)_2$ are all shorter than this; in addition, they are shorter than those found in the following compounds: $SnCl_2(btbm)_2$ [17], $SnCl_2(tacac)_2$ [17] and $[Sn(OPr^i)_3(acac)]_2$ [29] (Table 6). They are similar to the Sn–O bond distances in $SnCl_2(acac)_2$ [21] and $Cl_2Sn(ONPh{\cdot}COPh)_2$ [23]. It can therefore be concluded that the bulky dibenzoylmethane ligand is more strongly chelated to the tin atom than either benzoyl(thiobenzoyl)methane or monothioacetylacetone and is not exhibiting the anisobidentate behaviour observed for the dimethyltin complexes with the latter two diketonates [17] and that the strength of the interaction is similar to that observed for $SnCl_2(acac)_2$ and $Cl_2Sn(ONPh{\cdot}COPh)_2$. This is in agreement with the observation that similar Mössbauer isomer shift values and ν(Sn–O) values were obtained for $SnCl_2(bzbz)_2$ and $SnCl_2(acac)_2$. However, from the assignments made, $SnCl_2(tacac)_2$ has a much higher Sn–O stretching vibration than $SnCl_2(bzbz)_2$, which would not be expected on comparing the Sn–O bond lengths.

Gable *et al.* [27] found that, in $Br_2Sn(S{\cdot}CS{\cdot}OEt)_2$ and $I_2Sn(S{\cdot}CS{\cdot}OEt)_2$, mutually *trans* Sn–S distances were shorter than the Sn–S distances *trans* to the halides. However, this feature was not observed for $SnCl_2(bzbz)_2$, since only the Sn–O(2) bond distance [2.074(4) Å] was appreciably greater than the other three [2.062(4), 2.063(4) and 2.063(4) Å]. $SnCl_2(bzbz)_2$ therefore differs from $SnCl_2(acac)_2$ [21], $[Sn(OPr^i)_3(acac)]_2$ [29], $SnCl_2(btbm)_2$ [17] and $SnCl_2(tacac)_2$ [17], for which similar bond lengths are obtained for like bonds. However, considerable irregularity in the Sn–O bond distances was observed for tin(IV) tetraacetate, $Sn(OAc)_4$ [32], an eight coordinate tin compound, in order to relieve overcrowding. It may be that the slight lengthening of one of the Sn–O bonds in $SnCl_2(bzbz)_2$ is also due to steric effects.

All the angles subtended by the carbon and oxygen atoms of the chelate rings are larger than the ideal 120°, and range from 123.7(5)° [C(12)–C(13)–O(2), O(3)–C(31)–C(30)] to 128.5(4)° [Sn–O(2)–C(13)]. This indicates an opening of the angles after chelation and has been observed in other complexes [17,21].

Both Sn–Cl distances are shorter than those of $SnCl_2(tacac)_2$ [17] and are comparable to those observed in $SnCl_2(acac)_2$ [21], in agreement with the far infrared data, where ν_a and ν_s (Sn–Cl) for $SnCl_2(bzbz)_2$ are similar to those of $SnCl_2(acac)_2$ [21] and higher than those of $SnCl_2(tacac)_2$ [17]. According to Sreelatha *et al.* [17] these short Sn–Cl bond distances confirm that a strong complex has been formed.

The angle subtended by the two chloro groups is 95.1(1)° and is greater than the ideal 90°, probably because of the steric requirements of the chloro groups and the small bite of the diketonate rings. It has been suggested [8,9] that, for metallocene dichlorides of the type, $(\eta^5\text{-}C_5H_5)_2MCl_2$, where M = Ti, Zr, Hf, V or Mo, the Cl–M–Cl angle must lie within the range 82.0–94.5°, and, hence, the non-bonding Cl.....Cl distance(bite) must be less than 3.6 Å and may be important for their anti-tumour activity, since this is the upper limit for DNA–metal crosslinks. This criterion has been applied to some inorganic tin complexes [22], none of which were active as anti-tumour agents and none of which had Cl–Sn–Cl angles within the range specified. The Cl–Sn–Cl bond angle of $SnCl_2(bzbz)_2$ is just outside this range, and, on this basis, this complex would not be expected to show anti-tumour activity.

Evaluation of Anti-tumour Properties

The results of *in vivo* anti-tumour testing against P388 leukaemia are detailed in Table 7. The results show that neither of the tin complexes were active against this tumour, despite the high doses used.

Figure 2 shows the results of *in vitro* testing of the complexes against B16 murine melanoma. A statistically significant inhibition of cell growth was observed after 24 and 48 h exposure to 10^{-4} M $SnCl_2(bzac)_2$ or $SnCl_2(bzbz)_2$, the percentage cell growth being reduced to *c.* 70% in the case of $SnCl_2(bzac)_2$ and to *c.* 80% for $SnCl_2(bzbz)_2$. However, lower concentrations did not cause a significant reduction of cell proliferation.

As stated previously, the Cl–Sn–Cl angle of tin compounds containing *cis* chlorine atoms may be important in determining their effectiveness as anti-

TABLE 7. Results of P388 anti-tumour testing

Complex	Dose (mg/kg)	*MST*[a] (days)	*T/C* (%)
$SnCl_2(bzac)_2$	240	10.2	108
	120	10.0	106
	60	10.0	106
$SnCl_2(bzbz)_2$	240	10.5	111
	120	10.0	106
	60	9.4	

[a] Median Survival Time.

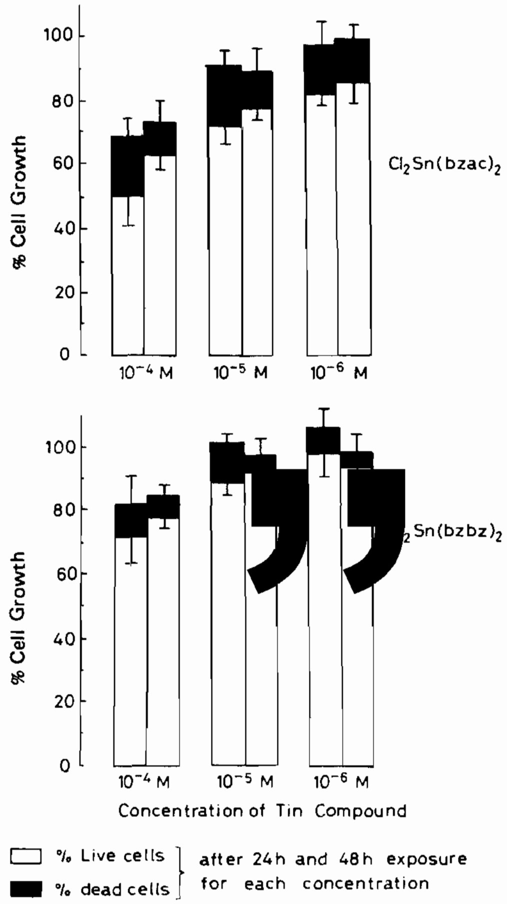

Fig. 2. Antitumour activity of $Cl_2Sn(bzac)_2$ and $Cl_2Sn(bzbz)_2$ against B16 murine melanoma.

tumour agents. The Cl–Sn–Cl bond angle of $SnCl_2$-$(bzbz)_2$ [95.1(1)°] is just outside of the range required for anti-tumour activity (82.1–94.5°) [8, 9], and, thus, it would not be expected to be active. This is in agreement with the results obtained on testing against P388 leukaemia but is not in accord with the activity observed against B16 murine melanoma. Activity for tin complexes with Cl–Sn–Cl bond angles $\geqslant 94.5°$ has been noted for some organotin adducts of the type, $R_2SnX_2 \cdot L_2$ (R = alkyl or aryl group; X = F, Cl, Br, I or NCS; L = N- or O-donor ligand) [33], and it has been concluded that the formation of metal–base crosslinks with DNA takes place via a different route for the organotin compounds. A similar conclusion may be drawn in this case. An alternative suggestion results from the observation that, for $R_2SnX_2 \cdot L_2$ (where L = N-donor ligand), the more stable complexes, i.e. those with shorter Sn–N bond lengths, had lower activities [33]. This implies that predissociation of the bidentate ligand may be a crucial step in the formation of a tin–DNA complex. However, from the values of the Sn–O bond lengths of $SnCl_2(bzbz)_2$, it appears that this may not be the case for this complex which contains a strongly chelating ligand and yet is still active against B16 murine melanoma.

Supplementary Material

Additional material available from the authors comprise thermal parameters, H atom coordinates, mean plane equations and structure factors.

Acknowledgements

The International Tin Research Institute, Uxbridge, is thanked for permission to publish this work, and the authors would like to express their appreciation to Professor L. Cima and Dr M. Carrara, Pharmacology Department, University of Padua, for anti-tumour testing.

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