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Dihalodimethyltin(IV) complexes of 2-(pyrazol-1-ylmethyl)pyridine

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Reaction of dichloro- and dibromodimethyltin(IV) with 2-(pyrazol-1-ylmethyl)pyridine (PMP) afforded [$SnMe_2Cl_2$(PMP)] and [$SnMe_2Br_2$(PMP)] respectively. The new complexes were characterized by elemental analysis and mass spectrometry and by IR, Raman and NMR (^{1}H, ^{13}C) spectroscopies. Structural studies by X-ray diffraction techniques show that the compounds consist of discrete units with the tin atom octahedrally coordinated to the carbon atoms of the two methyl groups in a *trans* disposition (Sn–C = 2.097(5), 2.120(5) Å and 2.110(6), 2.121(6) Å in the chloro and in the bromo compounds respectively), two *cis* halogen atoms (Sn–Cl = 2.4908(16), 2.5447(17) Å; Sn–Br = 2.6875(11), 2.7464(9) Å) and the two donor atoms of the ligand (Sn–N = 2.407(4), 2.471(4) Å and 2.360(5), 2.455(5) Å). In both cases, the Sn–N(pyridine) bond length is markedly longer than the Sn–N(pyrazole) distance. Copyright © 2003 John Wiley & Sons, Ltd.

KEYWORDS: tin; X-ray diffractometry; 2-(pyrazol-1-ylmethyl)pyridine

INTRODUCTION

The antitumour activity of platinum compounds, in particular *cis*-platin, has been extensively studied. However, the secondary effects of these types of compound have motivated the search for metal complexes possessing a lesser toxicity.[1]

Among these, complexes of the type [SnR_2X_2(LL)], where LL is a bidentate ligand, have been considered.[2] To try to modulate the Sn–N bond length, a parameter that influences the activity of the compounds,[2] in our laboratory we have used some ligands incorporating N-donor rings with a substituent in a position close to the nitrogen atom.

In this way, we have previously reported the synthesis of compounds [SnR_2X_2(M)] [M = 4-methoxy-2-(5-methoxy-3-methyl-pyrazol-1-yl)-6-methylpyrimidine, mepirizole] containing a five-membered chelate ring and with Sn–N bond distances >2.40 Å for the dimethyl and diphenyl derivatives. Their antitumour activity against the cell line KB, in the case of the butyl derivatives, was higher than that of *cis*-platin.[3,4]

Similar values for Sn–N bond lengths were obtained by using bis(1-methyl-2-imidazolylthio)methane, a ligand with no substituent close to the N-donor atom but able to give rise to an eight-membered chelate ring.[5] Following this strategy, we have now selected the ligand 2-(pyrazol-1-ylmethyl)pyridine (PMP), which provides a six-membered chelate ring and whose coordination chemistry has scarcely been studied.[6–9]

This paper describes the preparation and structural study of the dichlorodimethyltin(IV) and dibromodimethyltin(IV) complexes of this ligand; the Sn–N values found in the compounds suggest, having in mind previous data,[2–4] that the ethyl and butyl derivatives deserve consideration as potential antitumour agents.

EXPERIMENTAL

Materials

Dichlorodimethyltin(IV) (Aldrich), dibromodimethyltin(IV) (Alfa) and tetrabutylammonium hydroxide (Aldrich, 98%) were used as supplied. PMP was synthesized in benzene (**caution**) by reacting 2-(chloromethyl)pyridine hydrochloride (Aldrich) with pyrazole (Aldrich) in the presence of NaOH and tetrabutylammonium hydroxide.[10] After 6 h refluxing, the organic phase was separated, dried with Na_2SO_4 and concentrated *in vacuo* (Scheme 1).

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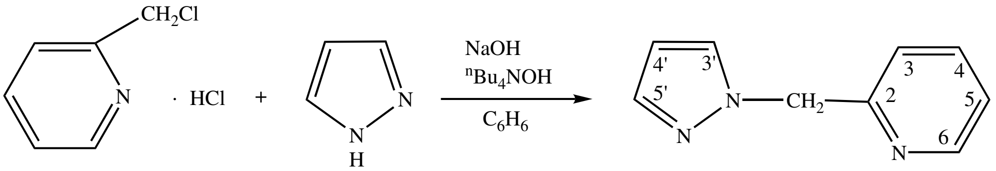

PMP

Scheme 1.

The product was purified by chromatography and characterized by mass spectrometry (M^+, 159.08) and IR (1595, 1450, 1400, 1040, 750, 630 cm^{-1}) and NMR spectroscopies. ^1H NMR: 5.47 (CH_2); 6.30t (H4′); 6.97d (H3); 7.2m (H5); 7.56 m (H4, H3′, H5′); 8.57d (H6). ^{13}C NMR: 57.4 (CH_2); 156.7 (C2); 122.7 (C3); 137.0 (C4); 121.7 (C5); 149.3 (C6); 139.8 (C3′); 106.2 (C4′); 130.0 (C5′). Solvents were dried by the usual methods.

Synthesis of complexes

The complexes were synthesized by the slow addition of a solution of the donor in dichloromethane (5 ml) to a solution of the acceptor in the same solvent. After stirring for 24 h, a solid was separated in both cases and dried *in vacuo*.

[$SnMe_2Cl_2$(PMP)]

From 0.30 g (1.39 mmol) of dichlorodimethyltin(IV) and 0.22 g (1.39 mmol) of ligand. Anal. Found: C, 34.4; H, 4.4; N, 10.8. Calc. for $C_{11}H_{15}Cl_2N_3Sn$: C, 34.9; H, 4.0; N, 11.1%. Yield: 42%. M.p. 142 °C. MS: m/e (ion, intensity): 151 ([$SnMe_2 + H$], 21.4); 135 ([SnMe], 9.8); 120 ([Sn], 23.2). IR (Raman) spectra (cm^{-1}): 571m ν_{as}(Sn–C); (508vs) ν_s(Sn–C); 263s,b, 248s,b, (263m) ν(Sn–X). ^1H NMR: 5.42[s, (CH_2)]; 6.29[t, C(4′)H]; 6.95[C(3)H]; 8.51[d, C(6)H]; 1.02[s, (Sn–H_α)]; $^2J(^{117/119}Sn–^1H) = 108.9/113.6$]. ^{13}C NMR: 56.4 (CH_2); 156.9 [C(2)], 122.6 [C(3)], 137.0 [C(4)], 121.4 [C(5)], 149.0 [C(6)], 139.2 [C(3′)], 105.4 [C(4′)], 130.7 [C(5′)], 22.6 (CH_3). Single crystals suitable for X-ray diffraction were obtained by slow concentration of a dichloromethane solution of the complex.

[$SnMe_2Br_2$(PMP)]

From 0.55 g (1.79 mmol) of dibromodimethyltin(IV) and 0.28 g (1.79 mmol) of ligand. Anal. Found: C, 28.3; H, 3.1; N, 9.0. Calc. for $C_{11}H_{15}Br_2N_3Sn$: C, 28.2; H, 3.2; N, 9.0%. Yield: 86%. M.p. 153 °C. MS: m/e (ion, intensity): 135 ([SnMe], 10.0); 120 ([Sn], 20.0). IR (Raman) spectra (cm^{-1}): 569m ν_{as}(Sn–C); (501vs) ν_s(Sn–C); 202w, 168s,b, (183w) ν(Sn–X). ^1H NMR: 5.42 [s, (CH_2)]; 6.29 [t, C(4′)H]; 6.95 [C(3)H]; 7.28 [m, C(5)H] 8.51 [d, C(6)H]; 1.21 [s, (Sn–H_α); $^2J(^{117/119}Sn–^1H) = 108.7/112.9$]. ^{13}C NMR: 56.4 (CH_2); 156.9 [C(2)], 122.6 [C(3)], 136.9 [C(4)], 121.4 [C(5)], 149.0 [C(6)], 139.2 [C(3′)], 105.4 [C(4′)], 130.7 [C(5′)], 24.5 (CH_3). The slow concentration of a dichloromethane solution of the complex afforded single crystals suitable for X-ray diffractometry.

Physical measurements

Elemental analyses were performed with a Carlo Erba 1108 apparatus. Melting points were measured on a Gallenkamp apparatus. Mass spectra were recorded on a Kratos MS50TC spectrometer connected to a DS90 system and operating under either electron impact conditions (direct insertion probe, 70 eV, 250 °C) or in fast atom bombardment mode (*m*-nitrobenzyl alcohol, Xe, 8 eV; *ca* 1.28×10^{-15} J); ions were identified by DS90 software and the data characterizing the metallated peaks were calculated using the isotope ^{120}Sn. IR spectra were recorded in Nujol mulls, and Raman spectra in capillary tubes, on a Bruker IFS-66V FT-IR spectrometer equipped with an FRA-106 Raman module. ^1H (250.13 MHz) and ^{13}C (62.83 MHz) NMR spectra were recorded in DMSO-d_6 at room temperature on a Bruker WM-250 instrument, and were referred to tetramethylsilane (TMS).

Determination of the molecular structures

Crystallographic data were collected at 293 K in an Enraf–Nonius MACH3 automatic diffractometer using Mo Kα radiation ($\lambda = 0.71073$ Å). Cell constants were obtained by least-squares refinement of the diffraction data from 25 reflections in the range of $9.23 < \theta < 20.89°$ (for the chlorocompound) and of $8.76 < \theta < 11.18°$ (for the bromo compound).[11] Data were corrected for Lorentz and polarization effects.[12] A semi-empirical absorption correction (Psi-scans) was made.[13] The structures were solved by direct methods[14] and subsequent difference Fourier maps, and refined on F^2 by a full-matrix least-squares procedure using anisotropic displacement parameters.[15] All hydrogen atoms were located in their calculated positions (C–H = 0.93–0.97 Å) and refined using a riding model. Atomic scattering factors were taken from *International Tables for Crystallography*.[16] Molecular graphics were produced using PLATON 99.[17] A summary of the crystal data, experimental details and refinement results is given in Table 1.

Crystallographic data for the structural analysis of the complexes have been deposited with the Cambridge Crystallographic Data Centre (CCDC nos 201 407 and 201 408 for the chloro- and bromo-compounds respectively). Copies of the information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336 033; e-mail: deposit@ccdc.cam.ac.uk; or web:http://www.ccdc.cam.ac.uk).

Table 1. Crystal data and structure refinement for the complexes

Empirical formula	$C_{11}H_{15}Cl_2N_3Sn$	$C_{11}H_{15}Br_2N_3Sn$
Formula weight	378.85	467.77
Temperature (K)	293(2)	293(2)
Wavelength (Å)	0.710 73	0.710 73
Crystal system	Triclinic	Triclinic
Space group	$P\bar{1}$ (No. 2)	$P\bar{1}$ (No. 2)
Cell constants		
a (Å)	7.093(3)	8.0796(19)
b (Å)	9.066(3)	9.1927(15)
c (Å)	12.670(5)	10.627(3)
α (°)	70.69(3)	105.573(19)
β (°)	87.98(3)	90.75(3)
γ (°)	70.63(3)	103.96(2)
Cell volume (Å^3)	722.8(4)	735.3(3)
Formula units/unit cell	2	2
D_{calc} (g cm^{-3})	1.741	2.113
Absorption coefficient (mm^{-1})	2.120	7.155
$F(000)$	372	444
θ range	3.05 to 26.44°	2.61 to 26.48°
Crystal size (mm^3)	0.28 × 0.20 × 0.12	0.32 × 0.16 × 0.12
Reflections collected/unique	3114/2975 ($R_{\text{int}} = 0.0160$)	3210/3043 ($R_{\text{int}} = 0.0231$)
Absorption correction	Psi-scan	Psi-scan
Max./min. transmission factors	0.949/0.787	0.954/0.688
Data/restraints/parameters	2975/0/156	3043/0/156
Goodness of fit on F^2	1.083	1.037
Final *R* indices [$I > 2\sigma(I)$]	$R_1 = 0.0378$	$R_1 = 0.0341$
	$wR_2 = 0.0912$	$wR_2 = 0.0653$
R indices (all data)	$R_1 = 0.0477$	$R_1 = 0.0816$
	$wR_2 = 0.0958$	$wR_2 = 0.0795$
Largest diff. peak and hole ($\text{e}^-\,\text{Å}^{-3}$)	1.428 and −0.920	0.690 and −0.778

RESULTS AND DISCUSSION

Description of the structures

Table 2 lists selected bond distances and angles for both complexes; Figs 1 and 2 show the PLATON views of the chloro- and bromo-complex respectively, along with the atomic numbering and thermal ellipsoids. Both structures consist of discrete units in which each tin atom is coordinated to two methyl carbon atoms in a *trans* disposition, two *cis* halogen atoms and the two nitrogen donor atoms of the ligand, creating for all of them a distorted octahedral $C_2SnCl_2N_2$ kernel. The Sn–C bond lengths around the metal atom [2.097(5), 2.120(5) Å in the chloro compound and 2.110(6), 2.121(6) Å in the bromo compound] are slightly shorter than the sum of the corresponding covalent radii (2.17 Å),[18] whereas the Sn–Cl distances [2.4908(16), 2.5447(17) Å] are slightly longer than that sum (2.39 Å).[18] A similar situation occurs in the case of the Sn–Br bond lengths [2.6875(11), 2.7464(9) Å], which are moderately longer than the sum of the covalent radii (2.54 Å).[18] The Sn–N bond lengths, on the other hand, [2.407(4), 2.471(4) Å and 2.360(5), 2.455(5) Å for the chloro and the bromo complexes respectively] are much longer than the sum of their covalent radii (2.15 Å). Moreover, the N(pyrazole) atom is, in both compounds, appreciably closer (almost 0.1 Å) to the tin than the N(pyridine), in keeping with what has been found in other metal complexes of the same[8] and other similar ligands.[19,20]

Regarding the bond angles around the tin atom, their values are close to the 90° expected from an octahedral disposition, ranging from 86.53(19) to 92.2(2)° [i.e.: C(11)–Sn(1)–N(1) = 91.67(18)°, 92.2(2)°; C(11)–Sn(1)–N(3) = 87.73(19)°, 90.4(2)°; C(12)–Sn(1)–N(1) = 86.53(19)°, 89.2(2)°; C(12)–Sn(1)–N(3) = 86.7(2)°, 87.0(2)° for the chloro and bromo compounds respectively]. There are two important exceptions in both compounds: the angle involving the halogen atoms, which is the broadest around the metal atom [Cl(1)–Sn(1)–Cl(2) = 100.62(6)°; Br(1)–Sn(1)–Br(2) = 100.93(39)°], and the N(1)–Sn(1)–N(3) angle [76.87(14)° and 76.32(16)°], which is logically the narrowest due to the ligand bite. The angles along the axis of the octahedron deviate somewhat from 180°; for instance: C(11)–Sn(1)–C(12) = 174.4(2)°, N(3)–Sn(1)–Cl(1) = 167.26(10)°, N(1)–Sn(1)–Cl(2) = 168.64 (10)° in the chloro compound; C(11)–Sn(1)–C(12) = 176.6(2)°, N(3)–Sn(1)–Br(1) = 167.91(11)°, N(1)–Sn(1)–Br(2) = 167.14

Table 2. Selected bond lengths (Å) and angles (deg) in [SnMe$_2$Cl$_2$(PMP)] and [SnMe$_2$Br$_2$(PMP)]

Sn(l)–C(11)	2.097(5)	2.110(6)
Sn(1)–C(12)	2.120(5)	2.121(6)
Sn(1)–N(1)	2.407(4)	2.360(5)
Sn(1)–N(3)	2.471(4)	2.455(5)
Sn(1)–X(1)	2.4908(16)[a]	2.6875(11)[b]
Sn(1)–X(2)	2.5447(17)[a]	2.7464(9)[b]
C(11)–Sn(1)–C(12)	174.4(2)	176.6(2)
C(11)–Sn(1)–N(1)	91.67(18)	92.2(2)
C(12)–Sn(1)–N(1)	86.53(19)	89.2(2)
C(11)–Sn(1)–N(3)	87.73(19)	90.4(2)
C(12)–Sn(1)–N(3)	86.7(2)	87.0(2)
N(1)–Sn(1)–N(3)	76.87(14)	76.32(16)
C(11)–Sn(1)–X(1)	92.07(17)[a]	92.94(18)[b]
C(12)–Sn(1)–X(1)	93.22(19)[a]	90.07(18)[b]
N(1)–Sn(1)–X(1)	90.40(11)[a]	91.93(12)[b]
N(3)–Sn(1)–X(1)	167.26(10)[a]	167.91(11)[b]
C(11)–Sn(1)–X(2)	90.69(16)[a]	87.50(17)[b]
C(12)–Sn(1)–X(2)	90.07(17)[a]	90.44(18)[b]
N(1)–Sn(1)–X(2)	168.64(10)[a]	167.14(12)[b]
N(3)–Sn(1)–X(2)	92.12(10)[a]	90.83(11)[b]
C1(1)–Sn(1)–X(2)	100.62(6)[a]	100.93(3)[b]

[a] X = Cl.
[b] X = Br.

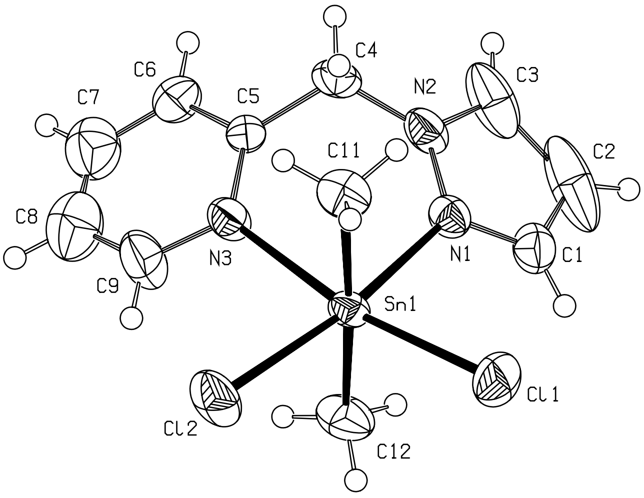

Figure 1. PLATON drawing of [SnMe$_2$Cl$_2$(PMP)] with the atom numbering scheme.

(12)° in the bromo complex. Finally, it is worth noting that the pyridine and pyrazole rings are both planar, and the angle between them is 52.99(0.24)° in the chloro compound and 54.08(0.23)° in the bromo compound. The tin atom is, in both cases, only slightly displaced (0.0267 Å and 0.0315 Å for the chloro and bromo compounds respectively) out of the plane containing the two nitrogen and the two halogen atoms.

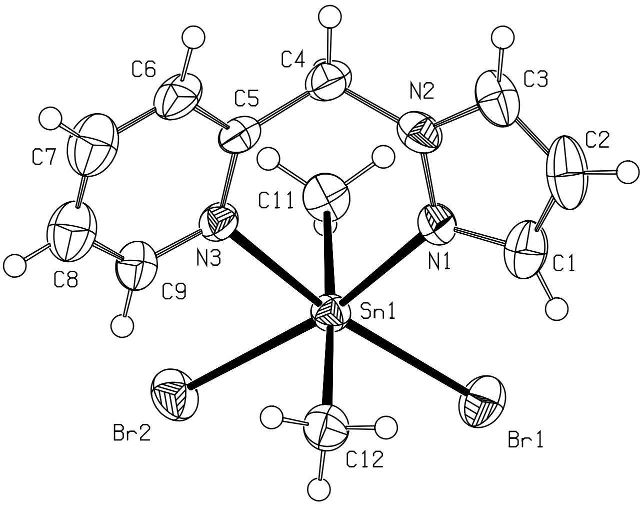

Figure 2. PLATON view of [SnMe$_2$Br$_2$(PMP)] showing the atom-labelling scheme.

IR and Raman spectroscopies

Vibrational spectroscopic studies were focused on the 700–100 cm^{-1} range, where the bands due to ν(Sn–C), ν(Sn–N) and ν(Sn–X) occur. Although the ν(Sn–N) bands are difficult to assign in these types of compound due to their low intensity and overlap with other bands, the Sn–X and Sn–C stretching modes are of great interest in order to propose a disposition of the ligands around the metal centre.

The ν_{asym}(Sn–C) and ν_{sym}(Sn–C) bands occur in the range 500–600 cm^{-1} and their number and coincidence in IR and Raman spectra provide information about the linearity of the C–Sn–C fragment. In this case, the quasi-linearity of this fragment shown by the X-ray studies leads to the occurrence of one single ν_{asym}(Sn–C) band in the IR spectrum and one ν_{sym}(Sn–C) band in the Raman spectrum for both compounds.

Regarding the metal–halogen stretching modes, the *cis* (X–Sn–X) fragment leads to two bands in both the IR and the Raman spectra; these bands occur at frequencies close to those found in other similar systems.[4,5]

NMR spectroscopy

The ^{1}H and ^{13}C NMR spectra were recorded in DMSO-d_6 and the δ values referred to TMS. The ligand signals (see Experimental section) remain practically unaltered upon coordination, whereas those corresponding to the acceptors [1.02 ppm (X = Cl) and 1.21 ppm (X = Br)] appear at the same positions as for the free SnMe$_2$X$_2$ species [1.03 ppm (Cl) and 1.23 ppm (Br)]. The coupling constants of the Me$_2$Sn fragment are also practically identical to those for the free acceptors [$^2J(^{117/119}$Sn–^{1}H) = 108.5/113.5 Hz for the chloride and 108.7/112.9 Hz for the bromide], suggesting a complete dissociation in DMSO-d_6 solution.

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