

Complexes of tin(IV) halides and diorganotin(IV) dihalides with 3,5-dimethyl-1-(2'-pyridyl)pyrazole

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Received 28 June 2002; accepted 26 February 2003

Abstract

3,5-Dimethyl-1-(2'-pyridyl)pyrazole (DMPP) reacts with SnX_4 and R_2SnX_2 ($\text{X}=\text{Cl}, \text{Br}, \text{I}$; $\text{R}=\text{Me}, \text{Et}, \text{Bu}, \text{Ph}$) to yield adducts of types $[\text{SnX}_4(\text{DMPP})]$ and $[\text{SnR}_2\text{X}_2(\text{DMPP})]$, respectively. The structure of $[\text{SnEt}_2\text{Br}_2(\text{DMPP})]$ has been determined by X-ray diffractometry. The crystal consists of discrete $[\text{SnEt}_2\text{Br}_2(\text{DMPP})]$ molecules with the metal atom octahedrally coordinated to two Br atoms [$\text{Sn}-\text{Br}=2.631(3), 2.703(3)$ Å; $\text{Br}-\text{Sn}-\text{Br}=98.00(10)^\circ$], two ethyl carbons [$\text{Sn}-\text{C}=2.11(3), 2.143(19)$ Å; $\text{C}-\text{Sn}-\text{C}=172.3(11)^\circ$] and the two donor N atoms of the ligand [$\text{Sn}-\text{N}=2.379(16), 2.387(16)$ Å; $\text{N}-\text{Sn}-\text{N}=66.8(6)^\circ$]. The IR data and Mössbauer parameters are consistent with all the organotin derivatives having, similar geometry whereas in the case of the $[\text{SnX}_4(\text{DMPP})]$ complexes the results of both techniques support the expectation of cis stereochemistry. The ^1H NMR data indicate significant dissociation in solution. The chlorobutyl derivative exhibited significant in vitro antitumour activity against the human carcinoma cell line KB.

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Keywords: Crystal structures; Cytostatic activity; Mössbauer spectroscopy; Diorganotin(IV) dihalide complexes

1. Introduction

A considerable number of metal-based compounds, including many organotin derivatives, have in recent years been synthesized and characterized in the search for compounds with greater antitumour activity and lower toxicity than platinum complexes [1]. For compounds $[\text{SnR}_2\text{X}_2(\text{LL})]$, where LL is an N,N' -didentate ligand, antitumour activity depends on the Sn–N distances (>2.39 and <2.39 Å for the active and

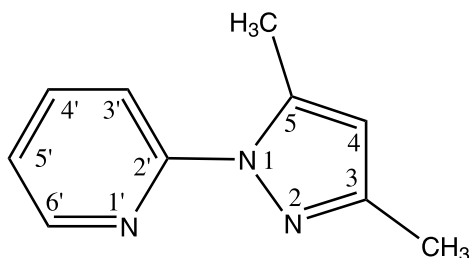
inactive compounds, respectively [2]), which suggests that dissociation of the ligand is a significant step in their mechanism of action.

In previous work [3], we synthesized compounds of this type either with the flexible ligand bis(1-methyl-2-imidazolylthio)methane as LL, in which case long Sn–N bonds resulted from the formation of an eight-membered ring; or with mepirazole [4-methoxy-2-(5-methoxy-3-methyl-pyrazol-1-yl)-6-methylpyrimidine], a ligand with substituents close to the donor N atoms that hinder the formation of strong Sn–N bonds [4,5]. In further pursuit of this second approach, we have now used the ligand 3,5-dimethyl-1-(2'-pyridyl)pyrazole (DMPP), a biologically active potentially N,N' -diden-

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tate compound [6], the coordination chemistry of which has scarcely been studied [7].



This paper describes the synthesis of the compounds $[\text{SnX}_4(\text{DMPP})]$ ($\text{X} = \text{Cl}, \text{Br}, \text{I}$) and $[\text{SnR}_2\text{X}_2(\text{DMPP})]$ ($\text{R} = \text{Me}, \text{Et}, \text{Bu}, \text{Ph}$; $\text{X} = \text{Cl}, \text{Br}$), the crystal structure of $[\text{SnEt}_2\text{Br}_2(\text{DMPP})]$ as determined by X-ray diffractometry, and the in vitro cytostatic activities of the ethyl, phenyl and butyl derivatives against the human carcinoma cell line KB. The compounds $[\text{SnMe}_2\text{Cl}_2(\text{DMPP})]$, $[\text{SnEt}_2\text{Cl}_2(\text{DMPP})]$ and $[\text{SnPh}_2\text{Cl}_2(\text{DMPP})]$ have been described previously [7c,7d].

2. Experimental

2.1. Materials

All tin(IV) halides and diorganotin(IV) dihalides except SnPh_2Br_2 were supplied by Ventron. SnPh_2Br_2 was prepared by reacting diphenyltin dichloride with sodium bromide. DMPP was synthesized by condensation of acetylacetone with 2-hydrazinepyridine in 1:1 mole ratio [6]; the two reagents were mixed and stirred until the reaction was practically complete and a bright yellow liquid had formed (b.p. 74°C , 0.4 mm of Hg).

2.2. Synthesis of complexes

All complexes were synthesized by slow addition of a solution of the donor in CH_2Cl_2 (10 ml) to a solution of the acceptor in the same solvent (10 ml). After 24 h stirring and another 24 h at low temperature, the solid product was filtered out and dried in vacuo.

2.2.1. $[\text{SnCl}_4(\text{DMPP})]$ (1)

From 0.260 g (1 mmol) of tin(IV) chloride and 0.173 g (1 mmol) of ligand. *Anal.* Found: C, 27.1; H, 2.5; N, 9.5. Calc. for $\text{C}_{10}\text{H}_{11}\text{Cl}_4\text{N}_3\text{Sn}$: C, 27.7; H, 2.5; N, 9.7%. Yield: 76%. M.p. 252°C . Mössbauer: I.S. 0.59, Q.S. 0.31, Γ 0.80. IR (Raman) (cm^{-1}): 1608vs (1606m), 1576m (1576s), 1489vs (1485m), $\nu(\text{ring})$; 328s,b, 284m (343s, 333s, 287s), $\nu(\text{Sn}-\text{Cl})$. ^1H NMR: 2.31 [s, C(3)- CH_3]; 6.21 [s, C(4)H]; 2.56 [s, C(5)- CH_3]; 7.41 [m, C(3')H]; 8.03 [m, C(4')H]; 7.75 [m, C(5')H]; 8.50 [m, C(6')H]. A_M (MeCN, 10^{-3} M): 12.8 S $\text{cm}^2 \text{mol}^{-1}$.

2.2.2. $[\text{SnBr}_4(\text{DMPP})]$ (2)

As above, from 0.438 g (1 mmol) of tin(IV) bromide and 0.173 g (1 mmol) of ligand. *Anal.* Found: C, 19.4; H, 1.7; N, 6.6. Calc. for $\text{C}_{10}\text{H}_{11}\text{Br}_4\text{N}_3\text{Sn}$: C, 19.6; H, 1.8; N, 6.9%. Yield: 72%. M.p. 286°C . Mössbauer: I.S. 0.87, Q.S. 0.30, Γ 0.79. IR (Raman) (cm^{-1}): 1604vs (1605m), 1575m (1574s), 1488vs (1485m), $\nu(\text{ring})$; 232s,b, 210m (244m, 230w, 208s), $\nu(\text{Sn}-\text{Br})$. ^1H NMR: 2.20 [s, C(3)- CH_3]; 6.11 [s, C(4)H]; 2.57 [s, C(5)- CH_3]; 7.29 [m, C(3')H]; 7.93 [m, C(4')H]; 7.80 [m, C(5')H]; 8.43 [m, C(6')H].

2.2.3. $[\text{SnI}_4(\text{DMPP})]$ (3)

From 0.626 g (1 mmol) of tin(IV) iodide and 0.173 g (1 mmol) of ligand. *Anal.* Found: C, 15.5; H, 1.3; N, 5.6. Calc. for $\text{C}_{10}\text{H}_{11}\text{I}_4\text{N}_3\text{Sn}$: C, 15.0; H, 1.4; N, 5.3%. Yield: 53%. M.p. 216°C . Mössbauer: I.S. 1.28, Q.S. 0.27, Γ 0.96. IR (Raman) (cm^{-1}): 1602vs (1600w), 1573m (1573m), 1484vs (1483w), $\nu(\text{ring})$; 188s, 177sh (193m, 182m, 167s), $\nu(\text{Sn}-\text{I})$. ^1H NMR: 2.43 [s, C(3)- CH_3]; 6.05 [s, C(4)H]; 2.67 [s, C(5)- CH_3]; 7.79 [m, C(3')H]; 7.83 [m, C(4')H]; 7.81 [m, C(5')H]; 7.85 [m, C(6')H].

2.2.4. $[\text{SnMe}_2\text{Cl}_2(\text{DMPP})]$ (4)

From 0.217 g (1 mmol) of dichlorodimethyltin(IV) and 0.173 g (1 mmol) of ligand. *Anal.* Found: C, 36.4; H, 4.5; N, 10.0. Calc. for $\text{C}_{12}\text{H}_{17}\text{Cl}_2\text{N}_3\text{Sn}$: C, 36.8; H, 4.4; N, 10.7%. Yield: 60%. M.p. 124°C . Mössbauer: I.S. 1.62, Q.S. 3.97, Γ 0.79, $A_{2/1}$ 1.12. IR (Raman) (cm^{-1}): 1604vs (1604m), 1575m (1575s), 1488vs (1488m), $\nu(\text{ring})$; 572m (570w), $\nu_{\text{as}}(\text{Sn}-\text{C})$; 510w (508vs), $\nu_{\text{s}}(\text{Sn}-\text{C})$; 275s (270m), 247s,b (250m), $\nu(\text{Sn}-\text{Cl})$. ^1H NMR: 2.35 [s, C(3)- CH_3]; 6.03 [s, C(4)H]; 2.62 [s, C(5)- CH_3]; 7.20 [m, C(3')H]; 7.82 [m, C(4')H]; 7.77 [m, C(5')H]; 8.56 [m, C(6')H]; 1.19 [s, (Sn- H_2)], $^2J(^{117/119}\text{Sn}-^1\text{H}) = 73.0/76.4$. A_M (MeCN, 10^{-3} M): 3.5 S $\text{cm}^2 \text{mol}^{-1}$.

2.2.5. $[\text{SnMe}_2\text{Br}_2(\text{DMPP})]$ (5)

From 0.308 g (1 mmol) of dibromodimethyltin(IV) and 0.173 g (1 mmol) of ligand. *Anal.* Found: C, 29.8; H, 3.5; N, 8.6. Calc. for $\text{C}_{12}\text{H}_{17}\text{Br}_2\text{N}_3\text{Sn}$: C, 29.9; H, 3.5; N, 8.7%. Yield: 84%. M.p. 115°C . Mössbauer: I.S. 1.71, Q.S. 4.07, Γ 0.80, $A_{2/1}$ 1.00. IR (Raman) (cm^{-1}): 1603vs (1603m), 1574m (1575m), 1487m (1487w), $\nu(\text{ring})$; 568m (570w), $\nu_{\text{as}}(\text{Sn}-\text{C})$; 510w (502vs), $\nu_{\text{s}}(\text{Sn}-\text{C})$; 207m (200m), 188s,b (182m), $\nu(\text{Sn}-\text{Br})$. ^1H NMR: 2.31 [s, C(3)- CH_3]; 6.00 [s, C(4)H]; 2.64 [s, C(5)- CH_3]; 7.15 [m, C(3')H]; 7.82 [m, C(4')H]; 7.77 [m, C(5')H]; 8.44 [m, C(6')H]; 1.38 [s, (Sn- H_2)], $^2J(^{117/119}\text{Sn}-^1\text{H}) = 63.9/66.7$. A_M (MeCN, 10^{-3} M): 7.2 S $\text{cm}^2 \text{mol}^{-1}$.

2.2.6. $[\text{SnEt}_2\text{Cl}_2(\text{DMPP})]$ (6)

From 0.247 g (1 mmol) of dichlorodiethyltin(IV) and 0.173 g (1 mmol) of ligand. *Anal.* Found: C, 39.1; H, 5.5; N, 9.7. Calc. for $\text{C}_{14}\text{H}_{21}\text{Cl}_2\text{N}_3\text{Sn}$: C, 40.0; H, 5.0; N, 10.0%. Yield: 78%. M.p. 63°C . Mössbauer: I.S. 1.79,

Q.S. 3.99, Γ 0.97, $A_{2/1}$ 0.95. IR (Raman) (cm^{-1}): 1603vs (1603m), 1575m (1576s), 1483vs (1483m), $\nu(\text{ring})$; 535m (534w), $\nu_{\text{as}}(\text{Sn}-\text{C})$; 490m (486vs), $\nu_{\text{s}}(\text{Sn}-\text{C})$; 267s,b (276m), 239s (236w), $\nu(\text{Sn}-\text{Cl})$. ^1H NMR: 2.45 [s, C(3)- CH_3]; 6.14 [s, C(4)H]; 2.62 [s, C(5)- CH_3]; 7.32 [m, C(3')H]; 7.99 [m, C(4')H]; 7.67 [m, C(5')H]; 8.90 [m, C(6')H]; 1.25 [t, (Sn-H $_{\beta}$)], 1.67 [q, (Sn-H $_{\alpha}$)]. A_{M} (MeCN, 10^{-3} M): 9.7 S $\text{cm}^2 \text{mol}^{-1}$.

2.2.7. [SnEt₂Br₂(DMPP)] (7)

From 0.336 g (1 mmol) of dibromodiethyltin(IV) and 0.173 g (1 mmol) of ligand. *Anal.* Found: C, 32.7; H, 4.1; N, 8.4. Calc. for C₁₄H₂₁Br₂N₃Sn: C, 33.0; H, 4.1; N, 8.3%. Yield: 80%. M.p. 89 °C. Mössbauer: I.S. 1.83, Q.S. 4.00, Γ 0.79, $A_{2/1}$ 1.06. IR (Raman) (cm^{-1}): 1605s (1609m), 1576m (1578s), 1483vs (1485m), $\nu(\text{ring})$; 526m, $\nu_{\text{as}}(\text{Sn}-\text{C})$; 475m (476s), $\nu_{\text{s}}(\text{Sn}-\text{C})$; 200sh, 170m (167m), $\nu(\text{Sn}-\text{Br})$. ^1H NMR: 2.34 [s, C(3)- CH_3]; 6.02 [s, C(4)H]; 2.63 [s, C(5)- CH_3]; 7.18 [m, C(3')H]; 7.78–7.83 [m, C(4')H]; 7.78–7.83 [m, C(5')H]; 8.53 [m, C(6')H]; 1.38 [t, (Sn-H $_{\beta}$)]; 1.84 [q, (Sn-H $_{\alpha}$)]. A_{M} (MeCN, 10^{-3} M): 12.0 S $\text{cm}^2 \text{mol}^{-1}$. A crystal suitable for X-ray diffraction was grown from the mother liquor.

2.2.8. [SnBu₂Cl₂(DMPP)] (8)

From 0.303 g (1 mmol) of dichlorodibutyltin(IV) and 0.173 g (1 mmol) of ligand. *Anal.* Found: C, 45.6; H, 6.6; N, 8.9. Calc. for C₁₆H₂₅Cl₂N₃Sn: C, 45.4; H, 6.1; N, 8.8%. Yield: 87%. M.p. 87 °C. Mössbauer: I.S. 1.75, Q.S. 4.04, Γ 0.82, $A_{2/1}$ 1.00. IR (Raman) (cm^{-1}): 1606s (1605m), 1578m (1578s), 1483vs (1483m), $\nu(\text{ring})$; 625w (625w), $\nu_{\text{as}}(\text{Sn}-\text{C})$; 590w (590vs), $\nu_{\text{s}}(\text{Sn}-\text{C})$; 238b (244m), $\nu(\text{Sn}-\text{Cl})$. ^1H NMR: 2.30 [s, C(3)- CH_3]; 6.00 [s, C(4)H]; 2.63 [s, C(5)- CH_3]; 7.15 [m, C(3')H]; 7.77–7.83 [m, C(4')H]; 7.77–7.83 [m, C(5')H]; 8.43 [m, C(6')H]; 0.95 [t, (Sn-H $_{\delta}$)]; 1.41 [m, (Sn-H $_{\gamma}$)]; 1.62–1.82 [m, (Sn-H $_{\alpha}$ H $_{\beta}$)]. A_{M} (MeCN, 10^{-3} M): 10.1 S $\text{cm}^2 \text{mol}^{-1}$.

2.2.9. [SnBu₂Br₂(DMPP)] (9)

From 0.392 g (1 mmol) of dibromodibutyltin(IV) and 0.173 g (1 mmol) of ligand. *Anal.* Found: C, 38.1; H, 6.0; N, 7.8. Calc. for C₁₆H₂₅Br₂N₃Sn: C, 38.2; H, 5.1; N, 7.4%. Yield: 26%. M.p. 75 °C. Mössbauer: I.S. 1.83, Q.S. 3.98, Γ 0.83, $A_{2/1}$ 1.03. IR (Raman) (cm^{-1}): 1605s (1606m), 1580m (1577s), 1483vs (1484m), $\nu(\text{ring})$; 632m (632w), $\nu_{\text{as}}(\text{Sn}-\text{C})$; 588w (586vs), $\nu_{\text{s}}(\text{Sn}-\text{C})$; 202m (212m), $\nu(\text{Sn}-\text{Br})$. ^1H NMR: 2.31 [s, C(3)- CH_3]; 6.00 [s, C(4)H]; 2.63 [s, C(5)- CH_3]; 7.15 [m, C(3')H]; 7.75–7.83 [m, C(4')H]; 7.75–7.83 [m, C(5')H]; 8.44 [m, C(6')H]; 0.95 [t, (Sn-H $_{\delta}$)]; 1.42 [m, (Sn-H $_{\gamma}$)]. A_{M} (MeCN, 10^{-3} M): 3.3 S $\text{cm}^2 \text{mol}^{-1}$.

2.2.10. [SnPh₂Cl₂(DMPP)] (10)

From 0.343 g (1 mmol) of dichlorodiphenyltin(IV) and 0.173 g (1 mmol) of ligand. *Anal.* Found: C, 51.6;

H, 4.1; N, 7.9. Calc. for C₂₂H₂₁Cl₂N₃Sn: C, 51.2; H, 4.1; N, 8.1%. Yield: 50%. M.p. 154 °C. Mössbauer: I.S. 1.45, Q.S. 3.47, Γ 0.80, $A_{2/1}$ 1.04. IR (Raman) (cm^{-1}): 1604s (1604m), 1573m (1574s), 1483vs (1486m), $\nu(\text{ring})$; 286s,b, $\nu(\text{Sn}-\text{C})$; 262s,b (270m), 230s (226w), $\nu(\text{Sn}-\text{Cl})$. ^1H NMR: 2.31 [s, C(3)- CH_3]; 6.02 [s, C(4)H]; 2.60 [s, C(5)- CH_3]; 7.15 [m, C(3')H]; 7.5–7.8 [m, C(4')H, C(5')H, Sn-Ph]; 8.42 [m, C(6')H]. A_{M} (MeCN, 10^{-3} M): 5.6 S $\text{cm}^2 \text{mol}^{-1}$.

2.2.11. [SnPh₂Br₂(DMPP)] (11)

From 0.432 g (1 mmol) of dibromodiphenyltin(IV) and 0.173 g (1 mmol) of ligand. *Anal.* Found: C, 42.9; H, 3.4; N, 6.9. Calc. for C₂₂H₂₁Br₂N₃Sn: C, 43.6; H, 3.5; N, 6.9%. Yield: 54%. M.p. 142 °C. Mössbauer: I.S. 1.56, Q.S. 3.57, Γ 0.80, $A_{2/1}$ 1.00. IR (Raman) (cm^{-1}): 1605s (1604m), 1580sh (1579s), 1485vs (1485m), $\nu(\text{ring})$; 288s,b, $\nu(\text{Sn}-\text{C})$; 162m,b (159m), $\nu(\text{Sn}-\text{Br})$. ^1H NMR: 2.31 [s, C(3)- CH_3]; 6.01 [s, C(4)H]; 2.64 [s, C(5)- CH_3]; 7.16 [m, C(3')H]; 7.51–7.84 [m, C(4')H, C(5')H, C(6')H, Sn-Ph]. A_{M} (MeCN, 10^{-3} M): 15.9 S $\text{cm}^2 \text{mol}^{-1}$.

2.3. Physical measurements

Elemental analyses were performed with a Carlo Erba 1108 apparatus. Melting points were measured on a Gallenkamp apparatus. IR spectra were recorded in Nujol mulls and Raman spectra in capillary tubes on a Bruker IFS-66V FT-IR apparatus equipped with an FRA-106 Raman module. Conductivities (10^{-3} M, CH₃CN) were measured in a CRISON micro CM 2200 conductimeter. Mössbauer spectra were determined at 80.0 K in a constant acceleration apparatus with a Ca^{119m}SnO₃ source, with isomer shifts (I.S.) referred to BaSnO₃. ^1H (250.13 MHz) NMR spectra were recorded in CDCl₃ at room temperature on a Bruker WM-250 spectrometer, and were referred to TMS.

2.4. Determination of the structure of [SnEt₂Br₂(DMPP)]

A colourless prismatic crystal of the complex was mounted on a glass fibre and used for data collection in an Enraf–Nonius MACH3 automatic diffractometer [8]. Cell constants and an orientation matrix for data collection were obtained by least-squares refinement of the diffraction data from 25 reflections in the range $9.182 < \theta < 12.926^\circ$. Data were collected at 293 K using Mo K α radiation ($\lambda = 0.71073 \text{ \AA}$) and the ω - 2θ scan technique, and were corrected for Lorentz and polarization effects [9]. A semi-empirical absorption correction was also made [10].

The structure was solved by direct methods [11], which revealed the positions of all non-hydrogen atoms, and was refined on F^2 by a full-matrix least-squares

procedure using anisotropic displacement parameters [12]. All hydrogen atoms were located in their calculated positions ($C-H = 0.93-0.97 \text{ \AA}$) and were refined using a riding model. Atomic scattering factors were taken from International Tables for X-ray Crystallography [13]. Molecular graphics were obtained with PLATON-98 [14]. Table 1 summarizes the crystal data, experimental details and refinement results.

2.5. *In vitro* cytostatic activity

Cytostatic activity was assayed against the established cell line KB, which derives from a human oral epidermoid carcinoma. Stock cultures were grown in 25 cm^3 flasks containing 10 ml of buffered Eagle's Minimum Essential Medium (MEM) supplemented with glutamine, non-essential aminoacids (1%) and newborn calf serum (10%), as previously described [15]. The cell population doubling time was approximately 24 h. The cells were dissociated with 0.05% trypsin solution, plated at a density of 5×10^5 cells per well in 24-well cell culture clusters (Costar) containing 1.0 ml of MEM per well, and preincubated for 24 h to allow adhesion to the substrate. Subsequently, the compounds to be tested

were dissolved immediately before use in Me_2SO and these solutions were diluted with the growth medium to the desired concentrations before addition to the wells. At least five concentrations of each compound were used, with eight cell culture wells for each concentration. Each compound was assayed on at least three separate occasions. Each assay included a blank containing complete medium without cells.

The cells were incubated with the compounds to be tested at 37°C in an atmosphere that was 5% CO_2 and had a relative humidity of 100%. The incubation time was 72 h, during which period the control cells showed exponential growth.

Cell growth was terminated by *in situ* fixation and followed by staining with the protein-binding dye sulforhodamine B (SRB) [16]. Specifically, adherent cell cultures were fixed *in situ* by addition of 250 μl of cold 50% (wt/vol) trichloroacetic acid (TCA) and were kept for 60 min at 4°C . The supernatant was then discarded and the plates were washed three times with deionized water and dried. SRB solution (500 μl , 0.4% wt/vol in 1% AcOH) was added to each well, and the cells were allowed to stain for 20–30 min at room temperature. Unbound SRB was removed by washing three times with 1% AcOH, and the plates were then air-dried while bound stain was solubilized with unbuffered Tris base [tris(hydroxymethyl)aminomethane]. Optical densities at 565 nm were read on a Perkin–Elmer 550 SE spectrophotometer.

The SRB assay was also used to measure the cell population density at time 0 (the time at which the test compounds were added).

Cytostatic activity was evaluated from the inhibition of cell growth in the treated cultures with respect to the controls. IC_{50} , the concentration of test compound at which cell proliferation was 50% of that observed in control cultures, was determined by linear regression analysis. The statistical significance of these results was estimated by means of Student's *t*-test ($P < 0.01$).

Table 1
Crystal and structure refinement data for $[\text{SnEt}_2\text{Br}_2(\text{DMPP})]$

Empirical formula	$\text{C}_{14}\text{H}_{21}\text{Br}_2\text{N}_3\text{Sn}$
Formula weight	509.85
Temperature (K)	293(2)
Wavelength (\AA)	0.71073
Crystal system	monoclinic
Space group	$P2_1/c$
Cell constants	
<i>a</i> (\AA)	8.197(7)
<i>b</i> (\AA)	13.297(5)
<i>c</i> (\AA)	16.797(7)
β ($^\circ$)	96.70(5)
<i>V</i> (\AA^3)	1818.2(18)
<i>Z</i>	4
D_{calc} (g cm^{-3})	1.863
Absorption coefficient (mm^{-1})	5.795
<i>F</i> (000)	984
Theta range ($^\circ$)	2.44–24.19
Crystal size (mm)	$0.20 \times 0.15 \times 0.10$
Index ranges	$-9 \leq h \leq 0,$ $0 \leq k \leq 15,$ $-19 \leq l \leq 19$
Reflections collected	3144
Unique reflections	2920 [$R_{\text{int}} = 0.1300$]
Absorption correction	Psi-Scans
Max/min transmission factors	0.962, 0.916
Refinement method	full-matrix least-squares on F^2
Data/restraints/parameters	2920/0/185
Goodness-of-fit on F^2	0.978
Final <i>R</i> indices [$I > 2\sigma(I)$]	$R_1 = 0.0605, wR_2 = 0.1330$
<i>R</i> indices (all data)	$R_1 = 0.3206, wR_2 = 0.2108$
Largest difference peak and hole (e \AA^{-3})	0.892 and -1.419

3. Results and discussion

3.1. Description of the structure of $[\text{SnEt}_2\text{Br}_2(\text{DMPP})]$ (7)

Fig. 1 shows the PLATON representation of the molecular structure of the complex, together with the atomic numbering scheme. Table 2 lists selected bond lengths and angles.

The crystal consists of isolated $\text{SnEt}_2\text{Br}_2(\text{DMPP})$ units. In each unit the coordination sphere around the tin atom is formed by two donor N atoms, two mutually trans ethyl carbon atoms and two cis Br atoms in a pseudo-octahedral distribution. Whereas the Sn–C distances, 2.11(3) and 2.143(19) \AA , are slightly shorter than

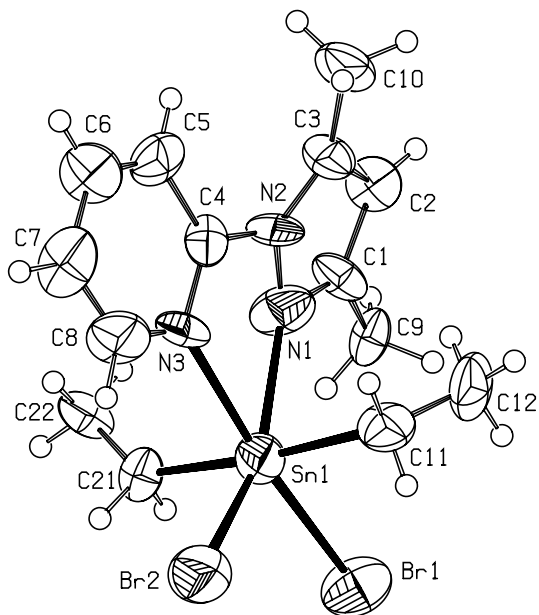


Fig. 1. The crystal structure of $[\text{SnEt}_2\text{Br}_2(\text{DMPP})]$, showing the numbering scheme.

the sum of the covalent radii (2.17 Å) [17], the Sn–N and Sn–Br bonds are significantly longer than the corresponding covalent radii sums (2.15 and 2.54 Å, respectively [17]): Sn–N = 2.379(16) and 2.387(16) Å, and Sn–Br = 2.631(3) and 2.703(3) Å. Although there are no known *trans*- SnC_2 , *cis*- SnN_2 , *cis*- SnBr_2 complexes of SnEt_2Br_2 with which to compare **7**, it may be compared with $[\text{SnMe}_2\text{Br}_2(\text{M})]$ (M = mepirizole) [5], in which one of the two donor N atoms belongs to a pyrimidine ring (cf. pyridine in DMPP), and the other, as in DMPP, to a pyrazole ring with a methyl substituent on a vicinal C atom. As in the mepirizole complex, the pyrazole nitrogen is the more closely bound to the Sn atom and lies *trans* to the longer Sn–Br bond, although both the Sn–N bonds are shorter and both the Sn–Br bonds longer than in the mepirizole complex.

Although some bond angles are close to the 90° proper to ideal octahedral geometry [C(11)–Sn(1)–N(1) = 87.1(7); C(21)–Sn(1)–N(3) = 89.9(9); C(11)–Sn(1)–Br(1) = 90.2(5)°], Br(1)–Sn(1)–Br(2) is wider [98.00(10)°] because of the bulk of the Br atoms, and N(1)–Sn(1)–N(3), is much narrower [66.8(6)°] because of the rigidity of the bidentate ligand.

The pyridine and pyrazole rings of the ligand lie at an angle of about 30° to each other, and the Sn atom lies slightly out of the least-squares plane defined by the two N and two Br atoms.

The structural parameters of the ligand rings differ only slightly from those found by Phillips and Steel [18] in free 2,2'-bis(3,5-dimethyl)-pyrazol-1-yl-4,4'-bipyridine, a dimer consisting of two DMPP molecules linked via the C(4) atoms of the pyridine rings. Even around

Table 2

Selected bond lengths (Å) and angles (°) in $[\text{SnEt}_2\text{Br}_2(\text{DMPP})]$, with e.s.d.s in parentheses

(a) Tin environment

Bond lengths			
Sn(1)–C(21)	2.11(3)	Sn(1)–C(11)	2.143(19)
Sn(1)–N(1)	2.379(16)	Sn(1)–N(3)	2.387(16)
Sn(1)–Br(2)	2.631(3)	Sn(1)–Br(1)	2.703(3)
Bond angles			
C(21)–Sn(1)–C(11)	172.3(11)	C(21)–Sn(1)–N(1)	85.6(10)
C(11)–Sn(1)–N(1)	87.1(7)	C(11)–Sn(1)–N(3)	89.0(6)
C(21)–Sn(1)–N(3)	89.9(9)	C(21)–Sn(1)–Br(2)	96.1(11)
N(1)–Sn(1)–N(3)	66.8(6)	N(1)–Sn(1)–Br(2)	156.4(4)
C(11)–Sn(1)–Br(2)	91.4(5)	C(21)–Sn(1)–Br(1)	89.8(8)
N(3)–Sn(1)–Br(2)	89.7(4)	N(1)–Sn(1)–Br(1)	105.5(4)
C(11)–Sn(1)–Br(1)	90.2(5)	Br(2)–Sn(1)–Br(1)	98.0(10)
N(3)–Sn(1)–Br(1)	172.3(4)	C(22)–C(21)–Sn(1)	131.0(3)
C(12)–C(11)–Sn(1)	119.8(13)		

(b) DMPP ligand

Bond lengths			
N(1)–C(1)	1.32(3)	N(1)–N(2)	1.41(2)
N(2)–C(3)	1.32(2)	N(2)–C(4)	1.41(2)
N(1)–C(8)	1.32(2)	N(3)–C(4)	1.34(2)
C(1)–C(2)	1.41(3)	C(1)–C(9)	1.56(3)
C(2)–C(3)	1.41(3)	C(3)–C(10)	1.51(2)
C(4)–C(5)	1.42(2)	C(5)–C(6)	1.33(2)
C(6)–C(7)	1.37(3)	C(7)–C(8)	1.39(3)
C(11)–C(12)	1.50(2)	C(21)–C(22)	1.24(4)
Bond angles			
C(1)–N(1)–N(2)	100.1(18)	C(1)–N(1)–Sn(1)	136.0(16)
N(2)–N(1)–Sn(1)	114.9(12)	C(3)–N(2)–C(4)	131.7(17)
C(3)–N(2)–N(1)	115.3(17)	C(4)–N(2)–N(1)	112.8(15)
C(8)–N(3)–C(4)	116.1(17)	C(8)–N(3)–Sn(1)	125.6(13)
C(4)–N(3)–Sn(1)	118.3(13)	N(1)–C(1)–C(2)	115.0(2)
N(1)–C(1)–C(9)	122.0(2)	C(2)–C(1)–C(9)	123.0(2)
C(3)–C(2)–C(1)	103.6(19)	N(2)–C(3)–C(2)	105.6(18)
N(2)–C(3)–C(10)	127.0(2)	C(2)–C(3)–C(10)	127.0(2)
N(3)–C(4)–N(2)	117.4(16)	N(3)–C(4)–C(5)	122.8(18)
N(2)–C(4)–C(5)	119.3(18)	C(6)–C(5)–C(4)	117.0(2)
C(5)–C(6)–C(7)	122.0(2)	C(6)–C(7)–C(8)	117.1(19)
N(3)–C(8)–C(7)	124.5(18)		

the donor atoms, the bond lengths are only slightly different: in the pyridine ring, for example, N(3)–C(4) = 1.34(2) Å as against 1.32 Å in the dimer, and N(3)–C(8) = 1.32(2) Å as against 1.34 Å; while in the pyrazole ring: N(1)–N(2) = 1.41(2) and N(1)–C(1) = 1.32(3) Å as against 1.37–1.38 and 1.31 Å, respectively in the dimer. Nor does coordination significantly change the C(8)–N(3)–C(4) bond angle [116.2(1) and 115.9(1)° in the dimer, 116.1(17)° in the complex], although coordination of the pyrazole N makes the C(1)–N(1)–N(2) angle narrow from 103.9(4) or 104.9(4)° in the dimer to 100.1(18)° in the complex. In $[\text{Fe}(\text{DMPP})_3](\text{ClO}_4)_2$ and $[\text{Ni}(\text{DMPP})_3](\text{BF}_4)_2$, the two DMPP compounds that have been studied previously by X-ray diffractometry [7b], the N(3)–C(4), N(3)–C(8), N(1)–N(2) and N(1)–C(1) bonds have mean lengths of 1.35, 1.34, 1.37 and 1.28 Å, respectively; the angles C(8)–N(3)–C(4) and C(1)–N(1)–N(2) are respectively 114(1) and 108(1)° in

the Ni compound and 115(1) and 107(2)° in the Fe compound (measured at 294 K); and the bite angles are 77.7(3) and 80.5(5)° in the Ni and Fe compounds, respectively.

3.2. Infrared and Raman spectra

The DMPP ring bands at 1590vs (1592s), 1579vs (1578s) and 1475vs (1479s) are shifted to similar extents in the spectra of all the complexes, which suggests that in all of them DMPP has the same *N,N'*-didentate behaviour as was observed in **7** by X-ray diffractometry. In the 650–100 cm⁻¹ range the $\nu(\text{Sn-X})$ and the $\nu(\text{Sn-C})$ stretching bands appear. None of the spectra of the [SnX₄(DMPP)] compounds show all the four $\nu(\text{Sn-X})$ bands ($2A_1 + B_1 + B_2$) that would be expected in both the IR and Raman spectra if there were local *C*_{2v} symmetry around the metal atom, and neither do all the [SnR₂X₂(DMPP)] spectra show the two IR and two Raman bands expected for a *cis*-(X-Sn-X) fragment. However, all the bands observed are very close to bands found in systems with this fragment [7c,19,20]. For the [SnR₂X₂(DMPP)] compounds, the number and activity of the $\nu_s(\text{Sn-C})$ and $\nu_{as}(\text{Sn-C})$ bands in the IR and Raman spectra are in keeping with the presence of a bent trans C-Sn-C fragment, as was found by X-ray diffractometry in the case of the bromoethyl derivative.

3.3. Mössbauer spectra

The Mössbauer spectra of all the compounds show singlets or doublets with narrow linewidths (0.79–0.96 mm s⁻¹) suggesting the existence of a single tin site. The hyperfine parameters (isomer shift and quadrupole splitting) are typical of [SnX₄(LL)] and [SnR₂X₂(LL)] complexes. The I.S. decrease as the electronegativity of the ligands increases (from I to Cl and from alkyl to aryl groups), in accordance with the expected trend in the charge density in the s-orbital of the metal atom. The dependence of the I.S. on the Mulliken electronegativity of the halogen in the [SnX₄(DMPP)] series is in fact linear, as expected, but the slope (-0.94) is much steeper than has been reported for similar compounds [21,22]. This increase in slope may be due to the strong asymmetry introduced in the structure by the small N-Sn-N angle imposed by the ligand. It is also noteworthy that the I.S. values themselves are somewhat higher than expected [22,23], as is also the case for the organometallic derivatives [24].

Quadrupole splitting (Q.S.) reflects the field gradient generated around the tin nucleus by the σ and π bonds formed with the six donor atoms, and provides information about the charge distribution arising from the arrangement of the ligands around the metal. The [SnX₄(DMPP)] compounds have Q.S. values near zero, as is expected for *cis* derivatives. Although their being

less than half a linewidth means they have a large relative error, the Sn-X bond lengths can be calculated, using published formulae [25], as 2.43 and 2.60 Å for the chloride and bromide derivatives, respectively. The Q.S. values for the [SnR₂X₂(DMPP)] derivatives are much larger (around 4 mm s⁻¹), and are fully in keeping with the trans arrangement of the R groups around the tin centre and with the C-Sn-C angles being quite close to the ideal 180°, since values close to 2 mm s⁻¹ are expected for *cis* C-Sn-C [26] and the values calculated using the point charge formalism with the C-Sn-C angle observed for **7** are around 3.9 mm s⁻¹.

3.4. Conductimetric measurements

The molar conductivities of 10⁻³ M solutions of the compounds in acetonitrile indicate that they are non-ionic in this solvent [27].

3.5. NMR spectroscopy

¹H NMR spectra of the complexes were recorded in CDCl₃. The DMPP signals at 2.30 [s, C(3)H₃], 6.00 [s, C(4)H], 2.63 [s, C(5)H₃], 7.14 [m, C(3')H], 7.82 [m, C(4')H], 7.77 [m, C(5')H] and 8.42 [m, C(6')H] ppm are only slightly shifted upon coordination, particularly in the SnR₂X₂ complexes. The ¹H NMR data obtained for these complexes are close to those of the free acceptors. In the case of the methyl derivatives, for example, singlets are observed at 1.19 ppm (X = Cl) and 1.38 ppm (X = Br), at the same or nearly the same positions as for SnMe₂Cl₂ (1.21 ppm) and SnMe₂Br₂ (1.38 ppm), respectively, and the values of ²J(^{117/119}Sn-¹H) (73.0/76.4 Hz for X = Cl; 63.9/66.7 Hz for X = Br) are also close or almost identical to those reported previously [28] for the free acceptors in the same solvent (65.7/68.7 and 63.2/66.1 Hz, respectively). These and the analogous data for the Et, Bu and Ph derivatives suggest that the chloride complexes are significantly dissociated in CDCl₃ and the bromide complexes almost completely, as is found in similar systems [7c,29].

Table 3
Results of in vitro cytostatic assays against cell line KB

Compound	IC ₅₀ (μg ml ⁻¹ medium)	IC ₅₀ (μM)
[SnEt ₂ Cl ₂ (DMPP)]	0.39	0.92
[SnEt ₂ Br ₂ (DMPP)]	4.49	8.81
[SnBu ₂ Cl ₂ (DMPP)]	0.13	0.30
[SnBu ₂ Br ₂ (DMPP)]	0.31	0.57
[SnPh ₂ Cl ₂ (DMPP)]	0.18	0.35
[SnPh ₂ Br ₂ (DMPP)]	0.39	0.65
<i>cis</i> -[PtCl ₂ (NH ₃) ₂]	0.11	0.37

3.6. *In vitro* cytostatic activity

Table 3 lists the IC₅₀ values of the compounds, expressed in μM, together with that of *cis*-[PtCl₂(NH₃)₂] for comparison. The butyl derivatives were the most active, and the ethyl derivatives the least. In particular, [SnBu₂Cl₂(DMPP)] was even more active than *cis*-[PtCl₂(NH₃)₂]. However, all the [SnR₂X₂(DMPP)] compounds except [SnEt₂Cl₂(DMPP)] were less active than the corresponding complexes of mepirizole, which in previous work were tested against the same cell line [4]. The bromide derivatives were less active than the chlorides.

4. Supplementary material

Complete crystallographic data for the structure reported in this paper have been deposited at the Cambridge Crystallographic Data Centre CCDC No. 187415. Copies of this data may be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336-033, e-mail: deposit@ccdc.cam.ac.uk or www: <http://www.ccdc.cam.ac.uk>).

Acknowledgements

We thank the Xunta de Galicia, Spain, for financial support of this work.

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