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Technetium complexes of capped tetradentate ligands
I. The synthesis and crystal and molecular structure of $[TcBr_2N\{(pyCH_2)_2NCH_2CMe_2SCH_2Ph\}]$ (py = 2-pyridyl) and its behaviour in solution

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Abstract

Reaction of $[TcBr_2N(PPh_3)_2]$ with $(pyCH_2)_2NCH_2CMe_2SCH_2Ph$ (L^1) in acetonitrile gives $[TcBr_2N(L^1)]$ in good yield. Crystal data: triclinic, space group $P\bar{1}$ (No 2), $a = 7.458(1)$, $b = 10.852(3)$, $c = 16.598(6)$ Å; $\alpha = 84.07(2)$, $\beta = 86.24(2)$, $\gamma = 72.44(2)°$; $U = 1273.1$ Å^3, $\lambda = 1.5406$ Å, $Z = 2$; $D_{calc} = 1.694$ g cm^{-3}; $F(000) = 644$. A total of 4204 unique reflections was collected; 3173 were used for structure solution and refinement to give $R = 0.070$. The geometry about the Tc atom is pseudo-octahedral with L^1 functioning as a tridentate ligand, the S atom being uncoordinated. However, NMR spectroscopy shows that in solution there is an equilibrium between this form and one in which a bromide ion is expelled and the thioether sulphur is ligated. The related unmethylated ligand, $(pyCH_2)_2NCH_2CH_2SCH_2Ph$ (L^2) behaves similarly.

Introduction

There continues to be considerable interest in the coordination chemistry of technetium with polydentate ligands in the context of developing new complexes with potential uses in diagnostic nuclear medicine [1]. Although many tetradentate ligands have been investigated, the majority of these have coordinated in a planar or near planar manner around the metal ion. We here report the initial findings of a programme to study the chemistry of a wide range of capped tetradentate ligands in the hope that these will impose novel geometries and coordination numbers on the technetium. Investigation of the chemistry of pyridine thiolate ligands has been restricted to studies of binuclear molybdenum oxo-complexes [2] and a binuclear nickel complex $[Ni_2(L^1)_2(OAc)_2]^{2+}$ which has a disulfide bridge [3].

Experimental

Caution: technetium^{99} is a weak β-emitter and should be handled at all times in an appropriate radiochemical laboratory. Technetium was provided in the form of aqueous pertechnetate solution by Amersham International and was used as supplied. The complex $[TcBr_2N(PPh_3)_2]$ was prepared by the literature method [4]. NMR spectra were obtained on a JEOL EX270 spectrometer operating at 270MHz for protons. HPLC was carried out using a Gilson chromatograph fitted with β- and UV detectors. Microanalyses were performed by Butterworth laboratories.

Ligand synthesis

2-Benzylmercapto-2-methylpropionyl chloride

A mixture of 2-benzylmercapto-2-methylpropionic acid [5] (10 g, 48 mmol), thionyl chloride (5.7 g, 48 mmol) and toluene (150 cm^3) was stirred at room temperature for 2 days. A further quantity of thionyl

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chloride (5 g) was then added and the stirring continued for a further day. Volatile components were removed under reduced pressure to give the acid chloride (10.25 g, 93%) which was sufficiently pure to be used without additional purification.

$\delta(^{13}C)(CDCl_3)$ 25.7(×2), 34.7, 57.3, 127.3, 128.5(×2), 129.0(×2), 135.7, 175.1.

Bis(2-pyridylmethyl)amine

2-Chloromethylpyridine (16.5 g, 130 mmol) was added in portions with stirring to 2-aminomethylpyridine (70.3 g, 650 mmol). The reaction was slightly exothermic, and the temperature rose to approx 45 °C. After 0.5 h chloroform (100 cm^3) was added and the resulting solution shaken with aqueous sodium hydroxide solution (40 cm^3, 2M). The aqueous phase was separated, extracted with chloroform, and the chloroform extracts combined with the original chloroform solution. After removal of the chloroform, the excess 2-aminomethylpyridine was removed under reduced pressure (80 °C, 0.01 mmHg) to give bis(2-pyridylmethyl)amine (22.7 g, 88%), in a sufficiently pure state to be used without further purification.

$\delta(^{13}C)$ $(CDCl_3)$ 54.3, 121.7, 122.1, 136.2, 149.0, 159.0.

N, N-Bis(2-pyridylmethyl)-2-benzylmercapto-2-methylpropionamide

To a mixture of bis(2-pyridylmethyl)amine (7.5 g, 38 mmol), chloroform (70 cm^3) and aqueous sodium hydroxide (30 cm^3; 12.5 M) was added 2-benzylmercapto-2-methylpropionyl chloride (8.9 g, 39 mmol) in small quantities, with vigorous shaking after each addition. The organic layer was separated and the aqueous layer extracted with chloroform. The combined chloroform extracts were dried and the solvent removed under reduced pressure (60 °C at 0.05 mmHg) to give the amide (14.4 g, 94%) as an oil which solidified on cooling. When necessary further purification was achieved by chromatography on florisil using an ethyl acetate/petrol (b.p. 60–80 °C) mixture (1:1) as eluant. *Anal.* Found: C, 70.26; H, 6.54; N, 10.72. Calc. for $C_{23}H_{25}N_3OS$: C, 70.56; H, 6.44; N, 10.73%.

$\delta(^{13}C)$ $(CDCl_3)$ 28.2(×2), 34.4, 48.6, 52.8(br), 55.0(br), 122.0(×2), 122.2(br), 126.9, 128.4(×2), 129.1(×2), 136.5(br×2), 137.1, 149.3(br×2), 157.5(×2), 173.4.

2-Benzylmercapto-2-methylpropyl-bis(2-pyridylmethyl)amine

To a solution of *N*, *N*-bis(2-pyridylmethyl)-2-benzylmercapto-2-methylpropionamide (7.8 g, 20 mmol) in dry tetrahydrofuran (15 cm^3) under dry nitrogen was added a solution of a borane/tetrahydrofuran complex in tetrahydrofuran (110 cm^3, 1M) and the mixture heated under reflux for 4 h. Excess borane complex was then destroyed by the careful addition of absolute ethanol The solvent was removed and the residue dissolved in ethanol (100 cm^3) and heated under reflux for 2 h. The solvent and other volatile components were then removed under reduced pressure (50 °C at 0.01 mmHg) to give 2-benzylmercapto-2-methylpropyl-bis(2-pyridylmethyl)amine (6.8 g, 90%). *Anal.* Found: C, 72.88; H, 7.28; N, 11.1. Calc. for $C_{23}H_{27}N_3S$: C, 73.17; H, 7.2; N, 11.13%.

$\delta(^{13}C)$ $(CDCl_3)$ 27.0(×2), 32.8, 47.9, 62.1(×2), 64.1, 121.9(×2), 123.4(×2), 126.7, 128.4(×2), 128.9(×2), 136.2(×2), 138.4, 148.9(×2), 159.7(×2).

2-[Bis(2-pyridylmethyl)amino]ethylthiol

A modification of the literature method was used [2]. Bis(2-pyridylmethyl)amine (3 g, 15 mmol) and ethylene sulfide (1.08 g, 18 mmol) in ethanol (15 cm^3) were heated and stirred at 70 °C for 16 h. The resulting mixture was filtered and the solvent and volatile components removed under reduced pressure (20 °C at 0.01 mmHg) to give 2-[bis(2-pyridylmethyl)amino]ethylthiol (3.5 g, 90%) which was sufficiently pure to be used without further purification.

$\delta(^{13}C)$ $(CDCl_3)$ 21.8, 56.2, 59.3(×2), 121.3(×2), 122.3(×2), 135.7(×2), 148.3(×2), 158.5(×2).

2-Benzylmercaptoethyl-bis(2-pyridylmethyl)amine

To a stirred mixture of 2-bis(2-pyridylmethyl)aminoethylthiol (0.82 g, 3.2 mmol) and benzyl chloride (0.6 g, 4.7 mmol) was added dropwise a solution of sodium ethoxide in ethanol (10 cm^3; 1 M). The mixture was stirred for 30 min and then poured into aqueous hydrochloric acid (20 cm^3; 2M). The aqueous phase was washed with diethyl ether (2×15 cm^3) and then made slightly basic by the addition of sodium hydroxide. The resulting solution was extracted with dichloromethane (3×15 cm^3) and the combined extracts dried (K_2CO_3). Removal of the solvent and other volatile components under reduced pressure (50 °C at 0.01 mmHg) gave 2-benzylmercaptoethyl-bis(2-pyridylmethyl)amine (1 g, 91%) as a viscous oil.

$\delta(^{13}C)$ $(CDCl_3)$ 28.5, 35.9, 53.1, 59.8(×2), 121.7(×2), 122.6(×2), 126.6, 128.1(×2), 128.5(×2), 136.0(×2), 138.0, 148.6(×2), 159.1(×2).

Dibromonitridobis(2-pyridylmethyl)-2-benzylthio-2,2-dimethylethylaminetechnetium(V) [$TcBr_2N(L^1)$]

[$TcBr_2N(PPh_3)_2$] (0.140 g; 0.176 mmol) and L^1 (0.30 g; 0.300 mmol) were heated under reflux in methyl cyanide (10 cm^3) until all the nitride precursor had dissolved (*c.* 3 h). Further heating causes decomposition. HPLC indicates the presence of a single Tc species at this stage. Diethyl ether (20 cm^3) was added and the resulting orange solid was filtered in air, washed with ether and dried. Yield 0.114 g, 60%. *Anal.* Found: C, 42.3; H, 4.0; N, 8.7. Calc. for $C_{23}H_{27}N_4Br_2STc$: C, 42.5; H, 4.2; N, 8.6%.

Dibromonitrido(2-pyridylmethyl)-2-benzylthioethylaminetechnetium(V), [TcBr$_2$N(L^2)]

This complex was prepared in analogous fashion to that above, using $[TcBr_2N(PPh_3)_2]$ (0.147 g, 0.184 mmol) and L^2 (0.110 g, 0.315 mmol), in 58% yield. *Anal.* Found: C, 41.0; H, 3.5; N, 9.0. Calc. for $C_{21}H_{23}N_4Br_2STc$: C, 40.5; H, 3.7; N, 9.0%.

Results and discussion

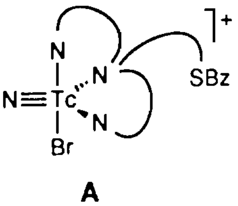
Synthesis of ligands and complexes

The benzylated thioether ligands were prepared from bis(2-pyridylmethyl)amine, by reaction with 2-benzylmercapto-2-methylpropioyl chloride and susequent reduction with borane in thf (see Scheme 1). The methyl substituents adjacent to the sulfur were introduced to minimise the possibility of thiolate bridging by providing steric bulk. The corresponding unmethylated version was obtained by the preparation of the free thiol by a variant of the literature method followed by benzylation.

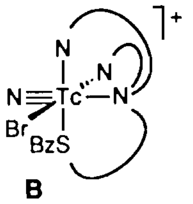
Previously it has been shown that benzyl protecting groups can be removed in reaction with technetium oxo precursors to generate thiolato complexes [6]. However in this instance the benzyl group is maintained on reaction with $[TcBr_2N(PPh_3)_2]$ to give the title complex. In order to investigate if the failure to deprotect the sulfur was due to the steric effect of the adjacent methyl groups, the corresponding unmethylated ligand L^2 was reacted with the nitride; but this also retained the benzyl group. Reaction of the free thiol gave an untractable mixture with multiple HPLC peaks and the individual components could not be separated. The potentially tridentate bis(2-pyridyl)amine also failed to give characterisable products, but this may have been due to the deprotonation of the amine nitrogen in the course of the reaction.

The complexes were isolated as air and moisture stable orange solids, soluble in most polar organic solvents. Their IR spectra showed the presence of the nitride ligand with a medium intensity bands at 1072 (L^1) and 1065 (L^2) cm^{-1} and none of the characteristic bands due to triphenylphosphine.

The 270 MHz ^1H NMR spectrum of $[TcBr_2N(L^1)]$ in $CDCl_3$ solution shows two signals of equal intensity at 1.21 and 1.57 ppm with a shoulder at 1.55 ppm, assigned to the gem-dimethyl groups. However, the structure as determined by X-ray diffraction (see below) would have equivalent methyl groups. In addition, the 5-protons of the pyridyl residue give rise to three signals at 9.41, 9.24 and 8.76 ppm in the ratio 1:3:3 (see Fig. 1) whereas the solid state structure requires only one environment for this proton. Moreover, the conductivity of the complex in MeCN was found to approach that of a 1:1 electrolyte at infinite dilution. It was a little lower than that of $[PPh_4]Br$ at concentrations comparable with those used for the NMR.



A



B

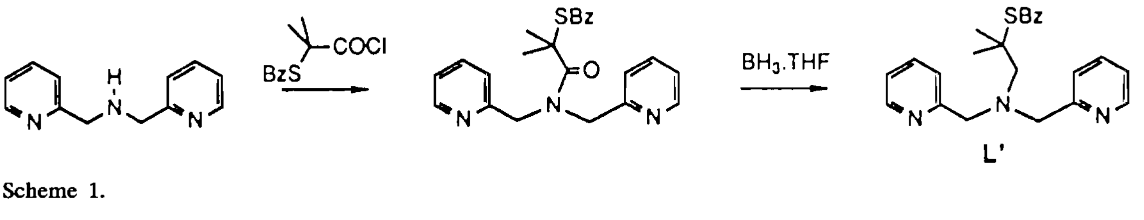
Two structures, A and B, can be drawn to rationalise the conductivity and NMR data. Structure A seems less probable, as it would require a highly distorted trigonal bipyramidal geometry to accommodate the ligand bite angles. Also the large shift difference between the two methyl signals suggests they are relatively close to the site of the asymmetry. The presence of the *three* resonances for the pyridyl 5-protons is therefore attributed to an equilibrium in solution involving structure B together with a small concentration of the solid state structure.

X-ray crystal and molecular structure of [TcBr$_2$N(L^1)]

Structure determination

A pale yellow needle was sealed in a capillary and mounted on a Enraf-Nonius CAD4, diffractometer.

Crystal data. $C_{23}H_{27}N_4SBr_2Tc$, $M=649.38$, triclinic, space group $P\bar{1}$ (No. 2), $a=7.458(1)$, $b=10.852(3)$, $c=16.598(6)$ Å, $\alpha=84.07(2)$, $\beta=86.24(2)$, $\gamma=72.44(2)$°, $U=1273.1$ Å^3 (from 20 values of 100 reflections), $\lambda=1.54056$ Å, $T=293$ K, $Z=2$. $D_{calc}=1.694$ g cm^{-3}, $\mu=92.81$ cm^{-1}, $F(000)=644$.



Scheme 1.

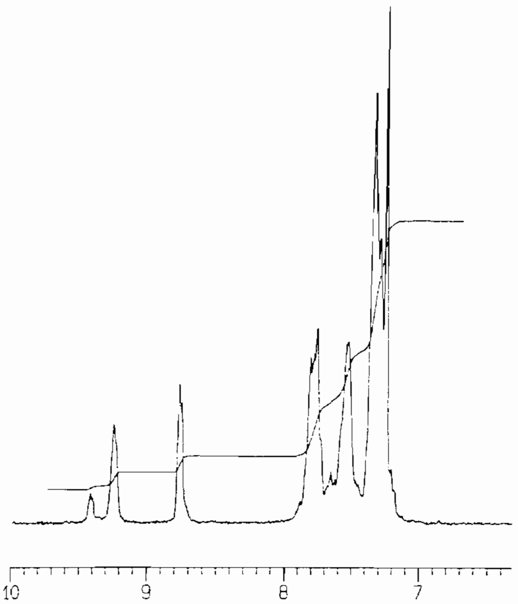


Fig. 1. 270 MH_2 ^{1}H NMR spectrum of $[TcBr_2N(L^1)]$ in $CDCl_3$ solution showing resonances due to pyridyl protons.

Data collection and processing. CAD4 diffractometer, graphite-monochromated Cu Kα radiation, $T=293$ K, ω–2θ scans, 4204 unique data collected, $\theta_{max}=69°$, h $0\rightarrow 9$, $k-13\rightarrow 13$, $l-20\rightarrow 20$, 3173 reflections with $(I>3\sigma(I))$ for use in all calculations. No significant crystal decay was observed.

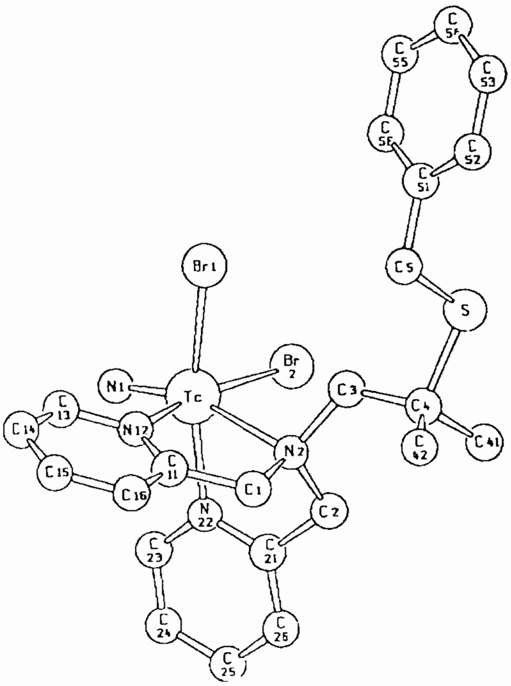


Fig. 2. Representation of the structure of $[TcBr_2N(L^1)]$ showing the atom numbering scheme.

TABLE 1. Selected bond lengths and angles for $[TcBr_2N(L^1)]$

Bond lengths (Å)			
Tc–Br1	2.539(2)	Tc–N2	2.47(1)
Tc–Br2	2.530(2)	Tc–N12	2.116(9)
Tc–N1	1.61(1)	Tc–N22	2.166(9)
Bond angles (Å)			
Br1–Tc–Br2	92.36(5)	Br2–Tc–N22	87.6(2)
Br1–Tc–N1	100.7(4)	N1–Tc–N2	161.4(2)
Br1–Tc–N2	92.3(3)	N1–Tc–N12	93.9(4)
Br1–Tc–N12	86.3(3)	N1–Tc–N22	93.1(5)
Br1–Tc–N22	166.0(4)	N2–Tc–N12	74.5(3)
Br2–Tc–N2	90.3(2)	N2–Tc–N22	72.7(4)
Br2–Tc–N12	164.7(3)	N12–Tc–N22	90.0(3)

Numbers in parentheses are e.s.d.s. in the least significant digits.

Structure solution and refinement. The structure was solved by a Patterson synthesis and subsequent iterative cycles of least-squares refinement and difference Fourier synthesis [7]. At isotropic convergence, corrections (min. 0.473, max. 2.089) for absorption were applied using DIFABS [8]. Final refinement (on F) with anisotropic displacement parameters for all non-hydrogen atoms and with hydrogen atoms in fixed, calculated positions converged at $R=0.070$ and $R_\omega=0.070$, respectively. $S=3.123$ for 281 refined parameters; a secondary extinction coefficient [9] refined to $1.0(6)\times 10^{-7}$. A graphic representation [10] of the structure of the complex is shown in Fig. 2, together with an atom labelling scheme. Table 1 gives selected bond lengths and angles. The geometry about the technetium is best described as distorted octahedral with the relatively small bite angles of the dipyridylamine moiety providing the principal distorting force. This is reflected in the N(2)–Tc–N(12) and N(2)–Tc–N(22) angles of 74.5(3) and 72.7(4)°, respectively. The technetium–nitride distance of 1.61(1) Å lies well within the range found for other Tc(V) nitride complexes [11–15] and there is a particularly long Tc–N bond (2.47(1) Å) *trans* to the nitride group. This is further manifestation of the well documented high *trans*-influence of the N^{3-} ligand shown in complexes such as $[TcN(NCS)_2(MeCN)(PPh_3)_2]$ where the corresponding Tc–N distance is 2.491(4) Å, and is unconstrained by chelate ring effects.

Supplementary material

Further details of the structure determination (atomic positional parameters, displacement factor coefficients and F_o/F_c tables) may be obtained from: Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-7514 Eggenstein-Leopoldshafen 2, by quoting the Registry-No. CSD 55066, the names of the authors and the journal citation.

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