



Note

Reactions of the tridentate and tetradentate amine ligands di-(2-picolyl)(*N*-ethyl)amine and 2,5-bis-(2-pyridylmethyl)-2,5 diazohexane with technetium nitrosyl complexes

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ABSTRACT

The reaction of the Tc(II) nitrosyl complex (Bu₄N)[Tc(NO)Cl₄] with di-(2-picolyl)(NEt)amine in methanol yields the neutral complex [Tc(NO)Cl(py-N(Et)-py)]. The reaction of the Tc(I) nitrosyl complex [Tc(NO)Cl₂(HOMe)(PPh₃)₂] with this tridentate ligand yields cationic [Tc(NO)Cl(py-N(Et)-py)(PPh₃)₂]⁺Cl⁻. These two complexes have been structurally characterized. The reaction of [Tc(NO)Cl₂(HOMe)(PPh₃)₂] with the tetradentate ligand 1,4-bis-(2-pyridylmethyl)-1,4-diazobutane yields a mixture of products including cationic [Tc(NO)Cl(py-NH-NH-py)]⁺Cl⁻ and cationic [Tc(NO)Cl(PPh₃)(py-NH-NH-py)]⁺Cl⁻, with a pyridyl terminus left dangling.

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1. Introduction

We recently began studies of Tc-nitrosyl chemistry which represents a new and novel core for radiopharmaceutical development. To gain a better understanding of the nature of the ligand donor-set and coordination geometries necessary for the synthesis of ^{99m}Tc-nitrosyl complexes, the long-lived macroscopic ⁹⁹Tc=N=O core was studied, starting initially with the redox active Tc(II) precursor (Bu₄N)[⁹⁹Tc(NO)Cl₄]. Previous results from the reaction with the neutral, tridentate ligand {Ph₂PCH₂CH₂N(R)CH₂CH₂PPh₂}, (PNP) highlight the many hurdles encountered when employing this highly reactive Tc(II)-nitrosyl precursor. This reaction yielded both the *mer*- and *fac*-structural isomers of [Tc(NO)Cl₂(PNP)], which were isolated and structurally characterized. Both of these species are present in equilibrium during the course of the reaction, as determined by infrared spectroscopy [1]. Herein we describe studies with the Tc(I) nitrosyl precursor [Tc(NO)Cl₂(HOMe)(PPh₃)₂] and its reactions with various ligands and their coordination geometries.

2. Experimental

ESI Mass Spectrometry was performed on a Bruker Daltonics APEX IV FT-ICR-MS (Fourier Transform-Ion Cyclotron

Resonance–Mass Spectrometer) with ESI (Electrospray Ionization) or DART (Direct Analysis in Real Time – made by IonSense) ion source. ESI condition: Drying gas (N₂) at 30 psi, heated to 230 °C; Nebulizing gas (N₂) at 40 psi, with no heat. Voltage applied to Capillary at –3724 V, End-plate at –3281 V, and CapExit at 112.4 V. DART condition: Drying gas (N₂) at 10 psi; reaction gas (He) at 2.2 L/min and heated up to 200–500 °C, depending on the sample's molecular weight (higher temperature for higher MW). Sample solution: Most samples were dissolved in 50–100 μL of dichloromethane, then methanol added.

2.1. [Tc(NO)Cl₂(pyN(Et)py)] complex (1)

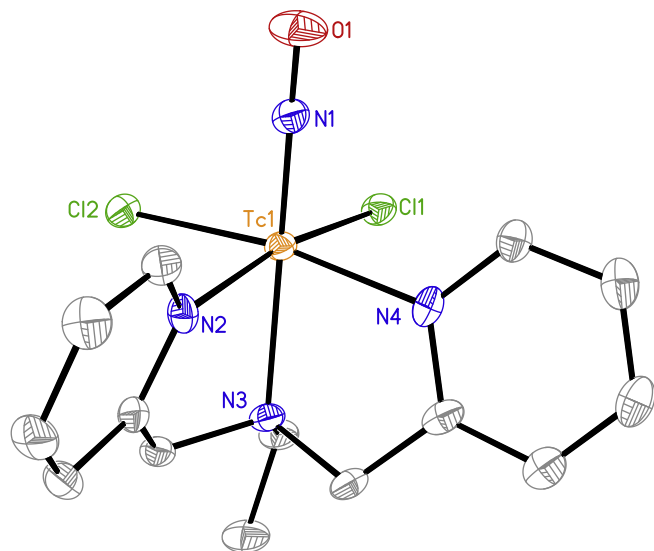
To a solution of (Bu₄N)[Tc(NO)Cl₄] [2] (45 mg, 0.09 mmole) in 45 mL of CH₂Cl₂ was added di-(2-picolyl)(*N*-ethyl)amine (20 mg, 0.092 mmole), which was stirred overnight at room temperature. The resulting orange solution was concentrated under vacuum and chromatographed, yielding 2 yellow bands in addition to an insoluble residue. The major band was evaporated to dryness, redissolved in dichloromethane and layered with methanol and ether to give a deep orange crystalline product. Yield: 23%. ESI-MS(+) (*m/z*): 426 [Tc(NO)Cl₂(pyN(Et)py)]⁺, 391 [Tc(NO)Cl(pyN(Et)py)]⁺. IR (neat): ν(N=O) 1788 (vs).

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Table 1
Selected bond lengths (Å) and angles (°) for [Tc(NO)Cl₂(pyN(Et)py)].

Bond lengths (Å)		Bond angles (°)			
Tc–N1	1.744(4)	Tc1–N1–O1	172.5(4)	N4–Tc1–Cl2	168.85(12)
N1–O1	1.187(6)	N1–Tc1–N4	94.60(18)	N2–Tc1–Cl2	89.78(11)
Tc–N3 _(ali)	2.233(4)	N1–Tc1–N2	92.56(18)	N3–Tc1–Cl2	90.73(11)
Tc–N2 _(py)	2.109(4)	N4–Tc1–N2	91.79(16)	N1–Tc1–Cl1	97.90(14)
Tc–N4 _(py)	2.097(4)	N1–Tc1–N3	166.23(17)	N4–Tc1–Cl1	86.28(12)
Tc–Cl1	2.4404(12)	N4–Tc1–N3	78.98(16)	N2–Tc1–Cl1	169.48(12)
Tc–Cl2	2.4349(12)	N2–Tc1–N3	75.62(15)	N2–Tc1–Cl1	90.17(4)
		N1–Tc1–Cl2	96.36(14)	N3–Tc1–Cl1	93.86(11)

**Fig. 1.** ORTEP diagram of neutral complex (1) [Tc(NO)Cl₂(pyN(Et)py)].**Table 2**
Selected bond lengths (Å) and angles (°) for [Tc(NO)Cl(pyN(Et)py)(PPh₃)Cl].

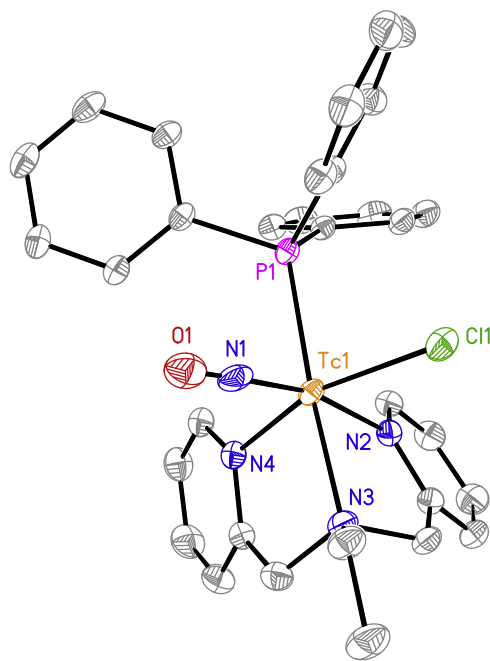
Bond lengths (Å)		Bond angles (°)			
Tc–N1	1.796(3)	O1–N1–Tc1	178.4(2)	N4–Tc1–Cl1	159.77(6)
N1–O1	1.088(3)	N1–Tc1–N4	96.94(9)	N3–Tc1–Cl1	89.65(6)
Tc–N3 _(ali)	2.215(2)	N1–Tc1–N3	94.08(9)	N2–Tc1–Cl1	85.31(6)
Tc–N2 _(py)	2.221(2)	N4–Tc1–N3	80.19(9)	N1–Tc1–P1	87.20(7)
Tc–N4 _(py)	2.138(2)	N1–Tc1–N2	168.57(9)	N4–Tc1–P1	103.08(6)
Tc–P1	2.4133(7)	N4–Tc1–N2	75.35(8)	N3–Tc1–P1	176.33(7)
Tc–Cl1	2.3984(8)	N3–Tc1–N2	76.46(8)	N2–Tc1–P1	102.65(6)
		N1–Tc1–Cl1	101.22(8)	Cl1–Tc1–P1	86.72(2)

2.2. [Tc(NO)Cl(pyN(Et)py)(PPh₃)Cl] complex (2)

To a solution of [Tc(NO)Cl₂(HOME)(PPh₃)₂] [3] (55 mg, 0.072 mmole) in 60 mL of CH₂Cl₂ was added di-(2-picoly) (*N*-ethyl)amine (17 mg, 0.075 mmole), which was stirred overnight at room temperature. The resulting dark orange solution was concentrated under vacuum and washed with ether. The residue was dissolved in dichloromethane and layered with methanol and ether to give a red crystalline product. Yield: 47%. ESI-MS(+) (*m/z*): 653 [Tc(NO)Cl(pyN(Et)py)(PPh₃)]⁺. IR (neat): ν(N=O) 1786 (vs).

2.3. [Tc(NO)Cl(pyNH-NHpy)]Cl complex (3)

To a solution of [Tc(NO)Cl₂(HOME)(PPh₃)₂] (68 mg, 0.090 mmole) in 55 mL of CH₂Cl₂ was added 2,5-bis-(2-pyridylmethyl)-2,5 diazo-

**Fig. 2.** ORTEP diagram of cationic complex (2) [Tc(NO)Cl(pyN(Et)py)(PPh₃)Cl]. The chloride counter ion has been omitted.

hexane (23 mg, 0.095 mmole) which was stirred overnight at room temperature. The resulting orange solution was concentrated and chromatographed on silica gel, yielding two distinctly separate yellow bands in addition to a significant immobile residue. The major band was evaporated to dryness, redissolved in dichloromethane and layered with methanol and ether to give orange crystalline product. Yield 18%. ESI-MS(+) (*m/z*): 406 [Tc(NO)Cl(pyNH-NHpy)]⁺, 370 [Tc(NO)(pyNH-NHpy)]⁺. IR (neat): ν(N=O) 1710 (vs).

2.4. [Tc(NO)Cl(pyNH-NHpy)(PPh₃)Cl] complex (4)

From the preparation of complex (3), the second yellow band from the chromatographic plate was evaporated to dryness, dissolved in methanol and layered with ether. Upon sitting for 7 days, small green crystals of complex (4) appeared from the yellow solution. Yield 7%. ESI-MS(+) (*m/z*): 668 [Tc(NO)Cl(PPh₃)(pyNH-NHpy)]⁺ 632 [Tc(NO)(PPh₃)(pyNH-NHpy)]⁺, 406 [Tc(NO)Cl(pyNH-NHpy)]⁺, 370 [Tc(NO)(pyNH-NHpy)]⁺. IR (neat): ν(N=O) 1727 (vs).

3. Results and discussion

We recently reported *fac*- and *mer*-isomers of the Tc(I) complex [TcCl₂NO(PNP)], which were isolated and structurally characterized from the reaction of the Tc(II) species (Bu₄N)[TcNOCl₄] and the neutral tridentate phosphine-amine ligand PNP [1]. This product displays oxidation state Tc(I) which suggests there are redox reactions competing with the desired substitution chemistry when employing this Tc(II) precursor.

Similarly, the reaction of the Tc(II) complex (Bu₄N)[TcNOCl₄] with the neutral, tridentate ligand *N*-ethyl-bis(2-picoly)amine in dichloromethane yields a mixture of yellow-brown products which are evident in the infrared spectrum of the crude product as multiple nitrosyl absorptions in the 1700–1900 cm⁻¹ region. Chromatography of this crude reaction mixture on silica produced a prominent yellow band, in addition to a large fraction of insoluble, intractable material. This yellow complex yielded X-ray quality crystals when layered with methanol and diethylether. The single

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