



The synthesis and X-ray structural characterization of *mer* and *fac* isomers of the technetium(I) nitrosyl complex [TcCl₂(NO)(PNPpr)]

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ABSTRACT

The nitrosyl complex H[TcNOCl₄] reacts with the tridentate ligand bis[(2-diphenylphosphino)propyl]amine (PNPpr) to yield a mixture of the *mer* or *fac* isomers of [TcCl₂(NO)(PNPpr)]. In acetonitrile, where the ligand is freely soluble, reaction occurs at room temperature to yield mostly the *mer* isomer with the linear nitrosyl ligand *cis* to the amine ligand; and the phosphine ligands arranged in a mutually *trans* orientation. The reaction in methanol requires reflux to dissolve the lipophilic ligand and generates the *fac* isomer of [TcCl₂(NO)(PNPpr)] as the major product, with the tridentate ligand in a facial arrangement, leaving the chlorides and nitrosyl ligand in the remaining facial sites. The steric bulk of the tridentate ligand's diphenylphosphino-moieties results in a significant distortion from octahedral geometry, with the P–Tc–P bond angle expanded to 99.48(4)°. The infrared spectra display absorptions from these nitrosyl ligands in the 1700 and 1800 cm⁻¹ regions for the *fac* and *mer* isomers, respectively. The ESI(+) mass spectra each display the parent ion at 647 *m/z*.

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1. Introduction

The nitrosyl ligand has been observed to adopt three modes of coordination. In its more common linear bonding mode, the nitrosyl consists of a metal ion doubly bonded to the nitrogen atom which is in turn doubly bonded to the oxygen atom. In its bent conformation, the nitrogen atom is singly bonded to the metal ion which results in a lone pair of electrons residing on the sp² hybridized nitrogen. The third bonding mode is a bridging conformation with the nitrogen atom bridging the two metal ions [1]. The oxygen atom is sp² hybridized in all three structural modes Fig. 1.

The majority of technetium nitrosyl chemistry reported in the literature to date has been synthesized from [Bu₄N][Tc(NO)Cl₄] [2–7]. The preparation of [Bu₄N][Tc(NO)Cl₄] involves reacting [Bu₄N][TcOCl₄] with a slight stoichiometric excess of hydroxylamine hydrochloride in methanol followed by a crystallization from dichloromethane under ether to yield the analytically pure product. The recrystallization is critical when employing [Bu₄N][Tc(NO)Cl₄] as a synthetic intermediate since residual hydroxylamine can cause unintended redox chemistry in subsequent reactions.

Recently, nitrosyl complexes containing the [TcNO(CO)₃]²⁺ core have been reported, synthesized from [Tc(H₂O)₃(CO)₃]⁺ [8], and renewing interest in technetium nitrosyl coordination chemistry for application in radiopharmaceutical development.

The nitrosyl core, in its linear coordination mode, unlike the neutral carbonyl ligands, introduces a mono-positive charge to the complex, which could provide a new handle with which to manipulate biodistributions.

2. Experimental

Caution: Technetium-99 is a weak β-emitter (*E* = 0.292 MeV, *t*_{1/2} = 2.12 × 10⁵ years). All work has been done in laboratories approved for the use of low levels of radioactive materials. Precautions have been detailed elsewhere [9]. Reagents and solvents were used as received unless otherwise stated. Routine infrared spectra were obtained on a Perkin Elmer Spectrum One FTIR Spectrometer. Mass spectra were recorded on a Bruker Daltonics APEXII 3 Tesla Fourier Transform Mass Spectrometer (Ion Cyclotron Resonance Mass Spectrometer). The ligand preparation has been published previously [10].

2.1. X-ray crystallographic data collection parameters

2.1.1. *fac*-[TcCl₂(NO)(PNPpr)]·(1/2CH₂Cl₂)

The crystal data and some experimental details of the structure determination are given in Table 1. A yellow plate shaped crystal of *fac*-[TcCl₂(NO)(PNPpr)] was isolated from the CH₂Cl₂/MeOH/Et₂O mixture as described below. The dimensions of the crystal used were 0.22 × 0.20 × 0.05 mm. The diffractometer employed was a Siemens three-circle diffractometer/Bruker APEX CCD with the

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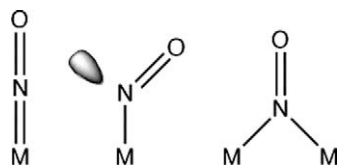


Fig. 1. Nitrosyl bonding conformations, linear on the left, bent in the middle and bridging on right.

Table 1
X-ray data collection parameters.

	Complex (1)	Complex (2)
Empirical formula	C _{31.25} H _{35.50} Cl _{2.50} N ₂ OP ₂ Tc	C ₃₄ H _{39.50} Cl ₂ N _{3.50} OP ₂ Tc
Formula weight	702.718	743.064
Crystal system	orthorhombic	orthorhombic
Space Group	<i>Pna</i> 2(1)	<i>Pna</i> 2(1)
<i>a</i> (Å)	11.5189	19.1840
<i>b</i> (Å)	23.6427	17.0729
<i>c</i> (Å)	12.7998	21.2377
<i>V</i> (Å ³)	3485.87(10)	6955.91
<i>Z</i>	4	8
<i>D</i> _{calc} (Mg/m ³)	1.339	1.419
<i>T</i> (°C)	−173	−173
<i>R</i> , <i>R</i> _w	0.056, 0.166	0.028, 0.060
Goodness of fit (GOF)	1.162	1.049

data set collected at −173 °C. The scan mode used was 2ω , with a maximum 2θ of 60°. A total of 13 679 reflections were collected of which 9756 were of $I > 2\sigma(I)$ and were used in the final refinement. The technetium atom was located using the direct methods. Neutral atomic scattering factors were used throughout the analysis. Extinction effects were not observed. Final hydrogen atom positions were calculated. All non-hydrogen atoms were refined anisotropically.

2.1.2. *mer*-[TcCl₂(NO)(PNPpr)]·(3/2CH₃CN)

The crystal data and some experimental details of the structure determination are given in Table 1. An orange needle shaped crystal of *mer*-[TcCl₂(NO)(PNPpr)] was isolated from the acetonitrile mixture as described below. The crystals dimensions were 0.25 × 0.05 × 0.05 mm. The diffractometer employed was a Siemens three-circle diffractometer/Bruker APEX CCD with the data set collected at −173 °C. The scan mode used was 2ω , with a maximum 2θ of 58°. A total of 18 728 reflections were collected of which 17 420 were of $I > 2\sigma(I)$ and were used in the final refinement. The technetium atom was located using the direct methods. Neutral atomic scattering factors were used throughout the analysis. Extinction effects were not observed. Final hydrogen atom positions were calculated. All non-hydrogen atoms were refined anisotropically. The two crystallographically independent molecules of the *mer* structure are almost related by an inversion center, making the pseudo space group *Pbcn* (after a unit cell transformation). This inversion center is only fulfilled by about 90% of all ordered atoms and refinement in the centrosymmetric space group is not stable. Two of the three CH₃CN solvent molecules are disordered.

3. Synthesis

3.1. *fac*-[TcCl₂(NO)(PNPpr)]

A sample of H[TcNOCl₄] was dissolved in 50 mL MeOH. To this was added 40 mg, (1 equivalent) of PNPpr. The reaction mixture was stirred at room temperature for 90 min, which failed to completely dissolve the ligand. This suspension was then brought

to reflux yielding a yellow–brown solution. The solution was allowed to evaporate at room temperature, yielding first a dull peach colored precipitate. This solid contained exclusively the *fac* isomer as determined by infrared spectroscopy. The both isomers are however present in the mother liquor and the recrystallized product, as determined by infrared spectroscopy.

Anal. Calc. Results^a for TcCl₂P₂ON₂C₃₂H₃₇: C, 55.12; H, 5.31; N, 4.02. Found: C, 54.19[10]; H, 5.38; N, 3.88%. IR(neat): $\nu(\text{N}=\text{O})$, 1789 cm^{−1}. ESI(+) Mass spectrum: 647 *m/z*, [TcCl₂(NO)(PNPpr)]⁺ (PNPbu ligand employed for analytical preparation).

3.2. *mer*-[TcCl₂(NO)(PNPpr)]

A sample of H[TcNOCl₄] was dissolved in 50 mL MeCN. To this was added 42 mg, (1 equivalent) of PNPpr, which rapidly dissolved yielding a yellow–orange solution. The solution was stirred at room temperature for 90 min and then refluxed with no further color change. The solution was reduced in volume to 5 mL, and then allowed to evaporate slowly at room temperature, yielding rod shaped, orange crystals. The mother liquor contains both structural isomers as determined by infrared spectroscopy.

IR(neat): $\nu(\text{N}=\text{O})$, 1689 cm^{−1}. ESI(+) Mass spectrum: 647 *m/z*, [TcCl₂(NO)(PNPpr)]⁺, 1331 *m/z*, [TcCl₂(NO)(PNPpr)]/[TcCl₃(NO)(PNPpr)]⁺.

4. Discussion

The search for new coordination complexes of technetium, and to a lesser extent rhenium, for evaluation as diagnostic imaging and therapeutic agents in nuclear medicine continues, *albeit* at a significantly diminished pace with technetium, due to licensing and regulatory hurdles now in place for the long-lived isotope⁹⁹Tc. Reports of Group 7 coordination complexes incorporating the nitrosyl ligand have been few and far between [7,11–18], which is due to the lack of easily prepared synthetic precursors. We recently reported the facile synthesis of H[TcNOCl₄] in a ‘one-pot’ preparation from pertechnetate [19], making the second row nitrosyl chemistry more accessible.

A representation of the tridentate bis-phosphine-amine ligand PNPpr is shown in Fig. 2 [20].

The reaction of H[TcNOCl₄] with one equivalent of PNPpr in refluxing methanol yields predominantly the facial complex [TcCl₂(NO)(PNPpr)]. This dull yellow colored species crystallizes from the slow evaporation of this solution. The sterically hindered, tridentate ligand occupies three *facial* coordination sites with the amine nitrogen coordinated *trans* to the nitrosyl ligand, in a distorted octahedral geometry. The Tc–N bond to the nitrosyl nitrogen atom is 1.751(5) Å and the N–O bond length is 1.163(6) Å, both of which are within the expected range for this type of multiply bonded species. The Tc–N–O bond angle is 177.9(4)° which confirms the linear nature of the nitrosyl core. The Tc–Cl bond lengths are somewhat elongated, with (Tc–Cl1) at 2.4695(11) Å and

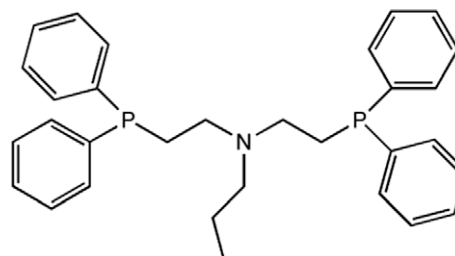


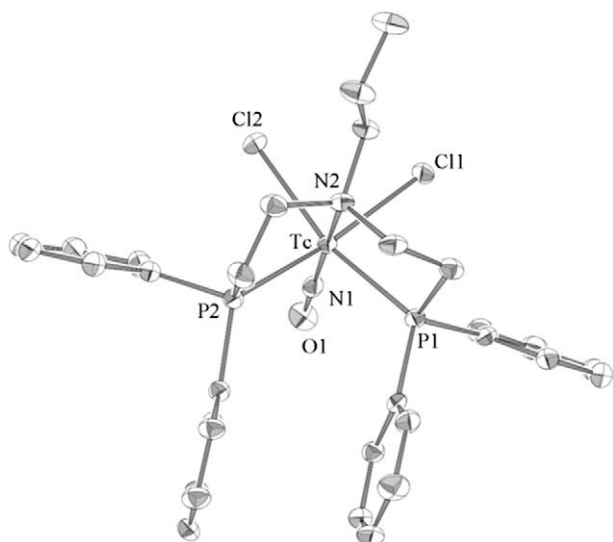
Fig. 2. Representation of the tridentate ligand bis[(2-diphenylphosphino)propyl]amine (PNPpr) where R = *n*-propyl.

Table 2
Select bond lengths (Å) and angles (°) for *fac*-[TcCl₂(NO)(PNPpr)], complex (1).

Tc1	N1	1.751(5)		
Tc1	N2	2.364(4)		
Tc1	P1	2.3647(12)		
Tc1	P2	2.3688(13)		
Tc1	Cl2	2.4671(12)		
Tc1	Cl1	2.4695(11)		
N1	O1	1.163(6)		
Tc1	N1	O1	177.9(4)	
N1	Tc1	N2	171.75(17)	
N1	Tc1	P1	94.54(14)	
N2	Tc1	P1	81.59(10)	
N1	Tc1	P2	92.02(14)	
N2	Tc1	P2	81.49(10)	
P1	Tc1	P2	99.48(4)	
N1	Tc1	Cl2	99.17(14)	
N2	Tc1	Cl2	85.85(10)	
P1	Tc1	Cl2	163.76(4)	
P2	Tc1	Cl2	88.75(4)	
N1	Tc1	Cl1	96.78(14)	
N2	Tc1	Cl1	90.03(10)	
P1	Tc1	Cl1	83.24(4)	
P2	Tc1	Cl1	170.57(4)	
Cl2	Tc1	Cl1	86.52(4)	

(Tc–Cl₂) at 2.4671(12) Å. The bonds from the technetium to the remaining three atoms are within the expected ranges, with (Tc–N amine) at 2.364(4) Å, (Tc–P1) at 2.3647(12) Å and (Tc–P2) at 2.3688(13) Å. The steric bulk at the diphenylphosphine termini of the tridentate ligand, which coordinate in a *cis* fashion, results in a significant deviation from octahedral coordination geometry. The P1–Tc–P2 bond angle has been expanded to 99.48(4)° while the Cl1–Tc–Cl2 bond angle has contracted to 86.52(4)°. Table 2 lists selected bond lengths and angles for *fac* complex. Fig. 3 displays an ORTEP diagram of the X-ray crystal structure of *fac*-[TcCl₂(NO)(PNPpr)] with the solvent molecule and hydrogen atoms omitted for clarity. The infrared spectrum of the solution as the *mer* complex precipitates and/or crystallizes displays $\nu(\text{N}=\text{O})$ from both isomers.

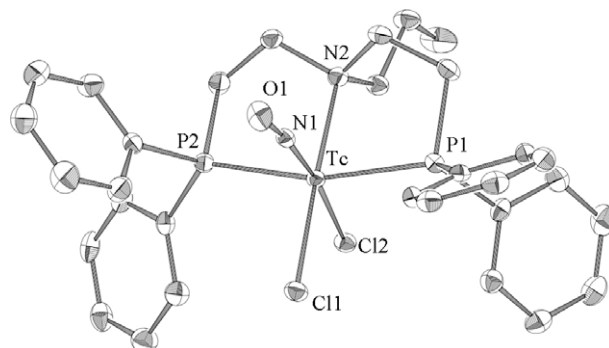
The reaction of H[TcNOCl₄] with one equivalent of PNPpr in refluxing acetonitrile yields a precipitate of the meridional complex [TcCl₂(NO)(PNPpr)] cleanly. This yellow–orange complex crystallizes from the slow evaporation of the acetonitrile reaction

**Fig. 3.** The ORTEP diagram for the facial [TcCl₂(NO)(PNPpr)].**Table 3**
Select bond lengths (Å) and angles (°) for *mer*-[TcCl₂(NO)(PNPpr)], complex (2).

Tc1	N1	1.758(4)		
Tc1	N2	2.2322(18)		
Tc1	P2	2.3979(6)		
Tc1	Cl2	2.4197(15)		
Tc1	P1	2.4253(6)		
Tc1	Cl1	2.4707(6)		
N1	O1	1.184(6)		
N1	Tc1	N2	91.26(12)	
N1	Tc1	P2	88.42(12)	
N2	Tc1	P2	83.64(5)	
N1	Tc1	Cl2	173.28(12)	
N2	Tc1	Cl2	93.00(6)	
P2	Tc1	Cl2	86.88(3)	
N1	Tc1	P1	91.76(12)	
N2	Tc1	P1	79.89(5)	
P2	Tc1	P1	163.53(2)	
Cl2	Tc1	P1	94.11(3)	
N1	Tc1	Cl1	88.56(11)	
N2	Tc1	Cl1	177.60(5)	
P2	Tc1	Cl1	98.75(2)	
Cl2	Tc1	Cl1	87.40(4)	
P1	Tc1	Cl1	97.72(2)	
O1	N1	Tc1	173.0(4)	

mixture to yield needle shaped crystals which contain two molecules of [TcCl₂(NO)(PNPpr)] and three molecules of acetonitrile per asymmetric unit. There is the usual site disorder within the molecule between the nitrosyl ligand and the chloride located *trans* to it. (See the *cif* file for a discussion of how the disorder was addressed during refinement.) The Tc–N bond to the nitrosyl nitrogen is 1.758(4) Å and the N–O bond is 1.184(6) Å, indicative of multiple bonding within the nitrosyl unit. The Tc–Cl bonds are again somewhat elongated at 2.4707(6) and 2.4197(15) Å. The Tc–N(amine) bond is 2.2322(18) Å and the elongated Tc–P bonds are 2.4253(6) and 2.3979(6) Å. The P–Tc–P bond angle for this complex is 163.53(2)° which deviates from octahedral due to the small bite angle imposed by the chelating tridentate ligand. The Cl–Tc–Cl bond angle is 87.40(4)° which shows a slight contraction due to the steric bulk of the diphenylphosphino moieties on the chelating ligand. Table 3 lists selected bond lengths and angles for *mer*-[TcCl₂(NO)(PNPpr)]. Fig. 4 displays an ORTEP diagram of *mer*-[TcCl₂(NO)(PNPpr)] with a single molecule displayed and solvent molecules and hydrogen atoms omitted for clarity.

Neither isomer is formed cleanly in their respective preparations detailed above. In each instance, a small absorption assigned to the other structural isomer is observed in the infrared spectra. These nitrosyl absorptions are strong, relatively sharp bands. And purification by thin layer chromatography on silica results in significant decomposition of the complexes, so removing the contaminating

**Fig. 4.** The ORTEP diagram for the meridional [TcCl₂(NO)(PNPpr)].

isomer by this method was not reasonable. The only instance where one isomer can be isolated cleanly is by filtering off the precipitate of *fac* complex which precipitates from solution and displays only the 1789 cm^{-1} absorption in the infrared spectrum. The absorption from the precursor $(\text{Bu}_4\text{N})[\text{TcNOCl}_4]$ falls at 1822 cm^{-1} region [20].

5. Conclusion

The reaction of $\text{H}[\text{TcNOCl}_4]$ with the tridentate ligand PNPpr gives a mixture of *mer* or *fac* isomers of $\text{TcCl}_2(\text{NO})(\text{PNPpr})$. Both complexes display linear nitrosyl ligands with the expected multiple bonding throughout the Tc–N–O linkage. The infrared spectra display the absorptions associated with the nitrosyl ligand in the 1700 and 1800 cm^{-1} regions, the 100 cm^{-1} difference being attributed to *trans* effect. Formation of different structural isomers may result from a number of factors including the significant difference in ligand solubility in the chosen solvent. The ligand is freely soluble in acetonitrile and the reaction proceeds in just a few minutes at room temperature. In methanol however, the reaction requires being brought to reflux to fully dissolve the PNPpr. Another factor that comes into play is the pH of the reaction mixture. Reaction in methanol of $\text{H}[\text{TcNOCl}_4]$ with PNPpr yields a mixture of the two isomers with the *fac* isomer cleanly precipitating from solution, as determined by infrared spectroscopy. However, the analogous reaction of $(\text{Bu}_4\text{N})[\text{TcNOCl}_4]$ with PNPpr in methanol yields no precipitate. Isomerization between the two structures in solution does occur with the spectroscopically clean *fac* isomer gradually displaying absorptions in both 1700 and 1800 cm^{-1} regions.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ica.2009.04.017.

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