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LETTER

Structure proof of *syn/anti* isomerism in N-alkylated diaminedithiol (DADT) complexes of technetium

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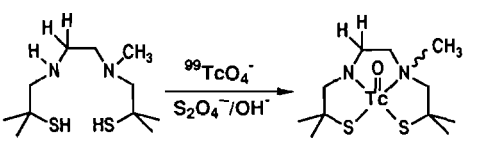
Within the past six years, progress in synthetic chemistry has produced new technetium complexes which are neutral, lipid-soluble and capable of crossing cell membranes [1]. The diaminedithiol (DADT) ligand system has proved the most versatile in the preparation of the new generation of technetium radiopharmaceuticals [2–4]. To date, no crystallographic analyses have been performed on the isomeric mixture of complexes derived from N-substituted DADT ligands. In fact, only limited data have been reported for any Tc–DADT complex [1a, 2b, e]. Structural data are essential to lay a strong foundation for assessment of biological and clinical studies. In this paper, we report the synthesis and structure of the isomers of 4-*N*-methyl-2,9-dimethyl-4,7-diaza-2,9-decanedithiolato oxotechnetium(V), the first documentation of *syn/anti* isomerism in N-substituted DADT technetium complexes.

Reduction of aqueous $NH_4{}^{99}TcO_4$ with sodium dithionite in aqueous sodium hydroxide in the presence of the ligand afforded two lipophilic complexes, **I** and **II**, in a 79:21 ratio, respectively, which were purified by preparative thin layer chromatography on silica gel (Scheme 1). IR (KBr pellet, cm^{-1}): Tc=O: **I**, 916 cm^{-1}; **II**, 924 cm^{-1}. ^1H NMR (300 MHz, CD_2Cl_2): N-CH_3: **I**, 3.4 ppm; **II**, 1.9 ppm. Crystal data for **I**: monoclinic $P2_1/n$; $a=21.21(1)$, $b=7.611(3)$, $c=21.409(6)$ Å, $\beta=115.14(2)°$, $V=3129(2)$ Å^3, $Z=8$, $F(000)=1488$. Structure solution and refinement based on 5947 reflections with ($I>3\sigma(I)$) (Mo Kα, $\lambda=0.71069$ Å) converged at $R=0.035$, $R_w=0.074$. Crystal data for **II**: orthorhombic $Fdd2$, $a=24.767(3)$, $b=32.391(3)$, $c=7.782(3)$ Å, $\beta=115.14(2)°$, $V=6243(2)$ Å^3, $Z=16$, $F(000)=2976$. Structure solution and refinement based on 1340 reflections which were considered observed ($I>3\sigma(I)$) (Mo Kα, $\lambda=0.71069$ Å) converged at $R=0.023$, $R_w=0.029$.



I and **II**

Scheme 1.

Upon complexation to the technetium, the N-methyl substituent can assume a *syn* or *anti* configuration with respect to the oxo–metal group. In the high field ^1H NMR spectra, the N-methyl substituent of **I** is found in a deshielded environment at 3.4 ppm, relative to the N-methyl group of **II** which is found upfield at 1.9 ppm. The ^1H NMR results suggest that the protons of the N-methyl group in **I** lie within the deshielding cone of the oxo–metal core, and thus, would be in the *syn* configuration. In complex **II**, the upfield position of the N-methyl protons suggests the N-methyl group lies outside the deshielding cone, which is consistent with an *anti* configuration.

The X-ray crystallographic data conclusively establishes the *syn* configuration of the N-methyl side chain in **I** (Fig. 1(a)) and the *anti* configuration in **II** (Fig. 1(b)). Upon complexation, the unsubstituted nitrogen becomes deprotonated, resulting in neutral complexes. The bond distances reflect this fact, where the Tc–unsubstituted N bonds are 0.288(9) and 0.198(9) Å shorter in **I** and **II**, respectively than the Tc–substituted N bonds.

Considering the product distributions observed from the complexation reaction and the structure proofs presented here, the *syn* configuration seems to be thermodynamically more stable than the *anti* configuration. This information, in conjunction with the ^1H NMR spectroscopic differences observed for **I** and **II**, will prove useful for determining the stereochemical configurations in other N-substituted DADT complexes of technetium which have biomedical significance.

Supplementary material

Atom coordinates, bond lengths and angles, anisotropic thermal parameters, hydrogen atom coordinates, and short intermolecular contacts are available from author S.Z.L. upon request.

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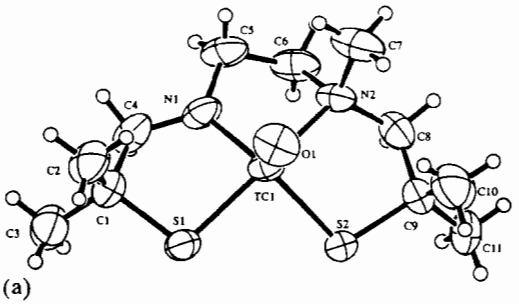
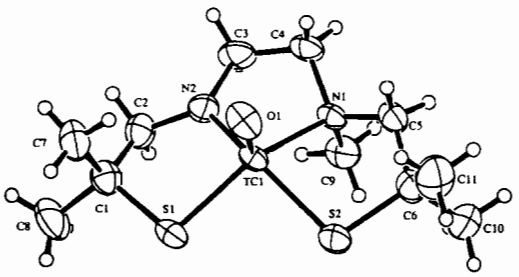


(a)



(b)

Fig. 1. (a) ORTEP drawing of **I** (50% probability ellipsoids), selected lengths (Å) and angles (°): Tc–O 1.678(4), Tc–N(1) 1.909(5), Tc–N(2) 2.197(4), Tc–S(1) 2.271(2), Tc–S(2) 2.298(2), N(2)–C(6) 1.498(7), N(2)–C(7) 1.477(8), N(2)–C(8) 1.503(7); O(1)–Tc–N(2) 102.4(2), Tc–N(2)–C(7) 109.0(4), C(7)–N(2)–C(8) 110.3(5), C(6)–N(2)–C(7) 108.3(5); (b) ORTEP drawing of **II** (50% probability ellipsoids), selected lengths (Å) and angles (°): Tc–O 1.671(4), Tc–N(1) 2.132(4), Tc–N(2) 1.934(5), Tc–S(1) 2.264(1), Tc–S(2) 2.314(2), N(1)–C(4) 1.506(8), N(1)–C(9) 1.497(7), N(1)–C(5) 1.485(8); O(1)–Tc–N(1) 113.8(2), Tc–N(1)–C(9) 114.0(3), C(5)–N(1)–C(9) 111.4(4), C(4)–N(1)–C(9) 108.3(5).

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