

Synthesis and structural characterization of an oxotechnetium(V) N,N' -ethylenebis(2-phenoxyacetamido) complex

Michael J. Abrams*

Pharmaceuticals Research, Materials Technology Division, Johnson Matthey Corporation, 1401 King Road, West Chester, PA 19380 (U.S.A.)

Shahid N. Shaikh and Jon Zubieta*

Department of Chemistry, Syracuse University, Syracuse, NY 13244-4100 (U.S.A.)

(Received February 28, 1991)

Abstract

The reaction of $[(n\text{-C}_4\text{H}_9)_4\text{N}][\text{TcOCl}_4]$ with N,N' -ethylenebis(2-phenoxyacetamide), H_4epa , in methylene chloride, yields orange crystals of $[(n\text{-C}_4\text{H}_9)_4\text{N}][\text{TcO}(\text{epa})]$. The X-ray structure reveals an oxotechnetium(V) core with the oxo group occupying the apical position of a distorted square pyramid whose base is defined by the oxygen and nitrogen donors of the quadruply deprotonated ligand. Crystal data: triclinic space group, $P\bar{1}$, with $a = 12.067(3)$, $b = 12.110(4)$, $c = 12.289(3)$ Å, $\alpha = 109.59(1)$, $\beta = 111.11(1)$, $\gamma = 92.09(1)^\circ$, $V = 1656.4(3)$ Å³, $Z = 2$, $D_{\text{calc}} = 1.34$ g cm⁻³. Structure solution and refinement based on 4177 reflections with $F_o \geq 6\sigma(F_o)$ converged at $R = 0.039$.

Introduction

The continuing interest in the coordination chemistry of technetium reflects the importance of the metastable isomer ^{99m}Tc in nuclear medicine [1–3]. ^{99m}Tc remains the radioisotope of choice for diagnostic imaging by virtue of its ideal γ photon energy of 140 keV, half-life of 6 h, lack of particulate radiation and ready availability [4]. Furthermore, the long-lived isotope ⁹⁹Tc may be used for preparative scale studies using conventional techniques.

As part of our continuing investigations of the coordination chemistry of technetium [5–9], we have prepared complexes of the $[\text{TcO}]^{3+}$ core. This d^2 metal–oxo center is prominent in the aqueous chemistry of technetium and displays a strong affinity for S-containing ligands. Consequently, numerous examples of square-pyramidal Tc(V) complexes with thiolate or amide/thiolate ligation have been characterized and shown to possess $[\text{TcOS}_4]$ and $[\text{TcO}(\text{S}_2\text{N}_2)]$ metal geometries respectively [10–16]. Square-pyramidal geometry is also favored by tetradentate nitrogen donor ligands, such as amine/oxime donors, which stabilize the $[\text{TcON}_4]$ geometry [17]. On the other hand, ‘classical’ tetradentate Schiff base ligands have been found to yield distorted

octahedral Tc(V) centers with the *trans* oxoqua-technetium(V) core, $[\text{TcO}(\text{H}_2\text{O})(\text{N}_2\text{O}_2)]$, or the *trans* chlorooxotechnetium(V) core, $[\text{TcOCl}(\text{N}_2\text{O}_2)]$ [18]. Quinquidentate Schiff base ligands likewise yield distorted octahedral Tc(V) sites, $[\text{TcO}(\text{N}_3\text{O}_2)]$ [19]. No example of square-pyramidal Tc(V) complexes with the $[\text{TcO}(\text{N}_2\text{O}_2)]$ core have been structurally characterized to date.

In this paper we report the synthesis of $(\text{Bu}_4\text{N})[\text{TcO}(\text{epa})]$ from the reaction of $(\text{Bu}_4\text{N})[\text{TcOCl}_4]$ with N,N' -ethylenebis(2-phenoxyacetamide) (H_4epa) in methanol. X-ray crystallographic analysis has revealed that the complex possesses the square-pyramidal $[\text{TcO}(\text{N}_2\text{O}_2)]$ core.

Experimental

Materials and methods

All reactions were performed in freshly dried and distilled solvents under an atmosphere of argon. Dichloromethane was technical grade and was distilled from CaCl_2 and P_2O_{10} . All reagents were obtained from standard commercial sources. $[(n\text{-C}_4\text{H}_9)_4\text{N}][\text{TcOCl}_4]$ was prepared by the literature method [20].

The following instruments were used in the study: IR, Perkin-Elmer 283B IR spectrophotometer; X-ray crystallography, Siemens R3m/V diffractometer.

*Authors to whom correspondence should be addressed.

Preparation of compounds

Preparation of [(n-C₄H₉)₄N][TcO(epa)]·H₂O

(TBA)[TcOCl₄] (0.037 g, 0.074 mmol) was dissolved in MeOH (2 ml). To this solution was added ethylene glycol (33 ml) followed by 2 N sodium acetate in MeOH (7 ml) causing the mixture to turn deep violet, the characteristic color of the [TcO(ethanediolato)₂]⁻ ion [21]. This solution was added dropwise to a stirred solution of 1,2-bis(2-hydroxybenzamido)ethane [22] (H₄epa) (0.071 g, 0.24 mmol) dissolved in MeOH/H₂O (15 ml, 50/50 vol./vol. with a few drops of 1 N NaOH to improve the solubility of the ligand). After 10 min the reaction mixture was bright red–orange. Slow evaporation of the mixture gave a red solid which was recrystallized from acetone/ether. Yield 0.02 g, 41% based on Tc. *Anal.* Calc. for C₃₂H₅₀H₃O₆Tc: C, 57.21; H, 7.51; N, 6.26. Found: C, 57.49; H, 7.55; N, 6.31%. IR (KBr): $\mu_{\text{Tc=O}}$, 965 cm⁻¹.

Preparation of [(n-C₄H₉)₄N][ReO(epa)]·2H₂O

A mixture of [ReOCl₃(PPh₃)₂] [23] (0.3 g, 0.36 mmol), K(CH₃CO₂) (0.14 g) and H₄epa (0.11 g, 0.37 mmol) were mixed with EtOH (50 ml) and heated to reflux for 30 min. After cooling to room temperature the mixture was filtered to remove KCl and treated with Et₂O to precipitate a yellow solid. This material was redissolved in H₂O (10 ml) and treated with tetrabutylammonium bromide (0.5 g) and sufficient acetone to yield a homogeneous solution. Slow evaporation yielded yellow crystals, 0.07 g. *Anal.* Calc for C₃₂H₅₂N₃O₇Re: C, 50.30; H, 6.48; N, 5.50. Found: C, 50.39; H, 6.77; N, 5.49%. IR (KBr): $\mu_{\text{Re=O}}$ 970 cm⁻¹.

Crystal data

C₃₂H₅₀N₂O₆Tc: formula weight = 657.7; triclinic, *PI*, *a* = 12.067(3), *b* = 12.220(4), *c* = 12.1189(3) Å, α = 109.59(1), β = 111.11(1), γ = 92.09(7)°, *V* = 1656.4(3) Å³, *Z* = 2, *D*_{calc} = 1.34 g cm⁻³, $\lambda(\text{Mo K}\alpha)$ = 0.71073 Å (graphite monochromator), μ = 4.35 cm⁻¹, *T* = 296 K, crystal dimensions: 1.00 × 0.51 × 0.22 mm.

X-ray structure determination

Full details of the crystallographic methodologies may be found in ref. 24. For full details of the crystal data, data collection and refinement procedures see 'Supplementary material'.

In no instance was an extinction correction applied to the data. Idealized hydrogen atom positions were used throughout the analysis, with the C–H distances set at 0.96 Å. All non-hydrogen atoms of the [(n-C₄H₉)₄N][TcO(epa)]·H₂O species were refined an-

isotropically. All other atoms were treated isotropically. The final discrepancy factor was 0.039 for 4177 reflections with $F_o \geq 6\sigma(F_o)$ (5222 collected).

Results and discussion

Synthesis and spectroscopic properties

The reaction of [(n-C₄H₉)₄N][TcOCl₄] with HOC₆H₄C(O)NHCH₂CH₂NHC(O)C₆H₄OH (H₄epa) yields the diamagnetic species [(n-C₄H₉)₄N][TcO(epa)]·H₂O as an orange crystalline product. The IR spectrum of (TBA)[TcO(epa)]·H₂O (TBA = (n-C₄H₉)₄N) exhibits the expected Tc=O stretch at 925 cm⁻¹. The complex is soluble in common polar organic solvents such as DMF, CH₃CN and CH₂Cl₂.

Attempts to replace the oxo group with a hydrazido(2-) unit, =N=NR₂, or a diazenido moiety, =N=NR, by exploiting the usual condensation-type reaction [6–9] resulted in intractable mixtures of products. Although the IR spectrum of the products clearly revealed the presence of the multiply bonded N–N unit, $\nu(\text{N=N})$ at 1580–1625 cm⁻¹, and the absence of $\nu(\text{Tc=O})$ in the 780–950 cm⁻¹ region, analytically pure compositions were not isolated. The organohydrazine reagents served not only to displace the oxo group of the parent [TcO(epa)]¹⁻ complex but also as reducing agents, such that mixtures of the desired [Tc^v(NNR₂)(epa)]⁻ complex and other products with reduced Tc centers were isolated. Furthermore, the [Tc(NNR₂)₃]³⁺ core of these species dissociates over time in solution to give mixtures of nitrido, [TcN]²⁺, and other unidentified products. Although reactions of metal–oxo species with organohydrazine ligands often proceed by condensation type reactions, resulting in displacement of the oxo group as H₂O and the formation of the chemically robust metal–hydrazido, M=NNR₂, or metal–diazenido, M=NNR, unit [25, 26], the hydrazine chemistry of the Tc–oxo group has been demonstrated to be complicated by a tendency to promote N–N bond cleavage and subsequent formation of Tc–nitrido and Tc–imido species [7] and by reduction of the Tc(V) core.

Description of the structure

Atomic coordinates for the structure of (TBA)[TcO(epa)]·H₂O are given in Table 1 while Table 2 lists selected bond lengths and angles. This structure of the anionic complex is illustrated in Fig. 1.

The coordination geometry about the Tc(V) site of the discrete molecular anionic complex is square-pyramidal with the oxo group in the apical position

TABLE 1. Atomic positional parameters ($\times 10^4$) and isotropic temperature factors ($\text{\AA}^2 \times 10^3$) for $[(n\text{-C}_4\text{H}_9)_4\text{N}][\text{TcO}(\text{epa})] \cdot \text{H}_2\text{O}$

	<i>x</i>	<i>y</i>	<i>z</i>	U_{eq}^a
Tc	984(1)	2415(1)	4833(1)	42(1)
O(1)	506(3)	1032(3)	4581(3)	60(2)
O(2)	1371(3)	2411(3)	3487(3)	51(1)
O(3)	-314(3)	3110(3)	4006(3)	55(2)
O(4)	4721(3)	2862(4)	6306(3)	85(2)
O(5)	41(4)	4375(4)	7581(3)	80(2)
N(1)	2731(3)	2820(3)	5854(3)	47(2)
N(2)	916(4)	3427(3)	6347(3)	52(2)
C(1)	2391(4)	2244(4)	3355(4)	45(2)
C(2)	2357(5)	1947(4)	2208(4)	58(2)
C(3)	3364(5)	1751(5)	1971(5)	71(3)
C(4)	4461(5)	1855(5)	2872(6)	73(3)
C(5)	4513(5)	2166(4)	4010(5)	61(3)
C(6)	3507(4)	2350(4)	4281(4)	48(2)
C(7)	3681(4)	2702(4)	5559(4)	53(2)
C(8)	3025(5)	3253(6)	7143(5)	81(3)
C(9)	1986(6)	3557(6)	7418(5)	82(3)
C(10)	18(5)	3939(4)	6560(5)	55(2)
C(11)	-1042(4)	4002(4)	5554(5)	53(2)
C(12)	-1975(5)	4503(4)	5808(6)	68(3)
C(13)	-2993(6)	4604(5)	4951(7)	78(4)
C(14)	-3072(5)	4205(5)	3797(7)	78(4)
C(15)	-2172(5)	3727(5)	3506(5)	68(3)
C(16)	-1136(4)	3599(4)	4377(5)	52(2)
N(3)	2150(3)	7980(3)	1984(3)	42(2)
C(21)	2827(4)	8848(4)	3260(3)	45(2)
C(22)	2355(4)	8724(4)	4154(4)	50(2)
C(23)	3076(4)	9674(4)	5373(4)	52(2)
C(24)	2644(5)	9596(5)	6302(5)	76(3)
C(25)	799(4)	7976(4)	1559(4)	49(2)
C(26)	409(4)	9159(4)	1648(4)	55(2)
C(27)	-927(5)	9056(5)	1375(5)	64(3)
C(28)	-1396(5)	10177(5)	1331(5)	71(3)
C(29)	2616(4)	8345(4)	1184(4)	52(2)
C(30)	3918(5)	8258(6)	1411(5)	76(3)
C(31)	4195(7)	8475(9)	380(8)	131(7)
C(32)	5135(14)	8122(13)	179(13)	136(5)
C(33)	2380(4)	6769(4)	1976(4)	46(2)
C(34)	8140(5)	4232(4)	9314(4)	62(2)
C(35)	7849(5)	5400(4)	9243(5)	68(3)
C(36)	6549(6)	5474(6)	8903(7)	119(5)
O(6)	9635(5)	3099(5)	1502(4)	85(2)

^aEquivalent isotropic U defined as one third of the trace of the orthogonalized U_{ij} tensor.

and the basal plane defined by the nitrogen and oxygen donors of the quadruply deprotonated epa ligand. The technetium rests 0.65 Å above the N_2O_2 plane of the ligand. The average Tc–N distance of 1.977(6) Å is similar to Tc–amido-nitrogen distances in the ‘ TcON_2S_2 ’ complexes $[\text{TcO}(\text{meg})]^-$ [16], $[\text{TcO}(\text{PIC})]$ [27] and $[\text{TcO}(\text{ema}(\text{morph}))]$ [14], which exhibit distances of 1.979(6), 1.965(6) and 1.982(6) Å, respectively. There are no directly comparable ‘ TcON_2O_2 ’ structural types, the nitrogen in the struc-

TABLE 2. Selected bond lengths (Å) and angles (°) for $[(n\text{-C}_4\text{H}_9)_4\text{N}][\text{TcO}(\text{epa})] \cdot \text{H}_2\text{O}$

Tc–O1	1.648(3)	C7–O4	1.238(5)
Tc–O2	1.963(3)	C7–N1	1.331(6)
Tc–O3	1.956(3)	N1–C8	1.474(6)
Tc–N1	1.979(4)	C10–O5	1.242(6)
Tc–N2	1.975(4)	C10–N2	1.339(6)
		N2–C9	1.474(6)
O1–Tc–O2	107.3(2)	O2–Tc–N1	144.5(1)
O1–Tc–O3	111.5(1)	O3–Tc–N1	140.3(1)
O1–Tc–N1	108.2(2)	O3–Tc–N2	88.4(1)
O1–Tc–N2	89.3(1)	N1–Tc–N2	80.8(2)
O2–Tc–O3	77.7(1)		
O2–Tc–N1	108.2(2)	Tc–N1–C7	130.1(3)
		Tc–N1–C8	114.9(3)
		C7–N1–C7	114.9(4)
		Tc–N2–C9	114.7(3)
		Tc–N2–C10	130.2(3)
		C9–N2–C10	114.9(4)

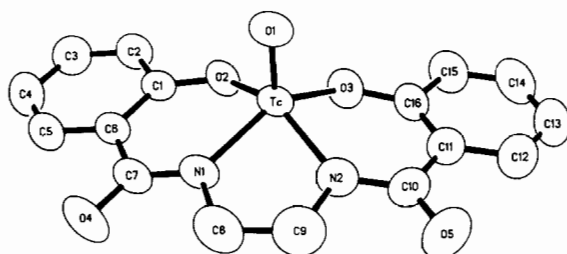


Fig. 1. ORTEP view of the structure of the molecular anion, $[\text{TcO}(\text{epa})]^{1-}$.

turally characterized complexes of this type possessing iminato nitrogen donors [17, 19] or amine and oxime nitrogen donors [18]. Iminato donors exhibit Tc–N distances in the 2.04–2.19 Å range [19], while oxime nitrogen donors and amine nitrogen ligands display Tc–N distances in the 2.06–2.09 and 1.89–2.05 Å ranges, respectively.

The average Tc–O ligand distance, 1.960(4) Å, is considerably shorter than those found in the six-coordinate $[\text{TcO}(\text{H}_2\text{O})((\text{acac})_2\text{en})]^+$, $[\text{TcO}((\text{sal})_2\text{en})\text{Cl}]$ [18] and $[\text{TcO}(\text{C}_{18}\text{H}_{18}\text{N}_3\text{O}_2)]$ [19] complexes which fall in the range 2.01–2.12 Å. The distance is comparable to those reported for the $[\text{TcCl}(\text{NO}_2)]$ core of $[\text{TcO}(\text{phsal})\text{Cl}]$ with an average Tc–O ligand distance of 1.948(5) Å [27].

Since a variety of substituted derivatives of H_4epa may be prepared, the synthetic procedure adopted in this work should be applicable to the production of a range of related Tc(V) complexes exhibiting a gradual modification of structural and electronic properties which may correlate with corresponding changes in the biological activity of the Tc complexes. The complex provides a square-pyramidal $[\text{Tc}^*\text{O}(\text{N}_2\text{O}_2)]$ core analogous to that reported for

the [Tc^vO(N₂S₂)] series, with hydroxyl ligands substituting for the thiolate donors of the latter. Since the [TcO(N₂S₂)] complexes are known to possess useful biodistributions, such modifications may prove fruitful. Furthermore, [TcO(epa)]¹⁻ provides the first structurally characterized example of an anionic Tc(V) species with a square-pyramidal [TcO(N₂O₂)] core [28].

Acknowledgement

This work was supported by a grant from Johnson Matthey to Jon Zubieta.

References

- 1 E. Deutsch, K. Libson, S. Jurrison and L. F. Lindoy, *Prog. Inorg. Chem.*, **30** (1983) 75.
- 2 M. J. Clarke and L. Podbielski, *Coord. Chem. Rev.*, **78** (1987) 253.
- 3 M. Nicolini, G. Bandoli and U. Mozzi (eds.), *Technetium in Chemistry and Nuclear Medicine*, Raven, New York, 1986.
- 4 S. Baum and R. Bramlet, *Basic Nuclear Medicine*, Appleton-Century-Crobits, New York, 1975; G. Subramanian, B. A. Rhodes and J. F. Cooper, V. J. Sodd (eds.), *Radiopharmaceuticals*, The Society of Nuclear Medicine, New York, 1978.
- 5 M. J. Abrams, S. N. Shaikh and J. Zubieta, *Inorg. Chim. Acta*, **171** (1990) 133.
- 6 M. J. Abrams, S. K. Larsen and J. Zubieta, *Inorg. Chim. Acta*, **173** (1990) 133.
- 7 M. J. Abrams, Q. Chen, S. N. Shaikh and J. Zubieta, *Inorg. Chim. Acta*, **176** (1990) 11.
- 8 M. J. Abrams, S. K. Larsen and J. Zubieta, *Inorg. Chem.*, **30** (1991) 2031.
- 9 M. J. Abrams, C. Costello, S. N. Shaikh and J. Zubieta, unpublished results.
- 10 J. E. Smith, E. F. Byrne, F. A. Cotton and J. C. Sekutowski, *J. Am. Chem. Soc.*, **100** (1978) 5571.
- 11 B. V. DePamphilis, A. G. Jones, M. A. Davis and A. Davison, *J. Am. Chem. Soc.*, **100** (1978) 5570.
- 12 A. Davison, C. Orvig, H. C. Trop, M. Sohn, B. V. DePamphilis and A. G. Jones, *Inorg. Chem.*, **19** (1980) 1988.
- 13 M. Kawashima, M. Koyama and T. Fujinaga, *J. Inorg. Nucl. Chem.*, **38** (1976) 801.
- 14 N. J. Bryson, D. Brenner, J. Lister-James, A. G. Jones, J. C. Dewan and A. Davison, *Inorg. Chem.*, **28** (1989) 3825.
- 15 H. F. Kung, Y.-Z. Guo, C.-C. Yu, J. Billings, V. Subramanyam and J. C. Calabrese, *J. Med. Chem.*, **32** (1989) 433.
- 16 T. N. Rao, D. Adhikesavalu, A. Camerman and A. R. Fritzberg, *J. Am. Chem. Soc.*, **112** (1990) 5798.
- 17 S. Jurrison, E. O. Schlemper, D. E. Troutner, L. R. Canning, D. P. Nowotnik and R. D. Neirinckz, *Inorg. Chem.*, **25** (1986) 543.
- 18 S. Jurrison, L. F. Lindoy, K. P. Dancy, M. McPartlin, P. A. Tasher, D. K. Uppal and E. Deutsch, *Inorg. Chem.*, **23** (1984) 227.
- 19 F. Refosco, F. Tisato, U. Mazzi, G. Bandoli and M. Nicolini, *J. Chem. Soc., Dalton Trans.*, (1988) 611.
- 20 A. Davison, H. S. Trop, B. V. DePamphilis and A. J. Jones, *Inorg. Synth.*, **21** (1982) 160.
- 21 B. V. DePamphilis, *Ph. D. Thesis*, Massachusetts Institute of Technology, 1981.
- 22 G. Daidone, R. Raffa, B. Maggio, S. Plescia, M. Matera and A. Caruso, *Farmaco*, **45** (1990) 285.
- 23 G. W. Parshall, *Inorg. Synth.*, **17** (1977) 110.
- 24 T. Nicholson and J. Zubieta, *Polyhedron*, **7** (1988) 171.
- 25 D. Sutton, *Chem. Soc. Rev.*, **4** (1975) 443.
- 26 J. R. Dilworth, *Coord. Chem. Rev.*, **21** (1976) 29.
- 27 G. Bandoli, B. Mazzi, B. E. Wilcox, S. Jurrison and E. Deutsch, *Inorg. Chim. Acta*, **95** (1984) 217.
- 28 M. Melnik and J. E. van Lier, *Coord. Chem. Rev.*, **77** (1987) 275.