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Synthesis and Characterization of Complexes Containing the Bis(1,2-diolato)-oxotechnetium(V) Core

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Abstract

The complexes $(Bu_4N)[TcO(O_2C_6H_4)_2]$ (1) and $Na[TcO(OCH_2CH_2O)_2]$ (2) have been prepared by reacting $TcOCl_4^-$ with respective diols in methanol. Compound 2 was identified by its elemental analysis and field desorption mass spectrum. Crystals of compound 1 are monoclinic, *C*2/*c*, with cell dimensions $a = 10.393(3)$, $b = 13.835(3)$, $c = 20.643(5)$ Å, $\beta = 101.74(3)^\circ$ and four formula units in the unit cell. The crystal structure was determined by standard methods and refined to $R_1 = 0.0694$, $R_2 = 0.0613$, on the basis of 2887 independent reflections. The data were collected with use of Mo Kα radiation and a Syntex $P2_1$ diffractometer. The anion of 1 is square pyramidal with a short Tc–O(oxo) bond (1.648(5) Å). Tc–O distances to the diolate groups are longer (1.956(3), 1.958(3) Å). The technetium atom lies 0.7014(4) Å out of the plane of the four diolate oxygen atoms. Compound 2 is hydrolytically unstable in pure water, but can be stabilized by the addition of a several-fold molar excess of ethylene glycol. Compound 1 decomposes minimally in pure water after 24 h. These complexes are shown to be good structural models for ^{99m}Tc-radiopharmaceuticals containing purely oxygen-donor ligands. Comparison of the physical properties of the structurally characterized members of the series of complexes with core structures $TcOS_xO_{(4-x)}$ ($x = 0, 2, 4$) shows a shift to low energy in the frequency of the terminal oxygen–technetium band in the IR correlated with increasing softness of the basal plane donor atom set.

Introduction

Nuclear medicine [1] is relying increasingly upon radiopharmaceuticals containing the metastable isomer of technetium (^{99m}Tc) as agents of choice for imaging organ systems in the diagnosis of disease [2]. This widespread use [3] is because of the favorable nuclear properties of ^{99m}Tc, which decays by emission of a 140 keV gamma ray and has a half-life of only 6 h. The energy of the gamma ray is optimal for detection by current instrumentation, and the combination of gamma energy and short half-life allows a relatively large amount to be administered for better image quality [4a, b], with very low radiation does [5a, b, c] to the patient. Chemically, the element has been combined with a variety of ligands to produce highly specific radiopharmaceuticals for imaging bones, kidney, liver, gall bladder, blood pool, etc.

We are using the long-lived radionuclide ^{99}Tc, a β^--emitter with a half-life of 213 000 years, to investigate the chemistry of technetium on a scale amenable to the use of commonly available methods of study. By isolating macroscopic amounts of ^{99}Tc-containing complexes, and determining their structures and reactivity, we are increasing our knowledge of the chemistry of this element to permit the design and synthesis of the improved radiopharmaceuticals of the future.

In our previous investigations of the chemistry of ^{99}Tc pertinent to radiopharmaceuticals containing ^{99m}Tc, the syntheses of bis(1,2-dithiolato) [6a, b] and bis(2-mercaptoethanolato) [7] complexes of oxotechnetium(V) were demonstrated. Both classes of complexes can be readily synthesized by the dithionite reduction, in aqueous alkaline medium, of stoichiometric amounts of pertechnetate (TcO_4^-) and the dithiol or β-mercaptoethanol. X-ray crystallographic studies [6a, 7] have established the core structures of these complexes to be square pyramids, with the oxo-oxygen occupying the apical position and either four sulfur atoms or two oxygen atoms and two sulfur atoms constituting the basal plane.

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It seems logical to investigate the possibility of the existence of a Tc(V)OO_4 core structure. There are a number of ^{99m}Tc-containing radiopharmaceuticals with ligands that are purely oxygen donors. A ^{99m}Tc-complex of citrate ion was used by Yeh and Kriss [8] as a renal agent; ^{99m}Tc-glucoheptonate is used as a renal- and brain-imaging agent, and ^{99m}Tc-gluconate [9a, b, 10] has been used for imaging kidney and myocardial infarctions. Lebowitz *et al.* [11] reported the use of ^{99m}Tc-mannitol as a renal agent. At the outset of this research there was no structural information available for these agents, and, in fact, the oxidation state of the technetium in the polyol complexes was assumed [12] to be +4.

By utilizing the lability of $TcOCl_4^-$ towards ligand exchange, first described ty Trop *et al.* [6b] for the case of 1,2-dithiols, we have been able to isolate and characterize oxotechnetium(V) complexes of ethylene glycol and catechol.

Experimental

Water was passed through a cartridge (Barnstead D8904) to remove organic compounds, then through an ion-exchanger (Corning 3508-B), and finally distilled. All other reagents were used as received, except as noted. Pertechnetate (as $NH_4{}^{99}TcO_4$) was obtained from New England Nuclear. Catechol was obtained from Aldrich, as was 1,2-cyclohexyldiol. The latter was crystallized from hot ethyl acetate. Ethylene glycol was obtained from Fischer. The starting material for the ligand exchange preparations, $(n\text{-}Bu_4N)[TcOCl_4]$, was prepared by the published method [6b, 13].

Microanalyses of elements other than Tc were performed by Spang Microanalytical Laboratory, Eagle Harbor, Michigan. The ^{99}Tc analysis of $Na[TcO(OCH_2CH_2O)_2]$ was done by a liquid scintillation counting method [14]. A standard solution of $Na[TcO(OCH_2CH_2O)_2]$ was oxidized to $NaTcO_4$ and an aliquot mixed with a commercial scintillation cocktail (Biofluor^R, New England Nuclear) and counted in a liquid scintillation counter (Packard Tri-carb Model 3385). This was compared with a standard solution of TcO_4^- [15]. The technetium content of $Na[TcO(OCH_2CH_2O)_2]$ was 37.80% Tc.

Infrared spectra were recorded on a Perkin-Elmer 180 grating spectrophotometer as KBr pellets. Optical spectra were obtained with a Cary 17 spectrophotometer. The field desorption mass spectrum (FDMS) of $Na[TcO(OCH_2CH_2O)_2]$ was obtained [16] with a Varian MAT 731 double focusing mass spectrometer fitted with a combination EI/FI/FD ion source. Carbon activated tungsten wire emitters were loaded by dipping them into a methanol solution of the compound.

Preparation of Tetrabutylammonium Bis(catecholato)oxotechnetium(V)

A solution of 0.09137 g (0.8301 mmol) catechol in 6.2 ml MeOH was added dropwise to a solution of 0.20674 g (0.4143 mmol) $(n\text{-}Bu_4N)[TcOCl_4]$ with constant stirring. The deep red–purple reaction mixture was treated with approximately 0.5 ml of 0.63 N NaOH, until it was a stable red–orange colour. The dropwise addition of 1 ml of 50% *w/v* Bu_4NCl/H_2O and 25 ml of H_2O resulted in a large mass of small golden crystals. These were filtered from the reaction mixture, washed with water (2 X 5 ml) and then dried *in vacuo*. The yield of $(n\text{-}Bu_4N)[TcO(O_2C_6H_4)_2]$ was 0.09244 g, 81% based on Tc.

The product is easily recrystallized from methanol–water or acetone–water. Crystals suitable for X-ray diffraction analysis were grown by slow recrystallization from acetone–isobutanol. *Anal.* Calc. for $C_{28}H_{44}NO_5Tc$: C, 58.6; H, 7.7; N, 2.4. Found: C, 58.6; H, 7.3; N, 2.8%.

Preparation of Sodium Bis(1,2-ethanediolato)oxotechnetium(V)

A 2.85 ml aliquot of neat ethylene glycol (50.91 mmol) was added in one portion to a solution of 1.02307 g (2.05 mmol) of $(n\text{-}Bu_4N)[TcOCl_4]$ in 20 ml of MeOH. A solution of 0.77627 g (9.46 mmol) of anhydrous sodium acetate in 20 ml MeOH was added dropwise to the reaction mixture. The addition of 300 ml of Et_2O to this solution affords a light purple precipitate, which was separated by filtration, and extracted with three 50 ml portions of boiling EtOH. The combined filtered extracts were reduced in volume on a rotary evaporator until a substantial yield of small blue–purple crystals was produced. The crystals were carefully filtered from the mother liquor, washed with 5 ml of cold EtOH and dried *in vacuo*. This synthesis yielded 0.23242 g of $Na[TcO(OCH_2CH_2O)_2]$, 44% based on Tc. *Anal.* Calc. for $C_4H_8NaO_5Tc$: C, 18.6; H, 3.1; Na, 8.9; Tc, 38.4. Found: C, 19.2; H, 3.2; Na, 8.6; Tc, 37.8%.

Collection of the X-ray Data

Precession photographs showed the crystals of $[(n\text{-}C_4H_9)_4N][TcO(O_2C_6H_4)_2]$ were monoclinic, space group *C2/c* or *Cc*. The centric space group was chosen and justified by the successful solution of the structure. Unit cell parameters were obtained from least-squares fit of χ, ϕ and 2θ for 15 reflections in the range of $23.6° < 2\theta < 31.9°$ recorded on a Syntex $P2_1$ diffractometer using graphite-monochromated Mo Kα radiation (λ 0.71069 Å). Crystal data and other data collection numbers are summarised in Table I. The density was obtained by flotation in an aqueous zinc bromide solution. Intensities were measured on the Syntex $P2_1$ diffractometer using a coupled θ(crystal) 2θ(counter)

TABLE I. Crystal Data

Compound $[(n\text{-}C_4H_9)_4N]^+[TcO(O_2C_6H_4)_2]^-$	$(C_{16}H_{36}N)^+(C_{12}H_8O_5Tc)^-$
Formula weight	573.66
Crystal size (mm)	approx. cylinder, $r = 0.11$, $l = 0.25$
Systematic absences	$h\,k\,l, h + k = 2n + 1, h\,0\,l, l = 2n + 1, 0\,k\,0, k = 2n + 1$
Space group	$C2/c$
Unit cell parameters (Å and °)	$a = 10.392(3)$; $\beta = 101.74(3)$
	$b = 13.835(3)$
	$c = 20.643(5)$
Volume (Å^3)	2906(1)
Z	4
ρ_{calc}, ρ_{obs} (g cm^{-3})[a]	1.28, 1.27(1)
Linear absorption coefficient (cm^{-1})	5.29
Max 2θ, reflection collected	55°, $\pm h, k, \pm l$
Standard reflections (e.s.d.%)	3, 1, 1 (2.04) −1, −1, 5 (2.04)
Temperature (°C)	−55
No. of independent reflections	2887
No. with $I > 0$	2755
$I < 0$ rejected	132
Final R_1[b], R_2[b]	0.0694, 0.0613
Final shift/error max. (average)	0.081(0.017)
Final difference map	
Highest peak (eÅ^{-3}); location	0.55, 0.05, 0.09, 0.22
Lowest trough (eÅ^{-3}); location	−0.40; 0.49; 0.40; 0.72
Weighting	$w = [\sigma^2 + (0.0249F_o)^2]^{-1}$
Error in an observation of unit wt	1.0589

[a]The density was measured at room temperature. Unit cell parameters used to calculate density were measured at 22 °C and were $a = 10.423(2)$, $b = 14.009(2)$, $c = 20.897(3)$ Å, $\beta = 101.86(2)$°. [b]$R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$; $R_2 = \{\Sigma w(|F_o| - |F_c|)^2/\Sigma w F_o^2\}^{1/2}$.

scan. Methods of selection of scan rates and initial data treatment have already been described [17, 18]. Corrections were made for Lorentz-polarization effects but not for absorption. This will introduce a maximum error of <1.0% in F_o.

Solution of the Structure

The coordinates were found from a three-dimensional Patterson synthesis and a series of full-matrix least-squares refinements followed by three-dimensional electron density synthesis revealed all the non-hydrogen atoms. Temperature factors of two carbon atoms (C(13), C(14)) suggested they were disordered, so each was replaced by two carbon atoms and the parameters, including the occupancy, allowed to vary. Geometric calculations showed that the two sets of atoms had to be correlated and so the occupancy of each disordered atom was fixed at 0.5. In further refinements using full-matrix least-squares and minimizing $\Sigma w(|F_o| - |F_c|)^2$, the temperature factors of all atoms were made sequentially anisotropic. Tests were made to show the use of increased parameters was significant [19]. When the shift/error had dropped to <0.2, a search was made for hydrogen atoms and all were detected. In final refinements the hydrogen atoms were placed at the positions found above and given temperature factors 20% greater than the atoms to which they were attached but only the non-hydrogen atoms were refined. Refinement was terminated when the shift/error fell below 0.1. Throughout, the scattering curves were taken from ref. 20 and anomalous dispersion corrections from ref. 21 were applied to the curve for technetium. The positional parameters for non-hydrogen atoms are listed in Table II. See also 'Supplementary Material'.*

Results and Discussion

The synthetic utility of (n-Bu$_4$N)[TcOCl$_4$] as precursor to the large class of bis(1,2-dithiolato)-oxotechnetate complexes was conclusively demonstrated [6b] by Trop *et al.* We have now extended its utility by reacting it with catechol and ethylene glycol, and have isolated and characterized the first examples of bis(1,2-diolato) complexes of oxotechnetium(V).

Tetrabutylammonium bis(catecholato)oxotechnetium(V) (**1**) was positively identified by X-ray crystallography. The anion is shown in Fig. 1 and

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*All calculations were carried out on a CYBER 170/730 computer. The structure was solved with use of SHELX [22a]. Planes and interplanar angles were calculated with use of NRC-22 [22b]. Diagrams were prepared by using ORTEP-II [22c].

TABLE II. Positional Parameters for Non-hydrogen Atoms ($\times 10^4$)

	x	*y*	*z*
Tc	0	939.4(3)	2500
O(1)	0	2131(3)	2500
O(2)	1741(2)	389(2)	2519(1)
C(1)	2378(4)	125(3)	3137(2)
C(2)	1641(4)	189(3)	3624(2)
O(3)	369(3)	469(2)	3414(1)
C(3)	2192(5)	−49(4)	4273(2)
C(4)	3488(5)	−355(4)	4416(3)
C(5)	4208(5)	−446(4)	3939(3)
C(6)	3656(4)	−205(3)	3286(2)
N	5000	2466(3)	2500
C(7)	4069(4)	1803(3)	2039(2)
C(8)	3007(4)	2284(3)	1521(2)
C(9)	3210(5)	1522(3)	1051(2)
C(10)	1162(5)	1916(5)	549(3)
C(11)	4262(4)	3115(3)	2887(3)
C(12)	3513(6)	2602(4)	3339(3)
C(13)[a]	3039(11)	3387(8)	3775(5)
C(14)[a]	2431(10)	2908(8)	4317(5)
C(13a)[a]	2470(9)	3227(9)	3574(7)
C(14a)[a]	3289(14)	3811(12)	4141(7)

[a]Disordered carbon atoms with site occupancy factors fixed at 0.5.

pertinent bond lengths and bond angles are given in Table III. The coordination geometry is square pyramidal, just like the $TcOS_4$ and $TcOS_2O_2$ complexes studied [6, 7] previously, with the Tc atom 0.701(1) Å above the plane of the four oxygen atoms. Because each pair of catechol oxygen atoms is nearly coplanar with their benzene ring, the rings are bent away from the oxo-group, making a dihedral angle of 162° with the base of the square pyramid and 144° with each other. The Tc–O distances (Tc–O(1) 1.648(5), Tc–O(2) 1.956(3), Tc–O(3) 1.958(3) Å) are consistent with values found previously for Tc=O (range 1.610(4)–1.679(5) Å) [6, 7, 23–27] and Tc–O bonds (1.950(6) Å) [7], C(1)–C(2) (1.385(7) Å) and both C–O distances (1.362(5), 1.361(5) Å) correlate well with those found in oxo–molybdenum complexes and Co(3,5-DBcat)-(3,5-DBSQ)bipy (range 1.376(12)–1.396(6) Å, 1.358(10)–1.37(2) Å respectively) [28]. However, the C–O distances are longer than those normally found in complexes of many metals not containing oxogroups (range 1.32(1)–1.355(6) Å) [28], and the C(1)–C(2) is generally shorter than those found in the same large group of metal complexes (1.402(7)–1.414(5) Å), although there are three exceptions (1.348(10)–1.366(11) Å) [28].

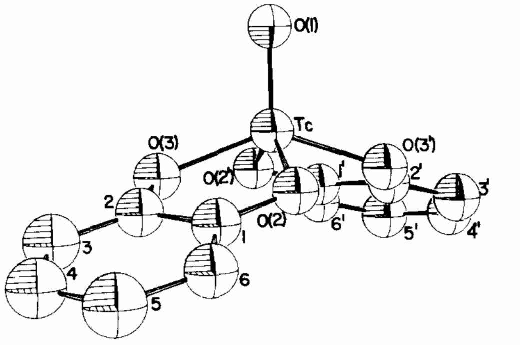

Fig. 1. Structure of the anion $(n\text{-}Bu_4N)[TcO(O_2C_6H_4)_2]$ showing the atom numbering. Carbon atoms are shown by numbers only.

A structurally analogous low spin d^2 complex is found in the oxoosmium(VI) diester $OsO(O_2C_2H_4)_2$ [29]. The Os–O (terminal) bond length is 1.66(1) Å; the Os–O(ester) average bond length is 1.89(1) Å; and the average O(terminal–Os–O(ester) bond angle is 110°. There is an Os=O stretch at 992 cm^{-1} in the IR. All of these parameters agree well with those of $TcO(O_2C_6H_4)_2^-$.

The packing of compound **1** within the unit cell is shown in Fig. 2. The cation and anion form an ion pair. The cation, which has the n-butyl groups arranged in a flat cross, lies below the anion (the oxo group is defined as up) with the cross parallel to the base of the square pyramid. One pair of n-butyl groups eclipses the two catechol rings and the alternate pair of n-butyl groups lies between the catechol rings. The former pair is thus restricted

TABLE III. Selected Interatomic Distances (Å) and Angles (°)

Tc–O(1)	1.648(5)	Tc–O(2)	1.956(3)	Tc–O(3)	1.958(3)
O(2)–C(1)	1.362(5)	O(3)–C(2)	1.361(5)	C(1)–C(2)	1.385(7)
C(2)–C(3)	1.384(6)	C(3)–C(4)	1.385(7)	C(4)–C(5)	1.359(8)
C(5)–C(6)	1.394(7)	C(6)–C(1)	1.379(6)		
O(1)–Tc–O(2)$_1$	112.93(8)	O(1)–Tc–O(3)$_1$	109.40(9)	O(2)–Tc–O(3)$_1$	81.5(1)
O(2)–Tc–O(3)	83.6(1)	O(2)–Tc–O(2)	134.1(1)	O(3)–Tc–O(3)	141.2(1)
Tc–O(2)–C(1)	113.2(3)	O(2)–C(1)–C(2)	115.3(3)	O(2)–C(1)–C(6)	124.0(4)
Tc–O(3)–C(2)	112.9(3)	O(3)–C(2)–C(1)	115.5(4)	O(3)–C(2)–C(3)	124.0(4)
C(2)–C(1)–C(6)	120.6(4)	C(1)–C(6)–C(5)	118.9(5)	C(6)–C(5)–C(4)	120.0(4)
C(1)–C(2)–C(3)	120.4(4)	C(2)–C(3)–C(4)	118.2(5)	C(3)–C(4)–C(5)	121.9(5)

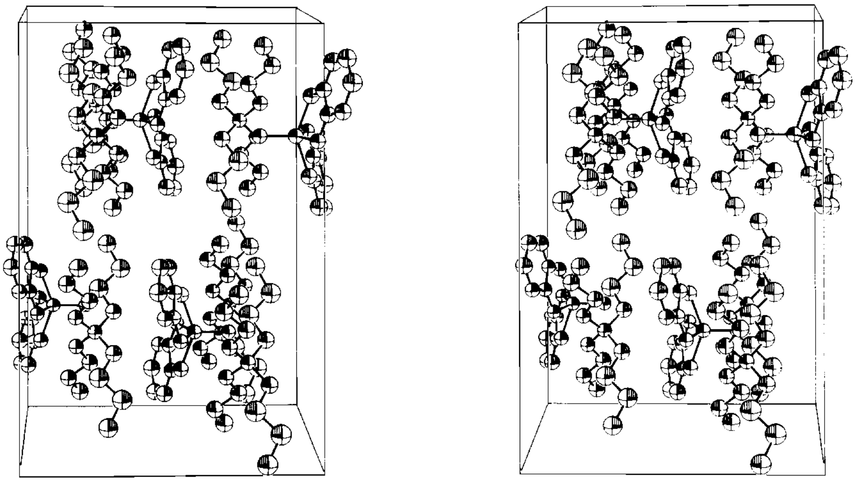

Fig. 2. Packing of (n-Bu_4N)[$TcO(O_2C_6H_4)_2$] within the unit cell. *b* and *c* are parallel to the bottom and side of the page respectively and the view is down *c**.

TABLE IV. Comparison of Bond Distances and ν(Tc=O) for some $TcOX_4{}^{n-}$ Ions

Ions [ref.]	Tc–oxo (Å)	Tc–S (average) (Å)	Tc–O (average) (Å)	Tc to basal plane (Å)	ν(Tc=O) (cm^{-1})
$TcO(O_2C_6H_4)_2{}^-$	1.648(5)		1.957(3)	0.701(1)	970
$TcO(S(CH_2)_2O)_2{}^-$ [7]	1.662(5)	2.290(3)	1.957(6)	0.720(1)	948
$TcO(SCH_2COS)_2{}^-$ [6a]	1.672(8)	2.320(4)		0.791	950
$TcO(S(CH_2)_2S)_2{}^-$ [25, 28]	1.64(1)	2.300(13)		0.761(2)	940
$TcOCl_4{}^-$ [24]	1.610(4)			0.66	1016
$TcO(\underline{S}CH_2CO\underline{N}CH_2{}^-)_2$ [23]	1.679(5)	2.287(3)		0.771(5)	945
$TcO(HBPz_3)Cl_2$ [29]	1.656(3)				970
$TcO(Dpen)_2$ [30]	1.657(4)	2.289(2)			958

in its geometry; the latter pair is not and shows the disorder mentioned above. The ion pairs are packed in layers parallel to the *ab* plane at roughly $z = 1/4$, $3/4$. Each layer is composed of rows of ion pairs along the *a* direction with the oxo-groups of one layer lying between cation pairs in the next row. Layers at $z = 1/4$ and $3/4$ have the oxo-groups pointing in opposite directions along *b*. Forces between layers are van der Waals.

There is a strong band in the infrared spectrum of **1** at 970 cm^{-1} which can be assigned to the Tc–oxo (apical) stretch. It is instructive at this point to compare the relevant structural parameters and ν(Tc=O) of representative members of the class of complexes with the $TcOS_xO_{4-x}$ core (Table IV). The average Tc–S bond length seems to be the same in the $TcOS_4$ and $TcOS_2O_2$ cores and the average Tc–O (ligand) distance also seems to be independent of core type, be it $TcOS_2O_2$ or $TcOS_4$. The Tc–oxo bond length varies slightly but significantly across the series, although the distance of the metal from the basal plane varies a substantial amount from core to core.

There also seems to be a systematic variation in the Tc=O stretch across the series, which correlates with this bond length change. As sulphur atoms are replaced by oxygen atoms, the band shifts to higher energy, at least for the ethanedithiolato-2-mercaptoethanolato-catecholato series. Thus as the average ligating atom becomes 'harder' the Tc=O bond gets stronger. The result is expected since an inverse bond length –ν(M=O) relationship has already been demonstrated by Cotton and Wing [31] for molybdenum and by Howard-Lock *et al.* for rhenium [32].

The optical spectrum of **1** in MeCN is dominated by a single, intense, unsymmetrical band (λ_{max} = 278 nm; $\epsilon = 13000$ l mol^{-1} cm^{-1}). It should be recalled that the major spectral feature of the toluene-dithiolato member of the $TcOS_4$ series [33] was also intense ($\epsilon = 13000$ l mol^{-1} cm^{-1}).

The compound $Na[TcO(OCH_2CH_2O)_2]$ (**2**) was prepared by reacting $TcOCl_4{}^-$ with a 2-fold excess of ethylene glycol and a greater-than 4-fold excess of sodium acetate. Unlike the reaction [6b] of 1,2-dithiols with $TcOCl_4{}^-$, there is no visible change in the color of the reaction mixture when a stoichiometric amount of ethylene glycol is added. Even at large molar excesses of the ligand, when the complex is formed, the addition of water and Bu_4NCl or Ph_4AsCl did not effect precipitation of the product as salts of these cations. In an effort to make the product less water-soluble, 1,2-cyclohexyldiol was used as the ligand in a similar preparation. Treatment of the reaction mixture with four equivalents of sodium acetate in the absence of additional counterions caused the precipitation of an amorphous blue powder, which was insoluble in all the common solvents tried, and thus could not be crystallized. It was finally possible to bring **2** out of the solution by the addition of a large quantity of Et_2O, and the product was recrystallized easily from hot EtOH.

Identification of **2** depends on its elemental analysis and its field desorption mass spectrum [16]. Peaks are observed in the cation FDMS of this compound at $m/e = 235$ ($[TcO(OCH_2CH_2O)_2]^+$), 258 ($Na[TcO(OCH_2CH_2O)_2]^+$), and 271 ($Na_2[TcO(OCH_2CH_2O)_2]^+$). The infrared spectrum of **2** has a number of strong bands in the 900–1000 cm^{-1} region. Although the strongest of these is at 972 cm^{-1} and is a very likely candidate for the Tc=O stretch, the presence of bands at 955 and 989 cm^{-1} makes this assignment ambiguous.

The optical spectrum of **2** in MeOH is characterized in the visible region by a weak band at 535 nm ($\epsilon = 60$ l mol^{-1} cm^{-1}). There is also an inflection at 355 nm ($\epsilon = 50$ l mol^{-1} cm^{-1}). At higher energy, there is an almost-resolved inflection at 250 nm ($\epsilon = 3500$ l mol^{-1} cm^{-1}). The extinction coefficient of this band is similar to that of the main spectral features of $TcO(SCH_2CH_2O)_2^-$ (**3**) and $TcO(SCH_2CH_2S)_2^-$ (**4**) and the progression in values of λ_{max} for each of these (250 nm for **2**, 357 nm for **3** [7], and 400 nm for **4** [28b]), suggests a red shift as sulfur atoms are added to, and the oxygen atoms removed from, the $TcOS_xO_{(4-x)}$ core. The complex $(n\text{-}Bu_4N)[TcOCl_4]$ instantly decomposes [34] in water to TcO_4^- and TcO_2. By contrast, a solution of **2** in water turns brown over several minutes. It can be stabilized indefinitely by the addition of some ethylene glycol to the solution. Furthermore, if a methylene chloride solution of **1** is extracted with aqueous $NaBPh_4$, the $TcO(O_2C_6H_4)_2^-$ now in the aqueous phase is substantially stable for 24 h, after which there is only slight decomposition. Surprisingly, when TcO_4^- is reacted with a stoichiometric amount of ethylene glycol and sodium dithionite in alkaline medium, a purple solution is formed and persists for several minutes, before decomposition sets in. This attests to the stabilization of Tc in solution by ethylene glycol under conditions where normal TcO_4^- would be instantly reduced to $TcO_2 \cdot xH_2O$.

The synthesis and characterization of **1** and **2** are relevant to our understanding of ^{99m}Tc radiopharmceuticals already in use. The large ligand-to-Tc ratios in all such preparations suggest that complexes of the $TcOO_4$-type will be readily formed and stable under the reducing conditions used.

Recently, de Kieviet investigated [35] the structure of ^{99m}Tc-glucoheptonate (a renal agent) by studying the properties of a ^{99}Tc complex formed by Sn(II) reduction of a solution of $^{99}TcO_4^-$ and excess glucoheptonate. The product (which was not isolated) had absorptions in its optical spectrum at 502 nm ($\epsilon = 65$ l mol^{-1} cm^{-1}) and 270–280 nm (ϵ 2800 l mol^{-1} cm^{-1}). Bands in the IR at 930 and 970 cm^{-1} suggested the presence of the Tc=O moiety, and it was deduced from the IR spectrum that the carboxylate-oxygen of the ligand was involved in the binding. The final identification [35] of this unisolated species as bis(glucoheptonato)oxotechnetium(V) is consistent with what we now understand about **1** and **2**.

The results reported here establish that stable bis(1,2-diolato)oxotechnetium(V) complexes can be prepared and are resistant to hydrolysis in the presence of excess diol. They clearly suggest that the same type of core structure can exist in ^{99m}Tc-radiopharmaceuticals with oxygen-donor ligands.

Supplementary Material

Temperature factors and parameters for hydrogen atoms have been deposited with the Editor-in-Chief.

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