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## Synthesis and Characterization of a Pentadentate Schiff Base N<sub>3</sub>O<sub>2</sub> Ligand and Its Neutral Technetium(V) Complex. X-ray Structure of {N,N'-3-Azapentane-1,5-diylbis(3-(1-iminoethyl)-6-methyl-2H-pyran-2,4(3H)-dionato)(3-)-O,O',N,N',N'}oxotechnetium(V)

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Received May 29, 1991

Preparations of a potentially pentadentate ligand, N,N'-3-azapentane-1,5-diylbis(3-(1-iminoethyl)-6-methyl-2H-pyran-2,4(3H)-dione) (H<sub>3</sub>apa), and its neutral technetium(V) complex, [TcO(apa)], are described. The <sup>13</sup>C and <sup>1</sup>H NMR, infrared, optical, and mass spectra of the pentadentate ligand and its technetium(V) complex are reported. The X-ray structure of [TcO(apa)] has been determined. Crystals are orthorhombic, space group *Pbca*, with *a* = 12.833 (2) Å, *b* = 33.320 (5) Å, *c* = 9.942(4) Å, *V* = 4251 (2) Å<sup>3</sup>, and *Z* = 8. The structure was solved by Patterson and Fourier methods and was refined by full-matrix least-squares procedures to *R* = 0.028 and *R*<sub>w</sub> = 0.032 for 4054 reflections with *I* ≥ 3σ(*I*). The technetium(V) complex has a highly distorted octahedral coordination geometry comprising a [TcO]<sup>3+</sup> core and the triply deprotonated pentadentate ligand wrapping around the metal center. One of the two oxygen donor atoms of the pentadentate ligand is located trans to the Tc=O bond while the remaining four donor atoms, N<sub>3</sub>O, occupy the equatorial sites. The distance between the deprotonated N(1) atom to the Tc center (1.880 (2) Å) is significantly shorter than a normal Tc—N single bond length of 2.10 Å, but longer than that for a Tc=N triple bond (1.61 Å). <sup>1</sup>H NMR spectral data reveal a rigid solution structure for the complex, which undergoes no conformational and configurational exchange at temperatures up to 50 °C.

### Introduction

A burgeoning interest in technetium coordination chemistry has been spurred by its widespread use in diagnostic nuclear medicine.<sup>2,3</sup> Recent focus has been on the design and preparation of new technetium complexes, the lipophilicity, polarity, and overall charge of which can be readily altered by simple substitutions in the molecular framework of the ligand in order to optimize the biodistribution of the potential pharmaceutical. Of particular significance are cationic and neutral technetium complexes, since it has been shown that cationic technetium complexes can accumulate in the myocardial tissue,<sup>4</sup> while neutral complexes have found application in brain imaging.<sup>5-7</sup>

We have been pursuing a continuing study of the coordination chemistry of tris(ligand)gallium and -indium complexes that are water soluble, are hydrolytically stable, and have varying lipophilicity.<sup>8-11</sup> This combination of properties and the great mobility of these complexes *in vivo* have suggested their potential application as heart-imaging agents.<sup>11</sup> In an effort to extend these properties to technetium compounds, we have prepared a potentially pentadentate ligand (H<sub>3</sub>apa), which contains both lipophilic hydrocarbon chains and polar carbonyl groups, and its neutral technetium(V) complex. The pentadentate ligand (H<sub>3</sub>apa), derived from the condensation of diethylenetriamine (dien) and two equivalents of dehydroacetic acid (dha), and its technetium(V) complex, [TcO(apa)], have been characterized by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy, mass spectrometry, UV/visible spectrophotometry, infrared spectrometry, and, for [TcO(apa)], X-ray crystallography.

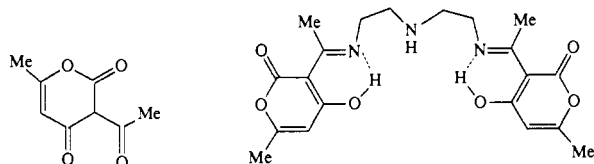
The ease of synthesis of polydentate Schiff base ligands has led to extensive investigation of their technetium coordination chemistry. The facility with which one can vary physical properties, coordination geometries, donor atoms, and backbones makes it possible to synthesize a wide variety of technetium complexes with different configurations, in which Tc is found in different oxidation states. Because of the strong trans effect of the oxygen in the [Tc=O]<sup>3+</sup> core, many technetium(V) complexes show a preference for five-coordination in a square-pyramidal geometry with the oxo oxygen in an apical position.<sup>2,3</sup> Six-coordination is possible only when a delicate balance is reached between the bond length to the metal center and the nucleophilic character of the group trans to the Tc=O bond.<sup>3,12</sup> Although many technetium(V) complexes with bidentate,<sup>12-14</sup> tridentate,<sup>12,14-19</sup> and tetradentate<sup>20-22</sup> Schiff base ligands have been well studied, only one structurally characterized six-coordinate technetium(V) complex

with a pentadentate ligand has been reported;<sup>23</sup> the pentadentate ligand was prepared by the Schiff base condensation of diethylenetriamine with 2 equiv of salicylaldehyde instead of dehydroacetic acid (dha, 3-acetyl-6-methyl-2H-pyran-2,4(3H)-dione) in our case. In fact, the present study presents the first structurally

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characterized dha-based Schiff base ligand complex, to our knowledge.



Dehydroacetic acid (dha)

 $H_3\text{apa} = (\text{dha})_2\text{dien}$ 

### Experimental Section

**Materials.**  $[\text{NH}_4][^{99}\text{TcO}_4]$  was obtained from the Du Pont Merck Pharmaceutical Company. Dehydroacetic acid and diethylenetriamine (both from Aldrich) were used without further purification.  $[\text{n-Bu}_4\text{N}][\text{TcOCl}_4]$  was prepared according to Davison's procedure.<sup>24</sup>

**Caution!**  $^{99}\text{Tc}$  is a low energy (0.292 MeV)  $\beta^-$  emitter with a half-life of  $2.12 \times 10^5$  years. All manipulations of solutions and solids were performed in a laboratory approved for the handling of low-level radioisotopes, and normal safety procedures must be used at all times to prevent contamination.

**Instrumentation.** Proton NMR spectra were recorded on a Bruker AC-200E ( $^1\text{H}$ - $^1\text{H}$  COSY, 200 MHz), a Varian XL 300 ( $^1\text{H}$ ,  $^{13}\text{C}$ , and APT  $^{13}\text{C}$  NMR, 300 MHz), or a Varian XL 500 ( $^1\text{H}$ - $^{13}\text{C}$  heteronuclear correlation, 500 MHz) spectrometer. Mass spectra were obtained with either a Kratos MS 50 (electron-impact ionization, EI) or an AEI MS-9 (fast atom bombardment ionization, FAB) instrument. Infrared spectra were recorded as KBr disks in the range 4000–200  $\text{cm}^{-1}$  on a Perkin-Elmer PE 783 spectrophotometer and were referenced to polystyrene. UV/visible spectra were recorded on a Shimadzu UV-2100 spectrophotometer. Melting points were measured on a Mel-Temp apparatus and are uncorrected. Analyses for CHN were performed by Peter Borda (for  $H_3\text{apa}$ ) in this department and by Canadian Microanalytical Services Ltd. (for the Tc complex). HPLC analyses were performed with a Waters system incorporating two 501 pumps, a Berthold LB 505 radioactivity monitor, and a Lambda-Max 481 LC spectrophotometer. The eluant was 60:40 methanol/water (flow rate 1  $\text{mL min}^{-1}$ ) on a  $\mu$ -Bondapak  $C_{18}$  column and Guard-Pak precolumn.

**Preparation of  $N,N'$ -3-Azapentane-1,5-diylbis(3-(1-iminoethyl)-6-methyl-2H-pyran-2,4(3H)-dione) ( $H_3\text{apa}$ ).** To a hot solution of dehydroacetic acid (8.4 g, 50 mmol) in 150 mL methanol was added diethylenetriamine (2.5 g, 25 mmol). The solution was refluxed for 30 min and then concentrated to about 50 mL under reduced pressure as a white solid was formed. The mixture was cooled to room temperature, and the solid was collected by filtration, washed with methanol and diethyl ether, and dried in air. The yield was 8.5 g (84.4%) with mp 143.5–144.5  $^\circ\text{C}$ . The white powder was soluble in chloroform and dichloromethane, slightly soluble in alcohols, and insoluble in diethyl ether. No recrystallization was necessary to obtain an analytically pure sample. Anal. Calcd (found) for  $\text{C}_{20}\text{H}_{25}\text{N}_3\text{O}_6$ : C, 59.54 (59.71); H, 6.25 (6.36); N, 10.42 (10.47). Mass spectrum (EI):  $m/e = 403$  (molecular ion  $[\text{C}_{20}\text{H}_{25}\text{N}_3\text{O}_6]^+$ ). Infrared spectrum ( $\text{cm}^{-1}$ , KBr disk): 3600–3300 ( $\nu_{\text{O-H}}$ ); 3000–2800 ( $\nu_{\text{C-H}}$ ); 1695, 1660, 1600, 1570 (all vs, mixed  $\nu_{\text{C=O}}$  and  $\nu_{\text{C=C}}$ ). Optical spectrum (in  $\text{CHCl}_3$ )  $\lambda_{\text{max}}$ , nm ( $\epsilon$ ,  $\text{L mol}^{-1} \text{cm}^{-1}$ ): 317 (29 300), 244 (20 300).

**Preparation of  $[\text{TcO}(\text{apa})]$ . Method A.** To a solution of  $[\text{n-Bu}_4\text{N}][\text{TcOCl}_4]$  (45 mg, 0.09 mmol) in 5 mL of methanol was added the ligand (40.3 mg, 0.1 mmol) in 5 mL of chloroform. To the resulting red solution was added sodium acetate trihydrate (40 mg, 0.3 mmol) in methanol (3 mL). The mixture was heated at 50  $^\circ\text{C}$  for 10 min and then left to stand at room temperature; purple-red crystals deposited as the solvent evaporated. These were collected by filtration, washed with methanol and diethyl ether, and dried in air to yield 25 mg of product (54% based on Tc). The product was soluble in chloroform and dichloromethane, but was insoluble in diethyl ether and water. Recrystallization of the product from  $\text{CHCl}_3/\text{Et}_2\text{O}$  by vapor diffusion afforded crystals for X-ray analysis.

**Method B.** The salt  $[\text{n-Bu}_4\text{N}][\text{TcOCl}_4]$  (34 mg, 0.068 mmol) was dissolved in methanol (5 mL); ethylene glycol ( $\text{H}_2\text{eg}$ , 0.5 mL) was added to the solution with stirring at room temperature, followed by sodium acetate trihydrate (66 mg, 0.5 mmol) in methanol (2 mL). The initial green color turned to turquoise and then to violet, producing the  $[\text{TcO}(\text{eg})_2]^-$  anion in situ.<sup>25</sup>  $H_3\text{apa}$  (32 mg, 0.08 mmol) in chloroform (3 mL)

**Table I.** Selected Crystallographic Data for  $[\text{TcO}(\text{apa})]$

formula	$\text{C}_{20}\text{H}_{22}\text{N}_3\text{O}_7\text{Tc}$	$Z$	8
fw	513.41	$T$ , $^\circ\text{C}$	21
cryst syst	orthorhombic	$\rho_c$ , $\text{g/cm}^3$	1.604
space group	$Pbca$	$\lambda$ , $\text{Å}$	0.710 69
$a$ , $\text{Å}$	12.833 (2)	$\mu(\text{Mo K}\alpha)$ $\text{cm}^{-1}$	6.93
$b$ , $\text{Å}$	33.320 (5)	transm factors	0.94–1.00
$c$ , $\text{Å}$	9.942 (4)	$R$	0.028
$V$ , $\text{Å}^3$	4251 (2)	$R_w$	0.032

**Table II.** Final Atomic Coordinates (Fractional) and  $B_{\text{eq}}$  ( $\text{Å}^2$ )<sup>a</sup>

atom	$x$	$y$	$z$	$B_{\text{eq}}$
Tc(1)	0.19734 (1)	0.114861 (6)	0.14914 (2)	2.592 (8)
O(1)	0.2189 (1)	0.09984 (6)	0.3078 (2)	3.90 (9)
O(2)	0.3606 (1)	0.10356 (5)	0.1268 (2)	2.75 (7)
O(3)	0.2301 (1)	0.13669 (5)	-0.0498 (2)	2.64 (7)
O(4)	0.4995 (1)	0.04543 (6)	-0.1806 (2)	3.99 (9)
O(5)	0.4805 (1)	0.20950 (5)	-0.0966 (2)	3.39 (8)
O(6)	0.3560 (2)	0.01758 (6)	-0.2533 (2)	4.5 (1)
O(7)	0.4409 (2)	0.24777 (6)	0.0750 (2)	4.6 (1)
N(1)	0.0524 (2)	0.12175 (6)	0.1341 (2)	3.2 (1)
N(2)	0.1666 (1)	0.06436 (6)	0.0414 (2)	2.72 (8)
N(3)	0.1852 (2)	0.17684 (7)	0.1731 (2)	3.5 (1)
C(1)	-0.0096 (2)	0.09103 (8)	0.0691 (3)	3.7 (1)
C(2)	0.0549 (2)	0.05295 (8)	0.0558 (3)	3.7 (1)
C(3)	0.2325 (2)	0.04197 (7)	-0.0258 (2)	2.7 (1)
C(4)	0.1954 (2)	0.00182 (8)	-0.0766 (3)	3.8 (1)
C(5)	0.3410 (2)	0.05379 (7)	-0.0470 (2)	2.6 (1)
C(6)	0.3934 (2)	0.03692 (8)	-0.1623 (3)	3.2 (1)
C(7)	0.5545 (2)	0.06804 (9)	-0.0912 (3)	3.5 (1)
C(8)	0.5086 (2)	0.08432 (8)	0.0150 (3)	3.3 (1)
C(9)	0.3977 (2)	0.08104 (7)	0.0353 (2)	2.6 (1)
C(10)	0.6652 (2)	0.0727 (1)	-0.1321 (3)	5.0 (2)
C(11)	0.0032 (2)	0.16042 (9)	0.1631 (3)	4.1 (1)
C(12)	0.0833 (2)	0.1851 (1)	0.2396 (3)	4.6 (1)
C(13)	0.2434 (2)	0.20517 (8)	0.1223 (3)	3.4 (1)
C(14)	0.2218 (3)	0.2488 (1)	0.1527 (4)	5.7 (2)
C(15)	0.3227 (2)	0.19460 (7)	0.0250 (3)	2.8 (1)
C(16)	0.4125 (2)	0.21951 (7)	0.0075 (3)	3.2 (1)
C(17)	0.4607 (2)	0.17922 (7)	-0.1849 (3)	3.0 (1)
C(18)	0.3747 (2)	0.15681 (7)	-0.1743 (2)	2.9 (1)
C(19)	0.3052 (2)	0.16193 (6)	-0.0632 (2)	2.48 (9)
C(20)	0.5468 (2)	0.17413 (9)	-0.2825 (3)	4.0 (1)

$$^a B_{\text{eq}} = (8/3)\pi^2 \sum \sum U_{ij} a_i^* a_j^* (\mathbf{a}_i \cdot \mathbf{a}_j)$$

was added to this mixture, and the solution became purple-red immediately. Upon evaporation of the solvents at room temperature, a purple-red solid was deposited. The solid was separated and then redissolved in chloroform (2 mL). Diffusion of diethyl ether into the chloroform solution afforded a product identical to that obtained by Method A with a yield of 17 mg (49% based on Tc). Anal. Calcd (found) for  $\text{C}_{20}\text{H}_{22}\text{N}_3\text{O}_7\text{Tc}$ : C, 46.58 (46.49); H, 4.30 (4.29); N, 8.16 (8.12). Mass spectrum (FAB):  $m/e = 515$  (molecular ion  $[\text{TcO}(\text{apa})]^+$ ). Infrared spectrum ( $\text{cm}^{-1}$ , KBr disk): 1695, 1665, 1645, 1580(s), 1550 (all vs, mixed  $\nu_{\text{C=O}}$  and  $\nu_{\text{C=C}}$ ), 915, 910 (s,  $\nu_{\text{Tc=O}}$ ). Optical spectrum (in  $\text{CHCl}_3$ )  $\lambda_{\text{max}}$ , nm ( $\epsilon$ ,  $\text{L mol}^{-1} \text{cm}^{-1}$ ): 460 (sh), 373 (21 200), 313 (sh), 280 (23 000), 247 nm (42 100).

**X-ray Crystallographic Analysis.** A summary of crystal data for  $[\text{TcO}(\text{apa})]$  is given in Table I. The final unit-cell parameters were obtained by least-squares refinement on the setting angles for 25 reflections with  $2\theta = 46.1$ – $51.9^\circ$  measured with Mo  $K\alpha$  radiation. The intensities of three standard reflections, measured every 200 reflections throughout the data collection, showed only small random variations. A total of 6193 reflections with  $2\theta \leq 60^\circ$  was collected on a Rigaku AFC6S diffractometer; of these, 4054 had  $I \geq 3\sigma(I)$  and were employed in the solution and refinement of the structure. The data were processed<sup>26</sup> and corrected for Lorentz and polarization effects and for absorption (empirical, based on azimuthal scans for four reflections).

The structure was solved by Patterson and Fourier methods, the coordinates of the Tc atom being determined from the Patterson function

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(26) TEXSAN/TEXRAY structure analysis package which includes versions of the following: MITHRIL, integrated direct methods, by C. J. Gilmore; DIRDIF, direct methods for difference structures, by P. T. Beurskens; ORFLS, full-matrix least-squares refinement, and ORFFE, function and errors, by W. R. Busing, K. O. Martin, and H. A. Levy; ORTEP II, illustrations, by C. K. Johnson.

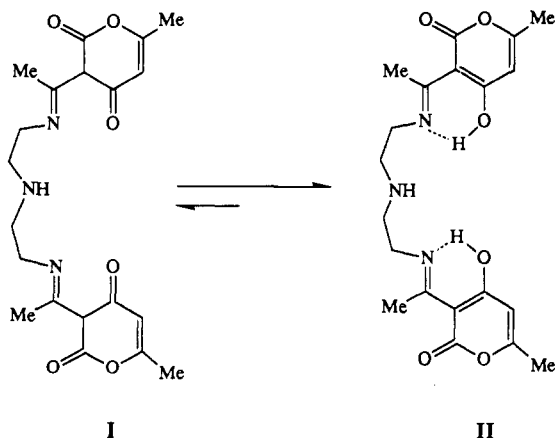
**Table III.** Bond Lengths (Å) with Estimated Standard Deviations for [TcO(apa)]

Tc(1)-O(1)	1.678 (2)	N(3)-C(12)	1.492 (3)
Tc(1)-O(2)	2.141 (2)	N(3)-C(13)	1.305 (3)
Tc(1)-O(3)	2.149 (2)	C(1)-C(2)	1.521 (4)
Tc(1)-N(1)	1.880 (2)	C(3)-C(4)	1.507 (3)
Tc(1)-N(2)	2.033 (2)	C(3)-C(5)	1.463 (3)
Tc(1)-N(3)	2.085 (2)	C(5)-C(6)	1.442 (3)
O(2)-C(9)	1.271 (3)	C(5)-C(9)	1.423 (3)
O(3)-C(19)	1.286 (3)	C(7)-C(8)	1.325 (4)
O(4)-C(6)	1.404 (3)	C(7)-C(10)	1.486 (4)
O(4)-C(7)	1.363 (3)	C(8)-C(9)	1.442 (3)
O(5)-C(16)	1.394 (3)	C(11)-C(12)	1.520 (4)
O(5)-C(17)	1.361 (3)	C(13)-C(14)	1.511 (4)
O(6)-C(6)	1.211 (3)	C(13)-C(15)	1.448 (3)
O(7)-C(16)	1.213 (3)	C(15)-C(16)	1.431 (3)
N(1)-C(1)	1.449 (3)	C(15)-C(19)	1.416 (3)
N(1)-C(11)	1.463 (3)	C(17)-C(18)	1.337 (3)
N(2)-C(2)	1.489 (3)	C(17)-C(20)	1.480 (3)
N(2)-C(3)	1.311 (3)	C(18)-C(19)	1.430 (3)

and those of the remaining non-hydrogen atoms from a subsequent difference Fourier synthesis. All non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were fixed in calculated positions (methyl group orientations based on difference map peaks,  $d_{C-H} = 0.98$  Å,  $B_H = 1.2B_{\text{bonded atom}}$ ). Neutral-atom scattering factors and anomalous dispersion corrections for the non-hydrogen atoms were taken from ref 27. Final atomic coordinates and equivalent isotropic thermal parameters, bond lengths, and bond angles appear in Tables II-IV, respectively. A more detailed table of crystallographic data (Table SI), and tables of hydrogen atom parameters (Table SII), anisotropic thermal parameters (Table SIII), intramolecular distances involving hydrogen atoms (Table SIV), intramolecular bond angles involving hydrogen atoms (Table SV), torsion angles (Table SVI), intermolecular contacts (Table SVII), least-squares planes (Table SVIII), and measured and calculated structure factor amplitudes (Table SIX) are included as supplementary material (see paragraph at the end of the paper).

### Results and Discussion

A new ligand ( $H_3apa$ ) has been prepared by the Schiff base condensation of diethylenetriamine (dien) with 2 equiv of dehydroacetic acid (dha). The potentially pentadentate ligand contains a ONNNO donor set in which an amine group is located in the middle of the chain joining two lateral imine groups. The analytical data are consistent with the proposed stoichiometry of  $[C_{20}H_{25}N_3O_6]$  for the ligand. Since the infrared spectrum of the free ligand shows a very broad band at  $3500\text{ cm}^{-1}$  due to O-H stretching vibrations, the molecule probably exists mainly as the imine-enol form (II). This conclusion is also supported by the enol proton  $^1\text{H NMR}$  signal, which is stabilized by intramolecular hydrogen bonding and lies far downfield ( $\delta$  14 ppm) as a broad singlet.



The technetium(V) complex has been prepared from the reaction of  $[\text{TcOCl}_4]^-$  with  $H_3apa$  and 3 equiv of sodium acetate

**Table IV.** Bond Lengths (deg) with Estimated Standard Deviations for [TcO(apa)]

O(1)-Tc(1)-O(2)	83.33 (7)	C(4)-C(3)-C(5)	119.4 (2)
O(1)-Tc(1)-O(3)	159.08 (7)	C(3)-C(5)-C(6)	117.0 (2)
O(1)-Tc(1)-N(1)	105.91 (9)	C(3)-C(5)-C(9)	125.1 (2)
O(1)-Tc(1)-N(2)	106.28 (9)	C(6)-C(5)-C(9)	117.9 (2)
O(1)-Tc(1)-N(3)	101.6 (1)	O(4)-C(6)-O(6)	113.3 (2)
O(2)-Tc(1)-O(3)	76.84 (6)	O(4)-C(6)-C(5)	118.5 (2)
O(2)-Tc(1)-N(1)	169.01 (8)	O(6)-C(6)-C(5)	128.1 (3)
O(2)-Tc(1)-N(2)	89.41 (7)	O(4)-C(7)-C(8)	121.1 (2)
O(2)-Tc(1)-N(3)	105.02 (7)	O(4)-C(7)-C(10)	112.0 (2)
O(3)-Tc(1)-N(1)	94.53 (7)	C(8)-C(7)-C(10)	126.9 (3)
O(3)-Tc(1)-N(2)	80.40 (7)	C(7)-C(8)-C(9)	121.3 (2)
O(3)-Tc(1)-N(3)	77.56 (7)	O(2)-C(9)-C(5)	126.7 (2)
N(1)-Tc(1)-N(2)	82.36 (8)	O(2)-C(9)-C(8)	115.2 (2)
N(1)-Tc(1)-N(3)	79.30 (9)	C(5)-C(9)-C(8)	118.2 (2)
N(2)-Tc(1)-N(3)	149.95(9)	N(1)-C(11)-C(12)	106.4 (2)
Tc(1)-O(2)-C(9)	123.0 (1)	N(3)-C(12)-C(11)	105.8 (2)
Tc(1)-O(3)-C(19)	117.6 (1)	N(3)-C(13)-C(14)	120.9 (2)
C(6)-O(4)-C(7)	122.0 (2)	C(16)-C(13)-C(15)	119.0 (2)
C(16)-O(5)-O(17)	122.6 (2)	C(14)-C(13)-C(15)	119.8 (3)
Tc(1)-N(1)-C(1)	119.5 (2)	C(13)-C(15)-C(16)	120.4 (2)
Tc(1)-N(1)-C(11)	121.3 (2)	C(13)-C(15)-C(19)	119.3 (2)
C(1)-N(1)-C(11)	118.2 (2)	C(16)-C(15)-C(19)	119.9 (2)
Tc(1)-N(2)-C(2)	110.3 (2)	O(5)-C(16)-O(7)	114.1 (2)
Tc(1)-N(2)-C(3)	127.9 (2)	O(5)-C(16)-O(15)	117.1 (2)
C(2)-N(2)-C(3)	121.7 (2)	O(7)-C(16)-C(15)	128.7 (3)
Tc(1)-N(3)-C(12)	107.4 (2)	O(5)-C(17)-C(18)	121.1 (2)
Tc(1)-N(3)-C(13)	129.0 (2)	O(5)-C(17)-C(20)	111.6 (2)
C(12)-N(3)-C(13)	122.7 (2)	C(18)-C(17)-C(20)	127.2 (2)
N(1)-C(1)-C(2)	109.2 (2)	C(17)-C(18)-C(19)	120.6 (2)
N(2)-C(2)-C(1)	108.6 (2)	O(3)-C(19)-C(15)	123.9 (2)
N(2)-C(3)-C(4)	118.2 (2)	O(3)-C(19)-C(18)	118.0 (2)
N(2)-C(3)-C(5)	122.3 (2)	C(15)-C(19)-C(18)	118.1 (2)

trihydrate in a mixture of methanol and chloroform. It was also prepared from the reaction of the ligand with  $[\text{TcO}(\text{eg})_2]^-$  (eg = ethylene glycolate),<sup>25</sup> which was produced in situ from  $[\text{TcOCl}_4]^-$ . The complex is soluble in chloroform and acetonitrile, but only slightly soluble in methanol. It is stable in the solid state and in methanol solution for 2 weeks with no hydrolysis detected by HPLC (the retention time for the complex was 4.25 min). The complex is diamagnetic in both solid and solution states.

The electronic spectrum of the complex in chloroform shows absorption bands at  $\lambda_{\text{max}}$  of 460 (sh), 373, 313 (sh), 280, and 247 nm. Only two bands are seen for the free ligand in the same solvent ( $\lambda_{\text{max}} = 317$  and 244 nm); the two new higher energy bands at 373 and 280 nm are assigned to the ligand-to-metal or/and metal-to-ligand charge transfers while the low-energy band at 460 nm as a shoulder is tentatively assigned to a d-d transition.

The infrared spectrum of the complex exhibits two Tc=O stretching vibrations at 915 and 910  $\text{cm}^{-1}$ ; this is very likely to be a solid-state effect since the presence of two enantiomers in the solid should not give a separate band for each optical isomer and the bands really appear as one which has been split. This split appearance varies from KBr disk to KBr disk. For monooxo square-pyramidal technetium(V) complexes, the Tc=O stretching band falls in the range 930-1020  $\text{cm}^{-1}$ .<sup>2,3</sup> The  $\nu_{\text{Tc=O}}$  band in  $[\text{TcO}(\text{apa})]$  occurs at the low end of the expected range, suggesting that the complex may contain a donor atom from the potentially pentadentate ligand in the position trans to oxo ligand. An envelope of bands between 1695 and 1580  $\text{cm}^{-1}$  (mixed C=O and C=N stretches in the ligand) has been blue-shifted about 20  $\text{cm}^{-1}$  when the ligand is coordinated to the Tc center; the other parts of the spectrum remain largely unchanged. The FAB mass spectrum showed a molecular ion at  $m/e$  515, suggesting that the complex is monomeric  $[\text{TcO}(\text{apa})]$  with a  $[\text{Tc=O}]^{3+}$  core and a triply deprotonated ligand wrapping around the metal center. The stoichiometry of  $[\text{C}_{20}\text{H}_{22}\text{N}_3\text{O}_7\text{Tc}]$  for the complex was confirmed by elemental analysis, and the structure of the complex was determined by X-ray diffraction methods.

The ORTEP stereo drawing of the complex is illustrated in Figure 1. The unit cell contains eight discrete  $[\text{TcO}(\text{apa})]$  molecules (four of each enantiomer), each of which has the  $[\text{Tc=O}]^{3+}$  core coordinated by all five donor atoms of the ligand. The central

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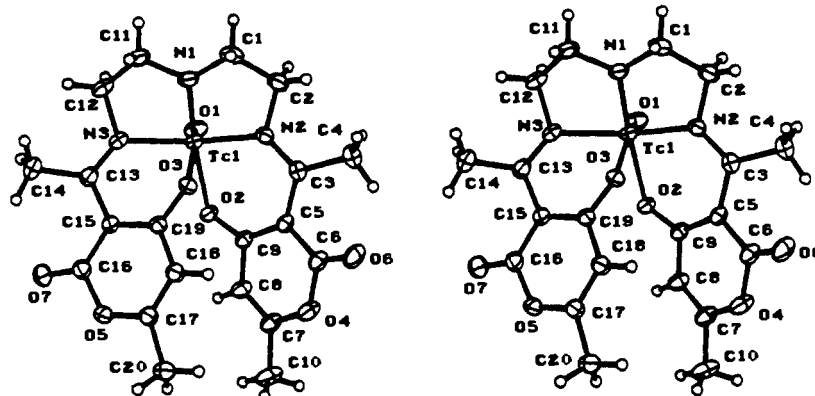


Figure 1. ORTEP stereoview of [TcO(apa)]; 33% probability ellipsoids are shown for the non-hydrogen atoms.

secondary amine nitrogen atom of the free ligand has been deprotonated upon coordination to the [Tc=O]<sup>3+</sup> core in the presence of the weak base acetate to give a neutral complex. A similar observation was reported for [TcO((sal)<sub>2</sub>dien)]<sup>23</sup> ((sal)<sub>2</sub>dien = *N,N'*-3-azapentane-1,5-diylbis(salicylideneamine(3-))), and is quite unusual under such mild conditions. Clearly, the highly electrophilic [Tc=O]<sup>3+</sup> core renders the coordinated central amine group very acidic. Therefore, the oxo ligand strongly influences not only the ligand in the trans position but also those in the equatorial plane perpendicular to the Tc=O bond.

The coordination geometry is a highly distorted octahedron with one of the two oxygen donors located in the position trans to the Tc=O and the remaining four N<sub>3</sub>O donor atoms occupying equatorial sites. The technetium atom lies 0.28 Å above the least-squares plane defined by the four equatorial N<sub>3</sub>O donor atoms. In part this is the effect of the strongly bonded oxo-ligand, which repels four equatorial donor atoms, N(1)-Tc(1)-O(2) and N(2)-Tc(1)-N(3) angles being 169 and 150°, respectively. In part this is caused by the small angles: N(1)-Tc(1)-N(2) (82°) and N(1)-Tc(1)-N(3) (79°), which are enforced by the NC-H<sub>2</sub>CH<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>N fragment of the pentadentate ligand, as is often found in five-membered chelate rings of technetium complexes.<sup>23,28</sup> O(2) is pinched up toward the oxo O(1) as evinced in the contrast between the O(1)-Tc(1)-O(2) angle of 83° and the angles with the other equatorial atoms O(1)-Tc(1)-N(1,2,3) which range from 101 to 106°. The Tc=O bond (1.678 Å) is slightly longer than the normal range of Tc=O distances (1.645–1.670 Å)<sup>3</sup> because of the oxygen coordination to the technetium atom in the trans position. The Tc–O bond lengths are normal with the Tc(1)–O(2) and Tc(1)–O(3) distances being 2.141 and 2.149 Å, respectively. The lengths of the Tc–N(2) and Tc(1)–N(3) bonds are 2.033 and 2.085 Å, respectively, while the Tc(1)–N(1) bond length is 1.880 Å. The results compare well with those for the [TcO((sal)<sub>2</sub>dien)]<sup>23</sup> complex, in which Tc=O = 1.685 Å, and the three Tc–N bond distances are 1.894, 2.044 and 2.101 Å, while the average equatorial Tc–O bond length is 2.125 Å.

The Tc–N bond lengths in oxotechnetium(V) complexes vary from 1.89 to 2.26 Å depending on ligand and the coordination number.<sup>12–23</sup> A typical Tc–N single bond in a six-coordinate oxotechnetium(V) complex is about 2.10 Å<sup>23</sup> whereas 1.61 Å is acceptable for a Tc≡N triple bond in nitridotechnetium(V) complexes.<sup>28</sup> In [TcO(apa)], the Tc(1)–N(1) distance is 1.880 (2) Å, between the bond length of a Tc–N single bond and that of a Tc≡N triple bond, indicating some double-bond character for the Tc=N(1) bond as is found in [TcO((sal)<sub>2</sub>dien)]<sup>23</sup> and in some tetradentate amine–oxime complexes (Tc=N, 1.90–1.92 Å).<sup>29,30</sup> Moreover, the central deprotonated nitrogen atom lies

Table V. 300-MHz <sup>1</sup>H NMR Data (δ in ppm from TMS, CDCl<sub>3</sub>) for H<sub>3</sub>apa and [TcO(apa)] with Numbering As Shown in Figure 2

H <sub>3</sub> apa	assignt	[TcO(apa)]	assignt <sup>a</sup>
1.45 (bs)	N–H		
2.00 (s, 6 H)	H9, H10, H11, H20, H21, H22	1.95 (s, 3 H), 2.10 (s, 3 H)	
2.56 (s, 6 H)	H5, H6, H7, H16, H17, H18	2.85 (s, 3 H), 2.89 (s, 3 H)	
2.92 (t, 4 H)	H1, H2, H12, H13	3.90 (m, 2 H), 4.10 (m, 3 H)	H4, H14, H2, H12, H15
3.48 (m, 4 H)	H3, H4, H14, H15	4.38 (m, 1 H), 4.70 (m, 1 H), 4.85 (m, 1 H)	H3, H1, H13
5.50 (s, 2 H)	H8, H19	5.00 (s, 1 H), 5.70 (s, 1 H)	
14.00 (bs, 2 H)	enol-OH		

<sup>a</sup> Same as in H<sub>3</sub>apa unless otherwise noted.

Table VI. <sup>13</sup>C NMR Data (δ in ppm from TMS, CDCl<sub>3</sub>) for H<sub>3</sub>apa and [TcO(apa)] with Numbering As Shown in Figure 2

H <sub>3</sub> apa	assignt	[TcO(apa)]	H <sub>3</sub> apa	assignt	[TcO(apa)]
18.2	C10, C20	19.2, 19.6	108.0	C8, C18	104.4, 107.5
19.5	C4, C14	18.8, 23.7	162.4	C7, C17	161.5, 164.1
44.0	C1, C11	59.3, 59.7	163.8	C3, C13	163.4, 165.0
47.3	C2, C12	63.6, 67.4	176.1	C6, C16	173.6, 179.5
96.5	C5, C15	103.0, 106.9	184.2	C9, C19	175.8, 179.6

exactly in the plane defined by Tc(1), C(1), and C(11) and all the bond angles around N(1) are very close to 120°, exactly as one would expect for sp<sup>2</sup> hybridization of the N(1) atom; the corresponding angles around N(2) and N(3) vary from 107 to 129°. The double-bond character can also be seen by comparing the bond length of Tc(1)–O(2) (2.141 Å, trans to the deprotonated nitrogen N(1)) to those trans to imino nitrogen atoms (Tc–O(phenol oxygen), 1.90 Å) found in [TcO(salen)]<sub>2</sub>O.<sup>20</sup>

The 500-MHz <sup>1</sup>H NMR spectrum is illustrated in Figure 2. The <sup>1</sup>H NMR spectral data for the pentadentate ligand and its technetium(V) complex are listed in Table V. Spectral assignments were made on the basis of <sup>1</sup>H–<sup>1</sup>H COSY, <sup>1</sup>H–<sup>13</sup>C heteronuclear correlation, and the normal expectation that coordination to a metal ion will deshield nearby hydrogens.<sup>12–23</sup> In some cases, the two hydrogens on a single carbon atom were distinguished by the fact that ring hydrogens in pseudoaxial environments are usually more shielded than those in pseudoequatorial environments.<sup>31</sup>

In the free ligand, hydrogen atoms H8 and H19 are equivalent and so are the hydrogens on methyls C4 and C14, and those on methyls C10 and C20. Upon coordination to the metal atom, however, H8 and H19 become nonequivalent as do the methyl hydrogens on C4 and C14 and those on C10 and C20; this results from the chirality of the pentadentate ligand bonding to the

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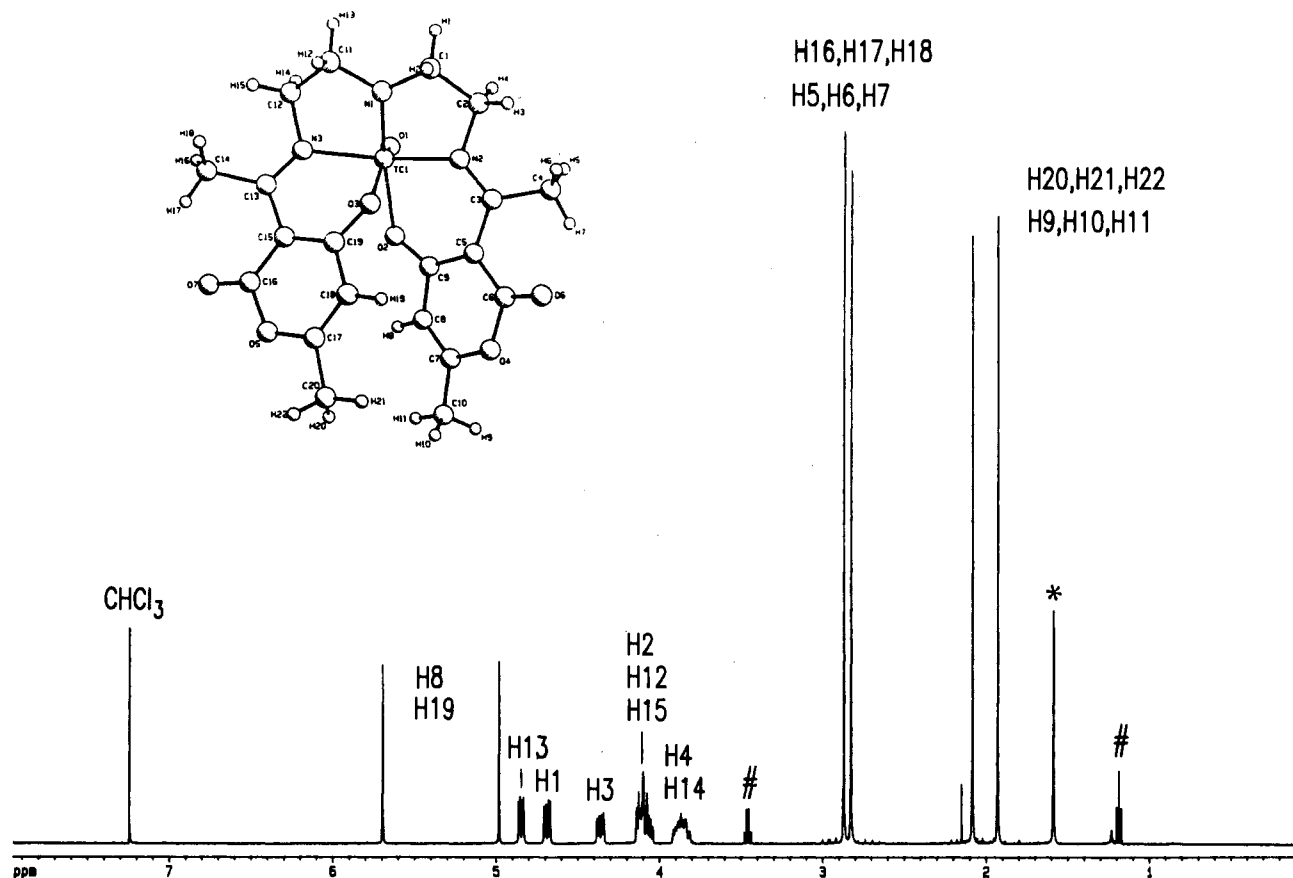


Figure 2. Room-temperature 500-MHz  $^1\text{H}$  NMR spectrum of  $[\text{TcO}(\text{apa})]$  in  $\text{CDCl}_3$ . Key: # =  $\text{Et}_2\text{O}$  peaks; \* = impurity peak.

$[\text{Tc}=\text{O}]^{3+}$  core. Consequently, the resonance at  $\delta$  5.50 (H8 and H19 of the free ligand) is split into two singlets at  $\delta$  5.00 and  $\delta$  5.70 (we still cannot assign these peaks as one or the other, however), and two resonances are observed for the hydrogens on C4 and C14 ( $\delta$  2.85 and 2.89) and for those on C10 and C20 ( $\delta$  1.95 and 2.10). This suggests a rigid structure for the complex in solution, with no fluxionality of the coordinated pentadentate ligand. The  $^{13}\text{C}$  NMR spectrum (Table VI) also supports this conclusion showing 20 distinct signals; the 10 pairs of carbon atoms in the bound ligand were assigned by  $^1\text{H}$ - $^{13}\text{C}$  heteronuclear correlation and the attached proton test (APT). If the coordinated pentadentate ligand were fluxional, only 10 signals would be expected as was observed in the spectrum of the free ligand.

The remainder of the proton NMR spectrum of  $[\text{TcO}(\text{apa})]$  involves separate signals for each of the eight hydrogens in the two  $\text{NCH}_2\text{CH}_2\text{N}$  units. Because of the rigidity of the molecule, the conformations available to the five-membered chelate rings  $\text{TcNCH}_2\text{CH}_2\text{N}$  are strictly limited. For example, half-chair conformations are not possible since the double-bond character of the  $\text{Tc}(1)=\text{N}(1)$  bond forces C(1), N(1), C(11), and Tc(1) to be almost coplanar. Also the pseudolibration movements of carbon atoms, C(1) and C(11) or C(2) and C(12), are prevented by the presence of the apical  $\text{Tc}=\text{O}$  bond and the double bond character of the imine  $\text{C}=\text{N}$  bonds. Therefore, only one envelope conformation is available for each of the five-membered chelate rings, as is found in the solid state (Figure 1), and one ABCD pattern is expected for each  $\text{NCH}_2\text{CH}_2\text{N}$  unit. This is supported by the observation of two overlapping ABCD spectra in the range  $\delta$  3.80–4.85, one for each  $\text{NCH}_2\text{CH}_2\text{N}$  unit. A  $^1\text{H}$  NMR temperature dependence study (21–55  $^\circ\text{C}$ ) was carried out for the Tc(V) complex to check for sharpening, broadening, and/or disappearance of this inequivalence. There was no significant change in the spectral parameters except that there were some slight shifts and broadening of the signals due to hydrogens on C4 and C14. The broadening of these signals is probably caused

by the vibrations of the two carbon atoms C4 and C14.

In conclusion, ligand substitution reactions of  $[\text{TcOCl}_4]^-$  or  $[\text{TcO}(\text{eg})_2]^-$  with the pentadentate ligand ( $\text{H}_3\text{apa}$ ) yield the same neutral well-characterized  $[\text{TcO}(\text{apa})]$  product. Upon coordination, the central amine group becomes very acidic due to the strongly electrophilic character of the  $[\text{Tc}=\text{O}]^{3+}$  core, and is deprotonated to give a neutral technetium(V) complex. If the hydrogen atom of the central amine group is substituted by an alkyl group, a cationic technetium(V) complex may be expected as has been found by other work.<sup>23</sup> Therefore, the present example provides an easy way to control the complex charge, which is very important for the localization properties of potential technetium radiopharmaceuticals. Further studies on technetium(V) complexes with a series of pentadentate ligands containing an ONN-NO donor set and on the biological properties of their  $^{99\text{m}}\text{Tc}$  complexes are in progress.

**Acknowledgment** is made to the Natural Sciences and Engineering Research Council of Canada for an NSERC Postdoctoral Fellowship (S.L.), to the U.S. Public Health Service for an operating grant (CA 48964), and to the Du Pont Merck Pharmaceutical Co. for continuing support and supply of  $\text{NH}_4^{99}\text{TcO}_4$ . We also thank Professor J. Trotter for the very kind use of his crystallographic facilities.

**Registry No.**  $\text{H}_3\text{apa}$ , 137465-46-4;  $[\text{TcO}(\text{apa})]$ , 137465-45-3;  $[n\text{-Bu}_4\text{N}][^{99}\text{TcOCl}_4]$ , 92622-25-8; dehydroacetic acid, 520-45-6; diethylenetriamine, 111-40-0.

**Supplementary Material Available:** A more detailed table of crystallographic data (Table SI) and tables of hydrogen atom parameters (Table SII), anisotropic thermal parameters (Table SIII), intramolecular distances involving hydrogen atoms (Table SIV), intramolecular bond angles involving hydrogen atoms (Table SV), torsion angles (Table SVI), intermolecular contacts (Table SVII), and least-squares planes (Table SVIII) (16 pages); a table of measured and calculated structure factor amplitudes (Table SIX) (21 pages). Ordering information is given on any current masthead page.