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Synthesis and Characterization of Technetium(III) and Technetium(II) Complexes with Mixed Phosphine-, Chloride-, and Nitrogen-Donor Ligands. X-ray Crystal Structure of $TcCl_3(PPh_3)(bpy)$[1]

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The synthesis and characterization of Tc(III) complexes of the types $TcCl_3(PMe_2Ph)(LL)$ and $TcCl_2(PMe_2Ph)_2(LL)^+$, the neutral Tc(II) series $TcCl_2(PMe_2Ph)_2(LL)$, and the Tc(II) complex $TcCl(PMe_2Ph)_3(bpy)^+$ are reported (LL = 2,2'-bipyridine (bpy), 1,10-phenanthroline (phen), 2,2'-bipyrimidine (bpm)). The Tc(III) complexes exhibit contact-shifted ^1H NMR spectra with relatively narrow line widths; the Tc(II) species give less well-defined spectra. The electrochemistry of these complexes is discussed as well. An X-ray structure determination of $TcCl_3(PPh_3)(bpy)$ was performed. Crystal data for $C_{28}H_{23}Cl_3N_2PTc$: monoclinic, space group = $P2_1/n$, a = 10.980 (2) Å, b = 24.336 (5) Å, c = 10.172 (2) Å, β = 106.89 (1)°, V = 2600.9 (8) Å^3 to give Z = 4. Structure solution and refinement based on 4366 reflections converged at R = 0.057 and R_w = 0.074.

Introduction

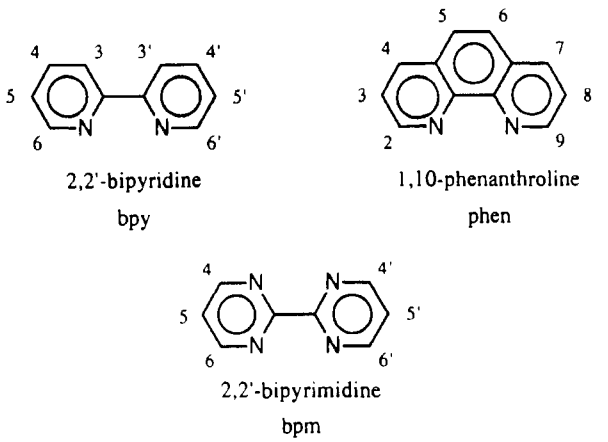
The growing interest in the inorganic coordination chemistry of the second-row transition-metal technetium has its roots in the widespread use of the γ-emitting isomer ^{99m}Tc in nuclear medicine.[3] While the wide diversity of this element's chemistry is becoming apparent, until recently[4] few lower oxidation state technetium complexes with nitrogen-donor ligands have been reported.[5-7] We have been exploring the chemistry of technetium with the aromatic amine ligands 2,2'-bipyridine (bpy), 1,10-phenanthroline (phen), and 2,2'-bipyrimidine (bpm), the structures, abbreviations, and numbering schemes of which are illustrated in Chart I. We describe here the synthesis and characterization of Tc(III) complexes of the types $TcCl_3(P)(LL)$ and $TcCl_2(PMe_2Ph)_2(LL)^+$, of the Tc(II) complexes in the $TcCl_2(PMe_2Ph)_2(LL)$ series, and of the Tc(II) species $TcCl(PMe_2Ph)_3(bpy)^+$ (P is PMe_2Ph or PPh_3; LL represents the N-donor ligand bpy, phen, or bpm). The X-ray structure of $TcCl_3(PPh_3)(bpy)$ is also reported. Additional members of the Tc(III) cationic class have recently been structurally characterized.[8]

Experimental Section

Caution! Technetium-99 is a weak β-emitter (E = 0.292 MeV, $t_{1/2}$ = 2.12 × 10^5 y). All manipulations involving radioactive materials were performed in laboratories approved for low-level radiation following precautions detailed elsewhere.[9]

Instrumentation. Elemental analyses were performed by Atlantic Microlab Inc., Norcross, GA. UV-visible spectra were recorded on a Hewlett Packard 8451A photodiode array spectrophotometer. Fast atom bombardment mass spectra (FABMS) were obtained with a MAT 731 mass spectrometer operating at an accelerating voltage of 8 kV and equipped with an Ion Tech B11N FAB gun, which produced a beam of 6-8-keV xenon neutrals. The samples were dissolved in a 3-nitrobenzyl alcohol matrix. Proton NMR spectra were recorded at 300 MHz on a Varian XL-300 spectrometer, with spectral windows ranging from 30000 to 50000 Hz. For each compound, several different sweep widths were used to detect and to avoid spectral folding. Electrochemical measurements were performed on N_2-purged acetonitrile solutions of the metal complexes with 0.1 M tetrabutylammonium perchlorate (TBAP, GFS Chemicals) as supporting electrolyte. The acetonitrile was of spectrophotometric grade and was kept over 3-Å molecular sieves. Experiments were conducted by using a one-compartment cell with a Pt disk as the working electrode, a Pt wire as the counter electrode, and an SCE (Fisher) as the reference. The potentiostat employed was a PAR Model 174 polarographic analyzer, and the data were plotted with a Hewlett Packard 7044A XY recorder.

Chart I



Materials. Ammonium pertechnetate was supplied as a gift by Du Pont/Biomedical Products. The complexes $TcCl_4(PPh_3)_2$ and $TcCl_3(PMe_2Ph)_3$ were obtained by the method of Mazzi.[10] All solvents were of reagent grade and were used as received without further purification. The ligands 2,2'-bipyridine (bpy) and dimethylphenylphosphine (PMe_2Ph), as well as ammonium hexafluorophosphate (NH_4PF_6), were obtained from Aldrich Chemical Co.; 1,10-phenanthroline (phen) was obtained from Fluka Chemie, and 2,2'-bipyrimidine (bpm), from Alfa. Column chromatography was performed with ICN Biomedicals Alumina N, Activity I.

$TcCl_3(PPh_3)(bpy)$. A solution of 81 mg of $TcCl_4(PPh_3)_2$ in acetonitrile (10 mL) was brought to reflux, and 49 mg of bpy was added. After 5 min, the volume of the reaction mixture was halved and the resulting precipitate filtered out, rinsed with acetonitrile until the washes were no longer red, and dried in vacuo. ^1H NMR (CD_2Cl_2): δ 42.12 (d, 2 H, bpy 5,5'), 15.49 (s, 6 H, Ph ortho), 9.88 (t, 3 H, Ph para), 8.24 (s, 6 H, Ph meta), -1.74 (s, 2 H, bpy 3,3'), -4.70 (d, 2 H, bpy 4,4'), -12.33 (s, 2 H, bpy 6,6'). FABMS(+), m/z: 622, $(M)^+$; 587, $(M - Cl)^+$; 325, $(M - Cl - PPh_3)^+$.

$TcCl_3(PMe_2Ph)(bpy)$. The general preparation is as follows: Under an atmosphere of dinitrogen, an excess of N-donor ligand was reacted with $TcCl_3(PMe_2Ph)_3$ in refluxing toluene or diglyme for 1-3 h, during which time the product was deposited as a microcrystalline solid. Proton NMR spectroscopy indicated the presence of only one compound.

Specifically, conditions were as follows: for bpy, 132 mg of $TcCl_3(PMe_2Ph)_3$ and 211 mg of bpy were reacted in toluene (10 mL) for 3 h to yield 79 mg of product (74%). This material cannot be chromato-

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graphed, as it decomposes on alumina, but it can be recrystallized by slow solvent reduction (by rotary evaporator) of a methylene chloride/ethanol solution. Anal. Calcd for $C_{18}H_{19}Cl_3N_2PTc$: C, 43.28; H, 3.80; N, 5.61; Cl, 21.29. Found: C, 43.21; H, 3.84; N, 5.59; Cl, 21.22; UV–vis (MeCN) [λ_{max}, nm (ϵ, M^{-1} cm^{-1})]: 204 (41 000), 244 (22 000), 300 (16 000), 398 (3200), 432 sh, 606 (2200). FABMS(+), m/z: 616, (M − Cl + NBA matrix)$^+$; 498, $(M)^+$; 463, (M − Cl)$^+$; 360, (M − PMe_2Ph)$^+$; 325, (M − Cl − PMe_2Ph)$^+$.

$TcCl_3(PMe_2Ph)(phen)$. For phen, 86 mg of $TcCl_3(PMe_2Ph)_3$ and 163 mg of phen were reacted in 10 mL of diglyme for 1 h to yield 26 mg of product (50%). UV–vis (MeCN) [λ_{max}, nm (ϵ, M^{-1} cm^{-1})]: 202 (42 000), 228 (36 000), 268 (27 000), 294 sh, 354 (3500), 390 sh, 436 (2400), 600 (3000). FABMS(+), m/z: 522, $(M)^+$; 487, (M − Cl)$^+$; 349, (M − Cl − PMe_2Ph)$^+$.

$TcCl_3(PMe_2Ph)(bpm)$. For bpm, 69 mg of $TcCl_3(PMe_2Ph)_3$ and 51 mg of bpm in toluene (10 mL) with a 2 h reflux gave 30 mg of product (54%). Anal. Calcd for $C_{16}H_{17}Cl_3N_4PTc$: C, 38.30; H, 3.42; N, 11.17; Cl, 21.20. Found: C, 38.40; H, 3.41; N, 11.08; Cl, 21.13. UV–vis (MeCN) [λ_{max}, nm (ϵ, M^{-1} cm^{-1})]: 204 (51 000), 244 (30 000), 325 sh, 446 (4000), 652 (2000). FABMS(+), m/z: 500, $(M)^+$; 465, (M − Cl)$^+$; 327 (M − Cl − PMe_2Ph)$^+$.

$[TcCl_2(PMe_2Ph)_2(bpy)](PF_6)$. Method 1. To 123 mg of $TcCl_3(PMe_2Ph)_3$ and 238 mg of bpy was added 10 mL of absolute ethanol. The reaction mixture was refluxed for 1 h under an atmosphere of dinitrogen, the solution changing color from orange to violet. It was then allowed to cool to room temperature and an ethanol solution of 160 mg of NH_4PF_6 added. The volume of the solution was reduced slightly on the rotary evaporator until the product began to precipitate out of solution. After the mixture was chilled at 0 °C, the black microcrystalline solid was filtered out, washed with cold ethanol and then diethyl ether, and dried in vacuo. Yield: 127.0 mg (85%). The complex can be chromatographed on alumina with acetonitrile as eluant, but this purification step appears to be generally unnecessary. Anal. Calcd for $C_{26}H_{30}Cl_2F_6N_2P_3Tc$: C, 41.79; H, 4.02; N, 3.75; Cl, 9.49. Found: C, 41.67; H, 4.07; N, 3.74; Cl, 9.20. UV–vis (EtOH) [λ_{max}, nm (ϵ, M^{-1} cm^{-1})]: 200 (40 000), 264 (31 000), 300 (14 000), 345 sh, 544 (2300). FABMS(+), m/z 601, $(M)^+$; 566, (M − Cl)$^+$; 463, (M − PMe_2Ph)$^+$; 428, (M − Cl − PMe_2Ph)$^+$; 325, (M − 2PMe_2Ph)$^+$.

Method 2. To a stirred ethanolic solution of aqueous $NH_4[TcO_4]$ (0.10 mmol) and concentrated HCl (0.10 mL) was slowly added a solution of 60 mg of bpy and 0.24 mL of PMe_2Ph in 6 mL of ethanol; the reaction mixture immediately turned yellow and began to darken. After being refluxed 1.5 h, the dark purple-brown solution was allowed to cool to room temperature, and an ethanol/water solution of 130 mg of $(NH_4)PF_6$ was added. The cloudy solution was left to stand overnight, and by morning, dark crystals had formed. Yield: 64.2 mg (86%). The product is spectroscopically identical with that obtained by method 1.

$[TcCl_2(PMe_2Ph)_2(phen)](PF_6)$. This was prepared according to method 1 above, using 64 mg of $TcCl_3(PMe_2Ph)_3$ and 140 mg of phen with a 1.25-h reflux. After addition of 85 mg of $(NH_4)PF_6$, the reaction mixture was stripped to dryness, redissolved in methylene chloride, and chromatographed on alumina with methylene chloride/acetone as eluant; the red-pink product remained immobile on the column while a brown byproduct was removed. Acetone was then used to elute the desired material, which was recrystallized from acetone/diethyl ether to give dark needles. Yield: 20.1 mg (26%). Anal. Calcd for $C_{28}H_{30}Cl_2F_6N_2P_3Tc$: C, 43.59; H, 3.93; N, 3.63; Cl, 9.19. Found: C, 43.60; H, 3.91; N, 3.60; Cl, 9.24. UV–vis (MeCN) [λ_{max}, nm (ϵ, M^{-1} cm^{-1})]: 200 (49 000), 226 (38 000), 266 (40 000), 390 (2700), 410 sh, 460 sh, 538 (2400), 600 sh. FABMS(+), m/z: 625, $(M)^+$; 590, (M − Cl)$^+$; 487, (M − PMe_2Ph)$^+$; 452, (M − Cl− PMe_2Ph)$^+$; 349, (M − 2PMe_2Ph)$^+$; 314, (M − Cl − 2PMe_2Ph)$^+$.

$[TcCl_2(PMe_2Ph)_2(bpm)](PF_6)$. To 11 mg of $TcCl_2(PMe_2Ph)_2$(bpm) dissolved in 10 mL of acetonitrile was added 2.0 mL of 6.0 M HCl. The reaction mixture was left at room temperature overnight; by morning, the originally orange-brown solution had turned deep blue-green. Adding methylene chloride (10 mL) and water (10 mL) to the reaction mixture extracted all the color into the organic layer. The organic portion was then separated, washed first with brine and next with an aqueous solution of $(NH_4)PF_6$, and finally dried over Na_2SO_4. The solution was then reduced in volume to about 5 mL and flooded with diethyl ether. By the next day, the product had crystallized as dark needles, which were filtered out, washed with diethyl ether, and dried in vacuo. Yield: 9.88 mg (74%). Anal. Calcd for $C_{24}H_{28}Cl_2F_6N_4P_3Tc$: C, 38.48; H, 3.78; N, 7.48; Cl, 9.46. Found: C, 38.60; H, 3.82; N, 7.47; Cl, 9.64. UV–vis (MeCN) [λ_{max}, nm (ϵ, M^{-1} cm^{-1})]: 196 (20 000), 210 (18 000), 262 (25 000), 325 sh, 418 sh, 594 (1500). FABMS(+), m/z: 603, $(M)^+$; 568, (M − Cl)$^+$; 465, (M − PMe_2Ph)$^+$; 430, (M − Cl − PMe^2Ph)$^+$; 327, (M − 2PMe_2Ph).

$TcCl_2(PMe_2Ph)_2(bpy)$. Aqueous concentrated KOH (20 mL) was added to 81 mg of $[TcCl_2(PMe_2Ph)_2(bpy)](PF_6)$ dissolved in 20 mL of acetonitrile. The violet solution was allowed to stand at room temperature for 2 days, during which time olive green plates were deposited. The product was filtered out, washed with water, and dried in vacuo. Yield: 43.43 mg (67%). The material can be chromatographed on alumina with acetone, but this purification step is generally unnecessary. Anal. Calcd for $C_{26}H_{30}Cl_2N_2P_2Tc$: C, 51.88; H, 5.03; N, 4.65; Cl, 11.78. Found: C, 51.72; H, 5.06; N, 4.64; Cl, 11.81. UV–vis (MeCN) [λ_{max}, nm (ϵ, M^{-1} cm^{-1})]: 200 (39 000), 248 (28 000), 294 (14 000), 397 sh, 448 (5200), 540 sh, 670 (2000). ^1H NMR (acetone-d_6): δ 15.42 (br s, 1 H), 8.00 (s, 1 H), 5.75 (s, 2 H), 4.72 (br s, 2 H), −8.65 (br s, 6 H). FABMS(+), m/z: 601, $(M)^+$; 463, (M − PMe_2Ph)$^+$.

$TcCl_2(PMe_2Ph)_2(phen)$. This was prepared analogously to the bpy analogue. To an acetonitrile solution of 17 mg of $[TcCl_2(PMe_2Ph)_2(phen)](PF_6)$ was added an equal volume of aqueous KOH. The reaction was left at room temperature overnight; by morning, a black microcrystalline solid had formed, which was filtered out, washed with water, and dried in vacuo. Yield: 8.4 mg (61%). Anal. Calcd for $C_{28}H_{30}Cl_2N_2P_2Tc$: C, 53.68; H, 4.84; N, 4.47; Cl, 11.32. Found: C, 53.71; H, 4.84; N, 4.44; Cl, 11.40. UV–vis (MeCN) [λ_{max}, nm (ϵ, M^{-1} cm^{-1})]: 206 (40 000), 226 (31 000), 256 (28 000), 332 (4000), 398 (2000), 516 (4000), 654 (3000). ^1H NMR ($CDCl_3$): δ 8.43 (s, 1 H), 8.00 (s, 1 H), 5.59 (s, 2 H), 4.70 (br s, 2 H), −8.60 (v br s, 5 H). FABMS(+), m/z 625, $(M)^+$.

$TcCl_2(PMe_2Ph)_2(bpm)$. The following reaction was performed under an atmosphere of dinitrogen. To 53 mg of $TcCl_3(PMe_2Ph)_3$ and 22 mg of bpm was added 10 mL of methanol. The reaction mixture was refluxed for 5 h and then cooled to room temperature and stripped to a brown oil. This was dissolved in a minimum volume of methylene chloride and chromatographed on alumina with acetone. The desired complex was the first band eluted from the column and was recrystallized from acetone/hexane to give a dark microcrystalline solid. Yield: 33.0 mg (64%). Anal. Calcd for $C_{24}H_{28}Cl_2N_4P_2Tc$: C, 47.69; H, 4.68; N, 9.27; Cl, 11.73. Found: C, 47.55; H, 4.74; N, 9.25; Cl, 11.78. UV–vis (MeCN) [λ_{max}, nm (ϵ, M^{-1} cm^{-1})]: 196 (48 000), 250 (34 000), 430 (4800), 484 (5700). ^1H NMR (acetone-d_6): δ 8.07 (s, 1 H), 5.90 (s, 2 H), 4.90 (br s, 1 H), −8.60 (br s, 5 H). FABMS(+), m/z: 603, $(M)^+$; 568, (M − Cl)$^+$; 465, (M − PMe_2Ph)$^+$; 325, (M − 2PMe_2Ph)$^+$.

$[TcCl(PMe_2Ph)_3(bpy)](PF_6)$. To 37 mg of $[TcCl_2(PMe_2Ph)_2(bpy)](PF_6)$ dissolved in methanol (10 mL) was added 7 drops of PMe_2Ph. The reaction mixture was allowed to reflux for 20 h under an atmosphere of dinitrogen. After the brown solution cooled to room temperature, a methanol/water solution of 32 mg of $(NH_4)PF_6$ was added. Solvent was removed under reduced pressure and the resulting oil chromatographed on alumina with 10% methylene chloride/acetone (v/v) as eluant. The desired complex was the brown band, the second fraction eluted from the column. This was recrystallized from acetone/hexane as dark needles, washed with hexane and diethyl ether, and dried in vacuo. Yield: 27.62 mg (65%). Anal. Calcd for $C_{34}H_{41}ClF_6N_2P_4Tc$: C, 48.04; H, 4.87; N, 3.30; Cl, 4.17. Found: C, 48.09; H, 5.14; N, 3.09; Cl, 3.92. UV–vis (MeCN) [λ_{max}, nm (ϵ, M^{-1} cm^{-1})]: 226 (41 000), 250 sh, 300 (17 000), 378 (4200), 430 sh, 524 (2200), 660 (1000). ^1H NMR (acetone-d_6): δ 35.8 (br s, 1 H), 23.2 (br s, 1 H), 23.0 (br s, 1 H), 20.5 (br s, 1 H), 17.7 (br s, 1 H), 16.9 (s, 1 H), 8.3 (br s, 2 H), 7.9 (s, 1 H), 7.5 (s, 2 H), 7.0 (s, 2 H), 5.5 (s, 4 H), 3.3 (br s, 4 H), −7.5 (v br s, 6 H, methyl), −10.6 (vbr s, 6 H, methyl), −11.0 (vbr s, 6 H, methyl). FABMS(+), m/z: 704, $(M)^+$; 566, (M − PMe_2Ph)$^+$; 428, (M − 2PMe_2Ph)$^+$.

Table I. X-ray Data for the Structure Determination of $TcCl_3(PPh_3)(bpy)$

$C_{28}H_{23}Cl_3N_2PTc$	space group = $P2_1/n$
fw = 623.35	T = 22 °C
a = 10.980 (2) Å	λ = 0.710 69 Å, graphite monochromated
b = 24.336 (5) Å	ρ_{calcd} = 1.59 g/cm^3
c = 10.172 (2) Å	μ = 9.22 cm^{-1}
β = 106.89 (1) deg	transm coeff = 1.00 − 0.79
V = 2600.9 (8) Å^3	R = 0.057
Z = 4	R_w = 0.074

X-ray Crystal Structure Determination. Crystal data are presented in Table I, atomic positional parameters are given in Table II, selected bond distances and angles are listed in Table III, and an ORTEP diagram is shown in Figure 1. Dichroic green/purple plates suitable for X-ray diffraction were grown by slow evaporation of a dilute CD_3CN solution of $TcCl_3(PPh_3)(bpy)$. A crystal with approximate dimensions of 0.5 × 0.2 × 0.4 mm was selected, and the space group was determined to be $P2_1/n$. A total of 6488 reflections (of which 6182 were unique, R_{int} = 0.012) were collected on a Rigaku AFC6R diffractometer (max 2θ = 55.1°, octants collected $+h,+k,\pm l$, scan mode ω–2θ). Solution and refinement of the structure were carried out by using SHELX-76 and TEXSAN programs of the Molecular Structure Corp. Neutral-atom scattering

Table II. Atomic Positional Parameters for $TcCl_3(PPh_3)(bpy)$

atom	x	y	z
Tc	0.17098 (4)	0.13317 (2)	0.03106 (4)
Cl(1)	0.3941 (1)	0.13752 (6)	0.1015 (2)
Cl(2)	0.1656 (1)	0.15348 (7)	0.2623 (1)
Cl(3)	0.1618 (1)	0.03882 (6)	0.0725 (2)
P(1)	0.1917 (1)	0.11956 (6)	−0.2016 (1)
N(1)	−0.0287 (4)	0.1427 (2)	−0.0373 (5)
N(2)	0.1460 (4)	0.2179 (2)	−0.0056 (4)
C(1)	−0.1133 (5)	0.1020 (3)	−0.0447 (7)
C(2)	−0.2412 (6)	0.1089 (3)	−0.1017 (8)
C(3)	−0.2850 (6)	0.1598 (4)	−0.1536 (8)
C(4)	−0.2022 (6)	0.2028 (3)	−0.1400 (6)
C(5)	−0.0728 (5)	0.1938 (2)	−0.0796 (5)
C(6)	0.0235 (5)	0.2364 (2)	−0.0560 (5)
C(7)	−0.0022 (6)	0.2921 (3)	−0.0797 (7)
C(8)	0.0957 (7)	0.3291 (3)	−0.0509 (7)
C(9)	0.2183 (7)	0.3105 (3)	0.0022 (7)
C(10)	0.2399 (6)	0.2558 (3)	0.0225 (6)
C(11)	0.0535 (5)	0.0940 (2)	−0.3341 (5)
C(12)	0.0310 (6)	0.1078 (3)	−0.4724 (6)
C(13)	−0.0672 (7)	0.0825 (3)	−0.5705 (6)
C(14)	−0.1450 (7)	0.0452 (3)	−0.5331 (7)
C(15)	−0.1230 (6)	0.0313 (3)	−0.3971 (7)
C(16)	−0.0219 (6)	0.0553 (3)	−0.2979 (6)
C(21)	0.2326 (5)	0.1857 (3)	−0.2579 (5)
C(22)	0.1409 (6)	0.2238 (3)	−0.3259 (6)
C(23)	0.1763 (7)	0.2758 (3)	−0.3514 (7)
C(24)	0.3031 (8)	0.2918 (3)	−0.3098 (8)
C(25)	0.3942 (7)	0.2539 (3)	−0.2412 (7)
C(26)	0.3597 (6)	0.2024 (3)	−0.2159 (7)
C(31)	0.3145 (5)	0.0736 (3)	−0.2303 (6)
C(32)	0.3554 (7)	0.0293 (3)	−0.1482 (6)
C(33)	0.4422 (8)	−0.0073 (4)	−0.1765 (7)
C(34)	0.4898 (7)	0.0007 (4)	−0.281 (1)
C(35)	0.4499 (8)	0.0450 (4)	−0.364 (1)
C(36)	0.3614 (7)	0.0831 (3)	−0.3409 (8)

Table III. Selected Bond Distances and Angles for $TcCl_3(PPh_3)(bpy)$

	Bond Lengths, Å		
Tc–Cl(1)	2.347 (1)	Tc–N(1)	2.112 (4)
Tc–Cl(2)	2.421 (2)	Tc–N(2)	2.099 (5)
Tc–Cl(3)	2.342 (2)	Tc–P(1)	2.465 (2)
	Bond Angles, deg		
N(1)–Tc–N(2)	76.4 (2)	N(2)–Tc–P(1)	90.3 (1)
N(1)–Tc–Cl(1)	171.0 (1)	Cl(1)–Tc–Cl(2)	90.68 (5)
N(1)–Tc–Cl(2)	88.9 (1)	Cl(1)–Tc–Cl(3)	94.87 (6)
N(1)–Tc–Cl(3)	94.1 (1)	Cl(1)–Tc–P(1)	85.40 (5)
N(1)–Tc–P(1)	94.3 (1)	Cl(2)–Tc–Cl(3)	90.62 (6)
N(2)–Tc–Cl(1)	94.6 (1)	Cl(2)–Tc–P(1)	174.51 (6)
N(2)–Tc–Cl(2)	86.2 (1)	Cl(3)–Tc–P(1)	93.55 (6)
N(2)–Tc–Cl(3)	170.0 (1)		

factors were used throughout,[11] and no extinction effects were observed. The structure was solved by using Patterson methods, an absorption correction was applied by using DIFABS, and all non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined from their calculated positions. Final residuals are $R = 0.057$ and $R_w = 0.074$.

Results and Discussion

Syntheses. The PPh_3 complex, *fac*-$TcCl_3(PPh_3)(bpy)$, was obtained in low yield from reaction of $TcCl_4(PPh_3)_2$ with excess bpy in refluxing acetonitrile; however, reactions of this Tc(IV) complex with bpy give a mixture of products containing technetium in a range of oxidation states.[12] We have found the Tc(III) complex $TcCl_3(PMe_2Ph)_3$ to be a much more useful starting material, and the Tc(III) complexes reported here are easily obtained by extension of the synthetic methods used by Meyer and co-workers[13] to prepare mono(bipyridyl) complexes of Re(III). Characterization data such as FABMS(+), UV–vis spectra, and elemental analyses are given in the Experimental Section.

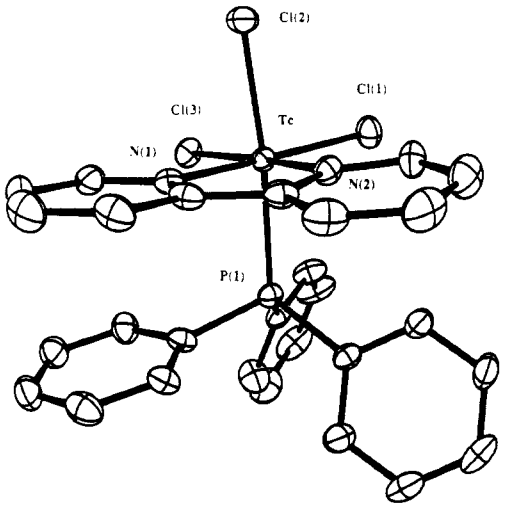

Figure 1. ORTEP diagram of $TcCl_3(PPh_3)(bpy)$ showing the partial atom-labeling scheme.

The green *fac*-$TcCl_3(PMe_2Ph)(LL)$ complexes were prepared by reaction of *mer*-$TcCl_3(PMe_2Ph)_3$ with excess N-donor ligand in a refluxing nonpolar solvent, precipitating out of solution as they formed. Diglyme was used as the solvent for preparation of *fac*-$TcCl_3(PMe_2Ph)(phen)$ because toluene gave the product as a mixture of facial and meridional isomers, as determined from ^1H NMR data. The relative amounts of the isomers depended upon length of reflux and are apparently due to the greater solubility of the phen complex as compared to the bpy and bpm analogues, for which no meridional isomers were observed. In the syntheses of the $TcCl_3(PMe_2Ph)(LL)$ complexes, the neutral $Tc^{II}Cl_2(PMe_2Ph)_2(LL)$ species were always obtained as byproducts.

The cationic $TcCl_2(PMe_2Ph)_2(LL)^+$ complexes (LL = bpy or phen) were prepared by reaction of *mer*-$TcCl_3(PMe_2Ph)_3$ with excess N-donor ligand in ethanol and isolated as PF_6^- salts. The bpy complex was also made directly from pertechnetate in a one-pot synthesis using excess PMe_2Ph as the reducing agent. The X-ray structures have recently been reported for these cations[8] and confirm the cis (chloride) and trans (phosphine) arrangement of ligands as deduced from the ^1H NMR spectra. The Tc(III) complexes could be purified by chromatography on alumina; this procedure was mandatory for the phen complex due to the numerous side products in the reaction mixture. With more than 1-h reflux, the neutral Tc(II) complex became a significant byproduct. The same procedure with bpm as the N-donor ligand resulted in only a trace of the Tc(III) cation, the major product being the neutral $Tc^{II}Cl_2(PMe_2Ph)_2(bpm)$ species due to the significantly different reduction potentials of $TcCl_2(PMe_2Ph)_2(bpm)^+$ and its bpy and phen analogues (see below). However, the cationic $TcCl_2(PMe_2Ph)_2(bpm)^+$ species could be obtained in good yield by oxidation of the neutral Tc(II) complex with dilute acid.

As discussed above, the neutral Tc(II) species $TcCl_2(PMe_2Ph)_2(LL)$ were present as byproducts in the preparations of $TcCl_3(PMe_2Ph)(LL)$ and $TcCl_2(PMe_2Ph)_2(LL)^+$. Under certain reaction conditions, the neutral Tc(II) complexes could be isolated as the major products in good yield. For bpm, reaction of the N-donor with $TcCl_3(PMe_2Ph)_3$ in ethanol gave the Tc(II) material directly. For bpy and phen, the corresponding $TcCl_2(PMe_2Ph)_2(LL)$ complexes were obtained as crystalline solids from the room-temperature reaction of $TcCl_2(PMe_2Ph)_2(LL)^+$ with aqueous KOH in acetonitrile solution. Hydroxide ion has been shown to be an effective one-electron reducing agent,[14,15] particularly for polypyridyl systems of group VIII transition metals,[16–18] and is apparently the reductant in this reaction. The Tc(II)

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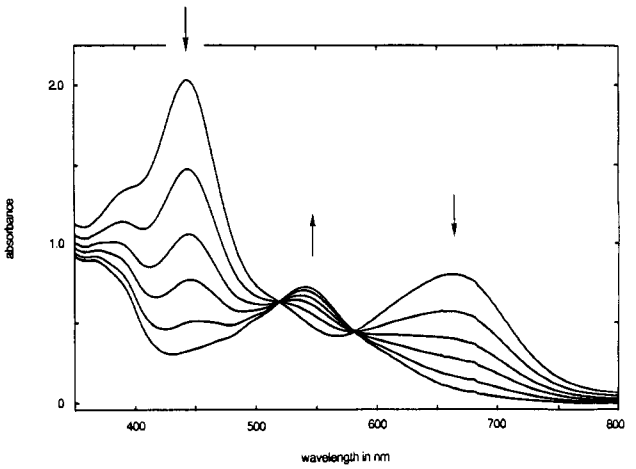

Figure 2. Spectral changes upon oxidation of $Tc^{II}Cl_2(PMe_2Ph)_2(bpy)$ to $Tc^{III}Cl_2(PMe_2Ph)_2(bpy)^+$ with dilute H_2SO_4 in acetonitrile/water solution.

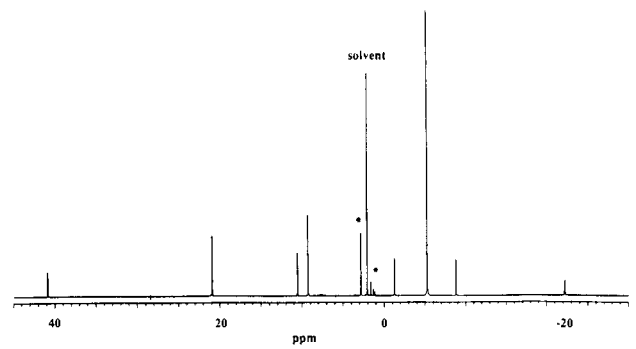

Figure 3. ^1H NMR spectrum of $[TcCl_2(PMe_2Ph)_2(bpy)](PF_6)$ in acetone-d_6.

complexes can be oxidized cleanly to the Tc(III) cations with dilute acid or water (Figure 2).

The other Tc(II) complex described here, $TcCl(PMe_2Ph)_3(bpy)^+$, was synthesized in good yield by reacting $TcCl_2(PMe_2Ph)_2(bpy)^+$ with excess PMe_2Ph in refluxing methanol and was isolated as the PF_6^- salt. This complex could be purified by chromatography on alumina and is quite stable to oxidation.

Proton NMR Spectra. Both the $TcCl_3(PMe_2Ph)(LL)$ and $TcCl_2(PMe_2Ph)_2(LL)^+$ complexes contain a Tc(III) metal center with a d^4 electronic configuration in an octahedral environment; the molecules are therefore paramagnetic. However, the electronic relaxation time (T_{1e}) of the technetium is sufficiently short ($\leq 10^{-11}$ s)[19] to permit observation of contact-shifted ^1H NMR spectra with relatively narrow line widths (Figure 3). Unambiguous assignments of the resonances can be made from the relative integrations, spin–spin splittings, relative line widths, and two-dimensional homonuclear shift correlation (COSY) experiments.[20] For each complex, the broad upfield singlet of the N-donor resonances is assigned as that for the ring 6,6′-protons (2,9 for the phen analogues). These protons are closest to the paramagnetic metal center and thus relaxing most rapidly, as seen by their relatively large line width. In the COSY experiment, coupling between the 6,6′-protons and their immediate neighbors, the 5,5′-protons, can be detected, allowing the 5,5′-protons to be distinguished from the 3,3′-protons. Assignments of the remaining signals are quite straightforward and reveal the plane of symmetry that bisects the N-donor ligand in each complex. No coupling to phosphorus was observed.

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Table IV. ^1H NMR Chemical Shifts and Splittings for Technetium(III) Complexes

	chem shift for LL complex, ppm		
resonance	bpy	phen	bpm
	$TcCl_3(PMe_2Ph)(LL)^a$		
methyl	−14.65 s	−16.28 s	−16.41 s
ortho	23.12 d	22.79 d	22.50 d
meta	10.06 t	9.64 t	9.88 t
para	12.06 t	12.13 t	11.91 t
3,3′ (5,6)[b]	−3.22 d	(−3.10) s	
4,4′ (4,7)	−0.07 t	(0.87) d	−0.06 s
5,5′ (3,8)	41.01 d	(35.19) d	56.40 s
6,6′ (2,9)	−6.51 s	(−14.30) s	−12.52 s
	$[TcCl_2(PMe_2Ph)_2(LL)]^{+c}$		
methyl	−5.27 s	−6.28 s	−7.10 s
ortho	20.91 d	19.80 d	19.93 d
meta	9.23 t	8.54 t	9.10 t
para	10.51 t	10.29 t	10.35 t
3,3′ (5,6)[b]	−1.28 d	(−2.94) s	
4,4′ (4,7)	−8.83 t	(−7.99) d	−9.24 s
5,5′ (3,8)	40.84 d	(33.33) d	55.56 s
6,6′ (2,9)	−22.22 s	(−29.18) s	−24.61 s

[a] In CD_2Cl_2. [b] Parentheses refer to the 1,10-phenanthroline numbering scheme. [c] In acetone-d_6.

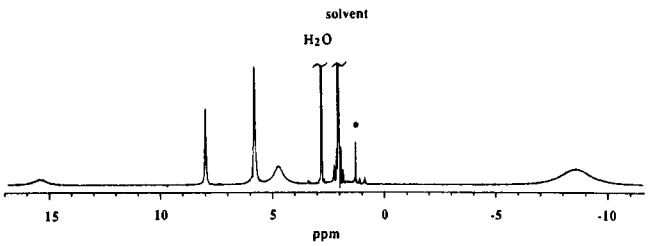

Figure 4. ^1H NMR spectrum of $TcCl_2(PMe_2Ph)_2(bpy)$ in acetone-d_6 at ambient temperature.

Table IV presents the chemical shift values and spin–spin splitting patterns for the Tc(III) complexes. The ^1H NMR spectra of the cationic complexes are quite similar to those of the neutral complexes, the most notable difference being the chemical shifts of the methyl groups on the PMe_2Ph ligand. For the neutral complexes, the methyl groups resonate around −15 ppm and are the furthest upfield signals. In the case of the $TcCl_2(PMe_2Ph)_2(LL)^+$ complexes, however, the methyl groups have moved to significantly lower field and resonate around −6 ppm. In the neutral species, the phosphine ligand is trans to a chloride, which cannot compete with the phosphine for electron density from the technetium center through back-bonding. However, in the $TcCl_2(PMe_2Ph)_2(LL)^+$ complexes, the mutually trans phosphine ligands are competing against each other. Thus, the chemical shifts of the methyl groups reflect the relative amounts of electron density on the phosphine ligands.

Comparison of the N-donor protons's chemical shifts shows slight variation within the $TcCl_3(PMe_2Ph)(LL)$ and $TcCl_2(PMe_2Ph)_2(LL)^+$ families due to the nature of the N-donor ligand. For each Tc(III) complex, the signals at highest field correspond to the protons α to the chelating nitrogen atoms, with the β-position protons resonating at lowest field. The relative shifts of the remaining ring protons are different for the $TcCl_3(PMe_2Ph)(LL)$ species as compared to the $TcCl_2(PMe_2Ph)_2(LL)^+$ complexes. In the former, the protons γ to the chelating nitrogen atom are immediately upfield of the protons in the δ ring position; for the $TcCl_2(PMe_2Ph)_2(LL)^+$ complexes, the situation is reversed. This phenomenon is not dependent on the identity of the N-donor ligand and suggests that the relative contributions of the contact and pseudocontact interactions to the chemical shift of the N-donor ring protons are different for the neutral Tc(III) complexes as compared to the cationic complexes.

The Tc(II) complexes also give observable ^1H NMR spectra, though the T_{1e} of the technetium center is longer than in the case of the Tc(III) species. As a result, the ^1H NMR spectra of the

Table V. Cyclic Voltammetry Results for Reported Complexes

complex	$E_{1/2}$,[a] V
$TcCl_3(PPh_3)(bpy)$	+0.71, −0.47,[b] −1.43[b]
$TcCl_3(PMe_2Ph)(bpy)$	+0.61, −0.56,[b] −1.51[b]
$TcCl_3(PMe_2Ph)(phen)$	+0.61, −0.55,[b] −1.49[b]
$TcCl_3(PMe_2Ph)(bpm)$	+0.77, −0.40,[b] −1.28,[b] −1.69[b]
$TcCl_2(PMe_2Ph)_2(bpy)^+$	+1.04, −0.13, −1.60[b]
$TcCl_2(PMe_2Ph)_2(phen)^+$	+1.05, −0.12, −1.59[b]
$TcCl_2(PMe_2Ph)_2(bpm)^+$	+1.22, +0.05, −1.34
$TcCl(PMe_2Ph)_3(bpy)^+$	+1.76,[c] +0.30, −0.82

[a] In CH_3CN solution with 0.1 M TBAP as supporting electrolyte. $E_{1/2}$ values were calculated from the average of the anodic and cathodic peak potentials, $E_{1/2} = (E_{p,a} + E_{p,c})/2$. $E_{1/2}$ values were measured relative to SCE and are uncorrected for junction potentials. [b] Irreversible peak potential, $E_{p,c}$. [c] Irreversible peak potential, $E_{p,a}$.

neutral $TcCl_2(PMe_2Ph)_2(LL)$ complexes are not readily interpretable due to the large line widths of the signals and the necessary conclusion that several resonances have been broadened into the base line (Figure 4). In the case of $TcCl_2(PMe_2Ph)_2$(bpy), this intermediate T_{1e} value also permits detection of a poorly resolved EPR signal at room temperature, which is more easily observed at liquid nitrogen temperatures. Recently, the isoelectronic Re(II) porphyrin complex $Re(TTP)(PMe_3)_2$ (TTP is 5,10,15,20-tetra-*p*-tolylporphyrinato dianion) has been reported[21] to give both ^1H NMR and EPR spectra at room temperature. The ^1H NMR spectrum of $TcCl(PMe_2Ph)_3(bpy)^+$ is more clearly defined, but there, two resonances are missing; presumably those arising from the ring 6,6′-positions on the bpy ligand are too broad to detect. Of the resonances that are observed, definitive assignments can only be made for the methyl groups, which give the three very broad signals at highest field. Two of these resonances overlap by varying amounts in different solvents.

When the Tc(III) $[TcCl_2(PMe_2Ph)_2(bpy)](PF_6)$ and the Tc(II) $TcCl_2(PMe_2Ph)_2(bpy)$ species are combined in solution, the ^1H NMR spectrum of the mixture reveals that rapid electron transfer is occurring between the two oxidation states. Rather than the distinct resonances of both the neutral and the cationic complexes, an averaged spectrum, which depends upon the molar ratio of the Tc(II) and the Tc(III) species, is recorded. Superficially, the self-exchange spectrum appears to be that of the Tc(II) complex, but closer examination reveals that the Tc(III) cation is functioning as a shift reagent, its presence drastically affecting the chemical shift values of the broader "Tc(II)-type" resonances.

Electrochemistry. The results of cyclic voltammetry experiments in acetonitrile solution with 0.1 M TBAP as supporting electrolyte are presented in Table V for neutral and cationic Tc(III) complexes. For both types of complexes, a reversible oxidation is seen, presumably the Tc(III) to Tc(IV) metal-based process, from comparison with data for rhenium complexes.[13] This oxidation occurs from about +0.6 to +0.8 V (vs SCE) in the neutral $TcCl_3(P)(LL)$ series and from about +1.0 to +1.3 V in the cationic $TcCl_2(PMe_2Ph)_2(LL)^+$ series. Both types of complexes also display metal- and ligand-centered reductions, the Tc(III) to Tc(II) process occurring from about −0.4 to about −0.46 V for the neutral series and at about −0.1 V for the cationic bpy and phen complexes. This reduction is irreversible for the $TcCl_3(P)(LL)$ complexes and gives rise to a new reversible redox couple centered about −0.1 V, suggesting loss of chloride in the original reduction process; this behavior is well-documented for similar complexes.[22] The Tc(II) oxidation state is found to be quite easily accessible from the Tc(III) complexes $TcCl_2(PMe_2Ph)_2(bpy)^+$ and $TcCl_2(PMe_2Ph)_2(phen)^+$, as could be deduced from the byproducts in the syntheses used to obtain the Tc(III) complexes. It also is clear from the $E_{1/2}$ values why the synthetic method used to obtain $Tc^{III}Cl_2(PMe_2Ph)_2(LL)^+$ does not work for the bpm analogue, producing instead the neutral $Tc^{II}Cl_2(PMe_2Ph)_2(bpm)$, which has a reversible metal-based oxidation at +0.05 V. Ligand-centered reductions, irreversible except in the case of $TcCl_2(PMe_2Ph)_2(bpm)^+$, occur from about −1.3 to about −1.6 V, with $TcCl_3(PMe_2Ph)(bpm)$ undergoing an additional irreversible reduction at −1.69 V. The more positive $E_{1/2}$ values obtained for the $TcCl_2(PMe_2Ph)_2(LL)^+$ as compared to the $TcCl_3(P)(LL)$ series reflect the effects of a positive charge and substitution of a good π-acceptor, the PMe_2Ph ligand, for a chloride, an electron-donating ligand.

The $E_{1/2}$ values for $[TcCl(PMe_2Ph)_3(bpy)](PF_6)$ are also given in Table V. This complex undergoes a reversible reduction at −0.82 V, presumably the Tc(II) to Tc(I) process. A reversible oxidation, Tc(II) to Tc(III), is seen at +0.30 V, and at +1.76 V an irreversible oxidation occurs. As seen for the $TcCl_2(PMe_2Ph)_2(LL)^{+/0}$ series, here again electrochemical interconversion between the Tc(II) and Tc(III) oxidation states is relatively facile.

Comparison of the $E_{1/2}$ values obtained for the Tc(III) complexes with those reported by Meyer and co-workers[13] for analogous Re(III) complexes shows the expected trends: second-row technetium complexes are easier to reduce (and more difficult to oxidize) than their third-row rhenium counterparts. For example, in acetonitrile solution, $Re^{III}Cl_3(PMe_2Ph)(bpy)$ is reported to undergo oxidation at +0.47 V and reduction at −0.74 V; the Tc(III) values are +0.61 and −0.56 V, respectively (all values vs SCE). Likewise, $Re^{III}Cl_2(PMe_2Ph)_2(bpy)^+$ has $E_{1/2}$ values of +0.88, −0.39, and −1.69 V compared to +1.04, −0.13, and −1.60 V for the Tc(III) analogue. Comparison of the Tc(III) $E_{1/2}$ values with those of $TcCl_3(PMe_2Ph)_3$, the starting material from which the Tc(III) complexes reported in this paper are derived, is also valuable. The compound $TcCl_3(PMe_2Ph)_3$ has been reported to undergo a reversible one-electron oxidation[23] at +0.86 V and a one-electron reduction,[24] followed by rapid loss of chloride, at −0.75 V vs SCE in acetonitrile solution. This $E_{1/2}$ value for the oxidation to Tc(IV) is intermediate between those measured for the $TcCl_3(P)(LL)$ and $TcCl_2(PMe_2Ph)_2(LL)^+$ complexes, reflecting the neutrality of $TcCl_3(PMe_2Ph)_3$ and the effect of substituting N-donor ligands for PMe_2Ph. The presence of bpy, phen, or bpm ligands serves to make reduction of Tc(III) complexes easier, and the appropriate combination of PMe_2Ph and N-donor ligands, as seen from the electrochemical behavior of $TcCl_2(PMe_2Ph)_2(LL)^+$ and $TcCl(PMe_2Ph)_3(bpy)^+$, permits reversible interconversion between Tc(III) and Tc(II).

X-ray Structure Determination. Suitable X-ray-quality crystals of $TcCl_3(PPh_3)(bpy)$ were obtained from a CD_3CN solution, and a crystal structure determination was performed. The compound has a slightly distorted octahedral coordination geometry with a facial arrangement of chloride ligands (Figure 1). Selected bond distances and angles are presented in Table III. Due to the strong trans influence of the phosphine, the chloride opposite the PPh_3 ligand has the longest of the three Tc–Cl bond distances (2.421 [2] Å). For the chelated bpy ligand, the two Tc–N bond distances are found to be unequal (2.112 [4] versus 2.099 [5] Å). The bond lengths are typical of those seen for Tc(III) complexes.[25]

Recently, Wilcox et al. have provided a detailed structural study[8] of three members of the closely related cationic series $TcCl_2(P)_2(LL)^+$ (P = PMe_2Ph, $PEtPh_2$; LL = bpy, phen). It is interesting to note that a comparison of these cations with the neutral complex described above shows that, with the exception of the Tc–Cl bond distance involving the unique trans-to-phosphorus chloride in $TcCl_3(PPh_3)(bpy)$, the Tc–N, Tc–P, and Tc–Cl bond distances for the two series are in close agreement.

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Supplementary Material Available: Figure S.1, showing an ORTEP diagram, and Tables S.I-S.V, listing respectively complete X-ray data, hydrogen atom positional parameters, thermal parameters, intramolecular atomic distances, and intramolecular angles for $TcCl_3(PC_{18}H_{15})(N_2C_{10}H_8)$ (7 pages); Table S.VI, listing calculated and observed structure factors for $TcCl_3(PC_{18}H_{15})(N_2C_{10}H_8)$ (41 pages). Ordering information is given on any current masthead page.

Contribution from the Medical Research Division, American Cyanamid Company, Lederle Laboratories, Pearl River, New York 10965, and Department of Chemistry and Biochemistry, University of Colorado, Boulder, Colorado 80309

(Malonato)bis[sulfinylbis[methane]-*S*']platinum(II) Compounds: Versatile Synthons for a New General Synthesis of Antitumor Symmetrical and Dissymmetrical (Malonato)platinum(II) Complexes

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New (malonato)platinum(II) compounds, *cis*-[Pt(OOCACOO)$(Me_2SO)_2$] (A = CH_2, cycloalkyl), have been prepared, and their reactions with various amines have led to a new general synthesis of antitumor symmetrical and dissymmetrical (malonato)platinum(II) complexes. Reaction of *trans*-(-)-1,2-cyclohexanediamine (CHDA*) with the cyclobutanedicarboxylate (CBDC) complex *cis*-[Pt(CBDC)$(Me_2SO)_2$] has been studied in detail, and crystallographic molecular structure determinations have been carried out on the Pt(CHDA*)(Me_2SO)(CBDC) intermediate and the Pt(CHDA*)(CBDC) product. Crystals of Pt(CHDA*)(Me_2SO)(CBDC) grown from aqueous solution form as unstable hydrates, which rapidly lose water molecules of crystallization upon removal from the crystallization solution at room temperature. X-ray data were collected on a crystal at -100 °C. The complex crystallizes in the noncentrosymmetric triclinic unit cell *P*1 with four independent Pt(CHDA*)(Me_2SO)(CBDC) molecules and thirteen independent water molecules per unit cell. Unit cell dimensions are a = 10.998 (3) Å, b = 13.946 (5) Å, c = 15.163 (5) Å, α = 65.39 (2)°, β = 88.21 (2)°, γ = 79.64 (2)°, and V = 2078 (1) Å^3. Complex molecules form as two independent hydrogen-bonded dimers, $[Pt(CHDA^*)(Me_2SO)(CBDC)]_2$, with hydrogen-bonded water molecules linking the two complex units. Platinum atoms of the complex are four-coordinate, bonded to the two nitrogens of the CHDA* ligand, the sulfur atom of the DMSO ligand, and one of the carboxylate oxygen atoms of the monodentate CBDC ligand. Crystals of Pt(CHDA*)(CBDC) obtained from aqueous solution form as hydrates in the noncentrosymmetric centered monoclinic unit cell *C*2. Unit cell dimensions are a = 24.889 (16) Å, b = 5.382 (2) Å, c = 11.426 (4) Å, β = 106.97 (2)°, and V = 1464 (1) Å^3, with one independent complex molecule and two half water molecules per asymmetric region of the unit cell. Displacement of the DMSO ligand of Pt(CHDA*)(Me_2SO)(CBDC) results in chelation of the CBDC ligand in Pt(CHDA*)(CBDC). The two half water solvate molecules are hydrogen bonded to oxygen atoms of adjacent complex molecules.

Introduction

cis-Diamminedichloroplatinum(II) (cisplatin)[1] is one of the most effective oncolytic agents against cancers of the testes, ovaries, bladder, and head and neck.[2-4] It is also an important adjunct for cancers of the cervix, lung, and breast.[2] Its most spectacular success has been in the treatment of testicular cancer,[3] a form of cancer previously resistant to any therapy but now considered to be curable in most cases. However, cisplatin has three drawbacks that limit its usefulness: (1) it has severe toxicities[5-7] such as nephrotoxicity, nausea/vomiting, myelosuppression, ototoxicity, and neurologic complications, (2) it only affects a narrow range of tumors, and (3) it causes the development of resistance in the tumor cell.

cis-Diammine(1,1-cyclobutanedicarboxylato)platinum(II) (carboplatin)[8-10] is the only clinically successful second-generation platinum complex. It does not exhibit significant nephrotoxicity and emesis, and its relatively lower toxicities as compared to those of cisplatin have been related to the greater pharmacokinetic stability of its 1,1-cyclobutanedicarboxylate ligand in solution.[11,12] Nevertheless, it still has two other drawbacks. Just like cisplatin, it only affects a narrow range of tumors and causes the development of resistance in the tumor cell.

In recent years, there has been an intense interest in developing third-generation platinum complexes with a broader spectrum of activity, improved clinical effectiveness, lack of cross-resistance to cisplatin, and enhanced water solubility. In our search for third-generation platinum complexes, we have encountered the following technical problems: (1) (malonato)platinum(II) complexes synthesized by literature procedures[13] were often contaminated with byproducts (sodium nitrate or silver chloride depending on the reaction employed and the solubility of the product), (2) no efficient synthesis of dissymmetrical platinum(II) complexes[14,15]

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