$\Delta H^{\ddagger}$. When there is a spin change during the ionization step, as with Fe(TPP)(1-MeIm)N_3,[29] the $\Delta S^{\ddagger}$ value is very different from the values given in Table I.

Perhaps the most important comparison of cobalt and iron deals with the role of hydrogen bonding in the chloride ionization step. In this regard the two metals behave similarly. Changing the imidazole from 1-MeIm to HIm causes a large rate acceleration, and in acetone the rate constant ratio k_2/k_1 is 300 for cobalt and 130 for iron. The increase in the rate of reaction of M(TPP)(1-MeIm)Cl as the solvent is changed from acetone to dichloromethane is also ascribed to hydrogen bonding, and this increase is a factor of 13 for cobalt and 20 for iron.

Conclusions. Hydrogen bonding plays a major role in chloride ionization from Co(TPP)(RIm)Cl. While analogous iron complexes react much more rapidly, both metals follow the same mechanism and display similar sensitivities to hydrogen-bonding interactions involving the chloride. Imidazoles bearing a 2-Ph or 2-Me substituent exhibit steric interactions with the porphyrin ligand in Co(TPP)(RIm)Cl that result in a ca. 10-fold increase in the lability of the trans chloride.

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Registry No. 1-MeIm, 616-47-7; 1-PhIm, 7164-98-9; 1-Me-2-PhIm, 3475-07-8; 1-Me-5-PhIm, 2154-38-3; 1,2-Me_2Im, 1739-84-0; HIm, 288-32-4; 4-PhIm, 670-95-1; 2-PhIm, 670-96-2; 2-MeIm, 693-98-1; 2-EtIm, 1072-62-4; Co(TPP)Cl, 60166-10-1; Co(TPP)Br, 60166-11-2.

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Neutral Technetium(V) Complexes with Amide-Thiol-Thioether Chelating Ligands

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General methods for the preparation of ligands of the type $R'SCH_2CONHCH_2CH_2NHCOCH_2SR$, $H_2ema(R)(R')$, where R = alkyl, aminoalkyl, and carboxyalkyl and R' = H, benzoyl, acetamidomethyl, and benzamidomethyl are described. New methods for the protection and deprotection of thiols with triphenylmethyl and amidomethyl groups have been developed. These ligands have been reacted with $(Bu_4N)[TcOCl_4]$ and $Na[TcO(eg)_2]$ (eg = ethylene glycolato), and for the cases where R = Me, CH_2Ph, $(CH_2)_{10}COOH$, and $CH_2CH_2(NC_4H_8O)$, neutral complexes, [TcO(emaR)], have been isolated and characterized. The complex $[TcO(ema(CH_2CH_2NC_4H_8O))]$ was crystallized as a monohydrate, and a single-crystal X-ray structure determination was performed. For all of the $[TcO(ema(CH_2CH_2NR_2))]$ complexes, an intramolecular dealkylation occurred to cleanly form $[TcO(ema)]^-$, which can be isolated as the $AsPh_4^+$ salt. Furthermore, $[TcO(ema(CH_2Ph))]$ and [TcO(ema(Me))] were reacted with amines, water, and halides to give the dealkylated products. Crystal data for $C_{12}H_{20}N_3O_4S_2Tc\cdot H_2O$: monoclinic, a = 12.120 (1) Å, b = 7.172 (1) Å, c = 18.933 (2) Å, β = 94.29 (1)°, V = 1641.1 Å^3, space group = $P2_1/n$ (No. 14), Z = 4, R = 0.042, R_w = 0.055.

Introduction

The coordination chemistry of amide and thiolate ligands has a strong basis in both biology and chemistry, and reviews have been dedicated to the field.[2] We are particularly interested in this area of chemistry as it pertains to the preparation of new classes of chelate complexes of technetium that can direct the biodistribution of the radiotracer ^{99m}Tc (γ = 140 keV, $t_{1/2}$ = 6 *h*), for purposes in diagnostic nuclear medicine.[3] Similar strategies by ourselves and others have lead to useful radiopharmaceutical preparations of ^{99m}Tc complexes for imaging renal function,[4] cerebral perfusion,[5] myocardial perfusion,[6] and other purposes.[7]

Studying the chemistry of technetium, by using macroscopic quantities of the long-lived isomer, ^{99}Tc (β = 0.292 MeV, $t_{1/2}$ = 2.12×10^5 years) has been particularly fruitful and has provided a powerful tool for the design, preparation, and characterization of potential radiopharaceuticals.

Previous work with bis(amide)-bis(thiol) chelates, such as *N*,*N'*-ethylenebis(2-mercaptoacetamide) (H_4ema), showed that the oxotechnetium(V) square-pyramidal core is readily accessible either by reduction from pertechnetate or by ligand exchange from $(Bu_4N)[TcOCl_4]$ or $Na[TcO(eg)_2]$ (eg = ethylene glycolato) to give anionic "$TcON_2S_2$" complexes, which result from deprotonation of the thiol and amide groups on the ligand.[8,9] As these amide-thiol ligands are very amenable to derivatization and as other workers have shown that five-coordinate neutral oxotechnetium(V) complexes of bis(amine)-bis(thiol)[5b] and bis(amine)-bis(oxime)[5c,5d] chelates are extremely useful for evaluating cerebral perfusion and can aid in diagnoses of physiological disorders, we modified the chelate H_4ema to give a series of trianionic mono-S-alkylated derivatives, H_3emaR. These ligands react to give the five-coordinate neutral oxotechnetium(V) complexes [TcO(emaR)], and in some instances, when R = $CH_2CH_2NR_2$, these complexes react further to give the thioether-dealkylated product, $TcO(ema)^-$. The following report describes the preparation of the ligands and the corresponding complexes derived from their reaction with technetium(V).

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Experimental Section

Caution! ^{99}Tc is a weak β emitter with a half-life of 2.12×10^5 years. All manipulations were carried out in laboratories approved for low-level radioactivity and precautions followed were as detailed previously.[10,11]

Ammonium pertechnetate was supplied as a gift by Du Pont Biomedical Products. Elemental analyses were performed by Atlantic Microlab, Atlanta, GA. Column chromatography was performed by using Kieselgel TLC grade silica. Melting points were obtained with a Melt-Temp apparatus and are uncorrected. IR spectra were measured from 4800 to 400 cm^{-1} on an IBM System 9000 FTIR spectrophotometer with a DTGS detector and 2-cm^{-1} resolution. ^1H and ^{13}C NMR spectra were recorded on Bruker WM 250- and 270-MHz spectrometers, respectively. UV–vis absorption spectra were recorded with a Hewlett-Packard 8451A photodiode array spectrophotometer. Routine mass spectra were measured on samples dissolved in a *p*-nitrobenzyl alcohol matrix with a MAT731 mass spectrometer equipped with an Ion Tech B11N FAB gun and operating at an accelerating voltage of 8 keV.

N-(2-Aminoethyl)-2-thioacetamide,[12] acetamidomethanol,[13,14] benzamidomethanol,[13,15] $(Bu_4N)[TcOCl_4]$[16] and $Na[TcO(eg)_2]$[17] were prepared as described previously. All other reagents and solvents were of reagent grade and used as received.

Preparation of Ligands. *N*-(2-Aminoethyl)-2-[(triphenylmethyl)thio]acetamide (1). To a solution of *N*-(2-aminoethyl)-2-mercaptoacetamide (14.56 g, 0.11 mol) in trifluoroacetic acid (100 mL) was added triphenylmethanol (28.25 g, 0.11 mol). The resultant brown solution was stirred for 30 min and evaporated to give a brown oil. The latter was triturated with ether (500 mL) to give the trifluoroacetate salt of (**1**) as a white solid, which was filtered, washed with ether, and dried; yield 49.5 g (93%).

The trifluoroacetate salt of (**1**) (10.06 g, 20.5 mmol) was partitioned between 1 M aqueous NaOH (30 mL) and ethyl acetate. The organic phase was washed with water and saturated aqueous NaCl, dried over K_2CO_3, evaporated to a gum, and crystallized from ethyl acetate to give (**1**) (7.42 g, 96%). Recrystallization from ethyl acetate afforded an analytically pure sample. Mp: 130–132 °C. Anal. Calcd for $C_{23}H_{24}N_2OS$: C, 73.37; H, 6.42; N, 7.44; S, 8.52. Found: C, 73.11; H, 6.49; N, 7.31; S, 8.46. IR: ν_{max} 3260, 3090, 3080, 3050, 1630, 1550, 1485, 1440, 760, 750, 740, 695 cm^{-1}. ^1H NMR: δ 1.13 (br s, 2 H), 2.63 (m, 2 H), 2.99 (m, 2 H), 3.13 (s, 2 H), 6.36 (m, 1 H), 7.1–7.5 (m, 15 H).

2-(Benzoylthio)acetic Acid (2). Compound **2** was prepared in 95% yield by Schotten–Baumann benzoylation of freshly distilled 2-mercaptoacetic acid. Mp: 103–105 °C (lit.[18] mp 106 °C). Electronic spectrum (dioxane): λ_{max} (ϵ, M^{-1} cm^{-1}) 264 (8100) nm. IR: ν_{max} 3000, 1710, 1665, 1300, 1205, 1170, 920, 775, 680, 645 cm^{-1}. ^1H NMR: δ 3.93 (s, 2 H), 7.48 (m, 3 H), 7.92 (m, 2 H), 10.48 (s, 1 H).

***N*-[2-((2-((Triphenylmethyl)thio)acetyl)amino)ethyl]-2-(benzoylthio)acetamide, H_2ema(Tr)(Bz) (3).** To a cooled solution of amine **1** (3.59 g, 9.53 mmol), acid **2** (1.87 g, 9.54 mmol) and *N*-hydroxysuccinimide (1.11 g, 9.65 mmol) in CH_2Cl_2 (100 mL) was added a solution of DCC (2.25 g, 10.92 mmol) in CH_2Cl_2 (10 mL) such that the temperature remained below −5 °C. After 15 min the cooling bath was removed, and the reaction was allowed to stir at room temperature for 2 h. The precipitated DCU was filtered and washed with CH_2Cl_2. The combined filtrate and washings were washed with 5% aqueous $NaHCO_3$, 1 M aqueous $KHSO_4$, water, and saturated aqueous NaCl and then dried over $MgSO_4$. Evaporation of the solvent, chromatography (MPLC 1–5% CH_3OH/CH_2Cl_2 over silica), and crystallization from CH_2Cl_2 gave **3** (3.67 g, 91%). Mp: 133–135 °C. Anal. Calcd for $C_{32}H_{30}N_2O_3S_2$: C, 69.29; H, 5.45; N, 5.05; S, 11.56. Found: C, 69.10; H, 5.50; N, 5.00; S, 11.55. IR: ν_{max} 3280, 3080, 3060, 1650, 1550, 1450, 1210, 930, 740, 700, 670 cm^{-1}. ^1H NMR: δ 3.04 (s, 2 H), 2.9–3.2 (m, 4 H), 3.66 (s, 2 H), 6.41 (m, 1 H), 6.93 (m, 1 H), 7.1–8.0 (m, 20 H). Electronic spectrum (dioxane): λ_{max} (ϵ, cm^{-1} M^{-1}) 264 (8800) nm.

***N*-[2-((2-Thioacetyl)amino)ethyl]-2-[(triphenylmethyl)thio]acetamide, H_3ema(Tr) (4).** A solution of benzoyl derivative **3** (4.96 g, 8.95 mmol) in 0.1 M methanolic sodium methoxide (90 mL, 9.0 mmol) was stirred for 20 min, diluted with water (150 mL), and neutralized with 1 M HCl to give **4** as a white solid, which was filtered, washed with water and ether, and dried (3.67 g, 91%). Mp: 170–172 °C. Anal. Calcd for $C_{25}H_{26}N_2O_2S_2$: C, 66.64; H, 5.82; N, 6.22; S, 14.23. Found: C, 66.59; H, 5.86; N, 6.16; S, 14.21. IR: ν_{max} 3260, 3080, 3060, 1655, 1570, 1445, 1230, 745, 700, 695 cm^{-1}. ^1H NMR: δ 1.86 (tr, 1 H), 2.9–3.5 (m, 6 H), 3.13 (s, 2 H), 6.36 (m, 1 H), 7.07 (m, 1 H), 7.0–7.5 (m, 15 H).

***N*-[2-((2-(Methylthio)acetyl)amino)ethyl]-2-[(triphenylmethyl)thio]acetamide, H_2ema(Me)(Tr) (5).** To a solution of thiol **4** (0.900 g, 2.00 mmol) in 0.11 M methanolic sodium methoxide (20 mL, 2.20 mmol) was added methyl iodide (125 μL, 2.01 mmol), and the reaction was stirred for 10 min. Then, 1 M aqueous HCl (2.20 mL) and water (20 mL) were added, causing a precipitate. The white solid (**5**) was filtered, washed with water and ether, and dried (0.749 g, 76%). Mp: 154–157 °C. IR: ν_{max} 3228, 3057, 2924, 2852, 1738, 1657, 1535, 1387, 1232, 750, 735, 703 cm^{-1}. ^1H NMR: δ 2.03 (s, 3 H), 3.05 (s, 4 H), 4.00 (m, 4 H), 6.22 (br, 1 H), 7.20 (m, 16 H).

***N*-[2-((2-((10-Carboxyundecyl)thio)acetyl)amino)ethyl]-2-[(triphenylmethyl)thio]acetamide, H_2ema(undec)(Tr) (6).** To a solution of thiol **4** (2.25 g, 5.00 mmol) in 0.11 M methanolic sodium methoxide (100 mL, 0.11 mmol) was added 11-bromoundecanoic acid (1.33 mL, 5.00 mmol). The resultant solution was refluxed for 2.5 h and then acidified with 1 M aqueous HCl (11 mL). Dilution with water gave an oil, which was extracted into CH_2Cl_2, washed with water and saturated aqueous NaCl, dried over $MgSO_4$, and evaporated to an oil. Trituration with ether gave **6** (2.27 g, 72%). Recrystallization from acetone/water gave an analytically pure sample. Mp: 88–91 °C. Anal. Calcd for $C_{36}H_{46}N_2O_4S_2$: C, 68.10; H, 7.30; N, 4.41; S, 10.10. Found: C, 68.08; H, 7.32; N, 4.39; S, 10.14. IR: ν_{max} 3380, 3080, 3060, 2970, 2930, 1710, 1650, 1560, 1490, 1445, 1435, 1335, 1240, 745, 705, 695 cm^{-1}. ^1H NMR: δ 1.26 (br s, 12 H), 1.45–1.71 (m, 4 H), 2.31 (m, 2 H), 2.46 (m, 2 H), 3.08 (m, 2 H), 3.13 (s, 2 H), 3.16 (s, 2 H), 3.23 (m, 2 H), 6.44 (br tr, 1 H), 7.1–7.5 (m, 16 H).

***N*-[2-((2-Thioacetyl)amino)ethyl]-2-(methylthio)acetamide, H_3ema(Me) (7).** To a solution of triphenylmethyl derivative **5** (0.557 g, 1.20 mmol) in trifluoroacetic acid (5 mL) was added triethylsilane (0.2 mL, 1.26 mmol). The reaction mixture was partitioned between hexanes (5 mL) and water (10 mL). The water layer was separated and filtered through Celite. The solvent was removed under reduced pressure to give a clear oil. Trituration with ether and recrystallization from 2-propanol/ether gave **7** (0.150 g, 91%). Mp: 112–113 °C. Anal. Calcd for $C_7H_{14}N_2O_2S_2$: C, 37.82; H, 6.35; N, 12.60; S, 28.84. Found: C, 37.88; H, 6.37; N, 12.58; S, 28.77. IR: ν_{max} 3286, 3086, 2983, 2947, 2918, 2548, 1641, 1558, 1447, 1336, 1303, 1239, 948, 739, 686 cm^{-1}. ^1H, NMR: δ 1.88 (tr, 1 H), 2.11 (s, 3 H), 3.17 (s, 2 H), 3.20 (d, 2 H), 3.44 (m, 4 H), 7.08 (br, 1 H), 7.18 (br, 1 H).

***N*-[2-((2-Thioacetyl)amino)ethyl]-2-[(10-carboxyundecyl)thio]acetamide, H_3ema(undec) (8).** A solution of triphenylmethyl derivative **6** (1.08 g, 1.70 mmol) in trifluoroacetic acid (7 mL) was treated with triethylsilane (0.32 mL, 2.00 mmol). Addition of hexanes and water precipitated **8**, which was filtered, washed with water, and dried. Recrystallization from aqueous methanol and then chloroform gave analytically pure material (0.54 g, 81%). Mp: 124–127 °C. Anal. Calcd for $C_{17}H_{32}N_2O_4S_2$: C, 52.01; H, 8.22; N, 7.14; S, 16.33. Found: C, 52.18; H, 8.26; N, 7.11; S, 16.36. IR: ν_{max} 3270, 2960, 2925, 1720, 1695, 1640, 1550, 1240 cm^{-1}. ^1H NMR (DMSO): δ 1.24 (br s, 12 H), 1.50 (m, 4 H), 2.19 (tr, 2 H), 2.53 (m, 3 H), 3.07 (m, 2 H), 3.13 (m, 4 H), 8.03 (m, 1 H), 8.16 (m, 1 H), 11.98 (s, 1 H). ^{13}C NMR: δ 24.5, 27.2, 28.6, 28.8, 31.7, 22.7, 34.6, 169.2, 169.7, 174.5.

***N*-[2-((2-(Benzoylthio)acetyl)amino)ethyl]-2-[(2-morpholinoethyl)thio]acetamide, H_2ema(morph)(Bz) (9).** To a solution of *N*-(2-aminoethyl)-2-mercaptoacetamide (0.505 g, 2.00 mmol) in 0.30 M methanolic sodium methoxide (25 mL) was added *N*-(2-chloroethyl)morpholine hydrochloride (0.702 g, 3.77 mmol). The reaction mixture was heated at reflux for 1.5 h and then cooled to −5 °C, at which time 2-benzoylthioacetic acid succinate ester (1.10 g, 3.77 mmol) was added, and the reaction was allowed to come to room temperature while being stirred over a period of 4 h. The solvent was removed under reduced pressure, and the residue was dissolved in CH_2Cl_2, washed with 5% $NaHCO_3$ and saturated aqueous NaCl, and dried over K_2CO_3. Chromatography (1–20% CH_3OH/CH_2Cl_2 over silica) and recrystallization from ethyl acetate gave **9** (0.493 g, 29%). Mp: 111–113 °C. Anal. Calcd for $C_{19}H_{27}N_3O_4S_2$: C, 53.62; H, 6.40; N, 9.87; S, 15.08. Found: C, 53.71, H, 6.43; N, 9.87; S, 15.02. IR: ν_{max} 3285, 3084, 2945, 2855, 2808, 1643, 1553, 1444, 1306, 1248, 1203, 1113, 918, 866, 692 cm^{-1}. ^1H NMR: δ

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2.40 (br tr, 4 H), 2.59 (A_2B_2 m, 4 H), 3.18 (s, 2 H), 3.40 (m, 4 H), 3.70 (m, 6 H), 6.48 (br, 1 H), 7.45 (m, 3 H), 7.50 (tr, 1 H), 7.95 (d, 2 H).

***N*-[2-((2-(((Benzoylamino)methyl)thio)acetyl)amino)ethyl]-2-[(2-piperidinoethyl)thio]acetamide, H_2ema(pip)(Bzm) (10).** To a solution of thiol **4** (1.00 g, 2.20 mmol) in methanol (40 mL) were added *N*-(2-chloroethyl)piperidine hydrochloride (0.41 g, 2.20 mmol) and 0.44 M methanolic sodium methoxide (10.1 mL). The reaction mixture was heated at reflux for 2 h and cooled and the solvent removed under reduced pressure. The residue was redissolved in trifluoroacetic acid (50 mL), and benzamidomethanol (0.35 g, 2.3 mmol) was added with stirring. After 30 min, triethylsilane (0.50 mL) was added, and then 50 mL of hexanes was added. Separation of the acid layer and evaporation gave a yellow oil, which was chromatographed (1–20% CH_3OH/CH_2Cl_2 over silica) and recrystallization from ethyl acetate to give **10** (0.65 g, 65%). Mp: 132–134 °C. Anal. Calcd for $C_{21}H_{32}N_4O_3S_2$: C, 55.76; H, 7.07; N, 12.38; S, 14.17. Found: C, 55.68; H, 7.13; N, 12.34; S, 14.22. IR: ν_{max} 3299, 3063, 2934, 2851, 2799, 1641, 1665, 1603, 1531, 1242, 694 cm^{-1}. ^1H NMR: δ 1.39 (m, 2 H), 1.55 (m, 4 H), 2.40 (br, 4 H), 2.50 (tr, 2 H), 2.71 (tr, 2 H), 3.19 (s, 2 H), 3.25 (s, 2 H), 3.40 (m, 4 H), 4.60 (d, 2 H), 7.42 (m, 3 H), 7.65 (br, 1 H), 7.80 (d, 2 H), 7.95 (br, 1 H), 8.15 (tr, 1 H).

***N*-[2-((2-(((Benzoylamino)methyl)thio)acetyl)amino)ethyl]-2-[(2-pyrrolidinoethyl)thio]acetamide, H_2ema(pyr)(Bzm) (11).** This compound was prepared according to the procedure for **10** and was recrystallized from acetonitrile (32%). Mp: 104–105 °C. Anal. Calcd for $C_{20}H_{30}N_4O_3S_2$: C, 54.80; H, 6.84; N, 12.78; S, 14.63. Found: C, 54.80; H, 6.91; N, 12.77; S, 14.59. IR: ν_{max} 3296, 3063, 2956, 2785, 1664, 1641, 1603, 1244, 694 cm^{-1}. ^1H NMR: δ 1.73 (m, 4 H), 2.45 (m, 4 H), 2.64 (m, 4 H), 3.18 (s, 2 H), 3.24 (s, 2 H), 3.35 (m, 4 H), 4.61 (d, 2 H), 7.43 (m, 3 H), 7.62 (br, 1 H), 7.83 (d, 2 H), 7.98 (br tr, 1 H), 8.15 (br, 1 H).

***N*-[2-((2-(((Benzoylamino)methyl)thio)acetyl)amino)ethyl]-2-[(2-(dimethylamino)ethyl)thio]acetamide, H_2ema(dma)(Bzm) (12).** This compound was prepared according to the procedure for **10** and was recrystallized from acetonitrile (70%). Mp: 99–101 °C. Anal. Calcd for $C_{18}H_{28}N_4O_3S_2$: C, 52.43; H, 6.79; N, 13.58; S, 15.55. Found: C, 52.48; H, 6.88; N, 13.54; S, 15.47. IR: ν_{max} 3294, 3061, 2938, 2772, 1666, 1645, 1535, 1242, 708, 694 cm^{-1}. ^1H NMR: δ 2.20 (s, 6 H), 2.45 (tr, 2 H), 2.63 (tr, 2 H), 3.21 (s, 2 H), 3.24 (s, 2 H), 3.39 (br m, 4 H), 4.64 (d, 2 H), 7.40–7.60 (m, 4 H), 7.80 (m, 3 H), 8.08 (br, 1 H).

***N*-[2-((2-(((Benzoylamino)methyl)thio)acetyl)amino)ethyl]-2-(benzylthio)acetamide, H_2ema(Bzl)(Bzm) (13).** This compound was prepared according to the procedure for **10**, substituting benzyl chloride for the S-alkylating agent, and was recrystallized from acetonitrile (84%). Mp: 141–143 °C. Anal. Calcd for $C_{21}H_{25}N_3O_3S_2$: C, 58.47; H, 5.80; N, 9.74; S, 14.86. Found: C, 58.38; H, 5.86; N, 9.74; S, 14.79. IR: ν_{max} 3297, 3059, 2945, 2922, 1655, 1603, 1531, 1282, 1240, 704 cm^{-1}. ^1H NMR (DMSO): δ 3.08 (s, 2 H), 3.17 (m, 4 H), 3.32 (s, 2 H), 3.39 (s, 4 H), 3.83 (s, 2 H), 4.55 (m, 2 H), 7.30 (m, 2 H); 7.33 (d, 3 H), 7.55 (m, 3 H), 7.90 (m, 2 H), 8.15 (br m, 2 H), 9.25 (tr, 1 H).

Preparation of Complexes. [TcO(ema(Me))] (14). To a purple methanolic solution of $Na[TcO(eg)_2]$ (0.236 mmol in 5 mL) was slowly added to a solution of ligand **8** (53.8 mg, 0.242 mmol) in methanol (2 mL) and 1 M aqueous NaOH (0.01 mL) to give a dark red solution, which was concentrated under reduced pressure, diluted with CH_2Cl_2, and chromatographed (1–5% CH_3OH/CH_2Cl_2 over silica). The resultant red solution was evaporated to an oil and crystallized from CH_2Cl_2/hexanes to give deep red needles of **14** (43.5 mg, 55%). Mp: 191–193 °C. Anal. Calcd for $C_7H_{11}N_2O_3S_2Tc$: C, 25.16; H, 3.32; N, 8.38; S, 19.19. Found: C, 25.16; H, 3.34; N, 8.37; S, 19.11. IR: ν_{max} 1631, 1326, 1299, 1072, 978, 958, 446, 407 cm^{-1}. ^1H NMR: δ 2.52 (s, 3 H), 3.61 (m, 1 H), 3.83 (m, 1 H), 3.90 (AB q, J(AB) = 17 Hz, 2 H), 4.16 (m, 2 H), 4.20 (m, 1 H), 5.16 (m, 1 H). ^{13}C NMR: δ 24.75, 38.51, 41.58, 54.70, 56.52, 180.43, 184.35. Electronic spectrum: λ_{max} (ϵ, cm^{-1} M^{-1}) 210 (16 000), 258 (12 600), 350 (sh 2640), 512 (106) nm. FAB^+ MS: m/z 335. $\Lambda(CH_3CN)$ = 2.74 Ω^{-1} m^2 mol^{-1}.

[TcO(ema(undec))] (15). This complex was prepared according to the procedure for **14** and recrystallized from methanol (56%). Mp: 130–133 °C. Anal. Calcd for $C_{17}H_{29}N_2O_5S_2Tc$: C, 40.48; H, 5.79; N, 5.52; S, 12.66. Found: C, 40.69; H, 5.67; N, 5.52; S, 12.66. IR: ν_{max} 2930, 2860, 1710, 1630, 1305, 1075, 955, 450 cm^{-1}. ^1H NMR: δ 1.29 (br s, 16 H), 1.60 (m, 4 H), 2.35 (tr, 2 H), 2.60 (m, 1 H), 3.20 (m, 1 H), 3.61 (m, 1 H), 3.83 (m, 1 H), 3.97 (AB q, J(AB)= 17 Hz, 2 H), 4.18 (m, 3 H), 5.16 (m, 1 H). ^{13}C NMR: δ 24.5, 27.4, 28.2, 28.6, 28.7, 28.9, 33.8, 38.7, 41.4, 54.4, 56.2, 178.6, 181.4, 184.7. Electronic spectrum: λ_{max} (ϵ, cm^{-1} M^{-1}) 375 (2900), 510 (103) nm. FAB^+ MS: m/z 319, 321, 505.

[TcO(ema(morph))]·H_2O (16). This complex was prepared according to the procedure for **14** and recrystallized from ethyl acetate (18%). Diffraction quality crystals were obtained by slow diffusion of hexanes into a CH_2Cl_2 solution of the complex. Mp: 163 °C dec. Anal. Calcd for $C_{12}H_{22}N_3O_4S_2Tc$: C, 31.93; H, 4.91; N, 9.31; S, 14.21. Found: C, 32.25; N, 4.66; N, 9.18; S, 14.00. IR: ν_{max} 3420, 2995, 2949, 2849, 1616, 1302, 1145, 1113, 1082, 1068, 951, 447 cm^{-1}. ^1H NMR: δ 1.60 (br s, 2 H), 2.46 (m, 4 H), 2.75 (m, 3 H), 3.40 (m, 1 H), 3.60 (m, 1 H), 3.70 (tr, 4 H), 3.85 (m, 1 H), 4.15 (m, 5 H), 5.15 (m, 1 H). ^{13}C NMR: δ 38.5, 38.6, 39.7, 53.4, 54.6, 56.1, 56.2, 66.6, 180.7, 184.4. Electronic spectrum: λ_{max} (ϵ, cm^{-1} M^{-1}) 260 (9100), 360 (2200), 508 (92) nm. FAB^+ MS: m/z 434, 867. $\Lambda(CH_3CN)$ = 15.5 Ω^{-1} m^2 mol^{-1}.

[TcO(ema(Bzl))] (17). This complex was prepared according to the procedure for **14**. Analytically pure material precipitated from the reaction mixture on standing (77%). Mp: 183–184 °C. Anal. Calcd for $C_{13}H_{15}N_2O_2S_2Tc$: C, 38.06; H, 3.66; N, 6.82; S, 15.63. Found: C, 37.97; H, 3.71; N, 6.79; S, 15.71. IR: ν_{max} 2932, 1651, 1445, 1440, 1350, 1296, 1242, 1103, 1026, 976, 949, 706, 447 cm^{-1}. ^1H NMR (CD_2Cl_2): δ 3.50 (m, 1 H), 3.78 (AB q, J(AB) = 17 Hz, 2 H), 3.80 (m, 1 H), 4.02 (AB q, J(AB) = 14 Hz, 2 H), 4.14 (m, 3 H), 5.10 (m, 1 H), 7.30 (m, 2 H), 7.45 (m, 3 H). ^{13}C NMR: δ 37.0, 38.5, 45.6, 54.6, 56.3, 129.6, 129.8, 131.0, 180.3, 184.4. Electronic spectrum: λ_{max} (ϵ, cm^{-1} M^{-1}) 264 (10 530), 388 (2540), 516 (109). FAB^+ MS: m/z 319, 321, 411, 821. $\Lambda(CH_3CN)$ = 1.59 Ω^{-1} m^2 mol^{-1}.

Reaction of Ligands 10, 11, and 12 with $(Bu_4N)[TcOCl_4]$. To a stirred solution of $(Bu_4N)[TcOCl_4]$ or $Na[TcO(eg)_2]$ (prepared in situ) in absolute methanol was added 1 molar equiv of ligand in methanol. The solution was allowed to stir until it became bright yellow, at which time 1 equiv of $AsPh_4Cl·H_2O$ was added with five additional volumes of water. The resultant solution was allowed to stand overnight, and the yellow precipitate was isolated in quantitative yield. Melting point, IR, ^1H NMR, and analytical data are identical with those of an authentic sample of $AsPh_4[TcO(ema)]$.[8]

Crystallography. Structure of [TcO(ema(morph))]·H_2O (16). X-ray data were collected from a red crystal of **16** at room temperature on a Enraf-Nonius CAD4F-11 κ-geometry diffractometer by using graphite-monochromated Mo Kα radiation (λ = 0.710 73 Å). Details of the data collection, reduction, and refinement procedure were similar to those described elsewhere.[19] A total of 3773 reflections ($+h,+k,\pm l$) were collected in the range $3° < 2\theta < 55°$ with the 3034 reflections having $I_o > 2\sigma(I_o)$ being used in the structure refinement, which was performed by full-matrix least-squares techniques (199 variables) using SHELX-76. Final R = 0.042 and R_w = 0.055. Hydrogen atoms were ignored while all other atoms were refined anisotropically. A semiempirical absorption correction was applied. The largest peak on the final difference Fourier map was 0.73 e Å^{-3}. Crystal data are shown in Table I, and atomic coordinates are shown in Table II.

Table I. Crystal Data for Structure Determination of [TcO(ema(morph))] (**16**)

empirical formula	$C_{12}H_{22}N_3O_5S_2Tc$
fw	435.25
cryst color, habit	red prisms
cryst dimens, mm	0.30 × 0.30 × 0.40
cryst syst	monoclinic
a, Å	12.120 (1)
b, Å	7.172 (1)
c, Å	18.933 (2)
β, deg	94.29 (1)
space group	$P2_1/n$
Z	4
ρ(calcd), g/cm^3	1.754
μ, cm^{-1}	10.3
diffractometer	Enraf-Nonius CAD4F-11
radiation (mono)	Mo Kα
temp, °C	23
scan mode	$\omega/2\theta$
max 2θ, deg	55
no. of reflcns measd	3773
cor	semiempirical abs; Lorentz–polarization
transmission factors	T_{max} = 1.0; T_{min} 0.91
structure soln	Patterson method
function minimized	$\sum w(\|F_o\| - \|F_c\|)^2$
anomalous dispersion	all non-hydrogen atoms
no. of observns with $I > 2\sigma(I)$	3034
no. variables	199
R, R_w	0.042, 0.055
max peak in final diff map, e Å^{-3}	0.73

(19) Silverman, L. D.; Dewan, J. C.; Giandomenico, C. M.; Lippard, S. J. *Inorg. Chem.* **1980**, *19*, 3379.

Table II. Atomic Coordinates for [TcO(ema(morph))] (**16**)

	x	y	z
Tc	0.29450 (3)	−0.34599 (6)	0.40591 (2)
S1	0.43004 (11)	−0.18060 (19)	0.46572 (7)
S2	0.37398 (11)	−0.28730 (17)	0.29642 (6)
O1	0.1756 (3)	−0.2315 (6)	0.39267 (19)
O2	0.3352 (4)	−0.5034 (6)	0.61584 (19)
O3	0.3550 (4)	−0.8340 (5)	0.2982 (2)
O4	0.6499 (4)	−0.4430 (8)	0.0702 (2)
N1	0.2961 (4)	−0.4826 (6)	0.4963 (2)
N2	0.2997 (3)	−0.6077 (6)	0.3726 (2)
N3	0.5515 (4)	−0.2520 (7)	0.1822 (2)
C1	0.4063 (5)	−0.2389 (10)	0.5566 (3)
C2	0.3436 (4)	−0.4237 (8)	0.5597 (3)
C3	0.2452 (6)	−0.6690 (9)	0.4930 (3)
C4	0.2620 (6)	−0.7563 (8)	0.4208 (4)
C5	0.3461 (4)	−0.6697 (7)	0.3146 (3)
C6	0.3963 (6)	−0.5247 (8)	0.2670 (3)
C7	0.5113 (4)	−0.1842 (7)	0.3062 (3)
C8	0.5433 (5)	−0.1076 (8)	0.2350 (3)
C9	0.6508 (5)	−0.3674 (10)	0.1962 (3)
C10	0.6494 (6)	−0.5245 (11)	0.1401 (4)
C11	0.5554 (6)	−0.3246 (11)	0.0560 (3)
C12	0.5537 (5)	−0.1689 (9)	0.1115 (3)

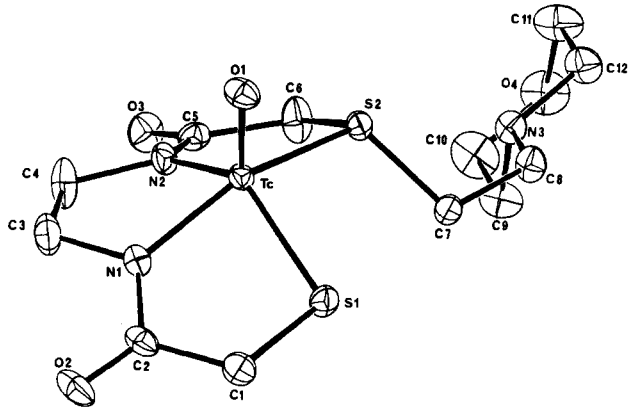


Figure 1. ORTEP drawing of [TcO(ema(morph))] (**16**) showing thermal ellipsoids at 30% probability.

Results

A series of tetradentate chelate ligands, H_2ema(R)(R′), where R = alkyl group and R′ = H, benzoyl (Bz), acetamidomethyl (Acm) or benzamidomethyl (Bzm), have been prepared according to the routes shown in Schemes I and II. These approaches are versatile for the preparation of a variety of ligands by choice of alkylating agents. Chelates containing alkyl, alkylamino and fatty acid side chains have been prepared and characterized.

A new and significant feature of the ligand preparations, which simplifies the synthesis of these protected thiol ligands, is a method that allows the clean removal of the triphenylmethyl (Tr) protecting group in concentrated trifluoroacetic acid. The free thiol ligand can be isolated cleanly by dissolving the Tr-protected derivative in trifluoroacetic acid, titrating the red-orange Tr^+ cation with triethylsilane until the solution is colorless, and evaporating the solvent. Alternatively, the ligand can be reprotected with the Acm- or Bzm-protecting group by the addition of the corresponding amidomethanol prior to the addition of silane.

Reaction of the ligands H_3ema(Me) (**7**), H_3ema(undec) (**8**), H_2ema(morph)(Bz) (**9**), and H_2ema(Bzl)(Bzm) (**13**) with $(Bu_4N)[TcOCl_4]$ or $Na[TcO(eg)_2]$ gave the neutral oxotechnetium(V) complexes that are formulated as [TcO(emaR)], where R = Me (**14**), undec (**15**), morph (**16**), and Bzl (**17**). These complexes are red-orange air-stable solids, which are soluble in polar organic solvents and have been characterized by analysis, conductivity, IR, UV–visible, ^{1}H NMR, and ^{13}C NMR spectroscopy, and positive-mode fast-atom-bombardment mass spectrometry (FAB^+ MS). In addition, a structural analysis has been performed on single crystals of [TcO(ema(morph))]·H_2O (**16**), for which an ORTEP drawing is shown in Figure 1. Selected bond angles and distances are shown in Table III and as supplementary material.

Table III. Selected Bond Lengths (Å) and Angles (deg) for [TcO(ema(morph))] (**16**)

Tc–O1	1.658 (3)	Tc–N1	1.975 (4)
Tc–S1	2.257 (1)	Tc–N2	1.989 (4)
Tc–S2	2.387 (1)		
O1–Tc–S1	114.3 (1)	S1–Tc–N1	82.3 (1)
O1–Tc–S2	100.7 (1)	S1–Tc–N2	127.9 (1)
O1–Tc–N1	109.2 (2)	Tc–S2–C6	100.5 (2)
O1–Tc–N2	117.7 (2)	Tc–S2–C7	114.1 (2)
S1–Tc–S2	91.1 (0)	C6–S2–C7	104.0 (3)

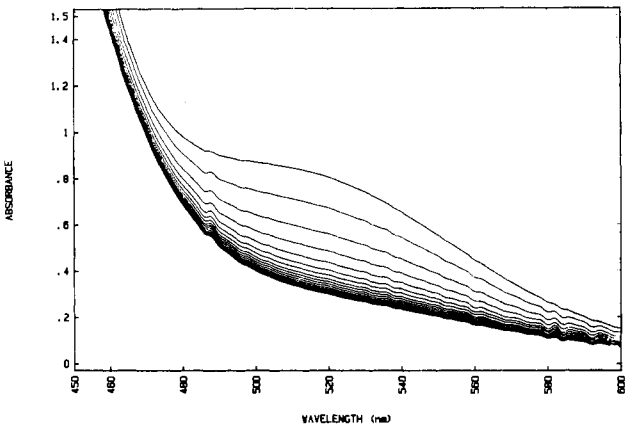


Figure 2. Electronic spectrum for the conversion of [TcO(ema(pip))] to [TcO(ema)]$^-$ in methanol at 22 °C.

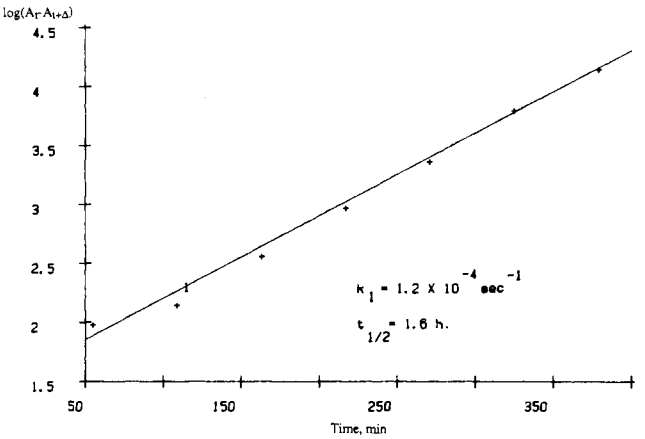
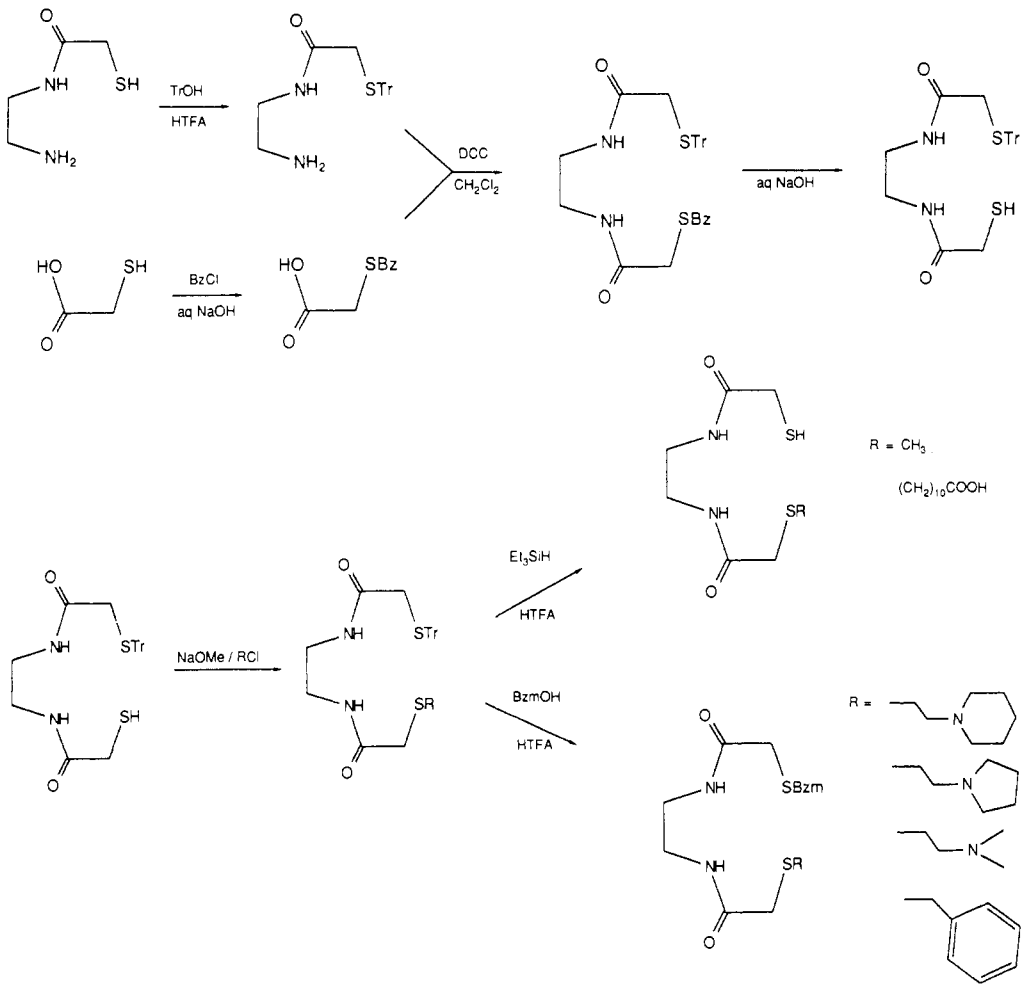


Figure 3. Plot of log $(A_t - A_{t+\Delta})$ at λ_{520nm} vs time for the conversion of [TcO(ema(pip))] to [TcO(ema)]$^-$ in methanol at 22 °C.

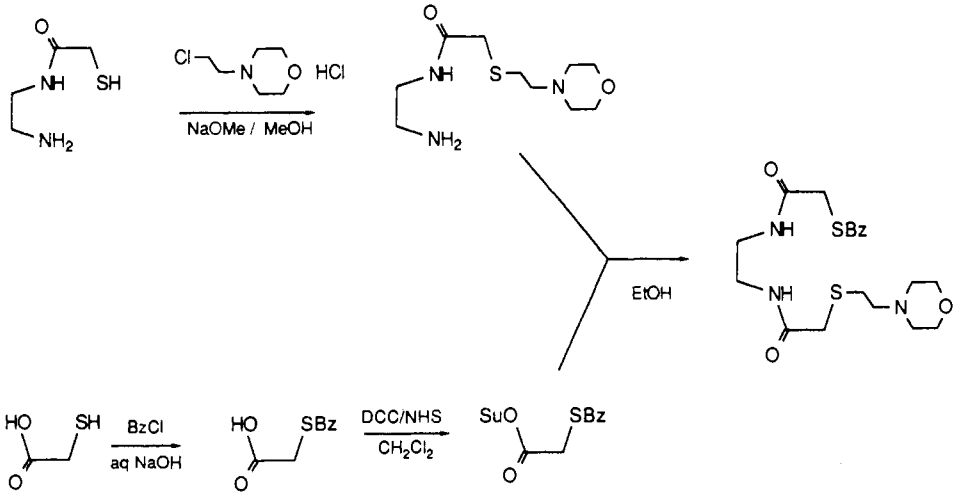
Infrared spectra of these neutral complexes showed the characteristic absorption due to the TcO stretch in the range 940–970 cm^{-1}. Conductivity measurements in acetonitrile ranged from 1.59 to 15.5 Ω^{-1} m^2 mol^{-1}, indicative of neutral complexes. FAB^+ mass spectra of all of the complexes showed ions corresponding to MH^+. ^{1}H and ^{13}C NMR spectra are consistent with formulation as the neutral compounds. These complexes react with water, amines, and halogens to give a yellow anionic complex, which is isolated after addition of $AsPh_4Cl$. Melting point IR and ^{1}H NMR spectroscopy, and analysis identified the yellow product as $AsPh_4$[TcO(ema)], which has been isolated previously by other routes.[8]

Reaction of H_2ema(pip)(Bzm) (**10**) with $(Bu_4N)[TcOCl_4]$ or $Na[TcO(eg)_2]$ gave a red solution, which was evaporated in vacuo to give an impure sample of a neutral $TcON_2S_2$ complex, characterized by a TcO stretch at 961 cm^{-1}, a visible band at 512 nm, and FAB^+ mass spectrum with a molecular ion, MH^+, at m/z 432. Solutions of this red complex slowly changed to yellow over the period of a few hours and $AsPh_4$[TcO(ema)] was isolated as the sole product of the reaction. Conversion of the red complex to [TcO(ema)]$^-$ was monitored by disappearance of the UV–visible

Scheme I



Scheme II



band at 512 nm and a first-order rate constant (k_1(22 °C) = 1.2 × 10^{-4} s^{-1}, $t_{1/2}$ = 1.6 h) for the reaction was obtained (see Figures 2 and 3).

Reaction of H_2ema(pyr)(Bzm) (**11**) or H_2ema(dma)(Bzm) (**12**) resulted only in the formation of the yellow anion, $[TcO(ema)]^-$. No other intermediates were observed.

Discussion

The amide–thiol ligands H_2ema(R)(R′) (R′ = H, Bz, Acm, Bzm) function as trianionic tetradentate chelates and were chosen to span the basal plane of the oxotechnetium(V) square-pyramidal core to produce the neutral complexes [TcO(emaR)]. The ligands were prepared by methods common to peptide synthesis, namely the use of activated esters and coupling reagents for the formation of amide bonds[20] and the use of protecting groups for selective protection and deprotection of thiols.[21] In addition, new methods for the convenient deprotection and swapping of protecting groups were developed. All three routes that were used are described as they show the progressively different strategies we took to obtain the desired neutral complexes. The thioether side-chain R groups were chosen to show the versatility of this series of ligands.

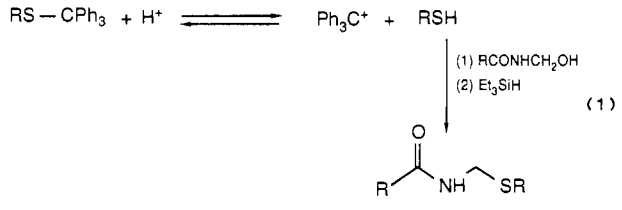
(20) Bodansky, M.; Klausner, Y. S.; Ondetti, M. A. *Peptide Synthesis*; Wiley: New York, 1976.
(21) For a list of general methods see: Green, T. In *Protective Groups in Organic Synthesis*; Wiley: New York, 1981; pp 193–217.

Initially, we prepared the mono-S-alkylated ema ligands in the form H_3emaR and H_2ema(R)(Bz). Dissolution of these ligands in aqueous base gave the corresponding thiolate anion (H_2emaR$^-$) and subsequent reaction by addition of $(Bu_4N)[TcOCl_4]$ or $Na[TcO(eg)_2]$ to this solution resulted in the formation of brown insoluble products that showed no evidence for a TcO stretch in IR spectra of the products. FAB$^+$ mass spectra were complicated and showed peaks assigned as monomeric and dimeric fragments of metal complexes of the ligand. There was no ESR signal observed between room temperature and −78 °C.

The reaction was also performed in the reverse manner by addition of stoichiometric amounts of the ligands, H_3emaR and H_2ema(R)(Bz), to $Na[TcO(eg)_2]$ dissolved in methanol and aqueous NaOH. This resulted in the formation of dark solutions from which moderate yields of bright red-orange complexes could be isolated. These complexes were characterized and formulated as the desired neutral complexes [TcO(emaR)]. Subsequent reaction of these neutral complexes with added equivalents of ligand or other organic thiols gave insoluble products similar to those described above. In addition, the neutral complexes also reacted readily with other reducing agents, such as $SnCl_2$ and $Na_2S_2O_4$, to give products that do not exhibit a TcO stretch in the IR. We believe that these insoluble compounds formed from reactions of the metal with an excess ligand are lower oxidation state complexes of technetium, resulting from reduction of the metal complex by the thiolate group of the ligand.

To prevent this type of reductive decomposition of the metal center in preparations where an excess of a thiol-containing ligand might be necessary, we utilized chemistry studied previously[22] for the preparation of the neutral dimeric complex $[Tc_2O_2(edt)_3]$ (edt = ethanedithiolato). This complex could be prepared by a reaction of 2 mol of $(Bu_4N)[TcOCl_4]$ with 3 mol of ethanedithiol. Addition of excess ethanedithiol in acetone at room temperature yielded the anionic monomeric complex $[TcO(edt)]^-$.[23] Alternatively, the neutral complex could be prepared by ligand exchange of $(Bu_4N)[TcOCl_4]$ with the di-S-protected ligand, $(Acm)_2$edt; however, in this case, an excess of the ligand did not cause the formation of the anionic monomer. This reaction was significant and provided a means of masking the thiolate moiety.

We then prepared the Acm-protected as well as the Bzm-protected chelates, H_2ema(R)(Acm) and H_2ema(R)(Bzm), in hopes that this modification would prevent the neutral metal complex from further reacting with the excess ligand in solution. As we had already devised methods for the preparation of the Tr-protected derivatives of these ligands during the course of this work, it was convenient to develop a method that would allow a facile "swapping" of the Tr-protecting group for an Acm or Bzm group, so that it was not necessary to do a two-step deprotection and reprotection of the thiol. Taking advantage of the equilibrium established upon dissolution of the Tr-protected ligand in acid, giving the thiol and the red-orange Tr^+ cation,[24] and the usual method for the preparation of Acm- and Bzm-protected thiols,[14,15,21] we added a stoichiometric amount of AcmOH or BzmOH to a solution of the Tr-protected derivative in concentrated trifluoroacetic acid. This gave the corresponding protected Acm-SR and Bzm-SR derivatives in good yield. The reaction of the thiol with the stabilized *N*-methyleneacetamide cation is stoichiometric and drives the reaction to completion.



(1)

As these amidomethyl-protected compounds are stable to hydrolysis and aerial oxidation, isolation and storage was significantly easier than for the thiol- or benzoyl-protected ligands. In addition, because these derivatives very effectively masked the thiolate and allowed the isolation of the desired neutral complexes, [TcO(emaR)], from reactions containing an excess of the protected ligand, they became the ligands of choice for the subsequent complexation chemistry.

Complexation. Whereas the previously isolated anionic amide–thiol complex $(AsPh_4)[TcO(ema)]$ could be prepared directly from pertechnetate and a reducing agent,[8] the mono-S-alkylated ligands H_3emaR, H_2emaR(Bz), H_2emaR(Acm), or H_2emaR(Bzm) did not form neutral chelate complexes under these conditions. As $TcO_2 \cdot xH_2O$ was the sole product of the reaction, the lack of formation of the desired neutral complexes was most likely due to the poorer donor quality of the thioether groups on the ligands and not due to decomposition of the neutral chelated complex by the reducing agent, which would have lead to products that contain both the metal and the ligand.

These chelates underwent ligand exchange with complexes such as $(Bu_4N)[TcOCl_4]$ and $Na[TcO(eg)_2]$, and in the cases where the ligand contained the side-chain groups methyl (**7**), 10-undecanoic acid (undec) (**8**), 2-morpholinoethyl (morph) (**9**), and benzyl (Bzl) (**13**), neutral complexes were formed. The products were isolated by evaporation of the solvent, chromatography over silica, and recrystallization. These complexes are red-orange air-stable solids, which are soluble in polar organic solvents and have been characterized by analysis, conductivity, IR, UV-visible, ^{1}H NMR, and ^{13}C NMR spectroscopy and $^+$FAB mass spectrometry. All data are consistent with the formulations of neutral complexes.

Characterization. Infrared spectra of the neutral complexes [TcO(emaR)] (**R** = Me (**14**), undec (**15**), morph (**16**), Bzl (**17**)) show strong absorptions corresponding to the TcO stretch in the range 949–960 cm^{-1}. These are within the accepted range, 860–970 cm^{-1}, for five-coordinate oxotechnetium(V) complexes and are shifted slightly to higher energy than that for the corresponding anion, $(AsPh_4)[TcO(ema)]$, which is found at 945 cm^{-1}. This difference might be attributable to the greater polarizability of the dithiolate ligand and a corresponding charge buildup in the anionic complex. This would cause a weakening of the metal–oxo bond with a resultant lower energy TcO stretching frequency in the IR spectrum of this complex. The broad amide NH bands at 3300 cm^{-1} found in the free ligands are not seen in the spectra of the neutral complexes, indicating that the amide groups are deprotonated and coordinated. Furthermore, there is a concomitant shift in the amide CO band from 1640 cm^{-1} for the free ligand to around 1620 cm^{-1} for the neutral complexes. This lowering in the amide carbonyl stretching frequency indicates that the nitrogen lone pair is strongly associated with the carbonyl moiety and might only be weakly involved in π-bonding to the metal atom.

The ^{1}H NMR ($CDCl_3$) spectra of these complexes show the resonances characteristic of the $OTcN_2S_2$ chelates. The square-pyramidal oxotechnetium core causes the $COCH_2S$ methylene units to be diastereotopic, and as result, these groups appeared in ^{1}H NMR spectra as AB quartets at δ 3.40–3.97 (methylene adjacent to the thioether) and 4.02–4.18 (methylene adjacent to the thiolate) with a geminal coupling constant of J_{AB} = 14–17 Hz. In addition, a set of four complex multiplets of equal intensity are observed at δ 3.50–3.60, 3.80–3.85, 4.14–4.20, and 5.10–5.16. These are assigned to the NCH_2CH_2N portion of the ligand and suggest a twisted conformation of the TcNCCN five-membered ring, a feature that is observed in the crystal structure of $[TcO(ema(morph))] \cdot H_2O$ (**16**). The remainder of the spectra for each of the complexes consists of one set of resonances assignable to the alkyl and/or aryl portions of the side chain.

It might be expected that the prochiral nature of the thioether would lead to diastereomers in which the alkyl side chain could be syn or anti with respect to the oxo ligand. However, for all of the neutral complexes isolated ^{1}H and ^{13}C NMR spectra showed

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only a single set of resonances assignable to the alkyl side chains. Diastereomers have been characterized in other systems for thioether complexes of Pt,[25,26] Re, Ru, and W,[27] and as variable temperature has previously been used as a probe to induce and/or detect fluxionality arising from inversion of a coordinated thioether,[28] ^{1}H NMR spectra of [TcO(ema(Me))] (**14**) were recorded on a 250-MHz Bruker NMR spectrometer between −60 and 125 °C and the resonance at 2.52 ppm (SCH_3) was monitored. None of the spectra showed any evidence of broadening of the signal in the range of temperature mentioned and we believe that this suggests the presence of only one isomer with a high barrier to inversion and that this isomer is the sterically favored anti isomer. In order to confirm our assignment and as subsequent chemistry of the alkylamino complexes warranted, single crystals of [TcO(ema(morph))]·H_2O (**16**) were grown for X-ray diffraction (see Crystallography section below).

The $^{13}C\{^1H\}$ NMR spectra were unambiguous and showed chelate backbone resonances at δ 38.5 and 41.5 for the thiolate and thioether methylene units and δ 54.7 and 56.5 for the ethylene portion. The amide carbonyl carbons were found at δ 180.4 and 184.3. The methyl group for [TcO(emaMe)] (**14**) appeared as a single resonance at δ 24.75. With this value as a reference and by the use of ^{13}C chemical shift addition tables, the resonances for the alkyl and aryl groups for the other neutral complexes were readily assigned.

Further characterization was provided by FAB^+ mass spectrometry, and spectra of the neutral complexes showed strong molecular ions and ions at double mass, M_2H^+. The double mass ions were interpreted as due to association of a cation/neutral pair, MH^+/M, and not due to dimeric impurities in the sample. This phenomenon has recently been observed in FAB^+ mass spectra of neutral complexes of other metals.[29] Fragmentation of the molecular ion was observed for [TcO(ema(undec))] (**15**) and [TcO(ema(Bzl))] (**17**), and peaks corresponding to loss of the side chain, R, were identified.

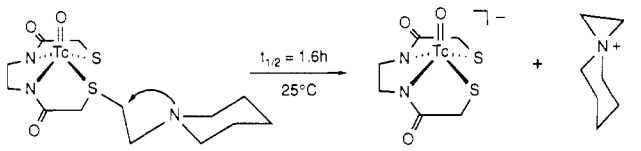
Crystallography. As there are few structurally characterized technetium–thioether complexes and no structurally characterized thioether complexes of technetium(V)[30] and as the dealkylation chemistry warranted a structural confirmation, single crystals of [TcO(ema(morph))]·H_2O (**16**) were prepared. X-ray diffraction revealed a distorted square-pyramidal $OTcN_2S_2$ core with the ethylmorpholine side chain occupying the least sterically hindered position, anti with respect to the oxo ligand.

The Tc–N(amide) bond distances of 1.975 (4) and 1.989 (4) Å are close to those observed for similar complexes.[30] The Tc–S distances are also within the ranges of typical M–S bond lengths, and as expected, the weaker Tc–S(thioether) bond (2.387 (1) Å) is 0.13 Å longer than the Tc–S(thiolate) bond (2.257 (1) Å). The C6–S_2–C7 angle about the thioether ligand is 104.0 (3)° and is consistent with sp^3 hybridization at the sulfur atom. The Tc–O bond distance of 1.658 (3) Å is shorter than that for the [TcO(ema)]$^-$ anion, which is 1.679 (5) Å, consistent with the increased Tc–O stretching frequency observed in the IR spectra of **16**. Other distances and angles about the molecule are unexceptional.

Dealkylation. The (dialkylamino)ethyl-derivatized ligands H_2emaR(Bzm), where R = $CH_2CH_2NMe_2$ (dma) (**12**) and $CH_2CH_2(NC_4H_8)$(pyr) (**11**), show a somewhat more complicated coordination chemistry with technetium(V), giving upon reaction with $(Bu_4N)[TcOCl_4]$ or $Na[TcO(eg)_2]$ the dealkylated anionic complex, [TcO(ema)]$^-$. Addition of the ligands H_2emaR(Bzm), where R = dma (**12**) or pyr (**11**), to a solution of the metal starting material at room temperature gave a bright yellow solution. Addition of $AsPh_4Cl$ to the reaction mixture precipitated [TcO(ema)]$^-$, which was the sole product of the reaction. No intermediates were observed.

When the ligand was H_2ema(pip)(Bzm) (**10**) and the reaction was performed at or below room temperature, a dark red solution persisted. This solution was quickly filtered through diatomaceous earth to remove polar impurities and evaporated to give a red oil, which was characterized by IR and UV–visible spectroscopy and FAB^+ mass spectrometry. The IR spectrum of the crude product showed a TcO stretch at 961 cm^{-1}, electronic spectra showed a band at 512 nm, and FAB^+ mass spectra showed ions corresponding to H[TcO(ema(pip))]$^+$, H_2[TcO(ema)]$^+$, and [TcO(ema)]$^+$. All of these data are consistent with the presence of [TcO(ema(pip))] in this impure mixture. This neutral product was not stable in solution at room temperature and slowly decomposed to cleanly give [TcO(ema)]$^-$. We monitored this reaction spectroscopically and obtained a first-order rate constant (k_1(22 °C) = 1.2 × 10^{-4} s^{-1}) for the conversion.

The formation of [TcO(ema)]$^-$ from reactions of the H_2ema($CH_2CH_2NR_2$)(Bzm) ligands with technetium(V) suggests that dealkylation must be occurring subsequent to complexation of the thioether by a mechanism that involves nucleophilic attack of the pendant amine functionality.



(2)

Nucleophilic attack at the carbon adjacent to a coordinated thioether is a fairly well-documented reaction, and there are examples for a variety of different metals and thioether ligands.[31] In fact, recently, Roundhill and co-workers measured the kinetics of dealkylation of a Pt(II) complex of *o*-(diphenylphosphino)-thiophenetole with a series of primary, secondary, and tertiary amines.[32] The kinetics suggested that the thioether group is polarized such that the metal thiolate complex becomes a good leaving group. Attack of the amine nucleophile at the α-carbon then results in the formation of the corresponding alkylated amine and the metal–thiolate complex.

Because the rate of dealkylation has been shown to increase with the oxidation state of the metal[33] and because the amino group on the ligands, presented in this study, are positioned such that entropic factors would favor the formation of the three-membered aziridinium ring, we have created a situation where dealkylation would be expected to occur and that the reaction might be quite fast for more nucleophilic amines. The rate of dealkylation is slowed by choice of a weaker and consequently less nucleophilic base, such as *N*-ethylmorpholine (pK_a = 7.13), such that the complex [TcO(ema(morph))] (**16**) is stable indefinitely in refluxing organic solutions.

On further examination of the reactivity of the other neutral complexes, [TcO(emaR)], where R = Me (**14**), and Bzl (**17**), we observed that dealkylation occurred in these systems as well. In fact, for [TcO(ema(Bzl))] (**17**), where it is already known that the benzyl groups is "activated" toward nucleophilic displacement at the methylene carbon, dealkylation occurred readily at room temperature with amines, halides, and water. Attempts to quantitate the kinetics of these reactions were complicated by the presence of new species possibly arising from coordination of the nucleophile to the metal, a problem that has been observed by Roundhill when studying the dealkylation of Pd(II) complexes of thioethers.[34]

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Conclusions

The neutral complexes [TcO(emaR)] show some very interesting features of the chemistry of technetium(V) that may be useful for the rational design of radiopharmaceutical tracers. In nuclear medicine one of the more important factors in the selection of a radiotracer is the efficiency with which it is "trapped" in a specific region of the body. The complexes prepared in this study display two mechanisms by which this might be realized, namely, reduction and dealkylation.

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Supplementary Material Available: Tables of anisotropic thermal parameters, bond distances, and bond angles (3 pages); a table of structure factors (13 pages). Ordering information is given on any current masthead page.

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Low-Temperature Synthesis of the Fluorite Modification of Lanthanoid(II) Chlorides

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Fluorite-type MCl_2 phases for M = Sm and Eu, previously reported to be stable only at elevated temperatures, have been prepared at room temperature by solvolytic decomposition reactions on mixed-valence lanthanoid chloride phases. The metastable character of these phases, which is evidenced by the transformation they undergo upon heating, and the synthesis and characterization of the mixed-valence phases $Sm_{14}Cl_{33}$, $Sm_9Gd_5Cl_{33}$, and $Sm_9Nd_5Cl_{33}$ are reported. Previously reported Sm_3Cl_7 is found to be $Sm_{14}Cl_{33}$. Lattice parameters and a probable space group for $YbCl_2$·THF are reported.

Introduction

It has long been known that by solvolytic decomposition (leaching) high oxidation state oxides can be synthesized from mixed-valence oxides.[1-5] For example, insoluble PrO_2 was prepared by selectively dissolving the Pr^{3+} ions from "Pr_6O_{11}" according to (1).[1,2] We wondered if lower valent compounds could

$$Pr_{12}O_{22}(s) + 12H^+(aq) = 4Pr^{3+}(aq) + 6H_2O + 8PrO_2(s) \quad (1)$$

be prepared by a comparable reaction in which the higher valent species was solvated preferentially. Crystal lattice energy considerations suggest that, for a given cation, salts with large, monovalent anions should dissociate more easily than salts in which the anion has a higher charge.[6] Hence heavy-metal mixed-valence chlorides, bromides, and iodides appeared to be a profitable area in which to initiate research. In the last decade numerous mixed-valence lanthanoid halide phases have been characterized. Examples include the vernier-type structures of the general formula M_nX_{2n+1} (M = lanthanoid; X = Cl, Br; n = 4–6)[7-10] and the $M_{14}X_{33}$ cluster-type compound.[9,10] Lanthanoid(III) chlorides are known to be soluble in tetrahydrofuran (THF); solubilities range from 0.5 to 1.9 g/100 mL of THF.[11] The dichlorides of samarium and europium are reported to be sparingly soluble in THF. They can be produced in THF by lithium metal/naphthalene reduction of the trichlorides. For Ln = Sm and Eu, the $LnCl_2$ phases are solvent-free, whereas for Ln = Yb, a solvate, $YbCl_2$·THF results.[12] We therefore investigated solvolytic decomposition reactions of lanthanoid chloride systems. Our primary goal was synthesis of $LnCl_2$ according to (2). An unexpected but interesting result

$$Ln^{II}_xLn^{III}_yCl_{2x+3y}(s) + ym\text{THF} = xLnCl_2(s) + yLnCl_3{\cdot}m(\text{THF}) \quad (2)$$

was the preparation at room temperature of the fluorite-type modification of $SmCl_2$ and $EuCl_2$. This modification had been reported previously to exist only at elevated temperatures. The low-temperature synthesis of this fluorite-type modification is presented and discussed.

Experimental Section

Chemical Reagents. Eu_2O_3 and Yb_2O_3: 99.99%, Research Chemicals, Phoenix, AZ. Sm_2O_3: 99.9%, Alfa Inorganics, Inc., Beverly, MA. Gd_2O_3: 99.9%, Michigan Chemical Corp., principal impurity of 500 ppm Ca. THF: "Baker Analyzed" reagent, J. T. Baker Chemical Co., Phillipsburg, NJ, was refluxed over sodium metal chips (benzophenone as indicator), distilled, and deoxygenated repeatedly prior to use by first

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