Bis(ligand) Rhenium(V) and Technetium(V) Complexes of Two Naturally Occurring Binding Moieties (Oxazoline and Thiazoline)

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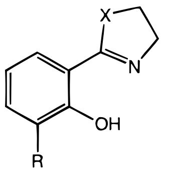
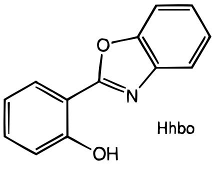
Attempts to prepare tris(ligand) metal complexes of technetium in intermediate oxidation states with potentially bidentate oxazoline- and thiazoline-containing ligands were unsuccessful; when pertechnetate was reduced in the presence of excess ligand, $TcO_2 \cdot xH_2O$ was produced. Instead, by reaction with preformed M•O cores, a series of oxotechnetium(V) and oxorhenium(V) complexes of the formula $MOXL_2$ (M = Re, X = Br; M = Tc, X = Cl) and HL = 2-(2′-hydroxyphenyl)-2-oxazoline (Hoz), 2-(2′-hydroxy-3′-methylphenyl)-2-oxazoline (Hmoz), 2-(2′-hydroxyphenyl)-2-thiazoline (Hthoz), and 2-(2′-hydroxyphenyl)-2-benzoxazoline (Hhbo) have been prepared. These compounds have been characterized by a variety of techniques including single-crystal X-ray diffraction. Crystals of Hthoz (C_9H_9NOS) are monoclinic, with space group $P2_1/n$, $a = 7.5342(6)$ Å, $b = 12.2187(6)$ Å, $c = 9.3942(8)$ Å, $\beta = 94.233(7)°$, and $Z = 4$; those of $TcOCl(thoz)_2$ ($C_{18}H_{16}ClN_2O_3S_2Tc$) are monoclinic, with space group $P2_1/n$, $a = 16.506(1)$ Å, $b = 7.664(1)$ Å, $c = 16.3216(6)$ Å, $\beta = 111.154(4)°$, and $Z = 4$; those of $ReOBr(oz)_2$ ($C_{18}H_{16}BrN_2O_5Re$) are orthorhombic, with space group *Pbca*, $a = 12.864(2)$ Å, $b = 25.369(2)$ Å, $c = 11.025(2)$ Å, and $Z = 8$. The structures were solved by direct (Hthoz) or Patterson (metal complexes) methods and were refined by full-matrix least-squares procedures to $R = 0.033$, 0.032, and 0.028 for 1600, 3152, and 2651 reflections with $I \geq 3\sigma(I)$, respectively. In the two complexes, the geometry around the metals is distorted octahedral with the halide ligands in each bound *cis*, and one phenolate oxygen from one ligand in each bound *trans* to the metal−oxo linkage. In $ReOBr(oz)_2$, the two oxazoline nitrogens are coordinated *trans* to one another; in $TcOCl(thoz)_2$, the two thiazoline nitrogens are found *cis* to one another.

Introduction

The application of technetium and rhenium radioisotopes in diagnostic and therapeutic nuclear medicine (^{186}Re, ^{188}Re, and especially ^{99m}Tc) has spawned a widespread interest in the coordination chemistry of these elements. Integral factors that are considered prior to the synthesis of a metal complex for use as a radiopharmaceutical are the polarity and lipophilicity of the ligand and the resulting metal complex, as well as overall complex charge. All these factors in part determine biodistribution properties of the radiopharmaceutical,[1,2] as is evinced by the fact that many lipophilic monocationic ^{99m}Tc complexes localize in heart muscle, and some neutral complexes accumulate in the brain.



	X	R
Hoz	O	H
Hthoz	S	H
Hmoz	O	CH_3



Hhbo

As part of a project to study metal complexes of naturally occurring chelators, bidentate ligands containing some of the less common binding moieties found in siderophores (microbial iron scavengers) are reported herein to form bis(ligand) complexes with rhenium and technetium. The affinity of siderophores for Fe(III) is predicated by chelating groups such as catecholates and hydroxamates and, to a lesser extent, derivatives of 2-(2′-hydroxyphenyl)-2-oxazoline (Hoz). 2-(2′-Hydroxyphenyl)-2-thiazoline (Hthoz) is found in *S*(−)-desferrithiocin and also forms stable iron(III) complexes.[3] Hoz and 2-(2′-hydroxy-3′-methylphenyl-2-oxazoline (Hmoz) contain a binding moiety found in the siderophores mycobactin and agrobactin.[4] While not found in siderophores, 2-(2′-hydroxyphenyl)benzoxazoline (Hhbo) is a more lipophilic and sterically demanding analog whose group 13 complexes have recently been reported by our laboratory.[5] The synthesis and characterization of tris(ligand) Al, Ga, and In complexes of the oxazoline-containing ligands have also been reported recently.[6] Bis(ligand) complexes of rhenium and technetium with bidentate Schiff base ligands[7,8] and mono- and bis(2-(2′-hydroxyphenyl)-2-benzothiazolinato) complexes of Re(V) and Tc(V) have been reported,[9,10] as have Co, Ni, and Zn bis(ligand) metal(II) complexes of Hoz.[11] The crystal structure of agrobactin was reported in 1980.[4]

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Experimental Section

Materials and Methods. All chemicals were reagent grade and were used as received. $[(n\text{-Bu})_4N][ReOBr_4]$[12] and $[(n\text{-Bu})_4N][TcOCl_4]$[13] were prepared from NH_4ReO_4 (a gift from Johnson Matthey, Inc.) and NH_4TcO_4 (a gift from the Du Pont Merck Pharmaceutical Company), respectively. The ligands 2-(2′-hydroxyphenyl)-2-oxazoline (Hoz) and 2-(2′-hydroxy-3′-methylphenyl)-2-oxazoline (Hmoz) were prepared as previously reported.[6] 2-(2′-Hydroxyphenyl)-2-benzoxazole (Hhbo) was obtained from Aldrich.

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

Instrumentation. NMR spectra were recorded on either a Bruker AC-200E or a Bruker WH-400 instrument. ^{1}H NMR data are reported as ppm downfield from an external TMS reference. Infrared spectra were recorded as KBr disks in the range 4000−400 cm^{-1} on a Perkin-Elmer 783 spectrophotometer with polystyrene as a reference. Mass spectra (Cs$^+$ LSIMS) were obtained on a Kratos Concept II H32Q instrument with 3-nitrobenzyl alcohol or thioglycerol as the matrix. Expected isotope ratios were observed for all Br-, Re-, and/or S-containing compounds; only the most intense peak in a given isotope pattern is reported. Melting points were recorded on a Mel-Temp apparatus and are uncorrected. Elemental analyses were performed by Mr. P. Borda using an in-house Carlo Erba instrument, except for the ^{99}Tc complexes, which were sent to Canadian Microanalytical Services Ltd., Delta, British Columbia.

2-(2′-Hydroxyphenyl)-2-thiazoline (Hthoz). To a solution of 2-cyanophenol (1.00 g, 8.39 mmol) in 30 mL of methanol was added 2-aminoethanethiol hydrochloride (1.91 g, 16.8 mmol) and Et_3N (1.87 g, 18.5 mmol). The resulting solution was refluxed for 5 h under N_2. The methanol was then removed under reduced pressure, and the residue obtained was redissolved in 60 mL of diethyl ether. Filtration of the triethylammonium chloride precipitate, removal of Et_2O, and column chromatography on silica gel of the residue thus obtained (eluant: 10% Et_2O in pentane, $R_f = 0.78$) furnished Hthoz (0.80 g, 53%) as a yellow crystalline solid, mp 44−46 °C. Crystals suitable for X-ray analysis were obtained by slow recrystallization from a Et_2O/pentane (1:9) solution. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.44 (t, 2H, $J = 8$ Hz), 4.60 (t, 2H, $J = 8$ Hz), 6.90−6.99 (m, 2H), 7.37−7.44 (m, 2H), 12.6 (s, 1H, O*H*). IR: 3400−2600 (br, ν_{OH}), 1623 (s, $\nu_{C=N}$), 1590 ($\nu_{C=C}$), 1570 ($\nu_{C=C}$), 1490 ($\nu_{C=C}$), 1450, 1405, 1318, 1310, 1220, 1150, 1120, 1010, 930, 805, 755 cm^{-1}. Exact mass calcd (Found): 179.0405 (179.0405). Anal. Calcd (found) for C_9H_9NOS: C, 60.31 (60.33); H, 5.06 (5.03); N, 7.81 (7.76).

Bromobis[2-(2′-hydroxyphenyl)-2-oxazolinato]oxorhenium(V), $ReOBr(oz)_2\cdot H_2O$. To a solution of $[(n\text{-Bu})_4N][ReOBr_4]$ (150 mg, 0.20 mmol) in 30 mL of ethanol was added Hoz (0.131 g, 0.80 mmol); the solution turned a dark green color. After 1 h at reflux, the solution was allowed to cool to room temperature. Slow evaporation of ethanol led to the precipitation of green needles of the monohydrate; these were isolated by filtration, washed with 5 mL of ether, and dried *in vacuo*, yield 0.045 g (37%). X-ray quality crystals were obtained by recrystallization from CH_2Cl_2/pentane. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.78−4.48 (m, 4H), 4.73−5.26 (m, 4H), 6.8−8.1 (m, 8H). IR: 1625 ($\nu_{C=N}$), 1610 ($\nu_{C=C}$), 1585 ($\nu_{C=C}$), 1485 ($\nu_{C=C}$), 1400, 1260, 1240, 1090, 970 ($\nu_{Re=O}$), 860, 755 cm^{-1}. EIMS: $m/z = 527$ (MOL_2^+), 606 ($MOBrL_2^+$). Anal. Calcd (found) for $C_{18}H_{18}BrN_2O_6Re$: C, 34.62 (34.51); H, 2.91 (2.80); N, 4.49 (4.37); Br, 12.8 (12.6).

Bromobis[2-(2′-hydroxyphenyl)-2-thiazolinato]oxorhenium(V), $ReOBr(thoz)_2$. To 25 mL of ethanol was added $[(n\text{-Bu})_4N][ReOBr_4]$ (150 mg, 0.20 mmol). Upon dissolution to form an orange-yellow solution, Hthoz (0.075 g, 0.42 mmol) was added, and the solution turned a dark green color. Slow evaporation of solvent yielded green needles (0.072 g, 57%). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 3.8−4.10 (m, 4H) 4.18−4.62 (m, 4H) 6.35−7.90 (series of overlapping m, 8H). IR: 1600 ($\nu_{C=N}$), 1570 ($\nu_{C=C}$), 1540 ($\nu_{C=C}$), 1470 ($\nu_{C=C}$), 1320, 1240, 1225, 1045, 960 ($\nu_{Re=O}$), 850, 765 cm^{-1}. EIMS: $m/z = 559$ (MOL_2^+), 638 ($MOBrL_2^+$). Anal. Calcd (found) for $C_{18}H_{16}BrN_2O_3ReS_2$: C, 33.86 (33.69); H, 2.53 (2.68); N, 4.39 (4.44); Br, 12.51 (12.33).

Bromobis[2-(2′-hydroxy-3′-methylphenyl)-2-oxazolinato]oxorhenium(V), $ReOBr(moz)_2$. To $[(n\text{-Bu})_4N][ReOBr_4]$ (153 mg, 0.20 mmol) in 20 mL of 1:1 $CHCl_3$/MeOH was added 2.1 equiv of Hmoz (0.075 g, 0.42 mmol). Following brief stirring, the green solution was refluxed overnight and then allowed to cool to room temperature. After slow evaporation of the solvent, a light green precipitate was isolated, washed with 10 mL of Et_2O, and dried *in vacuo* for 24 h to yield 56 mg (46%) $ReOBr(moz)_2$. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.94 (s, 3H), 2.11 (s, 3H), 4.30 (t, 2H), 4.80−5.10 (m, 6H), 6.69 (t, 1H, $J = 9$ Hz), 6.86 (t, 1H, $J = 9$ Hz), 7.10 (d, 1H, $J = 8$ Hz), 7.28 (m, 1H, $J = 8$ Hz), 7.53 (d, 1H, $J = 8$ Hz), 7.76 (dd, 1H, $J = 8$ Hz). IR: 1625 ($\nu_{C=N}$), 1605 ($\nu_{C=C}$), 1595 ($\nu_{C=C}$), 1555 ($\nu_{C=C}$), 1435, 1400, 1265, 1230, 1185, 975 ($\nu_{Re=O}$), 755 cm^{-1}. EIMS: $m/z = 555$ (MOL_2^+), 634 ($MOBrL_2^+$). Anal. Calcd (found) for $C_{20}H_{20}BrN_2O_5Re$: C, 37.86 (38.11); H, 3.18 (3.32); N, 4.42 (4.65); Br, 12.59 (12.73).

Bromobis[2-(2′-hydroxyphenyl)benzoxazolinato]oxorhenium(V), $ReOBr(hbo)_2$. This compound was prepared in a procedure analogous to that for $ReOBr(oz)_2$ using $[(n\text{-Bu})_4N][ReOBr_4]$ (150 mg, 0.20 mmol) and Hhbo (86 mg, 0.41 mmol) to yield 79 mg (56%). ^{1}H NMR (DMSO-d_6, 400 MHz): δ 6.3−8.3 (series of overlapping m). IR: 1610 ($\nu_{C=N}$), 1565 ($\nu_{C=C}$), 1520 ($\nu_{C=C}$), 1475 ($\nu_{C=C}$), 1430, 1325, 1245, 1165, 970 ($\nu_{Re=O}$), 870, 810, 755 cm^{-1}. EIMS: $m/z = 413$ (MOL^+), 623 (MOL_2^+), 702 ($MOBrL_2^+$). Anal. Calcd (found) for $C_{26}H_{16}BrN_2O_5Re$: C, 44.45 (44.33); H, 2.30 (2.43); N, 3.99 (3.89); Br, 11.37 (11.19).

Chlorobis[2-(2′-hydroxyphenyl)-2-oxazolinato]oxotechnetium(V), $TcOCl(oz)_2$. To $[(n\text{-Bu})_4N][TcOCl_4]$ (80 mg, 0.16 mmol) in 40 mL of methanol was added Hoz (57 mg, 0.35 mmol). The solution, which quickly turned a dark red color, was refluxed overnight. The volume of methanol was reduced to 5 mL by evaporartion under reduced pressure. A crystalline red solid was precipitated by layering hexane above the methanol and storing the solution at 0 °C for a week. Following the removal of hexane, additional product was precipitated by the addition of diethyl ether to the solution. The product was isolated by filtration, washed with ether, and dried *in vacuo* to yield 40 mg (57%). ^{1}H NMR (CD_2Cl_2, 300 MHz): δ 4.4−5.4 (m, 8H), 6.5−8.2 (series of overlapping m, 8H). IR: 1625 ($\nu_{C=N}$), 1605 ($\nu_{C=C}$), 1580, ($\nu_{C=C}$) 1545 ($\nu_{C=C}$), 1410, 1395, 1255, 1240, 1085, 960 ($\nu_{Tc=O}$), 945, 860 cm^{-1}. LSIMS: $m/z = 439$ (MOL_2^+). Anal. Calcd (found) for $C_{18}H_{16}ClN_2O_5Tc$: C, 45.54 (45.67); H, 3.40 (3.61); N, 5.90 (5.84).

Chlorobis[2-(2′-hydroxyphenyl)-2-thiazolinato]oxotechnetium(V), $TcOCl(thoz)_2\cdot 0.5EtOH$. In 20 mL of ethanol, dried over 4 Å molecular sieves, was mixed $[(n\text{-Bu})_4N][TcOCl_4]$ (50 mg, 0.10 mmol) and Hthoz (38 mg, 0.21 mmol). Refluxing the dark red solution for 24 h and then cooling yielded a red precipitate that was isolated, washed with diethyl ether, and dried *in vacuo* for 18 h to yield 50 mg (72%). IR: 1600 ($\nu_{C=N}$), 1575 ($\nu_{C=C}$), 1555 ($\nu_{C=C}$), 1540 ($\nu_{C=C}$), 1525 ($\nu_{C=C}$), 1225, 1045, 970 ($\nu_{Tc=O}$), 935, 835 cm^{-1}. LSIMS: $m/z = 471$ (MOL_2^+) 506 ($MOClL_2^+$). Anal. Calcd (found) for $C_{19}H_{19}ClN_2O_{3.5}TcS_2$: C, 43.07 (42.89); H, 3.61 (3.93); N, 5.29 (5.20).

Chlorobis[2-(2′-hydroxy-3′-methylphenyl)-2-oxazolinato]oxotechnetium(V), $TcOCl(moz)_2\cdot 0.5H_2O$. A solution (15 mL) of $[(n\text{-Bu})_4N][TcOCl_4]$ (75 mg, 0.15 mmol) and Hmoz (56 mg, 0.31 mmol) in methanol (15 mL) was refluxed for 24 h. Red crystals were isolated by filtration, washed with diethyl ether, and dried *in vacuo* to yield 50 mg (65%). IR: 1630 ($\nu_{C=N}$), 1605 ($\nu_{C=C}$) 1585 ($\nu_{C=C}$), 1555 ($\nu_{C=C}$), 1425, 1395, 950 ($\nu_{Tc=O}$), 755 cm^{-1}. LSIMS: $m/z = 467$ (MOL_2^+). Anal. Calcd (found) for $C_{20}H_{21}ClN_2O_{5.5}Tc$: C, 46.94 (46.76); H, 4.14 (3.94); N, 5.47 (5.48).

Chlorobis[2-(2′-hydroxyphenyl)benzoxazolinato]oxotechnetium(V), $TcOCl(hbo)_2\cdot 1.5H_2O$. With $[(n\text{-Bu})_4N][TcOCl_4]$ (60 mg, 0.12 mmol) and Hhbo (54 mg, 0.26 mmol) mixed in 10 mL of methanol, a red product was isolated in a manner identical to that for $TcOCl(thoz)_2$ (yield 50 mg, 72%). ^{1}H NMR ($CDCl_3$, 200MHz): δ 6.2−8.3 (series of m). IR: 1600 ($\nu_{C=N}$), 1530, 1470, 1240, 945 ($\nu_{Tc=O}$), 650 cm^{-1}. LSIMS: $m/z = 325$ (MOL^+), 535 (MOL_2^+), 570 ($MOClL_2^+$). Anal. Calcd (found) for $C_{26}H_{19}ClN_2O_{6.5}Tc$: C, 52.24 (52.23); H, 3.20 (2.80); N, 4.68 (4.77).

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Table 1. Selected Crystallographic Data for the Three Compounds

	Hthoz	$TcOCl(thoz)_2$	$ReOBr(oz)_2$
formula	C_9H_9NOS	$C_{18}H_{16}ClN_2O_3S_2Tc$	$C_{18}H_{16}BrN_2O_5Re$
fw	179.24	504.91	606.45
crystal system	monoclinic	monoclinic	orthorhombic
space group	$P2_1/n$	$P2_1/n$	Pbca
a, Å	7.5342(6)	16.506(1)	12.864(2)
b, Å	12.2187(6)	7.664(1)	25.369(2)
c, Å	9.3942(8)	16.3216(6)	11.025(2)
β, deg	94.233(7)	111.154(4)	90
V, Å^3	862.5(1)	1925.5(3)	3598.1(9)
Z	4	4	8
$\rho_{calc,}$ g/cm^3	1.380	1.742	2.239
T, °C	21	21	21
radiation	Cu	Cu	Mo
λ, Å	1.54178	1.54178	0.71069
μ, cm^{-1}	28.51	95.61	90.78
transm factors	0.81−1.00	0.45−1.00	0.66−1.00
$R(F)$	0.033	0.032	0.028
$R_w(F)$	0.040	0.041	0.024

X-ray Crystallographic Analyses of Hthoz, $TcOCl(thoz)_2$, and $ReOBr(oz)_2$. Selected crystallographic data for the three compounds appear in Table 1. The final unit-cell parameters were obtained by least-squares procedures on the setting angles for 25 reflections with $2\theta = 85.0-106.6°$ for Hthoz, 82.3−103.1° for $TcOCl(thoz)_2$, and 35.7−38.9° for $ReOBr(oz)_2$. The intensities of three standard reflections, measured every 200 reflections throughout the data collections, decayed uniformly by 4.9% for Hthoz and remained constant for the two metal complexes. The data were processed[14] and corrected for Lorentz and polarization effects, decay (for Hthoz), and absorption (empirical, based on azimuthal scans for three reflections).

The structure of Hthoz was solved by direct methods, and those of the two metal complexes were solved by conventional heavy atom methods, the coordinates of the heavy atoms being determined from the Patterson functions and those of the remaining non-hydrogen atoms from subsequent difference Fourier syntheses. All non-hydrogen atoms were refined with anisotropic thermal parameters. The hydrogen atoms of Hthoz were refined with isotropic thermal parameters and those of the metal complexes were fixed in calculated positions (C−H = 0.98 Å, $B_H = 1.2B_{\text{bonded atom}}$). Secondary extinction corrections were applied in all three cases, the final values of the extinction coefficient being $1.30(6) \times 10^{-4}$, $7.57(13) \times 10^{-6}$, and $5.6(2) \times 10^{-8}$, respectively, for Hthoz, $TcOCl(thoz)_2$, and $ReOBr(oz)_2$. Neutral-atom-scattering factors for all atoms and anomalous dispersion corrections for the nonhydrogen atoms were taken from the *International Tables for X-Ray Crystallography*.[15,16] Final atomic coordinates and equivalent isotropic thermal parameters for the three structures appear in the supporting information. Selected bond lengths and bond angles for each of the three structures appear in Tables 2−4, respectively. Complete tables of crystallographic data, final atomic coordinates and isotropic thermal parameters, bond lengths, bond angles, hydrogen atom parameters, anisotropic thermal parameters, torsion angles, and least squares planes are included as supporting information (see Supporting Information section at the end of this paper).

Results and Discussion

2-(2′-Hydroxyphenyl)-2-thiazoline. The synthesis of Hthoz was effected by analogy to, and improvement of, a literature procedure.[17] In a single-step preparation, refluxing 2-cyanophenol with 2-aminoethanethiol (free-based *in situ* with 1.1 equiv of Et_3N) in methanol under N_2, followed by experimental workup, resulted in a modest (53%) yield of the desired product.

Table 2. Bond Lengths (Å) and Angles (deg) in Hthoz

Bond Lengths			
S(1)−C(1)	1.758(2)	C(4)−C(5)	1.409(2)
S(1)−C(3)	1.787(2)	C(4)−C(9)	1.389(2)
O(1)−C(5)	1.349(2)	C(5)−C(6)	1.384(3)
N(1)−C(1)	1.275(2)	C(6)−C(7)	1.376(3)
N(1)−C(2)	1.461(2)	C(7)−C(8)	1.380(3)
C(1)−C(4)	1.465(2)	C(8)−C(9)	1.378(3)
C(2)−C(3)	1.522(3)		
Bond Angles			
C(1)−S(1)−C(3)	90.94(9)	C(5)−C(4)−C(9)	118.4(2)
C(1)−N(1)−C(2)	113.4(1)	O(1)−C(5)−C(4)	122.1(2)
S(1)−C(1)−N(1)	117.2(1)	O(1)−C(5)−C(6)	118.3(1)
S(1)−C(1)−C(4)	120.3(1)	C(4)−C(5)−C(6)	119.6(2)
N(1)−C(1)−C(4)	122.5(1)	C(5)−C(6)−C(7)	120.6(2)
N(1)−C(2)−C(3)	111.0(2)	C(6)−C(7)−C(8)	120.6(2)
S(1)−C(3)−C(2)	107.3(1)	C(7)−C(8)−C(9)	119.3(2)
C(1)−C(4)−C(5)	120.0(1)	C(4)−C(9)−C(8)	121.5(2)
C(1)−C(4)−C(9)	121.5(1)		

Table 3. Selected Bond Lengths (Å) and Angles (deg) in $TcOCl(thoz)_2$

Bond Lengths			
Tc(1)−Cl(1)	2.362(1)	O(1)−C(5)	1.332(4)
Tc(1)−O(3)	1.661(3)	C(4)−C(5)	1.405(6)
Tc(1)−O(1)	1.977(3)	C(1)−C(4)	1.462(6)
Tc(1)−O(2)	1.978(3)	S(2)−C(10)	1.751(4)
Tc(1)−N(1)	2.103(4)	C(10)−N(2)	1.284(5)
Tc(1)−N(2)	2.115(3)	N(2)−C(12)	1.480(5)
S(1)−C(1)	1.747(4)	C(12)−C(11)	1.482(6)
C(1)−N(1)	1.296(5)	C(11)−S(2)	1.790(6)
N(1)−C(3)	1.464(6)	O(2)−C(14)	1.328(4)
C(3)−C(2)	1.471(8)	C(14)−C(13)	1.409(5)
C(2)−S(1)	1.808(6)	C(13)−C(10)	1.464(5)
Bond Angles			
O(3)−Tc(1)−Cl(1)	102.6(1)	Cl(1)−Tc(1)−N(2)	86.2(1)
O(3)−Tc(1)−O(1)	103.0(1)	Tc(1)−O(1)−C(5)	125.6(3)
O(3)−Tc(1)−O(2)	163.7(1)	Tc(1)−N(1)−C(1)	124.4(3)
O(3)−Tc(1)−N(1)	86.5(1)	O(1)−C(5)−C(4)	126.1(4)
O(3)−Tc(1)−N(2)	89.5(1)	C(5)−C(4)−C(1)	123.2(4)
N(1)−Tc(1)−O(1)	89.1(1)	C(4)−C(1)−N(1)	124.8(4)
N(1)−Tc(1)−O(2)	80.4(1)	Tc(1)−O(2)−C(14)	128.5(2)
N(2)−Tc(1)−O(1)	167.0(1)	Tc(1)−N(2)−C(10)	127.8(3)
N(2)−Tc(1)−O(2)	82.2(1)	O(2)−C(14)−C(13)	121.8(3)
Cl(1)−Tc(1)−N(1)	170.88(9)	C(14)−C(13)−C(10)	119.7(3)
Cl(1)−Tc(1)−O(1)	87.58(9)	C(13)−C(10)−N(2)	124.9(3)
Cl(1)−Tc(1)−O(2)	90.94(9)		

The H-bonding of the phenolic OH group to the 2-thiazoline ring nitrogen is evident, in the solid state by IR spectral data and in solution ($CDCl_3$) by ^1H NMR spectroscopy—the OH chemical shift is 12.62 ppm, and the IR spectrum of Hthoz displays a broad ν_{OH} band from 2600 to 3400 cm^{-1}.

Bis(ligand) Complexes. Attempts to prepare tris(ligand) technetium complexes by the addition of 2−5 equiv of a reducing agent (sodium dithionite or sodium bisulfite)[18,19] to a basic aqueous methanol solution containing NH_4TcO_4 and from 3 to 10 equiv of Hthoz were not successful. Over the trials performed, the primary product was invariably the black, insoluble $TcO_2{\cdot}xH_2O$ and no reduced metal−ligand complex was ever isolated.

Combination of 2 equiv of ligand with preformed rhenium or technetium MOX_4^- cores (X = Br and Cl, respectively) led to the synthesis of the neutral $MOXL_2$ compounds. The green rhenium and red technetium compounds formed were all air stable. Elemental analyses for C, H, and N in all samples, and Br for the Re complexes, were consistent with the formulas

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Table 4. Selected Bond Lengths (Å) and Angles (deg) in $ReOBr(oz)_2$

Bond Lengths			
Re(1)−Br(1)	2.5804(7)	O(2)−C(5)	1.346(6)
Re(1)−O(5)	1.681(4)	C(5)−C(4)	1.412(8)
Re(1)−O(2)	1.988(4)	C(4)−C(1)	1.482(8)
Re(1)−O(4)	2.013(4)	O(3)−C(10)	1.329(7)
Re(1)−N(1)	2.098(5)	C(10)−N(2)	1.311(8)
Re(1)−N(2)	2.045(5)	N(2)−C(12)	1.499(7)
O(1)−C(1)	1.337(6)	C(12)−C(11)	1.515(9)
C(1)−N(1)	1.284(7)	C(11)−O(3)	1.460(8)
N(1)−C(3)	1.484(8)	O(4)−C(14)	1.327(6)
C(3)−C(2)	1.514(9)	C(14)−C(13)	1.419(8)
C(2)−O(1)	1.442(8)	C(13)−C(10)	1.437(8)

Bond Angles			
O(5)−Re(1)−Br(1)	90.7(1)	Br(1)−Re(1)−O(4)	169.7(1)
O(5)−Re(1)−O(2)	170.8(2)	Re(1)−O(2)−C(5)	136.7(4)
O(5)−Re(1)−O(4)	98.5(2)	Re(1)−N(1)−C(1)	130.3(5)
O(5)−Re(1)−N(1)	90.9(2)	O(2)−C(5)−C(4)	121.0(6)
O(5)−Re(1)−N(2)	99.5(2)	C(5)−C(4)−C(1)	119.2(5)
N(1)−Re(1)−O(2)	81.5(2)	C(4)−C(1)−N(1)	126.4(6)
N(1)−Re(1)−O(4)	85.9(2)	Re(1)−O(4)−C(14)	127.9(4)
N(2)−Re(1)−O(2)	88.3(2)	Re(1)−N(2)−C(10)	125.4(4)
N(2)−Re(1)−O(4)	90.0(2)	O(4)−C(14)−C(13)	125.3(6)
Br(1)−Re(1)−N(1)	89.3(1)	C(14)−C(13)−C(10)	122.5(5)
Br(1)−Re(1)−N(2)	93.2(1)	C(13)−C(10)−N(2)	127.8(6)
Br(1)−Re(1)-O(2)	84.0(1)		

proposed. The positive LSIMS mass spectra of all the Re complexes as well as $TcOCl(thoz)_2$ and $TcOCl(hbo)_2$ contained the molecular ion $[MOXL_2]^+$; for the rest of the complexes, $[MOL_2]^+$ was the highest mass peak which could be assigned. For all spectra, this $[MOL_2]^+$ was the parent peak, being of greater intensity than the molecular ion. The ^1H NMR spectra of these complexes were indicative of the two ligands in each complex residing in different chemical environments (i.e., a *cis* arrangement). For example, the ^1H NMR spectrum of $ReOBr(moz)_2$ had two triplets and four doublets in the aromatic region, corresponding to the six different hydrogens on the 2′-hydroxy-3′-methylphenyl rings of the two ligands; singlet methyl resonances were at 1.94 and 2.11 ppm. This NMR spectrum indicated that there were one equatorial ligand and one axial ligand bound to the metal; higher temperature spectra evinced decomposition before fluxionality. ^1H NMR spectra of $TcOCl(thoz)_2$ and $TcOCl(moz)_2$ were consistently of poor quality, as can be the case for low-symmetry $Tc^V{=}O$ complexes of the quadrupolar ^{99}Tc nucleus.

Crystal Structure of Hthoz. An ORTEP diagram is shown in Figure 1, while distances and angles are given in Table 2. The X-ray structural data of Hthoz reveal noticeable characteristics of the 2-(2′-hydoxyphenyl)-2-thiazoline ring as a chelating functionality. Being very similar in length to the C(3)−S(1) bond distance of 1.787(2) Å, the C(1)−S(1) bond of length 1.758(2) Å of the 2-thiazoline ring has no double-bond character. The C(1)−N(1) bond distance of 1.275(2) Å is significantly shorter than the C(2)−N(1) distance of 1.465(2) Å, which leads to the primary resonance structure having the double bond of the 2-thiazoline ring located between C(1) and N(1). Unlike that of Hthoz, the crystal structure of agrobactin shows that the 5-methyl-*trans*-2-oxazoline ring contains two resonance structures in which the double bond of the oxazoline ring resonates between the C−O and C−N linkages in the ring.[4]

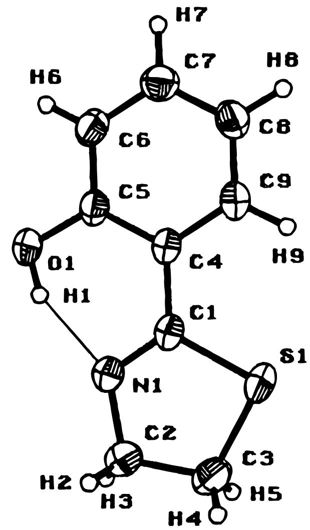

Figure 1. ORTEP diagram of Hthoz showing the crystallographic numbering. Thermal ellipsoids for the non-hydrogen atoms are drawn at the 33% probability level.

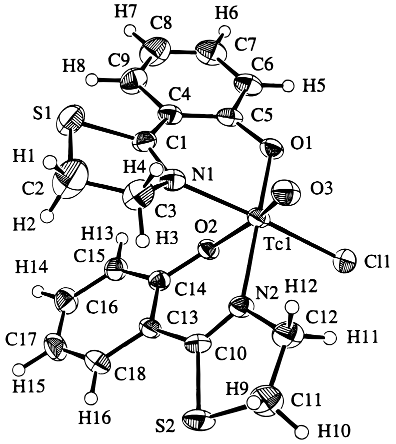

Figure 2. ORTEP diagram of $TcOCl(thoz)_2$ showing the crystallographic numbering. Thermal ellipsoids for the non-hydrogen atoms are drawn at the 33% probability level.

The intramolecular ring H-bond between the phenolic hydrogen and the thiazoline ring nitrogen has an important consequence for the ligating ability of the ligand; it stabilizes the chelating conformation of the appropriate rotomer, thereby preorganizing the ligand for bidentate chelation with a metal ion, and in doing so it further enhances the stability of the bicyclic conjugated (thus planar) ring systems. The virtually planar nature of the compound is denoted by the dihedral angles between the least-squares planes of atoms of the molecule. The plane of the thiazoline ring [S(1), N(1), C(1), C(2), and C(3)] has a dihedral angle of 2.5° with the aromatic ring [C(4), C(5), C(6), C(7), C(8), and C(9)]. The plane defined by the atoms joining the potential chelating functionalities [O(1), N(1), C(1), C(4), and C(5)] has a dihedral angle of 2.0° with the thiazoline ring and a dihedral angle of 0.5° with the aromatic ring.

Crystal Structures of $TcOCl(thoz)_2$ and $ReOBr(oz)_2$. ORTEP diagrams are shown in Figures 2 and 3, respectively. These structures are of discrete complexes without significant intermolecular interactions. Both complexes crystallize in a distorted octahedral configuration having two bidentate ligands and one halide about the metal−oxo centers. In each of these complexes, the metal atom is located 0.19 Å above the equatorial plane formed by the two nitrogens, one oxygen, and one halide atoms. In $TcOCl(thoz)_2$, the Tc−O(3) bond distance is 1.661(3) Å, close to the average of 1.65 Å for a Tc═O bond.[1,2] In both compounds, phenolate oxygens are *trans* to the M═O bonds. The Tc−O(2) bond length of 1.978(3) Å is typical of a Tc−O bond *trans* to an oxo group.[1,2] In the equatorial plane of $TcOCl(thoz)_2$, a second phenolate oxygen atom, the two nitrogen atoms, and the chloride are coordinated to the metal ion. The thiazoline nitrogen atoms, coordinated *cis* to one

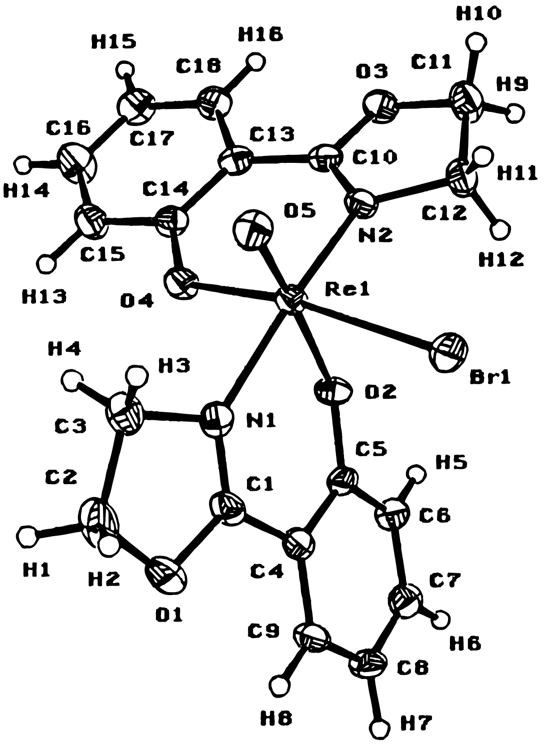

Figure 3. ORTEP diagram of $ReOBr(oz)_2$ showing the crystallographic numbering. Thermal ellipsoids for the non-hydrogen atoms are drawn at the 33% probability level.

another, have Tc−N bond distances of 2.103(4) and 2.115(3) Å, which are standard for nitrogens singly bound to Tc.[1,2] The O(3)−Tc−O(2) angle of 163.7(1)° is below the ideal of 180° for an octahedral complex. The Tc═O linkage significantly opens up the angles to the equatorial oxygen and chloride atoms (O(3)−Tc−O(1) = 103.0(1)°, and O(3)−Tc−Cl(1) = 102.6(1)°), but not those to the equatorial nitrogen atoms (O(3)−Tc−N(1) = 86.5(1)°, and O(3)−Tc−N(2) = 89.5(1)°). The O(1)−Tc−N(1) bite angle of the equatorially coordinated ligand is 89.1(1)°, while the O(2)−Tc−N(2) bite angle for the axial ligand is 82.2(1)°.

Comparison of the bond lengths and bond angles of Hthoz with the ligand $thoz^-$ in $TcOCl(thoz)_2$ shows that there are small changes upon complexation. All bond lengths among carbon, nitrogen, and sulfur atoms remain within 0.02 Å of those in Hthoz upon complexation to Tc, with the exception of C(2)−C(3) in the oxazoline ring, which decreases from 1.522(3) Å in Hthoz to 1.471(8) Å in the equatorial and 1.482(6) Å (C(11)−C(12)) in the axial ligands. The angles through the chelate ring portion of Hthoz (O(1)−C(5)−C(4) = 122.1(2)°, C(5)−C(4)−C(1) = 120.0(1)°, and C(4)−C(1)−N(1) = 122.5(1)°) increase in value upon complexation of the equatorial ligand (126.1(4)°, 123.2(4)°, and 124.8(4)°, respectively); in the axial ligand the corresponding values are 121.8(3)°, 119.7(3)°, and 124.9(3)°. This suggests that there is more strain in the equatorial ligand because there are greater deviations from the ideal bond angles of 120° for sp^2-hybridized carbon atoms in the equatorial ligand. Orthogonal coordination of the ligands and the *cis* orientation of the complexed nitrogen atoms about the technetium center are identical to the coordination of the bidentate 2-(2′-hydroxyphenyl)benzothiazolinato (hbt^-) ligand in the bis(ligand) complex $TcOCl(hbt)_2$.[10]

The crystal structure of $ReOBr(oz)_2$ shows that one ligand coordinates in the equatorial plane with respect to Re═O, while the second ligand has its phenolate oxygen atom bound axially and its oxazoline nitrogen atom bound equatorially with respect to the oxo bond. The Re═O bond distance is Re−O(5) = 1.681(4) Å, typical for a rhenium−oxygen double bond. The Re−O(2) bond length of 1.988(4) Å is consistent with the *trans* influence for an oxygen from an axially bound ligand *trans* to the Re═O linkage. In the equatorial plane, the two bound nitrogens coordinate *trans* to one another (Re−N(1) = 2.098(5) Å, and Re−N(2) = 2.045(5) Å), while the bromide is *trans* to the equatorial coordinated oxygen (Re−O(4) = 2.013(4) Å). The bond angles show that the rhenium complex is closer to a perfectly octahedral complex than the technetium species (for example, O(5)−Re−O(2) = 170.8(2)°). With an O(4)−Re−N(2) bite angle of 90.0(2)° for the equatorial ligand and a O(2)−Re−N(1) angle of 81.5(2)°, the axial and equatorial ligands in $ReOBr(oz)_2$ and $TcOCl(thz)_2$ have very similar bite angles.

In conclusion, bis(ligand) rhenium and technetium complexes of ligands containing naturally occurring binding groups derived from siderophores have been prepared and characterized. The crystal structures of the rhenium and technetium complexes show that the two ligands in each complex coordinate in a different orientation to each other. Curiously, we were unsuccessful in preparing tris(ligand) Tc complexes by reduction from pertechnetate, the thermodynamically favored $TcO_2{\cdot}xH_2O$ being formed instead.

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Supporting Information Available: Complete tables of crystallographic data, final atomic coordinates and isotropic thermal parameters, bond lengths, bond angles, hydrogen atom parameters, anisotropic thermal parameters, torsion angles, and least-squares planes (45 pages). Ordering information is given on any current masthead page.

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