

## Synthesis and Characterization of Mixed-Ligand Oxorhenium Complexes with the SNN Type of Ligand. Isolation of a Novel ReO[SN][S][S] Complex

A. Rey,<sup>\*,†</sup> I. Pirmettis,<sup>‡</sup> M. Pelecanou,<sup>§</sup> M. Papadopoulos,<sup>‡</sup> C. P. Raptopoulou,<sup>||</sup> L. Mallo,<sup>⊥</sup> C. I. Stassinopoulou,<sup>§</sup> A. Terzis,<sup>||</sup> E. Chiotellis,<sup>‡</sup> and A. León<sup>†</sup>

Cátedra de Radioquímica, Facultad de Química, C.C. 1157, Montevideo, Uruguay, Departamento de Radiofarmacia, CIN, Facultad de Ciencias, Montevideo, Uruguay, and Institute of Radioisotopes–Radiodiagnostic Products, Biology and Materials Science, NCSR “Demokritos”, 15310 Athens, Greece

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A new series of mixed-ligand oxorhenium complexes **4–9**, with ligands **1–3** (LH<sub>2</sub>) containing the SNN donor set and monodentate thiols as coligands (L<sub>2</sub>H), is reported. All complexes were synthesized using ReOCl<sub>3</sub>(PPh<sub>3</sub>)<sub>2</sub> as precursor. They were isolated as crystalline products and characterized by elemental analysis and IR and NMR spectroscopy. The ligands **1** and **2** (general formula RCH<sub>2</sub>CH<sub>2</sub>NHCH<sub>2</sub>CH<sub>2</sub>SH, where R = N(C<sub>2</sub>H<sub>5</sub>)<sub>2</sub> in **1** and pyrrolidin-1-yl in **2**) act as tridentate SNN chelates to the ReO<sup>3+</sup> core, leaving one open coordination site cis to the oxo group. The fourth coordination site is occupied by a monodentate aromatic thiol which acts as a coligand. Thus, three new “3+1” [SNN][S] oxorhenium complexes **4–6** (general formula ReO[RCH<sub>2</sub>CH<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>S]-[SX], where R = N(C<sub>2</sub>H<sub>5</sub>)<sub>2</sub> and X = phenyl in **4**, R = N(C<sub>2</sub>H<sub>5</sub>)<sub>2</sub> and X = *p*-methylphenyl in **5**, and R = pyrrolidin-1-yl and X = *p*-methylphenyl in **6**) were prepared in high yield. Complex **4** adopts an almost perfect square pyramidal geometry ( $\tau = 0.07$ ), while **6** forms a distorted square pyramidal geometry ( $\tau = 0.24$ ). In both complexes **4** and **6**, the basal plane is formed by the SNN donor set of the tridentate ligand and the S of the monodentate thiol. On the other hand, the ligand **3**, [(CH<sub>3</sub>)<sub>2</sub>CH]<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>NHCH<sub>2</sub>CH<sub>2</sub>SH, acts as a bidentate ligand, probably due to steric hindrance, and it coordinates to the ReO<sup>3+</sup> core through the SN atoms, leaving two open coordination sites cis to the oxo group. These two vacant positions are occupied by two molecules of the monodentate thiol coligand, producing a novel type of “2+1+1” [SN][S][S] oxorhenium mixed-ligand complexes **7–9** (general formula ReO{[(CH<sub>3</sub>)<sub>2</sub>CH]<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>NHCH<sub>2</sub>CH<sub>2</sub>S}[SX][SX], where X = phenyl in **7**, *p*-methylphenyl in **8**, and benzyl in **9**). The coordination sphere about rhenium in **7** and **8** consists of the SN donor set of ligand **3**, two sulfurs of the two monodentate thiols, and the doubly bonded oxygen atom in a trigonally distorted square pyramidal geometry ( $\tau = 0.44$  and  $0.45$  for **7** and **8**, respectively). Detailed NMR assignments were determined for complexes **5** and **8**.

### Introduction

During the last two decades, continuous investigation of the coordination chemistry of technetium has led to a rapid development of many Tc-99m radiopharmaceuticals, which became very useful tools in routine nuclear medicine imaging methods.<sup>1</sup> Extensive studies on the TcO<sup>3+</sup> core with linear tetradentate ligands possessing a N<sub>4</sub> (PhAO),<sup>2</sup> a N<sub>2</sub>S<sub>2</sub> (BAT or DADT),<sup>3</sup> a N<sub>2</sub>S<sub>2</sub> (DATS),<sup>4</sup> or a N<sub>3</sub>S<sup>5</sup> donor set have produced significant Tc-99m radiopharmaceuticals, such as the Tc-99m-HMPO,<sup>6</sup> Tc-99m-ECD,<sup>7</sup> and Tc-99m-MAG<sub>3</sub>,<sup>8</sup> for brain imaging and renal function studies.

The coordination chemistry of rhenium is currently drawing much attention not only because it is analogous to that of technetium but also because of the existence of the  $\beta$ -emitting radionuclides <sup>188</sup>Re and <sup>186</sup>Re. These radionuclides have become

\* Corresponding author. E-mail: arey@bilbo.edu.uy.

<sup>†</sup> Cátedra de Radioquímica, Facultad de Química.

<sup>‡</sup> Institute of Radioisotopes–Radiodiagnostic Products.

<sup>§</sup> Institute of Biology.

<sup>||</sup> Institute of Materials Science.

<sup>⊥</sup> CIN, Facultad de Ciencias.

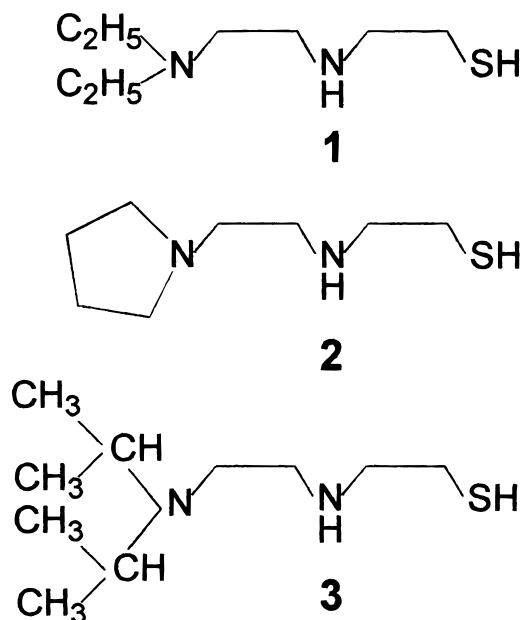
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two of the most promising candidates for therapeutic applications in nuclear medicine due to their attractive nuclear properties ( $E_{\max} = 2.12$  and  $1.1$  MeV,  $t_{1/2} = 17$  h with a  $\gamma$ -line of  $155$  keV (15%) and  $90.64$  h with a  $\gamma$ -line of  $137$  keV (9.5%) for  $^{188}\text{Re}$  and  $^{186}\text{Re}$ , respectively) and the availability of  $^{188}\text{Re}$  from a  $^{188}\text{W}/^{188}\text{Re}$  radionuclide generator at noncarrier levels.<sup>9</sup>

In the past decade, a very interesting concept, the “3+1” combination, was applied to the preparation of neutral penta-coordinated oxotechnetium and oxorhenium complexes for potential application in diagnosis and radiotherapy. Tridentate ligands with different donor atom sets (SSS, SOS, SNO, and SN(R)S) have been used with aromatic or aliphatic monodentate thiols on a suitable oxorhenium or oxotechnetium precursor, producing many “3+1” mixed-ligand complexes.<sup>10,11</sup> The coordination geometry of the [SSS][S], [SOS][S], and [SNO][S] mixed-ligand complexes is usually distorted square pyramidal. When the tridentate ligand has the SN(R)S donor set, two stereoisomers are expected, syn and anti, depending on the orientation of the R-functionality with respect to the Tc=O or Re=O core. However, our findings demonstrated that usually only the syn isomer is formed that adopts a trigonal bipyramidal geometry. In the few cases<sup>11c,d</sup> where the anti isomer was isolated, in very low yield (<2%), it was shown to have a square pyramidal geometry. The advantage of the mixed-ligand concept in the design of radiopharmaceuticals lies in the variety of possible tridentate/monodentate complexes that can be synthesized either by modifying the tridentate or by changing the monodentate ligand. So far, interesting “3+1” Tc-99m complexes have been developed by this approach and evaluated either as brain perfusion agents<sup>12</sup> or as specific brain receptor imaging agents.<sup>13</sup>

Scheme 1



Recently, we have reported the synthesis of a new class of  $\text{TcO}[\text{SNN}][\text{S}]$  mixed-ligand oxotechnetium complexes with tridentate ligands containing the SNN donor atom set and various monodentate thiols as coligands.<sup>14</sup> In this study, we applied the above ligand system in which the tridentate ligand contains one thiol and one secondary and one tertiary amine to the oxorhenium core. Symmetrical substitution of the tertiary amine was chosen to avoid the formation of stereoisomers during complexation with oxorhenium. Depending on the substituents of the tertiary amine, the ligands (Scheme 1) can act either as tridentate (ligands **1**, **2**) or bidentate (ligand **3**). The synthesis and characterization of three complexes **4–6** of the general formula  $\text{ReO}[\text{SNN}][\text{S}]$  and three complexes **7–9** of a novel combination  $\text{ReO}[\text{SN}][\text{S}][\text{S}]$  are reported herein (Scheme 2).

### Experimental Section

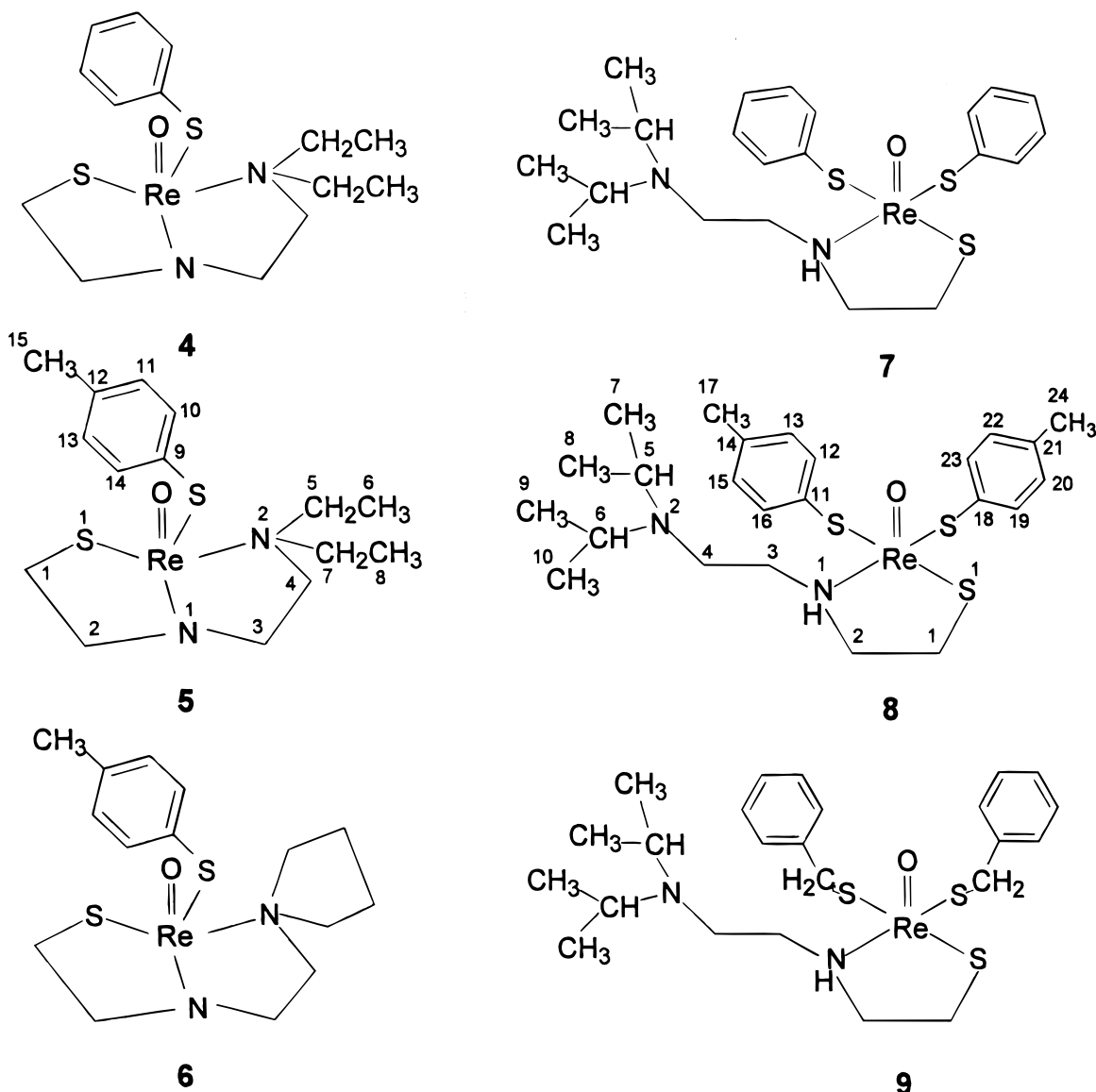
IR spectra were recorded as KBr pellets in the range of  $4000\text{--}500$   $\text{cm}^{-1}$  on a Perkin-Elmer 1600 FT-IR spectrophotometer and were referenced to polystyrene.

The NMR spectra were recorded in deuteriochloroform on a Bruker AC 250E spectrometer. Chemical shifts are reported with respect to TMS. Parameters for the 2D experiments have been previously reported.<sup>11c,14</sup>

All laboratory chemicals were reagent grade. The thiophenol and thioresol used as coligands were purchased from Fluka. The tridentate ligands **1**, **2**, and **3** were synthesized according to a published

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Scheme 2



procedure<sup>15</sup> reacting *N,N*-diethylethylenediamine, 1-(2-aminoethyl)-pyrrolidine, or *N,N*-diisopropylethylenediamine with ethylene sulfide in an autoclave at 110 °C. After the reaction was completed, the compounds were purified by vacuum distillation. The three ligands were characterized by IR and <sup>1</sup>H NMR. The analytical data were consistent with the assigned structures. ReOCl<sub>3</sub>(PPh<sub>3</sub>)<sub>2</sub> was prepared according to the literature.<sup>16</sup>

**Synthesis of Rhenium Complexes 4–9.** The typical synthetic procedure for all six compounds is given in detail for complex 4: To a stirred suspension of trichlorobis(triphenylphosphine)rhenium(V) oxide (166 mg, 0.2 mmol) in methanol (10 mL) was added 1 N CH<sub>3</sub>-COONa in methanol (2 mL, 2 mmol). A mixture of 0.2 mmol of *N,N*-diethyl-*N'*-(2-mercaptoethyl)ethylenediamine 1 and 0.2 mmol of thiophenol was added under stirring. The solution was refluxed until the green-yellow color of the precursor turned to dark-red. After being cooled to room temperature, the reaction mixture was diluted with CH<sub>2</sub>-Cl<sub>2</sub> (30 mL) and washed with water. The organic layer was separated from the mixture and dried over MgSO<sub>4</sub>. The volume of the solution was reduced to 5 mL, and then 5 mL of methanol was added.

TLC showed the formation of one complex in all cases. Slow evaporation of the solvents at room temperature afforded the products of the reaction as red or brown solids.

**[Thiophenolato][*N*-(2-mercaptoethyl)(2-diethylamino)ethylamine]oxorhenium(V) (4).** Red crystals, yield 40%. Anal. Calcd for C<sub>14</sub>H<sub>23</sub>N<sub>2</sub>OS<sub>2</sub>Re: C, 34.62; H, 4.77; N, 5.77; S, 13.20. Found: C, 34.42; H, 4.35; N, 5.63; S, 12.96. FT-IR (cm<sup>-1</sup>, KBr pellet): 954 (Re=O). <sup>1</sup>H NMR (ppm, CDCl<sub>3</sub>): 7.63–7.17 (5H, m), 4.08 (1H, m), 3.94–3.67 (3H, m), 3.59–3.19 (6H, m), 2.92 (1H, m), 1.91 (1H, m), 1.52 (3H, t), 1.08 (3H, t).

**[*p*-Methylbenzenethiolato][*N*-(2-mercaptoethyl)(2-diethylamino)ethylamine]oxorhenium(V) (5).** Red crystals, yield 45%. Anal. Calcd for C<sub>15</sub>H<sub>25</sub>N<sub>2</sub>OS<sub>2</sub>Re: C, 36.05; H, 5.04; N, 5.61; S, 12.83. Found: C, 35.73; H, 4.86; N, 5.31; S, 12.42. FT-IR (cm<sup>-1</sup>, KBr pellet): 953 (Re=O). For <sup>1</sup>H and <sup>13</sup>C NMR data, see Table 3.

**[*p*-Methylbenzenethiolato][*N*-(2-mercaptoethyl)(2-pyrrolidin-1-yl)ethylamine]oxorhenium(V) (6).** Red-brown crystals, yield 42%. Anal. Calcd for C<sub>15</sub>H<sub>23</sub>N<sub>2</sub>OS<sub>2</sub>Re: C, 36.20; H, 4.66; N, 5.63; S, 12.88. Found: C, 36.11; H, 4.89; N, 5.37; S, 12.59. FT-IR (cm<sup>-1</sup>, KBr pellet): 931 (Re=O). <sup>1</sup>H NMR (ppm, CDCl<sub>3</sub>): 7.51 (2H, m), 7.15 (2H, m), 4.59 (1H, m), 4.08 (1H, m), 3.88 (1H, m), 3.69–3.24 (7H, m), 2.96 (1H, m), 2.59 (1H, m), 2.40 (3H, t), 2.34–2.03 (4H, m).

**Bis[thiophenolato][*N*-(2-mercaptoethyl)(2-diisopropylamino)ethylamine]oxorhenium(V) (7).** Brown crystals, yield 60%. Anal. Calcd for C<sub>22</sub>H<sub>33</sub>N<sub>2</sub>OS<sub>2</sub>Re: C, 42.35; H, 5.33; N, 4.49; S, 15.42. Found: C, 42.67; H, 5.59; N, 4.56; S, 15.18. FT-IR (cm<sup>-1</sup>, KBr pellet): 961 (Re=O). <sup>1</sup>H NMR (ppm, CDCl<sub>3</sub>): 7.60–7.16 (10H, m), 4.68 (1H, m),

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3.76 (1H, m), 3.39–3.35 (2H, m), 3.23 (2H, m), 3.02 (2H, m), 2.85 (1H, m), 2.58 (1H, m).

**Bis[*p*-methylbenzenethiolato][*N*-(2-mercaptoethyl)(2-diisopropylamino)ethylamine]oxorhenium(V) (8).** Brown crystals, yield 69%. Anal. Calcd for C<sub>24</sub>H<sub>37</sub>N<sub>2</sub>OS<sub>3</sub>Re: C, 44.08; H, 6.01; N, 4.28; S, 14.71. Found: C, 44.40; H, 5.67; N, 4.36; S, 14.71. FT-IR (cm<sup>-1</sup>, KBr pellet): 954 (Re=O). For <sup>1</sup>H and <sup>13</sup>C NMR data, see Table 4.

**Bis[ $\alpha$ -toluenethiolato][*N*-(2-mercaptoethyl)(2-diisopropylamino)ethylamine]oxorhenium(V) (9).** Violet crystals, yield 54%. Anal. Calcd for C<sub>24</sub>H<sub>37</sub>N<sub>2</sub>OS<sub>3</sub>Re: C, 44.08; H, 6.01; N, 4.28; S, 14.71. Found: C, 43.99; H, 5.49; N, 4.28; S, 13.78. FT-IR (cm<sup>-1</sup>, KBr pellet): 951 (Re=O). <sup>1</sup>H NMR (ppm, CDCl<sub>3</sub>): 7.42 (2H, t), 7.28–7.20 (8H, m), 5.24 (1H, m), 4.60–4.50 (2H, m), 3.32 (2H, m), 3.20–3.15 (m, 4H), 2.7 (1H, m), 1.06 (6H, d), 1.04 (6H, d).

**X-ray Crystal Structure Determination.** Diffraction measurements for **4**, **6**, and **8** were performed on a Crystal Logic Dual Goniometer diffractometer using graphite-monochromated Mo radiation, while compound **7** was measured on a P21, Nicolet upgraded by Crystal Logic using Ni-filtered Cu radiation. Unit cell dimensions were determined and refined by using the angular settings of 25 automatically centered reflections in the ranges of 11 < 2 $\theta$  < 23° (for **4**, **6**, and **8**) and 24 < 2 $\theta$  < 54° (for **7**), and they appear in Table 1. Intensity data were recorded using the  $\theta$ -2 $\theta$  scan. Three standard reflections monitored every 97 reflections showed less than 3% variation and no decay. Lorentz, polarization, and  $\psi$ -scan absorption corrections were applied using Crystal Logic software. The structures were solved by direct methods using SHELXS-86<sup>17</sup> and refined by full-matrix least-squares techniques on  $F^2$  with SHELXL-93.<sup>18</sup>

Further crystallographic details for **4**: 2 $\theta$  = 53°; scan speed 4.0°/min; scan range 2.5 +  $\alpha_1\alpha_2$  separation; reflections collected/unique/used = 3704/3426( $R_{\text{int}}$  = 0.0232)/3425; 237 parameters refined;  $R_1/wR_2$  (for all data) = 0.0460/0.1204;  $[\Delta\rho]_{\text{max}}/[\Delta\rho]_{\text{min}}$  = 0.735/-0.625 e/Å<sup>3</sup>;  $[\Delta/\sigma]_{\text{max}}$  = 0.173. All hydrogen atoms (except those on C1, C5, C6, C8, and C13, which were introduced at calculated positions as riding on bonded carbon) were located by difference maps and refined isotropically. All non-hydrogen atoms were refined anisotropically.

Further crystallographic details for **6**: 2 $\theta$  = 54°; scan speed 3.5°/min; scan range 2.5 +  $\alpha_1\alpha_2$  separation; reflections collected/unique/used = 3871/3749( $R_{\text{int}}$  = 0.0092)/3746; 273 parameters refined;  $R_1/wR_2$  (for all data) = 0.0349/0.0962;  $[\Delta\rho]_{\text{max}}/[\Delta\rho]_{\text{min}}$  = 0.741/-0.942 e/Å<sup>3</sup>;  $[\Delta/\sigma]_{\text{max}}$  = 0.018. All hydrogen atoms (except those of the methyl group, which were introduced at calculated positions as riding on bonded atoms) were located by difference maps and refined isotropically. All non-hydrogen atoms were refined anisotropically.

Further crystallographic details for **7**: 2 $\theta$  = 130°; scan speed 3.0°/min; scan range 2.4 +  $\alpha_1\alpha_2$  separation; reflections collected/unique/used = 4534/4261( $R_{\text{int}}$  = 0.0495)/4261; 348 parameters refined;  $R_1/wR_2$  (for all data) = 0.0427/0.1145;  $[\Delta\rho]_{\text{max}}/[\Delta\rho]_{\text{min}}$  = 0.728/-0.895 e/Å<sup>3</sup>;  $[\Delta/\sigma]_{\text{max}}$  = 0.610. Hydrogen atoms on methyl groups C6, C7, C9, and C10, as well those on C1, were introduced at calculated positions as riding on bonded atoms; the rest were located by difference maps and refined isotropically. All non-hydrogen atoms were refined anisotropically.

Further crystallographic details for **8**: 2 $\theta$  = 50°; scan speed 3.2°/min; scan range 2.5 +  $\alpha_1\alpha_2$  separation; reflections collected/unique/used = 5062/4814( $R_{\text{int}}$  = 0.0299)/4814; 420 parameters refined;  $R_1/wR_2$  (for all data) = 0.0292/0.0636;  $[\Delta\rho]_{\text{max}}/[\Delta\rho]_{\text{min}}$  = 0.561/-0.559 e/Å<sup>3</sup>;  $[\Delta/\sigma]_{\text{max}}$  = 0.293. All hydrogen atoms (except those on C17 methyl, which were introduced at calculated positions as riding on bonded carbon) were located by difference maps and refined isotropically. All non-hydrogen atoms were refined anisotropically.

## Results and Discussion

**Synthesis.** The syntheses of the tridentate ligands **1**, **2**, and **3** were performed according to the procedure reported by

Marabella et al.<sup>15</sup> for mercaptoethylation of amines with ethylene sulfide.

Complexes **4–9** were prepared under the same experimental conditions by reacting the tridentate ligands **1–3** and monodentate thiols with ReOCl<sub>3</sub>(PPh<sub>3</sub>)<sub>2</sub> in a ratio of 1:1:1 in methanol. The reaction was monitored by TLC, and in all cases, only one product was formed. The complexes were extracted in dichloromethane and isolated as crystalline products by slow evaporation from CH<sub>2</sub>Cl<sub>2</sub>/MeOH.

As expected according to our previous experience with the corresponding oxotechnetium complexes,<sup>14</sup> the ligands **1** and **2** act as tridentate ligands and coordinate to the oxometal core through the sulfur, the secondary amine, and the tertiary amine nitrogens. The coordination sphere of the metal is completed by a monodentate thiol to produce complexes **4–6**. The complexes are neutral and lipophilic, as indicated by their quantitative extraction from the aqueous to the dichloromethane layer during isolation. They are soluble in CH<sub>2</sub>Cl<sub>2</sub> and CHCl<sub>3</sub>, slightly soluble in EtOH and MeOH, and insoluble in ether, pentane, and water. The complexes are stable in the solid state and organic solutions, as shown by NMR.

The tridentate ligand **3**, however, acts in a different way and, in the presence of the corresponding thiol, leads to the formation of complexes **7–9**. The elemental analysis and NMR spectroscopy of **7–9** showed the existence of two aromatic thiols in the complex. Accordingly, the presence in the IR spectra of a very strong band at approximately 810 cm<sup>-1</sup> indicated the presence of more than one aromatic thiol in the complexes. In addition, in the IR spectra, a peak at approximately 3100 cm<sup>-1</sup> indicated the presence of an NH group in the molecules. X-ray studies of complexes **7** and **8** demonstrated that the tertiary nitrogen of ligand **3** does not participate in the coordination sphere of the metal, and therefore, two molecules of the aromatic thiols occupy the two vacant positions of the ReO<sup>3+</sup> core, resulting in complexes of the [SN][S][S] type. The secondary amine is not deprotonated during complexation, and the total charge of the complex is zero. Complexes **7–9** are lipophilic and stable in dichloromethane and chloroform solutions as shown by NMR. In methanol, a slight decomposition is noted with time. In these complexes, the remaining free chain on the coordinated nitrogen may be locked in either the syn or anti configuration with respect to the oxometal core, and two stereoisomers are theoretically possible. However, only one complex was isolated from the reaction mixture in each case, and that proved to be the syn isomer.

The failure of the diisopropylamine group of ligand **3** to coordinate to the metal must be attributed to steric hindrance. Differences in basicity between the R groups of the ligands **1–3** cannot account for the observed differentiation in behavior, since the pK<sub>a</sub> values of all tertiary amines are comparable.

The infrared spectra of all complexes exhibit a strong Re=O vibration at 931–961 cm<sup>-1</sup>. These values are consistent with other values reported for well-characterized monooxo-Re(V) species.<sup>14,20</sup>

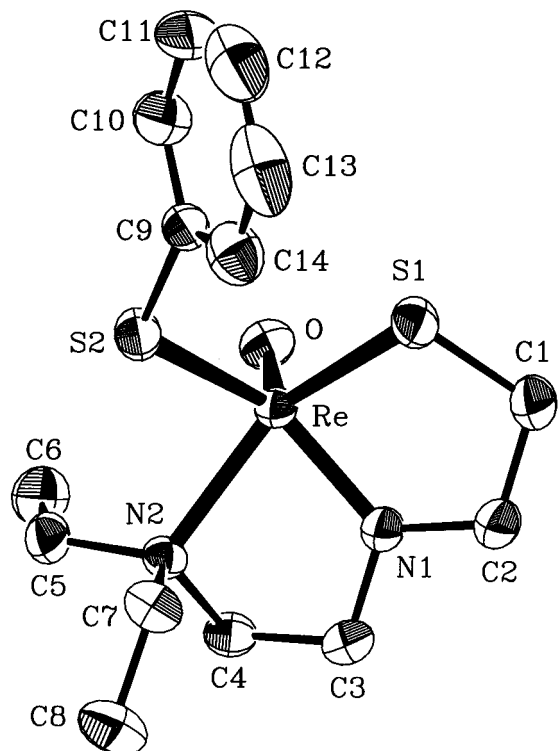
**X-ray Studies of Compounds 4, 6, 7, and 8.** ORTEP diagrams of the compounds **4**, **6**, **7**, and **8** are shown in Figures 1–4, respectively. A summary of crystal data is given in Table 1, and selected bond distances and angles are listed in Table 2. The coordination geometry about rhenium in **6**, which is

(17) Sheldrick, G. M. *SHELXS-86: Structure Solving Program*; University of Göttingen: Göttingen, Germany, 1986.

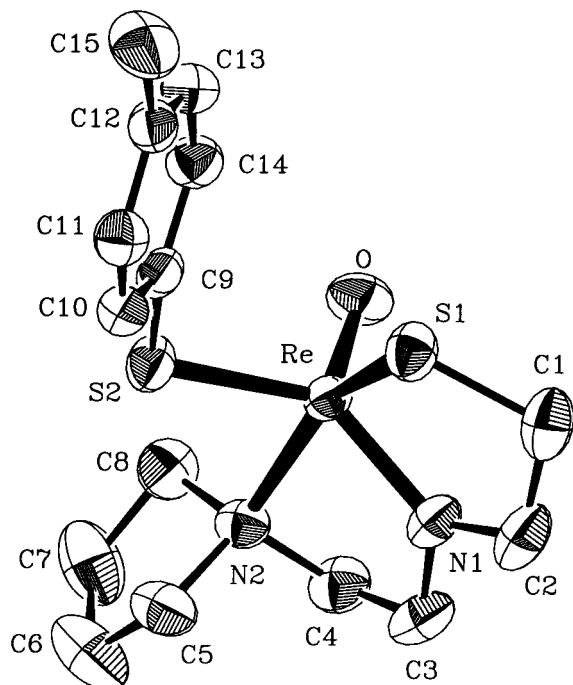
(18) Sheldrick, G. M. *SHELXL-93: Crystal Structure Refinement*; University of Göttingen: Göttingen, Germany, 1993.

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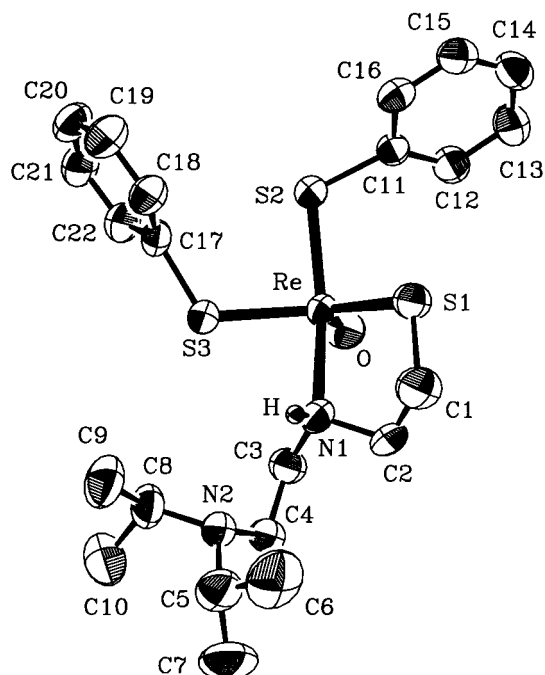


**Figure 1.** ORTEP diagram of complex **4** with 50% thermal probability ellipsoids showing the atomic labeling scheme.

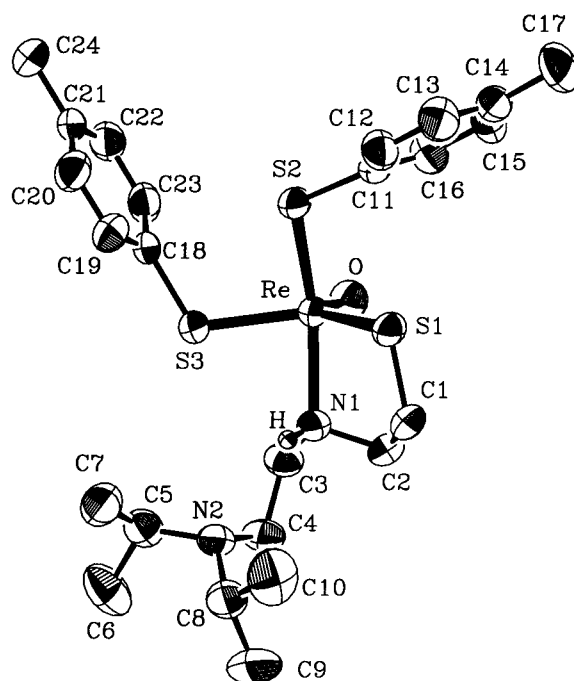


**Figure 2.** ORTEP diagram of complex **6** with 50% thermal probability ellipsoids showing the atomic labeling scheme.

isostructural to the technetium analogue,<sup>14</sup> is formed by two nitrogens, two sulfur atoms, and the doubly bonded oxygen, which is directed in the apex of a distorted square pyramid. Examining the N(2)–Re–S(1) and N(1)–Re–S(2) angles in the basal plane of the square pyramid of **6** (149.8(1)° and 135.4(1)°, respectively), we can calculate a value of 0.24 for the trigonality index<sup>19</sup> ( $\tau = 0$  for a perfect square pyramid,  $\tau = 1$  for a perfect trigonal bipyramid). This intermediate value has also been calculated for the analogous oxotechnetium and oxorhenium compounds<sup>14,20</sup> having the same [SNN][S]



**Figure 3.** ORTEP diagram of complex **7** with 50% thermal probability ellipsoids showing the atomic labeling scheme.



**Figure 4.** ORTEP diagram of complex **8** with 50% thermal probability ellipsoids showing the atomic labeling scheme.

coordination environment. On the other hand, in **4**, which has the same donor atoms set as **6**, the calculated trigonality index is  $\sim 0.07$ , indicating an almost perfect square pyramidal geometry around the metal. This may be attributed to the lack of steric effects on the substituents on N(2). Rhenium lies  $\sim 0.68$  Å out of the basal plane toward the oxo group in both complexes. The five-membered rings in the coordination sphere adopt the stable envelope configuration with C1 and C4 being  $\sim 0.66$  Å out of the mean plane of the remaining four atoms in **6**, while C1 and N2 are displaced by 0.66 and 0.80 Å, respectively, in the case of **4**. The pyrrolidine ring in **6** also exists in the envelope form with N2 being the “flap” atom (displacement 0.56 Å). The dihedral angles of the tridentate

**Table 1.** Summary of Crystal Data for **4**, **6**, **7**, and **8**

	<b>4</b>	<b>6</b>	<b>7</b>	<b>8</b>
formula	C <sub>14</sub> H <sub>23</sub> N <sub>2</sub> OReS <sub>2</sub>	C <sub>15</sub> H <sub>23</sub> N <sub>2</sub> OReS <sub>2</sub>	C <sub>22</sub> H <sub>33</sub> N <sub>2</sub> OReS <sub>3</sub>	C <sub>24</sub> H <sub>37</sub> N <sub>2</sub> OReS <sub>3</sub>
fw	485.66	497.67	623.88	651.94
<i>a</i> (Å)	6.888(2)	10231(6)	9.500(1)	11.687(7)
<i>b</i> (Å)	28.080(8)	9.277(5)	16.385(1)	14.462(7)
<i>c</i> (Å)	8.694(2)	18.316(9)	16.254(1)	16.272(8)
β (deg)	100.064(7)	97.60(1)	95.905(2)	92.11(2)
<i>V</i> (Å <sup>3</sup> )	1655.6(8)	1723.2(2)	2516.7(3)	2748.6(2)
<i>Z</i>	4	4	4	4
<i>D</i> <sub>calcd</sub> / <i>D</i> <sub>measd</sub> , (M gm <sup>-3</sup> )	1.948/1.93	1.918/1.89	1.647/1.62	1.575/1.55
space group	<i>P</i> 2 <sub>1</sub> / <i>n</i>	<i>P</i> 2 <sub>1</sub> / <i>n</i>	<i>P</i> 2 <sub>1</sub> / <i>n</i>	<i>P</i> 2 <sub>1</sub> / <i>n</i>
temp (K)	298	298	298	298
radiation, λ (Å)	Mo Kα, 0.71073	Mo Kα, 0.71073	Cu Kα, 1.5418	Mo Kα, 0.71073
abs coeff, μ (mm <sup>-1</sup> )	7.589	7.294	11.882	4.667
octants collected	-h, k, ±1	±h, -k, 1	-h, -k, ±1	-h, k, ±1
GOF on <i>F</i> <sup>2</sup>	1.121	1.086	1.109	1.100
R1	0.0408 <sup>a</sup>	0.0323 <sup>b</sup>	0.0387 <sup>c</sup>	0.0240 <sup>d</sup>
wR2	0.1138 <sup>a</sup>	0.0929 <sup>b</sup>	0.1100 <sup>c</sup>	0.0608 <sup>d</sup>

<sup>a</sup> For 3106 reflns with *I* > 2σ(*I*). <sup>b</sup> For 3749 reflns with *I* > 2σ(*I*). <sup>c</sup> For 3834 reflns with *I* > 2σ(*I*). <sup>d</sup> For 4282 reflns with *I* > 2σ(*I*).

backbone—i.e., S1—C1—C2—N1 and N1—C3—C4—N2—are 41.4° and -43.7° for **6**, and -41.3° and 43.8° for **4**. The Re=O and Re—S bond distances are in the ranges observed for other well-characterized complexes.<sup>14,20</sup> The Re—N(1) bond (1.931(4) and 1.938(5) Å in **6** and **4**, respectively) has a double-bond character, since the typical values for Re—N singlet<sup>21,22</sup> and triplet<sup>23</sup> bond lengths are 2.15 and 1.69 Å, respectively. The three bond angles around the amide nitrogen are close to 120°, ranging from 113.4(4) to 125.0(3)° and 113.0(5) to 124.8(4)° in **6** and **4**, respectively, as expected for the sp<sup>2</sup> hybridization of this atom. As a result, rhenium, N(1), and the adjacent carbon atoms are nearly coplanar. On the other hand, the Re—N(2) bond distance (2.198(5) and 2.223(5) Å in **6** and **4**, respectively) is in the range for typical Re—N amine single bonds,<sup>21</sup> while the angles about N(2) are close to 109°, as expected for the sp<sup>3</sup> hybridization of this atom.

The coordination environment about rhenium in **7** and **8** consists of the SN donor atom set of the bidentate ligand, the sulfurs of the two monodentate thiols, and the doubly bonded oxygen atom in a trigonally distorted square pyramidal geom-

**Table 2.** Selected Bond Distances (Å) and Angles (deg) for **4**, **6**, **7**, and **8**

	<b>4</b>	<b>6</b>	<b>7</b>	<b>8</b>
	Distances			
Re—O	1.687(5)	1.699(4)	1.679(4)	1.688(3)
Re—N(1)	1.938(5)	1.931(4)	2.187(4)	2.195(3)
Re—X	2.223(5) <sup>a</sup>	2.198(5) <sup>a</sup>	2.301(1) <sup>b</sup>	2.300(1) <sup>b</sup>
Re—S(1)	2.277(2)	2.286(2)	2.273(2)	2.290(1)
Re—S(2)	2.339(2)	2.321(2)	2.293(2)	2.304(1)
	Angles			
O—Re—N(1)	110.7(2)	113.4(2)	96.9(2)	97.4(1)
O—Re—X	107.2(2)	99.7(2)	113.3(1)	112.9(1)
N(1)—Re—X	77.4(2)	78.6(2)	81.7(1)	83.3(1)
O—Re—S(1)	107.6(2)	109.5(2)	115.3(1)	116.7(1)
N(1)—Re—S(1)	82.9(2)	82.9(1)	82.6(1)	81.1(1)
X—Re—S(1)	144.2(2)	149.8(1)	130.3(1)	129.4(1)
O—Re—S(2)	108.6(2)	110.5(1)	106.3(1)	106.4(1)
N(1)—Re—S(2)	140.1(2)	135.4(1)	156.7(1)	156.1(1)
X—Re—S(2)	84.9(1)	86.9(1)	87.8(1)	88.5(1)
S(1)—Re—(2)	91.7(1)	89.9(1)	88.5(1)	87.1(1)

<sup>a</sup> X = N(2). <sup>b</sup> X = S(3).

etry, as indicated by the trigonality index (0.44 and 0.45 for **7** and **8**, respectively). Rhenium lies 0.68 and 0.70 Å out of the basal plane toward the oxo group in **7** and **8**, respectively. The five-membered ring in the coordination sphere, defined by Re, S1, C1, C2, and N1, adopts in both compounds the stable envelope form with C2 displaced by 0.65 and 0.67 Å (for **7** and **8**, respectively) out of the mean plane of the remaining four atoms. The dihedral angle of the chelating agent (S1—C1—C2—N1) is -51.1 and -48.4° for **7** and **8**, respectively. The Re=O, Re—S, and Re—N bond distances are in the ranges observed for analogous complexes. The amine hydrogen is directed 3.55 Å trans to the oxo group.

**NMR Studies of Complexes 5 and 8.** The NMR studies of complexes **5** and **8** were conducted in CDCl<sub>3</sub>, and the assignments were based on a series of 2D homo- and heterocorrelation spectra. <sup>1</sup>H and <sup>13</sup>C chemical shifts of complexes **5** and **8** appear in Tables 3 and 4, respectively. The numbering of the atoms is shown in the structures of complexes **5** and **8** in Scheme 2.

Apart from the slow exchange of the NH proton of complex **8** with traces of water in the solvent, no signs of dynamic processes were observed.

**Complex 5.** Due to the asymmetry of the molecule, all protons and carbons of the SN<sub>2</sub> ligand of complex **5** have distinct resonances (Figure 5). The <sup>1</sup>H NMR spectrum of complex **5** at room temperature consists of sharp, well-resolved peaks with fine structures indicative of a time-averaged conformation.

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**Table 3.**  $^1\text{H}$   $\delta_{\text{H}}$  (ppm) and  $^{13}\text{C}$   $\delta_{\text{C}}$  (ppm) Chemical Shifts for Complex **5** in  $\text{CDCl}_3$  at 298 K

H1 endo	3.51 <sup>a</sup>	C1	46.00
H1 exo	2.92	C2	69.32
H2 endo	4.06	C3	60.52
H2 exo	3.39 <sup>a</sup>	C4	64.20
H3 endo	3.76 <sup>a</sup>	C5	55.35
H3 exo	3.44 <sup>a</sup>	C6	12.46
H4 endo	3.87 <sup>a</sup>	C7	51.20
H4 exo	3.46 <sup>a</sup>	C8	8.03
H5	3.74 <sup>a</sup>	C9	142.94
H5'	3.49 <sup>a</sup>	C10, C14	133.88
H6	1.63	C11, C13	128.62
H7	1.87	C12	136.12
H7'	3.26	C15	21.12
H8	1.07		
H10, H14	7.51		
H11, H13	7.15		
H15	2.40		

<sup>a</sup> Chemical shifts of overlapping multiplets were defined from the correlation peaks of the 2D experiments.

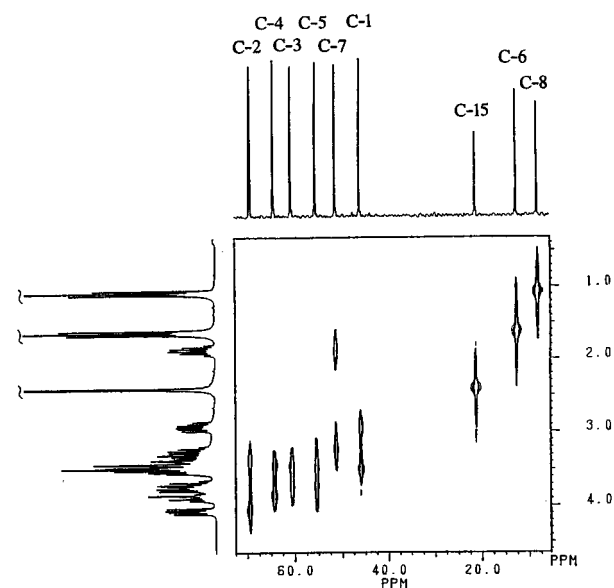
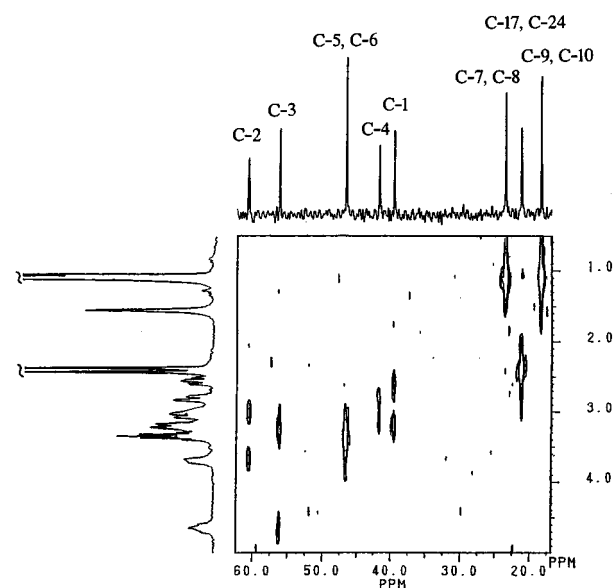
**Table 4.**  $^1\text{H}$   $\delta_{\text{H}}$  (ppm) and  $^{13}\text{C}$   $\delta_{\text{C}}$  (ppm) Chemical Shifts for Complex **8** in  $\text{CDCl}_3$  at 298 K

H1	3.18, 2.54	C1	39.51
H2	3.68, 3.02 <sup>a</sup>	C2	60.54
H3	4.64, 3.24 <sup>a</sup>	C3	56.15
H4	3.15, 2.79	C4	41.67
H5, H6	3.34	C5, C6	46.52
H7, H8	1.09	C7, C8	23.46
H9, H10	1.06	C9, C10	18.33
H12, H16	7.45	C11	137.45
H13, H15	7.19	C12, C16	134.18
H17	2.42	C13, C15	128.96
H19, H23	7.33	C14	136.02
H20, H22	7.12	C17	21.21
H24	2.36	C18	137.45
NH	5.5	C19, C23	133.61
		C20, C22	128.57
		C21	136.02
		C24	21.14

<sup>a</sup> Chemical shifts of overlapping multiplets were defined from the correlation peaks of the 2D experiments.

Protons are differentiated according to their orientation as endo (facing the oxygen of the  $\text{ReO}$  core) or exo (remote from the oxygen of the  $\text{ReO}$  core). Furthermore, the methylene protons of the ethyl groups on N2 (protons on C5 and C7) are distinguished according to their orientation toward the coligand: those facing the coligand are indicated in Table 3 with a prime. A detailed assignment procedure for the [SNN][S] ligand system has been previously reported from our team for analogous complexes of the oxotechnetium core,<sup>14</sup> and similar arguments have been employed in the peak assignments of complex **5**. The definition of the spatial arrangement of the protons on C5 and C7 of the ethyl substituents was based on the presence of an nOe peak between the exo H4 and one of the peaks assigned to H7 at 1.87 ppm. Consequently, the peak at 1.87 ppm was assigned to the H7 proton nearest to the SNN ligand, and its geminal at 3.26 ppm to the H-7 proton was oriented toward the aromatic coligand. The finding that protons oriented toward the aromatic coligand appear downfield compared to their geminals is in agreement with the observations of our previous studies on oxotechnetium complexes<sup>14</sup> and applies also to protons on C5.

**Complex 8.** The NMR study of the ligand system [SN][S]-[S] of complex **8** is of particular interest, since it has not previously appeared in the literature. A few points on the assignment procedure are presented below:

**Figure 5.**  $^{13}\text{C}$ - $^1\text{H}$  correlation (HETCOR) spectrum of complex **5** (range  $\delta_{\text{C}}$  72.52–5.41, range  $\delta_{\text{H}}$  4.65–0.32).**Figure 6.**  $^{13}\text{C}$ - $^1\text{H}$  correlation (HETCOR) spectrum of complex **8** (range  $\delta_{\text{C}}$  62.42–17.11, range  $\delta_{\text{H}}$  4.99–0.52).

In the HETCOR spectrum (Figure 6), carbon peaks close to the coordination sphere (carbons C1, C2, and C3) are easily distinguished from the rest, since the geminal protons on these carbons appear at substantially different chemical shifts due to their different orientations, principally with respect to the  $\text{ReO}$  core. On the basis of the relative electronegativity of the heteroatoms to which these carbons are attached (S vs N), the most upfield peak at 39.51 ppm was assigned to C1. The assignment of C1 and its attached protons at 3.18 and 2.54 ppm leads, through the coupling scheme displayed in the COSY spectrum, to protons H2 and, consequently, to C2. The assignment of C1 and C2 leaves the third carbon peak, which, in the HETCOR spectrum, has correlation peaks with protons at 4.64 and 3.24 ppm, to C3. The chemical shift of C4 at 41.67 ppm is comparable to the shift value of the corresponding methylene carbon of *N,N*-diisopropylethylamine (39.08 ppm) recorded in  $\text{CDCl}_3$  in our laboratory.

When the NMR spectra were taken in treated  $\text{CDCl}_3$  from which acidic impurities and residual water were removed to

slow the NH–water exchange, the presence of correlation peaks between the amine hydrogen and the neighboring protons on C2 and C3 confirmed the assignments. In the COSY spectrum in treated  $\text{CDCl}_3$  at 298 and 228 K, the NH proton has a strong correlation peak with the H2 proton at 3.02 ppm and a weak one with the H2 proton at 3.68 ppm. Since we know from crystallography that the  $\text{H}-\text{N1}-\text{C2}-\text{H2}_{\text{endo}}$  dihedral angle is  $177.7^\circ$  and the  $\text{H}-\text{N1}-\text{C2}-\text{H2}_{\text{exo}}$  angle is  $55.4^\circ$ , it is reasonable to assume that the proton with the stronger correlation peak at 3.02 ppm is the  $\text{H2}_{\text{endo}}$ .<sup>24</sup> This assignment, however, is in disagreement with what has been observed in our studies so far with the “tris” chelating  $[\text{SNS}][\text{S}]$  and  $[\text{SNN}][\text{S}]$  systems, as well as in the “tetra” chelating diaminedithiol  $[\text{SNNS}]$  system, where the endo protons appear downfield compared to their exo geminals. Since the observed chemical shifts of protons of the  $\text{S1}-\text{C1}-\text{C2}-\text{N1}$  part as well as the  $\Delta\delta(\text{endo}-\text{exo})$  difference of 0.65 ppm are within the values typically observed in our previous studies with oxorhenium complexes,<sup>25</sup> a reversal of the relative position of the exo/endo chemical shifts cannot be easily justified. Therefore, additional experimental evidence on the behavior of the  $\text{S1}-\text{C1}-\text{C2}-\text{N}$  chelated system is required from the study of suitably substituted analogues. Thus, in Table 4, geminal protons on C2 and C1 are not distinguished as endo or exo.

Due to the asymmetry of the molecule, the two isopropyl groups as well as the two phenylthiol substituents are in different magnetic environments and appear at different chemical shifts. Distinction of the absolute position of each of the isopropyl and thiophenyl groups is not possible from the NMR data and, consequently, chemical shifts reported in Table 4 are not position specific.

In summary, the isolation of the novel oxorhenium complexes **7–9** demonstrated the importance of the tertiary amine substituents of the ligand SNN (general formula  $\text{RCH}_2\text{CH}_2\text{NHCH}_2\text{CH}_2\text{SH}$ , where  $\text{R} = \text{N}(\text{C}_2\text{H}_5)_2$ ,  $\text{N}[\text{CH}(\text{CH}_3)_2]_2$ , or pyrrolidin-1-yl) in defining the structure of the generated complex in the presence of a monodentate thiol coligand. When  $\text{R} = \text{N}(\text{C}_2\text{H}_5)_2$  or pyrrolidin-1-yl, the tertiary nitrogen atom acts as a donor

atom, and it gives rise to complexes **4–6** of the “3+1”  $[\text{SNN}][\text{S}]$  type. Complexes of this type have been isolated before with the oxotechnetium core and the same ligand system with  $\text{R} = \text{N}(\text{CH}_3)_2$ , pyrrolidin-1-yl, and piperidin-1-yl.<sup>14</sup> The X-ray studies of **4** and **6** showed that the coordination environment of rhenium is formed by the SNN donor set of the tridentate ligand, the sulfur of the monodentate aromatic thiol, and the doubly bonded oxygen in an almost perfect square pyramidal geometry for **4** ( $\tau = 0.07$ ) or a distorted square pyramidal geometry for **6** ( $\tau = 0.24$ ). When  $\text{R} = \text{N}[\text{CH}(\text{CH}_3)_2]_2$ , the presence of the two bulky isopropyl groups prevents the tertiary nitrogen from acting as a donor atom and from participating in the coordinating sphere of rhenium. Thus, a novel class of complexes of the “2+1+1”  $[\text{SN}][\text{S}][\text{S}]$  type is generated. X-ray studies of **7** and **8** demonstrated that the coordination sphere of rhenium is formed by the SN donor set of the ligand, two sulfur atoms of the two aromatic thiol coligands, and the doubly bonded oxygen atom in a distorted squared pyramidal geometry ( $\tau = 0.44$  and  $0.45$  for **7** and **8**, respectively).

All synthesized complexes are neutral, lipophilic, and stable during manipulation. NMR studies of **5** and **8** revealed that the complexes are stable in  $\text{CDCl}_3$  solution over a period of months. Due to the asymmetry of the complexes and the anisotropic environment around rhenium, all protons and carbons have distinct NMR resonances.

This study further explores the parameters associated with the formation of the mixed-ligand oxorhenium complexes and is expected to be helpful in the preparation and characterization of biologically significant molecules with  $^{188}\text{Re}$  or  $^{99\text{m}}\text{Tc}$ . Studies at the tracer level with these radionuclides and their radiopharmaceutical chemistry are in progress.

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**Supporting Information Available:** Tables of crystal, intensity collection, and refinement data; positional and equivalent thermal parameters for all non-H atoms; anisotropic thermal parameters of all non-H atoms; and full bond lengths and angles for complexes **4**, **6**, **7**, and **8**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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