New Mixed-Ligand Re^V Complexes with Bis(2-mercaptoethyl) Sulfide and Functionalized Thioimidazolyl Ligands

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The preparation of the mixed-ligand Re^V complexes [Re(O)(κ^3-SSS)(κ^1-Simz)] (**1**), [Re(O)(κ^3-SSS)(κ^1-Simz)]·HCl (**2**) and [Re(O)(κ^3-SSS)(κ^1-SimzCOGlyGly)] (**3**) are described. These [3+1] type compounds are stabilized by tridentate bis(2-mercaptoethyl) sulfide (HSSSH) and by monodentate functionalized thioimidazolyl ligands. Complexes **1**, **2** and **3** were fully characterized by IR and ^{1}H NMR spectroscopy, and by X-ray diffraction analysis in the case of **1** and **2**. In complexes **1** and **2** the Re atom is five-coordinate, presenting a distorted square pyramidal coordination geometry. Based on the angular structural parameter, τ, this distortion lies towards a trigonal bipyramidal geometry (τ = 0.40, **1**; τ = 0.46, **2**).

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Introduction

The development of mixed-ligand complexes of Re and Tc, of the so-called [3+1] type, has been thoroughly investigated for labeling biomolecules, namely CNS receptor ligands. For this purpose different tridentate ligands and mono thiol co-ligands have been used.[1−7] This approach can be considered to be greatly advantageous since the combination of different ligands has allowed the synthesis of complexes with a wide variety of chemical and biochemical properties. However, in spite of this versatility they show a remarkable *in vivo* reactivity against nucleophiles, namely SH-group containing compounds like glutathione. This instability arises not only from ligand-exchange reactions between the co-ligand and nucleophiles, but also from the presence of a vacant coordination site trans to the oxo group.[3,6] Both processes depend on the nature and the concentration of the tridentate and monodentate ligands. In order to overcome this problem we studied the chemistry of Re and Tc using the well-known tridentate ligand bis(2-mercaptoethyl) sulfide (HSSSH) and functionalized thioimidazolyl molecules as co-ligands. This type of co-ligands can coordinate through the nitrogen and sulfur atoms. This bidentate coordination mode could provide complexes with higher stability against substitution.[3,6] The functionalized thioimidazolyl molecules will also allow the labelling of small peptides with $[^{99m}Tc(O)]^{3+}$. In this paper, we report on the synthesis and characterization of the mixed-ligand Re^V complexes, stabilized with these co-ligands, including one bearing a dipeptide (GlyGly): [Re(O)(κ^3-SSS)(κ^1-Simz)] (**1**), [Re(O)(κ^3-SSS)(κ^1-Simz)]·HCl (**2**) and [Re(O)(κ^3-SSS)(κ^1-SimzCOGlyGly)] (**3**).

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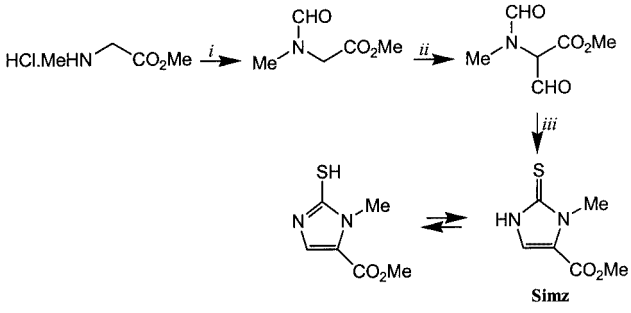
Results and Discussion

Synthesis and Characterization of the Simz, SimzCOOH and SimzCOGlyGly Co-Ligands

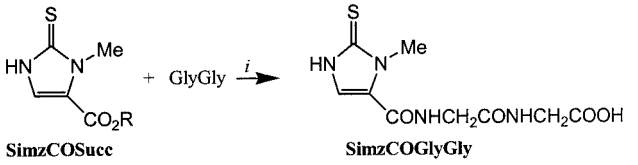
Methyl (2-mercapto-3-methylimidazol-4-yl)methanoate (**Simz**) was obtained, in a fair yield (68%), by a slight modification of a previously reported method.[9] The synthetic pathway for its preparation involves the formation of *N*-formyl and *C*-formyl intermediates, followed by ring formation with KSCN (Scheme 1).



Scheme 1. Synthesis of the **Simz** co-ligand; (*i*) NEt_3, HCOOH, THF, reflux; (*ii*) $NaOCH_3$, CH_3OCHO, room temperature; (*iii*) HCl, KSCN, 65−70° C

2-(Mercapto-3-methylimidazol-4-yl)methanoic acid (**SImzCOOH**) was isolated as a white precipitate in an almost quantitative yield (97%) by classical hydrolysis of the **Simz** ester under basic conditions, followed by acidification of the reaction solution. The compound glycylglycine (2-

mercapto-3-methylimidazol-4-yl)methanamide (**SimzCOGlyGly**) was obtained by reacting [(2-mercapto-3-methylimidazol-4-yl)methyloxy]succinimide (**SimzCOSucc**)[10,11] with Glycylglycine (**GlyGly**) (Scheme 2). For the coupling reaction to proceed, it is necessary of the presence of a deprotonating agent such as triethylamine. The compound **SimzCOGlyGly** is poorly soluble in most organic solvents, and is readily soluble in aqueous alkaline solutions only (pH ≈ 12).



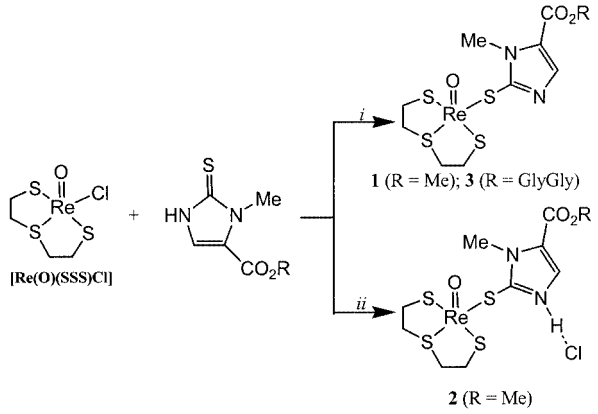
Scheme 2. Synthesis of **SimzCOGlyGly**; R = *N*-succinimido; (*i*) NEt_3, THF, DMF, H_2O, room temperature

The most important features in the IR spectra of **Simz** and derivatives is the existence of strong bands in the 1630−1765 cm^{-1} range, and medium intensity bands in the 735−760 cm^{-1} range, which are assigned to the ν(C=O) and ν(C=S) stretching vibrations, respectively.

The ^1H NMR spectra of **Simz**, **SimzCOOH** and **SimzCOSucc** in CD_3OD present one singlet at δ = 3.81, 3.81 and 3.78 ppm, respectively, assigned to the methyl group attached to one of the nitrogen atoms of the thioimidazolyl ring. **Simz** presents another singlet at δ = 3.83 ppm, which is assigned to the methyl group of the ester. In all spectra, one resonance assigned to the methylenic proton of the ring system can also be observed (**Simz**: δ = 7.61 ppm; **SimzCOOH**: δ = 7.57 ppm; **SimzCOsucc**: δ = 8.05 ppm). The NH proton of the thioimidazolyl ring is also observed when $CDCl_3$, CD_3CN or $[(CD_3)_2SO]$ is used as solvent. For instance, in the case of the **Simz** ligand, that signal appears as a broad singlet at δ = 12.08 ppm in $CDCl_3$ and at δ = 10.28 ppm in CD_3CN. In the IR spectrum, the (glygly)-functionalized thioimidazolyl ligand (**SimzCOGlyGly**) presents two strong bands at 1630 cm^{-1} and 1715 cm^{-1}, assigned to the ν(C=O) stretching vibrations of the amide functionalities and of the free carboxylic acid of the dipeptide. A characteristic medium band at 760 cm^{-1} also appears, which is assigned to the $\tilde{\nu}$(C=S) stretching vibration. The ^1H NMR spectrum in $[(CD_3)_2SO]$ of this ligand compares well with the above mentioned thioimidazolyl derivatives: a singlet at δ = 3.66 ppm assigned to the methyl group, a singlet at δ = 7.58 ppm assigned to the methylenic proton of the ring, and a broad singlet at δ = 12.55 ppm assigned to the NH group of the ring. The signals corresponding to the dipeptide are also clearly observed: two sets of doublets at δ = 3.75 and 3.83 ppm are assigned to the CH_2 groups, and two sets of triplets at δ = 8.23 and 8.60 ppm are assigned to the protons of the amide.

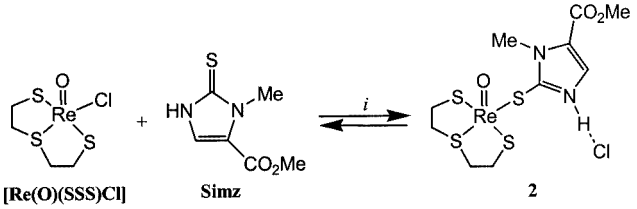
Synthesis and Characterization of the Complexes

Reactions of **Simz** and **SimzCOGlyGly** with the (chloro)oxorhenium(V) complex [ReO(SSS)Cl],[8] under different conditions, afforded the mixed-ligand complexes [Re(O)(κ³-SSS)(κ¹-Simz)] (**1**), [Re(O)(κ³-SSS)(κ¹-Simz)]·HCl (**2**) and [Re(O)(κ³-SSS)(κ¹-SimzCOGlyGly)] (**3**) (Scheme 3).



Scheme 3. Synthesis of complexes **1**, **2** and **3**; (*i*) NEt_3, CH_2Cl_2 (**1**), CH_3CN (**3**), reflux; (*ii*) CH_3CN, reflux

The neutral oxo complex **1** was obtained in a 68% yield, after appropriate workup, by refluxing [Re(O)(SSS)Cl] with **Simz** in CH_2Cl_2, with NEt_3 as the deprotonating agent. In this complex, the monodentate thioimidazolyl co-ligand is mononegative. When the reaction is run in CH_3CN, and in the absence of a base, the ^1H NMR spectrum of the product obtained, after workup, indicates a mixture of three species. Two of these species are unambiguously identified as [Re(O)(SSS)Cl] and free functionalized thioimidazolyl. The third species presented an ^1H NMR spectrum that is consistent with the presence of one tridentate SSS and one neutral **Simz** ligand (^1H NMR (δ, CD_3CN): 10.43 (1 H, s, br., NH), 7.84 (1 H, s, CH), 4.10−4.05 (2 H, m, CH_2), 3.88 (3 H, s, CH_3), 3.85 (3 H, s, CH_3), 3.13 (2 H, m, CH_2)). Recrystallization of the crude product of this reaction, from CH_3CN/hexane, led to the formation of violet crystals and to the precipitation of a blue solid. The blue solid was identified by ^1H NMR spectroscopy as [Re(O)(SSS)Cl]. The X-ray diffraction analysis of the violet crystals allowed the formulation of complex **2**, where the Simz is not deprotonated and is neutral. These crystals, after being washed with CH_3CN to remove any [Re(O)(SSS)Cl] present, were analyzed by NMR spectroscopy. The spectrum was identical to the one observed for the crude product. This result can only be explained by assuming that in solution **2** dissociates as indicated in Scheme 4.



Scheme 4. (*i*) CH_3CN

The neutral oxo complex **3** was obtained in a 60% yield by refluxing [ReO(SSS)Cl] and **SimzCOGlyGly** in dry

CH_3CN in the presence of NEt_3. Complex **1** is soluble in chlorinated solvents and insoluble in methanol and water. Complex **3**, which bears a GlyGly moiety, is soluble in methanol, relatively soluble in water and insoluble in chlorinated solvents. Both complexes **1** and **3** are air- and moisture-stable.

Complexes **1**, **2** and **3** present strong bands in the IR spectra at 970 cm^{-1}, which are assigned to the ν(Re=O) stretching vibrations. This value compares well with those found in other compounds of the [3+1] type, previously described (930−980 cm^{-1}).[7] Strong bands at 1715, 1725, and at 1535 cm^{-1}/1645 cm^{-1} are assigned to the ν(C=O) stretching vibrations of complexes **1**, **2** and **3**, respectively.

In the ^1H NMR spectra of **1** and **3**, four sets of multiplets appear, which are assigned to the methylenic protons of the tridentate ligand HSSSH; most of these signals are shifted upfield relative to those of the corresponding free ligand. For complex **2**, the identification of all methylenic protons of the tridentate ligand was not possible since two of the resonances are superimposable with those of [ReO(SSS)Cl], which is also present due to the equilibrium depicted in Scheme 4.

The chemical shifts corresponding to the monodentate ligand of the complexes **1** (δ = 7.73, 3.85 and 3.82 ppm) and **2** (δ = 10.43, 7.84, 3.88 and 3.85 ppm) in CD_3CN are shifted downfield relative to those of the free ligand (δ = 10.28, 7.45, 3.78 and 3.73 ppm) in the same solvent. The same holds true for complex **3** in CD_3OD (**3**: δ = 7.76, 4.05, 3.94 and 3.89 ppm; **SimzCOGlyGly**: δ = 7.51, 4.00, 3.88 and 3.79).

Crystal Structures of [Re(O)(κ³-SSS)(κ¹-Simz)] (1) and [Re(O)(κ³-SSS)(κ¹-Simz)]·HCl (2): Suitable crystals for X-ray structural analysis were obtained for complexes **1** and **2**. ORTEP views are shown in Figure 1 and Figure 2, and selected bond lengths and angles for both complexes are presented in Table 1.

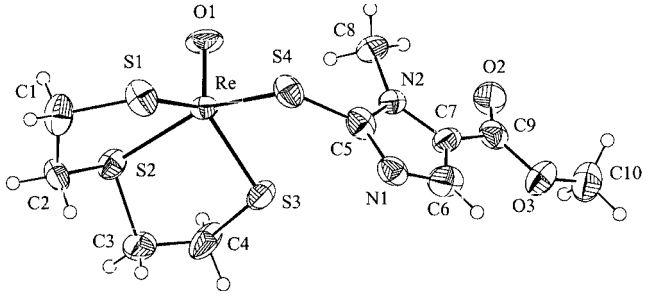


Figure 1. ORTEP drawing of complex **1** with the atom numbering scheme; thermal ellipsoids are drawn at the 40% probability level. Hydrogen atoms were introduced in calculated positions.

Complex **2** is monocationic with a chloride atom as the counterion, while complex **1** is neutral. In both compounds the coordination geometry around the five-coordinate Re^v atom is best described as distorted square-pyramidal, with the axial Re−O(1) bond length significantly shorter than the Re−L(basal) distances. The Re=O(1) bond lengths in **1** [1.683(8) Å] and **2** [1.673(5) Å] are comparable, and are in the range (1.67−1.70 Å) so far observed for this type of

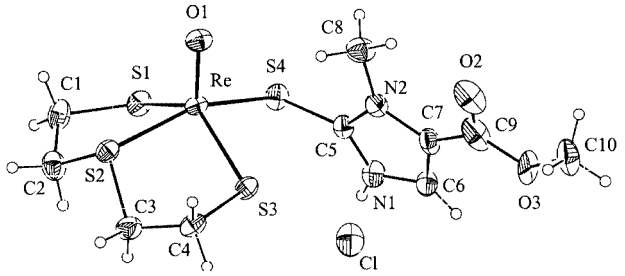


Figure 2. ORTEP drawing of complex **2** with the atom numbering scheme; thermal ellipsoids are drawn at the 30% probability level. Hydrogen atoms were introduced in calculated positions.

Table 1. Selected bond lengths (Å) and Angles (°) for [Re(O)(κ³-SSS)(κ¹-Simz)] (**1**), and [Re(O)(κ³-SSS)(κ¹-Simz)]·HCl (**2**)

	1	2
Re−O(1)	1.683(8)	1.673(5)
Re−S(1)	2.285(3)	2.290(2)
Re−S(2)	2.367(3)	2.364(2)
Re−S(3)	2.285(3)	2.282(2)
Re−S(4)	2.327(3)	2.345(2)
S(4)−C(5)	1.745(13)	1.734(7)
O(1)−Re−S(1)	114.5(3)	116.6(2)
O(1)−Re−S(2)	100.6(3)	99.3(2)
O(1)−Re−S(3)	115.1(3)	115.4(2)
O(1)−Re−S(4)	105.3(3)	105.1(2)
S(1)−Re−S(3)	130.35(14)	127.86(7)
S(3)−Re−S(4)	87.64(12)	88.29(7)
S(1)−Re−S(4)	82.38(12)	81.15(7)
S(3)−Re−S(2)	84.25(11)	84.44(7)
S(1)−Re−S(2)	84.18(11)	84.76(7)
S(4)−Re−S(2)	154.00(11)	155.29(7)
Re−S(4)−C(5)	110.7(4)	110.1(2)

3+1 compounds.[1−6,12−16] The C−S bond lengths [1.745(13) Å (**1**), 1.734(7) Å (**2**)] are comparable and are similar to those found previously,[17] which range from 1.68 to 1.73 Å. Additionally, provided that the values found for the best least-square planes through the atoms S(1)−S(2)−S(3)−S(4) (RMSD = 0.218 Å for **1**, RMSD = 0.253 Å for **2**) show significant deviations from planarity, we conclude that these atoms in both structures do not define a basal plane. The chloride ion is hydrogen bonded to N(1) and the distance between them [3.023(8) Å] allows for the presence of a hydrogen atom [N(1)−H(1): 0.86 Å, H(1)···Cl: 2.18 Å]. The angle N(1)−H(1)−Cl is 166.7°, which can be considered to be linear. Relative to the coordination positions, in both complexes (**1** and **2**), only one of the axial positions is occupied by the oxo group. The equatorial positions are defined by sulfur atoms, three from the tridentate and dianionic ligand $(SSS)^{2-}$, and a thione sulfur atom belonging to the monodentate thioimidazolyl co-ligand.

The Re−S(4) bond lengths in **1** [2.327(3) Å] and **2** [2.345(2) Å] are comparable and typical of a monothiolate. The Re−S bonds within the tridentate ligand in **1** [2.285(3), 2.367(3) and 2.285(3) Å] and **2** [2.290(2), 2.364(2) and 2.282(2) Å] compare with the values found for the same

Table 2. Crystallographic data for complexes **1** and **2**

	1	**2**
Empirical formula	$C_{10}H_{15}N_2O_3S_4Re{\cdot}CHCl_3$	$C_{10}H_{16}ClN_2O_3S_4Re$
Formula mass	645.05	578.14
Crystal size, mm	0.18 × 0.17 × 0.17	0.34 × 0.18 × 0.10
Temperature, K	293(2)	293(2)
Crystal system	Monoclinic	Triclinic
Space group	$P2_1/c$	$P\bar{1}$
a, Å	8.275(2)	8.069(2)
b, Å	17.287(2)	9.935(2)
c, Å	14.373(3)	12.664(2)
α, deg		96.830(10)
β, deg	98.37(2)	92.000(10)
γ, deg		109.80(2)
V, Å^3	2034.2(7)	945.3(3)
Z	4	2
Density (calcd.), g·cm^{-3}	2.106	2.031
Absorption coefficient, mm^{-1}	6.791	7.024
2θ Range, deg	3.7−56.00	3.24−54.00
Reflections collected	5082	4385
Independent reflections	4896 [*R*(int) = 0.0502]	4140 [*R*(int) = 0.0201]
Parameters	217	223
Observed reflections [$I>2\sigma(I)$]	2917	3539
Final *R* indices [$I>2\sigma(I)$]	$R1$[a] = 0.0637 $wR2$[b] = 0.0995	$R1$[a] = 0.0390 $wR2$[b] = 0.0869
Goodness-of-fit	1.087	1.052

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [b] $wR2 = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$; $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$, where $P = (F_o^2 + 2F_c^2)/3$.

type of bond in complexes of the 3+1 type, stabilized by SSS chelates.[1,18]

The five-membered rings, formed by the atoms Re, S(1), C(1), C(2) and S(2) are in the twisted form in both complexes. Relative to the plane [Re−S(1)−S(2)], C(1) is 0.53 and 0.50 Å above the plane for **1** and **2**, respectively, and C(2) is −0.25 and −0.21 Å below the plane for **1** and **2**, respectively.

The five-membered rings, formed by the atoms Re, S(2), C(3), C(4) and S(3) are in the twisted form in both complexes. Relative to the plane [Re−S(2)−S(3)], C(3) and C(4) are equally far from the plane by 0.37 Å in complex **1,** and in **2** are 0.30 and −0.39 Å above and below the plane, respectively.

In terms of the trigonality index, τ, the values are 0.40 and 0.46 for **1** and **2**, respectively (τ = 0 for a regular square pyramid, τ = 1 for a regular trigonal bipyramid).[19] According to the results in this work and those obtained earlier for complexes with a SSS/S donor atom set,[1,18] the τ values remain between 0.253−0.473. This means that the majority of structures in this study may be classified as intermediate between the square pyramidal and trigonal bipyramidal limiting geometries, but in agreement with the structural index parameter (τ) adopted, all of the structures are described as distorted square pyramidal rather than distorted trigonal bipyramidal. The major distortions from the regular square pyramidal geometry arise from the chelate bite angles of the tridentate ligand (see Table 2).

We also note that one of the reasons that the thioimidazolyl co-ligand acts as a monodentate ligand may be due to the existence of a wide angle [Re−S(4)−C(5): 110.7(4)° (for **1**) and 110.1(2)° (for **2**)] that prevents N(1) from coordinating to the metal.

Concluding Remarks

Using the tridentate bis(2-mercaptoethyl) sulfide ligand and functionalized thioimidazolyl co−ligands, it was possible to isolate and characterize oxorhenium(V) complexes of the [3+1] type. The complexes are stable in solution when the monodentate thioimidazolyl co-ligands are monoanionic. The functionalization of the thioimidazolyl with a dipeptide leads to a water soluble complex, which is promising for biomedical applications.

Experimental Section

General Procedures: All chemicals were of reagent grade. Solvents were dried and distilled prior to use, according to described procedures. Methyl (2-mercapto-3-methylimidazol-4-yl) methanoate (**Simz**) was prepared by a modification of a reported method and [Re(O)(SSS)Cl] as described in the literature.[8,9] The reactions were run in air unless otherwise indicated. ^{1}H NMR spectra were recorded on a Varian Unit 300 MHz spectrometer. ^{1}H chemical shifts were referenced to the residual solvent resonance relative to tetramethylsilane. The NMR samples were prepared in $CDCl_3$, CD_3OD, $[(CD_3)_2SO]$ and CD_3CN. Infrared spectra were recorded in the range 4000−200 cm^{-1} on a Perkin−Elmer 577 spectrometer with KBr pellets. Elemental analyses were performed on a Perkin−Elmer automatic analyser.

Methyl (2-Mercapto-3-methylimidazol-4-yl)methanoate (Simz). i. Methyl *N*-Formylsarcosinate: Triethylamine (48 mL, 0.344 mol) and formic acid (4.8 mL, 0.127 mol) were added to a solution of sarcosine methyl ester hydrochloride (16.0 g, 0.115 mol) in THF (30 mL). The suspension was stirred at 125° C overnight, cooled to room temperature, filtered, and the obtained solid rinsed with THF. The filtrate was collected and the solvent evaporated to dryness. The obtained yellow oil was dissolved in water (20 mL) and a solution of NaOH (1 N) was added dropwise until pH = 7. After extracting with CH_2Cl_2 (3 × 20 mL), the solution was dried over magnesium sulfate, filtered and concentrated to dryness. A white solid was obtained. Yield: 8.53 g (57%). ^{1}H NMR (δ, $CDCl_3$) two rotamers: 2.62 (s, 3 H, NCH_3), 2.77 (s, 3 H, NCH_3), 3.46 (s, 2 H, CH_2), 3.49 (s, 2 H, CH_2), 3.79 (s, 1 H, OCH_3), 3.82 (s, 1 H, OCH_3), 7.76 (s, 1 H, CHO), 7.83 (s, 1 H, CHO).

ii. Methyl (2-Mercapto-3-methylimidazol-4-yl)methanoate (Simz): A solution of methyl *N*-formylsarcosinate (8.52 g, 65.0 mmol) in methyl formate (14 mL, 0.227 mol) was added dropwise to a solution of sodium methoxide (4.11 g, 76.1 mmol) in distilled THF (40 mL), at 10-15° C. The resulting mixture was stirred overnight at room temperature. The solvent was removed under vacuum and the residue diluted with 150 mL MeOH/H_2O (1:1). The solution was treated with activated carbon, filtered and cooled in ice. Hydrochloric acid (12 N, 13 mL) and a solution of potassium thiocyanate (7.92 g, 81.5 mmol) in a minimum amount of water were added, and the resulting solution heated at 65°-70° C for 24 hours. The precipitate formed was removed by filtration, and the solvent was evaporated to dryness affording a white solid that corresponds to the pure product. Yield: 7.57 g (68%). ^{1}H NMR ($CDCl_3$): δ = 3.84 (s, 3 H, CH_3), 3.87 (s, 3 H, CH_3), 7.42 (s, 1 H, CH), 12.08 (br. s, 1 H, NH) ppm. ^{1}H NMR (CD_3OD): δ = 3.81 (s, 3 H, CH_3), 3.83 (s, 3 H, CH_3), 7.61 (s, 1 H, CH) ppm. ^{1}H NMR (CD_3CN): δ = 3.73 (s, 3 H, CH_3), 3.78 (s, 3 H, CH_3), 7.45 (s, 1 H, CH), 10.28 (br. s, 1 H, NH) ppm. IR (KBr): $\tilde{\nu}$ = 1715 cm^{-1} (vs, C=O), 755 cm^{-1} (m, C=S).

(2-Mercapto-3-methylimidazol-4-yl)methanoic Acid (SImzCOOH): Methyl (2-mercapto-3-methylimidazol-4-yl)methanoate (Simz) (6.00 g, 34.8 mmol) was dissolved in a NaOH solution (50 mL, 2.1 M). After 3 hours at room temperature, whilst stirring, HCl (3 N) was added dropwise until pH = 1−2. A white solid precipitated that was collected by filtration, washed with water and dried. Yield: 5.33 g (97%). ^{1}H NMR (CD_3OD): δ = 3.81 (s, 3 H, CH_3), 7.57 (s, 1 H, CH) ppm. IR (KBr): $\tilde{\nu}$ = 1670 cm^{-1} (vs, C=O), 755 cm^{-1} (m, C=S). $C_5H_6N_2O_2S$ (158.2): calcd. C 37.97, H 3.82, N 17.71, S 20.27; found C 38.13, H 4.11, N 17.55, S 20.52.

[(2-Mercapto-3-methylimidazol-4-yl)methyloxy]succinimide (SimzCOSucc): *N*-hydroxysuccinimide (0.71 g; 6.2 mmol) was added to a suspension of SimzCOOH (0.89 g; 5.6 mmol) in CH_2Cl_2 (15 mL) in an ice bath, and the mixture was stirred for 15 minutes. On addition of *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimidehydrochloride (1.19 g; 6.2 mmol) and after stirring for 63 hours, the reaction was complete. The solvent was evaporated to dryness, and the urea formed and the excess *N*-hydroxysuccinimide were removed by washing the residue with water. The compound was then vacuum-dried for several hours and used without further purification. Yield: 1.35 g (95%). ^{1}H NMR (CD_3OD): δ = 2.88 (s, 4 H, C_2H_2), 3.78 (s, 3 H, CH_3), 8.05 (s, 1 H, CH) ppm. ^{1}H NMR [$(CD_3)_3SO$]: δ = 2.86 (s, 4 H, C_2H_2), 3.66 (s, 3 H, CH_3), 8.34 (s, 1 H, CH), 13.21 (br. s, 1 H, NH) ppm. IR (KBr): $\tilde{\nu}$ = 1725 cm^{-1}, 1765 cm^{-1} (vs, C=O), 735 cm^{-1} (m, C=S). $C_9H_9N_3O_4S{\cdot}H_2O$ (273.3): calcd. C 39.56, H 4.06, N 15.38, S 11.73; found C 40.02, H 3.92, N 15.52, S 12.03.

Glycylglycine (2-Mercapto-3-methylimidazol-4-yl)methanamide (SimzCOGlyGly): A mixture of glycylglycine (0.25 g; 1.9 mmol) and triethylamine (0.30 mL, 2.2 mmol) in THF/H_2O 3:4 (7 mL) was added dropwise, at room temperature, to a stirred solution of SimzCOSucc (0.25 g; 0.97 mmol) in THF/DMF 1:1 (4 mL). After 20 hours, whilst stirring at room temperature, the solvent was evaporated to dryness and the white solid obtained was washed with water. Yield: 0.053 g (20%). ^{1}H NMR (CD_3OD): δ = 3.79 (s, 3 H, CH_3), 3.88 (s, 2 H, CH_2), 4.00 (s, 2 H, CH_2), 7.51 (s, 1 H, CH). ^{1}H NMR [$(CD_3)_2SO$]: δ = 3.66 (s, 3 H, CH_3), 3.75 (d, 2 H, CH_2), 3.83 (d, 2 H, CH_2), 7.58 (s, 1 H, CH), 8.23 (t, 1 H, NH), 8.60 (t, 1 H, NH), 12.55 (br. s, 1 H, NH) ppm. IR (KBr): $\tilde{\nu}$ = 3060 cm^{-1}, 3220 cm^{-1}, 3320 cm^{-1}(m, N−H), 1630 cm^{-1}, 1715 cm^{-1} (vs, C=O), 760 cm^{-1} (m, C=S). $C_9H_{12}N_4O_4S$ (272.3): calcd. C 39.70, H 4.44, N 20.58, S 11.77; found C 38.97, H 4.32, N 20.01, S 11.18.

[Re(O)(κ^3-SSS)(κ^1-Simz)] (1): A solution of **Simz** (0.071 g; 0.41 mmol) and triethylamine (68 μL, 0.49 mmol) in dichloromethane (2 mL) was added dropwise, at room temperature, to a stirred solution of [Re(O)Cl(SSS)] (0.080 g; 0.21 mmol) in the same solvent (9 mL). After several minutes the color of the solution turned brown. The mixture was refluxed under a nitrogen atmosphere for 4 hours. A brown solid was obtained after evaporation of the solvent and washing with methanol. Brown crystals suitable for X-ray diffraction analysis were obtained by slow diffusion of hexane to a solution of the complex in chloroform. Yield: 0.072 g (67%). ^{1}H NMR (CD_3CN): δ = 2.28−2.18 (m, 2 H, CH_2), 3.14−3.04 (m, 2 H, CH_2), 3.82 (s, 3 H, CH_3), 3.85 (s, 3 H, CH_3), 4.07−4.02 (m, 2 H, CH_2), 4.24−4.18 (m, 2 H, CH_2), 7.73 (s, 1 H, CH) ppm. IR (KBr): $\tilde{\nu}$ = 1715 cm^{-1}, (vs, C=O), 970 cm^{-1} (s, Re=O), 740 cm^{-1}, 760 cm^{-1}, 770 cm^{-1}. $C_{10}H_{15}N_2O_3S_4Re{\cdot}3CHCl_3$ (883.8): calcd. C 17.67, H 2.05, N 3.17 S 14.51; found C 17.52 H 1.98, N 3.08, S 14.02.

[Re(O)(κ^3-SSS)(κ^1-Simz)]·HCl (2): A suspension of Simz (0.022 g, 0.13 mmol) in CH_3CN (2 mL) was added dropwise, at room temperature, to a blue solution of [Re(O)Cl(SSS)] (0.050 g, 0.13 mmol) in the same solvent (9 mL). The violet mixture was refluxed under a nitrogen atmosphere for 4 hours. The solvent was evaporated, the crude product was washed with CH_3CN and, after drying under vacuum, analyzed by ^{1}H NMR spectroscopy. The NMR spectrum indicates a mixture of three species, two of them identified as **Simz** and [Re(O)Cl(SSS)]. Recrystallization of the crude solid from CH_3CN/hexane led to violet crystals, which were formulated as complex **2** by X-ray diffraction analysis. IR (KBr): $\tilde{\nu}$ = 1725 cm^{-1} (vs, C=O), 965 cm^{-1}(s, Re=O), 750 cm^{-1}, 760 cm^{-1}.

[Re(O)(κ^3-SSS)(κ^1-SimzCOGlyGly)] (3): A mixture of **SimzCOGlyGly** (0.029 g, 0.11 mmol) and triethylamine (18 μL, 0.13 mmol) in acetonitrile (2 mL) and a few drops of dry dimethylformamide was added dropwise, at room temperature, to a stirred solution of [Re(O)Cl(SSS)] (0.050 g, 0.13 mmol) in acetonitrile (9 mL). After several minutes the color of the solution turned brown. The reaction mixture was refluxed under a nitrogen atmosphere overnight and the solvent evaporated to dryness. The residue obtained was extracted with methanol and a brown solid was obtained after evaporation of the solvent. This compound was then washed with acetonitrile and further purified by recrystallization from methanol/dichloromethane. Yield: 0.044 g (64%). ^{1}H NMR (CD_3OD): δ = 2.32−2.22 (m, 2 H, CH_2), 3.13−3.03 (m, 2 H, CH_2), 3.89 (s, 3 H, CH_3), 3.94 (s, 2 H, CH_2), 4.05 (s, 2 H, CH_2), 4.13−4.08 (m, 2 H, CH_2), 4.26−4.20 (m, 2 H, CH_2), 7.76 (s, 1 H, CH) ppm. IR (KBr): $\tilde{\nu}$ = 1645 cm^{-1}, 1535 cm^{-1} (vs, C=O), 970 cm^{-1} (s, Re=O). $C_{13}H_{19}N_4O_5S_4Re{\cdot}2CH_2Cl_2$ (795.6): calcd. C 22.64, H 2.91, N 7.04, S 16.12; found C 22.69, H 2.64, N 7.32, S 16.35.

X-ray Crystallographic Analysis: A brown crystal of **1** was obtained by recrystallization from $CHCl_3$/hexane, and a violet crystal of **2** was obtained from CH_3CN/hexane. Both were mounted in thin-walled glass capillaries. Data were collected at room temperature on an Enraf−Nonius CAD-4 diffractometer with graphite-monochromatized Mo-K_α radiation, using a ω-20 scan mode. The crystallographic data for both complexes are summarized in Table 2. Unit cell dimensions were obtained by least-squares refinement of the setting angles of 25 reflections with $14.85<2\theta<27.28°$ for **1** and $15.30<2\theta<26.87°$ for **2**. Data were corrected for Lorentz and polarization effects, for linear decay (for **1**) and for absorption by empirical corrections based on ψ scans.[20] The heavy atom positions were located by Patterson methods using SHELXS-86.[21] The remaining atoms were located by successive different Fourier maps and refined by least-squares refinements on F^2 using SHELXL-93.[22] One $CHCl_3$ molecule of crystallization was also located in the Fourier difference map for **1**. In **2**, the atoms O(2), C(3) and C(10) are disordered over two positions rotated about the C(7)−C(9) bond, which refined with site occupancy factors of 0.69 and 0.31, respectively (in the interests of clarity only one site is shown in Figure 2). In the residual electron density of **2**, the highest peak was assumed to be an oxygen atom of a water molecule, which presents a high thermal motion. All the non-hydrogen atoms were refined with anisotropic thermal motion parameters and the contribution of the hydrogen atoms was included in calculated positions, (except the hydrogens of the water molecule in **2**). The drawings were made with ORTEP-3 and the calculations were performed on a DEC α 3000 computer.[23] CCDC-178292 (**1**) and CCDC-178293 (**2**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) +44−1223/336−033; E-mail: deposit@ccdc.cam.ac.uk].

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