Crystal Structure of a Bis(amido)bis(thiolato)oxorhenium(V) Complex That Forms a Methanol-Solvated Salt with Calcium Extracted from Silica Gel

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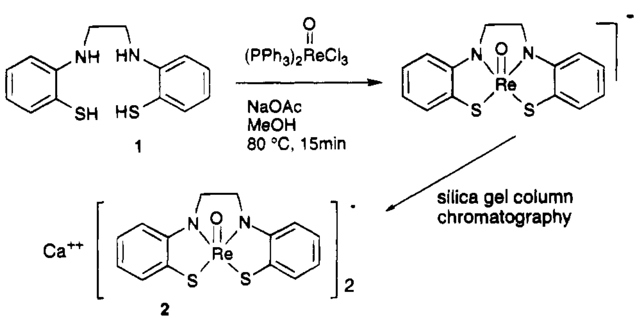
Complexes of oxorhenium(V) and oxotechnetium(V) with bis(amine)−bis(thiols) have been actively studied in the development of agents for diagnostic imaging (utilizing technetium-99m) or radiotherapy (utilizing rhenium-186 and 188).[1] In the preliminary stages of preparing complexes that might mimic the structure of nonsteroidal estrogens,[2] we prepared complex **2** of the aromatic bis(amine) bis(thiol) chelate **1**. The chelate **1** itself was prepared by standard methods (Scheme 1),[3] and the complex **2**, isolated after chromatography over silica gel, was obtained as a salt, and was shown by X-ray crystallography, unexpectedly, to have calcium as its counterion. The calcium counterion appears to originate from the chromatographic medium, and in the crystal structure of complex **2**, it is solvated by seven molecules of methanol in a novel capped trigonal prism geometry.

Complex **2** was prepared by warming chelate **1** (55.2 mg, 0.20 mmol) with trichlorobis(triphenylphosphine)oxorhenium(V) (166.6 mg, 0.20 mmol) and 2.0 mL of 1 N methanolic NaOAc (2.0 mmol) at 80 °C for 15 min. A yellow solid (100.0 mg) was collected by flash chromatography[4] (silica gel, 10% MeOH/CH_2Cl_2). Recrystallization from 50% MeOH/EtOH provided a good yield of complex **2**[5] as red single crystals, suitable for X-ray crystallography; these crystals were readily soluble in EtOH, but only sparingly soluble in MeOH.

The neutral form of most tetradentate (N_2S_2) oxorhenium(V) complexes is typically unsymmetrical, having three heteroatom metal bonds and one dative bond (the latter being to a protonated nitrogen atom), and therefore gives a complex ^1H NMR spectrum.[6] The ^1H NMR spectrum of rhenium complex **2**, by contrast, is very simple,[5] suggesting that it exists as a symmetrical anion formed by deprotonation of both nitrogen atoms.[7] The four methylene protons between the two nitrogens resonate at δ 4.30−4.40 and 4.62−4.70. According to an earlier precedent,[6] we assigned the downfield signal to the two protons that are on the same face of the complex as the oxygen of the Re=O core (*syn* to Re=O), and the upfield group to those on the opposite face (*anti* to Re=O). The large magnetic anisotropy of the metal−oxide bond effects a strong deshielding of protons that are close to the periphery of the π electron system.[6]

Scheme 1



The X-ray crystal structure[8] of complex **2** is shown in Figures 1 and 2 and Table 1. Two aspects of the structure are of note: (1) Complex **2** is in the bis(aminato) form and therefore is an anion; the sp^2 hybridization state of both nitrogens is evident from their planar geometry and their N−Re bond lengths of 1.957 and 1.940 Å, which are typical $N(sp^2)$−Re bonds but are 0.2 Å shorter than typical $N(sp^3)$•••Re dative bonds.[9] This result confirmed our presumption of the symmetry of complex **2**, based on the simplicity of its ^1H NMR spectrum. (2) The counterion appeared as a center of high electron density surrounded by seven molecules of methanol, in a stoichiometry of 1 to 2 with the rhenium complex.

Because of this stoichiometry, it appeared most likely that this density was due to a dication, and in structural refinement calcium produced the lowest residuals. Verification of calcium as the counterion was obtained by ICP analysis of the complex, which indicated 3.22% calcium (calculated 3.30%) for $Ca(CH_3OH)_7{\cdot}2C_{14}H_{12}N_2OReS_2$.

There are three curious issues concerning the structure of complex **2** and its formation: (1) there was no deliberate exposure of complex **2** to a source of calcium ion; (2) the calcium ion is heptasolvated with a capped trigonal prism geometry (Figure 2); (3) only methanol solvates the calcium ion, even though 50% MeOH/EtOH was used for crystallization of complex **2**.

The material first isolated from the reaction mixture prior to chromatography is most likely the sodium salt of the oxorhenium

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(5) ^1H NMR (300 MHz, CD_2Cl_2 + CD_3OD): δ 4.30−4.40 (m, 4, 2(*anti* protons of NCH_2CH_2N to Re=O)), 4.62−4.70 (m, 4, 2(*syn* protons of NCH_2CH_2N to Re=O)), 6.56−6.63 (m, 4, 4(C4 or C5-H)), 6.84−6.94 (m, 8, 4C6-H+4(C4 or C5-H)), 7.43 (d, 4, J = 7.6 Hz, 4C3-H). UV and vis λ_{max} (CH_2Cl_2): 654, 318, 238 nm. MS (FAB): *m*/*e* 451 (M^+ + 1, 8), 450 (M^+, 20), 449 (M^+ + 1, 20), 448 (M^+, 18).

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(7) Oxorhenium and oxotechnetium N_2S_2 complexes generally adopt an unsymmetrical neutral form with three metal−heteroatom bonds and one dative bond to $N(sp^3)$ when the nitrogens are of the more basic amine type (pK_a 39 for deprotonation), but form anions by a fourth deprotonation if both nitrogens are of the more acidic amide type (pK_a 17) (cf. ref 1a). In the case of chelate **1**, where both nitrogens are of an aniline type, with an intermediate pK_a estimated to be 27, it was not possible to predict whether the neutral or anionic form of the oxorhenium complex would predominate.

(8) Crystal data for $Ca(CH_3OH)_7{\cdot}2C_{14}H_{12}N_2OReS_2$, **2**: A red and prismatic single crystal of **1** was triclinic at −75 °C, space group $P\bar{1}$, with a = 12.870(2) Å, b = 13.735(3) Å, c = 13.880(5) Å, α = 71.48(2)°, β = 86.18(2)°, γ = 67.65(2)°, V = 2147.6(10) Å^3 and d_{calcd} = 1.877 cm^{-3} for Z = 2. A total of 6264 intensities were measured (Mo Kα 2θ < 46°, 5969 unique, R_i = 0.0378) on an Enraf-Nonius CAD4 automated κ-axis diffractometer using ω/θ scans with angles of 1.50[1.10 + 0.35 tan (θ)]. These data were corrected for Lorentz-polarization effects, anomalous dispersion and absorption [μ_a(Mo Kα) = 5.997 mm^{-1}]. The structure was solved by Patterson methods (SHELXS-86; Sheldrick, G. M. SHELXS-86. In *Crystallographic Computing 3*; Sheldrick, G. M., Kruger, C., Goddard, R., Oxford University Press: London, 1986; pp 175−189), and refined by least-squares (SHELXL-93; Sheldrick, G. M. SHELXL-93. Manuscript in preparation for *J. Appl. Crystallogr.*) to convergence [$R(F)$ = 0.052 and $\omega R(F^2)$ = 0.127 for 4904 observed reflections ($I > 2\sigma(I)$)].

(9) The bond lengths of Re−N bonds are 1.950 (normal bond) and 2.154 (dative bond) Å for (*N*-(2-mercapto-2-(methylpropyl))-*N*-(4′-methoxyphenyl)aminato)(2-mercaptomethylpyridinato)oxorhenium(V),[2a] 1.978 and 2.182 Å for *syn*-Bn-MAMA′-ReO,[6] and 1.990 and 2.151 Å for *anti*-Bn-MAMA′-ReO.[6]

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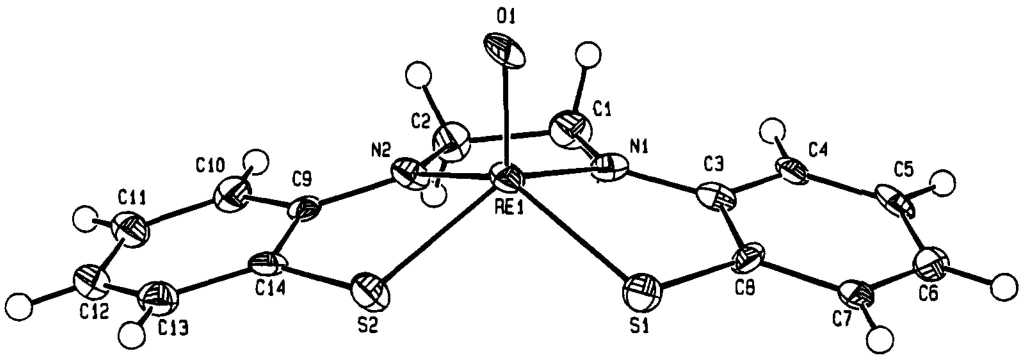

Figure 1. Anion structure $(C_{14}H_{12}N_2OReS_2)^-$ of **2**.

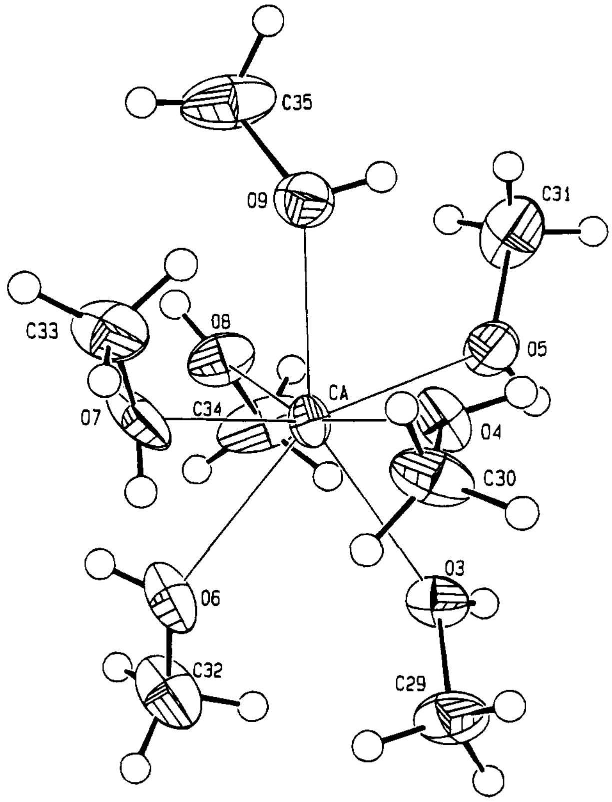

Figure 2. Methanol-solvated calcium cation structure, $Ca(CH_3OH)_7{}^{2+}$, of **2**.

Table 1. Selected Structural Parameters for **2**

	Distance, Å		
Re1–O1	1.750(8)	Re1–N1	1.957(10)
Re1–N2	1.940(10)	Re1–S1	2.310(3)
Re1–S2	2.312(3)	S1–C8	1.752(13)
S2–C14	1.766(13)	N1–C1	1.47(2)
N1–C3	1.39(2)	N2–C2	1.46(2)
N2–C9	1.40(2)	C1–C2	1.53(2)
Re2–O2	1.706(10)[a]	Re2–N3	1.965(9)
Re2–N4	1.952(9)	Re2–S3	2.308(3)
Re2–S4	2.310(4)	S3–C22	1.778(12)
S4–C28	1.782(11)	N3–C15	1.45(2)
N3–C17	1.40(2)	N4–C16	1.46(2)
N4–C23	1.42(2)	C15–C16	1.52(2)
C1–O3	2.452(11)	Ca–O4	2.355(10)
Ca–O5	2.372(11)	Ca–O6	2.421(10)
Ca–O7	2.398(10)	Ca–O8	2.338(11)
Ca–O9	2.401(11)		
	Angles, deg		
O1–Re1–N1	108.8(4)	O1–Re1–N2	111.5(4)
O1–Re1–S1	109.3(3)	O1–Re1–S2	108.4(3)
N1–Re1–N2	79.7(4)	N1–Re1–S1	81.9(3)
N1–Re1–S2	142.5(3)	N2–Re1–S1	138.7(3)
N2–Re1–S2	82.5(3)	S1–Re1–S2	90.34(12)
O2–Re1–N3	109.3(5)	O2–Re2–N4	111.6(4)
O2–Re2–S3	110.2(3)	O2–Re2–S4	108.0(3)
N3–Re2–N4	79.5(4)	N3–Re2–S3	81.8(3)
N3–Re2–S4	142.4(3)	N4–Re2–S3	137.8(3)
N4–Re2–S4	82.5(3)	S3–Re2–S4	90.20(12)

[a] The data for Re2 are from the second anion.

complex, with the cation coming from the NaOAc used as a buffer in the complexation reaction. While the chemical shifts of the protons of the NCH_2CH_2N system before and after chromatography are almost the same, the crystalline material obtained after silica gel chromatography was the heptasolvated calcium salt. This pointed to the silica gel as the only likely source of calcium ion. ICP analysis of the ion composition of the silica gel used in this purification (manufactured by E. Merck, 40–63 μm silica gel, No. 9385) showed that it contained 1.51 mg of calcium per gram. The residual amount of this ion is not unexpected, considering that silica gel is manufactured by alkaline erosion of various metal carbonates from a mixed carbonate-silicate soft glass. The fact that the calcium counterion is heptasolvated by MeOH suggests that a soft–soft interaction between the large delocalized rhenium and a well solvated calcium ion is preferred in the crystalline state to a soft–hard interaction that would take place between the anion and an unsolvated calcium ion. Finally, the selective solvation of calcium by MeOH rather than EtOH probably derives from steric constraints on the cation in the crystal lattice. We have found two heptacoordinate calcium compounds in the literature (both distorted pentagonal bispyramid structures),[10] but we have not found any precedent for a heptasolvated calcium ion nor have we found any calcium structure with a capped trigonal prism geometry.

In conclusion, ligand exchange of an oxorhenium(V) precursor with a tetradentate bis(*o*-mercaptoaniline) chelate forms an anionic complex which, after chromatographic purification over silica gel, gives high quality crystals of a salt with a calcium counterion solvated in a novel capped trigonal prism geometry by seven molecules of methanol. The calcium comes, apparently, from the silica gel.

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Supplementary Material Available: Proton NMR spectra of complex **2** before and after silica gel chromatography, ORTEP structure of complex **2**, various views of the solvated calcium ion and unit cell, and tables of atomic coordinates, hydrogen coordinates, anisotropic displacements, and bond lengths and angles (19 pages). Ordering information is given on any current masthead page.

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