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An unexpected '4+2' [N₃S]:[NS] rhenium(IV) complex formed upon cleavage of a Re(V) imido bond

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Abstract

The reaction of [Re(NMe)Cl₃(PPh₃)₂] with the pentadentate [N₃S₂] ligand pyN₂H₂S₂-H₂ [2,6-bis(2-mercaptophenylamino)dimethylpyridine] (**1**) in the presence of triethylamine did not yield the anticipated six-coordinate complex [Re(NMe)(η⁵-pyN₂HS₂)] (**2**), but rather resulted in cleavage of the Re(V)=NMe bond. A novel six-coordinate Re(IV) [N₃S]/[NS] complex [Re(η⁴-SC₆H₄-2-NCH₂-C₅H₃N-C=NC₆H₄-2-S)(η²-NHC₆H₄-2-S)] (**4**) was thus obtained with the simultaneous coordination of 2-aminothiophenol, a dianionic bidentate [NS] donor resulting from the decomposition of the parent ligand and ligand **3**, a dianionic tetradentate [N₃S] donor formed by partial self-condensation and subsequent oxidation of the parent ligand **1**. Crystal data for **4**: C₂₅H₁₈N₄S₃Re·CH₂Cl₂, monoclinic, space group *P*2₁/*n*, *a* = 9.255(2) Å, *b* = 11.181(2) Å, *c* = 25.316(4) Å, β = 97.434(3)°, *V* = 2587.8(7) Å³ and *Z* = 4.

Keywords

Crystal structures; '4 + 2' Rhenium(IV) chemistry; Re(V)=NMe bond cleavage; Skew-trapezoidal-bipyramidal geometry; Thiazolidine

1. Introduction

The continuing expansion of the coordination chemistry of the Group VII elements technetium and rhenium reflects the application of their radionuclides to the development of radiopharmaceuticals [1–5]. ^{99m}Tc-based radiopharmaceuticals continue to provide the mainstay in diagnostic nuclear medicine due to the optimal nuclear properties (*t*_{1/2} = 6.02 h, *E*_g = 142 keV) and easy availability from ⁹⁹Mo/^{99m}Tc generator [6]. Furthermore, the β-emitting radionuclides ¹⁸⁶Re (*t*_{1/2} = 90.64 h, *E*_g = 1.07 MeV, *E*_g = 137 keV) and ¹⁸⁸Re (*t*_{1/2} = 17 h, *E*_g = 2.12 MeV, *E*_g = 155 keV) of the Group VII congener of technetium have become the logical choices for therapeutic applications [7]. The accessibility of multiple oxidation states of Tc and Re, −3 to +7 [8], makes it possible to accommodate a variety of polydentate, multi-anionic ligands. The most successful strategy to the development of diagnostic imaging agents of Tc and potential therapeutic reagents based on Re has exploited ligands to stabilize the oxometal [MO]³⁺ core (where M = Tc and Re), utilizing tetradentate N_xS(4−*x*) (*x* = 0 to 3) chelates [9], '3+1' [10] and '3+2' [11] mixed thiolate ligands. However, the recent introduction of technetium and rhenium complexes with alternative functional cores, such as diazenido-, hydrazido-, imido- and nitrido- [12], at the 'carrier free' level has made this class of compounds featuring M–N multiple bonds more

attractive for the development of ^{99m}Tc and $^{186/188}\text{Re}$ radiopharmaceuticals, whose production had been focused in the past primarily on oxometal complexes (Scheme 1).

Due to the weaker *trans* influence of the nitrogen donor ligand with comparison to the oxo ligand, methylimido complexes of technetium and rhenium containing the linear $\{\text{M}=\text{NMe}\}$ unit prefer six-coordinate octahedral geometry at the imidometal(V) core rather than five-coordinate square-pyramidal or trigonal bipyramidal geometry which is invariably encountered in oxometal(V) complexes in the presence of a tetradentate chelator. The imido complexes are inclined to incorporate a solvent molecule at the apical position *trans* to the relatively weak σ - and π -donating methylimido group to attain the maximum electron count (EAN rules) [13] of 18. An ideal conceptual design would provide six-coordinate $\{\text{Re}=\text{N}-\text{R}\}$ complexes with maximum stability, which hold a pre-organized pentadentate ligand with four coplanar donor atoms and the fifth group perpendicular to the basal plane and *trans* to the metal–imido bond. Coordination modes of the pentadentate $[\text{N}_3\text{S}_2]$ ligand $\text{pyN}_2\text{H}_2\text{S}_2-\text{H}_2$ [2,6-bis(2-mercaptophenylamino)dimethylpyridine] (**1**) [14] with Fe(II), Ru(II) and Ni(II) ions suggest that this specific ligand may be suitable to bind the $\{\text{Re}=\text{NMe}\}$ core in either tetradentate or pentadentate modes. However, the unexpected cleavage of the $\{\text{Re}=\text{NMe}\}$ bond was observed upon reaction of the precursor $[\text{Re}(\text{NMe})\text{Cl}_3(\text{PPh}_3)_2]$ with **1** utilizing triethylamine as base to neutralize the HCl produced in situ. We herein report the synthesis of a novel ‘4+2’ rhenium(IV) complex **4** whose structure is defined by a highly distorted six-coordinate geometry featuring the $[\text{N}_3\text{S}]$ donor set of ligand **3**, a partially self-condensed thiazolidine derivative of ligand **1**, whose N_3S donors define a trapezoidal plane and the $[\text{NS}]$ donors of the doubly deprotonated form of 2-aminothiophenol, $(\text{NHC}_6\text{H}_4\text{S})^{2-}$, in the apical positions.

2. Experimental

2.1. General considerations and materials

NMR spectra were recorded on a Bruker DPX 300 (^1H 300.10 MHz) spectrometer in CDCl_3 (δ 7.27 ppm). IR spectra were recorded as KBr pellets with a Perkin-Elmer Faragon 1000 FT-IR spectrometer. Elemental analyses for carbon, hydrogen and nitrogen were carried out by Oneida Research Services, Whitesboro, NY. Analytical thin layer chromatography (TLC) was performed with Merck silica gel F-254 glass-backed plates. Visualization was achieved by UV illumination. Flash chromatography was performed according to Still et al. [15] using Aldrich silica gel (70–230 mesh). All chemicals were purchased from Aldrich Chemicals and used without further purification. Methyl imidorhenium(V) precursor $[\text{Re}(\text{NMe})\text{Cl}_3(\text{PPh}_3)_2]$ [16] and the pentadentate $[\text{N}_3\text{S}_2]$ ligand 2,6-bis(2-mercaptophenylamino)-dimethylpyridine, $\text{pyN}_2\text{H}_2\text{S}_2-\text{H}_2$ (**1**) [17] were prepared according to the reported procedures.

2.2. Preparation of the ‘4+2’ $[\text{N}_3\text{S}]/[\text{NS}]$ complex $[\text{Re}(\eta^4-\text{SC}_6\text{H}_4-2-\text{NCH}_2-\text{C}_5\text{H}_3\text{N}-\text{C}=\text{NC}_6\text{H}_4-2-\text{S})(\eta^2-\text{NHC}_6\text{H}_4-2-\text{S})]\cdot\text{CH}_2\text{Cl}_2$ (**4**)

To a refluxing solution of $[\text{Re}(\text{NMe})\text{Cl}_3(\text{PPh}_3)_2]$ (91 mg, 0.1 mmol) in chloroform (50 cm^3) was added the pentadentate ligand **1** in chloroform (0.5 M, 2.2 cm^3). The color of the solution changed immediately from sky-blue to brownish. Triethylamine (five drops) was then added and the resulting reaction mixture was refluxed for an additional 30 min. After cooling to room temperature, the reaction mixture was washed with water. The organic layer was separated from the mixture and dried over Na_2SO_4 . The volume was reduced to 3 cm^3 and then purified on silica gel column using a gradient eluent (from 100% CHCl_3 to 90/10 CHCl_3 /acetone). Yield: 39%. $R_f = 0.86$. Slow evaporation of ether into complex **4** in minimum amount of CH_2Cl_2 afforded brown plates suitable for X-ray analysis. IR (KBr, v cm^{-1}): 1709, 1588, 1508, 1437, 1316, 1194, 1119, 997, 811, 720, 695, 543. ^1H NMR

(CDCl₃, ppm): 8.6–7.9 (m, 3H, pyH), 7.7–7.3 (m, 12H, ArH), 5.26 (s, 2H, CH₂Cl₂), 5.1–4.9 (m, 2H, CH₂). *Anal.* Found: C, 41.95; H, 2.82; N, 7.63. Calc. for C₂₆H₂₀N₄S₃Cl₂Re: C, 42.11; H, 2.70; N, 7.56%.

2.3. X-ray structure determination

The selected crystal of **4** was measured with a Siemens P4 diffractometer equipped with the SMART CCD system [18] and using graphite monochromated Mo K α radiation ($\lambda = 0.071073\text{\AA}$). The data collection was carried out at 89(5) K. The data were corrected for Lorentz and polarization effects, and absorption corrections were made using SADABS [19]. Neutral atom scattering factors were taken from Cromer and Waber [20]. Anomalous dispersion corrections were taken from Creagh and McAuley [21]. All calculations were performed using SHELXL [22]. The structures were solved by direct methods [23] and all of the non-hydrogen atoms were located from the initial solution. After locating all the initial non-hydrogen atoms in the structure, the models were refined against F^2 , initially using isotropic and later anisotropic thermal displacement parameters until the final value of $\Delta/\sigma_{\text{max}}$ was less than 0.001. At this point the hydrogen atoms were located from the electron density difference map and a final cycle of refinements was performed, until the final value of $\Delta/\sigma_{\text{max}}$ was again less than 0.001. No anomalies were encountered in the refinement of the structure. The relevant parameters for crystal data, data collection, structure solution and refinement are summarized in Table 1, and important bond lengths and angles in Table 2. A complete description of the details of the crystallographic methods is given in Section 4.

3. Results and discussion

The reaction of [Re(NMe)Cl₃(PPh₃)₂] with the pentadentate [N₃S₂] ligand 2,6-bis(2-mercaptophenylamino)-dimethylpyridine (**1**) in the presence of triethylamine did not result in the anticipated six-coordinate complex [Re(NMe)(η^5 -pyN₂HS₂)] (**2**), but rather yielded a novel [N₃S]/[NS] Re(IV) complex [Re(η^4 -SC₆H₄-2-NCH₂-C₅H₃N-C=NC₆H₄-2-S)(η^2 -NHC₆H₄-2-S)] (**4**) in 39% yield after purification by column chromatography. The cleavage of the {Re=NMe} bond is confirmed by the fact that a triplet at $\delta = 0.38$ ppm ($J = 4.5$ Hz), characteristic of =NMe protons in the [Re(NMe)Cl₃(PPh₃)₂] precursor, disappeared in the ¹H NMR spectrum of the complex obtained. Due to the symmetry of the '4+2' complex, the geminal protons on the methylene carbon backbone were distinguished as *endo* and *exo* protons. A singlet at 4.40 ppm in the free ligand **4** was thus downfield shifted to the region of 4.9–5.1 ppm as two broad humps. The integration of only two methylene protons in this region indicated the condensation of one of the two 2-mercaptophenylaminomethylene groups to form a benzothiazolato group. Despite the presence of paramagnetic d³ Re(IV) species, we were still able to observe reasonably sharp proton NMR resonances. A strong vibration at 1588 cm⁻¹ in the IR spectrum is ascribed to the C=N stretching of this unit. An integration of 12 protons in the aromatic phenyl region suggests the simultaneous coordination of the doubly deprotonated ligand **3** and (NHC₆H₄S)²⁻. The downfield shift and convergence of proton resonances of the aromatic rings interposed between the N and S donors of the ligands are observed as a consequence of the delocalization of the π -electron density in the chelate rings.

Single crystals of [Re(η^4 -SC₆H₄-2-NCH₂-C₅H₃N-C=NC₆H₄-2-S)(η^2 -NHC₆H₄-2-S)]·CH₂Cl₂ (**4**) of X-ray quality were obtained from diffusion of ether into methylene chloride solution. The compound crystallizes with one molecule of solvent CH₂Cl₂. A representation of the structure of complex **4** is shown in Fig. 1 along with the associated atom numbering scheme. The terminal methylimido ligand has been replaced by the bidentate amino/thiolate ligand. The overall geometry about the central rhenium atom is best described as skew-trapezoidal-bipyramidal [24,25] with the tetradentate [N₃S] ligand occupying the equatorial plane and the nitrogen and sulfur donors of the bidentate ligand taking the apical positions.

The Re(IV) lies 0.89 Å out of the equatorial plane. The C(13)–N(3) bond distance of 1.33(1) Å is considerably shorter than a characteristic C–N single bond of 1.45 Å but somewhat longer than the expected C–N double bond length of 1.27 Å which may be attributed to the delocalization of the five-membered chelate ring Re(1)–N(1)–C(5)–C(13)–N(3) [26]. One of the 2-mercaptophenylaminomethyl groups was stabilized by coordination to the rhenium ion center, while the other uncoordinated 2-mercaptophenylaminomethyl group may first condense to the benzothiazoline group, and subsequently oxidize to the benzothiazolato group with the evolution of molecular hydrogen [27]. The Re(1)–N(2) distance of 2.047(7) Å is about 0.1 Å shorter than Re(1)–N(3), a characteristic observation for the deprotonation of a secondary amine upon coordination with the rhenium core. The Re(1)–N(4) distance of 1.961(8) Å is about 0.2 Å shorter than a characteristic Re–N single bond length, but 0.2–0.25 Å longer than the length of a Re=N double bond, thus the bond order of Re(1)–N(4) may be estimated as 1.5 [28].

In conclusion, the cleavage and replacement of the {Re(V)=NMe} bond with nitrogen and sulfur donors of an amino/thiolato bidentate ligand, formed by decomposition of the pentadentate [N₃S₂] ligand **1** was observed. Furthermore, the potentially pentadentate ligand only serves as a tetradentate [N₃S] donor set, as a consequence of condensation of the unbound thiol group with the secondary amino group to form a benzothiazoline intermediate which undergoes further oxidative reaction to form a stable benzothiazolato group, accompanied by the production of molecular hydrogen. The structure of the title '4+2' complex is best described in terms of skew–trapezoidal–bipyramidal geometry about the tetravalent rhenium center. To the best of our knowledge, this is the first example of cleavage of the {Re=NMe} unit and the reduction of Re(V) to Re(IV) under such mild reaction conditions.

4. Supplementary material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Fig. 1. ORTEP diagram of the '4 + 2' $[N_3S]/[NS]$ complex $[Re(\eta^4-SC_6H_4-2-NCH_2-C_5H_3N-C=NC_6H_4-2-S)(\eta^2-NHC_6H_4-2-S)]$ (**4**) showing the crystallographic numbering scheme. Thermal ellipsoids for the non-hydrogen atoms are drawn at the 50% probability level.

1

Scheme 1.

Table 1

Selected crystallographic data for the '4+2' [N₃S]/[NS] complex [Re(η^4 -SC₆H₄-2-NCH₂-C₅H₃N-C=NC₆H₄-2-S)(η^2 -NHC₆H₄-2-S)](4)

Formula	C ₂₅ H ₁₈ N ₄ S ₃ Re·CH ₂ Cl ₂
Formula weight	741.73
Crystal system	Monoclinic
Space group	<i>P</i> 2 ₁ / <i>n</i>
<i>a</i> (Å)	9.255(2)
<i>b</i> (Å)	11.181(2)
<i>c</i> (Å)	25.316(4)
β (°)	97.434(3)
<i>V</i> (Å ³)	2597.8(7)
<i>Z</i>	4
ρ_{calc} (Mg m ⁻³)	1.894
<i>T</i> (°C)	90(2)
Radiation	Mo K α
λ (Å)	0.71073
μ (cm ⁻¹)	5.149
Goodness-of-fit, <i>S</i> (<i>F</i> ²)	1.015
Final indices (2 σ data), <i>R</i> ₁ (<i>wR</i> ₂) ^a	0.0569, 0.1196

$$^a R_1 = \Sigma(|F_o| - |F_c|)/\Sigma|F_o|, wR_2 = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}.$$

Table 2Selected bond lengths (Å) and angles (°) in complex **4**

<i>Bond lengths</i>			
Re(1)–N(4)	1.961(8)	S(3)–C(25)	1.766(9)
Re(1)–N(1)	1.998(7)	N(1)–C(1)	1.378(12)
Re(1)–N(2)	2.047(7)	N(1)–C(5)	1.391(12)
Re(1)–N(3)	2.140(8)	N(2)–C(6)	1.364(11)
Re(1)–S(1)	2.331(3)	N(2)–C(7)	1.408(12)
Re(1)–S(3)	2.374(2)	N(3)–C(13)	1.327(13)
S(1)–C(12)	1.770(9)	N(3)–C(14)	1.406(14)
S(2)–C(13)	1.717(11)	N(4)–C(20)	1.416(11)
S(2)–C(19)	1.764(13)		
<i>Bond angles</i>			
N(4)–Re(1)–N(1)	90.0(3)	N(2)–Re(1)–S(1)	80.4(2)
N(4)–Re(1)–N(2)	82.4(3)	N(3)–Re(1)–S(1)	92.5(2)
N(1)–Re(1)–N(2)	73.4(3)	N(4)–Re(1)–S(3)	79.3(2)
N(4)–Re(1)–N(3)	137.7(3)	N(1)–Re(1)–S(3)	129.5(2)
N(1)–Re(1)–N(3)	73.6(3)	N(2)–Re(1)–S(3)	150.3(2)
N(2)–Re(1)–N(3)	126.6(3)	N(3)–Re(1)–S(3)	81.9(2)
N(4)–Re(1)–S(1)	125.3(2)	S(1)–Re(1)–S(3)	91.22(9)
N(1)–Re(1)–S(1)	132.5(2)		