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Investigations of the $\{\text{ReO}\}^{3+}$ core: A '2+2' complex from bidentate and potentially trident ligands: $[\text{ReO}(\eta^2\text{-HOC}_6\text{H}_4\text{-2-CH}_2\text{NC}_6\text{H}_4\text{S})(\eta^2\text{-SC}_5\text{H}_4\text{N})(\text{PPh}_3)]$

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Abstract

The reaction of $[\text{ReOCl}_3(\text{PPh}_3)_2]$ with *N*-(2-hydroxybenzyl)-2-mercaptoaniline (H_3hbma) (**2**) and 2-mercaptopyridine in hot CHCl_3 yields $[\text{ReO}(\eta^2\text{-HOC}_6\text{H}_4\text{-2-CH}_2\text{NC}_6\text{H}_4\text{S})(\eta^2\text{-SC}_5\text{H}_4\text{N})(\text{PPh}_3)]$ (**3**). The structure of **3** consists of distorted octahedral Re(V) monomers. The coordination geometry at the rhenium is defined by a terminal oxo-group, the nitrogen and sulfur donors of the chelating mercaptopyridine, the nitrogen and sulfur donors of a bidentate (Hhbma)²⁻ ligand, and the phosphorus of the PPh_3 group. The $-\text{C}_6\text{H}_4\text{OH}$ arm of (Hhbma)²⁻ is pendant, and the coordinated nitrogen of this ligand is present as a deprotonated amido nitrogen.

Keywords

Crystal structures; Rhenium complexes; Oxo complexes; Thiolate complexes

1. Introduction

The contemporary interest in the coordination chemistry of rhenium derives from the applications of the radioisotopes ^{186}Re and ^{188}Re to radiotherapy [1-5]. The discovery of novel radiopharmaceuticals is driven by synthesis of new materials. In this connection, one approach has focused on the robust $\{\text{ReO}\}^{3+}$ core in combination with ligands possessing different donor sets and denticities. The most extensively developed strategy exploits '3+1' ligand combinations, which contain a dianionic tridentate ligand with various donor atoms, but requiring at least one thiolate sulfur, and a monodentate thiol [6-9]. In addition, '2+2' ligand combinations [10] and more recently '3+2' chelates have been exploited [11,12].

In the course of our investigations of the coordination chemistry of the $\{\text{ReO}\}^{3+}$ core with chelating ligands of varying denticity and different donor groups, several observations were made. Firstly, tridentate Schiff base ligands were effective for the expansion of the '3+1' approach [13]. Secondly, dianionic tridentate ligands with alkoxo rather than thiol donors favored the isolation of '3+2' chelate frameworks [12]. In an effort to conflate these two

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5. Supplementary material

All atomic and thermal parameters and all inter-atomic angles are available from the authors upon request. Crystallographic data (excluding structure factor) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Center as publication No. CCDC-139495. Copies of the data can be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB21EQ, UK (Fax: +44-1223-336-033; deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

strategies, the chemistry of the ligand $\text{HOC}_6\text{H}_4\text{-2-CH}_2\text{NHC}_6\text{H}_4\text{SH}$, *N*-(2-hydroxybenzyl)-2-mercaptoaniline (**2**), the reduced form of the Schiff base *N*-(2-mercaptophenyl)salicylideneimine (**1**), with the $\{\text{ReO}\}^{3+}$ core in the presence of the potentially bidentate ligand 2-mercaptopyridine was investigated. Two possible structural results were considered: (i) the **2** ligand would adopt a dianionic tridentate mode and the mercaptopyridine the common monodentate mode to provide a '3+1' species with the conventional distorted square pyramidal geometry (**A**); (ii) the flexibility of the tridentate ligand together with the tendency of aryloxo and alkoxo ligands to occupy positions *trans* to the oxo-group would allow expansion of the coordination sphere to provide a '3+2' complex (**B**). Curiously, neither expectation was realized, but rather the unusual six-coordinate '2+2+1' complex $[\text{ReO}(\eta^2\text{-HOC}_6\text{H}_4\text{-2-CH}_2\text{NC}_6\text{H}_4\text{S})(\eta^2\text{-SC}_5\text{H}_4\text{N})(\text{PPh}_3)]$ (**3**) was isolated.

2. Experimental

2.1. General considerations

NMR spectra were recorded on a Bruker DPX 300 (^1H 300.10 MHz) spectrometer in CDCl_3 (δ 7.27 ppm). Elemental analysis for carbon, hydrogen and nitrogen were carried out by Oneida Research Services, Whitesboro, NY. Ammonium perrhenate, 2-mercaptopyridine, salicylaldehyde and 2-aminobenzenethiol were purchased from Aldrich and used without further purification. Reagent grade solvents, distilled and dried by standard methods, were used in all cases. Solutions were deaerated with 99.997% N_2 . $[\text{ReOCl}_3(\text{PPh}_3)_2]$ was prepared according to the literature [14]. Schiff base *N*-(2-mercaptophenyl)salicylideneimine (**1**) was prepared previously in this laboratory [13] and initially by Corbin and Work [15].

2.2. Preparation of ligand 2

The ligand **2** was prepared from the Schiff base *N*-(2-mercaptophenyl)salicylideneimine (**1**) by the method of Rajan [16] with minor modifications. The completeness of the reaction was monitored by the disappearance of $\text{C}=\text{N}$ stretching band in the IR spectrum. The resulting thick, yellow, oily liquid was kept in a solution of CHCl_3 and covered with N_2 . (yield: 35%). ^1H NMR (CDCl_3 , ppm): 4.28 (s, 1H, SH); 4.44 (s, 2H, $\text{HOC}_6\text{H}_4\text{CH}_2\text{NH}$); 6.75–6.95 (m, 4H, ArH); 7.15–7.45 (m, 4H, ArH). *Anal.* Calc. for $\text{C}_{13}\text{H}_{13}\text{NOS}$: C, 67.53; H, 5.63; N, 6.06. Found: C, 68.01; H, 5.71; N, 5.96%.

2.3. Preparation of $[\text{ReO}(\eta^2\text{-HOC}_6\text{H}_4\text{CH}_2\text{NC}_6\text{H}_4\text{S})(\eta^2\text{-C}_5\text{H}_4\text{N-2-S})(\text{PPh}_3)]$ (**3**)

To a solution of 23.1 mg (0.1 mmol) of **2** in dry, deaerated CHCl_3 (20 cm^3) was added $\text{ReOCl}_3(\text{PPh}_3)_2$ (83 mg, 0.1 mmol) and subsequently 2-mercaptopyridine (12 mg, 0.11 mmol). The solution was heated to 60°C for 30 min. The resulting dark brown solution was evaporated to dryness under reduced pressure. The brown residue was dissolved in warm acetonitrile (10 cm^3). Upon slow cooling, dark green-brown crystals were formed. (Yield: 38 mg, 45%). IR (KBr, cm^{-1}): 1560(m), 1481(s), 1438(m), 1095(m), 920(m), 746(m). ^1H NMR (CDCl_3 , ppm): 2.00 (s, 3H, CH_3CN); 5.36 (d, $J=6.7\text{ Hz}$, 1H, $\text{HOC}_6\text{H}_4\text{CH}_2\text{N}$ eq); 5.95 (d, $J=6.7\text{ Hz}$, 1H, $\text{HOC}_6\text{H}_4\text{CH}_2\text{N}$ ax); 7.33 (s, 15H, PPh_3); 6.7–7.7 (m, 12H, ArH). A few

crystals were selected for X-ray analysis. *Anal.* Calc. for $C_{36}H_{30}N_2O_2S_2\text{-Pre}\cdot\text{CH}_3\text{CN}$: C, 54.02; H, 3.91; N, 4.98. Found: C, 53.87; H, 3.97; N, 5.10%.

2.4. X-ray crystallography

Crystallographic data for **3** were collected with a Siemens P4 diffractometer equipped with the SMART CCD system [17] and using Mo K α radiation (γ 0.71073 Å). The data were collected at 100 K. The data were corrected for Lorentz and polarization effects, and absorption corrections were made using *SADABS* [18]. The structure solution and refinement were carried out using the *SHELXL-96* [19] software package. The structure was solved using direct methods and all of the non-hydrogen atoms were located from the initial solution. After locating all of the non-hydrogen atoms in each structure, the model was 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. Crystallographic data are summarized in Table 1. Selected bond lengths and bond angles for **3** are given in Table 2.

3. Discussion

The reaction of $[\text{ReOCl}_3(\text{PPh}_3)_2]$ with H_3hbma and 2-mercaptopyridine in hot CHCl_3 yields, after appropriate work-up, green-brown crystals of $[\text{ReO}(\eta^2\text{-HOC}_6\text{H}_4\text{-2-CH}_2\text{NC}_6\text{H}_4\text{S})(\eta^2\text{-SC}_5\text{H}_4\text{N})(\text{PPh}_3)]\cdot\text{CH}_3\text{CN}(\mathbf{3}\cdot\text{CH}_3\text{-CN})$ in 45% yield (Scheme 1). The observation of both the axial and equatorial protons of the $-\text{CH}_2-$ group in the ^1H NMR spectrum at 5.95 and 5.36 ppm, respectively, confirms that the ligand has not been oxidized to the Schiff base. Furthermore, the absence of bands attributable to $\nu(\text{N-H})$ in the infrared suggests that the nitrogen has been deprotonated in the course of the reaction. Finally, the presence of a resonance at 7.33 ppm in the ^1H NMR spectrum, integrating to 15 protons, establishes that one PPh_3 ligand remains coordinated to the rhenium.

As shown in Fig. 1, the structure of **3** consists of discrete mononuclear units with the Re(V) center in a distorted octahedral geometry. The coordination about the rhenium is defined by the terminal oxo-group, the nitrogen and sulfur donors of the dianionic $(\text{Hhbma})^{2-}$ ligand, the nitrogen and sulfur donors of the 2-mercaptopyridine, and the phosphorus of the PPh_3 ligand.

Several features of the structure are noteworthy. The first is the retention of one PPh_3 ligand. The common substitution pattern of the $[\text{ReOCl}_3(\text{PPh}_3)_2]$ precursor in the presence of chelating ligands results in loss of the sterically demanding PPh_3 ligands. While stepwise substitution is relatively common, providing an intermediate which retains the $\{\text{ReOCl}_2(\text{PPh}_3)\}^+$ core (Scheme 2) [20], addition of the second chelating ligand almost invariably results in displacement of the second PPh_3 group. Related to this observation is the bidentate coordination mode of the $(\text{Hhbma})^{2-}$ ligand. A tridentate geometry with the phenoxy oxygen donor occupying the position *trans* to the oxo-group and concomitant loss of the PPh_3 ligand (structure **B**) was the naive expectation. In fact, the hydroxyl group assumes a pendant role with the oxygen protonated. Consequently, the coordinated N1 nitrogen of the $(\text{Hhbma})^{2-}$ ligand is deprotonated and binds as an amido ligand. The ability of transition metals in high oxidation states to deprotonate coordinated amino nitrogen ligands is well documented [16,21,22], and several examples of amido coordination to the $\{\text{ReO}\}^{3+}$ core, subsequent to amino deprotonation, have been discussed [23,24]. The Re–N1 bond distance of 1.993(5) Å, compared to Re–N2 of 2.157(4) Å, the valence angles at N1 of 116.1(4), 120.7(4) and 123.2(3)° are consistent with an sp^2 hybridized amido site.

Finally, it is curious that the chelating 2-mercaptopyridine is so disposed that the thiolate sulfur is *trans* to the terminal oxo-group. The π -donating thiolate ligand invariably occupies positions *cis* to the oxo-group, suggesting that the observed geometry is the consequence of steric constraints about the six-coordinate $\{\text{Re}(\text{ON}_2\text{S}_2\text{P})\}$ core of **3**. The *trans* influence of the oxo-group is evident in the lengthening of the Re–S2 bond to 2.572(2) Å, compared to 2.300(1) Å for Re–S1.

4. Conclusion

The reaction of $[\text{ReOCl}_3(\text{PPh}_3)_2]$ with the potentially bidentate 2-mercaptopyridine and the potentially tridentate *N*-(2-hydroxybenzyl)-2-mercaptoaniline (**2**) yields neither the ‘3+1’ nor the ‘3+2’ complex which was anticipated, but rather an unusual ‘2+2+1’ species with four different donor atoms about the Re(V) center to produce $\{\text{Re}(\text{ON}_2\text{S}_2\text{P})\}$ coordination geometry. The result not only illustrates the structural diversity of the $\{\text{ReO}\}^{3+}$ core, but also reinforces observations that variable protonation sites and pendant groups can introduce significant structural complications in the design of radiopharmaceutical reagents.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Fig. 1.
A view of the structure of **3**, showing the atom-labeling scheme and 50% thermal ellipsoids.

Scheme 1.

Scheme 2.

Table 1

Summary of crystallographic data of $[\text{ReO}(\eta^2\text{-HOC}_6\text{H}_4\text{-2-CH}_2\text{NC}_6\text{H}_4\text{S})(\eta^2\text{-SC}_5\text{H}_4\text{N})\text{PPh}_3]\cdot\text{CH}_3\text{CN}$
($3\cdot\text{CH}_3\text{CN}$)

Empirical formula	$\text{C}_{38}\text{H}_{33}\text{N}_3\text{O}_3\text{PS}_2\text{Re}$
Formula weight	844.96
Crystal system	monoclinic
Space group	$P2_1/n$
Unit cell dimensions	
a (Å)	8.462(2)
b (Å)	25.099(7)
c (Å)	15.964(5)
β (°)	90.208(7)
V (Å ³)	3390(2)
Z	4
D_{calc} (g cm ⁻³)	1.655
μ (cm ⁻¹)	37.93
R_1^a	0.0456
wR_2^b	0.0736

$$^a R_1 = \Sigma(F_o - F_c) / \Sigma(F_o).$$

$$^b wR_2 = \left[\Sigma \left[w(F_o^2 - F_c^2)^2 \right] / \Sigma w(F_o^2)^2 \right]^{1/2}.$$

Table 2Selected bond lengths (Å) and angles (°) for **3**

<i>Bond lengths</i>	
Re(1)–O(1)	1.702(3)
Re(1)–N(1)	1.993(5)
Re(1)–N(2)	2.157(4)
Re(1)–S(1)	2.3004(14)
Re(1)–S(2)	2.5715(15)
O(2)–C(9)	1.384(7)
S(1)–C(1)	1.762(6)
S(2)–C(14)	1.729(5)
N(1)–C(6)	1.415(7)
N(1)–C(7)	1.472(7)
N(2)–C(18)	1.358(7)
N(2)–C(14)	1.364(7)
<i>Bond angles</i>	
O(1)–Re(1)–N(1)	105.79(17)
O(1)–Re(1)–N(2)	87.70(17)
N(1)–Re(1)–N(2)	91.29(17)
O(1)–Re(1)–S(1)	107.32(13)
N(1)–Re(1)–S(1)	82.37(13)
N(2)–Re(1)–S(1)	164.77(12)
O(1)–Re(1)–P(1)	90.70(13)
N(1)–Re(1)–P(1)	163.51(13)
N(2)–Re(1)–P(1)	89.36(12)
S(1)–Re(1)–P(1)	92.85(5)
O(1)–Re(1)–S(2)	148.49(12)
N(1)–Re(1)–S(2)	88.85(13)
N(2)–Re(1)–S(2)	63.77(12)
S(1)–Re(1)–S(2)	102.11(5)
P(1)–Re(1)–S(2)	76.67(5)
C(6)–N(1)–C(7)	116.1(4)
C(6)–N(1)–Re(1)	120.7(4)
C(7)–N(1)–Re(1)	123.2(3)