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Note

Synthesis and structural characterization of two *cis*-dioxorhenium(V) $ReO_2[SN][P]$ mixed-ligand complexes

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Abstract

Two novel five-coordinate *cis*-dioxorhenium(V) complexes of the general formula $ReO_2[R_2NCH_2CH_2S][PPh_3]$ ($R_2N = Et_2N$, complex **1** and $R_2N = (o\text{-}CH_3O\text{–}C_6H_4N(CH_2CH_2)_2N$, complex **2**) have been synthesized by reacting $ReOCl_3(PPh_3)_2$ with the respective bidentate ligands $R_2NCH_2CH_2SH$. The complexes have been characterized by elemental analysis, IR, NMR spectroscopies and X-ray crystallography. X-ray crystallographic studies showed that the coordination geometry around rhenium is distorted trigonal bipyramidal. The basal plane is defined by the two doubly bonded oxygen atoms and the sulfur of the bidentate ligand, while the nitrogen of the ligand and the phosphorus occupy the apical positions. © 2001 Elsevier Science B.V. All rights reserved.

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1. Introduction

The coordination chemistry of rhenium and technetium is currently attracting much attention due to the radionuclide-based application in radiopharmaceuticals [1]. ^{99m}Tc is the radionuclide of choice for use in diagnostic nuclear medicine due to its almost ideal physical properties ($t_{1/2} = 6.02$ h, gamma-energy = 140 keV) [2]. Recently, $^{186/188}$Re have been introduced in this field as suitable β-emitting radionuclides for use in therapy. Rhenium belongs to the same group of the periodic table (VII) as technetium and therefore exhibits similar chemical properties. It is often used as a non-radioactive alternative to technetium for structural characterization [3].

The mixed ligand concept and particularly the SNS/S combination has been applied for the preparation of neutral pentacoordinated oxorhenium and oxotechnetium complexes of the general formula MO[SN(R)S][S] [4]. The major advantage of using the SNS/S mixed ligand complex system in the design of radiopharmaceuticals is the ease of derivatization by the modification of either the tridentate and/or the monodentate ligand. Based on this approach, numerous ^{99m}TcO[SNS][S] derivatives have been synthesized and evaluated in experimental animals as potential brain perfusion agents [5]. Furthermore, the incorporation of the appropriate receptor seeking group on the mixed

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ligand oxometal core led to the generation of complexes with affinity for the 5-HT_{2A} serotonin receptor [6], the dopamine transporter system [7] as well as melanoma lesions [8].

In our attempts to elucidate the mechanism of the mixed-ligand reactions, two rare *cis*-dioxorhenium(V) complexes have been isolated. In this work, the synthesis and characterization of these two novel complexes of the general formula $ReO_2[R_2NCH_2CH_2S][PPh_3]$, where $R_2N = Et_2N$ (complex **1**) and $R_2N =$ (o-CH_3O–$C_6H_4N(CH_2CH_2)_2N$ (complex **2**) are presented.

2. Experimental

2.1. Materials and methods

IR spectra were recorded as KBr pellets in the range 4000–500 cm^{-1} on a Perkin–Elmer 1600 FTIR spectrophotometer. Elemental analyses were performed on a Perkin–Elmer 2400/II automatic analyzer.

NMR spectra were obtained in $CDCl_3$ at 298 K on a Bruker AC 250E spectrometer. Chemical shifts (δ, ppm) are relative to internal TMS. Assignments were based on 1D and 2D (COSY, HETCOR, NOESY) experiments as well as proton homodecoupling.

$ReOCl_3(PPh_3)_2$ precursor was prepared according to literature [9]. 2-Diethylaminoethylthiol and *N*-*o*-methoxyphenyl-*N′*-2-mercaptoethylpiperazine were prepared according to methods reported in literature [10,11].

Table 1
Crystal data and structure refinement parameters for **1** and **2**

	1	**2**·MeOH
Empirical formula	$C_{24}H_{29}NO_2PReS$	$C_{32}H_{38}N_2O_4PReS$
Formula weight	612.71	763.87
Temperature (K)	298	298
Wavelength (Å)	Mo Kα 0.710730	Mo Kα 0.710730
Space group	$P2_1/c$	$P2_1/n$
Unit cell dimensions		
a (Å)	15.041(7)	11.49(1)
b (Å)	9.247(4)	18.39(2)
c (Å)	17.141(8)	15.90(1)
β (°)	92.64(2)	109.43(3)
V (Å^3)	2381(1)	3167(5)
Z	4	4
D_{calc}/D_{meas} (Mg m^{-3})	1.709/1.68	1.602/1.58
Absorption coefficient (mm^{-1})	5.278	3.991
F(000)	1208	1528
R indices	$R_1 = 0.0238$ [a], $wR_2 = 0.0623$ [a]	$R_1 = 0.0250$ [b], $wR_2 = 0.0644$ [b]
Goodness-of-fit on F^2	1.124	1.060

[a] For 4117 reflections with $I > 2\sigma(I)$.

[b] For 4816 reflections with $I > 2\sigma(I)$.

2.2. Preparation of the complexes

To a 1 M AcONa solution in MeOH (4 ml) $ReOCl_3(PPh_3)_2$ (166.6 mg, 0.2 mM) and 2-diethylaminoethylthiol (26.6 mg, 0.2 mM, complex **1**) or *N*-*o*-methoxyphenyl-*N′*-2-mercaptoethylpiperazine (50.5 mg, 0.2 mM, complex **2**) are added under stirring. The mixture is refluxed until a clear red solution forms. After addition of CH_2Cl_2 the organic phase is washed with H_2O, dried, concentrated to a small volume and submitted to purification by chromatography over silica gel, with CH_2Cl_2 as the solvent. Crystals separate by slow evaporation from CH_2Cl_2–MeOH.

Complex **1**: reddish-brown crystals. Yield: 55%; *Anal.* Found: C, 46.61; H, 4.98; N, 2.07; S, 5.02. Calc. for $C_{24}H_{29}NO_2PReS$: C, 47.04; H, 4.77; N, 2.29; S, 5.23%. IR (KBr, cm^{-1}): ν (O=Re=O) 831, 902. ^1H NMR ($CDCl_3$, δ ppm): 7.84–7.56 (m, 6H, P-*ortho*-phenyl); 7.44–7.41 (m, 9H, *P*-*meta*-phenyl and *P*-*para*-phenyl); 2.94 (m, 4H, $ReNCH_2CH_3$); 2.71 (m, 2H, SCH_2CH_2N); 2.60 (m, 2H, SCH_2CH_2N); 1.20 (t, 6H, $ReNCH_2CH_3$). ^{13}C NMR ($CDCl_3$, δ ppm): 134.53 (2C, *P*-*ortho*-phenyl, [$^2J_{CP} = 10.5$ Hz]); 132.75 (*P*-*ipso*-phenyl, [$^1J_{CP} = 52.6$ Hz]); 130.70 (*para*-phenyl, [$^4J_{CP} = 1.7$ Hz]); 128.57 (2C, *P*-*meta*-phenyl, [$^3J_{CP} = 10.2$ Hz]); 60.59 (SCH_2CH_2N), 47.57 ($ReNCH_2CH_3$); 38.29 (SCH_2CH_2N); 8.39 ($ReNCH_2CH_3$).

Complex **2**: dark red crystals. Yield: 59%; *Anal.* Found: C, 50.89; H, 4.61; N, 4.11; S, 4.36. Calc. for $C_{32}H_{38}N_2O_4PReS$: C, 50.31; H, 5.01; N, 3.67; S, 4.20%. IR (KBr, cm^{-1}): ν (O=Re=O) 828, 904. ^1H NMR ($CDCl_3$, δ ppm): 7.67–7.55 (m, 6H, *P*-*ortho*-phenyl); 7.48–7.38 (m, 9H, *P*-*meta*-phenyl and *P*-*para*-phenyl); 7.07–6.84 (m, 4H, *N*-*o*-OCH_3–phenyl); 3.86 (s, 3H, OCH_3); 3.48, 3.37 (m, 4H, $ReNCH_2CH_2N$); 3.51, 2.92 (m, 4H, $ReNCH_2CH_2N$); 2.79 (m, 2H, SCH_2CH_2N); 2.72 (m, 2H, SCH_2CH_2N). ^{13}C NMR ($CDCl_3$, δ ppm): 152.10, 140.55, 123.09, 121.00, 118.48, 111.07 (*N*-*o*-OCH_3–phenyl); 134.53 (2C, *P*-*ortho*-phenyl, [$^2J_{CP} =$ 10.5 Hz]); 132.48 (*P*-*ipso*-phenyl, [$^1J_{CP} = 53.7$ Hz]); 130.82 (*para*-phenyl, [$^4J_{CP} = 1.6$ Hz]); 128.62 (2C, *P*-*meta*-phenyl, [$^3J_{CP} = 10.4$ Hz]); 68.66 (SCH_2CH_2N); 57.04 ($ReNCH_2CH_2N$); 55.39 (OCH_3); 48.02 ($ReNCH_2CH_2N$); 37.99 (SCH_2CH_2N).

2.3. X-ray crystallography

Crystals of **1** and **2** suitable for X-ray analysis were mounted in air on a Crystal Logic Dual Goniometer diffractometer using graphite monochromated Mo Kα radiation. Unit cell dimensions were determined by using the angular settings of 25 automatically centered reflections in the range $11 < 2\theta < 23°$ and they appear in Table 1. Intensity data were recorded using a θ–2θ scan. Three standard reflections monitored every 97 reflections showed less than 3% variation and no decay.

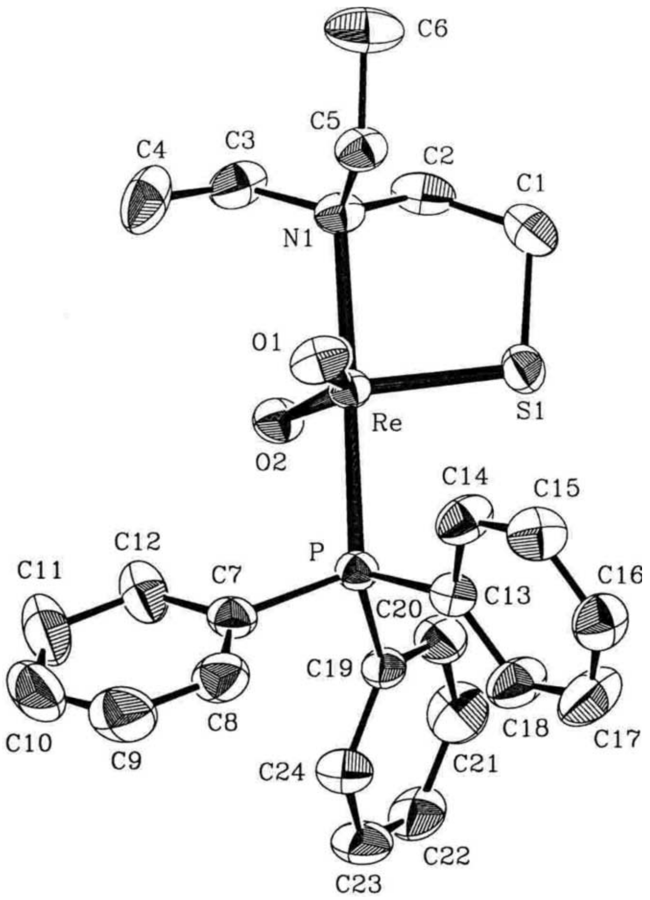

Fig. 1. ORTEP diagram of complex **1**.

Lorentz, polarization and psi-scan absorption corrections were applied using Crystal Logic software. The structures were solved by direct methods using SHELXS-86 [12] and refined by full-matrix least-squares techniques on F^2 using SHELX-93 [13].

3. Results and discussion

The complexes were prepared by reacting the bidentate aminethiols over $ReOCl_3(PPh_3)_2$, which acts as the ReO^{3+} precursor. The neutral and lipophilic complexes were extracted in dichloromethane and isolated as dark-red crystalline products. Both complexes are readily soluble in dichloromethane and chloroform, poorly soluble in methanol, ethanol and insoluble in diethylether and hexane. They are stable in the solid phase and in solution, and their stability is not affected by the presence of air or moisture.

The IR spectra of the complexes each showed two characteristic peaks, at 902 and 831 cm^{-1}, and at 904 and 828 cm^{-1}, for complexes **1** and **2**, respectively. These values are typical of the *cis*-O=Re=O group of the *cis*-dioxorhenium(V) coordinated complexes [14–16].

The NMR spectra of the complexes revealed that the geminal protons on C1 and C2 of the chelated N–C1–C2–S part of the ligand are essentially equivalent. The usually observed [17] chemical shift differentiation between geminal protons of the chelated aminothiol backbone in oxorhenium and oxotechnetium complexes is not present in these complexes, which feature a second Re=O bond in their core. Corresponding protons and carbons of the three aromatic rings of the phosphine moiety are magnetically equivalent due to the rotation around the Re–P and the $P–C_{arom}$ bonds.

ORTEP diagrams of **1** and **2** are given in Figs. 1 and 2, respectively, and selected bond distances and angles are listed in Table 2. The coordination geometry around rhenium is trigonal bipyramidal, with the two doubly bonded oxygens and the sulfur atom of the bidentate ligand occupying the basal plane while the nitrogen of the ligand and the phosphorous occupy the apical positions. Analysis of the shape determining angles using the approach of Addison et al. [18] yields a value for trigonality index, τ, of 0.66 for both **1** and **2** ($\tau = 0$ for perfect square pyramidal and $\tau = 1$ for perfect trigonal bipyramidal geometry). Rhenium is slightly displaced out of the basal plane of the trigonal bipyramid by 0.046 and 0.033 Å in **1** and **2**, respectively, towards the coordinated phosphine. The five-membered ring in the coordination sphere adopts the stable envelope configuration with C2 being ~0.65 Å

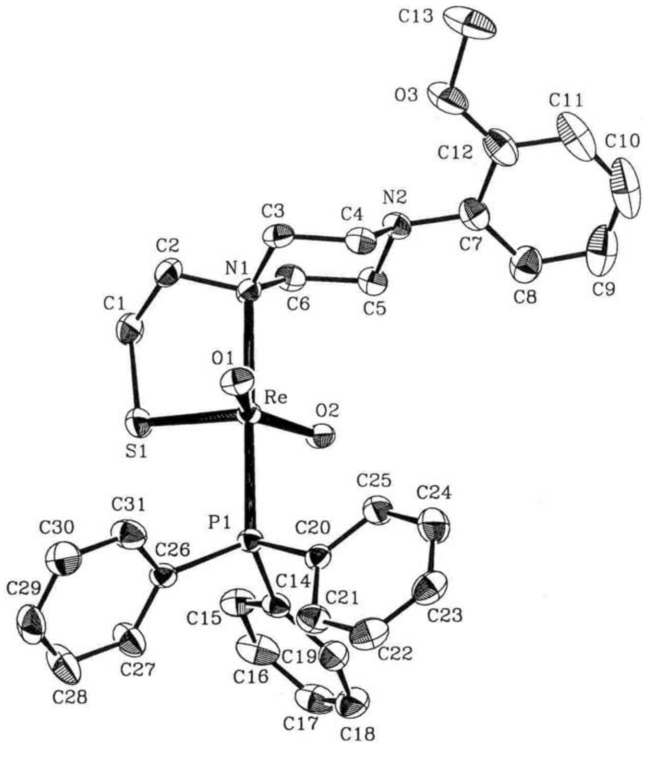

Fig. 2. ORTEP diagram of complex **2**.

Table 2
Selected bond distances (Å) and bond angles (°) for **1** and **2**

	1	**2**
Re–O(1)	1.742(3)	1.749(3)
Re–O(2)	1.746(3)	1.731(3)
Re–N(1)	2.267(4)	2.299(4)
Re–S(1)	2.274(1)	2.263(2)
Re–P	2.404(2)	2.406(2)
O(1)–Re–O(2)	135.4(1)	138.5(2)
O(1)–Re–N(1)	89.5(1)	88.6(1)
O(2)–Re–N(1)	90.6(1)	92.0(1)
O(1)–Re–S(1)	113.7(1)	111.3(1)
O(2)–Re–S(1)	110.7(1)	110.0(1)
N(1)–Re–S(1)	84.6(1)	85.3(1)
O(1)–Re–P	85.7(1)	90.1(1)
O(2)–Re–P	92.8(1)	88.5(1)
N(1)–Re–P	175.2(1)	178.4(1)
S(1)–Re–P	97.3(1)	96.0(1)

(for both **1** and **2**) out of the best mean plane of the remaining four atoms. The dihedral angle of the chelating atoms of the bidentate ligand (N1–C2–C1–S1) is 51.7(5) (for **1**) and 56.5(6)° (for **2**). The six-membered ring of the piperazine exists in the stable chair conformation with N1 and N2 being 0.66 and 0.69 Å out of the mean plane of the four carbon atoms. The Re=O bond distances ($\sim$ 1.74 Å) are in the long range observed for oxorhenium complexes [19]. The Re–N bond distance (2.267(4) and 2.299(4) Å for both **1** and **2**) is slightly longer than that found in other rhenium complexes where the metal is coordinated to a sp^3 nitrogen atom [19]. The Re–S and Re–P bond distances are in the range found in other well characterized rhenium complexes [14,19]. The bond angles between atoms in the basal plane deviate from the ideal value of 120°. The N–Re–P is close to the ideal 180° (175.2(1) and 178.4(1)° for **1** and **2**, respectively).

Previous studies regarding the formation of dioxo complexes of this type show that the origin of the additional oxo group is the water in the reaction mixture [14]. This type of complexes can be easily transformed into the well-known '3 + 1' monooxo complexes, ReO(SNS)(S), by the addition of a tridentate SNS ligand (subject of a future publication).

4. Supplementary material

Tables of crystallographic data, fractional atomic coordinates and anisotropic thermal parameters and a full listing of bond distances and angles are available upon request. A CIF in ASCII format is also available.

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References

[1] A. Duatti, in: M. Nicolini, U. Mazzi (Eds.), Technetium, Rhenium and other Metals in Chemistry and Nuclear Medicine, vol. 5, SGEditoriali, Padua, Italy, 1999, p. 3.

[2] S. Jurisson, J. Lyndon, Chem. Rev. 99 (1999) 2205.

[3] J. Dilworth, S. Parrot, Chem. Soc. Rev. 27 (1998) 43.

[4] H. Spies, J.H. Pietzsch, B. Johannsen, in: M. Nicolini, U. Mazzi (Eds.), Technetium, Rhenium and other Metals in Chemistry and Nuclear Medicine, vol. 5, SGEditoriali, Padua, Italy, 1999, p. 101.

[5] I. Pirmettis, I.M. Papadopoulos, E. Chiotellis, J. Med. Chem. 40 (1997) 2539.

[6] H.-J. Pietzsch, M. Scheunemann, M. Kretzschmar, S. Elz, H.H. Pertz, S. Seifert, P. Brust, H. Spies, R. Syhre, B. Johannsen, Nucl. Med. Biol. 26 (1999) 865.

[7] S. Meegalla, K. Plössl, M.-P. Kung, S. Chumpradit, A.A. Stevenson, D. Frederick, H.F. Kung, Bioconjugate Chem. 7 (1996) 421.

[8] M. Friebe, A. Mahmood, H. Spies, R. Berger, B. Johannsen, A. Mohammed, M. Eisenhut, C. Bolzati, A. Davison, A. Jones, J. Med. Chem. 43 (2000) 2745.

[9] J. Chatt, G.A. Rowe, J. Chem. Soc. (1962) 4019.

[10] H.R. Snyder, J.M. Steward, J.B. Ziegler, J. Am. Chem. Soc. 69 (1947) 72.

[11] D. Papagiannopoulou, I. Pirmettis, T. Maina, M. Pelecanou, A. Nikolopoulou, El. Chiotellis, C. Raptopoulou, A. Vlahos, A. Terzis, M. Papadopoulos, E. Chiotellis, J. Biol. Inorg. Chem. 6 (2001) 256.

[12] G.M. Sheldrick, SHELXS-86, Structure solving Program, University of Göttingen, Germany, 1993.

[13] G.M. Sheldrick, SHELXS-86, Program of Crystal Structure Refinement, University of Göttingen, Germany, 1993.

[14] M. Friebe, R. Jankowsky, H. Spies, W. Seichter, M. Papadopoulos, E. Chiotellis, B. Johannsen, Polyhedron 17 (1998) 3711.

[15] G.F. Ciani, G. D'Alfonso, P.F. Romiti, A. Sironi, M. Freni, Inorg. Chim. Acta 72 (1983) 29.

[16] M.S. Ram, J.T. Hupp, Inorg. Chem. 30 (1991) 130.

[17] M. Pelecanou, K. Chryssou, C.I. Stassinopoulou, J. Inorg. Biochem. 79 (2000) 347.

[18] A.W. Addison, T.N. Rao, J. Reedijk, J. Rijn, G.C. Verschoor, J. Chem. Soc., Dalton Trans. (1984) 1349.

[19] M. Papadopoulos, I. Pirmettis, M. Pelecanou, C.P. Raptopoulou, A. Terzis, C.I. Stassinopoulou, E. Chiotellis, Inorg. Chem. 35 (1996) 7377.