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Oxo-rhenium(V) mixed-ligand complexes with bidentate functionalized phosphines and tridentate Schiff base ligands

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Abstract

A series of monooxo-rhenium(V) mixed-ligand complexes containing bidentate functionalized phosphines and tridentate Schiff base (SB) ligands have been synthesized via ligand-exchange reactions starting from labile Re(V) precursors. A convenient route of synthesis is provided by the isolation of intermediate species such as $[Re(O)(L^n)Cl_3]^-$ (**1**–**3**), (L^n = bidentate phosphino-phenolato or phosphino-carboxylato ligands). Subsequent addition of the relevant SB affords neutral mixed-ligand complexes of general formula $[Re(O)(L^n)(SB^m)]$ (**1**–**3m**). By reversing the addition of the two ligands, i.e. SB first followed by functionalized phosphine, the resulting mixed-ligand species do not change formulation. Conventional spectroscopic techniques and the single-crystal X-ray structure determination of the two representative compounds ($[Re(O)(L^1)(SB^a)]$ (**1a**) and $[Re(O)(L^1)(SB^b)]$ (**1b**)) reveal a distorted octahedral geometry around the rhenium center, with the phosphino-phenolato oxygen located *trans* to the oxo group and the equatorial sites filled by the SB donors and the phosphine phosphorus. It is worth noting that technetium chemistry works quite differently under the same reaction conditions. In fact, no intermediate species of the type $[Tc(O)(L^n)Cl_3]^-$ can be isolated with $[Tc(O)Cl(L^1)_2]$ and reduced $[Tc(L^n)_3]$ being the major compounds.

Keywords: Rhenium complexes; Oxo complexes; Crystal structures; Bidentate phosphine complexes; Schiff base complexes

1. Introduction

Rhenium is often used as a technetium surrogate to study the macroscopic chemistry of potentially useful agents in nuclear medicine because of the chemical similarities of these Group 7 elements. Although remarkable differences have been observed in terms of redox behavior and kinetics of substitution [1], the advantage of operating with 'cold' materials (the natural isotopic mixture of ^{185}Re and ^{187}Re), instead of using a radioactive nuclide (the soft β-emitter ^{99g}Tc), makes rhenium chemistry, at macroscopic level, very attractive for researchers involved in the radiopharmaceutical field. In addition, the recent advent of the two β-emitters ^{186}Re and ^{188}Re in the therapeutic field [2] makes even more obvious the use of the third-row congener itself, in order to elucidate the molecular structure of 'hot' rhenium agents relevant to nuclear medicine.

Very recently a new concept has emerged in the design of substitution-inert technetium and rhenium agents. In this connection, it is necessary to generate a robust 'metal-fragment', to which small bifunctional ligands bearing specific pharmacophores can be eventually coordinated. The metal-fragment contains the ion stabilized in an appropriate oxidation state by means of a suitable ligand framework, which only partially fills the coordination sphere. Examples of application of this concept include the recently developed low valent Tc-tricarbonyl $[Tc^I(CO)_3]^+$ [3] and the high valent

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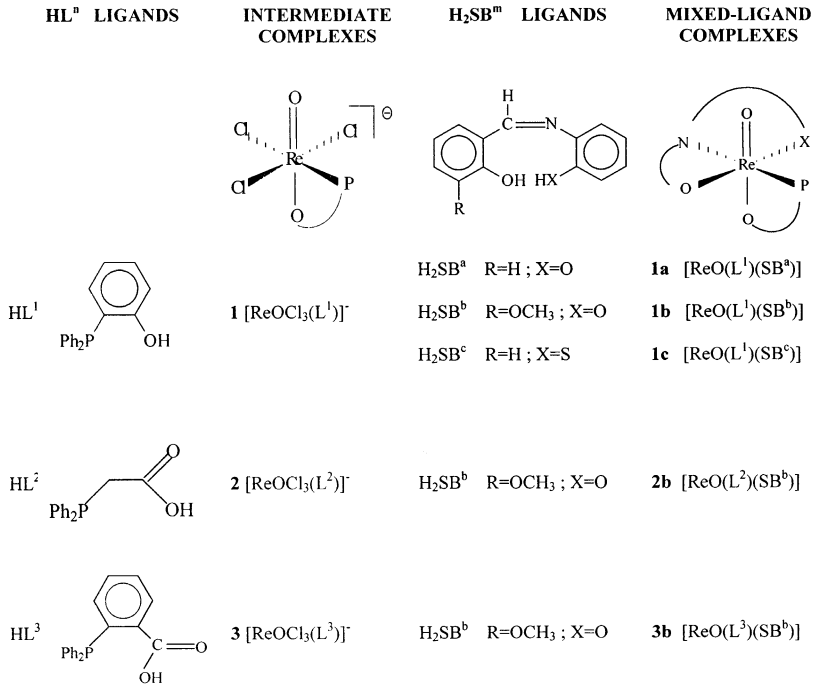
'super-nitrido' $[Tc^{V}(N)(PNP)]^{2+}$ [4] (PNP = tridentate aminediphosphine ligand) fragments. On the opposite side of the molecule these substitution-inert moieties accommodate labile ligands, i.e. water molecules and/or related hydroxyl functions or halide groups. These monodentate ligands can be readily replaced by incoming small chelate ligands, either bidentate or tridentate as in the examples detailed above, which may balance the positive charge of the moiety and fill completely the final octahedral coordination sphere. In this connection, technetium and rhenium systems, named '3 + 1' [5], can also join the metal-fragment concept if we consider the $[M^{V}(O)(SNS)]^{+}$ group (SNS = tridentate aminedithiolate ligand) a substitution-inert moiety to which a monodentate thiolate group can be attached. However, the $[M^{V}(O)(SNS)]^{+}$ moiety and related neutral and lipophilic '3 + 1'-$[M^{V}(O)(SNS)(SR)]$ compounds do not appear to be stable enough both in vivo and in vitro, given that hydrophilic adducts are generated during incubation of these agents with physiologically relevant molecules such as cysteine or glutathione [6].

Looking for additional stable metal-fragments including the monooxo core, we have studied the suitability of the $[Re^{V}(O)(L^{n})]^{2+}$ framework as a new potential building-block for producing mixed-ligand heterocomplexes (HL^{n} is a bidentate functionalized phosphine, in detail HL^{1} = *o*-diphenylphosphinophenol, HL^{2} = diphenylphosphino acetic acid and HL^{3} = *o*-diphenylphosphino benzoic acid). Previous efforts in this direction have generated a class of monooxo-rhenium mixed-ligand complexes of general formulation $[Re^{V}(O)(L^{1})('T')]$, where 'T' is a tridentate aminedithiolate or diaminethiolate ligand (see Refs. [21–23]).

Reactions of the $[Re^{V}(O)(L^{n})]^{2+}$ metal-fragments with the Schiff base (SB) ligands *N*-(2-hydroxyphenyl)salycilideneimine (H_2SB^{a}), *N*-(2-hydroxy-3-metoxhyphenyl)salycilideneimine (H_2SB^{b}) and *N*-(2-mercaptophenyl)salycilideneimine (H_2SB^{c}) afford stable oxorhenium'3 + 2' mixed-ligand complexes $[Re^{V}(O)(L^{n})(SB^{m})]$, as outlined in Scheme 1.

Despite the general assumption that rhenium and technetium exhibit similar synthetic chemistries, we report here on the remarkable different reactivity of bidentate functionalized phosphines toward oxo-rhenium compounds compared to oxo-technetium analogs. The strategy adopted for the synthesis of these rhenium mixed-ligand heterocomplexes appears to be not suitable for radiodiagnostic technetium at 'no carrier added' conditions (vide infra). On the contrary, by using specific phosphines, such strategy might be useful for rhenium also at 'no carrier added' level. Until now only oxo-rhenium agents including tetradentate frameworks such as N_2S_2-diaminodithiols and N_3S-MAG_3-type ligands [7] have been tested for radiotherapeutic application. Our proposed [Re(O)(L^{n})] moiety constitutes a novel substitution-inert metal-fragment which may eventually conjugate bioactive molecules on the coordination vacant sites.



Scheme 1.

Table 1
Selected spectral parameters of the rhenium complexes prepared in this work

Complex	ν(Re=O) (cm^{-1})	^{31}P (ppm)	$^{1}H_{imine}$	$^{1}H_{aromatic}$	^{1}H, others
[*n*-bu_4N][$ReOCl_3(L^1)$] (**1**)	963	−8.6 (s)		7.9–6.4	0.90, 1.31, 1.53, 3.19 [butyl-*H*]
[*n*-bu_4N][$ReOCl_3(L^2)$] (**2**)	985	−14.2 (s)		8.2–7.0	0.90, 1.31, 1.65, 3.29 [butyl-*H*]
[*n*-bu_4N][$ReOCl_3(L^3)$] (**3**)	983	−22.8 (s)		8.2–7.0	0.92, 1.33, 1.65, 3.29 [butyl-*H*]
[$ReO(L^1)(SB^a)$] (**1a**)	964	10.3 (s)	8.89 (d), J_{HP} = 17 Hz	8.1–6.4	
[$ReO(L^1)(SB^b)$] (**1b**)	959	8.1 (s)	8.91 (d), J_{HP} = 17 Hz	8.1–6.4	3.61 (s), O*Me*
[$ReO(L^1)(SB^c)$] (**1c**)	949	8.0 (s)	9.02 (d), J_{HP} = 19 Hz	8.4–6.2	3.65 (s), O*Me*
[$ReO(L^2)(SB^b)$] (**2b**)	989	−1.5 (s)	8.90 (d), J_{HP} = 16 Hz	8.1–6.6	3.80 (s), O*Me*, 3.91 (dd, CH_2)
[$ReO(L^3)(SB^b)$] (**3b**)	978	−8.3 (s)	8.91 (d), J_{HP} = 17 Hz	8.4–6.7	3.68 (s), O*Me*

2. Experimental

2.1. General

All chemicals were of reagent grade and used as such without prior purification. The synthesis of *o*-diphenylphosphinophenol (HL^1) [8], diphenylphosphino acetic acid (HL^2) [9] and *o*-diphenylphosphino benzoic acid (HL^3) [10] were performed according to published protocols. Tridentate SB ligands *N*-(2-hydroxyphenyl)salycilideneimine (H_2SB^a), *N*-(2-hydroxy-3-metoxhyphenyl)salicylideneimine (H_2SB^b) and *N*-(2-mercaptophenyl)salicylideneimine (H_2SB^c) were synthesized as reported previously [11]. Rhenium was purchased from Aldrich as $KReO_4$ and was converted first to the labile precursor [$(n\text{-}C_4H_9)_4N$][$ReOCl_4$] according to published methods [12]. IR spectra were recorded on KBr pellets on a Mattson 3030 Fourier-transform spectrophotometer in the region 400–4000 cm^{-1}. ^1H and ^{31}P NMR spectra were recorded on a Bruker AC-200 instrument, using $SiMe_4$ as internal reference (for ^1H) and 85% aqueous H_3PO_4 as external reference (for ^{31}P). Samples were dissolved in deuterated chloroform at a concentration of approximately 1–2%. Elemental analyses for C, H, N and S were conducted on a Fisons EA1108 elemental analyzer.

2.2. Synthesis of intermediate $[ReO(L^n)Cl_3]^-$ complexes

2.2.1. $[ReO(L^1)Cl_3]^-$ (**1**) and $[ReO(L^3)Cl_3]^-$ (**3**)

Complexes **1** and **3** were prepared as reported previously [13,14]. For these two complexes selected spectral parameters are reported in Table 1.

2.2.2. $[ReO(L^2)Cl_3]^-$ (**2**)

A solution of [*n*-bu_4n][$ReOCl_4$] (100.6 mg, 0.171 mmol) in EtOH (10 ml) was treated with a slight excess of HL^2 (50 mg, 0.204 mmol) under stirring at room temperature (r.t.). The solution became suddenly blue and deposited within a few minutes a turquoise solid, which was filtered off and washed with EtOH (3 ml) and Et_2O (3 × 5 ml). No recrystallization was necessary to obtain a pure compound. Yield: 75 mg, 55%. *Anal.* Found: C, 45.45; H, 6.01; N, 1.67. Calc. for $C_{30}H_{48}NO_3PReCl_3$: C, 45.36; H, 6.09; N, 1.76%. IR (KBr, ν, cm^{-1}): 2962, 2874, 1639 (s, ν[COO]), 1483, 1314, 1285, 1097, 985 (s, ν[Re=O]), 853, 755, 693, 504. ^1H NMR (200 MHz, $CDCl_3$, δ ppm): 0.90 (t, 12H); 1.31 (m, 8H); 1.65 (m, 8H); 3.29 (m, 8H) [*n*-Bu_4N]; 3.82 (d, 2H, $^2J_{HP}$ = 11.0 Hz, P–CH_2–COO); 7.0–8.2 (10H, Ar-*H*). ^{13}C NMR (200 MHz, $CDCl_3$, δ ppm): 13.70, 19.72, 24.05, 58.68 [*n*-bu_4N]; 37.68 (d, P–CH_2–COO); 128.70, 130.71, 131.52, 133.26 (Ar-*C*); 172.62 (P–CH_2–*C*OO); ^{31}P NMR (200 MHz, $CDCl_3$, ppm): −22.8 (s). The product is soluble in chlorinated solvents, sparingly soluble in alcohols and insoluble in Et_2O.

2.3. Synthesis of mixed-ligand oxo-Re(V) complexes $[ReO(L^n)(SB^m)]$

The three mixed-ligand compounds containing the phosphinophenolato fragment (L^1) were prepared using the same procedure, detailed below for **1a**.

2.3.1. $[ReO(L^1)(SB^a)]$ (**1a**)

The emerald [*n*-bu_4N][$ReOCl_3(L^1)$] intermediate complex **1** (120 mg, 0.145 mmol) is suspended in EtOH (15 ml). An equimolar amount of solid *N*-(2-hydroxyphenyl)salicylideneimine H_2SB^a (31 mg, 0.145 mmol) is added under stirring at r.t. The darkened mixture was refluxed for 30 min. On cooling a dark-red precipitate appeared. The solid was filtered off and washed with a few drops of EtOH and Et_2O (3 × 10 ml). Recrystallization from CH_2Cl_2–EtOH mixtures gave 81 mg of pure **1a**. Yield 81%. *Anal.* Found: C, 53.06; H, 3.64; N, 1.87. Calc. for $C_{31}H_{23}NO_4PRe$: C, 53.88; H, 3.35; N, 2.02%. IR (KBr, ν, cm^{-1}): 1604, 1582, 1454, 1432, 1380, 1297, 1248, 1126, 964 (s, ν[Re=O]), 855, 840, 755. ^1H NMR (200 MHz, $CDCl_3$, δ ppm): 6.4–8.1 (22H, Ar-*H*), 8.89 (s, 1H; –C*H*=N–). ^{31}P NMR (200 MHz, $CDCl_3$, δ ppm): 10.3 (s). The product is soluble in chlorinated solvents, insoluble in alcohols and in Et_2O. Crystals suitable for X-ray diffraction analysis were grown from CH_2Cl_2–MeOH mixtures.

*2.3.2. [ReO(L^1)(SB^b)] (**1b**)*

Yield 76%. *Anal*. Found: C, 50.12; H, 3.51; N, 1.82. Calc. for $C_{33}H_{27}NO_5PCl_2Re$: C, 49.18; H, 3.38; N, 1.74. IR (KBr, ν, cm^{-1}): 1585, 1543, 1456, 1426, 1381, 1253, 1242, 959 (s, ν[Re=O]), 855, 832, 740, 511. ^1H NMR (200 MHz, $CDCl_3$, δ ppm): 3.61 (s, 3H; –OCH_3); 6.4–8.1 (21H, Ar-*H*); 8.91 (s, 1H; –C*H*=N–). ^{31}P NMR (200 MHz, $CDCl_3$, δ ppm): 8.1 (s). The product is soluble in chlorinated solvents, sparingly soluble in alcohols and insoluble in Et_2O. Crystals suitable for X-ray diffraction analysis were grown from CH_2Cl_2 solutions layered with MeOH.

*2.3.3. [ReO(L^1)(SB^c)] (**1c**)*

Yield 85%. *Anal*. Found: C, 51.97; H, 3.25; N, 1.89; S, 4.43. Calc. for $C_{31}H_{23}NO_3SPRe$: C, 52.66; H, 3.28; N, 1.98; S, 4.53%. IR (KBr, ν, cm^{-1}): 1606, 1583, 1541, 1426, 1386, 1253, 1219, 1177, 949 (s, ν[Re=O]), 853, 746, 511. ^1H NMR (200 MHz, $CDCl_3$, δ ppm): 3.65 (s, 3H; –OCH_3); 6.2–8.4 (21H, Ar-*H*); 9.02 (s, 1H; –C*H*=N–). ^{31}P NMR (200 MHz, $CDCl_3$, δ ppm): 8.0 (s). The product is soluble in chlorinated solvents, insoluble in alcohols and in Et_2O.

Table 2
Structure determination summary of complexes **1a** and **1b**

	Complex **1a**	Complex **1b**
Empirical formula	$C_{31}H_{23}NO_4PRe$	$C_{33}H_{27}Cl_2NO_5PRe$
Formula weight	690.67	805.63
Crystal system	monoclinic	triclinic
Space group	$P2_1/c$	$P\bar{1}$
Unit cell dimensions		
a (Å)	9.890(4)	10.204(5)
b (Å)	15.792(5)	11.586(7)
c (Å)	16.949(6)	13.832(6)
α (°)	90.00	71.95(4)
β (°)	99.34	75.12(4)
γ (°)	90.00	71.99(4)
Volume (Å^3)	2612(2)	1455(1)
Z	4	2
Temperature (K)	293(2)	293(2)
ρ_{calcd} (g cm^{-3})	1.756	1.839
Absorption coefficient (mm^{-1})	4.75	4.46
F(000)	1352	792
Independent reflections	2812	3824
Observed reflections [$I \geq 2\sigma(I)$]	2016	3163
Refinement method	full matrix least-squares on F^2	
Final R indices [$I \geq 2\sigma(I)$]	R_1 [a] = 0.045	R_1 [a] = 0.046
	wR_2 [b] = 0.068	wR_2 [b] = 0.057
Goodness-of-fit	0.925	1.061

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

*2.3.4. [ReO(L^2)(SB^b)] (**2b**)*

The turquoise [n-bu_4N][$ReOCl_3(L^2)$] intermediate complex **2** (90 mg, 0.118 mmol) is suspended in EtOH (15 ml). An equimolar amount of solid *N*-(2-hydroxy-3-metoxhyphenyl)salycilideneimine H_2SB^b (29 mg, 0.119 mmol) is added under stirring at r.t. The mixture quickly darkened and was refluxed for 30 min. On cooling a bright-red precipitate appeared, which was filtered off and washed with a few drops of EtOH and Et_2O (3×10 ml). Recrystallization from CH_2Cl_2–EtOH mixtures gave 63 mg of pure **2b**. Yield 69%. *Anal*. Found: C, 49.12; H, 3.47; N, 1.92. Calc. for $C_{28}H_{23}NO_6PRe$: C, 48.96; H, 3.37; N, 2.04%. IR (KBr, ν, cm^{-1}): 1663, 1595, 1546, 1480, 1435, 1389, 1256, 989 (s, ν[Re=O]), 742, 518. ^1H NMR (200 MHz, $CDCl_3$, δ ppm): 3.80 (s, 3H; –OCH_3); 3.91 (dd, 2H; P–CH_2–, AB system); 6.6–8.1 (17H, Ar-*H*); 8.90 (s, 1H; –C*H*=N–). ^{31}P NMR (200 MHz, $CDCl_3$, δ ppm): -1.5 (s). The product is soluble in chlorinated solvents, insoluble in alcohols and in Et_2O.

*2.3.5. [ReO(L^3)(SB^b)] (**3b**)*

The turquoise [n-bu_4N][$ReOCl_3(L^2)$] intermediate complex **3** (135 mg, 0.157 mmol) is suspended in EtOH (15 ml). An equimolar amount of solid *N*-(2-mercaptophenyl)salycilideneimine (H_2SB^c) (36 mg, 0.157 mmol) is added under stirring at r.t. The mixture becomes dark within a few minutes. It is then refluxed for 30 min. On cooling a bright-red precipitate appeared, which is filtered off and washed with a few drops of EtOH and Et_2O (3×10 ml). Recrystallization from CH_2Cl_2–EtOH mixtures gave 109 mg of pure **3b**. Yield 92%. *Anal*. Found: C, 52.86; H, 3.53; N, 1.80. Calc. for $C_{33}H_{25}NO_6PRe$: C, 52.92; H, 3.36; N, 1.87%. IR (KBr, ν, cm^{-1}): 1652, 1595, 1546, 1480, 1434, 1385, 1303, 1283, 1253, 1098, 978 (s, ν[Re=O]), 837, 747, 694, 534, 506. ^1H NMR (200 MHz, $CDCl_3$, δ ppm): 3.68 (s, 3H; –OCH_3), 6.7–8.4 (21H, Ar-*H*); 8.91 (s, 1H; –C*H*=N–). ^{31}P NMR (200 MHz, $CDCl_3$, δ ppm): –8.3 (s). The product is soluble in chlorinated solvents, insoluble in alcohols and in Et_2O.

*2.4. X-ray diffraction data and crystal structure determination and refinement for **1a** and **1b***

The experimental X-ray data for **1a** and **1b** are summarized in Table 2, while some selected bond lengths and angles are given in Table 3. Data for both complexes were collected at r.t. (293 K) on a Siemens Nicolet R3m/V diffractometer with Mo Kα radiation ($\lambda = 0.71073$ Å) in the restricted range $2.1 \leq \Theta \leq 22.5°$. In fact, much of the higher angle data collected were weak and bore negative intensity. The final cell parameters were determined from 50 reflections at $\Theta > 10°$. Data were corrected for Lorentz polarization and absorption effects. Both structures were solved by heavy-

Table 3
Selected bond length (Å) and angles (°) for complexes **1a** and **1b**

	Complex **1a**	Complex **1b**
Re–P(1)	2.425(4)	2.432(3)
Re–O(1)	1.69(1)	1.651(9)
Re–O(2)	2.01(1)	2.008(8)
Re–O(3)	2.03(1)	2.047(8)
Re–O(4)	2.035(9)	2.039(8)
Re–N(1)	2.12(1)	2.08(1)
O(1)–Re–P(1)	88.6(3)	90.4(3)
O(1)–Re–O(2)	98.3(4)	99.3(4)
O(1)–Re–N(1)	110.0(5)	108.6(5)
O(1)–Re–O(3)	97.8(4)	93.6(4)
O(1)–Re–O(4)	166.2(4)	167.9(4)
O(2)–Re–N(1)	78.2(5)	80.2(5)
N(1)–Re–O(3)	91.8(5)	91.1(5)
P(1)–Re–O(4)	77.7(3)	77.8(2)

atom methods and refined using the SHELXTL/PC [15] and SHELXL-93 [16] suite of programs. To ensure a good observation/parameters ratio, anisotropy was not applied to carbon atoms of phenyl rings in **1a**, while in **1b** all the non-hydrogen atoms, apart the carbon atom of the disordered CH_2Cl_2 solvent molecule, were refined anisotropically. The hydrogen atoms were included in the calculated positions and refined as riding atoms using the SHELXL-93 default parameters. The final Fourier difference maps did not show any significant features, showing some electron density residuals (up to 1 e $Å^{-3}$) in the vicinity of Re.

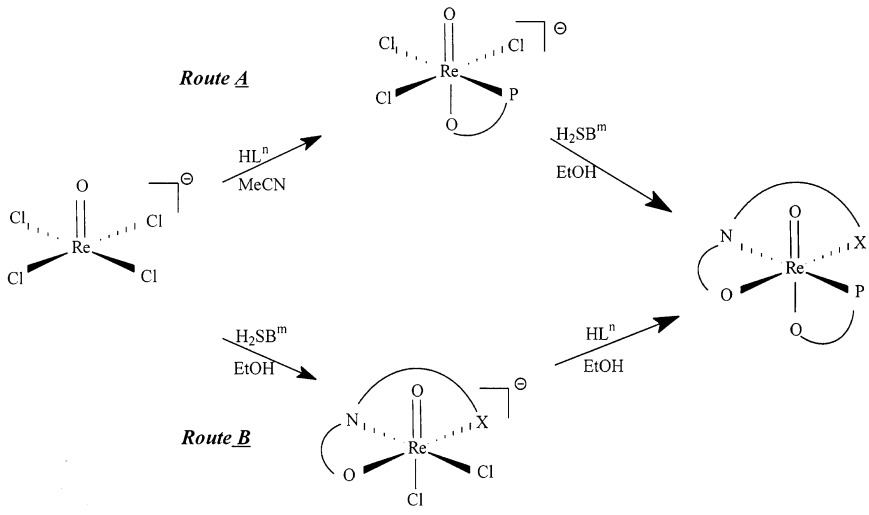
3. Results and discussion

3.1. Synthesis and general considerations

As sketched in Scheme 2, stable mixed-ligand oxorhenium heterocomplexes $[Re^{V}(O)(L^{n})(SB^{m})]$ (**1**–**3m**) can be prepared in alcoholic solutions using two alternative routes by changing the sequential addition of the ligands. In both cases intermediate compounds of the type $[Re^{V}(O)(L^{n})Cl_3]^{-}$ (**1**–**3**) or $[Re^{V}(O)(SB^{m})Cl_2]^{-}$ are isolated; they further react with the other ligand to give the heterocomplexes in high yields.

Simultaneous addition of the two different ligands, HL^{n} and H_2SB^{m}, to $[ReOCl_4]^{-}$ solutions (1:1:1 metal:HL^{n}:H_2SB^{m} ratio) still affords the heterocomplexes (in lower yield than above) contaminated by small amounts of the intermediate species. When an excess of the two ligands is utilized (1:2:2 metal:HL^{n}:H_2SB^{m} ratio), different results are obtained depending on the functionalized phosphine employed. While reaction mixtures containing the phosphino-carboxylic ligands HL^{2} or HL^{3} and the relevant SB yield the heterocomplexes, the phosphino-phenol ligand HL^{1} produces the bis-substituted compound $[Re^{V}(O)(L^{1})_2Cl]$ as the major product, contaminated by several impurities including the intermediate SB complex $[Re^{V}(O)(SB^{m})Cl_2]^{-}$. This challenge reaction indicates that the phosphino-phenol is by far the kinetic donor, and that $[Re^{V}(O)(L^{1})_2Cl]$ is thermodynamically favored over the heterocomplex. In fact, prolonged reflux does not induce significant change in the final products. The reactivity of rhenium with HL^{1} parallels the chemistry exhibited by technetium with phosphino-phenol ligands, where the phosphine-rich $[Tc^{V}(O)(L^{1})_2Cl]$ [17] and eventually the reduced tris-substituted *mer*-$[Tc^{III}(L^{1})_3]$ [18] complexes are the predominant species under the synthetic conditions utilized above for rhenium.

On the contrary, when phosphino-carboxylic ligands are employed, a remarkably different reactivity toward the two metals is observed. While reduced *mer*-$[Tc^{III}(L^{2})_3]$ and *mer*-$[Tc^{III}(L^{3})_3]$ are collected [9], confirming the tendency toward the stabilization of lower



Scheme 2.

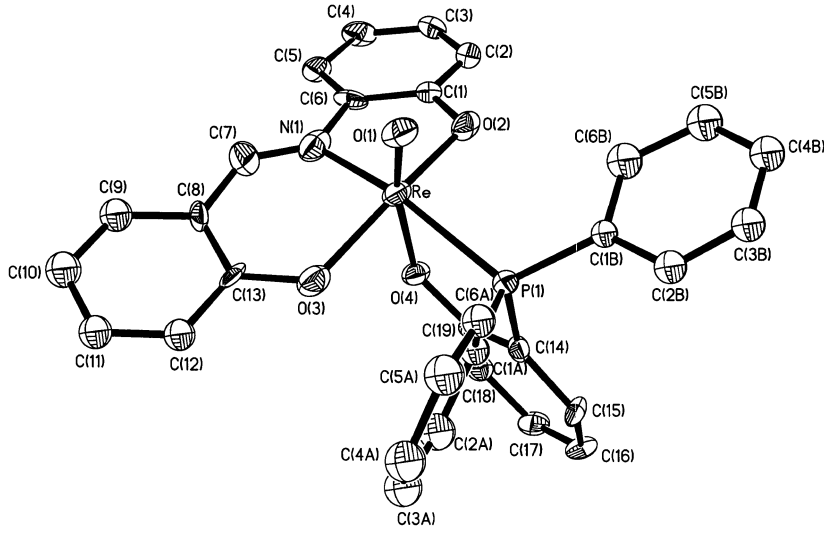


Fig. 1. ORTEP view of complex **1a** showing the atom labeling scheme. The thermal ellipsoids are drawn at 40% probability.

oxidation states for technetium, only the mono-substituted complexes $[Re^{V}(O)(L^{2})Cl_3]^-$ (**2**) and $[Re^{V}(O)(L^{3})Cl_3]^-$ (**3**) are recovered with rhenium, even in the presence of a large excess of phosphine, a condition usually met during the reconstitution of any radiopharmaceutical.

In this view and according to the results detailed above, the mono-substituted species $[Re(O)(L^{n})Cl_3]^-$ ($n = 2$, 3) containing the phosphino-carboxylato groups appear to be promising candidates for application in therapy. Studies to explore this possibility are in progress.

3.2. Characterization

Elemental analyses, as reported in Section 2, are in good agreement with the proposed formulation. IR spectra of all synthesized rhenium complexes show the characteristic Re=O stretching vibration in the range 949–989 cm^{-1}, values in accordance with those exhibited by six-coordinated monooxo-rhenium compounds [12,19]. Additional absorptions typical of coordinated arylphosphines are shown in the range 900–580 cm^{-1} [13], while complexes containing the phosphino-carboxylato groups exhibit an intense vibration in the 1663–1639 cm^{-1} region, bathocromic shifted by approximately 40 cm^{-1} with respect to those observed in uncoordinated HL^2 and HL^3. Negative charged intermediate complexes **1**–**3** show the presence of the tetrabutylammonium counterion (strong absorption just below 3000 cm^{-1}).

The ^{31}P NMR signal of uncoordinated phosphinophenol (HL^1, −20.8 ppm) moves significantly downfield in the intermediate complex **1** and in the final mixed-ligand compounds **1m**, according to the strong acid character of the $[ReO]^{3+}$ moiety. Conversely, the phosphino-carboxylate seems to work as π-acceptor in intermediate complexes **2** and **3**, the ^{31}P singlet signal falling at −14.2 and −22.8 ppm, respectively, compared to the signals observed for uncoordinated HL^2 and HL^3 (−17.4 and −4.0 ppm). Again a predominant downfield shift trend is observed in mixed-ligand species (see Table 1). The unusual ^{31}P upfield signals exhibited by complex **3** may be ascribed to the steric constrains introduced by the six-membered ring of the L^3 ligand bite compared to the five-membered rings of the L^1 and L^2 ligands. The presence of the distinctive *n*-Butyl protons in the ^{1}H NMR spectra allow to easily distinguish intermediate species, while mixed-ligand compounds exhibit an additional imine proton signal in the narrow range of 8.89–9.02 ppm indicating coordination of the SB.

3.2.1. Description of the crystal structures

The molecular structure of complexes **1** and **3** have been elucidated recently and reported in separate contributions [13,14]. The distorted octahedral arrangement (see Scheme 2) resulting from the analyses of the spectroscopic data for the series of mixed-ligand complexes is confirmed by single-crystal X-ray investigations of two representative compounds. Both structures **1a** and **1b** contain discrete monomeric octahedral monooxo-rhenium(V) complex units (Figs. 1 and 2, respectively), in which the ONO donor atoms from the tridentate dinegative ligand, along with the phosphorus of the chelating moiety, occupy the equatorial plane. The phenolate oxygen atom of the bidentate ligand, *trans* to the oxo atom, completes the octahedral coordination sphere. The $Re–O_{oxo}$ axis is inclined at 80.1 and 81.5° in **1a** and **1b**, respectively, with respect to the mean equatorial plane. Distortion from an ideal Re-

centered octahedron mainly results in a non-linear O(4)–Re–O(1) angle of 166.2 and 167.9° in **1a** and **1b**, respectively, accomplished by P(1)–Re–N(1) and O(2)–Re–O(3) angles of 161.3 and 163.2° in **1a** and 160.6 and 166.2° for **1b**, respectively. In both complexes the five-membered Re–P(1)–C(14)–C(19)–O(4) ring (in a somewhat envelope form) is virtually normal to the equatorial plane (dihedral angle of 92.9 and 87.8° in **1a** and **1b**, respectively), while the atomic displacements from the mean plane determined by the (5 + 6 member) rings of the tridentate ligand range from +0.20 (for Re) to −0.18 (for O(3)) in **1a** and from +0.13 (for Re) to −0.09 (for O(3)) in **1b**. As expected, the coordination spheres in both structures are practically superimposable (Fig. 3), the weighted root-mean-squares deviation being only 0.065 Å, when the fitting is performed using the octahedron atoms.

Bond lengths and angles, which are cumulated in Table 2, show no unusual features being within the range expected from the comparison of about 50 other six-coordinate monooxo-Re(V) complexes retrieved from the Cambridge Structural Database [20], although the Re–O (*trans* to O_{oxo}) deserves a comment. In fact, the Re–O distances (2.035(9) and 2.039(8) Å in **1a** and **1b**, respectively) are somewhat shorter than the values reported for other seven '3 + 2' oxorhenium complexes [20–24] incorporating the [ReO(L^1)] fragment (from 2.048(3) Å in [ReO(L^1)(N{$CH_2CH_2NH_2$}$_2$)]$^+$ [22] to 2.117(6) Å in [ReO(L^1)(EtN{CH_2CH_2S}$_2$)] [23]. The Re–P(1) distances (2.425(4) and 2.432(3) Å in **1a** and **1b**, respectively) are within the normal range (2.400–2.470 Å) found in this type of complexes and closely parallel the value of 2.428(1) Å found in [ReO(L^1){(*o*-C_6H_4)$_2$PPh}] [24], where the oxygen phenolate atom is

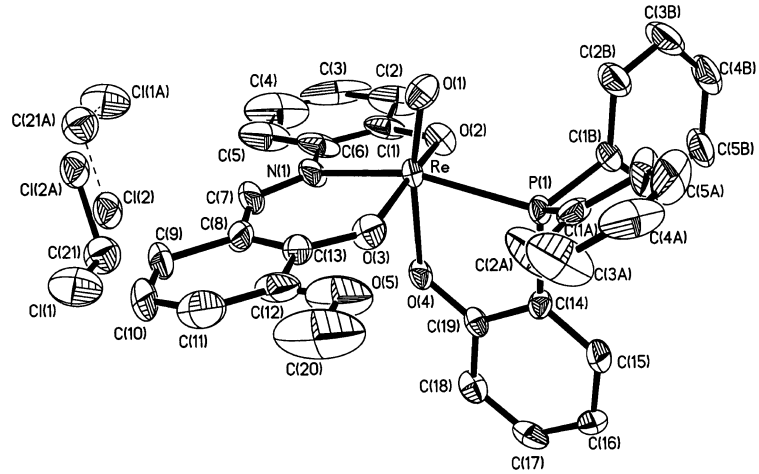


Fig. 2. ORTEP view of complex **1b** showing the atom labeling scheme. Dashed lines indicate the second equipopulated orientation of the CH_2Cl_2 molecule.

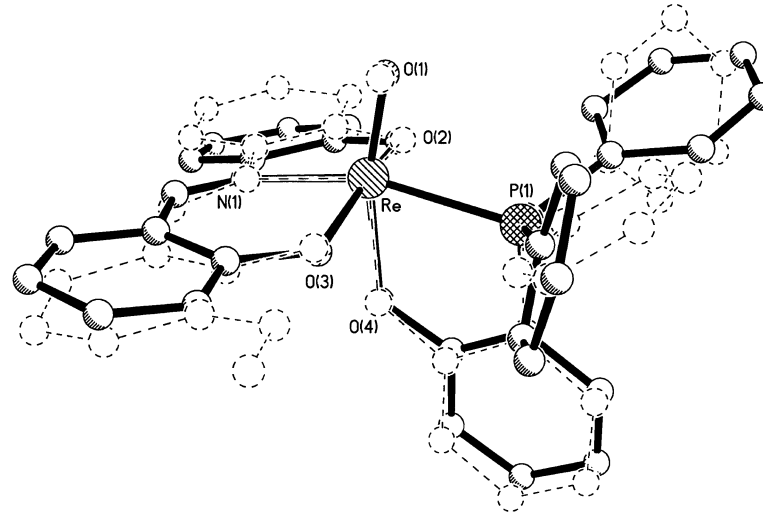


Fig. 3. Superimposition of complexes **1a** (—) and **1b** (- - -).

trans to the phosphorus of the OPO tridentate dinegative ligand.

4. Supplementary material

Crystallographic data (excluding structure factors) for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 157026 for compound **1a** and No. 157027 for compound **1b**. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

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References

[1] E.A. Deutsch, K. Libson, J.-L. Vanderheyden, in: M. Nicolini, G. Bandoli, U. Mazzi (Eds.), Technetium and Rhenium in Chemistry and Nuclear Medicine, vol. 3, Raven Press, New York, 1990, p. 13.
[2] (a) S. Jurisson, D. Berning, J. Wei, M. Dangshe, Chem. Rev. 93 (1993) 1137. (b) S. Liu, D.S. Edwards, Chem. Rev. 99 (1999) 2235. (c) J.C. Reubi, J. Nucl. Med. 36 (1995) 1825.
[3] R. Alberto, R. Schibli, A.P. Schubiger, U. Abram, J. Am. Chem. Soc. 121 (1999) 6076.
[4] C. Bolzati, A. Boschi, A. Duatti, S. Prakash, L. Uccelli, F. Refosco, F. Tisato, G. Bandoli, J. Am. Chem. Soc. 122 (2000) 4510.
[5] (a) H.-J. Pietzsch, H. Spies, S. Hoffmann, J. Stach, Inorg. Chim. Acta 161 (1989) 15. (b) D.M. Spyriounis, M. Pelecanou, C.I. Stassinopoulou, C.P. Raptopoulou, A. Terzis, E. Chiotellis, Inorg. Chem. 34 (1995) 1077. (c) M. Papadopoulos, I. Pirmettis, M. Pelecanou, C.P. Raptopoulou, A. Terzis, C.I. Stassinopoulou, E. Chiotellis, Inorg. Chem. 35 (1996) 7377. (d) I. Pirmettis, M.S. Papadopoulos, S.G. Mastrostamatis, C.P. Raptopoulou, A. Terzis, E. Chiotellis, Inorg. Chem. 35 (1996) 1685.
[6] B. Nock, S. Maina, D. Yannoukakos, I. Pirmettis, M. Papadopoulos, E. Chiotellis, J. Med. Chem. 42 (1999) 1066.
[7] P. Blower, S. Prakash, The Chemistry of Rhenium in Nuclear Medicine, in: R.W. Hay, J.R. Dilworth, K.B. Nolan (Eds.), Perspectives on Bioinorganic Chemistry, vol. 4, JAI Press, Stamford, CT, 1999 (and references therein).
[8] (a) T.B. Rauchfuss, Inorg. Chem. 16 (1977) 2966. (b) J. Yardley, H. Fletcher III, Synthesis (1975) 244.
[9] T. Jarolim, J. Podlahova, J. Inorg. Nucl. Chem. 38 (1976) 125.
[10] F. Refosco, F. Tisato, G. Bandoli, E. Deutsch, J. Chem. Soc., Dalton Trans. (1993) 2901.
[11] F. Tisato, F. Refosco, U. Mazzi, G. Bandoli, M. Nicolini, J. Chem. Soc., Dalton Trans. (1987) 1693.
[12] G. Rouschias, Chem. Rev. 74 (1974) 531.
[13] C. Bolzati, F. Tisato, F. Refosco, G. Bandoli, A. Dolmella, Inorg. Chem. 35 (1996) 6221.
[14] J. Correia, A. Domingos, I. Santos, C. Bolzati, F. Refosco, F. Tisato, Inorg. Chim. Acta, 2000, submitted for publication.
[15] G.M. Sheldrick, SHELXTL/PC ver. 5.03, Siemens Analytical X-ray Instruments, Madison, WI, 1994.
[16] G.M. Sheldrick, SHELXL-93, Program for the Refinement of Crystal Structures, University of Göttigen, Germany, 1993.
[17] C. Bolzati, F. Tisato, F. Refosco, G. Bandoli, Inorg. Chim. Acta 247 (1996) 125.
[18] C. Bolzati, F. Refosco, F. Tisato, G. Bandoli, A. Dolmella, Inorg. Chim. Acta 201 (1992) 7.
[19] F. Refosco, F. Tisato, G. Bandoli, C. Bolzati, A. Dolmella, A. Moresco, M. Nicolini, J. Chem. Soc., Dalton Trans. (1993) 605.
[20] (a) CSD Database, Release 5.19, 2000. (b) F.H. Allen, J.E. Davies, J.J. Galloy, O. Johnson, O. Kennard, C.F. Macrae, E.M. Mitchell, J.M. Smith, D.G. Watson, J. Chem. Inf. Compt. Sci. 31 (1991) 187.
[21] B. Nock, T. Maina, F. Tisato, C.P. Raptopoulou, A. Terzis, E. Chiotellis, Inorg. Chem. 39 (2000) 5197.
[22] B. Nock, T. Maina, F. Tisato, M. Papadopoulos, C.P. Raptopoulou, A. Terzis, E. Chiotellis, Inorg. Chem. 39 (2000) 2178.
[23] B. Nock, T. Maina, F. Tisato, M. Papadopoulos, C.P. Raptopoulou, A. Terzis, E. Chiotellis, Inorg. Chem. 38 (1999) 4197.
[24] H. Luo, I. Setyawati, S.J. Rettig, C. Orvig, Inorg. Chem. 34 (1995) 2287.