



HAL
open science

Synthesis and structural characterization of new oxorhenium and oxotechnetium complexes with XN₂S-tetradentate semi-rigid ligands (X = O, S, N)

Julien Le Gal, Francesco Tisato, Giuliano Bandoli, Marie Gressier, Joël Jaud, Sandra Michaud, Michèle Dartiguenave, Eric Benoist

► To cite this version:

Julien Le Gal, Francesco Tisato, Giuliano Bandoli, Marie Gressier, Joël Jaud, et al.. Synthesis and structural characterization of new oxorhenium and oxotechnetium complexes with XN₂S-tetradentate semi-rigid ligands (X = O, S, N). Dalton Transactions, 2005, 23, pp.3800-3807. 10.1039/b508661b . hal-03600003

HAL Id: hal-03600003

<https://hal.science/hal-03600003v1>

Submitted on 7 Mar 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Open Archive Toulouse Archive Ouverte (OATAO)

OATAO is an open access repository that collects the work of Toulouse researchers and makes it freely available over the web where possible.

This is a publisher-deposited version published in: <http://oatao.univ-toulouse.fr/>
Eprints ID: 3982

To link to this article: DOI:10.1039/b508661b

URL: <http://dx.doi.org/10.1039/b508661b>

To cite this version: Le Gal, Julien and Tisato, Francesco and Bandoli, Giuliano and Gressier, Marie and Jaud, Joël and Michaud, Sandra and Dartiguenave, Michèle and Benoist, Eric (2005) *Synthesis and structural characterization of new oxorhenium and oxotechnetium complexes with XN₂S-tetradentate semi-rigid ligands*(X = O, S, N). Dalton Transactions (n° 23). pp. 3800-3807. ISSN 1477-9226

Any correspondence concerning this service should be sent to the repository administrator:
staff-oatao@inp-toulouse.fr

Synthesis and structural characterization of new oxorhenium and oxotechnetium complexes with XN_2S -tetradentate semi-rigid ligands ($\text{X} = \text{O}, \text{S}, \text{N}$)

Julien Le Gal,^a Francesco Tisato,^{*b} Giuliano Bandoli,^c Marie Gressier,^a Joël Jaud,^d Sandra Michaud,^a Michèle Dartiguenave^a and Eric Benoist^{*a}

^a Laboratoire de Chimie Inorganique, EA 807, Université Paul Sabatier, Bat. IIR1, 118, route de Narbonne, 31062, Toulouse, France. E-mail: benoist@chimie.ups-tlse.fr; Fax: 33 561 556 118

^b ICIS-CNR, Corso Stati Uniti, 4, 35127, Padova, Italy. E-mail: tisato@icis.cnr.it; Fax: 39 049 870 2911

^c Dept. Pharmaceutical Sciences, University Padova, Via Marzolo, 5, 35131, Padova, Italy

^d CEMES-CNRS, 29, rue Jeanne Marvig, BP 4347, 31055, Toulouse, France

Twelve novel oxo-technetium and oxo-rhenium complexes based on N_2S_2 -, N_2SO - or N_3S -tetradentate semi-rigid ligands have been synthesised and studied herein. By reacting the ligands with a slight excess of suitable $[\text{MO}]^{3+}$ precursor ($\text{ReOCl}_3(\text{PPh}_3)_2$ or $[\text{NBu}_4][^{99\text{g}}\text{TcOCl}_4]$), the monoanionic complexes of general formula $[\text{MO}(\text{Ph}-\text{XN}_2\text{S})]^-$ could be easily produced in high yield. The complexes have been characterized by means of IR, electrospray mass spectrometry, elemental analysis, NMR and conductimetry. The crystal structures of $[\text{PPh}_4][\text{ReO}(\text{Ph}-\text{ON}_2\text{S})]$ **1b** and $[\text{NBu}_4][^{99\text{g}}\text{TcO}(\text{Ph}-\text{ON}_2\text{S})]$ **1c** have been established. The $[\text{MO}]^{3+}$ moiety was coordinated *via* the two deprotonated amide nitrogens, the oxygen and the terminal sulfur atoms in **1b** and **1c**. In both compounds, the ON_2S coordination set is in the equatorial plane, and the complexes adopted a distorted square-pyramidal geometry with an axial oxo-group. The chemical and structural identity of the different prototypic complexes (rhenium, $^{99\text{g}}\text{Tc}$ complexes and their corresponding $^{99\text{m}}\text{Tc}$ radiocomplexes) have been also established by a comparative HPLC study.

Introduction

Technetium and rhenium are known for their useful applications in nuclear medicine. $^{99\text{m}}\text{Tc}$ (140 keV γ emitter, $t_{1/2}$ 6.02 h, convenient availability from the $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator) is widely used for diagnostic imaging, while ^{186}Re (1.07 MeV β^- emitter, $t_{1/2}$ 90 h) and ^{188}Re (2.12 MeV β^- emitter, $t_{1/2}$ 17 h) are two of the most attractive isotopes for applications in targeted radionuclide therapy.^{1,2} The efforts made in this field in recent years have led to the synthesis of novel, selective and effective chelates.^{2,3} Among them, N_2S_2 , N_2O_2 or N_3S frameworks are the most common chelate systems used to bind the $[\text{TcO}]^{3+}$ and $[\text{ReO}]^{3+}$ cores.⁴

In connection with our interest in the preparation of new substitution-inert technetium and rhenium compounds, we have recently reported the synthesis of a new family of semi-rigid N_2S_2 , N_2OS or N_3S tetradentate ligands, which are characterised by the presence of an aromatic cycle in the framework (Scheme 1). This design (i) enhances the sp^2 character of the nitrogen atom bonded to the metal, (ii) promotes rigidity to the square-pyramidal base which can favour and stabilise the chelate ring by an entropic effect,⁵ and (iii) avoids the formation of isomers. Thus, coordination of selected tetraanionic tetradentate ligands (Scheme 1) towards usual rhenium ($\text{ReOCl}_3(\text{PPh}_3)_2$ or $[\text{NBu}_4][\text{ReO}_4]$) and technetium ($[\text{NBu}_4][^{99\text{g}}\text{TcOCl}_4]$) precursors gave straightforwardly complexes of the general formula $[\text{C}][\text{MO}(\text{Ph}-\text{XN}_2\text{S})]$ (C is Na, NBu_4 , Et_3NH , PPh_4 ; X = O, S, NH, NMe) under mild conditions. Complexes $[\text{PPh}_4][\text{ReO}(\text{Ph}-$

$\text{ON}_2\text{S})]$ **1b** and $[\text{NBu}_4][^{99\text{g}}\text{TcO}(\text{Ph}-\text{ON}_2\text{S})]$ **1c** were characterised by single-crystal X-ray analyses, the latter constituting the first example of $^{99\text{g}}\text{Tc}$ crystal structure with this kind of semi-rigid ligands.

The reactivity of these ligands with $^{99\text{m}}\text{Tc}$ and the stability of the corresponding radiocomplexes, were also investigated. While trianionic tetradentate ligands gave quite stable $[\text{M}^{3+}\text{TcO}]^{3+}$ complexes with two *syn/anti* epimers,⁶ these tetraanionic tetradentate ligands produced unique and highly stable $[\text{M}^{3+}\text{TcO}]^{3+}$ species,⁷ in accordance to a recent contribution of Papachristou *et al.*⁸ Moreover, our new tetraanionic chelating ligands can be functionalized through the aromatic ring (by amine or acid function) to obtain bifunctional chelating agents (BCAs) for targeting purposes.

The structural identity of the corresponding Re, $^{99\text{g}}\text{Tc}$ and $^{99\text{m}}\text{Tc}$ compounds was assessed by means of HPLC studies.

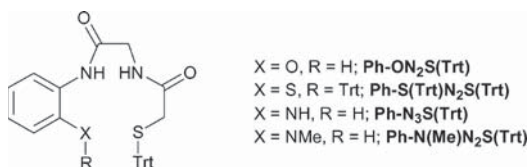
Results and discussion

The ligands

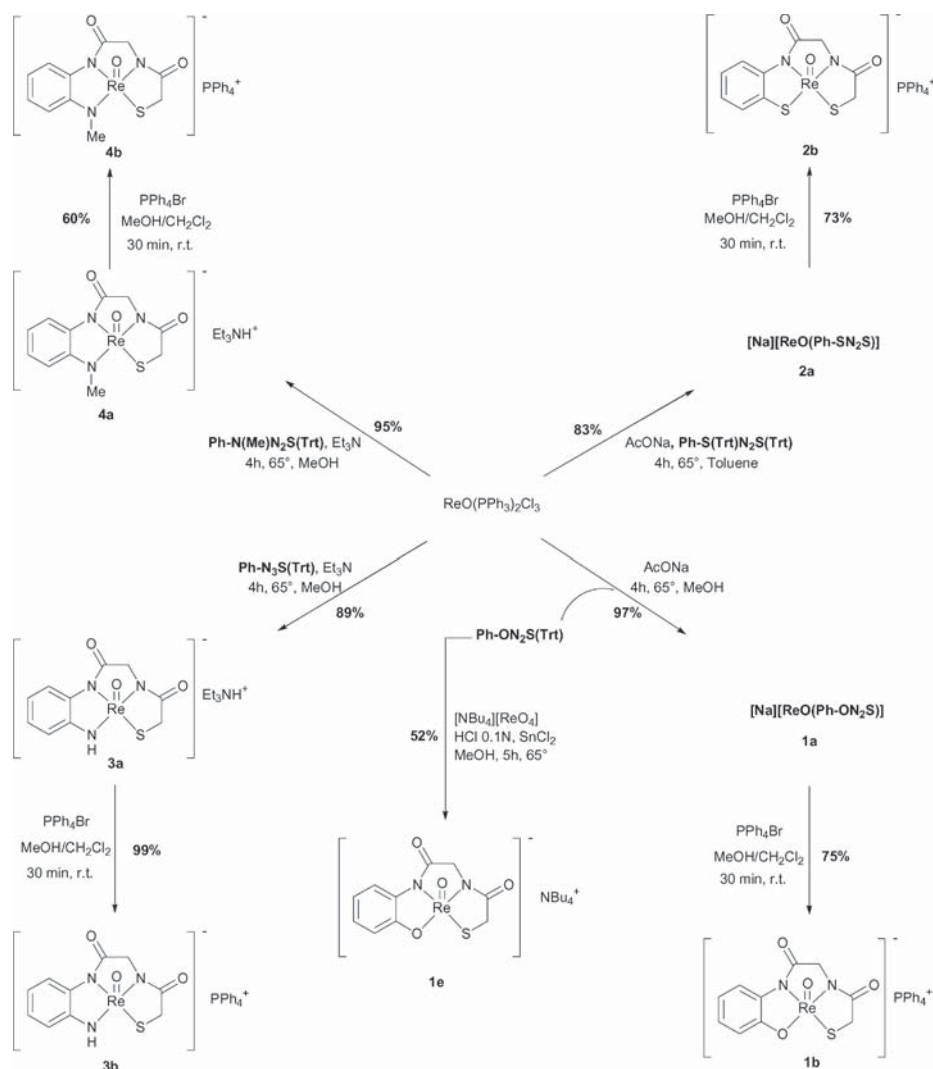
Four tetradentate semi-rigid ligands ($\text{Ph}-\text{ON}_2\text{S}(\text{Trt})$, $\text{Ph}-\text{S}(\text{Trt})\text{N}_2\text{S}(\text{Trt})$, $\text{Ph}-\text{N}_3\text{S}(\text{Trt})$, $\text{Ph}-\text{N}(\text{Me})\text{N}_2\text{S}(\text{Trt})$, general abbreviation, $\text{Ph}-\text{XN}_2\text{S}$; Trt = trityl) have been used as chelating agents in the present work. They were synthesised in good yield *via* multistep reactions as previously described.⁷ $\text{Ph}-\text{XN}_2\text{S}$ ligands act as tetraanionic ligands $\text{X}^- \text{N}^- \text{N}^- \text{S}^-$, by coordination *via* the charged X aromatic function, the two amide nitrogens and the sulfur atoms. Very preliminary studies on radiolabelling of these ligands showed that they form stable $^{99\text{m}}\text{Tc}$ complexes **1d–4d** at tracer level.⁷

Preparation of rhenium(v) complexes

Ligand-exchange reactions of labile $\text{ReOCl}_3(\text{PPh}_3)_2$ ⁹ with a slight excess of the relevant tetradentate ligand (1 : 1.3 metal : ligand ratio) in the presence of a deprotonating agent (Scheme 2)



Scheme 1 Ph-XN₂S Ligands.



Scheme 2 Preparation of the rhenium complexes.

gave $[\text{MO}(\text{Ph-XN}_2\text{S})]^-$ compounds in high yield. In more detail, reactions of $\text{Ph-ON}_2\text{S}(\text{Trt})$ or $\text{Ph-S}(\text{Trt})\text{N}_2\text{S}(\text{Trt})$ with $\text{ReOCl}_3(\text{PPh}_3)_2$ in the presence of sodium acetate in methanol or toluene resulted in oxorhenium complexes **1a** or **2a** as the sodium salts in 97 and 83% yield, respectively. The cleavage of trityl group was accomplished during the coordination of the ligand to the ReO^{3+} core and this is in agreement with the acidic contribution of the metal in the mechanism of sulfur detritylation.¹⁰

By using the above detailed conditions with $\text{Ph-N}_3\text{S}(\text{Trt})$ or $\text{Ph-N}(\text{Me})\text{N}_2\text{S}(\text{Trt})$, only a mixture of several rhenium complexes were obtained. However, use of triethylamine instead of sodium acetate as deprotonating agent determined a quite rapid change of the methanol solution colour from greenish-yellow to the final reddish-brown. The coordination took place in 4 h at reflux and led, for each ligand, to a unique oxorhenium complex (**3a**, **4a**) as the triethylammonium salt, in good yield (>85%). The presence of triethylammonium chloride as a persistent contaminant, even after column chromatography purification, suggested the replacement of the counter-cation with larger PPh_4^+ . Metathesis reactions were performed in dichloromethane/methanol solutions at room temperature. Under these conditions, analytically pure complexes **1b-4b** were obtained in high yield. Complex **1b** gave red crystals suitable for X-ray analysis from dichloromethane-methanol solution. This compound, as well as all other complexes prepared in this

study, contains a metal-monooxo core with no additional group coordinated *trans* to the yl-oxygen. This behaviour is typical of anionic five-coordinated complexes in which the ligand contains good π donor atoms.^{11,12}

Rhenium complexation of the trityl protected $\text{Ph-ON}_2\text{S}(\text{Trt})$ ligand was also performed in refluxing methanol by direct reduction of tetrabutylammonium perrhenate in the presence of an excess of tin chloride,¹³ giving $[\text{NBu}_4][\text{Ph-ON}_2\text{S}]$, **1e**.

These oxo-rhenium compounds are soluble in dichloromethane, chloroform, methanol and insoluble in water. They are indefinitely stable in the solid state as well as in organic solvents (for a period of months) as shown by HPLC and NMR. The stability is not affected by the presence of air or moisture.

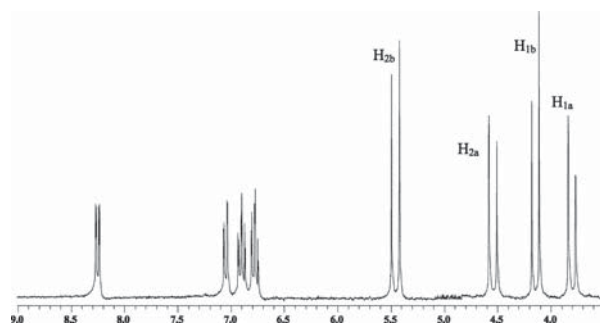
All the oxo-rhenium complexes were unambiguously identified by conventional analytical and spectroscopic techniques. In particular, IR spectra showed an intense band in the range 948–969 cm^{-1} attributable to the Re=O stretching vibration,¹⁴ and two strong bands in the range 1618–1667 cm^{-1} assigned to $\nu_{\text{C=O}}$ of both amides (Table 1). No multiple strong bands were detected in the ranges 1500–1560 and 3200–3400 cm^{-1} of complexes **1a**, **1b**, **1e**, **2a** and **2b**, confirming that the amides were deprotonated.¹⁵ Conversely, complexes **3a**, **4a** and **3b** exhibited vibrations in the 3200–3400 cm^{-1} range, due to the presence of the triethylammonium counter-cation and/or of the aromatic amine N–H stretching vibrations, respectively. The IR spectra of complexes **1b-4b** exhibited five additional bands of the PPh_4^+ moiety.

Table 1 Selected ^1H , ^{13}C NMR and IR data of oxorhenium and oxotechnetium complexes **1–4**

	NMR			IR	
	CH_2S	CH_2N	$\text{C}=\text{O}$	$\text{C}=\text{O}$	$\text{M}=\text{O}$
	$\delta_{\text{H}}(\text{H}_{\text{exo}}/\text{H}_{\text{endo}})$ (ppm); $J_{\text{H-H}}/\text{Hz}$			δ_{C} (ppm)	ν/cm^{-1}
1a	3.81/4.15; $J = 17.2$	4.54/5.46; $J = 18.3$	187.3/194.5	1661/1624	968
2s	3.71/3.90; $J = 17.4$	4.54/4.94; $J = 18.9$	190.5/194.8	1662/1620	964
3a	3.81/4.02; $J = 17.2$	4.55/5.12; $J = 18.7$	188.1/194.0	1635/1613	956
4a	3.83/3.99; $J = 17.1$	4.49/5.04; $J = 18.6$	187.6/193.4	1647/1622	953
1e	3.79/4.13; $J = 17.1$	4.57/5.53; $J = 18.4$	186.9/193.1	1664/1641	968
1b	3.71/4.01; $J = 16.8$	4.44/5.37; $J = 18.3$	187.5/193.9	1667/1638	969
2b	3.72/3.87; $J = 17.1$	4.56/4.88; $J = 18.9$	188.7/192.2	1665/1625	962
3b	3.77/3.93; $J = 16.8$	4.43/5.04; $J = 18.3$	187.7/192.8	1648/1618	948
4b	3.79/3.97; $J = 17.1$	4.39/5.01; $J = 18.6$	187.8/193.2	1649/1625	954
1c	3.85/4.04; $J = 16.9$	4.61/5.19; $J = 18.3$	182.5/185.9	1654/1634	953
2c	3.85/4.10; $J = 16.9$	4.72/4.82; $J = 18.9$	184.0/186.4	1655/1638	945
3c	3.72/4.07; $J = 16.7$	4.58/4.93; $J = 18.6$	183.3/186.2	^a	^a

^a Not realised.

Proton NMR of Re-complexes revealed the loss of both amide and XR (XR = OH, NH₂ or NHMe) hydrogens indicating deprotonation and coordination. In complexes **3a,b** and **4a,b** the loss of aromatic amine nitrogen hydrogens, which is unusual in amines, may be attributed to the greater acidity imparted to the aniline-like amine hydrogens by conjugation with the aromatic ring.¹⁶ Moreover, only a unique signal for hydrogen (**3a,b**) and the methyl group (**4a,b**) of the aromatic nitrogen, respectively, was detected indicating sp² hybridization for the aromatic amine nitrogen. Methylene protons of the tetradentate ligand framework were found to be diastereotopic (AB pattern) with coupling constants in the range 17–19 Hz. *Exo* and *endo* α protons of the glycine residue were detected at 4.54 (H_{2a}) and 5.46 ppm (H_{2b}) for **1a**, downfield shifted compared to the corresponding protons in the uncoordinated ligand (3.76 ppm). Similarly, the α protons close to the thiolate group were deshielded from 3.21 ppm in the uncoordinated ligand to 3.81 (H_{1a}) and 4.15 ppm (H_{1b}) for **1a** (Fig. 1).

**Fig. 1** Proton NMR spectra for complex **1a** (MeOD, 25 °C).

Similar magnetic inequivalence of CH₂ protons attached to amide donor atoms was observed in MAG₃Re type complexes.¹⁷ According to the literature,¹⁰ we assigned the downfield signal of both AB patterns to the *endo* protons (*syn* to the Re=O

group) and the upfield signals to the *exo* ones (*anti* to the Re=O group).¹⁸ ^{13}C NMR spectra confirmed coordination of the ligands showing remarkable downfield shifts of the carbon signals nearby the ligating atom set compared to those of the corresponding carbons in the free ligand. For example, the amide carbons were downfield shifted by 20–25 ppm upon coordination,¹⁹ and, analogously, the glycine α carbons moved from 42–45 ppm in the free ligands to 60–62 ppm in the complexes.

Negative-ion ESI-MS spectra of each Re-complex showed the parent peak with the correct isotope distribution pattern consistent with the monomeric anion, without significant fragmentation. Conductivity measurements gave values in methanol consistent with a 1 : 1 electrolyte type.

Synthesis of $^{99\text{g}}\text{Tc}$ complexes

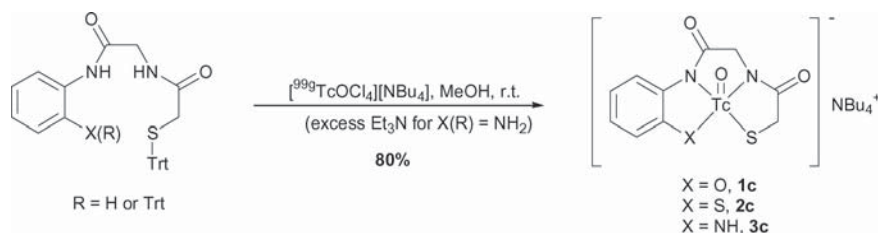
$^{99\text{g}}\text{Tc}$ complexes **1–3c** were synthesised by ligand-exchange reactions starting from $[\text{NBu}_4][^{99\text{g}}\text{TcOCl}_4]$ ²⁰ and the relevant ligand in methanol at room temperature. Addition of triethylamine was necessary to isolate pure **3c**. In contrast, complex **4c** was always collected as a mixture of two species (Scheme 3).

The IR features of **1c–3c** were similar to those observed in oxorhenium analogues. The Tc=O stretching vibration appeared consistently at 950 cm⁻¹, *ca.* 15–20 cm⁻¹ ipsochromic shifted compared to the vibrations observed in the corresponding oxorhenium compounds. This difference is common in series of isostructural mono-oxo Tc and Re species.^{21,22}

Analogously, ^1H and ^{13}C NMR values do not change significantly on going from oxorhenium to oxotechnetium complexes, indicating structural similarity (Table 1) that was confirmed by the X-ray analysis of complex **1c**.

X-Ray crystallography

The $[\text{PPh}_4][\text{ReO}(\text{Ph}-\text{ON}_2\text{S})]$ **1b** and $[\text{NBu}_4][^{99\text{g}}\text{TcO}(\text{Ph}-\text{ON}_2\text{S})]$ **1c** complexes were crystallised by slow evaporation of a dichloromethane–ethanol and a dichloromethane–isopropanol solution, respectively. Crystallographic data and structure

**Scheme 3** Synthesis of $^{99\text{g}}\text{Tc}$ complexes **1c**, **2c**, **3c**.

refinement as well as selected bond distances and angles involving the atoms of the anions are summarised in Tables 2 and 3, respectively. Perspectives drawings of the two complexes are shown in Figs. 2 and 3.

Both compounds are monoanionic, the $[\text{MO}]^{3+}$ core charge being balanced by the four hydrolysable functions of the tetradentate ligand. Each asymmetric unit cell contains only one metal complex, and the absolute configuration around the metal is clockwise. The stereochemical notation to describe this situation is $(SP-5-24-C)-\mathbf{1b}$ and $(SP-5-24-C)-\mathbf{1c}$.²³ The acronym means that the complex assumes a square-pyramidal geometry with coordination number 5, 24 is the configuration

number according to the CIP (Cahn–Ingold–Prelog) rules,²⁴ and the symbol *C* is assigned to that configuration in which the CIP priority numbers of the ligating atoms in the equatorial plane increase proceeding in a clockwise manner when viewing the plane from the ligating atom on the C_4 axis.

Thus, $[\text{MO}(\text{Ph}-\text{ON}_2\text{S})]^-$ complexes exhibit a distorted square-pyramidal geometry with yl-oxygen in the apical position. The square planes defined by the combination of nitrogen, oxygen and sulfur atoms are little distorted, with the two amide nitrogens and the phenolate oxygen in the plane and the sulfur atom lying below the plane by about 0.28 and 0.30 Å in **1b** and **1c**, respectively. Re and Tc lie above the mean plane by 0.67 and

Table 2 Crystal data and structure refinement for **1b** and **1c** complexes

Complex	$[\text{PPh}_4][\text{ReO}(\text{Ph}-\text{ON}_2\text{S})] \mathbf{1b}$	$[\text{NBu}_4][^{99\text{m}}\text{TcO}(\text{Ph}-\text{ON}_2\text{S})] \mathbf{1c}$
Formula	$\text{C}_{34}\text{H}_{28}\text{N}_2\text{O}_4\text{PReS}$	$\text{C}_{26}\text{H}_{44}\text{N}_3\text{O}_4\text{STc}$
<i>M</i>	777.85	592.70
Crystal system	Orthorhombic	Monoclinic
Color	Dark red	Brown
Crystal size/mm	$0.21 \times 0.14 \times 0.64$	$0.20 \times 0.12 \times 0.06$
Space group	$P2_12_12_1$	$P2_1/n$
<i>a</i> /Å	9.600(4)	9.114(2)
<i>b</i> /Å	14.588(3)	18.383(4)
<i>c</i> /Å	21.525(9)	17.360(4)
$\beta/^\circ$	90	91.32(3)
<i>V</i> /Å ³	3015(2)	2907.8(9)
<i>Z</i>	4	4
<i>T</i> /K	298	293
<i>D_c</i> /g cm ⁻³	1.714	1.354
<i>F</i> (000)	1536	1248
Total reflections	35340	7250
Independent reflections	9963	7250
Observed reflections [<i>I</i> > 2σ(<i>I</i>)]	6195	3700
Data/restraints/parameters	6195/0/378	3700/0/315
Final <i>R</i> indices [<i>I</i> > 2σ(<i>I</i>)]	$R_1 = 0.0505, wR_2 = 0.0962$	$R_1 = 0.0454, wR_2 = 0.1064$
<i>R</i> indices (all data)	$R_1 = 0.1070, wR_2 = 0.1080$	$R_1 = 0.0900, wR_2 = 0.1286$
GOF	0.947	0.881

Table 3 Selected bond lengths (Å) and angles (°) in complexes **1b** and **1c**

	$[\text{PPh}_4][\text{ReO}(\text{Ph}-\text{ON}_2\text{S})] \mathbf{1b}$	$[\text{NBu}_4][^{99\text{m}}\text{TcO}(\text{Ph}-\text{ON}_2\text{S})] \mathbf{1c}$
M(1)–O(4)	1.675(4)	1.653(2)
M(1)–O(3)	2.000(4)	1.986(2)
M(1)–N(2)	1.999(5)	1.984(3)
M(1)–N(1)	1.983(6)	1.960(3)
M(1)–S(1)	2.276(2)	2.276(1)
C(1)–S(1)	1.788(9)	1.822(4)
C(2)–O(1)	1.208(9)	1.219(4)
C(2)–N(1)	1.356(9)	1.365(5)
C(4)–O(2)	1.225(9)	1.216(5)
C(4)–N(2)	1.388(9)	1.375(5)
C(5)–N(2)	1.398(8)	1.414(5)
C(10)–O(3)	1.347(8)	1.359(4)
O(4)–M(1)–N(1)	110.9(3)	109.7(1)
O(4)–M(1)–O(3)	109.3(2)	110.8(1)
O(4)–M(1)–N(2)	114.1(2)	114.3(1)
O(4)–M(1)–S(1)	110.4(2)	110.9(1)
O(3)–M(1)–N(2)	78.6(2)	79.2(1)
N(2)–M(1)–N(1)	78.4(2)	78.9(1)
N(1)–M(1)–S(1)	83.2(2)	82.81(9)
O(3)–M(1)–S(1)	89.9(1)	88.64(8)
N(2)–M(1)–S(1)	135.4(2)	134.66(9)
O(3)–M(1)–N(1)	139.1(2)	139.0(1)
M(1)–S(1)–C(1)	100.4(3)	99.7(1)
M(1)–N(1)–C(2)	125.2(5)	125.9(3)
M(1)–N(2)–C(4)	117.6(5)	118.5(3)
M(1)–N(2)–C(5)	116.0(4)	115.7(3)
M(1)–O(3)–C(10)	113.9(4)	113.5(2)
N(2)–C(4)–O(2)	123.1(8)	126.0(4)
N(1)–C(2)–O(1)	123.5(9)	123.6(4)
C(3)–C(4)–O(2)	125.3(8)	122.9(4)
C(1)–C(2)–O(1)	122.4(8)	122.2(4)

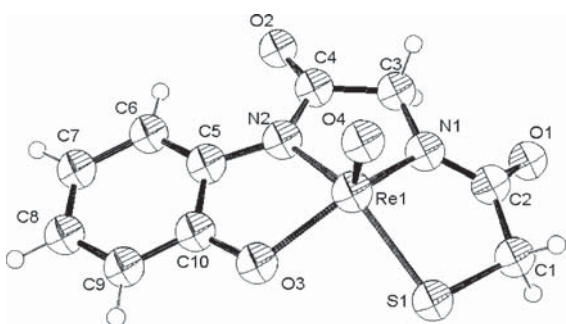


Fig. 2 An ORTEP drawing of the asymmetric anionic unit $[\text{ReO}(\text{Ph-ON}_2\text{S})]^-$ of complex **1b** with its numbering scheme. Thermal ellipsoids are drawn at the 50% probability level.

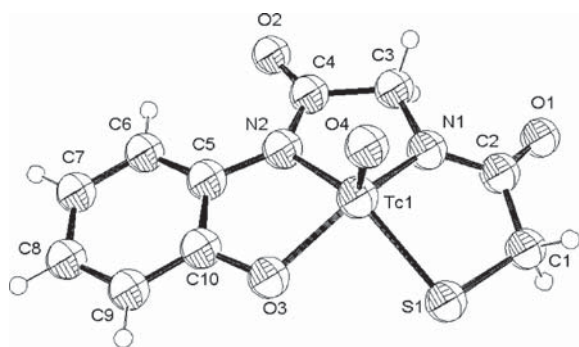


Fig. 3 Perspective view and atom-labelling scheme of the asymmetric anionic unit $[\text{}^{99\text{g}}\text{TcO}(\text{Ph-ON}_2\text{S})]^-$ of complex **1c**. All non hydrogen atoms are represented by their 50% thermal probability ellipsoids.

0.70 Å, respectively. The angles between the opposite atoms of the equatorial plane deviate from the ideal value of 180°, N(2)–M–S(1) and N(1)–M–O(3) being 135.4(2) and 139.1(2)° for **1b** and 134.66(9) and 139.0(1)° for **1c**. In addition, the trigonality index τ , defined by Addison *et al.*,²⁵ was 0.07 and 0.06 for **1b** and **1c**, respectively. The M–N(1) and M–N(2) bond distances, *ca.* 1.98 Å, are shorter than typical M–N single bonds, *ca.* 2.15 Å,²⁶ suggesting multiple bonding character. These bonds lengths are within the range observed for M–N_{amide} bonds in M^{VO} five-coordinate square-pyramidal complexes,^{10,21,22} as well as M–S_{thiolate} bond distances (both 2.276 Å).²⁷ For each complex, two of the three five-membered rings in the coordination sphere, *i.e.* those defined by MO(3)C(10)C(5)N(2) and MN(2)C(4)C(3)N(1) adopt the stable envelope conformation. The metal is 0.34 and 0.53 Å for **1b** and 0.39 Å and 0.53 Å for **1c** out of the mean plane of the remaining four atoms. On the contrary, the third five-membered ring defined by N(1)C(2)C(1)S(1)M tends to the envelope conformation, due to the sulfur atom having the largest displacement of 0.49 Å (**1b**) and 0.44 Å (**1c**) out of the best mean plane. Moreover, the O_{phenolate}–M–N_{amide} and N_{amide}–M–N_{amide} bond angles are all approximately 79° which is comparable with those found in analogous complexes. Then, the M=O bond distances (1.675(4) in **1b** and 1.653(2) Å in **1c**) are similar with those found for square-pyramidal M^{VO} complexes such as the MAG₃ derivatives ($d_{\text{Re=O}} = 1.653(2)^\circ$)^{27a} and analogous semi-rigid complexes recently developed by Papadopoulos *et al.*²² ($d_{\text{Re=O}} = 1.673(5)$ Å, $d_{\text{Tc=O}} = 1.657(3)$ Å).

HPLC profiles of Re-, ^{99g}Tc- and ^{99m}Tc-complexes (Fig. 4), obtained by using a combination of UV-vis and radiometric detections, revealed that these three species possessed similar retention times (Table 4), thereby indicating identity of their molecular structures.^{7,28}

The minor difference of retention times observed between Tc and Re complexes could be explained by the different polarities of the $[\text{Tc=O}]^{3+}$ and $[\text{Re=O}]^{3+}$ group.²⁹ These results indicate

Table 4 HPLC retention times of the ^{99m}Tc, ^{99g}Tc and ^{185/187}Re complexes

Ligand	Metallic complexes		
	^{99m} TcO	^{99g} TcO	ReO
Ph–ON ₂ S(Trt) ^a	4.31 (1d)	4.21 (1c)	3.89 (1b)
Ph–S(Trt)N ₂ S(Trt) ^b	2.74 (2d)	2.64 (2c)	2.51 (2b)
Ph–N ₂ S(Trt) ^a	3.59 (3d)	3.50 (3c)	3.87 (3b)
Ph–N(SMe)N ₂ S(Trt) ^b	2.98 (4d)	—	2.87 (4b)

^a Eluent: MeOH–H₂O–TFA (55 : 45 : 0.1). ^b Eluent: MeOH–H₂O–TFA (70 : 30 : 0.1).

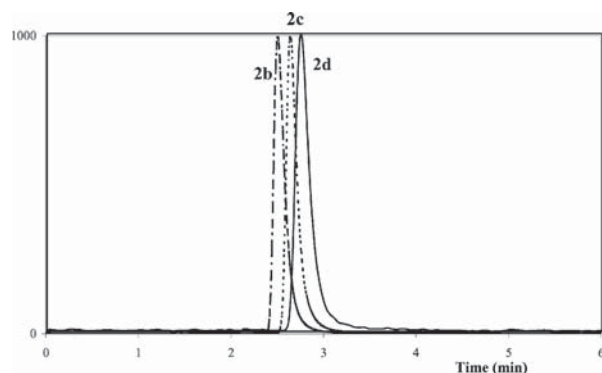


Fig. 4 Comparative reverse-phase HPLC chromatograms: **2b** (rhenium complex, UV recording at 270 nm, $t_r = 2.51$ min), **2c** (^{99g}Tc complex, UV recording at 270 nm, $t_r = 2.64$ min), **2d** (^{99m}Tc complex, radiometric detection, $t_r = 2.74$ min).

that our semi-rigid ligands form similar 1 : 1 complexes at macroscopic (Re/^{99g}Tc) and at tracer level (^{99m}Tc).

To conclude, in this paper we have shown that semi-rigid Ph–XN₂S-type ligands allow stabilization of identical mono-oxo Re and Tc species both in the solid and in the solution states. The incorporation of an aromatic ring fused into the chelate backbone imparts rigidity to a portion of the ligand enhancing the formation and stability of the resulting complex by an entropy effect. The high *in vivo* stability of the corresponding ^{99m}Tc complexes established before⁷ with the structural details and correlations reported here provide support for the potential development of agents as diagnostic (^{99m}Tc)/therapeutic (¹⁸⁸Re) matched pairs. Incorporation of biologically active fragments into this kind of chelate for the development of *in vivo* target-specific radiopharmaceuticals remains our main objective.

Experimental

Safety note

CAUTION! ^{99g}Tc is a weak β -emitter ($E_{\beta^-} = 0.292$ MeV, $t_{1/2} = 2.12 \times 10^5$ years). All manipulations were carried out in laboratories approved for low-level radioactivity using monitored hoods and glove-boxes. When handled in milligram amounts, ^{99g}Tc does not present a serious health hazard because common laboratory glassware provides adequate shielding. *Bremsstrahlung* is not a significant problem due to the low energy of the β -particles. However, normal radiation safety procedures must be used at all times, especially with solid samples, to prevent contamination and inhalation.

General

All chemicals were of the highest purity commercially available. Solvents were purified by standard methods before use and stored over 0.3 nm molecular sieves. Technetium as $[\text{NH}_4][\text{}^{99\text{g}}\text{TcO}_4]$ was obtained from Oak Ridge National Laboratory. Samples were dissolved in water and treated with

an excess of aqueous ammonia and H₂O₂ (30%) at 80 °C prior to use to oxidise residual TcO₂. Slow evaporation of the solvent with heating at 40 °C afforded [NH₄]^{99m}TcO₄ as a white powder which was converted to the [NBu₄][TcOCl₄] precursor following a literature method.²⁰ Rhenium(VII) oxide was purchased from Aldrich Chem. Co. It was converted to ReOCl₃(PPh₃)₂ according to published protocols.⁹ The ligands *N*-(2-hydroxyphenyl)-2-[(triphenylmethylthio)methylcarbonylamino]ethanamide, Ph-ON₂S(Trt); *N*-[2-(triphenylmethylthio)phenyl]-2-[(triphenylmethylthio)methylcarbonylamino]ethanamide, Ph-S(Trt)N₂S(Trt); *N*-(2-aminophenyl)-2-[(triphenylmethylthio)methylcarbonylamino]ethanamide, Ph-N₂S(Trt); *N*-[2-(*N*-methylamino)phenyl]-2-[(triphenylmethylthio)methylcarbonylamino]ethanamide, Ph-N(Me)N₂S(Trt) and the corresponding ^{99m}Tc complexes have been prepared as described previously.⁷

Instrumentation

For rhenium compounds, NMR spectra were recorded on a Bruker AC 200 (50.323 MHz for ¹³C and 200.133 MHz for ¹H) or 250 apparatus (62.896 MHz for ¹³C and 250.133 MHz for ¹H). Chemical shifts are indicated in δ values (ppm) downfield from internal TMS. ¹H NMR and ¹³C NMR spectra of each complex were recorded at room temperature in CDCl₃ except for **1a**, **2a** which were performed in MeOD. Unambiguous assignments, were established by two-dimensional [¹H, ¹H] COSY and [¹H, ¹³C] HMQC and HMBC experiments (Table 1).

IR spectra were recorded as KBr pellets on a Bruker Vector 22 spectrophotometer in the range 4000–400 cm⁻¹. Negative electrospray mass spectra were obtained on a NERMAG R 10–10 mass spectrometer. Microanalysis was performed by the microanalytical department of the Ecole Nationale Supérieure de Chimie de Toulouse. TLC was performed using precoated Kieselgel 60 plates F₂₅₄ (TLC plates, Merck) and was visualised by UV. Column chromatography was carried out using “gravity” silica (SDS silica gel).

For technetium compounds, NMR spectra were collected on a Bruker AC-300 apparatus (75.467 MHz for ¹³C and 300.13 MHz for ¹H) using SiMe₄ as internal reference (¹H). FT IR spectra were recorded on a Nicolet 510P Fourier transform spectrometer in the range 4000–400 cm⁻¹ in KBr pellets using a Spectra-Tech diffuse-reflectance collector accessory. Mass spectra of selected technetium compounds (*ca.* 10⁻⁶ M solutions) were recorded on a LCQ instrument (Finnigan, Palo Alto, CA). The complexes have been directly injected by a syringe pump at a flow of 5 μ L min⁻¹. Thin-layer chromatography (TLC) was performed using sheets from Riedel de Haen (Silica gel 60 F₂₅₄).

HPLC comparison was achieved on a waters 600E gradient chromatography with a Waters Lambda Max UV detector, a SAIP radioactivity detector and an ICS dual integrator for effluent monitoring and a Satisfaction RP18AB column using MeOH–H₂O–TFA (55 : 45 : 0.1 or 70 : 30 : 0.1) as eluent (flow rate of 1 mL min⁻¹). The eluate was monitored by UV absorbance at 270 nm for Re and ^{99m}Tc complexes, or γ -ray detection for ^{99m}Tc complexes.

X-Ray crystal structure determination for compounds **1b** and **1c**

Diffraction measurements for **1b** were performed on a Nonius Kappa CCD diffractometer using graphite-monochromated Mo-K α radiation ($\lambda = 0.71073$ Å) while, for **1c**, diffraction data were collected on a Nicolet R3m/V diffractometer (Mo-K α radiation; $\lambda = 0.71073$ Å). The structures were solved by direct methods for **1b** and by heavy-atom methods for **1c**. Both were refined with full-matrix least-squares procedure based on F^2 . Structure determination and refinement were performed using the SIR97,³⁰ Maxus³¹ and SHELX-97³² programs. 7350 and 3700 independent reflections with $I \geq 2\sigma(I)$ were used for refinement of the unit cell for **1b** and **1c**, respectively. Hydrogens for the disordered chain of the tBu molecule in compound **1c** were not located. The most significant details of the crystallography study

are reported in Table 2. A collection of selected bond distance and angles are shown in Table 3.

CCDC reference numbers 275918 and 275919.

See <http://dx.doi.org/10.1039/b508661b> for crystallographic data in CIF or other electronic format.

Synthesis of complexes

[Na][ReO(Ph-ON₂S)] **1a** and [Na][ReO(Ph-SN₂S)] **2a**. The synthesis and characterisation of the two complexes **1a** and **2a** have been reported previously.⁷

[PPh₄][ReO(Ph-ON₂S)] **1b**. **1a** (100.0 mg, 0.22 mmol) and tetraphenylphosphonium chloride (89.2 mg, 0.24 mmol) were dissolved in a mixture of MeOH (15 mL) and CH₂Cl₂ (15 mL). The solution was stirred for 30 min at room temperature and then allowed to precipitate during 2 days. A red solid was filtered and washed with cold water and dried under vacuum (126.3 mg, yield = 75%).

Found: C, 52.23; H, 3.63; N, 3.46. C₃₄H₂₈N₂O₄PreS requires C, 52.50; H, 3.63; N, 3.60%; IR: $\nu_{\max}/\text{cm}^{-1}$ 1667, 1638 (CO); 969 (ReO); ¹H NMR (250 MHz, CDCl₃): δ_{H} 3.71 (d, ² $J_{\text{HH}} = 16.8$ Hz, 1 H, CH₂S), 4.01 (d, ² $J_{\text{HH}} = 16.8$ Hz, 1 H, CH₂S), 4.44 (d, ² $J_{\text{HH}} = 18.3$ Hz, 1 H, CH₂N), 5.37 (d, ² $J_{\text{HH}} = 18.3$ Hz, 1 H, CH₂N), 6.63 (dt, ³ $J_{\text{HH}} = 7.6$ Hz, ⁴ $J_{\text{HH}} = 1.2$ Hz, 1 H, CH_{Ar}), 6.75 (dt, ³ $J_{\text{HH}} = 7.6$ Hz, ⁴ $J_{\text{HH}} = 1.5$ Hz, 1 H, CH_{Ar}), 6.99 (dd, ³ $J_{\text{HH}} = 7.6$ Hz, ⁴ $J_{\text{HH}} = 1.2$ Hz, 1 H, CH_{Ar}), 7.52 (m, 8 H, CH_{Ar} PPh₄), 7.69 (m, 8 H, CH_{Ar} PPh₄), 7.83 (m, 4 H, CH_{Ar} PPh₄), 8.22 (dd, ³ $J_{\text{HH}} = 7.6$ Hz, ⁴ $J_{\text{HH}} = 1.5$ Hz, 1 H, CH_{Ar}); ¹³C{¹H} NMR (62.5 MHz, CDCl₃): δ_{C} 40.9 (CH₂S), 61.8 (CH₂N), 116.1, 118.7, 119.5, 123.4 (4 CH_{Ar}), 117.3 (4 C_{Ar} PPh₄), 131.2, 131.4, 134.9, 135.0, 136.3, 136.4 (20 CH_{Ar} PPh₄), 141.4, 171.1 (2 C_{Ar}), 187.5, 193.9 (2 CO); MS (ES⁻): m/z (%) 437 (60), 439 (100) [M⁻].

[NBu₄][ReO(Ph-ON₂S)] **1c**. To a boiling solution of Ph-ON₂S(Trt) (148.8 mg, 0.30 mmol) in 40 mL of MeOH was added a solution of tin(II) chloride (143.5 mg, 0.63 mmol, in 1 mL of 0.1 M HCl), followed immediately by a solution of tetrabutylammonium perchlorate (310.6 mg, 0.63 mmol, in 1 mL of MeOH). Refluxing was continued for 5 h, the solution cooled at room temperature and washed with 20 mL of hexane. MeOH was removed and the crude solid was dissolved in CH₂Cl₂ (20 mL), then washed with water (20 mL). The organic layer was dried with solid Na₂SO₄, filtered and concentrated to dryness. The crude material was purified by column chromatography on silica gel (eluent CH₂Cl₂–MeOH (95 : 5)) followed by two crystallisations in methanol–ether mixture (3 : 1 v/v). Under these conditions, [Bu₄N]Cl remained in solution and the complex was obtained as a red–orange powder (105 mg, 52%).

Found: C, 45.75; H, 6.60; N, 5.72. C₂₇H₄₈N₃O₄ReS requires C, 46.53; H, 6.94; N, 6.03%; IR: $\nu_{\max}/\text{cm}^{-1}$ 1641 (CO), 968 (ReO); ¹H NMR (250 MHz, CDCl₃): δ_{H} 0.99 (m, 12 H, CH₃), 1.49 (m, 16 H, CH₂), 3.07 (m, 8 H, CH₂), 3.79 (d, ² $J_{\text{HH}} = 17.1$ Hz, 1 H, CH₂S), 4.13 (d, ² $J_{\text{HH}} = 17.1$ Hz, 1 H, CH₂S), 4.57 (d, ² $J_{\text{HH}} = 18.4$ Hz, 1 H, CH₂N), 5.53 (d, ² $J_{\text{HH}} = 18.4$ Hz, 1 H, CH₂N), 6.75 (dt, ³ $J_{\text{HH}} = 7.8$ Hz, ⁴ $J_{\text{HH}} = 1.2$ Hz, 1 H, CH_{Ar}), 6.86 (dt, ³ $J_{\text{HH}} = 7.8$ Hz, ⁴ $J_{\text{HH}} = 1.5$ Hz, 1 H, CH_{Ar}), 7.05 (dd, ³ $J_{\text{HH}} = 7.8$ Hz, ⁴ $J_{\text{HH}} = 1.2$ Hz, 1 H, CH_{Ar}), 8.33 (dd, ³ $J_{\text{HH}} = 7.8$ Hz, ⁴ $J_{\text{HH}} = 1.5$ Hz, 1 H, CH_{Ar}); ¹³C{¹H} NMR (75.5 MHz, CDCl₃): δ_{C} 13.6 (4 CH₃), 19.7, 23.8 (8 CH₂), 40.0 (CH₂S), 58.6 (4 CH₂), 61.2 (1 CH₂N), 115.5, 118.3, 119.3, 123.0 (4 CH_{Ar}), 140.9, 170.5 (2 C_{Ar}), 186.9, 193.1 (2 CO); m/z (%) 437 (60), 439 (100) [M⁻].

[PPh₄][ReO(Ph-SN₂S)] **2b**. **2a** (105.0 mg, 0.22 mmol) and tetraphenylphosphonium chloride (89.2 mg, 0.24 mmol) were dissolved in a mixture of MeOH (15 mL) and CH₂Cl₂ (15 mL). After 30 min under stirring, the solvent was removed and the crude was purified by column chromatography on silica gel (eluent: CH₂Cl₂–MeOH (95 : 5 then 90 : 10)) to yield the complex **2b** as an orange powder (121.0 mg, yield = 73%).

Found: C, 50.86; H, 3.48; N, 3.17. C₃₄H₂₈N₂O₃PreS₂ requires C, 51.44; H, 3.55; N, 3.53; IR: $\nu_{\max}/\text{cm}^{-1}$ 1665, 1625 (CO); 962

(ReO); $^1\text{H NMR}$ (250 MHz, CDCl_3): δ_{H} 3.72 (d, $^2J_{\text{HH}} = 17.1$ Hz, 1 H, CH_2S), 3.87 (d, $^2J_{\text{HH}} = 17.1$ Hz, 1 H, CH_2S), 4.56 (d, $^2J_{\text{HH}} = 18.9$ Hz, 1 H, CH_2N), 4.88 (d, $^2J_{\text{HH}} = 18.9$ Hz, 1 H, CH_2N), 6.85 (m, 2 H, CH_{Ar}), 7.49 (m, 9 H, 1 $\text{CH}_{\text{Ar}} + 8 \text{CH}_{\text{Ar PPh}_4}$), 7.65 (m, 8 H, $\text{CH}_{\text{Ar PPh}_4}$), 7.80 (m, 4 H, $\text{CH}_{\text{Ar PPh}_4}$), 8.75 (m, 1 H, CH_{Ar}); $^{13}\text{C}\{^1\text{H}\}$ NMR (75.5 MHz, CDCl_3): δ_{C} 39.3 (CH_2S), 60.3 (CH_2N), 116.8, 118.0 (4 $\text{C}_{\text{Ar PPh}_4}$), 120.6, 122.9, 124.1, 128.1 (4 C_{Ar}), 130.6, 130.7, 134.3, 134.4, 135.7, 135.8 (20 $\text{CH}_{\text{Ar PPh}_4}$), 147.3, 152.2 (2 C_{Ar}), 188.7, 192.2 (2 CO); MS (ES^-): m/z (%) 453 (60), 455 (100) [M^-].

[Et₃NH][ReO(Ph–N₃S)] 3a. To a stirred suspension of Ph–N₃S(Trt) (144.3 mg, 0.30 mmol) and $\text{ReOCl}_3(\text{PPh}_3)_2$ (324.5 mg, 0.39 mmol) in MeOH (40 mL) neat Et₃N (148.1 μL , 1.20 mmol) was added. The mixture was refluxed for 4 h and then cooled to room temperature. The solvent was removed and the crude purified by column chromatography on silica gel (eluent: CHCl_3 –MeOH (95 : 5 then 90 : 10)) to afford the complex **3a** as a red–orange powder (114.2 mg, yield = 89%).

Found: C, 35.16; H, 4.52; N, 10.68. $\text{C}_{16}\text{H}_{25}\text{N}_4\text{O}_3\text{ReS}$ requires C, 35.61; H, 4.67; N, 10.38%; IR: $\nu_{\text{max}}/\text{cm}^{-1}$ 1635, 1613 (CO); 956 (ReO); $^1\text{H NMR}$ (250 MHz, CDCl_3): δ_{H} 1.23 (t, $^3J_{\text{HH}} = 7.4$ Hz, 9 H, CH_3), 3.09 (q, $^3J_{\text{HH}} = 7.4$ Hz, 6 H, NCH_2), 3.81 (d, $^2J_{\text{HH}} = 17.2$ Hz, 1 H, CH_2S), 4.02 (d, $^2J_{\text{HH}} = 17.2$ Hz, 1 H, CH_2S), 4.55 (d, $^2J_{\text{HH}} = 18.7$ Hz, 1 H, CH_2N), 5.12 (d, $^2J_{\text{HH}} = 18.7$ Hz, 1 H, CH_2N), 6.62 (m, 1 H, CH_{Ar}), 6.88 (m, 2 H, CH_{Ar}), 8.21 (m, 1 H, CH_{Ar}); $^{13}\text{C}\{^1\text{H}\}$ NMR (75.5 MHz, CDCl_3): δ_{C} 7.8 (3 CH_3), 40.4 (CH_2S), 46.5 (3 CH_2), 60.0 (1 CH_2N), 114.2, 117.5, 117.8, 123.1 (4 CH_{Ar}), 140.9, 158.9 (2 C_{Ar}), 188.1, 194.0 (2 CO); MS (ES^-): m/z (%) 436 (60), 438 (100) [M^-].

[PPh₄][ReO(Ph–N₃S)] 3b. To a stirred solution of **3a** (118.8 mg, 0.22 mmol) in 10 mL of MeOH and 10 mL of CH_2Cl_2 was added tetraphenylphosphonium chloride (71.2 mg, 0.19 mmol). The mixture was stirred for 15 min and then treated with H_2O (20 mL). The solution was extracted twice with CH_2Cl_2 (20 mL). The organic layers were dried with MgSO_4 , filtered and dried under vacuum to give a red powder (170.9 mg, yield = 99%).

Found: C, 52.14; H, 3.66; N, 4.89. $\text{C}_{34}\text{H}_{29}\text{N}_3\text{O}_3\text{PReS}$ requires C, 52.57; H, 3.76; N, 5.41%; IR: $\nu_{\text{max}}/\text{cm}^{-1}$ 1648, 1618 (CO); 948 (ReO); $^1\text{H NMR}$ (250 MHz, CDCl_3): δ_{H} 3.77 (d, $^2J_{\text{HH}} = 16.8$ Hz, 1 H, CH_2S), 3.93 (d, $^2J_{\text{HH}} = 16.8$ Hz, 1 H, CH_2S), 4.43 (d, $^2J_{\text{HH}} = 18.3$ Hz, 1 H, CH_2N), 5.04 (d, $^2J_{\text{HH}} = 18.3$ Hz, 1 H, CH_2N), 6.50 (m, 1 H, CH_{Ar}), 6.71 (m, 2 H, CH_{Ar}), 7.57 (m, 8 H, $\text{CH}_{\text{Ar PPh}_4}$), 7.71 (m, 8 H, $\text{CH}_{\text{Ar PPh}_4}$), 7.83 (m, 4 H, $\text{CH}_{\text{Ar PPh}_4}$), 8.22 (m, 1 H, CH_{Ar}), 8.79 (s, 1 H, NH); $^{13}\text{C}\{^1\text{H}\}$ NMR (75.5 MHz, CDCl_3): δ_{C} 40.2 (CH_2S), 60.4 (CH_2N), 116.9, 118.0 (4 $\text{C}_{\text{Ar PPh}_4}$), 114.2, 117.6, 118.2, 122.4 (4 CH_{Ar}), 130.6, 130.8, 134.3, 134.4, 135.7, 135.8 (20 $\text{CH}_{\text{Ar PPh}_4}$), 140.1, 158.3 (2 C_{Ar}), 187.7, 192.8 (2 CO); MS (ES^-): m/z (%) 436 (60), 438 (100) [M^-].

[Et₃NH][ReO(Ph–N(Me)N₂S)] 4a. Using the same procedure adopted for **3a**, Ph–N(Me)N₂S(Trt) (148.5 mg, 0.30 mmol) gave the complex as a red solid (157.5 mg, yield = 95%) which was contaminated by traces of residual Et₃NHCl salt.

IR: $\nu_{\text{max}}/\text{cm}^{-1}$ 1647, 1622 (CO); 953 (ReO); $^1\text{H NMR}$ (250 MHz, CDCl_3): δ_{H} 1.25 (t, 9 H, $^3J_{\text{HH}} = 7.3$ Hz, CH_3), 3.01 (q, $^3J_{\text{HH}} = 7.3$ Hz, 6 H, CH_2), 3.83 (d, $^2J_{\text{HH}} = 17.1$ Hz, 1 H, CH_2S), 3.99 (d, $^2J_{\text{HH}} = 17.1$ Hz, 1 H, CH_2S), 4.14 (s, 3 H, CH_3), 4.49 (d, $^2J_{\text{HH}} = 18.6$ Hz, 1 H, CH_2N), 5.04 (d, $^2J_{\text{HH}} = 18.6$ Hz, 1 H, CH_2N), 6.66 (m, 1 H, CH_{Ar}), 6.87 (m, 2 H, CH_{Ar}), 8.28 (m, 1 H, CH_{Ar}); $^{13}\text{C}\{^1\text{H}\}$ NMR (75.5 MHz, CDCl_3): δ_{C} 9.1 (3 CH_3), 40.8 (1 CH_2S), 47.3 (3 CH_2), 49.9 (CH_3), 60.3 (CH_2N), 110.9, 117.7, 118.2, 123.3 (4 CH_{Ar}), 142.9, 160.0 (2 C_{Ar}), 187.6, 193.4 (2 CO); MS (ES^-): m/z (%) 450 (60), 452 (100) [M^-].

[PPh₄][ReO(Ph–N(Me)N₂S)] 4b. This complex was prepared analogously to **2b** in 60% yield using CH_2Cl_2 –MeOH (98 : 2) as eluent for column chromatography purification.

Found: C, 52.27; H, 3.89; N, 4.93. $\text{C}_{35}\text{H}_{31}\text{N}_3\text{O}_3\text{PReS}$ requires C, 53.15; H, 3.95; N, 5.31%; IR: $\nu_{\text{max}}/\text{cm}^{-1}$ 1649, 1625 (CO); 954

(ReO); $^1\text{H NMR}$ (250 MHz, CDCl_3): 3.79 (d, $^2J_{\text{HH}} = 17.1$ Hz, 1 H, CH_2S), 3.97 (d, $^2J_{\text{HH}} = 17.1$ Hz, 1 H, CH_2S), 4.14 (s, 3 H, NCH_3), 4.39 (d, $^2J_{\text{HH}} = 18.6$ Hz, 1 H, CH_2N), 5.01 (d, $^2J_{\text{HH}} = 18.6$ Hz, 1 H, CH_2N), 6.53 (m, 1 H, CH_{Ar}), 6.80 (m, 2 H, CH_{Ar}), 7.53 (m, 8 H, $\text{CH}_{\text{Ar PPh}_4}$), 7.67 (m, 8 H, $\text{CH}_{\text{Ar PPh}_4}$), 7.82 (m, 4 H, $\text{CH}_{\text{Ar PPh}_4}$), 8.28 (m, 1 H, CH_{Ar}); $^{13}\text{C}\{^1\text{H}\}$ NMR (75.5 MHz, CDCl_3): 40.2 (CH_2S), 49.8 (CH_3), 60.3 (CH_2N), 110.4 (CH_{Ar}), 116.8, 118.0 (4 $\text{C}_{\text{Ar PPh}_4}$), 110.4, 117.4, 117.7, 122.4 (4 CH_{Ar}), 130.6, 130.8, 134.2, 134.4, 135.8, 135.9 (20 $\text{CH}_{\text{Ar PPh}_4}$), 143.4, 160.2 (2 C_{Ar}), 187.8, 193.2 (2 CO); MS (ES^-): m/z (%) 450 (60), 452 (100) [M^-].

[NBu₄][TcO(Ph–ON₂S)] 1c. To a stirred green solution of $[\text{NBu}_4][\text{TcOCl}_4]$ (31 mg, 0.062 mmol) in MeOH (3 mL) Ph–ON₂S(Trt) (30 mg, 0.062 mmol) was added. The solution turned orange suddenly. After 1 h stirring at room temperature, the solvent was removed by a gentle stream of N₂ and the crude was purified by column chromatography on silica gel (eluent: CH_2Cl_2 –MeOH (95 : 5)) to afford a yellow powder (29.4 mg, 80%).

IR: $\nu_{\text{max}}/\text{cm}^{-1}$ 1654, 1634 (CO); 953 (TcO); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ_{H} 0.98 (m, 12 H, CH_3), 1.36 (m, 16 H, CH_2), 2.95 (m, 8 H, CH_2), 3.85 (d, $^2J_{\text{HH}} = 16.9$ Hz, 1 H, CH_2S), 4.04 (d, $^2J_{\text{HH}} = 16.9$ Hz, 1 H, CH_2S), 4.61 (d, $^2J_{\text{HH}} = 18.3$ Hz, 1 H, CH_2N), 5.19 (d, $^2J_{\text{HH}} = 18.3$ Hz, 1 H, CH_2N), 6.75 (dt, $^3J_{\text{HH}} = 7.8$ Hz, $^4J_{\text{HH}} = 1.1$ Hz, 1 H, CH_{Ar}), 6.89 (dt, $^3J_{\text{HH}} = 7.8$ Hz, $^4J_{\text{HH}} = 1.4$ Hz, 1 H, CH_{Ar}), 7.23 (dd, $^3J_{\text{HH}} = 7.8$ Hz, $^4J_{\text{HH}} = 1.1$ Hz, 1 H, CH_{Ar}), 8.24 (dd, $^3J_{\text{HH}} = 7.8$ Hz, $^4J_{\text{HH}} = 1.4$ Hz, 1 H, CH_{Ar}); $^{13}\text{C}\{^1\text{H}\}$ NMR (75.5 MHz, CDCl_3): δ_{C} 13.6 (4 CH_3), 19.6 (4 CH_2), 23.8 (4 CH_2), 36.9 (CH_2S), 58.6 (4 CH_2), 59.9 (CH_2N), 114.7, 118.3, 118.6, 122.9 (4 CH_{Ar}), 139.5, 165.2 (2 C_{Ar}), 182.5, 185.9 (2 CO); MS (ES^-): m/z (%) 351 (100) [M^-].

[NBu₄][TcO(Ph–SN₂S)] 2c. As for **1c**, 25 mg (0.05 mmol) of Ph–S(Trt)N₂S(Trt) gave the complex as a yellow–brown oil.

IR: $\nu_{\text{max}}/\text{cm}^{-1}$ 1655, 1638 (CO); 945 (TcO); $^1\text{H NMR}$ (300 MHz, CDCl_3): δ_{H} 0.94 (m, 12 H, CH_3), 1.33 (m, 16 H, CH_2), 2.86 (m, 8 H, CH_2), 3.85 (d, $^2J_{\text{HH}} = 16.9$ Hz, 1 H, CH_2S), 4.10 (d, $^2J_{\text{HH}} = 16.9$ Hz, 1 H, CH_2S), 4.72 (d, $^2J_{\text{HH}} = 18.9$ Hz, 1 H, CH_2N), 4.82 (d, $^2J_{\text{HH}} = 18.9$ Hz, 1 H, CH_2N), 6.96 (t, $^3J_{\text{HH}} = 7.6$ Hz, 1 H, CH_{Ar}), 7.06 (t, $^3J_{\text{HH}} = 7.6$ Hz, 1 H, CH_{Ar}), 7.48 (d, $^3J_{\text{HH}} = 7.6$ Hz, 1 H, CH_{Ar}), 8.75 (d, $^3J_{\text{HH}} = 7.6$ Hz, 1 H, CH_{Ar}); $^{13}\text{C}\{^1\text{H}\}$ NMR (75.5 MHz, CDCl_3): δ_{C} 13.6 (4 CH_3), 19.6 (4 CH_2), 23.7 (4 CH_2), 37.3 (CH_2S), 58.5 (4 CH_2), 59.3 (CH_2N), 120.6, 122.8, 124.3, 127.0 (4 CH_{Ar}), 140.3, 150.1 (2 C_{Ar}), 184.0, 186.4 (2 CO); MS (ES^-): m/z (%) 367 (100) [M^-].

[NBu₄][TcO(Ph–N₃S)] 3c. To a stirred green solution of $[\text{NBu}_4][\text{TcOCl}_4]$ (16.0 mg, 0.032 mmol) in MeOH (3 mL) was added Ph–N₃S(Trt) (15.4 mg, 0.032 mmol) and an excess of triethylamine (22.5 μL , 0.160 mmol). The reaction was stirred for 30 min and the solution turned dark orange. The crude solution was then treated twice with hexane (2 \times 3 mL) and then the solvents were removed. The solid was dissolved in CH_2Cl_2 (5 mL), treated with water (5 mL), and the organic layers were separated, dried and concentrated to dryness. The title compound was obtained as a yellow–orange solid (15 mg, 79%).

$^1\text{H NMR}$ (300 MHz, CDCl_3): δ_{H} 0.95 (m, 12 H, CH_3), 1.30 (m, 16 H, CH_2), 2.84 (m, 8 H, CH_2), 3.72 (d, $^2J_{\text{HH}} = 16.7$ Hz, 1 H, CH_2S), 4.07 (d, $^2J_{\text{HH}} = 16.7$ Hz, 1 H, CH_2S), 4.58 (d, $^2J_{\text{HH}} = 18.6$ Hz, 1 H, CH_2N), 4.93 (d, $^2J_{\text{HH}} = 18.6$ Hz, 1 H, CH_2N), 6.65 (t, $^3J_{\text{HH}} = 7.2$ Hz, 1 H, CH_{Ar}), 6.80 (m, 2 H, CH_{Ar}), 8.03 (s, 1 H, NH), 8.28 (d, $^3J_{\text{HH}} = 7.2$ Hz, 1 H, CH_{Ar}); $^{13}\text{C}\{^1\text{H}\}$ NMR (75.5 MHz, CDCl_3): δ_{C} 13.6 (4 CH_3), 19.6 (4 CH_2), 23.6 (4 CH_2), 37.3 (CH_2S), 58.3 (4 CH_2), 59.4 (CH_2N), 113.6, 117.8, 118.1, 122.8 (4 CH_{Ar}), 139.9, 153.8 (2 C_{Ar}), 183.3, 186.2 (2 CO); MS (ES^-): m/z (%) 350 (100) [M^-].

Acknowledgements

We are grateful to Prof. R. Chauvin (LCC, Toulouse, France) for helpful discussions.

References

- (a) J. R. Dilworth and S. J. Parrot, *Chem. Soc. Rev.*, 1998, **27**, 43–55; (b) K. Schwochau, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 2258–2267; (c) B. Johannsen and H. Spies, *Top. Curr. Chem.*, 1996, **176**, 79–121.
- (a) S. Liu, *Chem. Soc. Rev.*, 2004, **33**, 445–461, and references therein; (b) R. Schibli and P. A. Schubiger, *Eur. J. Nucl. Med.*, 2002, **29**, 1529–1542, and references therein; (c) S. Jurisson and J. D. Lydon, *Chem. Rev.*, 1999, **99**, 2205–2218, and references therein.
- (a) F. Mevellec, A. Roucoux, N. Noiret, A. Moisan, H. Patin and A. Duatti, *J. Label. Compd. Radiopharm.*, 2003, **46**, 319–331; (b) L. Kurti, D. Papagiannopoulou, M. Papadopoulos, I. Permettis, C. P. Raptopoulou, A. Terzis, E. Chiolettis, M. Harmata, R. R. Kuntz and R. S. Pandurangi, *Inorg. Chem.*, 2003, **42**, 2960–2967; (c) F. Mevellec, A. Roucoux, N. Noiret and H. Patin, *J. Chem. Soc., Dalton Trans.*, 2001, 3603–3610; (d) B. J. Cleyhens, G. M. Bormans, H. P. Vanbilloen, D. V. Vanderghinste, D. M. Kieffer, T. J. de Groot and A. M. Verbruggen, *Tetrahedron Lett.*, 2003, **44**, 2597–2600; (e) S. Jurisson, M. M. Halilan, J. D. Lydon, C. L. Barnes, D. P. Nowotnik and A. D. Nunn, *Inorg. Chem.*, 1998, **37**, 1922–1928; (f) R. Schibli, R. La Bella, R. Alberto, E. Garcia-Garayoa, K. Ortner and U. Abram, *Inorg. Chem.*, 1998, **37**, 1922–1928; P. A. Schubiger, *Bioconjugate Chem.*, 2000, **11**, 345–351; (g) G. Jaouen, S. Top, A. Vessieres, P. Pigeon, G. Leclercq and I. Laios, *Chem. Commun.*, 2001, 383–384.
- (a) L. Fourteau, E. Benoist and M. Dartiguenave, *Synlett*, 2001, **1**, 126–128; (b) C. Decristoforo and S. J. Mather, *Bioconjugate Chem.*, 1999, **10**, 431–438; (c) R. Rajagopalan, G. D. Grummon, J. Bugaj, L. S. Halleman, E. G. Webb, M. E. Marmion, J. L. Vanderheyden and A. Srinivasan, *Bioconjugate Chem.*, 1997, **8**, 407–415; (d) R. K. Hom and J. A. Katzenellenbogen, *J. Org. Chem.*, 1997, **62**, 6290–6297.
- J. Le Gal, E. Benoist, M. Gressier, Y. Coulais and M. Dartiguenave, *Tetrahedron Lett.*, 2002, **43**, 9295–9297.
- J. Le Gal, PhD thesis, University of Toulouse, 2004.
- J. Le Gal, L. Latapie, M. Gressier, Y. Coulais, Dartiguenave and E. Benoist, *Org. Biomol. Chem.*, 2004, **2**, 876–883.
- M. Papachristou, I. Permettis, T. Siatra-Papastaikoudi, M. Pelecanou, C. Tsoukalas, C. P. Raptopoulou, A. Terzis, E. Chiotellis and M. Papadopoulos, *Eur. J. Inorg. Chem.*, 2003, 3826–3830.
- J. Chatt and G. A. Rowe, *J. Chem. Soc.*, 1962, **2**, 4019–4033.
- R. Visentin, R. Rossin, M. C. Giron, A. Dolmella, G. Bandoli and U. Mazzi, *Inorg. Chem.*, 2003, **42**, 950–959.
- (a) J. E. Smith, E. F. Byrne, F. A. Cotton and J. C. Sekutowsky, *J. Am. Chem. Soc.*, 1978, **100**, 5571–5572; (b) B. V. DePamphilis, A. G. Jones, M. A. Davis and A. Davison, *J. Am. Chem. Soc.*, 1978, **100**, 5570–5571.
- (a) H. S. Trop, A. G. Jones and A. Davison, *Inorg. Chem.*, 1980, **19**, 1993–1997; (b) A. Davison, C. Orvig, H. S. Trop, M. Sohn, B. V. DePamphilis and A. G. Jones, *Inorg. Chem.*, 1980, **19**, 1988–1992.
- W. Zhen, H. Han, M. Anguiano, C. A. Lemere, C.-G. Cho and P. T. Lansbury, *J. Med. Chem.*, 1999, **42**, 2805–2815.
- G. Bandoli, U. Mazzi, E. Roncari and E. Deutsch, *Coord. Chem. Rev.*, 1982, **44**, 191–227.
- J. B. Lambert, H. F. Shurvell, D. Lightner and R. Graham Cooks, *Introduction to Organic Spectroscopy*, Macmillan Publishing Company, New York, 1987.
- L. M. Schultze, L. J. Torado, R. M. Baldwin, E. F. Byrne and B. J. McBride, *Inorg. Chem.*, 1994, **33**, 5579–5585.
- M. Lipowska, L. Hanson, X. Xu, P. Marzilli, A. Taylor and L. G. Marzilli, *Inorg. Chem.*, 2002, **41**, 3032–3041.
- J. P. O'Neil, S. R. Wilson and J. A. Katzenellenbogen, *Inorg. Chem.*, 1994, **33**, 319–323.
- R. A. Bell, B. E. McCarry and J. F. Valliant, *Inorg. Chem.*, 1998, **37**, 3517–3520.
- A. Davison, H. S. Trop, B. V. DePamphilis and A. G. Jones, *Inorg. Synth.*, 1982, **21**, 160–162.
- (a) M. Papadopoulos, I. Permettis, M. Pelecanou, C. Raptopoulou, A. Terzis, C. Stassinopoulou and E. Chiotellis, *Inorg. Chem.*, 1996, **35**, 7377–7383; (b) A. Mahmood, K. E. Baidoo and S. Z. Lever, in *Technetium and Rhenium in Chemistry and Nuclear Medicine 3*, ed. M. Nicolini, G. Bandoli and U. Mazzi, Raven Press, New York, 1990, p. 119; (c) T. N. Rao, D. Adhikesavalu, A. Camerman and A. R. Fritzberg, *J. Am. Chem. Soc.*, 1990, **112**, 5798–5804.
- M. Papadopoulos, B. Nock, T. Maina, I. Permettis, C. Raptopoulou, A. Tasiopoulos, A. Troganis, T. Kabanos, A. Terzis and E. Chiotellis, *J. Biol. Inorg. Chem.*, 2001, **6**, 159–165.
- M. F. Brown, B. R. Cook and T. E. Sloan, *Inorg. Chem.*, 1975, **14**, 1273–1278.
- (a) R. S. Cahn, C. Ingold and V. Prelog, *Angew. Chem., Int. Ed. Engl.*, 1966, **5**, 385–415; (b) V. Prelog and G. Helmchen, *Angew. Chem., Int. Ed. Engl.*, 1982, **21**, 567.
- A. W. Addison, T. N. Rao, J. Reedijk and G. C. Verschoor, *J. Chem. Soc., Dalton Trans.*, 1984, 1349–1356.
- (a) M. E. Kastner, M. J. Lindsay and M. J. Clarke, *Inorg. Chem.*, 1982, **21**, 2037–2040; (b) A. J. Blake, J. A. Greig and M. Schroder, *J. Chem. Soc., Dalton Trans.*, 1988, 2645–2647.
- (a) G. Grummon, R. Rajagopalan, G. J. Palenik, A. E. Koziol and D. L. Nosco, *Inorg. Chem.*, 1995, **34**, 1764–1772; (b) P. J. Blower, J. R. Dilworth, J. P. Hutchinson, T. Nicholson and J. Zubieta, *J. Chem. Soc., Dalton Trans.*, 1986, 1339–1345; (c) F. Tisato, F. Refosco, U. Mazzi, G. Bandoli and M. Nicolini, *J. Chem. Soc., Dalton Trans.*, 1987, 1693–1699.
- C. M. Archer, J. R. Dilworth, D. Vaughan Griffiths, M. J. Al-Jeboori, J. Duncan Kelly, C. Lu, M. J. Rosser and Y. Zheng, *J. Chem. Soc., Dalton Trans.*, 1997, 1403–1410.
- C. S. Hilger, B. Noll, F. Blume, P. Leibnitz and B. Johannsen, in *Technetium, Rhenium and Other Metals in Chemistry and Nuclear Medicine 5*, ed. M. Nicolini and U. Mazzi, SGEditionali, Padova, Italy, 1999, pp. 221–224.
- A. Altomare, M. C. Burla, M. Camalli, G. L. Cascarano, C. Giacovazzo, A. Guagliardi and A. G. G. Moliterni, *J. Chem. Soc., Dalton Trans.*, 1997, **34**, 1403–1410; R. Spagna, *J. Appl. Crystallogr.*, 1999, **32**, 115–119.
- S. Mackay, C. J. Gilmore, C. Edwards, N. Stewart and K. Shankland, *maXus, Computer Program for the Solution and Refinement of Crystal Structures*, Nonius, The Netherlands; MacScience, The University of Glasgow, 1999.
- G. M. Sheldrick, *SHELXL-97. Program for the Refinement of Crystal Structures*, University of Göttingen, Germany, 1997.