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Synthesis and characterisation of new homoleptic rhenium thiosemicarbazone complexes

Andrew R. Cowley,[a,b] Jonathan R. Dilworth,*[a] Paul S. Donnelly[a] and John Woollard-Shore[a]

[a] *Inorganic Chemistry Laboratory, University of Oxford, South Parks Road, Oxford, UK OX1 3QR. E-mail: jon.dilworth@chem.ox.ac.uk*

[b] *Chemical Crystallography Laboratory, University of Oxford, Parks Road, Oxford, UK OX1 3PD*

Received 25th October 2002, Accepted 4th December 2002
First published as an Advance Article on the web 21st January 2003

A series of new rhenium(III) complexes, $[ReL_2]^+$, where LH = a 2-formylpyridine thiosemicarbazone have been synthesised and characterised. The complexes have been synthesised from the Re(V) starting material $[ReOCl_3(PPh_3)_2]$ and from $[ReO_4]^-$ in the presence of triphenylphosphine. All of the new compounds have been characterised by X-ray crystallography, NMR and mass spectroscopy. In all cases the Re atom is in a distorted octahedral environment with two tridentate deprotonated thiosemicarbazones binding as monoanionic ligands through the sulfur, pyridyl nitrogen and azamethinic nitrogen in a *mer* (azomethine nitrogen atoms *trans*) configuration. Electrochemical measurements show that the complexes undergo two reversible reductions at biologically accessible potentials. Under certain conditions the 2-formylpyridine thiosemicarbazone ligands undergo reductive cleavage of the hydrazinic N–N bond resulting in the formation of a rhenium complex of methyl(2-pyridyl)methyleneimine which has been characterised by X-ray crystallography.

Introduction

Thiosemicarbazones are of considerable pharmacological interest since a number of derivatives have shown a broad spectrum of chemotherapeutic properties. In particular heterocyclic thiosemicarbazones (Fig. 1) have antibacterial, antimalarial,

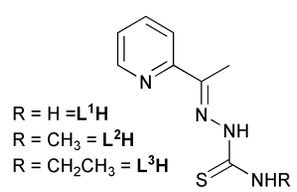


Fig. 1 Thiosemicarbazone ligands.

antiviral and antitumour activities.[1] It has been suggested that the antitumour activity of heterocyclic thiosemicarbazones is due to the compounds modifying the reductive conversion of ribonucleotides to deoxyribonucleotides resulting in inhibition of DNA synthesis.[1–3] Although the uncomplexed thiosemicarbazones show interesting biological activity, metal complexes of thiosemicarbazones show a marked increase in activity.[4,5] In particular, the platinum and palladium complexes of heterocyclic thiosemicarbazones exhibit significant antitumour activity[2,6,7] and copper, platinum and palladium complexes of tetradentate bis(thiosemicarbazones) have also shown promising anticancer properties.[3,8] It is, however, the use of bis(thiosemicarbazone) ligands as delivery vehicles for radioactive copper and the development of new copper-based radiopharmaceuticals that has attracted much recent interest.[9–14]

Conventional radiotherapy involves the external delivery of a sterilising dose of radiation to the cancer site. An attractive alternative to the external use of radiation to treat cancer is the internal specific delivery of a β-emitting radionuclide to the cancerous area.[15] Rhenium has two β-emitting isotopes, ^{188}Re and ^{186}Re, which have shown potential to act as radionuclides suitable for therapeutic agents.[16] The choice of a suitable nuclide for a radiopharmaceutical depends on number of factors including availability, half-life, type of emitted radiation and the size of tumour. ^{188}Re can be relatively readily obtained from a ^{188}W/^{188}Re generator and this coupled with its other properties means that it offers real possibilities in therapeutic nuclear medicine.[16,17] One way of administering ^{188}Re *in vivo* is in the form of a stable coordination complex. With this in mind we and others have been investigating the synthesis of stable rhenium complexes in which the metal is in intermediate to low oxidation states.[18–22]

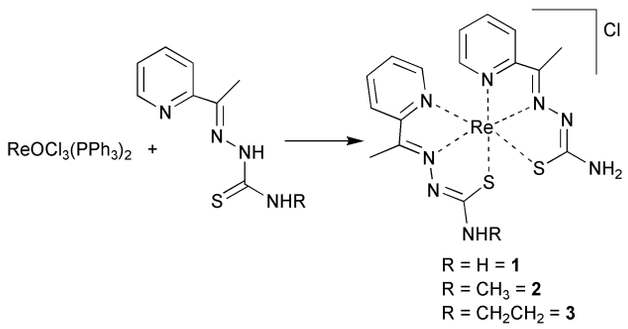
In this study we report the synthesis of several new rhenium complexes of tridentate formylpyridyl thiosemicarbazones (**LH**[1–3] see Fig. 1) which since they are metal complexes of heterocyclic thiosemicarbazones could not only show intrinsic anticancer activity but also provide a possible pathway into the synthesis of new rhenium based radiotherapeutics. The thiosemicarbazone ligands also have the potential to be functionalised to allow the tethering of a biologically active molecule to the complex which could provide *in vivo* specificity or to control the lipophilicity and biodistribution.[23] The use of tridentate Schiff base ligands derived from S-methyl dithiocarbazate to form neutral oxorhenium(V) complexes has been reported recently.[18,19,24] A preliminary report of a Re thiosemicarbazone derivative coupled to an antibody fragment has been reported but the Re species present was not characterised[25] and an oxorhenium complex containing a tridentate thiosemicarbazone was recently reported but the compound was not structurally characterised.[26] Rhenium complexes of ferrocenylcarbaldehyde thiosemicarbazones have also been very recently reported.[27] The complexes described below are the first fully characterised homoleptic complexes of rhenium with thiosemicarbazone ligands, and have interesting redox behaviour.

Results and discussion

Several new rhenium thiosemicarbazone complexes (**1**–**3**) were synthesised by the reaction of $[ReOCl_3(PPh_3)_2]$ with 2 equivalents of the tridentate ligands **LH**[1–3] in methanol, heated at reflux under an atmosphere of nitrogen. The lime green colour of the starting material was replaced by the dark colour of the product almost as soon as heating commenced. The black products could be readily isolated as they precipitated in good yields from the reaction mixture. In all cases the major product proved to be the monocationic complexes $[Re^{(III)}\mathbf{L}_2]Cl$ (Scheme 1). Reduction to Re(III) is somewhat surprising, the PPh_3 liberated in the reaction is presumably the reductant.

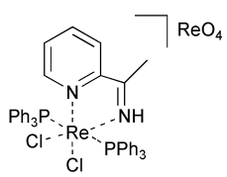
Once the initial black crystalline precipitate had been collected the filtrate was left to stand which resulted in the precipitation of a very small amount of red needle-like crystals.

DOI: 10.1039/b210540n



Scheme 1 Synthesis of complexes **1**–**4**.

X-Ray studies revealed that this second precipitate was $[ReCl_2L^4(PPh_3)_2][ReO_4]$, **4**, where L^4 was the product of a N–N cleavage reaction of the original 2-acetylpyridine thiosemicarbazone ligand to give a rhenium complex of methyl-(2-pyridyl)methyleneimine (Fig. 2).



4

Fig. 2 Complex **4**.

The formation of the imine complex from the thiosemicarbazone presumably proceeds *via* a two-electron reductive cleavage of the hydrazinic N–N bond. It is also interesting to note the anion of this minor product is $[ReO_4]^-$ despite the use of the Re(v) starting material which indicates that the mechanism of the cleavage reaction could involve complex redox processes. Metal complexes of the imine of a 2(N)-heterocyclic ketone are very rare with only one previous example, a ruthenium complex of methyl(2-pyridyl)-methyleneimine which was also formed by the N–N cleavage of a tridentate pyridyl thiosemicarbazone.[28]

Rhenium complexes of phenyl and methyl thiosemicarbazides[29] and rhenium complexes of N-methyl substituted dithiocarbazates[24] also undergo N–N bond cleavage but these result in nitride complexes.

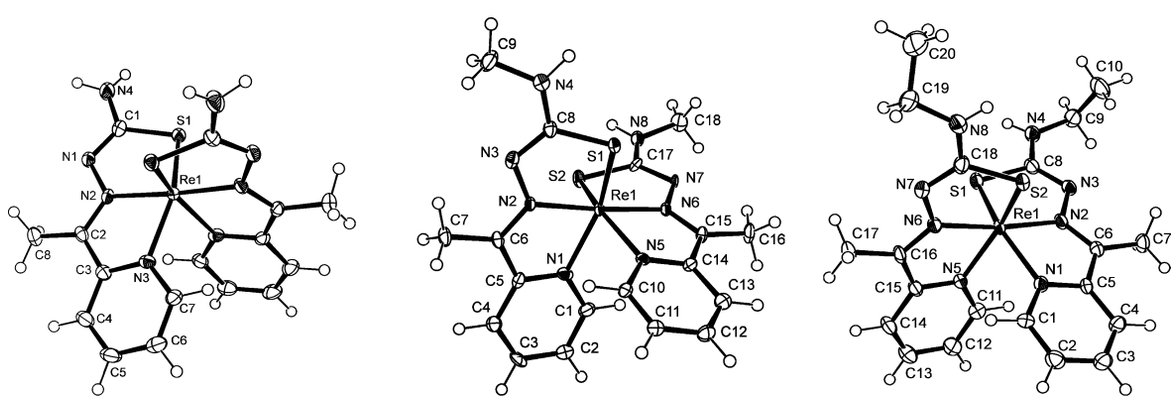
Complex **4** can be synthesised reproducibly, and in reasonable yield from the reaction of $[Bu_4N][ReO_4]$ with PPh_3 and L^2H, in ethanol made mildly acidic with HCl. Attempts to synthesise **2** from $[ReO_4]^-$ in acidic ethanol always resulted in the isolation of **4**. This suggests that the N–N cleavage reaction is dependent on pH as has been found with other systems which involve the cleavage of N–N bonds in hydrazine-derived species resulting in the formation of nitride species.

Representations of the X-ray crystal structures of the $[Re(L^{1-3})_2]Cl$ complexes are shown in Fig. 3 and pertinent crystallographic data is summarised in Table 1. In all cases the Re atom is in a distorted octahedral environment with two tridentate deprotonated thiosemicarbazones binding as monoanionic ligands through the sulfur, pyridyl nitrogen and azamethinic nitrogen in a *mer* (azomethine nitrogen atoms *trans*) configuration. In the case of **1** the rhenium atom and the Cl counterion both lie on a crystallographic twofold axis running parallel to the *c* axis. Much of the ligand (N1, N2, C2, C3 and the aromatic ring) and the Re atom lie in a single plane (rms deviation 0.035 Å), which is inclined at 33.6° to the *c* axis. The remaining atoms of the ligand lie on the side of the plane remote from the other ligand (distances from plane: C1 0.32, N1 0.29, and S1 0.85 Å). In the cases of **2** and **3** the complexes have no crystallographic symmetry, but closely approximate local twofold symmetry.

A selection of bond lengths are given in Table 2 which shows that the bond lengths that are common in each compound are all very similar. The deprotonation of the ligands results in extensive delocalisation of charge and as a consequence the C–S bond lengths (1.777(7)–1.792(4) Å) are much closer in length to a C–S single bond (1.82 Å) than the free ligand, which has partial double bond character (for example, in L^2 C–S = 1.675(4)).[30] As a consequence the C–N bond length of the N–N–C–SN fragment is shorter (1.315(5)–1.332(8) Å) than it is in the free ligand (1.366(3) Å)[30] consistent with an increase in the bond order. In agreement with this the Re–S bond lengths (2.2743(9)–2.2908(12) Å) are similar to that of Re-thiolate type coordination.[31] The Re–N bond with pyridyl nitrogen (2.080(3)–2.091(3) Å) is slightly longer than the Re–N bond with the azo-methine nitrogen (2.056(5)–2.078(5) Å).

Structures **2** and **3** display some interesting hydrogen bonding networks. In the case of **2** the cations are stacked in layers running parallel to the *bc* plane (Fig. 4). The local twofold axes run perpendicularly to this plane. The two NH groups of the Re complex each form a hydrogen bond to a different Cl anion (N(4) ··· Cl(1) 3.167(6) Å, N(8) ··· Cl(1)′ 3.141(6) Å). These interactions join the molecules to form chains running parallel to the crystallographic *b* axis. The solvent is also hydrogen bonded to Cl (O(1) ··· Cl(1) 3.172(8) Å). In **3** once again each of the NH groups is hydrogen-bonded to a different Cl anion (N(4) ··· Cl(1)′ 3.111(4) Å, N(8) ··· Cl(1) 3.199 Å). These bonds again link the complexes to form chains but this time running parallel to the crystallographic *a* axis. Each of the two positions of the solvent also forms a hydrogen bond to Cl^- (O(1) ··· Cl(1) 3.014(6), O(101) ··· Cl(1) 3.204(10) Å).

The nature of the hydrogen bonding interactions within these complexes may be relevant to their possible interactions with nucleoside bases and peptide bonds that may be important in any biological activity.[32] The flat, conjugated ligand may be also able to interact with DNA *via* the intercalative interaction well known for many metal polypyridyl complexes. This is currently under investigation.



1 **2** **3**

Fig. 3 ORTEP-3 representations of the cations present in **1**, **2** and **3**.

Table 1 Crystallographic data

Crystal identification	$[Re(L^1)_2]$ **1**	$[Re(L^2)_2]$ **2**	$[Re(L^3)_2]$ **3**	$[ReCl_2(L^4)(PPh_3)_2]$ **4**
Chemical formula	$C_{18}H_{26}ClN_8O_2ReS_2$	$C_{19}H_{26}ClN_8OReS_2$	$C_{21}H_{30}ClN_8OReS_2$	$C_{44}H_{42}Cl_2N_2O_5P_2Re_2$
M	672.24	668.24	696.32	1184.09
Crystal system	Orthorhombic	Monoclinic	Triclinic	Triclinic
Space group	*Pccn*	$P2_1/c$	$P\bar{1}$	$P\bar{1}$
a/Å	8.6587(2)	12.8385(5)	8.8775(2)	13.3321(2)
b/Å	12.7664(2)	8.5154(3)	11.9729(2)	17.7129(3)
c/Å	21.9866(4)	22.3598(8)	12.6197(3)	19.3778(4)
α/°	90	90	96.4542(11)	106.4656(8)
β/°	90	96.2545(17)	93.2383(11)	100.6320(8)
Γ/°	90	90	103.1595(9)	93.6732(8)
Cell volume/Å^3	2430.4	2429.9	1293.2	4280.1
Z	4	4	2	4
R_{int}	0.033	0.060	0.047	0.068
R	0.0197	0.0478	0.0268	0.0451
wR	0.0259	0.0461	0.0316	0.0484
Residual electron density (min, max)/e Å^{-3}	−1.03, 0.65	−1.94, 1.68	−1.65, 1.10	−4.32, 3.55

Table 2 Selected bond distances (Å) in complexes **1**–**3**

1	**2**	**3**
Re(1)–S(1) 2.2840(7)	Re(1)–N(1) 2.089(6)	Re(1)–N(1) 2.088(3)
Re(1)–N(2) 2.059(3)	Re(1)–N(2) 2.056(5)	Re(1)–N(2) 2.057(3)
Re(1)–N(3) 2.091(3)	Re(1)–S(1) 2.2778(18)	Re(1)–S(1) 2.2821(9)
	Re(1)–N(5) 2.090(5)	Re(1)–N(5) 2.080(3)
	Re(1)–N(6) 2.078(5)	Re(1)–N(6) 2.064(3)
	Re(1)–S(2) 2.2908(17)	Re(1)–S(2) 2.2743(9)

Table 3 Selected bond distances (Å) in **4**

Re(1)–Cl(1)	2.3744(18)	Re(2)–Cl(3)	2.3611(17)
Re(1)–Cl(2)	2.3485(16)	Re(2)–Cl(4)	2.3542(17)
Re(1)–N(1)	2.065(6)	Re(2)–N(3)	2.038(6)
Re(1)–N(2)	2.121(6)	Re(2)–N(4)	2.110(6)
Re(1)–P(1)	2.4824(17)	Re(2)–P(3)	2.4788(18)
Re(1)–P(2)	2.4849(16)	Re(2)–P(4)	2.4740(17)

The X-ray crystal structure of the complex formed as a consequence of N–N bond cleavage, **4** is shown in Fig. 5 (Table 3). The asymmetric unit of the crystal contains two crystallographically-distinct cationic complexes, two distinct $[ReO_4]^-$ ions and solvent molecules, none of which have any crystallographic symmetry. The identification of the chelating ligand as the imine of 2-acetylpyridine and not as the free ketone is strongly indicated by location of the imine hydrogen atoms and subsequent refinement of their coordinates. In addition, replacement of the imine nitrogen by O leads to a small reduction of the agreement of the model with the X-ray data and to refined O thermal parameters significantly larger than those of the other ligand atoms. This also agrees with the electrospray mass spectrum of the complex. The central regions of the two cations have very similar geometries, but the relative orientations of the phenyl substituents differ. The C_8N_2Re units are almost exactly planar (the rms deviations from best plane are 0.04 Å for Re(1) *etc.*, 0.02 Å for Re(2) *etc.*). The coordination geometries of the Re atoms deviate substantially from regular octahedra. The $[ReO_4]^-$ anions have approximately regular tetrahedral geometry. Both anions exhibit large thermal motion as shown by the large thermal parameters of their O atoms. The thermal parameters of the Re atoms are also relatively large and this, together with the large peaks and troughs of electron density (which lie close to the Re atoms), suggest that the ions may be disordered.

Attempts to model this, however, did not lead to any improvement of the agreement with the X-ray data. The solvent molecules may also be disordered but again this could not be satisfactorily modelled. Each imine N forms a hydrogen bond to an O atom of a nearby $[ReO_4]^-$ anion (apparent N ··· O distances: N(1) ··· O(2) 2.946(8), N(3) ··· O(6) 2.889(9) Å, but note the previous comment). One of the solvent molecules is similarly hydrogen-bonded to an anion (O(10) ··· O(5) 2.86(2) Å). The second solvent exists as pairs of hydrogen-bonded molecules related by a crystallographic centre of inversion (O(9) ··· O(9′) 3.05(4) Å). Note that this requires the solvent hydroxyl group to be disordered, but only a single position for the hydrogen has been modelled as there is no information available to determine the other site.

NMR studies

The Re(III) complexes **1**–**3** are diamagnetic and their ^{1}H and ^{13}C NMR spectra show well defined narrow lines which is somewhat surprising for these formally d^4 octahedral systems and

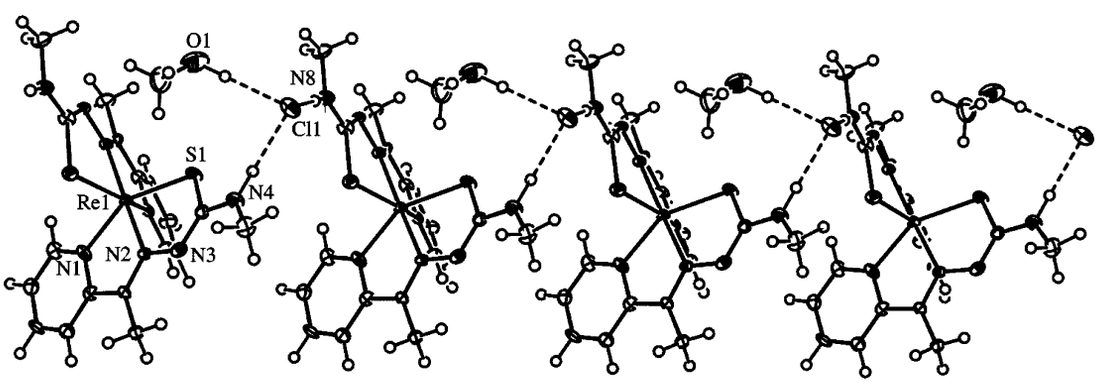


Fig. 4 Hydrogen bonding network in **2**.

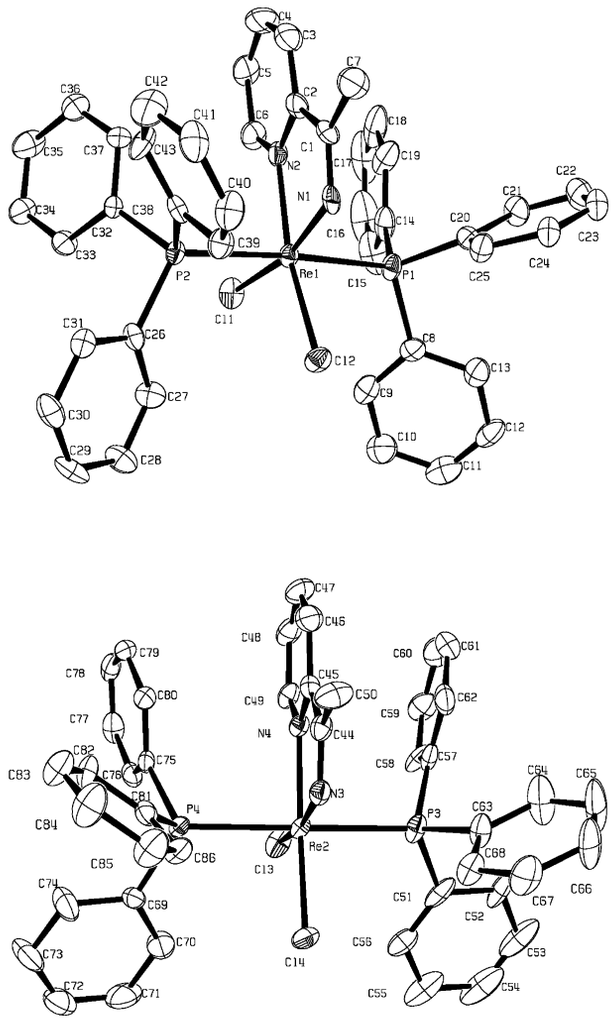


Fig. 5 The two crystallographically-distinct cations present in **4**, each viewed along an arbitrary axis. H atoms, anions and solvent are not shown.

might reflect the special nature of the delocalised ligand. Systems in which Re(III) is coordinated to a chelated pyridyl hydrazine ligand, $[Re(NNpy)(PPh_3)_2Cl_2]$, are also diamagnetic.[33] For these systems it was suggested that binding of pyridine nitrogen to form a chelate may account for the diamagnetic nature of the complexes due to the π- system in which the lone pair of electrons is donated by the pyridine nitrogen into the t_{2g} set of the metal.[33] Similar mechanisms may be involved in these thiosemicarbazone systems but it should be noted that other Re(III) systems which do not involve coordination to a pyridyl nitrogen but do involve coordination to a conjugated ligand are also diamagnetic.[34] Interestingly, the minor product, **4** which is also formally Re(III), is paramagnetic.

The nmr spectra of the **1**–**3** are consistent with the symmetric nature of the complexes. The ^{13}C NMR of **1** is shown in Fig. 6 and exhibits 8 resonances. The signals for C4, C2, C3 and C1 are all significantly deshielded occurring at lower fields than they do in the free ligand. The shifts of about 10 ppm are much larger than for Pt(II) complexes with the same ligand.[30] This is probably as a consequence of the enhanced inductive effects of the relatively highly charged metal(III) centre. In all of the complexes the signal for the C–S carbon comes at about δ = 188 ppm compared with δ = 179 ppm in the free ligand which is consistent with thiolate like coordination to the rhenium rather than thione. The deprotonation of the ligand is confirmed in the ^1H NMR spectra of the complexes by the absence of a resonance attributable to the hydrazinic proton which is readily detectable in the spectra of the free ligands at very low field (at δ = 10.3 ppm). The singlet due to the CCH_3 group is significantly deshielded in the metal complexes, shifting downfield to δ = ~4.5 ppm from δ = ~2.5 ppm in the free ligands. The large shift is due to the inductive effects of the highly charged metal(III) centre and an increase in delocalisation of charge associated with complexation as observed in the crystal structures. Coordination of the pyridyl group results in the resonances for the protons of the aromatic ring being more shielded than in the free ligand presumably due to a reduction of the diamagnetic anisotropy of the pyridyl ring fragment.[35]

Table 4 Table of reduction potentials for complexes **1**–**3**. Potentials are quoted relative to SCE. Scan rate 0.2 V s^{-1}

Compound	$E_{1/2}$ for first reduction/V	$E_{1/2}$ for second reduction/V
1	−0.51	−1.07
2	−0.50	−1.08
3	−0.48	−1.04

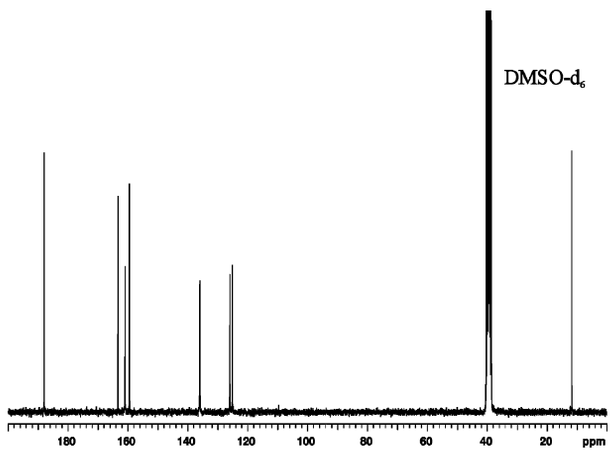


Fig. 6 ^{13}C NMR of complex **1**.

Electrochemistry

Copper complexes of copper bis(thiosemicarbazones) exhibit interesting electrochemistry which results in some derivatives being hypoxic selective.[14,36] The rhenium thiosemicarbazone complexes **1**–**3** also exhibit extensive electrochemistry. Cyclic voltammetry measurements show that each of the complexes undergo two fully reversible one electron reductions (Fig. 7, Table 4). In all cases the peak separations are approximately 63 mV and the I_{pa}/I_{pc} ratios are very close to unity. We have tentatively assigned the peaks to Re(III)/Re(II) and Re(II)/Re(I) processes but it should be noted that the thiosemicarbazone ligands themselves may be 'non-innocent'[37] and participating in the reductive processes. This well defined electrochemistry indicates that the complexes are capable of acting as double electron acceptors and this could be of importance to any

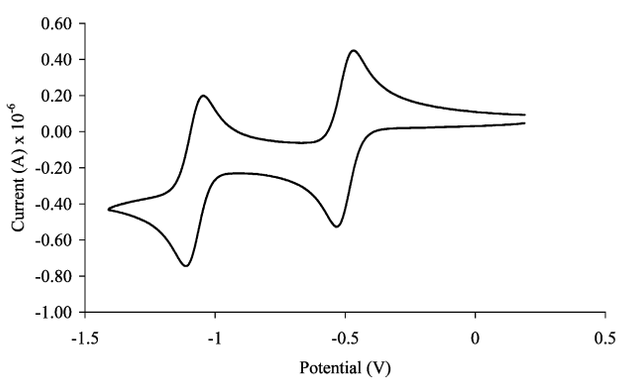


Fig. 7 Cyclic voltammogram of **2**. Scan rate 0.2 V s^{-1}. Potentials are quoted relative to a SCE.

biological activity since the mechanism of anticancer activity of NNS heterocyclic tridentate thiosemicarbazone metal complexes is thought to involve action of these complexes on the free radical present in the enzyme, ribonucleoside diphosphate reductase (RDR).[38] The fully reversible electrochemistry, providing that neutral complexes can be made, means that the development of hypoxic selective rhenium complexes could be realised.

Synthesis from $[ReO_4]^-$

If these complexes are to be suitable for use as rhenium radiopharmaceuticals it is essential that they can be synthesised directly from $[ReO_4]^-$. Heating $[ReO_4]^-$ and PPh_3 in the presence of hydrochloric acid in methanol for 30 minutes results in the formation of a green solid. Neutralisation of the acid, addition of $\mathbf{L^2}$, and gentle heating (at about 60 °C) results in the disappearance of the green solid and the formation of a black solution. Electrospray mass spectrometry of this mixture reveals only one peak with a rhenium isotope pattern at m/z = 601 which corresponds to $[Re\mathbf{L^2_2}]^+$. Concentration of the mixture and cooling allowed the isolation of black crystals with identical properties to those isolated from the reaction of $[ReOCl_3(PPh_3)_2]$ with $\mathbf{L^2}$.

Conclusions

The new Re(III)(thiosemicarbazone) complexes can be readily prepared from $[ReO_4]^-$ or $[ReOCl_3(PPh_3)_2]$ in very high yield provided the pH is kept near neutrality. Use of more acidic solutions leads to reductive N–N bond cleavage and formation of a pyridyl-methyleneimine complex. The complexes readily and reversibly reduce at biologically accessible reduction potentials which may confer interesting biological behaviour. The use of two tridentate chelating ligands binding in a *mer* fashion to form octahedral rhenium complexes does not result in *syn*/*anti* isomeric mixtures which complicate the radiolabelling and pharmacokinetic properties of the well known oxorhenium complexes formed with N_2S_2 ligands.[26]

Experimental

General procedures

Nuclear magnetic resonance spectra (NMR) spectra were acquired with a Varian Mercury VX300 spectrometer (^{1}H at 300 MHz and ^{13}C at 75.4 MHz). All chemical shifts were referenced to residual solvent peaks and are quoted in ppm relative to TMS. Mass spectra were recorded using the electrospray technique (positive ion) on a Micromass LCT Time of Flight Mass Spectrometer.

Cyclic voltammograms were recorded on a CH instruments Electrochemical Analyser equipped with Chi600 software employing a platinum working electrode, a platinum counter electrode and a silver pseudo reference electrode. All measurements were carried out in DMF. All solutions were 5 mmol L^{-1} of analyte in 0.1 mol L^{-1} tetrabutylammoniumtetrafluoroborate solution. DMF was obtained from standard commercial sources and then dried over 4 Å sieves before use. Each solution was purged with nitrogen prior to analysis and measured at ambient temperatures. Each sample was referenced to an internal reference of ferrocene, which was taken as having a $E_{1/2}$ = 0.53 V in DMF *versus* SCE.

All reagents and other solvents were obtained from standard commercial sources and were used as received.

Synthesis

$[ReOCl_3(PPh_3)_2]$ was prepared by a literature procedure.[39] The ligands $\mathbf{LH^{1-3}}$ were synthesised by conventional procedures,[40] for example $\mathbf{L^1}$: 2-formylpyridine (6.0 g. 5.5 mL, 0.050 mol) and thiosemicarbazide (4.56 g, 0.050 mol) were added to methanol (25 mL). The mixture was heated at reflux under an atmosphere of nitrogen for 4–5 hours. The reaction mixture was allowed to cool to room temperature. A crystalline precipitate formed which was collected by filtration and washed with a small amount of cold methanol and copious quantities of diethyl ether to give 2-acetylpyridinethiosemicarbazone as large beige crystals (7.38 g, 0.38 mmol, 75%). ^{1}H NMR (d_6-DMSO): δ 2.42, 3H, s, CH_3; 7.41. 1H, m, ArH; 8,13, 1H, s, NH_2; 8.37, d, $^3J_{HH}$ = 6 Hz, ArH; 8.6, d, $^3J_{HH}$ = 6 Hz, ArH; 10.3, s, 1H, NH.

General procedure: $[Re(L^1)_2]Cl$. $[ReOCl_3(PPh_3)_2]$ (0.200 g, 0.24 mmol) and $\mathbf{LH^1}$ (0.093 g, 0.48 mmol) were added to methanol (45 mL). The mixture was heated at reflux under an atmosphere of nitrogen for 4 hours. The reaction mixture was filtered whilst it was still hot and then allowed to cool to room temperature. A black precipitate formed which was collected by filtration and washed with a small amount of cold methanol and diethyl ether to give $[Re(\mathbf{L^1})_2]Cl{\cdot}2H_20$ as black crystals (0.108 g, 0.17 mmol, 71%). (Found: C, 30.0; H, 3.7; N, 17.7. Calc. for $ReC_{16}H_{18}N_8ClS_2.2H_2O$: C, 29.8; H, 3.4; N, 17.4%).

^{1}H NMR (DMSO-d_6): δ 4.48, 3H, s, CH_3; 6.92, 2H, m, ArH; 7.12, 2H, d, $^3J_{HH}$ = 6 Hz ArH; 7.45, 2H, m, ArH; 8.29, d, $^3J_{HH}$ = 6 Hz, ArH; 8.75, 2H, broad s, NH_2. ^{13}C{^{1}H} NMR: δ 11.5 methyl, 125.4, 126.2, 136.3, 159.9, 161.3, 163.7 and 188.5 CS.

IR: ν_{max}/cm^{-1} 3360,3150 (NH), 1614 (C=N), 1303 (C–S), 1002 (N–N), 847 (C–S). MS: m/z 573 = $[Re(\mathbf{L^1})_2]^+$.

Crystals suitable for single crystal X-ray crystallography were grown by slow evaporation of a MeOH solution of the complex.

Leaving the filtrate to evaporate at room temperature resulted in precipitation of a very small amount of red needle-like crystals suitable for X-ray studies. An X-ray structure determination revealed that the red crystals were $[ReCl_2\mathbf{L^4}(PPh_3)_2][ReO_4]$, **4**.

$[Re(L^2)_2]Cl$. As per general procedure except with $[ReOCl_3(PPh_3)_2]$ (0.800 g, 0.96 mmol) and $\mathbf{LH^2}$ (0.402 g, 1.92 mmol).

$[Re(\mathbf{L^2})_2]Cl$ was isolated as black crystals (0.340 g, 0.27 mmol, 56%). (Found: C, 34.4; H, 3.4; N, 17.6. Calc. for $ReC_{18}H_{22}N_8ClS_2$: C, 33.98; H, 3.48; N, 17.61%). ^{1}H NMR (DMSO-d_6): δ 2.92, 6H, d, $^3J_{HH}$ = 6 Hz, NHCH_3; 4.54, 6H, s, CCH_3; 6.92, 2H, m, ArH; 7.14, 2H, d, $^3J_{HH}$ = 6 Hz ArH; 7.42, 2H, m, ArH; 8.24, d, $^3J_{HH}$ = 6 Hz, ArH; 9.03, 2H, broad s, NHCH_3. ^{13}C{^{1}H} NMR: δ 11.5 CCH_3, 33.1 $NHCH_3$, 125.5, 126.3, 136.4, 160.0, 161.3, 164,4 and 187.9 CS.

IR (ν_{max}/cm^{-1}): 3100–3200 (NH), 1600 (C=N), 1271 (C–S), 982 ν(N–N), 813 (C–S). MS: m/z 601 = $[Re(\mathbf{L^2})_2]^+$.

Crystals suitable for single crystal X-ray crystallography were grown by slow evaporation of a MeOH solution of the complex.

$[Re(L^3)_2]Cl$. As per general procedure except using $[ReOCl_3(PPh_3)_2]$ (0.800 g, 0.96 mmol) and $\mathbf{LH^3}$ (0.212 g, 1.92 mmol).

$[Re(\mathbf{L^3})_2]Cl$ was isolated as black crystals (0.425 g, 0.62 mmol, 65%). (Found: C, 36.0; H, 4.0; N, 16.9. Calc. for $ReC_{20}H_{26}N_8ClS_2$: C, 36.16; H, 3.94; N, 16.87%).

^{1}H NMR (DMSO-d_6): δ 1.21, 6H, t, $^3J_{HH}$ = 7 Hz, CH_2CH_3; 3.33, 4H, q, $^3J_{HH}$ = 7 Hz, CH_2CH_3; 4.48, 3H, s, CCH_3; 6.89, 2H, m, ArH; 7.09, 2H, d, $^3J_{HH}$ = 6 Hz, ArH; 7.44, 2H, m, ArH; 8.25, 2H, d, $^3J_{HH}$ = 6 Hz, ArH; 8.96, 2H, broad s, NH. ^{13}C{^{1}H} NMR: δ 12.2 CH_2CH_3, 14.8 NCH_3, 42.4 CH_2CH_3, 125.9, 126.1, 136.7, 160.1, 160.2, 161.7 and 186.6 CS. MS. m/z 629 = $[Re(\mathbf{L^3})_2]^+$.

Crystals suitable for single crystal X-ray crystallography were grown by slow evaporation of a MeOH solution of the complex.

Synthesis of 4 from $[NH_4][ReO_4]$. $[NH_4][ReO_4]$ (0.1 g, 0.373 mmol) was added to a mixture of ethanol (5 mL) and

concentrated HCl (1 mL). A mixture of triphenylphosphine (0.39 g, 1.49 mmol) and $\mathbf{L^2}$H (0.155 g, 0.746 mmol) in ethanol (10 mL) was added and the mixture heated at 65 °C under an atmosphere of nitrogen for 2 hours. The mixture was filtered hot and then allowed to cool to room temperature. The precipitate was collected by filtration and washed with diethyl ether to give **4** as red needle-like crystals (0.06 g). Microanalytical results suggested that this compound was a mixture of the chloride and perrhenate salts of the catioic complex.

^{1}H NMR signals were broad and indicative of a paramagnetic species.

M.S. m/z 901 = $[ReC_{43}H_{38}Cl_2N_2P_2]^+$

Synthesis of 2 from $[Bu_4N][ReO_4]$. $[Bu_4N][ReO_4]$ (0.183 g, 0.373 mmol) was added to methanol (15 mL). Triphenylphosphine (0.39 g, 1.49 mmol) and concentrated HCl (1 mL) were added and the mixture was heated at reflux under an atmosphere of nitrogen for 45 minutes. The mixture was allowed to cool to room temperature and triethylamine (1.4 mL) was added followed by $\mathbf{L^2}$H (0.155 g, 0.746 mmol) in methanol (10 mL) and the mixture was heated at 60 °C under an atmosphere of nitrogen for 1.5 hours. An aliquot of the reaction mixture was taken and analysed by electrospray MS (positive ion mode). The only rhenium containing species present was at m/z = 601 = $[Re(\mathbf{L^2})_2]^+$. The mixture was filtered hot and the volume reduced to about 12 mL by evaporation under reduced pressure. The mixture was left to stand at 4 °C for two hours. The black crystals that precipitated were collected by filtration and washed with a small amount of methanol and diethyl ether to give $[Re(\mathbf{L^2})_2]Cl$ (0.08 g, 33%). Analytical data was consistent with the material synthesised from $[ReOCl_3(PPh_3)_2]$.

Crystallography

Crystals were mounted on glass fibres using perfluoropolyether oil and cooled rapidly to 150 K in a stream of cold N_2 using an Oxford Cryosystems CRYOSTREAM unit. Diffraction data were measured using an Enraf-Nonius KappaCCD diffractometer (graphite-monochromated MoKα radiation, λ = 0.71073 Å). Intensity data were processed using the DENZO-SMN package.[41]

The structures were solved using the direct-methods program SIR92,[42] which located all non-hydrogen atoms. Subsequent full-matrix least-squares refinement was carried out using the CRYSTALS program suite.[43]

1. Examination of the systematic absences of the intensity data showed the space group to be *Pccn*. Coordinates and anisotropic thermal parameters of all non-hydrogen atoms were refined. The H atoms of the amine and hydroxyl substituents were located in a difference Fourier map and their coordinates and isotropic thermal parameters subsequently refined. Other hydrogen atoms were positioned geometrically after each cycle of refinement. A 3-term Chebychev polynomial weighting scheme was applied. Refinement converged satisfactorily to give R = 0.0197, wR = 0.0259.

2. Examination of the systematic absences of the intensity data showed the space group to be $P2_1/c$. Coordinates and anisotropic thermal parameters of all non-hydrogen atoms were refined. Hydrogen atoms were positioned geometrically after each cycle of refinement. A 4-term Chebychev polynomial weighting scheme was applied. Refinement converged satisfactorily to give R = 0.0478, wR = 0.0461.

3. The structure was solved in the space group $P\bar{1}$ using the direct-methods program SIR92,[42] which located all non-hydrogen atoms. Coordinates and anisotropic thermal parameters of all non-hydrogen atoms were refined. The thermal parameters of the solvent refined to extremely large values, suggesting this molecule to be disordered. It was modelled as disordered over two positions, the coordinates, anisotropic thermal parameters and site occupancies of which were refined. The C–O distances were restrained to be 1.41(1) Å and the sum of the two site occupancies was constrained to be unity. The N–H hydrogen atoms were located in a difference Fourier map and their coordinates and isotropic thermal parameters subsequently refined. Other hydrogen atoms were positioned geometrically after each cycle of refinement. A 3-term Chebychev polynomial weighting scheme was applied. Refinement converged satisfactorily to give R = 0.0268, wR = 0.0316.

4. The structure was solved in the space group $P\bar{1}$ using the direct-methods program SIR92,[42] which located all Re, Cl and P atoms together with many other non-hydrogen atoms. All remaining non-hydrogen atoms were located in a difference Fourier map. Coordinates and anisotropic thermal parameters of all non-hydrogen atoms were refined. The hydrogen atoms of the imine groups were located in a difference Fourier map and their coordinates and isotropic thermal parameters subsequently refined. Remaining hydrogen atoms were positioned geometrically after each cycle of refinement. A 4-term Chebychev polynomial weighting scheme was applied. Refinement converged satisfactorily to give R = 0.0451, wR = 0.0484.

CCDC reference numbers 196178–196181.

See http://www.rsc.org/suppdata/dt/b2/b210540n/ for crystallographic data in CIF or other electronic format.

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