DALTON
FULL PAPER

Preparation and structural studies of neutral oxorhenium(V) complexes with D-penicillamine methyl ester

Sylvia Kirsch,[a] Bernhard Noll,[a] Hartmut Spies,[a] Peter Leibnitz,[b] Dieter Scheller,[c] Torsten Krueger[c] and Bernd Johannsen*,†,[a]

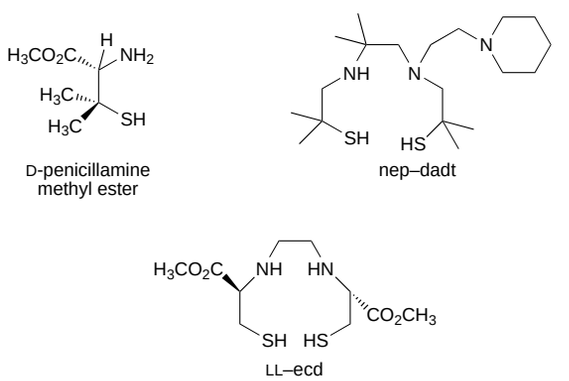
[a] *Forschungszentrum Rossendorf, Institut für Bioanorganische und Radiopharmazeutische Chemie, PF 510119, D-01314 Dresden, Germany*
[b] *Bundesanstalt für Materialforschung, D-12489 Berlin, Germany*
[c] *Fachrichtung Chemie, Technische Universität Dresden, D-01062 Dresden, Germany*

Reaction of oxorhenium(V) gluconate with D-penicillamine methyl ester (methyl 3-sulfanylvalinate) yielded three neutral 1:2 complexes. For two complexes (**1** and **2**) the ^{1}H NMR spectrum in $(CD_3)_2SO$ shows the presence of a deprotonated and a neutral nitrogen donor group in the $ReO(NS)_2$ system which is an unusual co-ordination mode for bidentate N,S ligands. Complex **1**, $[ReO\{SC(CH_3)_2CH(CO_2CH_3)NH_2\}\{SC(CH_3)_2CH(CO_2CH_3)NH\}]$, possibly containing in non-co-ordinating solvents an ester oxygen co-ordinated *trans* to the Re=O group, is able to bind a water molecule *trans* to the oxo core to give species **2**. In aqueous solution the mixed-ligand complex $[ReO\{SC(CH_3)_2CH(CO_2CH_3)NH_2\}\{SC(CH_3)_2CH(CO_2)NH_2\}]$ **3** was unexpectedly formed out of **1** and **2**. It contains bidentate D-penicillamine methyl ester and tridentate D-penicillamine in a co-ordination geometry similar to that of the known D-penicillamine complex $[ReO\{SC(CH_3)_2CH(CO_2H)NH_2\}\{SC(CH_3)_2CH(CO_2)NH_2\}]$ **4**. Complexes **3** and **4** were structurally characterized by X-ray diffraction.

Ligands containing both amine and thiol donor groups play an important role in technetium(V) chemistry as relevant to nuclear medicine.[1] Particularly tetradentate N_2S_2 ligands such as diamine dithiols are most valuable in the design of brain imaging ^{99m}Tc radiopharmaceuticals which should be neutral and lipophilic in order to be able to cross the blood–brain barrier. This class of ligand, and in particular nep-dadt[2] and LL-ecd,[3] shown in Scheme 1, has a strong propensity for co-ordinating the $[Tc^VO]^{3+}$ core in such a way that neutral complexes result. Upon interaction with the metal core the chelate ligands adopt a trianionic form by deprotonation of the two thiol groups and of one of the two NH groups. If there are also ester groups in the ligand molecule such as in ecd they will not be involved. The structures of the five-co-ordinate, square-pyramidal complexes were investigated in detail, using rhenium as a non-radioactive surrogate for technetium as well as the long-lived technetium isotope ^{99}Tc.[3]

The exclusive formation of such neutral N_2S_2 complexes by concerted action of a neutral and a deprotonated amine-N donor atom is obviously interfered with or abolished by pendant carboxyl groups.[4] Likewise, bidentate NS ligands instead of tetradentate diamine dithiols are thought to differ by not being able to provide deprotonated amine-N donors. As for the latter case, we have recently found that cysteamine favours in aqueous solution the formation of a cationic 1:2 oxorhenium(V) species at low pH and builds an oxo-bridged complex at higher pH.[5] The facility of NH deprotonation of one cysteamine portion in the 1:2 complex and hence straightforward formation of a neutral complex is not pronounced. Thus, the amine groups typically remain protonated. This difference between the $ReO(N_2S_2)$ and $ReO(NS)_2$ type complexes is also expected for ester group-bearing derivatives or analogous ligands.

Compared with tetradentate N_2S_2 ligands having pendant carboxyl groups,[4,6] very few studies have been devoted to the composition and structure of oxo complexes of Tc^V and Re^V with mercaptoamino acids and their derivatives, despite a continuous interest in the biological behaviour of ^{99m}Tc complexes of cysteine and derivatives.[7–12] Recently profound solution studies of the oxorhenium(V) penicillamine complex have been described,[13,14] including the observation that NH deprotonation does not occur in this system up to a very high pH value. Having studied the complexation behaviour of Tc^V and Re^V with cysteamine as the simple N,S-donor building block of the ligands of interest, we extended our investigations to D-penicillamine methyl ester. By analogy with cysteamine,[5] it was anticipated that D-penicillamine methyl ester should be amenable to the formation of cationic or dinuclear oxorhenium(V) complexes. We now report the results of our studies which have shed some more light on the subtle interplay of the O,N,S donor groups of ligands such as D-penicillamine methyl ester upon co-ordination with the $[Re^VO]^{3+}$ core.



Scheme 1 Molecular structure of D-penicillamine methyl ester (methyl 3-sulfanyl D-valinate) in comparison with two tetradentate N_2S_2 ligands used in nuclear medicine, nep-dadt [2,5,5,9-tetramethyl-7-(2-piperidinoethyl)-4,7-diazadecane-2,9-dithiol][2] and LL-ecd [*N*,*N*′-ethylenebis(L-cysteine ethyl ester)][3]

Results and Discussion

D-Penicillamine methyl ester reacted with the recently described precursor oxorhenium(V) gluconate, $[ReO\{OCH_2[CH(OH)]_4CO\}_2]$,[15] in acidic aqueous solution giving a mixture of two

† E-Mail: johannsen@fz-rossendorf.de

Table 1 Selected bond distances (Å) and angles (°) of complexes **3** and **4**

	3	**4**
Re–O(1)	1.663(5)	1.687(6)
Re–N(2)	2.162(6)	2.186(6)
Re–O(2)	2.179(4)	2.184(6)
Re–N(1)	2.194(6)	2.214(7)
Re–S(2)	2.280(2)	2.286(2)
Re–S(1)	2.300(2)	2.296(2)
O(1)–Re–N(2)	97.9(2)	98.2(3)
O(1)–Re–O(2)	157.9(2)	157.3(3)
N(2)–Re–O(2)	74.3(2)	73.5(2)
O(1)–Re–N(1)	90.2(2)	90.2(3)
N(2)–Re–N(1)	93.2(2)	93.8(3)
O(2)–Re–N(1)	70.1(2)	69.9(2)
O(1)–Re–S(2)	106.0(2)	106.8(2)
N(2)–Re–S(2)	83.1(2)	83.0(2)
O(2)–Re–S(2)	93.71(13)	93.3(2)
N(1)–Re–S(2)	163.8(2)	163.0(2)
O(1)–Re–S(1)	104.6(2)	105.8(2)
N(2)–Re–S(1)	157.3(2)	155.9(2)
O(2)–Re–S(1)	83.77(12)	83.30(15)
N(1)–Re–S(1)	84.6(2)	83.9(2)
S(2)–Re–S(1)	92.80(7)	92.17(10)

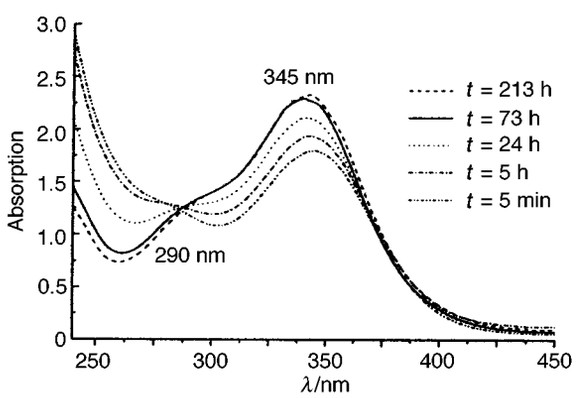


Fig. 1 Ultraviolet spectra indicating the conversion of complex **1** into **3** recorded in water–ethanol (50 : 50)

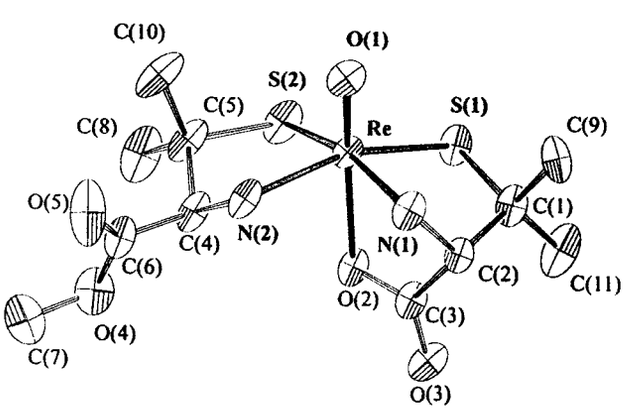


Fig. 2 An ORTEP[16] view of complex **3**

neutral complexes **1** and **2**. They were extracted with $CHCl_3$ and isolated as powders after flash chromatography on silica gel 60 in acetone. When the product mixture was allowed to react with water for a longer time another neutral complex **3** was obtained. Fig. 1 shows UV spectra recorded in water–ethanol (50 : 50), indicating the conversion of **1** into **3** within 3 d. Crystallization of **3** from aqueous solution at pH 2 yielded violet needles suitable for X-ray analysis. The crystal structure is shown in Fig. 2. Complex **3**, being surprisingly a mixed-ligand rhenium complex, contains one D-penicillamine carboxylate ligand co-ordinated *via* the N, S and O sites and one D-penicillamine carboxylate ligand co-ordinated through N and S only and shows some interesting resemblance to a known Re^{V}=O species of D-penicillamine[13] or D-penicillamine/L-penicillamine.[14] Therefore, we also synthesized the related oxorhenium(V) complex **4** with D-penicillamine as ligand. It was similarly purified and crystallized from a red aqueous solution at pH 2. The results of a single-crystal X-ray diffraction study of **4** are presented in Fig. 3. It can be seen from Table 1 that **3** and **4** show very similar bond angles and lengths. As expected, **4** resembles in its crystal structure the analogous technetium-99 complex described by Franklin *et al.*[8] in 1982. This complex is characterized by a carboxyl group of tridentate D-penicillamine bound *trans* to the oxide ligand and the two N-donor groups in the N_2S_2 plane are protonated (as NH_2). Likewise, in the crystal structure of $[ReO\{SC(CH_3)_2CH(CO_2H)NH_2\}\{SC(CH_3)_2CH(CO_2)NH_2\}]$ **4** the H_2N and S atoms in the basal plane are *cis* co-ordinated, and one of the carboxyl groups is ligated *trans* to the oxo group. Hansen *et al.*[13,14] have recently described the six-co-ordinate complex in solution and its intricate changes occurring at higher pH. Similarly, we observed in the ^{1}H NMR spectrum of **3** and **4** four NH signals indicating that the amine groups remain protonated (as NH_2). So it seems that in aqueous solution this octahedral, six-co-ordinate form is favoured within this type of complex.

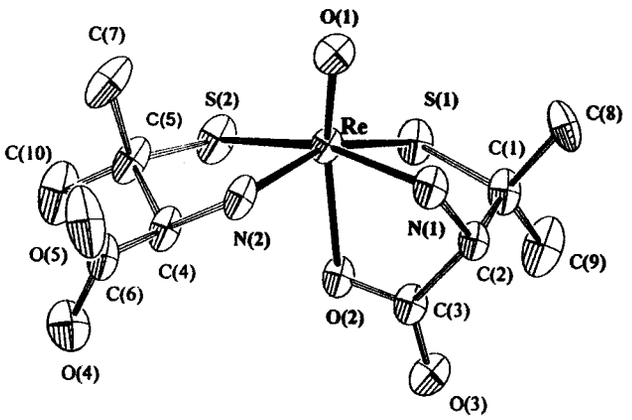


Fig. 3 An ORTEP view of complex **4**

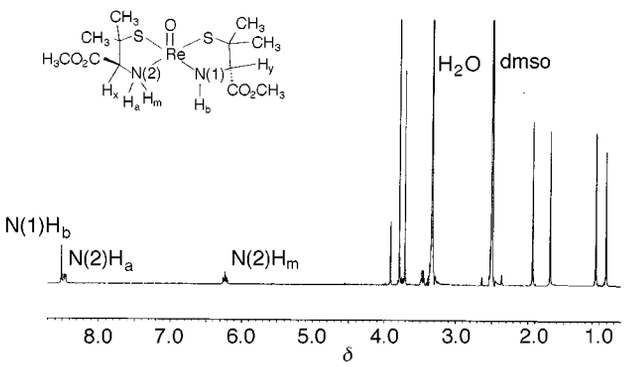


Fig. 4 Proton NMR spectrum of complex **1** in $(CD_3)_2SO$

Unlike **3** and **4**, the oxorhenium(V) complexes **1** and **2** which convert in water into **3** exhibit a different ^{1}H NMR spectrum. In the spectrum of **1** (Fig. 4) two methoxy signals are observed at δ 3.71 and 3.79. Furthermore, there are only three NH signals, each belonging to one proton: a triplet at δ 6.23, a doublet at 8.46 and a singlet at 8.50 in contrast to **3** and **4** with four NH signals. These facts demonstrate that one amine group was deprotonated during complex formation of **1**. For the $N(2)H_a$ group a pair of doublets is obtained at δ 8.46. Its coupling constant $^3J_{HH}$ with CH_x is relatively small (3.5 Hz) and therefore, with respect to the Karplus–Conroy curve,[17] the dihedral angle between these protons must be almost 50°. The coupling constants $^3J_{HH}$ of $N(2)H_m$ with CH_x and $^2J_{HH}$ for the two pro-

Table 2 Proton NMR chemical shifts (δ in ppm) of complexes **1**–**4** in $(CD_3)_2SO$

1		**2***		**3**		**4**	
0.91 (s)	CH_3	0.94 (s)	CH_3	1.29 (s)	CH_3	1.31 (s)	CH_3
1.05 (s)	CH_3	1.08 (s)	CH_3	1.48 (s)	CH_3	1.49 (s)	CH_3
1.69 (s)	CH_3	1.69 (s)	CH_3	1.68 (s)	CH_3	1.65 (s)	CH_3
1.93 (s)	CH_3	1.81 (s)	CH_3	1.89 (s)	CH_3	1.99 (s)	CH_3
3.47 (dd)	CH_x	3.74 (dd)	CH_x	3.10 (dd)	CH	3.00 (dd)	CH
3.91 (s br)	CH_y	4.01 (s br)	CH_y	3.64 (s br)	CH	3.63 (s br)	CH
3.71 (s)	OCH_3	3.74 (s)	OCH_3				
3.79 (s)	OCH_3	3.76 (s)	OCH_3	3.81 (s)	OCH_3		
6.23 (t)	$N(2)H_m$	5.82 (t)	$N(2)H_m$	5.80 (d)	N(1)H	5.75 (d)	N(1)H
				6.79 (t)	N(2)H	6.54 (t)	N(2)H
8.46 (dd)	$N(2)H_a$	8.34 (dd)	$N(2)H_a$	7.60 (dd)	N(2)H	7.60 (dd)	N(2)H
8.50 (s)	$N(1)H_b$	9.78 (s)	$N(1)H_b$	7.75 (d)	N(1)H	7.80 (d)	N(1)H

* Obtained from the ^1H NMR spectrum in $(CD_3)_2SO$ (see Fig. 6) showing a mixture of complex **2** and a species similar or identical to **1** in the same solvent.

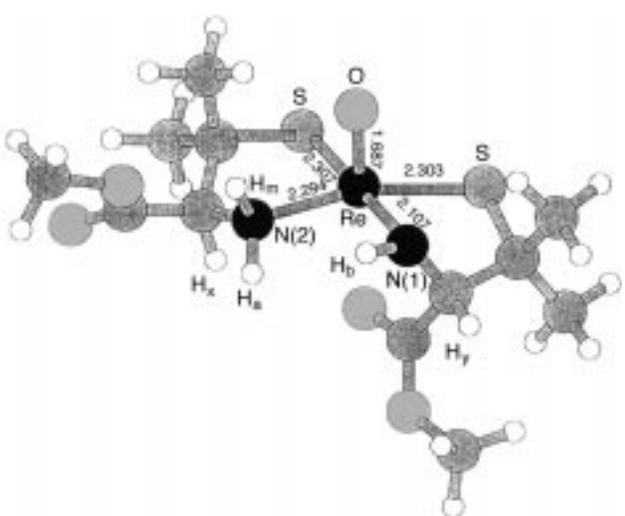


Fig. 5 Postulated structure of complex **1** obtained by *ab initio* and density functional calculations showing some calculated bond lengths (Å)

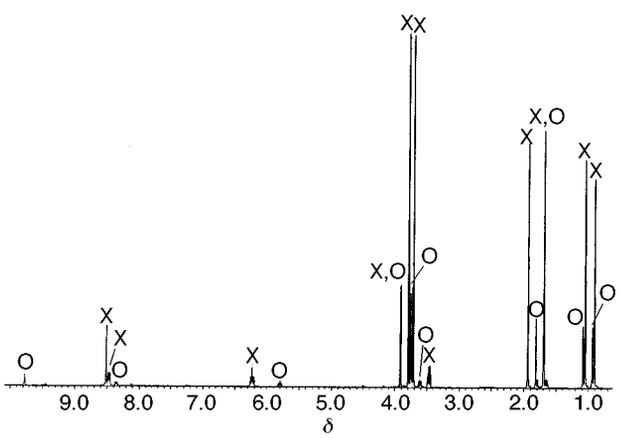
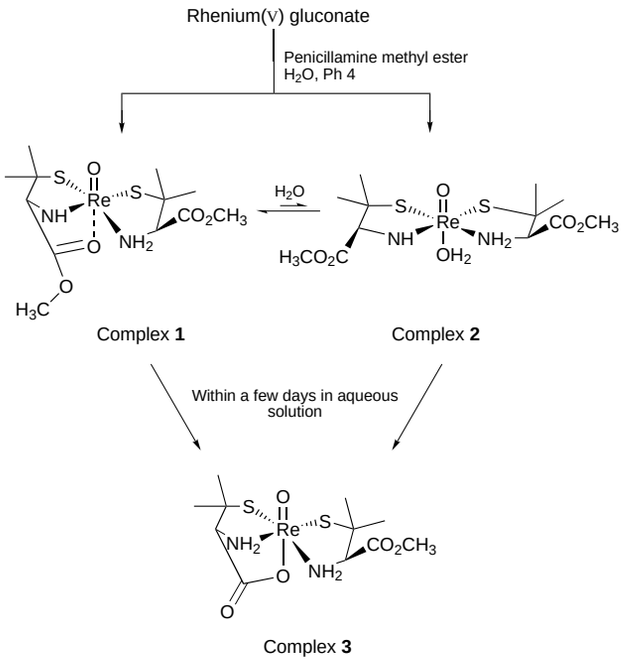


Fig. 6 Proton NMR spectrum of pure complex **2** redissolved in $(CD_3)_2SO$. The spectrum obtained is assumed to be a mixture of that of **2** and a species similar or identical to **1** in this solvent. O, signals belonging to **2**, X, signals similar or identical to those of **1**

tons of the NH_2 group are equal which results in a triplet at δ 6.23 instead of the expected pair of doublets. Its coupling constant $^3J_{HH} = 12.5$ Hz is quite large. This fact indicates a dihedral angle of 180° between the $N(2)H_m$ and CH_x proton. No coupling is observed between the CH_y group at δ 3.91 and its neighbouring $N(1)H_b$ group at δ 8.50. These two signals are therefore not doublets as expected but singlets. Consequently the dihedral angle between these two protons must be nearly 90°. For a better comparison in Table 2 the chemical shifts of all four complexes are listed. In the two-dimensional nuclear Overhauser enhancement spectroscopy (NOESY) NMR spectrum of complex **1** cross-peaks are obtained between $N(2)H_a$ and $N(2)H_m$ (strong), $N(2)H_a$ and CH_x, $N(1)H_b$ and CH_y (very weak), CH_x and $CH_3^{(2)}$, $CH_3^{(1)}$ and $CH_3^{(3)}$, $CH_3^{(2)}$ and $CH_3^{(4)}$. The last three cross-peaks with CH_3 groups indicate that the CH_x group belongs to $CH_3^{(2)}$ and $CH_3^{(4)}$. Therefore, $CH_3^{(1)}$ and $CH_3^{(3)}$ belong to the deprotonated ligand. All these conclusions are in good agreement with density functional calculated data for the H–N–C–H dihedral angles[18] and result in the proposed structure shown in Fig. 5. The usefulness of the applied computer methods has been verified in a comparison of calculated and crystal structure data for complex **3** (for more details see Experimental section). Interestingly, the ester oxygen of one ester group is located opposite to the oxide ligand and may therefore interact with the central atom.

In water-containing solvents complex **1** partly converts into and coexists with **2** prior to ultimate conversion into **3**. For **2** we first recorded the ^1H NMR spectrum in $CDCl_3$ and found, additionally to the expected CH and NH signals similar to those of complex **1**, a water signal at δ 1.60 integrating for two protons. Therefore, the *trans* position of **2** seems to be occupied by one molecule of water. This has a great effect on the co-ordinatively bonded deprotonated $N(1)H_b$ group which becomes apparent from the extremely shifted singlet at δ 10.94 belonging to this proton. After the measurement $CDCl_3$ was evaporated and the residue dissolved in $(CD_3)_2SO$ (Fig. 6). Surprisingly, little complex **2** still exists in this solvent, with the extremely shifted $N(1)H_b$ group being at δ 9.77. The main portion of the complex is apparently transformed into a species that possesses an identical ^1H NMR spectrum to that of **1** in $(CD_3)_2SO$. Obviously, the co-ordinated water in *trans* position is partly replaced by $(CD_3)_2SO$ and the pertinent chemical shifts are identical with those of complex **1** in $(CD_3)_2SO$. Thus, in co-ordinating solvents like $(CD_3)_2SO$ or water a dynamic equilibrium seems to exist with varying replacement of solvent molecules in the *trans* position. These results show that the bidentate N,S ligand, D-penicillamine methyl ester, is unexpectedly able to establish neutrality of the 1 : 2 complex(es) by virtue of deprotonation of one amine group upon complexation. Both complexes (**1** and **2**) exhibit a donor set arrangement that was thought to be a privilege of tetradentate ligands such as nep-dadt and ecd, namely a combination of deprotonated and protonated amine groups. This characteristic remains when a water molecule is bound *trans* to the oxide ligand in **2**. Complexes **1** and **2** were further characterized by FAB mass and IR spectral studies. However, a comparison of the mass data failed

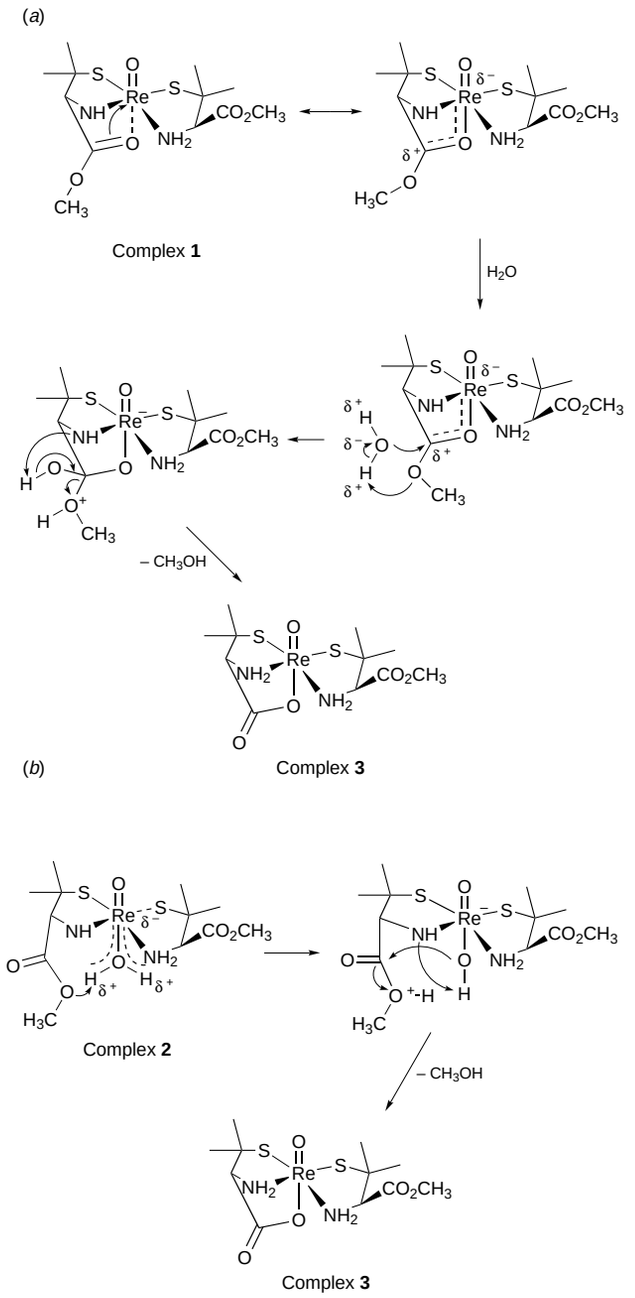


Scheme 2 Preparation of the two neutral complexes **1** and **2** from oxorhenium(V) gluconate, its interconversion and ultimate conversion into **3**. The crystal structure of **3** is established; the structures of **1** and **2** are based on ^{1}H NMR and IR data

to distinguish between the two complexes. The detected M^+ peak corresponds to complex **1**. Obviously, this technique is not sensitive enough to detect the M^+ peak for intact **2**. The IR absorptions for ν(Re=O) are around 940 cm^{-1} for both complexes and are in a similar range to that postulated by Hansen *et al.*[13] for a corresponding five-co-ordinate oxorhenium(V) penicillamine complex with one deprotonated amine group. Whether the *trans* position in complex **1** is actually free is questionable because there are hardly any differences in IR data between **1** and **2**. However, this fact could be explained by the assumption that **1** may contain an ester oxygen co-ordinated *trans* to the Re=O group, exerting a similar effect on the oxo group as that of the co-ordinated water molecule in **2**. So, as illustrated in Scheme 2 it is suggested that in complex **1** prepared from oxorhenium(V) gluconate by ligand exchange the ester oxygen permanently competes with solvent molecules co-ordinating *trans* to the oxo group. With water as the solvent complex **2** is obtained. A dynamic equilibrium seems to exist between **1** and **2**. We managed to isolate these two forms from aqueous solution because both complexes are insoluble in water but soluble in non-co-ordinating solvents such as $CHCl_3$ or acetone. Furthermore, in aqueous solution both complexes are ultimately converted into **3**. This unexpected hybrid complex is formed because the parent ligand is partly saponified under the conditions used. Obviously, saponification takes place only at the ester group which is arranged *anti* to the oxo group. In Scheme 3 two proposed mechanisms are outlined for the formation of **3** from **1** and **2**.

Conclusion

The studies of new rhenium complexes of D-penicillamine methyl ester confirm a great tendency of 2(N,S) aminethiol ligands to form neutral oxorhenium(V) complexes. Accordingly, in aprotic, non-co-ordinating solvents such as $CHCl_3$, one amine group in the 1:2 oxorhenium(V) complex **1** is deprotonated and thus contributes to the compensation of the positive charge at the oxorhenium core. In the presence of co-ordinating solvents like water, the *trans* position is occupied by a solvent molecule (**2**) without any change in the NH/NH_2 co-ordination mode. In water, however, the kinetically favoured complexes are slowly converted into the thermodynamically



Scheme 3 Proposed mechanisms for the formation of complex **3** from (*a*) **1** and (*b*) **2**

more favoured complex represented by **3**, avoiding NH deprotonation. One of the ester group-bearing ligands is hydrolysed and assumes a higher denticity. The generated carboxyl group binds *trans* to the oxide ligand. The co-ordination geometry of the mixed-ligand complex **3** is similar to that of the known D-penicillamine complex **4**, the crystal structure of which is also reported. It is evident that a NH_2/NH_2 co-ordination is preferred to the asymmetric NH/NH_2 co-ordination, if charge compensation can be provided by an appropriate donor group such as carboxyl that binds *trans* to the oxo group.

Experimental

Materials and methods

D-Penicillamine hydrochloride and D-penicillamine methyl ester hydrochloride (Fluka) were used as received without further purification. Oxorhenium(V) gluconate solution was prepared as recently described.[15]

Elemental analyses were performed on a LECO CHNS-932 elemental analyser. The UV/VIS spectra were recorded on a

Table 3 Crystal data and structure refinement for complexes **3** and **4***

	3	**4**
Empirical formula	$C_{11}H_{21}N_2O_5ReS_2$	$C_{10}H_{19}N_2O_5ReS_2$
M	511.61	497.59
T/K	293(2)	295(2)
λ/Å	0.71069	0.71073
a/Å	6.085(2)	5.930(4)
b/Å	13.880(4)	11.709(4)
c/Å	19.702(3)	21.750(4)
U/Å^3	1664.0(8)	1510.1(12)
D_c/mg m^{-3}	2.042	2.189
μ/mm^{-1}	7.573	8.342
F(000)	992	960
Crystal size/mm	0.36 × 0.20 × 0.14	0.63 × 0.27 × 0.18
2θ/° data collection	1.79 to 26.96	1.87 to 27.47
Index ranges	$0 \leqslant h \leqslant 7$, $0 \leqslant k \leqslant 17$, $-25 \leqslant l \leqslant 25$	$0 \leqslant h \leqslant 7$, $0 \leqslant k \leqslant 15$, $-28 \leqslant l \leqslant 28$
Reflections collected	4140	3956
Independent reflections (R_{int})	3624 (0.025)	3420 (0.022)
Data, restraints, parameters	3622, 0, 198	3420, 0, 185
Goodness of fit on F^2	1.032	1.131
Final *R*1, *wR*2 [$I > 2\sigma(I)$]	0.0314, 0.0810	0.0299, 0.0754
(all data)	0.0364, 0.0828	0.0316, 0.0768
Absolute structure parameter	0.004(12)	−0.0022(14)
Extinction coefficient	0.0003(2)	0.0024(2)
Largest difference peak and hole/e Å^{-3}	1.036 and −0.933	2.652 and −1.858
A_{max}, A_{min}	1.1972, 0.7642	1.1896, 0.8826

* Details in common: orthorhomic, space group $P2_12_12_119$; $Z = 4$; full-matrix least-squares refinement on F^2. The largest peak and hole are located near to Re atoms (0.9 Å) and cannot be explained by additional atoms. Carbon atoms in Fourier-difference syntheses gave electron-density peaks of more than 5 e Å^{-3}. Therefore, the relatively high difference and hole may be caused by the unfavourable crystal shape.

Specord S 10 instrument from Zeiss Jena, infrared spectra (KBr pellets) on a Specord M80, proton NMR spectra on a Bruker DRX 500 [solvent $(CD_3)_2SO$, $CDCl_3$] and mass spectra using a Finnigan MAT 95 spectrometer.

Crystallography

X-Ray crystallographic data were obtained at 294 K on an ENRAF-Nonius CAD-4 diffractometer, using graphite-monochromated Mo-Kα radiation (λ = 0.71069 Å). Full details are given in Table 3. Direct methods (Re and S atoms) followed by normal heavy-atom procedures were used. Most of the hydrogen atoms were found in subsequent Fourier-difference synthesis, but owing to the resulting inaccurate bond distances and angles all H atoms were calculated corresponding to their geometrical conditions and refined using the riding model. For absorption correction an empirical method using the DIFABS program was applied. For programs used and sources of scattering factor data see ref. 19.

CCDC reference number 186/805.

See http://www.rsc.org/suppdata/dt/1998/455/ for crystallographic files in .cif format.

Molecular modelling

The structure of complex **1** has been determined by *ab initio* and density functional calculations (see Fig. 5).[18] The molecules were completely geometry optimized to a gradient norm less than 0.0001 kcal mol^{-1} Å^{-1} (cal = 4.184 J). The *ab initio* calculations were carried out with GAUSSIAN 94[20] using the 6-31G, 6-31G* basis sets at the Hartree–Fock level. The density functional calculations were done with ADF[21] using the II(DZ) and IV(DZ) large-core basis sets in the generalized gradient approximations method (non-located).

Preparations

[ReO{SC(CH$_3$)$_2$CH(CO$_2$CH$_3$)NH$_2$}{SC(CH$_3$)$_2$CH(CO$_2$-CH$_3$)NH}] 1 and [ReO{SC(CH$_3$)$_2$CH(CO$_2$CH$_3$)NH$_2$}{SC-(CH$_3$)$_2$CH(CO$_2$CH$_3$)NH}(H$_2$O)] 2. D-Penicillamine methyl ester hydrochloride (40 mg, 0.2 mmol) in water (2 cm^3) was added to oxorhenium(V) gluconate solution (2 cm^3, 0.1 mmol). The reddish brown residue was filtered off and redissolved in acetone (2–3 cm^3). The solution was purified by flash chromatography on silica gel 60 in acetone. Two fractions were isolated: **1** as a violet powder and **2** as a light red powder, soluble in almost all organic solvents. The yield of **2** was about 20% of the total yield of **1** [Found: C, 28.0; H, 4.8; N, 5.1; S, 11.9. $C_{12}H_{23}N_2O_5ReS_2$ **1** requires C, 27.4; H, 4.6; N, 5.3; S, 12.2%. UV/VIS: λ_{max}/nm (in CH_2Cl_2) 531 and 358. IR (KBr)/cm^{-1} 1732vs (C=O ester) and 940m (Re=O). Mass spectrum (FAB, negative ion): *m*/*z* 525 (60), 396 (20) and 183 (100%). Found: C, 26.3; H, 4.55; N, 5.1; S, 11.7. $C_{12}H_{25}N_2O_6ReS_2$ **2** requires C, 26.5; H, 4.6; N, 5.15; S, 11.8%. UV/VIS: λ_{max}/nm (CH_2Cl_2) 517 and 315. IR (KBr)/cm^{-1}: 1728vs (C=O) and 936s (Re=O). Mass spectrum (FAB, negative ion) similar to that of **1**].

[ReO{SC(CH$_3$)$_2$CH(CO$_2$CH$_3$)NH$_2$}{SC(CH$_3$)$_2$CH(CO$_2$)-NH$_2$}] 3. D-Penicillamine methyl ester hydrochloride (40 mg, 0.2 mmol) in water (2 cm^3) was added to oxorhenium(V) gluconate solution (2 cm^3, 0.1 mmol). A reddish brown precipitate was obtained as above, filtered off and redissolved in acetone (2–3 cm^3). Water (3 cm^3) was added and the solution allowed to crystallize by slow evaporation at 25 °C. Yield: 25 mg (24%) of dark violet needles suitable for X-ray analysis (Found: C, 26.0; H, 4.1; N, 5.4; S, 12.6. $C_{11}H_{21}N_2O_5ReS_2$ requires C, 25.3; H, 4.1; N, 5.5; S, 12.6%). UV/VIS absorption: λ_{max}/nm (water) 499, 340 and 290(sh). IR (KBr)/cm^{-1}: 1732s (C=O, free ester group), 1630s (C=O, *trans* co-ordinated) and 976s (Re=O). Mass spectrum (desorption chemical ionization, DCI): *m*/*z* 512 (M^+, 100%).

[ReO{SC(CH$_3$)$_2$CH(CO$_2$H)NH$_2$}{SC(CH$_3$)$_2$CH(CO$_2$)NH$_2$}] 4. D-Penicillamine (30.0 mg, 0.4 mmol) in water (2–3 cm^3) was added to oxorhenium(V) gluconate solution (2 cm^3, 0.2 mmol) while stirring under nitrogen for 45 min. The mixture was concentrated to 0.5 cm^3 in a vacuum evaporator and loaded on a column filled with Dowex 50 WX 4 cation-exchange resin (5 × 1 cm, mesh size 100–200, counter ion H^+). The eluted red solution (pH 2) was allowed to crystallize by slow evaporation at 25 °C. Yield: 31.7 mg (31%) of dark red crystals suitable for

X-ray analysis (Found: C, 24.1; H, 3.8; N, 5.5; S, 12.9. $C_{10}H_{19}N_2O_5ReS_2$ requires C, 24.2; H, 3.65; N, 5.6; S, 12.9%). UV/VIS: λ_{max}/nm (water) 502, 345 and 290(sh). IR (KBr)/cm^{-1}: 1692s (C=O), 1660s (C=O, *trans* co-ordinated) and 984s (Re=O). Mass spectrum (DCI): *m*/*z* 498 (M^+, 100), 480 (80) and 382 (65%).

References

1 B. Johannsen and H. Spies, *Top. Curr. Chem.*, 1996, **176**, 77.
2 L. A. Epps, H. D. Burns, S. Z. Lever, H. W. Goldfarb and H. N. Wagner, jun., *Appl. Radiat. Isot.*, 1987, **38**, 661.
3 D. S. Edwards, E. H. Cheesman, M. W. Watson, L. J. Maheu, S. A. Nguyen, L. Dimitre, T. Nason, A. D. Watson and R. Walovitch, in *Technetium and rhenium in chemistry and nuclear medicine*, eds. M. Nicolini, G. Bandoli and U. Mazzi, Cortina International, Verona, Raven Press, New York, 1990, p. 433.
4 L. G. Marzilli, M. G. Banaszcyk, L. Hansen, Z. Kuklenyik, R. Cini and A. Taylor, jun., *Inorg. Chem.*, 1994, **33**, 4850.
5 S. Kirsch, B. Noll, D. Scheller, K. Klostermann, P. Leibnitz, H. Spies and B. Johannsen, Annual Report of the Institute of Bioinorganic and Radiopharmaceutical Chemistry, Rossendorf, 1995, pp.110–114.
6 L. Hansen, M. Lipowska, A. Taylor, jun. and L. G. Marzilli, *Inorg. Chem.*, 1995, **34**, 3579.
7 B. Johannsen, R. Syhre, H. Spies and R. Münze, *J. Nucl. Med.*, 1978, **19**, 816.
8 K. J. Franklin, H. E. Howard-Lock and C. J. L. Lock, *Inorg. Chem.*, 1982, **21**, 1941.
9 A. Marchi, R. Rossi and L. Marvelli, *Inorg. Chem.*, 1993, **32**, 4673.
10 A. Wang and R. Liu, *Nucl. Med. Biol.*, 1995, **22**, 937.
11 J. Bonnyman, *Nucl. Med. Biol.*, 1995, **22**, 943.
12 S. Mansur, M. Jehangir, S. Stathaki, M. Papadopoulos, S. Mastrostamatis and E. Chiotellis, *Nucl. Med. Biol.*, 1993, **20**, 819.
13 L. Hansen, X. Xu, K. T. Yue, Z. Kuklenyik, A. Taylor, jun. and L. G. Marzilli, *Inorg. Chem.*, 1996, **35**, 1958.
14 L. Hansen, X. Xu, K. T. Yue, A. Taylor, jun. and L. G. Marzilli, *Inorg. Chem.*, 1996, **35**, 2785.
15 B. Noll, T. Kniess, M. Friebe, H. Spies and B. Johannsen, *Isot. Environ. Health Stud.*, 1996, **32**, 21.
16 C. K. Johnson, ORTEP, Report ORNL-5138, Oak Ridge National Laboratory, Oak Ridge, TN, 1976.
17 M. Karplus, *J. Am. Chem. Soc.*, 1963, **85**, 2870; Karplus equation: $J(\theta) = A\ \cos^2\theta + B\ \cos\theta + C$ where θ is the dihedral angle, the values *A*, *B*, *C* depend on the precise system under investigation and in particular are sensitive to the electronegativity of the substituents on the carbons *etc*.
18 T. Krueger, unpublished work.
19 N. Walker and D. Stuart, DIFABS, *Acta Crystallogr.*, *Sect. A*, 1983, **39**, 158; G. Reck and R. G. Kretschmer, CELLGRAF, a program for representation of organic and inorganic crystal structures, *Analytisches Zentrum Berlin* 1989/1991; *CAD4 Operations Manual*, Enraf-Nonius, Delft, 1977; C. K. Fair, MOLEN, An Interactive Intelligent System for Crystal Structure Analysis, User Manual, Enraf-Nonius, Delft, 1990; W. H. Zachariasen, *Acta Crystallogr.*, 1963, **16**, 1139; P. Main, S. J. Fiske, S. E. Hull, L. Lessinger, G. Germain, J. P. DeClerq and M. M. Woolfson, MULTAN 80, University of York, 1980.
20 M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. W. Gill, B. G. Johnson, M. A. Robb, J. R. Cheeseman, T. Keith, G. A. Petersson, J. A. Montgomery, K. Raghavachari, M. A. Al-Laham, V. G. Zakrzewski, J. V. Ortiz, J. B. Foresman, J. Cioslowski, B. B. Stefanov, A. Nanayakkara, M. Challacombe, C. Y. Peng, P. Y. Ayala, W. Chen, M. W. Wong, J. L. Andres, E. S. Replogle, R. Gomperts, R. L. Martin, D. J. Fox, J. S. Binkley, D. J. Defrees, J. Baker, J. P. Stewart, M. Head-Gordon, C. Gonzalez and J. A. Pople, GAUSSIAN 94, Revision B.2, Gaussian Inc., Pittsburgh, PA, 1995.
21 Amsterdam Density Functional (ADF): E. J. Baerends, D. E. Ellis and P. Ros, *Chem. Phys.*, 1973, **2**, 42; E. J. Baerends and P. Ros, *Chem. Phys*., 1973, **2**, 51; *Int. J. Quantum Chem*., 1978, **512**, 169; P. M. Boerrigter, G. te Velde and E. J. Baerends, *Int. J. Quantum Chem*., 1988, **33**, 87; G. te Velde and E. J. Baerends, *J. Comput. Phys*., 1992, **99**, 84.

Received 21*st August* 1997; *Paper* 7/06127G