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[2-Carboxy-2,2′,2″-nitrilotris(ethanethiolato)-κ^4N,S,S',S''](triphenylphosphine-κP)rhenium(III) acetone solvate

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Key indicators

Single-crystal X-ray study
T = 273 K
Mean σ(C–C) = 0.018 Å
Disorder in main residue
R factor = 0.074
wR factor = 0.214
Data-to-parameter ratio = 16.8

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

The title compound, $[Re(C_7H_{12}NO_2S_3)(C_{18}H_{15}P)]\cdot C_3H_6O$, crystallizes from a solution in chloroform–acetone–cyclohexane with enantiomers disordered equally over each molecular site. Hydrogen bonds between the carboxyl groups form dimers in the crystal structure.

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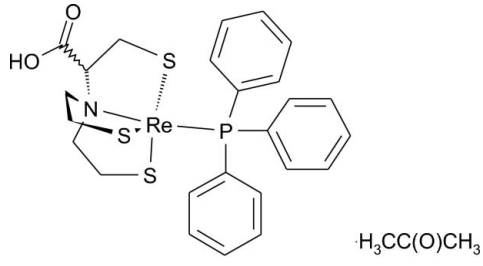
Comment

The application of radionuclides for the internal radiotherapy of cancer has been intensely investigated over the last decade (Larson & Krenning, 2005). Among the multitude of potential radionuclides suitable for therapeutic application in nuclear medicine, rhenium-188 is one of the most attractive (Knapp, 1998). This is due to its nuclide properties and its daily availability from a $^{188}W/^{188}Re$ generator. The major drawbacks in internal radionuclide therapy have been low target uptake and accumulation of radioactivity in non-target organs, such as kidney and liver. To overcome these problems, several strategies have been suggested. Increasing hydrophilicity of the ligands and coupling of hydrophilic molecules are possible approaches.

Rhenium complexes with tetradentate/monodentate NS_3/P ('4+1') coordination are promising candidates for the development of rhenium-188 complexes of high *in vivo* stability. 4+1 complexes containing the tris-(2-mercaptoethyl)amine chelator (NS_3) are of high lipophilicity, giving rise to accumulation of these compounds in the liver (Pietzsch *et al.*, 2001). These unfavourable biodistribution characteristics were diminished by the introduction of a carboxyl group into the NS_3 framework, resulting in increased hydrophilicity of the corresponding rhenium complexes (Seifert *et al.*, 2004). The new ligand can easily be modified by coupling different amines *via* an amide bond, thus increasing the variability of the 4+1 approach. The crystal structure of the first rhenium 4+1 complex with a carboxyl group containing a tripodal tetradentate NS_3 ligand, the title complex, (I), is reported here.



(I)

Compound (I) crystallizes as a disordered racemic structure. For clarity, only the structure of one component molecule

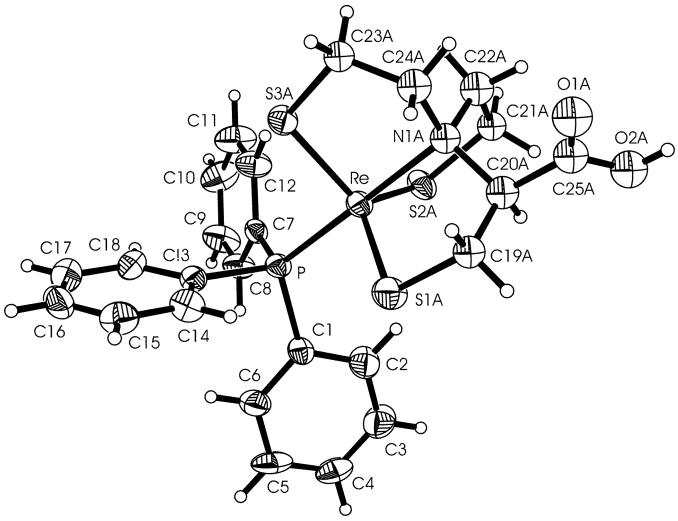


Figure 1
The structure of one of the two disordered complexes in (I), showing 30% probability displacement ellipsoids.

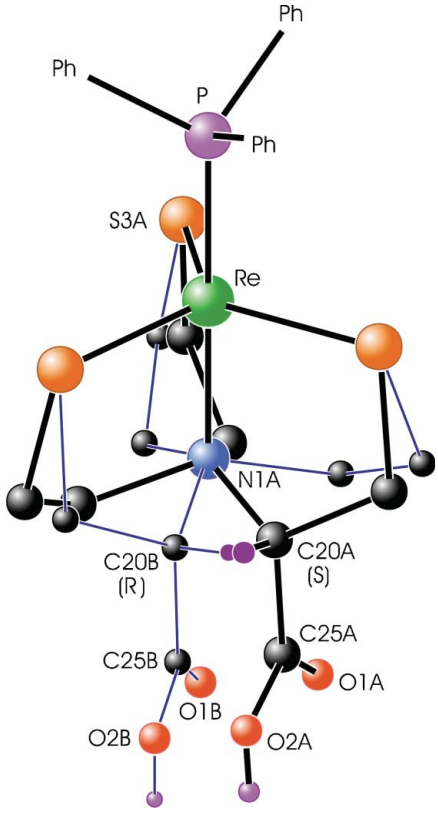


Figure 2
Superimposition of two disordered molecules of (I) having different absolute configurations.

is depicted in Fig. 1. With respect to the triphenylphosphine group, there are two different arrangements of the NS_3 chelator, which occupy the same site in the disordered crystal structure, as shown in Fig. 2. The two arrangements are approximately related by a partial mirror plane through atoms Re, S3*A*, P and N1*A*. This mirror plane converts the 20(*R*) configuration of the molecule into a 20(*S*) configuration.

Fig. 3 shows the linkage of two molecules *via* hydrogen bonds between the carboxyl groups, forming a dimer in the crystal structure. There are four possibilities for this dimer formation, namely linkage of two 20(*R*) molecules, 20(*S*) pairs, and two different combinations of 20(*R*) and 20(*S*) molecules, disordered over the centre of symmetry of the space group. The corresponding symmetry-independent hydrogen bonds are given in Table 2. From the geometry of the hydrogen bonds, it can be concluded that the formation of 20(*R*)–20(*R*) and 20(*S*)–20(*S*) dimers is energetically favoured. Nevertheless, the refinement of (I) in the space group *P*1 as an ordered twinned structure with two symmetry-independent molecules gave no satisfactory results.

Experimental

The title compound was prepared according to the method published by Spies *et al.* (1995). Slow solvent evaporation of a solution of (I) in chloroform–acetone–cyclohexane (8:1:1) gave green crystals suitable for X-ray analysis. Spectroscopic analysis: ^{1}H NMR (400 MHz, methanol-d_4/$CDCl_3$, δ, p.p.m.): 2.44 (*td*, J = 12.54 and 5.31 Hz, 1H), 2.73 (*m*, 2H), 2.86 (*td*, J = 13.05 and 4.30 Hz, 1H), 3.08 (*m*, 2H), 3.20 (*m*, 1H), 3.37 (*m*, 1H), 3.44 (*m*, 1H), 3.65 (*m*, 2H), 7.27 (*m*, 9 H_{arom}), 7.43 (*m*, J = 8.70 and 8.70 Hz, 6 H_{arom}); ^{13}C NMR (101 MHz, methanol-d_4/$CDCl_3$, δ, p.p.m.): 46.76 (*d*, J = 4.6 Hz, 1C, SCH_2), 49.14 (*d*, J = 4.6 Hz, 1C, SCH_2), 50.70 (*d*, J = 4.6 Hz, 1C, SCH_2), 55.81 (*s*, 1C, NCH_2), 57.11 (*s*, 1C, NCH_2), 70.78 (*s*, 1C, NCH), 127.85 (*d*, J = 9.1 Hz, 6 C_{arom}), 129.02 (*s*, 3 C_{arom}), 134.34 (*d*, J = 11.4 Hz, 6 C_{arom}), 144.04 (*d*, J = 46.2 Hz, 3 C_{arom}), 172.00 [*s*, 1C, C(O)]; ^{31}P NMR (162 MHz, methanol-d_4/$CDCl_3$, δ, p.p.m.): 31.80 (*s*); IR (KBr, cm^{-1}): 1435 (ν P—C_{arom}), 1714 (ν C═O); ESI$^+$ MS (*m*/*z*): 687 M^+.

Crystal data

$[Re(C_7H_{12}NO_2S_3)(C_{18}H_{15}P)]\cdot C_3H_6O$
M_r = 744.90
Triclinic, $P\overline{1}$
a = 9.624 (6) Å
b = 12.811 (7) Å
c = 13.392 (9) Å
α = 112.231 (5)°
β = 96.527 (6)°
γ = 90.078 (6)°
V = 1516.8 (17) Å^3
Z = 2
D_x = 1.631 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 928 reflections
θ = 2.9–28.2°
μ = 4.29 mm^{-1}
T = 273 (2) K
Plate, green
0.17 × 0.15 × 0.02 mm

Data collection

Bruker SMART CCD area-detector diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.452, T_{max} = 0.914
7570 measured reflections
5244 independent reflections
4168 reflections with $I > 2\sigma(I)$
R_{int} = 0.063
θ_{max} = 25.0°
$h = -11 \rightarrow 11$
$k = -14 \rightarrow 15$
$l = -13 \rightarrow 15$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.074
$wR(F^2)$ = 0.214
S = 0.99
5244 reflections
312 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1647P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 2.46 e Å^{-3}
$\Delta\rho_{min}$ = −2.02 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

Re—S1*A*	2.219 (11)	S2*A*—C21*A*	1.862 (18)
Re—S3*A*	2.216 (12)	S3*A*—C23*A*	1.862 (18)
Re—N1*A*	2.228 (15)	O1*A*—C25*A*	1.220 (9)
Re—S2*A*	2.243 (12)	O2*A*—C25*A*	1.297 (9)
Re—P	2.315 (3)	N1*A*—C20*A*	1.511 (17)
P—C7	1.822 (11)	N1*A*—C22*A*	1.526 (17)
P—C1	1.829 (12)	N1*A*—C24*A*	1.529 (17)
P—C13	1.835 (12)	C20*A*—C25*A*	1.53 (3)
S1*A*—C19*A*	1.860 (17)		
S1*A*—Re—S3*A*	124 (3)	N1*A*—Re—S2*A*	83.8 (7)
S1*A*—Re—N1*A*	86.0 (8)	C7—P—Re	117.2 (3)
S3*A*—Re—N1*A*	86.6 (10)	C1—P—Re	117.3 (3)
S1*A*—Re—S2*A*	115 (3)	C13—P—Re	114.2 (3)
S3*A*—Re—S2*A*	119 (3)		

Table 2
Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2*A*—H16···O1*B*^{i}	0.82	1.83	2.64 (3)	176
O2*B*—H28···O1*A*^{i}	0.82	1.82	2.64 (2)	179
O2*A*—H16···O1*A*^{i}	0.82	2.18	2.88 (3)	144
O2*B*—H28···O1*B*^{i}	0.82	2.24	2.93 (2)	142

Symmetry code: (i) $-x+1, -y+1, -z+2$.

The atoms of the disordered ligand were refined isotropically and with restrained bond lengths. All H atoms were positioned geometrically and refined as riding, with C—H = 0.93–0.97 Å and O—H = 0.82 Å, and with U_{iso}(H) = 1.2U_{eq}(parent atom) (1.3U_{eq} for OH and methyl groups). There is one acetone molecule in the asymmetric unit. This solvent molecule is disordered over two positions, assumed to have equal site occupancy, and was refined with isotropic displacement parameters. The highest peak and the deepest hole in the final difference Fourier map are located 0.59 Å from C28*A* (in the disordered solvent molecule) and 0.88 Å from Re, respectively.

Data collection: *SMART* (Bruker, 1997); cell refinement: *SAINT* (Bruker, 1997); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 1997); software used to prepare material for publication: *SHELXTL*.

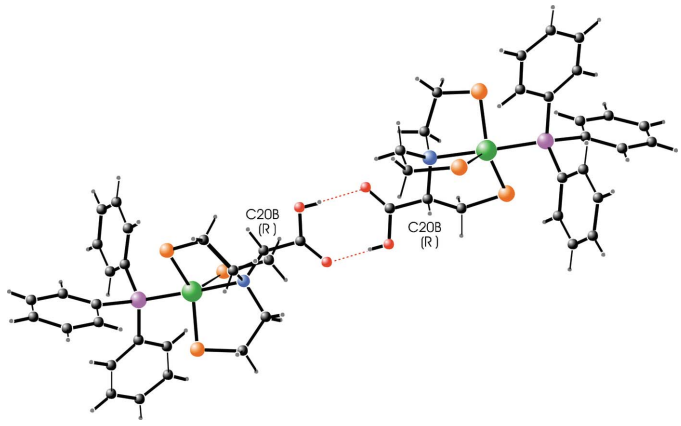


Figure 3
A molecular dimer of (I), shown here with two 20(*R*) molecules. Dashed lines indicate hydrogen bonds.

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