Application of technetium and rhenium carbonyl chemistry to nuclear medicine. Preparation of $[NEt_4]_2[TcCl_3(CO)_3]$ from $[NBu_4][TcO_4]$ and structure of $[NEt_4][Tc_2(\mu\text{-}Cl)_3(CO)_6]$; structures of the model complexes $[NEt_4][Re_2(\mu\text{-}OEt)_2(\mu\text{-}OAc)(CO)_6]$ and $[ReBr(\{\text{-}CH_2S(CH_2)_2Cl\}_2)(CO)_3]$

Roger Alberto[†‡], Roger Schibli[†], Daniela Angst[†] and P. August Schubiger*[†]

[†]*Division of Radiopharmacy, Paul Scherrer Institute, CH-5232 Villigen Switzerland, and* [‡]*Institute of Inorganic Chemistry, University of Zürich, Winterthurerstr. 190, CH-8057-Zürich, Switzerland*

Ulrich Abram and Sonja Abram

Institute of Inorganic Chemistry, University of Tübingen, Auf der Morgenstelle 18, D-72076 Tübingen, Germany

Th. A. Kaden

Institute of Inorganic Chemistry, University of Basel, Spitalstrasse 51, CH-4056 Basel, Switzerland

Summary

A detailed investigation of the one-pot synthesis of $[NEt_4]_2[MX_3(CO)_3]$ [M = Tc *(1a)* or Re *(1b)*; X = Cl^-, Br^-] is presented. The intermediates $[NEt_4][Tc_2(\mu\text{-}Cl)_3(CO)_6]$ *(2a)*, $[NBu_4][Tc_3(\mu_3\text{-}H)(\mu\text{-}H)_3(CO)_9]$ *(3)* and $[Tc_3(\mu\text{-}H)_3(CO)_{12}]$ *(4)* have been isolated and characterized. The X-ray structure of *(2a)* is described. Complex *(2a)* crystallizes in the monoclinic space group $P2_1/c$ with a = 19.491(6), b = 18.323(2) and c = 17.497(9) Å, and β = 97.59(2)°. Quantitative conversion of *(2a)*, *(3)* and *(4)* into the aqua-ion $[M(OH_2)_3(CO)_3]^+$ [M = Tc *(5a)* or Re *(5b)*] is described. To evaluate an optimal and simple chelating group for the "*fac*-$M(CO)_3$" moiety, the reaction with the bidentate thioether ligand $Cl(CH_2)_2S(CH_2)_2S(CH_2)_2Cl$ (qyp) has been investigated and the structure of the neutral complex $[ReBr(qyp)(CO)_3]$ *(6)* is described. Complex *(6)* crystallizes in the monoclinic space group $P2_1/c$ with a = 15.935(6), b = 2.788(4) and c = 7.955(10) Å, and β = 98.57(1)°. To extend the knowledge about substitution chemistry of organometallic complexes in aqueous solution, the acetato ligand $[OOCCH_3]^-$ has been reacted with *(1b)*, resulting in the formation of the dinuclear, acetato-bridged complex $[NEt_4][Re_2(\mu\text{-}OH)_2(\mu\text{-}OAc)(CO)_6]$, which converted into $[Re_2(\mu\text{-}OEt)_2(\mu\text{-}OAc)(CO)_6]^-$ *(7)* after recrystallization from EtOH. The X-ray structure of *(7)* has been determined. Complex *(7)* crystallizes in the monoclinic space group $P2_1/c$ with a = 16.288(3), b = 12.4272(10) and c = 13.620(3) Å, and β = 76.63(1)°. For a future application of the small "*fac*-$M(CO)_3$" moiety, it seems thus advantageous to combine these two ligand groups in one simple chelating function.

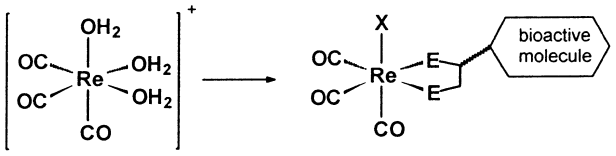
Introduction

The application of metal complexes with a wide variety of radionuclides in the field of nuclear medicine has become a major tool in diagnosis and also more recently in therapy[1–3]. Beside the potential for routine application of various radioisotopes such as ^{67}Cu, ^{105}Rh or ^{111}Ag, complexes with ^{99m}Tc or $^{186/188}Re$ are in widespread use or have reached the stage of preclinical evaluation. To develop stable tailor made bifunctional chelators, complexes or precursors linkable to small or large biomolecules, retaining their bioactivity, is a challenge to inorganic chemistry. A number of reviews covering this interdisciplinary field have appeared recently[4–7]. The most successful approaches with Tc or Re are focused mainly on complexes with the valency +V, typically containing the $[Tc{=}O]^{3+}$ moiety and readily achieved by reducing $[^{99m}TcO_4]^-$ with, for example, $[Sn]^{2+}$. For $[^{186}ReO_4]^-$ more vigorous conditions have to be used. Further attempts to achieve flexibility and convenience, based on the $[Tc{=}O]^{3+}$ moiety, are based on the so-called [3 + 1] strategies[8–11]. Three coordination sites around this core are protected, whereas the fourth site is coordinated with the biomolecule. This approach requires only derivatization with one single group and not with a tetradentate ligand. A further attractive approach, not based on the $[Tc{=}O]^{3+}$ moiety, is the application of hydrazides, which can provide very stable TcN multiple bonds. The monodentate "hynic" ligand is a good example of this strategy[12–14].

Whether thermodynamic or kinetically stable complexes are preferable for a radiopharmaceutical application is not yet very clear, but the potential of inertness has impressively been demonstrated with $[^{99m}Tc(CN\text{–}R)_6]^+$[15,16]. The $[^{99m}Tc(CN\text{–}R)_6]^+$ complexes are rare examples where radioactive organometallic compounds have been applied successfully, and several inactive investigations have demonstrated the potential of homoleptic isocyanide complexes of technetium(I) and rhenium(I)[17–20]. Application of organometallics suffers from a drawback, namely that most of potential precursors are prepared form $[MBr(CO)_5]$. To avoid $[MBr(CO)_5]$, we have developed a one-pot synthesis of the d^6 precursor $[MX_3(CO)_3]^{2-}$ directly from $[MO_4]^-$ under ambient conditions. The halides are labilized by the *trans* standing COs and are easily exchanged by incoming ligands. Both *(1a)* and *(1b)* form $[M(OH_2)_3(CO)_3]^+$ readily in water. A classical exchange can occur with ligand groups potentially bearing a biomolecule (Scheme 1).

* Author to whom all correspondence should be directed.

0340–4285



Scheme 1. The principle of anchor groups.

In order to develop convenient anchor groups or fragments, substitutions with a carboxylic acid and a bidentate thioether ligand have been performed.

Experimental

Crystallographic studies

The selected crystals of *(6)*, *(2a)* and *(7)* were measured on an Enraf-Nonius CAD-4 diffractometer. The unit cells were determined from 25 reflections each. During data collection, the crystals were monitored for decay every 100 reflections with three controls. No decay was observed in any of the crystals. Absorption corrections were applied from *psi*-scans. Additional relevant parameters for crystal data, data collection, structure solution and refinement are given in Table 1, and important bond lengths and angles in Table 2.

[NBu$_4$][Tc$_2$(μ-Cl)$_3$(CO)$_6$] (2a)

A 1 M $BH_3 \cdot THF$ solution (6 cm^3) was added to a THF solution (15 cm^3) of [NBu_4]Cl (0.38 g, 1.36 mmol) under N_2. Subsequently, CO was bubbled and [NBu_4][TcO_4] (0.19 g, 0.45 mmol) in THF (2 cm^3) was added dropwise over 15 min. The solution turned yellow after each addition but lost this colour within minutes. Stirring at r.t. for 5 h or boiling under reflux for 1 h completed the reaction. THF was removed by evaporation and the oily residue dissolved in CH_2Cl_2 (10 cm^3). Water (5 cm^3) was added and the mixture stirred for 4 h. The organic layer was separated and the solvent evaporated. Mixing the residue with H_2O caused precipitation of the colourless product (yield: 0.13 g, 79%). I.r. (KBr/cm^{-1}): 2036, 1940 and 1914 [ν(CO)]; ^{99}Tc NMR (δ, $[TcO_4]^-$ in D_2O = 0 p.p.m.): −965 (s, $\Delta_{1/2}$ = 25 Hz).

[NEt$_4$][Re$_2$(μ-OC$_2$H$_5$)$_2$(OAc)(CO)$_6$] (7)

Complex *(1b)* (0.15 g, 0.18 mmol) was dissolved in water (3 cm^3) and Ag(OAc) (0.095 g, 0.56 mmol), dissolved in H_2O, was added. The precipitate (AgBr) was removed by filtration and H_2O evaporated *in vacuo*. The residue was dissolved in EtOH and slow diffusion of Et_2O resulted in crystals (yield: 0.063 g) of X-ray quality within a few days (75%). I.r. (KBr cm^{-1}): 1984, 1864 and 1838 [ν(CO)].

[ReBr(qyp)(CO)$_3$] (6)[†]

(1b) (0.123 g, 0.16 mmol) was dissolved in MeOH (5 cm^3) and qyp (0.035 g, 0.16 mmol) added. The solution was stirred over night at r.t., the solvent evaporated *in vacuo* and the waxy residue obtained stirred with Et_2O to form a crystalline solid. The solvent was separated and the product extracted from [NEt_4]Br with THF. Slow diffusion of hexane yielded crystals (78 mg) of

Table 1. Crystal data, data collection and solution refinement parameters for the X-ray structures of $[Re_2(\mu\text{-OEt})_2(OAc)(CO)_6]^-$ *(7)*, $[Tc_2(\mu\text{-Cl})_3(CO)_6]^-$ *(2a)* and [ReBr(qyp)$(CO)_3$] *(6)*[a]

	(7)	*(2a)*	*(6)*
Crystal data			
Formula	$C_{20}H_{33}NO_{10}Re_2$	$C_{22}H_{36}Cl_3NO_6Tc_2$	$C_9H_{12}BrCl_2O_3S_2Re$
M (g/mol)	819.87	712.87	569.32
Crystal system	monoclinic	monoclinic	monoclinic
Space group (Nr.)	$P2_1/c$ (14)	$P2_1/c$ (14)	$P2_1/c$ (14)
a (Å)	16.228(3)	19.491(6)	15.935(6)
b (Å)	12.4272(10)	18.323(2)	2.788(4)
c (Å)	13.620(3)	17.497(9)	7.955(10)
β (°)	76.63(1)	97.59(2)	98.57(1)
V (Å^3)	2672.3(8)	6194(4)	1602(2)
Z	4	8	4
ρ_{calc} (g cm^{-3})	2.038	1.529	2.359
μ, (mm^{-1})	9.100	1.184	10.663
F(000)	15600	2880	1064
Data collection			
2θ range (°)	3.04–28.92	3.06–25.00	3.04–26.98
h,k,l	−22/21; 0/16; −18/1	−24/24; −2/0; −1/22	−19/19; −16/0; −1/10
Nr. of reflections	7910	12029	4085
Independent reflections	7079	10888	3356
R_{int} (%)	2.24	1.3356	2.43
Observed reflections [$I > 2\sigma(I)$]	5877	8553	2860
Structure solution and refinement			
Goodness of fit (GooF)	1.162	1.076	1.149
$R1$ (%)	3.4	4.79	2.77
$wR2$ (%)	8.0	12.48	5.80
Rest electron density (e Å^{-3})	2.125; −1.371	1.273; −0.808	1.297; −1.356

[a] Details in common: diffractometer, CAD 4 Enraf-Nonius; radiation, MoK_α λ = 0.70930 Å; graphite monochromator; absorption correction, *psi* scans; temperature, 203(2) K.

[†] *Caution*! qyp Is a blister-causing vessicant.

Table 2. Important bond lengths (Å) and angles (°) in the complexes *(7)*, *(2a)* and *(6)*

(7)		*(2a)*		*(6)*	
Bond lengths					
Re(1)—C(3)	1.886(6)	Tc(1)—C(1)	1.904(8)	Re—C(10)	1.979(6)
Re(1)—C(1)	1.901(7)	Tc(1)—C(2)	1.889(7)	Re—C(20)	1.936(6)
Re(1)—C(2)	1.901(7)	Tc(1)—C(3)	1.884(7)	Re—C(30)	1.917(11)
Re(1)—O(10)	2.100(4)	Tc(1)—Cl(3)	2.520(2)	Re—S(2)	2.525(3)
Re(1)—O(20)	2.111(4)	Tc(1)—Cl(1)	2.5477(13)	Re—Br(1)	2.6087(10)
Re(1)—O(31)	2.176(4)	Tc(1)—Cl(2)	2.506(2)	Re—S(1)	2.537(2)
Re(2)—C(5)	1.886(8)	Tc(2)—C(4)	1.891(8)		
Re(2)—C(4)	1.886(6)	Tc(2)—C(5)	1.891(9)		
Re(2)—C(6)	1.898(7)	Tc(2)—C(6)	1.895(8)		
Re(2)—O(32)	2.169(4)	Tc(2)—Cl(1)	2.5658(13)		
Re(2)—O(20)	2.117(4)	Tc(2)—Cl(2)	2.503(2)		
Re(2)—O(10)	2.114(4)	Tc(2)—Cl(3)	2.520(2)		
Bond angles					
Re(1)—O(20)—Re(2)	105.7(2)	C(1)—Tc(1)—Cl(1)	96.3(2)	C(10)—Re—S(1)	173.2(2)
Re(1)—O(10)—Re(2)	106.3(2)	C(1)—Tc(1)—Cl(2)	93.3(2)	C(20)—Re—S(1)	89.0(2)
O(20)—Re(1)—O(31)	81.6(2)	C(1)—Tc(1)—Cl(3)	173.5(2)	C(30)—Re—S(1)	96.1(2)
O(10)—Re(1)—O(31)	82.1(2)	C(2)—Tc(1)—Cl(2)	95.2(2)	C(10)—Re—S(2)	92.8(2)
C(3)—Re(1)—O(10)	98.8(2)	C(2)—Tc(1)—Cl(3)	93.4(2)	C(20)—Re—S(2)	175.2(2)
C(1)—Re(1)—O(10)	99.3(2)	C(3)—Tc(1)—Cl(1)	93.6(2)	C(30)—Re—S(2)	90.2(3)
C(2)—Re(1)—O(10)	171.0(2)	C(3)—Tc(1)—Cl(2)	175.4(3)	C(10)—Re—Br(1)	90.6(2)
O(10)—Re(1)—O(20)	73.7(2)	C(3)—Tc(1)—Cl(3)	97.9(3)	C(30)—Re—Br(1)	177.3(2)
C(1)—Re(1)—O(20)	172.7(2)	Cl(2)—Tc(1)—Cl(1)	81.93(5)	C(20)—Re—Br(1)	87.4(2)
C(2)—Re(1)—O(20)	99.6(2)	Cl(2)—Tc(1)—Cl(3)	80.43(6)	S(2)—Re—S(1)	86.17(8)
C(3)—Re(1)—O(20)	97.6(2)	Cl(3)—Tc(1)—Cl(1)	81.19(5)		
C(3)—Re(1)—O(31)	178.7(2)	Tc(1)—Cl(1)—Tc(2)	81.55(4)		
C(1)—Re(1)—O(31)	95.4(2)	Tc(2)—Cl(2)—Tc(1)	83.63(5)		
C(2)—Re(1)—O(31)	91.0(2)	Tc(2)—Cl(3)—Tc(1)	82.98(5)		

X-ray quality (86%). I.r. (KBr/cm^{-1}): 2032, 1942, 1908 and 1892 [ν(CO)].

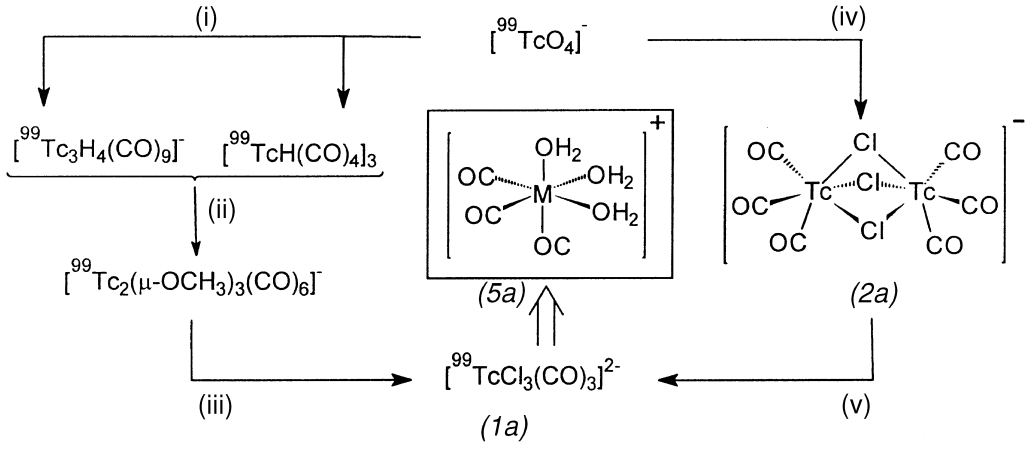
Results and discussion

Low-pressure carbonylation

The synthesis of *(1a)* and *(1b)* is one of the rare examples where a low-valent carbonyl complex is prepared directly from its permetallate[21,22]. Although the overall process includes a 6e$^-$ reduction, no defined compounds in the intermediate oxidation states could be trapped. As is evident from reactions with [^{188}ReO$_4$]$^-$, however, the different end-products were convertable into *(5)* by acid or alkaline hydrolysis. In order to elucidate the nature of these products, similar reactions were performed with [^{99}TcO$_4$]$^-$. Scheme 2 depicts the products characterized by X-ray structure or chemical analysis.

Performing the reaction in THF in the presence of halide yielded, as a direct precursor of *(1a)*, the dinuclear complex *(2a)*. Complex *(1a)* remained in solution due to the presence of the [NBu$_4$]$^+$ counter-ion. Isolation of *(2a)* was successful due to its insolubility in H$_2$O. Complex *(1a)* can be precipitated by addition of [NEt$_4$]$^+$ and *(2a)* is slowly converted into *(1a)* by cleaving the Cl$^-$ bridges and subsequent precipitation with [NEt$_4$]Cl in EtOH. The structure of *(2a)* was elucidated and an *ORTEP* presentation is given in Figure 1. The Re analogue was already known from the standard approach, starting with [Re$_2$(CO)$_{10}$][23].

The reaction with [^{188}ReO$_4$]$^-$ gave no unambiguous evidence for the identity of one of the byproducts with *(2a)*. For this reason the reaction was performed with ^{99}Tc in the absence of halide in order to mimic the very small halide concentration with ^{188}Re. By this approach the two carbonyl hydride complexes [TcH(CO)$_4$]$_3$ *(4)*



Scheme 2. General conditions to prepare Tc^I-carbonyl precursors: (i) CO (1 atm), THF, BH$_3$·THF, 30–50 °C; (ii) NaOH/MeOH r.t.; (iii) 1 M HCl/H$_2$O; (iv) CO (1 atm), THF, BH$_3$·THF, [NBu$_4$]Cl, 30–50 °C; (v) ex. [NEt$_4$]Cl, EtOH.

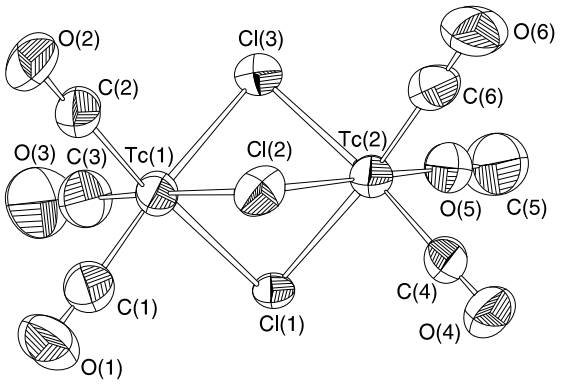


Figure 1. *ORTEP* presentation of the complex anion $[Tc_2(\mu\text{-}Cl)_3(CO)_6]^-$ *(2a)*. Thermal ellipsoids are drawn on the 30% level.

and $[NBu_4][Tc_3(\mu\text{-}H)_3(\mu_3\text{-}H)(CO)_9]$ *(3)* were isolated. Complex *(4)* was characterized by X-ray structure analysis, and *(3)* by spectroscopic methods[24]. Complex *(3)* exhibits a single resonance in the ^{99}Tc-n.m.r. spectrum at −1006 p.p.m. (relative to $[TcO_4]^-$ in D_2O), a typical "*fac*-$M(CO)_3$" pattern at 2023 and 1924 cm^{-1}, two singlets in the ^{1}H-n.m.r. and an additional set of $[NBu_4]^+$ signals in the correct ratio. The nature of the two byproducts containing ^{188}Re allowed us to develop a strategy for their conversion into *(1b)* and hence into *(5b)*, which is a base suitable for further coordination chemistry studies. The same procedure, as with ^{188}Re, is also possible with ^{99m}Tc. The reaction occurred in the latter case much faster and radiolysis, as observed with higher ^{188}Re activities, did not lead to decomposition.

We conclude ultimately that this synthesis of low valent Re- and Tc-carbonyls will open the way to their application in nuclear medical fields.

Substitution of (5a) and (5b) with acetate and qyp

The aquo-ions *(5a)* and *(5b)*, or the correspondingly solvated complexes, *e.g.* with methanol, have several distinct advantages over the usual precursors. In contrast to [MO(gluco)], for example, they are stable over a long period without the necessity of multidentate stabilizing ligands such as glucoheptonate or citrate and only monodentate solvent ligands such as H_2O or MeOH have to be substituted, which are additionally labilized by the *trans* CO ligands. Although a wide variety of complexes containing the "*fac*-$M(CO)_3$" moiety are known, hardly any resulted from ligand exchange based on solvent equilibrium, but instead from CO release in $[MX(CO)_5]$ at high temperature in non-coordinating solvents. It was thus necessary to study such reactions to investigate the kinetics and thermodynamics of complex formation. We have already described the reaction with thiols, isocyanides and aromatic or aliphatic amines in this respect[21,22,25]. For the design of anchor groups, the two aspects of charge and softness have to be considered. The d^6 systems of group 7 transition elements are generally characterized as soft, resulting in a preference for soft ligand atoms, *e.g.* thioethers or isocyanides. The strong π-backbonding of the CO ligands results in electron deficiency and an enhanced preference for weak donating ligands such as carboxylic acids or amines can be expected. The concerted donating/accepting properties of different atoms is highly important in designing an optimal anchor ligand.

The ligand $Cl(CH_2)_2S(CH_2)_2S(CH_2)_2Cl$ (qyp) has been chosen since it offers two moderately donating thioether functions that are easily derivatized at the non-coordinating terminal chlorides. The monopositive charge of *(5a)* or *(5b)* is expected to be neutralized by Cl^- present, in particular, in aqueous solution.

The reaction of qyp with *(1b)* in methanol, present as $[Re(HOMe)_3(CO)_3]^+$, was straightforward but slow. As evident from i.r. spectroscopy, $[Re(HOMe)qyp(CO)_3]^+$ formed initially, followed by Br^- substitution of the last MeOH, resulting in the neutral complex [ReBr(qyp)$(CO)_3$] *(6)*. An *ORTEP* presentation of the complex molecule is given in Figure 2.

Similar behaviour was observed in water. The ease of product formation with bidentate thioether groups make them versatile as anchor groups for biomolecules, since their preparation and derivatization is also convenient. The reaction with $[Re(HOMe)_3(CO)_3]^+$ occurred at a reasonable rate ($t_{1/2}$ = *ca.* 30 min) and under controlled conditions. Preliminary investigations at the n.c.a. level revealed that ligand concentration can be decreased to an almost stochiometric level, which represents significant progress from the above-mentioned protocols.

The carboxylato group is a typical anionic ligand, able to provide different modes of coordination. Alone or in combination with other groups, it is advantageous for our purposes in two respects. The monopositive charge of $[M(Sol)_3(CO)_3]^+$ is neutralized and additional electron density is shifted to the metal centre, supporting π-backbonding and inertness in combination with other ligand groups. It is easily included in a potential bidentate ligand for the same purposes, thus resulting in a simple, probably even naturally occurring, anchor group. To obtain fundamental information we have investigated the coordinative properties of ethanoic acid in water. The halides were previously precipitated with three equivalents of Ag(OAc). I.r. spectroscopic investigations in water revealed the formation of a neutral or anionic species as evident from the redshift of the CO stretching vibrations. T.l.c. showed the formation of a single species. This complex could be isolated and, after recrystallization from ethanol, structurally characterized. An *ORTEP* presentation of $[NEt_4][Re_2(\mu\text{-}OEt)_2(OAc)(CO)_6]$ *(7)* is given in Figure 3. The acetato group

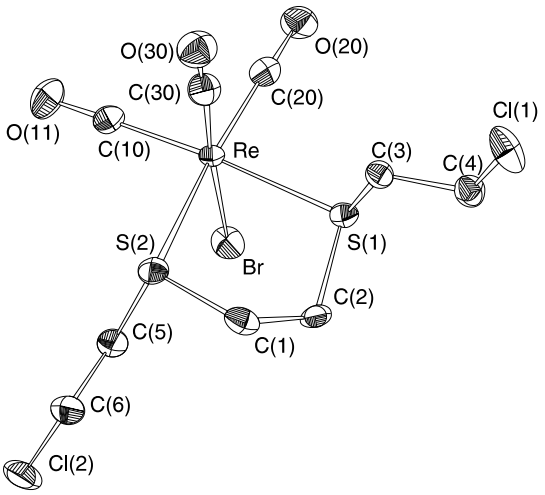


Figure 2. *ORTEP* presentation of the complex [ReBr(qyp)$(CO)_3$]. Thermal ellipsoids are drawn on the 30% level.

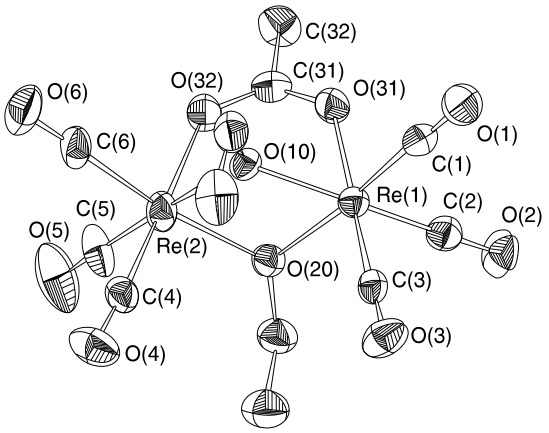


Figure 3. *ORTEP* presentation of the complex anion $[Re_2(\mu\text{-}OEt)_2(OAc)(CO)_6]^-$. Thermal ellipsoids are drawn on the 30% level.

acts as a bridging ligand between two Re centres to form a dinuclear complex. Two bridging ethanolato ligands occupy the remaining coordination sites.

After isolation from aqueous media, a sharp O—H stretching vibration could be detected. Recrystallization from ethanol resulted in the substitution of (μ-OH) groups by the corresponding alcoholato functions without touching the acetato ligand. Potentiometric titration of *(1b)* in water yielded the tri- and dinuclear species $[Re_3(\mu\text{-}OH)_3(\mu_3\text{-}OH)(CO)_9]^-$ and $[Re_2(\mu\text{-}OH)_3(CO)_6]^-$[26], respectively. It was obvious from those experiments that the hard $2e^-$ donating ligand $[OH]^-$ tends to form bridges between metal centres. The "*fac*-$M(CO)_3$" moiety is not able to accept the provided high-electron density from a single ligand, but tries to distribute the charge over different cations. The same behaviour was found to be true with the much weaker donating acetato group and only bridging allowed coordination to the "*fac*-$M(CO)_3$" moiety. Since acetate can act as a OH^- source the remaining positions are predominantly occupied by this ligand. From these observation carboxylato groups are not very convenient as single ligands. Ligands have to include other groups of backbonding properties that provide chelation to the metal centre. Reaction of *(5a)* or *(5b)* in water with picolinic acid, for example, did not result in a bridged species but in the formation of a mononuclear complex of composition $[ReBr(pic)(CO)_3]$, exhibiting exceptional stability towards acid[25].

Conclusion

The synthesis of *(1a)* or *(1b)* from $[TcO_4]^-$ or $[ReO_4]^-$ under 1 atm of CO at ambient temperature is an important step towards the application of organometallic complexes in nuclear medicine. It is possible to prepare these precursors on the n.c.a. as well as on the macroscopic level. Since *(1a)* and *(1b)* are converted into the "semi-aquo-ions" *(5a)* and *(5b)*, simple ligand exchange reactions with easily available anchor groups can be performed. Owing to their "soft" nature, ligands such as thioethers are preferred as exemplified by the synthesis of *(6)*. Single carboxylato groups such as acetate were shown to bridge two metal centres. Thus, single carboxylato groups seemed not to be particularly advantageous since one "*fac*-$M(CO)_3$" moiety can not accept the high-electron density provided by acetate. The fact that the carboxylate is able to coordinate to the soft "*fac*-$Re(CO)_3$" moiety mirrors, however, its usefulness in combination with other ligand groups, *i.e.* those derived from thioether functions.

Supporting material

Complete information about crystal data, data collection, structure solution and refinement and tables of bond lengths, bond angles, positional and thermal parameters of compounds *(2a)*, *(6)* and *(7)* have been deposited with the Editor.

References

(1) W. A. Volkert, G. J. Goeckeler, and A. R. Ketring, *J. Nucl. Med.*, **32**, 174 (1991).
(2) P. A. Schubiger, R. Alberto and A. Smith, *Bioconjugate Chem.*, **7**, 165 (1996).
(3) S. Jurisson, D. Berning, W. Jia and D. Ma, *Chem. Rev.*, **93**, 1137 (1993).
(4) E. Deutsch and K. Libson, *Commun. Inorg. Chem.*, **3**, 83 (1984).
(5) M. J. Clarke and J. Podbielsky, *Coord. Chem. Rev.*, **78**, 253 (1987).
(6) W. C. Eckelman, *The Chemistry of Technetium in Medicine*, National Academic Press, Washington, 1992.
(7) A. M. Verbruggen, *Eur. J. Nucl. Med.*, **17**, 346 (1990).
(8) H. J. Pietzsch, H. Spies, S. Hoffmann and D. Scheller, *Appl. Radiat. Isot.*, **41**, 185 (1990).
(9) G. Bandoli, U. Mazzi, H. J. Pietzsch and H. Spies, *Acta Crystallogr., Sect. C*, **48**, 1422 (1992).
(10) H. J. Pietzsch, H. Spies and S. Hoffmann, *Inorg. Chim. Acta*, **168**, 7 (1990).
(11) H. Spies and B. Johannsen, *Analyst*, **120**, 775 (1995).
(12) M. J. Abrams, S. K. Larsen, J. Zubieta, *Inorg. Chim. Acta*, **173**, 133 (1990).
(13) R. Pasqualini, C. Veronique, E. Bellande, A. Duatti and A. Marchi, *Appl. Radiat. Isot.*, **11**, 1329 (1992).
(14) C. M. Archer, J. R. Dilworth, P. Jobanputra, R. M. Thompson, M. McPartlin, D. C. Povey and J. D. Kelly, *Polyhedron*, **9**, 1497 (1990)
(15) M. J. Abrams, A. Davison, A. G. Jones, C. E. Costello and H. Pang, *Inorg. Chem.*, **22**, 2798 (1983).
(16) R. Taillefer, L. Laflamme and G. Dupras, *Eur. J. Nucl. Med.*, **13**, 515 (1988).
(17) W. H. Soine, C. E. Guyer and F. F. Knapp, *J. Med. Chem.*, **27**, 803 (1984).
(18) D. Vichard, M. Gruselle, H. E. Amouri and G. Jaouen, *J. Chem. Soc., Chem. Commun.*, **46**, (1991).
(19) M. Salmain, M. Gunn, A. Gorfti, S. Top and G. Jaouen, *Bioconjugate Chem.*, **4**, 425 (1993).
(20) A. Gorfti, M. Salmain, G. Jaouen, M. J. McGlinchey, A. Bennouna and A. Mousser, *Organometallics*, **15**, 142 (1996).
(21) R. Alberto, R. Schibli, A. Egli, P. A. Schubiger, W. A. Herrmann, G. Artus, U. Abram and T. A. Kaden, *J. Organometal. Chem.*, **493**, 119 (1995).
(22) R. Alberto, R. Schibli, P. A. Schubiger, U. Abram and T. A. Kaden, *Polyhedron*, **15**, 1079 (1996).
(23) T. Beringhelli, G. D'Alfonso and M. Zarini, *J. Chem. Soc., Dalton Trans.*, 2407 (1995).
(24) R. Alberto, R. Schibli, P. A. Schubiger, U. Abram, R. Hübener, H. Berke and T. A. Kaden, *J. Chem. Soc., Chem. Commun.*, 1291 (1996).
(25) R. Alberto, R. Schibli, U. Abram, P. A. Schubiger and T. A. Kaden, submitted for publication in *Inorg. Chem.*
(26) R. Alberto, A. Egli, U. Abram, K. Hegetschweiler, V. Gramlich and P. A. Schubiger, *J. Chem. Soc., Dalton Trans.*, 2815 (1994).

(Received 27 March 1997
Accepted 9 May 1997) TMC 3949