# Synthesis and Characterization of Oxorhenium and Oxotechnetium Complexes with a Novel Tetradentate $N_3O$ Bifunctional Agent

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The novel tetradentate $N_3O$ bifunctional agent 3-hydroxy-4-[2-(2′-pyridinecarboxamido)acetylamino]benzoic acid (**1**), reacts with $[Bu_4N][ReOCl_4]$ or $[Bu_4N][^{99g}TcOCl_4]$ in EtOH resulting in neutral and stable oxorhenium **2** or oxotechnetium-99 g **3** complexes. Both complexes were characterized by elemental analysis, IR, $^1H$ and $^{13}C$ NMR spectroscopy. X-ray analysis of **2** showed that the rhenium atom is pentacoordinate presenting a distorted square-pyramidal coordination geometry. The analogous oxotechnetium-99m complex **4** was also prepared quantitatively by the reaction of ligand **1** with $Na^{99m}TcO_4$ in isotonic saline using tin chloride as reducing agent. Its identity was established by chromatographic comparison to the oxorhenium **2** and oxotechnetium **3** complexes.

## Introduction

Technetium belongs to Group 7 of the Periodic Table and its chemistry has been explored extensively over the past years primarily because of the importance of the radioisotope $^{99m}Tc$ in the field of diagnostic nuclear medicine.[1,2] Rhenium, which also belongs to Group 7, exhibits similar chemical properties to technetium and is often used as a nonradioactive alternative to working with technetium radionuclides.[2] Furthermore, the β-emitting radionuclides $^{186}Re$ ($t_{1/2}$ = 90 h) and $^{188}Re$ ($t_{1/2}$ = 17 h) are of great interest to nuclear medicine as they possess physical and nuclear properties favourable for use in systemic radiotherapy.[3] In fact, $^{99m}Tc$ and $^{186/188}Re$ can be considered to be a matched pair for imaging and therapy.

The bifunctional strategy for the development of technetium and rhenium radiopharmaceuticals has become the most widely used method for producing well-defined technetium- and rhenium-labelled receptor ligands capable of highly specific in vivo localization in target tissues.[4] In this strategy a bifunctional coupling agent (BFCA) is used for the chelation of the radionuclide ($^{99m}Tc$ or $^{188}Re$) and the conjugation of the receptor ligand. An ideal BFCA is one which is able to form stable and inert $^{99m}Tc$ or $^{188}Re$ complexes in high yield at low concentration without the formation of isomers.

In this work, we report the synthesis and characterization of the new BFCA 3-hydroxy-4-[2-(2′-pyridinecarboxamido)acetylamino]benzoic acid and of the corresponding oxorhenium(V) and oxotechnetium(V) complexes. Studies at tracer level using $^{99m}Tc$ are also reported. This ligand is designed with the purpose of chelating to oxorhenium and oxotechnetium with an $N_3O$ donor system involving the pyridine nitrogen, the amide nitrogens and the phenolate oxygen. For coupling to the target molecule, the carboxyl group is selected since many biomolecules contain amino groups available for formation of amide bonds. Furthermore, this ligand system does not lead to formation of *syn-anti* isomers.

## Results and Discussion

Condensation of ethyl 4-amino-3-hydroxybenzoate, N-Boc-glycine and 2-carboxypyridine in the presence of DCC resulted in the novel tetradentate ligand 3-hydroxy-4-[2-(2′-pyridinecarboxamido)acetylamino]benzoic acid (**1**; Scheme 1).[5] The product was purified by flash column chromatography and characterized by elemental analysis, $^1H$ and $^{13}C$ NMR spectroscopy (Table 1 and Figure 1).

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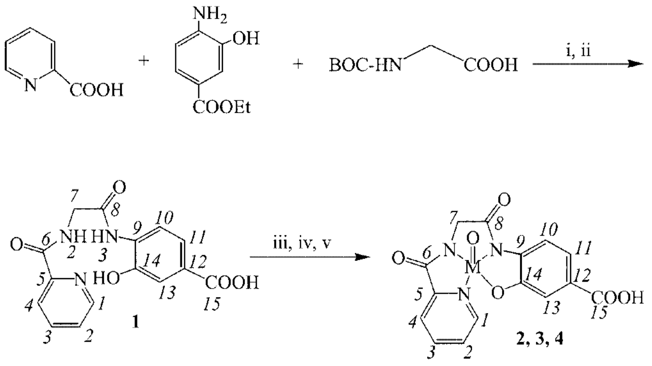

Scheme 1. Synthesis of ligand and complexes studied: (i) DCC, THF, 25 °C, 4 h; (ii) $NaHCO_3$, $CH_3COOH$ (yield 42%); (iii) M = Re, $[Bu_4N][ReOCl_4]$ for **2**; (iv) M = $^{99g}$Tc, $[Bu_4N][^{99g}TcOCl_4]$ for **3**; (v) M = $^{99m}$Tc, $Na^{99m}TcO_4$, $SnCl_2$ for **4**

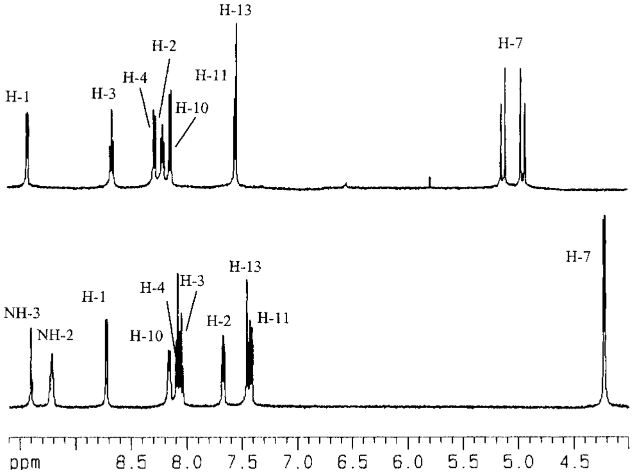

Figure 1. $^1$H NMR spectra of ligand **1** (bottom) and complex **3** (top) in [D$_6$]DMSO (range 9.60−4.00 ppm) at 25 °C

The oxorhenium complex **2** was prepared by reacting ligand **1** with the $[Bu_4N][ReOCl_4]$ precursor in EtOH (Scheme 1). A similar reaction was employed for the preparation of the oxotechnetium complex **3** using $[Bu_4N][^{99g}TcOCl_4]$ as a precursor. Complexes **2** and **3** were characterized by elemental analysis, IR, UV/Vis, $^1$H and $^{13}$C NMR spectroscopy (Table 1 and Figure 1). Complex **2** was also characterized by X-ray crystallography. Both complexes are soluble in DMSO, slightly soluble in dichloromethane, methanol and ethanol and insoluble in water. They are stable in the solid state as well as in organic solvents (for a period of months), as shown by HPLC and NMR spectroscopy. Their stability is not affected by the presence of air or moisture.

The IR spectra of the complexes show characteristic peaks at 981 cm$^{-1}$ and 972 cm$^{-1}$ that can be attributed to oxorhenium and oxotechnetium bond stretches respectively.[6] The Re=O stretch in **2** is higher than the Tc=O stretch in **3**. This shift to higher frequencies of the Re=O compared to Tc=O complex has been attributed to the greater orbital overlap of the 5d orbitals of rhenium as compared to the 4d orbitals of technetium.[7] The electronic absorption spectra of the oxorhenium and oxotechnetium complexes were determined upon HPLC analysis by using a photodiode array detector. The UV/Vis spectrum of complex **2** is characterized by an intense band at 380 nm, while the UV/Vis spectra of the oxotechnetium complex **3** is characterized by an intense band at 480 nm.

An ORTEP diagram of complex **2** is given in Figure 2. Selected distances and angles are listed in Table 2. The coordination geometry about the metal is distorted square pyramidal with the pyridine nitrogen, the two amide nitrogens and the phenolate oxygen of the tetradendate ligand occupying the equatorial plane and the oxo group directed in the apical position. The carboxylate group of the tetradentate ligand remains uncoordinated. Rhenium lies 0.76 Å out of the equatorial plane toward the oxo group. The angles between the opposite atoms of the equatorial plane severely deviate from the ideal value of 180° [N(1)−Re−N(3) = 135.3(3)°, N(2)−Re−O(3) = 134.7(3)°]. Inspection of the shape-determining angles about the metal

Table 1. $^1$H and $^{13}$C NMR chemical shifts (ppm) for ligand **1** and complexes **2** and **3** in [D$_6$]DMSO at 25 °C; the numbering used is shown in Scheme 1 and is according to the crystallographic structure of Figure 2

| | **1** | **2** | **3** | | **1** | **2** | **3** |
|---|---|---|---|---|---|---|---|
| H-1 | 8.72 | 9.55 | 9.42 | C-1 | 148.64 | 159.40 | 151.69 |
| H-2 | 7.67 | 8.31 | 8.21 | C-2 | 126.97 | 128.63 | 129.22 |
| H-3 | 8.05 | 8.56 | 8.66 | C-3 | 138.00 | 144.34 | 146.02 |
| H-4 | 8.09 | 8.15 | 8.28 | C-4 | 121.98 | 124.86 | 125.05 |
| H-7 | 4.23 | 5.24, | 5.13, | C-5 | 149.29 | 152.68 | 151.87 |
| | | 4.83 ($^2J$ = 18.3 Hz) | 4.95 ($^2J$ = 18.0 Hz) | C-6 | 163.59 | 179.05 | 170.74 |
| | | | | C-7 | 43.58 | 59.88 | 58.22 |
| H-10 | 8.16 | 8.29 | 8.14 | C-8 | 168.01 | 184.05 | 181.07 |
| H-11 | 7.42 | 7.45 | 7.56 | C-9 | 146.13 | 147.56 | 145.14 |
| H-13 | 7.45 | 7.54 | 7.54 | C-10 | 119.72 | 116.89 | 116.90 |
| NH-2 | 9.22 | – | – | C-11 | 120.96 | 120.64 | 121.57 |
| NH-3 | 9.40 | – | – | C-12 | 125.83 | 126.01 | 126.62 |
| OH | 10.35 | – | – | C-13 | 115.44 | 116.04 | 115.09 |
| COOH | 12.69 | 12.73 | 12.74 | C-14 | 146.03 | 173.35 | 165.12 |
| | | | | C-15 | 166.62 | 167.75 | 166.63 |

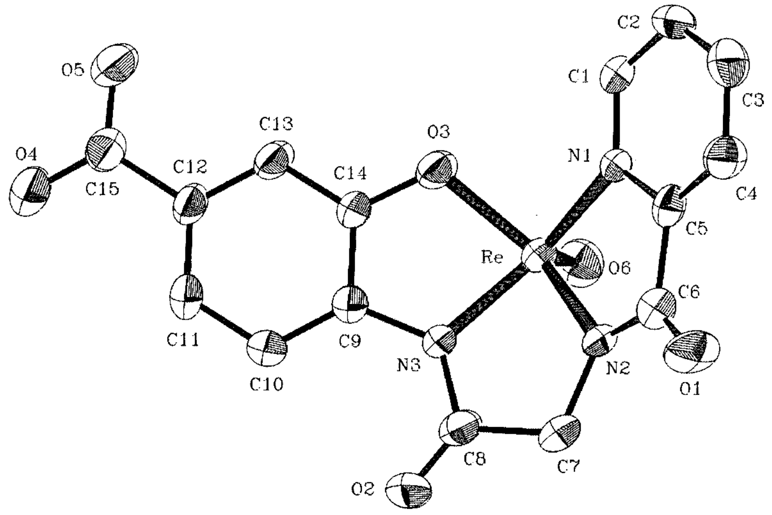

Figure 2. ORTEP diagram of **2** with 50% probability thermal ellipsoids showing the atomic labelling scheme

according to the analysis of Addison et al.[8] gives a value of 0.01 for the trigonality index, τ. The $Re-N_{amide}$ bond lengths are 1.965(6) Å while the $Re-N_{pyridine}$ bond length is slightly longer at 2.076(6) Å. The $Re-O_{oxo}$ and the $Re-O_{phenolate}$ bond lengths are 1.685(6) and 1.962(5) Å respectively. These values are in agreement with those found in analogous pentacoordinate oxorhenium complexes.[9] However, the $Re-N_{pyridine}$ and the $Re-O_{phenolate}$ bond lengths are shorter than heptacoordinated oxorhenium complexes with similar donor centers.[10] The two five-membered rings in the coordination sphere, i.e. those defined by Re−N2−C7−C8−N3 and Re−N3−C9−C14−O3 adopt the stable envelope configuration, with the metal being 0.53 and 0.35 Å, respectively, out of the mean plane of the remaining four atoms. On the contrary, the five-membered ring defined by Re−N1−C5−C6−N2 is planar, with C5 having the largest displacement of 0.028 Å out of the best mean plane.

Table 2. Selected bond lengths (Å) and angles (°) for complex **2**

| Distances (Å) | | | |
|---|---|---|---|
| Re−O(6) | 1.685(6) | Re−N(2) | 1.965(6) |
| Re−O(3) | 1.962(5) | Re−N(3) | 1.965(6) |
| Re−N(1) | 2.076(6) | | |
| **Angles (°)** | | | |
| O(6)−Re−O(3) | 112.9(3) | N(3)−Re−N(2) | 79.1(3) |
| O(6)−Re−N(3) | 113.1(3) | O(6)−Re−N(1) | 111.3(3) |
| O(3)−Re−N(3) | 80.4(2) | O(3)−Re−N(1) | 87.8(2) |
| O(6)−Re−N(2) | 112.2(3) | N(3)−Re−N(1) | 135.3(3) |
| O(3)−Re−N(2) | 134.7(3) | N(2)−Re−N(1) | 79.4(2) |

The two amide functions of the tetradentate ligand are planar, as indicated by the values of the $\omega_1$ (C-C-*N*-C), $\omega_2$ (O-C-*N*-M) and $\omega_3$ (O-C-*N*-C) torsion angles and the values of the parameters $\tau\ [(\omega_1 + \omega_2)/2(|\omega_1 - \omega_2| < \pi)]$, $\chi_N\ [(\omega_2 - \omega_3 + \pi)\mathrm{mod}2\pi]$ and $\chi_C\ [(\omega_1 - \omega_3 + \pi)\mathrm{mod}2\pi]$, where τ is the approximate measure of the angles between the nitrogen and carbonyl carbon π orbitals and $\chi_N$ and $\chi_C$ describe the out-of-plane bending at the amide nitrogen and at the amide carbon respectively.[11] The torsion angles for the one amide group are: $\omega_1$ = C5−C6−N2−C7 = −165.47°, $\omega_2$ = O1−C6−N2−Re = 173.14° and $\omega_3$ = O1−C6−N2−C7 = 11.32° thus, the calculated parameters are τ = 3.84°, $\chi_N$ = −18.18° and $\chi_C$ = 3.21°. For the second amide function these angles are: $\omega_1$ = C7−C8−N3−C9 = −158.85°, $\omega_2$ = O2−C8−N3−Re = −167.91° and $\omega_3$ = O2−C8−N3−C9 = 22.33° thus, the calculated parameters are τ = −163.38°, $\chi_N$ = −10.24° and $\chi_C$ = −1.18°.

The short interatomic distance between the carboxylate oxygens O(4)···O(5′) (1 − *x*, 1 − *y*, −*z*) = 2.603 Å belonging to adjacent molecules is probably indicative of a hydrogen bonding interaction, although the hydrogen atom was not located in the difference map.

The synthesis of the complex was successfully transferred at tracer level ($^{99m}Tc$). Ligand **1** reacted with $Na^{99m}TcO_4$ in isotonic saline using tin chloride as reducing agent (Scheme 1) to give the oxotechnetium-99m complex **4**. The radiochemical purity of the reaction mixture was checked by HPLC and the radioactivity of the major peak was more than 85%, while the recovery of radioactivity from the column was quantitative. The characterization of complex **4** was accomplished by chromatographic comparison (HPLC) to the analogous oxorhenium (**2**) and oxotechnetium-99 g (**3**) complexes adopting parallel radiometric and photometric detection. Thus, by co-injection of the respective $^{99m}Tc$ and $Re/^{99g}Tc$ complexes, identical retention times were obtained revealing the structural analogy of the three complexes (Figure 3).

In conclusion, the novel tetradentate ligand 3-hydroxy-4-[2-(2′-pyridinecarboxamido)acetylamino]benzoic acid (**1**) was synthesized and successfully used for the synthesis of stable and neutral complexes with rhenium and technetium at carrier ($Re/^{99g}Tc$) and at tracer level ($^{99m}Tc$). The carboxyl group does not coordinate to the metal and thus it

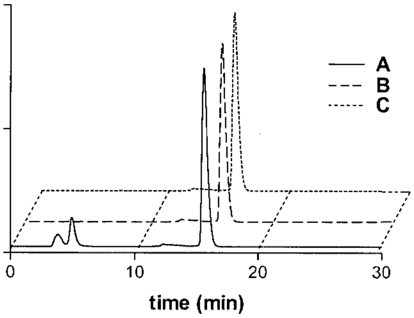

Figure 3. Comparative reverse-phase HPLC chromatograms: **A** (radiometric detection): reaction mixture from the preparation at tracer level ($^{99m}$Tc), complex **4** ($t_R$: 15.58 min, 85%); **B** (UV recording at 254 nm): complex **2** ($t_R$: 15.04 min); **C** (UV recording at 254 nm): complex **3** ($t_R$: 15.34 min)

could be used for the conjugation of the receptor ligand to develop target-specific radiopharmaceuticals for diagnosis and therapy.

## Experimental Section

*Caution!!!* Technetium-99 g is a weak β-emitter (0.292 MeV) with a half life of $2.12 \times 10^5$ years. All manipulations of solutions and solids were carried out in a laboratory approved for the handling of low-level radioisotopes. Normal safety procedures were followed at all times to prevent contamination.

IR spectra were recorded as KBr pellets in the range 4000−500 cm$^{-1}$ on a Perkin−Elmer 1600 FT-IR spectrophotometer. NMR spectra were recorded in [D$_6$]DMSO, at 25 °C on a Bruker 500 MHz Avance DRX spectrometer using TMS as internal standard. Chemical shift assignments were based on a series of 2D homo- and heteronuclear correlation spectra. Elemental analyses were performed on a Perkin−Elmer 2400/II automated analyser. $^{99g}$Tc was purchased as ammonium pertechnetate from the Oak Ridge National Laboratory. The impure black solid was purified prior to use by overnight treatment with hydrogen peroxide and ammonium hydroxide in methanol. Evaporation of the solvent gave ammonium pertechnetate as a white powder. Na$^{99m}$TcO$_4$ was obtained in isotonic saline as commercial $^{99}$Mo/$^{99m}$Tc generator eluate (Cis International). The precursors [Bu$_4$N][ReOCl$_4$] and [Bu$_4$N][$^{99g}$TcOCl$_4$] were synthesized by literature methods.[12,13] Ethyl 4-amino-3-hydroxybenzoate was prepared by refluxing 4-amino-3-hydroxybenzoic acid in EtOH in the presence of HCl. All laboratory chemicals were reagent grade.

High performance liquid chromatography (HPLC) analysis was performed on a Waters 600E Chromatography System coupled to both a Waters 991 photodiode array detector (UV trace for $^{99g}$Tc, Re and ligands) and a GABI gamma detector from Raytest (γ trace for $^{99m}$Tc). Separations were achieved on a Techsil C18 (10 µm, 250 mm × 4 mm) column eluted with a binary gradient system at a 1.0 mL/min flow rate. Mobile phase A was water containing 0.1% trifluoroacetic acid while mobile phase B was methanol. The elution profile was: 0 min 5% B followed by a linear gradient to 70% in 8 min; this composition was held for another 12 min. Prior to each injection the column was washed with 95% B for 5 min and re-equilibrated by applying the initial conditions (5% B) for 15 min.

NMR spectroscopic data for **1**, **2** and **3** are given in Table 1.

**Synthesis of Ligand 1:** A solution in THF (40 mL) of ethyl 4-amino-3-hydroxybenzoate (1.81 g, 0.01 mol), N-Boc-glycine (1.75 g, 0.01 mol), 2-carboxypyridine (1.23 g, 0.01 mol) and *N*,*N*′-dicyclohexylcarbodiimide (2.48 g, 0.012 mol) was stirred at room temperature for 4 hours. The insoluble urea was removed by filtration, the solvent was replaced by ethyl acetate and the solution was washed with dilute acetic acid and aqueous sodium hydrogencarbonate. The solvent was removed and the product was purified by flash column chromatography (silica gel 60, CHCl$_3$/MeOH/CH$_3$COOH, 77:15:8). Yield 42%. $C_{15}H_{13}N_3O_5$ (315.28): calcd. C 57.14, H 4.16, N 13.33; found C 57.07, H 4.22, N 13.17.

**Synthesis of Oxorhenium Complex 2:** A solution of ligand **1** (40 mg, 0.1 mmol) in MeOH (3 mL) was added to a solution of [Bu$_4$N][ReOCl$_4$] (58.6 mg, 0.1 mmol) in MeOH (15 mL). The reaction mixture was refluxed for 1 h. After cooling to room temperature the reaction mixture was diluted with CH$_2$Cl$_2$ and then washed with water. The organic layer was collected and dried over MgSO$_4$. The volume of the solution was reduced and then 5 mL of MeOH was added. Slow evaporation of the solvents at room temperature afforded the product as red crystals. Recrystallization from CH$_2$Cl$_2$/MeOH afforded crystals of **2** suitable for X-ray crystallography. Yield: 50%; $R_f$ (SiO$_2$, CH$_2$Cl$_2$): 0.5; HPLC retention time: 15.04 min. FT-IR (KBr): $\tilde{\nu}$ = 981 cm$^{-1}$ (Re=O). UV/Vis: $\lambda_{max}$ = 229 nm, 271, 380. $C_{15}H_{10}N_3O_6Re$ (514.46): calcd. C 35.02, H 1.96, N 8.17; found C 34.95, H 1.94, N 8.04.

**Synthesis of Oxotechnetium-99g Complex 3:** A solution of **1** (40 mg, 0.1 mmol) in MeOH (2 mL) was added to a solution of [Bu$_4$N][$^{99g}$TcOCl$_4$] (50 mg, 0.1 mmol) in MeOH (10 mL) and the mixture was stirred at room temperature for 1 h. Upon standing, a brown solid precipitated that was collected and washed with Et$_2$O. Yield: 40%; $R_f$ (SiO$_2$,CH$_2$Cl$_2$): 0.5; HPLC retention time: 15.34 min. FT-IR (KBr): $\tilde{\nu}$ = 972 cm$^{-1}$ (Tc=O). UV/Vis: $\lambda_{max}$ = 229 nm, 265, 480. $C_{15}H_{10}N_3O_6Tc$ (427.16): calcd. C 42.18, H 2.36, N 9.84; found C 42.08, H 2.29, N 9.73.

**Synthesis of Oxotechnetium-99m Complex 4:** Ligand **1** (0.5 mg in 100 µL saline solution) and Na$^{99m}$TcO$_4$ (40 mCi in 600 µL saline solution) were added to a vial containing a 0.1 м solution of sodium citrate (100 µL). A fresh solution of SnCl$_2$ in EtOH (20 µg, 20 µL) was subsequently added and the mixture was left to react at room temperature for 15 min. The pH was then brought to 7.0 and the reaction was analysed by HPLC. HPLC retention time: 15.58 min. Labelling yield >85%. The identity of the $^{99m}$Tc complex was established by comparative HPLC studies using samples of the well-characterized corresponding oxorhenium and oxotechnetium complexes as references.

**X-ray Crystal Structure Determination:** A red crystal of **2** with approximate dimensions 0.04 × 0.20 × 0.40 mm was mounted in air. Diffraction measurements were made on a Crystal Logic Dual Goniometer diffractometer using graphite monochromated Mo-$K_\alpha$ radiation. Complete crystal data and parameters for data collection and refinement are listed in Table 3. Unit cell dimensions were determined and refined by using the angular settings of 25 automatically centered reflections in the range $11 < 2\theta < 23°$.

Intensity data were recorded using the θ-2θ scan method. Three standard reflections monitored every 97 reflections showed less than 3% variation and no decay. Lorentz, polarization and ψ-scan absorption corrections were applied using the Crystal Logic software.

Table 3. Summary of crystal data for complex **2**

| Parameter | **2** |
|---|---|
| Empirical formula | $C_{15}H_{10}N_3O_6Re$ |
| Mol. wt. | 514.46 |
| Crystal system | Monoclinic |
| Space group | $P2_1/n$ |
| $a$ (Å) | 9.836(6) |
| $b$ (Å) | 21.60(1) |
| $c$ (Å) | 7.606(5) |
| β (°) | 111.99(2) |
| $V$ (Å$^3$) | 1498(2) |
| Z | 4 |
| ρ (Mg·m$^{-3}$) | 2.281 |
| $T$ (°C) | 25 |
| λ (Mo-$K_{\alpha}$) (Å) | 0.71073 |
| μ (mm$^{-1}$) | 8.151 |
| $F$(000) | 976 |
| $2\theta_{\max}$ (°) | 50 |
| Index ranges | $-11 \leq h \leq 8$, $-25 \leq k \leq 0$, $0 \leq l \leq 9$ |
| No. of reflections collected | 2682 |
| No. of indep. refls./ Rint | 2519/0.0303 |
| Data with $I > 2\sigma(I)$ | 2184 |
| $(\Delta/\sigma)_{\max}$ | 0.041 |
| $GOF$ (on $F^2$) | 1.089 |
| $R1$[a] | 0.0376 |
| $wR2$[b] | 0.0947 |
| Residuals (e·Å$^{-3}$) | 0.798/−0.403 |

[a] $R1 = \Sigma(|F_o| - |F_c|)/\Sigma(|F_o|)$. [b] $wR2 = \{\Sigma[w[(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$.

The structure was solved by direct methods using SHELXS-86[14] and refined by full-matrix least-squares techniques on $F^2$ with SHELXL-93.[15] All hydrogen atoms (except that of the carboxylate group which was not included in the refinement) were located by difference maps and their positions were refined isotropically. All non-hydrogen atoms were refined anisotropically.

CCDC-208922 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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[1] S. Jurisson, J. D. Lydon, *Chem. Rev.* **1999**, *99*, 2205−2218.

[2] S. Jurisson, D. B. Berning, W. Jia, D. Ma, *Chem. Rev.* **1993**, *93*, 1137−1156.

[3] J. Dilworth, S. Parrot, *Chem. Soc. Rev.* **1998**, *27*, 43−55.

[4] S. Liu, D. S. Edwards, *Chem. Rev.* **1999**, *99*, 2235−2268.

[5] J. Sheehan, G. Hess, *J. Am. Chem. Soc.* **1955**, *77*, 1067−1068.

[6] [6a] U. Mazzi, *Polyhedron* **1989**, *8*, 1683−1688. [6b] T. N. Rao, D. Adhikesavalu, A. Camerman, A. R. Fritzberg, *J. Am. Chem. Soc.* **1990**, *112*, 5798−5804. [6c] J. O'Neil, S. Wilson, J. Katzenellenbogen, *Inorg. Chem.* **1994**, *33*, 319−325. [6d] M. Pelecanou, I. Pirmettis, M. Papadopoulos, C. P. Raptopoulou, A. Terzis, E. Chiotellis, C. I. Stassinopoulou, *Inorg. Chim. Acta* **1999**, *287*, 142−151.

[7] A. Davison, C. Orving, H. S. Trop, M. Sohn, B. V. DePamphilis, A. G. Jones, *Inorg. Chem.* **1980**, *19*, 1988−1992.

[8] A. W. Addison, T. N. Rao, J. Reedijk, G. C. Verschoor, *J. Chem. Soc., Dalton Trans.* **1984**, 1349−1356.

[9] M. Papadopoulos, B. Nock, T. Maina, I. Pirmettis, C. Raptopoulou, A. Tasiopoulos, A. Troganis, T. Kabanos, A. Terzis, E. Chiotellis, *J. Biol. Inorg. Chem.* **2001**, *6*, 159−165.

[10] L. Xu, I. Setyawati, J. Pierreroy, M. Pink, V. Young Jr, B. Patrick, S. Rettig, C. Orvig, *Inorg. Chem.* **2000**, *39*, 5958−5963.

[11] F. C. Anson, T. J. Collins, S. L. Gipson, J. T. Keech, T. E. Kraft, G. T. Peake, *J. Am. Chem. Soc.* **1986**, *108*, 6593−6605.

[12] R. Alberto, R. Schibli, A. Egli, A. Schubiger, W. A. Herrmann, G. Artus, U. Abram, T. Kaden, *J. Organomet. Chem.* **1995**, *492*, 217−224.

[13] A. Davison, H. S. Trop, B. V. DePamphilis, A. G. Jones, *Inorg. Synth.* **1982**, *21*, 160−162.

[14] G. M. Sheldrick, *SHELXS-86, Program for the Solution of Crystal Structures*, University of Göttingen, Germany, **1986**.

[15] G. M. Sheldrick, *SHELXL-93, Program for the Refinement of Crystal Structures*, University of Göttingen, Germany, **1993**.

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