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Preliminary communication

Formation of a rhenium(III) carbonyl complex by electrophilic attack on rhenium isocyanides. Synthesis and molecular structure of {Re[N(CH$_2$CH$_2$S)$_3$][CNC(CH$_3$)$_3$]} and {Re[N(CH$_2$CH$_2$S)$_3$](CO)}

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Abstract

Treatment of the trigonal-bipyramidal complex {Re[N(CH$_2$CH$_2$S)$_3$](CNCH$_2$COOEt)} (**1a**) with LiOH in THF leads to ester hydrolysis and yields the complex {Re[N(CH$_2$CH$_2$S)$_3$](CNCH$_2$COOH)} (**2**). Attempts to hydrolyze the ester in **1a** in the two-phase system toluene/concentrated hydrochloric acid proceeded under electrophilic attack at the isocyanide nitrogen atom and formation of the carbonyl complex {Re[N(CH$_2$CH$_2$S)$_3$](CO)} (**3**). Complex **3** was also obtained by treatment of {Re[N(CH$_2$CH$_2$S)$_3$][CNC(CH$_3$)$_3$]} (**1b**) with toluene/hydrochloric acid. The molecular structures of **1b** and **3** were established by X-ray structure analysis.

Keywords: Isocyanide complexes; Carbonyl complexes; Rhenium; X-ray crystallography

Only a few technetium and rhenium complexes with tripodal ligands containing sulfur donors are known [1–3]. Recently we reported the syntheses and crystal structures of some trigonal bipyramidal rhenium und technetium complexes with the *tris*(2-mercaptoethyl)amine ligand [4]. Attempts to hydrolyze the ester function in the isocyanide complex {Re[N(CH$_2$CH$_2$S)$_3$](CNCH$_2$COOEt)} (**1a**) with LiOH in THF led to the complex {Re[N(CH$_2$CH$_2$S)$_3$](CNCH$_2$COOH)} (**2**) containing an isocyanide ligand functionalized with a carboxylic acid group. Treatment of **1a** with hydrochloric acid did not lead to ester hydrolysis but gave the unexpected carbonyl complex {Re[N(CH$_2$CH$_2$S)$_3$](CO)} (**3**). **3** was also obtained, when complexes with oxygen-free isocyanides like {Re[N(CH$_2$CH$_2$S)$_3$][CNC(CH$_3$)$_3$]} (**1b**) were treated with hydrochloric acid. In this paper we describe the synthesis of **3** together with the crystal structures of **1b** and **3**.

In our search for rhenium complexes which can be coupled to biological relevant molecules we studied complexes of type 1a (Scheme 1) containing functionalized iscyanide ligands. The ester group in **1a** could be used for coupling of the complex to a primary amine via formation of an amide bond. In addition, the neutral complex **1a** can be converted into an anionic derivative via ester hydrolysis and deprotonation of the carboxylic acid. Such behavior can influence the in vivo biodistribution of the complex. Technetium complexes with hydrolyzable ester groups are currently under investigation as cerebral perfusion imaging agents [5].

Complexes of type **1** with various isocyanide ligands can be synthesized by substitution of the phosphine in {Re[N(CH$_2$CH$_2$S)$_3$](PR$_3$)} for an isocyanide. They are green, air-stable crystalline solids with a trigonal-bipyramidal coordination geometry at the rhenium atom [4].

Reaction of **1a** in THF with LiOH · H$_2$O at room temperature results in ester hydrolysis and gives the lithium salt {Re[N(CH$_2$CH$_2$S)$_3$](CNCH$_2$COOLi} which was converted without isolation or purification into the isocyanacetic acid complex **2** by means of a cation-exchange resin (Scheme 1) [6]. The analytical and spectroscopic data for **2** are consistent with a trigonal-bipyramidal molecular structure as shown in Scheme 1.

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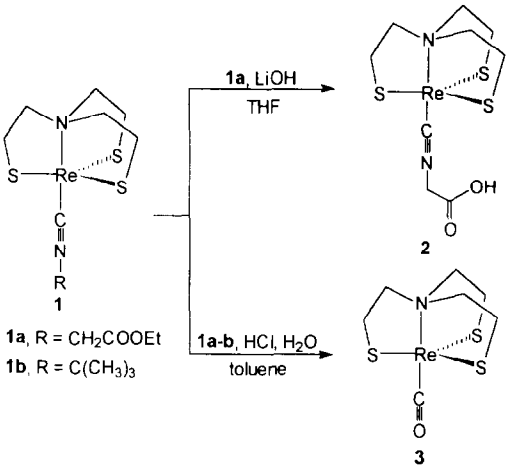


Scheme 1. Synthesis of the complexes **2** and **3**.

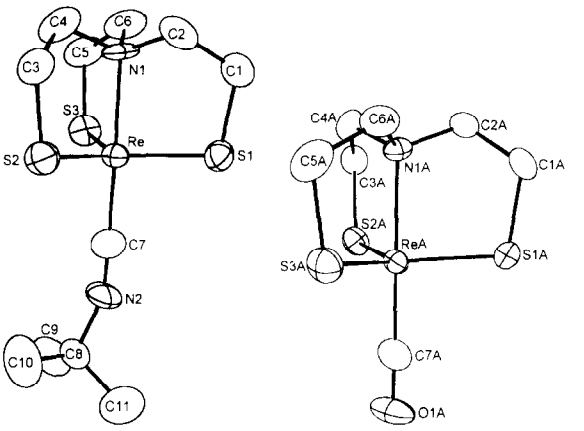
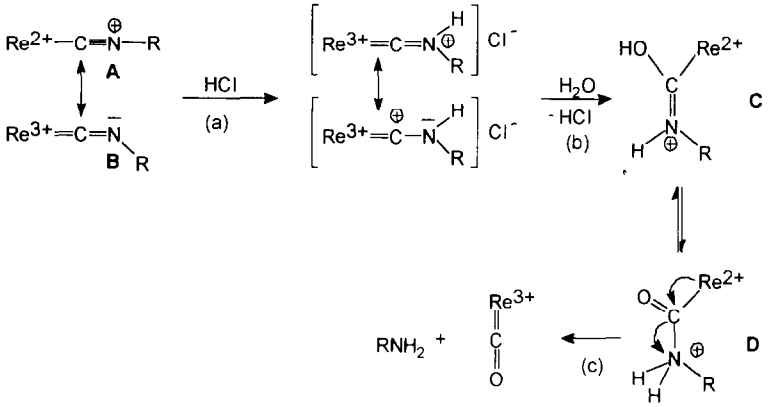


Fig. 1. ORTEP drawings of complexes {Re[N($CH_2CH_2S)_3$][CNC-($CH_3)_3$]} **1b** and {Re[N($CH_2CH_2S)_3$](CO)} **3**. (only molecule A is shown). Selected bond distances [Å] and angles [deg] for **1b**: Re–S1 2.236(2), Re–S2 2.234(2), Re–S3 2.227(2), Re–N1 2.215(6), Re–C7 1.949(10), N2–C7 1.174(12), N2–C8 1.433(12), S1–Re–S2 120.49(9), S1–Re–S3 118.30(9), S1–Re–N1 85.5(2), S1–Re–C7 95.9(3), S2–Re–S3 119.36(9), S2–Re–N1 85.0(2), S2–Re–C7 93.0(3), S3–Re–N1 86.0(2), S3–Re–C7 94.7(3), N1–Re–C7 177.9(4) Re–C7–N2 179.6(12), C7–N2–C8 154.0(10). Molecular structure of {Re[N($CH_2CH_2S)_3$](CO)} **3**. Selected bond distances [Å] and angles [deg] for molecule A [molecule B] of **3**: Re–S1 2.226(2) [2.224(2)], Re–S2 2.243(2) [2.242(2)], Re–S3 2.241(2) [2.239(2)], Re–N1 2.227(5) [2.221(5)], Re–C7 1.888(7) [1.877(7)], O1–C7 1.152(9) [1.163(8)], S1–Re–S2 117.35(6) [117.35(7)], S1–Re–S3 120.27(7) [120.22(7)], S1–Re–N1 85.46(13) [86.08(13)], S1–Re–C7 94.4(2) [94.3(2)], S2–Re–S3 120.60(7) [120.69(6)], S2–Re–N1 85.45(14) [85.07(14)], S2–Re–C7 96.4(2) [96.3(2)], S3–Re–N1 85.79(14) [85.66(14)], S3–Re–C7 92.6(2) [92.7(2)], N1–Re–C7 178.0(2) [178.2(2)], Re–C7–O1 178.8(6) [177.7(6)].

In principle, a nucleophile like OH^- can attack complex **1a** at two sites: (i) at the ester group or (ii) at the isocyanide carbon atom. The latter attack, which constitutes the oldest method for the synthesis of heteroatom-stabilized carbene complexes [7], is only possible for isocyanides which are not deactivated for nucleophilic attack by (d → p)π backbonding from the metal center [8]. Such a strong deactivation of the isocyanide carbon atom against nucleophilic attack is observed in complexes of type **1**. The $N(S^-)_3$ coordination generates an electron-rich Re(III) center which engages in very strong backbonding to the isocyanide ligand. This can be seen by the low wave numbers for the N≡C stretch in the IR spectrum (2150 cm^{-1} and 2137 cm^{-1} for the free ligands [9], 1976 cm^{-1} for **1a** and 1976 cm^{-1} for **1b** [6]). Another indication of strong backbonding is a significant deviation from linearity for the C≡N-C bond. The X-ray crystal structure analysis [10] with crystals of **1b** (Fig. 1) shows a significantly bent isocyanide [angle C7–N2–C8 154.0(10)°]. Similar behavior was observed for the complex {Re[N(CH_2CH_2-$S)_3$](CNCH$_2$COOMe)}, which differs form **1a** only in the presence of a methyl ester group instead of an ethyl ester group at the isocyanide [angle C≡N–C 150.8(9)°] [4]. As desired for a high in vivo stability, nucleophilic attack at the isocyanide carbon is impossible for complexes of type **1** with an electron rich $N(S^-)_3$ ligand and in the presence of an ester substituted isocyanide, hydroxyl ions will only hydrolyze the ester to the carboxylic acid.

An attempt to hydrolyze the ester group in **1a** in the two-phase system toluene/concentrated hydrochloric acid gave unexpected results. After heating of **1a** in



Scheme 2. Proposed mechanism for the conversion of **1** to **3**.

toluene/hydrochloric acid for one hour [11], the original green color of the organic phase bleached and the water phase turned orange. Continued heating of the reaction mixture lead to a lipophilic compound, which redissolved in the toluene phase. The toluene phase turned red in the process. Standard workup of the toluene solution led to the isolation of a deep red crystalline compound. The IR spectrum of this compound showed no absorptions which could be attributed to an isocyanide complex but instead a strong absorption at 1876 cm^{-1}, suggesting the formation of complex **3** with a a coordinated carbonyl group (Scheme 1). An X-ray structure analysis [10] with crystals of **3** confirmed this conclusion (Fig. 1). The asymmetric unit of **3** contains two, almost identical molecules. The rhenium atoms in these molecules are pentacoordinated by the tetradentate tripodal ligand and one CO ligand.

Formation of **3** was also observed upon treatment of the oxo-free complex **1b** with hydrochloric acid [11]. For the formation of **3** from both **1a** and **1b** we propose the mechanism depicted in Scheme 2. Due to the strong backbonding from rhenium atom to the isocyanide carbon in **1a** and **1b** (vide supra) these complexes are best represented by resonance formula **B** with a partly sp^2-hybridized isocyanide nitrogen. In the first reaction step (a) the isocyanide nitrogen atom is protonated, leading to the orange, water soluble species. The color change from green to red corroborates a general change at the rhenium chromophor during the protonation. In the water phase, the carbon atom of the protonated isocyanide is attacked by a water molecule (step b) and HCl is eliminated. The resulting complex can be formulated as Re(II) derivative which can exist in two tautomeric forms **C** and **D**. Elimination of a primary amine (step c) from **D** gives complex **3**.

The observation of an electrophilic H^+ attack at the isocyanide nitrogen followed by a nucleophilic attack of OH^- at the carbon atom of the protonated isocyanide is unprecedented. The only reported conversion of a coordinated isocyanide ligand into a carbonyl is reported to proceed via nucleophilic attack at the isocyanide carbon followed by amine elimination [12]. Various examples for the electrophilic attack at the isocyanide nitrogen (reaction a in Scheme 2) by H^+ or alkyl halides have been reported. These lead either to stable cationic carbene type complexes [13] or, in case of protonation of the isocyanide, can rearrange to give metal hydrides [14]. A protonated isocyanide can be regarded as an iminiocarbene which have been shown to be strongly electron withdrawing ligands [13a]. Thus the subsequent nucleophilic attack at the carbene carbon by a water molecule (reaction b in Scheme 2), although not reported previously, becomes feasible. Any reaction mechanism based on an initial nucleophilic attack at the isocyanide carbon can be ruled out since we have shown that the reaction of **1a** with aqueous LiOH leads exclusively to ester hydrolysis and not to nucleophilic attack at the isocyanide. Finally it should be noted, that the $Re(NS_3)$ chelate unit remains unchanged in both base and acid catalyzed reactions at the isocyanides which is another testatment to the stability of this coordination type.

Acknowledgements

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[6] Correct elemental analyses (C, H, N) for all new compounds. The isocyanide complexes of type **1** were synthesized from phosphine complexes $\{Re[N(CH_2CH_2S)_3](PR_3)\}$ and the corresponding iosocyanide by substitution reaction [4]. Selected spectroscopic data for **1a**: ^1H NMR (90 MHz, $CDCl_3$, δ): 5.45 (s, 2H, $CNCH_2$), 4.28 (q, 2H, OCH_2), 3.02 (m, 12H, SCH_2 and NCH_2), 1.31 (t, 3H, CH_3); IR (KBr, ν): 1976 (CN), 1744 (CO) cm^{-1}; for **1b**: ^1H NMR (90 MHz, CDCl3, δ): 2.98 (m, 12H, SCH_2 and NCH_2), 1.54 (s, 9H, CH_3); IR (KBr, ν): 1976 (CN) cm^{-1}. For the synthesis of **2** 50 mg (0.101 mmol) of **1a** were dissolved in 5 ml of THF. To this were added 7 mg (0.167 mmol $LiOH \cdot H_2O$ dissolved in 0.5 ml water). The reaction mixture was stirred for 1 h at room temperature and then the THF was removed by nitrogen stream. 10 ml of cation exchange resin suspension (DOWEX 50 WX8) were added to the remaining aqueous phase. After stirring for 2 h complex **2** was extracted with acetonitrile (4×2 ml). Recrystallization from acetonitrile/water (10:1, v:v) gave olive green needles (27.4 mg, 58%), m.p. 197–205°C (decomp.). ^1H NMR (90 MHz, $CDCl_3$, δ): 11.81 (s; 1H, $COOH$), 5.37 (s, 2H, $CNCH_2$), 2.88 (m, 12H, SCH_2 and NCH_2); IR (KBr, ν): 1924 (CN), 1720 (CO) cm^{-1}.

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[10] X-ray structure determinations. Crystals of **1b** (green plates) and **3** (red cubes) were grown from CH_2Cl_2/methanol at room temperature. Selected crystallographic details for **1b** [3]: size of data crystal $0.40\times0.35\times0.15$ [$0.35\times0.25\times0.25$] mm, formula $C_{11}H_{21}N_2ReS_3$ [$C_7H_{12}NOReS_3$], $M = 463.70$ [408.57] amu, monoclinic [triclinic], space group $P2_1/c$ [$P\bar{1}$], $a = 12.084(2)$ [7.924(2)], $b = 11.915(2)$ [10.467(3)], $c = 12.244(3)$ [13.556(2)] Å, $\alpha = 90.0$ [96.61(2)], $\beta = 114.31(2)$ [90.47(2)], $\gamma = 90.0$ [101.68(2)]°, $V = 1606.6(12)$ [1093.2(9)] Å^3, $Z = 4$ [4, 2 independent molecules per asymmetric unit], $\rho_{exp} = 1.93$ [2.50], $\rho_{Calc.} = 1.917$ [2.482] g cm^{-3}, Mo Kα-radiation ($\lambda = 0.71073$ Å, monochromator graphite), μ(Mo Kα) = 80.26 [117.82] cm^{-1}. 2822 [2863] symmetry independent diffraction data were measured at 20(2) [20(2)]°C in the 2Θ-range 2–50 [2–45]°. Structure solution with Patterson and refinement with Fourier methods, refinement of positional parameters of all non-hydrogen atoms with anisotropic thermal parameters. Hydrogens on calculated positions [d(C–H) = 0.95 Å] with B_{eq}(H) = $1.3B_{eq}$(C). $R = 4.62$ [2.50], $Rw = 6.55$ [3.71] for 2425 [2543] absorption corrected structure factors $F_o^2 \geq 3\sigma(F_o^2)$ and 155 [236] refined parameters. Neutral atomic scattering factors [15] were used and all scattering factors were corrected for anomalous dispersion [15]. All calculations were carried out with the MolEn program package [16]. Further details of the crystal structure investigation may be obtained from the Fachinformationszentrum Karlsruhe, D-76344 Eggenstein-Leopoldshafen (FRG) on quoting the depository number CSD-58979 and the journal citation.

[11] 50 mg (0.101 mmol) of **1a** were dissloved in a mixture of dichlormethane (1 ml) and toluene (10 ml) and concentrated hydrochloric acid (1 ml, 37%) was added under nitrogen. The mixture was heated under reflux for 2 h. The organic layer was separated, washed with water (3 × 5 ml) and dried over Na_2SO_4. Recrystallization from dichlormethane/ethanol gives cube shaped, red crystals (24.4 mg, 64%), m.p. 235–237°C (decomp.). Correct elemental analysis (C, H, N). ^{1}H NMR (90 MHz, $CDCl_3$, δ): 3.22 (m, 12H, SCH_2 and NCH_2); IR (KBr, ν): 1876 (CO) cm^{-1}. The same reaction conditions were employed for the conversation of **1b** to **3** (yield 37%). The identity of the product was established by its melting point and IR spectrum.

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