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Article

Water-Exchange Study Revealed Unexpected Substitution Behavior of $[(CO)_2(NO)Re(H_2O)_3]^{2+}$ in Aqueous Media

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The pH-dependent water-exchange rates of $[(CO)_2(NO)Re(H_2O_{cis})_2(H_2O_{trans})]^{2+}$ (**1**) in aqueous media were investigated by means of ^{17}O NMR spectroscopy at 298 K. Because of the low pK_a value found for **1** (p$K_a = 1.4 \pm 0.3$), the water-exchange rate constant $k_{obs}{}^{H_2O_{trans/cis}}$ was analyzed with a two-pathway model in which $k_{Re}{}^{H_2O_{trans/cis}}$ and $k_{ReOH}{}^{H_2O_{trans/cis}}$ denote the water-exchange rate constants in trans or cis position to the nitrosyl ligand on **1** and on the monohydroxo species $[(CO)_2(NO)Re(H_2O)_2(OH)]^+$ (**2**), respectively. Whereas the rate constants $k_{ReOH}{}^{H_2O_{trans}}$ and $k_{ReOH}{}^{H_2O_{cis}}$ were determined as $(4.2 \pm 2) \times 10^{-3}$ s^{-1} and $(5.8 \pm 2) \times 10^{-4}$ s^{-1}, respectively, $k_{Re}{}^{H_2O_{trans}}$ and $k_{Re}{}^{H_2O_{cis}}$ were too small to be determined in the presence of the much more reactive species **2**. Apart from the water exchange, an unexpectedly fast $C{\equiv}^{16}O \rightarrow C{\equiv}{}^*O$ exchange was also observed via NMR and IR spectroscopy. It was found to proceed through **1** and **2**, with rate constants $k_{Re}{}^{CO}$ and $k_{ReOH}{}^{CO}$ of $(19 \pm 4) \times 10^{-3}$ s^{-1} and $(4 \pm 3) \times 10^{-3}$ s^{-1}, respectively. On the other hand, $N{\equiv}^{16}O \rightarrow N{\equiv}{}^*O$ exchange was not observed.

Introduction

Over the past decade, low-oxidation-state complexes of technetium and rhenium have attracted a growing interest because of their potential use in diagnostic and therapeutic nuclear medicine.[1] Particularly, the tricarbonyl precursors $[(CO)_3M(H_2O)_3]^+$ (M = Tc, Re) have significantly impacted the development of new organometallic radiopharmaceuticals. Many efforts are currently being devoted to the design and preparation of chelating ligand systems for the $\{(CO)_3M\}^+$ fragment (M = Tc, Re).[2−9] The unique features of the organometallic tricarbonyl cores of Tc(I)/Re(I) (e.g., small size, high kinetic inertness, in vivo stability, efficient labeling of bioactive molecules) prompted us and others to set out to develop other water-soluble and water-stable organometallic precursors for potential radiopharmaceutical use. In this regard, the substitution of one of the three carbonyl ligands in the $\{(CO)_3M\}^+$ core by the isolable nitrosyl ligand, forming a $\{(CO)_2(NO)M\}^{2+}$ core, was considered.[10−15] The resulting mixed dicarbonyl−nitrosyl

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complexes could lead to compounds with different and/or improved chemical and biological properties compared to those radiolabeled with the tricarbonyl fragment. The additional positive charge renders the metal center harder, and thus, a preference for different chelating ligand systems may result. Furthermore, the linearly coordinated NO^+ ligand is considered to have a lower σ-donor and higher π-acceptor strength than the CO ligand, resulting in a higher electron-acceptor strength as an overall effect. Finally, the presence of the nitrosyl ligand can considerably affect transition-metal centers and their coordination sphere, particularly the substitution lability of ligands in trans position.[16]

$[(CO)_2(NO)ReX_3]^-$ complexes (X = Cl, Br, I) are convenient starting materials for the precursor $[(CO)_2(NO)Re(H_2O)_3]^{2+}$ (**1**).[10,13] They are generally synthesized in organic solvents via nitrosylation of $[(CO)_2ReX]_2$ or $[(CO)_3ReX_2]_2$.[14,17−20] To develop novel radiopharmaceuticals, however, it is of crucial importance to achieve the synthesis of the precursors and understand their reactivity and properties in aqueous media. We elaborated new synthetic routes for producing $[(CO)_2(NO)MX_3]^-$ (M = Tc, Re; X = Cl, Br) starting from $[(CO)_3M(H_2O)_3]^+$ (M = Tc, Re) in water.[12] Berke and Alberto recently reported some aspects of the aqueous behavior of **1**.[10,13] With the aim of better comprehending the reactivity and properties of the latter in aqueous media, and particularly assessing the intrinsic lability of the coordinated water molecules, we studied the water exchange by means of ^{17}O NMR spectroscopy.

We present, herein, the first study of the water exchange on **1** by ^{17}O NMR spectroscopy as a function of the acidity, as well as the oxygen exchange of the two carbonyl ligands. The effect of the nitrosyl ligand on the lability of the coordinated water molecules in trans and cis positions is discussed, and a comparison of the reactivity of **1** with that of the previously reported congener complexes $[(CO)_3M(H_2O)_3]^{n+}$ (M= Re(I),[21] Tc(I),[22] Mn(I),[23] and Ru(II)[24,25]) is presented.

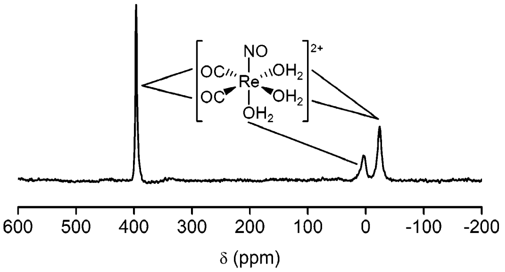

Figure 1. ^{17}O NMR spectrum (54 MHz) of a solution of $[(CO)_2(NO)Re(H_2O)_3]^{2+}$ (**1**) in CF_3SO_3H 1 M recorded at 298 K, 23 h after the addition of ^{17}O-enriched water (3% enrichment) in the presence of Mn^{2+}.

Results and Discussion

Preparation and Structural Characterization of $[(CO)_2(NO)Re(H_2O)_3]^{2+}$ (1). The complex $[(CO)_2(NO)ReBr_3](NEt_4)$ is a useful starting material for the preparation of aqua complex **1**. Dehalogenation of $[(CO)_2(NO)ReBr_3](NEt_4)$ in aqueous media using $AgCF_3SO_3$ and subsequent separation of AgBr gives solutions of **1** suitable for kinetic experiments. To prevent the formation of oligomers by hydrolysis,[10,13] we performed the synthesis in an acidic aqueous medium using triflic acid ($[H^+]$ ranging from 3.0 to 0.01 M), because of the weakly coordinating properties and redox stability of the $CF_3SO_3^-$ anion.

Solutions of **1** were analyzed by means of HATR−IR at different pH values (see the Supporting Information, Figure S3). At pH < 0, the spectra revealed absorption bands at 2122, 2054 (ν_{CO}), and 1824 cm^{-1} (ν_{NO}), which could be unambiguously attributed to aqua ion **1**. The spectrum of a solution of **1** at pH 1, on the other hand, displayed additional absorption bands at 2106 and 2036 cm^{-1} (ν_{CO}) and a very broad absorption band for ν_{NO} at 1820 cm^{-1}, which most likely correspond to the monohydroxo species $[(CO)_2(NO)Re(H_2O)_2(OH)]^+$ (**2**).[10] At pH 2, the IR spectrum showed that **2** prevails with absorption bands at 2106, 2036 (ν_{CO}), and 1783 cm^{-1} (ν_{NO}).

An ^{17}O NMR spectrum of an isotopically equilibrated aqueous, acidic solution of **1** (3% enrichment), recorded at 298 K, is shown in Figure 1. Signals at 4 and −24 ppm (1:2) are in accordance with the usual chemical shifts of water molecules coordinated to transition-metal ions.[21−25] They were assigned to the coordinated water molecules in trans and cis, respectively, to the nitrosyl ligand. The ^{17}O signal at 396 ppm could be attributed unambiguously to the two equivalent carbonyl oxygens. The signal of the bulk water was suppressed by the addition of Mn^{II} (See Experimental Section). No nitrosyl oxygen signal could be detected in the ^{17}O NMR spectra, even after several days.

To observe a possible nitrosyl oxygen exchange, we added $H_2{}^{18}O$ to a solution of **1** in 1.0 M CF_3SO_3H (48% enrichment) and analyzed it by means of HATR−IR as a function of time (Figure 2).[26] Although additional absorption bands for ν_{CO} could be observed within 10 min, confirming the oxygen exchange of the carbonyl ligand, no change in the NO region could be noticed, even after 3 days. This indicates an

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[26] $H_2{}^{18}O$ was used instead of $H_2{}^{17}O$ because of its higher enrichment (98% instead of 10%).

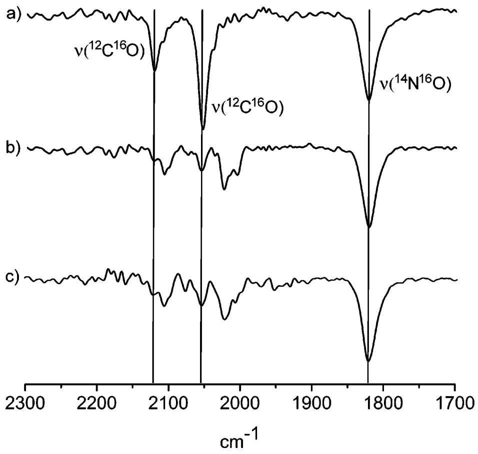
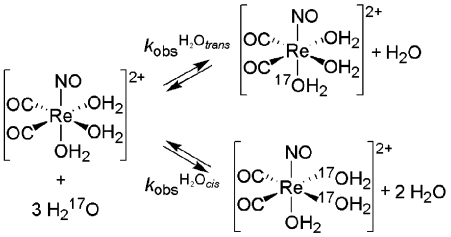


Figure 2. IR spectra of solutions of $[(CO)_2(NO)Re(H_2O)_3]^{2+}$ (**1**) in CF_3SO_3H 1.0 M: (a) reference solution, diluted twice with normal water; (b) 10 min after the addition of $H_2{}^{18}O$ (48% enrichment); (c) same solution as that in (b), but 3 days after the addition of $H_2{}^{18}O$.

Scheme 1. Water-Exchange Reactions in trans and cis Positions to the Nitrosyl Ligand in $[(CO)_2(NO)Re(H_2O_{cis})_2(H_2O_{trans})]^{2+}$ (**1**)[a]



[a] $k_{obs}{}^{H_2O_{trans}}$ and $k_{obs}{}^{H_2O_{cis}}$ represent the observed rate constants of the coordinated water molecules in trans and cis positions, respectively, to the nitrosyl ligand.

extremely slow or nonexisting oxygen exchange of the nitrosyl ligand and corroborates the ^{17}O NMR observations. Similar findings were reported by Emel'yanov et al., who investigated solutions of ruthenium nitrosyl complexes in $H_2{}^{17}O$ by ^{17}O NMR. After 35 days, the spectra revealed only very small signals in the 382−324 ppm range, resulting from an oxygen exchange of the nitrosyl ligand. It was found that after one year, equilibrium was still not reached.[27]

In addition, the enriched complex $[(CO)_2(^{15}NO)Re(H_2O)_3]^{2+}$ was prepared and analyzed by ^{15}N NMR spectroscopy in 1 M CF_3SO_3H. A single resonance at −33.9 ppm was observed ($CH_3{}^{15}NO_2$ 0.0 ppm, internal reference) and was assigned to the nitrosyl ^{15}N. The ^{13}C NMR spectrum of an aqueous solution of **1** exhibits a single signal at 188 ppm, confirming the equivalence of the two carbonyl oxygens.

No decomposition of solutions of **1** in CF_3SO_3H was observed over a period of several weeks, as monitored via NMR and IR spectroscopy.

2. Water-Exchange Rates of $[(CO)_2(NO)Re(H_2O)_3]^{2+}$ (1). The pH dependence of the water-exchange rates in trans and cis positions to the nitrosyl ligand on $[(CO)_2(NO)Re(H_2O_{cis})_2(H_2O_{trans})]^{2+}$ (**1**) was investigated (Scheme 1).

To follow the water-exchange reactions on **1**, we added $H_2{}^{17}O$ (10% enrichment) to acidic solutions of **1** (final concentrations: [**1**] = 0.05 M; $[H^+]$ ranging from 3 to 0.001 M, ^{17}O 3%) at 298 K using a fast-injection device.[28] The increase in the intensity of the ^{17}O NMR signals of the coordinated water molecules, resulting from the ^{17}O-enriching exchange process, was monitored as a function of time, and the experimental signal integrals of the coordinated water in trans and cis positions to NO^+ were least-squares-fitted according to eq 1 (Figure 3).

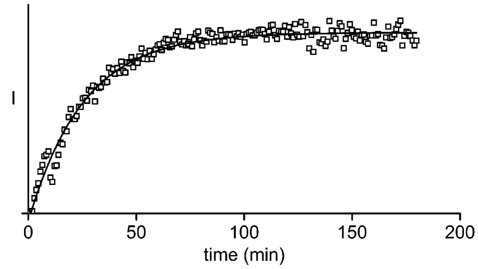


Figure 3. Increase in the experimental ^{17}O NMR signal integrals I (□) of the coordinated water in cis position to NO^+ in $[(CO)_2(NO)Re(H_2O_{cis})_2(H_2O_{trans})]^{2+}$ (**1**) as a function of time (1 M CF_3SO_3H; I = 1 M), at 298 K. The best fit according to eq 1 is shown as a solid line (—).

$$I = I_\infty\left[1 - \exp\left(\frac{k_{obs}}{1 - X_\infty}t\right)\right] \qquad (1)$$

I and I_∞ denote the integrals of the coordinated $H_2{}^{17}O$ peak at time t and t_∞, respectively, and X_∞ is the mole fraction of coordinated $H_2{}^{17}O$ at t_∞.

Unfortunately, $k_{obs}{}^{H_2O_{trans}}$ could not be determined at pH > 1 because of substantial broadening of the corresponding signal. The observed rate constants $k_{obs}{}^{H_2O_{trans}}$ and $k_{obs}{}^{H_2O_{cis}}$, however, were found to increase with decreasing acidity (Figure 4a). This points out that the triaqua (**1**) as well as the monohydroxo species (**2**) contribute to the exchange process, in a ratio determined by the acid dissociation constant K_a (Scheme 2). In contrast to $[(CO)_3Re(H_2O)_3]^+$,[21] the dependence of $k_{obs}{}^{H_2O_{trans}}$ and $k_{obs}{}^{H_2O_{cis}}$ as a function of $1/[H^+]$ was found to be nonlinear. A similar behavior was also reported for $[(CO)_3Ru(H_2O)_3]^{2+}$ and was ascribed to a proton dissociation taking place in the $[H^+]$ range covered by the study.[25]

As illustrated in Figure 4b, the observed ^{17}O transverse relaxation rates $1/T_{2,obs}{}^{H_2O_{trans}}$ and $1/T_{2,obs}{}^{H_2O_{cis}}$ as a function of the acidity show the same curvature as the observed rate constants (Figure 4a). This confirms the existence of a very fast acid−base equilibrium (Scheme 2) and implies that the observed ^{17}O NMR signals are weighted average signals of **1** and **2**. It is important to note that the observed curves in Figure 4b cannot be due to changes in viscosity, because the ^{17}O NMR line width of the CO ligand remains invariant with respect to proton concentration. The fact that the signal of the coordinated water molecule trans to the nitrosyl ligand is more affected by the line broadening suggests that the proton dissociation process occurs on H_2O_{trans} (Scheme 2).

The observed rate constants $k_{obs}{}^{H_2O_{trans}}$ and $k_{obs}{}^{H_2O_{cis}}$ and the ^{17}O transverse relaxation rates $1/T_{2,obs}{}^{H_2O_{trans}}$ and $1/T_{2,obs}{}^{H_2O_{cis}}$ can therefore be related to eqs 2 and 3, respectively, with

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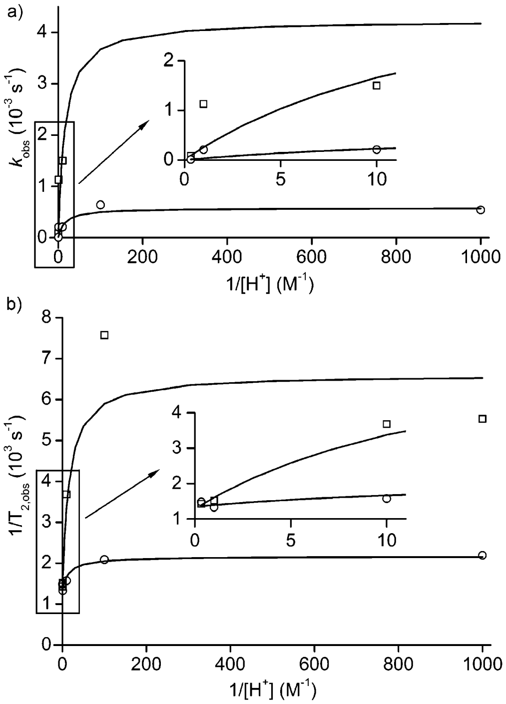
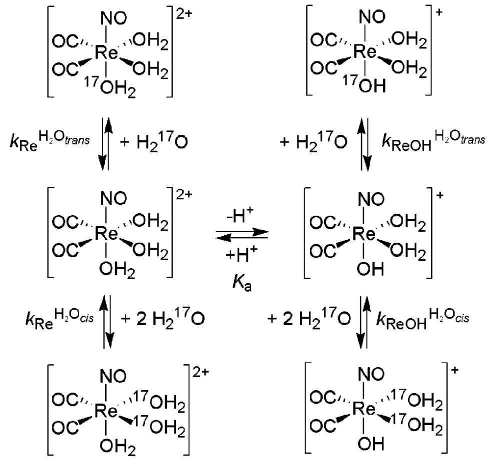


Figure 4. (a) Observed rate constants $k_{obs}^{H_2O_{trans}}$ (□) and $k_{obs}^{H_2O_{cis}}$ (○) and (b) observed ^{17}O transverse relaxation rates $1/T_{2,obs}^{H_2O_{trans}}$ (□) and $1/T_{2,obs}^{H_2O_{cis}}$ (○) for the water-exchange reactions in trans and cis positions to the nitrosyl ligand in $[(CO)_2(NO)Re(H_2O_{cis})_2(H_2O_{trans})]^{2+}$ (**1**) as a function of the acidity at 298 K. The solid lines (−) correspond to the best fits according to eqs 2−5.[29]

Scheme 2



the populations of **1** (p_{Re}) and **2** (p_{ReOH}) given by eqs 4 and 5.

$$k_{obs} = p_{Re}k_{Re} + p_{ReOH}k_{ReOH} \tag{2}$$

$$\frac{1}{T_{2,obs}} = p_{Re}\left(\frac{1}{T_{2,Re}}\right) + p_{ReOH}\left(\frac{1}{T_{2,ReOH}}\right) \tag{3}$$

$$p_{Re} = \frac{[H^+]}{[H^+] + K_a} \tag{4}$$

$$p_{ReOH} = \frac{K_a}{[H^+] + K_a} \tag{5}$$

Simultaneously fitting the nine adjustable parameters of eq 2 to eq 5 and to the experimental data gives $k_{Re}^{H_2O_{trans}}$ and $k_{Re}^{H_2O_{cis}}$ values equal to zero within experimental error.[30] This indicates that these rates are too low to be determined experimentally in the presence of the much more reactive monohydroxo species **2**. For $[(CO)_3Ru(H_2O)_3]^{2+}$, a similar situation was found; however, the rate constant for the water exchange could be estimated (10^{-4}/10^{-3} s^{-1}) from a comparison of ^{17}O NMR chemical shifts and Ru−O bond lengths with other carbonyl aqua complexes.[25] In the case of **1**, such estimation appears more difficult because of the lack of structural data. The rate constants $k_{Re}^{H_2O_{trans}}$ and $k_{Re}^{H_2O_{cis}}$ were therefore neglected, and the fitting procedure was repeated with only seven adjustable parameters. Results are summarized in Table 1.

Table 1. Rate Constants ($k_{Re}^{H_2O_{trans/cis}}$ and $k_{ReOH}^{H_2O_{trans/cis}}$) and ^{17}O Transverse Relaxation Rates ($1/T_{2,Re}^{H_2O_{trans/cis}}$ and $1/T_{2,ReOH}^{H_2O_{trans/cis}}$) for Water Exchange in trans and cis Positions to the Nitrosyl Ligand on $[(CO)_2(NO)Re(H_2O)_3]^{2+}$ (**1**) and $[(CO)_2(NO)Re(H_2O)_2(OH)]^+$ (**2**), Respectively, and the Acid Dissociation Constant Resulting from Fit of eq 2 to eq 5 at 298 K

	H_2O_{trans}	H_2O_{cis}
k_{Re} (s^{-1})	0^a	0^a
k_{ReOH} (s^{-1})	$(4.2 \pm 2) \times 10^{-3}$	$(5.8 \pm 2) \times 10^{-4}$
$1/T_{2,Re}$ (s^{-1})	1282 ± 414	1345 ± 364
$1/T_{2,ReOH}$ (s^{-1})	6610 ± 1605	2162 ± 574
K_a (M)	$(6.5 \pm 3) \times 10^{-2}$	

[a] $k_{Re} \ll k_{ReOH}$.

It is interesting to analyze the influence the nitrosyl ligand exerts on the water-exchange rates. The substitution of a CO ligand in the monohydroxo complex $[(CO)_3Re(H_2O)_2(OH)]$ by a NO$^+$ ligand indeed has a dramatic impact: the water-exchange rates in the trans and cis positions were decreased by 4 and 5 orders of magnitude, respectively.[31] The water-exchange rates of $[(CO)_2(NO)Re(H_2O)_2(OH)]^+$ (**2**) are even smaller than that of $[(CO)_3Ru(H_2O)_2(OH)]^+$, for which a $k_{RuOH}^{H_2O}$ of 5.3 × 10^{-2} s^{-1} at 262 K was reported.[25,32] The effect of the nitrosyl ligand on the water-exchange rate in cis is slightly stronger than that in trans. The different trans and cis effects of the CO ligand on the water-exchange rates were also investigated for complexes of Ru^{II}.[25,33] In $[(CO)Ru(H_2O_{eq})_4(H_2O_{ax})]^{2+}$, it was found that the CO ligand predominantly exerts a cis effect. Indeed, the lability of the H_2O bound in cis positions (equatorial) is significantly reduced compared to that of $[Ru(H_2O)_6]^{2+}$, whereas that of the trans H_2O (axial) is only slightly increased.[33] When a second or third H_2O is substituted by a CO ligand, the H_2O reactivity seems to be less predictable. For example, the water-exchange rate constant of the axial H_2O in $[(CO)_2Ru$-

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(29) All four curves in panels a and b of Figure 4 were obtained from a simultaneous fit of eq 2 to eq 5 with seven adjustable parameters. More data points at lower [H$^+$] could not be obtained because of the significant broadening of the ^{17}O signal of H_2O_{trans}. A table with values of $k_{obs}^{H_2O_{trans}}$, $k_{obs}^{H_2O_{cis}}$, $1/T_{2,obs}^{H_2O_{trans}}$, and $1/T_{2,obs}^{H_2O_{cis}}$ as a function of the acidity can be found in the Supporting Information.

(30) Values of (0.06 ± 57) × 10^{-6} s^{-1} and (0.0003 ± 9000) × 10^{-9} s^{-1} were, indeed, found for $k_{Re}^{H_2O_{trans}}$ and $k_{Re}^{H_2O_{cis}}$, respectively.

(31) A water-exchange rate constant k_{ReOH} of 27 ± 1 s^{-1} was reported for $[(CO)_3Re(H_2O)_2(OH)]$ at 298 K. See ref 21.

(32) One can estimate that rate constants increase by of a factor 2 when the temperature increases by 10 °C.

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$(H_2O_{eq})_2(H_2O_{ax})_2]^{2+}$, which has one CO ligand in cis position and one CO ligand in trans position, corresponds to the estimated rate constant for the H_2O substitution on $[(CO)_3Ru(H_2O)_3]^{2+}$, which has two CO ligands in cis position and one in trans position.[25] In the case of $[(CO)_2(NO)Re(H_2O)_2(OH)]^+$ (**2**), the NO^+ ligand seems to overrule the two CO ligands. Indeed, the water-exchange rate of H_2O_{cis} is nearly 10 times smaller than that for H_2O_{trans}. The former has one CO ligand in trans position and one NO^+ ligand and one CO ligand in cis position, whereas the latter has one NO^+ ligand in trans position and two CO ligands in cis position. The higher rate constant for the exchange of H_2O_{trans} compared to that for H_2O_{cis} is surprising. One might have expected that the OH^- ligand is exchanging slower because it is more tightly bound. However, this is only true if the exchange proceeds via a dissociatively activated mechanism. In the case of an associatively activated mechanism, a proton exchange in the transition state may help to labilize the OH^- and exchange it by a water molecule. Because a mechanism could not be assigned at this point in the investigations, those considerations remain hypothetical.

The pK_a value derived from our NMR experiments was determined to be (1.2 ± 0.2). This clearly shows that (**1**) is much more acidic than the related $[(CO)_3Re(H_2O)_3]^+$, for which a pK_a value of 7.5 ± 0.2 was reported.[34] In this respect, **1** more likely resembles $[(CO)_3Ru(H_2O)_3]^{2+}$ ($pK_a = -0.14$).[25] The strong acidity of **1** is due to the π-acceptor properties of the CO and NO^+ ligands, which decrease the electron density at the metal center. The electron density at the Re^I metal center in **1** is reduced compared to that in $[(CO)_3Re(H_2O)_3]^+$ because NO^+ has a higher π-acceptor strength than CO. As a consequence, the O−H bonds, and particularly that in trans to the NO^+ ligand, are more polarized than in the case of $[(CO)_3Re(H_2O)_3]^+$. Therefore, the acidity of the coordinated water is increased. Spectrophotometric titrations, performed in parallel to the NMR studies, revealed a pK_a value of (1.6 ± 0.1), which corroborates that obtained by the ^{17}O NMR experiments (See Experimental Section and the Supporting Information).[35]

3. Fast Oxygen Enrichment of the Carbonyl Ligands. To our surprise, we observed, in the case of $[(CO)_2(NO)Re(H_2O)_3]^{2+}$ (**1**), an oxygen exchange between enriched H_2O and the carbonyl oxygens, as evidenced by the presence of the signal at 396 ppm in the ^{17}O NMR spectra and the absorption bands for $\nu_{C^{18}O}$ in the IR spectra (See above). This type of exchange was not found for $[(CO)_3Re(H_2O)_3]^+$ in acidic solutions[21] but was reported for $[(CO)_3Mn(H_2O)_3]^{+}$[23] and $[(CO)_nRu(H_2O)_{6-n}]^{2+}$ ($n = 1-3$).[25] This exchange was proposed to occur by a nucleophilic attack by H_2O, forming a metallacarboxylic acid intermediate (Scheme 3).[23,25,36−39]

As already observed for the water exchange, the rate constant k_{CO}^{obs} for the CO oxygen exchange on **1** also depends on the proton concentration. However, opposite to the water-exchange behavior, k_{obs}^{CO} decreases with decreasing proton concentration, as illustrated in Figure 5.

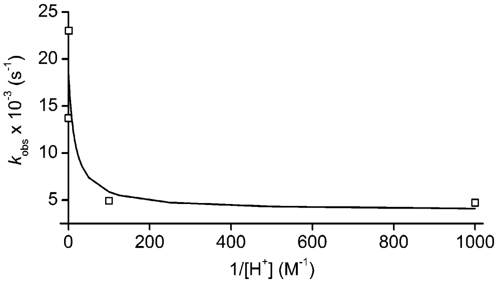
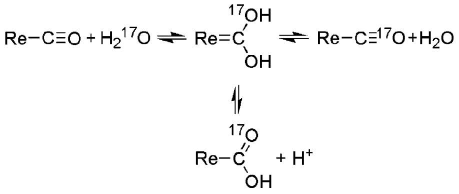


Figure 5. Observed rate constant k_{obs}^{CO} for the exchange between ^{17}O-enriched water and the carbonyl oxygens on $[(CO)_2(NO)Re(H_2O)_3]^{2+}$ (**1**) as a function of the acidity at 298 K. The solid line corresponds to the best fit obtained using eqs 2, 4, and 5.

Scheme 3



To analyze the acid dependence, we considered exchanges on both **1** and the monohydroxo species **2** (eq 2). Fitting eqs 2, 4, and 5 to k_{obs}^{CO} with k_{Re}^{CO} and k_{ReOH}^{CO} as adjustable parameters and K_a determined from the water-exchange rate (see above) as a fixed parameter gives $k_{Re}^{CO} = (19 \pm 4) \times 10^{-3}\ s^{-1}$ and $k_{ReOH}^{CO} = (4 \pm 3) \times 10^{-3}\ s^{-1}$ at 298 K. A faster exchange on **1** than on **2** is not surprising, because the electrophilic character of the carbon atom in **2** is reduced compared to that in **1**. Contrary to **1**, in the case of $[(CO)_3Ru(H_2O)_3]^{2+}$, the carbonyl oxygen exchange was found to proceed mainly through the hydrolyzed species $[(CO)_3Ru(H_2O)_2(OH)]^+$, with $k_{Ru}^{CO} = (3 \pm 2) \times 10^{-3}\ s^{-1}$ and $k_{RuOH}^{CO} = (24 \pm 3) \times 10^{-3}\ s^{-1}$ at 262 K.[25] However, in this case, the water exchange on $[(CO)_3Ru(H_2O)_2(OH)]^+$ is approximately two times faster than the CO oxygen exchange ($k_{RuOH}^{H_2O} = (53 \pm 6) \times 10^{-3}\ s^{-1}$ at 262 K). This unexpected behavior was attributed to a probable intramolecular nucleophilic attack at the CO carbon atoms by a coordinated H_2O, the latter being much more labile in $[(CO)_3Ru(H_2O)_2(OH)]^+$ than in $[(CO)_3Ru(H_2O)_3]^{2+}$.[40] In the case of the slower ^{17}O carbonyl exchange on $[(CO)_3Ru(H_2O)_3]^{2+}$, the latter should occur by a nucleophilic attack by the bulk water.

Conclusion

The present investigation demonstrated the dramatic effect of the replacement of one of the three carbonyl ligands by the isolable nitrosyl ligand in the precursor $[(CO)_3Re(H_2O)_3]^+$ on the reactivity of $[(CO)_2(NO)Re(H_2O)_3]^{2+}$ (**1**) in aqueous media. This was clearly demonstrated by the following

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(35) Potentiometric titrations seem, indeed, inadequate with respect to the low pK_a value.

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(40) For $[(CO)_3Ru(H_2O)_3]^{2+}$, the water-exchange rate $k_{Ru}^{H_2O}$ was estimated to be between 1×10^{-4} and $1 \times 10^{-3}\ s^{-1}$ at 298 K and between 1×10^{-6} and $1 \times 10^{-5}\ s^{-1}$ at 262 K. See ref 25.

aspects: (i) The 4 and 5 orders of magnitude decreases in the water-exchange rate constants on the monohydroxo species $[(CO)_2(NO)Re(H_2O)_2(OH)]^+$ (**2**) in trans and cis positions, respectively. (ii) The much-lower pK_a value. (iii) The high reactivity of the carbonyl oxygen atoms. We are, currently, investigating the substitution of the water molecules in **1** by mono- and polydendate ligands with different functional groups in order to assess the potential of this new $\{(CO)_2(NO)M\}^{2+}$ metal fragment for biological application.[11]

Experimental Section

General. $^{17}O-H_2O$ (10.5% ^{17}O, 49.3% ^{18}O) was obtained from the National High Technology Center of Georgia. $Na^{15}NO_2$ (≥98%) was purchased from Cambridge Isotope Laboratories, Inc., CF_3SO_3H (≥99%) and $AgCF_3SO_3$ (≥98%) from Fluka, and $NaCF_3SO_3$ (98%) from Aldrich. Solutions of commercial $NaCF_3SO_3$ were found to be basic, probably because of alkaline traces. Therefore, $NaCF_3SO_3$ was neutralized by the addition of CF_3SO_3H. After evaporation of the neutralized solution, $NaCF_3SO_3$ was stored in a desiccator over P_2O_5. $Mn(CF_3SO_3)_2$ was prepared by dissolving Mn (metallic) in aqueous 0.5 M CF_3SO_3H. Once evolution of H_2 had stopped, unreacted Mn was removed by filtration. The filtrate was then concentrated until crystallization. Crystals were recovered by filtration and dried under vacuum to yield a white powder. The precursors $[(CO)_2(NO)ReBr_3](NEt_4)$[14,17−20] and $[(CO)_3ReBr_3](NEt_4)_2$[41] were prepared according to previously published procedures. For the NMR and spectrophotometric data treatment, the pH was defined as $-\log [H^+]$.

$[(CO)_2(^{15}NO)ReBr_3](NEt_4)$. To a solution of $[(CO)_3ReBr_3](NEt_4)_2$ (500 mg, 0.65 mmol) in a mixture of H_2O:1 M HBr: concentrated H_2SO_4 (2:1:0.1 v/v; 5 mL) was added a solution of $Na^{15}NO_2$ (90 mg, 1.30 mmol) in the same mixture (2.8 mL). After being stirred at 70 °C for 50 min, the resulting solution was evaporated to dryness to give a yellow powder, which was then extracted with H_2O. The insoluble yellow powder was then filtered, washed twice with water, and dissolved in EtOH. The procedure was repeated with the filtrate as long as more product could be collected. After evaporation of the EtOH phase, the product was recrystallized from EtOH/hexane to give a yellow powder. Yield: 192 mg (46%).

Solutions of $[(CO)_2(NO)Re(H_2O)_3]^{2+}$ (1) Suitable for NMR Measurements. Acidic aqueous solutions of complex **1** were prepared under nitrogen using $[(CO)_2(NO)ReBr_3](NEt_4)$ as precursor. To $[(CO)_2(NO)ReBr_3](NEt_4)$ (80 mg, 0.12 mmol) in CF_3SO_3H (0.001−1.0 M, 2 mL) were added 3 equiv of $AgCF_3SO_3$. After the solution was stirred overnight at room temperature, AgBr was removed by filtration to yield yellow solutions of **1** ([**1**] = 0.06 M). For the preparation of the solution of **1** in 3.0 M CF_3SO_3H, we first prepared a solution of **1** in 1.0 M CF_3SO_3H as described above. $CF_3SO_2-O-SO_2CF_3$ was then added to reach the desired $[H^+]$ concentration. To all solutions of **1** in CF_3SO_3H (0.001−3.0 M) was added $Mn(CF_3SO_3)_2$ ($[Mn(CF_3SO_3)_2] = 0.1$ M) to suppress the signal of the bulk water. The ionic strength was then adjusted to 1.0 M with $NaCF_3SO_3$.

NMR Measurements. NMR spectra were measured on Bruker ARX-400 and DPX-400 spectrometers with resonance frequencies at 400.13 MHz for ^1H, 100.63 MHz for ^{13}C, 54.25 MHz for ^{17}O, and 40.54 MHz for ^{15}N. ^1H and ^{13}C chemical shifts are referenced to TMS (water soluble), ^{15}N chemical shifts to $CH_3{}^{15}NO_2$, and ^{17}O chemical shifts to H_2O.

Kinetic Data Treatment. Kinetic experiments were conducted by following the evolution of NMR signals with time. The NMR integrals were obtained by fitting the signals to a Lorentzian function with the program NMRICMA 3.1 for MATLAB.[42] The time-dependent concentrations were extracted from the integrals, and the experimental data were fitted using the programs VISUALISEUR 2.3.5 and OPTIMISEUR 2.3.5 for MATLAB.[43]

IR Measurements. Infrared spectra of aqueous solutions of **1** in CF_3SO_3H were recorded on a Perkin-Elmer FT-IR 16PC spectrometer using an HATR device or on a Perkin-Elmer FT-IR Spectrum One spectrometer equipped with a Diamond ATR Golden Gate device.

Spectrophotometric Titrations. The first pK_a of aqua ion **1** was determined by continuous titrations. Solutions (10 mL) containing 2×10^{-3} M **1** and 0.1 M CF_3SO_3H were prepared as described above and placed in a water-jacketed beaker at 298 K. A total of 19 aliquots (45 μL each) of 1.0 M KOH (Merck Titrisol) were then subsequently added under continuous stirring. Before the first aliquot and after each aliquot, UV−vis spectra ($200 < \lambda < 1000$ nm) were recorded with an immersion probe (HELLMA) connected to a diode array spectrophotometer (J&M, TIDAS−UV/NIR/100-1). The program SPECFIT/32[44] was used to evaluate the spectrophotometric data. Only absorption data with $300 < \lambda < 500$ nm were used for the determination of the first pK_a of **1**, and an auto-zero correction of the baseline at 500 nm was performed. The experimental spectrophotometric data were least-squares fitted for the reaction $L + H^+ \rightarrow HL$ ($L = [(CO)_2(NO)Re(H_2O)_2(OH)]^+$), and an average value of 1.6 ± 0.1 was found for the first pK_a (See the Supporting Information).

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Supporting Information Available: Values of $k_{obs}{}^{H_2O_{trans}}$, $k_{obs}{}^{H_2O_{cis}}$, $1/T_{2,obs}{}^{H_2O_{trans}}$ and $1/T_{2,obs}{}^{H_2O_{cis}}$ for the water-exchange reactions in **1** as a function of the acidity; determination of the first pK_a of **1** by continuous spectrophotometric titrations; IR spectra of aqueous solutions of **1** in CF_3SO_3H at different pH. This material is available free of charge via the Internet at http://pubs.acs.org.

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