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Generation of a Hydroperoxidochromium Complex from Nitratochromium(III) Ions and Hydrogen Peroxide

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Accelerated substitution at chromium(III) in $Cr_{aq}ONO_2^{2+}$ provides the basis for a novel route to the corresponding hydroperoxidochromium complex in aqueous solutions. Despite the great concentration advantage of water, the reaction of $Cr_{aq}ONO_2^{2+}$ with 10–100 mM H_2O_2 generates >50 % yields of $Cr_{aq}OOH^{2+}$, which makes this reaction useful for preparative purposes, and may also represent a potential source of high-valent chromium in biological environments. In a minor, parallel path, small concentrations of a superoxidochromium(III) complex, $Cr_{aq}OO^{2+}$, are also produced.

Introduction

Peroxido and hydroperoxido transition metal complexes are key intermediates in various catalytic and biological transformations involving oxygen.[1–5] Typically, metal hydroperoxides are generated by reduction of the superoxido precursors or by direct substitution by hydrogen peroxide at the metal atom.[6] The latter approach is obviously limited to substitutionally labile metals and excludes inert complexes such as hexaaquachromium(III) ion. Consequently, the only practical route to the hydroperoxido complex $Cr_{aq}OOH^{2+}$ until now has been the one-electron reduction of the superoxido complex $Cr_{aq}OO^{2+}$, itself generated in small concentrations (≤0.1 mM) from Cr_{aq}^{2+} and O_2[6] [Equation (1)]. Here we report a successful preparation of higher concentrations of $Cr_{aq}OOH^{2+}$ by a novel method that should be applicable to other substitutionally inert complexes as well.

$$Cr_{aq}^{2+} + O_2 \longrightarrow Cr_{aq}OO^{2+} \xrightarrow{e^-,\,H^+} Cr_{aq}OOH^{2+} \tag{1}$$

The chemistry described here may also lead to high-valent chromium under physiologically relevant conditions. Cr^V intermediates[7] are known to be generated from N_4-macrocyclic hydroperoxido complexes in a process mimicking the formation of reactive iron species in the cytochrome P450 cycle.[8] It has not been confirmed that $Cr_{aq}OOH^{2+}$ also leads to high-valent chromium intermediates, but they are strongly implicated by the formation of chromate as a product.[9] The carcinogenicity of chromate, and the likelihood that Cr^V is involved in the mechanism of carcinogenesis,[10] are two factors that make it critical to identify potential sources of high-valent chromium and/or its precursors, including the hydroperoxido species.

Chromium(III) ions in aqueous solutions are typically quite unreactive and are considered safe to use in food supplements. The substitution at Cr^{III} can be, however, quite rapid as a result of *cis*[11,12] and *trans*[13,14] labilization by various ligands. This feature was exploited in the present work, and large, non-equilibrium concentrations of a hydroperoxidochromium complex were generated by accelerated substitution at Cr^{III}.

Results and Discussion

A mixture of acidic aqueous solutions of H_2O_2 with $(H_2O)_5CrONO_2^{2+}$ (hereafter $Cr_{aq}ONO_2^{2+}$), prepared as described in the Supporting Information, generated the characteristic UV spectrum of a long-lived superoxidochromium complex, $Cr_{aq}OO^{2+}$ (λ_{max} = 290 and 245 nm)[15] (Figure S1, see Supporting Information). Additional confirmation of the nature of the product came from its decomposition kinetics, which were identical to those of the authentic compound under our experimental conditions.

The kinetics and amplitude of the absorbance increase at 290 nm were comparable under argon, air, and oxygen (Figure S2), ruling out any mechanism that would depend on the Cr_{aq}^{2+}/O_2 reaction as a source of $Cr_{aq}OO^{2+}$.

The yield of $Cr_{aq}OO^{2+}$ was typically about 8 % based on the initial (limiting) concentration of $Cr_{aq}ONO_2^{2+}$, requiring that other product(s) also be formed. Increased absorbance in the UV spectrum suggested the presence of $Cr_{aq}OOH^{2+}$. Because this complex, unlike $Cr_{aq}OO^{2+}$, does not exhibit unique spectral features that would unequivocally identify it, we resorted to kinetic identification. For

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that purpose, we used the characteristic reactions of $Cr_{aq}OOH^{2+}$ with halide ions, shown in Equation (2) (X = I or Br).[16–18]

$$Cr_{aq}OOH^{2+} + 2X^-/3X^- + 2H^+ \rightarrow Cr_{aq}OH^{2+} + X_2/X_3^- + H_2O \quad (2)$$

Upon addition of iodide to reaction solutions, the absorbance increased in two stages. A sudden initial jump (corresponding to the $Cr_{aq}OOH^{2+}$/iodide reaction) at 350 nm[17] was followed by a much slower increase caused by the H_2O_2/iodide reaction (Figure S3). The kinetics of the initial jump were measured separately in stopped-flow experiments. The reaction obeyed a mixed third-order rate law (rate = $k[Cr_{aq}OOH^{2+}][I^-][H^+]$) and yielded k = $(943 \pm 25)\ \text{M}^{-2}\,\text{s}^{-1}$, in good agreement with the known rate constant for the $Cr_{aq}OOH^{2+}/I^-/H^+$ reaction $(988 \pm 16\ \text{M}^{-2}\,\text{s}^{-1})$.[19]

In a similar set of experiments with Br^- as a scavenger for $Cr_{aq}OOH^{2+}$, the measured rate constant was $0.47 \pm 0.05\ \text{M}^{-2}\,\text{s}^{-1}$, in agreement with the reported value of $0.54 \pm 0.05\ \text{M}^{-2}\,\text{s}^{-1}$.[20] The good kinetic match in reactions with both halides identifies the product as $Cr_{aq}OOH^{2+}$. Some $Cr_{aq}{}^{3+}$ was also observed, so that the overall reaction between $Cr_{aq}ONO_2{}^{2+}$ and H_2O_2 is described by Equation (3).

$$Cr_{aq}ONO_2{}^{2+} + H_2O_2 \rightarrow \{Cr_{aq}OOH^{2+} + Cr_{aq}OO^{2+} + Cr_{aq}{}^{3+} + NO_3{}^-\} \quad (3)$$

The kinetics of reaction (3) were studied under pseudo-first order conditions with H_2O_2 in large excess over $Cr_{aq}ONO_2{}^{2+}$. The increase in absorbance at 290 nm (maximum for $Cr_{aq}OO^{2+}$) was followed by a decrease as $Cr_{aq}OO^{2+}$ and $Cr_{aq}OOH^{2+}$ decomposed at longer times.[21] The fit to a double exponential equation yielded rate constants for the two reaction steps. Only the rate constant for absorbance increase showed a dependence on $[H_2O_2]$ as illustrated in Figure S4. There was no dependence on $[H^+]$ in the range $0.10\ \text{M} \le [H^+] \le 0.50\ \text{M}$ (Figure S5). The straight line drawn through the data in Figure S4 has a slope k_3 = $(0.043 \pm 0.002)\ \text{M}^{-1}\,\text{s}^{-1}$. The points at the lowest $[H_2O_2]$ deviate somewhat from the line, which we believe is caused by imperfect fit to consecutive kinetics (see analysis in Supporting Information). This interpretation is strengthened by the fact that an excellent fit is obtained when initial rates, which should be unaffected by the events in the decay stage, are plotted against the product of initial concentrations $[Cr_{aq}ONO_2{}^{2+}]_0[H_2O_2]_0$ (Figure S6). Given the complexity of the system, a realistic standard deviation for k_3 is about 25%.

To confirm that $Cr_{aq}OO^{2+}$ and $Cr_{aq}OOH^{2+}$ were formed simultaneously in parallel reactions, the rate of growth of $Cr_{aq}OOH^{2+}$ was determined directly. For this purpose, aliquots of a reaction solution were analylzed for $Cr_{aq}OOH^{2+}$ by the iodide method[18] at different times and plotted in Figure 1. Also shown in Figure 1 is the absorbance/time trace for the same solution measured at 290 nm, and a biexponential fit. The two curves, one dominated by the growth of $Cr_{aq}OOH^{2+}$, the other by $Cr_{aq}OO^{2+}$ (290-nm trace), clearly follow the same pattern on the same time scale, showing that the two products are generated in the same kinetic process.

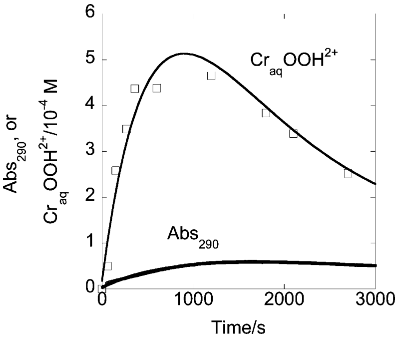

Figure 1. Change of absorbance at 290 nm [dominated by buildup of $Cr_{aq}OO^{2+}$ (bottom) and buildup of $Cr_{aq}OOH^{2+}$ (top)] with time for a reaction between 3.5 mM $Cr_{aq}ONO_2{}^{2+}$ and 9.0 mM H_2O_2. The rising portions of the two traces have the same rate constant.

Theoretical yields of $Cr_{aq}OOH^{2+}$ were obtained from simulations of the reaction scheme that took into account all the known reactions for the formation and loss of $Cr_{aq}OOH^{2+}$ (see Supporting Information). At 360 s after the mixing of the reagents in Figure 1 (25% reaction completed), the calculated concentration of $Cr_{aq}OOH^{2+}$ was 0.67 mM. The experimental value was 0.44 mM (66%). Comparable results were obtained at other times in Figure 1. No other absorbing species were detected, suggesting that the remaining chromium was present as the non-absorbing $Cr_{aq}{}^{3+}$, as shown in Equation (3) and discussed below.

Several exploratory experiments with $Cr_{aq}(OAc)^{2+}$ (OAc = CH_3COO^-), which also has labile *cis* positions,[13] showed that this complex also reacted with H_2O_2 and produced $Cr_{aq}OOH^{2+}$ and small amounts of $Cr_{aq}OO^{2+}$.

Despite the great concentration advantage of water (55 M) over hydrogen peroxide (10–100 mM), the yields of $Cr_{aq}OOH^{2+}$ in the reaction of H_2O_2 with $Cr_{aq}ONO_2{}^{2+}$ and $Cr_{aq}(OAc)^{2+}$ are large (exceeding 60%), and many orders of magnitude greater than the equilibrium amounts that could be generated from $Cr_{aq}{}^{3+}$ and H_2O_2. In fact, the latter reaction would not produce observable quantities of $Cr_{aq}OOH^{2+}$.

A mechanism consistent with these results is shown in Scheme 1, according to which the coordinated nitrate labilizes one or more positions at the metal atom, most likely the four *cis* sites.[12] This allows the entry of H_2O_2 and the formation of the mixed nitrato peroxido intermediate **I** (where the peroxide ion could be coordinated either as H_2O_2 or $HO_2{}^-$). The peroxido ligand is apparently more labilizing than the nitrato ligand, so that the latter is preferentially eliminated from **I**. In other words, the ligand being replaced is the one whose own *cis*-labilizing effect had initiated the entire process.

Intermediate **I** is probably also the source of the superoxido complex. One possibility, shown in Scheme 1, has **I** react in two competing reactions: substitution to generate $Cr_{aq}OOH^{2+}$, and internal electron transfer to yield Cr^{V}. The latter will disproportionate to Cr^{IV} and chromate, both of

$$\begin{tikzcd}
\mathrm{Cr^{III}{}_{aq}ONO_2{}^{2+}} + \mathrm{H_2O_2} \arrow[r, shift left] & \underset{\mathbf{I}}{\mathrm{Cr^{III}{}_{aq}(H_2O_2)ONO_2{}^{2+}}} \arrow[l, shift left] \arrow[r] \arrow[d] & \mathrm{Cr^{III}{}_{aq}OOH^{2+}} + \mathrm{NO_3{}^-} + \mathrm{H^+} \\
 & \mathrm{Cr^{V}{}_{aq}O(OH)(ONO_2)^+} + \mathrm{H^+} \arrow[r, "\text{fast}"] & \mathrm{Cr^{V}{}_{aq}O(OH)^{2+}} + \mathrm{NO_3{}^-}
\end{tikzcd}$$

Scheme 1.

which react with H_2O_2 to give $Cr_{aq}OO^{2+}$.[6] The hydroperoxido-to-Cr^V conversion in Scheme 1 should be facilitated by anionic ligands (nitrato and acetato), just as the electron-rich macrocyclic N_4 ligands induce the formation of Cr^V.[7,22]

The incomplete formation of $Cr_{aq}OOH^{2+}$ and $Cr_{aq}OO^{2+}$ in the $Cr_{aq}ONO_2{}^{2+}/H_2O_2$ reaction indicates that another pathway operates for the loss of **I**. Most likely, this involves hydrolysis to $Cr_{aq}{}^{3+}$. Based on the amount of "missing" $Cr_{aq}ONO_2{}^{2+}$, about 20% of the intermediate decays by that route.

Both $Cr_{aq}OOH^{2+}$ and $Cr_{aq}OO^{2+}$ are potential precursors of Cr^V. A proposal that H_2O_2 and Cr^{III} may generate hydroperoxido species at biological pH values has been considered by Lay et al.,[10] although no experimental evidence was found for such a reaction. The effects of nitrate (product of NO metabolism and a potential contaminant in drinking water) and acetate reported here add even more credence to such ideas, and suggest that these and other species (e.g. carboxylic and amino acids) present in biological milieu may assist the oxidation of Cr^{III}.

Conclusions

The reaction between $Cr_{aq}ONO_2{}^{2+}$ and H_2O_2 generates large, non-equilibrium yields of the hydroperoxido complex $Cr_{aq}OOH^{2+}$. The *cis* effect exhibited by the nitrate ion is believed to play an important mechanistic role, suggesting that related reactions with other metals and oxido anions may also take place and provide a route to novel hydroperoxido compounds.

Supporting Information (see footnote on the first page of this article): Experimental details, spectral and kinetic data (Figures S1–S6), and complete kinetic scheme and results of kinetic simulations.

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