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Fast Ligand Substitution at a Chromium(III) Hydroperoxo Complex

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The hydroperoxo group in $(H_2O)_5CrOOH^{2+}$ is replaced with selected anions (acetate, nitrate, and sulfate) at rates that are unprecedented for substitution at a pentaaquachromium(III) complex. The chemistry is noteworthy in that it interchanges low-concentration, weak ligands between a Cr(III) coordination sphere and solution in the presence of a large excess of water. We attribute this chemistry and the fast kinetics to the hydroperoxo cis effect. Each of the entering anions follows a different rate law in support of H^+-assisted dissociation of the hydroperoxo group from a mixed-ligand intermediate. The dependence on $[H^+]$ is first-order for nitrate, zero-order for acetic acid, and changes from first- to zero-order for sulfate in the acidity range $0.015\ M < [H^+] < 0.20\ M$. At 1.0 M H^+, the second-order rate constants are 3.0 (nitrate), 2.49 (sulfate), and 0.90 (acetic acid) $M^{-1}\ s^{-1}$. The similarity in rate constants supports a mechanism featuring rate-limiting substitution at chromium. The equilibrium constant for the reaction $(H_2O)_5CrOOH^{2+} + NO_3^- + H^+ \rightleftarrows (H_2O)_5CrONO_2^{2+} + H_2O_2$, $K = 62\ M^{-1}$, was obtained from the kinetics of forward and reverse reactions.

Introduction

Transition metal hydroperoxo complexes are key intermediates in oxygen activation in catalytic and biological systems.[1−9] In the laboratory, they are generated[1] by a number of methods, including one-electron reduction of superoxide precursors, insertion of O_2 into metal−hydrogen bonds,[8−11] direct ligand replacement by H_2O_2 at sufficiently labile metal centers, and others.[12] Recently, we reported a fast reaction between a nitratochromium(III) ion, $(H_2O)_5CrONO_2^{2+}$, and H_2O_2 that generated $(H_2O)_5CrOOH^{2+}$ in > 50% yield.[13] Small amounts of the superoxo complex $(H_2O)_5CrOO^{2+}$ were also observed.

$$(H_2O)_5CrONO_2^{2+} + H_2O_2 \rightarrow (H_2O)_5CrOOH^{2+} + NO_3^- + H^+$$

The rapid substitution at the typically inert Cr(III) was attributed to the cis effect of the nitrato group, whereby the binding of nitrate alternates between monodentate and bidentate and thus labilizes the four neighboring positions.[13−16] It was postulated that a mixed hydroperoxo nitrato intermediate $(H_2O)_4Cr(ONO_2)(H_2O_2)^{2+}$ was formed, followed by the elimination of nitrate. The surprisingly high yields of $(H_2O)_5CrOOH^{2+}$ at only ~0.01 M H_2O_2 in H_2O suggested that the hydroperoxo group itself must be more labilizing than nitrate, resulting in preferential dissociation of the latter. If only nitrate, but not H_2O_2, exhibited a cis effect, then the product of the above reaction would be $(H_2O)_{5-n}Cr(ONO_2)(H_2O_2)_n^{2+}$, where n should reflect the proportion of H_2O_2 in bulk solution, that is, about 1 in 5500 for 0.01 M H_2O_2. To address this potentially novel aspect of hydroperoxo chemistry and to look for additional evidence for the cis effect of coordinated hydroperoxide, we examined the reaction between $(H_2O)_5CrOOH^{2+}$ and several anions including NO_3^-. The results are described herein.

Experimental Section

Solutions of $(H_2O)_5CrONO_2^{2+}$ were prepared as previously described.[13] Acidic aqueous solutions of $(H_2O)_5CrOO^{2+}$ were prepared from $Cr(H_2O)_6^{2+}$ and excess O_2 in dilute aqueous $HClO_4$ containing 0.05−0.10 M methanol as a stabilizer and scavenger of $(H_2O)_5Cr^{IV}O^{2+}$.[12] Solutions of $(H_2O)_5CrOO^{2+}$ were briefly purged with argon to remove the majority of O_2

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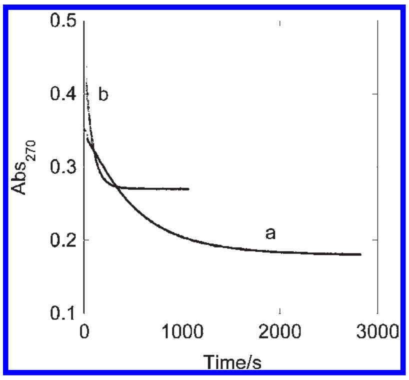

Figure 1. Plots of absorbance against time for the disappearance of $(H_2O)_5CrOOH^{2+}$ (0.22 mM) in the absence (a) and presence (b) of 0.040 M NO_3^- in 0.090 M $HClO_4$ at 25.0 ^{0} C.

and reduced with stoichiometric amounts of $Ru(NH_3)_6^{2+}$ to generate $(H_2O)_5CrOOH^{2+}$. It was found that a 2 min purge was sufficient to prevent the oxidation of $Ru(NH_3)_6^{2+}$ with O_2 in competition with the desired $Ru(NH_3)_6^{2+}/(H_2O)_5CrOO^{2+}$ reaction. Longer purging times were avoided to prevent the decomposition of $(H_2O)_5CrOO^{2+}$. Reactions initiated by the addition of nitrate to $(H_2O)_5CrOOH^{2+}$ thus contained only limited amounts of O_2 ($\leq$0.01 mM). Those initiated by the addition of H_2O_2 to $(H_2O)_5Cr(ONO_2)^{2+}$ were typically run in air-saturated solutions after it had been established that the presence of O_2 had no effect on the kinetics and products. The constant ionic strength of 0.20 M was maintained with lithium perchlorate. In-house distilled water was further purified by passage through a Barnstead EASY pure III system.

Equilibrium concentrations of $(H_2O)_5CrOOH^{2+}$ in the presence of excess H_2O_2 were determined iodometrically by monitoring the kinetics of I_3^- formation at 351 nm ($\varepsilon = 2.6 \times 10^4$ M^{-1} cm^{-1}).[17] The reaction of the chromium complex (k/M^{-1} s^{-1} = 988[H^+])[18] is much faster than that of H_2O_2 (k/M^{-1} s^{-1} = 0.0115 + 0.173[H^+]),[19] so that the absorbance change associated with the $(H_2O)_5CrOOH^{2+}/I^-$ reaction in the initial fast stage could be obtained either by direct inspection of the trace or by a fit to consecutive kinetics. The latter treatment was adopted for experiments with a large excess of H_2O_2.

UV−vis spectra and kinetics were recorded with a Shimadzu 3101 PC spectrophotometer at a constant temperature of 25 ± 0.2 °C. For fast reactions, an Applied Photophysics stopped flow spectrophotometer was used. Most of the kinetics data were acquired at 270 nm, where $(H_2O)_5CrOOH^{2+}$ exhibits a molar absorptivity of 1.0 (±0.1) × 10^3 M^{-1} cm^{-1}.[13] Kinetic analyses were performed with KaleidaGraph 4.05 PC software.

Results

Nitrate. The first-order rate constant for the spontaneous decay[20,21] of $(H_2O)_5CrOOH^{2+}$ (0.22 mM) in 0.090 M $HClO_4$ at 25 °C is k_{dec} = 1.90 × 10^{-3} s^{-1}, trace *a* in Figure 1. Upon the addition of 0.040 M nitrate, the kinetics still followed an exponential rate law, but the rate constant increased to 1.30 × 10^{-2} s^{-1}, trace *b* in Figure 1. The kinetics of spontaneous decay are somewhat sensitive to the change in initial concentrations[21] but were much slower than the reaction with added ligands in all of the experiments. Also, in the range of [H^+] used, the decomposition reaction generates only minor amounts of H_2O_2.[21]

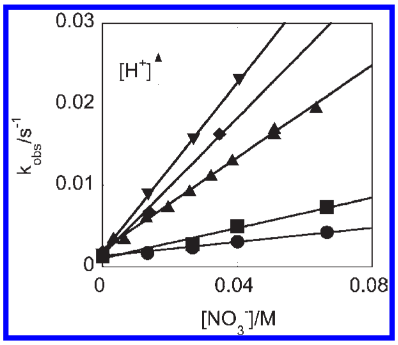

Figure 2. Plots of pseudo-first-order rate constants against [NO_3^-] for the reaction with $(H_2O)_5CrOOH^{2+}$ at [H^+] = 0.018 M (circles), 0.036 (squares), 0.09 (triangles), 0.135 (diamonds), and 0.18 (inverted triangles). Conditions: 25 °C, $[(H_2O)_5CrOOH^{2+}]_0$ = 0.22−0.36 mM, μ = 0.20 M ($HClO_4$ + $LiClO_4$ + $NaNO_3$).

Products. Upon completion of the reaction between 0.32 mM $(H_2O)_5CrOOH^{2+}$ and 0.050 M nitrate in 0.090 M $HClO_4$, the products were separated on a column of Sephadex C25 cation exchange resin. The behavior of the major chromium-containing fraction on the resin indicated a +2 charge. The UV spectrum was consistent with $(H_2O)_5CrONO_2^{2+}$ in ca. 70% yield based on the absorbance at 260 nm (ε = 100 M^{-1} cm^{-1}).[22] The yield is satisfactory in view of the small volumes, low concentrations, and weak spectral features of the complexes involved. The remaining chromium was presumed to be present as $Cr(H_2O)_6^{3+}$.

The identification of $(H_2O)_5CrONO_2^{2+}$ on the basis of its UV spectrum, which shows increased intensity below 300 nm but no characteristic transitions, is not unambiguous. To confirm that the $(H_2O)_5CrOOH^{2+}/NO_3^-$ reaction indeed takes place as in eq 1, we carried out the reverse reaction between the ion-exchanged product and excess (33 mM) H_2O_2. As expected,[13] a mixture of $(H_2O)_5CrOOH^{2+}$ (major) and $(H_2O)_5CrOO^{2+}$ (minor) was generated with a rate constant of 2 × 10^{-3} s^{-1}, which is within 20% of that expected for the $(H_2O)_5CrONO_2^{2+}/H_2O_2$ reaction.

$$(H_2O)_5CrOOH^{2+} + NO_3^- + H^+ \underset{k_{H2O2}}{\overset{k_{NO3}}{\rightleftharpoons}} (H_2O)_5CrONO_2^{2+} + H_2O_2 \quad K_1 \qquad (1)$$

Kinetics. The dependence on NO_3^- was examined at a constant, 0.20 M ionic strength. As shown in Figure 2, the plots of k_{obs} against [NO_3^-] at constant [H^+] were linear with a small intercept (k_{dec}) corresponding to the spontaneous decomposition of $(H_2O)_5CrOOH^{2+}$. The slope of each line in Figure 2 yielded the second-order rate constant *k* for the $(H_2O)_5CrOOH^{2+}/NO_3^-$ reaction at a given [H^+]. As is clear from Figure 2, *k* increases with [H^+]. The relationship is linear, Figure S1 (Supporting Information), and the overall rate law is given in eq 2.

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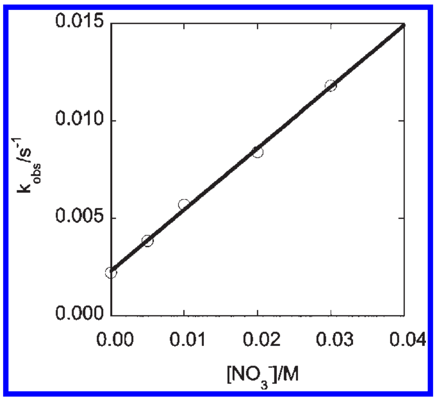

Figure 3. Plot of the observed rate constant for the reaction of $(H_2O)_5CrONO_2^{2+}$ (0.25 mM) with a mixture of H_2O_2 (0.046 M) and NO_3^- against the concentration of NO_3^- in 0.10 M $HClO_4$ ($\mu = 0.20$ M), according to eq 3.

From the slope of the line in Figure S1, we obtain $k_{NO3} = 3.0 \pm 0.07\ M^{-2}\ s^{-1}$.

$$-d[(H_2O)_5CrOOH^{2+}]/dt = k_{NO3}[H^+][NO_3^-][(H_2O)_5CrOOH^{2+}] \quad (2)$$

The kinetics of the reverse of reaction 1 were determined in our earlier work at 0.50 M ionic strength ($k_{H2O2} = 0.043\ M^{-1}\ s^{-1}$) and again here at 0.20 M ionic strength ($k_{H2O2} = 0.048\ M^{-1}\ s^{-1}$), a condition used in the measurement of k_{NO3} in this work. The equilibrium constant K_1 was calculated from the ratio of the rate constants for the forward and reverse reactions, $K_1 = k_{NO3}/k_{H2O2} = 62 \pm 4\ M^{-1}$.

The reversibility of reaction 1 was confirmed by running kinetics experiments with mixtures of H_2O_2 and NO_3^- and starting with either $(H_2O)_5CrONO_2^{2+}$ or $(H_2O)_5CrOOH^{2+}$. In the example in Figure 3, the $(H_2O)_5CrONO_2^{2+}/H_2O_2$ reaction was studied in the presence of increased amounts of nitrate. As expected for the equilibrium in eq 1, the absorbance changes decreased, and rate constants increased with increasing $[NO_3^-]$. The expression for equilibrium kinetics in eq 3 identifies the slope of the line in Figure 3 as $k_{NO3}[H^+]$ and the intercept as the pseudo-first-order rate constant $k_{H2O2}[H_2O_2]$.

$$k_{obs} = k_{H2O2}[H_2O_2] + k_{NO3}[NO_3^-][H^+] \quad (3)$$

By substituting appropriate concentrations, the data in Figure 3 yielded $k_{NO3} = 3.2 \pm 0.1\ M^{-2}\ s^{-1}$ and $k_{H2O2} = 0.050 \pm 0.002\ M^{-1}\ s^{-1}$, in good agreement with independently determined values. Similar experiments at constant 0.020 M NO_3^- and varying $[H_2O_2]$ (0–0.058 M) yielded $k_{NO3} = 2.6 \pm 0.2\ M^{-2}\ s^{-1}$ and $k_{H2O2} = 0.053 \pm 0.002\ M^{-1}\ s^{-1}$.

The concentration of $(H_2O)_5CrOOH^{2+}$ at equilibrium was determined in all of the above kinetic experiments either from the overall absorbance change or iodometrically at the conclusion of the reaction. Concentrations of the remaining species at equilibrium were obtained by mass balance. These values were used in the expression in eq 4 to calculate the equilibrium constant K_1. All of the data are summarized in Table 1.

$$K_1 = \frac{[(H_2O)_5CrONO_2^{2+}][H_2O_2]}{[(H_2O)_5CrOOH^{2+}][NO_3^-][H^+]} \quad (4)$$

Table 1. Summary of Kinetic and Equilibrium Data for Reaction 1

method	$k_{H2O2}/M^{-1}\ s^{-1}$	$k_{NO3}/M^{-2}\ s^{-1}$	K_1/M^{-1}
k_{H2O2}/k_{NO3}[a]	0.048 ± 0.002	3.0 ± 0.1	62 ± 4
k_{H2O2}/k_{NO3} 0.020 M NO_3^-[b]	0.050 ± 0.003	3.2 ± 0.1	64 ± 6
k_{H2O2}/k_{NO3} 0.046 M H_2O_2[c]	0.053 ± 0.005	2.6 ± 0.2	49 ± 10
ΔAbs_{270}[d]			57 ± 8
$[Cr_{aq}OOH^{2+}]_{eq}$[e]			63 ± 8

[a] Forward and reverse of reaction 1 were monitored separately. [b] Equilibrium conditions, constant $[NO_3^-]$, vary $[H_2O_2]$. [c] Equilibrium conditions, constant $[H_2O_2]$, vary $[NO_3^-]$. [d] From the extent of reaction by absorbance change at 270 nm. [e] From equilibrium concentrations of $(H_2O)_5CrOOH^{2+}$ determined iodometrically, see text.

The good agreement between the values obtained by kinetic and equilibrium measurements confirms the chemistry in eq 1. The third entry in Table 1, $K_1 = 49 \pm 10\ M^{-1}$, is the least reliable. It was obtained from the kinetics of the unfavorable reverse reaction in the presence of added NO_3^- that made the equilibrium concentration of $(H_2O)_5CrOOH^{2+}$ and the accompanying absorbance change quite small.

Sulfate. Excess sulfate reacted with $(H_2O)_5CrOOH^{2+}$ to yield $(H_2O)_5CrSO_4^+$ in about 70% (recovered) yield, as determined from the UV–vis spectrum[23] of the product after ion exchange on a Sephadex C25. The kinetics of disappearance of $(H_2O)_5CrOOH^{2+}$ were first-order in total [sulfate], Figure S2 (Supporting Information). The dependence of the second-order rate constant (obtained by dividing the corrected pseudo-first-order rate constant by $[sulfate]_{tot}$) on $[H^+]$ in the range $0.015\ M \le [H^+] \le 0.19$ M is shown in Figure 4. The rate constant increases with $[H^+]$ in a nonlinear fashion and exhibits saturation at higher H^+ concentrations. Also shown in Figure 4 are the $[H^+]$-dependence data for the acetato and nitrato complexes.

The fit of the data to a general equation for saturation kinetics, eq 5, yielded $A = 2.49 \pm 0.10\ M^{-1}\ s^{-1}$ and $B = 0.048 \pm 0.006$ M. The value of B is close to the literature data for the acid dissociation constant of HSO_4^- ($K_a = 0.010$ M ($\mu = 0$), 0.028 ($\mu = 0.10$ M), and 0.048 ($\mu = 0.5$ M)).[24]

$$k = \frac{k_{obs} - k_{dec}}{[sulfate]_{tot}} = \frac{A[H^+]}{B + [H^+]} \quad (5)$$

Acetic Acid. Acetic acid also reacted with $(H_2O)_5CrOOH^{2+}$. By analogy with other anions, we expect the product to be $(H_2O)_5CrOAc^{2+}$, but this has not been verified experimentally. The kinetics were first-order in [HOAc] and independent of $[H^+]$ in the range $0.20\ M \ge [H^+] \ge 0.017$ M. The plot in Figure S3 (Supporting Information) yielded the rate constant $k_{OAc} = 0.900 \pm 0.012\ M^{-1}\ s^{-1}$.

Chloride and dimethyl sulfoxide (0.03–0.07 M) had no noticeable reactivity toward $(H_2O)_5CrOOH^{2+}$.

Discussion

The well-established cis-labilizing effect of nitrate and acetate[14–16] can accelerate the substitution at Cr(III) by several orders of magnitude as compared to the parent $Cr(H_2O)_6^{3+}$ ion. As an example, Table 2 summarizes the

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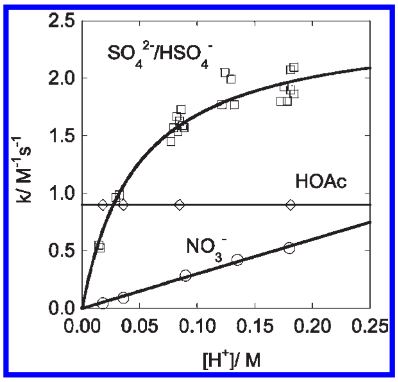

Figure 4. Plot of the rate constants for the reactions of $(H_2O)_5CrOOH^{2+}$ with sulfate, acetic acid, and nitrate against $[H^+]$ at $\mu = 0.20$ M. The line for sulfate is a fit to eq 5.

rate constants for the replacement of X in $(H_2O)_5CrX^{n+}$ with nitrate. The acceleration by coordinated OH^- is mainly a result of the trans effect,[25] which, although significant, is clearly much smaller than the cis effect exhibited by acetate. The nitrate cis effect is even greater.[14] The comparison between various complexes in Table 2 is not totally straightforward because some of reactions are acid-catalyzed and exhibit a third-order rate law, while others are second-order. A good measure of relative reactivities can be obtained, however, at constant $[H^+]$. Moreover, all of the numerical values in Table 2 are directly comparable at 1.0 M H^+.

With the addition of our new data for the hydroperoxo complex, the range of rate constants in Table 2 has been extended by a factor of 300. A strict comparison between the acetato and hydroperoxo complexes is valid because the two obey the same general rate law. Without a doubt, the HOO^- group has the greatest labilizing effect of all of the potentially bidentate ligands explored with Cr(III) so far.[26−28] Even though the binding mode in hydroperoxo complexes is normally end-on, transient chelation or side-on geometry may provide a mechanism for labilizing the cis sites.

Also listed in Table 2 are data for the substitution of −OOH by acetate and sulfate. The values are similar to that for nitrate, but once again, the strict comparison can be made only at a specific $[H^+]$. In fact, the dependence on $[H^+]$ for the reactions of $(H_2O)_5CrOOH^{2+}$ with the three entering ligands Y^n is quite instructive. There is a clear requirement for a proton in the transition state, undoubtedly because the dissociation of hydroperoxide can take place only with the assistance of H^+.

We begin our mechanistic analysis under the assumption that the dominant chemical forms are the reactive ones. As explained later, this interpretation provides the most consistent mechanistic picture, although other possibilities do exist and will be discussed for all three entering ligands in view of the potential proton ambiguity. The general mechanism is outlined in Scheme 1, where $n = -1$ (NO_3^- and OAc^-) or -2 (SO_4^{2-}).

Table 2. Rate Constants for the Reaction of Some Chromium(III) Complexes with Nitrate at 25° C

Cr(III) complex	k	source
$(H_2O)_5Cr(H_2O)^{3+}$	7.1×10^{-7} M^{-1} s^{-1}	ref 25
$(H_2O)_5CrOH^{2+}$	1.5×10^{-4} M^{-1} s^{-1}	ref 25
$(H_2O)_5CrOC(O)CH_3^{2+}$	0.01 M^{-2} s^{-1}	ref 14
$(H_2O)_5CrOOH^{2+}$	3.0 M^{-2} s^{-1}	this work
$(H_2O)_5CrOOH^{2+}$	0.90 M^{-1} s^{-1} [a]	this work
$(H_2O)_5CrOOH^{2+}$	2.49 M^{-1} s^{-1} [b]	this work

[a] For reaction with CH_3COOH. [b] For reaction with HSO_4^-/SO_4^{2-}.

On the basis of the stated premise, a ligand that is unprotonated in bulk solution, such as nitrate, coordinates to $(H_2O)_5CrOOH^{2+}$ to generate $(H_2O)_4Cr(NO_3)OOH^+$, eq I in Scheme 1. This intermediate loses either nitrate in a $[H^+]$-independent reverse process or the hydroperoxide in a $[H^+]$-catalyzed forward process of eq III. The steady-state approximation for the concentration of $(H_2O)_4Cr(NO_3)OOH^+$ leads to the rate law in eq 6. For $k_{-I} \gg k_{III}[H^+]$, the order in $[H^+]$ becomes strictly first-order, as observed experimentally, and $k_{NO3} = k_I k_{III}/k_{-I}$.

$$-d[(H_2O)_5CrOOH^{2+}]/dt = \frac{k_I k_{III}[NO_3^-][H^+]}{k_{-I} + k_{III}[H^+]}[(H_2O)_5CrOOH^{2+}] \qquad (6)$$

The inequality $k_{-I} \gg k_{III}[H^+]$ is also required to rationalize the lack of $[H^+]$ dependence in the reverse reaction between $(H_2O)_5CrONO_2^{2+}$ and H_2O_2 to generate $(H_2O)_5CrOOH^{2+}$,[13,29] confirming the internal consistency of the mechanistic scheme.

For an incoming ligand that is almost fully protonated in bulk solution, such as acetic acid, the coordination step includes deprotonation, eq II in Scheme 1. Both the reverse of this step and the forward step in eq III are $[H^+]$-assisted, which makes the kinetics of formation of $(H_2O)_5Cr(OAc)^{2+}$ independent of $[H^+]$. According to this mechanism, the experimental rate constant $k_{OAc} = 0.900$ M^{-1} s^{-1} is identified in eq 7 as $k_{II}k_{III}/(k_{-II} + k_{III})$.

$$-d[(H_2O)_5CrOOH^{2+}]/dt = k_{obs}[(H_2O)_5CrOOH^{2+}] = \frac{k_{II}k_{III}[HOAc]}{(k_{-II} + k_{III})}[(H_2O)_5CrOOH^{2+}] \qquad (7)$$

The sulfate reaction represents an intermediate case, where the need for an external proton changes with the pH in concert with changes in the protonation state of the major

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(29) The back reaction is

$$(H_2O)_5CrONO_2^{2+} + H_2O_2 \rightleftarrows (H_2O)_4Cr(OOH)(ONO_2)^+ + H^+ + H_2O \quad k_{-III}, k_{III}$$

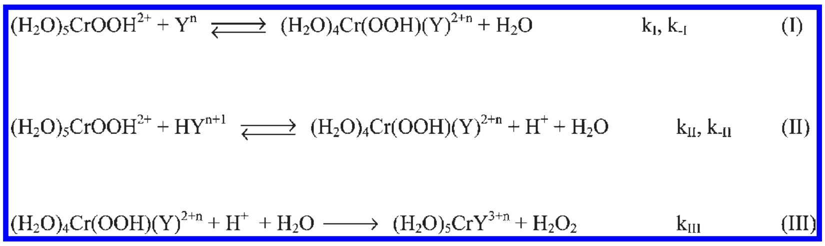
$$(H_2O)_4CrOOH(ONO_2)^+ + H_2O \rightarrow (H_2O)_5CrOOH^{2+} + NO_3^- \quad k_{-I}$$

and

$$k_{obs} = \frac{k_{-I}k_{-III}}{k_{-I} + k_{III}[H^+]}$$

which reduces to the observed $[H^+]$-independent form by setting $k_{-I} \gg k_{III}$. The rate constants are numbered as in Scheme 1.

Scheme 1



$$(H_2O)_5CrOOH^{2+} + Y^n \rightleftharpoons (H_2O)_4Cr(OOH)(Y)^{2+n} + H_2O \qquad k_I, k_{-I} \qquad (I)$$

$$(H_2O)_5CrOOH^{2+} + HY^{n+1} \rightleftharpoons (H_2O)_4Cr(OOH)(Y)^{2+n} + H^+ + H_2O \qquad k_{II}, k_{-II} \qquad (II)$$

$$(H_2O)_4Cr(OOH)(Y)^{2+n} + H^+ + H_2O \longrightarrow (H_2O)_5CrY^{3+n} + H_2O_2 \qquad k_{III} \qquad (III)$$

form in solution, as expressed by the acidity constant in eq 8. Here, both eq I and eq II must be considered as valid pathways to the mixed-ligand intermediate. This results in the rate law in eqs 9 and 10, which is equivalent to eq 5 with $B = K_a$ for HSO_4^- and $A = k_{III}(P)$, where (P) is the term in parentheses in eq 10.

$$HSO_4^- \rightleftarrows H^+ + SO_4^{2-} \quad K_a \tag{8}$$

$$-d[(H_2O)_5CrOOH^{2+}]/dt = k_{obs}[(H_2O)_5CrOOH^{2+}][\text{sulfate}]_{tot} \tag{9}$$

$$k_{obs} = \frac{k_{III}[H^+]}{(K_a + [H^+])}\left(\frac{k_I K_a + k_{II}[H^+]}{(k_{-I} + (k_{-II} + k_{III})[H^+])}\right) = \frac{k_{III}[H^+]}{(K_a + [H^+])}(P) \tag{10}$$

In the limits of low and high $[H^+]$, that is, $K_a \gg [H^+]$ and $K_a \ll [H^+]$, the expression for k_{obs} reduces to those in eqs 11 and 12, respectively, matching the experimentally observed first- and zero-order dependence on $[H^+]$:

$$K_a >> [H^+], k_{obs} = \frac{k_{III}[H^+]}{K_a}(P) \tag{11}$$

$$K_a << [H^+], k_{obs} = k_{III}(P) \tag{12}$$

The validity of eqs 11 and 12 and the fact that all of the data, including those in the intermediate regime, are fitted well with eq 5 (see Figure 4) and yield a reasonable value for K_a require the (P) term to be $[H^+]$-independent.

This can be achieved by having one path dominate throughout. The charge advantage should make SO_4^{2-} a more reactive form, and given that its concentration never drops below 20% of total sulfate, the term $k_I K_a$ should be much grater than $k_{II}[H^+]$. The reverse reaction is somewhat more complicated to analyze, because one path (k_{-I}) is a unimolecular dissociation of SO_4^{2-} from $(H_2O)_4Cr(SO_4)(OOH)$, and the other ($k_{-II}[H^+]$) involves the protonation of coordinated sulfate followed by the dissociation of HSO_4^-. The basicity of sulfate will be greatly diminished upon coordination and a loss of the negative charge, which should make the k_{-II} path less favorable than k_{-I}. As with the other ligands, the k_{III} step is taken to be kinetically slow, so that $k_{-I} \gg (k_{-II} + k_{III})[H^+]$, and the P term in eq 10 becomes $[H^+]$-independent, that is, $P = k_I K_a / k_{-I}$.

On the basis of the preceding discussion, the mechanism in Scheme 1 can be summarized as follows. The substitution at $(H_2O)_5CrOOH^{2+}$ is dissociatively activated, which results in limited discrimination between hydrolytic forms of the entering ligands. If one or the other form greatly dominates in solution, then the dominant form is also the one that reacts, that is, NO_3^- (rather than HNO_3) and CH_3COOH (rather than CH_3COO^-). When the two forms are present in comparable amounts, as is the case with HSO_4^-/SO_4^{2-}, then the better ligand, namely SO_4^{2-}, will be the one that reacts.

Further support for this mechanism comes from the analysis of the actual rate constants. Table 3 summarizes the kinetic data and provides kinetic expressions in terms of elementary steps for each of the two pathways, that is, I−III or II−III in Scheme 1.

In each of the rate laws in Table 3, the composite rate constant is a product of k_I or k_{II} and a factor that is a combination of rate and equilibrium constants. The composite rate constants are either second-order or third-order overall and are not directly comparable. The order is determined by the units of the multiplication factor, the value of which varies from case to case but is always less than or equal to 1. [As a corollary, the experimental rate constant cannot be greater than any specific rate constant for an elementary step in the forward direction for a "normal" (nonchain) reaction.] Thus, the values of composite rate constants calculated in Table 3 represent lower limits for k_I and k_{II}, both of which are second-order.

For nitrate, $k_I \geq 3\ M^{-1}\ s^{-1}$ and $k_{II} \geq 75\ M^{-1}\ s^{-1}$. Clearly, a mechanism that requires HNO_3 to coordinate to Cr(III) with a rate constant of $\geq 75\ M^{-1}\ s^{-1}$ seems much less favored than one that requires the anion NO_3^- to substitute with $k_I \geq 3\ M^{-1}\ s^{-1}$. On that basis, we prefer the sequence I−III for nitrate.

With acetate, the numerical difference is much greater and requires the anionic form to react much faster. Even though this possibility cannot be ruled out, the absolute value of the rate constant, $k_I \geq 4.5 \times 10^4\ M^{-1}\ s^{-1}$, does seem unreasonably large for substitution at a pentaaqua chromium(III) center, even if it has been labilized. The II−III sequence is thus preferred for acetate. This analysis does not entirely rule out some contribution from the I−III path at the lowest acid concentrations, but the importance of that route should be minor.

As shown in eqs 6 and 7, the assignment of different paths for acetate and nitrate includes a different dependence on $[H^+]$ for the reverse reactions −I and −II. Nitrate dissociates by a $[H^+]$-independent path (k_{-I} dominates), but acetate utilizes assistance by H^+. This outcome is exactly as one might have predicted on the basis of the known Bronsted and Lewis basicities of the two ligands and further supports our proposed mechanism. In fact, the pentaaqua analogs of our

Table 3. Kinetic Expressions for Various Substitution Pathways

		reactive form		
ligand	$k_{obs}/M^{-1}\,s^{-1}$	rate law		K_a/M
NO_3^-/HNO_3	$k_{NO3} = 3.0\,[H^+]$	$NO_3^{-\,a}$ $k_Ik_{III}/k_{-I} = 3.0\ M^{-2}\,s^{-1}$	HNO_3^{a} $k_{II}k_{III}/k_{-II}K_a = 3.0\ M^{-2}\,s^{-1}$ $k_{II}k_{III}/k_{-II} = 75\ M^{-1}\,s^{-1}$	24^{b}
$HOAc/OAc^-$	$k_{OAc} = 0.90$	OAc^- $k_Ik_{III}K_a/(k_{-I} + k_{III}) = 0.90\ M^{-1}\,s^{-1}$ $k_Ik_{III}/(k_{-I} + k_{III}) = 4.5 \times 10^4\ M^{-2}\,s^{-1}$	HOAc $k_{II}k_{III}/(k_{-II} + k_{III}) = 0.90\ M^{-1}\,s^{-1}$	$1.8 \times 10^{-5\,b}$
HSO_4^-/SO_4^{2-}	$k_{SO4} = 2.49[H^+]/(0.048 + [H^+])$	$SO_4^{2-\,c}$ $[H^+] \gg K_a$ $k_Ik_{III}K_a/k_{-I} = 2.49\ M^{-1}\,s^{-1}$ $k_Ik_{III}/k_{-I} = 52\ M^{-2}\,s^{-1}$ $[H^+] \ll K_a$ $k_Ik_{III}/k_{-I} = 52\ M^{-2}\,s^{-1}$	$HSO_4^{-\,c}$ $[H^+] \gg K_a$ $k_{II}k_{III}/k_{-II} = 2.49\ M^{-1}\,s^{-1}$ $[H^+] \ll K_a$ $k_{II}k_{III}/k_{-II}K_a = 52\ M^{-2}\,s^{-1}$	0.048^{d}

[a] Second denominator term, $k_{III}[H^+]$, is small and was dropped, see text. [b] Reference 30. [c] Assuming that the term $k_{III}[H^+]$ was negligible compared to other denominator terms, k_{-I} or $k_{-II}[H^+]$. [d] Identified as *B* in eq 5.

intermediate exhibit the same behavior, so that nitrate dissociates from $(H_2O)_5CrONO_2^{2+}$ in an $[H^+]$-independent reaction,[31] but the major path for aquation of $(H_2O)_5CrOAc^{2+}$ is first-order in $[H^+]$.[32] The protonation of the singly charged $(H_2O)_4Cr(OOH)(OAc)^+$ in this work should be even more facile and the H^+-catalyzed route for the back reaction more favorable than that observed for the doubly charged $(H_2O)_5CrOAc^{2+}$.[32]

For the sulfate case, none of the numerical limits in Table 3 can automatically rule out one form or the other. Our earlier analysis of the full rate law in eq 10, however, suggests that one path should be dominant, and chemical reasoning makes the I−III path a more reasonable option.

Still other combinations of various hydrolytic forms of the reactants in this work would result in a correct general rate law. For example, the $(H_2O)_5CrOOH^{2+}$/HOAc reaction can be expressed in terms of $(H_2O)_5Cr(OOH_2)^{3+}$ and OAc^-, as in eqs 13 and 14. In this case, the rate constant k_{13} would have to be $> 10^5\ M^{-1}\,s^{-1}$, which again seems unreasonably large for an aqua complex of Cr(III). This limit on the rate constant arises from the small concentrations of both reactive species ($pK_{a(CrOOH2)}$ for $(H_2O)_5CrOOH_2^{3+} < 0$,[1] pK_a for HOAc = 4.8).

$$\begin{aligned}&(H_2O)_5Cr(OOH_2)^{3+} + OAc^-\\ &\underset{k_{-13}}{\overset{k_{13}}{\rightleftharpoons}} cis\text{-}(H_2O)_4Cr(OOH)(OAc)^+ + H_2O + H^+\\ &\overset{k_{13}'}{\rightarrow} (H_2O)_5CrOAc^{2+} + H_2O_2 \qquad (13)\end{aligned}$$

$$\begin{aligned}&-d[(H_2O)_5CrOOH^{2+}]/dt\\ &= \frac{K_{a(HOAc)}k_{13}k_{13}'}{K_{a(CrOOH2)}(k_{-13} + k_{13}')}[HOAc][(H_2O)_5CrOOH^{2+}] \qquad (14)\end{aligned}$$

Similarly, the nitrate reaction could be written in terms of $(H_2O)_5Cr(OOH_2)^{3+}$ and NO_3^-. The protonated hydroperoxo complex was invoked earlier as a more reactive oxygen atom donor.[5,33] In that case, the reactivity was greatly increased by protonation, which changed the leaving group from OH^- to H_2O. In the present case, the protonation would improve the electrostatics for the initial encounter. Even though we cannot completely dismiss this option, the benefits of replacing a +2/−1 pair with a +3/−1 pair would seem to be too small given that $(H_2O)_5Cr(OOH_2)^{3+}$ is only a minute fraction of the hydroperoxochromium pool.

The dissociatively activated substitution at $Cr(H_2O)_5OOH^{2+}$ proposed here explains why the substitution rates in the initial step are not greatly affected by the degree of protonation of the reacting ligand. The final step in the reaction, eq III, is a H^+-assisted dissociation of hydroperoxide from complexes of similar composition and charge and could also be expected to differ only moderately for the three cases. In fact, the reverse reactions, k_{-I} and k_{-II}, which include acid-independent and acid-promoted dissociation of charged and uncharged ligands from the hydroperoxochromium cation are probably the step where the kinetic difference between the three ligands is the greatest.

Throughout this analysis, the accelerated substitution at chromium has been attributed to the hydroperoxo cis effect. The justification for this assignment is based on the known cis effect[14−16] of nitrate and acetate which, we believe, provides the mechanism for the formation of the hydroperoxo complex in the reverse of reaction 1. The principle of microscopic reversibility requires for the forward of that reaction to occur by the same mechanism and same transition state.

A reviewer suggested a possibility of redox-activated substitution. In principle, this is an attractive idea, but one that is difficult to accommodate with the known chemistry. Clearly, some redox chemistry takes place and generates small amounts of $(H_2O)_5CrOO^{2+}$. This appears to be a side reaction, however, and is unimportant to substitution for several reasons. Most importantly, if the chromium coordination sphere were redox-labilized, either by electron transfer or by a contribution of Cr(II) and Cr(IV) canonical forms to the ground state of the resonance hybrid, then all of the ligands would be labilized and equilibrated with the environment, yielding $Cr(H_2O)_6^{3+}$. This is contrary to the observed chemistry which interchanges two low-concentration, weak ligands (e.g., NO_3^- and OOH^-), between the Cr(III) coordination sphere and solution, producing $Cr(H_2O)_5X^{3+n}$.

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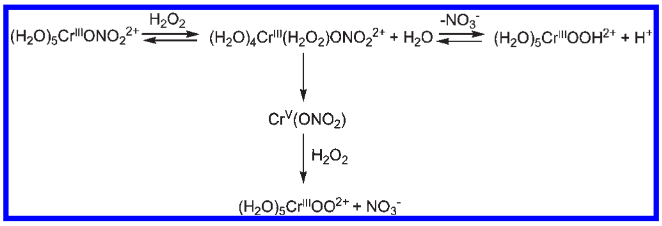
A bimolecular reaction between $(H_2O)_5CrOOH^{2+}$ and a labile chromium complex by ligand-bridged electron-transfer, in analogy with the known $Cr(H_2O)_6^{2+}$-catalyzed substitutions at inert metal centers, might yield the observed products, but a mechanism that would reproducibly generate and maintain a labile oxidation state of chromium under the experimental conditions is not obvious. $Cr(H_2O)_6^{2+}$ could not be efficient in a system that contained variable amounts of O_2 and H_2O_2, both of which rapidly oxidize $Cr(H_2O)_6^{2+}$. The former reaction generates $(H_2O)_5CrOO^{2+}$ ($k = 1.6 \times 10^8\ M^{-1}\ s^{-1}$),[34] and the latter, $Cr(H_2O)_6^{3+}$ and hydroxyl radicals ($k = 7 \times 10^4\ M^{-1}\ s^{-1}$),[35] which would further initiate complicated autoxidation of both methanol (present at 0.10 M level) and H_2O_2 and generate oxidizing intermediates. The reproducibility of our data and clean kinetics and stoichiometry argue vehemently against such a possibility. If Cr(IV) were important in the substitution reaction, the kinetics would have to be much faster than the rapid reduction of Cr(IV) by methanol to yield $Cr(H_2O)_6^{2+}$ ($k = 52\ M^{-1}\ s^{-1}$)[36] and by H_2O_2 to yield $(H_2O)_5CrOO^{2+}$ ($k = 190\ M^{-1}\ s^{-1}$).[37] Small amounts of the latter have been observed and attributed precisely to this reaction as a minor side path. In other words, when Cr(IV) is involved, it generates different products and not $Cr(H_2O)_5X^{3+n}$.

Finally, Cr(V) is believed to be formed from $Cr(H_2O)_5OOH^{2+}$ in a minor but real reaction that ultimately yields $Cr(H_2O)_5OO^{2+}$, but not $Cr(H_2O)_5X^{3+n}$. This reaction is a part of k_{dec} and is much slower (at least 10 times) than the observed substitution reactions reported here, as illustrated in Figure 1.

The mechanism presented in Scheme 1, on the other hand, can account for all of the observations. It can also explain the failure of Cl^- and DMSO to react[38] with $(H_2O)_5CrOOH^{2+}$. According to this picture, the four positions cis to $-OOH$ are labilized and available to any incoming ligand. Once the intermediate is formed, the weaker ligand will be lost, resulting either in the regeneration of $(H_2O)_5CrOOH^{2+}$ or in the formation of the product. Monodentate ligands, such as Cl^-, which themselves have no obvious mechanism to eliminate the hydroperoxo group, will be lost rapidly by the same cis effect that allowed them to coordinate. When the incoming ligand is potentially bidentate, and therefore potentially cis-labilizing, as is the case with nitrate, the ligand with the stronger cis effect will remain coordinated. In the nitrato−hydroperoxo example, either one or the other ligand can be lost, depending on concentrations. This is also true for the nitrato−DMSO complex, as reported earlier,[16] but not for the hydroperoxo−DMSO complex where DMSO is lost preferentially. This is consistent with our estimate of the much stronger cis effect of the hydroperoxo relative to that of the nitrato group.

Scheme 2



As commented previously, rapid substitution at nitratochromium(III) and related complexes may provide a path to high-valent chromium in biological systems.[13] The discovery of an even faster reverse reaction in this work not only strengthens that argument but also allows for the faster formation of reactive chromium intermediates. This is especially true for the combination of Cr(III) with carboxylic acids and H_2O_2, both of which are available in biological systems and may engage in the chemistry shown in eq 1. That reaction leads to measurable amounts of superoxochromium(III) ions, either from the mixed-ligand intermediate, as shown in Scheme 2, or in a parallel reaction, to generate Cr(V). Subsequent disproportionation or reduction would generate $(H_2O)_5CrO^{2+}$, which is known to react with H_2O_2 and yield the observed $(H_2O)_5CrOO^{2+}$.

Intramolecular electron transfer will be facilitated by the presence of anionic ligands, such as nitrate, acetate, sulfate, and so forth. Moreover, our most recent results suggest that $Cr_{aq}OOH^{2+}$ engages in this type of chemistry even in the absence of added anions.[21] Thus, the "innocuous" Cr(III) may not be innocuous in biological environments. High-valent chromium intermediates, such as Cr(IV) and Cr(V), are believed to be responsible for the carcinogenic action of chromate.[39] We have now shown that these same intermediates can be generated from Cr(III), without even involving chromate, which suggests that the ever-increasing amounts of chromium in food supplements should perhaps be reconsidered, an issue that has been raised by other authors as well.[40]

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Supporting Information Available: Figures S1−S3. This material is available free of charge via the Internet at http://pubs.acs.org.

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