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Biomimetic Chemistry of Chromium. Intramolecular Conversion of Hydroperoxochromium(III) to Oxochromium(V)

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Transition metal hydroperoxo complexes, LMOOH (L = ligand system, M = transition metal), are important intermediates in many catalytic oxidations by molecular oxygen and hydrogen peroxide. In the catalytic cycle of cyt P450, an intermediate (P)Fe^{III}OOH complex (P = porphyrin) undergoes intramolecular electron transfer producing a reactive "oxene", [P$^{\bullet+}$]Fe^{IV}O or PFe^{V}=O.[1,2] Methane monooxygenase, ribonucleotide reductase, and heme peroxidases are also believed to produce transient high valent oxo-species from peroxo or hydroperoxo precursors,[2] and a hydroperoxo complex of bleomycin causes strand scission in DNA in a scheme involving Fe(IV) or Fe(V) intermediates.[3,4]

Some synthetic hydroperoxometal complexes[5−9] persist in solution for several minutes or even hours in the absence of reducing substrates and decompose mainly by dissociation of H_2O_2 from the metal. These complexes typically react as electrophiles and one-electron oxidants[5] and show no tendency to form oxenes, presumably because the nonparticipating ligands do not stabilize the metal in the 4+ or 5+ oxidation state. We now report that a synthetic hydroperoxochromium(III) complex of a non-porphyrin, saturated macrocycle undergoes intramolecular conversion to Cr(V).

The complex *trans*-$(H_2O)L^1CrOO^{2+}$ [10] (L^1 = [14]aneN$_4$ = 1,4,8,11-tetraazacyclotetradecane) reacts with Cr_{aq}^{2+} in acidic aqueous solutions as in eq 1.[11,12] The reaction with Fe_{aq}^{2+}, on the other hand, has 1:1 stoichiometry.

$$(H_2O)L^1CrOO^{2+} + 3Cr_{aq}^{2+} + 4H^+ \rightarrow L^1Cr(H_2O)_2^{3+} + 3Cr_{aq}^{3+} + H_2O \quad (1)$$

The reduction of similar superoxometal(III) complexes $LMOO^{n+}$ [13] by Fe_{aq}^{2+} produces peroxo or hydroperoxo intermediates, which engage in Fenton-type chemistry, eqs 2−3.

$$LMOO^n + Fe_{aq}^{2+} + H^+ \rightarrow LMOOH^n + Fe_{aq}^{3+} \quad (2)$$

$$LMOOH^n + 2Fe_{aq}^{2+} + 3H^+ \rightarrow LM(H_2O)^{n+1} + 2Fe_{aq}^{3+} + H_2O \quad (3)$$

We hypothesized that the reductions of $(H_2O)L^1CrOO^{2+}$ with Cr_{aq}^{2+} and with Fe_{aq}^{2+} also start out as 1e processes yielding $(H_2O)L^1CrOOH^{2+}$ (or a binuclear peroxide), eq 2. The further reduction by Cr_{aq}^{2+} results in an overall 3:1 stoichiometry. In contrast, Fe_{aq}^{2+} does not react with $(H_2O)L^1CrOOH^{2+}$, suggesting that this hydroperoxide is unusually short-lived and can be intercepted only by potent reductants like Cr_{aq}^{2+}.

This proposal was confirmed by allowing $(H_2O)L^1CrOO^{2+}$ to react with 1 equiv of Fe_{aq}^{2+}, after which the spent reaction solution was titrated with Cr_{aq}^{2+}. Only one oxidizing equivalent, corresponding to Fe_{aq}^{3+} of eq 2, was found. The hydroperoxide had clearly decomposed during the 2−3 min that elapsed between its formation and addition of Cr_{aq}^{2+}.[14]

Kinetically, the reaction of $(H_2O)L^1CrOO^{2+}$ with Fe_{aq}^{2+} is a three-stage process,[15,16] Figure S1. The first step corresponds to eq 2, with the rate law $-d[(H_2O)L^1CrOO^{2+}]/dt = k_{Fe}[Fe^{2+}][(H_2O)L^1CrOO^{2+}]$, where $k_{Fe} = (3.52 \pm 0.25) \times 10^3$ M^{-1} s^{-1} at 0.02 M HClO$_4$. This value is almost identical to that for the reduction of $(H_2O)_5CrOO^{2+}$ to $(H_2O)_5CrOOH^{2+}$ by Fe_{aq}^{2+}.[5]

The next two stages correspond to the formation and decay of an intermediate,[17] which we show below to be a Cr(V) species. The formation stage obeys a two-term rate law, $k_{obs} = k' + k''[Fe^{2+}]$, with $k' = 0.17 \pm 0.03$ s^{-1} and $k'' = 58 \pm 14$ M^{-1} s^{-1}. At a constant ionic strength, both k' and k'' are independent of [H$^+$] in the range 0.02−0.2 M. The value of k'' is remarkably similar[6] to the rate constants for the reduction of H_2O_2 ($k = 58$ M^{-1} s^{-1}) and $(H_2O)_5CrOOH^{2+}$ ($k = 48$ M^{-1} s^{-1}) by Fe_{aq}^{2+}, supporting the notion that k'' path is the reduction of $(H_2O)L^1CrOOH^{2+}$ by Fe_{aq}^{2+}.[6] At low Fe_{aq}^{2+} concentrations, such as those used in the spectrophotometric titrations ([Fe_{aq}^{2+}] < 0.1 mM), only the [Fe^{2+}]-independent term contributes.

The decay of the intermediate, $k_{Cr(V)} = 0.19 \pm 0.03$ s^{-1}, is independent of [H$^+$] (0.02−0.2 M) and [Fe_{aq}^{2+}] (0.28−4.2 mM). The difference between the UV−visible spectra of the intermediate and final products shows an intense band at 296 nm and several maxima in the visible region (400, 440, and 518 nm), Figure S2.[16] These features, especially a strong band at ~300 nm, are typical of Cr(V) complexes.[18]

The ESR spectrum[19] of the intermediate, Figure 1, in water/propylene glycol glass at 120 K indicates that the molecule has axial symmetry and yields $g_\perp = 1.99$ and $g_\parallel = 1.96$. Values slightly under 2 are as expected for Cr(V),[18,20−26] and we assign the formula L^1CrO^{3+} to the intermediate. The peaks are broad

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[11] Spectrophotometric titrations were carried out at pH 1−2 (HClO$_4$ or CF$_3$SO$_3$H) and monitored at 290 nm, where the molar absorptivity for $(H_2O)L^1CrOO^{2+}$ is 2900 ± 300 M^{-1} cm^{-1}, somewhat larger than reported previously.[10]

[12] Data were corrected for ~10% background decomposition of $(H_2O)L^1CrOO^{2+}$ during the titration under air-free conditions.

[13] LM = $(H_2O)_5Cr^{2+}$ (Brynildson, M. E.; Bakac, A.; Espenson, J. H. *Inorg. Chem.* **1988**, *27*, 2592), $(H_2O)L^1Co^{2+}$ (Kumar, K.; Endicott, J. F. *Inorg. Chem.* **1984**, *23*, 2447. Munakata, M.; Endicott, J. F. *Inorg. Chem.* **1984**, *23*, 3693), and $(H_2O)(Me_6\text{-}[14]aneN_4)Co^{2+}$.[7]

[14] The titration was carried out at the 240 nm absorption maximum of Fe^{3+}, $\epsilon = 4160$ M^{-1} cm^{-1}. After the equivalence point was reached, the addition of more Cr_{aq}^{2+} caused no absorbance change in the 200−300 nm range.

[15] The reaction was monitored at the 290-nm maximum of $(H_2O)L^1CrOO^{2+}$ using 0.028−0.045 mM L^1CrOO^{2+}, 0.28−4.2 mM Fe_{aq}^{2+}, and 0.020 M H$^+$.

[16] Supporting Information.

[17] The two stages were resolved by fitting the data to a biexponential equation.

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[19] A small excess of Fe_{aq}^{2+} was added to an ice-cold solution of 0.1 mM $(H_2O)L^1CrOO^{2+}$ in 0.02 M HClO$_4$. The green color of $(H_2O)L^1CrOO^{2+}$ disappeared immediately. Within the next several seconds the solution turned red, at which point it was mixed with an equal volume of propylene glycol, transferred to an ESR tube, and frozen to a glass by immersion into liquid nitrogen. The spectrum was recorded by use of a Bruker ER 200 D-SRC spectrometer.

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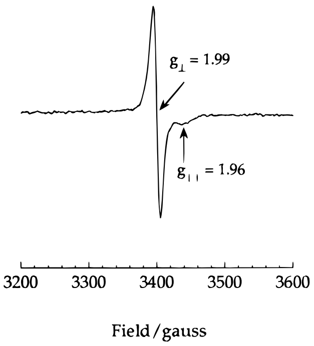
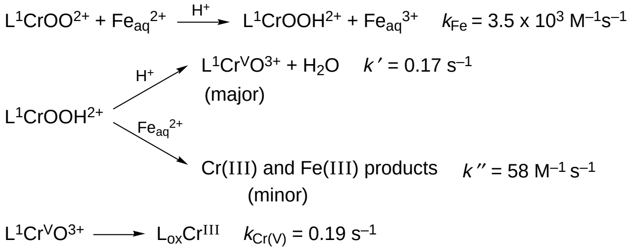


Figure 1. First derivative ESR spectrum of $L^1Cr^VO^{3+}$ (L^1 = [14]aneN_4) in 1:1 H_2O/propylene glycol glass at 120 K: $g_\perp = 1.99$, $g_\parallel = 1.96$.

Scheme 1



(11 G maximum-to-minimum separation in the perpendicular component), accounting for the absence of hyperfine splitting by ^{53}Cr ($S = 3/2$, 9.5% natural abundance). The intensity of the Cr(V) peak was somewhat greater than that of 0.1 mM diphenylpicrylhydrazine, demonstrating that significant amounts of Cr(V) were formed.

The data support the mechanism of Scheme 1, where L_{ox}-Cr^{III} represents a Cr(III) product with a modified macrocyclic ligand.

The most intriguing step in Scheme 1 is the conversion of $(H_2O)L^1CrOOH^{2+}$ to L^1CrO^{3+}, and we sought additional experimental support for this step. According to Scheme 1, any species that will reduce $(H_2O)L^1CrOO^{2+}$ to $(H_2O)L^1$-$CrOOH^{2+}$ but not react directly with $(H_2O)L^1CrOOH^{2+}$ should produce L^1CrO^{3+} with the rate constant $k' = 0.17\ s^{-1}$. This was confirmed by use of an outer-sphere reductant, $ABTS^{2-}$.[27] The reduction of $(H_2O)L^1CrOO^{2+}$, monitored at the 650 nm maximum of $ABTS^{\bullet-}$, is a biphasic process, Figure S3.[16] The rate constant for the first stage has a value $k_A = (2.53 \pm 0.01) \times 10^4\ M^{-1}\ s^{-1}$. The second stage is strictly first order, $k' = 0.17 \pm 0.02\ s^{-1}$, at 0.1 mM ≤ $[ABTS^{2-}]$ ≤ 5.0 mM. The absorbance increase in the second stage was exactly twice as large as that in the first. The results strongly support Scheme 2, in which the intramolecular conversion of $(H_2O)L^1CrOOH^{2+}$ to L^1CrO^{3+} is followed by rapid oxidation of two additional moles of $ABTS^{2-}$.

Scheme 2

$$L^1CrOO^{2+} + ABTS^{2-} \xrightarrow{H^+} L^1CrOOH^{2+} + ABTS^{\bullet-}$$
$$k_A = 2.53 \times 10^4\ M^{-1}\,s^{-1}$$

$$L^1CrOOH^{2+} \xrightarrow{H^+} L^1Cr^VO^{3+} + H_2O \quad k' = 0.17\ s^{-1}$$

$$L^1Cr^VO^{3+} + 2ABTS^{2-} \xrightarrow{H_2O,\ H^+} L^1Cr(H_2O)_2^{\ 3+} + 2ABTS^{\bullet-}$$
$$\text{fast}$$

One experiment used only a 2-fold excess of $ABTS^{2-}$ over $(H_2O)L^1CrOO^{2+}$. After all of the $ABTS^{2-}$ was oxidized to $ABTS^{\bullet-}$, further oxidation of $ABTS^{\bullet-}$ to $ABTS^0$ (λ_{max} 518 nm) took place, again with a rate constant $k' = 0.17\ s^{-1}$. Thus even $ABTS^{\bullet-}$ reacts rapidly with L^1CrO^{3+}. The reduction potential of the couple $ABTS^0/ABTS^{\bullet-}$ is 1.09 V vs NHE,[27] which places the lower limit for the one-electron potential of L^1CrO^{3+} at ~1.1 V.

Attempts were made to characterize $L_{ox}Cr(III)$, the decomposition product of L^1CrO^{3+}. After the reaction with $Fe_{aq}^{\ 2+}$ was complete, the reaction mixture was ion-exchanged on Sephadex C25 cation-exchange resin. The elution behavior of the product indicated a 3+ charge. Complete separation from unreacted $L^1Cr(H_2O)_2^{3+}$ [28] was not achieved, but early fractions showed bands at 482 and 369 nm, significantly removed from the 510- and 350-nm maxima of $L^1Cr(H_2O)_2^{3+}$. Intramolecular oxidations of N_4-macrocycles usually result in the formation of monoimine complexes or the rupture of the macrocycle.[29,30] An interesting possibility for L^1CrO^{3+} is the oxidation of the macrocycle by oxygen atom insertion into a C−H bond, in analogy to cyt P450. The extreme solubility of the product in water is consistent with the presence of an additional OH group in the macrocycle. We continue to work on the characterization of the product as well as the chemistry of L^1CrO^{3+}.

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Supporting Information Available: Figures S1−3 (3 pages). See any current masthead page for ordering and Internet access instructions.

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