On the Mechanism of *cis*-Dioxovanadium(V)-Catalyzed Oxidation of Bromide by Hydrogen Peroxide: Evidence for a Reactive, Binuclear Vanadium(V) Peroxo Complex

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Abstract: Bromide oxidation by hydrogen peroxide is catalyzed by *cis*-dioxovanadium(V) in acidic, aqueous and aqueous/ethanolic solution. Hydrogen peroxide consumption is stoichiometric with bromide oxidation. Bromide is oxidized by two electrons and can undergo further reaction with organic substrates or hydrogen peroxide. The dependence of the rate of bromide oxidation is second order in vanadium concentration and first order in bromide concentration. Coordination of hydrogen peroxide by vanadium(V) gives rise to an equilibrium mixture of oxomonoperoxo- and oxodiperoxovanadium(V), whose composition is dependent on the concentrations of acid and hydrogen peroxide. Kinetic and spectroscopic analyses suggest that catalysis occurs by dimerization of oxomonoperoxo- and oxodiperoxovanadium(V) to form a binuclear, triperoxo vanadium(V) complex followed by oxidation of bromide. Ethanol increases the rate of the reaction by increasing the formation of the vanadium(V) dimer. The bimolecular rate of bromide oxidation by the vanadium dimer is 4.1 ± 0.1 M^{-1} s^{-1}. The relevance of this catalytic system to vanadium bromoperoxidase and to other metal-catalyzed halide oxidations is discussed.

Introduction

Interest in understanding transition metal-catalyzed oxidation of halide by hydrogen peroxide has increased recently,[1–8] after a lull following the initial reports of iodide oxidation.[9,10] In part, this interest stems from the discovery of vanadium bromoperoxidase,[11] a vanadium enzyme which catalyzes the oxidation of chloride,[12] bromide, and iodide by hydrogen peroxide.[13,14] All the halides except fluoride can be oxidized by hydrogen peroxide under neutral and acidic conditions. The redox potentials of halide oxidation by hydrogen peroxide are pH-dependent, such that hydrogen peroxide is able to oxidize the less electronegative halides under more basic conditions.

Vanadium bromoperoxidase, which is isolated primarily from marine macro-algae, is an acidic protein[15,16] with 1 mol of vanadium(V) per mol of subunit.[15,17,18] Bromide oxidation is the first step in the catalytic cycle, and the reactions following bromide oxidation are established:[19,20] (1) the oxidized product reacts with an organic substrate, which in some cases is enzyme-associated,[21] or (2) it oxidizes an additional equivalent of hydrogen peroxide, to yield singlet oxygen and halide (Scheme 1).[22] The steady-state kinetic parameters from these two reactions agree within a factor of 2, which implies that both pathways proceed through a common intermediate, the production of which is rate-limiting.[19] Although formally the equivalent of a "Br^+" ion, the precise identity of this intermediate (*e.g.*, HOBr, Br_2, Br_3^-, V_{enz}–OBr, enz-Br) is not known. The proposed mechanism involves the ordered binding of one substrate followed by binding of the other substrate. Although the order of substrate binding cannot be determined from the steady-state kinetic measurements, the UV spectrum is changed on addition of hydrogen peroxide and restored following bromide addition.[23] On the basis of these observations, de Boer and Wever suggested that hydrogen peroxide binds to the enzyme before bromide is oxidized.[24]

Several functional mimics of vanadium bromoperoxidase have been reported in which the metal is vanadium,[1–3,5] molybdenum,[6,7] rhenium,[4] and tungsten.[6] We reported recently that *cis*-dioxovanadium(V), *cis*-VO_2^+, catalyzes the oxidation of bromide by hydrogen peroxide[1] under acidic conditions (*e.g.*, 0.05 M $HClO_4$). In this reaction, hydrogen peroxide consumption is stoichiometric with bromide oxidation. The oxidation of

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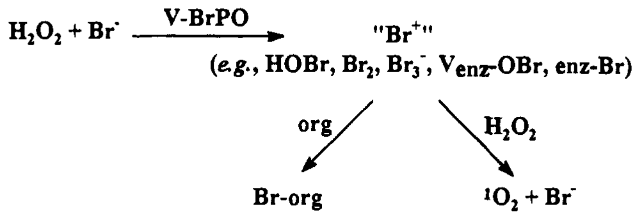
Scheme 1



bromide yields a two-electron oxidized intermediate ("Br^+"). This unstable "Br^+" species either brominates a suitable organic substrate or reacts with additional hydrogen peroxide to yield dioxygen and regenerate bromide. These two pathways mimic those observed in the enzymatic reaction: peroxidative bromination and halide-assisted disproportionation of hydrogen peroxide.[25] The reduction of hypobromous acid by hydrogen peroxide to produce dioxygen and bromide occurs under acidic conditions by the direct reaction:[26]

$$HOBr + H_2O_2 \rightarrow O_2 + Br^- + H_3O^+ \qquad (1)$$

HOBr rapidly equilibrates with Br_2 and Br_3^-. Consequently, the reduction of HOBr can be suppressed under conditions of high bromide and acid, which lower the concentration of HOBr by shifting the equilibrium to Br_2 and Br_3^-. Then the rate of bromide oxidation can be measured by the rate of formation of tribromide (Br_3^-). This pathway constitutes a third method for monitoring the oxidation of bromide over several minutes. In our previous communication, we established the stoichiometry and reactivity of the *cis*-VO_2^+-catalyzed oxidation of bromide by hydrogen peroxide.[1] Herein, we consider mechanistic questions and report a kinetic analysis and some related spectroscopic studies of the same system.

The speciation and equilibria of aqueous vanadium(V) and oxoperoxovanadium(V) species are both complex and well-studied. Under neutral and alkaline conditions, at vanadium concentrations below 0.5 mM, vanadium(V) exists primarily as a monomeric oxyanion (VO_4^{3-}, HVO_4^{2-}, $H_2VO_4^-$),[27,28] while under acidic conditions ($[H^+] > 5 \times 10^{-4}$ M), the predominant species is *cis*-VO_2^+.[29] Under neutral and basic conditions, coordination of hydrogen peroxide to vanadate gives anionic peroxovanadates, with one to four coordinated peroxide ligands, and peroxodivanadates.[30-32] Under acidic conditions, addition of hydrogen peroxide to VO_2^+ gives the red oxomonoperoxo $VO(O_2)^+$ and the yellow oxodiperoxo $VO(O_2)_2^-$ species, as described by eqs 2 and 3.

$$VO_2^+ + H_2O_2 \rightleftarrows VO(O_2)^+ + H_2O \qquad K_1 \qquad (2)$$

$$VO(O_2)^+ + H_2O_2 \rightleftarrows VO(O_2)_2^- + 2H^+ \qquad K_2 \qquad (3)$$

The coordination of the first equivalent of hydrogen peroxide to VO_2^+ is acid-independent. When the second equivalent of peroxide coordinates, two equivalents of acid are released. Consequently, the relative concentrations of $VO(O_2)^+$ and $VO(O_2)_2^-$ depend on acid concentration as well as hydrogen peroxide concentration. $VO(O_2)_2^-$ is favored by low acid and high hydrogen peroxide concentrations, while $VO(O_2)^+$ is favored by high acid and low hydrogen peroxide concentrations. On the basis of spectrophotometric measurements, the equilibrium constants K_1 and K_2 are $(3.7 \pm 0.4) \times 10^4$ M^{-1} and 0.6 ± 0.1 M, respectively, at 0.3 M ionic strength and 25 °C.[9] At 1.0 M ionic strength and 25 °C, K_1 and K_2 are 3.5×10^4 M^{-1} and 1.3 M, respectively, showing that K_2, but not K_1, is sensitive to ionic strength.[33]

Several dimeric peroxo vanadium(V) complexes are formed in aqueous solution over the entire pH range, of which two are well-characterized. Over the pH range 4.5−7, dioxotetraperoxodivanadate is the predominant dimeric species.[30,31] Under more acidic conditions (pH ≤ 2), dioxotriperoxodivanadium(V), $(VO)_2(O_2)_3$, is the predominant dimeric complex, which has been proposed to form from the dimerization of $VO(O_2)^+$ and $VO(O_2)_2^-$:[34]

$$VO(O_2)^+ + VO(O_2)_2^- \rightleftarrows (VO)_2(O_2)_3 \qquad K_3 \qquad (4)$$

From ^{51}V NMR measurements, a value for K_3 of *ca.* 9 M^{-1} was obtained at pH 0−2 in the presence of $NaClO_4$ ($\mu = 2.0$ M) and in the absence of added $NaClO_4$.[31] The equilibria defined by eqs 2−4 describe the formation and decomposition of $VO(O_2)^+$, $VO(O_2)_2^-$, and $(VO)_2(O_2)_3$ and provide the basis for understanding the kinetics of the vanadium(V)-catalyzed oxidation of bromide in acidic, aqueous solution (see Results and Interpretation, below).

In other systems, vanadium(V) peroxo complexes are also versatile oxidants.[35] They catalyze oxidation and oxygenation reactions by radical and electrophilic mechanisms. Some monoperoxo complexes are more reactive than their diperoxo analogues,[36] while others are significantly less reactive.[37] Efforts to develop a comprehensive explanation of these differences in reactivity have been stymied by the fact that changes in solvent, as well as minor changes in coordination environment, can alter both mechanisms and patterns of reactivity.[35-37]

cis-VO_2^+-catalyzed bromide oxidation by hydrogen peroxide initially appeared to be an excellent system to address questions regarding the relative reactivities of mono- and diperoxo vanadium complexes.[1] Iodide oxidation was reported[9] to proceed through differently protonated states of $VO(O_2)^+$ and $VO(O_2)_2^-$, with the latter being more reactive. Oxidation of a thiolato Co^{III} complex was reported to occur only from the reaction of differently protonated states of $VO(O_2)_2^-$.[37] By contrast and to our surprise, our kinetic and spectroscopic results are consistent with a mechanism in which bromide is oxidized by the binuclear, oxotriperoxodivanadium(V) species. Our results show that the mechanism of bromide oxidation in this system differs from the mechanisms of other vanadium-

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(25) Bromide was shown to be required for the disproportionation reaction, distinguishing this reaction from the much slower reaction which is not bromide dependent.[46]

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catalyzed[36,38–40] or vanadium-mediated[41,42] oxidations, bromide-oxidation reactions catalyzed by other metals,[1–10] and the enzymatic reaction.[13]

Materials and Methods

General. All chemicals were reagent grade or better and were used as received. Distilled water was further purified by ion-exchange and charcoal filtration (Barnstead NANOpureII). Hydrogen peroxide was standardized spectrophotometrically by measuring the oxidation of iodide to triiodide (λ_{max} = 353 nm, ϵ = 26 400 M^{-1} cm^{-1}), catalyzed by chloroperoxidase, using the method of Cotton and Dunford.[43]

Kinetic Measurements. The initial-rate kinetic measurements were performed on a 3-mL scale in 1-cm path length quartz cuvettes. Tribromide (Br_3^-) formation was measured at 268 nm (ϵ = 36 100 M^{-1} cm^{-1}).[51] Spectra were collected primarily on a Hewlett Packard 8452a diode array spectrophotometer. The participation of photochemical side reactions was considered by reducing the sampling time 10-fold; no alteration in the rate of bromide oxdation was observed on the time scale (≤2 min) of the kinetic measurements. Xylene cyanole bromination was measured by the decrease in absorbance at 616 nm ($\Delta\epsilon$ = 6010 M^{-1} cm^{-1} at 0.05 M $HClO_4$).[44] The kinetics of monochlorodimedone (2-chloro-5,5-dimethyl-1,3-cyclohexanedione; MCD) bromination were measured by the decrease in absorbance on bromination of MCD to bromochlorodimedone on a Kontron Uvikon 860 at 270 nm [$\Delta\epsilon$ = 12 800 M^{-1} cm^{-1} under acidic (0.01–0.20 M) conditions[4]]; the absorbance maximum and the extinction coefficient of MCD differ under the acidic conditions employed in this work from those under the near-neutral conditions used for enzymatic assays. For each reaction, stock solutions of ammonium vanadate (5.0 mM) and perchloric acid (0.429 and 4.29 M) were mixed and allowed to equilibrate for 5 min to ensure the complete dehydration of vanadate to *cis*-dioxovanadium(V) cation. The other reagents (ammonium bromide, sodium perchlorate, water, and, as needed, ethanol and organic substrates) were added (except the initiator, hydrogen peroxide) and the cuvettes were incubated in a water bath (23.0 ± 0.1 °C) for 5 min. Reactions were generally initiated by the addition of hydrogen peroxide, and identical results were obtained from initiation with ammonium bromide. The reactions in which the kinetics were analyzed over the entire time-course were measured on a quarter-milliliter scale in 0.1-cm path length cells under otherwise identical conditions.

Kinetic Analyses. Initial-rate data were fit using the software of the HP or Kontron spectrophotometers or the data analysis and plotting program PSI-plot (Polysoft International, Inc., Salt Lake City, UT). The initial-rate data were corrected for the vanadium-independent reaction (except where noted). This reaction has also been referred to as an acid-catalyzed reaction.[45] The rate of this reaction is described by the rate law $d[Br^+]/dt = k_H[H^+][H_2O_2][Br^-]$. The calculation of the rate of the vanadium-independent reaction relies on the value of the concentration of uncomplexed hydrogen peroxide, $[H_2O_2]_u$, in solution. The concentration of uncomplexed hydrogen peroxide was obtained by subtracting the concentration of vanadium-bound peroxide (in $VO(O_2)^+$ and $VO(O_2)_2^-$) from the total added hydrogen peroxide, $[H_2O_2]_0$.

$$[H_2O_2]_u = [H_2O_2]_0 - [VO(O_2)^+] - 2[VO(O_2)_2^-] \qquad (5)$$

By expressing $[VO(O_2)^+]$ and $[VO(O_2)_2^-]$ in terms of the acid, hydrogen peroxide, and total vanadium, $[V_T]$, concentrations, the expression for the concentration of uncomplexed hydrogen peroxide becomes

$$[H_2O_2]_u = [H_2O_2]_0 - [V_T]\left\{1 + \frac{K_2[H_2O_2]'}{K_2[H_2O_2]' + [H^+]^2}\right\} \qquad (6)$$

The concentration of hydrogen peroxide in solution was obtained using this equation iteratively. In the first iteration, $[H_2O_2]'$ was set equal to $[H_2O_2]_0$. In subsequent iterations, the value derived for $[H_2O_2]_u$ was used as $[H_2O_2]'$. $[H_2O_2]_u$ generally converged after two iterations. The difference between $[H_2O_2]_0$ and $[H_2O_2]_u$ is dependent on the concentrations of oxomonoperoxovanadium(V) and oxodiperoxovanadium(V), and hence on the concentrations of hydrogen peroxide and acid. The amount of peroxide bound to vanadium varies between 1 and 2 mol per mol of vanadium. Since the hydrogen peroxide concentration was generally 25-fold greater than the vanadium concentration, the correction for bound peroxide was usually small (5–8%, depending on the acid concentration). It became substantial at low hydrogen peroxide concentrations: for instance, when $[H_2O_2]_0$ = 1 mM, $[V_T]$ = 200 μM, and $[H^+]$ = 0.05 M, the correction in converting $[H_2O_2]_0$ to $[H_2O_2]_u$ was *ca.* 25%.

The fitting and interpretation of the initial rates of the vanadium-dependent oxidation of bromide by hydrogen peroxide depend on the value of K_2 (see Results and Interpretation, below). The initially chosen value of K_2 was determined by ^{51}V NMR (see below); the data were fit to eq 14, giving values for kK_3 and K_2. This refined value for K_2 was then used iteratively until it converged. Data manipulation was performed with the spreadsheet program Quattro-Pro. Non-linear curve fitting was performed using the Simplex and Marquadt-Levenberg fitting routines in PSI-Plot.

^{51}V NMR Measurements of K_2 and K_3. ^{51}V NMR spectra were collected at 79 MHz with a GE GN300 spectrometer on unlocked, non-spinning, 2-mL samples, in 10-mm tubes, at 25 °C using $VOCl_3$ as an external reference. Typically, 1–2000 scans were collected. The exponential multiplier was 20 Hz. Reactions were made by allowing ammonium (or sodium) vanadate and perchloric acid to equilibrate as described above. Ionic strength was adjusted with $NaClO_4$. Hydrogen peroxide was added immediately prior to insertion in the magnet. Signal areas for the determination of K_2 and K_3 were obtained using GEMCAP, an interactive curve-fitting routine supplied in the GN software. The total signal areas were constant within 10%, indicating that all the vanadium was observed under these conditions. Using eq 3, values for K_2 were calculated from the fitted curve areas, the known acid concentration, and the uncomplexed hydrogen peroxide concentration ($[H_2O_2]_u$). The equilibrium constant for dimer formation, K_3, was calculated from eq 4 using the fitted ^{51}V NMR signal areas.

^{35}Cl and ^{79}Br NMR Measurements. ^{35}Cl and ^{79}Br NMR spectra were collected at 29 and 75 MHz, respectively, with a GE GN300 spectrometer on unlocked, non-spinning, 2-mL samples, in 10-mm tubes, at 25 °C. The exponential multiplier was 5 Hz. Line widths were calculated based on a Lorentzian function and compared to identical chloride and bromide samples, prepared without vanadium(V) and hydrogen peroxide.

Results and Interpretation

Vanadium Dependence of Bromide Oxidation. Acidic solutions of hydrogen peroxide, with catalytic amounts of vanadium(V), oxidize bromide. The concentration of bromide oxidized is stoichiometric with hydrogen peroxide consumption.[1] Initial rates of bromide oxidation were measured by following the appearance of Br_3^- at 268 nm (ϵ = 36 100 M^{-1} cm^{-1}). Reactions were performed under conditions of 25- to 200-fold excess of hydrogen peroxide over vanadium(V) (25–200 μM NH_4VO_3) and a 200-fold excess of ammonium bromide (1 M) over hydrogen peroxide (5 mM). Under these conditions, the initial rate of Br_3^- formation is second order with respect to vanadium concentration (Figure 1). The second-order depen-

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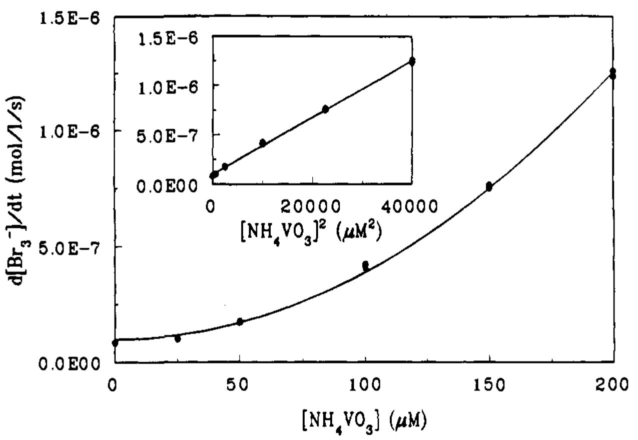

Figure 1. Initial rate of tribromide formation as a function of vanadium concentration. Inset: Rate plotted against vanadium concentration to the second power. Reaction conditions: 25–200 μM NH_4VO_3, 0.05 M $HClO_4$, 1.0 M NH_4Br, 5.08 mM H_2O_2; $\mu = 2.0$ M ($NaClO_4$); 23 °C. The fit (i.e., the curved line) is $d[Br_3^-]/dt = 9.88 \times 10^{-8}$ M s^{-1} + (28.9 M^{-1} s^{-1})$[NH_4VO_3]^2$. $r^2 = 0.9994$.

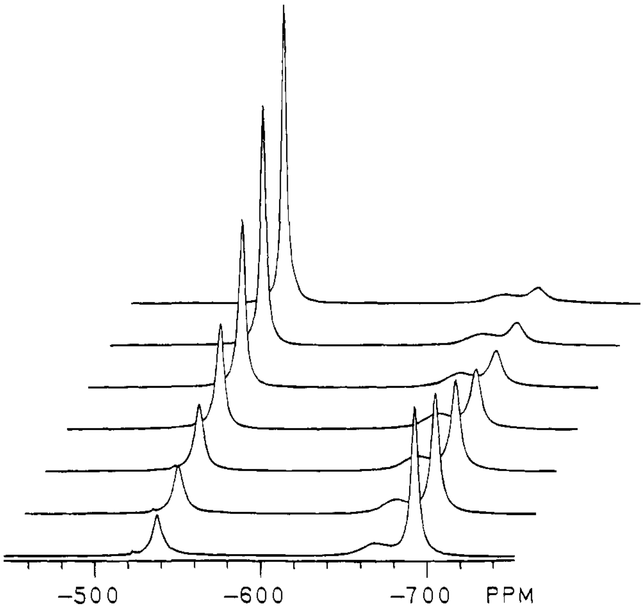

Figure 2. ^{51}V NMR spectra of oxoperoxovanadium(V) complexes. The signals are assigned[1,30,31,50] as follows: −540 ppm, $VO(O_2)^+$; −670 ppm, dioxotriperoxodivanadium(V); −698 ppm, $VO(O_2)_2^-$. Conditions: 40 mM NH_4VO_3, 0.13 M $HClO_4$, *ca.* 100 mM hydrogen peroxide (initial concentration); $\mu = 2.0$ M ($NaClO_4$); 25 °C.[47] Spectra were collected on the same sample over time without a delay between successive spectra. Acquisition time was *ca.* 4 min per spectrum. Sample preparation is described in the Methods section.

dence on vanadium concentration suggests the possible involvement of a vanadium(V) dimer.

Under acidic conditions, at vanadium concentrations up to 20 mM and several-fold excess of hydrogen peroxide, ^{51}V NMR spectroscopy reveals resonances at −540 and −698 ppm, which are assigned[1,31,32] to $VO(O_2)^+$ and $VO(O_2)_2^-$, respectively. A solution of 40 mM sodium (or ammonium) vanadate and 100 mM hydrogen peroxide shows the same, two resonances, at −540 and −698 ppm, from the oxomonoperoxo- and oxodiperoxovanadium(V) complexes, respectively, and a third, broad resonance at *ca.* −670 ppm (Figure 2), which has been previously assigned to dioxotriperoxodivanadium(V).[31] The resonance at −670 ppm is not observed at 0.5 mM ammonium vanadate, 5 mM hydrogen peroxide, and 0.05 M perchloric acid, which are the conditions under which we originally investigated *cis*-VO_2^+-catalyzed oxidation of bromide by hydrogen peroxide.[1] To measure a formation constant for the dimer, we took advantage of the vanadium(V)-catalyzed decomposition of hydrogen peroxide to obtain varied concentrations of $VO(O_2)^+$, $VO(O_2)_2^-$, and the dimer, $(VO)_2(O_2)_3$.[46] ^{51}V NMR spectra were recorded over time as the peroxide decomposed (Figure 2). The formation constant of the dimer, K_3, is defined by the concentrations of $VO(O_2)^+$, $VO(O_2)_2^-$, and the dimer:

$$K_3 = \frac{[(VO)_2(O_2)_3]}{[VO(O_2)^+][VO(O_2)_2^-]} \qquad (7)$$

K_3 was determined by measuring the signal areas of the three vanadium species ($VO(O_2)^+$, $VO(O_2)_2^-$, and $(VO)_2(O_2)_3$). A value for K_3 of 32 ± 4 M^{-1} was calculated from the ^{51}V NMR signal areas at 0.13 M $HClO_4$ added (0.05 M $HClO_4$ after dehydration of vanadate),[47] 40 mM $NaVO_3$, and *ca.* 100 mM H_2O_2. At a higher perchloric acid concentration (0.21 M added, 0.13 M after dehydration of vanadate)[47] and otherwise identical conditions, the ^{51}V NMR spectra were qualitatively similar, except that the initial concentration of $VO(O_2)_2^-$ was reduced with respect to $VO(O_2)^+$, as predicted by eq 3; here the value of K_3 was 32 ± 5 M^{-1}, showing the K_3 is independent of acid concentration [$\mu = 2.0$ M ($NaClO_4$) in both reactions]. Our value compares reasonably well with the K_3 value of *ca.* 9 M^{-1} determined by Harrison and Howarth using $NaVO_3$ concentrations up to 0.5 M and the same ionic strength (2.0 M ($NaClO_4$)) over a pH range of 0.1–1.7.[31] Consistent with their findings, our determination of K_3 is independent of ionic strength (K_3 = 26 ± 6 and 32 ± 4 M^{-1} at μ = 0.3 and 2.0 M ($NaClO_4$), respectively). Another determination of K_3 using NH_4ClO_4 in place of $NaClO_4$ to control ionic strength (to *ca.* 1 M)[48] yielded a value of 30 ± 5 M^{-1}.[49] Since the composition (with respect to hydration) and the structure of this dimer are not known, we use the formulation $(VO)_2(O_2)_3$ for simplicity.

Decreasing the temperature decreased the ^{51}V NMR line width of the dimer. At 25 °C, the line width of the dimer was 1310 Hz at 25 °C, 595 Hz at 8 °C, and 561 Hz at −5 °C. By contrast, the change in the line widths of the monomeric species was negligible. The excess line width of the dimer at higher temperature is likely due to exchange-broadening, suggesting that the dimer is in rapid equilibrium with $VO(O_2)^+$ and $VO(O_2)_2^-$.

Bromide Dependence. The initial rate of V(V)-catalyzed bromide oxidation was found to depend on the bromide

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(46) The kinetics of the vanadium-catalyzed decomposition of hydrogen peroxide have been partially characterized at neutral pH.[59] Recently, they have also been investigated in some detail at pH 0: Bonchio, M.; Conte, V.; Di Furia, F.; Modena, G.; Moro, S.; Edwards, J. O. *Inorg. Chem.* **1994**, *33*, 1631–7. The vanadium(V)-catalyzed disproportionation of hydrogen peroxide under acidic conditions must be distinguished from the vanadium(V)-catalyzed, *halide-assisted* disproportionation of hydrogen peroxide. The disproportionation reaction in the absence of bromide is much slower than in the presence of bromide, where the initial reaction is the oxidation of bromide, followed by oxidation of hydrogen peroxide.

(47) The acid concentration upon equilibration is reduced in this experiment from the initial concentration by the reaction $VO_3^- + 2H^+ \rightarrow VO_2^+ + H_2O$, see: LaSalle, M. J.; Cobble, J. W. *J. Phys. Chem.* **1955**, *59*, 519–24. With the sodium vanadate concentration equal to 0.04 M, this reaction results in a decrease in the acid concentration of 0.08 M, see: Dean, G. A. *Can. J. Chem.* **1961**, *39*, 1174–83.

(48) NH_4ClO_4 was prepared *in situ* by neutralizing perchloric acid with ammonium hydroxide. Limited solubility made it impossible to maintain the ionic strength at 2.0 M. *Caution!* NH_4ClO_4 is known to detonate upon heating in the solid state. Appropriate safety measures should be observed.

(49) Although the value of K_3 is unaffected by ammonium ion, at 40 mM $NaVO_3$, 0.05 M $HClO_4$, and *ca.* 100 mM H_2O_2, oligomeric species are visible in the ^{51}V NMR, suggesting that ammonium ion affects the value of K_1 or of the formation constants for multimeric vanadates. The result should not affect the kinetics described here, as these kinetic reactions are done using at least 100-fold less vanadium.

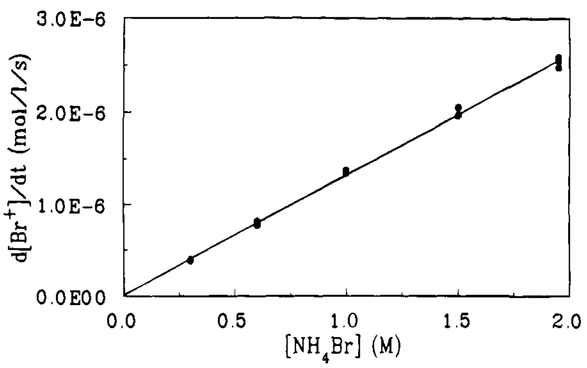

Figure 3. Initial rate of vanadium-catalyzed tribromide formation as a function of bromide concentration. Reaction conditions: 200 μM NH_4VO_3, 0.05 M $HClO_4$, 0.3−1.95 M NH_4Br, 5.08 mM H_2O_2; μ = 2.0 M ($NaClO_4$); 23 °C. The equation of the fitted line is $d[Br^+]/dt = 1.75 \times 10^{-8}\ M^{-1}\ s^{-1} + (1.30 \times 10^{-6}\ s^{-1})[NH_4Br]$. $r^2 = 0.999$.

concentration (Figure 3). The observed data were corrected in two ways for analysis of the dependence on bromide and determination of the fundamental rate constants. First, the observed rate of tribromide formation is a combination of the rate of bromide oxidation and the rapidly-established equilibrium between bromine and tribromide:

$$Br_2 + Br^- \rightleftarrows Br_3^- \qquad (8)$$

The equilibrium constant is 17 M^{-1},[50,51] so the fraction of oxidized bromine which exists as tribromide varies from 0.84 at 0.3 M bromide to 0.97 at 1.95 M bromide. The observed rates of tribromide formation ($d[Br_3^-]/dt$) are converted[52] to rates of "Br^+" formation ($d[Br^+]/dt$).[53] The magnitude of this correction is variable, increasing the rate 16% at 0.3 M Br^- and 3% at 1.95 M Br^-. Second, the observed rate of bromide oxidation was corrected for the rate of the vanadium-independent oxidation of bromide by hydrogen peroxide (see below). Under these conditions (Figure 3, caption), the correction for the vanadium-independent reaction is 5% of the observed rate of tribromide formation. The corrected data are shown in Figure 3. The fit to the corrected data shows a first-order dependence on bromide concentration.

Vanadium-Independent Reaction. The non-zero intercept in Figure 1 indicates that a vanadium-independent reaction is operative under the conditions of the kinetic measurements. The oxidation of bromide by hydrogen peroxide in acidic solution was studied by Mohammed and Liebhafsky.[45] The products of bromide oxidation (HOBr, Br_2, Br_3^-) undergo further reaction with hydrogen peroxide under their conditions of high hydrogen peroxide and low bromide concentrations to evolve dioxygen. The net reaction is thus the disproportionation of hydrogen peroxide, and the acid serves as a catalyst. At 0.4 M ionic strength, the rate law for the uncatalyzed and acid-catalyzed oxidation of bromide by hydrogen peroxide is[45]

$$\frac{d[O_2]}{dt} = \frac{d[Br^+]}{dt} = \{3.8 \times 10^{-7} + (2.3 \times 10^{-4})[H^+]\}[H_2O_2][Br^-] \qquad (9)$$

Thus, the dominant pathway under at least mM acid concentrations is the acid-catalyzed portion.

It was necessary for us to determine the rate of the vanadium-independent oxidation of bromide by hydrogen peroxide under our conditions (0, 15, and 25% ethanol and 2.0 M ionic strength). The initial rates of tribromide formation were measured spectrophotometrically and converted to rates of Br^+ formation[52] under the following conditions: 1−50 mM hydrogen peroxide, 0.3−1.95 M ammonium bromide, and 0.005−0.2 M perchloric acid in 0, 15, and 25% (v/v) ethanolic solution. Under these acidic conditions, only an acid-dependent reaction is observed, as expected from eq 9. The observed rate law is

$$\frac{d[Br^+]}{dt} = k_H[H^+][H_2O_2][Br^-] \qquad (10)$$

where $k_H = (2.92 \pm 0.08) \times 10^{-4}\ M^{-2}\ s^{-1}$ in the absence of ethanol at 23 °C and μ = 2.0 M. The reported error is the standard deviation in the determinations of k_H from the three fits of rate *vs* reactant concentration. Recently, Espenson *et al.*[4] determined a value for k_H of $(4.9 \pm 0.3) \times 10^{-4}\ M^{-2}\ s^{-1}$ by measuring the steady-state concentration of bromine at 1.0 M perchloric acid, 25 °C, and μ = 2.0 M.

Acid and Hydrogen Peroxide Dependences. The dependences of the initial rate of vanadium(V)-catalyzed oxidation of bromide by hydrogen peroxide on the concentrations of acid and hydrogen peroxide are more complex than the vanadium and bromide dependences (Figures 4a and 5a). The initial rate of MCD bromination was measured as a function of acid concentration at three hydrogen peroxide concentrations (Figure 4a). At low concentrations of acid, the initial rate of bromide oxidation is slow. The rate increases with increasing acid concentration until a maximum is reached. At still higher concentrations, the rate decreases. The value of the acid concentration at which the maximal rate occurs depends on the hydrogen peroxide concentration [Figure 4a, curves A (5 mM H_2O_2), B (15 mM H_2O_2), and C (25 mM H_2O_2)]. Similar to the dependence of the initial rate on acid concentration, the dependence on hydrogen peroxide concentration shows a maximal rate at an intermediate hydrogen peroxide concentration (Figure 5a). That is, at low H_2O_2 concentration (at a fixed acid concentration), the rate is slow, increases to a maximum, and then decreases at high [H_2O_2].

Since the equilibrium between oxomonoperoxo- and oxodiperoxovanadium(V) is dependent on both acid and hydrogen peroxide concentrations (eq 3) and the initial rate of bromide oxidation has a second-order dependence on the vanadium concentration, it seemed possible that both oxomonoperoxo- and oxodiperoxovanadium might be required for catalytic turnover. If we consider the hypothesis that bromide is oxidized by a vanadium(V) dimer formed from $VO(O_2)^+$ and $VO(O_2)_2^-$, then maximal rates should be observed when the concentrations of $VO(O_2)^+$ and $VO(O_2)_2^-$ are equal. From eq 3, it is apparent that this condition (*i.e.*, $[VO(O_2)^+] = [VO(O_2)_2^-]$) should be satisfied at a particular acid concentration for each fixed hydrogen peroxide concentration. Indeed, increased hydrogen peroxide concentration requires increased acid concentration to achieve the maximal rate (Figure 4a). Also, the maximal rate at each of the three hydrogen peroxide concentrations (Figure 4a) is the same, which is consistent with the formation of a

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(50) Griffith, R. O.; McKeown, A.; Winn, A. G. *Trans. Faraday Soc.* **1932**, *28*, 101−7.

(51) For a useful review of aqueous halogen chemistry, see: Thompson, R. C. In *Advances in Inorganic and Biochemical Mechanisms*; Academic Press Inc.: New York, 1986; Vol. 4, pp 65−106.

(52) From the equilibrium expression of tribromide (eq 8), it can be seen that $K_{Br}[Br^-] = [Br_3^-]/[Br_2]$. Since $[Br^+] = [Br_3^-] + [Br_2]$, multiplying $[Br_2]$ by $[Br_3^-]/[Br_3^-]$ and factoring gives $[Br^+] = [Br_3^-]\{1 + ([Br_2]/[Br_3^-])\}$. Substituting $K_{Br}[Br^-]$ for $[Br_2]/[Br_3^-]$ yields the necessary multiplicative factor, $1 + 1/(17[Br^-])$, to convert $d[Br_3^-]/dt$ to $d[Br^+]/dt$.

(53) $d[Br^+]/dt$ is the notation used for the rate of formation of all the oxidized bromine species (HOBr, Br_2, Br_3^-), which undergo rapid equilibration or trapping by an organic substrate.

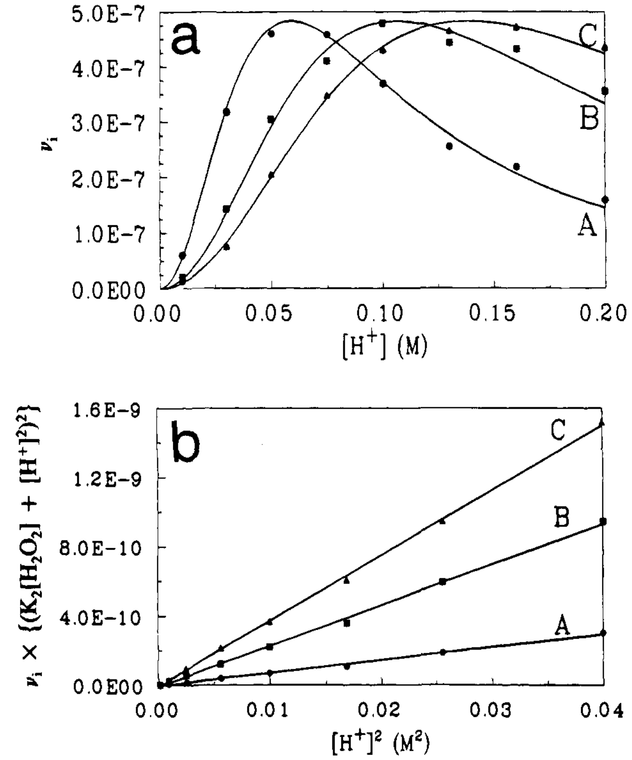

Figure 4. (a) Initial rate of vanadium-catalyzed MCD bromination as a function of acid concentration. Fit is calculated as described in the text and yields values for kK_3 of 120 M^{-2} s^{-1} and $K_2 = 0.79 \pm 0.01$ M. (b) Initial rate multiplied by $(K_2[H_2O_2] + [H^+]^2)^2$ and plotted against $[H^+]^2$ ($K_2 = 0.79 \pm 0.01$ M). Reaction conditions: 400 μM NH_4VO_3, 0.01–0.2 M $HClO_4$, 0.1 M NH_4Br, 5.0, 15, and 25 mM H_2O_2; $\mu = 2.0$ M ($NaClO_4$); 23 °C. The slopes of the fitted lines are (A) 7.49×10^{-9} M^4 s^{-1}, (B) 2.35×10^{-8} M^4 s^{-1}, and (C) 3.77×10^{-8} M^4 s^{-1}. The intercepts are -4.29×10^{-12} M^5 s^{-1}, -9.07×10^{-12} M^5 s^{-1}, and -5.81×10^{-12} M^5 s^{-1}, respectively. r^2 values are 0.998, 0.999, and 0.9996, respectively.

dimer from $VO(O_2)^+$ and $VO(O_2)_2^-$ at constant total vanadium concentration.

The data shown in Figures 4 and 5 are corrected for the vanadium-independent reaction. The magnitude of this correction generally varies from less than 2% to about 15%. At the highest acid concentration (0.2 M) with the highest hydrogen peroxide concentration (25 mM), the correction reaches 30%. The fits to the data in Figures 4a and 5a (the solid black lines) and Figures 4b and 5b are discussed below.

Kinetic Model. The initial-rate data can be fit with a model in which $(VO)_2(O_2)_3$ and bromide are kinetically essential components:

$$\frac{d[H_2O_2]}{dt} = \frac{d[Br^+]}{dt} = k[(VO)_2(O_2)_3][Br^-] \qquad (11)$$

Using the equilibrium expression for $(VO)_2(O_2)_3$ in eq 7, eq 11 can be expressed as

$$\frac{-d[H_2O_2]}{dt} = \frac{d[Br^+]}{dt} = kK_3[VO(O_2)^+][VO(O_2)_2^-][Br^-] \qquad (12)$$

A rate expression can be derived by casting the equilibrium expressions for $[VO(O_2)^+]$ and $[VO(O_2)_2^-]$ in terms of the total vanadium concentration, $[V_T]$.

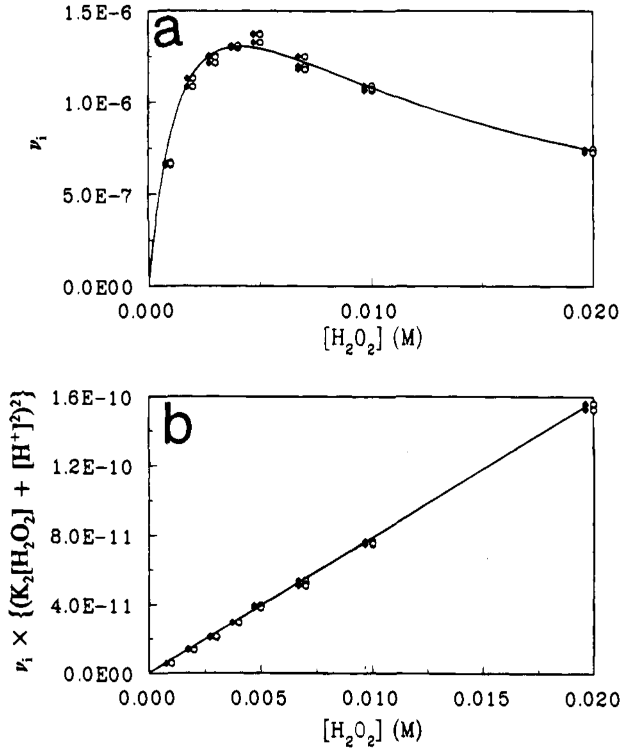

Figure 5. (a) Initial rate of vanadium-catalyzed tribromide formation as a function of hydrogen peroxide concentration. Data are corrected and fitted as described in the text, giving values for $kK_3 = 130$ M^{-2} s^{-1} and $K_2 = 0.61$ M. Open circles: plotted using $[H_2O_2]_0$. Closed diamonds: plotted using $[H_2O_2]_u$. (b) Initial rate multiplied by $(K_2[H_2O_2] + [H^+]^2)^2$ and plotted against hydrogen peroxide (*i.e.*, $[H_2O_2]_u$, concentration ($K_2 = 0.61$ M)). Reaction conditions: 200 μM NH_4VO_3, 0.05 M $HClO_4$, 1.0 M NH_4Br, 1–20 mM H_2O_2; $\mu = 2.0$ M ($NaClO_4$); 23 °C. The solid line in (b) is the fit using $[H_2O_2]_u$; its equation is $v_i\{(K_2[H_2O_2] + [H^+]^2)^2\} = -1.72 \times 10^{-12}$ M^5 s^{-1} + (7.81×10^{-9} M^4 s^{-1})$[H_2O_2]$. $r^2 = 0.9997$.

$$\frac{-d[H_2O_2]}{dt} = \frac{d[Br^+]}{dt} = \frac{kK_1^2K_2K_3[V_T]^2[H^+]^2[H_2O_2]_u^3[Br^-]}{\{[H^+]^2 + K_1[H^+]^2[H_2O_2]_u + K_1K_2[H_2O_2]_u^2\}^2} \qquad (13)$$

Since $[H^+]^2$ is small with respect to the terms containing K_1 in the denominator, the rate law simplifies to

$$\frac{-d[H_2O_2]}{dt} = \frac{d[Br^+]}{dt} = \frac{kK_2K_3[V_T]^2[H^+]^2[H_2O_2]_u[Br^-]}{\{[H^+]^2 + K_2[H_2O_2]_u\}^2} \qquad (14)$$

This expression was used to generate the fits (*i.e.*, the solid lines) to the data in Figures 4a and 5a. Plots of the observed initial rates multiplied by the denominator, (*i.e.*, $v_i\{(K_2[H_2O_2]_u + [H^+]^2)^2\}$), *vs* $[H^+]^2$ (Figure 4b) and *vs* $[H_2O_2]$ (Figure 5b) are linear, showing the second-order dependence on $[H^+]$ and the first-order dependence on $[H_2O_2]$ required from eq 14.

The speciation of vanadium(V) into $VO(O_2)^+$ and $VO(O_2)_2^-$, calculated using eq 3, as a function of acid concentration is shown in Figure 6. At low acid concentrations, $VO(O_2)_2^-$ is favored over $VO(O_2)^+$ (Figure 6, curve A), while at high acid concentrations, $VO(O_2)^+$ is favored over $VO(O_2)_2^-$ (Figure 6, curve B). Under both of these conditions, bromide oxidation is slow. The vanadium is equally partitioned between $VO(O_2)^+$ and $VO(O_2)_2$ at an intermediate, fixed acid concentration, the value of which is determined by the hydrogen peroxide

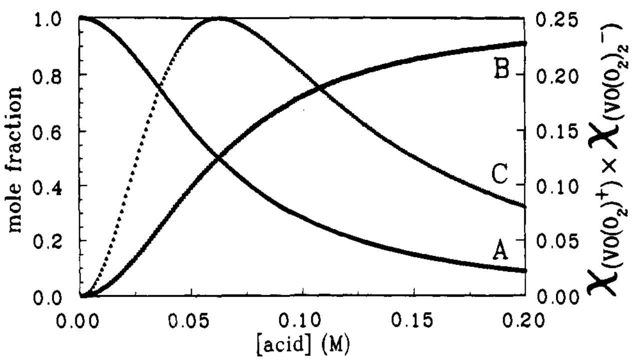

Figure 6. Calculation of the mole fractions of $VO(O_2)_2^-$ (curve A) and $VO(O_2)^+$ (curve B) from eq 3, using $K_2 = 0.79$ M, $[H_2O_2] = 5$ mM, and $[H^+] = 0.001-0.200$ M. Curve C depicts the product of the mole fractions of $VO(O_2)_2^-$ and $VO(O_2)^+$, which is proportional to $[VO(O_2)_2^-][VO(O_2)^+]$ and to $[(VO)_2(O_2)_3]$. The left-hand *y* axis is for curves A and B; the right-hand *y* axis is for curve C.

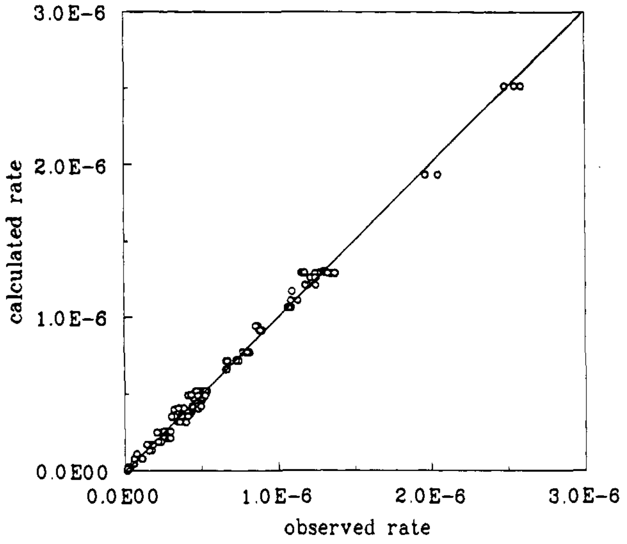

Figure 7. Plot of the calculated *vs* observed rates. The data are fitted to eq 14. The refined parameters are $K_2 = 0.64 \pm 0.01$ M and $kK_3 = 130.0 \pm 0.6$ M^{-2} s^{-1}. The equation of the fitted line is the following: calculated rate = 1.005(observed rate) − 7.9×10^{-9}. $r^2 = 0.996$.

concentration. The product of the mole fractions, $\chi_{VO(O_2)^+} \times \chi_{VO(O_2)_2^-}$ (Figure 6, curve C), is proportional to the concentration of dioxotriperoxodivanadium(V) as expected from eq 7. This variation of dimer concentration matches the variation of the initial rate of bromide oxidation with acid concentration (Figure 4a, curve A).

A further test of this model is the relationship between the observed and calculated rates (Figure 7). Two parameters can be determined by fitting the kinetic data to eq 14: K_2, the formation constant of $VO(O_2)_2^-$, and kK_3, the product of *k*, the bimolecular rate constant for the reaction of $(VO)_2(O_2)_3$ and bromide, and K_3, the formation constant of $(VO)_2(O_2)_3$. From fitting all the kinetic data (about 135 runs) to eq 14, values for kK_3 and K_2 are derived: $kK_3 = 130.0 \pm 0.6$ M^{-2} s^{-1} and $K_2 = 0.64 \pm 0.01$ M.

Equilibrium and Kinetic Parameters: K_2, K_3, and *k*. The value of K_2, derived from the fit of all the initial-rate data (*i.e.*, $K_2 = 0.64 \pm 0.01$ M), differed somewhat from the literature values of K_2,[9,33] and was sensitive to the concentration of NH_4Br. The initial-rate data, measured as a function of acid concentration, were fit with a value of $K_2 = 0.79 \pm 0.01$ M where $[NH_4Br] = 0.1$ M (Figure 4), while a value of $K_2 = 0.70 \pm 0.01$ M was determined where $[NH_4Br] = 1.0$ M (data not shown). Given the known sensitivity of K_2 to ionic strength,[9,33] we needed to measure K_2 under conditions as close as possible to those of the kinetic measurements. The ionic strength was 2.0 M in all the kinetic and ^{51}V NMR measurements; it was maintained with $NaClO_4$ (except where noted below). The differences in the conditions between the kinetic measurements and the ^{51}V NMR measurements of K_2 are (1) a 10-fold increase in the vanadium concentration in the ^{51}V NMR experiments and (2) the replacement of ammonium bromide in the kinetic reactions by sodium perchlorate in the NMR experiments; this replacement was necessary to maintain the ionic strength at 2.0 M in the absence of ammonium bromide. Determinations were made by measuring $[VO(O_2)^+]$ and $[VO(O_2)_2^-]$ using ^{51}V NMR spectroscopy under conditions of 2 mM total ammonium vanadate, 8 mM hydrogen peroxide, and 0.04−0.2 M perchloric acid. We found $K_2 = 1.0 \pm 0.2$ M at 2.0 M ionic strength ($NaClO_4$). Our values are consistent with the spectrophotometric determinations of Wilkins[33] and Secco.[9] The determination of K_2 by ^{51}V NMR using NH_4Cl, instead of $NaClO_4$, to control ionic strength (2.0 M) resulted in a value of 0.7 ± 0.1 M. This variability in K_2 with different salts may account for the difference between the value for K_2 (0.64 M^{-1}) determined from the kinetic measurements and that from the ^{51}V NMR measurements (0.7−1.0 M^{-1}).

The other parameter derived from the kinetic data is kK_3. Separating the two components is possible through an independent measurement of K_3, the dimer formation constant. Since K_3 is measured by ^{51}V NMR with at least a 100-fold increase in vanadium concentration over the kinetic measurements, it was of interest to determine how well the value derived from ^{51}V NMR data held under the conditions of the kinetic measurements. Furthermore, the K_3 determination from the ^{51}V NMR data has a standard deviation greater than 10%. Therefore, the composite value, kK_3, is known with greater precision than the bimolecular rate constant, *k*. The values ($K_3 = 32 \pm 4$ M^{-1}) measured at different ionic strengths and in the presence of ammonium ion are identical within experimental error (see Vanadium Dependence of Bromide Oxidation, above). A value of $k = 4.1 \pm 0.1$ M^{-1} s^{-1} is obtained for the bimolecular rate constant for the reaction of $(VO)_2(O_2)_3$ and Br^- at 23 °C and $\mu = 2.0$ M ($NaClO_4$).

Effect of Ethanol. The rate of the *cis*-VO_2^+-catalyzed oxidation of bromide by hydrogen peroxide was found to increase upon addition of ethanol (15% and 25% v/v). However, the overall mechanism of bromide oxidation was unchanged from that in the absence of ethanol. The values of k_H, K_2, K_3, kK_3, and *k*, determined at 0%, 15%, and 25% ethanol are summarized in Table 1. The parameters k_H, K_2, and K_3 increase with increasing ethanol concentration. The bimolecular rate constant, *k*, remains constant (4.1 ± 0.1 M^{-1} s^{-1}) up to 25% ethanol, which further suggests that the vanadium dimer does not strongly coordinate ethanol.

Bromination of MCD over the Entire Time Course of the Reaction. The integrated form of eq 13 was used to analyze data collected over the full time course of the reaction to check our model, arising from initial-rate measurements, that $(VO)_2(O_2)_3$ is the oxidant of bromide. Reactions were performed using MCD as the organic substrate because MCD traps the oxidized bromine species to yield bromochlorodimedone. Tribromide measurements are not suitable because the side reactions of tribromide interfere over long periods of time (up to 4 h); xylene cyanole bromination is not a suitable measure because at mM concentrations, xylene cyanole no longer obeys Beer's law, as it does at less than 200 μM. The bromination of MCD is stoichiometric with hydrogen peroxide consumption, so with excess [MCD] over $[H_2O_2]$, it was possible to monitor

Table 1. A Compilation of Rate and Equilibrium Constants for the *cis*-VO_2^+-Catalyzed Peroxidative System in Acidic, Aqueous Solution as a Function of Ethanol Concentration[a]

	kinetic parameters				^{51}V NMR parameters	
	k_H (M^{-2} s^{-1})	kK_3 (M^{-2} s^{-1})	k (M^{-1} s^{-1})[b]	K_2 (M)	K_2 (M)	K_3 (M^{-1})
0% EtOH (v/v)	(2.92 ± 0.08) × 10^{-4}	130.0 ± 0.6	4.06	0.64 ± 0.01	1.0 ± 0.2	32 ± 4
15% EtOH (v/v)	(3.82 ± 0.07) × 10^{-4}	225 ± 1	4.24	0.92 ± 0.1	1.4 ± 0.2	53 ± 6
25% EtOH (v/v)	(4.3 ± 0.4) × 10^{-4}	369 ± 6	4.10	1.3 ± 0.05	1.7 ± 0.3	90 ± 6
average			4.1 ± 0.1			

[a] Constants are defined in the text. [b] k is calculated from kK_3/K_3.

the oxidation of bromide over the entire reaction. The conditions were similar to the conditions employed for the initial rate measurements, except the acid concentration was kept low (0.01−0.05 M) to minimize the vanadium-independent reaction and the hydrogen peroxide concentration that could be used was limited by the solubility of MCD ([MCD] needed to be greater than [H_2O_2]). Conditions were 100 or 150 μM NH_4VO_3, 0.01, 0.03, or 0.05 M $HClO_4$, 1.17, 1.76, or 2.35 mM H_2O_2, and 0.5, 1.0, or 1.95 M NH_4Br at $\mu = 2.0$ M ($NaClO_4$).

Since the rate of disappearance of MCD (−d[MCD]/d*t*) is equal to the rate of disappearance of hydrogen peroxide (−d[H_2O_2]/d*t*), the absorbance (270 nm) *vs* time data can be analyzed using the integrated form of eq 13:

$$\frac{[H^+]^4}{2}\left\{\frac{1}{[H_2O_2]_0{}^2} - \frac{1}{[H_2O_2]_{u,t}{}^2}\right\} + 2K_1[H^+]^4\left\{\frac{1}{[H_2O_2]_0} - \frac{1}{[H_2O_2]_{u,t}}\right\} - (2K_IK_2[H^+]^2 + K_I{}^2[H^+]^4)[\ln([H_2O_2]_0) - \ln([H_2O_2]_{u,t})] - 2K_1{}^2K_2[H^+]^2([H_2O_2]_0 - [H_2O_2]_{u,t}) - \frac{1}{2}K_1{}^2K_2{}^2([H_2O_2]_0{}^2 - [H_2O_2]_{u,t}{}^2) = kK_1{}^2K_2K_3[V_T]^2[H^+]^2[Br^-]t \quad (15)$$

where [H_2O_2]$_0$ is the initial concentration of hydrogen peroxide and [H_2O_2]$_{u,t}$ is the concentration of uncomplexed hydrogen peroxide at time *t*. Similarly to [H_2O_2]$_u$ in the initial-rate analysis, [H_2O_2]$_{u,t}$ is calculated from the difference between the concentration of hydrogen peroxide added initially and the concentration of peroxide bound to vanadium. Since the oxidation of bromide is stoichiometric with hydrogen peroxide consumption,[1] the bromination of MCD and the consequent loss of absorbance at 270 nm provide data from which to calculate the concentration of hydrogen peroxide consumed over time. The concentration of uncomplexed hydrogen peroxide at time *t*, [H_2O_2]$_{u,t}$, is thus the initial concentration of hydrogen peroxide, [H_2O_2]$_0$, less the concentration of brominated MCD (which is measured as the disappearance of MCD at 270 nm) and the concentration of peroxide bound to vanadium (which is calculated using K_2 as described in Materials and Methods):

$$[H_2O_2]_{u,t} = [H_2O_2]_0 - (-[MCD]) - [V_T]\left\{1 + \frac{K_2[H_2O_2]'}{K_2[H_2O_2]' + [H^+]^2}\right\} \quad (16)$$

It should be noted that the contribution of the vanadium-independent reaction is not included in this analysis (i.e., eqs 13 and 15). In the worst case (0.5 M $HClO_4$), the vanadium-independent reaction has an initial contribution of less that 7%. More typically (e.g., 0.03 M $HClO_4$), the initial contribution is less that 3%. Plots of the left-hand side of eq 15 using values for [H_2O_2]$_0$ and [H_2O_2]$_{u,t}$ *vs* time (under the conditions listed above) are linear for 70−80% of the reaction (data not shown). The parameter, kK_3, is calculated from the slope, $kK_1{}^2K_2K_3[V_T]^2[H^+]^2[Br^-]$, since all other quantities are known. The calculated values of kK_3, 126 ± 20 M^{-1} s^{-1}, from the slope of these plots, agree with the value of kK_3, 130.0 ± 0.6 M^{-1} s^{-1}, derived from the initial-rate analysis, demonstrating the validity of our proposed mechanism.

Electrophilic Bromination. To determine whether the initial product of bromide oxidation is oxidized by one or two electrons, the product of bromination of 2,3-dimethoxytoluene (DMT) was examined. DMT reacts with bromine radical ($Br^{\bullet}$) to give 2,3-dimethoxybenzyl bromide and with "Br^+" to yield bromo-2,3-dimethoxytoluene.[2,54] Only a single product, bromo-2,3-dimethoxytoluene, was observed under turnover conditions: 400 μM NH_4VO_3, 5 mM H_2O_2, 0.05 M $HClO_4$, 1 M NH_4Br, 6 mM DMT, 25% ethanol, $\mu = 2.0$ M. Thus, bromination occurs by an electrophilic mechanism and not a radical mechanism.

^{35}Cl and ^{79}Br NMR Experiments. Halogen NMR (*e.g.*, ^{35}Cl, ^{37}Cl, ^{79}Br, ^{81}Br, ^{127}I) is a useful technique to study reversible halide binding.[55,56] Line broadening requires rapid exchange between bound and free states. The ^{79}Br NMR resonance of bromide showed no line broadening (*i.e.*, 2041 ± 48 Hz) under turnover conditions (1.0 mM NH_4VO_3, 5.0 mM H_2O_2, 0.05 M $HClO_4$, 1.0 M NH_4Br, 5.3 mM trimethoxybenzene, 25% ethanol, $\mu = 2.0$ M) beyond the line width in the absence of either hydrogen peroxide (1944 ± 43 Hz) or hydrogen peroxide and vanadium (1988 ± 43 Hz). All of these line widths are greater than in the absence of ethanol: the ^{79}Br line width was 602 ± 2 Hz for 1.0 M NH_4Br at 2.0 M ionic strength ($NaClO_4$) and 619 ± 2 Hz for 1.0 M NH_4Br conditions of 1 mM NH_4VO_3, 0.1 M $HClO_4$, and 1.0 M NH_4Br ($\mu = 2.0$ M ($NaClO_4$)). Trimethoxybenzene was used in bromide oxidation reactions to trap "Br^+", otherwise Br_3^- contributed to substantial line broadening: 100 μM Br_3^- added to either of the two solutions just described resulted in line widths in excess of 2200 Hz. Similar to the ^{79}Br results, no change was observed in the line width of the ^{35}Cl chloride resonance under similar, turnover conditions: 1.0 mM NH_4VO_3, 2.0 mM H_2O_2, 1.0 M NH_4Cl; $\mu = 2.0$ M ($NaClO_4$). The ^{35}Cl line width was 20 ± 0.5 Hz in the absence of hydrogen peroxide and vanadium(V) and 18 ± 0.4 Hz under turnover conditions. Because chloride oxidation is so much slower than bromide oxidation,[1] addition of an organic substrate to trap oxidized chlorine species was not necessary and ethanol was not included.

Discussion

The oxidation of bromide by hydrogen peroxide is catalyzed by *cis*-dioxovanadium(V). The reaction rate shows a first-order dependence on bromide concentration and a second-order

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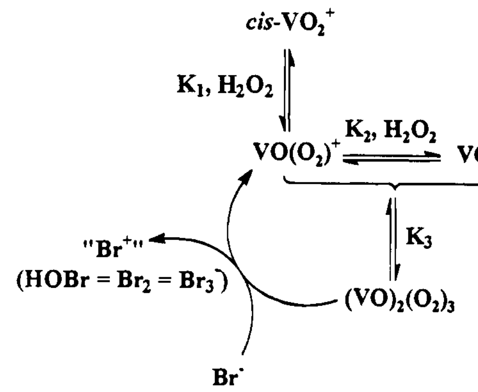
(54) Volhardt, K. P. C. *Organic Chemistry*; W. H. Freeman and Co.: New York, 1987; pp 1090−2.

(55) For a general treatment, see: *Multinuclear NMR*, Mason, J., Ed.; Plenum Press: New York, 1987; Chapter 17.

(56) Bryant, R. G. *J. Am. Chem. Soc.* **1969**, *91*, 976−81.

Scheme 2



dependence on vanadium(V) concentration. The dependences of the rate on acid and hydrogen peroxide concentrations are superficially complex, but arise from the equilibrium between oxomonoperoxo- and oxodiperoxovanadium(V) complexes (eq 3), which is dependent on acid and hydrogen peroxide concentrations. The maximal rate of bromide oxidation occurs when the concentrations of $VO(O_2)^+$ and $VO(O_2)_2^-$ are equal. These two complexes combine to give dioxotriperoxodivanadium(V), which appears to be the actual oxidant of bromide. The proposed mechanism (Scheme 2), consistent with all of the kinetic data, is coordination of peroxide to VO_2^+ to generate $VO(O_2)^+$ and $VO(O_2)_2^-$; dimerization of $VO(O_2)^+$ and $VO(O_2)_2^-$ to produce $(VO)_2(O_2)_3$; oxidation of bromide and concomitant production of 2 equiv of $VO(O_2)^+$; and re-equilibration of $VO(O_2)^+$ according to eqs 2−4. Alternatively, oxidation of bromide by $(VO)_2(O_2)_3$ could result in 1 equiv each of VO_2^+ and $VO(O_2)_2^-$, which would also re-equilibrate according to eqs 2−4.

Catalytic oxidation by a vanadium peroxo dimer is unprecedented in vanadium peroxo chemistry. Many peroxo vanadium complexes oxidize a wide variety of substrates.[35] In each of the systems that has been investigated kinetically, a first-order vanadium dependence is observed.[36,38−40] This first-order dependence is retained across a variety of solvents, substrates, and ligands, and even in reactions that proceed via both radical and non-radical intermediates. An interesting exception to mononuclear catalysis is a titanium complex $[Ti(tartrate)(OR)_2]_2$, which catalyzes the asymmetric epoxidation of allylic alcohols by alkyl hydroperoxides. On the basis of spectroscopic evidence, Sharpless and co-workers suggest it is dimeric in its active conformation.[57] Over a 10-fold range of titanium concentrations, this catalyst has a kinetic order of one, rather than two, because the association of the titanium monomers is so strong.[58]

The formation constants of $VO(O_2)_2^-$ and $(VO)_2(O_2)_3$, K_2 and K_3, are sensitive to ethanol (Table 1). The source of this ethanol effect is not known. While ethanol coordinates to vanadate under neutral conditions, giving rise to species with distinct ^{51}V NMR resonances,[27] under these acidic conditions, ethanol does not affect the ^{51}V NMR chemical shifts of the peroxo complexes relevant to this work. Inclusion of ethanol does alter the equilibrium constants, K_2 (determined kinetically or spectroscopically) and K_3, and the composite parameter, kK_3. Further, the rate constant for the vanadium-independent peroxidative oxidation of bromide, k_H, is sensitive to ethanol. By contrast, the bimolecular rate constant, k, for the reaction of dioxotriperoxodivanadium(V) and bromide is not dependent on the ethanol concentration.

We reported previously[1] that the *cis*-VO_2^+-catalyzed oxidation of bromide by hydrogen peroxide occurs under significantly different conditions from those of vanadium bromoperoxidase. The *cis*-VO_2^+ system requires lower pH (≤2 compared to pH 5−7 for the enzymatic reaction) and functions much more slowly. Under neutral conditions, even though bromide oxidation by hydrogen peroxide is still thermodynamically feasible, it is not catalyzed by vanadium(V). This result can now be rationalized: at neutral pH, the binding constant of vanadium for the second peroxide is 100-fold larger than for the first. Consequently, the concentration of monoperoxovanadate is insignificant and thus dioxotriperoxodivanadium(V) does not form. Additionally, at neutral pH, the monoperoxo vanadium(V) is anionic[59] instead of cationic[33] and the peroxo vanadium(V) dimer that has been reported contains four peroxide ligands.[30−32] An understanding of the differences in reactivity of these dimers awaits their further characterization.

The determination of the bimolecular rate constant for the reaction of $(VO)_2(O_2)_3$ and Br^- ($k = 4.1 \pm 0.1\ M^{-1}\ s^{-1}$) permits us to make some detailed comparisons regarding the rates and mechanism of the oxidation of bromide in this and several other systems. The kinetic analysis described here reveals that the bimolecular reaction of the oxidant, $(VO)_2(O_2)_3$, with Br^- is not acid-dependent: the acid participates in the overall catalytic cycle by maintaining vanadium(V) as *cis*-dioxovanadium(V) rather than vanadate ($H_2VO_4^-$, HVO_4^{2-}, VO_4^{3-}) and in the peroxo vanadium(V) equilibria (eqs 2−4). Wever *et al.* estimated a lower limit for the bimolecular rate constant of the V−BrPO−H_2O_2 complex with bromide.[24] This value, $k_{cat}/K_m^{H_2O_2}$, is strongly pH-dependent, primarily because $K_m^{H_2O_2}$ is sensitive to pH. The calculated bimolecular rate constant varies from 2.78×10^3 at pH 7.9 to $1.75 \times 10^5\ M^{-1}\ s^{-1}$ at pH 4.0, which is $10^3−10^5$ times larger than the rate constant ($4.1 \pm 0.1\ M^{-1}\ s^{-1}$) derived in this work for the reaction of dioxotriperoxodivanadium(V) and bromide. $MoO(O_2)_2(H_2O)_2$ and $MoO(O_2)_2(H_2O)(OH)^-$ react with Br^- with bimolecular rate constants of 1.5×10^{-2} and $2.4 \times 10^{-3}\ M^{-1}\ s^{-1}$, respectively.[6] The oxalato complex, $MoO(O_2)_2(C_2O_4)^{2-}$, reacts with bromide with a bimolecular rate constant of $9.2 \times 10^{-3}\ M^{-1}\ s^{-1}$ at pH 5.1, 20% methanol, $\mu = 2.0$ M ($NaClO_4$)[6] and $4.8 \times 10^{-3}\ M^{-1}\ s^{-1}$ at pH 5.0, $\mu = 1.0$ M ($LiClO_4$).[7] The tungstate-catalyzed, like the molybdate-catalyzed, reaction is faster at higher acid concentrations, but the low pK_a (0.2) prevented determination of rate constants for the two, analogous species. The $MeReO_3$-catalyzed oxidation of bromide by hydrogen peroxide was found to occur by bimolecular reactions of the monoperoxo and diperoxo complexes with bromide ($k_{Re} = 3.5 \times 10^2$ and $1.9 \times 10^2\ M^{-1}\ s^{-1}$, respectively).[4] This rhenium system differs from the vanadium system in that the equilibrium between the monoperoxo and diperoxo complexes of $MeReO_3$ is not acid-dependent.

Several possibilities for the detailed mechanism of bromide oxidation merit consideration: (1) bromide is oxidized in two one-electron steps; (2) bromide coordinates to one of the vanadium(V) ions prior to oxidation by coordinated peroxide; (3) bromide reacts directly with a coordinated peroxide by nucleophilic attack. Although one-electron chemistry might result in substoichiometric bromide oxidation as a result of radical decomposition of hydrogen peroxide, the stoichiometry of hydrogen peroxide consumed to bromide oxidized is 1:1. Further, electrophilic bromination was demonstrated through product analysis using DMT as a substrate. With respect to

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(57) Finn, M. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1991**, *113*, 113−126.

(58) Woodard, S. S.; Finn, M. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1991**, *113*, 106−113.

(59) Jaswal, J. S.; Tracey, A. S. *Inorg. Chem.* **1991**, *30*, 3718−22.

bromide coordination to vanadium(V), we see no rate saturation up to 1.95 M bromide and no line broadening by ^{79}Br NMR. Thus, bromide oxidation by hydrogen peroxide seems likely to occur in this system by the same mechanism as has been proposed in other systems: nucleophilic attack of bromide on a vanadium-bound peroxide oxygen.

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Supplementary Material Available: Four plots of MCD bromination *vs* time and of the integrated rate expression (the left-hand side of eq 15) *vs* time over the full reaction (8 pages). This material is contained in many libraries, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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