

## Electron Transfer. 133. Copper Catalysis in the Sulfite Reduction of Peroxynitrite<sup>1</sup>

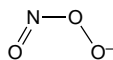
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Received August 1, 1996<sup>⊗</sup>

Peroxynitrite (O=NOO<sup>-</sup>) is formed by the reaction of cold aqueous solutions of hydrogen peroxide and nitrous acid, followed by rapid quenching with base. Reduction of this peroxy anion with sulfite (O=NOO<sup>-</sup> + SO<sub>3</sub><sup>2-</sup> → NO<sub>2</sub><sup>-</sup> + SO<sub>4</sub><sup>2-</sup>) at pH 12–14 is slow but is catalyzed markedly by dissolved Cu(II), which, in this medium, exists predominantly as Cu(OH)<sub>4</sub><sup>2-</sup>. Nonexponential kinetic profiles for 10 runs, carried out with [OH<sup>-</sup>] = 0.005–0.50 M, [O=NOO<sup>-</sup>] = 0.16–0.58 mM, [SO<sub>3</sub><sup>2-</sup>] = 7.5–75 mM, and [Cu<sup>II</sup>] = 1.0–4.0 μM, are consistent with a sequence (eqs 8–13 in the text) in which Cu(I) is generated from the one-electron reduction of Cu(II) by SO<sub>3</sub><sup>2-</sup>, after which Cu(I) reduces peroxynitrite to NO<sub>2</sub> by competing protonated and nonprotonated paths. Subsequent reduction of NO<sub>2</sub> is taken to be rapid. The proposed sequence then attributes the catalytic role of copper, in this system, to its ability to support a single-electron route to supplement the uncatalyzed path, which has been taken to entail direct oxygen atom transfer. Vanadium(V) and molybdenum(VI), which exist in this medium predominantly as the oxo anions VO<sub>4</sub><sup>3-</sup> and MoO<sub>4</sub><sup>2-</sup>, are devoid of catalytic action. The couples Fe(II,III) and Mn(II,III) are also catalytically inactive, presumably due to the very low solubility of several of the metal hydroxides at the high pH values employed.

Peroxynitrite (O=NOO<sup>-</sup>), the anion of the weak acid peroxynitrous acid (pK<sub>a</sub> 6.5),<sup>2</sup> is formed by the rapid combination ( $k = 6 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$  at 25 °C)<sup>3</sup> of the two biologically important<sup>4</sup> odd-electron diatomic species nitric oxide and superoxide (O<sub>2</sub><sup>-</sup>). Although the acid is unstable, the anion can be preserved for weeks in a strongly basic media at -18 °C.<sup>5</sup> Raman spectra<sup>6</sup> support a predominant *cis* structure for this ion.



The production of peroxynitrite, which has been found to be cytotoxic,<sup>7</sup> in biosystems has been confirmed,<sup>8</sup> and it has been proposed as an active agent in reactions associated with vascular injuries<sup>9</sup> and in the development of atherosclerotic lesions.<sup>10</sup>

Several activation paths come to mind for the O=NOO<sup>-</sup>/O=NO<sub>2</sub>H couple. The N–O bond may be broken heterolytically to yield the NO<sup>+</sup> cation, a powerful nitrosating agent. In addition, evidence has been presented that reactions of the acid may proceed, at least in part, via excitation of its predominant *cis*- to a more reactive *trans*-form<sup>11</sup> or formation of a cyclic

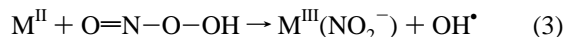
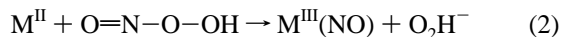
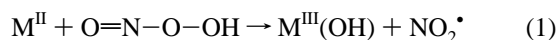
(three-membered ring) intermediate.<sup>12</sup> Spontaneous homolysis of the O–O bond to form the unusually reactive hydroxyl radical appears to be ruled out thermodynamically.<sup>13</sup>

Although an array of reports is at hand describing oxidations by peroxynitrite of both inorganic<sup>14</sup> and organic<sup>15</sup> coreagents, all quantitative studies, with but two exceptions,<sup>14b,c</sup> have been carried out with care taken to exclude contamination by transition metal ions. This expedient is likely to bypass mechanistic features of such oxidations. Moreover, extensions to bioconversions should deal with the possibility of trace metal species in such systems. Past experience with reactions of hydroperoxides,<sup>16</sup> peroxy acids,<sup>17</sup> and metal–peroxo complexes<sup>18</sup> demonstrate striking changes in reaction rates, kinetic patterns, and product distributions resulting from the intervention of metal centers at low concentrations.

Transition metal ions open additional routes. Reactions 1–3 feature oxidative changes at the metal center analogous to the familiar Fenton-type activation of peroxy compounds.<sup>19</sup> Each

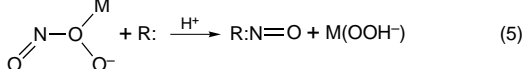
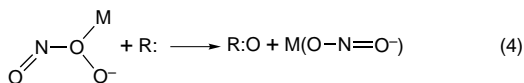
- <sup>⊗</sup> Abstract published in *Advance ACS Abstracts*, January 15, 1997.
- (1) Sponsorship of this work by the National Science Foundation (Grant 9414113) is gratefully acknowledged.
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- (14) See, for example: (a) Halfpenny, E.; Robinson, P. L. *J. Chem. Soc. A* **1952**, 928 (Br<sup>-</sup>). (b) Hughes, M. N.; Nicklin, H. G.; Sackrile, W. A. *J. Chem. Soc. A* **1971**, 3722 (I<sup>-</sup>, SCN<sup>-</sup>). (c) Hughes, M. N.; Nicklin, H. G. *J. Chem. Soc. A* **1970**, 925 (CN<sup>-</sup>, NH<sub>2</sub>OH). (d) Goldstein, S.; Czapski, G. *Inorg. Chem.* **1995**, *34*, 4041 (Fe(CN)<sub>6</sub><sup>4-</sup>, Ni<sup>II</sup>(cyclam).)
- (15) See, for example: (a) Radi, R.; Beckman, J. S.; Bush, K. M.; Freeman, B. A. *J. Biol. Chem.* **1991**, *266*, 4244 (thiols). (b) Pryor, W. A.; Jin, X.; Squadrito, G. L. *Proc. Natl. Acad. Sci. U.S.A.* **1994**, *91*, 11173 (thioethers). (c) Beckman, T. W.; Chen, J.; Marshall, P. A.; Freeman, B. A. *Proc. Natl. Acad. Sci. U.S.A.* **1990**, *87*, 1620 (1,2-glycols). (d) Ischiropoulos, H.; Zhu, L.; Chen, M.; Tsai, M.; Martin, J. C.; Smith, C. D.; Beckman, J. S. *Arch. Biochem. Biophys.* **1992**, *298*, 431 (amino acids). (e) Bartlett, D.; Church, D. F.; Bounds, P. L.; Koppenol, W. H. *Free Radical Biol. Med.* **1995**, *18*, 85 (ascorbate).
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- (17) Allen, T. L. *J. Am. Chem. Soc.* **1951**, *73*, 3589.
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requires a metal having at least two accessible oxidation states differing by one unit (e.g.,  $\text{M}^{\text{II}}$ ,  $\text{M}^{\text{III}}$ ).

In other cases, a metal center may activate the transfer of an electrophilic fragment to a reductant (R:), via preliminary coordination, but with no change in the oxidation state (eqs 4 and 5), a route which is characteristic of such oxyphilic d<sup>0</sup> centers as Ti(IV) and Mo(VI).<sup>20</sup>



There are constraints associated with the study of metal catalysis in such systems. The very low solubilities of many transition metal hydroxides at pH's great enough to allow peroxynitrite to persist dictate using these metals as slightly dissociated complexes rather than as their aqua ions. A number of the most effective d-block sequestrants feature hydroxamic acid units or catecholates residues,<sup>21</sup> neither of which is expected to survive under strongly oxidative conditions. Moreover, some degree of substitution-lability at the metal ion should be retained, since the action of these centers is customarily initiated by coordination to the peroxide function.

In the present study, which deals with the reduction of peroxynitrite with sulfite as catalyzed by copper, conversions are carried out in strongly basic solutions (pH 12–14) to minimize the complications that are associated with the uncatalyzed reaction<sup>22</sup> and the self-decomposition of the oxidant, since both processes are markedly accelerated by  $\text{H}^+$ . These experiments are possible because Cu(II) exhibits an appreciable amphoteric character in aqueous alkaline media.<sup>23</sup>

## Experimental Section

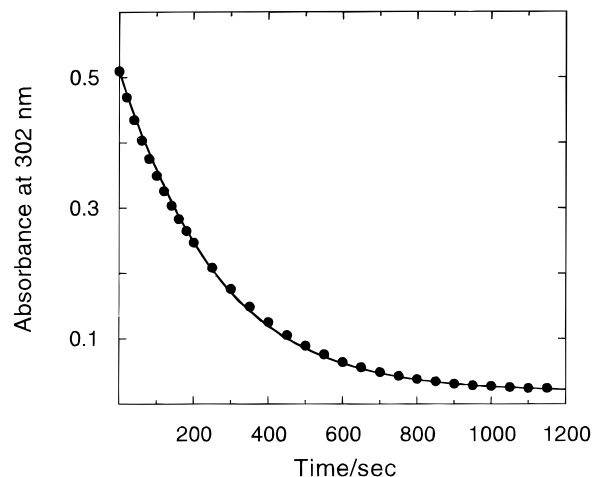
**Materials.** All solutions were prepared from Millipore water, which was treated with zinc amalgam, as described, to remove  $\text{Cu}^{2+}$ ,<sup>24</sup> boiled for 2 h, and then purged with  $\text{N}_2$  for 2 h more to remove dissolved  $\text{O}_2$ . Sodium perchlorate and standard solutions of NaOH (1.0 M) (Aldrich products) and sodium sulfite (MCB) were used as received. Sulfite solutions were prepared with deaerated water, kept under  $\text{N}_2$ , and standardized daily iodometrically.<sup>25</sup> Copper sulfate was crystallized once from water. Peroxynitrite solutions were prepared using slight modifications of the literature methods,<sup>14a,d,22</sup> were kept at  $-18^\circ\text{C}$ , and were standardized spectrophotometrically each day ( $\epsilon_{302} = 1670 \text{ M}^{-1} \text{ cm}^{-1}$ ).<sup>14d</sup>

- (19) See, for example: (a) Sosnovsky, G.; Rawlinson, D. J. In *Organic Peroxides*; Swern, D., Ed.; Wiley: New York, 1971; Vol. II, pp 153–268. (b) Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidation of Organic Compounds*; Academic Press: New York, 1981; pp 34–49.
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**Table 1.** Stoichiometry of the Reaction of Peroxynitrite with Sulfite As Catalyzed by Copper<sup>a</sup>

[O=NOO <sup>-</sup> ], mM	[SO <sub>3</sub> <sup>2-</sup> ], mM	$\Delta[\text{O}=\text{NOO}^-]$ , mM <sup>b</sup>	$\Delta[\text{O}=\text{NOO}^-]/\Delta[\text{SO}_3^{2-}]$
1.80	1.00	0.95	0.95
2.25	1.80	1.77	0.98
4.15	3.00	2.86	0.95
5.54	3.00	2.89	0.96

<sup>a</sup> Reactions were carried out at  $24^\circ\text{C}$  under  $\text{N}_2$  in 0.025 M NaOH;  $\mu = 1.0 \text{ M}$  ( $\text{NaClO}_4$ );  $[\text{Cu}^{\text{II}}] = 2.0 \times 10^{-6} \text{ M}$ . Indicated concentrations are initial values. <sup>b</sup> Measured at 302 nm (optical path length 0.20 cm) and corrected for loss of  $\text{O}=\text{NO}_2^-$  resulting from its Cu(II)-catalyzed self-decomposition (see Experimental Section).



**Figure 1.** Kinetic profile at 302 nm for the reduction of peroxynitrite ( $3.1 \times 10^{-4} \text{ M}$ ) with sulfite ( $7.5 \times 10^{-3} \text{ M}$ ), as catalyzed by Cu(II) ( $2.0 \times 10^{-6} \text{ M}$ ) in 0.025 M NaOH at  $24^\circ\text{C}$ ;  $\mu = 1.0 \text{ M}$  ( $\text{NaClO}_4$ ). The circles are experimental values, whereas the solid line represents absorbances calculated from numerical integration of differential equations based on reaction 6 and sequence 8–16, taking the parameters from Table 3. The extinction coefficient used for peroxynitrite is  $1.67 \times 10^3 \text{ M}^{-1} \text{ cm}^{-1}$ , and the other species were considered to be negligibly absorbent. Optical path length = 1.00 cm.

**Stoichiometric Studies.** The stoichiometry of the peroxynitrite–sulfite reaction, as catalyzed by copper, was examined under  $\text{N}_2$  in 0.025 M NaOH in a short path length (0.20 cm) spectrophotometric cell. Deficient quantities of sulfite were added to a known concentration of peroxynitrite. After a 40 min waiting period, the decreases in absorbance at 302 nm were measured. These changes, after minor adjustments to reflect the (much slower) Cu<sup>II</sup>-catalyzed self-decomposition of the oxidant in the same time period, were compared to those occurring when peroxynitrite was treated with excess sulfite. Results are summarized in Table 1.

**Kinetic Studies.** Reactions were monitored from measurements of absorbance decreases at 302 nm using a Shimadzu 1601 recording spectrophotometer. Temperatures were kept at  $24.0 \pm 0.2^\circ\text{C}$ . Conversions were carried out in basic solutions (0.005–0.50 M NaOH),<sup>26</sup> and the ionic strength was maintained at 1.0 M using  $\text{NaClO}_4$ . Excess sulfite was used in all kinetic runs. Decay profiles were curved but not exponential, generally exhibiting an approach toward linearity during the first third of the reaction but becoming more nearly exponential during the latter stages (Figure 1). Comparisons of initial rates throughout the series of runs suggested a first-order dependence on  $[\text{SO}_3^{2-}]$  at low concentrations of this reductant but an approach to kinetic saturation at higher levels, as well as inhibition by  $\text{OH}^-$ . Variation with  $[\text{O}=\text{NOO}^-]$  was less marked than that corresponding to unit order, whereas rates appeared to be proportional to  $[\text{Cu}^{\text{II}}]$  at

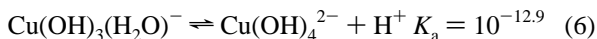
- (26) Reactions at lower pH's, which proceed at rates measurable by flow methods, were not examined in detail since reagents appeared to become irreproducibly contaminated, on mixing, with traces of dissolved copper arising from corroded surfaces of the metal valves in our flow system.

concentrations of Cu<sup>II</sup> less than 5.0 μM but reached a (reproducible) maximum at levels slightly above this value.

The peroxyxynitrite-sulfite reactions were also catalyzed perceptibly by Co<sup>III</sup> (added as (NH<sub>3</sub>)<sub>6</sub>Co(ClO<sub>4</sub>)<sub>3</sub> or (NH<sub>3</sub>)<sub>5</sub>Co(H<sub>2</sub>O)(ClO<sub>4</sub>)<sub>3</sub>) but not by VO<sub>4</sub><sup>3-</sup>, MoO<sub>4</sub><sup>-</sup>, or ReO<sub>4</sub><sup>-</sup>. Experiments to establish catalysis by Fe<sup>III</sup> or Mn<sup>II</sup> were not informative due to precipitation of the hydroxides of these metals in the basic media employed.

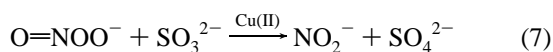
## Results and Discussion

Gubeli and co-workers<sup>23b</sup> have studied the speciation of dilute solutions of Cu(II) at high pH and report formation constants of 10<sup>14.5</sup> and 10<sup>15.6</sup> for the hydroxo complexes Cu(OH)<sub>3</sub><sup>-</sup> and Cu(OH)<sub>4</sub><sup>2-</sup> (25 °C, 1.0 M). Combination of these values with K<sub>H<sub>2</sub>O</sub> leads to the acidity constant for Cu(OH)<sub>3</sub>(H<sub>2</sub>O)<sup>-</sup>.



The tetrahydroxo complex is then nearly half-protonated in 0.08 M NaOH. The steady increase in rates as [catalyst] is raised to 5 × 10<sup>-6</sup> M, in conjunction with the observed ceiling at slightly greater concentrations, suggests a maximum set by the solubility of Cu(II) in this medium, in agreement with the limit (5 μM at pH 13) documented by Gubeli.

The close approach to 1:1 reactant ratios for these oxidations (Table 1) indicates that conversions are predominantly to nitrite and sulfate

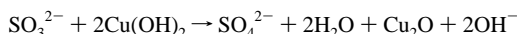


The slight departures from unit stoichiometry probably reflect uncertainties in the extrapolation procedure used to accommodate the self-decomposition of the oxidant.

The progressive change in the character of the decay profiles as each reaction proceeds implies a gradual shift in the rate-limiting step in the catalytic sequence. Shortly after mixing, rates are determined principally by a process not involving peroxyxynitrite, yielding an active catalytic species, which then reacts rapidly with the oxidant. During this stage of reaction, the action of peroxyxynitrite resembles that of a scavenger. However, as the oxidant is depleted, it is consumed more slowly and its disappearance becomes more nearly rate determining, approaching exponential behavior. The observed deceleration of the net reaction with increasing pH points to one or more protonation equilibria in the reaction path.

The recognized ease with which sulfite reduces Cu(II) to Cu(I) in highly basic media<sup>27,28</sup> strongly suggests that the active reductant in the catalytic sequence is a Cu(I) species. Catalysis then involves recycling between the oxidation states of the copper, and a key question is whether the higher state is Cu(II) or Cu(III). The latter is much less usual, but a rapidly growing array of Cu(III) complexes have been characterized,<sup>29</sup> a number of which are prepared by oxidation in basic media.<sup>30</sup> Since, however, stabilization of this hypervalent state appears to require

(27) The strongly positive potential, 0.71 V, for the reaction



at pH 14, calculated from data of Bard,<sup>28</sup> should not be greatly altered by the partial conversion of the copper species to soluble hydroxo complexes.

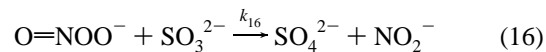
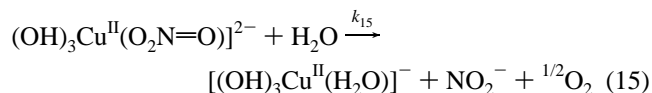
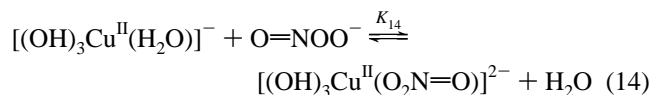
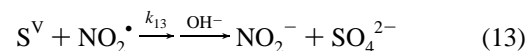
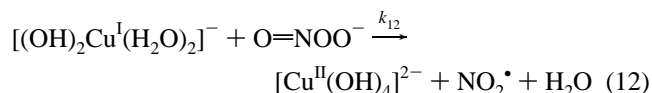
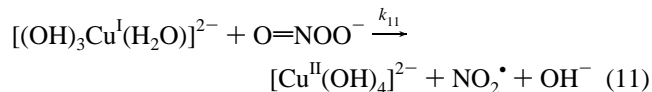
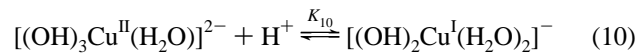
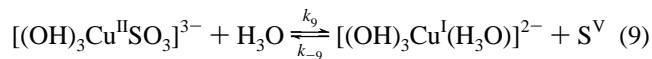
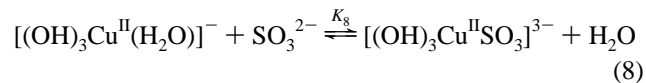
(28) *Standard Potentials in Aqueous Solutions*; Bard, A. J., Parsons, R., Jordan, J., Eds.; Marcel Dekker: New York, 1985; pp 102, 292.

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either a medium with a high oxidizing potential<sup>31</sup> or such unusual ligands as periodate,<sup>32</sup> tellurate,<sup>33</sup> dialkyl dithiocarbamates,<sup>34</sup> biuret,<sup>35</sup> deprotonated peptides,<sup>36</sup> or dioximate anions,<sup>37</sup> none of which is present in the system at hand, interpretation of our data in terms of a Cu(I,II) cycle is taken to be more reasonable.

Data for all runs are consistent with sequence 8–13, in which S<sup>V</sup> is an abbreviation for the radical anion SO<sub>3</sub><sup>•-</sup>. It is further assumed that Cu(I) in these solutions exists at two protonation levels, designated [(OH)<sub>3</sub>Cu<sup>I</sup>(H<sub>2</sub>O)]<sup>2-</sup> and [(OH)<sub>2</sub>Cu<sup>I</sup>(H<sub>2</sub>O)<sub>2</sub>]<sup>-</sup>. Net rates at the beginning of each run are set mainly by the generation of Cu(I) (step 9), whereas rates near the end depend also on steps 11 and 12, both of which involve O=NOO<sup>-</sup>. In addition, reactions 14–16 have been included to accommodate minor contributions from the catalyzed self-decomposition of the oxidant (which is very nearly first order in substrate in the time frame considered) and the uncatalyzed O=NOO<sup>-</sup>–SO<sub>3</sub><sup>2-</sup> reaction, rates of which, at the various [OH<sup>-</sup>] values, were previously determined.<sup>22</sup>



The reduction of peroxyxynitrite by Cu<sup>I</sup> is taken to proceed via a combination of a protonated route (steps 10 and 12) and a deprotonated path (step 11). The rapid reaction of the two odd-electron species, SO<sub>3</sub><sup>•-</sup> and NO<sub>2</sub><sup>•</sup> (step 13), occurs after all of the rate-determining processes and is kinetically silent. No

(31) See, for example: Bour, J. J.; Steggerda, J. J. *J. Chem. Soc., Chem. Commun.* **1967**, 85.

(32) Malatesta, L. *Gazz. Chim. Ital.* **1941**, *71*, 467.

(33) Balinkungeri, A.; Pelletier, M.; Monnier, D. *Inorg. Chim. Acta* **1977**, *22*, 7.

(34) See, for example: Golding, R. M.; Harris, C. M.; Jessop, K. J.; Tennant, W. C. *Aust. J. Chem.* **1972**, *25*, 2567.

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**Table 2.** Representative Kinetic Data for the Oxidation of Sulfite by Peroxynitrite As Catalyzed by  $\text{Cu}^{2+}$  <sup>a</sup>

$[\text{Cu}^{2+}]$ , $\mu\text{M}$	$[\text{S}^{\text{IV}}]$ , $\text{mM}$	$[\text{ONOO}^-]$ , $\text{mM}$	$[\text{NaOH}]$ , $\text{M}$	$K_8$ , $\text{M}^{-1}$	$k_9$ , $\text{s}^{-1}$	$k_{-9}$ , $\text{M}^{-1} \text{s}^{-1}$	$K_{10}$ , $\text{M}^{-1} \text{s}^{-1}$	$k_{11}$ , $\text{M}^{-1} \text{s}^{-1}$	$k_{12}$ , $\text{M}^{-1} \text{s}^{-1}$	$k_{13}$ , $\text{M}^{-1} \text{s}^{-1}$	$K_{14}k_{15}$ , $\text{M}^{-1} \text{s}^{-1}$	$k_{16}$ , <sup>b</sup> $\text{M}^{-1} \text{s}^{-1}$
1.0	7.5	0.33	0.025	52	14	$1 \times 10^5$	4.8	440	$8.0 \times 10^4$	$1 \times 10^9$	75	0.059
2.0	7.5	0.31	0.025	50	12	$1 \times 10^5$	5.1	475	$8.5 \times 10^4$	$1 \times 10^9$	75	0.059
4.0	7.5	0.30	0.025	52	12	$1 \times 10^5$	5.0	450	$8.0 \times 10^4$	$1 \times 10^9$	75	0.059
2.0	25.0	0.29	0.025	50	12	$1 \times 10^5$	5.0	480	$8.5 \times 10^4$	$1 \times 10^9$	75	0.059
2.0	75.0	0.28	0.025	50	13	$1 \times 10^5$	5.1	480	$8.5 \times 10^4$	$1 \times 10^9$	75	0.059
2.0	7.5	0.58	0.025	48	11	$1 \times 10^5$	5.0	475	$8.4 \times 10^4$	$1 \times 10^9$	75	0.059
2.0	7.5	0.16	0.025	52	13	$1 \times 10^5$	5.2	480	$8.6 \times 10^4$	$1 \times 10^9$	75	0.059
2.0	7.5	0.18	0.025	50	12	$1 \times 10^5$	5.0	460	$8.3 \times 10^4$	$1 \times 10^9$	75	0.076
2.0	7.5	0.20	0.20	51	13	$1 \times 10^5$	5.0	450	$8.2 \times 10^4$	$1 \times 10^9$	75	0.053
2.0	7.5	0.17	0.50	47	11	$1 \times 10^5$	4.8	420	$8.0 \times 10^4$	$1 \times 10^9$	75	0.051

<sup>a</sup> Reactions were carried out under  $\text{N}_2$  at 24 °C and at ionic strength = 1.0 M ( $\text{NaClO}_4$ ). Parameters were obtained from the best fit of integrated forms of sequence 8–16 to experimental curves (see text and ref 38). <sup>b</sup> Values from the measured variation, with acidity, of the rate constant for the uncatalyzed redox reaction.<sup>22</sup>

**Table 3.** Rate Constants and Equilibrium Quotients Contributing to the Oxidation of Sulfite by Peroxynitrite As Catalyzed by Dissolved Copper<sup>a</sup>

$K_6$	$1.3 \times 10^{-13} \text{ M}^b$	$k_{11}$	$4.6 \times 10^2 \text{ M}^{-1} \text{ s}^{-1}$
$K_8$	$50 \text{ M}^{-1}$	$k_{12}$	$8.3 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$
$k_9$	$12 \text{ s}^{-1}$	$k_{13}$	$1 \times 10^9 \text{ M}^{-1} \text{ s}^{-1} \text{ }^c$
$k_{-9}$	$1 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$	$K_{14}k_{15}$	$75 \text{ M}^{-1} \text{ s}^{-1} \text{ }^d$
$K_{10}$	$5.0 \times 10^{10} \text{ M}^{-1}$	$k_{16}$	$0.051\text{--}0.076 \text{ M}^{-1} \text{ s}^{-1} \text{ }^e$

<sup>a</sup> Parameters pertain to reaction and sequence 8–16 in text. Reactions were run at 24 °C;  $\mu = 1.00 \text{ M}$  ( $\text{NaClO}_4$ ).  $[\text{OH}^-] = 0.005\text{--}0.50 \text{ M}$ ,  $[\text{SO}_3^{2-}] = 7.5\text{--}75 \text{ mM}$ ,  $[\text{O}=\text{NOO}^-] = 0.16\text{--}0.58 \text{ mM}$ ,  $[\text{Cu}^{\text{II}}] = 1.0\text{--}4.0 \mu\text{M}$ ,  $\lambda = 302 \text{ nm}$ . Values listed are those giving optimum agreement between calculated and observed absorbances for 10 runs in which concentrations of reagents, catalyst, and acidity were varied. <sup>b</sup> Reference 23. <sup>c</sup> Value set at diffusion-controlled limit. <sup>d</sup> Steps for the  $\text{Cu}^{\text{II}}$ -catalyzed decomposition of peroxynitrite. The observed acidity dependence for this competing reaction also reflects equilibrium  $K_6$ . <sup>e</sup> Acid-dependent uncatalyzed redox reaction.<sup>22</sup>

details concerning the route for the catalyzed self-decomposition of the oxidant (step 15) are suggested since this constitutes only a small fraction of the entire change.

Expression of this sequence as a series of differential equations and numerical integration using an adaptation of the program KINSIM<sup>38</sup> yield concentrations of the participating species at appropriate time intervals during the course of each reaction. Incorporation of the molar absorbance of peroxynitrite (the only species absorbing appreciably at 302 nm) yields calculated values of the absorbance of the reaction solutions at each point.

Rate constants and equilibrium constants leading to optimal agreement between calculated and observed absorbances are listed in Table 2 and summarized in Table 3. The parameters pertaining to this sequence are not wholly independent; our experiments allow an estimate of  $K_{14}k_{15}$  but not of the individual constants. The bimolecular rate constant,  $k_{13}$ , for the reaction of the two odd-electron species, which is set near the diffusion-controlled limit, does not affect the quality of fit. Absorbances calculated from the parameters in Table 3 are compared to a representative experimental curve in Figure 1.<sup>39,40</sup>

The proposed mechanistic sequence thus ascribes the catalytic role of copper in this system to its ability to support a single-

electron path. This supplements the uncatalyzed route which, based on earlier evidence,<sup>22</sup> has been taken to entail direct oxygen atom transfer. At the same time, the observed absence of catalytic activity associated with vanadium(V) and molybdenum(VI) species is not unexpected. These  $d^0$  states, when active, are thought generally to promote peroxide heterolyses via metal–peroxy complexation and resultant polarization of the O–O bond. At the low catalyst concentrations and the very high basicities employed here, these metal states exist predominantly as the strongly negative oxo complexes  $\text{MoO}_4^{2-}$  and  $\text{VO}_4^{3-}$ , in which the electrophilic character of the metal centers has been severely diminished. Since the O–O bond in peroxynitrite is already markedly polarized by the electron-attracting nitrosyl function, further external enhancement of this effect is vanishingly small.

Some catalytic action by the single-electron couples  $\text{Fe}(\text{II,III})$  and  $\text{Mn}(\text{II,III})$  might be anticipated. Because of the negligible amphotericism exhibited by these states, experiments in basic media require that such centers be utilized as slightly dissociated complexes. Whether available sequestrants will accomplish the necessary solubilization without shifting the interconversion potentials beyond the effective range or curtailing the substitution lability needed for rapid metal–peroxy coordination remains to be seen.

**Acknowledgment.** The authors are grateful to Mrs. Arla McPherson for technical assistance.

IC960907R

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(39) Note that the indicated  $\text{p}K_a$  (10.7) pertaining to the hydroxocopper(I) interconversion (eq 10) is lower than that recorded<sup>23</sup> for the hydroxocopper(II) deprotonation (12.9), probably reflecting the smaller number of  $\text{OH}^-$  units associated with the  $\text{Cu}(\text{I})$  center. Attempts to reproduce the observed kinetic profiles using a somewhat simplified sequence, in which the reaction of the  $[(\text{OH})_2\text{Cu}(\text{H}_2\text{O})]^{2-}$  complex with peroxynitrite ( $k_{11}$ ) was neglected, were not successful.

(40) A reviewer has asked whether we have considered the possibility that dimerization of the  $\text{SO}_3^{\cdot-}$  radical anion ( $\text{S}^{\text{V}}$ ) to form  $\text{S}_2\text{O}_6^{2-}$  competes significantly with the indicated  $\text{S}^{\text{V}}\text{--NO}_2^{\cdot}$  reaction (13). Although we cannot rule out such a dimerization as a minor path, a major contribution of this type would not be compatible with what is observed as the stoichiometry approaches 1:1.