

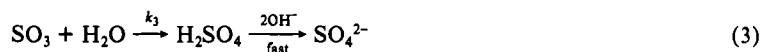
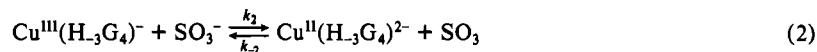
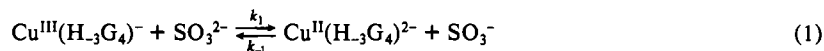
Contribution from the Department of Chemistry,
Purdue University, West Lafayette, Indiana 47907

Trivalent Copper Catalysis of the Autoxidation of Sulfite. Kinetics and Mechanism of the Copper(III/II) Tetraglycine Reactions with Sulfite

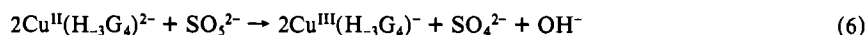
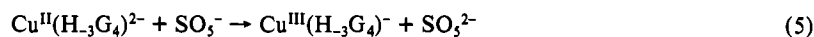
JOHN M. ANAST and DALE W. MARGERUM*

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Copper(III) tetraglycine reacts rapidly with sulfite in two reversible one-electron steps to give copper(II) tetraglycine and aquated sulfur trioxide, which hydrolyzes to sulfate ion (eq 1-3). Suppression of the rate by the copper(II) complex shows



that the sulfite radical anion is an intermediate and indicates a maximum value of 0.89 V for the reduction potential: $\text{SO}_3^- + e^- \rightleftharpoons \text{SO}_3^{2-}$. In the proposed mechanism $k_1 = 3.7 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$, $k_2/k_{-1} = 1.66$, and $k_{-2}/k_3 = 177 \text{ M}^{-1}$. Oxygen intercepts the sulfite radical to produce an oxidizing intermediate which in turn regenerates $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ by reactions with the $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ complex. As a result sulfite addition to $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ in the presence of $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ and O_2 can result in a net increase in the $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ concentration. Observed oscillations in the $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ concentration suggest that the dominant pathway alternates between the reaction of eq 2, which leads to loss of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$, and that of eq 4, which leads to formation of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$. The Cu(III/II) tetraglycine couple catalyzes the autoxidation of sulfite to sulfate.



Introduction

Since the discovery of the stabilization of trivalent copper by deprotonated peptide ligands,^{1,2} many peptide complexes of this oxidation state have been reported.³ The triply deprotonated tetraglycine complex $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ has been well characterized in solution.²⁻⁵ Its acid, base, and photochemical decomposition reactions have been reported recently.⁶ The complex, which is moderately stable in neutral solution, undergoes very rapid one-electron-transfer reactions with IrCl_6^{3-} ,^{7,8} $\text{Co}(\text{phen})_3^{2+}$,⁹ $\text{Cu}^{\text{I}}(\text{dmp})_2^+$, and $\text{Cu}^{\text{I}}(\text{dpmp})_2^{3-}$.¹⁰ Electron-transfer studies of this copper(III) complex have been extended to nonmetallic reducing agents in its reaction with iodide ion¹¹ and in the present case with sulfite ion. It was of special interest to see if any evidence could be found for a two-electron reduction of Cu(III) to Cu(I) with sulfite oxidation to sulfate.

Previously reported transition-metal reductions by sulfite have been carried out in acid media with HCrO_4^- ,¹² IrCl_6^{2-} ,¹³

$\text{Fe}^{3+}(\text{aq})$, and $\text{Fe}(\text{phen})_3^{3+}$.¹⁴⁻¹⁹ Although sulfite reductions in base have been performed with $\text{Mo}(\text{CN})_8^{3-}$, $\text{Mn}(\text{P}_2\text{O}_7)_3^{9-}$,²⁰ and $\text{Fe}(\text{CN})_6^{3-}$, the kinetics and mechanism for the Mo(V) and Mn(III) reactions were not reported, and the reduction of $\text{Fe}(\text{CN})_6^{3-}$ was complicated by attachment of sulfite to a coordinated cyano ligand.²¹ The $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ complex is sufficiently stable to allow the study of sulfite or hydrogen sulfite as the predominant species, and there is no sulfite interaction with tetraglycine.

The introduction of oxygen into reaction mixtures of sulfite and copper tetraglycine causes an induced oxidation of copper(II) to copper(III). This oxidation is autocatalytic, with the rate being proportional to the concentration of the product, $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$. A net gain in copper(III) concentration can result when $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ is initially present with O_2 and sulfite ion.

Experimental Section

Reagents. Copper(II) perchlorate, prepared from CuCO_3 and HClO_4 , was standardized by EDTA titration with a murexide indicator. Tetraglycine (Biosynthetika, Oberdorf, Switzerland) was found to be greater than 95% pure by reverse-phase liquid chromatography using the ion-pairing mode.^{22,23} The chromatographic system consists of an Eldex high-pressure pump, a Rheodyne 7121 injector valve, and a modified Beckman DU variable-wavelength detector set

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at 205 nm. An Altex Ultrasphere-IP, 250 mm by 4.6 mm, 5- μ m octyldecylsilica column was used with a mobile phase of 1.0 mM sodium octyl sulfate and 50 mM NaClO₄ and the pH adjusted to 4.0 with HClO₄.

Peroxonosulfate was supplied courtesy of Du Pont, Wilmington, DE, in the form of the triple salt 2KHSO₅·KHSO₄·K₂SO₄. Sodium perchlorate was prepared by neutralizing Na₂CO₃ with HClO₄. All other chemicals were of analytical reagent grade.

Generation of Cu^{III}(H₃G₄)⁻. Solutions of Cu^{II}(H₃G₄)²⁻ were prepared by addition of 10% molar excess of tetraglycine to stock Cu(ClO₄)₂ solutions and then adjusted to 0.1 M ionic strength with NaClO₄ and to pH 10.5. Since Cu^{II}(H₃G₄)²⁻ is known to undergo autoxidation,⁵ fresh solutions were prepared immediately prior to use.

The Cu^{II}(H₃G₄)²⁻ solutions were electrolyzed at a potential of 0.70 V vs. Ag-AgCl reference, with use of a flow-through electrode consisting of a graphite powder working electrode packed in a porous glass column wrapped externally with a platinum counterelectrode.²⁴ Typical Cu^{III}(H₃G₄)⁻ yields were greater than 98% on the basis of spectrophotometric analysis, $\epsilon_{365 \text{ nm}} = 7400 \text{ M}^{-1} \text{ cm}^{-1}$.⁶ Solutions showing thermal decomposition of greater than 10% were replaced with fresh solutions. All experiments were conducted in light that was passed through a Kodak 1A filter to avoid wavelengths less than 580 nm, which cause photochemical decomposition of Cu^{III}(H₃G₄)⁻.⁶

Preparation of Standard Sulfite Solutions. Anaerobic conditions were strictly observed during the use, handling, and storage of aqueous sulfite solutions as the trace-metal-catalyzed autoxidation of sulfite is well-known.²⁵⁻²⁹ Reagent grade Na₂SO₃ was weighed into a solid-addition arm for a 150-mL three-neck flask. Buffer solution was added to the flask, and the flask was purged with argon for 30 min prior to the addition of the solid Na₂SO₃. Sulfite solutions were transferred by standard syringe techniques and were standardized immediately prior to use by iodometric titration.³⁰ With use of these procedures, the sulfite titer could be maintained within 0.5% for 48 h or more.

The autoxidation of sulfite was briefly investigated under conditions used in this study to test for possible interferences. A half-life of approximately 25 min was found for the loss of sulfite at pH 9.2. This trace-metal-catalyzed autoxidation was effectively suppressed by addition of the strong chelating agent *trans*-1,2-diaminocyclohexanetetraacetic acid (CyDTA) such that less than 1% was lost over 30 min. However, CyDTA could not be used in this study as it is capable of displacing tetraglycine from the copper(II) complex. It is important to note that the trace-metal-catalyzed autoxidation of sulfite is much slower than any of the reactions observed with the copper peptide complex. Tetraglycine, used in 10% molar excess, is a strong chelator of some trace metals, including copper, which has been found to be the most efficient trace-metal catalyst for the sulfite autoxidation.²⁹

Stoichiometric Measurements. The stoichiometry of the reduction was determined by using two methods of spectrophotometric titration, the results of which are termed *normal* and *reverse* stoichiometries. The normal stoichiometry was determined by using a standard sulfite solution as the titrant and monitoring the loss of Cu^{III}(H₃G₄)⁻ absorbance at 365 nm. Freshly prepared Cu^{III}(H₃G₄)⁻ buffered at an appropriate pH was added to a 2.00-cm optical cell, and the cell was purged for 10 min with Ar. The absorbance was then monitored by a Cary 14 spectrophotometer thermostated at 25.0 °C. The sulfite titrant was added to the cell by the injection of microliter quantities with a Hamilton N701 syringe. The titration was limited to approximately 4 min to minimize errors caused by the thermal decomposition of Cu^{III}(H₃G₄)⁻.

For the reverse stoichiometry the Cu^{III}(H₃G₄)⁻ was used as the titrant, and the appearance of the Cu^{III}(H₃G₄)⁻ absorbance at 365 nm was taken as the end point. The titration was carried out by injecting a small quantity of oxygen-free sulfite solution into an optical cell containing purged buffer solution, with microliter additions of

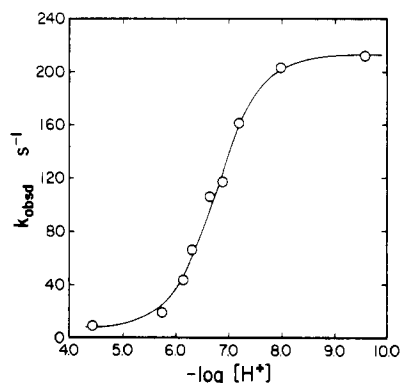


Figure 1. Dependence of the first-order rate constant (initial-rate method) for the loss of Cu^{III}(H₃G₄)⁻ in the presence of excess sulfite upon $-\log [\text{H}^+]$. The solid line is calculated from eq 8 with $k_{\text{HB}} = 2.3 \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$, $k_{\text{B}} = 6.9 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$, and $K_{\text{H}} = 6.3 \times 10^6 \text{ M}^{-1}$. Conditions: $1 \times 10^{-5} \text{ M}$ [Cu^{III}(H₃G₄)⁻], $3.13 \times 10^{-3} \text{ M}$ [SO₃]_T, $\mu = 0.10 \text{ M}$ (NaClO₄) at 25.0 °C.

Table I. Initial-Rate Data for the Reduction of Cu^{III}(H₃G₄)⁻ by SO₃²⁻ ^a

| $10^4 [\text{SO}_3]_{\text{T}}, \text{M}$ | $k_{\text{obsd}}, \text{s}^{-1}$ | $10^4 [\text{SO}_3]_{\text{T}}, \text{M}$ | $k_{\text{obsd}}, \text{s}^{-1}$ |
|---|----------------------------------|---|----------------------------------|
| 1.00 | 6.9 ± 0.8 | 10.00 | 76 ± 12 |
| 2.00 | 21 ± 4 | 20.0 | 150 ± 16 |
| 6.00 | 38 ± 2 | 30.0 | 224 ± 7 |

^a $2k_1 = 7.5(\pm 0.2) \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$. $-\log [\text{H}^+] = 9.12$; [Cu^{III}(H₃G₄)⁻] = $1 \times 10^{-5} \text{ M}$.

purged Cu^{III}(H₃G₄)⁻ following. The slope of the absorbance vs. titrant added after the end point was used to calculate the concentration of Cu^{III}(H₃G₄)⁻ used. The error associated with the thermal decomposition of the copper(III) titrant was minimized by limiting the titration time to approximately 4 min and storing the titrant in an ice bath.

Kinetic Measurements. The kinetics were determined on a Durrum stopped-flow spectrophotometer with on-line digital data acquisition and analysis carried out by a Hewlett-Packard 2115A general-purpose minicomputer.³¹ Non-first-order kinetic data were analyzed off-line with use of least-squares regression programs written in this laboratory. The reactions were monitored at 365 nm, which is the wavelength of maximum absorbance for Cu^{III}(H₃G₄)⁻. All solutions were thermostated at $25.0 \pm 0.1 \text{ °C}$, and the ionic strength was maintained at 0.10 M with NaClO₄. Anaerobic solutions were delivered to the stopped-flow instrument through minimal lengths of Teflon tubing by applying positive argon pressure to purged reservoir flasks. In order to minimize oxygen interference, we measured the final pH values of the reaction mixtures as rapidly as possible using a Radiometer 26 pH meter and microelectrodes. The pH electrode was calibrated to yield $-\log [\text{H}^+]$ from pH readings by titrating a 4.3 mM HClO₄ solution ($\mu = 0.10 \text{ M}$ (NaClO₄)) with 0.10 M NaOH and treating the data as suggested by Molina et al.³² The correction equation followed the form $-\log [\text{H}^+] = \text{pH}_{\text{obsd}} - 0.06$.

Results

Kinetics. The data in Figure 1 show the pH dependence of the pseudo-first-order rate constants for the reduction of Cu^{III}(H₃G₄)⁻ by excess sulfite. The reaction followed a clean first-order rate dependence up to pH 5.8. Above this pH the reaction appeared to become reversible, showing signs of product inhibition. Initial-rate data analysis was used for all reactions giving this behavior. The sulfite dependence at pH 9.2 indicates that sulfite is a first-order reactant. Analysis of the data in Table I gave an observed rate constant of $(7.5 \pm 0.2) \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$ with the sulfite-independent term deemed

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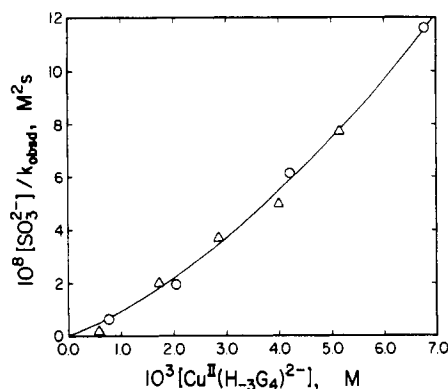


Figure 2. Dependence of the inverse of the second-order rate constant, normalized by the sulfite concentration, upon the concentration of $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$, showing inhibition by the latter with a first-order and second-order dependence. The $[\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}]$ is calculated from $[\text{Cu}^{\text{II}}\text{G}_4]_{\text{T}}$ with use of $\log K_{\text{H}} = 9.15$: (Δ) pH 10.4, 0.01 M carbonate buffer; (\circ) pH values given in Table II. The solid line is calculated from eq 10 with $A = 8.01 \times 10^{-6} \text{ M s}$ and $B = 1.42 \times 10^{-3} \text{ s}$. Conditions: $(2.3\text{--}2.9) \times 10^{-5} \text{ M} [\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^{-}]$, $4.9 \times 10^{-4} \text{ M} [\text{SO}_3^{2-}]$, $\mu = 0.10 \text{ M}$ (NaClO_4) at 25.0°C , $\text{Cu}^{\text{II}}\text{G}_4$ buffer.

Table II. Kinetic Data for the Dependence upon $[\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}]$ of the Reduction of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^{-}$ by SO_3^{2-} ^a

| $10^4 \times [\text{SO}_3]_{\text{T}}, \text{M}$ | $10^3 \times [\text{Cu}^{\text{II}}\text{G}_4]_{\text{T}}, \text{M}$ | $-\log [\text{H}^+]$ | $10^4 k'_{\text{obsd}}, \text{M}^{-1} \text{s}^{-1}$ |
|--|--|----------------------|--|
| 4.97 | 0.605 | 10.30 | 28.2 |
| 4.97 | 1.82 | 10.30 | 2.47 |
| 4.97 | 3.02 | 10.30 | 1.35 |
| 4.97 | 4.24 | 10.30 | 0.995 |
| 4.97 | 5.45 | 10.30 | 0.640 |
| 4.90 | 2.00 | 8.92 | 7.40 |
| 4.90 | 5.00 | 8.98 | 2.50 |
| 4.90 | 10.0 | 9.00 | 0.790 |
| 4.90 | 15.0 | 9.05 | 0.420 |

^a $[\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^{-}] = 1 \times 10^{-5} \text{ M}$. Buffers are 0.01 M carbonate for $-\log [\text{H}^+] = 10.3$; all others use $\text{Cu}^{\text{II}}\text{G}_4$ as buffer.

negligible at $0.8 \pm 3 \text{ s}^{-1}$. The pH dependence and the sulfite dependence at pH 9.2 follow the expressions given in eq 7 and 8, where $[\text{SO}_3]_{\text{T}} = [\text{HSO}_3^-] + [\text{SO}_3^{2-}]$. The calculated fit of

$$-\frac{d[\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^{-}]}{dt} = k_{\text{obsd}}[\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^{-}] \quad (7)$$

$$k_{\text{obsd}} = \frac{k_{\text{HB}}K_{\text{H}}[\text{H}^+] + k_{\text{B}}}{1 + K_{\text{H}}[\text{H}^+]}[\text{SO}_3]_{\text{T}} \quad (8)$$

the pH data to eq 8 yields a K_{H} value of $(6.3 \pm 0.9) \times 10^6 \text{ M}^{-1}$. This value is slightly lower than the values reported by Cuta et al.,³³ $7.8 \times 10^6 \text{ M}^{-1}$ ($\mu = 0.10 \text{ M}$ (NaCl)), and Tartar et al.,³⁴ $1.0 \times 10^7 \text{ M}^{-1}$ ($\mu = 0.10 \text{ M}$ (NaCl)). However, Tartar reported a specific anion dependence with a higher value of K_{H} found when NaBr was used to control the ionic strength ($2.8 \times 10^7 \text{ M}^{-1}$ for $\mu = 0.10 \text{ M}$ (NaBr)).

The resolved rate constants of eq 8 correspond to the two reduction pathways, which involve HSO_3^- (k_{HB}) and SO_3^{2-} (k_{B}) with respective values of $(2.3 \pm 0.5) \times 10^3$ and $(6.9 \pm 0.4) \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$.

Effect of Added $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$. The reversible reduction kinetics were studied at pH values from 9 to 10.4 with both $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ and sulfite concentrations in excess over the $[\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^{-}]$. At these pH values 36–95% of the copper(II) complex is in the triply deprotonated form.³⁵

Table III. Determination of the Rate Constant for the Reaction of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^{-}$ and SO_3^{2-} under Pseudo-First-Order Conditions with Excess $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ ^a

| $[\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}], \text{M}$ | $k_{\text{obsd}}, \text{s}^{-1}$ | $10^{-4}k_1, \text{M}^{-1} \text{s}^{-1}$ |
|--|----------------------------------|---|
| 1.15×10^{-4} | 7.68 | 6.68 |
| 1.04×10^{-4} | 6.42 | 6.17 |
| 8.17×10^{-5} | 6.58 | 8.05 |
| 6.28×10^{-5} | 4.89 | 7.79 |
| | | av 7.2 (± 0.9) |

^a $[\text{SO}_3^{2-}] = 4.38 \times 10^{-6} \text{ M}$; $-\log [\text{H}^+] = 9.12$.

Table IV. Stoichiometry of the Reaction of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^{-}$ and SO_3^{2-} ^a

| mode | $[\text{Cu}^{\text{III}}\text{G}_4], \text{M}$ | $[\text{SO}_3]_{\text{T}}, \text{M}$ | atm pH ^b | $[\text{Cu}^{\text{III}}\text{G}_4] / [\text{SO}_3]_{\text{T}}$ | addn size, μL |
|-----------------------|--|--------------------------------------|-----------------------|---|--------------------------|
| normal | 8.28×10^{-5} | 5.33×10^{-3} | Ar 6.86 | 1.94 ± 0.04 | 2 |
| | 8.14×10^{-5} | 5.33×10^{-3} | Ar 6.86 | 2.0 ± 0.1 | 2 |
| | 6.69×10^{-5} | 5.28×10^{-3} | Ar 9.18 | 2.0 ± 0.1 | 10 |
| | 5.23×10^{-5} | 5.28×10^{-3} | Ar 9.18 | 1.9 ± 0.1 | 5 |
| | 6.75×10^{-5} | 5.28×10^{-3} | Ar 9.18 | 1.9 ± 0.3 | 2 |
| | 7.94×10^{-5} | 5.28×10^{-3} | Ar 9.18 | 1.9 ± 0.2 | 2 |
| | 7.64×10^{-5} | 5.28×10^{-3} | Ar 9.18 | 2.0 ± 0.4 | 2 |
| | 9.24×10^{-5} | 5.33×10^{-3} | O ₂ 6.86 | 0.56 ± 0.09 | 5 |
| | reverse | 1.64×10^{-3} | 1.63×10^{-5} | Ar 6.86 | 1.5 |
| 1.91×10^{-3} | | 1.63×10^{-5} | O ₂ 6.86 | 0.44 | 10 |
| 1.98×10^{-3} | | 1.63×10^{-5} | O ₂ 6.86 | 0.34 | 5 |
| 1.99×10^{-3} | | 1.63×10^{-5} | O ₂ 6.86 | 0.18 | 1 |

^a $\mu = 0.10 \text{ M}$ (NaClO_4) at 25.0°C . ^b Buffers: 0.01 M phosphate, pH 6.86; 0.01 M borate, pH 9.18.

The added $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ effectively suppressed the reaction rate and shifted the rate law to pseudo second order in the loss of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^{-}$ as in eq 9. The dependence of the inverse

$$-\frac{d[\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^{-}]}{dt} = k'_{\text{obsd}}[\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^{-}]^2 \quad (9)$$

of the rate constant, normalized by the sulfite concentration, upon the concentration of $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ is illustrated in Figure 2. The data, summarized in Table II, were found to obey a summed first-order and second-order dependence on the $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ concentration, as in eq 10.

$$[\text{SO}_3^{2-}] / k'_{\text{obsd}} = A[\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}] + B[\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}]^2 \quad (10)$$

The results of the least-squares regression gave values of $A = 8.01 \times 10^{-6} \text{ M s}$ and $B = 1.42 \times 10^3 \text{ s}$. This relationship indicates that there are at least two steps that are inhibited by the product, $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$.

Pseudo-First-Order Kinetics in Sulfite. The high absorptivity at 365 nm and the thermal decomposition of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^{-}$ made the use of this reagent in excess difficult. The reaction did, however, follow a first-order rate law at pH 9.2. The data in Table III are the observed first-order rate constants and the calculated second-order rate constants based on the $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^{-}$ concentration. The resulting average rate constant of $(7.2 \pm 0.9) \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$ is in fair agreement with the value determined by initial rates. Interestingly, $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^{-}$ acts as a first-order oxidant when it is in excess over sulfite and $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$, but as a second-order oxidant when $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ is in excess over the sulfite and $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^{-}$.

Stoichiometry. The anaerobic and aerobic stoichiometric data are presented in Table IV. As is apparent when the values listed are compared, significant deviations from the expected stoichiometry were found for solutions not purged with an inert gas. Argon was found to be somewhat more

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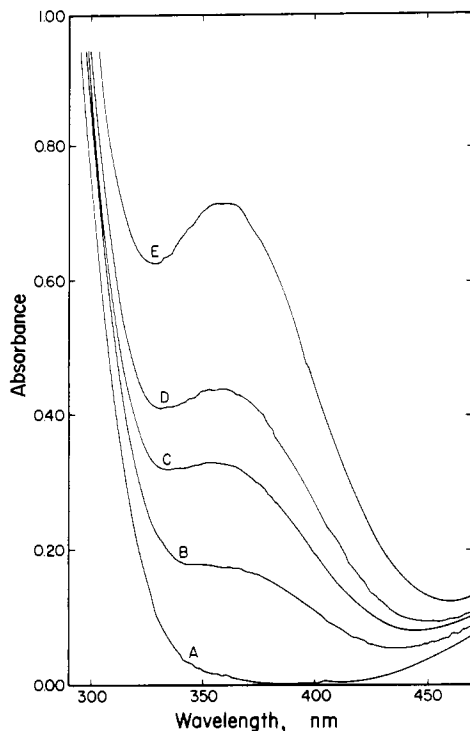
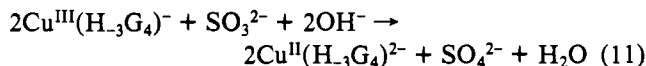


Figure 3. Sulfite-induced reaction of oxygen with $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ to produce $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$. Each spectral scan was taken immediately after the addition of small quantities of $1.27 \times 10^{-3} \text{ M } [\text{SO}_3^{2-}]$: A, 0; B, 10 μL ; C, 10 μL ; D, 10 μL ; E, 20 μL . Conditions: $1.10 \times 10^{-3} \text{ M } [\text{Cu}^{\text{II}}\text{G}_4]$, $1.3 \times 10^{-3} \text{ M } [\text{O}_2]$, total initial volume 6.00 mL, 0.01 M borate buffer at pH 9.2, $\mu = 0.10 \text{ M } (\text{NaClO}_4)$ at 25.0 $^\circ\text{C}$.

efficient at purging than nitrogen. Initial reverse stoichiometric titration using nitrogen as a purge gas showed little difference from the oxygen-sparged titrations of Table IV; hence nitrogen was abandoned in favor of argon.

The normal stoichiometry under argon gave results consistent with a 2-equiv reductant reacting with a 1-equiv oxidant as in eq 11. The larger standard deviation at pH 9.2 was due



in part to the decreased stability of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ at the higher pH value. The titration of oxygen-saturated solutions gave much higher ratios of sulfite oxidized per $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ added than did Ar-purged solutions. Although the reaction of sulfite and oxygen is well-known²⁵⁻²⁹ ($t_{1/2} \sim 25$ min in this work), it is much too slow to be the interference observed here, suggesting the complication is synergistic with sulfite, oxygen, and the copper peptide. Since sulfite autoxidation is trace-metal catalyzed, the copper peptide is presumably catalyzing the sulfite autoxidation.

The reverse stoichiometry provides more dramatic evidence for this effect, as the titration is extremely sensitive to the oxygen in solution. The 1.5:1.0 ratio of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ to SO_3^{2-} for Ar-purged solution was the lowest consumption of sulfite per $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ found for a reverse stoichiometric determination, still well above the normal stoichiometric consumption. It is reasonable to assume that a reverse stoichiometry of 2:1 $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-:\text{SO}_3^{2-}$ could be attained with use of an optimized system to lower the trace levels of oxygen.

The oxygen-saturated solutions all show large ratios of sulfite consumed per $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ added, with the maximum of 7.8 occurring when the smallest additions of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ were made (see Table IV). Hence the oxygen interference has a kinetic dependence in $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ that affects the stoichiometry. This effect was also noted near the end of a normal

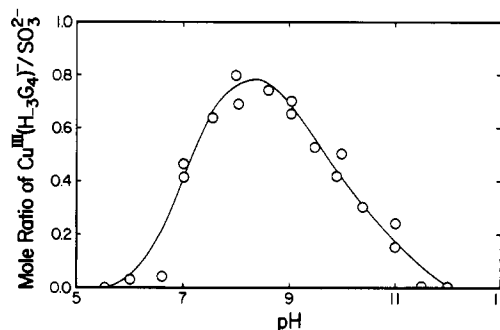


Figure 4. Dependence of the mole ratio between the $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ formed and the sulfite added upon the pH for the sulfite-induced oxidation of $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$. Conditions: $1.10 \times 10^{-3} \text{ M } [\text{Cu}^{\text{II}}\text{G}_4]$, $8.4\text{--}9.0 \times 10^{-6} \text{ M } [\text{SO}_3^{2-}]$, $2.6 \times 10^{-4} \text{ M } [\text{O}_2]$, initial volume 6.00 mL, $\text{Cu}^{\text{II}}\text{G}_4$ buffer, $\mu = 0.10 \text{ M } (\text{NaClO}_4)$ at 25.0 $^\circ\text{C}$.

stoichiometric determination where the concentration of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ was low.

Aerobic Reaction

In order to clarify the oxygen reaction, we studied the effects of sulfite on the product of the reaction, $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$. Figure 3 shows the results of the addition of sulfite to an oxygen-containing solution of $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ at pH 9.2. When oxygen was excluded, no significant spectral changes were found upon multiple injections of sulfite. The same additions to the oxygen-saturated solution produced an intense absorption centered at 365 nm, which increased with each increment of sulfite until a maximum absorbance was reached. At that point, further addition of sulfite rapidly reduced the absorbance to its initial value. This cycle could be repeated provided that the solution was resaturated with oxygen between each cycle. Five to six cycles have been observed with little change in the absorbance yield or behavior. The absorbance generated at 365 nm is characteristic of the charge-transfer band of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$, while the initial rate of decay of that absorbance ($8 \times 10^{-5} \text{ s}^{-1}$, $\mu = 0.10 \text{ M } (\text{NaClO}_4)$) between additions of sulfite corresponds to the rate of the base decomposition of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ at pH 9.2 of $1.6 \times 10^{-4} \text{ s}^{-1}$ ($\mu = 1.0 \text{ M } (\text{NaClO}_4)$).⁶ This, together with the evidence of an oxidizing species when excess sulfite was added, indicates $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ is being oxidized to $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ in the presence of sulfite, a good reducing agent. The ability to reduce the $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ formed in this manner with excess sulfite and carry out the cycle again by oxygen resaturation indicates that oxygen is a limiting reactant.

The pH dependence of the induced sulfite oxidation is depicted in Figure 4. The maximum net generation of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ was found at pH 8, which also corresponds to the maximum rate of formation of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$, with the rate decreasing at both higher and lower pH values.

The kinetics of this reaction proved to be quite complex. Large variations in the kinetics were found, depending on the relative concentrations of the $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ and sulfite reactants. As many as four distinct reaction-rate processes were found for a single kinetic run. However, for the set of conditions given in Figure 5 a rate law was found that was autocatalytic, that is, accelerated by a path that is first order in product, as in eq 12. The observed rate constant was

$$d[\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-]/dt = k_{\text{obsd}}[\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-] \quad (12)$$

calculated to be 0.38 s^{-1} . The intercept of the logarithmic plot in Figure 5 was extrapolated to time zero since for the first 5 s the value of $A_t - A_0$ was so small that $\ln(A_t - A_0)$ was indeterminate. The value of the intercept revealed that $5 \times 10^{-9} \text{ M } \text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ was initially present. Attempts to study the dependence of the sulfite or $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ concentrations

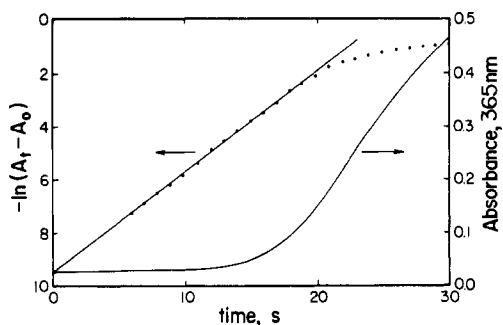


Figure 5. Autocatalytic formation of $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^-$ where the reaction is first order in product. A_0 and A_t correspond to the initial absorbance and the absorbance at any time t . Conditions: 5.50×10^{-4} M $[\text{Cu}^{\text{II}}\text{G}_4]_{\text{T}}$, 2.2×10^{-4} M $[\text{SO}_3^{2-}]$, 6.5×10^{-4} M $[\text{O}_2]$, total volume 6.00 mL, $\lambda = 365$ nm, 0.01 M borate buffer at pH 9.2, $\mu = 0.10$ M (NaClO_4) at 25.0°C .

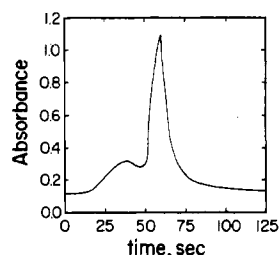


Figure 6. Triphasic kinetic trace of the sulfite-induced oxidation of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^{2-}$ in the presence of O_2 . Conditions: 1.00×10^{-3} M $[\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^{2-}]$, 1.00×10^{-3} M $[\text{SO}_3^{2-}]$, 6.5×10^{-4} M $[\text{O}_2]$, 0.01 M borate buffer at pH 9.2, $\mu = 0.10$ M (NaClO_4) at 25.0°C .

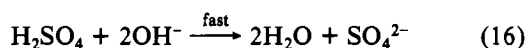
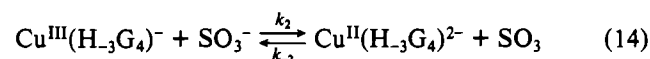
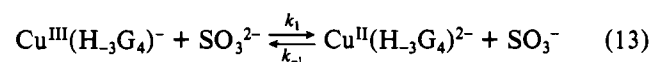
lead to the complex behavior of the type illustrated in Figure 6. The triphasic reaction gave two apparent autocatalytic segments and a pseudo-second-order decay of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$. As already seen, in the absence of oxygen and with excess $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$, the reduction of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ by excess sulfite occurs by a second-order process; hence oxygen again appears to be a limiting reagent.

Product Analysis

The reaction products were analyzed with use of reverse-phase ion-pairing liquid chromatography. No evidence was found to indicate that the tetraglycine ligand was involved in the sulfite reduction of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ or in the $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ -catalyzed oxidation of $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ by sulfite. Greater than 85% of the ligand could be recovered intact in all cases. The remaining unrecovered tetraglycine gave products which are typical of the thermal decomposition of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$.⁵ It therefore appears that the ligand is not involved in the sulfite reactions but is modified by the thermal decomposition of the copper(III) peptide as previously suggested.⁵

Discussion

The mechanism proposed in eq 13–16 is consistent with the



anaerobic kinetic and stoichiometric relationships in basic solution. The generation of the sulfite free-radical species, SO_3^- , has been suggested^{12–15,18,29,36} in several transition-metal

Table V. Summary of Kinetically Determined Constants

Equilibrium and Rate Constants from the pH Variation

$$K_{\text{H}} = (6.3 \pm 0.9) \times 10^6 \text{ M}^{-1}$$

$$k_{\text{HB}} = (2.3 \pm 0.5) \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$$

$$k_{\text{B}} = (6.9 \pm 0.4) \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$$

Determination of k_1

| source | $k_1, \text{M}^{-1} \text{s}^{-1}$ |
|---|------------------------------------|
| pH variation ($k_{\text{B}}/2$) | $(3.5 \pm 0.2) \times 10^{-4}$ |
| excess SO_3^{2-} | $(3.8 \pm 0.1) \times 10^{-4}$ |
| excess $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ | $(3.6 \pm 0.5) \times 10^{-4}$ |
| weighted mean | $(3.7 \pm 0.1) \times 10^{-4}$ |
| pH variation ($k_{\text{HB}}/2$) for HSO_3^- | $(1.2 \pm 0.3) \times 10^{-3}$ |

Ratios of Other Rate Constants

$$k_2/k_{-1} = 1.66$$

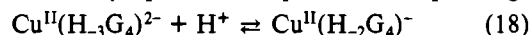
$$k_{-2}/k_3 = 177 \text{ M}^{-1}$$

redox systems, but no direct evidence has been presented. However, the sulfite radical anion has been produced by pulse radiolysis,³⁷ flash photolysis,³⁸ and fast-flow techniques³⁹ and subsequently characterized by EPR spectroscopy. The reversible kinetics suggested by the inhibitory effects of $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ in the work presented here provide conclusive evidence that the sulfite radical is indeed produced as a product of the initial one-electron reduction of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$.

When the proposed mechanism is treated by the double steady-state approximation, with the steady-state species being SO_3^- and SO_3 , the rate law in eq 17 results.

$$2d[\text{SO}_3]/dt = -d[\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-]/dt = \{2k_1k_2k_3[\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-]^2[\text{SO}_3^{2-}]/\{k_2k_3[\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-] + k_{-1}k_3[\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}] + k_{-1}k_{-2}[\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}]^2\} \} \quad (17)$$

Two protonations have been eliminated for clarity. Hydrogen sulfite has been shown to be reactive but was only briefly investigated, and attention will be focused on the sulfite dianion. Secondly, $\text{Cu}^{\text{II}}\text{G}_4$ undergoes stepwise deprotonation of the peptide nitrogens with successive pK values of 5.41, 6.81, and 9.15 ($\mu = 0.10$ M (NaClO_4)).³⁵ This system has been extensively studied by Youngblood and co-workers⁴⁰ with the proton-transfer rates and mechanism elucidated. Equation 18 represents the only equilibrium important in the pH range



of 9–10.5 where the hydrogen sulfite concentration can be neglected. The rate constant of the forward reaction in eq 18 is $1.6 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$.⁴⁰ The rapid scavenging of $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ by acid accounts for the lack of product inhibition during the reduction of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ below pH 5.8; that is, the $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ protonation, eq 12, is faster than the reverse of the hydrogen sulfite reduction when the pH is less than 5.8.

Under the conditions of excess sulfite and with the use of initial rate determinations so that eq 19 holds, the observed

$$k_2k_3[\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-] \gg k_{-1}k_3[\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}] + k_{-1}k_{-2}[\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}]^2 \quad (19)$$

rate constant for the loss of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ is given in eq 20.

$$k_{\text{obsd}} = 2k_1[\text{SO}_3^{2-}] \quad (20)$$

From the results of the sulfite dependence in Table I the value of k_1 is calculated to be $(3.8 \pm 0.1) \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$. Likewise when $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ is in excess the rate constant reduces to the expression in eq 21. From the results of the $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$

$$k_{\text{obsd}} = 2k_1[\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-] \quad (21)$$

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dependence in Table III the value of k_1 can be calculated to be $(3.6 \pm 0.5) \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$. These two values for k_1 as well as the initial rate value of k_1 determined from the pH variation ($k_B/2$) are summarized in Table V. The weighted mean is $(3.7 \pm 0.1) \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$. The corresponding rate constant for HSO_3^- becomes $k_{\text{HB}}/2 = (1.2 \pm 0.3) \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$.

In the presence of excess $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ and sulfite the rate of loss of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ becomes second order, as predicted by the proposed rate law, eq 11. When $k_{-1}k_3[\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}] + k_{-1}k_2[\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}]^2 \gg k_2k_3[\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-]$, the observed rate constant is that given in eq 22. The dependence of the

$$k'_{\text{obsd}} = \frac{2k_1k_2k_3[\text{SO}_3^{2-}]}{k_{-1}k_3[\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}] + k_{-1}k_2[\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}]^2} \quad (22)$$

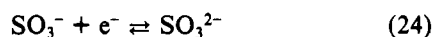
inverse of the rate constant, normalized by the sulfite concentration, upon the concentration of $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$, shown in eq 23, can be fit to the data illustrated in Figure 2. Com-

$$\frac{[\text{SO}_3^{2-}]}{k'_{\text{obsd}}} = \frac{k_{-1}}{2k_1k_2}[\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}] + \frac{k_{-1}k_2}{2k_1k_2k_3}[\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}]^2 \quad (23)$$

parison of eq 10 and 23 allows the calculation of the ratios of the rate constants where k_2/k_{-1} and k_{-2}/k_3 are 1.66 and 177 M^{-1} , respectively.

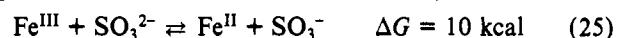
Furthermore, the fact that both sets of data shown in Figure 2 can be fit to the same dependence confirms that the reaction step involving SO_3 is attack by water, eq 15, and not hydroxide. If hydroxide were involved, a large difference in the rates at pH 9 and 10.4 would be expected. Subsequent steps must therefore be the rapid neutralization reactions to yield the final product, sulfate.

The absence of dithionate production from anaerobic reaction conditions indicates that the copper(III) peptide is much more efficient at scavenging the sulfite radical than is a second sulfite radical. Such is not the case in the studies of the sulfite reactions with IrCl_6^{3-} ¹³ and $\text{Fe}(\text{phen})_3^{3+}$ ¹⁹ where production of dithionate was found. However, the thermodynamic driving forces of the IrCl_6^{3-} and $\text{Fe}(\text{phen})_3^{3+}$ reductions appear to be smaller in the acidic media in which these reactions were run, and the reduced reaction rates favor the dimerization of SO_3^- . As seen in this study, HSO_3^- is 30 times less reactive than SO_3^{2-} . The electrode potentials of these species (HSO_3^- vs. SO_3^{2-}) reflect this trend as the reduction potential ranges from -0.93 V in basic solution to $+0.17 \text{ V}$ in acidic media.⁴¹ Thus, sulfite might be expected to produce sulfate as a product, whereas hydrogen sulfite would yield greater amounts of dithionate. Although no quantitative relationships can be drawn, it is clear from studies reported of SO_3^{2-} reductions involving other transition-metal complexes that the rate of reduction increases as the redox potential of the metal complex increases.^{13,19,21} The dependence on the redox potential suggests that the electron transfer could be involved in the rate-determining step. The application of free energy relationships such as the Marcus theory,⁴² while being advantageous for detailing sulfite electron transfer, suffers from the necessity of knowing the as yet undetermined formal potential of the sulfite radical anion, eq 24. With the use of the estimate of



Brown and Higginson⁴³ for the free energy of the reaction in

eq 25 and an E° value of 0.77 V for $\text{Fe}(\text{III}/\text{II})$,⁴¹ the sulfite

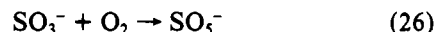


potential, eq 24, can be calculated to be $+1.2 \text{ V}$. However, with use of this formal potential for the sulfite radical and the formal potential of the copper(III/II) tetraglycine couple of 0.63 V ,³ the equilibrium constant for the reaction in eq 13 becomes 2.3×10^{-10} . Since k_1 has a value of $3.7 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$, k_{-1} becomes $1.6 \times 10^{14} \text{ M}^{-1} \text{ s}^{-1}$, clearly exceeding the diffusion-controlled limit of the reverse rate constant. The diffusion limit for two reactants of 1- and 2- charges in 0.10 M ionic medium, on the assumption of a closest approach of 5 \AA , is approximately $1 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$.

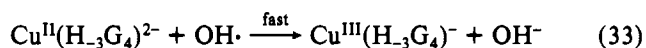
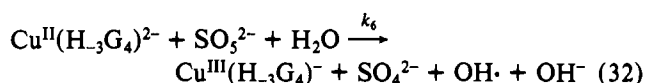
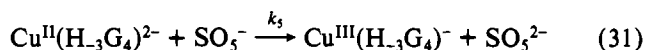
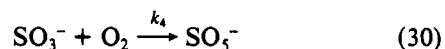
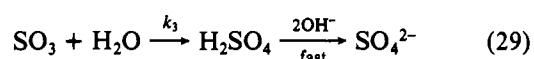
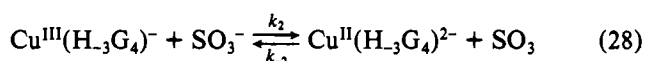
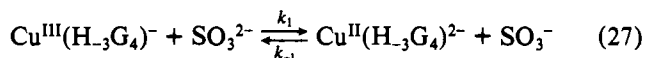
With use of this diffusion-limited value for k_{-1} , the formal potential for the reduction of the sulfite radical, eq 24, is calculated to be $+0.89 \text{ V}$. It is evident that this potential must be an upper limit for the sulfite radical anion.

The Oxygen Reaction

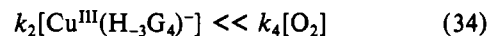
The direct reactions of oxygen with SO_3^{2-} , $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$, and $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ are slow and cannot explain the observed aerobic behavior. However, Hayon et al.⁴⁴ have suggested from pulse-radiolysis and flash-photolysis experiments that the formation of peroxomonosulfate radicals from sulfite radicals and oxygen, eq 26, occurs with a rate constant of $10^9 \text{ M}^{-1} \text{ s}^{-1}$.



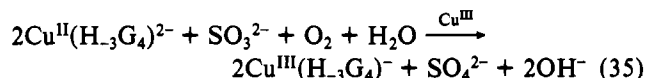
A much slower reaction of SO_5^- with ethanol occurs with $k \leq 10^3 \text{ M}^{-1} \text{ s}^{-1}$ at pH 9. With this in mind the scheme of eq 27–33 is postulated for the aerobic mechanism.



Under conditions where the concentration of oxygen is much larger than that of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ so that



the SO_3^- produced in eq 27 preferentially reacts via the aerobic pathway (eq 30–33) rather than the anaerobic pathway (eq 28 and 29). With the summation of eq 27 and 30–33, the aerobic stoichiometry becomes that shown in eq 35, which



corresponds to the autocatalytic generation of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$. As noted in the reverse stoichiometry, the highest consumption of sulfite was found at the lowest concentration of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$. This is consistent with the relationship in eq 34.

For most of the aerobic experiments oxygen was the limiting reagent. As $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ is generated and the oxygen is depleted, the relationship in eq 34 will become reversed,

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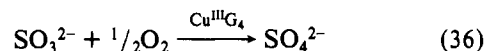
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shifting the reaction to the anaerobic pathway. Thus, depending on the ratio of the concentrations of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ and oxygen, the stoichiometry can shift from 2:1 $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$: SO_3^{2-} for the anaerobic pathway to a very large number of SO_3^{2-} per $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$, as suggested by eq 35. While a highly efficient catalytic role for $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ has not been observed (this is in part due to the use of oxygen as a limiting reagent), the high consumption of sulfite in the aerobic reverse stoichiometric determination indicates that considerable cycling of the copper oxidation states has occurred. Likewise when the $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ concentration is held high (normal stoichiometric determination) the pathway in eq 28 and 29 occurs even in the presence of traces of O_2 , so that each sulfite equivalent reacts with $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ only.

The observed oscillations in the $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ concentration during the reaction illustrated in Figure 6 suggest that this system could be explained in terms of other chemical oscillators.^{45,46} Consider the overall reaction as given in eq 36.



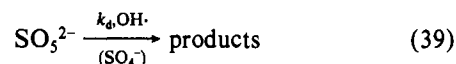
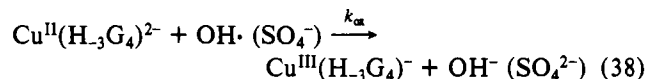
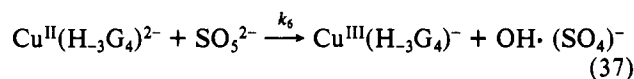
First, the reactant (SO_3^{2-} and O_2) and product (SO_4^{2-}) concentrations do not oscillate, but the rates of consumption and production do. Second, there is indirect feedback; that is, the autocatalytic regeneration of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ serves to regulate the shifting in the relationship of eq 34. Third, the system contains irreversible steps, as the products of eq 29 and 30 cannot exert direct feedback control on preceding reactions.

This is important in that the generation of $\text{Cu}^{\text{III}}\text{G}_4$ can occur somewhat independently of factors governing the reduction of $\text{Cu}^{\text{III}}\text{G}_4$, such that the two processes can become out of step with each other to produce the type of behavior shown in Figure 6. This is in sharp contrast to the steady state in $\text{Cu}(\text{III})$ concentration expected if both the loss and gain of $\text{Cu}^{\text{III}}\text{G}_4$ were regulated by common factors. Finally, the concentration of the intermediate undergoes oscillations. This final fact has been experimentally shown for one to two cycles of the generation and loss of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$, and while it appears theoretically possible for this system to support prolonged oscillations, the speed at which the reaction proceeds makes it difficult in practice. The problem becomes one of heterogeneous transfer of oxygen into solution being too slow to maintain high enough levels to sustain the reaction for more than the two oscillations observed.

Intermediates in the Aerobic Reaction. The evidence for SO_5^- and for SO_5^{2-} in the reaction mechanism is indirect. First, SO_3^- and O_2 are known⁴⁴ to react rapidly to give SO_5^- , and there is good evidence for SO_3^- as an intermediate. Second, SO_5^{2-} is able to oxidize $\text{Cu}(\text{II})$ peptides to $\text{Cu}(\text{III})$ peptides. Third, alternative mechanisms with HO_2 and H_2O_2 are not attractive because H_2O_2 reduces $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$.⁴⁷ Finally, Ettel and co-workers⁴⁸ have found that mixtures of SO_3^{2-} and O_2 have sufficient oxidizing power to oxidize $\text{Ni}(\text{OH})_2$ whereas hydrogen peroxide had no effect. Sizable amounts of SO_5^{2-} were produced from aerated Na_2SO_3 slurries in the absence of $\text{Ni}(\text{OH})_2$. It is interesting that in both the $\text{Ni}(\text{OH})_2$ study and the present work a strong oxidant can be produced in the presence of a strong reductant. This suggests that the reaction between SO_3^{2-} and O_2 to form sulfate is not rapid despite the favorable thermodynamics.

The oxidation of excess $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ by peroxomonosulfate, SO_5^{2-} , at pH 10.4 was carried out to estimate the rates at which the reactions in eq 32 and 33 occur. The rate of

production of the characteristic absorbance of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ at 365 nm was found to increase with increasing $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ concentration. However, at this pH only 4% of the oxidizing equivalents of SO_5^{2-} resulted in the oxidation of $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$. Maruthamutha and Neta⁴⁹ in the study of the radiolytic chain decomposition of peroxomonosulfate raise two important points. First, peroxomonosulfate was found⁵⁰ to react with aquated electrons to form SO_4^{2-} and OH^- radicals as products 4 times more frequently than it did to form SO_4^- and OH^- as products. Hence the reaction in eq 32 could have a parallel path to produce SO_4^- and OH^- . Second, it was observed that the resulting radicals, either SO_4^- or OH^- , rapidly attacked the remaining SO_5^{2-} reactant by a chain-reaction mechanism, giving chain lengths as large as 60 at pH 12. Thus the low yield of the SO_5^{2-} oxidation of $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ can result from the products (OH^- or SO_4^-) of the first oxidation, eq 32, decomposing the SO_5^{2-} by a chain mechanism before it can further react with the copper(II) peptide as in eq 37–39. This low oxidation yield is reflected in the limited efficiency of the copper(III) peptide catalysis of the sulfite autoxidation.



Dependence on pH of the $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ Formation. The yield of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ from the induced sulfite oxidation reaction exhibits a complex dependence on pH as shown in Figure 4. The sharp rise in the rate of formation and yield of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ from pH 5 to 8 parallels the increase in the fraction of copper(II) tetraglycine that is in the form of the $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ species. An increase in the $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ concentration serves to accelerate the rates of the reactions in eq 31–33. The decrease in the rate of formation and the yield above pH 8 can be attributed to the decomposition of SO_5^{2-} . A further consequence of the radiolytic decomposition of SO_5^{2-} was that the chain length for decomposition exhibited a pH dependence with a sharp increase occurring at pH 9. The increase was explained⁴⁹ by a higher susceptibility of SO_5^{2-} (over HSO_5^- , $\text{p}K_a = 9.4^{51}$) to the chain decomposition. The overall pH dependence of the sulfite-induced oxidation of $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ is the sum of the pH dependences of the two competing pathways, eq 31–33 vs. eq 39.

Furthermore $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ becomes increasingly unstable as the pH rises above 7. Since the induced oxidation is autocatalytic in $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$, the reaction can be stopped by the thermal decomposition of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ during the induction period where the reaction rate is very slow. (This is essentially the same effect that light has in preventing the $\text{Cu}(\text{III})$ -catalyzed autoxidation of $\text{Cu}(\text{II})$ tetraglycine.⁵) The base-catalyzed $\text{Cu}^{\text{III}}\text{G}_4$ decomposition may also contribute to the lower yields at pH values greater than 8. Thus, in more basic media, $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ becomes increasingly susceptible to loss by a pathway other than the sulfite reduction, and lower $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ yields are observed.

Initiation Reaction. The autocatalytic formation of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ is consistent with the proposed mechanism; however, the integrated rate expression derived from eq 12 requires some finite initial concentration of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$. The aerobic re-

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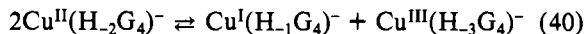
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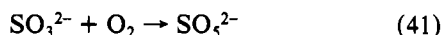
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action in Figure 5 began with only copper(II) tetraglycine. An initiation reaction is required in order to produce the initial 5×10^{-9} M $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ found from the intercept of the log plot in Figure 5. The initiation reaction proposed for the autocatalytic autoxidation of copper(II) tetraglycine is the disproportionation of $\text{Cu}^{\text{II}}(\text{H}_2\text{G}_4)^-$ as in eq 40. The equi-



librium constant was estimated to be 10^{-8} ($\mu = 1.0$ M (NaClO₄)).⁵ From the conditions used for the reaction illustrated in Figure 5, the equilibrium constant for the reaction in eq 40 predicts 1.4×10^{-8} M $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^-$ initially, certainly a reasonable initiation step. The reaction of sulfite and oxygen, eq 41, is also a reasonable initiation step. The SO_5^{2-} produced



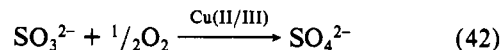
can then generate the initial $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ by oxidizing the $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$ reactant. The mechanism by which the reaction in eq 41 occurs is not entirely clear. The possibility of a multistep process in which trace-metal catalysis takes part has not been ruled out; however, this type of catalysis must be considerably slower than the copper peptide catalysis.

Conclusions

The anaerobic reduction of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ by sulfite proceeds stoichiometrically via two reversible one-electron-transfer steps.

Kinetic evidence strongly supports the sulfite radical anion as a product of the first electron transfer. An upper limit for the formal potential of the sulfite radical anion has been estimated from kinetic considerations to be +0.89 V. Hydrogen sulfite was found to be 30 times slower as a reductant than sulfite.

Oxygen, in the presence of added $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$, prompts a sulfite-induced oxidation to form $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$. The $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ autocatalytically accelerates the induced oxidation reaction. The switching redox nature of the sulfite-O₂ reaction and the observed oscillations in the concentration of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ are regulated by the relative rates at which $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$ and oxygen compete for the sulfite radical. Facile electron transfer makes the copper peptide complex a catalyst for the autoxidation of sulfite. The efficiency of the catalysis



is limited, however, by the rate at which sulfur-based oxidizing intermediates are lost by pathways other than those leading to the autocatalytic formation of $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$.

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Registry No. $\text{Cu}^{\text{III}}(\text{H}_3\text{G}_4)^-$, 57692-61-2; SO_3^{2-} , 14265-45-3; HSO_3^- , 15181-46-1; $\text{Cu}^{\text{II}}(\text{H}_3\text{G}_4)^{2-}$, 57603-18-6; O_2 , 7782-44-7.

Contribution from the Department of Chemistry, East Texas State University, Commerce, Texas 75428

Kinetic and Equilibrium Study of the Reaction of (*meso*-Tetrakis(*p*-sulfonatophenyl)porphyrinato)diaquocobaltate(III) with Pyridine in Aqueous Solution

KENNETH R. ASHLEY* and JOHAN G. LEIPOLDT¹

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The reaction of pyridine (py) with (*meso*-tetrakis(*p*-sulfonatophenyl)porphyrinato)diaquocobaltate(III) ($\text{Co}(\text{TPPS})(\text{H}_2\text{O})_2^{3-}$) has been investigated between pH 2 and 13 at $\mu = 1.00$ M (NaClO₄). Scheme I best depicts the reactions deduced to be important. The values of all of the parameters in Scheme I were determined and are reported. The k_1^{py} path is second order with $k_1^{\text{py}} = (9.56 \pm 0.30) \times 10^2 \text{ M}^{-1} \text{ s}^{-1}$ at 25 °C and the values of the activation parameters are $\Delta H^{\ddagger}_1 = 17.6 \pm 0.4$ kcal/mol and $\Delta S^{\ddagger}_1 = 14.4 \pm 1.3$ cal/(deg mol). These parameters imply dissociative (d) activation. The k_4^{py} path is second order with $k_4^{\text{py}} = (1.22 \pm 0.12) \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ at 25 °C, and the values of the activation parameters are $\Delta H^{\ddagger}_4 = 11.5 \pm 0.5$ kcal/mol and $\Delta S^{\ddagger}_4 = 6.4 \pm 1.6$ cal/(deg mol). The parameters imply d activation and the OH⁻ ligand has labilized the $\text{Co}(\text{TPPS})(\text{OH})(\text{H}_2\text{O})^+$ by a factor of 10^3 compared to $\text{Co}(\text{TPPS})(\text{H}_2\text{O})_2^{3-}$. The k_2^{py} path has a pseudo-first-order rate law with the pseudo-first-order rate constant $k_{\text{obs}} = (E[\text{py}] + FG)/(G + [\text{py}])$ at pH 13. This is interpreted to imply a dissociative (D) mechanism. The parameter E represents the first-order rate constant for formation of the 5-coordinate intermediate and has a value of $(1.57 \pm 0.13) \times 10^3 \text{ s}^{-1}$ at 25 °C. The values of ΔH^{\ddagger}_2 and ΔS^{\ddagger}_2 are 11.6 ± 3.1 kcal/mol and -5.1 ± 10.1 cal/(deg mol). The values of K_{a1} , K_{a2} , and K_{a1}^{py} at 25 °C are $(9.4 \pm 0.6) \times 10^{-8}$, $(1.7 \pm 0.2) \times 10^{-10}$, and $(5.6 \pm 0.2) \times 10^{-10}$ M, respectively. The values of K_1^{py} , K_2^{py} , K_4^{py} , K_5^{py} , and K_6^{py} at 25 °C are $(9.1 \pm 0.9) \times 10^8 \text{ M}^{-1}$, $(1.2 \pm 0.1) \times 10^5 \text{ M}^{-1}$, $(5.4 \pm 0.8) \times 10^6 \text{ M}^{-1}$, $(1.3 \pm 0.2) \times 10^2$, and 3.4 ± 0.7 , respectively. In summary, the kinetic and equilibrium properties of $\text{Co}(\text{TPPS})(\text{H}_2\text{O})_2^{3-}$ are very similar to those of (*meso*-tetrakis(4-*N*-methylpyridyl)-porphyrin)diaquocobalt(III) and (*meso*-tetrakis(4-carboxyphenyl)porphyrinato)diaquocobaltate(III). However there are some significant differences.

Introduction

The substitution reactions of cobalt(III) porphyrins have been of continuing interest.²⁻¹⁰ The most striking thing about

these reactions is the unusual lability of the compounds. The anation reactions were concluded to occur by a D or an I_d mechanism. Ashley and Au-Young have reported the results of the anation reactions of NCS⁻, I⁻, Br⁻, and Cl⁻ with (*meso*-tetrakis(*p*-sulfonatophenyl)porphyrinato)diaquocobaltate(III), ($\text{Co}(\text{TPPS})(\text{H}_2\text{O})_2^{3-}$).⁹ This paper reports the results of the investigation of the reaction of C₅H₅N(py), between pH 2 and 13.0 with $\text{Co}(\text{TPPS})(\text{H}_2\text{O})_2^{3-}$.

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