Oxyhalogen−Sulfur Chemistry: Oxidation of Taurine by Chlorite in Acidic Medium[1]

Cordelia R. Chinake*

Department of Chemistry, University of Natal, P.O. Box X01, Scottsville 3209, South Africa

Reuben H. Simoyi*,†

Department of Chemistry, West Virginia University, Morgantown, West Virginia 26506-6045

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The reaction between chlorite and the aminosulfonic acid, taurine, has been studied in neutral to acidic pH. The stoichiometry of the reaction was deduced as $3ClO_2^- + H_2NCH_2CH_2SO_3H + 3H^+ \rightarrow Cl(H)NCH_2CH_2SO_3H + 2ClO_2 + 2H_2O$. The formation of chlorotaurine is rapid and is followed by a slower accumulation of chlorine dioxide. The chlorotaurine disproportionates at low pH to give dichlorotaurine and taurine. There is no appreciable reaction between chlorine dioxide and any of the amine species in solution. The reaction is characterized by an induction period during which the reactive species HOCl and $H(OH)NCH_2CH_2SO_3H$ are formed. This is followed by the autocatalytic production of chlorotaurine and chlorine dioxide. The autocatalysis is mediated through the formation of the intermediate Cl_2O_2, which is typical of the reactions of chlorite. One notable result obtained in this study was that the C−S bond in taurine does not cleave even when subjected to a strong oxidizing agent, HOCl.

Introduction

Taurine, $H_2NCH_2CH_2SO_3H$, is a sulfur-containing amino acid found ubiquitously in living organisms and often in concentrations exceeding those of all the other amino acids.[2] It is a crystalline, colorless compound which is soluble in water, but not in ethanol or ether. At 25 °C it has a pK_a of 1.5 and a pK_b of 8.74.[3] Taurine can be obtained from natural sources such as ox bile and molluscs or by organic synthesis.[4] Its derivatives include 2-aminoethanesulfinic acid, 2-guanidoethanesulfonic acid, 2-hydroxyethanesulfonic acid, 2-ureidoethanesulfonic acid, and 2-aminoethanethiosulfonic acid.[5] Although taurine was first identified in 1827,[6] the question of its functional importance in plant and animal physiology is still not completely resolved.

Many studies have implicated taurine and its derivatives in several physiological roles such as (i) osmoregulation in marine invertebrates, (ii) energy storage in certain worms, (iii) inhibition of nerve impulses in invertebrate and vertebrate nerve tissue, (iv) elimination of cholesterol in vertebrates, and (v) regulation of excitability in various tissues.[7] Taurine and isethionic acid, $HO-CH_2CH_2-SO_3H$, have been shown to inhibit calcium-activated respiration in rat liver mitochondria.[8] Taurine requirements can be met through dietary supplements or through several biosynthetic pathways in some organisms.[2] There is an equilibrium between newly synthesized taurine and taurine leaving the cells or being metabolized in other pathways.[2]

Taurine is involved in the killing of foreign microorganisms by the immune system.[9] The most abundant cells in the human body's defensive mechanism are the granulocytes which contain a multilobed nucleus and cytoplasmic granules containing potent enzymes.[10] There are three types of granulocytes: neutrophils, eosinophils, and basophils.

Stimulated granulocytes produce oxidizing agents (e.g., H_2O_2) and secrete granular proteins, which contribute to their antimicrobial, cytotoxic, and cytolytic activities, into the extracellular medium.[9] Each group of cells contains a specific peroxidase which catalyzes the reactions of hydrogen peroxide with halogens. The enzyme myeloperoxidase, which is abundant in neutrophils, catalyzes the oxidation of Cl^- ions by H_2O_2 to yield HOCl:

$$H_2O_2 + Cl^- \xrightarrow{\text{myeloperoxidase/H}^+} HOCl + H_2O \qquad \text{(R1)}$$

HOCl is capable of destroying a variety of microoganisms and mammalian cell targets.[11] It is also believed to be involved in the inflammatory response.[11] HOCl is, however, a short-lived oxidant. It has been demonstrated that HOCl generates longer-lived oxidizing species through its reaction with nitrogen compounds to yield chlorinated nitrogen derivatives with a N−Cl bond.[12] The most important of such compounds is the β-amino acid taurine:

$$HOCl + \underset{\text{taurine (Tau)}}{H_2NCH_2CH_2SO_3H} \rightarrow \underset{\substack{\text{Taurine chloramine}\\ \text{(TauNHCl)}}}{ClHNCH_2CH_2SO_3H} + H_2O \qquad \text{(R2)}$$

A second chlorine atom can be added to give dichlorotaurine ($TauNCl_2$), which is a stronger lytic agent.[12]

The chloramine derivatives can thus continue to moderate the neutrophil toxicity long after HOCl has been depleted. The N−Cl derivatives contain oxidized chlorine (Cl^+).[12] The toxicity of a particular N−Cl is determined by its overall structure and not just the N−Cl bond. The reaction of taurine with HOCl prevents the attack of cellular components by HOCl.[12] Erythrocytes take up and detoxify TauNHCl and $TauNCl_2$.[12] However, at very high concentrations of TauNHCl and $TauNCl_2$, they both attack the cells by oxidizing heme and protein sulfhydryl groups, thus inhibiting energy metabolism.[12]

Recent work by Folkes et al. has looked at the myeloperoxidase-catalyzed reactions of HOCl with glutathione, ascorbate, and taurine.[13] Their experimental data on the HOCl−taurine system confirm that the reaction follows an electrophilic rather

† Author to whom correspondence should be addressed.

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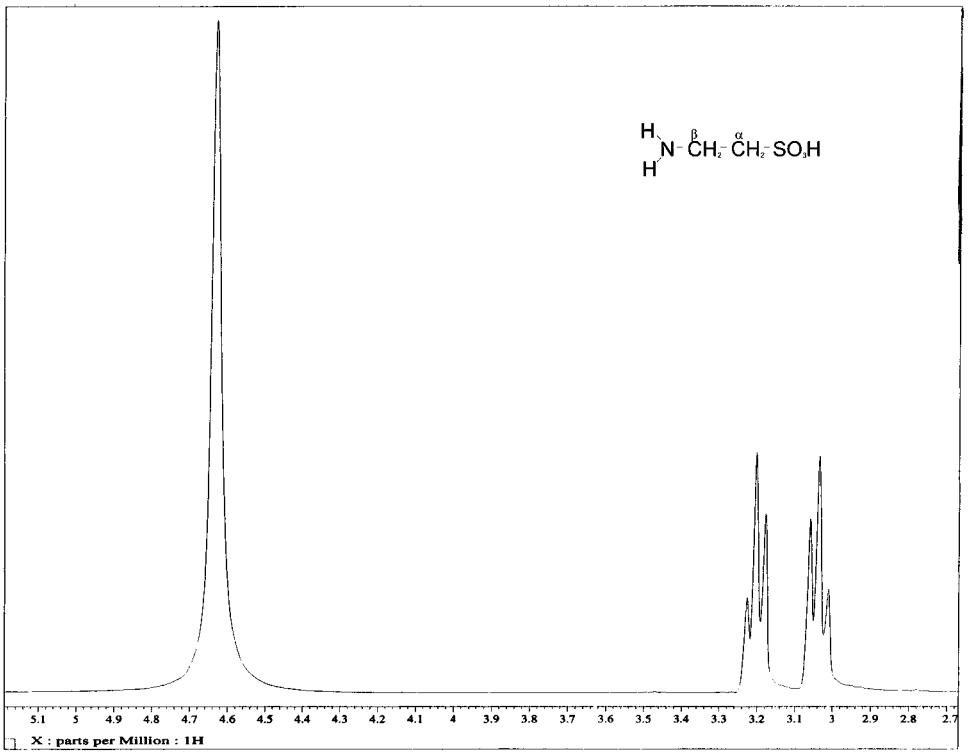


Figure 1. (a) NMR spectrum of taurine in D_2O showing the two triplets from the α- and β- sets of methylene protons. The sharp peak at $\delta = 4.67$ ppm is from the solvent. (b) Structure of taurine showing the α-, β-, and γ-protons. Due to rapid exchange, γ-protons are not observed.

than a free radical mechanism. ^{13}C-NMR studies of the HOCl-taurine reaction have shown that N-chlorotaurine is formed and is stable at pH 7.0.[14] The ^{13}C-NMR of [^{13}C]taurine (28% of [1-^{13}C]taurine + 72% of [2-^{13}C]taurine) shows two methylene singlets at 49.9 and 37.9 ppm.[14] These are assigned to HO_3SCH_2- and $-CH_2NH_2$, respectively. When ^{13}C-labeled taurine and HOCl are mixed, two new peaks are obtained at 53.1 ($-CH_2NHCl$) and 51.3 ppm (HO_3SCH_2-).[14]

Although the presence of TauNHCl and $TauNCl_2$ in intact cells has been demonstrated, their chemical characterisitics and complete functions are not fully understood. A full understanding of the reactivity of taurine can help in our understanding of its unique physiological role. We present in this paper a pure reaction kinetics and mechanism study of the reaction of taurine with chlorite because there is a need to understand the basic chemical reaction kinetics of taurine and chlorotaurine. There are several studies which focus on the physiological role of taurine, but without a firm grasp of its in vitro reactivity, it is impossible to decipher the mechanism by which it acts in vivo.

Experimental Section

Materials. The following analytical grade chemicals were used without further purification: sodium perchlorate, perchloric acid (72%), potassium iodide, sodium thiosulfate (Fisher), D_2O, and taurine (Aldrich). Technical grade sodium chlorite (Aldrich, 81%) was recrystallized from an ethanol/water mixture. Recrystallized solutions of chlorite were standardized iodometrically by adding excess acidified iodide and titrating the liberated iodine against standard sodium thiosulfate.[16] Chlorine dioxide was prepared by oxidizing potassium chlorate in a sulfuric acid/oxalic acid mixture and then stored in perchloric acid at 4 °C.[17] It was standardized spectrophotometrically by using its molar absorptivity coefficient of 1265 M^{-1} cm^{-1} at 360 nm.[18]

Methods. The stoichiometric determinations were carried out by mixing various ratios of chlorite and taurine and leaving them overnight in stoppered volumetric flasks. The amount of chlorine dioxide formed was measured spectrophotometrically. ^{1}H-NMR spectra of taurine and chlorotaurine were obtained on a JEOL GX 270 spectrometer using D_2O as solvent and internal standard. Chlorotaurine was quantified by its ability to oxidize iodide to iodine.[19] Kinetics experiments were carried out at 25.0 ± 0.5 °C and an ionic strength of 0.5 M ($NaClO_4$). The reactions were followed spectrophotometrically by using the absorbance of ClO_2 at 360 nm. The first stage of the reaction which required stopped-flow techniques was followed on a Hi-Tech Scientific stopped-flow spectrophotometer. The reaction was also monitored by following the formation of chlorotaurine at 250 nm.[19] A conventional Perkin-Elmer Lambda 2S UV−vis spectrophotometer interfaced to a DEC 486/33 DX computer was used for slower experiments.

Results

Stoichiometry. The stoichiometry of the reaction in perchloric acid and excess chlorite was determined to be

$$3ClO_2^- + 3H^+ + H_2NCH_2CH_2SO_3H \rightarrow Cl(H)NCH_2CH_2SO_3H + 2H_2O + 2ClO_2 \quad (R3)$$

Qualitative tests for Cl^- and SO_4^{2-} were negative.[20] A test for glycine, NH_2CH_2COOH, using Sorensen's test for amino acids was negative, indicating that the C−S bond was not cleaved.[21] Identification of chlorotaurine was by UV−vis and NMR spectroscopy.[15,19] The NMR spectrum of taurine gave two triplets centered at 3.05 and 3.22 ppm at pH 4.5 (Figure 1a). The triplet at $\delta = 3.05$ ppm is from the α-protons while the triplet at 3.22 ppm is from the β-protons. Due to rapid exchange with the solvent, the γ-protons (on nitrogen) are not observed. The labeled structure of taurine is shown in the inset of Figure 1a.

The product's NMR spectrum was obtained after an incubation period of up to 2 days. Figure 2a shows the spectrum of the product solution. This spectrum shows three peaks: two

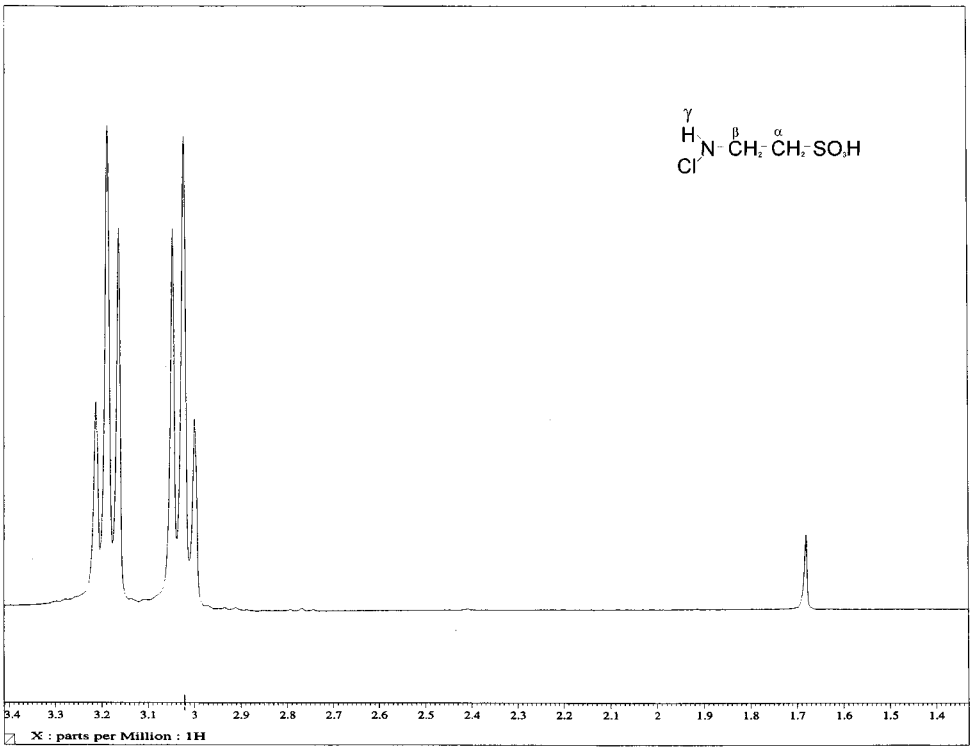


Figure 2. (a) NMR spectrum of the reaction products of the ClO_2^-−taurine reaction in excess ClO_2^-. The spectrum was taken after a 24 h incubation period. The triplets from the two methylene peaks are unchanged. The singlet peak at $\delta = 1.68$ ppm is from the N-bonded proton. (b) Structure of chlorotaurine derived from the NMR spectrum in Figure 2a.

triplets and a singlet in the ratio 2(t):2(t):1(s). There is a very slight shift in the two triplets from the original taurine spectrum. The NMR spectrum in Figure 2a confirms the structure of chlorotaurine as that shown the inset of in Figure 2a. The single γ-proton is the one that is observed at $\delta = 1.68$ ppm. This singlet disappeared in highly acidic solutions. The spectral data verify the results obtained by qualitative analysis which gave negative tests for amino acids, chloride, and sulfate. Taurine is thus a very special molecule in which the C−S bond is not easily cleaved. Its reactivity, which is centered on the nitrogen atom, gives it its special physiological importance.[13]

On prolonged standing and in acidic environments, TauNHCl disproportionated to give taurine and dichlorotaurine:[14]

$$2Cl(H)NCH_2CH_2SO_3H \rightarrow H_2NCH_2CH_2SO_3H + Cl_2NCH_2CH_2SO_3H \quad (R4)$$

The final product of the oxidation of taurine is TauNHCl. The final absorbance of ClO_2 at 360 nm gives the value expected from the stoichiometric equation, reaction R3.

TauNHCl has a maximum absorbance at 250 nm with a molar absorptivity of 398 M^{-1} cm^{-1}.[19] By scanning the spectrum at regular intervals, between 200 and 500 nm, activity was observed at 250 and 360 nm (Figure 3). The peak at 360 nm (chlorine dioxide) grew steadily with time. The absorbance peak at 250 nm (TauNHCl) rose rapidly in the initial stages and was then slowly depleted, but not to the background value. This peak could not decay to zero because there is a small contribution to the absorbance at 250 nm from ClO_2. Within the pH range of 4−7, TauNHCl was quantitatively formed according to the stoichiometry of reaction R3. Below pH 4.00 there was a mixture of both chlorotaurine and dichlorotaurine. The concentration of $TauNCl_2$ increased in higher acid concentration. The dichloroamine when formed absorbs at 300 nm.

Reaction Dynamics. In acidic environments the reaction of chlorite and taurine shows three stages. The first is a very short induction period during which neither chlorotaurine nor chlorine dioxide is formed (see Figure 4a). The induction period is about 0.05 s. TauNHCl is formed just after this induction period. The second is a rapid formation of chlorine dioxide and TauNHCl, and the third is a slower accumulation of chlorine dioxide and a very slow depletion of TauNHCl (at low pH and excess ClO_2^- conditions). Further increase in the absorbance of ClO_2 (after depletion of taurine) is due to pure oxyhalogen

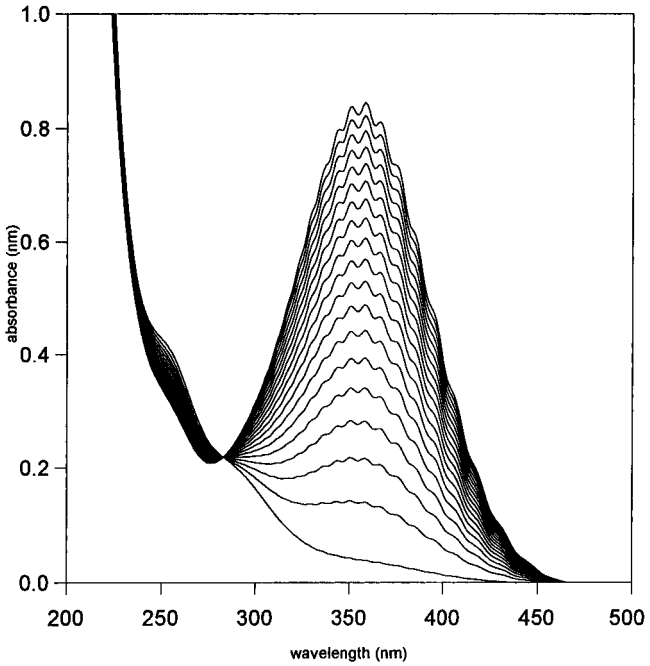


Figure 3. Spectral scans at 60 s intervals of the ClO_2^-−taurine reaction. Activity is observed only at $\lambda = 250$ and 360 nm. Absorbance at 250 nm shows a rapid increase followed by a slow decrease while a monotonic increase in absorbance is observed at 360 nm (ClO_2): $[ClO_2^-]_o = 4.0 \times 10^{-3}$ M, $[\text{taurine}]_o = 1.0 \times 10^{-3}$ M, $[H^+]_o = 0.025$ M.

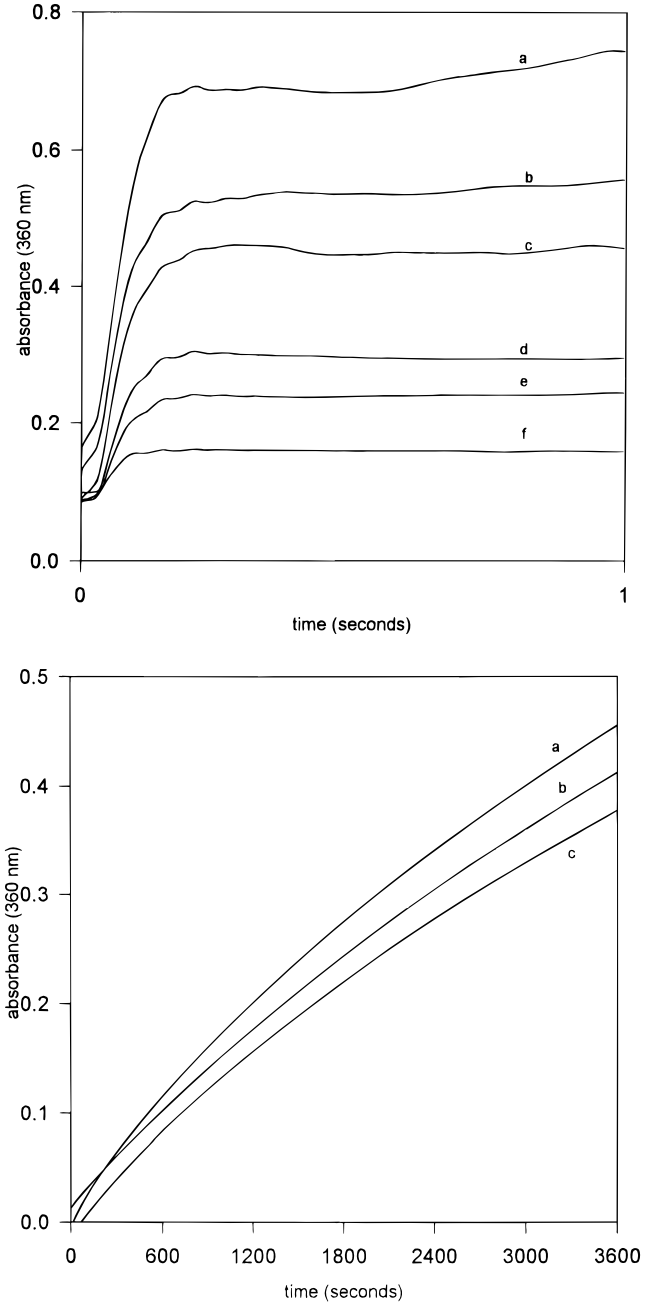


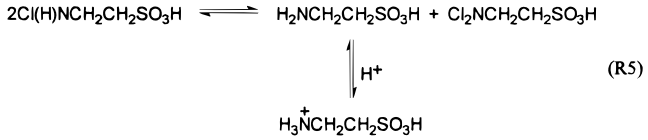
Figure 4. (a) Effect of chlorite on the initial absorbance of chlorine dioxide at 360 nm in conditions of excess taurine. A slower increase in absorbance follows this initial rapid increase: $[\text{taurine}]_o = 0.04$ M, $[H^+]_o = 1.0 \times 10^{-5}$ M, $[ClO_2^-]_o$: (a) 0.001, (b) 0.0009, (c) 0.0008, (d) 0.0007, (e) 0.0006, (f) 0.0005 M. (b) Effect of the addition of H^+ on the formation of chlorine dioxide over a longer time span.: $[ClO_2^-]_o = 0.004$ M, $[\text{taurine}]_o = 0.001$ M, $[H^+]_o =$ (a) 0.04, (b) 0.03, (c) 0.02 M.

chemistry involving the oxychlorine species only. Reaction mixtures of taurine and ClO_2 did not show any change in ClO_2 absorbance even on prolonged standing, indicating that there is no appreciable reaction between ClO_2 and taurine.

Data at 360 nm. The reaction was monitored at both 250 nm (TauNHCl) and 360 nm (ClO_2). Figure 4a shows the effect of chlorite on the first two stages of the reaction at 360 nm and in excess chlorite. This shows the very short induction period followed by the rapid formation of ClO_2. The start of the slower ClO_2 formation can be detected about 0.5 s into the reaction in traces a and b. Higher $[ClO_2^-]_o$ gave higher ClO_2 concentrations as predicted by the stoichiometry of reaction R3. This initial rapid formation of ClO_2 is more pronounced in low acid conditions. Figure 4b shows a set of absorbance traces at high acid concentrations. There is no initial rapid accumulation of ClO_2 under these conditions because of the high acid concentration, but rather ClO_2 continues to be formed slowly over a long period of time.

Data at 250 nm. Figure 5a shows the effect of acid on the formation of chlorotaurine at 250 nm. The initial rapid formation of TauNHCl can be observed as well as the subsequent very slow consumption of TauNHCl (trace a). As the acid is increased, formation of TauNHCl is suppressed. Figure 5b shows the effect of taurine on the formation of chlorotaurine at 250 nm, but in this case no acid has been added and taurine is in overwhelming excess over chlorite. Here, the formation of TauNHCl is nearly exponential. A test for pseudo-first-order kinetics failed because both $[H^+]$ and $[ClO_2^-]$ were reaction variables. Figure 5c shows the slow depletion of TauNHCl under the conditions used in Figure 3. The change in absorbance is within a very small range (0.41 > absorbance > 0.32) due to contribution from ClO_2 at 250 nm. Determining the contribution to the absorbance solely from TauNHCl is complicated by the lack of a mass balance equation between ClO_2 and TauNHCl. An approximation can be made by determining the absorbance at t_∞ and equating it solely to ClO_2 absorbance. Assuming second-order kinetics (reaction R4) and no interference from the acid, a rate constant for the depletion of TauNHCl was evaluated as 0.395 ± 0.05 M^{-1} s^{-1}.

The rate of depletion of TauNHCl gave complex dependencies on the initial concentrations of taurine, chlorite and acid. The initial rate of consumption of TauNHCl increased with initial taurine concentration (see Figure 6a). A log−log plot of initial rate (of consumption of TauNHCl) vs $[ClO_2^-]_o$ gave a straight line of slope slightly greater than 1 (Figure 6b). Another log−log plot of initial rate vs acid concentration gave a straight line of slope 0.33 ($R^2 = 0.99$) (see Figure 6c). The mechanism of such a complex acid catalysis can best be understood from the following reaction network:



(R5)

The depletion of taurine by protonation pushes the equilibrium for reaction R4 to the right, thus facilitating disproportionation.

Mechanism

The data in Figure 4a show that there is a rapid formation of chlorine dioxide after a short induction period. On prolonged standing and in mildly acidic conditions, ClO_2^- decomposes to give ClO_2 according to the following stoichiometry:[22]

$$5ClO_2^- + 4H^+ \rightarrow 4ClO_2(aq) + Cl^- + 2H_2O \quad \text{(R6)}$$

It has been demonstrated that Cl^-, which is always present as an impurity in ClO_2^- solutions,[23] is directly responsible for the decomposition of ClO_2^- via HOCl at low pH conditions:

$$ClO_2^- + Cl^- + 2H^+ \rightarrow 2HOCl \quad \text{(R7)}$$

Reaction R7 is, however, considered to be quite slow and would not be effective on the time scale of Figure 4a.

Thus, it is the interaction of ClO_2^- and taurine in the initial stages which produces the reactive intermediate HOCl:

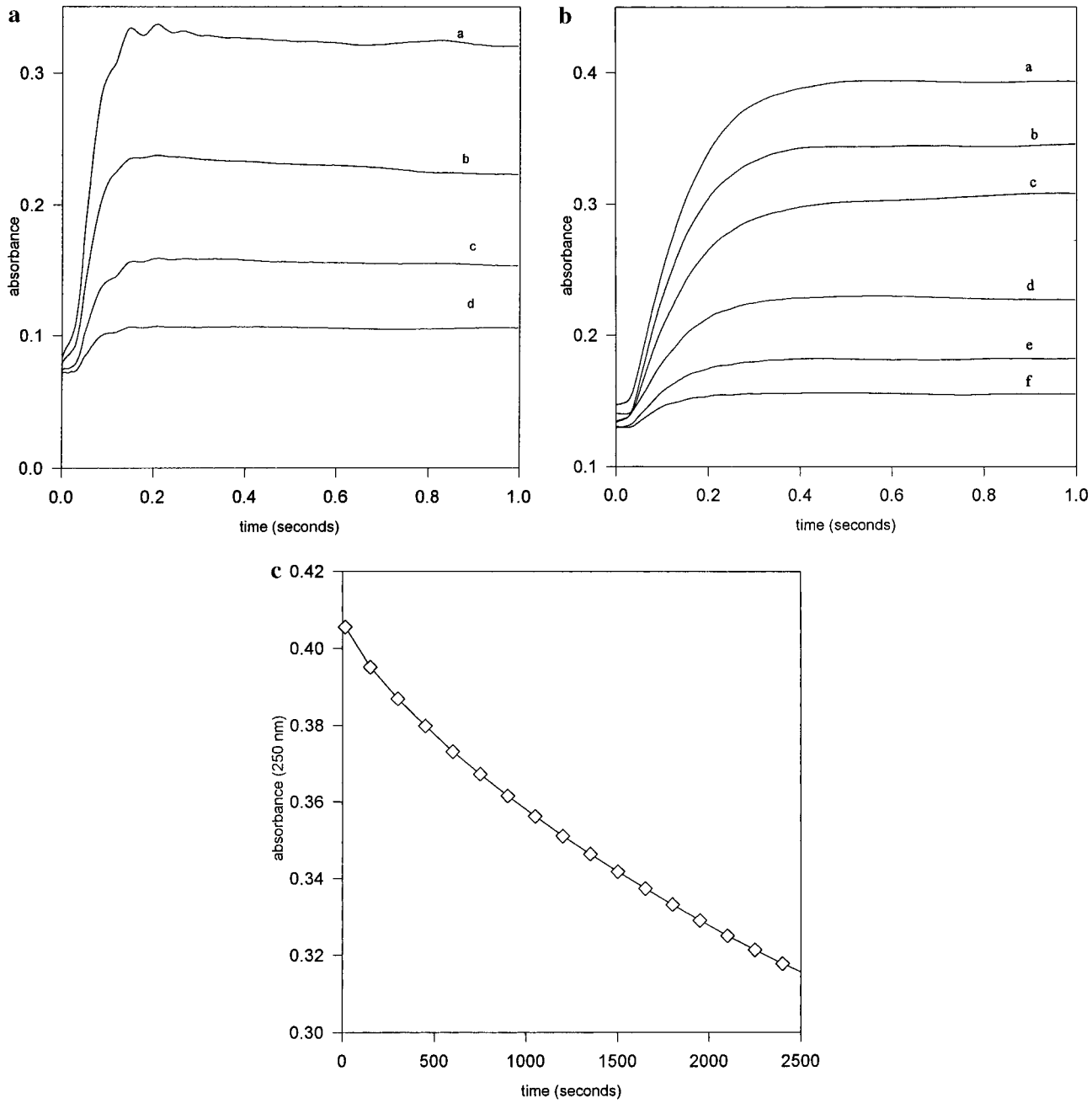


Figure 5. (a) Effect of acid on the absorbance activity at 250 nm. Major contributions to absorbance at 250 nm are from chlorotaurine. Acid inhibits the rapid formation of chlorotaurine: $[ClO_2^-]_o = 0.005$ M, $[taurine]_o = 0.04$ M, $[H^+]_o =$ (a) 4.0×10^{-6}, (b) 6.0×10^{-6}, (c) 8.0×10^{-6}, (d) 10.0×10^{-6} M. (b) Effect of $[taurine]_o$ on the rapid formation of chlorotaurine within the first second of the reaction. The absorbance started decreasing after about 10 s into the reaction. No acid was added: $[ClO_2^-]_o = 0.0005$ M, $[taurine]_o =$ (a) 0.060, (b) 0.050, (c) 0.040, (d) 0.030, (e) 0.020, (f) 0.010 M. (c) Depletion of chlorotaurine at 250 nm after the initial rapid increase shown in Figure 3: $[ClO_2^-]_o = 4.0 \times 10^{-3}$ M, $[taurine]_o = 1.0 \times 10^{-3}$ M, $[H^+]_o = 0.025$ M.

$$ClO_2^- + H_2NCH_2CH_2SO_3H + H^+ \rightarrow H(OH)NCH_2CH_2SO_3H + HOCl \quad (R8)$$

If reaction R8 is rate-determining, then the rate of reaction will be

$$-d[ClO_2^-]/dt = k_{R8}[ClO_2^-][H_2NCH_2CH_2SO_3H][H^+] \quad (1)$$

HOCl produced in reaction R8 will rapidly oxidize ClO_2^- to ClO_2:[22]

$$2ClO_2^- + HOCl + H^+ \rightarrow 2ClO_2 + Cl^- + H_2O \quad (R9)$$

The intermediate RNHOH[24] (where R is $-CH_2CH_2SO_3H$) is then converted to the more stable chlorotaurine:

$$RNHOH + Cl^- + H^+ \rightarrow RNHCl + H_2O \quad (R10)$$

Addition of reactions R8, R9, and R10 gives the observed stoichiometry of the following reaction:

$$3ClO_2^- + H_2NCH_2CH_2SO_3H + 3H^+ \rightarrow Cl(H)NCH_2CH_2SO_3H + 2ClO_2(aq) + 2H_2O \quad (R3)$$

Reactions R9 and R10 are fast and are not rate-determining.[23] Reaction R8 is a composite of three reactions: two protonation reactions (reactions R11 and R12) and an oxidation reaction (reaction R13):

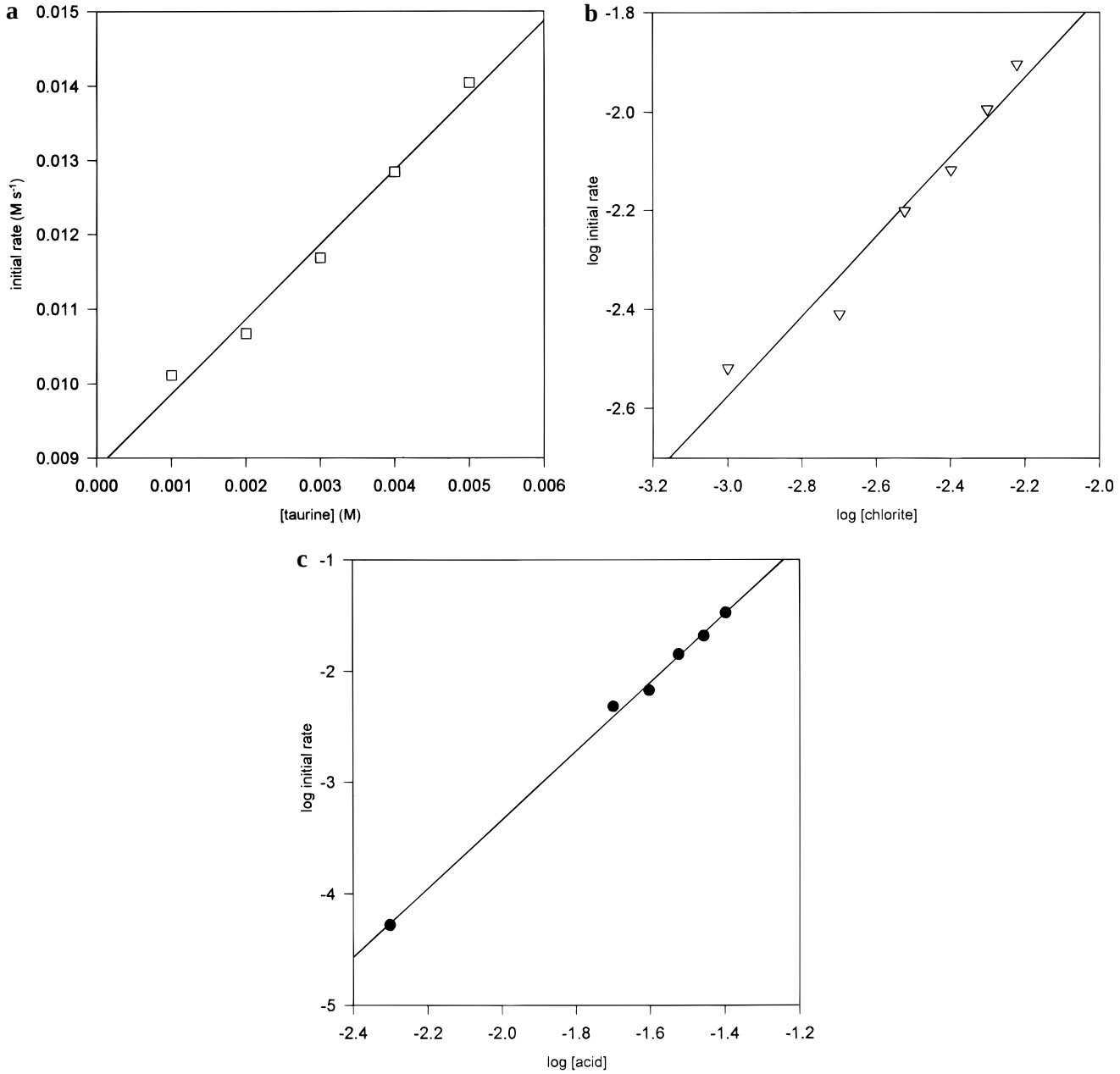


Figure 6. (a) Effect of taurine on the depletion (disproportionation) of chlorotaurine at $\lambda = 250$ nm. Higher initial taurine concentrations gave higher transient chlorotaurine concentrations: $[ClO_2^-]_o = 4.0 \times 10^{-3}$ M, $[H^+]_o = 0.02$ M. (b) A log−log plot of the initial rate of depletion of chlorotaurine vs the initial chlorite concentration: $[\text{taurine}]_o = 1.0 \times 10^{-3}$ M, $[H^+]_o = 0.02$ M. (c) A log−log plot of the initial rate of depletion of chlorotaurine vs the acid concentration: $[ClO_2^-]_o = 4.0 \times 10^{-3}$ M, $[\text{taurine}]_o = 1.0 \times 10^{-3}$ M.

$$H_2NCH_2CH_2SO_3H + H^+ \rightleftharpoons H_3\overset{+}{N}CH_2CH_2SO_3H \qquad K_{a_1} \qquad \text{(R11)}$$

$$H^+ + ClO_2^- \rightleftharpoons HClO_2 \qquad K_{a2} \qquad \text{(R12)}$$

followed by:

$$ClO_2^- + H_3\overset{+}{N}CH_2CH_2SO_3H \rightarrow H(OH)NCH_2CH_2SO_3H + HOCl \quad \text{(R13)}$$

HOCl then rapidly reacts with taurine to form chlorotaurine:

$$HOCl + H_2NCH_2CH_2SO_3H \rightarrow Cl(H)NCH_2CH_2SO_3H + H_2O \quad \text{(R2)}$$

Protolytic reaction R11 will dominate over reaction R12 due to the basic moiety on taurine and its pK_b. Reaction R12 will be significant below a pH of 2.5, which is the pK_a of chlorous acid.[23]

The rate of reaction, from rate-determining step R13, becomes

$$-d[ClO_2^-]/dt = k_{R13}K_{a1}[ClO_2^-][H_2NCH_2CH_2SO_3H][H^+] \qquad (2)$$

which is the same as eq 1.

The monochlorotaurine does not undergo any further oxidation except disproportionation as in reaction R4.[14] The establishment of reaction R8 as the rate-determining step leads to the deduction that rates of formation of monochlorotaurine and chlorine dioxide are controlled by eq 1.

$$d[RNHCl]/dt = {}^1/_2 d[ClO_2]/dt = k'[ClO_2^-][H_2NCH_2CH_2SO_3H][H^+] \qquad (3)$$

where $k' = k_{R13}K_{a1}$.

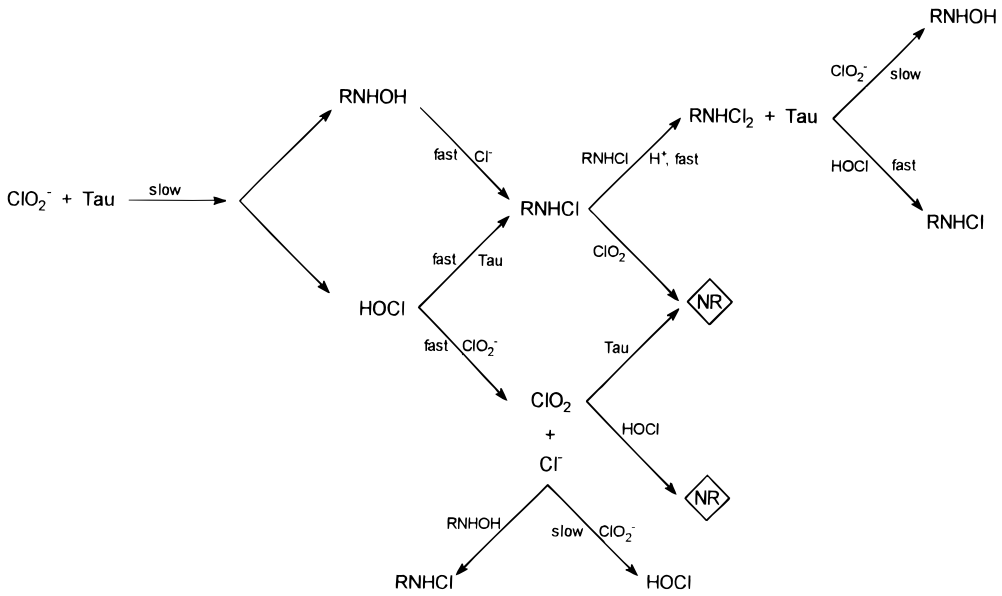


Figure 7. Schematic diagram showing the various reactions involved in the chlorite−taurine reaction. ClO_2(aq) acts as a Cl(IV) sink as it undergoes no further reaction with any other species in solution except Cl^-. Tau represents taurine, RNHCl is taurine monochloramine, $RNHCl_2$ is taurine dichloramine, and, RNHOH is the hydroxylamine formed from taurine while NR stands for no reaction.

Role of Acid. Acid has a complex role in the oxidation of taurine. The protonation equilibria of reactions R11 and R12 have opposite effects on the rate of reaction. With reaction R13 as the rate-determining step, it can be assumed that protonation of taurine will enhance the reaction. The total Cl(III) species $[Cl(III)]_T$ will be given by

$$[Cl(III)]_T = [HClO_2] + [ClO_2^-] \quad (4a)$$

and

$$[ClO_2^-] = [Cl(III)]_T/\{1 + K_{a2}[H^+]\} \quad (4b)$$

The rate of reaction now becomes:

$$\frac{d[RNHCl]}{dt} = \frac{k_{R13}K_{a1}[Cl(III)]_T}{1 + K_{a2}[H^+]}[H_2NCH_2CH_2SO_3H][H^+] \quad (5)$$

At low acid, where $K_{a2}[H^+] \ll 1$, eq 5 simplifies to eq 1. At high acid concentrations, eq 5 predicts that acid should have a reduced effect on the rate of reaction. Experimental results have shown that there is indeed a reduced but not complete loss of acid effect on the reaction rate as the acid concentration increases. This is also due to the fact that the reaction

$$HClO_2 + H_3\overset{+}{N}CH_2CH_2SO_3H \rightarrow H(OH)NCH_2CH_2SO_3H + HOCl + H^+ \quad (R14)$$

is not completely inert, but merely much slower than reaction R12.

Formation of N-chlorotaurine. Chlorotaurine is formed quite rapidly at the beginning of the reaction (see data at $\lambda = 250$ nm in Figures 5a,b). Its consumption, however, is relatively slow (Figure 5c) and is controlled by the pH of the solution. Experimental results show that this regeneration of taurine is also affected by the $[ClO_2^-]$/[Taurine] ratio. Formation of chlorotaurine is quantitative (with no subsequent formation of dichorotaurine) in low ratios (i.e., excess taurine over chlorite). In high ratios and low pH, taurine, mono-, and dichlorotaurine coexist.

TABLE 1: Mechanism of the Reaction between Taurine and Chlorite in Acidic Medium

M1	$ClO_2^- + HOCl + H^+ \rightleftharpoons Cl_2O_2 + H_2O$
M2	$HOCl + Cl^- + H^+ \rightleftharpoons Cl_2 + H_2O$
M3	$ClO_2^- + Cl^- + 2H^+ \rightleftharpoons 2HOCl$
M4	$Cl_2O_2 + ClO_2^- \rightleftharpoons 2ClO_2 + Cl^-$
M5	$ClO_2^- + H^+ \rightleftharpoons HClO_2$
M6	$H_2NCH_2CH_2SO_3H + H^+ \rightleftharpoons [H_3NCH_2CH_2SO_3H]^+$
M7	$ClO_2^- + [H_3NCH_2CH_2SO_3H]^+ \rightarrow H(OH)NCH_2CH_2SO_3H + HOCl$
M8	$H(OH)NCH_2CH_2SO_3H + Cl^- \rightarrow Cl(H)NCH_2CH_2SO_3H + OH^-$
M9	$H_2NCH_2CH_2SO_3H + HOCl \rightarrow Cl(H)NCH_2CH_2SO_3H + H_2O$
M10	$2ClHNCH_2CH_2SO_3H \rightarrow Cl_2NCH_2CH_2SO_3H + H_2NCH_2CH_2SO_3H$

Global Reaction Mechanism. The full reaction mechanism is shown in the schematic sketch in Figure 7. Reaction starts from left to right in the sketch. The initiation reaction is reaction R8, which is at the extreme left of the sketch. The global reaction characteristics are determined by the reactivities of the intermediate products of reaction R8, RNHOH and HOCl. A very fast reaction ensues which forms oxidatively inert ClO_2 from the reaction of HOCl with excess ClO_2^-. This explains the very rapid ClO_2 formation (see Figure 4a) after a very short induction period. The HOCl concurrently also reacts with taurine to form chlorotaurine, while Cl^- formed from reaction R9 reacts with the intermediate hydroxylamine RNHOH to also give the more stable chlorotaurine. The stoichiometry of the overall reaction is satisfied by the first two sets of reactions shown in the schematic diagram. The third set of reactions shows the disproportionation of chlorotaurine as well as the relatively slow oxyhalogen reaction, reaction R7. The third set shows that ClO_2 is a sink for oxyhalogen species as no appreciable reactions were observed between ClO_2 and taurine and HOCl and RNHCl. The regeneration of taurine from chlorotaurine can trigger reaction R8 and the whole process repeats itself.

The full set of reactions that controls this reaction is shown in Table 1. The first five reactions are pure oxyhalogen reactions, and the last five reactions involve reactions of the amino acid.

Nonlinearities. ClO_2^- oxidations have a well-established pathway which generates nonlinearities in the form of autocatalysis and clock mechanisms.[25] The production of ClO_2 and

chlorotaurine show nonlinearities in the form of an induction period followed by their rapid production.

The induction period can be explained as the period taken by the reaction system to generate the reactive species HOCl and RNHOH. The autocatalytic nature of the formation of ClO_2 and chlorotaurine can easily be explained by the formation of the intermediate species Cl_2O_2 which leads to HOCl autocatalysis:[26]

$$ClO_2^- + HOCl + H^+ \rightleftharpoons Cl_2O_2 + H_2O \qquad (R15)$$

$$Cl_2O_2 + 2e^- + H^+ \rightarrow 2HOCl \qquad (R16)$$

The reductant in reaction R16 can be taurine, chlorotaurine, or ClO_2^-.

Conclusion

The oxidation of taurine makes interesting comparison with the oxidation of thiocarbonyls which we have previously studied.[27] In thiourea, for example, the sulfur in the C═S bond is successively oxidized to the sulfonic acid $-C-SO_3H$, with the final step being the cleavage of the C−S bond to give sulfate, H^+, and large heat evolution. This step has been shown to be slow and was expected in the reactions of taurine. The work reported in this paper establishes that the C−S bond in taurine is not readily cleaved. Instead, all the chemical reactivity is at the nitrogen center. The sulfonc acid moeity has been implicated in cation transport in tissues.[8,15] TauNHCl is known to protect tissues against oxidative toxicity.[12] Thus, a study of the fundamental reaction kinetics such as undertaken here can only contribute to a better understanding of the biological mode of action of sulfur amino acids.

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References and Notes

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