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Oxyhalogen–sulfur chemistry: kinetics and mechanism of oxidation of formamidine disulfide by acidic bromate†

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Received 13th May 2003, Accepted 10th July 2003
First published as an Advance Article on the web 5th September 2003

The kinetics and mechanism of the oxidation of formamidine disulfide, FDS, a dimer and major metabolite of thiourea, by bromate have been studied in acidic media. In excess bromate conditions the reaction displays an induction period before formation of bromine. The stoichiometry of the reaction is: $7BrO_3^- + 3[(H_2N(HN=)CS-]_2 + 9H_2O \rightarrow 6NH_2CONH_2 + 6SO_4^{2-} + 7Br^- + 12H^+$ (A). In excess oxidant conditions, however, the bromide formed in reaction A reacts with bromate to give bromine and a final stoichiometry of: $14BrO_3^- + 5[(H_2N(HN=)CS-]_2 + 8H_2O \rightarrow 10NH_2CONH_2 + 10SO_4^{2-} + 7Br_2 + 6H^+$ (B). The direct reaction of bromine and FDS was also studied and its stoichiometry is: $7Br_2 + [(H_2N(HN=)CS-]_2 + 10H_2O \rightarrow 2NH_2CONH_2 + 2SO_4^{2-} + 14Br^- + 18H^+$ (C). The overall rate of reaction A, as measured by the rate of consumption of FDS, is second order in acid concentrations, indicating the dominance of oxyhalogen kinetics which control the formation of the reactive species $HBrO_2$ and HOBr. The reaction proceeds through an initial cleavage of the S–S bond to give the unstable sulfenic acids which are then rapidly oxidized through the sulfinic and sulfonic acids to give sulfate. The formation of bromine coincides with formation of sulfate because the cleavage of the C–S bond to give sulfate occurs at the sulfonic acid stage only. The mechanism derived is the same as that derived for the bromate–thiourea reaction, suggesting that FDS is an intermediate in the oxidation of thiourea to its oxo-acids as well as to sulfate.

Introduction

Invariably, the oxidation of thiourea gives exotic dynamics.[2] Nearly all reactions of thiourea with an oxyhalogen species give nonlinear kinetics characterized by clock reaction characteristics, autocatalysis and/or autoinhibition.[3] The oxidation of thiourea by acidic bromate, for example, gives oscillatory behavior in a continuously-stirred tank reactor, CSTR.[4] The reaction of thiourea with acidic iodate is oligooscillatory, and even the simple iodine–thiourea reaction is extremely complex and autoinhibitory. The chlorite–thiourea reaction has displayed the most varied complex dynamical behavior that can only be rivaled by the venerable Belousov–Zhabotinski reaction.[5] The chlorite–thiourea reaction is autocatalytic and bistable in batch, oscillatory in a CSTR and is the only chemical system to show homoclinic chaos.[6] In unstirred solutions it generates lateral instabilities that are derived from convective instabilities.[7]

Efforts at systematically designing chemical oscillators[8] were greatly enhanced by the introduction of two-component oscillators that involved oxyhalogen–sulfur systems.[9] While the relevant chemistry of oxyhalogens is well known, not much is known with respect to the sulfur-based set of reactions. It has been difficult to evaluate the genesis of nonlinearities in aqueous sulfur chemistry. We recently embarked on a series of studies aimed at evaluating the kinetics and mechanism of oxidation of sulfur compounds.[2] The major aim of this series of studies was to evaluate the mechanisms of the several systematically designed two-component oxyhalogen–sulfur oscillators. The rate of discovery of nonlinear dynamical behavior in chemistry based on sulfur chemistry has outgrown the basic knowledge of the general dynamical behavior of sulfur compounds. For example, our inability to derive the mechanism of the bromate–thiourea reaction rendered the derivation of the oscillatory mechanism for the bromate–thiourea reaction impossible.[4]

Previous studies on the oxidation of thiourea had postulated a series of 2-electron steps that involved the successive addition of oxygen to the sulfur center followed by the cleavage of the C–S bond after the formation of the aminoiminomethanesulfonic acid.[10] The oxidation of the sulfur center to sulfate involves an oxidation change of the sulfur center from −2 to +6. Many intermediates would occur over this large oxidation state change. One way of proving the veracity of a proposed mechanistic pathway is to utilize postulated intermediates in the mechanism as the starting materials. If the mechanism is correct, then the reactivity of the intermediate should be consistent with its role in the whole mechanism. In the bromate–thiourea reaction, the first postulated intermediate used was the stable and isolable aminoiminomethanesulfinic acid, AIMSA.[10] Kinetics experiments and subsequent simulations proved that it could be an intermediate in the complete oxidation of thiourea by excess oxidant.

Many studies have pointed out that the propensity of sulfur to polymerize and form extensive S–S bonds constitutes an in-built nonlinearity that should be factored into any meaningful evaluation of oxyhalogen–sulfur systems. While several polysulfides exist, for the bulkier molecules, dimerization is the maximum degree of polymerization that can be achieved. Several studies of the oxidation of thiocarbamides had concluded that the formation of the dimeric species can be quantitative, and that this could be a possible pathway towards the metabolic oxidation of most biologically active thiocarbamides.[11] This assertion was based on the fact that the first step of the S-oxygenation of an organosulfur compound

† Part 6 of 10 in the series to honor the memory of Dr. Cordelia R. Chinake (1965–1998). For Part 5 see ref. 1.

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(*e.g.* thiourea) will yield a highly unstable sulfenic acid:[12]

$$X_2(aq) + (H_2N)_2C{=}S + H_2O \rightarrow H_2N(=NH)CSOH + 2H^+ + 2X^- \quad (R1)$$

In this case X_2 could be a halogen or any 2-electron oxidant. The sulfenic acid being highly unstable, should, in the presence of further oxidant, be rapidly oxidized to the sulfinic acid:

$$X_2(aq) + H_2N(=NH)CSOH + H_2O \rightarrow H_2N(=NH)CSO_2\ H + 2H^+ + 2X^- \quad (R2)$$

In the absence of further oxidizing agent, however, the sulfenic acid can disproportionate into a number of thiosulfinates,[13] but the major pathway is towards dimerization:[14]

$$(H_2N)_2C{=}S + H_2N(=NH)CSOH \rightarrow H_2N(=NH)CS{-}SC(=NH)NH_2 + H_2O \quad (R3)$$

Formamidine disulfide exists as a doubly-protonated cation hydrochloride (with each positive charge delocalized over a carbon center and two nitrogens) under the conditions used because it is very unstable in alkaline conditions. However, we will represent it as a neutral molecule. Reaction (R3), which produces the dimer of thiourea, $H_2N(=NH)CS{-}SC(=NH)NH_2$ (which is written as $[(H_2N(HN{=})CS{-}]_2$) is also dominant in the presence of a weak oxidizing agent which might render reaction (R2) slow (or unfeasible). In such situations, quantitative formation of the dimeric species might be achieved. A further slow reaction will then occur with the dimeric species being oxidized further to the sulfinic and sulfonic acids. In alkaline conditions, the dimer is very unstable but exists as the doubly protonated cation in acidic medium. Oxidants such as hydrogen peroxide and peracetic acid can quantitatively oxidize thiourea to the dimer, formamidine disulfide, FDS, in exact stoichiometric equivalents.[15] However, with any oxidant, and in any quantity, there will always be a competition between reactions (R2) and (R3).

Our own research work on the mechanism of the oxidation of thiourea by bromate had postulated a mechanism that involved sulfenic, sulfinic and sulfonic acids without involving FDS. Here we report on a comprehensive kinetics and mechanistic study on the oxidation of FDS by acidic bromate. The fact that it was overlooked as a possible intermediate in the oxidation of thiourea could be explained if the FDS is labile enough to be easily oxidized to two sulfenic acids:

$$X_2 + [(H_2N(HN{=})CS{-}]_2 + 2H_2O \rightarrow 2H_2N(=NH)CSOH + 2H^+ + 2X^- \quad (R4)$$

If reaction (R4) is rapid (or in overwhelming excess of X_2), it will be kinetically inconsequential with respect to the rate of consumption of thiourea. However, this manuscript will examine if FDS is a viable intermediate in the oxidation of thiourea.

Experimental

Materials

The following reagents were used without further purification: sodium bromate, formamidine disulfide dihydrochloride (FDS), 97% (Aldrich), perchloric acid (70–72%), sodium bromide, bromine, sodium chloride, sodium thiosulfate (Fisher). All the major reactants were assumed to be of high enough purity with no need for further standardization. FDS solutions were prepared just before use and were not kept for more than 48 h. These solutions were stored in dark Winchester bottles and further protected from light by covering them with aluminum foil. Reaction solutions were prepared using singly distilled water.

Methods

Experiments were carried out at 25 ± 1.0 °C. The ionic strength was maintained at 1.0 M (NaCl) in all experiments. Most of the reactions were performed on a Hi-Tech Scientific SF-61 DX2 double mixing stopped flow spectrophotometer with an M300 monochromator and a spectrascan diode array control unit. The signal from the spectrophotometer was digitized *via* an Omega Engineering DAS-50/1 16-bit A/D board interfaced to a computer for storage and data analysis. Reaction progress was followed by monitoring the evolution of Br_2 at 390 nm. The direct reactions between bromine and FDS were also monitored by following the consumption of bromine at 390 nm on the stopped flow spectrophotometer using cells with a 1 cm path length.

Stoichiometric determinations

Stoichiometric determinations were performed by varying the amount of bromate while keeping concentrations of FDS constant. The required stoichiometry was determined as the point just before the reaction solution produced bromine as a final product.

Analyses for sulfate, bromate and bromine were also performed: sulfate was analyzed gravimetrically as $BaSO_4$ in excess bromate conditions. The reactions were allowed to sit for at least 24 h before addition of barium chloride. Subsequently the precipitate was allowed to sit for several hours in a vacuum desiccator before weighing. In these gravimetric analysis experiments; excess BrO_3^- was first removed iodometrically since it forms slightly insoluble $Ba(BrO_3)_2$ precipitate with $BaCl_2$, thus distorting the precipitation results. Excess bromate was acidified and mixed with excess iodide and the liberated iodine was titrated against standard sodium thiosulfate with starch as indicator. Bromine was evaluated from its absorbance at 390 nm (absorptivity coefficient 142 M^{-1} cm^{-1}).

Results

Stoichiometry

The reaction appeared to deliver two stoichiometries based on the ratio of the initial concentrations of oxidant to reductant, R. In excess bromate conditions, $R > 3$, yellow bromine is formed as a final product, but in conditions of excess reductant, no formation of bromine is observed. From our previous studies, it has been generally acknowledged that formation of bromine is derived from the reaction of one of the products, bromide, with excess bromate after all the reducing substrate has been oxidatively saturated. Hence the true stoichiometry of the reaction under study is one in which there is just enough bromate to oxidize FDS with no bromate left to conduct the bromate–bromide reaction and produce bromine. This ratio could be obtained by extrapolation: bromate was varied for fixed set of acid and FDS concentrations for ratios that produce bromine (excess oxidant). At the end of the reaction the excess oxidizing power was measured *via* an iodometric titration in which excess iodide was added and the liberated iodine titrated with standard thiosulfate:

$$BrO_3^- + 9I^- + 6H^+ \rightarrow Br^- + 3I_3^- + 3H_2O \quad (R5)$$

$$I_3^- + 2S_2O_3^{2-} \rightarrow S_4O_6^{2-} + 3I^- \quad (R6)$$

The bromate–bromide reaction will not alter the value of the thiosulfate titer obtained since it will be merely a rearrangement of oxidizing species. One can then plot the volume of titer obtained against the amount of bromate used. This plot will give a straight line. This line is extrapolated to the bromate volume axis for a value for zero titer and this intercept is the

exact amount of bromate needed to just consume FDS. This series of titrations was carried out for the bromate–FDS reaction and the results are shown in Fig. 1 where a fixed amount of 0.001 M FDS was used. The intercept obtained in this experiment is exactly 0.00233. The empirical ratio was thus deduced as 3 : 7. Gravimetric analysis showed that all the sulfur in FDS was collected as sulfate in which one mole of FDS gave two moles of sulfate. Combining these two results gave:

$$7BrO_3^- + 3[(H_2N(HN{=})CS{-}]_2 + 9H_2O \rightarrow 6NH_2CONH_2 + 6SO_4^{2-} + 7Br^- + 12H^+ \quad (R7)$$

In excess bromate conditions, the amount of bromine formed was observed to be proportional to the initial concentration of FDS used. This can be justified from the stoichiometry of reaction (R7) in which the bromide needed for the further reaction with bromate is proportional to initial FDS concentrations. By utilizing the final absorbance of bromine after prolonged standing, we could deduce stoichiometrically that one mole of FDS gave exactly 1.4 moles of aqueous bromine (empirically a ratio of 5 : 7). Sulfate production based on gravimetric analysis also showed the 1 : 2 ratio with FDS as found in the stoichiometry of reaction (R7). By calculating the oxidant equivalents needed to oxidize the sulfur centers, we could deduce the following stoichiometry in excess bromate environments:

$$14BrO_3^- + 5[(H_2N(HN{=})CS{-}]_2 + 8H_2O \rightarrow 10NH_2CONH_2 + 10SO_4^{2-} + 7Br_2 + 6H^+ \quad (R8)$$

This stoichiometry could also be obtained by a linear combination of 5R7 + 7R9 where R9 is the well known BrO_3^-/Br^- reaction:[16]

$$BrO_3^- + 5Br^- + 6H^+ \rightarrow 3Br_2(aq) + 3H_2O \quad (R9)$$

The stoichiometry of the direct bromine–FDS reaction was determined both spectrophotometrically and by direct titration. Aqueous bromine, in the burette was titrated into a conical flask with a solution of FDS with freshly-prepared starch. The end-point is when a persistent blue–black color is observed. The stoichiometry for this reaction was deduced to be:

$$7Br_2 + [(H_2N(HN{=})CS{-}]_2 + 10H_2O \rightarrow 2(H_2N)_2C{=}O + 2SO_4^{2-} + 14Br^- + 18H^+ \quad (R10)$$

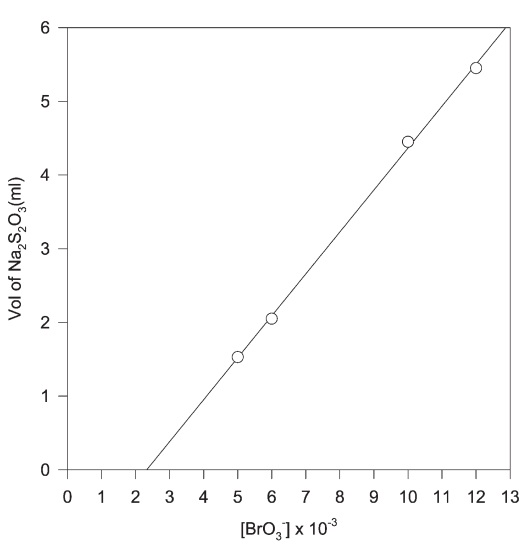

Fig. 1 Stoichiometric determinations by titration. The plot is the titer of thiosulfate obtained *vs.* the initial bromate concentrations. $[H^+]_0 = 0.10$ M, $[FDS]_0 = 0.001$ M, $[BrO_3^-]_0$ = (a) 0.005,(b) 0.006, (c) 0.010, (d) 0.012 M.

Reaction kinetics

The dynamics of this reaction mirror all other bromate oxidations in which there is a quiescent induction period followed by a rapid formation of bromine in stoichiometric excess of oxidant. This rapid formation of bromine is also accompanied by a rapid increase in the redox potential of the reaction mixture from approximately 600 to 1100 mV. A number of parameters could be measured for this reaction: induction period, rate of formation of bromine at the end of the induction period, and the amount of bromine formed. Fig. 2a shows a series of absorbance traces obtained from varying initial bromate concentrations while keeping all other parameters constant. The traces show a reduction in induction period with increasing bromate concentrations. Fig. 2b shows that there is a linear relationship between the initial bromate concentrations and the inverse of the induction period. This would seem to suggest that bromate is involved in the rate-determining step of the reaction that leads to the end of the induction period to the first power. Until the rate of the direct reaction of bromine and FDS is deduced, one can conjecture that the precursor reaction to the end of the induction period should be the oxidation of FDS by bromate. This reaction takes place during the induction period even though no noticeable activity is observed in redox potential and absorbance at 390 nm. It is

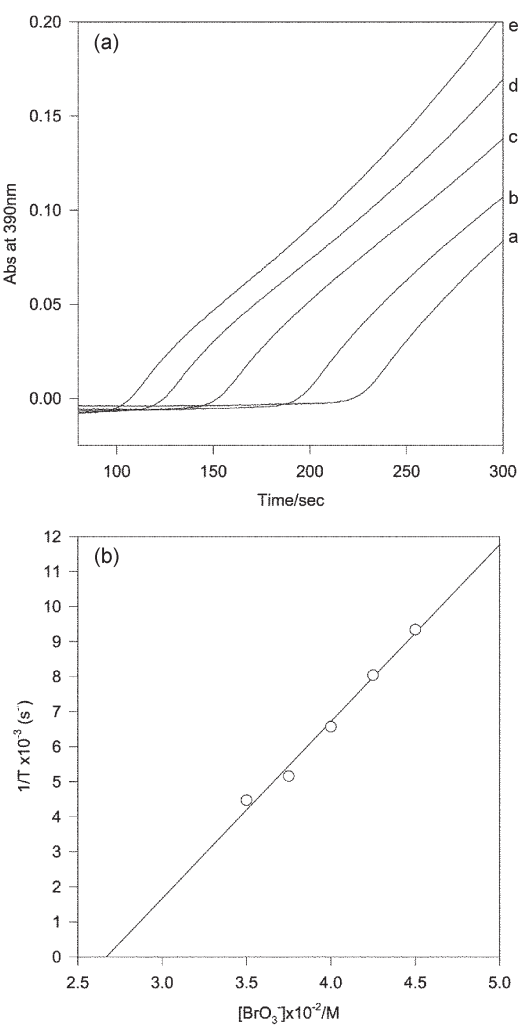

Fig. 2 (a) Effect of bromate variation on FDS depletion at 390 nm. In excess bromate the reaction displays an induction period before formation of bromine. $[H^+]_0 = 0.05$ M, $[FDS]_0 = 0.010$ M, $[BrO_3^-]_0$: (a) 0.035, (b) 0.0375, (c) 0.0400, (d) 0.0425, (e) 0.0450 M. (b) Plot of inverse of induction time *vs.* bromate concentration, for the data shown in Fig. 2a. The induction time is inversely proportional to initial bromate concentration.

difficult to use redox potentials as an analytical tool, but in general a single redox couple normally predominates in any reaction mixture. The final redox potential recorded after the induction period of 1100 mV appears to be derived from the $Br_2(aq)/2Br^-$ couple which has a redox potential of 1.08 V at standard conditions. Hence the post-induction period activity is the observation of reaction (R9) with no contribution from the reducing substrates in the reaction mixture which would have all been consumed. Although acid is not a reactant in this mechanism, it delivers a very powerful catalytic effect. In fact, this reaction will not proceed in pH conditions above 3.0. Fig. 3a shows that acid not only shortens the induction period, but also increases dramatically the rate of formation of bromine at the end of the induction period. Fig. 3b shows that there is a linear relationship between the inverse of the induction period and the square of the initial acid concentrations. Fig. 4a shows the effect of the reducing substrate, FDS, on the global dynamics of the reaction. The fact that lower FDS concentrations give shorter induction periods suggests, once again, that the complete consumption of FDS is a prerequisite to the end of the induction period. Higher FDS concentrations give longer induction periods and also give higher rates of formation of bromine at the end of the induction period. A plot of this rate of formation of bromine

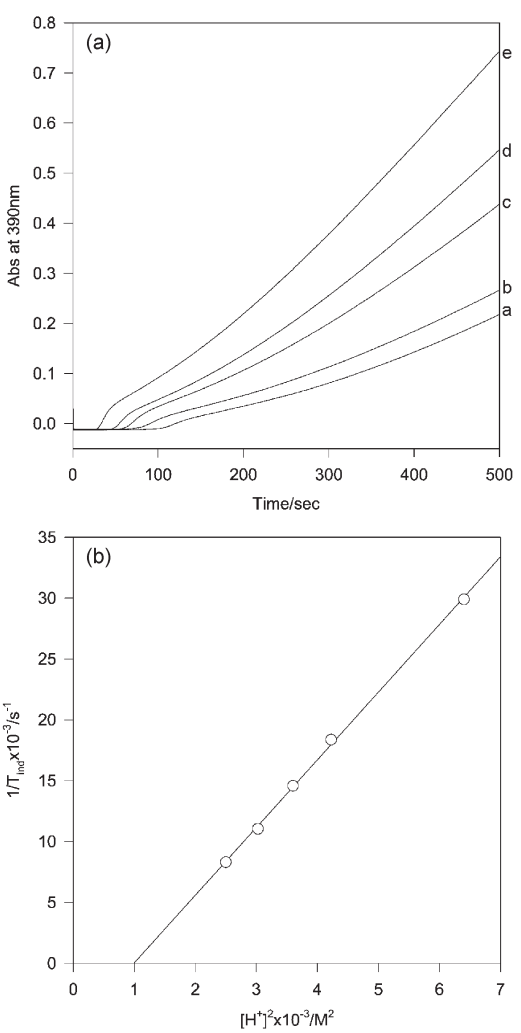

Fig. 3 (a) Effect of varying acid concentration on the absorbance traces observed at 390 nm. Acid simultaneously reduces the induction time and accelerates the rate of formation of bromine after the induction period. $[BrO_3^-]_0 = 0.035$ M, $[FDS]_0 = 0.005$ M, $[H^+]_0 =$ (a) 0.05, (b) 0.055, (c) 0.060, (d) 0.065, (e) 0.080 M. (b) Plot of dependence of inverse induction time *vs.* $[H^+]^2$, for the data shown in Fig. 3a. The reaction that consumes FDS has a second order dependence on acid.

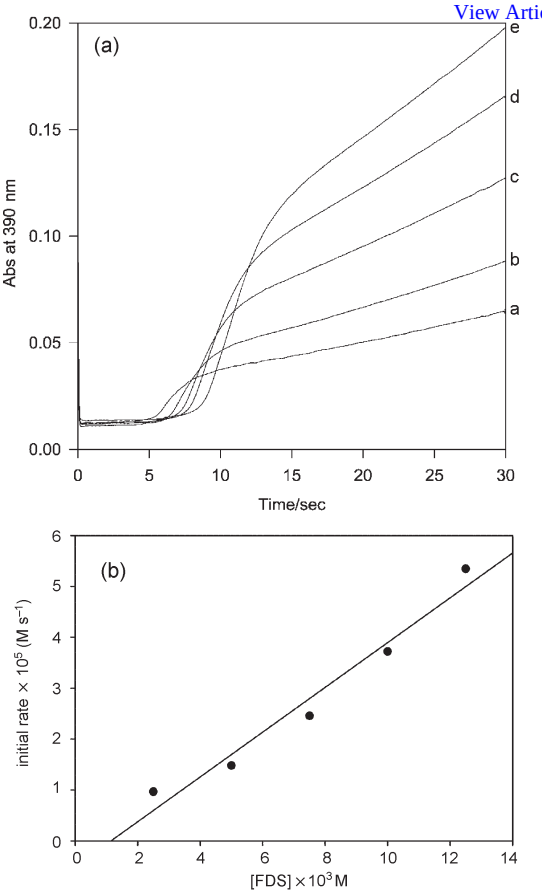

Fig. 4 (a) Effect of [FDS] variation. $[BrO_3^-]_0 = 0.008$ M, $[H^+]_0 =$ 0.10 M, $[FDS]_0 =$ (a) 0.0025, (b) 0.0050, (c) 0.0075, (d) 0.0100, (e) 0.0125 M. (b) Plot of initial rate dependence *vs.* $[FDS]_0$ concentration, for the data shown in Fig. 4a.

vs. the initial FDS concentration gives a straight line (see Fig. 4b), with an intercept that nearly coincides with the exact concentration of FDS required to satiate the stoichiometry of reaction (R7). This is important in the search of a plausible mechanism for this reaction. The amount of bromide available at the start of bromine formation (end of induction period) is related to the initial concentration of FDS according to the stoichiometry of reaction (R7); and thus, in our analysis of the rate of formation of bromine according to reaction (R9), we can replace the role of bromide by FDS. The direct oxidation of FDS by aqueous bromine is moderately fast (Fig. 5a) but not close to diffusion-limited as some reactions of bromine with other thiols and thiocarbamides.[12,17] The reaction appears to be mildly autoinhibitory. The Br_2–FDS reaction proceeds with the production of large amounts of acid which can lower the pH of the reaction solution from approximately 4.5 to 1.2 depending on the initial concentrations [see the stoichiometry of reaction (R10)]. Acid retardation has always been observed in conditions where electrophilic bromine atoms are supposed to attack a nucleophilic sulfur center. Previous studies involving thiourea and bromine showed a rapid initial step in which bromine is consumed in a diffusion-controlled rate to form the sulfenic acid which in turn is also rapidly oxidized to form the sulfonic acid which is then slowly oxidized to form sulfate and the organic residue.[12] Apart from trace e, all the experiments shown in Fig. 5a are in stoichiometric excess of reductant which yields a product with no bromine. The kinetics traces show a rapid initial step in which one mole of bromine is consumed before a second stage in which there is a slower consumption of bromine. This initial step is so rapid that it occurs within the mixing time of the stopped-flow spectrophotometer. Fig. 5b shows that this reaction is first order in

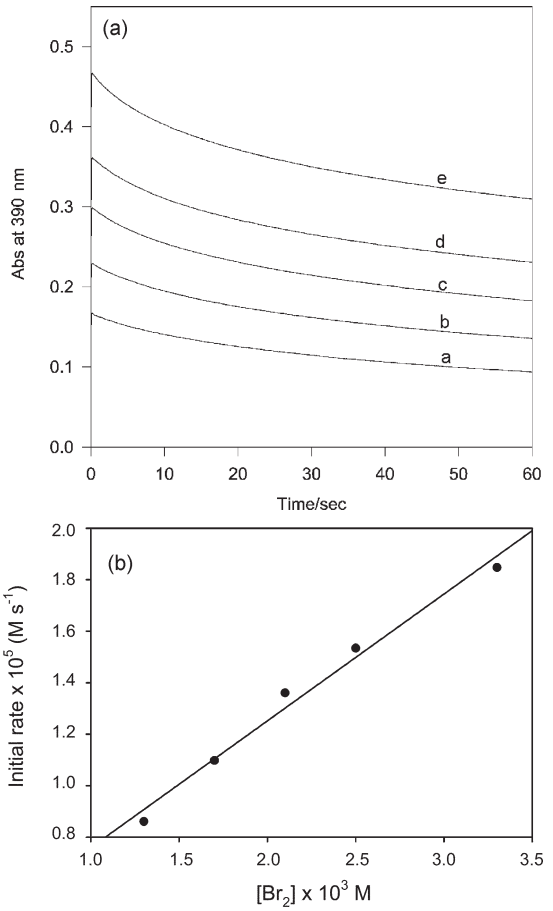

Fig. 5 (a) Direct reaction of [FDS] with bromine. $[FDS]_0 = 5 \times 10^{-4}$ M, $[H^+] = 0.005$ M $[Br_2]_0$ = (a) 0.0013, (b) 0.0017, (c) 0.0021, (d), 0.0025, (e) 0.0033 M. (b) Plot of initial rate of depletion of Br_2 *vs.* the concentration of bromine. The reaction is first order $[Br_2]_0$.

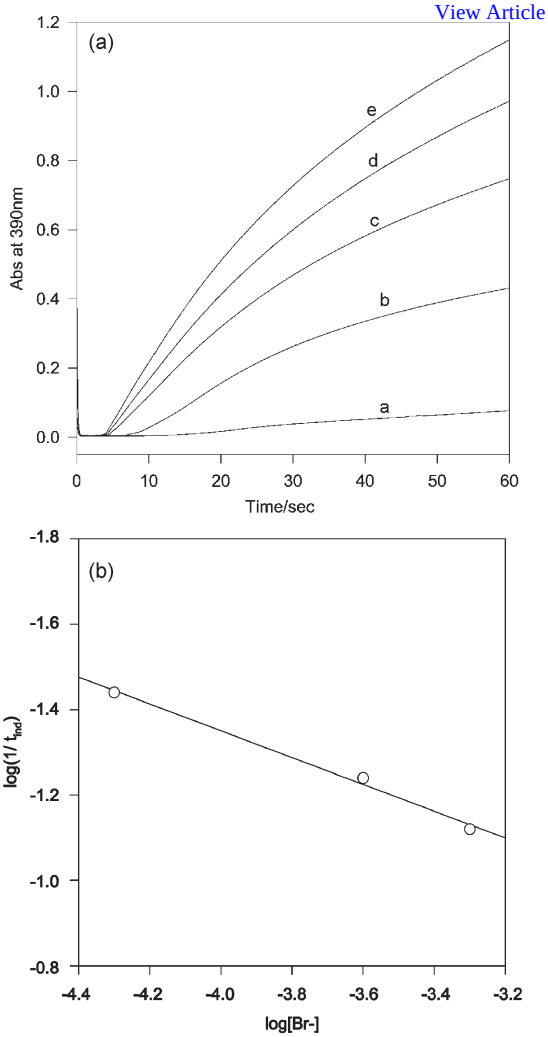

Fig. 6 (a) Effect of Br^- on the traces at 390 nm. Bromide has a catalytic effect on the reaction (as evidenced by the decrease in induction time). Higher bromide concentrations also increased the amount of Br_2 formed and the rate of bromine formation. $[FDS]_0 = 0.01$ M, $[BrO_3^-] = 0.008$ M, $[H^+] = 0.05$ M, $[Br^-]_0$ added = (a) 5.0×10^{-5}, (b) 2.5×10^{-4}, (c) 5.0×10^{-4} M. (d) A log–log plot of the inverse of the induction period *vs.* bromide concentrations. The data used are derived from Fig. 6a.

bromine concentration. A similar series of experiments showed that the reaction is also first order in FDS.

Apart from acid, bromide also seems to have a very strong catalytic effect on the whole reaction even though it is not a reactant according to the stoichiometries of reactions (R7) and (R8). Since it is a product in reaction (R7), its involvement in the acceleration of the reaction renders it as an autocatalyst. Fig. 6a shows the effect of bromide in which it drastically reduces the induction period and also increases the rate of formation of bromine after the induction period. Fig. 6a also shows that this catalytic effect quickly saturates. While there is a noticeable reduction in induction period in going from no added bromide to 5×10^{-5} and 1.5×10^{-4} M; further increases in initial bromide concentrations do not show an equally dramatic effect. A log–log plot of bromide concentrations *vs.* inverse of induction period gives a straight line as shown in Fig. 6b.

Proposed mechanism

The kinetics data summarized in Figs. 2 to 4 suggest a reaction with a rate law of the form:

$$\text{Rate} \propto [BrO_3^-][H^+]^2[FDS] \quad (1)$$

and the kinetics data in Fig. 6 also suggest the following relationship:

$$\text{Rate} \propto [Br^-] \quad (2)$$

The nucleophilic nature of the substrate suggests that reaction with the oxidant is initiated through the initial formation of bromic acid, which then attacks the S–S bond to commence the autocatalytic formation of the reactive species. This initial reaction only serves as a chain-initiation step.

$$BrO_3^- + H^+ \rightarrow HBrO_3 \quad (R11)$$

$$HBrO_3 + [(H_2N(HN{=})CS{-}]_2 + H_2O \rightarrow 2(H_2N(HN{=})CSOH + HBrO_2 \quad (R12)$$

Both the sulfenic acid, $(H_2N(HN{=})CSOH$ and bromous acid, $HBrO_2$, are very unstable and should disproportionate or react further to give the more stable sulfinic acid, $H_2N(HN{=})CSO_2H$, or bromide, Br^-, respectively

$$(H_2N(HN{=})CSOH + HBrO_2 \rightarrow (H_2N(HN{=})CSO_2H + HOBr \quad (R13)$$

$$(H_2N(HN{=})CSOH + HOBr \rightarrow (H_2N(HN{=})CSO_2H + Br^- + H^+ \quad (R14)$$

The sulfinic acid, aminoiminomethanesulfinic acid, is known to be very stable and is a well-known metabolite of thiourea. Addition of reactions R11 + R12 + R13 + R14 gives the overall reaction of:

$$BrO_3^- + [(H_2N(HN{=})CS{-}]_2 + H_2O \rightarrow 2(H_2N(HN{=})CSO_2H + Br^- \quad (R15)$$

The bromide formed in reaction (R15) can initiate the most important oxyhalogen reaction (R16) whose sole purpose in bromate oxidations is to form the reactive species $HBrO_2$ and HOBr that are responsible for the bulk of the oxidation:[18]

$$BrO_3^- + 2H^+ + Br^- \rightarrow HBrO_2 + HOBr \qquad (R16)$$

Both $HBrO_2$ and HOBr will end up as Br^-, which means that overall, there will be an autocatalytic production of bromide if reactions (R13) and (R14) are both faster than reaction (R12) because one mole of bromide in reaction (R16) will deliver two moles of bromide (quadratic autocatalysis). As bromide increases in concentration, however, $HBrO_2$ would rather rapidly decompose to hypobromous acid rather than participate as an oxidant as in reaction (R13):[19]

$$HBrO_2 + Br^- + H^+ \rightarrow 2HOBr;\ k_f = 2 \times 10^6,\ k_r \sim 0 \qquad (R17)$$

Addition, then, of reactions R11 + R12 + 2R14 + R17 will also deliver quadratic autocatalysis in bromide:

$$BrO_3^- + [(H_2N(HN{=})CS{-}]_2 + H_2O + Br^- \rightarrow 2(H_2N(HN{=})CSO_2H + 2Br^- \qquad (R18)$$

The autocatalytic production of bromide will render reaction (R16) as the rate-determining step instead of initiation reaction (R12). The kinetics and mechanism of this step have been studied in detail, and the rate law governing this step is:

$$\text{Rate} = k_0[BrO_3^-][Br^-][H^+]^2 \qquad (3)$$

Rate law (3) is supported by the data in Figs. 2b and 3b. The presence of [FDS] in the rate law [see eqn. (1)] is through composite reaction (R15). The rate of formation of bromide in this reaction will be directly proportional to the initial FDS concentration. Thus the bromide concentrations in eqn. (3) will be proportional to FDS concentrations, and the overall rate law for the reaction will be given by the rate equation:

$$\text{Rate} = k^{app}[BrO_3^-][H^+]^2[FDS] \qquad (4)$$

where k^{app} is the apparent rate constant if we were observing the rate of consumption of bromate or FDS. The observation of the rate of depletion of bromate or FDS could not be unambiguously observed due to their lack of absorptivity in the UV region.

Further oxidation

In the presence of excess oxidant, we expect the oxo-acids to be continuously oxidized *via* S-oxygenation until the C–S bond is cleaved and sulfate is formed.[20] Experiments with barium chloride as an indicator have shown that the formation of sulfate coincides with the formation of bromine. Thus there is a sequential and orderly oxidation from the sulfenic acid to the sulfinic, sulfonic, and finally to sulfate. We can safely assume that the major oxidant in getting FDS to sulfate is HOBr (if R17 is as fast as it is known to be in literature):

$$(H_2N(HN{=})CSO_2H + HOBr \rightarrow H_2N(HN{=})CSO_3H + Br^- + H^+ \qquad (R19)$$

$$(H_2N(HN{=})CSO_3H + HOBr + H_2O \rightarrow (H_2N)_2C{=}O + SO_4^{2-} + Br^- + 3H^+ \qquad (R20)$$

Formation of bromine

If we assume that there is only one reaction in solution producing bromine:

$$HOBr + Br^- + H^+ \rightarrow Br_2(aq) + H_2O \qquad (R21)$$

then the rate of formation of bromine will be determined by the rate of formation of HOBr. This whole section of the reaction will be bromide-controlled. In highly excess bromate conditions, $R \rightarrow 15$; then we can assume that the concentrations of bromate and acid will not have changed much at the point where bromine production commences; $[BrO_3]_t \approx [BrO_3]_0$, $[H^+]_t \approx [H^+]_0$. The only variables would be bromide concentrations and other reactive oxybromine species that might still be in the reaction mixture at the point where all the reductant has been consumed. Control experiments run with stoichiometric amounts of bromide as derived from the stoichiometry of reaction (R7) gave rates of formation of bromine according to the expected kinetics of reaction (R9) that were much slower than those observed in our experiments with FDS. This would suggest that there is no quantitative formation of bromide before formation of bromine commences: the true picture might involve a mixture of $HBrO_2$, HOBr and Br^- with no reducing species left in the reaction mixture. Without the concentrations of all the reacting species known to a certainty, one cannot evaluate kinetics constants for this process apart from extrapolations that can be derived from computer simulations. However, we managed to derive the dependence of the rates of formation of bromine with respect to the buffered species: bromate and acid *via* log–log plots. A log–log plot of rate of formation of bromine and initial acid concentrations gave a straight line of slope 2.0 and the same log–log plot with respect to bromate concentrations gave a straight line with a slope very close to unity. This suggests, again, that reaction (R16) is the rate-determining step with respect to the formation of bromine at the end of the induction period.

The bromine–FDS reaction

The oxidation of FDS by aqueous bromine was straightforward with the rate law:

$$-d[Br_2]/dt = k_{17}[Br_2][FDS] \qquad (5)$$

The initial step is the formation of the sulfenic acid:

$$Br_2(aq) + [(H_2N(HN{=})CS{-}]_2 + 2H_2O \rightarrow 2\ (H_2N(HN{=})CSOH + 2Br^- + 2H^+ \qquad (R22)$$

Reaction (R22) is a very rapid step with a lower limit bimolecular rate constant which we deduced to be $k_{22} = 6 \times 10^5\ M^{-1}\ s^{-1}$. The next step, though still quite rapid, will involve the formation of the sulfinic acid, and this portion of the reaction could be captured on a stopped-flow spectrophotometer. We experimentally evaluated a bimolecular rate constant for the second slower part of the reaction of $25 \pm 5\ M^{-1}\ s^{-1}$. As the reaction proceeds, it produces, as major products, protons and bromide ions. The mild autoinhibition observed is due to the formation of the tribromide anion which is a much poorer electrophile than molecular bromine:[21]

$$Br_2(aq) + Br^- \rightarrow Br_3^-;\ K_{eq} = 17 \qquad (R23)$$

Experiments undertaken of bromine oxidations with added bromide have shown a measurable retardation of the reaction. The continuous formation of bromide as the reaction proceeds pushes the equilibrium of reaction (R23) to the right with continuously less and less molecular bromide available for reaction. This tribromide equilibrium does not assert itself as much in the formation of bromine at the end of the induction period because the bromide formed in reaction (R7) will continuously be consumed by reaction (R9) to produce bromine.

Computer simulations

Our inability to experimentally follow the rate of consumption of FDS made computer simulations studies mandatory in this mechanism. Our experimental data allowed us to produce a very concise and abbreviated mechanism that could still adequately describe the observed reaction dynamics. Although

we are aware that there are four oxidizing species in the reaction mixture: BrO_3^-, $HBrO_2$, HOBr and Br_2(aq) as well as four reducing species: FDS, the sulfenic, sulfinic and sulfonic acids, there was no need to produce a mechanism with 16 oxidation–reduction reactions that permute all possible combinations because we could assume HOBr and Br_2(aq) as the major oxidizing species. This could be possible after our assertion that reaction (R16) was rate-determining and that reaction (R17) was fast. The full mechanism used for our modeling studies is shown in Table 1. It consists of three oxyhalogen reactions (P1–P3) whose kinetic constants have been deduced from previous studies,[19] a rapid protolytic reaction (P4), initiation reactions (P5–P8) and eight oxybromine–sulfur reactions (P7–P14) in which only aqueous bromine and HOBr have been utilized as oxidants. Sulfur–sulfur reactions were ignored in this mechanism because they would be inconsequential in excess oxidant. Reaction (P4) is known to be diffusion-controlled. The use of high diffusion-controlled rate constants in this mechanism greatly increased the stiffness of the generated ordinary differential equations resulting in simulations that needed up to 24 h on a Pentium IV 2.4 Ghz computer. The use of lower than diffusion-controlled rate constants increased computational efficiency without loss in the accuracy of the model for as long as the chosen rate constants did not render reaction (P4) rate-limiting. The stiff set of ordinary differential equations derived from the kinetics rate laws was integrated by semi-implicit forth order Runge–Kutta techniques derived from the CKS software generated by IBM's Almaden group as well as the *Kintecus* software developed by Ianni.[22] The simulations were most sensitive to the kinetics parameters used for reaction (P5) and the bimolecular rate constant of 400 M^{-1} s^{-1} was based on the best fit to the induction period. Kinetics parameters used for reactions (P6), (P7), (P8) and (P10) were chosen as lower limit values such that these reactions were not rate-determining. The values for (P12) and (P13) were deduced from this study. The 'kink' which is evident in Fig. 3a in which a two-stage formation of bromine is observed after the induction period could only be modeled if $k_{P14} > k_{P13}$. Thus the value of k_{P14} was guessed after the experimentally estimated k_{P13}. Fig. 7 shows that this simple mechanism can easily simulate the induction period and bromine formation. The data simulated is from Fig. 3a. The model was able to satisfactorily reproduce acid and bromate effects in induction periods and rate of formation of bromine at the end of the induction period.

Table 1 The reduced bromate–FDS mechanism used for computer simulations

Number	Reaction	k_f; k_r
P1	$BrO_3^- + 2H^+ + Br^- \rightleftharpoons HBrO_2 + HOBr$	2.1; 1×10^4
P2	$HBrO_2 + Br^- + H^+ \rightleftharpoons 2HOBr$	2×10^6; 2×10^{-5}
P3	$HOBr + Br^- + H^+ \rightleftharpoons Br_2(aq) + H_2O$	8.9×10^8; 110
P4	$BrO_3^- + H^+ \rightleftharpoons HBrO_3$	1×10^7; 1×10^5 [a]
P5	$HBrO_3 + [H_2N(HN{=})CS{-}]_2 + H_2O \rightarrow 2H_2N(HN{=})CSOH + HBrO_2$	400
P6	$HBrO_2 + [H_2N(HN{=})CS{-}]_2 + H_2O \rightarrow 2H_2N(HN{=})CSOH + HOBr$	5×10^4
P7	$HOBr + [H_2N(HN{=})CS{-}]_2 + H_2O \rightarrow 2H_2N(HN{=})CSOH + Br^- + H^+$	1×10^5
P8	$HOBr + H_2N(HN{=})CSOH \rightarrow H_2N(HN{=})CSO_2H + Br^- + H^+$	1×10^5
P9	$HOBr + H_2N(HN{=})CSO_2H \rightarrow H_2N(HN{=})CSO_3H + Br^- + H^+$	100
P10	$HOBr + H_2N(HN{=})CSO_3H + H_2O \rightarrow (H_2N)_2C{=}O + SO_4^{2-} + Br^- + 3H^+$	700
P11	$Br_2 + [H_2N(HN{=})CS{-}]_2 + 2H_2O \rightarrow 2H_2N(HN{=})CSOH + 2Br^- + 2H^+$	6×10^5
P12	$Br_2 + H_2N(HN{=})CSOH + H_2O \rightarrow H_2N(HN{=})CSO_2H + 2Br^- + 2H^+$	2×10^4
P13	$Br_2 + H_2N(HN{=})CSO_2H + H_2O \rightarrow H_2N(HN{=})CSO_3H + 2Br^- + 2H^+$	20
P14	$Br_2 + H_2N(HN{=})CSO_3H + 2H_2O \rightarrow (H_2N)_2C{=}O + SO_4^{2-} + 2Br^- + 4H^+$	120

[a] Though this reaction is diffusion-controlled, these values were lower-limit kinetics parameters that could be used without rendering this reaction rate-determining. The use of diffusion-controlled rate constants rendered the mechanism extremely stiff and computationally slow.

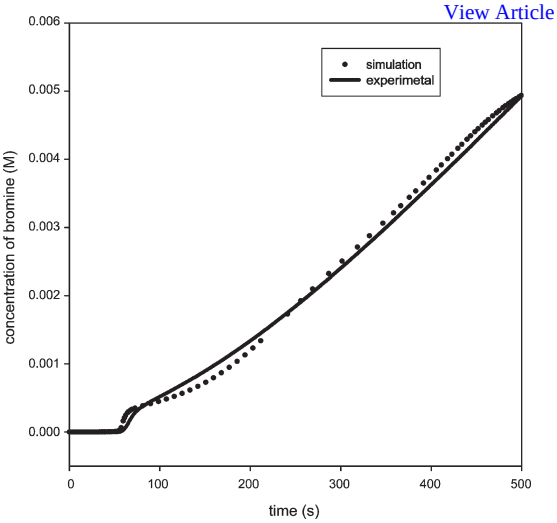

Fig. 7 Computer modeling of the reaction mechanism shown in Fig. 3a, trace e. $[FDS]_0 = 0.005$ M, $[BrO_3^-] = 0.035$ M, $[H^+] = 0.08$ M.

Conclusion

The oxidation of the thiourea dimer, FDS, by bromate has a mechanism that closely mimics the thiourea–bromate mechanism. The only difference lies in the stoichiometry and the fact that the bromate–FDS reaction is much faster than the corresponding bromate–thiourea reaction. This study clearly shows that in an oxidative environment, FDS would be one of the first intermediates formed from thiourea. The physiological environment also supports the formation of the dimer as the first step in the oxidative metabolism of thiocarbamides.

Acknowledgements

We would like to thank Dr. Ian Love of the University of Zimbabwe for alerting us to the existence of the *Kintecus* modeling software. This work was supported by grant number CHE-0137435 from the National Science Foundation.

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