ascribe the difference in reaction enthalpies to a bonding interaction more favorable in CuT^- than in H[CuT] compared with the change in overall bonding between $Cu(EDTA)^{2-}$ and $H[Cu(EDTA)]^-$. This might result from a reorientation of metal-ligand bonds in the CuT^- species resulting in either release of strain or more effective metal-ligand interaction. Some internal reorientation is consistent with the more negative $\Delta S°$ value for H[CuT] acidic dissociation compared with that for $H[Cu(EDTA)]^-$. Both processes restrict internal motion by binding a carboxylate group, but this restriction seems larger in the case of H[CuT]. $\Delta S°$ for the acidic dissociation reactions consists of contributions from several processes: (1) solvent ordering around H^+, common to both reactions; (2) increased secondary solvation around the copper complexes, a process that provides a larger negative contribution to $H[Cu(EDTA)]^-$ dissociation than to H[CuT] dissociation; (3) positive contributions due to solvent release from the sixth copper coordination; (4) loss of internal freedom. Of these factors the last might account for the more negative $\Delta S°$ value observed for H[CuT] dissociation. That is, differences in solvent binding at the sixth copper coordination site might result in a relatively more negative contribution to $\Delta S°$ for H[CuT] dissociation. However, the sixth coordination position on Cu^{2+} is known to be only weakly solvated so that differences between weakly solvated sites are not likely to provide for the observed result. Consequently, it appears possible that some distortion of Cu^{2+} ligation occurs upon CuT^- formation. This proposition seems supported by the X-ray crystallographic data, which indicate an unusually large trigonal distortion in CuT^- in which the locus of nitrogen atoms is twisted away from the carboxylate locus by about 30° from the idealized octahedral orientation. A large trigonal distortion of this kind would certainly influence the ligand field near Cu^{2+} and might profoundly effect the magnitude of the ligand field, thus accounting for the unusual difference between spectral properties of H[CuT] and CuT^-. As a final comparison we note that λ_{max} = 660 nm[2c] for aqueous $Cu[9]aneN_3^{2+}$, which we presume exists as a hexacoordinate species. Unfortunately, no crystallographic data is available for this complex. Nevertheless it seems unlikely that large trigonal distortions would be present and that the similar λ_{max} values of H[CuT] and $Cu[9]aneN_3(H_2O)_3^{2+}$ reflect approximately octahedral coordination. Thus, it appears that the large displacement of λ_{max} from 660 nm for H[CuT] to a value near 750 nm for CuT^- results from a substantial distortion of the ligand field in CuT^-, which we connect with a release of strain interactions in H[CuT]. The importance of these interactions is consistent with thermodynamic, X-ray crystallographic, and spectral evidence.

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Kinetics and Mechanism of General-Acid-Assisted Oxidation of Bromide by Hypochlorite and Hypochlorous Acid

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Received March 12, 1987

The rate expression for the oxidation of bromide by HOCl and OCl^- is $-d[OCl^-]_T/dt = k_{HA}[HA][OCl^-]_T[Br^-]$, where $[OCl^-]_T = [OCl^-] + [HOCl]$ and HA is a general acid (H_2O, HPO_4^{2-}, HCO_3^-, CH_3COOH, $ClCH_2COOH$, or H_3O^+). The k_{HA} value for $H_3O^+ + OCl^- + Br^-$ is 3.65×10^{10} M^{-2} s^{-1} (this path requires HOCl as an intermediate), while the k_{HA} value for $H_3O^+ + HOCl + Br^-$ is 1.32×10^6 M^{-2} s^{-1}. In terms of second-order expressions, the rate constant for HOCl and Br^- is 1.55×10^3 M^{-1} s^{-1}, while the rate constant for $OCl^- + Br^-$ is only 0.90×10^{-3} M^{-1} s^{-1}. The proposed mechanism for the acid-assisted reactions (except for $H_3O^+ + OCl^-$) is a simultaneous proton transfer (from HA to OCl^- or to HOCl) and Cl^+ transfer to Br^- (to give BrCl, which reacts rapidly to give OBr^- or Br_2 and Br_3^-). The Brønsted α value is 0.75 for the reactions of HA with OCl^- and Br^-, and the α value is 0.27 for the reactions of HA with HOCl and Br^-. The α values reflect the degree of proton transfer in the transition state.

Introduction

Many non-metal redox reactions take place by atom-transfer or ion-transfer processes. However, much less attention has been paid to the kinetics and mechanisms of these reactions than to electron-transfer reactions. This lack of study may have left the impression that the reactions are well understood. In reality, detailed knowledge of non-metal redox reaction kinetics and mechanisms is limited.

The oxidation of bromide ion by hypochlorite ion was studied by Farkas, Lewin, and Bloch[1] in the pH range 10.8-13.2 under second-order conditions. They verified the stoichiometry of eq 1 and studied the progress of the reaction by tritrimetric methods.

$$OCl^- + Br^- \rightleftarrows OBr^- + Cl^- \qquad (1)$$

They reported the rate-determining step to be the reaction between HOCl and Br^- with a rate constant of 2.95×10^3 M^{-1} s^{-1} at 25 °C. Their proposed mechanism (eq 2-4) implies nucleophilic attack by Br^- at oxygen, which is equivalent to an OH^+ transfer between Cl^- and Br^-.

$$OCl^- + H_2O \rightleftarrows HOCl + OH^- \qquad (2)$$

$$HOCl + Br^- \rightarrow HOBr + Cl^- \qquad (3)$$

$$HOBr + OH^- \rightleftarrows OBr^- + H_2O \qquad (4)$$

Recent studies in our laboratory indicate that Cl^+ transfer occurs in the reactions of NH_2Cl and $NHCl_2$ with iodide[2] and in the reaction of NH_2Cl with sulfite.[3] All of these reactions are general-acid assisted. (General-acid-catalyzed reactions can be considered to be a special case of general-acid-assisted reactions in which no acid is consumed or released.) The reaction of OCl^- with I^- is also general-acid assisted and appears to have a Cl^+-transfer mechanism.[2] We propose ICl as an intermediate in all the reactions with iodide. Recent pulsed-accelerated-flow studies[4] show that the reaction between ICl and I^- to form I_2 and I_3^- is extremely rapid.

Eigen and Kustin[5] determined the kinetics of halogen hydrolysis by temperature-jump relaxation methods. Their work shows that H_3O^+ assists the rate of reaction between Br^- and HOBr to form Br_2. Thus, H_3O^+ might well be expected to assist the reaction between Br^- and HOCl, but this has not been studied previously.

In the present work, we report the kinetics of the reaction in eq 1 in base (from 0.45 M NaOH to pH 9.5) and show that the

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(1) Farkas, L.; Lewin, M.; Bloch, R. *J. Am. Chem. Soc.* **1949**, *71*, 1988-1991.

(2) Kumar, K.; Day, R. A.; Margerum, D. W. *Inorg. Chem.* **1986**, *25*, 4344-4350.

(3) Yiin, B. S.; Walker, D. M.; Margerum, D. W., submitted for publication in *Inorg. Chem.*

(4) Margerum, D. W.; Dickson, P. N.; Nagy, J. C.; Kumar, K.; Bowers, C. P.; Fogelman, K. D. *Inorg. Chem.* **1986**, *25*, 4900-4904.

(5) Eigen, M.; Kustin, K. *J. Am. Chem. Soc.* **1962**, *84*, 1355-1361.

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Table I. Absorption Spectral Characteristics of Halogen Species

species	λ_{max}, nm	ϵ, M^{-1} cm^{-1}	ref
OCl^-	292	350	*a*
OBr^-	329	345	*b*
HOCl	230	100	*c*
HOBr	260	160	*b*
Br_2	390	175	*b*
Br_3^-	266	35000	*b*
$BrCl_2^-$	380	560	*d*

[a] Grey, E. T. Ph.D. Thesis, Purdue University, West Lafayette, IN, 1977. [b] Soulard, M.; Block, F.; Hatterer, A. *J. Chem. Soc. Dalton Trans.* **1981**, 2300–2310. [c] Anbar, M.; Dostrovdky, I. *J. Chem. Soc.* **1954**, 1105–1108. [d] Reference 7.

Table II. Protonation, Hydrolysis, and Formation Constants

equilibrium	*K*	ref
$OCl^- + H^+ \rightleftharpoons HOCl$	2.75×10^7	13
$OBr^- + H^+ \rightleftharpoons HOBr$	5×10^8	5
$OCl^- + H_2O \rightleftharpoons HOCl + OH^-$	5.2×10^{-7}	*a*
$Cl_2 + H_2O \rightleftharpoons HOCl + H^+ + Cl^-$	1.0×10^{-3}	13
$Br_2 + H_2O \rightleftharpoons HOBr + H^+ + Br^-$	4.4×10^{-9}	5
$Br_2 + Br^- \rightleftharpoons Br_3^-$	17	5
$BrCl + H_2O \rightleftharpoons HOBr + H^+ + Cl^-$	2.95×10^{-5}	*b*
$H_2O \rightleftharpoons H^+ + HO^-$	1.82×10^{-14}	13

[a] Calculated from pK_a of HOCl and pK_w of water. [b] Kanyaev, N.; Shilov, E. A. *Tr. Ivanov. Khim.-Tekhnol. Inst.* **1940**, *3*, 69.

reaction is general-acid catalyzed. The kinetics of the reaction of HOCl with Br^- (eq 5 and 6) is studied in acid (from pH 5.3

$$H^+ + HOCl + 2Br^- \rightarrow Br_2 + Cl^- + H_2O \quad (5)$$

$$Br_2 + Br^- \rightleftharpoons Br_3^- \quad (6)$$

to 1.0) and is shown to be general-acid assisted. We propose that these reactions occur by transfer of Cl^+ to give BrCl as an intermediate. Bromine chloride is a known compound that can be prepared in nonaqueous solutions by the reaction of *N*-chlorosuccinimide and bromide.[6] In aqueous solutions BrCl is not stable, but in high concentrations of chloride, $BrCl_2^-$ forms readily.[7]

Experimental Section

Reagents. A 5% (Baker) or 10% (Mallinckrodt) solution of sodium hypochlorite was used as the source of hypochlorite or hypochlorous acid. Stock solutions of hypochlorite were standardized by the measurement of the absorbance of OCl^- at 292 nm (Table I) or by the formation of I_3^- (λ_{max} = 353 nm, ϵ = 26 400 M^{-1} cm^{-1})[8] after the addition of excess iodide and acid. Solutions of sodium bromide (MCB) were standardized by argentimetric titrations[9] with 5% potassium chromate as an indicator.

Sodium perchlorate, prepared from Na_2CO_3 and $HClO_4$, was used to maintain the ionic strength of the solutions at μ = 0.5 M. Reagent grade acids, bases, and buffers were used. Distilled deionized water was used for the preparation of solutions. All solutions were freshly prepared to avoid any complication due to decomposition of hypochlorite or hypochlorous acid. The distribution of protonated, unprotonated, and hydrolyzed species was calculated from the equilibrium data given in Table II.

Methods. Absorbance measurements were made with a Perkin-Elmer Model 320 spectrophotometer interfaced to a Perkin-Elmer 3600 data station. Solution pH values were measured with a Corning Model 476051 combination glass electrode and an Orion Model 601 pH meter. All pH values were corrected to give –log [H^+] values at 25.0 °C and μ = 0.5 M, based on the electrode titrations with standard solutions of NaOH and $HClO_4$. Gran plots[10] were used in the calibration of the electrodes.

All reactions were run under pseudo-first-order conditions with Br^- in large excess. In base, the rates of the reaction were monitored by the disappearance of OCl^- at 292 nm with the Perkin-Elmer spectrophotometer. Reactions were followed for at least 4 half-lives, and 250 data points were collected for a least-squares linear regression analysis of ln $(A_t - A_\infty)$ vs. time, where A_∞ and A_t are the final absorbance and the absorbance at any time, respectively. First-order rate constants are given in Table III with the standard deviations for individual runs. Under acidic conditions, the reactions were monitored by following the formation of Br_2 at 390 nm or the formation of Br_3^- at 266 nm. At 390 nm, both Br_2 and Br_3^- (ϵ = 600 M^{-1} cm^{-1}) contribute to the absorbance. The formation equilibrium constant for Br_3^- is 17 M^{-1}. Absorbance vs. time data were obtained for more than 4 half-lives with a Durrum stopped-flow spectrometer interfaced to a Hewlett-Packard computer (HP 2100S).[11] First-order rate constants (k_{obsd}, s^{-1}) were determined from least-squares linear regression analysis of 250 data points. The first-order rate constants in Table IV are given for the average of at least five runs for each set of conditions with the standard deviations for these runs. Experimental rate constants (k'_{obsd}) larger than 80 s^{-1} were corrected for mixing effects[12] in accord with eq 7, where k_m is 1700 s^{-1}. The corrected values are given in Table IV.

Table III. Pseudo-First-Order Rate Constants for the Oxidation of Bromide by Hypochlorite in Base[a]

NaOH Solutions

[Br^-], M	[OH^-], M	k_{obsd}, s^{-1}
0.100	0.450	$(1.90 \pm 0.01) \times 10^{-4}$
0.100	0.350	$(2.09 \pm 0.01) \times 10^{-4}$
0.100	0.300	$(2.41 \pm 0.01) \times 10^{-4}$
0.100	0.250	$(2.65 \pm 0.01) \times 10^{-4}$
0.020	0.0972	$(2.12 \pm 0.08) \times 10^{-4}$
0.030	0.0972	$(2.57 \pm 0.01) \times 10^{-4}$
0.200	0.0972	$(1.87 \pm 0.01) \times 10^{-3}$
0.010	0.0493	$(1.731 \pm 0.003) \times 10^{-4}$
0.020	0.0493	$(2.705 \pm 0.004) \times 10^{-4}$
0.080	0.0493	$(1.28 \pm 0.01) \times 10^{-3}$
0.100	0.0493	$(1.42 \pm 0.01) \times 10^{-3}$
0.150	0.0493	$(2.037 \pm 0.001) \times 10^{-3}$
0.200	0.0493	$(2.738 \pm 0.002) \times 10^{-3}$
0.250	0.0493	$(3.14 \pm 0.01) \times 10^{-3}$
0.020	0.0756	$(1.942 \pm 0.002) \times 10^{-4}$
0.020	0.0256	$(5.783 \pm 0.003) \times 10^{-4}$
0.020	0.0106	$(1.278 \pm 0.003) \times 10^{-3}$
0.020	0.0056	$(2.410 \pm 0.002) \times 10^{-3}$

Buffer Solution[b]

[Br^-], M	–log [H^+]	$[buffer]_T$, M	k_{obsd}, s^{-1}
0.020	10.99	0.025 (P)	0.016 ± 0.001
0.050	10.99	0.025 (P)	0.035 ± 0.005
0.080	10.99	0.025 (P)	0.055 ± 0.002
0.100	11.01	0.025 (P)	0.066 ± 0.001
0.120	10.99	0.025 (P)	0.091 ± 0.005
0.150	10.99	0.025 (P)	0.107 ± 0.005
0.050	10.97	0.0125 (P)	0.0305 ± 0.0006
0.050	11.01	0.050 (P)	0.043 ± 0.001
0.050	11.01	0.0625 (P)	0.045 ± 0.002
0.100	9.48	0.005 (C)	1.6 ± 0.1
0.100	9.45	0.0125 (C)	1.88 ± 0.03
0.100	9.46	0.025 (C)	2.05 ± 0.03
0.100	9.46	0.0375 (C)	2.02 ± 0.08
0.100	9.48	0.0625 (C)	2.03 ± 0.07
0.100	9.48	0.075 (C)	2.25 ± 0.07
0.100	9.48	0.100 (C)	2.54 ± 0.07

[a] [OCl^-] = 6.00×10^{-4} M, μ = 0.5 M ($NaClO_4$), 25.0 °C, λ = 292 nm. [b] Buffers used are P = phosphate and C = carbonate.

$$k_{obsd} = k'_{obsd}/[1 - (k'_{obsd}/k_m)] \quad (7)$$

Commercial hypochlorite solutions are prepared from chlorine and NaOH and therefore contain approximately equimolar chloride ion concentrations. For the studies under acidic conditions, the HOCl solution was adjusted initially to pH 5 so that the Cl_2 formation (eq 8) was

$$HOCl + H^+ + Cl^- \rightleftharpoons Cl_2 + H_2O \quad (8)$$

negligible (Table II). The forward and reverse rate constants for eq 8

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(6) Wilbur, D. S.; Anderson, K. W. *J. Org. Chem.* **1982**, *47*, 358–359.
(7) Bell, R. P.; Pring, M. *J. Chem. Soc. A* **1966**, 1607–1609.
(8) Awtrey, A. D.; Connick, R. E. *J. Am. Chem. Soc.* **1951**, *73*, 1842–1843.
(9) Kolthoff, I. M.; Sandall, E. B.; Meehan, E. J.; Brukenstein, S. *Quantitative Chemical Analysis*, 4th ed.; Macmillan: London, 1969; p 796.
(10) Rossotti, F. J. C.; Rossotti, H. *J. Chem. Educ.* **1965**, *42*, 375–378.
(11) Willis, B. G.; Bittikofer, J. A.; Pardue, H. L.; Margerum, D. W. *Anal. Chem.* **1970**, *42*, 1340–1349.
(12) Dickson, P. N.; Margerum, D. W. *Anal. Chem.* **1986**, *58*, 3153–3158.

Table IV. Pseudo-First-Order Rate Constants for the Oxidation of Bromide by Hypochlorous Acid[a]

Buffer Solutions[b]

$[Br^-]$, M	$-\log [H^+]$	$[buffer]_T$, M	k_{obsd}, s^{-1}
0.010	5.23	0.05 (A)	24.7 ± 0.4
0.020	5.22	0.05 (A)	46.1 ± 0.5
0.050	5.22	0.05 (A)	115 ± 4[c]
0.100	5.30	0.05 (A)	245 ± 4[c]
0.0050	4.78	0.01 (A)	10.83 ± 0.07
0.0050	4.78	0.02 (A)	11.27 ± 0.13
0.0050	4.78	0.05 (A)	12.58 ± 0.05
0.0050	4.78	0.10 (A)	14.65 ± 0.06
0.0050	4.78	0.20 (A)	18.8 ± 0.8
0.0050	2.90	0.01 (C)	16.6 ± 0.2
0.0050	2.87	0.025 (C)	19.44 ± 0.08
0.0050	2.85	0.050 (C)	22.2 ± 0.5
0.0050	2.84	0.100 (C)	27.8 ± 0.4
0.0050	2.83	0.125 (C)	30.0 ± 0.4

Perchloric Acid Solutions

$[Br^-]$, M	$10^3[H^+]$, M	k_{obsd}, s^{-1}
0.0020	1.063	6.33 ± 0.05
0.003	1.063	9.75 ± 0.06
0.004	1.063	12.7 ± 0.2
0.005	1.063	16.3 ± 0.3
0.010	1.063	31.7 ± 0.4
0.020	1.063	63.2 ± 0.7
0.005	1.59	19.6 ± 0.2
0.005	2.66	26.4 ± 0.3
0.005	5.84	45.1 ± 0.4
0.005	11.16	81 ± 2[c]
0.005	21.79	154 ± 2[c]

[a] [HOCl] = (0.5–6.00) × 10^{-4} M, μ = 0.5 M ($NaClO_4$), 25.0 °C, λ = 266 or 392 nm. [b] Buffers used are A = acetic acid and C = chloroacetic acid. [c] Rate constants are corrected for mixing.[12]

are 2.8 × 10^4 M^{-2} s^{-1} and 28.6 s^{-1} at μ = 0.5, 25.0 °C.[13] Under all conditions, the calculated rate of formation of Cl_2 was less than the observed rate of formation of Br_2.

Results and Discussion

Reaction of Bromide with Hypochlorite in Base. Farkas et al.[1] used second-order unequal-concentration conditions, variable ionic strength (0.030–1.049), and a limited pH range (10.8–13.2) to measure the rate of reaction 1. They monitored the reaction by withdrawal of aliquots of the reaction mixture, followed by a dual-titration procedure to distinguish OCl^- from OBr^-. The data were fit to the rate expression $-d[OCl^-]/dt = k[HOCl][Br^-]$. They extrapolated the experimental data to zero ionic strength to obtain a value of 2.95 × 10^3 M^{-1} s^{-1} for k at 25 °C, based on a K_a value of 3.2 × 10^{-8} for HOCl. In the present work, reaction 1 is studied at constant ionic strength (0.50) under pseudo-first-order conditions with bromide ion in large excess. The bromide concentration is varied from 0.10 to 0.250 M, and the hydroxide ion concentration is varied from 0.0056 to 0.450 M (Table III). Individual reactions give excellent first-order plots, and the k_{obsd} values are proportional to the Br^- concentration (Figure 1). The k_{obsd} values are inversely proportional to OH^- concentration but have a small intercept (Figure 2). Farkas[1] did not observe a hydroxide-independent term, because of the limitations of the method of observation and the variation in ionic strength. Our experimentally observed rate expression is given in eq 9, where k_0 = (0.9 ± 0.1) × 10^{-3} M^{-1} s^{-1} and k_1 = (6.64

$$-d[OCl^-]/dt = [k_0 + (k_1/[OH^-])][Br^-][OCl^-] \quad (9)$$

± 0.09) × 10^{-4} s^{-1} at 25.0 °C. The base-dependent rate constant can be expressed in terms of $[H^+]$, $k_H = k_1/K_w$ = 3.65 × 10^{10} M^{-2} s^{-1} (pK_w = 13.74 at μ = 0.5, 25.0 °C),[13] or in terms of a second-order rate constant of 1.32 × 10^3 M^{-1} s^{-1} for the reaction of HOCl (pK_a = 7.44). Thus, HOCl is 1.5 × 10^6 times more reactive than OCl^- in its reaction with Br^-.

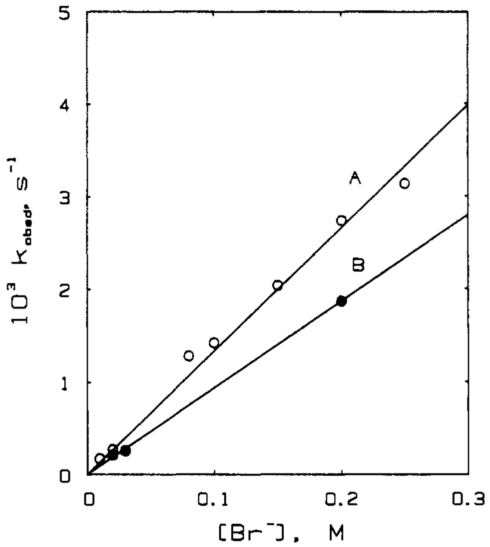

Figure 1. Pseudo-first-order rate constants (25.0 °C, μ = 0.50) for the reaction of OCl^- and Br^- in base: (A) 0.0493 M NaOH; (B) 0.0972 M NaOH.

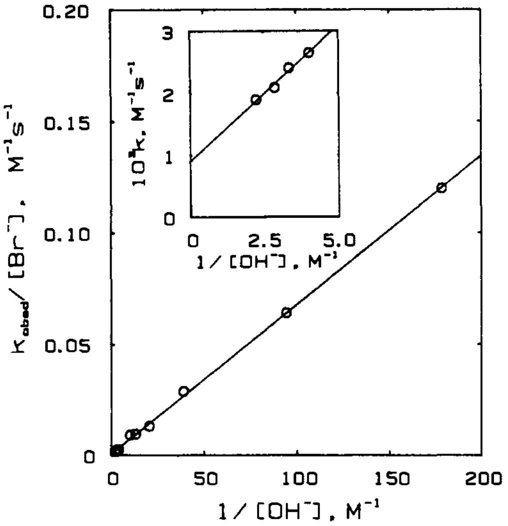

Figure 2. Inverse hydroxide ion dependence of $k_{obsd}/[Br^-]$ for the reaction of OCl^- + Br^- in base (25.0 °C, μ = 0.50). The insert shows $k = k_{obsd}/[Br^-]$ at high hydroxide concentrations, where the intercept is the small hydroxide-independent rate constant, k_0 = 0.9 × 10^{-3} M^{-1} s^{-1}.

The rate of reaction 1 is increased by an increase in buffer concentration at constant hydrogen ion concentration, as seen in Table III for hydrogen carbonate and hydrogen phosphate. This behavior is consistent with our previous studies,[2] and the data can be fit to eq 10 and 11, where HA is the acid form of the buffer,

$$k_{obsd} = (k_0 + k_H[H^+] + k_{HA}[HA])[Br^-] \quad (10)$$

$$(k_{obsd} - k_0)/([H^+][Br^-]) = k_H + k_{HA}[buffer]_T/(K_a + [H^+]) \quad (11)$$

$[buffer]_T$ is the total buffer concentration, and k_{HA} is the general-acid-catalyzed rate constant. Figure 3 shows the general-acid catalysis effect for HCO_3^-, k_{HA} = (1.25 ± 0.15) × 10^2 M^{-2} s^{-1}, and for HPO_4^{2-}, k_{HA} = 8.9 ± 1.3 M^{-2} s^{-1}.

Acid-Assisted Reactions of Bromide with Hypochlorous Acid. Equations 5 and 6 give the stoichiometry in acid, where the formation of Br_3^- (or Br_2) is followed by stopped-flow methods. The pseudo-first-order rate constants (Table IV) are directly proportional to the bromide concentration (Figure 4), but are now much larger because HOCl is the dominant species. Despite the

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[13] Margerum, D. W.; Gray, E. T.; Huffman, R. P. In *Organometals and Organometalloids, Occurrence and Fate in the Environment*; Brinckman, F. E., Bellama, J. M., Eds.; ACS Symposium Series 82; American Chemical Society: Washington, DC, 1978; pp 278–291.

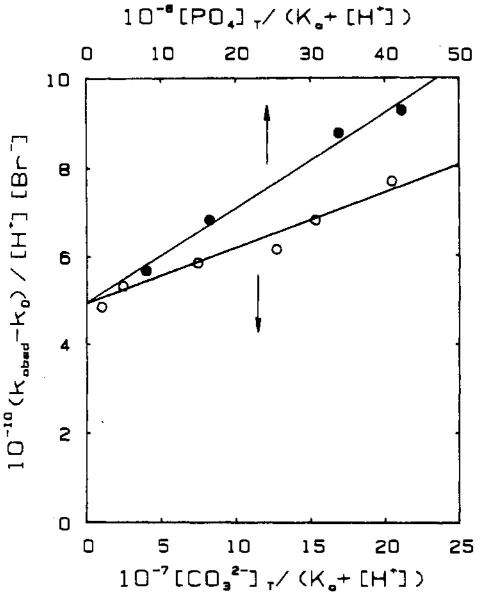


Figure 3. Plot of eq 11 for the general-acid-catalyzed reactions of OCl^- + Br^- by HPO_4^{2-} (top) and HCO_3^- (bottom).

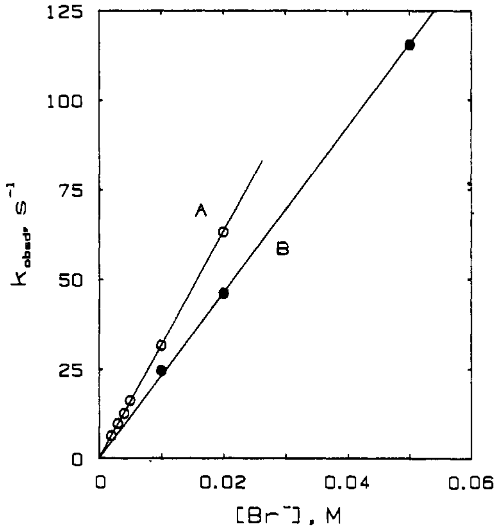


Figure 4. Pseudo-first-order rate constants (25.0 °C, $\mu = 0.50$) for the reaction of HOCl and Br^-: (A) $[H^+] = 1.063 \times 10^{-3}$ M; (B) $-\log [H^+] = 5.22$ (0.05 M acetate buffer).

fact that additional acid is not needed to give HOCl, the rates again increase with the concentration of general acids (eq 12).

$$\text{rate} = (k' + k'_H[H^+] + k'_{HA}[HA])[Br^-][HOCl] \quad (12)$$

The large increase in the second-order rate constant (for the HOCl reaction with Br^-) with increase in H_3O^+ concentration is shown in Figure 5. The intercept, $k' = 1.55 \times 10^3$ M^{-1} s^{-1}, is in excellent agreement with the value of 1.45×10^3 M^{-1} s^{-1} calculated for this rate constant from the high-pH data. The slope in Figure 5 gives a k'_H value of 1.32×10^6 M^{-2} s^{-1} for the reaction of H^+ + HOCl + Br^-.

The rates of reaction between HOCl and Br^- also increase in the presence of acetic acid and chloroacetic acid (Figure 6). The intercepts differ in this figure because different concentrations of H_3O^+ are present in the two cases. The k'_{HA} values, obtained from the slopes in Figure 6, are $(2.09 \pm 0.01) \times 10^4$ M^{-2} s^{-1} for CH_3COOH and $(6.1 \pm 0.3) \times 10^4$ M^{-2} s^{-1} for $ClCH_2COOH$.

Figure 7 shows the calculated dependence of the second-order rate constant between $[Br^-]$ and $[OCl^-]_T$ from 1 M H_3O^+ to 1 M OH^-, when no buffers are present (eq 13). At pH 14 the rate is due mostly to the reaction of OCl^- and Br^-. From pH 3 to 13 the rate is carried by HOCl + Br^-, but the pK_a of HOCl (7.44) affects the observed rate constant. Below pH 2 the rate increases due to the reaction of H^+ with HOCl and Br^-.

$$k = k_{obsd}/[Br^-] = (k_0 + k_H[H^+] + k'_H K_H[H^+]^2)/(1 + K_H[H^+]) \quad (13)$$

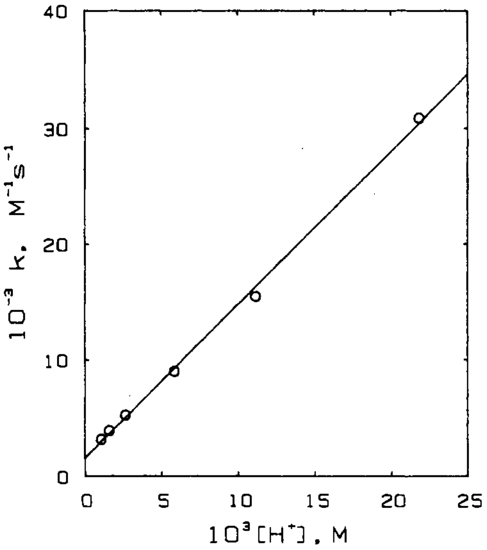


Figure 5. Dependence of the second-order rate constant (HOCl + Br^-) on $HClO_4$ concentration.

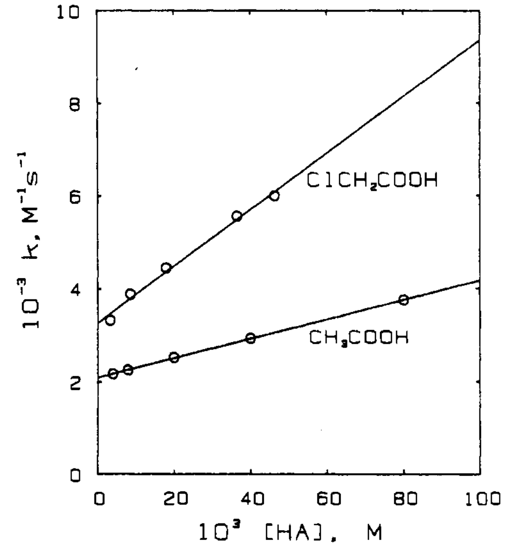


Figure 6. Dependence of the second-order rate constant (HOCl + Br^-) on the concentration of general acids.

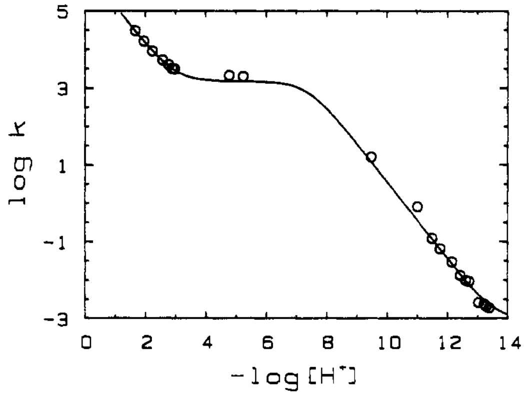


Figure 7. Dependence of the second-order rate constant (in terms of $[OCl^-]_T$ and $[Br^-]$) on the acidity (without buffer catalysis effects).

Brønsted Relationship. The buffer-catalyzed rates for these reactions increase with the strength of the general acids that are

Table V. Third-Order General-Acid-Catalyzed Rate Constants (M^{-2} s^{-1}) for the Oxidation of Bromide by Hypochlorite and Hypochlorous Acid[a]

HA	pK_a	k_{OCl^-}	k_{HOCl}
H_3O^+	−1.72[b]	$(3.65 \pm 0.05) \times 10^{10}$	$(1.32 \pm 0.03) \times 10^6$
$ClCH_3COOH$	2.6[c]		$(6.11 \pm 0.34) \times 10^4$
CH_3COOH	4.6[d]		$(2.09 \pm 0.01) \times 10^4$
HCO_3^-	9.8[e]	$(1.25 \pm 0.15) \times 10^2$	
HPO_4^{2-}	11.3[f]	8.9 ± 1.3	
H_2O	15.52[g]	$(1.6 \pm 0.3) \times 10^{-5}$	27.9 ± 5.5

[a] 25.00 °C, μ = 0.5 M. [b] Reference 14, p 300. [c] Martell, A. E.; Smith, R. M. *Critical Stability Constants*; Plenum: New York, 1982; Vol. 5, p 287. [d] Feldman, I.; Koval, L. *Inorg. Chem.* **1963**, *2*, 145–150. [e] MacInnes, D. A.; Belcher, D. J. *J. Am. Chem. Soc.* **1935**, *57*, 1683–1685. [f] Sillen, L. G.; Martell, A. E. *Spec. Publ.—Chem. Soc.* **1964**, *No. 17*, 180. [g] Lagerstrom, G. *Acta Chem. Scand.* **1959**, *13*, 722–736. The value is calculated by dividing K_w by the water molarity, 55.5 M.

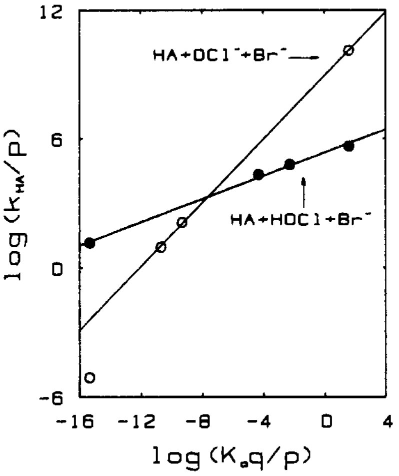


Figure 8. Brønsted plots for the general-acid-assisted reactions of OCl^- and Br^- and of HOCl and Br^-.

present in the solution. The rate constants (Table V) depend on the Brønsted relationship[14] in eq 14, where p is the number of

$$k_{HA}/p = G_A(K_aq/p)^\alpha \qquad (14)$$

equivalent acidic protons in HA, q is the number of equivalent basic sites in A, K_a is the acid dissociation constant of HA, G_A is a proportionality constant, and α is the Brønsted coefficient. Figure 8 shows the Brønsted plot for both reaction systems. The slope gives an α value of 0.75 for the HA + OCl^- + Br^- reaction, while the α value for the HA + HOCl + Br^- reaction is 0.27. The rate constant for the H_2O + OCl^- + Br^- reaction (the lower left-hand point in Figure 8) falls off the Brønsted correlation. If the immediate reaction products are OH^- + OH^- + BrCl, the difficulty in generating adjacent hydroxide ions may lower the effectiveness of this path. (A least-squares line through the three points for H_2O, HPO_4^{2-}, ane HCO_3^- gives an α value greater than unity, which is not possible. Even an α value of unity would be inconsistent with the experimentally observed general-acid catalysis.) The α value in the case of other HA + OCl^- reactions with Br^- is very close to the value observed in the case of the reaction of hypochlorite with iodide.[2] Although the α values are similar, the rates are 10^5 faster for iodide as compared to bromide. The reactivity of bromide is lower because bromide is a poor nucleophile compared to iodide. The much larger α value for HA + OCl^- + Br^- as compared to HA + HOCl + Br^- reflects the larger degree of proton transfer to OCl^-, which is a better base than HOCl. The pK_a value of H_2OCl^+ has been estimated to be in the region of −3 to −4.[15]

Proposed Mechansisms. General-acid-catalyzed kinetics are consistent with the mechanism given in eq 15 and 16 for the reactions in base.

$$HA + OCl^- + Br^- \rightarrow A^- + OH^- + BrCl \qquad (15)$$

$$BrCl + 2OH^- \xrightleftharpoons{\text{fast}} OBr^- + Cl^- + H_2O \qquad (16)$$

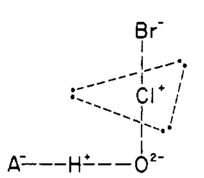
The proposed general-acid-assisted mechanism for the reactions in acid is given by eq 17–19.

$$HA + HOCl + Br^- \rightarrow A^- + H_2O + BrCl \qquad (17)$$

$$BrCl + Br^- \xrightleftharpoons{\text{fast}} Br_2 + Cl^- \qquad (18)$$

$$Br_2 + Br^- \xrightleftharpoons{\text{fast}} Br_3^- \qquad (19)$$

In these reactions, Cl^+ is transferred to Br^- to form BrCl, a highly reactive intermediate. The similarity of the reactions of OCl^-, NH_2Cl, and $NHCl_2$ with I^- to the reactions of OCl^- and HOCl with Br^- strongly suggests a parallel Cl^+-transfer mechanism.[2] The proposed transition states in structures I and II have an expanded coordination number for chlorine, which is not at all unusual for this atom. The fact that the reactions in eq 15 and 17 are general-acid catalyzed requires that proton transfer take place as the reactions pass through the transition state. A prior proton equilibration step would remove the dependence on the concentration of HA and result in catalysis only by H_3O^+. This distinction cannot be made when HA = H_3O^+, and in this case prior protonation is possible to give the reactions in eq 20 and 21. The third-order rate constant for H_3O^+ + OCl^- + Br^- equals 3.65×10^{10} M^{-2} s^{-1}. The magnitude of this rate constant requires some degree of prior association between two of the species, even if the third species reacts with this pair at a diffusion-controlled rate. Hence, the bimolecular steps in eq 20 and 21 are suggested and are consistent with the rate constant for reaction 21 (1.55×10^3 M^{-1} s^{-1}) that is measured directly in acid. Nevertheless, the H_3O^+ value for the third-order rate constant in eq 15 falls on the Brønsted plot with the other general acids.



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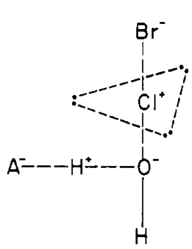
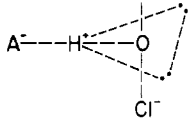


II

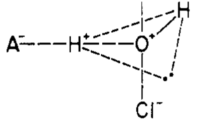
$$OCl^- + H_3O^+ \xrightleftharpoons{\text{fast}} HOCl + H_2O \qquad (20)$$

$$HOCl + Br^- \rightarrow OH^- + BrCl \qquad (21)$$

An alternate mechanism with transfer of HO^+ or H_2O^{2+} between Cl^- and Br^- is much less likely. It is more difficult to expand the coordination of oxygen as compared to chlorine, and the transition states in structures III and IV would be high-energy states. This path would be expected to have much smaller rate constants as is the case for carbon analogues.[2] Furthermore, it is not clear why protons should necessarily assist oxygen atom



III



IV

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Table VI. Third-order Rate Constants for the Oxidation of Halides by Hypochlorite and by Hypohalous Acids

reactants	k, $M^{-2}\ s^{-1}$	ref
$H^+ + OCl^- + Br^-$	3.65×10^{10}	*a*
$H^+ + OCl^- + I^-$	4.4×10^{15}	*b*
$H^+ + HOCl + Cl^-$	2.8×10^{4}	*c*
$H^+ + HOCl + Br^-$	1.3×10^{6}	*a*
$H^+ + HOBr + Br^-$	1.6×10^{10}	*d*
$H^+ + HOI + I^-$	4.4×10^{12}	*d*

[a] This work. [b] Reference 2. [c] Reference 13. [d] Reference 5.

transfer reactions (i.e. why HO^+ and H_2O^{2+} should react much more rapidly than the oxygen atom).

Reactions are known in which a halide reacts as a nucleophile at an oxygen atom, for example the bromide reactions with hydrogen peroxide:[16]

$$H_2O_2 + Br^- \xrightarrow{2.3 \times 10^{-5}\ M^{-1}\ s^{-1}} OH^- + HOBr \tag{22}$$

$$H^+ + H_2O_2 + Br^- \xrightarrow{1.4 \times 10^{-2}\ M^{-2}\ s^{-1}} H_2O + HOBr \tag{23}$$

In these cases OH^- and H_2O are leaving groups, in a manner similar to structures I and II where OH^+ replaces Cl^+. On the other hand, the above H_2O_2 rate constants are factors of 1.5×10^8 and 1.1×10^8 slower than the corresponding reactions of HOCl. This is consistent with a less favorable nucleophilic attack by bromide ion at oxygen as compared to chlorine.

In the Cl^+-transfer mechanism, protonation of the oxygen atom greatly assists the rate because OH^- and H_2O are suitable leaving groups. Since the O^{2-} ion is not an appropriate leaving group, water must donate a proton if the k_0 path ($H_2O + OCl^- + Br^-$) also occurs by Cl^+ transfer.

Table VI summarizes the third-order H_3O^+-assisted rate constants for the reactions of hypochlorite and hypohalous acids with halide ions. The relative reactivity for $H^+ + OCl^-$ with halides is $I^- \gg Br^-$ and for $H^+ + HOCl$ with halides is $Br^- \gg Cl^-$. The increase in reactivity with $I^- \gg Br^- \gg Cl^-$ reflects the relative nucleophilicity of the halide ions. The rate constants for $H^+ + HOX + Br^-$ show that HOBr is more reactive than HOCl, even though the HOCl reaction is more favorable thermodynamically. The relative reactivity of HOCl, HOBr, and HOI parallels the ability to more easily expand the coordination of X and transfer X^+ to the halide ion.

Acknowledgment. This work was supported by National Science Foundation Grants CHE-8319935 and CHE-8616666.

Registry No. Br^-, 24959-67-9; OCl^-, 14380-61-1; HOCl, 7790-92-3.

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Removal of Iron from Transferrin by Pyrophosphate and Tripodal Phosphonate Ligands

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Received September 18, 1986

The kinetics of iron removal from transferrin in 0.1 M hepes buffer at pH 7.4 and 25 °C have been studied by visible spectroscopy. Pseudo-first-order rate constants have been determined as a function of the ligand concentration for the ligands pyrophosphate, nitrilotris(methylenephosphonic acid), *N*-(phosphonomethyl)iminodiacetic acid, *N*,*N*-bis(phosphonomethyl)glycine, and nitrilotriacetic acid. The general equation that describes this ligand dependence is $k_{obsd} = k'[L]/(1 + k''[L]) + k'''[L]$. The results are discussed in terms of two parallel pathways for iron removal, one that is first order in ligand and another that shows saturation kinetics. Iron removal by the phosphonic acids proceeds predominately through the saturation pathway, while iron removal by the structurally related ligand nitrilotriacetic acid proceeds exclusively through the first-order pathway. Iron removal by pyrophosphate is relatively rapid through both pathways, so that the saturation process predominates at low ligand concentration and the first-order pathway predominates at higher ligand concentrations.

Introduction

Serum transferrin is the primary mammalian iron transport protein. The protein has been extensively studied, and several recent reviews of transferrin chemistry are available.[1-3] Transferrin consists of two major lobes, designated N-terminal and C-terminal, with a single high-affinity iron-binding site associated with each lobe. These sites are well separated, and although they are very similar, they are not identical.

Serum transferrin belongs to a small class of proteins that includes ovotransferrin and lactoferrin. The distinguishing characteristic of these proteins is the requirement of a synergistic anion for effective metal binding. Under physiological conditions the anion is (bi)carbonate, which binds simultaneously to the iron and to cationic side groups on the protein to form an $Fe-HCO_3-Tf$ ternary complex. Under carbonate-free conditions, reasonably stable ternary complexes can be formed with a variety of other anions.[4]

At sites of iron utilization, ferric transferrin binds to specific cell membrane receptors and releases its iron, although the process by which iron is removed from the very stable transferrin complex is still not clearly understood.[3] Iron removal from transferrin could also be important in chelation therapy for chronic iron overload. Certain genetic disorders such as β-thalassemia require frequent transfusions of whole blood. Since the body is unable to excrete the iron contained in this blood, it accumulates to lethal levels in organs such as the heart.[5] As a serum protein, transferrin is readily accessible to therapeutic chelating agents, but the rate of iron removal by desferrioxamine B, the current drug of choice, is quite slow.[5,6] Thus there is considerable interest in ligands that can remove iron from transferrin more quickly.

Rates of iron removal by several classes of ligands, including phosphonic acids,[7] catecholates,[8,9] hydroxamates,[10,11] and pyrophosphate,[12,13] have recently been reported. In all cases a hyperbolic dependence of the rate of iron removal on the concentration of ligand was reported. In enzyme kinetics this type of

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