4258 *Inorg. Chem.* **1982**, *21*, 4258–4263

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Rates of Formation of *N*-Bromo Amines in Aqueous Solution

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Received July 7, 1981

Rates of formation of NH_2Br, $(CH_3)_2NBr$, *N*-bromoglycine, and *N*-bromoglutamate from hypobromite and excess nitrogenous compound were determined in a stopped-flow rapid-kinetics spectrophotometer for the pH range 7–13. The variation of the observed second-order rate constants with pH is consistent with a mechanism in which HOBr and OBr^- react simultaneously with the free base of the amine. Specific rate constants are 7.5×10^7 and 7.6×10^4 $(mol/L)^{-1}$ s^{-1} for reaction of HOBr and OBr^- with ammonia at 20.0 °C, $>3 \times 10^9$ and $>3 \times 10^6$ $(mol/L)^{-1}$ s^{-1} for reaction with dimethylamine, 3.8×10^8 and 2.1×10^5 $(mol/L)^{-1}$ s^{-1} for reaction with glycine, and 3.5×10^8 and 5×10^4 $(mol/L)^{-1}$ s^{-1} for reaction with glutamate. Thus, *N*-bromo amines form 3–15 times more rapidly than the corresponding *N*-chloro amines. Rates of N-bromination tend to increase proportionately with increase in basicity (nucleophilicity) of the nitrogenous compound and with increase in electrophilicity of the bromine donor.

Aqueous bromine, like aqueous chlorine, reacts with ammonia and many nitrogenous organic compounds in dilute aqueous solution to form *N*-bromo amines.[1–4] With ammonia, for instance, bromamide (NH_2Br), bromimide ($NHBr_2$), and nitrogen tribromide (NBr_3) are formed sequentially[5] through reactions such as eq 1–3. The relative proportions of these

$$HOBr + NH_3 \rightarrow NH_2Br + H_2O \tag{1}$$

$$HOBr + NH_2Br \rightarrow NHBr_2 + H_2O \tag{2}$$

$$HOBr + NHBr_2 \rightarrow HBr_3 + H_2O \tag{3}$$

compounds present in solution for periods between 1 min and 1 h after mixing depend only on the initial ratio of bromine to ammonia and the pH.[6] Bromamide predominates at alkaline pH values or at small (<0.1) bromine-to-ammonia ratios, while nitrogen tribromide predominates in acidic solution or at great bromine-to-ammonia ratios. In contrast, the relative proportions of the corresponding chlorine derivatives found in freshly reacted, dilute aqueous solution are dependent upon their relative rates of formation.[7]

Primary amines react with aqueous bromine to form *N*-bromo or *N,N*-dibromo amines.[3] Secondary amines form *N*-bromo amines,[4,8] but tertiary amines do not appear to form *N*-bromo derivatives in aqueous solution.[9,10] Amino acids also react with aqueous bromine to form *N*-bromo amino acids.[11] In addition, the reaction of aqueous bromine with imides, to form compounds such as *N*-bromosuccinimide and *N,N'*-dibromocyanuric acid,[12] is well-known.

N-Bromo compounds form within seconds of mixing aqueous bromine and the nitrogenous reactant in dilute aqueous solution[5,13,14] but are not the stable end products of reaction. For example, the ammonia derivatives decompose completely to N_2 and H_2O within hours or days,[5,6,13–15] $NHBr_2$ being especially unstable. *N*-Bromo amino acids are also unstable, decomposing within minutes to hours.[11] *N*-Bromoalkylamines are considerable more stable, forming carboxylic acids or ketones only after several days,[3,8,9] while *N*-bromo imides are quite stable.[12]

Table I. Molar Absorptivities of Active Bromine Compounds in Aqueous Solution

	absorptivity/M^{-1} cm^{-1}					
compd	232 nm	261 nm	279 nm	290 nm	300 nm	331 nm
HOBr	45	85	65	50	40	25
OBr^-	150	25	40	80	145	315
NH_2Br	135	305	395	330	235	40
$NHBr_2$	2090	1110	730	630	560	390
$(CH_3)_2NBr$	470	180	305	400	430	215
N-bromoglycine	440	230	370	415	390	130
N-bromoglutamate	435	225	370	420	390	125

In this study, the rapid kinetics of the reactions for (6–60) × 10^{-5} M aqueous bromine and (1–18) × 10^{-4} M ammonia, dimethylamine, glycine, or glutamate, have been followed in a stopped-flow spectrophotometer. Rates of formation for the *N*-bromo products were determined at pH values greater than 10, where the *N*-monobromo derivative is the ultimate product,[6] and also, in the case of ammonia, at pH values less than 8, where the *N,N*-dibromo derivative is the ultimate product.

Experimental Methods

All solutions were made with chlorine demand-free water prepared from glass-distilled tap water. Solutions of HOBr (0.02 M) free of bromide and bromate were prepared from saturated solutions of purified[16] AR liquid bromine (Baker Chemical Co.) by distillation under reduced pressure after the addition of $AgNO_3$ solution. The solutions were stored in a low-actinic glass bottle at 2 °C, redistilled at 3-month intervals, and discarded after 1 year. Solutions of sodium bromite (5%) were obtained from Freeman Industries (Tuckahoe, NY). Solutions of nitrogenous compounds were prepared from 99.999% $NH_4H_2PO_4$, AR dimethylamine hydrochloride, AR glutamic acid (all Aldrich Chemical Co.), or glycine (Sigma Chemical Co.).

Spectra of NH_2Br, $NHBr_2$, $(CH_3)_2NBr$, *N*-bromoglycine, and *N*-bromoglutamate, prepared in the presence of excess nitrogenous compound, were determined on a Beckman DK-2 or a Perkin-Elmer 552 spectrophotometer. Absorption coefficients at selected wavelengths are presented in Table I.

Kinetic studies were performed in a Durrum Model 110 stopped-flow spectrophotometer in which 0.075-mL solutions of aqueous bromine and nitrogenous compound were mixed in a 2-cm path length, 0.066-mL cuvette with a dead time of 1.6 ms. Each reactant solution was equilibrated in the drive syringe for 4 min before reaction. The reaction temperature was controlled to ±0.05 °C at temperatures

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(1) Johannesson, J. K. *N. Z. J. Sci. Technol.* **1955**, *36*, 600.
(2) Johannesson, J. K. *Analyst* **1958**, *83*, 155.
(3) Johannesson, J. K. *Chem. Ind.* (*London*) **1958**, 97.
(4) Johannesson, J. K. *J. Chem. Soc.* **1959**, 2998.
(5) Galal-Gorchev, H.; Morris, J. C. *Inorg. Chem.* **1965**, *4*, 899.
(6) Johnson, J. D.; Overby, R. *J. Sanit. Eng. Div., Am. Soc. Civ. Eng.* **1971**, *97*, 617.
(7) Morris, J. C. In "Principles and Applications of Water Chemistry"; Faust, S. D., Hunter, J. V., Eds.; Wiley: New York, 1967; pp 28–53.
(8) Johannesson, J. K. *Nature* (*London*) **1958**, *181*, 1799.
(9) Deno, N. C.; Fruit, R. E. *J. Am. Chem. Soc.* **1968**, *90*, 3502.
(10) Lee, D. G.; Srinivasan, R. *Can. J. Chem.* **1973**, *51*, 2546.
(11) Wajon, J. E.; Morris, J. C. In "Water Chlorination: Environmental Impact and Health Effects"; Jolley, R. L., Brungs, W. A., Cumming, R. B., Eds.; Ann Arbor Science Publishers Inc.: Ann Arbor, MI, 1980; Vol. 3, pp 171–181.
(12) Gottardi, W. *Monatsh. Chem.* **1977**, *108*, 1067.
(13) Inman, G. W.; LaPointe, T. F.; Johnson, J. D. *Inorg. Chem.* **1976**, *15*, 3037.
(14) Cromer, J. L.; Inman, G. W.; Johnson, J. D. In "Chemistry of Wastewater Technology"; Rubin, A. J., Ed.; Ann Arbor Science Publishers, Inc: Ann Arbor, MI, 1978; pp 213–225.
(15) Galal, H. A. Ph.D. Dissertation, Harvard University, Cambridge MA, 1961.
(16) Bauer, W. H.; Daniels, F. *J. Am. Chem. Soc.* **1934**, *56*, 378.

0020-1669/82/1321-4258$01.25/0

between 10 and 35 °C, and to ±0.5 °C at other temperatures. Reaction was followed by measurement of UV absorbance, monitoring the disappearance of OBr^- or the appearance of *N*-bromo product at the absorption maximum with a Biomation 805 waveform recorder and an oscilloscope. The data from the least noisy of similar curves of absorbance vs. time spanning 95–99% of reaction were stored in a Data Graphics Datos 305 Interface and then transferred to a digital computer. The pH of a sample of reacted solution was determined at the reaction temperature with a Fisher Scientific Micro-Combination pH electrode and Model 420 digital pH meter.

Total concentrations of active bromine species (HOBr, OBr^-, BrO_2^-, and *N*-bromo compounds were determined by adding samples to excess phenylarsine oxide (PAO) (AR, Fisher Scientific Co.) in acetic acid–KI solution[17] and titrating excess PAO amperometrically with standard iodine on a Fisher Scientific Co. Model 393 Chlorine Titrator. Oxidant recoveries averaged 98%, while the standard deviations of analyses were about 5%.

Bromite determinations were performed on samples from which hypobromite and bromo amines had first been removed by the addition of phenol at pH 10.[18] Subsequently the samples were added to excess PAO and residual oxidant was determined as described previously. Reactant aqueous bromine solutions were found to be free of bromite.

Total ammonia was determined by a scaled-down version of the indophenol blue method[19] in which the absorbance of the analytical sample at 640 nm was measured with a Beckman DU spectrophotometer. Standard deviations of analyses averaged 5%.

Reactions were carried out with the nitrogenous compound present in at least twofold and up to 25-fold excess. The pseudo-first-order rate expression applicable to the initial stages of reaction is

$$-d[B_T]/dt = d[\mathrm{Prod}]/dt = k_2'[N_T][B_T] = k_{obsd}[B_T] \qquad (4)$$

where $[B_T]$ = total concentration of hypobromite (HOBr + OBr^-), $[N_T]$ = total concentration of nitrogenous compound, k_2' = second-order rate constant, and k_{obsd} = observed first-order specific rate.

Equation 4, after integration and substitution of absorbance relations for concentrations, can be expressed as

$$k_{obsd}t = \ln |A_\infty - A_0| - \ln |A_\infty - A| \qquad (5)$$

where A = absorbance at time t, A_0 = absorbance at time $t = 0$, and A_∞ = absorbance at time $t = \infty$.

First-order specific rates were determined by fitting the initial 10–20% of the absorbance–time data to eq 5 with the aid of the curve-fitting program of Dye and Nicely.[20] Both k_{obsd} and $\ln |A_\infty - A_0|$ were taken as adjustable parameters; A_∞ values were obtained experimentally as terminal A values following completion of initial reaction. Second-order rate constants k_2' were calculated from k_{obsd} by uslng eq 4. Initial rates used in establishing the kinetic order of the reaction were evaluated by fitting straight lines through the first 1–2% of absorbance–time data by linear regression.

Formation of NH_2Br

Reaction of aqueous bromine and ammonia was observed for the pH ranges 7.0–8.1 and 9.5–12.5 at 20.0 °C, for the pH range 10.4–12.7 at 5 °C, and for a number of temperatures between 5 and 45 °C at pH values near 11.7. At pH ≥9.9, NH_2Br was the only product observed, and its formation was complete within 10–200 ms. Some decomposition of NH_2Br, which seemed to be accelerated by light, occurred within 200 ms at pH >12.4 but was not sufficiently rapid at pH ≤ 12 to affect measurements of the rate of formation. Between pH 8.3 and pH 9.8, formation of NH_2Br was complete within the dead time of the apparatus. At pH ≤8.2, $NHBr_2$ was the ultimate product, on the basis of the absorbance measured at 232 nm, and was observed to form fully within 20–200 s. On the basis of the absorbance at 279 nm, however, formation of NH_2Br was complete within the first 10–100 ms. It appeared that NH_2Br was converted into $NHBr_2$, at a rate that increased with decrease in pH, and that, at pH 7, the formation of NH_2Br was almost complete before any $NHBr_2$ formed.

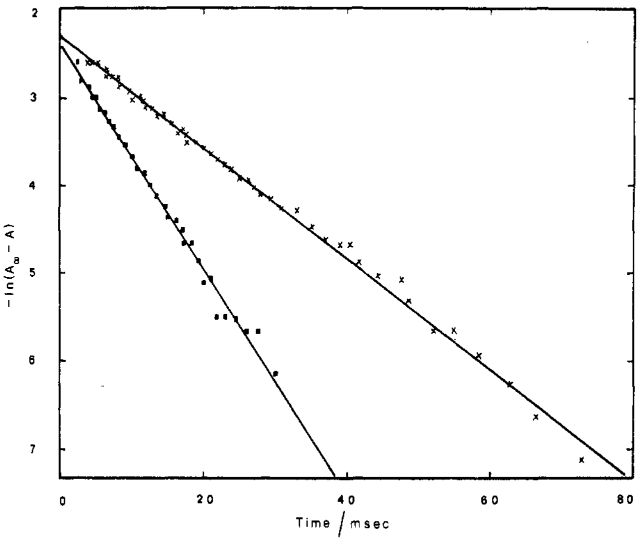

Figure 1. Absorbance measurements at 279 nm for formation of NH_2Br at pH 11.70, 20 °C: ×, $[N_T]_0 = 4.74 \times 10^{-4}$ M; $[B_T]_0 = 1.64 \times 10^{-5}$ M; ■, $[N_T]_0 = 9.06 \times 10^{-4}$ M, $[B_T]_0 = 1.64 \times 10^{-5}$ M.

Table II. Observed Second-Order Rate Constants, at 20.0 °C, for the Formation of NH_2Br

pH	$[B_T]_0/10^{-5}$ M	$[N_T]_0/10^{-4}$ M	$k_2'/M^{-1}\ s^{-1}$
10.43	7.55	2.27	1.14×10^6
10.43	7.60	2.40	1.21×10^6
10.43	7.70	2.32	1.09×10^6
10.46	7.50	4.68	1.00×10^6
10.46	7.50	4.68	1.02×10^6
10.46	7.50	4.66	1.07×10^6
10.45	14.4	4.48	1.02×10^6
10.45	14.2	4.50	1.01×10^6
10.45	14.4	4.82	1.01×10^6
7.10	5.2	4.14	3.39×10^5
7.10	5.2	4.14	3.31×10^5
7.11	4.8	1.30	3.35×10^5
7.11	4.8	1.30	3.56×10^5
7.13	5.0	2.10	3.52×10^5
7.13	5.0	2.10	3.42×10^5

Formation of NH_2Br at pH ≥10 was first order each with respect to ammonia and aqueous bromine and second order overall, on the basis of initial rate studies with varied initial conditions. Plots of $\ln |A_\infty - A|$ as a function of time were linear through 1 or more half-lives of the reaction at all pH values, in accord with the assumption of initial pseudo-first-order behavior. Typical plots, from which values of k_{obsd} were estimated, are shown in Figure 1. Rate constants (k_2'), calculated from k_{obsd} by the use of eq 4, exhibited no trends with varied initial concentrations, as shown in Table II, thus confirming second-order kinetic behavior. Values of k_2' based on both the appearance of NH_2Br and the disappearance of OBr^- were determined at pH ≥10 and were alike at all pH values except at pH ≥12.4, where significant decomposition of NH_2Br occurred.

Effect of pH on the Second-Order Rate Constant. Second-order rate constants (k_2') increased 10-fold for each unit pH increase for pH <8 and decreased similarly between pH 10 and 11 pH (see Table III and Figure 2). The variation of k_2' with pH at pH values less than 8 is similar to the variation of the observed rates of the hypochlorite–ammonia reaction with pH at pH values less than 8.[21] In contrast, however, to the hypochlorite–ammonia reaction, for which, at all pH values greater than 10, observed rates decrease

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[17] Carpenter, J. H.; Moore, C. A.; Macalady, D. L. *Environ. Sci. Technol.* **1977**, *11*, 992.

[18] Chapin, R. M. *J. Am. Chem. Soc.* **1934**, *56*, 2211.

[19] Strickland, J. D. H.; Parsons, T. H. "A Practical Handbook of Seawater Analysis"; Fisheries Research Board of Canada: Ottawa, 1972.

[20] Dye, J. L.; Nicely, V. A. *J. Chem. Educ.* **1971**, *48*, 443.

[21] Weil, I.; Morris, J. C. *J. Am. Chem. Soc.* **1949**, *71*, 1664.

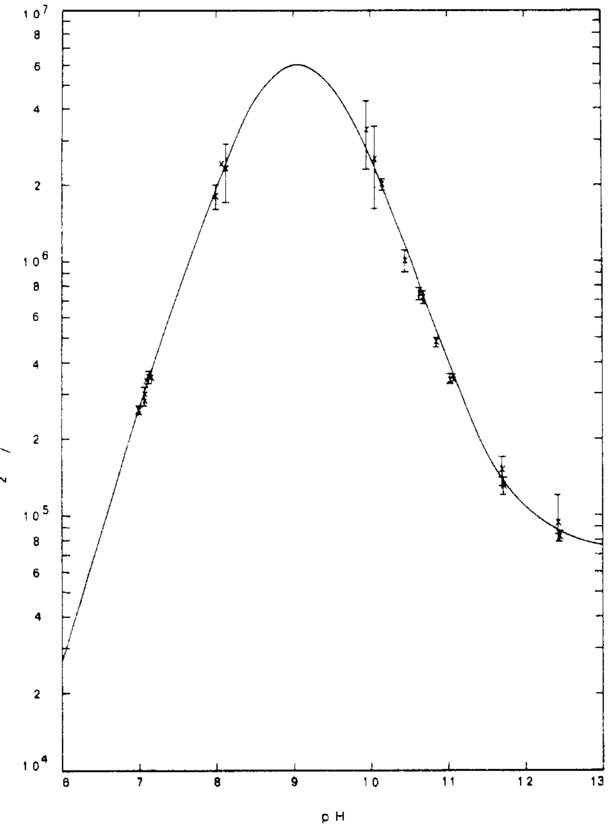

Figure 2. Variation in specific rate of formation of NH_2Br with pH at 20 °C.

10-fold for each unit increase in pH, the rate of the hypobromite–ammonia reaction levels off at pH >11.

The 10-fold variation of the observed rate of the hypochlorite–ammonia reaction with unit variation in pH has been attributed to a reaction mechanism in which the nonionic species HOCl and NH_3 are the direct reactants.[21] Reaction between the nonionic species appears to be the major pathway also for the hypobromite–ammonia reaction at pH <11, but the observed leveling-off in rate indicates reaction of OBr^- with NH_3 as well. That is, there are two simultaneous reactions

$$HOBr + NH_3 \xrightarrow{k_a} NH_2Br + H_2O \tag{6}$$

$$OBr^- + NH_3 \xrightarrow{k_b} NH_2Br + OH^- \tag{7}$$

that occur in strong basic solutions. For this mechanism the expression for the overall rate of formation of NH_2Br can be written

$$d[NH_2Br]/dt = k_2'[B_T][N_T] \tag{8}$$

$$= k_a(HOBr)(NH_3)/\gamma_x + k_b(OBr^-)(NH_3)/\gamma_{x^-} \tag{9}$$

$$= (k_a[HOBr]\gamma_{HOBr}/\gamma_x + k_b[OBr^-]\gamma_{OBr^-}/\gamma_{x^-})[NH_3]\gamma_{NH_3} \tag{10}$$

where γ_i indicates the activity coefficient of the species i, and x and x^- are the activated complexes of reactions 6 and 7, respectively. When expressions for the acid dissociation constants of HOBr (K_a) and NH_4^+ (K_b) are substituted in eq 10, eq 11 results by equating expressions 8 and 10. If it is

$$k_2' = \left(\frac{\gamma_{HOBr}\gamma_{OBr^-}}{K_a\gamma_{HOBr} + (H^+)\gamma_{OBr^-}}\right) \times \left(\frac{K_b\gamma_{NH_3}\gamma_{NH_4^+}}{K_b\gamma_{NH_4^+} + (H^+)\gamma_{NH_3}}\right)\left(\frac{k_a(H^+)}{\gamma_x} + \frac{k_bK_a}{\gamma_{x^-}}\right) \tag{11}$$

assumed that in dilute aqueous solution the activity coefficients

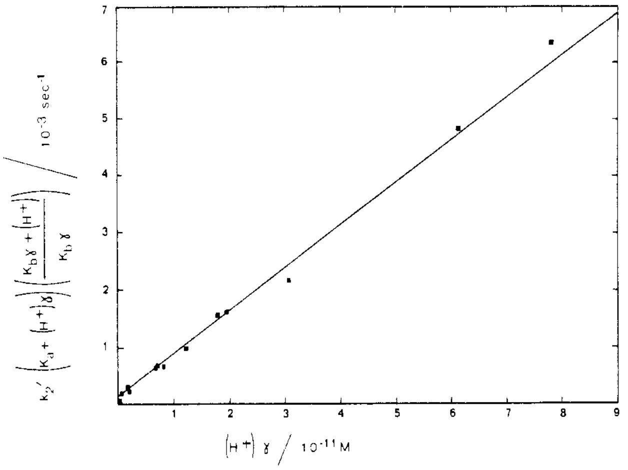

Figure 3. Evaluation of k_a for formation of NH_2Br at 20 °C.

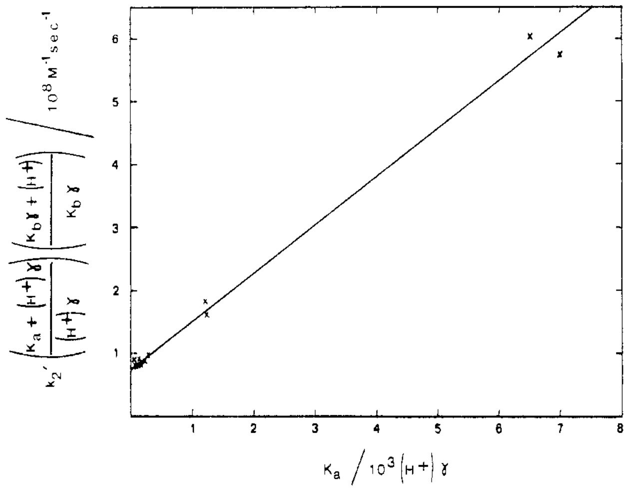

Figure 4. Evaluation of k_b for formation of NH_2Br at 20 °C.

of neutral molecules and neutral activated complexes are equal to unity, eq 11 can be rearranged to

$$k_2' = \left(\frac{k_a(H^+)\gamma_{\pm 1} + k_bK_a}{K_a + (H^+)\gamma_{\pm 1}}\right)\left(\frac{K_b\gamma_{\pm 1}}{K_b\gamma_{\pm 1} + (H^+)}\right) \tag{12}$$

where $\gamma_\pm$ refers to the activity coefficient for a monovalent ion, either positive or negative. This can be expressed as

$$k_2'(K_b\gamma_{\pm 1} + (H^+))(K_a + (H^+)\gamma_{\pm 1})/K_b\gamma_{\pm 1} = k_a(H^+)\gamma_{\pm 1} + k_bK_a \tag{13}$$

which can be arranged to

$$F(k_2') = k_a(H^+)\gamma_{\pm 1} + k_bK_a \tag{14}$$

Values of K_a were calculated from data of Kelley and Tartar,[22] and values of K_b were taken from Bates and Pinching.[23] Activity coefficients were calculated from the Guntelburg expression.[24]

The plot of $F(K_2')$ as a function of $(H^+)\gamma_{\pm 1}$ at 20.0 °C was linear over the pH range 10.1–12.5 (see Figure 3). The value of the slope, k_a, determined by linear regression ($r = 0.996$), was $(7.5 \pm 0.4) \times 10^7$ M^{-1} s^{-1}. Data for pH 7–8.1 also yielded a linear plot with an identical slope.

The function $F(k_2')/(H^+)\gamma_{\pm 1}$ was independent of $K_a/(H^+)\gamma_{\pm 1}$ for the pH range 7–8.1, where $[OBr^-]$ is very small, but gave a linear plot as a function of $K_a/(H^+)\gamma_{\pm 1}$, for the pH

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(22) Kelley, C. M.; Tartar, H. V. *J. Am. Chem. Soc.* **1956**, *78*, 5752.
(23) Bates, R. G.; Pinching, G. D. *J. Res. Natl. Bur. Std.* **1949**, *42*, 419.
(24) Robinson, R. A.; Stokes, R. H. "Electrolyte Solutions", 2nd ed.; Butterworths: London, 1968.

Table III. Observed Second-Order Rate Constants, at 20.0 °C, for the Formation of NH_2Br, Determined at 279 nm

pH	ionic strength/M	$k_2'/M^{-1}\ s^{-1}$	$k_2^{pred}/M^{-1}\ s^{-1}$ [a]
7.00	0.013	$(2.6 \pm 0.1) \times 10^5$	2.6×10^5
7.08	0.013	$(2.8 \pm 0.1) \times 10^5$	3.1×10^5
7.09	0.013	$(3.0 \pm 0.2) \times 10^5$	3.2×10^5
7.10	0.013	$(3.4 \pm 0.1) \times 10^5$	3.2×10^5
7.11	0.013	$(3.5 \pm 0.2) \times 10^5$	3.3×10^5
7.13	0.013	$(3.5 \pm 0.1) \times 10^5$	3.4×10^5
8.00	0.036	$(1.8 \pm 0.2) \times 10^6$	1.9×10^6
8.07	0.036	$(2.4 \pm 0.1) \times 10^6$	2.2×10^6
8.12	0.036	$(2.3 \pm 0.6) \times 10^6$	2.4×10^6
9.06	0.02		6.0×10^6
9.06	0.00		7.3×10^6
9.95	0.02	$(3.3 \pm 1.0) \times 10^6$	2.8×10^6
10.07	0.02	$(2.5 \pm 0.9) \times 10^6$	2.3×10^6
10.15	0.02	$(2.0 \pm 0.1) \times 10^6$	2.0×10^6
10.45	0.02	$(1.0 \pm 0.1) \times 10^6$	1.1×10^6
10.64	0.028	$(7.7 \pm 0.2) \times 10^5$	7.6×10^5
10.69	0.03	$(7.6 \pm 0.2) \times 10^5$	6.9×10^5
10.73	0.03	$(8.4 \pm 0.2) \times 10^5$	6.4×10^5
10.84	0.03	$(4.8 \pm 0.1) \times 10^5$	5.3×10^5
10.98	0.025	$(3.6 \pm 0.1) \times 10^5$	4.1×10^5
11.02	0.025	$(3.5 \pm 0.1) \times 10^5$	3.8×10^5
11.07	0.025	$(3.5 \pm 0.1) \times 10^5$	3.5×10^5
11.08	0.025	$(3.4 \pm 0.1) \times 10^5$	3.4×10^5
11.08	0.025	$(3.9 \pm 0.1) \times 10^5$	3.4×10^5
11.70	0.05	$(1.5 \pm 0.2) \times 10^5$	1.4×10^5
11.71[b]	0.05	$(1.3 \pm 0.1) \times 10^5$	1.4×10^5
12.42	0.07	$(9.3 \pm 0.9) \times 10^4$	8.7×10^4
12.45[b]	0.07	$(8.1 \pm 0.2) \times 10^4$	8.7×10^4

[a] Predicted on the basis of the proposed mechanism, eq 12. [b] Determined at 331 nm.

range 10.1–12.5. The slope, k_b, of the plot, Figure 4, was equal to $(7.6 \pm 0.4) \times 10^4\ M^{-1}\ s^{-1}$ ($r = 0.996$).

Values of k_2' calculated from these values of k_a and k_b for 20.0 °C on the basis of eq 12 are given in Table III and are shown by the solid line in Figure 2. The proposed mechanism predicts a maximum in the observed rate of reaction at pH 9.06 at 20.0 °C, with a rate constant k_2' equal to $7.3 \times 10^6\ M^{-1}\ s^{-1}$ at zero ionic strength.

Effect of Temperature on the Second-Order Rate Constant. The variation of the second-order rate constant (k_2') with pH at 5 °C in the range from 10 to 13 was similar to that at 20 °C. Consequently, a similar mechanism was postulated, and values of $k_a = (5.3 \pm 0.4) \times 10^7\ M^{-1}\ s^{-1}$ and $k_b = (2.6 \pm 0.5) \times 10^4\ M^{-1}\ s^{-1}$ were determined. Arrhenius expressions determined from the rate constants at 5 and 20.0 °C are

$$k_a = 4.7 \times 10^{10} \exp(-15.7/RT)\ M^{-1}\ s^{-1} \qquad (15)$$

$$k_b = 3.2 \times 10^{13} \exp(-48.4/RT)\ M^{-1}\ s^{-1} \qquad (16)$$

where the values of the activation energy are in kJ mol^{-1}.

Values for the second-order rate constants calculated by using eq 15, 16, and 12 agree well with measured values near pH 11.7 for the temperature range 5–20 °C, but are consistently greater than measured ones for temperatures higher than 20 °C.[25] This appears largely to be due to the large E_{act} value for k_b and reflects the imprecision with which k_b could be determined at 5 and 20 °C. Nonetheless, observed rates of N-bromination are not expected to vary significantly with temperature at pH <10 because of the small value of the temperature coefficient for k_a.

Effects of Bromide and Bromite. The addition of bromide ion to a solution of hypobromite is expected to increase the equilibrium concentration of Br_2. At pH ≥10.5, however, the addition of up to 1×10^{-2} M KBr to a reacting mixture of hypobromite and ammonia had no effect on the second-order rate constant. It appears, then, that the specific rate constant for reaction of Br_2 with NH_3 cannot be several orders of magnitude greater than k_a.

Table IV. Second-Order Rate Constants for *N*-Bromo Amine Formation, Determined at 290 nm

pH	ionic strength/M	$k_2'/M^{-1}\ s^{-1}$	$k_2^{pred}/M^{-1}\ s^{-1}$ [a]
(a) Formation of *N*-Bromoglycine at 20.0 °C			
10.28	0.022	$(9.4 \pm 1.8) \times 10^6$	6.6×10^6
10.83	0.030	$(2.5 \pm 0.3) \times 10^6$	2.5×10^6
11.58	0.05	$(7.4 \pm 0.7) \times 10^5$	7.4×10^5
11.59[b]	0.05	$(7.5 \pm 1.6) \times 10^5$	7.3×10^5
12.41	0.072	$(4.0 \pm 0.1) \times 10^5$	4.0×10^5
(b) Formation of *N*-Bromoglutamate at 20.3 °C			
11.58	0.055	$(4.9 \pm 0.2) \times 10^5$	4.8×10^5
11.70	0.055	$(4.0 \pm 0.5) \times 10^5$	3.9×10^5

[a] Predicted on the basis of the proposed mechanism, eq 20 or 22. [b] Determined at 331 nm.

There is considerable dispute in the literature as to whether bromite does[26] or does not[18,27] react with ammonia. When bromite solution (1.5×10^{-3} M) was added to a solution of ammonia at either pH 11.5 or pH 8.9 with N:Br molar ratios from 0.4 to 90, no formation of NH_2Br was observed spectrophotometrically, and there was no loss of oxidant. It is likely that, in the study in which the absorbance due to bromite was observed to disappear,[26] the investigators did not fully characterize the solutions and may have observed reactions leading to other bromine oxidants.

Formation of *N*-Bromo Organic Compounds

The reactions between hypobromite and dimethylamine, glycine, and glutamate to form bromo amines at pH >10 were more rapid than that between hypobromite and ammonia. Indeed, $(CH_3)_2NBr$ formed so rapidly at pH 11.7 that the rate of its formation could not be measured, even with the stopped-flow equipment.

***N*-Bromoglycine.** The formation of *N*-bromoglycine was followed in the pH range 10.3–12.4 at 20.2 °C and was found to be complete within 10–100 ms. Decomposition of *N*-bromoglycine was significant within 100 ms at pH 12.4 but was not sufficiently rapid at pH <12.4 to affect measurement of its formation kinetics. Formation of *N*-bromoglycine was second order, first order each with respect to aqueous bromine and glycine, on the basis of the linearity of plots of ln $|A_\infty - A|$ as a function of time and on the basis of the constancy of rate constants k_2' calculated by using eq 4 with varying initial glycine concentrations.

Second-order rate constants at 20.0 °C decreased with increasing pH at pH >10 like those for formation of NH_2Br (Table IV). A similar mechanism, in which the basic glycinate ion is the reactive nitrogenous species, is postulated. The overall rate of formation of *N*-bromoglycine (NBG) is, then

$$d[NBG]/dt = k_2'[N_T][B_T] \qquad (17)$$

$$= k_a(HOBr)(NH_2CH_2COO^-)/\gamma_{\pm1} + k_b(OBr^-)(NH_2CH_2COO^-)/\gamma_{\pm2} \qquad (18)$$

Substitution of the acid dissociation constants for HOBr (K_a) and glycine ($K_b = 1.23 \times 10^{-10}$ at 10.0 °C)[28] and rearrangement as before result in the equation

$$k_2'(K_b + (H^+)\gamma_{\pm1})(K_a + (H^+)\gamma_{\pm1})/K_b = k_a(H^+)\gamma_{\pm1} + k_bK_a\gamma_{\pm1}^2/\gamma_{\pm2} \qquad (19)$$

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(25) Wajon, J. E. Ph.D. Dissertation, Harvard University, Cambridge, MA, 1980.

(26) Andersen, T.; Lundager-Madsen, H. E. *Anal. Chem.* **1965**, *37*, 49.

(27) Hashmi, M. H., Ayaz, A. A. *Anal. Chem.* **1963**, *35*, 308.

(28) Perrin, D. D. "Dissociation Constants of Organic Bases in Aqueous Solution"; Butterworths: London, 1965.

Table V. Rate Constants for *N*-Halogenation Reactions

	HOBr				HOCl[a]		
compd	temp/°C	k_a/M^{-1} s^{-1} [b]	k_b/M^{-1} s^{-1} [b]	k_{obsd}/M^{-1} s^{-1} [c] (pH 7)	temp/°C	k_2/M^{-1} s^{-1}	k_{obsd}/M^{-1} s^{-1} [c] (pH 7)
NH_3	5	$(5.3 \pm 0.9) \times 10^7$	$(2.6 \pm 0.5) \times 10^4$	6.6×10^4	5	3.5×10^6	3.3×10^3
NH_3	20	$(7.5 \pm 0.4) \times 10^7$	$(7.6 \pm 0.4) \times 10^4$	2.9×10^5	20	4.7×10^6	2.1×10^4
$(CH_3)_2NH$	20	$\leqslant 3.0 \times 10^9$		$\leqslant 6.0 \times 10^5$	25	3.3×10^8	4.3×10^4
glycine	20	$(3.8 \pm 0.3) \times 10^8$	$(2.1 \pm 0.2) \times 10^5$	4.6×10^5	25	1.3×10^8	1.7×10^5
glutamate	20	3.5×10^8	5.0×10^4	3.0×10^5			

[a] Data from ref 7. k_2 for HOCl is equivalent to k_a for HOBr. [b] Listed errors are 95% confidence limits (two-tailed *t* test). [c] At zero ionic strength, predicted by the postulated reaction mechanism.

where $\gamma_{\pm 2}$ is the activity coefficient for a divalent ion. This equation can be written as

$$F(K_2') = k_a(H^+)\gamma_{\pm 1} + k_b K_a \gamma_{\pm 1}^2/\gamma_{\pm 2} \qquad (20)$$

For the pH range 10.8–12.4, the plots of $F(k_2')$ as a function of $(H^+)\gamma_{\pm 1}$ and of $F(k_2')/(H^+)\gamma_{\pm 1}$ as a function of $K_a\gamma_{\pm 1}/(H^+)\gamma_{\pm 2}$ were linear, and their slopes yielded values of $k_a = (3.8 \pm 0.3) \times 10^8$ M^{-1} s^{-1} and $k_b = (2.1 \pm 0.2) \times 10^5$ M^{-1} s^{-1}. The values of k_2' calculated from these values of k_a and k_b with eq 19 are given in Table IV. The proposed mechanism predicts a maximum in the observed rate of reaction at pH 9.30 at 20.0 °C with a rate constant k_2' equal to 1.5×10^7 M^{-1} s^{-1} at zero ionic strength.

***N*-Bromoglutamate.** The formation of *N*-bromoglutamate was followed at pH 11.58 and 11.70 and 20.3 °C; it was complete within 100 ms. Its formation was first order with respect to each reactant. The second-order rate constants obtained are shown in Table IV. A mechanism for the formation of *N*-bromoglutamate similar to that for formation of *N*-bromoglycine is postulated, giving as the overall rate of formation of *N*-bromoglutamate (NBGlu)

$$d[\mathrm{NBGlu}]/dt = k_2'[N_T][B_T] \qquad (21)$$

$$= [k_a(\mathrm{HOBr})\gamma_{\pm 2} + k_b(\mathrm{OBr^-})\gamma_{\pm 3}] \times (^-\mathrm{OOCCH_2CH_2CH(NH_2)COO^-}) \qquad (22)$$

With $K_b = 1.0 \times 10^{-10}$ for glutamate at 20.3 °C,[28] values of $k_a = 3.5 \times 10^8$ M^{-1} s^{-1} and $k_b = 5 \times 10^4$ M^{-1} s^{-1} were obtained as described previously. The values of k_2' calculated from these values of k_a and k_b are given in Table IV. The proposed mechanism predicts a maximum in the observed rate of reaction at pH 9.36 at 20.0 °C with a rate constant k_2' equal to 1.0×10^7 M^{-1} s^{-1} at zero ionic strength.

Discussion

Specific rate constants for reaction of HOBr with ammonia, amines, and amino acids lie in the range 7×10^7 to 3×10^9 M^{-1} s^{-1} at 20 °C (see Table V). Rate constants of this magnitude, together with the relatively small activation energy found for the reaction HOBr + NH_3, indicate that, while the slower reactions are chemically controlled, the faster reactions are approaching diffusion control. The considerably smaller specific rate constants for reaction of OBr^- with nitrogenous compounds mean that these are chemically controlled reactions. Furthermore, except under quite alkaline conditions (pH >11), the reaction of OBr^- is insignificant in the overall formation of *N*-bromo amines.

The reaction between a halogenating agent S–X and a nitrogenous compound R_2NH according to the equation

$$\mathrm{S{-}X} + \mathrm{R_2N{-}H} \rightarrow \mathrm{R_2N{-}X} + \mathrm{S^-} + \mathrm{H^+} \qquad (23)$$

can be considered as an electrophilic displacement of H by X. When it is chemically controlled rather than diffusion controlled, the reactivity of a halogenating agent with a given nitrogenous compound is expected to be related directly to the electrophilicity of the halogenating agent. Also, the order of electrophilicities of a series of brominating agents S–Br probably follows generally the acidities of the analogues compounds S–H. An exact correspondence is not necessarily exhibited.[29] The expected order of reactivity is, then

$$\mathrm{Br^+} > \mathrm{H_2OBr^+} > \mathrm{Br_2} > \mathrm{ROOBr} > \mathrm{HOBr} > \mathrm{NH_2Br} > \mathrm{R_2NBr} > \mathrm{OBr^-} \qquad (24)$$

This order of reactivity is in accord with the observed 1000-fold greater reactivity of HOBr toward NH_3, glycine, and glutamate as compared with that of OBr^-. The observed equilibrium distribution between NH_2Br and $NHBr_2$, in which $NHBr_2$ is favored at neutral pH values and NH_2Br is favored at alkaline pH values,[6] suggests that the order of reactivity of HOBr, NH_2Br, and OBr^- with NH_2Br to form $NHBr_2$ is also in accord with (24). Bromine (Br_2) is expected to be several times more reactive than HOBr; its reactions with nitrogenous compounds of the type R_2NH may be so rapid as to be diffusion controlled.

N-Bromo amines form more rapidly than do the *N*-chloro amines. The rate constants listed in Table V indicate that the specific rate constant for reaction of HOX with NH_3 is 15 times greater for X = Br than for X = Cl, while the specific rate constants for reaction of HOX with amines and amino acids are 3–5 times as great for X = Br as for X = Cl. Such an order of reactivity of HOBr and HOCl is in the direction expected from the electrophilicites of the hypohalous acids, HOX, wwich are in the order HOI > HOBr > HOCl because of the increasing electronegativities and decreasing polarizabilities in the same order. Analogous reasoning accounts, in part, for the observation that hypobromite ion is several orders of magnitude more reactive than hypochlorite ion. The observed rate law for N-chlorination does not suggest any reactivity of hypochlorite at pH <13.[21] In addition, the Br atom can better delocalize part of the total electron density of the negatively charge activated complex in its d orbitals than can the Cl atom, thus providing the transition state with additional stability.

Equation 23 may also be considered a nucleophilic displacement of S^- from the halogenating agent by the nitrogenous compound. If the reaction is chemically controlled, then the rates of reaction of a given halogen donor with a series of nitrogenous compounds should be related directly to the nucleophilicities of the nitrogenous compounds. Since nucleophilicity of nitrogen toward X^+ can be expected to parallel basicity of nitrogen toward H^+, a linear free energy relationship of the form

$$\log k_a = \mathrm{p}K_b + \log A \qquad (25)$$

may be found to correlate specific rates of N-halogenation (k_a) with the basicities of the nitrogenous compounds (K_b).

The extremely rapid N-bromination of very basic compounds such as $(CH_3)_2NH$ is probably diffusion controlled. Consequently, a linear relationship between rate and basicity is not expected for compounds much more basic than the

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(29) Gottardi, W. *Monatsh. Chem.* **1973**, *104*, 421.

amino acids. The value of 3×10^9 M^{-1} s^{-1}, which has been placed on the specific rate of reaction between HOBr and $(CH_3)_2NBr$ (Table V), on the basis of a linear extrapolation of the data for ammonia and glycine, should be regarded as an upper limit.

Free amino groups less basic than ammonia such as those of aniline, xanthine, cystine, and proteins are likely to be N brominated slightly less rapidly than ammonia. The amido nitrogen of amides and proteins is likely to be brominated slowly in neutral solution, while tertiary amines appear not to be N brominated at all.[9,10]

An *N*-bromo compound may react with another molecule of HOBr but can be expected to react several orders of magnitude more slowly because of its reduced basicity compared to that of the free amine. This is illustrated by the relatively slow formation of $NHBr_2$ during the formation of NH_2Br. Nevertheless, the overall reaction may be rather rapid in neutral solution.

In a neutral solution containing 1×10^{-6} M ammonia and 1×10^{-6} M nitrogenous organic compounds, a mixture of *N*-bromo compounds will be 99% formed within 1 s–1 min. The distribution among the bromo amines observed at the end of this time will be determined by their relative rates of formation, just as in the case of the *N*-chloro amines, so that as much as 60% of the mixture initially may be *N*-bromo organic compounds. However, the distribution among the bromo amines observed after several minutes is likely to be determined by equilibrium considerations[6] rather than by the relative rates of formation, which determine the distribution of *N*-chloro amines for up to several hours.[7]

Transfer reactions of the type shown in eq 26 are also likely to occur. Equilibrium lies far on the side of *N*-halo organic

$$NH_2{-}X + R_2NH \rightarrow R_2N{-}X + NH_3 \qquad (26)$$

compounds when X = chlorine[30-32] and probably does also for X = bromine. Johannesson, for instance, presented evidence to suggest the equilibrium between *N*-bromodimethylamine and NH_2Br favored *N*-bromodimethylamine.[4,8] The order of reactivity of brominating agents shown previously indicates that the transfer of bromine from NH_2Br to amines and amino acids is more rapid than the rate of reaction of OBr^- with these compounds. Furthermore, relative nucleophilicites suggest that the rate of reaction of NH_2Br with R_2NH is likely to be more rapid than the reaction of NH_2Br with NH_2Br to form $NHBr_2$, a reaction that has been observed to be complete with 1–3 min. So, it appears that transfer reactions probably have rate constants of the order of 10^6 M^{-1} s^{-1}. Kinetic measurements of Br^+ transfer from NH_2Br to a variety of nitrogenous organic compounds and determination of the resulting equilibrium positions are needed to validate this conclusion, however.

Conclusions

Formation of the bromo amines NH_2Br, $(CH_3)_2NBr$, *N*-bromoglycine, and *N*-bromoglutamate is very rapid with typical formation times of 1 s–1 min at 10^{-6} M concentrations. Variations of the observed second-order rate constants with pH are consistent with mechanisms in which both HOBr and OBr^- react with the most basic form of the nitrogenous compound. Specific rate constants for reaction of HOBr with these amines range from 10^7 to 10^9 M^{-1} s^{-1} at 20 °C, while OBr^- reacts 10^{-3} times as rapidly. So, the contribution of the OBr^- to the formation of *N*-bromo amines is insignificant at pH <11. The overall rate of formation of *N*-bromo amines varies only slightly with change in temperature.

N-Bromo amines form 3–15 times as rapidly as the corresponding *N*-chloro amines. This is consistent with the greater electrophilicity of HOBr. Electrophilicities of bromine donors, S–Br, and their rates of N-bromination of a given nitrogenous compound appear to increase with increasing acidity of the analogous acids, S–H. Conversely, rates of N-bromination by a given bromine donor appear to increase with increasing nucleophilicities or basicities of the nitrogenous compounds. The reactions of HOBr with very basic amines may be so rapid that they are diffusion controlled.

Transfer of bromine from NH_2Br to NH_2Br, forming $NHBr_2$, is also quite rapid. Bromine-transfer reactions between NH_2Br and other nitrogenous compounds also are expected to be rapid, so that the distribution among bromo amines in a mixture will be determined by equilibrium consideration within several minutes after formation.

Acknowledgment. Support for this research was provided under U.S. Army Medical Research and Development Command Contract No. DAMD-17-77-C-7051.

Registry No. HOBr, 13517-11-8; NH_3, 7664-41-7; Me_2NH, 124-40-3; glycine, 56-40-6; sodium glutamate, 142-47-2.

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(30) White, G. C. "Disinfection of Wastewater and Water for Reuse"; Van Nostrand-Reinhold: New York, 1978.

(31) Gray, E. Ph.D. Dissertation, Purdue University, Lafayette, IN, 1977.

(32) Isaac, R. A.; Morris, J. C. In "Water Chlorination: Environmental Impact and Health Effects"; Jolley, R. L., Brungs, W. A., Cumming, R. B., Eds.; Ann Arbor Science Publishers Inc.: Ann Arbor, MI, 1980; Vol. 3, pp 183–191.